Decreased Slow Wave Sleep Increases Risk of Developing Hypertension in Elderly Men

Maple M. Fung, Katherine Peters, Susan Redline, Michael G. Ziegler, Sonia Ancoli-Israel, Elizabeth Barrett-Connor, Katie L. Stone, for the Osteoporotic Fractures in Men Research Group

Abstract—The importance of sleep to health and cardiovascular disease has become increasingly apparent. Sleep-disordered breathing, sleep duration, and sleep architecture may all influence metabolism and neurohormonal systems, yet no previous study has evaluated these sleep characteristics concurrently in relation to incident hypertension. Our objective was to determine whether incident hypertension is associated with polysomnography measures of sleep-disordered breathing, sleep duration, and sleep architecture in older men. Participants were 784 community-dwelling, ambulatory men ≥65 years of age (mean age: 75.1±4.9 years) from the Outcomes of Sleep Disorders in Older Men Study who did not have hypertension at the time of their in-home polysomnography sleep studies (2003–2005) and who returned for follow-up (2007–2009). Of 784 older men included in this report, 243 met criteria for incident hypertension after a mean follow-up of 3.4 years. In unadjusted analyses, incident hypertension was associated with increased hypoxemia, increased sleep stages N1 and N2, and decreased stage N3 (slow wave sleep [SWS]). After adjustment for age, nonwhite race, study site, and body mass index, the only sleep index to remain significantly associated with incident hypertension was SWS percentage (odds ratio for lowest to highest quartile of SWS: 1.83 [95% CI: 1.18 to 2.85]). No attenuation of this association was seen after accounting for sleep duration, sleep fragmentation, and indices of sleep-disordered breathing. Percentage time in SWS was inversely associated with incident hypertension, independent of sleep duration and fragmentation, and sleep-disordered breathing. Selective deprivation of SWS may contribute to adverse blood pressure in older men. (Hypertension. 2011;58:596-603) ● Online Data Supplement

Key Words: hypertension ■ slow wave sleep ■ respiratory disturbance index ■ elderly ■ polysomnography

The importance of sleep to health, including hypertension (HTN) and cardiovascular disease, continues to be elucidated. HTN is present in ≥30% of the US adult population, with a much higher risk in the elderly; ≥65% of Americans age ≥60 years have been diagnosed with HTN.1 Sleep disturbances and disorders are also exceedingly common in older adults. Sleep disorders such as sleep-disordered breathing (SDB), sleep duration, and sleep architecture may affect neurohormonal axes, including the sympathetic nervous system, which contribute to elevated blood pressure and HTN. To our knowledge, a comprehensive evaluation of sleep characteristics and incident HTN in an elderly cohort has not been reported.

SDB, which includes obstructive sleep apnea, is strongly associated with HTN.2 In a study of veterans, 60% of obstructive sleep apnea patients had HTN,3 which is often refractory to treatment.4 Conversely, OSA may be present in ≥30% of adults with HTN.3 Previous studies have suggested that SDB, as determined by the respiratory disturbance index (RDI; number of respiratory events per hour of sleep), precedes incident HTN,6 although these associations may be partly attributable to obesity.7 Epidemiological studies of self-reported sleep have also found that sleep deprivation and/or short sleep duration are associated with both prevalent and incident HTN8,9 and that such associations may be most pronounced among premenopausal women.9 A case-control polysomnographic study showed that severity of HTN was associated with short sleep duration, lower sleep efficiency, and less rapid eye movement (REM) sleep.11 Sleep disruption may also lead to increased blood pressure.12

Human sleep is divided into REM and non-REM (NREM) sleep. NREM is further divided into the stages of N1 (previously called stage 1), N2 (previously stage 2), and N3 (previously stage 3 and 4; also called slow wave sleep [SWS]).13 Both NREM and REM sleep are assessed by the brain wave activity (frequency and amplitude) recorded with polysomnography (PSG). SWS is considered to be “restor-
We recently reported from the Outcomes of Sleep Disorders in Older Men Study (MrOS Sleep Study) that decreased percentage of time in SWS assessed by PSG was related to increased odds of obesity. Obesity and high blood pressure are very highly associated conditions with important public health consequences as major risk factors for both cardiovascular disease and death. To our knowledge, assessment of the association between SWS or other markers of sleep architecture with HTN has not yet been reported in prospective epidemiological studies.

