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Authors

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Figueiredo, Pedro
Gudnason, Vilmundur
et al.

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Associations of 24-hour sleep duration and CT-derived measurements of muscle and bone: the AGES-Reykjavik Study

Elisa A Marques[1], **Pedro Figueiredo**[1,2], **Vilmundur Gudnason**[3,4], **Thomas Lang**[5], **Gunnar Sigurdsson**[3,4,6], **Sigurdur Sigurdsson**[3], **Thor Aspelund**[3,7], **Kristin Siggeirsdottir**[3], **Lenore Launer**[1], **Gudny Eiriksdottir**[3], and **Tamara B Harris**[1]

[1]Laboratory of Epidemiology and Population Sciences, Intramural Research Program, National Institute on Aging, National Institutes of Health, 7201 Wisconsin Avenue, Gateway Building, Suite 2N212, Bethesda, MD 20892-9205 USA [2]Research Center in Sports Sciences, Health Sciences and Human Development, CIDESD, University Institute of Maia, ISMAI, Av. Carlos Oliveira Campos — Castelo da Maia 4475-690 Maia, Portugal [3]Icelandic Heart Association Research Institute, Holtasmari 1, IS-201 Kópavogur, Iceland [4]University of Iceland, Sæmundargata 2, 101 Reykjavík Ssn: 600169-2039, Iceland [5]Department of Radiology and Biomedical Imaging, University of California, 505 Parnassus Ave, San Francisco, CA 94143, USA [6]Landspitali-University Hospital, 101 Reykjavik, Iceland [7]Centre of Public Health Sciences, University of Iceland, Stapi v. Hringbraut, 107 Reykjavík, Iceland

Abstract

Background—Although the importance of sleep on preservation of several physiological functions is well known, the relationship with the two interconnected tissues — muscle and bone is less understood.

Objectives—This study aimed to examine the association of 24-hour sleep duration with mid-thigh muscle composition and proximal femur volumetric bone mineral density (vBMD).

Methods—2,438 men and 3326 women aged 66 to 96 years, residents in the Reykjavik area, were included in this cross-sectional study. Proximal femur integral vBMD, mid-thigh muscle area and muscle attenuation were assessed with computed tomography. Sleep and nap habits were assessed using a questionnaire.

Results—We found that after adjustment for age and BMI long sleep duration (>8 h/d) was negatively associated with thigh lean area in both men (B= −2.21, 95% confidence interval (CI): −4.01, −0.40) and women (B= −2.39, 95% CI: −3.75, −1.03) and with muscle attenuation (B= −0.95, 95% CI: −1.47, −0.43) only in women. After adjustments for age, health and lifestyle factors the association between long sleep duration and muscle lean area was attenuated and

Corresponding Author: Elisa A Marques, National Institute on Aging, National Institutes of Health, 7201 Wisconsin Avenue, Gateway Building, Suite 2N212, Bethesda, MD 20892-9205 USA, *Phone:* (301) 496-1178, *Fax:* (301) 496-4006, elisa.marques@nih.gov.

became nonsignificant while associations with muscle attenuation remained marginally significant (B= −0.51, 95% CI: −1.03, −0.002). Sleep duration was not associated with proximal femur integral vBMD in the multivariate models.

Conclusion—Long sleep duration, particularly in old women, can affect thigh muscle attenuation (increase in intramuscular fat). Whether optimization of sleep can ameliorate age-associated intramuscular or intermuscular adipose tissue warrants further studies.

