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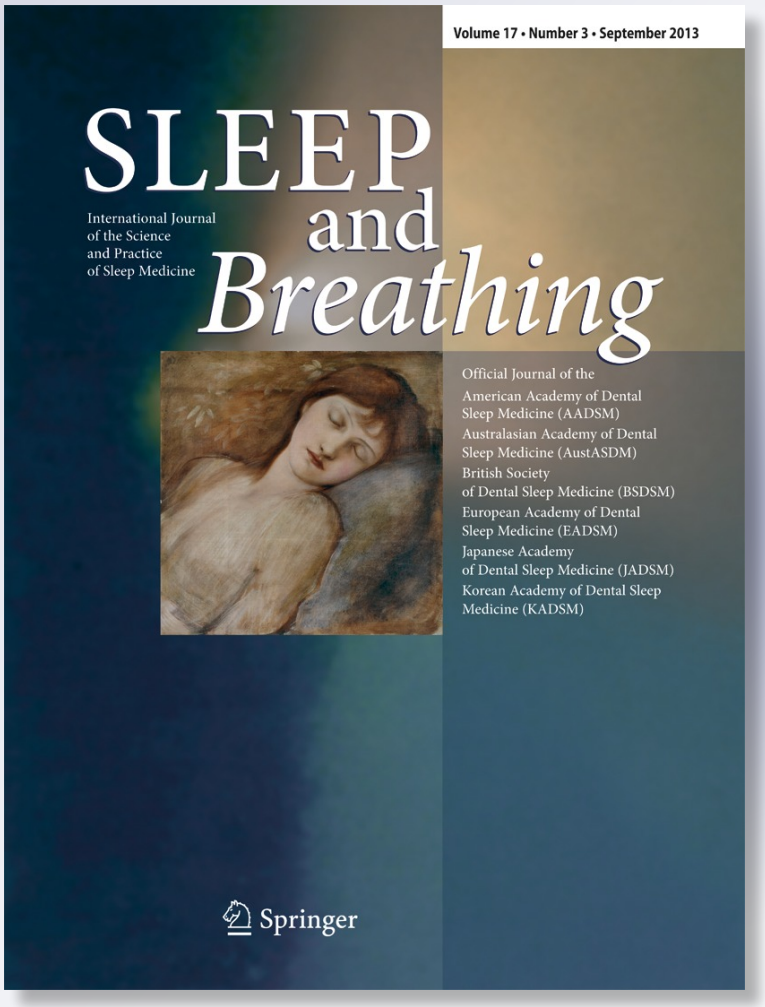

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ORIGINAL ARTICLE

The relationship between cephalometric carotid artery calcification and Framingham Risk Score profile in patients with obstructive sleep apnea

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Abstract
Purpose The morbidity rate of arteriosclerosis becomes clinically manifested as acute cardiovascular events. In the progress of atherosclerosis, the carotid artery calcifies and sometimes appears as a calcified mass on a cephalometric radiograph. This study was designed to evaluate cardiovascular risks according to the Framingham Risk Score (FRS) between subjects with and without visible carotid artery calcification on a cephalogram.
Methods Subjects diagnosed with obstructive sleep apnea (OSA) were divided into two groups according to whether or not calcification was visible on a cephalometric radiograph in the carotid artery area, and the characteristic differences between the two groups were analyzed. The evaluated variables included age, BMI, apnea–hypopnea index (AHI), SpO_2, ESS, blood pressure, medication history, diabetes mellitus (DM), drinking, smoking, and lipid-related measurements. FRSs for stroke, general cardiovascular disease (GCD), and coronary heart disease (CHD) were calculated. Statistical analyses were performed (SPSS 18.0) with significance defined as a two-tailed p value less than 0.05.
Results A total of 811 subjects completed the data collection (727 males, age 53.0±12.5 years, AHI 31.7±22.6, times/h). From FRSs, probabilities of a GCD, stroke, and CHD within 10 years were 16.0±9.7, 9.8±6.7, and 11.9±8.3 %, respectively. Some 84 subjects exhibited calcification in the carotid arterial area. Calcification subjects were higher GCD risk and older than subjects who had no identified calcification (20.3±10.1 vs 15.6±20.3 %, p=0.013, 58.8±11.4 vs. 52.3±12.5 years, p<0.001). Although there is no significant difference in OSA-related variables and FRSs, subjects with visible calcifications have higher prevalence of high blood pressure medication and DM (p<0.01).
Conclusion While the presence of a calcified mass on a cephalometric radiograph is not diagnostic of atherosclerosis, this information indicates some cardiovascular risk.

