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Arousal index as a marker of carotid artery atherosclerosis in patients with obstructive sleep apnea syndrome

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Abstract

Purpose It was shown in a previous cohort study that men with internal carotid artery (ICA) plaque, defined as focal wall thickness of ≥ 1.5 mm, had a threefold higher risk of stroke than those without plaque. We examined the relationship between arousal indices and sleep stages in patients with obstructive sleep apnea syndrome (OSAS) and carotid atherosclerosis.

Methods Carotid atherosclerosis severity was evaluated using the maximal carotid wall intima-media thickness of the ICA (ICA-maxIMT) and plaque in 83 patients with OSAS.

Results The ICA-maxIMT values were positively correlated with the apnea hypopnea index (AHI) ($\rho = 0.294$, $P = 0.007$), arousal index ($\rho = 0.289$, $P = 0.008$), oxygen desaturation index ($\rho = 0.298$, $P = 0.006$), percentage of visually scored total sleep time spent in nocturnal oxygen saturation < 90% ($SpO_2 < 90\%$) ($\rho = 0.246$, $P = 0.025$), and the percentage of visually scored total sleep time spent in non-REM sleep stage 1 ($\rho = 0.326$, $P = 0.003$) and were negatively correlated with the percentage of visually scored total sleep time spent in non-REM sleep stages 2 and 3. Arousal index, diabetes mellitus, and age were found to be independent predictors of ICA plaque presence (OR 1.052, $P = 0.003$; OR 8.705, $P = 0.026$; OR 1.064, $P = 0.023$, respectively).

Conclusions Several PSG variables that are indicative of sleep fragmentation, sleep disordered breathing, and poor sleep quality correlated with the occurrence of atherosclerosis, but total arousal index was the only independent predictive factor.

Keywords Arousal index · Sleep stage · IMT · Carotid atherosclerosis · Obstructive sleep apnea syndrome

Introduction

Obstructive sleep apnea syndrome (OSAS) is known to be associated with cardiovascular disease and stroke. In patients with OSAS, repetitive nocturnal hypoxemia, negative intrathoracic pressure, sympathetic activation, and frequent arousals are associated with a number of neural, humoral, thrombotic, and inflammatory changes, all of which are involved in the pathophysiology of endothelial dysfunction and atherosclerosis.

Carotid wall intima-media thickness (IMT) and plaque are useful markers for determining the degree of early atherosclerosis [1]. In a Japanese cohort study, men with plaque, defined as focal wall thickness > 1.5 mm in the internal carotid artery (ICA) had a threefold higher risk of stroke than those without plaque during the 4.5-year follow-up [2]. The carotid IMT value was reported to be significantly elevated in patients with OSAS as compared to control subjects, particularly in patients with moderate-to-severe OSAS [3–5]. Several studies have assessed the relationship between carotid IMT and the parameters of nocturnal hypoxia in patients with OSAS. The values of minimum nocturnal oxygen saturation (SpO_2 min), mean nocturnal oxygen saturation (SpO_2 mean), nocturnal oxygen desaturation index (ODI), and percentage of visually scored total sleep time with nocturnal oxygen saturation < 90% ($SpO_2 < 90\%$) were reported to be correlated with carotid

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IMT [3–8]. Ozdemir et al. included $SpO_2 < 90\%$, SpO_2 min, SpO_2 mean, and ODI in a regression model for IMT and observed that only ODI was an independent predictor [9]. Thus, intermittent hypoxemia appears to be the most significant factor influencing carotid atherosclerosis.