Keywords

computed tomography; proximal femur; muscle composition; fat infiltration

1. Introduction

Aging is associated with a degeneration of skeletal muscle and function (sarcopenia) and decrease in bone density and quality (osteoporosis). Although the relationships between bone and muscle are not fully understood, accumulated data suggests that the mechanisms and changes in these two tissues are highly interlinked. Recent findings suggest that the muscle-bone links are not only mechanical but also involve complex genetic and molecular pathways (Hamrick 2012). New evidence suggests that bone tissue can also modulate muscle metabolism (Brotto and Johnson 2014; Cianferotti and Brandi 2014). Combined, these findings provide support for a ‘bone-muscle crosstalk’ hypothesis and strengthen the rationale for research on the common risk factors that may be implicated in the pathogenesis of muscle and bone changes. Recently, age-related sleep patterns and sleep disturbances have been proposed as potential contributors to skeletal muscle decline (Piovezan et al. 2015a) and osteoporosis (Cunningham and Di Pace 2015).

Although based on limited evidence, studies in older adults have found an inverted U-shaped relationship between sleep duration and skeletal muscle mass (Auyeung et al. 2015; Chien et al. 2015). However, it is unclear how thigh lean mass and muscle attenuation, a noninvasive measure of muscle density obtained from computed tomography (CT) that has been linked to reduced strength and performance (Goodpaster et al. 2001; Visser et al. 2002), are affected by sleep.

In addition, recent evidence links self-reported sleep duration with increased risk of osteoporosis or lower bone mineral density (BMD) in older adults, but the results have been inconsistent (Chen et al. 2014; Cunningham and Di Pace 2015; Fu et al. 2011; Kim et al. 2014). The underlying mechanisms for a causal effect of sleep on osteoporosis risk and BMD are not fully understood, and the effect of sleep duration on CT-based proximal femur measures remains unexplored. Thus, testing the hypotheses that long and/or short sleep duration may be associated with age-related low bone mass, muscle atrophy and fat infiltration will help to understand the pathophysiological mechanisms underlying these geriatric phenomena.

In the present study we assessed whether sleep duration was associated with thigh soft tissue composition and proximal femur bone parameters in a population-based cohort of older men and women. We hypothesize that negative association of thigh lean area, muscle attenuation

and proximal femur volumetric BMD would be observed with both short and excessive sleep duration.

2. Methods

2.1. Study participants

The Age, Gene/Environment Susceptibility Study-Reykjavik Study (AGES-Reykjavik) is a random sample of 5,764 men and women nested in the Reykjavik Study, a single-center prospective population study of Icelandic men and women. Mean age of the participants at the time of enrollment (2002–2006) in the AGES-Reykjavik Study was 77 years (range 66–96). All variables were assessed at baseline. Details of the study design are provided elsewhere (Harris et al. 2007). Written informed consent was obtained from all participants, and the study was approved by the Icelandic National Bioethics Committee (VSN: 00–063) and the Institutional Review Board of the Intramural Research Program of the National Institute of Aging.

2.2. CT-derived Outcomes

CT measurements were performed at the mid-thigh and hip using the same four-row detector CT system (Sensation; Siemens Medical Systems, Erlangen, Germany), following a similar protocol as previously described (Sigurdsson et al. 2006). A single axial section through the mid-thigh (120 kVp, 10 mm slice thickness) was used to quantify the geometry of the mid-thigh (Johannesdottir et al. 2012). We report average values from the both thighs; if data on one leg was missing, then the non-missing thigh was used. We estimated lean area (cm^2) and muscle attenuation (HU). The cross-sectional area of nonadipose, nonbone tissue within the deep fascial plane was used as a measure of muscle mass. Lean area was segmented using the outline along the fascial plane between the muscle and subcutaneous fat as previously described (Lang et al. 2008). The upper and lower boundaries of the Hounsfield units (HU) threshold used to segment the lean region was set between 1 and 100. Intermuscular adipose tissue is the visible fat within the fascia surrounding skeletal muscles (Miljkovic and Zmuda 2010); lakes of adipose tissue between and within muscle were determined as the number of pixels with HU between −190 and −30 multiplied by the area of a pixel. The mean attenuation coefficient (measured in HU) of muscle tissue obtained by excluding intermuscular and intramuscular adipose tissue lying interior to the deep fascial plane surrounding the muscle, was used as an indicator of fat infiltration into the muscle. Lower HU indicates greater fat infiltration (Goodpaster et al. 2000a).