Keywords Atherosclerosis · Calcification · Sleep apnea · Radiograph

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Introduction

Obstructive sleep apnea (OSA) is highly prevalent in patients with established cardiovascular disease [1–3]. Although there are various pathways by which the symptoms of OSA may induce atherosclerosis, one of the mechanisms is thought to be the mechanical stress from vibrations [4] induced by snoring. Many epidemiologic studies have demonstrated an association between snoring and strokes [5–9], and have shown that the strength of this association is on par with traditional stroke risk factors such as hypertension, smoking, atrial fibrillation, and hypercholesterolaemia [10]. Hedner et al. proposed that the possible mechanism by which snoring could precipitate an embolic stroke is through vibrations transmitted to the arterial wall. If sleep apnea is involved in the development of atherosclerosis, mechanical factors such as vibration may well promote this

atherosclerosis by causing repetitive injury to the wall of the carotid arteries [11]. Lee et al. quantified snoring in a sleep lab and evaluated it with atherosclerosis in both the bilateral carotid and femoral arteries. After adjustment for age, sex, smoking history, and hypertension, this study demonstrated that heavy snoring was significantly associated with carotid atherosclerosis but not with femoral atherosclerosis. It was concluded that heavy snoring significantly increases the risk of carotid atherosclerosis. This increase was found to be independent of other risk factors, including nocturnal hypoxia and obstructive sleep apnea severity [12]. Furthermore, in a study on rabbits, it was demonstrated that pressure vibrations occur in the tissues surrounding the carotid artery wall during snoring and are transmitted to the carotid artery lumen itself [13]. In addition, recently Cho and colleges reported that carotid arteries subjected to 6 h of continuous peri-carotid vibration exhibited the reduction of endothelial function, suggesting a direct plausible mechanism linking snoring to the development of carotid atherosclerosis[14]. In general, as the arteriosclerosis progresses, the calcification on the vascular system frequently increases. Allison et al. reported that carotid calcification can be significantly correlated with the carotid intimal medial thickness [15], which is a useful marker for investigating the degree of early atherosclerosis [16]. Recently, many reports focus on continuous positive airway pressure (CPAP) effects for cardiovascular functions, and revealed the relationship between CPAP and cerebral blood flow or carotid–femoral pulse wave velocity [17, 18].

In dental clinics, dentists often obtain panoramic or cephalometric radiographs for diagnosis or the follow-up of patient oral symptoms. Many reports have examined carotid artery calcification (CAC) on panoramic dental radiographs [19–21], and these reports have found the prevalence of CAC in the general dental population to be 0.8 % [20]. Cohen et al. examined and followed patients whose panoramic radiographs showed carotid calcification, and these investigators demonstrated that 86 % of patients had preexisting risk factors, and 34 % had major end points of myocardial infarction, stroke, or death in an average mean time of 2.7 years [19]. Friedlander examined cerebrovascular accident patients, and found the CAC in 37 % of subjects [21]. Although some articles report that panoramic radiographs have moderate diagnostic accuracy in the detection of CAC, when compared to ultrasound [22] or CT [23], many calcifications shown on the panoramic radiographs were confirmed as CAC by ultrasonographic tests [24, 25].

When oral appliance therapy for OSA is indicated, the dentist obtains a cephalometric radiograph to analyze the patient's craniofacial characteristics, to monitor side effects, and the appearance of carotid artery calcification will sometimes be identified. Although the prevalence or importance of calcification is unclear, the information may be help in finding previously undiagnosed cardiovascular disease. We have previously identified a higher prevalence of CAC in OSA patients when compared to the general population[26].

The Framingham Heart Study, under the direction of the National Heart, Lung and Blood Institute, has identified common factors or characteristics that contribute to cardiovascular disease (CVD) and developed a CVD risk score[27]. This study was designed to evaluate the demographic data and the prevalence of calcification in cephalometric radiographs of OSA patients to identify cardiovascular risks according to the Framingham Risk Score (FRS) between subjects with and without visible carotid artery calcification on cephalograms. We hypothesize that cephalograms with the appearance of some calcification suggest the presence of cardiovascular risk more than the absence of calcification.