The aim of the present study was to determine whether sleep characteristics, including SDB, determined by RDI or hypoxemia, decreased sleep duration, or indices of sleep architecture (which include overall arousal index, time in each sleep stage, sleep efficiency, or sleep fragmentation), predict incident HTN among elderly community-dwelling men.

Methods

Study Subjects

Study subjects were participants in the MrOS Sleep Study conducted in 2003–2005, an ancillary study of the parent MrOS study, a cohort of 5994 community-dwelling men, aged 65 years, described previously. A total of 3135 participants in the MrOS Sleep Study had full in-home PSG. See the online Data Supplement for more details. Sleep stages (REM and stages 1 to 4 NREM, now N1 to N3) were scored using the standard criteria at the time of the studies. SWS was defined as the total sleep time scored as stage 3 plus stage 4, now N3, and expressed as percentage of total sleep time. RDI, an indication of the severity of SDB, was defined as the number of apneas and hypopneas (based on the Sleep Heart Health Study criteria) per hour of sleep, each associated with an oxygen desaturation of ≥4%. Hypoxemia was determined by sleep time spent with oxygen desaturation to <80% (PaO₂ <80%). Central apnea index was defined as the number of apneas per hour of sleep with no displacement of either chest or abdominal inductance channels, regardless of oxygen desaturation. Total sleep duration at night and sleep efficiency, defined as the percentage of the sleep period (time in bed) spent asleep, were also obtained from PSG. Overall arousal index was determined as number of arousals per hour of sleep. Wake after sleep onset (the minutes awake after having been asleep) was used as a marker of sleep fragmentation.

Statistical Analyses

Initial associations of sleep variables with incident HTN were examined using ANOVA, Kruskal-Wallis, or χ² tests. Sleep variables considered included indices of SDB (by RDI and percentage of sleep time with oxygen saturation <80%), nighttime sleep duration, and sleep architecture (sleep stage distributions, wake after sleep onset, sleep efficiency, and overall arousal index). Descriptive and inferential statistics were performed using SAS version 9.2 (SAS Institute, Inc, Cary, NC). To account for multiple end points that are highly correlated, we used the Dubey and Armitage-Parmar procedure.

Potential confounders were identified a priori. Summary statistics for variables believed to be related to the polysomnographic variables and/or incident HTN were performed. ANOVA, Kruskal-Wallis, or χ² tests were used to examine associations with the sleep characteristics and incident HTN for normal, nonparametric, and categorized variables, respectively. Variables that were significant at P<0.10 for both outcomes were included in a multivariable model. A list of potential confounders and sleep variables considered are shown in Tables 1 and 2, respectively.

To account for nonlinear associations, sleep variables were categorized as quartiles. Parameters with a high number of 0 values (central apnea index and hypoxemia [percentage of time with PaO₂ <80%]) were expressed as present or absent. Logistic regression was
The 784 men included in this report had a mean age of 75.1 years (SD 4.9 years) and mean BMI of 26.4 kg/m² (SD 3.4 kg/m²); ~90% were white. Demographic characteristics are shown in Table 1. The mean baseline SBP was 121.0 mm Hg (SD 10.6 mm Hg) and DBP was 76.4 mm Hg (SD 7.7 mm Hg). A majority of the participants (61%) were prehypertensive, classified as a SBP 120 to <140 mm Hg or DBP 80 to <90 mm Hg; 19.7% reported a history of cardiovascular disease, and 5.7% reported a history of diabetes mellitus. Almost all (92.3%) rated their health as “excellent” or “good.”