Analysis of the CT images was performed using specialized software developed at the University of California, San Francisco. Twenty-six randomly selected participants underwent a second CT scan after repositioning. The coefficient of variation (CV, %) was 1.3% for lean area and 1.5% for muscle attenuation. There was no significant difference between the repeated measurements.

A helical study of the left hip (120 kVp, 140 mA s, 1-mm slice thickness, pitch=1, coarsened to 3-mm slice thickness) encompassed the proximal femur from a point 1 cm superior to the acetabulum to a point 3–5 mm inferior to the lesser trochanter. Proximal femoral vQCT

images were processed to extract measures of integral volumetric BMD (vBMD) of total femur region and the ratio of the volume of the cortical femur region to the total bone volume (cvol/ivol), a fracture-related measure of the integrity of the proximal femoral cortex (Lang et al. 2012).

2.3. Exposure

Total 24-hour sleep duration was estimated base on the nighttime sleep duration and nap habits that were collected from the comprehensive questionnaire administered at the first clinic visit (Harris et al. 2007). The average (summer and winter) number of hours of nighttime sleep and daytime napping were calculated based on the following closed questions: “During a typical 24-h period during summer/winter months, how many hours do you spend sleeping at night?” and “During a typical 24-h period during summer/winter months, how many hours do you spend napping during the day?” Total 24-hour sleep duration was estimated as the sum of nighttime sleep hours and daytime nap hours.

2.4. Covariates and other risk factors

We adjusted our analyses for previously described variables (Marques et al. 2016) that are potentially confounding or are known to be associated with muscle and bone quality or sleep duration. These included age, body mass index (BMI), smoking and physical activity status, self-reported mobility disability status, use of medications known to affect bone density, and total 25-hydroxyvitamin D (25OHD). Based on biological plausibility or previous literature findings the following variables were also added: self-reported overall health status, history of chronic health conditions, cognitive function status, and high-sensitivity C-reactive protein (hs-CRP). Subjects reported their overall state of health on a scale of 1–5 with a score of 1 indicating excellent health and a score of 5 indicating poor health, and responses were dichotomized as good (≤3) vs poor (≥4). The sum of 13 chronic health conditions were determined using self-report with confirmation by treatment and medications. These conditions included osteoporosis, diabetes mellitus, kidney disease, thyroid diseases (low and high), arthritis, Parkinson disease, cancer, chronic obstructive pulmonary disease, myocardial infarction, hypertension, congestive heart failure, and stroke. Cognitive status was determined by professional consensus after reviewing results of cognitive examinations and categorized as normal, mild cognitive impairment and dementia (Vidarsdottir et al. 2014). HsCRP, as a marker of inflammation, was analyzed using reagents from Roche Diagnostics (Mannheim, Germany) on a Hitachi 912 analyzer according to manufacturer instructions. We additionally considered several other variables that may confound the association of interest including height, weight, current depression status, use of antidepressant and psycholeptics (including anxiolytics, hypnotics and sedatives) medication assessed based on medication bottles brought to the clinic, coffee consumption (recoded as “yes” for consumption ≥3 cups per day; otherwise, no), and alcohol consumption. Depressive symptomology was defined as a score of 6 or greater on the 15-item Geriatric Depression Scale (Sigurdsson et al. 2012). Current alcohol use, was first converted into grams per week using 14 g of alcohol as a standard drink, and afterwards participants were classified into three categories: none (currently not drinking), light-to-moderate (>0 and ≤ 75g/week for women and >0 and ≤ 150g/week for men) and heavy (>75 and >150 g/week for women and men, respectively).

