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SCIENTIFIC INVESTIGATIONS

Cerebral Microbleeds on MRI in Patients with Obstructive Sleep Apnea

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Study Objectives: Obstructive sleep apnea (OSA) is known to increase the risk of stroke. Cerebral microbleeds (CMBs) are considered one of the precursors to symptomatic stroke. We aimed to clarify the relationship between OSA and CMBs.

Methods: We recruited patients who visited our clinic for the evaluation of sleep-disordered breathing. All patients underwent both overnight polysomnography and brain magnetic resonance imaging, which included T2*-weighted gradient-recalled echo images. We applied multivariate logistic regression and partial correlation analysis to estimate the relationship between OSA and CMBs.

Results: A total of 75 (45 male, 30 female) patients were enrolled. Their mean age was 60.5 years. Patients with CMBs had a significantly higher apnea-hypopnea index (AHI) compared with those without CMBs. AHI equal to or greater than 15 was a significant independent predictor of CMBs (adjusted odds ratio, 4.51; 95% CI, 1.40–14.58; p = 0.012) in the multivariate regression analysis. In addition, a partial correlation analysis adjusted for age, hypertension, diabetes, and cardiovascular disease revealed a positive relationship between AHI and the number of CMBs (r = 0.585, p = 0.028).

Conclusions: Moderate-to-severe OSA can be one of the independent predictors of CMBs which are considered a surrogate marker of overt stroke.

Keywords:obstructive sleep apnea, apnea-hypopnea index, cerebral microbleeds, stroke

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INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by intermittent cessation of breathing during sleep due to complete or partial airway obstruction. Repetitive apneas and hypopneas cause intermittent hypoxemia, hypercapnia, microarousals, and fragmented sleep.[1,2] OSA is associated with cardiovascular and cerebrovascular morbidity and mortality, and increases the risk of cerebrovascular events and death.[3–7] Previous studies have determined that OSA is prevalent in more than 60% of stroke patients.[3,5]

Cerebrovascular disease is a leading cause of morbidity and is associated with increased mortality.[6] Although preventive measures of stroke have reduced the disease burden, stroke remains an important enemy of health. It has been reported that OSA increases the risk of stroke two- to four-fold independent of other factors.[7,8]

High-resolution magnetic resonance imaging (MRI) has enabled the identification of asymptomatic brain lesions. Previous studies have shown that silent cerebral infarcts increased the annual incidence of clinical strokes,[9] and one study has suggested that moderate to severe OSA was associated with silent cerebral infarctions and lacunar infarctions in elderly participants.[10] Cerebral microbleeds (CMBs) are asymptomatic brain lesions that are also associated with cerebral small vessel disease. Recent studies have revealed that patients with CMBs have a significantly higher incidence of symptomatic strokes than those without CMBs.[11,12] CMBs may also be a cause of cognitive decline and dementia, such as Alzheimer disease and vascular dementia.[13,14] However, the significance of CMBs has not been well investigated in patients with sleep-disordered breathing. We aimed to clarify the relationship between sleep-disordered breathing and CMBs.

BRIEF SUMMARY

Current Knowledge/Study Rationale: Cerebral microbleeds are considered as a surrogate marker of overt stroke. Obstructive sleep apnea is known to increase the risk of stroke and death, but the significance of cerebral microbleeds has not been well investigated in patients with obstructive sleep apnea.

