Obstructive Sleep Apnea With Objective Daytime Sleepiness Is Associated With Hypertension

Rong Ren,* Yun Li,* Jihui Zhang, Junying Zhou, Yuanfeng Sun, Lu Tan, Taomei Li, Yun-Kwok Wing, Xiangdong Tang

See Editorial Commentary, pp 1100–1102

Abstract—Subjective daytime sleepiness is considered a significant risk factor of hypertension in patients with obstructive sleep apnea (OSA). In this study, our goal was to examine the joint effect on hypertension of OSA and objective daytime sleepiness measured by the multiple sleep latency test (MSLT). A total of 1338 Chinese patients with OSA and 484 primary snorers were included in the study. All subjects underwent 1 night polysomnography followed by MSLT. The MSLT values were classified into 3 categories: >8 minutes, 5 to 8 minutes, and <5 minutes. Hypertension was defined based either on direct blood pressure measures or on diagnosis by a physician. After controlling for confounders, OSA combined with MSLT of 5 to 8 minutes increased the odds of hypertension by 95% (odds ratio, 1.95; 95% confidence interval, 1.10–3.46), whereas OSA combined with MSLT <5 minutes further increased the odds of hypertension by 111% (odds ratio, 2.11; 95% confidence interval, 1.22–3.31) compared with primary snorers with MSLT >8 minutes. In stratified analyses, the association of hypertension with MSLT in OSA patients was seen among both sexes, younger ages, both obese and nonobese patients, and patients with and without subjective excessive daytime sleepiness. We conclude that objective daytime sleepiness is associated with hypertension in patients with OSA. (Hypertension. 2016;68:1264-1270. DOI: 10.1161/HYPERTENSIONAHA.115.06941.) • Online Data Supplement

Key Words: arousal ■ asphyxia ■ baroreflex ■ blood pressure ■ daytime sleepiness ■ hypertension ■ obstructive sleep apnea

Obstructive sleep apnea (OSA) is a common disease that affects 2% to 4% of adult men and 1% to 2% of adult women,1 and among adults aged 30 to 70 years, the prevalence of OSA increases to 24% to 26% in men and 17% to 28% in women.2 Repetitive asphyxia events in sleep apnea result in brain arousal, intermittent hypoxemia, and increased sympathetic nervous system activity. Both cross-sectional and longitudinal studies have demonstrated that OSA is a risk factor for hypertension that is independent of age, sex, and body mass index.3–5 Furthermore, it has been shown that OSA is an important cause of hypertension.5–7 Several mechanisms, including increased sympathetic tone, inflammatory response, impaired arterial baroreflex sensitivity, and pleural pressure swings, induced by intermittent hypoxemia of OSA are involved in the relationship between OSA and hypertension.8–11

Excessive daytime sleepiness (EDS) is common in patients with OSA and an important criterion for diagnosis and treatment of OSA. EDS has a prevalence of 16% to 22% in OSA in epidemiological samples, and it is the most common complaint in clinical samples.1,12 Many studies have shown that OSA patients with subjective EDS have a higher prevalence of hypertension compared with those without EDS.13–15 Furthermore, a series of clinical trials have suggested that continuous positive airway pressure (CPAP) therapy is less effective in OSA patients without EDS than those with EDS in terms of decreasing blood pressure (BP) and preventing the occurrence of hypertension.16–20 These findings suggest that subjective EDS is associated with hypertension in OSA. However, in previous studies, EDS was determined by self-report, with the Epworth Sleepiness Scale (ESS)21 being most frequently used. Lombardi et al22 found that EDS determined by the multiple sleep latency test (MSLT) in OSA patients was associated with lower baroreflex sensitivity and higher low-to-high frequency power ratio of heart rate variability during overnight sleep compared with OSA patients without EDS. To our knowledge, this is the only existing study reflecting a possible association between objective EDS and cardiovascular events in OSA. The specific relationship between hypertension and objectively evaluated EDS has not been investigated.

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Sleepiness and Hypertension in OSA Patients

The ESS is a widely used, self-report questionnaire, helping subjects rate their feeling of daytime sleepiness and fatigue, whereas the MSLT is a laboratory-based tool designed to evaluate objective daytime sleepiness and physiological sleep propensity and arousal.\textsuperscript{21,22,25} Several studies examining the association between objective and subjective sleepiness in experimental and clinical samples have found inconsistent results, and the correlation between these 2 measures is relatively low.\textsuperscript{26–28} Furthermore, MSLT values have been shown associated with several biological indicators, whereas ESS scores are not. For example, a preliminary study of the underlying mechanism of subjective and objective daytime sleepiness in OSA patients has reported that objective, but not subjective, daytime sleepiness is associated with increased secretion of 24-hour mean interleukin-6.\textsuperscript{29} Bonnet and Arand\textsuperscript{30} also found that resting heart rate and sympathetic nervous system activity are associated with MSLT values but not with ESS scores in healthy subjects. In addition, Li et al\textsuperscript{24} have reported that MSLT values, but not ESS scores, were associated with higher odds of hypertension in insomnia patients. Thus, ESS and MSLT may reflect different dimensions of central nervous system functions. The extent to which objective EDS is related to hypertension in OSA patients and whether objective EDS has a greater predictive relationship to increased blood pressure (BP) regardless of OSA status or relative subjective EDS have not been determined.

On the basis of these observations, we speculate that objective daytime sleepiness may be an index of the biological severity of OSA and that OSA with objective daytime sleepiness could be associated with adverse medical outcomes. To test these hypotheses, we examined the joint effect of OSA and objective daytime sleepiness on hypertension in a large, cross-sectional, hospital-based sample. We hypothesized that OSA with objective daytime sleepiness would be associated with hypertension and that the comorbidity of OSA and hypertension would be enhanced by objective daytime sleepiness.