2.5. Statistical analysis

To be consistent with previous reports and because of the known differences in sleep, muscle and bone quality, all analyses were performed separately for women and men. Mean ± standard error (SE) or percentages for categorical variables were used to summarize subject characteristics. Variables with non-Gaussian distribution were normal-scored transformed using Van der Waerden's Formula. Total 24-hour sleep duration (hours/day) was divided into three categories: less than 6 (short sleepers), 6 to 8 (reference group), and more than 8 (long sleepers). Multivariable linear regression was used to determine the association between sleep duration and CT muscle and bone parameters (as dependent variable). The minimally adjusted model included age and BMI (model 1). The fully adjusted model (model 2) also include current physical activity level (low/high), current smoking status (yes/no), overall health status (poor/good), mobility disability (yes/no), number of chronic diseases, dementia (yes/no, based on cognitive status assessment), total 25OHD, and hs-CRP levels were added in the final model. Glucocorticoid or antiepileptic drugs (yes/no) and anti-bone loss drugs (yes/no) were included in the full-adjusted model the bone outcomes. Results are expressed as regression coefficient (B), 95% confidence interval (CI), and p-value for all models. Three additional (sensitivity) analyses were conducted, (i) repeating model 3 but covariates were retained if they had a significant contribution to the multivariate model (retention threshold of $p < 0.10$); (ii) BMI was replaced by weight and height, and (iii) several other potential confounders: depression status (yes/no), use of psycholeptics (yes/no), use of antidepressant medication (yes/no), alcohol consumption (none, light-to-moderate, heavy), and coffee intake (yes/no) were considered to test the robustness of our results. In an additional analysis we also examined the associated between sleep duration and cvol/ivol. To reduce bias and loss of information due to missing data, we used multiple imputation (20 new datasets) using the Fully Conditional Specification method by chained equations as implemented in SPSS, under the assumption that data were missing at random (MAR) (Lee and Carlin 2010). Statistical analyses were conducted using IBM SPSS Statistics, version 22.0 (Armonk, NY: IBM Corp).

3. Results

Of the 5,764 participants, 3,326 (57.7%) were women and mean age was similar between sexes (77.7 years). Mean BMI was in the overweight range (27.0 kg/m^2), and was significantly higher in women (27.2 kg/m^2) compared with men (26.8 kg/m^2). On average, nocturnal sleep duration (mean ± SE) was 7.02 ± 0.02 hours for the men and 6.91 ± 0.02 hours for the women. Napping habits were also significantly different between sexes; more women reported they did not nap daily compared to men (50.8% vs 31.5%). Only 5.9% of participants (8.1% men, 4.3% women) reported daily naps longer than 1 hour. Baseline data for men and women by 24-hour sleep duration are shown for men in Table 1. Among both men and women, long sleepers (>8h) were older, had less thigh lean mass and more fat infiltration, more likely to have poor health and less physically active compared to participants who slept 6–8 h sleep duration ($p<0.05$). Overall, most dependent variables and covariates were significantly different when stratified by 24-hour sleep duration, except for smoking status for men, bone variables and alcohol consumption for women, and height, weight, BMI, 25OHD, hs-CRP, coffee consumption, use of bone-altering drugs and use

psycholeptics for both men and women. Other relevant characteristics are summarized in Table 1.

Table 2 shows the results of the associations between sleep duration and thigh muscle composition and proximal femur vBMD. In men, the crude models showed that long sleep duration (> 8h) was negatively associated with both muscle outcomes. After adjusting for age and BMI (model 2) only the association with thigh lean area remained significant (coefficient = −2.21; 95% confidence interval (CI): −4.01, −0.40; p=0.017). The relation between sleep and thigh muscle lean area was mostly explained by differences in mobility status, as when this single confounding factor was added to model 2, the association was no longer significant (> 8h sleep p=0.199). The relation between long sleep duration and muscle attenuation was mostly affected by age and BMI (model 2) and mobility status and physical activity levels were the most relevant confounding factors from all the included covariates in model 3. Sleep duration was not associated with proximal femur integral vBMD in men (crude model: short sleep duration coefficient = 4.23; 95% CI: −2.57, 11.03; long sleep duration coefficient = −5.24; 95% CI: −10.79, 0.32).

