Association of cigarette smoking with radial augmentation index: the Circulatory Risk in Communities Study (CIRCS)

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ABSTRACT

This study aimed to assess association of cigarette smoking with radial augmentation index among Asian general population. We conducted a cross-sectional population-based study consisted of 1,593 men and 2,671 women aged 40-79 years. Smoking status was ascertained by interviewing and the pack-years of smoking were calculated. The radial augmentation index was defined as a ratio of central pulse pressure to brachial pulse pressure, and measured by an automated tonometer: the HEM-9000AI device (Omron Healthcare co., Kyoto, Japan). Compared with never smokers, current male smokers who smoked ⩾30 cigarettes/day and all female smokers had a higher prevalence of high values of radial augmentation index. After adjustment for known atherosclerosis risk factors, the multivariable odd ratio (OR) [95% confidence intervals (CI)] of high values of radial augmentation index for current male smokers who smoked ⩾30 cigarettes/day compared with never smokers was 1.9 (1.1-3.4). The multivariable ORs (95% CIs) of high values of radial augmentation index for former female smokers and current female smokers compared with never smokers were 1.8 (1.2-2.7) and 2.5 (1.6-3.9), respectively. Moreover, smoking pack-years was positively associated with the prevalence of high values of radial augmentation index for both genders. There were no associations of smoking status with the prevalence of high values of central or brachial pulse pressure in either gender. In conclusion, cigarette smoking and cumulative smoking exposure

were positively associated with increased radial augmentation index for men who smoked heavily, and women.

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Key words: arterial stiffness, radial augmentation index, central pulse pressure, cigarette smoking, epidemiology

INTRODUCTION

Despite the great improvement of the tobacco epidemic control, tobacco smoking continues to be one of the biggest public health problems, especially in low- and middle-income countries.[1] Cigarette smoking is a major cause of atherosclerosis[2,3] and cardiovascular diseases,[4] and passive smoking has been associated with prevalence of hypertension.[5] Mounting evidence indicated that atherosclerosis plays an important role in the pathophysiology of smoking-induced cardiovascular risk.[6-8]

The radial augmentation index, a ratio of central pulse pressure to brachial pulse pressure,[9] has been a widely used surrogate of wave reflection. A high value of augmentation index has been reported as a marker of increased arterial stiffness[10-12] and a predictive factor of cardiovascular events.[13] Several population-based studies have reported that cigarette smoking was positively associated with radial augmentation index.[14-17] In addition, smoking pack-years, a unit for measuring the amount of smoking exposure over a long period of time, was positively associated with aortic augmentation index for young men.[18] However, previous study failed to indicate a dose-response relationship for women, probably due to the small number of female smokers.[15]

A meta-analysis of 23 population-based studies has indicated that cigarette smoking was not associated with blood pressure.[19] A Japanese population-based study has also reported no association of smoking statue with brachial pulse pressure.[20] Another European

epidemiological study reported that current smokers had higher central pulse pressure than non-smokers, despite the similar values of brachial pulse pressure.[21] The impact of smoking pack-years on central or brachial pulse pressures has not yet been explored.

In view of the above limited evidence, we conducted a study using the data of a large community-based cohort study; the Circulatory Risk in Communities Study (CIRCS), and aimed to investigate: (1) the associations of cigarette smoking with high values of radial augmentation index, central and brachial pulse pressures for both men and women; (2) whether there is a cumulative impact of cigarette smoking on radial augmentation index, central and brachial pulse pressures.

METHODS

Study subjects

We used the data from the Circulatory Risk in Communities Study (CIRCS), a prospective community-based study of cardiovascular diseases in Japan since 1963.[22] Measurements of arterial stiffness were conducted for 1,593 men and 2,671 women aged 40-79 years enrolled in annual cardiovascular risk surveys in three communities: Kyowa town, Ibaraki Prefecture; Ikawa town, Akita Prefecture and Yao City, Osaka Prefecture between January 2010 and June 2011. For each subject, physicians, epidemiologists and trained staff members explained the protocol in detail. The informed consent was obtained from all subjects, and the study protocol was approved by the Ethics Committee of Osaka University.