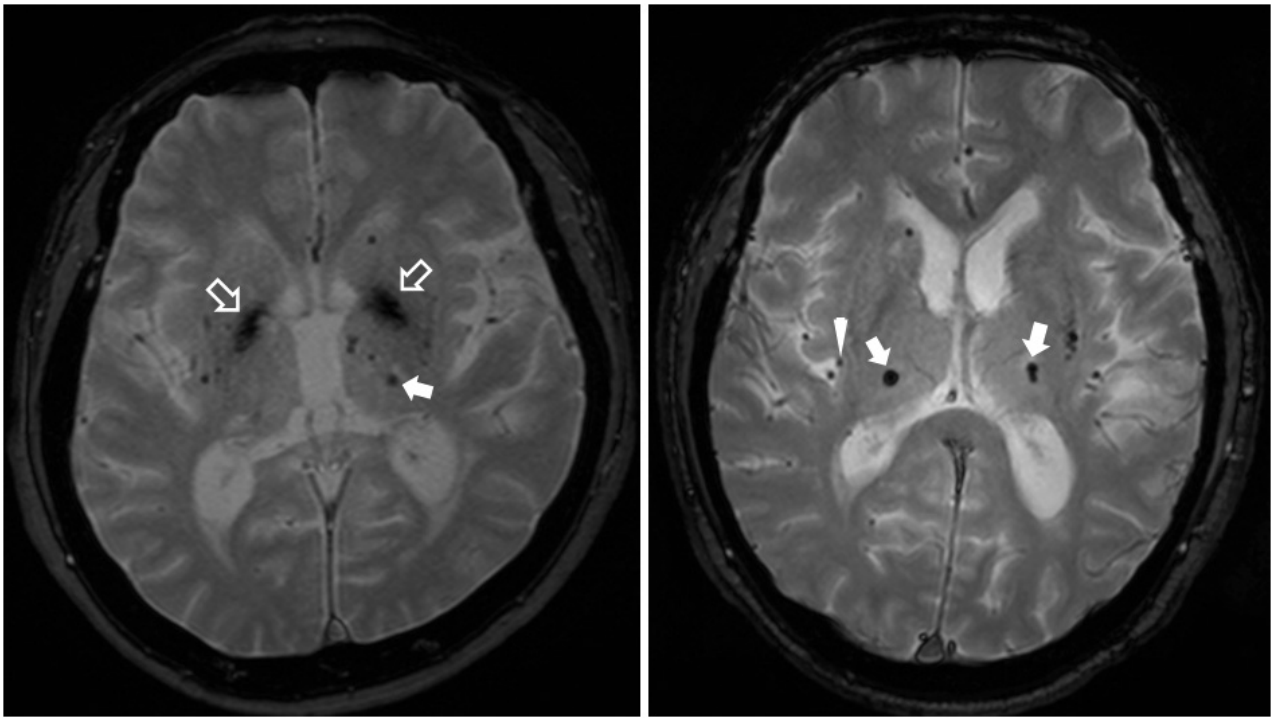
Study Impact: Moderate-to-severe obstructive sleep apnea is associated with the presence of cerebral microbleeds, and higher apnea-hypopnea index is correlated with more cerebral microbleeds. Preemptive stroke evaluations and preventive treatment may be necessary in patients with moderate-to-severe OSA.

METHODS

Study Participants

We recruited a total of 1,353 patients who underwent overnight polysomnography in our sleep center at the Boramae Hospital of Seoul National University between May 2004 and April 2014. Among these cases, we excluded 1,124 patients without a brain MRI and 81 patients without T2*-weighted gradient-recalled echo (GRE) imaging. We excluded 61 patients because the interval between MRI and PSG exceeded 12 months. We excluded 12 patients because they had a previous history of cerebrovascular disease: 8 patients had lacunar infarctions, 2 had large artery atherosclerotic strokes, 1 had a cardioembolism, and 1 had a transient ischemia attack. Finally, 75 patients were included in the analysis. None of the patients were taking antithrombotic medications. In this study, we considered hypertension to be present when a patient was taking an antihypertensive medication or had a record of high blood pressure at the time of PSG. We obtained

Figure 1—Examples of cerebral microbleeds on gradient-recalled echo images.



Examples of T2*-weighted gradient-recalled echo (GRE) images showing cerebral microbleeds (CMBs). Multiple CMBs are located in the thalamic regions (closed arrows). The CMBs are distinct from calcifications (open arrows) and cerebral vessels (arrowhead).

a detailed sleep history, past medical and medication history, family history, and body mass index (BMI) from all patients. Approval for this study was obtained from the Institutional Review Board at the Boramae Hospital of Seoul National University. We also obtained written informed consent from each patient or from his/her legal representative for participation in this study.

Polysomnography

PSG was recorded with the Twin-PSG software (Natus Neurology Incorporated, West Warwick, RI, USA) using a 6-channel electroencephalogram, a 4-channel electrooculogram, electromyogram, and electrocardiogram. A thermistor, a nasal air pressure monitoring sensor, an oximeter, piezoelectric bands, and a body position sensor were also applied to the patient. Apnea was defined as a reduction in airflow by 90% or more lasting ≥ 10 s. Hypopnea was defined as a reduction in airflow by 30% or more lasting ≥ 10 s and accompanied by ≥ 4% oxygen desaturation compared to baseline. OSA was graded according to the apnea-hypopnea index (AHI): AHI < 5 (events/h) was considered normal, 5 ≤ AHI < 15 was considered mild OSA, 15 ≤ AHI < 30 was considered moderate OSA, and AHI ≥ 30 was considered severe OSA.