Many studies have assessed the presence of nocturnal hypoxemia in patients with OSAS; however, only a few studies have examined the correlation between the arousal index (total number of arousals divided by the duration of sleep in hours) or sleep stages and carotid IMT. Saletu et al. investigated the association between excessive daytime sleepiness and cardiovascular risk factors, sleep-related respiratory variables, and carotid IMT. Defining the visually scored arousals that overlapped with, or were adjacent to, apneas/hypopneas defined as respiratory arousals, they found that the respiratory arousal index was importantly correlated with atherosclerosis evaluated by carotid IMT [10]. However, arousals also occur spontaneously or in association with snoring and body movements, some of which are not directly related to abnormal respiratory events. The effects of total arousals on carotid IMT were not examined in the study by Saletu et al. [10]. Furthermore, there have been no studies to investigate the association between the sleep stages determined by polysomnography examination and carotid IMT.

In the present study, we aimed to evaluate whether elevated total arousal index or poor sleep quality determined by the percent changes in total sleep time spent in each sleep stage influenced the occurrence of carotid artery atherosclerosis in patients with OSAS.

Methods

The present cross-sectional observational study evaluated 83 Japanese patients (19 female, 64 male) with OSAS who visited our sleep laboratory from August 2011 to May 2013. Inclusion criteria were (1) patients with OSAS who were newly diagnosed by a full-laboratory PSG examination and (2) patients who agreed to participate in the study with carotid ultrasonography before and after the treatment of OSAS. The exclusion criteria were diagnosis of other sleep disorder complications including central sleep apnea (CSA), restless leg syndrome, rapid eye movement (REM) sleep behavior disorders, periodic limb movement disorders, narcolepsy, and circadian rhythm sleep disorders. The study was approved by the ethical committee of Tokyo Women's Medical University, and written informed consent was obtained from all participants.

The patients were interviewed regarding their sleep and medical history, while specifically focusing on the presence of major cardiovascular risk factors and the current medications (i.e., antihypertensive, lipid-lowering, and anti-diabetic medications). In addition, the patients underwent physical examinations, including measurements of blood pressure, waist circumference, and body mass index (BMI).

Cardiovascular risk factors

Blood pressure was recorded with the patient in the sitting position, after a rest period of 15 min. Hypertension was diagnosed if the blood pressure values exceeded 140/90 mmHg or if the patient used antihypertensive medication [11]. In addition, waist circumference, BMI, and current smoking status were assessed.

Fasting blood screening tests for diabetes mellitus and hyperlipidemia were performed. The plasma levels of low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglyceride, glucose, and glycated hemoglobin (HbA1c) values were measured by LSI Medience Corporation; Tokyo, Japan. Patients were considered to have diabetes mellitus if they had an HbA1c value (National Glycohemoglobin Standardization Program, NGSP) of $\geq 6.5\%$, if they had a history of diabetes, or if they used antidiabetic medication or insulin therapy. Hyperlipidemia was defined as the presence of hypercholesterolemia, with LDL levels of > 140 mg/dl, or hypertriglyceridemia, with triglyceride levels of ≥ 150 mg/dl; hyperlipidemia was also considered to be present in all patients receiving lipid-lowering medication.

Blood sampling and high-sensitivity C-reactive protein analyses

For the analysis of serum surrogate markers, including high-sensitivity C-reactive protein (hs-CRP), blood samples were obtained in the fasting state. The hs-CRP levels were measured using a nephelometer.

PSG examinations

A full-laboratory PSG examination was conducted overnight in each subject using Neurofax EEG-9200 (Nihon Kohden; Tokyo, Japan). The sleep status was determined based on the data from electroencephalography, electrooculography, and submental electromyography, which were examined using the available software (Polysmith QP-260A, Neurotronics; Gainesville, FL, USA). Percutaneous oxyhemoglobin saturation (SpO_2) was measured using a pulse oximeter (JL-951T3, Nihon Kohden; Tokyo, Japan). The presence of apnea or hypopnea was determined by examining oral and nasal airflow in terms of thermocouples, nasal air pressure, and thoracic and abdominal motions recorded using piezoelectric belt sensors. Simultaneously, bipolar electrocardiogram (ECG) was recorded at a sampling frequency of 200 Hz to obtain the R-R interval (RRI) data during sleep.