Measurements

To assess arterial stiffness, trained technicians conducted measurements of radial augmentation index, central systolic blood and brachial blood pressure using the automated tonometer, HEM-9000AI (Omron, Healthcare Co., Kyoto, Japan) for all subjects in a sitting position after 5 minutes of rest, using a standard protocol.[23] Radial augmentation index was defined as central pulse pressure/brachial pulse pressure×100(%). Because radial augmentation index was influenced by heart rate, this index was normalized for 75 heart beats/minute according to previous guidelines.[24] Central pulse pressure was defined as the

central systolic blood pressure minus the brachial diastolic blood pressure, and brachial pulse pressure was defined as the brachial systolic minus the diastolic blood pressures.

Trained observers ascertained the smoking status, number of cigarettes smoked per day and the duration of smoking. Subjects who had quit smoking for at least the past 3 months were defined as former smokers, whereas those who currently smoke ≥1 cigarette/day were defined as current smokers and stratified as 1-19, 20-29 and ≥30 cigarettes/day for men, and 1-19 and ≥20 cigarettes/day for women. The smoking pack-years of current smokers was calculated as the mean number of smoked cigarettes packs per day multiplied by years of smoking, and stratified as <30, 30-44 and ≥45 for men, and <12, 12-23 and ≥24 for women according to the tertiles of pack-years for each gender.

During health checkups, height in stocking feet and weight in light clothing were measured. The usual weekly intake of alcohol was evaluated by units of "*go*", a traditional Japanese unit of volume corresponding to 23g of ethanol, and converted into grams of ethanol per day.[25] Seated right arm systolic and diastolic blood pressures were measured for all subjects who had rested for 5 minutes by trained observers using HEM-9000AI (Omron, Healthcare Co., Kyoto, Japan). Diabetes mellitus was defined as a fasting glucose level of ≥ 7.8 mmol/L, a non-fasting glucose level of ≥11.1 mmol/L or the use of medication for diabetes mellitus. For the measurement of serum lipids and glucose, non-fasting blood was drawn from seated subjects into a plain, siliconized glass tube, and the serum was separated

within 30 min. Serum glucose was measured by the hexokinase method and serum total and HDL-cholesterol were measured using enzymatic methods by an automatic analyzer (Hitachi 7250, Hitachi Medical Corp., Ibaraki, Japan) at the Osaka Medical Centre for Health Science and Promotion, an international member of the US National Cholesterol Reference Method Laboratory Network (CRMLN).[26]

Statistical analysis

We analyzed the sex-specific prevalence of high values of radial augmentation index, central and brachial pulse pressures according to smoking status to assess the impact of cigarette smoking on changes in arterial stiffness. In this study, values higher than the lower limit of the highest quintile values of radial augmentation index (≥88% for men and ≥94% for women) were defined as high values of radial augmentation index. The same concept was applied to define high values of central and brachial pulse pressures (≥55 mmHg for men and ≥56 mmHg for women central pulse pressure; and ≥65 mmHg for men and ≥64 mmHg for women brachial pulse pressure). Smoking status was divided into five groups (never-, former-, current smokers with 1-19, 20-29 and ≥30 cigarettes/day) for men, and four groups (never-, former-, current smokers with 1-19 and ≥20 cigarettes/day) for women. Dunnett's test was used to compare the difference of each measure value between never smokers and other smoking status. We calculated the age- and multivariable odds ratios (ORs)

[95% confidence intervals (CIs)] of high values of radial augmentation index, central and brachial pulse pressures according to smoking status using the logistic regression analysis. Tests for trend across smoking pack-years groups were conducted by assigning median values of smoking pack-years: 0 in never smokers, 21 in <30 pack-years group, 38 in 30-44 pack-years group and 54 in ⩾45 pack-years group for men; 0 in never smokers, 7.75 in <12 pack-years group, 16.875 in 12-23 pack-years group and 31.75 in ⩾24 pack-years group for women. The potential confounding factors included age (year), height (cm), weight (kg), serum non-HDL cholesterol and HDL cholesterol (mmol/L), heart rate (beats/min), alcohol intake (g/day), diabetes mellitus, and the use of antihypertension medication (yes or no). Because radial augmentation index was calculated by pulse pressures, we did not adjust blood pressure in the multivariable models. All analyses were conducted using the SAS statistical package version 9.4 (SAS Institute Inc., Cary, CA). All P values for statistical tests were two-tailed, and values of $P < 0.05$ were regarded as indicative of statistical significance.