Among women, long sleep duration (> 8h) was negatively associated with all outcomes in the crude linear models. Similar to men, in the fully adjusted model (model 3) the association with thigh muscle lean area was attenuated and became nonsignificant (coefficient = −1.15, 95% CI: −2.49, 0.19) in women. No single covariate can explain the attenuation observed in the association between long sleep duration and muscle lean area. In fact, in a fully-adjusted model not accounting for mobility status or cognitive status the association would remained significant (p=0.037 and p=0.045, respectively). Thus, except for vitamin D and smoking status, all covariates had a significant contribution in the model. The association was stronger between long sleep duration and muscle attenuation and persisted, although the association was statistically marginally significant (coefficient= −0.51; 95% CI: −1.03, −0.002) in the fully-adjusted model. Similar to the lean mass model, no single factor accounted for the observed attenuation in the relation between the exposure and outcome. In fact, results from the first sensitivity analysis showed that the association between long sleep duration and muscle attenuation was stronger (B, −0.53; 95% CI: −1.04, −0.02, p=0.043), when only covariates with a significant contribution to the multivariate model were retained (all covariates expect cognitive status and 25OHD levels). In all other models, this stepwise approach had no influence on the results (data not shown). In the second sensitivity analysis, associations remained virtually unchanged after replacing BMI by weight and height. Adjustment for additional covariates in produced similar results (data not shown). Results from the multivariate models were similar when the association between sleep duration and hip cvol/ivol, rather than integral vBMD, was tested (coefficients were nonsignificant). However, the crude models in both sexes showed significant negative associations between long sleep duration and cvol/ivol (B, −0.006; 95% CI: −0.012, −0.0004 in men and B, −0.007; 95% CI: −0.013, −0.001 in women).

4. Discussion

While there have been previous explorations of the relationship between sleep duration and muscle mass and bone density in older adults (Auyeung et al. 2015; Fex et al. 2012; Kim et

al. 2014; Niu et al. 2015), this is the first study of mid-thigh muscle composition and volumetric bone density. We expected to see a negative association between the three outcomes with both short and long sleep duration; however, our hypotheses were only partially supported. Long sleep duration was negatively associated with mid-thigh lean area and, particularly in women, long sleep duration was negatively associated with muscle attenuation, thus predicting a higher fat infiltration into the muscle. Furthermore, the associations between long sleep duration and integral vBMD at the proximal femur were not significant in the adjusted models. Unexpectedly, short sleep duration was not associated with any dependent outcomes. This suggests that only long sleep duration may be an important risk factor for muscle quality but less relevant for bone health.

This study explores a novel association between sleep duration and thigh composition, measured by CT imaging. The observed negative association between long sleep duration and thigh muscle lean area is consistent with data from previous studies measuring skeletal muscle mass (Auyeung et al. 2015; Chien et al. 2015; Fex et al. 2012; Kim et al. 2015). An inverted U-shaped relationship has been described between sleep duration and muscle mass in older men (Auyeung et al. 2015), and an equivalent U-shaped pattern for the association with sarcopenia (defined base on skeletal muscle index cutoff points) in older women (Chien et al. 2015). However, there is not a clear consensus on this association, as our results do not support a U-shape association, and depending on the level of confounder adjustment the shape of association may change. Recent findings also suggested that only older women with ≥8 h of sleep had higher odds for sarcopenia (Chien et al. 2015). The biological mechanisms linking long sleep duration with muscle mass remain unclear. Recent reviews have suggested that hormonal pathways involved in muscle metabolism (by modulating the expression of intramuscular proteins) are affected by sleep deprivation and disorders, and are the strongest candidates to explain how sleep impairment can impact muscle recovery, and promote muscle atrophy and sarcopenia (Dattilo et al. 2011; Piovezan et al. 2015b). These mechanisms may differ between short and long duration, but currently remains unresolved and warrants further discussion and research.