The sleep stages and disturbed respiratory events were scored by a trained sleep technician based on the recommendations of the American Academy of Sleep Medicine [12]. The apnea hypopnea index (AHI), arousal index (total number of respiratory and non-respiratory arousals divided by the duration of sleep in hours), SpO2 min, SpO2 mean, ODI as the number of times per hour of sleep that the blood's oxygen level drops by 3% or more from baseline, and SpO2 < 90% were recorded. The percentage of visually scored total sleep time spent in each sleep stage, i.e., non-REM sleep stage 1 (N1%), non-REM sleep stage 2 (N2%), non-REM sleep stage 3 (N3%), and REM sleep (N3%) were also determined.

Snores were automatically scored by detecting bursts longer than 0.6 s on the snore channel, and the snore index (snores per hour of sleep) was calculated.

Carotid IMT measurements

Atherosclerotic changes were measured using high-resolution B-mode ultrasonography and a 7.5-MHz linear array probe (LOGIQ-S8, GE Healthcare Japan; Tokyo, Japan). We adopted the ultrasonography protocol previously used in a Japanese cohort study [2]. Atherosclerosis was evaluated by measuring the carotid artery IMT, which was defined as the distance between the leading edge of the luminal echo and the media/adventitia echo. The imaging protocol involved obtaining a single longitudinal lateral view of the distal 10 mm of the right and left common carotid arteries (CCA) and three longitudinal views (anterior-oblique, lateral, and posterior-oblique) of each ICA. The ICA was defined as including the carotid bulb, identified by loss of the parallel wall present in the CCA, and the 10-mm segment of the ICA distal to the tip of the flow divider separating the internal from external carotid arteries [2].

The severity of carotid atherosclerosis was evaluated using the maximal carotid wall IMT of the ICA (ICA-maxIMT); ICA-maxIMT was defined as the single thickest wall based on three scan views of the right and left ICA. Plaque in the ICA wall was defined as a focal wall thickness of ≥ 1.5 mm. In cases with multiple plaques, only the thickest plaque was evaluated [2].

Data and statistical analysis

First, the Spearman's rank correlation coefficients were obtained for ICA-maxIMT with age, BMI, waist circumference, hs-CRP, AHI, arousal index, parameters of nocturnal hypoxemia (SpO_2 min, SpO_2 mean, ODI, SpO_2 < 90%), percentage of visually scored total sleep time spent in each sleep stage (N1%, N2%, N3%, and REM%), and snore index.

Second, the patients were assigned to two groups: ICA plaque+ group ($n = 37$) and ICA plaque− group ($n = 46$), with regard to whether or not a plaque was present in the ICA, respectively. The Epworth Sleepiness Scale (ESS) score was also recorded. Clinical variables, cardiovascular risk factors, and sleep variables from PSG were compared between the two groups using non-parametric analyses or the chi-square goodness of fit test.

Univariate logistic regression was performed to determine the independent predictors of carotid atherosclerosis (ICA plaque presence). The dependent variables included AHI, arousal index, parameters of nocturnal hypoxemia (SpO_2 min, SpO_2 mean, ODI, and SpO_2 < 90%), snore index, and cardiovascular risk factors (BMI, waist circumference, age, sex, smoking status, hypertension, diabetes mellitus, hyperlipidemia, HDL-cholesterol, hs-CRP). The independent variables that were significant in the univariate logistic regression analyses were included in stepwise multivariate logistic regression analysis to identify the independent predictors of an ICA plaque presence. Odds ratios (OR) with 95% confidence intervals (CI) were used to quantify the degree of association. All calculations were performed using SPSS 17 (SPSS Inc., Chicago, IL). Statistical significance was set at $P < 0.05$.

Results

The clinical variables and PSG data are shown in Table 1. The mean age and BMI of the patients were 56.1 ± 10.7 years and 25.4 ± 4.1 kg/m^2, respectively. The mean AHI value was 46.3 ± 22.5/h. Fifty-eight patients (70%) had severe OSAS (AHI ≥ 30/h), 23 patients (28%) had moderate OSAS (15/h ≤ AHI < 30/h), and two patients (2%) had mild OSAS (AHI < 15/h).