Results

Baseline Characteristics and Univariate Analyses

The 784 men included in this report had a mean age of 75.1 years (SD 4.9 years) and mean BMI of 26.4 kg/m² (SD 3.4 kg/m²); ~90% were white. Demographic characteristics are shown in Table 1. The mean baseline SBP was 121.0 mm Hg (SD 10.6 mm Hg) and DBP was 76.4 mm Hg (SD 7.7 mm Hg). A majority of the participants (61%) were prehypertensive, classified as a SBP 120 to <140 mm Hg or DBP 80 to <90 mm Hg; 19.7% reported a history of cardiovascular disease, and 5.7% reported a history of diabetes mellitus. Almost all (92.3%) rated their health as “excellent” or “good.”

At baseline, participants had a mean RDI of 10.0 (SD 12.0; median of 5.7), but 54.0% of men had an RDI >5, indicating at least mild SDB, shown with other sleep characteristics in Table 2. On average, the total sleep duration was 364 minutes (SD 66.4 minutes) or 6.1 hours. Average percentage of time in REM was 20.2% (SD 6.2%), stage 1 (N1) 6.5% (SD 4.2%), stage 2 (N2) 62.0% (SD 9.2%), and SWS (stages 3 and 4, N3) 11.2% (SD 8.5%).

Incident HTN Was Associated With Sleep Architecture

Over the 3.4-year follow-up interval, 243 men developed incident HTN; 59 (24.3%) were diagnosed by blood pressure criteria alone, 9 (3.7%) by self-report of HTN alone, 5 (2.1%) had both self-reported HTN and met blood pressure criteria, and 170 (70%) were taking ≥1 antihypertensive medication. Those with incident HTN were older (75.7 versus 74.9 years; \( P = 0.04 \)) and were more likely to report cardiovascular disease (24.1% versus 17.7%; \( P = 0.04 \)), shown in Table 1.

There was a nonsignificant trend toward higher mean RDI with incident HTN, shown in Table 2. Percentage of time in...
sleep stages 1 (N1), 2 (N2), and SWS (N3) were associated with incident HTN, shown in Table 2. Those with incident HTN had poorer sleep architecture, as evidenced by significantly less SWS (mean: 9.8% versus 11.2%; P=0.002) and correspondingly more stage 1 (N1) and stage 2 (N2) sleep (P=0.013 and P=0.033, respectively). After adjusting for age, race, BMI, and study site, only the association between SWS and incident HTN remained statistically significant (Table S1, available in the online Data Supplement).

**SWS and Incident HTN**

To further explore the associations between SWS and incident HTN, we first assessed the associations of covariates and other sleep variables with quartiles of time in SWS (Table 3). The lowest quartile of percentage of sleep time in SWS (<4.1%) was associated with increasing age (P<0.001), BMI (P=0.015), and neck circumference (P=0.012) but not baseline SBP and DBP. In those in the lowest quartile of SWS, we observed a higher mean RDI (P<0.001), a higher mean overall arousal index (P<0.001), lower mean total sleep duration (P=0.009), and lower mean sleep efficiency (P<0.001). Those in the lowest quartile of percentage of sleep time in SWS were also more likely to have any SDB (RDI ≥5) or moderate-severe SDB (RDI ≥15; P=0.048 and P=0.0005, respectively). Central apnea index was not associated with quartile of SWS. Men taking either an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker at follow-up (9.6% total) were more likely to be in the lowest quartile of SWS (P=0.034).

In unadjusted analyses, 41% of those in quartile 1 of SWS (Q1; least SWS) developed incident HTN compared with <30% in each of the other quartiles (Figure). We further examined the association of SWS and incident HTN in multivariate models (Table 4). After adjusting for age and BMI, those in Q1 of SWS experienced an ~80% increase in risk of incident HTN as compared with those in Q4 (odds ratio: 1.81 [95% CI: 1.18 to 2.80]). These results were unchanged after further adjustment for study site, race, history of cardiovascular disease, the polysomnographic sleep variables of overall arousal index, sleep time with PaO2 <80% saturation, RDI, sleep efficiency, total sleep duration, and smoking history and alcohol use. After adjusting for multiple correlated comparisons using the Dubey and Armitage-Parmar procedure, results were not significantly changed. In addition, substituting height and weight, waist circumference, hip circumference, or hip/waist ratio for BMI did not significantly change the results.