Methods

Databases of OSA patients from the Sleep Center at Kirigaoka Tsuda Hospital in Japan were used. The retrospective study was approved by the Behavioral Research Ethics Board of the Kyushu University Hospital and ethics board of Kirigaoka Tsuda Hospital. Patients attended the Sleep Center, Kirigaoka Tsuda Hospital, for an initial evaluation of their SDB, and all had digital cephalometric data collected (image size of 57×43 cm). Inclusion criteria were older than 30 years and younger than 84, having data from a baseline polysomnography (PSG), and having a cephalometric radiograph that clearly identified the area above C4. Two investigators observed the carotid artery area in each radiograph and counted the number of radiographs on which calcification appeared. During this examination, those investigators were blinded to all patient demographic information such as name, sex, age, body mass index (BMI), and apnea–hypopnea index (AHI) severity. Kappa for interrater reliability was calculated after the assessment (κ=0.86). The radiographs that had different results between two investigators were re-assessed together and judged. Demographic data such as age, sex, and BMI were collected from each patient's chart. The evaluated variables included age, BMI, Slow Wave Sleep (SWS) time (percentage), AHI, minimum and average SpO_2, Epworth Sleepiness Scale (ESS), systolic and diastolic blood pressures, medication history, diabetes mellitus (DM), previous CVD, drinking habit, smoking habit, and lipid-related measurements such as total lipoprotein and low- and high-density lipoprotein (LDL and HDL). FRSs for general cardiovascular disease (GCD), stroke, and coronary heart disease (CHD) were calculated based on the proposed criteria (Table 1). The data were presented as a mean±SD. After calculating the incidence of calcified masses in the cervical portion of the carotid artery, the subjects were divided into two groups, those who showed

Table 1 Parameters for Framingham Risk Score

Framingham Heart Study Indicator of Risk Score
General cardiovascular disease (10-year risk)
Age
Diabetes
Smoking
Treated and untreated systolic blood pressure
Total cholesterol
HDL cholesterol
BMI replacing lipid in a simpler model
Stroke (10-year risk)
Age
Systolic blood pressure
Diabetes mellitus
Cigarette smoking
Prior cardiovascular disease
Atrial fibrillation
Left ventricular hypertrophy
Use of hypertensive medication
Coronary heart disease (10-year risk)
Age
Diabetes
Smoking
JNC-V blood pressure categories
NCEP total cholesterol categories
LDL cholesterol categories

calcification and those who did not. The SPSS software program (version 18.0 for windows, SPSS Inc, Chicago, IL, USA) was used for statistical analysis with significance defined as a two-tailed p value less than 0.05. Unpaired t tests, Mann–Whitney U tests, and Pearson chi-square tests were used to assess the characteristic differences between the group that showed calcification and the group that did not. Spearman test was used to assess the correlations between PSG-related variables and FRSs ($|r|>0.2$) for all subjects.

Results

A total of 811 x-rays met the inclusion criteria. Demographic data are provided in Table 2. Eighty-four subjects had evidence of calcifications, and the prevalence of calcification for the total group was 10.4 %. Statistical analysis suggested that age ($p<0.001$), medication for hypertension ($p<0.01$), DM ($p<0.01$), and 10-year risk of GCD ($p<0.05$) identified significant differences between subjects who exhibited calcification or these who did not, although there is no significant difference in OSA-related variables and FRSs (Tables 2 and 3). The data of 10-year risk of GCD, stroke, and CHD divided by sex and age are shown in Table 4. In the 60 to 70 years female group, subjects with CAC scored higher risks of GCD and stroke than non-CAC subjects ($p<0.05$; Table 4). SWS time (percentage) identified significant correlations with 10-year risks of GCD and stroke ($p<0.001$), and BMI exhibited a significant correlation with age, AHI, minO2, aveO2, diastolic and systolic blood pressures, and LDL ($p<0.001$). Figure 1 presents the average 10-year risk of CHD in males and the patient numbers of score more than the age-matched average. Some 34.5 % male subjects and 25.0 % female subjects had a higher CHD risk score than the age-matched general population. In the age 30 to 34 male group, 85.7 % subjects exceeded the average CHD risk score.