The ICA-maxIMT values were significantly correlated with age, and hs-CRP levels ($\rho = 3.999$, $P < 0.001$; $\rho = 0.251$, $P = 0.023$, respectively). With regard to sleep variables in the PSG data, the ICA-maxIMT values were positively correlated with AHI, arousal index, ODI, SpO_2 < 90%, and N1% ($\rho = 0.294$, $P = 0.007$; $\rho = 0.289$, $P = 0.008$; $\rho = 0.298$, $P = 0.006$; $\rho = 0.246$, $P = 0.025$; and $\rho = 0.326$, $P = 0.003$, respectively). However, the ICA-maxIMT values were negatively correlated with N2% and N3% ($\rho = -0.255$, $p = 0.02$; $\rho = -0.249$, $p = 0.023$, respectively). The scatter plots for ICA-maxIMT with AHI, arousal index, ODI, and SpO_2 < 90% are shown in Fig. 1, whereas those for ICA-maxIMT with N1%, N2%, and N3% are shown in Fig. 2. The ICA-maxIMT were not significantly correlated with SpO_2 min, SpO_2 mean, REM%, and snore index ($\rho = -0.150$, $P = 0.175$; $\rho = 0.201$, $P = 0.068$; $\rho = -0.045$, $P = 0.686$; and $\rho = 0.031$, $P = 0.779$, respectively).

The comparisons of the clinical variables, cardiovascular risk factors, and sleep variables from PSG between the two groups are shown in Table 2. Compared to the ICA plaque− group, patients in the ICA plaque+ group were older, more likely to be male, and had a higher risk of developing diabetes mellitus and hypertension. Moreover, patients in the ICA

Table 1 General characteristics and PSG data of the entire study population ($n = 83$)

Variables	
Age (years)	56.1 ± 10.7[a]
Sex M/F (persons)	64 / 19
BMI (Kg/m^2)	25.4 ± 4.1[a]
Waist circumference (cm)	90.5 ± 10.4[a]
maxIMT (mm)	1.5 ± 0.6[a]
hs-CRP (mg/dl)	0.090 ± 0.098[a]
Smokers (%)	21
Hypertension (%)	52
Diabetes mellitus (%)	15
Hyperlipidemia (%)	61
HDL-cholesterol < 40 mg/dl (%)	13
AHI (/h)	46.3 ± 22.5[a]
Arousal index (/h)	47.1 ± 18.1[a]
SpO2min (%)	75.9 ± 10.0[a]
SpO2mean (%)	94.1 ± 2.4[a]
SpO2 < 90% (%)	6.7 ± 10.0[a]
ODI (%)	42.7 ± 24.1
Snore index (/h)	306.9 ± 190.8[a]
Total sleep time (min)	405.7 ± 64.5[a]
Sleep efficiency (%)	80.9 ± 9.9[a]
N1%	39.8 ± 18.0[a]
N2%	43.4 ± 15.1[a]
N3%	4.6 ± 5.1[a]
REM%	12.2 ± 4.7[a]

[a] mean ± S.D.

PSG polysomnography, *BMI* body mass index, *maxIMT* maximal carotid wall intima-media thickness, *hs-CRP* high-sensitivity C-reactive protein, *HDL* high-density lipoprotein, *AHI* apnea hypopnea index, *ODI* oxygen desaturation index, *REM* rapid eye movement

plaque+ group had higher AHI, arousal index, $SpO_2 < 90\%$, ODI, and N1%, as well as lower N2 and N3%.

The results from the univariate and stepwise multivariate logistic regression analysis are shown in Table 3. AHI, arousal index, $SpO_2 < 90\%$, ODI, age, male sex, hypertension, and diabetes mellitus were associated with the presence of an ICA plaque. Arousal index, diabetes mellitus, and age were found to be independent predictors of the presence of an ICA plaque in the stepwise multivariate logistic regression analysis (OR 1.052, 95% CI 1.018–1.088, $P = 0.003$; OR 8.705, 95% CI 1.291–58.681, $P = 0.023$ and OR 1.064, 95% CI 1.009–1.122, $P = 0.023$, respectively).

