Relationship between Severity of Obstructive Sleep Apnea Syndrome and Retinal Nerve Fiber Layer Thickness

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• PURPOSE: To determine whether there is a significant correlation among the peripapillary retinal nerve fiber layer (RNFL) thickness, foveal thickness, total macular volume, and severity of obstructive sleep apnea syndrome.

• DESIGN: Prospective study.

• METHODS: We studied 124 consecutive subjects who underwent polysomnography. Optical coherence tomography (OCT) was used to measure the peripapillary RNFL, foveal thickness, and total macular volume. The Pearson correlation coefficient was used to determine the relationship between the apnea-hypopnea index and OCT and other parameters. Multiple regression analysis was used to determine the independent factors for the RNFL sectors that were the most strongly correlated with the apnea-hypopnea index.

• RESULTS: The apnea-hypopnea index was significantly and negatively correlated (right eye, $r = -0.31$, $P = 0.0004$; left eye, $r = -0.39$, $P < 0.0001$) with the nasal RNFL thickness (Pearson correlation analysis). The foveal thickness and total macular volume were not correlated. The intraocular pressure, body mass index, plaque score, and incidence of hypertension were negatively correlated, and the lowest oxygen saturation and mean oxygen saturation were positively correlated with the nasal RNFL thickness in the left eye. Multiple regression analysis showed that the apnea-hypopnea index and age were independent contributors to the nasal RNFL thickness in the left eye (apnea-hypopnea index, standard regression coefficient, −0.30, t value, −2.76, $P = 0.007$; age, −0.24, −2.36, 0.02, respectively). The nasal RNFL thickness in both eyes decreased significantly based on the severity of the obstructive sleep apnea syndrome.

• CONCLUSION: Exacerbation of obstructive sleep apnea syndrome may produce unique retinal neurodegenerative disorders that decrease the nasal RNFL thickness. (Am J Ophthalmol 2014;157:1202–1208. © 2014 by Elsevier Inc. All rights reserved.)

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THE ASSOCIATION OF ARTERIOSCLEROTIC DISEASES with obstructive sleep apnea syndrome has been identified recently and may be a possible risk factor for macroangiopathies, such as hypertension, coronary artery disease, and cerebrovascular disease or microangiopathic disorders such as renal disease.[1–5]

In ophthalmology, obstructive sleep apnea syndrome is associated with glaucoma and optic neuropathy. Previous studies have reported that patients with obstructive sleep apnea syndrome had a high incidence of glaucoma.[6–8] However, the prevalence of glaucoma in patients with obstructive sleep apnea syndrome was similar to that in the general Caucasian population.[9,10] Optic neuropathy associated with glaucoma is characterized by decreased retinal nerve fiber layer (RNFL) thickness. Early detection of decreased RFNL thickness offers an opportunity to detect glaucoma in its early stages.[11,12] It has also been reported that patients with glaucoma can lose 40% of retinal ganglion cell axons before a measurable visual defect becomes evident.[13] Optical coherence tomography (OCT), a noninvasive imaging technique, provides reproducible, high-resolution, cross-sectional imaging of the RNFL. OCT is used for diagnosis and follow-up of various ophthalmologic disorders, including glaucoma.[14] Previous studies have found that the RNFL thickness levels in patients with obstructive sleep apnea syndrome decreased compared with control subjects.[15–19] However, it remains unclear whether the severity of obstructive sleep apnea syndrome is related to the RNFL thickness. The purpose of the current study was to determine whether there is a significant correlation between the RNFL thickness of the optic nerve head, the foveal thickness, and the total macular volume as determined by Stratus OCT (Carl Zeiss Meditec, Dublin, CA) and the severity of obstructive sleep apnea syndrome in Japanese patients. We also compared the carotid arteriosclerotic parameters obtained from high-resolution B-mode ultrasonography and serum arteriosclerotic risk factors.

METHODS

THE INSTITUTIONAL REVIEW BOARD OF TOHO UNIVERSITY Sakura Medical Center approved the current study. Design of this study was prospective, and all participants provided informed consent according to the Declaration of Helsinki.