RESULTS

Among the 1,593 male and 2,671 female participants, 436 (27.4%) were current smokers for men and 122 (4.6%) were current smokers for women. Table 1 shows the sex-specific, age-adjusted mean values ± standard errors and proportions of selected atherosclerosis risk factors according to smoking status. Compared with never smokers, current smokers were younger and had higher intake of alcohol for both genders. Current smokers had lower serum HDL cholesterol levels for women. Also, current smokers had higher radial augmentation index, while their central and brachial pulse pressures were similar with those of never smokers. There were no significant differences in mean values of systolic and diastolic blood pressures, heart rate, height, weight, serum non-HDL cholesterol, the proportions of diabetes mellitus, and the use of antihypertension medication according to smoking status in either gender.

Sex-specific, age- and multivariable ORs (95%CIs) of high values of radial augmentation index, central and brachial pulse pressures according to smoking status are shown in Table 2. Compared with never smokers, current male smokers who smoked ⩾30 cigarettes/day had a higher age-adjusted prevalence of high values of radial augmentation index, whereas former and current female smokers had a similar higher prevalence. These associations did not change substantially after further adjustment for known atherosclerosis risk factors: the multivariable OR (95% CI) of high values of radial augmentation index for

current male smokers who smoked ⩾30 cigarettes/day compared with never smokers was 1.9 (1.1-3.4). The multivariable ORs (95% CIs) of high values of radial augmentation index for former and current female smokers compared with never smokers were 1.8 (1.2-2.7) and 2.5 (1.6-3.9), respectively. Moreover, current female smokers who smoked ⩾20 cigarettes/day had a relatively higher prevalence of high values of radial augmentation index and the multivariable OR (95% CI) was 3.6 (1.7-7.6). There was no material difference in the prevalence of high values of central or brachial pulse pressure according to smoking status in either gender.

We also analyzed the impact of smoking pack-years on radial augmentation index, central and brachial pulse pressures, and the age- and multivariable ORs (95%CIs) of high values of those are shown in Table 3. Smoking pack-years was positively associated with the prevalence of high values of radial augmentation index in both genders, and the positive association was more evident for women than for men. Further adjustment for known atherosclerosis risk factors did not alter these associations materially: for men, the multivariable ORs (95% CIs) of high values of radial augmentation index in current smokers with smoking pack-years <30, 30-44 and ⩾45 compared with never smokers were 0.9 (0.5-1.4), 1.8 (1.2-2.8) and 1.6 (1.1-2.4), respectively; for women, the multivariable ORs (95% CIs) of high values of radial augmentation index in current smokers with smoking pack-years <12, 12-23 and ⩾24 compared with never smokers were 1.4 (0.6-3.2), 3.3

(1.7-6.5) and 2.3 (1.2-4.5), respectively. There were no significant differences in the prevalence of high values of central or brachial pulse pressure according to smoking pack-years in either gender.

DISCUSSION

In this population-based study of 4,264 participants aged 40-79 years, compared with never smokers, current male smokers who smoked ⩾30 cigarettes/day had two-fold higher prevalence of high values of radial augmentation index, and current female smokers had approximately two- to four-fold higher prevalence of high values of radial augmentation index. Furthermore, smoking pack-years was positively associated with the prevalence of high values of radial augmentation index for both genders. There were no associations of cigarettes smoking with the prevalence of high values of central pulse pressure or brachial pulse pressure in either gender.

Several previous studies have reported that cigarette smoking was positively associated with values of radial augmentation index. An epidemiological study of 143 Czech men and 148 women aged 25-65 years reported that current smokers had higher age-adjusted mean values of radial augmentation index than never smokers for both genders: 71.1% versus 62.9%; P value<0.01 for men and 84.0% versus 74.4%; P value<0.01 for women, respectively.[14] The Tanushimaru study of 769 Japanese men and 1,157 women aged 40-95 years reported a dose-response relationship between smoking status and age-adjusted mean values of radial augmentation index for men: 80.9% in never smokers, 81.5% in former smokers, 83.9% in current smokers who smoked 1-19 cigarettes/day and 84.6% in current smokers who smoked ⩾20 cigarettes/day, P for trend=0.01, but similar trend was not

observed for women, P for trend=0.127.[15] The Nagahama study of 8,557 Japanese men and women aged 30-75 years reported that cigarette smoking was positively associated with values of radial augmentation index for all subjects using multiple linear regression analysis, but that study did not provide the sex-specific results.[16] Another population-based study of 909 Japanese men whose mean age was 58 years reported that current smokers had a higher prevalence of high values of radial augmentation index, the multivariable OR (95% CI) of high values of radial augmentation index (>79.4%; the mean value) in current smokers compared with never smokers was 1.74 (1.27-2.43), P value < 0.001.[17]

In our study, we found that cigarette smoking was strongly associated with high values of radial augmentation index for women more than for men. Women have generally shorter stature and length of the arterial tree compared with those of men. These anatomical characteristics for women result in earlier return of the reflected wave to the central aorta in systole rather than diastole,[27] leading to increased pulse pressure and higher value of radial augmentation index. With such sex difference in the vascular tree, if a certain threshold of tobacco exposure is needed to affect the radial augmentation index for men, any exposure to tobacco for women seems to have a greater impact on radial augmentation index.