Definition of CMBs

CMBs were defined as round, low-signal intensity focal lesions with a diameter less than 10 mm on GRE imaging (**Figure 1**).[15,16] Hypointensities, which might represent either calcification or cerebral vessels, were excluded. The number of CMBs was counted in each GRE image.[17] Hypointense foci located in the subarachnoid spaces or symmetrically in the globus pallidus were excluded, because they are considered to be vessel markings or calcifications. To estimate interrater reliability, two independent raters evaluated the locations and numbers of CMBs, without any clinical information. The κ value of agreement was 0.854, and the locations and numbers of CMBs were coded based on the consensus of the two raters in cases in which there were rater discrepancies. Detailed information on the protocol used to identify microbleeds was described previously.[12,18–20]

Statistical Analysis

The participants in this study were divided into two groups based on the presence of CMBs. To compare the clinical and PSG parameters between the groups, we used *t*-tests for continuous variables and Pearson χ^2 and Fisher exact tests for categorical variables. All the continuous quantitative variables are summarized as the mean and standard deviation (SD). In addition, our subjects were divided 4 four groups according to the severity of OSA: normal (AHI < 5), mild (AHI 5 to < 15), moderate (AHI 15 to < 30), and severe (AHI ≥ 30). Differences in variables among these 4 groups were measured by one-way analyses of variance and χ^2 tests with adjustments for multiple comparisons using a Bonferroni correction. Variables with a significant p value ($p < 0.05$) in the univariate regression were considered as candidates in the multivariate models. Several multivariate

Table 1—Clinical and polysomnographic characteristics of patients with and without CMBs.

	Patients with CMBs	Patients without CMBs	p value
Clinical factors			
Subjects, n	18	57	
Age (years), mean (SD), range	65.9 (13.4), 39–87	59.0 (14.5), 20–85	0.183
Male, n (%)	13 (72.2)	32 (56.1)	0.228
BMI (kg/m^2), mean (SD)	24.6 (3.9)	24.5 (3.5)	0.553
ESS score, mean (SD)	9.6 (4.9)	7.5 (5.2)	0.310
SSS score, mean (SD)	3.2 (0.9)	2.9 (0.9)	0.171
Global PSQI score, mean (SD)	8.3 (3.1)	9.3 (7.5)	0.709
Hypertension, n (%)	12 (66.7)	21 (36.8)	0.027
Diabetes mellitus, n (%)	3 (16.7)	16 (28.1)	0.335
Cardiovascular disease, n (%)	4 (22.2)	3 (5.3)	0.032
Atrial fibrillation	2	1	
Cardiac arrhythmia	2	2	
Smoking, n (%)	4 (22.2)	13 (22.8)	0.964
Alcohol, n (%)	5 (27.8)	12 (21.1)	0.547
Polysomnographic parameters			
Time in bed (minutes), mean (SD)	404.7 (55.2)	427.9 (52.6)	0.029
Total sleep time (minutes), mean (SD)	252.7 (90.7)	305.8 (85.3)	0.035
N1 sleep (%), mean (SD)	25.5 (13.2)	17.8 (14.4)	0.018
N2 sleep (%), mean (SD)	41.2 (13.1)	46.4 (14.0)	0.456
N3 sleep (%), mean (SD)	18.0 (11.1)	19.0 (12.6)	0.628
REM sleep (%), mean (SD)	15.4 (9.2)	16.9 (9.2)	0.384
Sleep latency (minutes), mean (SD)	27.1 (38.9)	22.1 (47.2)	0.955
REM sleep latency (minutes), mean (SD)	137.4 (110.7)	134.3 (100.6)	0.995
Sleep efficiency (%), mean (SD)	62.4 (19.2)	71.7 (18.5)	0.071
Arousal index (events/h), mean (SD)	41.1 (21.8)	26.6 (19.5)	0.013
PLMS index (events/h), mean (SD)	9.8 (14.7)	11.8 (27.4)	0.518
RDI (events/h), mean (SD)	31.0 (23.8)	19.8 (17.7)	0.283
AHI (events/h), mean (SD)	27.5 (22.8)	13.7 (16.8)	0.018
AHI during NREM sleep, mean (SD)	27.8 (24.6)	13.5 (17.4)	0.048
AHI during REM sleep, mean (SD)	22.4 (22.5)	12.8 (18.4)	0.320
Supine AHI, mean (SD)	37.4 (29.6)	20.9 (23.4)	0.053
Lateral AHI, mean (SD)	10.0 (19.1)	4.0 (10.2)	0.370
Supine position (% of TST), mean (SD)	63.7 (31.0)	56.5 (36.3)	0.595
Apnea index (events/h), mean (SD)	10.7 (17.6)	3.8 (6.6)	0.023
Mixed apnea index, mean (SD)	4.2 (7.3)	0.4 (1.7)	0.002
Hypopnea index (events/h), mean (SD)	9.5 (9.1)	9.3 (12.4)	0.650
RERA (events/h), mean (SD)	5.7 (5.7)	5.5 (6.1)	0.890
Longest sleep apnea (seconds), mean (SD)	45.5 (33.7)	24.2 (25.2)	0.026
Time below 90% SpO_2 (% of TST), mean (SD)	14.0 (20.7)	8.5 (16.0)	0.093