Table 2 Demographic data

	Total	No calcification	Calcification
N	811	727	84
Sex (male/female)	677/134	612/115	65/19
Age (year)	53.0±12.5	52.3±12.5**	58.7±11.4**
BMI (kg/m^2)	26.3±4.2	26.4±4.3	25.8±3.7
AHI (events/h)	31.7±22.6	31.7±2.8	31.8±20.5
Ave O_2 (%)	95.9±2.2	95.9±2.3	96.0±1.5
SWS (%)	5.1±6.5	5.1±6.5	4.9±7.0
ESS	8.4±4.7	8.4±4.7	8.4±4.8
BP systolic (mmHg)	139.5±19.4	139.6±19.7	139.2±16.7
BP diastolic (mmHg)	86.2±12.8	86.4±12.9	84.8±12.1
Medication for hypertension	241	205*	36*
Smoking	226	201	25
Alcohol consumption	472	421	51
Diabetes mellitus	80	64*	16*
History of CVD	48	43	5
Total cholesterol	211.3±37.4	211.3±37.5	211.1±36.6
HDL cholesterol	52.4±14.0	52.7±14.2	49.7±11.9
LDL cholesterol	124.4±32.8	125.0±33.1	118.4±29.2

Data are shown as mean± standard deviation

*$p<0.01$, **$p<0.001$, statistical significance

Table 3 Framingham Risk Scores of general cardiovascular disease, stroke, and coronary heart disease

	Total	No calcification	Calcification
10-year risk of general cardiovascular disease (GCD) (%)	16.0±9.7	15.6±9.5*	20.3±10.1*
10-year risk of stroke (%)	9.8±6.7	9.7±6.9	10.1±5.5
10-year risk of coronary heart disease (CHD) (%)	11.9±8.3	11.7±8.3	14.3±8.7

Data are shown as mean±standard deviation

*$p<0.05$, statistical significance

Table 4 Framingham Risk Scores of general cardiovascular disease, stroke, and coronary heart disease in different sex and ages

		GCD		Stroke		CHD	
	Age	No calcification	Calcification	No calcification	Calcification	No calcification	Calcification
Male	30–40	5.0±3.2	5.9±2.8	N/A	N/A	5.6±3.2	7.0±4.2
	40–50	10.2±5.7	11.7±6.8	N/A	N/A	7.3±4.3	8.3±5.3
	50–60	20.5±7.3	23.5±7.7	7.0±3.0	7.1±2.5	14.4±7.5	14.4±7.7
	60–70	24.3±6.6	28.4±2.7	10.4±6.9	10.3±4.9	19.4±8.9	22.3±7.8
	70–	27.6±5.7	29.8±0.35	16.5±8.2	14.9±5.3	23.2±7.8	28.0±4.2
Female	30–40	7.43±3.7	N/A	N/A	N/A	2.0±0	N/A
	40–50	10.1±5.1	N/A	N/A	N/A	6.5±2.7	N/A
	50–60	11.5±7.5	3.9±0.4	3.3±1.7	4.3±0.5	8.6±4.4	7.0±0.7
	60–70	**13.3±6.7***	**25.3±8.1***	**5.7±3.2***	**9.4±5.7***	11.6±5.8	19.0±6.9
	70–	13.4±5.4	20.0±14.1	11.0±5.4	10.5±3.5	9.2±3.2	6.0±0

Data are shown as mean±standard deviation

*$p<0.05$, statistical significance

Discussion

This study identifies the prevalence of calcifications on cephalograms and a significant relationship between carotid artery calcifications and cardiovascular risks in patients with sleep apnea. By evaluating more than 800 x-rays, it was documented that 10.4 % of the Japanese digital cephalograms identified calcification in the carotid artery area. This prevalence is higher than that of the general dental population as reported in a panoramic radiograph study [20]. In this study, we could not identify significant sleep apnea-related variable differences between absence and presence of calcification. Similarly, Mason and collaborators did not find an association between the frequency of self-reported snoring and the presence of carotid atheroma [28]. As it is known that age and blood pressure are the dominant risks for systemic calcified atherosclerosis [29] and the association of OSA and hypertension has additive effects on markers of carotid atherosclerosis [30], this study design was not rigorous enough to clearly estimate the relationship between CAC and OSA symptoms.