Smoking pack-year is a marker for the amount of smoking exposure over a long period of time. Our findings indicated that smoking pack-years was positively associated with the prevalence of high values of radial augmentation index for both genders. The atherosclerosis

risk in young adults (ARYA) study of 330 men aged 27-30 years in Netherlands reported that smoking pack-years was positively associated with high values of aortic augmentation index, a ratio of the augmentation of central systolic pressure above the first systolic pressure to the central pulse pressure, using the SphygmoCor system; the aortic augmentation index was associated with a 0.31% increase for each additional smoking pack-year (P value < 0.05).[18] Regardless of different types of augmentation index measure, radial augmentation index was correlated well with aortic augmentation index (r=0.91, P value <0.001).[28] We conducted a similar linear regression analysis, and found that radial augmentation index was associated with a 0.04% increase for men (P value = 0.03) and a 0.12% increase for women (P value < 0.001), for each additional smoking pack-year.

Some epidemiological studies have reported that the central and brachial pulse pressures were associated with risk of cardiovascular events.[29,30] Cigarette smoking could increase the blood pressure acutely, but a few epidemiological studies suggested a chronic effect of cigarette smoking on the blood pressure.[31] A Mendelian randomization meta-analysis of 23 population-based studies has also reported no association between smoking and the blood pressure.[19] In a Japanese population-based study of 2,634 men and women aged ⩾68 years cigarette smoking was not associated with brachial pulse pressure.[20] Besides, a European epidemiological study of 299 men and women aged 25-84 years reported that current smokers had higher central pulse pressure than non-smokers (29.4mmHg versus 30.8mmHg,

p=0.043), but no difference in brachial pulse pressure was reported.[21] In our study, we analyzed the associations of cigarette smoking with higher values of central and brachial pulse pressures for both genders, and found no statistical difference of those pulse pressures according to smoking status.

Our study has several strengths: first, we had a large sample size, detailed smoking status and internal quality control for data collection,[22] to examine association of cigarette smoking with high values of radial augmentation index. Second, we used the data form a large community-based study, which is likely to make our findings extrapolated to general population. Third, not only radial augmentation index but also central and brachial pulse pressures were used to examine the impact of cigarette smoking on arterial stiffness. As for limitations of our study, arterial stiffness was centered in only radial augmentation index. Unfortunately, we did not measure other parameters of arterial stiffness, such as pulse wave velocity (PWV) and ankle-brachial pressure index (ABI) to assess the impact of cigarette smoking on changes of arterial stiffness, although these parameters have been associated with cigarette smoking.[32, 33] Last, we could not draw a causal association because of the cross-sectional design of the current study.

In conclusion, cigarette smoking and cumulative smoking exposure were positively associated with increased arterial stiffness evaluated by radial augmentation index for men who smoked heavily, and women.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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APPENDIX

CIRCS collaborators

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Table 1 Sex-specific, age-adjusted mean values ± standard errors and proportions of atherosclerosis risk factors according to smoking status.