Methods

Subjects

This was a between-group, cross-sectional, observational study conducted at the Sleep Medicine Center, West China Hospital, Sichuan University, China. The study procedure was approved by the University’s Institutional Review Board, and informed consent was obtained from each participant.

All participants were Chinese adults (aged >18 years) had habitual snoring with suspected OSA. All potential research subjects were interviewed with a comprehensive questionnaire. The questionnaire assessed history of sleep complaints, general health, and medication use.

To qualify for the study, patients with OSA had to meet an apnea-hypopnea index (AHI) criterion of >15 events/h. Snorers with an AHI ≤15 events/h were included in the primary snoring group. We excluded subjects who had (1) a chronic sleep-disrupting medical condition (ie, pain); (2) a current major psychiatric condition (ie, depression); (3) current use of hypnotics, anxiolytics, antidepressants, and any other antipsychotics or during the past 3 months; (4) evidence of narcolepsy; and (5) any other comorbid sleep disorder (ie, insomnia).

During the recruitment period, 2135 consecutive habitual snorers met the selection criteria for the present study. On the basis of these observations, we speculated that OSA with objective daytime sleepiness could be associated with adverse medical outcomes. To test these hypotheses, we examined the joint effect of OSA and objective daytime sleepiness on hypertension in a large, cross-sectional, hospital-based sample. We hypothesized that OSA with objective daytime sleepiness would be associated with hypertension and that the comorbidity of OSA and hypertension would be enhanced by objective daytime sleepiness.

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Multiple Sleep Latency Test

The MSLT was performed on the day immediately after the overnight polysomnography recording, and it comprised four 20-minute nap opportunities at intervals of 2 hours (9:00, 11:00, 13:00, and 15:00). Sleep onset required the presence of any sleep stage for a duration of ≥30 seconds. If no sleep occurred, the trial was terminated at 20 minutes, and a sleep latency of 20 minutes was assigned. The mean sleep latency was the average sleep latency from all 4 naps. Lower values of MSLT indicate EDS (eg, the mean sleep latency <8 minutes).\textsuperscript{25}

Hypertension

BP was measured at 2 time points: in the evening ≈2 hours before starting polysomnography (ie, 20:00–21:00) and in the morning after the end of polysomnography but before getting out of bed (ie, 06:00–07:00). We used a pneumoelectric microprocessor–controlled instrument with the appropriate-sized cuffs. The accuracy of this monitor is reported to be ±3 mm Hg; in addition, internal calibration was performed before each use, and the machine was checked against a mercury sphygmomanometer at least once a year. Recorded BP was the average of 3 consecutive readings during a 5-minute period after at least 10 minutes of rest in the supine position. Hypertension was defined as (1) a diastolic BP ≥90 mm Hg or a systolic BP ≥140 mm Hg at either evening or morning measurement, (2) use of antihypertensive medication, or (3) physician diagnosis of hypertension as per clinical history. Mean arterial pressure was defined as (systolic BP–diastolic BP)/3 in mm Hg. We used the average of evening and morning BP for analyzing.

Other Key Measurements

Subjective EDS was measured by ESS, a cutoff point of ESS >10 was defined as subjective EDS.\textsuperscript{21} Inclusion in diabetes mellitus was based on whether subjects were being treated for diabetes mellitus or had a physician diagnosis of diabetes mellitus as per clinical history. We also ascertained history of tobacco (current or past use of any type of tobacco product), alcohol (>2 alcohol drinks per day), and coffee usage (>2 coffee drinks per day). Body mass index was based on measured height (cm) and weight (kg) during the subjects’ sleep laboratory visit.

Statistical Analysis

Data are presented as the mean±SD for continuous variables and percent for categorical variables. Bivariate comparisons between groups were conducted using independent-sample t tests or Mann–Whitney U tests for normally and not normally distributed continuous variables, respectively, and with the \( \chi^2 \) test for categorical variables.

Logistic regression models were used to assess the independent associations between OSA and MSLT with hypertension. The covariates we adjusted for included major confounding factors expected to affect this relation. Furthermore, to examine the joint effect of OSA and objective daytime sleepiness, we performed logistic regression models that included 5 dummy variables to represent all 6 possible combinations of OSA and MSLT. We used primary snorers with MSLT >8 minutes as a reference group. We calculated the adjusted odds ratios (ORs) and the 95% confidence intervals (95% CIs) while adjusting for potential confounders from this model to estimate the odds of hypertension associated with OSA and MSLT. The interaction between AHI and MSLT was significant (\( P<0.05 \)).

To examine the observed association between different levels of objective EDS and frequency of hypertension and BP, we conducted an ANCOVA adjusted for potential confounders. Post hoc Dunnett
tests were used to control for type I errors in multiple comparisons; primary snorers with MSLT >8 minutes were the reference group. Linear regression models were used to explore the association between BP and MSLT values within patient with and without OSA, respectively. Data were analyzed using SPSS 19.0. Comparisons with \( P \) values <0.05 were considered statistically significant. Please see online-only Data Supplement detailing the sampling procedure, polysomnography, and statistical analysis of the study.

**Results**

The demographic, clinical, and sleep characteristics of primary snoring and OSA patients and different levels of objective daytime sleepiness are presented in Table 1. Table S1 in the online-only Data Supplement presents the demographic, clinical, and sleep characteristics of subgroups based on different levels of objective daytime sleepiness within primary snoring and OSA patient groups.

In Table 2, we present the association of OSA alone or the 3-level MSLT alone with hypertension after progressively adjusting for potential confounders. OSA showed a significant association with hypertension (OR=1.51; 95% CI, 1.15–1.99). In terms of MSLT, MSLT <5 minutes increased the odds of hypertension by 30% (OR=1.30; 95% CI, 1.02–1.69) as compared with those with MSLT >8 minutes. MSLT 5 to 8 minutes was marginally significantly associated with increased odds of hypertension (OR=1.27; 95% CI, 0.97–1.67; \( P=0.07 \)) as compared with those with MSLT >8 minutes.