Our results showed a possible link between long sleep (>8 h/day) and thigh muscle attenuation, an indicator of intramuscular fat, particularly in women and the result from our fully-adjusted model was only statistically marginally significant. There are no previous studies exploring the association between muscle fat infiltration and sleep duration. Although previous studies have only examined the link between sleep duration and obesity, a lower thigh muscle attenuation was found in obese subjects (Goodpaster et al. 2000b). For example, a cross-sectional study in older men reported a U-shaped association between percent body fat (measured by DXA) and sleep duration (Patel et al. 2008). However, results are not consistent, as only reduced sleep durations were associated with higher BMI and with higher odds of obesity in men and women the same study (Patel et al. 2008) and in older women, but not in men, in another study (Chien et al. 2015). Further studies are needed to confirm these findings and whether or not obesity and thigh muscle attenuation share other risk factors implicated in their pathophysiological mechanisms.

Previous studies have reported associations between sleep duration and areal BMD (Kim et al. 2014; Niu et al. 2015) and qualitative ultrasound index at the calcaneus (Wang et al.

2015), but conclusions remain inconsistent. We examined two different volumetric CT-derived measures of bone mass, one based on density and the other on volume, but the associations with sleeping >8 h/day were not significant after adjustment for covariates. Our results suggest that overall sleep duration does not play an important role in hip bone structure in older adults. Inconsistent findings have been previously reported, depending on the outcome being tested (continuous BMD measure or risk of osteoporosis). Thus some studies found a significant association with short sleep duration (Cunningham and Di Pace 2015; Fu et al. 2011), others with long sleep duration (Kim et al. 2014; Niu et al. 2015; Tian et al. 2015), and some reports with both, short and sleep durations (Chen et al. 2014; Wang et al. 2015). The plausible mechanisms include altered osteoblasts and osteoclasts circadian rhythmicity, overactivity of proinflammatory cytokines, increases in sympathetic tone and cortisol secretion, and altered growth hormone metabolism, which are important regulators of bone formation and resorption (Raggatt and Partridge 2010; Swanson et al. 2015).

The present study has several strengths, including the measurement of mid-thigh and proximal femur using CT imaging, large numbers of men and women, and a comprehensive collection of important covariates. In addition, daytime nap duration was included when calculating total 24-hour sleep duration because of the potential compensation effect of napping.

However, there are also some limitations in our study. First, our findings are cross-sectional, thus temporal relationship or causality could not be established. Secondly, we used self-reported sleep duration, giving rise to possible biased estimates. However, recall sleep and nap duration was obtained separately for summer and winter months to increase accuracy. Studies using objective measures of sleep duration, variability and timing are needed to support our findings. Also, comparisons with other studies are difficult, as there is no consensus for defining cut points for sleep categories and to select the appropriate reference group. Next, we did not measure sleep apnea and some relevant hormonal and inflammatory makers (such as insulin-like growth factor-1, testosterone, growth hormone, and IL-6), which could enable us to explore the potential biological mechanisms linking sleep duration to muscle composition and BMD. Finally, results are also limited to Caucasian with European ancestry, community-dwelling and relatively health older men and women. Therefore, the findings may not apply to nonwhite, frailer or institutionalized older adults.

In conclusion, long sleep duration is associated with thigh muscle composition, particularly intramuscular fat in older women. With increased life expectancy-which allows for greater decline in muscle and bone strength across the lifespan-the consequences of muscle and bone changes during aging have become a public health priority. Thus, sleep habits (mostly prolonged sleep patterns) should be further investigated for its potential adverse effect, particularly on muscle composition and consequently low physical performance in older adults.

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Highlights

- Long sleep duration is negatively associated with mid-thigh lean area.
- In women, long sleep duration was associated with mid-thigh fat infiltration.
- No associations were observed between sleep duration and hip bone density.
- Long sleep duration may be an important risk factor for muscle quality.

