Table 3
Multivariate linear regression model for predicting abdominal aortic calcification (AAC) scores.

Model	Variables	Log (AAC + 1)								
		Upper			Lower			Total		
		β	*P*	Adjusted model R^2	β	*P*	Adjusted model R^2	β	*P*	Adjusted model R^2
1	Age, years	0.53	<0.0001		0.50	<0.0001		0.54	<0.0001	
	BMI, kg/m^2	0.06	N.S.		0.02	N.S.		0.03	N.S.	
	OSA (vs. none/mild)									
	Moderate	0.01	N.S.		0.05	N.S.		0.06	N.S.	
	Severe	0.04	N.S.	25.8	0.15	0.01	25.2	0.14	0.01	29.0
2	Age, years	0.52	<0.0001		0.50	<0.0001		0.53	<0.0001	
	Visceral fat area, cm^2	0.17	0.0004		0.17	0.0004		0.18	<0.0001	
	OSA (vs. none/mild)									
	Moderate	0.004	N.S.		0.04	N.S.		0.04	N.S.	
	Severe	−0.01	N.S.	27.9	0.08	N.S.	28.5	0.08	N.S.	31.6
3	Age, years	0.46	<0.0001		0.45	<0.0001		0.48	<0.0001	
	Visceral fat area, cm^2	0.06	N.S.		0.07	N.S.		0.08	N.S.	
	OSA (vs. none/mild)									
	Moderate	−0.02	N.S.		0.01	N.S.		0.02	N.S.	
	Severe	−0.05	N.S.		0.02	N.S.		0.03	N.S.	
	Men	0.04	N.S.		0.07	N.S.		0.04	N.S.	
	Smoker	0.04	N.S.		0.22	<0.0001		0.20	<0.0001	
	Hypertension	0.18	<0.0001		0.13	0.002		0.14	0.0009	
	Dyslipidemia	0.07	N.S.		0.08	N.S.		0.08	N.S.	
	Diabetes	0.15	0.0005	33.4	0.09	0.03	36.7	0.09	0.04	39.0

OSA: obstructive sleep apnea.

and AAC. Second, many of the study participants had cardiometabolic disorders other than OSA. Although this heterogeneity may better reflect clinical settings where OSA is identified, our results merely indicated that the impact of OSA was negated by coexisting atherogenic risk factors, and thus did not necessarily deny the potential role of OSA in the development of atherosclerotic calcification. Third, as the study population was limited to Japanese participants with suspected sleep-disordered breathing, the results are prone to potential selection bias, thus may not be extrapolated to other populations. Fourth, because we only had a small number of participants who did not have OSA (AHI <5), we could not form a non-OSA group as a separate category of disease severity, which would have helped to achieve a better understanding of the relationship between OSA and AAC.

In conclusion, severe OSA was associated with a greater extent of AAC, which was dependent on coexisting atherogenic risk factors. Our findings support the concept that comorbid cardiometabolic disorders may largely mediate the association of OSA with subclinical atherosclerosis.

Sources of funding

This work was supported by grants from the Japanese Ministry of Education, Culture, Sports, Science and Technology (Grant number 26293198, 24621005), Respiratory Failure Research Group and Health Science Research Grants (Comprehensive Research on Life-Style Related Diseases including Cardiovascular Diseases and Diabetes Mellitus) from the Ministry of Health, Labor and Welfare, Japan (Tokyo, Japan) and the Japan Vascular Disease Research Foundation (Tokyo, Japan).

Conflicts of interest

This was not an industry-supported study. The Department of Respiratory Care and Sleep Control Medicine, Graduate School of Medicine, Kyoto University is funded by endowments from Philips-Respironics, Teijin Pharma, and Fukuda Denshi to Kyoto University. Chin K, Oga T, Tanizawa K, and Inouchi M belong to the department. The other authors have indicated no financial conflicts of interest.

Acknowledgment

We thank Mr. Kazuyuki Ueda, Ms. Yuko Yamanishi, Akemi Ishii, Yuri Masuda, and Yumiko Narita for analyzing polysomnographic data. We also thank Ms. Naoko Kimura, Satoko Tamura and Tomoko Toki for their contribution of inputting data.