Table 3 presents the joint effect of OSA and MSLT on hypertension. The odds of hypertension were significantly increased among OSA patients with objective EDS: OSA with MSLT 5 to 8 minutes and MSLT <5 minutes increased the odds of hypertension by \( \approx 95\% \) (OR=1.95; 95% CI, 1.10–3.46) and \( \approx 110\% \) (OR=2.11; 95% CI, 1.22–3.31) compared with primary snorers without objective EDS, respectively. In contrast, OSA patients without objective EDS and primary snorers with objective EDS did not have significantly increased odds of hypertension. Furthermore, Figure depicts the observed association between different levels of objective EDS and frequency of hypertension and BP, adjusted for confounders.

### Table 1. Demographic, Clinical, and Sleep Characteristics of Primary Snoring and OSA Groups and for Different Levels of Objective EDS

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Primary Snoring (n=484)</th>
<th>OSA (n=1338)</th>
<th>( P_1 ) Value</th>
<th>MSLT &gt;8 min (n=1089)</th>
<th>5 min≤MSLT≤8 min (n=377)</th>
<th>MSLT &lt;5 min (n=356)</th>
<th>( P_2 ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic and clinical</strong></td>
<td></td>
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<tr>
<td>Men, n (%)</td>
<td>319 (65.9)</td>
<td>1174 (87.7)</td>
<td>&lt;0.001</td>
<td>849 (78.0)</td>
<td>323 (85.7)</td>
<td>321 (90.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, y</td>
<td>41.0±11.19</td>
<td>44.7±11.26</td>
<td>&lt;0.001</td>
<td>44.2±11.74</td>
<td>43.56±10.90</td>
<td>42.23±10.51</td>
<td>0.013</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.98±3.24</td>
<td>27.38±3.49</td>
<td>&lt;0.001</td>
<td>26.02±3.69</td>
<td>26.48±3.44</td>
<td>27.86±3.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>147 (30.4)</td>
<td>761 (56.9)</td>
<td>&lt;0.001</td>
<td>512 (47.0)</td>
<td>197 (52.3)</td>
<td>199 (55.9)</td>
<td>0.008</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>120.63±14.35</td>
<td>127.23±15.13</td>
<td>&lt;0.001</td>
<td>125.63±15.30</td>
<td>126.82±15.12</td>
<td>127.07±14.96</td>
<td>0.234</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>77.33±9.27</td>
<td>83.57±11.21</td>
<td>&lt;0.001</td>
<td>81.56±10.96</td>
<td>83.19±11.23</td>
<td>84.80±11.28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>91.76±10.35</td>
<td>98.12±11.84</td>
<td>&lt;0.001</td>
<td>96.24±11.71</td>
<td>97.73±11.90</td>
<td>98.89±11.96</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>10 (2.1)</td>
<td>65 (4.9)</td>
<td>0.007</td>
<td>48 (4.4)</td>
<td>13 (3.5)</td>
<td>14 (3.9)</td>
<td>0.710</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>141 (29.1)</td>
<td>603 (45.1)</td>
<td>&lt;0.001</td>
<td>392 (36.0)</td>
<td>163 (43.2)</td>
<td>189 (53.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol drinking, n (%)</td>
<td>155 (32.0)</td>
<td>650 (48.6)</td>
<td>&lt;0.001</td>
<td>448 (41.1)</td>
<td>178 (47.2)</td>
<td>179 (50.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Coffee use, n (%)</td>
<td>97 (20.1)</td>
<td>415 (31.1)</td>
<td>&lt;0.001</td>
<td>282 (26.0)</td>
<td>108 (28.6)</td>
<td>117 (32.9)</td>
<td>0.010</td>
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<tr>
<td><strong>Nighttime sleep</strong></td>
<td></td>
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<tr>
<td>Sleep-onset latency, min</td>
<td>17.73±24.21</td>
<td>12.79±18.01</td>
<td>&lt;0.001</td>
<td>16.18±21.65</td>
<td>11.81±14.53</td>
<td>10.18±18.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total sleep time, min</td>
<td>417.98±69.33</td>
<td>432.70±67.41</td>
<td>&lt;0.001</td>
<td>418.65±68.49</td>
<td>438.79±63.80</td>
<td>449.24±65.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>82.95±12.10</td>
<td>85.46±10.61</td>
<td>&lt;0.001</td>
<td>83.07±11.45</td>
<td>86.21±10.23</td>
<td>88.56±9.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wake after sleep onset, min</td>
<td>68.46±56.25</td>
<td>60.97±49.88</td>
<td>0.010</td>
<td>69.83±54.21</td>
<td>56.92±46.75</td>
<td>48.34±44.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AHI, events/h</td>
<td>6.14±4.44</td>
<td>54.81±23.54</td>
<td>&lt;0.001</td>
<td>35.43±27.69</td>
<td>44.98±29.13</td>
<td>58.33±28.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T90%, %</td>
<td>1.13±5.29</td>
<td>23.35±23.73</td>
<td>&lt;0.001</td>
<td>13.13±19.83</td>
<td>19.72±24.31</td>
<td>28.24±25.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LSaO₂, %</td>
<td>85.46±10.36</td>
<td>64.65±18.51</td>
<td>&lt;0.001</td>
<td>72.85±18.17</td>
<td>69.30±19.29</td>
<td>62.91±19.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Daytime sleepiness</strong></td>
<td></td>
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<tr>
<td>ESS</td>
<td>7.14±5.39</td>
<td>9.86±6.06</td>
<td>&lt;0.001</td>
<td>8.03±5.76</td>
<td>9.69±5.73</td>
<td>11.93±6.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MSLT, min</td>
<td>11.18±4.50</td>
<td>9.01±4.58</td>
<td>&lt;0.001</td>
<td>12.96±3.15</td>
<td>6.52±0.86</td>
<td>3.32±1.19</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Categorical variables are represented as percentages, and other variables are represented as mean±SD. AHI indicates apnea/hypopnea index; DBP, diastolic blood pressure; EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; LSaO₂, the lowest oxygen saturation; MAP, mean arterial pressure; MSLT, multiple sleep latency test; OSA, obstructive sleep apnea; \( P_1, P_2 \) values for the comparisons between OSA and primary snoring; \( P \) values for the comparisons among 3 MSLT subgroups; SBP, systolic blood pressure; and T90%, percentage of time spent in sleep below 90% oxygen saturation.
The association between different MSLT categories with hypertension in subgroups defined according to sex, obesity (cutoff point of body mass index was 28 kg/m²), and subjective EDS are presented in Table 4. The interactions between MSLT and AHI were significant for men, in patients <55 years old, in patients with and without obesity, and in patients with ESS ≤ 0 (all P values <0.05) but were not significant for women, in patients ≥ 55 years old or with ESS >10 (all P values >0.05). As shown in Table 4, the association between hypertension and objective daytime sleepiness was present in both sexes, younger ages, both obese and nonobese patients, and patients with and without subjective EDS. Our findings showed a trend suggesting that OSA has larger effect on hypertension when MSLT is shorter in women and in patients with subjective EDS. However, the interaction between MSLT and AHI were not significant in these 2 subgroups, suggesting that there were no significant synergistic effect on OSA and MSLT in women and subjective EDS patients.