Table 1

Sample characteristics according to 24-hour sleep duration (hours/day)

	Men (n=2,438)				Women (n=3,326)			
	< 6 h (n=257)	**6–8 h (n=1,789)**	**> 8 h (n=392)**	**p-value**	**< 6 h (n=569)**	**6–8 h (n=2,338)**	**> 8h (n=419)**	**p-value**
Mean ± SE								
Age, years	76.8 ± 0.4[a]	76.7 ± 0.1[a]	78.6 ± 0.3	<0.001	77.0 ± 0.3[a]	76.8 ± 0.1[a]	78.1 ± 0.4	0.001
Weight, kg	83.5 ± 0.8	82.5 ± 0.3	82.4 ± 0.7	0.44	70.0 ± 0.6	69.9 ± 0.3	71.0 ± 0.7	0.26
Height, cm	175.4 ± 0.4	175.3 ± 0.2	174.7 ± 0.4	0.07	160.5 ± 0.3	160.6 ± 0.1	159.9 ± 0.3	0.06
BMI, kg/m^2	27.1 ± 0.2	26.8 ± 0.1	26.9 ± 0.2	0.30	27.1 ± 0.2	27.1 ± 0.1	27.7 ± 0.3	0.07
Thigh muscle lean area, cm^2	127.6 ± 1.3[a]	126.9 ± 0.5[a]	122.9 ± 1.2	<0.001	91.7 ± 0.7 [a]	91.7 ± 0.4[a]	89.2 ± 0.9	0.02
Thigh muscle attenuation, HU	41.2 ± 0.4	41.9 ± 0.1[a]	40.6 ± 0.3	<0.001	38.6 ± 0.2[a]	38.8 ± 0.1[a]	37.3 ± 0.3	<0.001
Integral vBMD, mg/cm^3	251.9 ± 3.3[a]	247.7 ± 1.2	242.5 ± 2.5	0.03	225.6 ± 2.0	226.3 ± 0.001	220.5 ± 2.7	0.06
cvol/ivol	0.36 ± 0.003[a]	0.36 ± 0.001	0.35 ± 0.003	0.03	0.35 ± 0.002	0.35 ± 0.001	0.34 ± 0.003	0.06
# of medical conditions	2.2 ± 0.1	2.0 ± 0.1[a]	2.2 ± 0.1	0.03	2.4 ± 0.06	2.3 ± 0.1[a]	2.4 ± 0.1	0.02
25OHD, nmol/L	55.2 ± 1.6	57.1 ± 0.6	55.0 ± 1.3	0.21	51.0 ± 1.1	51.3 ± 0.5	49.4 ± 1.2	0.35
Hs-CRP, mg/L	4.2 ± 0.5	3.7 ± 0.2	4.4 ± 0.4	0.19	3.7 ± 0.4	3.8 ± 0.2	4.8 ± 0.5	0.06
n (%)								
Current Smoker	15 (5.8)	101 (5.6)	27 (6.9)	0.60	53 (9.3)	282 (12.1)	70 (16.7)	0.003
High PA level status	49 (19.1)	387 (21.6)	52 (13.3)	0.001	84 (14.8)	332 (14.2)	29 (6.9)	<0.001
Poor health status	93 (36.2)	491 (27.4)	162 (41.3)	<0.001	233 (40.9)	842 (36.0)	198 (47.3)	<0.001
Mobility disability	29 (11.3)	127 (7.1)	67 (17.1)	<0.001	103 (18.1)	349 (14.9)	121 (28.9)	<0.001
Depressive symptoms	21 (8.2)	103 (5.8)	56 (14.3)	<0.001	56 (9.8)	186 (8.0)	58 (13.8)	0.006
Dementia	15 (5.8)	111 (6.2)	78 (19.9)	<0.001	30 (5.3)	149 (6.4)	69 (16.5)	<0.001
Use of oral glucocorticoid or antiepileptics	9 (3.5)	80 (4.5)	13 (3.3)	0.35	27 (4.7)	113 (4.8)	29 (6.9)	0.46
Use of anti-bone loss drugs	14 (3.9)	99 (5.5)	20 (5.1)	0.80	151 (26.5)	571 (24.4)	91 (21.7)	0.30
Use of antidepressants	24 (9.3)	181 (10.1)	92 (23.5)	<0.001	80 (14.1)	398 (17.0)	143 (34.1)	<0.001
Use of psycholeptics	34 (13.2)	208 (11.6)	40 (10.2)	0.48	133 (23.4)	458 (19.6)	90 (21.5)	0.25
Coffee consumption	144 (56.0)	999 (55.8)	202 (51.5)	0.42	270 (47.5)	1240 (53.0)	209 (49.9)	0.06
Light to moderate alcohol consumption	170 (66.1)	1251 (69.9)	258 (65.8)	0.03	321 (56.4)	1341 (57.4)	209 (49.9)	0.26