Discussion

In previous studies, intermittent hypoxia was considered to play an important role in atherosclerotic changes or endothelial dysfunction in patients with OSAS [6–9]. In line with the previous studies, we observed that the ODI and $SpO_2 < 90\%$ were correlated with the ICA-maxIMT values. Furthermore, the multivariate logistic regression analysis identified arousal index as one of the independent predictors of ICA plaque presence along with diabetes mellitus and age in patients with OSAS. These findings suggest that increases in arousals may lead to atherosclerosis even in the absence of intermittent hypoxia.

In animal models of severe OSAS, long-term sleep fragmentation induced vascular endothelial dysfunction and mild blood pressure increases [13]. In several studies, partial sleep deprivation has been consistently linked to decreased vasodilation [14–16]. Considering the findings of studies on endothelial dysfunction in sleep deprivation, the present study supports the notion that poor quality of sleep (fragmented sleep with an elevated arousal index) induces vascular endothelial dysfunction, which induces carotid atherosclerosis.

Increases in arousals may result in repeated activations of the sympathetic nervous system as well as cardiovascular changes (including surges in blood pressure), insulin resistance, impaired glucose tolerance, and increases in cortisol secretion and lipid levels. Chronic partial sleep deprivation caused by arousals may lead to an increase in the levels of inflammatory markers, which promote the atherosclerotic process [17, 18].

Sleep fragmentation appears to induce the suppression of growth hormone (GH) release in patients with OSAS; in particular, a decrease in the slow-wave sleep stage leads to suppression of GH release [19, 20]. GH and insulin-like growth factor 1 (IGF-1) were reported to be linked with the cardiovascular system, and an excess or deficiency of GH is associated with an increased risk of cardiovascular morbidity and mortality [21]. With regard to the relationship between carotid atherosclerosis and GH (the IGF-1 axis), one report showed that hypopituitary GH-deficient (GHD) adults had an increased number of atheromatous plaques in the carotid and femoral arteries [21]. Moreover, these patients had increased carotid artery IMT, even in the absence of classic risk factors for atherosclerosis [22]. In the present study, we did not evaluate the levels of GH and IGF-1. We noted that arousal index and N1% were positively correlated and that N3% was negatively correlated with the ICA-maxIMT values. It was speculated that an increase in arousal could lead to sleep fragmentation, which could affect the GH levels and IGF-1 axis in patients with OSAS and consequently increase the ICA-IMT.

In addition, heavy snoring is frequently observed in patients with OSAS, and snoring is considered a risk factor for cerebrovascular events [23–26]. Earlier studies have investigated the effects of snoring on carotid atherosclerosis; however, only a few studies have used an objective scoring method for snoring in patients with