Subgroup analysis of sleep architecture in normotensive men who progressed to pre-HTN or HTN, described in the online Data Supplement and Figure S1, revealed an association with decreased percentage of time in SWS (P=0.004) and percentage of increased time in stage 2 (N2; P=0.042) sleep as subjects either stayed normotensive or progressed to pre-HTN or HTN.

**Discussion**

Sleep disturbances are exceedingly common in older adults and may contribute to a number of adverse health outcomes, including HTN and cardiovascular disease through perturbations in a number of physiological systems. Most previous research on the relationship between incident HTN and sleep disturbances has focused on SDB, with some studies also addressing sleep duration. To our knowledge, this is the first large-scale analysis of comprehensive PSG data that assesses the association of indices of 3 key sleep domains, SDB, sleep duration, and sleep architecture, to incident HTN in an elderly cohort. In these community-dwelling older men, we found

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**Table 2. Sleep Characteristics Of Study Cohort: Overall and by Follow-Up HTN Status**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N=784)</th>
<th>Incident HTN (N=243)</th>
<th>No Incident HTN (N=541)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep-disordered breathing, mean±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RDI</td>
<td>10.0±12.0</td>
<td>10.8±13.5</td>
<td>9.7±11.3</td>
<td>0.256*</td>
</tr>
<tr>
<td>Hypoxemia (% sleep time PaO2 &lt;80%)</td>
<td>0.05±0.3</td>
<td>0.09±0.4</td>
<td>0.03±0.2</td>
<td>0.025†</td>
</tr>
<tr>
<td>Central apnea index</td>
<td>5±4.5</td>
<td>1.7±5.6</td>
<td>1.4±4.0</td>
<td>0.835*</td>
</tr>
<tr>
<td>RDI ≥15, n (%)</td>
<td>164 (20.9)</td>
<td>51 (21.0)</td>
<td>113 (20.9)</td>
<td>0.975</td>
</tr>
<tr>
<td>RDI ≤5, n (%)</td>
<td>423 (54.0)</td>
<td>133 (54.7)</td>
<td>290 (53.6)</td>
<td>0.770</td>
</tr>
<tr>
<td>Sleep duration, mean±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total sleep duration, min</td>
<td>364.1±66.4</td>
<td>365.5±72.3</td>
<td>363.5±63.7</td>
<td>0.715</td>
</tr>
<tr>
<td>Sleep architecture, mean±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall arousal index</td>
<td>22.9±11.3</td>
<td>23.1±12.3</td>
<td>22.8±10.8</td>
<td>0.724*</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>75.9±11.7</td>
<td>74.9±12.8</td>
<td>76.4±11.2</td>
<td>0.116</td>
</tr>
<tr>
<td>Wake after sleep onset, min</td>
<td>106.3±63.0</td>
<td>112.2±63.7</td>
<td>103.6±62.6</td>
<td>0.079</td>
</tr>
<tr>
<td>% time in stage 1 (N1) sleep</td>
<td>6.5±4.2</td>
<td>7.2±5.3</td>
<td>6.2±3.6</td>
<td>0.013†</td>
</tr>
<tr>
<td>% time in stage 2 (N2) sleep</td>
<td>62.0±9.2</td>
<td>63.1±9.2</td>
<td>61.6±9.2</td>
<td>0.033†</td>
</tr>
<tr>
<td>% time in slow wave (N3) sleep</td>
<td>11.2±8.5</td>
<td>9.8±8.1</td>
<td>11.8±8.5</td>
<td>0.002†</td>
</tr>
<tr>
<td>% time in REM</td>
<td>20.2±6.2</td>
<td>20.0±6.4</td>
<td>20.3±6.1</td>
<td>0.479</td>
</tr>
</tbody>
</table>

RDI indicates respiratory disturbance index; HTN, hypertension; REM, rapid eye movement sleep.