References

[1] L.F. Drager, L.A. Bortolotto, C. Maki-Nunes, et al., The incremental role of obstructive sleep apnoea on markers of atherosclerosis in patients with metabolic syndrome, Atherosclerosis 208 (2010) 490–495.
[2] L.F. Drager, V.Y. Polotsky, G. Lorenzi-Filho, Obstructive sleep apnea: an emerging risk factor for atherosclerosis, Chest 140 (2011) 534–542.
[3] S.S. Ali, E.T. Oni, H.J. Warraich, et al., Systematic review on noninvasive assessment of subclinical cardiovascular disease in obstructive sleep apnea: new kid on the block!, Sleep. Med. Rev. 18 (2014) 379–391.
[4] G. Sangiorgi, J.A. Rumberger, A. Severson, et al., Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: a histologic study of 723 coronary artery segments using non-decalcifying methodology, J. Am. Coll. Cardiol. 31 (1998) 126–133.
[5] R. Detrano, A.D. Guerci, J.J. Carr, et al., Coronary calcium as a predictor of coronary events in four racial or ethnic groups, N. Engl. J. Med. 358 (2008) 1336–1345.
[6] F. Bastos Goncalves, M.T. Voute, S.E. Hoeks, et al., Calcification of the abdominal aorta as an independent predictor of cardiovascular events: a meta-analysis, Heart 98 (2012) 988–994.
[7] D. Sorajja, A.S. Gami, V.K. Somers, T.R. Behrenbeck, A. Garcia-Touchard, F. Lopez-Jimenez, Independent association between obstructive sleep apnea and subclinical coronary artery disease, Chest 133 (2008) 927–933.
[8] S.H. Kim, G.Y. Cho, I. Baik, et al., Association of coronary artery calcification with obstructive sleep apnea and obesity in middle-aged men, Nutr. Metab. Cardiovasc. Dis. 20 (2010) 575–582.
[9] G. Weinreich, T.E. Wessendorf, T. Erdmann, et al., Association of obstructive sleep apnoea with subclinical coronary atherosclerosis, Atherosclerosis 231 (2013) 191–197.
[10] Y. Kwon, D.A. Duprez, D.R. Jacobs, et al., Obstructive sleep apnea and progression of coronary artery calcium: the multi-ethnic study of atherosclerosis study, J. Am. Heart Assoc. 3 (2014) e001241.
[11] A.S. Agatston, W.R. Janowitz, F.J. Hildner, N.R. Zusmer, M. Viamonte Jr., R. Detrano, Quantification of coronary artery calcium using ultrafast computed tomography, J. Am. Coll. Cardiol. 15 (1990) 827–832.
[12] K. Murase, K. Mori, C. Yoshimura, et al., Association between plasma neutrophil gelatinase associated lipocalin level and obstructive sleep apnea or nocturnal intermittent hypoxia, PLoS One 8 (2013) e54184.
[13] C. Iber, S. Ancoli-Israel, A. Chesson, S. Quan, The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications, American Academy of Sleep Medicine, Westchester, IL, USA, 2007.
[14] Y. Harada, T. Oga, Y. Chihara, M. Azuma, K. Murase, Y. Toyama, et al.,

Differences in associations between visceral fat accumulation and obstructive sleep apnea by sex, Ann. Am. Thorac. Soc. 11 (2014) 383–391.
[15] T. Teramoto, J. Sasaki, H. Ueshima, et al., Executive summary of Japan Atherosclerosis Society (JAS) guideline for diagnosis and prevention of atherosclerotic cardiovascular diseases for Japanese, J. Atheroscler. Thromb. 14 (2007) 45–50.
[16] R.W. Jayalath, S.H. Mangan, J. Golledge, Aortic calcification, Eur. J. Vasc. Endovasc. Surg. 30 (2005) 476–488.
[17] S.E. New, E. Aikawa, Cardiovascular calcification: an inflammatory disease, Circ. J. 75 (2011) 1305–1313.
[18] Natural history of aortic and coronary atherosclerotic lesions in youth, Findings from the PDAY study. Pathobiological determinants of atherosclerosis in youth (PDAY) research group, Arterioscler. Thromb. 13 (1993) 1291–1298.
[19] N.E. Jensky, M.H. Criqui, M.C. Wright, C.L. Wassel, S.A. Brody, M.A. Allison, Blood pressure and vascular calcification, Hypertension 55 (2010) 990–997.
[20] N.D. Wong, V.A. Lopez, M. Allison, et al., Abdominal aortic calcium and multisite atherosclerosis: the multiethnic study of atherosclerosis, Atherosclerosis 214 (2011) 436–441.
[21] C.S. Fox, S.J. Hwang, J.M. Massaro, et al., Relation of subcutaneous and visceral adipose tissue to coronary and abdominal aortic calcium (from the Framingham Heart Study), Am. J. Cardiol. 104 (2009) 543–547.
[22] A.M. Shaaban, A.J. Duerinckx, Wall shear stress and early atherosclerosis: a review, AJR Am. J. Roentgenol. 174 (2000) 1657–1665.
[23] L.I. Kauppila, J.F. Polak, L.A. Cupples, M.T. Hannan, D.P. Kiel, P.W. Wilson, New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study, Atherosclerosis 132 (1997) 245–250.