[a]Significantly different from longer sleep group (>8h/day);

[b] Significantly different from shorter sleep group (<6h/day) BMI = body mass index, cvol/ivol = cortical volume integral volume PA= physical activity, Hs-CRP = high-sensitivity C-reactive protein.

Table 2

Regression coefficients (B), 95% CI and *P* Value expressing associations of 24-hour sleep duration with outcome measures in men (2,438) and women (3,326)

			Men			Women		
CT-derived measures	**Model**	**Sleep hours**	**B**	**95% CI**	**p-value**	**B**	**95% CI**	**p-value**
Thigh muscle lean area, cm^2	1	<6h	0.70	−2.14, 3.53	0.63	−0.01	−1.54, 1.53	0.99
		>8h	−4.07	−6.49, −1.66	0.001	−2.50	−4.37, −0.62	0.009
	2	<6h	−0.20	−2.39, 1.99	0.86	0.13	−1.01, 1.26	0.83
		>8h	−2.21	−4.01, −0.40	0.017	−2.39	−3.75, −1.03	0.001
	3	<6h	0.79	−1.27, 2.85	0.45	0.27	−0.82, 1.37	0.62
		>8h	−0.22	−1.95, 1.50	0.80	−1.15	−2.49, 0.19	0.09
Thigh muscle attenuation, HU	1	<6h	−0.66	−1.39, 0.07	0.078	−0.27	−0.78, 0.24	0.30
		>8h	−1.27	−1.87, −0.66	<0.001	−1.56	−2.13, −0.98	<0.001
	2	<6h	−0.49	−1.13, 0.15	0.14	−0.17	−0.62, 0.28	0.47
		>8h	−0.48	−1.02, 0.06	0.08	−0.95	−1.47, −0.43	<0.001
	3	<6h	−0.27	−0.89, 0.35	0.39	−0.11	−0.55, 0.33	0.61
		>8h	−0.08	−0.61, 0.46	0.78	−0.51	−1.03, −0.002	0.049
Total hip integral vBMD, mg/cm^3	1	<6h	4.23	−2.57, 11.03	0.22	−0.69	−5.15, 3.77	0.76
		>8h	−5.24	−10.79, 0.32	0.07	−5.73	−11.32, −0.14	0.045
	2	<6h	3.41	−3.10, 9.91	0.30	−0.15	−4.21, 3.92	0.94
		>8h	−3.02	−8.39, 2.36	0.27	−3.87	−8.97, 1.23	0.14
	3	<6h	4.23	−2.23, 10.69	0.20	−0.06	−4.07, 3.94	0.98
		>8h	−1.39	−6.90, 4.12	0.62	−1.57	−6.68, 3.55	0.55

Reference category: 6–8h of sleep per 24-hour period; Model 1: unadjusted model; Model 2: adjusted for age and BMI; Model 3: further adjusted for physical activity level, smoking status, health status, mobility disability status, number of medical conditions, cognitive status, hs-CRP, 25OHD and bone medication (only in the vBMD predictor model).