CMBs = cerebral microbleeds, BMI = body mass index, ESS = Epworth Sleepiness Scale, SSS = Stanford Sleepiness Scale, PSQI = Pittsburgh Sleep Quality Index, REM = rapid eye movement, PLMS = periodic limb movements during sleep, RDI = respiratory disturbance index, AHI = apnea-hypopnea index, RERA = respiratory effort-related arousal, SpO_2 = arterial oxygen saturation, TST = total sleep time, n = number, SD = standard deviation.

models were applied to avoid overfitting and multicollinearity, and two variables were used due to the small number of CMBs. Partial correlations were calculated after controlling for possible confounding variables to estimate the relationship between the degree of AHI and the number of CMBs. Statistical analyses were performed with SPSS statistical software version 21 (SPSS Inc., Armonk, NY, USA). Two-sided p values less than 0.05 were considered statistically significant.

RESULTS

A total of 75 patients with complaints of sleep-disordered breathing were included in this analysis. CMBs were present in 18 patients (24%). Six patients exhibited a single CMB, 5 patients exhibited 2 to 4 CMBs, and 7 patients exhibited 5 or more CMBs. Patients with CMBs were primarily older males, but age and sex differences between patients with and without

Table 2—Demographic and polysomnographic characteristics based on OSA severity.

	AHI < 5	AHI 5 to < 15	AHI 15 to < 30	AHI ≥ 30
Subjects, n	29	19	13	14
Age (years) mean (SD)	58.0 (17.8)	67.9 (8.2)	56.7 (10.2)	59.5 (14.7)
Male, n (%)	13 (44.8)	11 (57.9)	9 (69.2)	12 (85.7)
BMI (kg/m^2), mean (SD)	23.5 (3.0)	23.5 (2.5)	25.3 (2.8)	27.3 (4.8) [a,b]
ESS score, mean (SD)	6.2 (4.6)	8.6 (5.6)	9.6 (4.2)	9.4 (6.1)
SSS score, mean (SD)	2.8 (0.7)	3.2 (1.1)	2.5 (0.8)	3.2 (1.0)
Global PSQI score, mean (SD)	7.3 (3.2)	8.3 (2.2)	7.4 (3.3)	7.4 (3.1)
Smoking, n (%)	6 (20.7)	1 (5.3)	5 (38.5)	5 (35.7)
Alcohol, n (%)	7 (24.1)	1 (5.3)	5 (38.5)	4 (28.6)
Hypertension, n (%)	13 (44.8)	8 (42.1)	3 (23.1)	9 (64.3)
Diabetes Mellitus, n (%)	6 (20.7)	8 (42.1)	1 (7.7)	4 (28.6)
Cardiovascular diseases, n (%)	2 (6.9)	1 (5.3)	1 (7.7)	3 (21.4)
Presence of CMBs, n (%)	5 (17.2)	2 (10.5)	5 (38.5)	6 (42.9)
AHI (events/h), mean (SD)	2.5 (1.7)	10.3 (3.1)	20.3 (4.5)	52.1 (12.6) [a,b,c]
Time below 90% SpO_2 (% of TST), mean (SD)	0.4 (0.7)	4.4 (5.4)	11.4 (9.5)	34.9 (25.1) [a,b,c]

[a] Significant difference compared with patients with AHI < 5, $p < 0.05$. [b] Significant difference compared with patients with 5 < AHI < 15, $p < 0.05$. [c] Significant difference compared with patients with 15 < AHI < 30, $p < 0.05$. OSA = obstructive sleep apnea, BMI = body mass index, ESS = Epworth Sleepiness Scale, SSS = Stanford Sleepiness Scale, PSQI = Pittsburgh Sleep Quality Index, AHI = apnea-hypopnea index, CMBs = cerebral microbleeds, SpO_2 = arterial oxygen saturation, TST = total sleep time, n = number, SD = standard deviation.