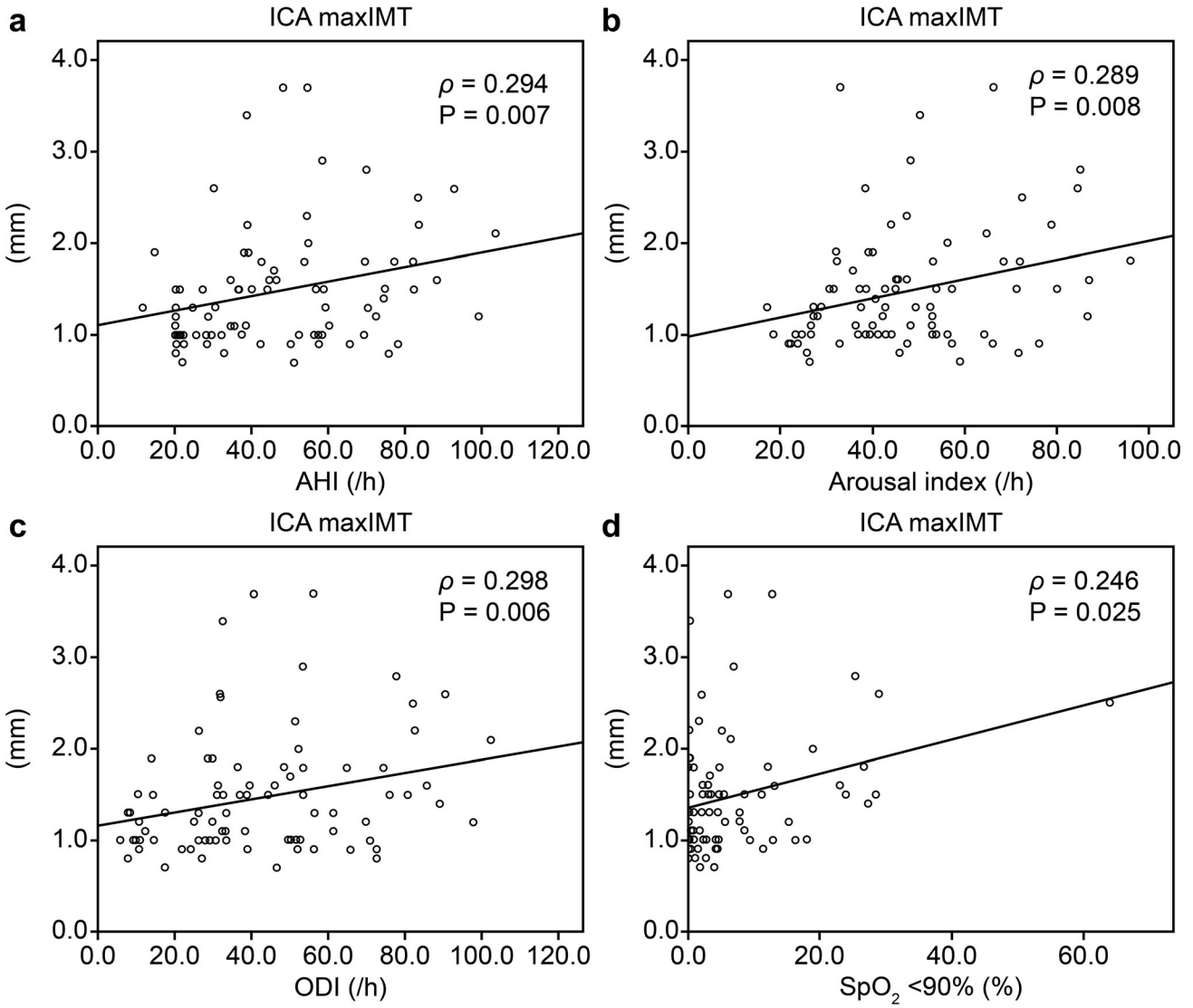

Fig. 1 Scatter plot showing the relationships between maxIMT and **a** AHI, **b** arousal index, **c** ODI, and **d** SpO2<90% maxIMT: maximal carotid wall intima-media thickness, AHI: apnea hypopnea index, ODI: oxygen desaturation index

OSAS. Lee et al. [27] used snoring time and the snore index in snorers and non-snorers with mild non-hypoxic OSAS and reported that heavy snoring was significantly associated with carotid atherosclerosis. Moreover, Salepci et al. [28] showed that the arousal index and snore index were significantly different between patients with OSAS with and without IMT hypertrophy as defined over 0 and 81 mm in CCA and/or ICA.

In a study with rabbits, Amatoury et al. [29] reported that the vibrations resulting from snoring can be detected at the carotid artery wall and within the artery lumen. Exposure to such vibrations may damage the arterial wall endothelial cells and thus trigger inflammatory processes leading to early atherosclerotic changes [30]. The associations between snoring and changes in blood pressure have also been evaluated [31]. Gregory et al. [31] indicated that baroreflex sensitivity was lower in the snoring group, which could lead to a decreased sensitivity to nocturnal blood pressure increases. Thus, snoring can induce carotid atherosclerosis through a direct effect via vibration or changes in blood pressure.