*Data show the use of Kruskal-Wallis statistic because of nonnormal distributions.

†P<0.05.
that men with SWS in the lowest quartile had an ≈1.8-fold increased incidence of HTN compared with men with the highest levels of SWS. This association persisted after adjusting for several covariates and after considering other sleep exposures, such as RDI, the overall arousal index, and total sleep duration. This study adds to the growing important body of literature regarding sleep and cardiovascular risks. Rather than noting associations alone, it describes more detailed associations of incident disease with sleep in particular stages.

Decreased SWS is increasingly recognized as a marker, possibly etiologically associated with several adverse health outcomes. Sleep architecture, particularly SWS, has been implicated in neurocognition and, more recently, in influencing endocrine function. Human metabolism is affected by changes in circadian rhythm, which includes the sleep-wake cycle. Low sleep quality and reduced SWS have been associated with insulin resistance and associated with the presence of diabetes mellitus, findings that may relate to the close interactions between the hypothalamic-pituitary-adrenal axis and sleep homeostasis. SWS may potentially be influencing endocrine function.

Calcium channel blocker use at follow-up, n (%) 17 (2.2) 5 (2.6) 6 (3.1) 2 (1.0) 4 (2.0) 0.57
Follow-up SBP, mm Hg 118.7 121.0 10.9 10.6 10.1 10.0 0.061
Follow-up DBP, mm Hg 68.1 ± 9.7 68.1 ± 9.8 68.6 ± 9.5 70.0 ± 9.5 68.4 ± 10.0 0.371
PACE score 160.8 ± 71.3 162.6 ± 71.9 152.5 ± 69.6 164.3 ± 71.6 163.9 ± 72.2 0.305
RDI 10.0 ± 10.0 13.3 ± 15.3 9.8 ± 10.9 19.3 ± 15.9 9.4 ± 11.6 7.7 ± 8.8 0.006‡
Overall arousal index 22.9 ± 11.3 26.5 ± 13.5 22.7 ± 11.1 21.8 ± 9.5 20.6 ± 9.8 < 0.001††
Central apnea index 1.5 ± 4.5 1.7 ± 6.1 1.5 ± 4.0 1.2 ± 2.9 1.4 ± 4.5 0.813†
Sleep efficiency, % 76.3 ± 11.1 75.9 ± 11.7 71.4 ± 12.5 70.9 ± 12.4 73.6 ± 11.9 78.7 ± 10.1 0.0001§
Total sleep duration, min 364.2 ± 66.4 350.2 ± 77.0 370.0 ± 58.7 368.6 ± 66.8 367.7 ± 60.4 0.009
Wake after sleep onset, min 106.3 ± 63.1 122.2 ± 64.0 109.5 ± 70.6 102.1 ± 57.5 91.6 ± 55.4 < 0.0001§
Time in SWS, min 41.4 ± 31.8 60.5 ± 50.0 25.7 ± 7.8 49.4 ± 11.2 83.7 ± 20.7 < 0.0001§
Nonwhite race, n (%) 68.7 (8) 22.1 (11.3) 16 (8.1) 22 (11.5) 8 (4) 0.027†
Current smoker, n (%) 22.8 (2) 9 (4.6) 4 (2.0) 1 (0.5) 8 (4) 0.058
Has ≥1 alcoholic drink per wk, n (%) 432 (55.4) 104 (53.9) 108 (55.4) 105 (54.7) 115 (57.5) 0.902
Use of sleep medication, n (%) 72.9 (92) 19 (9.7) 21 (10.7) 18 (9.4) 14 (7) 0.628
Diabetes mellitus, n (%) 45.5 (7.7) 13 (6.7) 9 (4.6) 13 (6.8) 10 (5.0) 0.708
History of cardiovascular disease, n (%) 154 (19.7) 39 (20.1) 40 (20.3) 33 (17.3) 42 (21.0) 0.80
Prehypertensive at baseline, n (%) 477 (60.8) 127 (65.1) 118 (59.9) 112 (58.3) 120 (60.0) 0.543
Self-rating of health: excellent or good, n (%) 723 (932.3) 188 (96.4) 183 (92.9) 168 (88.0) 184 (92.0) 0.0197
GDS score ≥6, n (%) 34 (4.3) 9 (4.6) 6 (3.0) 8 (4.17) 11 (5.5) 0.684
RDI ≥5, n (%) 423 (54.0) 119 (61.0) 111 (56.3) 94 (49.0) 99 (49.5) 0.048‡
Sleep time PaO2 < 80%, n (%) 0.05 ± 0.3 0.1 ± 0.5 0.2 ± 0.5 0.2 ± 0.5 0.04 ± 0.21 0.04 ± 0.24 0.013††
ACEI/ARB use at follow-up, n (%) 75 (9.0) 29 (14.9) 14 (7.1) 17 (7.8) 17 (8.5) 0.034†
Diacetic use at follow-up, n (%) 48 (6.1) 16 (8.2) 9 (4.6) 16 (8.3) 7 (3.5) 0.097
β-Blocker use at follow-up, n (%) 79 (10.1) 21 (10.8) 17 (8.6) 23 (12.0) 18 (9) 0.66
Calcium channel blocker use at follow-up, n (%) 17 (2.2) 5 (2.6) 6 (3.1) 2 (1.0) 4 (2.0) 0.57