CMBs were not statistically significant. Patients with CMBs had a significantly higher percentage of hypertension and cardiovascular disease than those without CMBs ($p = 0.027$ and $p = 0.032$, respectively). Among the PSG variables, patients with CMBs had substantially less total sleep time, a higher arousal index, and a higher AHI than those without CMBs. **Table 1** summarizes the clinical and PSG features of patients with and without CMBs.

Based on the AHI, 29 patients (38.7%) were normal and 46 had OSAs. Among those with OSA, 19 patients (25.3%) were mild, 13 (17.3%) were moderate, and 14 (18.7%) were severe. Patients with severe OSA had a significantly higher BMI compared with normal patients and patients with mild OSA ($p < 0.05$). The presence of CMBs was higher among patients with moderate and severe OSA compared to the other groups, but the statistical difference was not significant (**Table 2**).

Table 3 summarizes the results from univariate logistic regressions that estimate the risk of CMBs. The presence of hypertension or cardiovascular disease, shortened total sleep time, frequent arousals, and higher AHI all were significantly associated with the risk of CMBs. Importantly, moderate-to-severe OSA (AHI ≥ 15) was a significant predictor of the presence of CMBs (odds ratio [OR], 4.03; 95% CI, 1.33–12.23).

We adopted only two factors (hypertension and AHI) for consideration in the multivariate analysis due to the small number of patients with CMBs. Hypertension and AHI as continuous variables were significantly associated with higher odds of CMBs ($p = 0.044$ and, $p = 0.035$, respectively; Model 1 in **Table 4**). In the multivariate model with AHI ≥ 15, hypertension remained significant (adjusted OR, 3.88; 95% CI, 1.18–12.75; $p = 0.026$). Moderate to severe AHI (AHI ≥ 15) was a significant independent predictor of the presence of CMBs (adjusted OR, 4.51; 95% CI, 1.40–14.58; $p = 0.012$; Model 2 in **Table 4**). In Model 3 with AHI ≥ 15 and a combined score of hypertension and cardiovascular diseases, moderate to severe AHI and a combined score were significantly predictive of the presence of CMBs ($p = 0.018$ and, $p = 0.013$, respectively; **Table 4**). AHI ≥ 30 was not significant in the multivariate regression. In partial correlation analysis, residuals from the numbers of CMBs and AHI with adjusting for age, hypertension, diabetes, cardiovascular disease, have been calculated. Partial correlation plot revealed a positive relationship between regressing CMBs and regressing AHI ($r = 0.585$, $p = 0.028$) (**Figure 2**).

DISCUSSION

Our cross-sectional observational study demonstrates that moderate to severe AHI is positively associated with the presence of CMBs in patients with OSA. We adjusted for potential confounding factors for CMBs such as age, hypertension, and the presence of cardiovascular disease. The number of CMBs was positively correlated with the severity of OSA after controlling other variables. To the best of our knowledge, this is the first report to demonstrate the association between OSA and CMBs in patients without stroke history. One previous study showed a relationship between OSA and CMBs in patients with cerebral infarction.[21] However, we focused on patients with a primary complaint of sleep-disordered breathing without any history of ischemic or hemorrhagic stroke.

Previous studies demonstrated that OSA was associated with a higher mortality rate,[7,22,23] and cerebrovascular disease remains a major cause of death despite adequate control of traditional vascular risk factors. Bassetti and Aldrich first reported an association between stroke and OSA in 1999.[3] In a large cohort study published in 2005, Yaggi et al. revealed that

Table 3—Univariate logistic regression for clinical and polysomnographic predictors of CMBs.