Our result could not find the gender difference in CAC prevalence; however, older females with CAC had significantly higher FRSs than females without CAC. As Odink reported that the prevalence of calcification in the carotid artery was higher in males when compared to females [31], females may exhibit CAC only after the cardiovascular risk such as when atherosclerosis becomes more severe. In this study, number of females is smaller than males. Although it had 44 females with aged 60–70 and 6 subjects had calcification in their radiographs, it may need some consideration to discuss this result. Recent report from Franklin suggested that a prevalence of OSA in female aged 20–70 is 50 %, and female OSA is related to age, obesity, and hypertension but not to daytime sleepiness [32]. It means that female is not a small population in OSA patients. As not enough study has

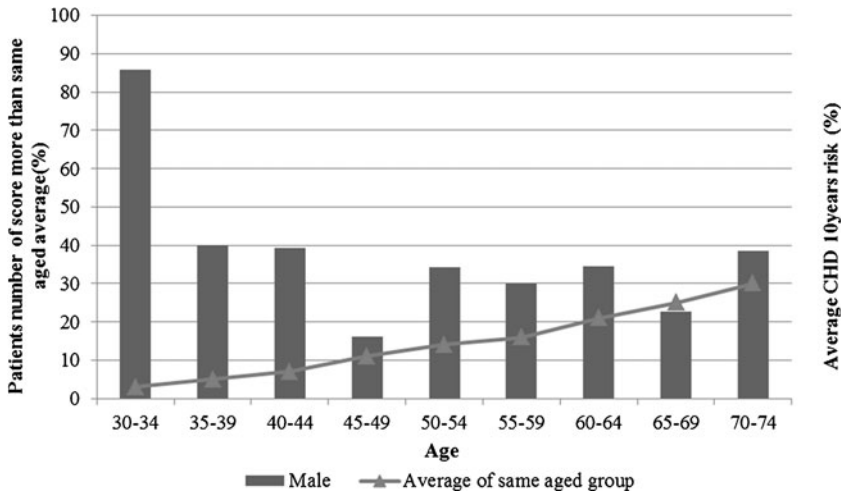

Fig. 1 Coronary heart disease risk in male subjects

been done for OSA in female, this study is considered to suggest a new sight for OSA research. It is exhibited that more than 30 % of male and 25 % of female subjects had higher coronary heart disease risk than age-matched data. As it is suggested that OSA patients frequently have comorbid DM, high blood pressure, and high cholesterol parameters for FRS of CHD, it is important to examine the probability of cardiovascular risk in a clinical setting.

There are some reports which doubt the risk of CAC. These studies have shown that symptomatic plaques are less calcified and more inflamed than asymptomatic plaques [33, 34]. Calcification appears to be a marker of stability within the atheromas [35], and the degree of carotid calcification does not independently predict future stroke risk [36]. Although Russell et al. also demonstrated the remodeling of unstable plaques with patients who had previously had a neurologic event, they cautioned that the future stroke risk of these patients could be high compared to that of the general population [37]. The clinical meaning of calcification and its exact prevalence could not be concluded from this study as there are many different and confounding factors as mentioned above. The presence of calcification does not confirm atherosclerosis as accurately as the gold standard of carotid intima-media thickness can [38]. One might suggest that the prevalence of calcification in the carotid artery area of OSA patients is higher than that of the general population, and there is a significant relationship between CAC and FRSs. It may be clinically useful to pay attention to this symptom when a physician or dentist evaluates an OSA patient's radiographs.

FRSs of stroke and GCD revealed significant correlations between SWS similar to Matthews's report [39]. Although this study result is not enough to discuss a cause–effect relationship between SWS and cardiovascular risk, sleep quality may be an important factor to consider for cardiovascular risk.

This study does not recommended using a radiograph to diagnose atherosclerosis nor should it be concluded that just because a patient's radiograph does not show calcification, he or she will have no symptoms of atherosclerosis. However, calcification should be noted when a cephalometric radiograph is taken for any purpose or used to screen for other symptoms related to airway collapsibility. After a dentist indentifies a possible CAC on a lateral head film, it would be appropriate to refer the patients to a radiologist experienced in the field to confirm the finding.