BMI indicates body mass index; PASE, physical activity score in the elderly; REM, rapid eye movement sleep; SBP, systolic blood pressure; DBP, diastolic blood pressure; RDI, respiratory disturbance index; GDS, geriatric depression scale; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

*Further categorization of alcoholic drinks per week 0, 1 to 2, 3 to 5, 6 to 13, or ≥14 did not significantly change results.
†P < 0.05.
The strengths of this study include the use of PSG for objectively measuring sleep characteristics and assessment in a large community-dwelling cohort of older men. However, given that the parent study (MrOS) was originally designed to exclude those with prevalent hypertension, this study suggests differences across the age span in the associations between sleep characteristics and health outcomes. Poor sleep quality may be measured by several different metrics, including an increased arousal index and increased wake after sleep onset, decreased sleep efficiency, and increased stages 1 and 2 (N1 and N2) sleep. Previous studies have focused on the arousal index as a metric for increased sympathetic activation and as a potential predictor of HTN. Our study suggests that a specific reduction of SWS, rather than nonspecific sleep disruption, may be a more critical factor that influences blood pressure.

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evaluate the risks of fractures in older men, this study must be considered exploratory in nature. We acknowledge that this observational study is challenged by many factors that influence both blood pressure and sleep, which also change over time. Additional study to confirm this association is necessary to determine the direction of the association after longer follow-up. Other limitations include the lack of 24-hour ambulatory blood pressure monitoring for HTN and the precise time of the blood pressure readings. Almost a quarter of those with incident HTN (24.3%) were classified based on a single blood pressure measurement; however, sensitivity analysis that excluded these participants showed similar results (data not shown).

In an exploratory study, we evaluated 11 sleep variables (Table s1) that raise questions about multiple comparisons. Because many of these indices are highly correlated (Pearson coefficients range from −0.86 to 0.64), we used the Dubey and Armitage-Parmar procedure\(^2\) to address the influence of testing for multiple correlated outcomes, and the results were not appreciably changed. These results in older men may not be generalizable to women or younger adults. It is uncertain whether there is a true association between the use of angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker and SWS (Table 3), but <10% of participants were taking these medications at follow-up (and none at baseline). Residual confounding because of other medications, activity, or comorbid conditions was not captured in this study. Also, use of PSG to determine sleep duration may not be optimal, because PSG monitoring, with possible disruptions of leads and electrodes, may not represent typical sleep patterns. However, previous work has shown that SWS has high night-to-night reproducibility.\(^2\)

**Perspectives**

This prospective study suggests that older community-dwelling men with a lower percentage of sleep time in SWS have an increased risk of incident HTN. In contrast, indices of breathing disturbances, level of hypoxemia, sleep duration, and arousal index were not independently associated with an increased risk of HTN after considering confounders. This article adds to the growing body of literature that associates sleep architecture with metabolic and physiological changes that may reflect altered neurohormones and inflammatory markers. Further studies are necessary to confirm these observations, elucidate the causal pathways, and determine whether modifications in SWS improve HTN.