Furthermore, non-respiratory arousals were accompanied by leg or body movements or other events. We found that total arousals as well as diabetes mellitus and age also played an important role in predicting carotid atherosclerosis. Hence, we concluded that arousals associated with respiratory and non-respiratory events acted as one of the most significant factors in promoting atherosclerotic processes in patients with moderate-to-severe OSAS.

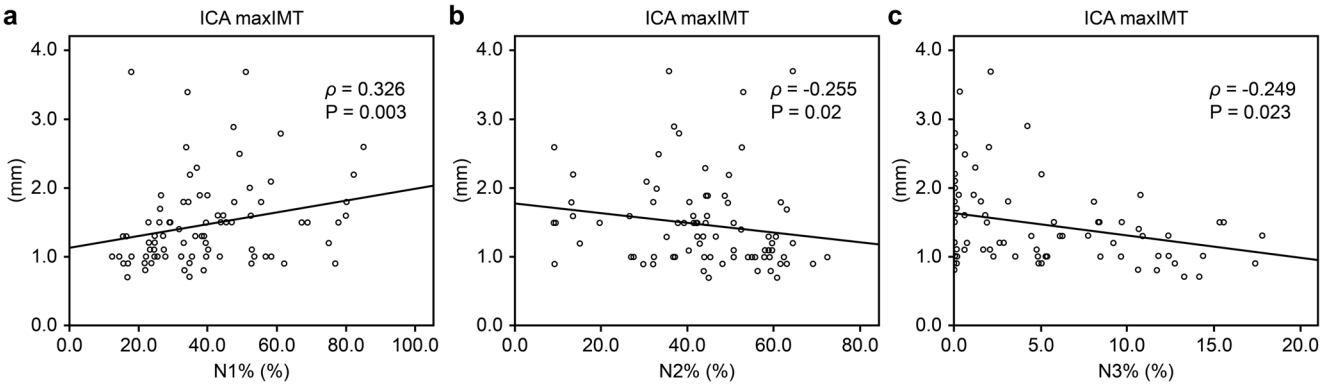

Fig. 2 Scatter plot showing the relationships between ICA-maxIMT and **a** non-REM stage 1/total sleep time (%) (N1%), **b** non-REM stage 2/Total sleep time (%) (N2%), and **c** non-REM stage 3/Total sleep time (%) (N3%). ICA: internal carotid artery, maxIMT: maximal carotid wall intima-media thickness, REM :rapid eye movement

The present study has certain limitations. This was an observational study with a small group size, and the severity of OSAS was biased. We did not examine cardiovascular risk factors, including their severity and management with specific

Table 2 General characteristics and PSG data of the ICA plaque (+) and ICA plaque (−) groups