	OR	95% CI	p value
Clinical variables			
Age in years	1.30	0.87–1.94	0.197
Male sex	2.03	0.64–6.46	0.230
BMI	1.01	0.87–1.17	0.947
ESS score	1.06	0.95–1.17	0.304
PSQI score	1.00	0.82–1.21	0.971
Presence of hypertension	3.43	1.12–10.49	0.031
Presence of diabetes mellitus	0.51	0.13–2.01	0.338
Presence of cardiovascular disease	5.14	1.03–25.7	0.046
Presence of smoking	1.01	0.28–3.62	0.993
Presence of alcohol	0.55	0.20–2.33	0.546
Polysomnographic variables			
Total sleep time	0.99	0.99–1.00	0.048
Proportion of N1 sleep	1.03	0.99–1.01	0.085
Proportion of N2 sleep	0.98	0.94–1.02	0.286
Proportion of N3 sleep	0.99	0.95–1.04	0.701
Proportion of REM sleep	0.98	0.93–1.04	0.487
Sleep latency	1.00	0.99–1.01	0.779
REM sleep latency	1.00	0.99–1.01	0.959
Sleep efficiency	0.98	0.95–1.01	0.125
Arousal index	1.03	1.01–1.06	0.021
PLMS index	1.00	0.97–1.02	0.769
RDI	1.02	0.99–1.05	0.156
AHI	1.03	1.00–1.06	0.024
AHI during NREM sleep	1.03	1.00–1.06	0.027
AHI during REM sleep	1.02	0.99–1.05	0.130
Supine AHI	1.02	1.00–1.04	0.047
Lateral AHI	1.03	0.99–1.07	0.138
AHI ≥ 5 events/h	1.89	0.59–6.02	0.281
AHI ≥ 10 events/h	2.39	0.79–7.24	0.125
AHI ≥ 15 events/h	4.03	1.33–12.23	0.014
AHI ≥ 30 events/h	3.06	0.89–10.50	0.075
Supine position	1.00	0.99–1.02	0.616
Apnea index	1.05	0.99–1.11	0.060
Mixed apnea index	1.25	1.04–1.51	0.018
Hypopnea index	1.00	0.95–1.05	0.997
RERA	0.99	0.89–1.10	0.842
Longest sleep apnea	1.02	1.00–1.04	0.025
Time below 90% SpO_2	1.01	0.99–1.04	0.332

CMBs = cerebral microbleeds, OR = odds ratio, CI = confidence interval, BMI = body mass index, ESS = Epworth Sleepiness Scale, PSQI = Pittsburgh Sleep Quality Index, REM = rapid eye movement, PLMS = periodic limb movements during sleep, RDI = respiratory disturbance index, AHI = apnea-hypopnea index, RERA = respiratory effort-related arousal, SpO_2 = arterial oxygen saturation.

OSA syndrome significantly increased the risk of stroke, and this increase was independent of other risk factors such as hypertension.[7] Another large cohort study showed that OSA was associated with a higher incidence of stroke.[24] It was also reported that OSA with AHI > 10 was independently associated with lacunar infarction localized in the internal capsule or in the pons.[25] Asymptomatic brain lesions such as silent cerebral infarctions, leukoaraiosis, and CMBs have been considered to be predictors of future stroke.[26] Many investigators, therefore, have tried to investigate the relationship between OSA and various preclinical state of strokes. Previous studies have revealed positive correlations between OSA and the presence of silent cerebral infarctions,[10,27–29] but have reported inconsistent findings regarding the association between OSA and leukoaraiosis.[28,30–32] However, few studies have examined an association between OSA and CMBs.

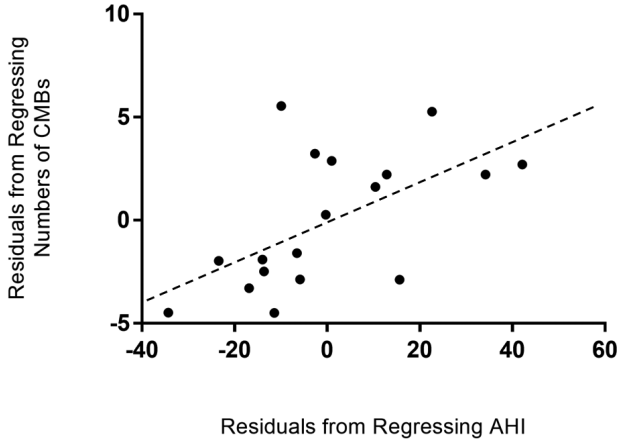
Several pathological mechanisms are presumed to be involved in the association between OSA and stroke. Possible

Table 4—Multivariate logistic regression models for the presence of CMBs.