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**References**


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DECREASED SLOW WAVE SLEEP INCREASES RISK OF DEVELOPING HYPERTENSION IN ELDERLY MEN

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Online supplemental methods.

Study participants.

2,860 participants from the original cohort did not participate in the sleep study as they were unwilling (1997), not screened because recruitment goals were met (332), death before the sleep study visit (334), ineligible due to exclusion criteria such as use of mechanical devices during sleep, including positive airway pressure devices, oral appliances for snoring or sleep apnea, or oxygen therapy (150), and quitting the MrOS study before the sleep study was offered (37). Among the 49 men who reported use of one of the sleep devices, 17 men were able to forego use of their sleep devices during the night of the in-home PSG study and had sleep studies performed. Of the 3,135 enrolled participants, 2,911 had valid PSG data. Of these, sleep staging could not be performed on 39 studies (due to poor EEG quality), and in 132 records there was difficulty differentiating stage 2 and SWS due to artifact; 5 people fell into both categories.

Other measures. Self-administered questionnaires were used at the time of the sleep study to ascertain participant demographic and lifestyle information and their personal and family medical history, including self-reported HTN, diabetes, and cardiovascular disease (which included history of myocardial infarction, angina, congestive heart failure, coronary bypass surgery, transient ischemic attack, stroke, or rheumatic heart disease). Race/ethnicity was self-reported using a questionnaire with a choice of 5 categories (Caucasian/White, African American/Black, Asian, Hispanic, and Other). Due to the small percentiles of non-Caucasian participants (<10% total) and no difference by SWS or incident hypertension, they were then simplified to Caucasian and Non-Caucasian. Interviews and examinations by trained study staff members included measures of functional status and anthropometric data. Physical activity was assessed by using the physical activity scale for the elderly (PASE)1. Depressed mood was assessed using the Geriatric Depression Scale (GDS), a 15 point scale of yes or no questions, and a standard cut point of >6 was used to define depressed mood2. Participants also reported tobacco use (current, past, or never) and alcohol use (drinks per week). Alcohol use was assessed by <1 or >1 drink per week and also by 0, <1, 1-2, 3-5, 6-13, or 14+ drinks per week). Participants were asked to bring in all current medications used within the preceding 30 days. All prescription and nonprescription medications were entered into an electronic database and each medication was matched to its ingredient(s) based on the Iowa Drug Information Service (IDIS) Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA)3. They were also asked whether each medication was used for sleep, and if so, the subject was considered to have “Use of Sleep Medication.” Zolpidem, diphenhidramine, acetaminophen, trazadone, and melatonin were the most common medications reported for this purpose.

Sleep studies.

The recording montage consisted of C3/A2 and C4/A1 electroencephalograms, bilateral electroculograms, electrocardiogram, a bipolar submental electromyogram, thoracic and abdominal respiratory inductance plethysmography, airflow (using nasal-oral thermocouple and nasal pressure cannula), finger pulse oximetry, electrocardiogram, body position (mercury switch sensor), and bilateral leg movements (piezoelectric sensors). Trained certified staff members performed home visits for setup of the sleep study units. After sensors were placed and calibrated, signal quality and impedance were checked, and sensors were repositioned as needed to improve signal quality, replacing electrodes if impedances were > 5000 ohms, using approaches similar to those in the Sleep Health Heart Study4. After studies were downloaded, they were transferred to the Case Western Reserve University Reading Center (Cleveland, OH) for centralized scoring by a trained technician using standard criteria5,6. PSG data quality was excellent, with > 70% of studies graded as being of excellent or outstanding quality and a failure rate < 4%. Quality codes for signals and studies were graded using previously described approaches, including coding of the duration of artifact-free data per channel and overall study quality (reflecting the combination of grades for each channel)7.