To compare the effect of MSLT within OSA and primary snoring patients on BP, we conducted linear regression models to examine the association between MSLT values and BP within primary snoring and OSA patients, respectively. Please see online-only Data Supplement and Table S2.

**Discussion**

By using a large sample size in the current study, we were able to classify primary snoring and OSA patients into 6 subgroups based on MSLT values to explore the relationship between objective EDS and hypertension. The large sample size also allowed us to conduct a stratified analysis in both sexes, younger and older ages, obese and nonobese individuals, and those with and without subjective sleepiness. Our findings suggest that OSA with objective EDS, as measured by the MSLT, is associated with hypertension regardless of whether or not the patients had subjective EDS. However, a similar association was not found among primary snorers.

As one of the most common complaints in patients with OSA, subjective EDS has been demonstrated to be a significant risk factor of hypertension. Recently, Feng et al13 found that subjective EDS was an indicator of BP profile in a study of 2297 consecutive Chinese OSA patients. Kapur et al15 found a significantly elevated OR for hypertension among OSA patients with a high AHI, low MSLT, and low ESS.

### Table 2. Adjusted ORs and 95% CIs for the Association of Hypertension With OSA or MSLT

<table>
<thead>
<tr>
<th>Predictors</th>
<th>n</th>
<th>OR (95% CI)</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Primary snoring</td>
<td></td>
<td></td>
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<tr>
<td>MSLT &gt;8 min</td>
<td>353</td>
<td>1.03 (0.61–1.75)</td>
<td>1.08 (0.64–1.84)</td>
<td>1.13 (0.66–1.92)</td>
<td></td>
</tr>
<tr>
<td>5 min ≤ MSLT ≤ 8 min</td>
<td>85</td>
<td>0.88 (0.44–1.80)</td>
<td>0.94 (0.46–1.89)</td>
<td>1.00 (0.49–2.04)</td>
<td></td>
</tr>
<tr>
<td>MSLT &lt;5 min</td>
<td>46</td>
<td>1.83 (1.36–2.47)</td>
<td>1.18 (0.59–2.34)</td>
<td>1.28 (0.65–2.54)</td>
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<tr>
<td>OSA</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>MSLT &gt;8 min</td>
<td>736</td>
<td>2.30 (1.61–3.28)</td>
<td>1.76 (1.01–3.11)</td>
<td>1.95 (1.10–3.46)</td>
<td></td>
</tr>
<tr>
<td>5 min ≤ MSLT ≤ 8 min</td>
<td>292</td>
<td>2.35 (1.62–3.32)</td>
<td>1.85 (1.13–3.03)</td>
<td>2.11 (1.22–3.31)</td>
<td></td>
</tr>
<tr>
<td>MSLT &lt;5 min</td>
<td>310</td>
<td>1.95 (1.15–1.99)</td>
<td>1.30 (0.97–1.67)</td>
<td>1.30 (0.97–1.67)</td>
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</tr>
</tbody>
</table>

Model 1 was adjusted for age, sex, and BMI; model 2 was adjusted for age, sex, BMI, tobacco use, alcohol drinking, coffee use, diabetes mellitus, ESS, T90%, LSao₂, and OSA (or MSLT); and model 3 was adjusted for age, sex, BMI, tobacco use, alcohol drinking, coffee use, diabetes mellitus, ESS, T90%, LSao₂, OSA (or MSLT), sleep-onset latency, sleep efficiency, and wake time after sleep onset. BMI indicates body mass index; CI, confidence interval; ESS, Epworth Sleepiness Scale; LSao₂, the lowest oxygen saturation; MSLT, multiple sleep latency test; OR, odds ratio; OSA, obstructive sleep apnea; and T90%, percentage of time spent in sleep below 90% oxygen saturation.