	ICA plaque (−)	ICA plaque (+)	*P*
n (persons)	46	37	
Waist circumference (cm)	89.1 ± 11.3[a]	92.3 ± 8.9[a]	
BMI (kg/m^2)	25.1 ± 4.5[a]	25.8 ± 3.4[a]	
Age (year)	53.4 ± 11.4[a]	60.0 ± 9.0[a]	< 0.05
Sex M: F (persons)	31 : 15	32 : 5	< 0.05
hs-CRP (mg/dl)	0.079 ± 0.094[a]	0.104 ± 0.102[a]	< 0.05
Smokers (%)	17%	24%	
Diabetes mellitus (%)	4%	27%	< 0.05
Hypertension (%)	41%	65%	< 0.05
Hyperlipidemia (%)	59%	68%	
HDL-cholesterol < 40 mg/dl (%)	11%	19%	
AHI	40.4 ± 21.3[a]	53.6 ± 22.0[a]	< 0.05
Arousal index	41.6 ± 16.0[a]	53.9 ± 18.3[a]	< 0.05
MinO2 (%)	77.3 ± 9.9[a]	74.1 ± 10.0[a]	
MeanO2 (%)	94.5 ± 1.7[a]	93.6 ± 3.1[a]	
SpO2 < 90% (%)	4.3 ± 5.8[a]	9.7 ± 12.9[a]	< 0.05
ODI (/h)	36.8 ± 23.6[a]	50.0 ± 22.9[a]	< 0.05
Snore index (/h)	323.5 ± 165.7[a]	293.6 ± 209.7[a]	
Total sleep time (min)	413.2 ± 65.2	396.3 ± 63.2	
Sleep efficiency (%)	83.9 ± 9.0	77.1 ± 9.8	< 0.05
Non-REM stage1 (N1) (%)	33.9 ± 15.8[a]	47.0 ± 18.0[a]	< 0.05
Non-REM stage2 (N2) (%)	47.9 ± 13.8[a]	37.7 ± 15.0[a]	< 0.05
Non-REM stage3 (N3) (%)	5.8 ± 5.4[a]	3.1 ± 4.4[a]	< 0.05
REM stage (%)	12.4 ± 4.5[a]	12.1 ± 5.1[a]	
ESS	8.5 ± 5.1[a]	10.2 ± 4.5[a]	< 0.05

[a] mean ± S.D.

PSG polysomnography, *ICA* internal carotid artery, *BMI* body mass index, *hs-CRP* high-sensitivity C-reactive protein, *HDL* high-density lipoprotein, *AHI* apnea hypopnea index, *ODI* oxygen desaturation index, *REM* rapid-eye movement, *ESS* Epworth Sleepiness Scale

Table 3 Univariate logistic regression analyses-independent variables of ICA plaque (+). Stepwise multivariate logistic regression-independent predictors of ICA plaque (+)

Dependent variable	OR	CI	*P*
Age	1.066	1.017–1.117	0.008
Male	3.097	1.004–9.550	0.049
Hypertension	2.623	1.073–6.417	0.035
Diabetes mellitus	8.148	1.658–40.036	0.01
AHI	1.028	1.007–1.050	0.01
Arousal index	1.043	1.014–1.073	0.003
SpO2 < 90%	1344.252	2.8430–635,679.073	0.022
ODI (/h)	1.024	1.005–1.045	0.016
Diabetes mellitus	8.705	1.291–58.681	0.026
Age	1.064	1.009–1.122	0.023
Arousal index	1.052	1.018–1.088	0.003

Diabetes mellitus, age, and arousal index were found to be independent predictors of ICA plaque (+)

OR odds ratio, *CI* confidence interval, *ICA* internal carotid artery, *AHI* apnea hypopnea index, *ODI* oxygen desaturation index, *REM* rapid eye movement

medications such as antihypertensive, lipid-lowering, and anti-diabetic medications, in detail. Moreover, we only considered current smoking status, i.e., current smokers or past smokers that included never-smokers. In addition, most patients in the present study had cardiovascular risk factors, which could increase inflammation and promote carotid atherosclerosis. The effects of each risk factor, number of complications, and the severity of these complications may affect the independent predictors of ICA plaque presence. It must also be noted that occasionally, patients can hear their own snoring during non-respiratory arousals. Respiratory effort-related arousal (RERA) is also included in non-respiratory arousal with and without snoring. However, in the present study, the presence of RERA via the monitoring of esophageal pressure was not evaluated; therefore, we cannot speculate on the effects of RERA. The abovementioned points emphasize that further assessment of a larger number of patients with minimal risk factors is paramount.

Conclusion

Our results show that the arousal index may not only serve as an index of daytime sleepiness or insomnia, but also as an index of atherosclerosis in patients with OSAS.

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Compliance with ethical standards

Ethical approval The study was approved by the ethical committee of Tokyo Women's Medical University, and written informed consent was obtained from all participants. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare that they have no conflict of interest.

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