Conclusion

This study could reveal the relationship between calcification on cephalometric radiographs and cardiovascular risks especially in female sleep apnea patients. While the presence of a calcified mass on a cephalometric radiograph is not diagnostic of atherosclerosis, this information suggests to us some cardiovascular risk when screening for the condition.

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References

1. Mooe T, Rabben T, Wiklund U, Franklin KA, Eriksson P (1996) Sleep-disordered breathing in men with coronary artery disease. Chest 109(3):659–663
2. Peker Y, Kraiczi H, Hedner J, Loth S, Johansson A, Bende M (1999) An independent association between obstructive sleep apnoea and coronary artery disease. Eur Respir J 14(1):179–184
3. Schafer H, Koehler U, Ewig S, Hasper E, Tasci S, Luderitz B (1999) Obstructive sleep apnea as a risk marker in coronary artery disease. Cardiology 92(2):79–84
4. Curry BD, Bain JL, Yan JG, Zhang LL, Yamaguchi M, Matloub HS, Riley DA (2002) Vibration injury damages arterial endothelial cells. Muscle Nerve 25(4):527–534
5. Koskenvuo M, Kaprio J, Telakivi T, Partinen M, Heikkila K, Sarna S (1987) Snoring as a risk factor for ischaemic heart disease and stroke in men. Br Med J (Clin Res Ed) 294(6563):16–19
6. Palomaki H (1991) Snoring and the risk of ischemic brain infarction. Stroke 22(8):1021–1025
7. Partinen M, Palomaki H (1985) Snoring and cerebral infarction. Lancet 2(8468):1325–1326
8. Leineweber C, Kecklund G, Janszky I, Akerstedt T, Orth-Gomer K (2004) Snoring and progression of coronary artery disease: The Stockholm Female Coronary Angiography Study. Sleep 27 (7):1344–1349
9. Hu FB, Willett WC, Manson JE, Colditz GA, Rimm EB, Speizer FE, Hennekens CH, Stampfer MJ (2000) Snoring and risk of cardiovascular disease in women. J Am Coll Cardiol 35 (2):308–313
10. Yaggi H, Mohsenin V (2004) Obstructive sleep apnoea and stroke. Lancet Neurol 3(6):333–342
11. Hedner J (1994) Speculations on the interaction between vascular disease and obstructive sleep apnea. In: SNaS C (ed) Sleep and breathing. Marcel Dekker, New York, pp 823–846
12. Lee SA, Amis TC, Byth K, Larcos G, Kairaitis K, Robinson TD, Wheatley JR (2008) Heavy snoring as a cause of carotid artery atherosclerosis. Sleep 31(9):1207–1213
13. Amatoury J, Howitt L, Wheatley JR, Avolio AP, Amis TC (2006) Snoring-related energy transmission to the carotid artery in rabbits. J Appl Physiol 100(5):1547–1553
14. Cho JG, Witting PK, Verma M, Wu BJ, Shanu A, Kairaitis K, Amis TC, Wheatley JR (2011) Tissue vibration induces carotid artery endothelial dysfunction: a mechanism linking snoring and carotid atherosclerosis? Sleep 34(6):751–757
15. Allison MA, Tiefenbrun J, Langer RD, Wright CM (2005) Atherosclerotic calcification and intimal medial thickness of the carotid arteries. Int J Cardiol 103(1):98–104
16. O'Leary DH, Polak JF (2002) Intima-media thickness: a tool for atherosclerosis imaging and event prediction. Am J Cardiol 90 (10C):18L–21L
17. Chung S, Yoon IY, Lee CH, Kim JW (2011) The effects of nasal continuous positive airway pressure on vascular functions and