### Table 3. Adjusted ORs and 95% CIs for the Association of Hypertension With OSA and MSLT

<table>
<thead>
<tr>
<th>Predictors</th>
<th>n</th>
<th>OR (95% CI)</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary snoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSLT &gt;8 min</td>
<td>353</td>
<td>1.52 (2.51)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 min ≤ MSLT ≤ 8 min</td>
<td>85</td>
<td>1.30 (1.64)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSLT &lt;5 min</td>
<td>46</td>
<td>1.38 (1.67)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OSA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSLT &gt;8 min</td>
<td>736</td>
<td>1.95 (1.15–1.99)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 min ≤ MSLT ≤ 8 min</td>
<td>292</td>
<td>1.28 (1.01–1.67)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSLT &lt;5 min</td>
<td>310</td>
<td>1.30 (1.02–1.69)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Model 1 was adjusted for age, sex, and BMI; model 2 was adjusted for age, sex, BMI, tobacco use, alcohol drinking, coffee use, diabetes mellitus, ESS, AHI, T90%, LSao₂, and interaction between AHI and MSLT; and model 3 was adjusted for age, sex, BMI, tobacco use, alcohol drinking, coffee use, diabetes mellitus, ESS, AHI, T90%, LSao₂, interaction between AHI and MSLT, sleep-onset latency, sleep efficiency, and wake time after sleep onset. The interaction between AHI and MSLT was significant, P < 0.05. AHI indicates apnea/hypopnea index; BMI, body mass index; CI, confidence interval; ESS, Epworth Sleepiness Scale; LSao₂, the lowest oxygen saturation; MSLT, multiple sleep latency test; OR, odds ratio; OSA, obstructive sleep apnea; and T90%, percentage of time spent in sleep below 90% oxygen saturation.
who reported sleepiness ≥5 days per week. In addition, 3 short-
term and 2 long-term randomized controlled trials have shown,
that the mild beneficial effect of CPAP on BP in nonsleepy
patients with OSA, even when they insisted on CPAP usage for
a longer period (3.6 hours or longer) each night. They did, however,
find significantly decreased BP in sleepy OSA patients
after CPAP treatment.16–20 Nevertheless, each of these studies
used self-reported questionnaires, such as the ESS, rather than
an objective measure such as the MSLT, to determine EDS.

The weak-to-moderate association between objective and
subjective sleepiness is not well understood. It has been pro-
posed that the discrepancy between the ESS and the MSLT
may be explained by a lack of sensitivity of the currently
used cutoff points or by the fact that they measure different
constructs, that is, the ESS estimates an overall trait, whereas
the MSLT assesses a state (ie, an exact time or situation).32
The MSLT is not selectively sensitive to either sleepiness or
alertness but is sensitive to both the sleep and the arousal sys-
tems.30,33 Accordingly, Fong et al34 suggested that the MSLT
assesses physiological sleep propensity associated with
impaired arousal mechanisms (ie, increased interleukin-6 and
decreased cortisol levels),36 whereas the ESS captures the sub-
jective complaint of daytime sleepiness/fatigue resulting from
impaired sustained attention.37 This hypothesis is supported
by a preliminary study demonstrating that objective EDS dif-
fers from subjective EDS in terms of its association with the
peripheral levels of arousal-related molecules, that is, in-
terleukin-6 and cortisol in patients with OSA.29

The MSLT has not been recommended as a measure of
EDS in the diagnosis and treatments guidelines of OSA.
However, our findings suggest that the MSLT may provide a
reliable index of the biological and medical significance and
severity of OSA. Furthermore, the finding of a significant
association between objective EDS and hypertension in OSA
patients without subjective EDS suggests that subjective mea-
sures of EDS may be of limited use in clinical practice for
determining which patients warrant immediate intervention.

![Figure](http://hyper.ahajournals.org/)

**Figure.** Frequency of hypertension (A), systolic blood pressure (SBP; B), diastolic blood pressure (DBP; C), and mean arterial pressure (MAP; D) across different levels of multiple sleep latency test (MSLT; >8 min, 5–8 min, and <5 min) in primary snoring and obstructive
sleep apnea (OSA) patients adjusted for age, sex, body mass index, tobacco use, alcohol drinking, coffee use, diabetes mellitus, Epworth Sleepiness Scale, apnea/hypopnea index, T90%, LSao2, interaction between AHI and MSLT, antihypertension medicine, sleep-onset
latency, sleep efficiency, and wake time after sleep onset. Error bars indicate SE. *P<0.05. LSao2 indicates the lowest oxygen saturation;
to and T90%, percentage of time spent in sleep below 90% oxygen saturation.)
The mechanisms for the significant association between objective EDS and hypertension are likely related to increased sympathetic tone, impaired nocturnal autonomic cardiac modulation, and systemic inflammation. It has been shown that OSA with objective EDS is associated with lower baroreflex sensitivity and impaired heart rate variability, which are indicators of sympathetic activity. Furthermore, Li et al have reported that OSA with objective EDS is associated with increased levels of proinflammatory cytokines (e.g., interleukin-6), which has been known associated with increased risk for cardiometabolic morbidity and mortality. Thus, the increased inflammatory response and dysregulated cardiac autonomic control may be the mechanisms underlying the association between objective EDS and increased odds of hypertension in OSA.

There are several strengths of this study, such as the large sample size, careful assessment of the subjects, and that measurements were not confounded by the use of sleep and other psychotropic medication or presence of other frequent sleep and mental disorders. However, several limitations should be addressed: (1) data are from one full-night polysomnography, and night-to-night variation/first night effects cannot be excluded; (2) BP measurements taken at 2 time points cannot approximate the entire 24-hour BP profile; (3) there is the possibility of a white coat bias effect as we conducted direct BP measures as one way to assess hypertension; and (4) our cross-sectional study examines only one point in time and cannot account for potential changes across time. Thus, we do not know whether CPAP, or other therapies, can reverse the deleterious effects of objective EDS on BP. Although a cross-sectional study cannot directly demonstrate causality, this study provided important data indicating a significant link between objective EDS and hypertension among OSA patients.

### Perspectives

In conclusion, our study suggests that OSA with objective daytime sleepiness is independently associated with hypertension. Further studies with longitudinal designs are warranted to delineate the temporal association between objective EDS and hypertension.