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TABLE 1. Clinical and Examination Characteristics of Study Subjects with Obstructive Sleep Apnea Syndrome

	Mean ± Standard Deviation	Range
Age (years)	61.7 ± 10.0	38 to 86
Men/women	88/36	
Spherical refraction (diopters)		
Right eye	−0.14 ± 2.12	−6.75 to 5.5
Left eye	−0.15 ± 2.22	−10.00 to 4.25
IOP (mm Hg)		
Right eye	12.7 ± 3.1	7 to 23
Left eye	12.7 ± 2.9	7 to 20
Body mass index (kg/m^2)	24.9 ± 3.6	18.2 to 35.8
HbA1C (%)	5.8 ± 1.0	4.4 to 10.8
Total cholesterol (mg/dL)	187.6 ± 29.6	104 to 253
Triglycerides (mg/dL)	140.7 ± 77.0	45 to 600
LDL-C (mg/dL)	108.7 ± 26.4	35 to 175
HDL-C (mg/dL)	51.8 ± 14.9	28 to 94
Cystatin C (mg/L)	0.82 ± 0.15	0.53 to 1.54
High-sensitivity C-reactive protein (mg/L)	0.12 ± 0.24	0.004 to 2.380
Intima-media thickness (mm)	0.90 ± 0.17	0.6 to 1.4
Plaque score	4.6 ± 4.5	0.0 to 20.1
Hypertension (%)	61.3	
Diabetes mellitus (%)	26.6	
Coronary artery disease (%)	21.8	
Apnea hypopnea index (times/hour)	33.2 ± 21.0	0.3 to 83.3
Lowest SpO2 (%)	83.1 ± 8.0	58 to 96
Mean SpO2 (%)	95.2 ± 1.7	90 to 98

HbA1C = glycated hemoglobin A1C; IOP = intraocular pressure; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; lowest SpO2 = lowest oxygen saturation (%) during sleep; mean SpO2 = average oxygen saturation (%) value during sleep.
n = 124.

We studied 147 consecutive patients who underwent standard overnight polysomnography at the Department of Cardiovascular Center of Toho University Sakura Medical Center between April 1, 2007, and March 1, 2010.

• **SLEEP STUDY:** Patients underwent polysomnography performed over a minimum of 6 hours in a quiet private room in our hospital. Electroencephalography, submental electromyography, electro-oculography, nasal and oral airflow measured using thermistors, and pulse oximetry measurements were recorded using a standard technique. The apnea-hypopnea index (times/hour) was calculated and used as an indicator of the severity of obstructive sleep apnea syndrome. An apneic event was defined as cessation of airflow for at least 10 seconds with effort to breathe. A hypoapneic event was defined as a minimal 30% reduction in thoracoabdominal movement or airflow compared with baseline lasting at least 10 seconds with 4% or greater oxygen desaturation.[20] The severity of obstructive sleep apnea syndrome was graded according to the following apnea-hypopnea index values: normal to mild, less than 15; moderate, 15 or higher to less than 30; severe, 30 or higher to less than 60; and very severe, over 60.[21] The lowest oxygen saturation during sleep (lowest SpO2) and the average oxygen saturation during sleep (mean SpO2) also were calculated.

• **MEASUREMENT OF CAROTID INTIMA-MEDIA THICKNESS AND PLAQUE SCORE:** High-resolution ultrasonographic imaging of the carotid artery using the B-scan mode was performed using the EUB-8500 ultrasound system (Hitachi, Tokyo, Japan) with the probe frequency set to 7.5 MHz. The patients were measured while in the supine position with their heads slightly turned away from the sonographer. The procedures involved scanning the near and far walls of the carotid artery every 1 cm proximal to the carotid bulb in the longitudinal view. The intima-media thickness was defined as the average of the maximal intima-media thickness 1 cm proximal and 1 cm distal to the carotid bulb.[22–24] The intima-media thickness of the thickened side of the carotid artery was used for data analyses. The plaque score was calculated as reported previously.[25] Briefly, plaques (localized increases in intima-media thickness ≥1.1 mm) were detected by cross-sectional and longitudinal scanning of the bilateral common and internal carotid arteries. The plaque score was computed by adding the maximal thickness of each plaque in the bilateral carotid arteries.