serum cardiovascular risk factors in obstructive sleep apnea syndrome. Sleep Breath 15(1):71–76
18. Yiallourou TI, Odier C, Heinzer R, Hirt L, Martin BA, Stergiopulos N, Haba-Rubio J (2012) The effect of continuous positive airway pressure on total cerebral blood flow in healthy awake volunteers. Sleep Breath. doi:10.1007/s11325-012-0688-0
19. Cohen SN, Friedlander AH, Jolly DA, Date L (2002) Carotid calcification on panoramic radiographs: an important marker for vascular risk. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 94(4):510–514
20. Lewis DA, Brooks SL (1999) Cartoid artery calcification in a general dental population: a retrospective study of panoramic radiographs. Gen Dent 47(1):98–103
21. Friedlander AH, Manesh F, Wasterlain CG (1994) Prevalence of detectable carotid artery calcifications on panoramic radiographs of recent stroke victims. Oral Surg Oral Med Oral Pathol 77(6):669–673
22. Madden RP, Hodges JS, Salmen CW, Rindal DB, Tunio J, Michalowicz BS, Ahmad M (2007) Utility of panoramic radiographs in detecting cervical calcified carotid atheroma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 103(4):543–548
23. Yoon SJ, Yoon W, Kim OS, Lee JS, Kang BC (2008) Diagnostic accuracy of panoramic radiography in the detection of calcified carotid artery. Dentomaxillofac Radiol 37(2):104–108
24. Almog DM, Illig KA, Khin M, Green RM (2000) Unrecognized carotid artery stenosis discovered by calcifications on a panoramic radiograph. J Am Dent Assoc 131(11):1593–1597
25. Ravon NA, Hollender LG, McDonald V, Persson GR (2003) Signs of carotid calcification from dental panoramic radiographs are in agreement with Doppler sonography results. J Clin Periodontol 30 (12):1084–1090
26. Tsuda H, Almeida FR, Tsuda T, Moritsuchi Y, Lowe AA (2010) Cephalometric calcified carotid artery atheromas in patients with obstructive sleep apnea. Sleep Breath 14(4):365–370
27. Framingham Heart Study http://wwwframinghamheartstudyorg/about/indexhtml Accessed 20 Sept 2012
28. Mason RH, Mehta Z, Fonseca AC, Stradling JR, Rothwell PM (2012) Snoring and severity of symptomatic and asymptomatic carotid stenosis: a population-based study. Sleep 35(8):1147–1151
29. Allison MA, Criqui MH, Wright CM (2004) Patterns and risk factors for systemic calcified atherosclerosis. Arterioscler Thromb Vasc Biol 24(2):331–336
30. Drager LF, Bortolotto LA, Krieger EM, Lorenzi-Filho G (2009) Additive effects of obstructive sleep apnea and hypertension on early markers of carotid atherosclerosis. Hypertension 53(1):64–69
31. Odink AE, van der Lugt A, Hofman A, Hunink MG, Breteler MM, Krestin GP, Witteman JC (2007) Association between calcification in the coronary arteries, aortic arch and carotid arteries: the Rotterdam study. Atherosclerosis 193(2):408–413
32. Franklin KA, Sahlin C, Stenlund H, Lindberg E (2012) Sleep apnoea is a common occurrence in females. Eur Respir J.
33. Shaalan WE, Cheng H, Gewertz B, McKinsey JF, Schwartz LB, Katz D, Cao D, Desai T, Glagov S, Bassiouny HS (2004) Degree of carotid plaque calcification in relation to symptomatic outcome and plaque inflammation. J Vasc Surg 40(2):262–269
34. Hunt JL, Fairman R, Mitchell ME, Carpenter JP, Golden M, Khalapyan T, Wolfe M, Neschis D, Milner R, Scoll B, Cusack A, Mohler ER 3rd (2002) Bone formation in carotid plaques: a clinicopathological study. Stroke 33(5):1214–1219
35. Nandalur KR, Hardie AD, Raghavan P, Schipper MJ, Baskurt E, Kramer CM (2007) Composition of the stable carotid plaque: insights from a multidetector computed tomography study of plaque volume. Stroke 38(3):935–940
36. Fanning NF, Walters TD, Fox AJ, Symons SP (2006) Association between calcification of the cervical carotid artery bifurcation and white matter ischemia. AJNR Am J Neuroradiol 27(2):378–383
37. Russell DA, Wijeyaratne SM, Gough MJ (2007) Changes in carotid plaque echomorphology with time since a neurologic event. J Vasc Surg 45(2):367–372
38. O'Leary DH, Bots ML (2010) Imaging of atherosclerosis: carotid intima-media thickness. Eur Heart J 31(14):1682–1689
39. Matthews KA, Strollo PJ Jr, Hall M, Mezick EJ, Kamarck TW, Owens JF, Buysse DJ, Reis SE (2011) Associations of Framingham risk score profile and coronary artery calcification with sleep characteristics in middle-aged men and women: Pittsburgh SleepSCORE study. Sleep 34(6):711–716