### Acknowledgments

We thank Dr Larry Sanford at Eastern Virginia Medical School for help in editing the article. Our technical staffs (F. Lei and L. Du) are especially commended for their efforts.

### Sources of Funding

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### Disclosures

None.

### References


Novelty and Significance

What Is New?

• This is the first study demonstrating the joint effect of obstructive sleep apnea (OSA) and objective excessive daytime sleepiness measured by multiple sleep latency test on hypertension, and we found that OSA with objective excessive daytime sleepiness is significantly associated with hypertension.

What Is Relevant?

• Excessive daytime sleepiness is often seen in OSA patients. Physicians may consider using multiple sleep latency test to evaluate the biological severity of OSA in terms of cardiometabolic comorbidities.
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Obstructive sleep apnea with objective daytime sleepiness is associated with hypertension

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bDepartment of Psychiatry, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong Special Administrative Region

*Rong Ren and *Yun Li made equal contributions to this work.

Short title: Sleepiness and hypertension in OSA patients

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ONLINE SUPPLEMENTAL METHODS

Subjects

This was a between-group, cross-sectional, observational study conducted at the Sleep Medicine Center, West China Hospital, Sichuan University, China. The study procedure was approved by the University’s Institutional Review Board and informed consent was obtained from each participant.

All participants were Chinese adults (age > 18 years) with suspected OSA. They were selected consecutively from January 2010 to July 2014. All potential research subjects were interviewed with a comprehensive questionnaire. The questionnaire assessed history of sleep complaints, general health, and medication use.

To qualify for the study, patients with OSA had to meet an apnea/hypopnea index (AHI) criterion of > 15 events/hour. Snorers with an AHI ≤ 15 events/hour were included in the primary snoring group. We excluded subjects who had (1) a chronic sleep-disrupting medical condition (i.e., pain); (2) a current major psychiatric condition (i.e., depression); (3) use of hypnotics, anxiolytics, antidepressants, and any other antipsychotics currently or during the past 3 months; (4) evidence of narcolepsy, that is, MSLT ≤ 8 minutes, ≥ 2 sleep onset rapid eye movement periods (SOREMPs) and/or cataplexy; and (5) any other comorbid sleep disorder (i.e., insomnia).

During the recruitment period, 2135 consecutive habitual snorers were studied in our sleep laboratory. After an overnight polysomnography and MSLT, 135 participants were excluded based on use of medication, and 118 participants were excluded based on MSLT ≤ 8 min and ≥ 2 SOREMPs. Smoking, caffeinated beverages, drinking alcohol and vigorous physical activity were normally restricted during the entire night and day of polysomnography and MSLT recording. A total of 1882 individuals, 1338 OSA and 484 primary snoring patients met the selection criteria for the present study.

Polysomnography

All subjects were evaluated for 1 night in the sleep laboratory in sound-attenuated, light- and temperature-controlled rooms. During this evaluation, subjects were allowed to sleep ad libitum based on their habitual sleep time, with the recording time range from 22:00–23:00 to 6:00–7:00. Sleep data were collected and scored via the Alice 5 Diagnostic Sleep System (Philips Respironics, Bend, OR, USA). Subjects were continuously monitored with 16-channel polygraphs, including electroencephalographic, bilateral electrooculography, electromyography, and electrocardiography. Respiration was monitored throughout the night with oronasal thermocouples, nasal pressure transducer and thoracic/abdominal strain gauges. Hemoglobin oxygen saturation (SpO₂) were obtained with an oximeter attached to the finger. All sleep parameters recorded by polysomnography were analyzed according to the international criteria of the American Academy of Sleep Medicine by a senior technician who was blind to any diagnosis. An apnea was defined as more than 90% reduction in airflow for at least 10s; whereas hypopnea was defined as 50% or more reduction of airflow for at least 10s associated with 3% or more reduction in oxygen
Multiple Sleep Latency Test

The MSLT was performed on the day immediately after the overnight polysomnography recording and was comprised of four 20-minute nap opportunities at intervals of 2 hours (9:00, 11:00, 13:00, and 15:00). Sleep onset required the presence of any sleep stage for a duration of ≥ 30 s. If no sleep occurred, the trial was terminated at 20 minutes and a sleep latency of 20 minutes was assigned. The mean sleep latency was the average sleep latency from all four naps. Lower values of MSLT indicate excessive daytime sleepiness (e.g., the mean sleep latency < 8 minutes)².

Hypertension

Blood pressure was measured at 2 time points: in the evening about 2 hours before starting polysomnography (i.e., 20:00–21:00) and in the morning after the end of polysomnography but before getting out of bed (i.e., 06:00–07:00). We used a pneumoelectric microprocessor–controlled instrument with the appropriate-sized cuffs. The accuracy of this monitor is reported to be ± 3 mm Hg; in addition, internal calibration was performed before each use and the machine was checked against a mercury sphygmomanometer at least once a year. Recorded blood pressure was the average of 3 consecutive readings during a 5-minute period following at least 10 minutes of rest in the supine position. Hypertension was defined as (1) a diastolic blood pressure (DBP) ≥ 90 mm Hg or a systolic blood pressure (SBP) ≥ 140 mm Hg at either evening or morning measurement, (2) use of antihypertensive medication, or (3) physician-diagnosis of hypertension as per clinical history. Mean arterial pressure (MAP) was defined as (SBP– DBP) / 3 + DBP in mmHg.

Other Key Measurements

Subjective EDS was measured by ESS. Total ESS scores range from 0 to 24 and higher scores indicate more subjective EDS³. A cut-off point of ESS> 10 was defined as subjective EDS. Inclusion in diabetes mellitus was based on whether subjects were being treated for diabetes mellitus or had a physician-diagnosis of diabetes mellitus as per clinical history. We also ascertained history of tobacco (current or past use of any type of tobacco product), alcohol ( > 2 alcohol drinks per day), and coffee usage ( > 2 coffee drinks per day). BMI was based on measured height (cm) and weight (kg) during the subjects’ sleep laboratory visit.