The inter-scorer reliability of percent time in SWS was high (intraclass correlation coefficient [ICC] = 0.958, 95% CI = 0.921-0.982). The intra-scorer reliability was also high, with the ICC ranging from 0.964-0.998.
**Pre-hypertension subgroup analysis.** In a subgroup analysis, determined whether the association between SWS and incident HTN persisted after excluding men who were pre-hypertensive at baseline. The normotensive participants were further divided into normotensive, pre-hypertensive or hypertensive groups at follow-up. ANOVA, Kruskal-Wallis and chi square tests were analyzed for significant differences in SWS and the other sleep stages in this subset.

**Results.**

**Subgroup analysis of sleep architecture in normotensive subjects.**

In evaluating only normotensive subjects at the start of the study (without blood pressure medication or other evidence of pre-hypertension), there was an association with decreased percent time in SWS ($P=0.004$) and percent increased time in stage 2 (N2; $P=0.042$) sleep as subjects either stayed normotensive, or progressed to pre-hypertension or HTN, shown in Online Supplemental Figure S1. There was no difference in percent time in REM sleep or stage 1 (N1) sleep and HTN progression. These results were unchanged after adjustment for age and covariates.
References:


Table S1. Adjusted odds ratios of incident hypertension (HTN) in the lowest quartile compared to the highest quartile in sleep characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio of lowest quartile to highest quartile</th>
<th>95% CI</th>
<th>P value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sleep disordered breathing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory disturbance index (RDI)</td>
<td>0.89</td>
<td>0.56, 1.42</td>
<td>0.82</td>
</tr>
<tr>
<td>Hypoxemia (% sleep time Pao2 &lt;80%)</td>
<td>0.62*</td>
<td>0.31, 1.24</td>
<td>0.18</td>
</tr>
<tr>
<td>Central apnea index</td>
<td>1.00*</td>
<td>0.73,1.38</td>
<td>0.98</td>
</tr>
<tr>
<td><strong>Sleep duration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total sleep duration (minutes)</td>
<td>0.68</td>
<td>0.44, 1.06</td>
<td>0.088</td>
</tr>
<tr>
<td><strong>Sleep architecture</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall arousal index</td>
<td>1.26</td>
<td>0.82, 1.94</td>
<td>0.26</td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>0.93</td>
<td>0.59, 1.47</td>
<td>0.81</td>
</tr>
<tr>
<td>Wake after sleep onset (minutes)</td>
<td>0.89</td>
<td>0.56, 1.40</td>
<td>0.57</td>
</tr>
<tr>
<td>% time in stage 1 (N1) sleep</td>
<td>0.69</td>
<td>0.44, 1.08</td>
<td>0.075</td>
</tr>
<tr>
<td>% time in stage 2 (N2) sleep</td>
<td>0.77</td>
<td>0.50, 1.19</td>
<td>0.068</td>
</tr>
<tr>
<td>% time in slow wave (N3) sleep</td>
<td>1.83</td>
<td>1.18, 2.85</td>
<td><strong>0.012</strong></td>
</tr>
<tr>
<td>% time in REM</td>
<td>0.97</td>
<td>0.62, 1.52</td>
<td>0.93</td>
</tr>
</tbody>
</table>

*Denotes variables dichotomized as zero or greater than zero rather than quartiles due to distributions not suitable for quartiles. Models are adjusted for age, non-white race, study site, and body mass index. (Models are not significantly changed when additionally adjusting for alcohol use or smoking).
Online Supplemental Figure S1 Legend

Sleep architecture of normotensive subjects at baseline based on hypertension progression ~3.4 years later. In subset analysis of participants who were normotensive at baseline (not pre-hypertensive but with SBP<120 mmHg and DBP <80 mmHg; N=307), we found an association with percent time in slow wave sleep (SWS; P=0.004) and stage 2 sleep (P=0.042) as subjects progressed to pre-hypertension or hypertension. There was no difference in percent time in REM sleep or stage 1 sleep.