Model	OR	95% CI	p value
Model 1			
Hypertension	3.29	1.04–10.47	0.044
AHI	1.03	1.00–1.06	0.035
Model 2			
Hypertension	3.88	1.18–12.75	0.026
AHI ≥ 15 events/h	4.51	1.40–14.58	0.012
Model 3			
Combined score of hypertension and cardiovascular diseases*	3.09	1.27–7.56	0.013
AHI ≥ 15 events/h	4.17	1.28–13.56	0.018

*Total scores range from 0 to 2: 0 (neither hypertension nor cardiovascular disease), 1 (hypertension or cardiovascular diseases), 2 (hypertension and cardiovascular diseases). CMBs = cerebral microbleeds, OR = odds ratio, CI = confidence interval, AHI = apnea-hypopnea index.

Figure 2—Partial correlation between the apnea-hypopnea index and the number of cerebral microbleeds.



The scatter plot shows the correlation (r = 0.585, p = 0.028) between the apnea-hypopnea index (AHI) and the number of cerebral microbleeds (CMB) controlling for age, hypertension, diabetes, cardiovascular disease. Each closed circle represents one patient.

mechanisms include acute hemodynamic changes during apnea/hypopnea events, paradoxical embolization, hypercoagulability, hypoxia-related cerebral ischemia, and atherosclerosis.[7] A decline in middle cerebral artery blood flow during obstructive apneas or hypopneas can also result in vascular injury.[33] CMBs are commonly observed in the healthy population as well as in patients with cerebrovascular disease.[15,34,35] Other studies have disclosed that the presence of CMBs was a potential predictor of hemorrhagic and ischemic strokes.[36,37] One recent study urged that CMBs might be an independent risk factor for subsequent ischemic stroke in patients who had experienced a transient ischemic attack.[12] Although the pathophysiologic link between CMBs and cerebrovascular disease remains unclear, the prevailing pathological mechanism of CMBs seems to be lipohyalinosis.[37,38] CMBs may be harmful to small vessels, resulting in in-situ thrombosis and decreased arterial flow distal to the CMBs.[39,40] CMBs may therefore be an early marker of cerebral vasculopathy prior to the clinical events of symptomatic strokes. The prevalence of CMBs varies from 3.1% to 23.5% among healthy individuals without cerebrovascular disease, and prevalence gradually increases with age.[11,34,41,42] In patients with dementia, CMBs are relatively common, with prevalence from 35% to 85%.[43,44] Our results demonstrated that the prevalence of CMBs was 28.2% in patients with OSA and 17.2% in patients without OSA. Our study has a limitation in differentiating CMBs from calcifications or vessels on a GRE image, although our MR protocol has been reported previously and the inter-rater reliability was also estimated. Further studies with advanced MR sequences should be followed to improve the accuracy of micro-bleeds confirmation.

To date, known risk factors for CMBs include older age and the presence of hypertension, cardiovascular disease, or stroke.[34,35] In the present study, AHI ≥ 15 was associated with a 4.5-fold increase in risk for the presence of CMBs after adjusting for hypertension. Furthermore, the severity of AHI was positively correlated with the number of CMBs in the partial correlation analysis, which controlled for potential confounding variables such as age, hypertension, diabetes, and cardiovascular disease. Thus, the main novel finding of this study is that moderate to severe AHI might be an independent predictor for the presence of CMBs. One previous study has suggested that CMBs shared risk factors with other small vessel diseases for future ischemic stroke,[37] and OSA is considered one such risk factors.[7] In a recent study, continuous positive airway pressure (CPAP) treatment for OSA was shown to reduce mortality in patients with moderate to severe OSA.[45] We assume that the benefit of CPAP is conferred at least partly through the prevention of preclinical and clinical strokes.

In conclusion, moderate-to-severe OSA is associated with the presence of CMBs. In addition, higher AHI is correlated with more CMBs. Moderate-to-severe OSA can be considered an independent predictor of CMBs, which are considered a surrogate marker of overt stroke. The necessity of preemptive stroke evaluations and preventive treatment in the moderate-to-severe OSA group needs to be investigated in future studies.

ABBREVIATIONS

AHI, apnea-hypopnea index
BMI, body mass index
CMBs, cerebral microbleeds

CPAP, continuous positive airway pressure
GRE, gradient-recalled echo
MRI, magnetic resonance imaging
OSA, obstructive sleep apnea
SD, standard deviation

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