Statistical analysis

Data are presented as the mean ± standard deviation (SD) for continuous variables and percent for categorical variables. Bivariate comparisons between groups were conducted using independent-sample t-tests or Mann–Whitney U tests for normally and not normally distributed continuous variables, respectively, and with the
χ² test for categorical variables.

Logistic regression models were used to assess the independent associations between OSA and MSLT with hypertension. The covariables we adjusted for included major confounding factors expected to affect this relation, i.e., age, sex, BMI, diabetes, tobacco, alcohol drinking, coffee use, ESS, percentage of time spent in sleep below 90% oxygen saturation (T90%), LSaO₂, sleep onset latency, sleep efficiency and wake time after sleep onset. Furthermore, to examine the joint effect of OSA and objective daytime sleepiness, we performed logistic regression models which included 5 dummy variables to represent all 6 possible combinations of OSA and MSLT. We used primary snorers with MSLT > 8 min as a common reference group. We calculated the odds ratios (ORs) and the 95% confidence intervals (95% CIs) from this model to estimate the odds of hypertension associated with OSA and MSLT. The interaction between AHI and MSLT was significant (p< 0.05). The covariables we adjusted for included major confounding factors expected to affect this relation, i.e., age, sex, BMI, diabetes, tobacco, alcohol drinking, coffee use, ESS, AHI, percentage of time spent in sleep below 90% oxygen saturation (T90%), LSaO₂, sleep onset latency, sleep efficiency, wake time after sleep onset and the interaction between AHI and MSLT.

In order to examine the observed association between different levels of objective EDS and frequency of hypertension and blood pressure, we conducted an analysis of covariance (ANCOVA) adjusted for age, sex, BMI, tobacco, alcohol drinking, coffee use, diabetes mellitus, ESS, AHI, T90%, LSaO₂, sleep onset latency, sleep efficiency and wake time after sleep onset, anti-hypertension medicine use and the interaction between AHI and MSLT. Post hoc Dunnett tests were used to control for type I errors in multiple comparisons; controls with MSLT > 8 minutes were the reference group.

Linear regression models were used to explore the association between blood pressure and MSLT values, adjusted for age, sex, BMI, tobacco, alcohol drinking, coffee use, diabetes mellitus, ESS, anti-hypertension medicine, sleep onset latency, sleep efficiency and wake time after sleep onset in primary snoring patients, and OSA patients, respectively. Within OSA patients, we further adjusted for the severity of OSA, T90% and LSaO₂.

Data were analyzed using SPSS 19.0. Comparisons with p values < 0.05 were considered statistically significant.
ONELINE SUPPLEMENTAL RESULTS

Results

The demographic, clinical, and sleep characteristics of primary snoring and OSA patients as well as different levels of objective daytime sleepiness are presented in Table 1. Table S1 presents the demographic, clinical and sleep characteristics of subgroups based on different levels of objective daytime sleepiness within primary snoring and OSA patient groups.

In Table 2, we present 2 logistic regression models that examined the association of OSA alone or the 3-level MSLT alone with hypertension after progressively adjusting for potential confounders. OSA showed a significant association with hypertension that changed slightly as we increased the number of confounding factors that we adjusted for (OR ranged from 1.95, 95% CI 1.52–2.51, P < 0.05, in the first model to OR = 1.51, 95% CI 1.15–1.99, P < 0.05, in the last model). In terms of MSLT, MSLT < 5 minutes increased the odds of hypertension by 30% (OR = 1.30, 95% CI 1.02–1.69, P < 0.05) as compared to patients with MSLT > 8 minutes. MSLT 5-8 min was marginally significantly associated with increased odds of hypertension (OR = 1.27, 95% CI, 0.97–1.67, P = 0.074) as compared to patients with MSLT > 8 minutes.

Table 3 presents the joint effect of OSA and MSLT on hypertension. The odds of hypertension were significantly increased among OSA patients with objective EDS: OSA with MSLT 5-8 min and MSLT < 5min increased the odds of hypertension by approximately 95% (OR = 1.95, 95% CI 1.10—3.46, P < 0.05) and 110% (OR = 2.11, 95% CI 1.22—3.31, P<0.05), respectively. In contrast, OSA patients without objective EDS (MSLT > 8 minutes), and primary snorers with objective EDS did not have significantly increased odds of hypertension. Furthermore, Figure 1 depicts the observed association between different levels of objective EDS and frequency of hypertension and blood pressure, adjusted for confounding factors.

The association between different MSLT categories with hypertension in subgroups defined according to sex, age, obesity (cutoff point of BMI was 28 kg/m²), and subjective EDS (cutoff point of ESS score was 10) are presented in Table 4. The interactions between MSLT and AHI were significant for men (P < 0.01), in patients less than 55 years old (p< 0.05), in patients with and without BMI ≥ 28kg/m² (p values< 0.05) and in patients with ESS≤ 10 (p< 0.05), but were not significant for women, in patients with age ≥ 55 years old or ESS > 10 (all P values > 0.05). As shown in Table 4, the association between hypertension and objective daytime sleepiness was present in both sexes, younger ages, both obese and non-obese patients and in patients with and without subjective EDS. Our findings showed a trend suggesting that OSA has larger effect on hypertension when MSLT is shorter in women and in patients with subjective EDS. However, the interaction between MSLT and AHI were not significant in these two subgroups, suggesting that there were no significant synergistic effect on OSA and MSLT in women and subjective EDS patients.

In order to compared the effect of MSLT in OSA and primary snoring patients on
blood pressure, we conducted multiples linear regression models to examine the association between MSLT values and blood pressure within primary snoring and OSA patients, respectively. As shown in Table S2, our findings suggest that DBP ($\beta=0.17$, $p=0.024$) and MAP ($\beta=0.15$, $p=0.035$) were significantly associated with the MSLT values in OSA patients. However, no significant correlations were found between blood pressure and MSLT values within primary snoring patients.
References:
Table S1. Demographic, clinical, and sleep characteristics of study sample

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Primary snoring</th>
<th>OSA</th>
<th>P1</th>
<th>P2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MSLT&gt;8min (n=353)</td>
<td>5min≤MSLT≤8min (n=85)</td>
<td>MSLT&lt;5min (n=46)</td>
<td>MSLT&gt;8min (n=736)</td>
</tr>
<tr>
<td><strong>Demographic and clinical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>228 (64.6)</td>
<td>58 (68.2)</td>
<td>33 (71.7)</td>
<td>0.558</td>
</tr>
<tr>
<td>Age (years)</td>
<td>41.02±11.61</td>
<td>41.36±10.50</td>
<td>40.26±9.14</td>
<td>0.865</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.84±3.23</td>
<td>24.29±3.13</td>
<td>24.45±3.51</td>
<td>0.308</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>107 (30.3)</td>
<td>27 (31.8)</td>
<td>13 (28.3)</td>
<td>0.915</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>121.14±14.72</td>
<td>119.60±15.09</td>
<td>118.50±9.51</td>
<td>0.617</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>77.79±9.19</td>
<td>76.24±10.71</td>
<td>75.75±6.98</td>
<td>0.429</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>7 (2.0)</td>
<td>2 (2.4)</td>
<td>1 (2.2)</td>
<td>0.976</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>95 (26.9)</td>
<td>29 (34.1)</td>
<td>17 (37.0)</td>
<td>0.199</td>
</tr>
<tr>
<td>Alcohol drinking, n (%)</td>
<td>120 (34.0)</td>
<td>21 (24.7)</td>
<td>14 (30.4)</td>
<td>0.250</td>
</tr>
<tr>
<td>Coffee using, n (%)</td>
<td>71 (20.2)</td>
<td>20 (23.5)</td>
<td>6 (13.0)</td>
<td>0.359</td>
</tr>
<tr>
<td><strong>Nighttime sleep</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep onset latency (min)</td>
<td>19.62±26.48</td>
<td>13.69±15.75</td>
<td>10.69±15.70</td>
<td>0.015</td>
</tr>
<tr>
<td>Total sleep time (min)</td>
<td>414.23±68.23</td>
<td>425.52±65.69</td>
<td>432.78±81.77</td>
<td>0.127</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>82.35±12.00</td>
<td>82.45±12.55</td>
<td>88.44±10.82</td>
<td>0.005</td>
</tr>
<tr>
<td>Wake after sleep onset (min)</td>
<td>70.56±55.66</td>
<td>70.08±57.12</td>
<td>49.35±56.81</td>
<td>0.053</td>
</tr>
<tr>
<td>AHI (events/h)</td>
<td>6.12±4.48</td>
<td>6.31±4.46</td>
<td>5.98±4.10</td>
<td>0.906</td>
</tr>
<tr>
<td>T90% (%)</td>
<td>1.10±5.30</td>
<td>1.62±6.48</td>
<td>0.43±1.17</td>
<td>0.461</td>
</tr>
<tr>
<td>Lowest-SaO2 (%)</td>
<td>85.41±10.61</td>
<td>85.85±6.60</td>
<td>85.11±13.83</td>
<td>0.915</td>
</tr>
<tr>
<td><strong>Daytime sleepiness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESS</td>
<td>6.60±5.13</td>
<td>7.76±5.45</td>
<td>10.13±6.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MSLT (min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td></td>
<td>13.29±3.15</td>
<td>6.60±0.94</td>
<td>3.42±1.40</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Percent for categorical variables and the other variables are presented with mean ± SD. SBP, mean systolic blood pressure; DBP, mean diastolic blood; MAP, mean arterial pressure; T90%, percentage of time spent in sleep below 90% oxygen saturation; Lowest-SaO₂, the lowest oxygen saturation. P₁: P values for the comparisons within primary snoring patients; P₂: P values for the comparisons within OSA patients.
Table S2 Association between MSLT values and blood pressure

<table>
<thead>
<tr>
<th>Sleep disturbance</th>
<th>Dependent variables</th>
<th>( \beta )</th>
<th>95% CIs</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary snoring</td>
<td>SBP</td>
<td>-0.03</td>
<td>-0.40 to 0.37</td>
<td>0.954</td>
</tr>
<tr>
<td></td>
<td>DBP</td>
<td>-0.09</td>
<td>-0.25 to 0.29</td>
<td>0.889</td>
</tr>
<tr>
<td></td>
<td>MAP</td>
<td>-0.04</td>
<td>-0.28 to 0.30</td>
<td>0.952</td>
</tr>
<tr>
<td>OSA</td>
<td>SBP</td>
<td>-0.12</td>
<td>-0.33 to 0.03</td>
<td>0.104</td>
</tr>
<tr>
<td></td>
<td>DBP</td>
<td>-0.17</td>
<td>-0.29 to -0.02</td>
<td>0.024</td>
</tr>
<tr>
<td></td>
<td>MAP</td>
<td>-0.15</td>
<td>-0.30 to -0.01</td>
<td>0.035</td>
</tr>
</tbody>
</table>

Adjusted \( \beta \) and \( P \) values of linear regression models were calculated after adjusting for age, sex, BMI, tobacco, alcohol drinking, coffee use, diabetes mellitus, ESS, anti-hypertension medicine, sleep onset latency, sleep efficiency and wake time after sleep onset in both primary snoring and OSA patients; OSA patients were further adjusted for severity of OSA, T90% and LSaO\(_2\). SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, arterial pressure.