	Men						Women				
	Never smokers	Former smokers	Current smokers	Cigarettes smoked (no./day)			Never smokers	Former smokers	Current smokers	Cigarettes smoked (no./day)	
				1-19	20-29	≥30				1-19	≥20
No. of subjects	312	845	436	160	178	98	2,372	177	122	90	32
Age, years	63.9 ± 0.5	64.5 ± 0.3	60.6 ± 0.4‡	62.5 ± 0.7	60.5 ± 0.7‡	57.7 ± 0.9‡	62.1 ± 0.2	60.0 ± 0.7‡	54.4 ± 0.8‡	54.0 ± 1.0‡	55.4 ± 1.6‡
Augmentation index, %	77.9 ± 0.6	78.1 ± 0.4	80.4 ± 0.5†	79.9 ± 0.8	80.5 ± 0.8*	81.1 ± 1.1*	86.1 ± 0.2	87.9 ± 0.7*	90.8 ± 0.9‡	90.9 ± 1.0‡	90.5 ± 1.7*
Central pulse pressure, mmHg	43.4 ± 0.8	43.7 ± 0.5	45.1 ± 0.6	44.2 ± 1.0	45.4 ± 1.0	45.9 ± 1.3	45.1 ± 0.3	46.9 ± 1.0	47.4 ± 1.2	47.2 ± 1.3	47.7 ± 2.2
Brachial pulse pressure, mmHg	52.9 ± 0.7	54.0 ± 0.4	54.6 ± 0.6	53.8 ± 1.0	54.8 ± 1.0	55.7 ± 1.3	52.2 ± 0.3	53.0 ± 1.0	53.1 ± 1.2	52.6 ± 1.3	54.6 ± 2.2
Systolic brachial blood pressure, mmHg	. 137.1 ± 1.0	. 138.5 ± 0.6	. 137.1 ± 0.9	. 135.5 ± 1.4	. 137.7 ± 1.3	. 138.7 ± 1.8	. 132.7 ± 0.4	. 134.0 ± 1.4	. 135.1 ± 1.6	. 133.8 ± 1.9	. 138.7 ± 3.2
Diastolic brachial blood pressure, mmHg	84.2 ± 0.6	84.5 ± 0.4	82.5 ± 0.5	81.7 ± 0.9	82.9 ± 0.8	83.0 ± 1.1	80.5 ± 0.2	80.9 ± 0.8	82.0 ± 1.0	81.2 ± 1.1	84.1 ± 1.9
Heart rate, beats/min	66.7 ± 0.6	68.2 ± 0.4	68.1 ± 0.5	68.7 ± 0.9	67.1 ± 0.9	68.8 ±1.2	70.2 ± 0.2	68.2 ± 0.8*	70.9 ± 1.0	70.2 ± 1.1	72.8 ± 1.9
Height, cm	163.8 ± 0.3	164.8 ± 0.2*	164.4 ± 0.3	164.4 ± 0.5	164.2 ± 0.4	164.6 ± 0.6	152.3 ± 0.1	153.5 ± 0.5	153.2 ± 0.6	153.1 ± 0.7	153.3 ± 1.2
Weight, kg	64.5 ± 0.5	65.2 ± 0.3	63.5 ± 0.4	63.5 ± 0.7	63.1 ± 0.7	64.2 ± 0.9	53.6 ± 0.2	54.5 ± 0.6	53.6 ± 0.8	52.7 ± 0.9	56.2 ± 1.5
Serum non-HDL cholesterol, mmol/L	3.72 ± 0.05	3.77 ± 0.03	3.69 ± 0.04	3.66 ± 0.07	3.67 ± 0.07	3.78 ± 0.09	3.92 ± 0.02	3.92 ± 0.07	4.09 ± 0.08	3.97 ± 0.10	4.41 ± 0.16†
Serum HDL cholesterol, mmol/L	1.57 ± 0.02	1.55 ± 0.01	1.46 ± 0.02	1.49 ± 0.03	1.46 ± 0.03	1.43 ± 0.04	1.70 ± 0.01	1.72 ± 0.04	1.56 ± 0.04†	1.63 ± 0.05	1.37 ± 0.08‡
Alcohol intake, g/day	15.3 ± 1.3	22.8 ± 0.8‡	26.9 ± 1.1‡	24.6 ± 1.8‡	28.4 ± 1.7‡	28.0 ± 2.3‡	1.59 ± 0.1	7.50 ± 0.5‡	8.20 ± 0.6‡	8.22 ± 0.7‡	8.15 ± 1.2‡
Diabetes mellitus, %	11.3	11.8	13.4	14.0	12.3	14.3	5.5	5.3	7.5	6.3	10.9
Antihypertensive medication use, %	28.2	32.2	28.1	28.4	27.4	28.9	24.4	27.9	22.9	22.3	24.7

*P<0.05, †P<0.01, ‡P<0.001 compared with never smokers (Dunnett's test).

Non-HDL cholesterol was calculated as serum total cholesterol minus HDL-cholesterol.

Table 2 Sex-specific, age- and multivariable ORs (95%CIs) of high values of radial augmentation index (rAI), central and brachial pulse pressure (cPP and bPP) according to smoking status.

	Men						Women				
	Never smokers	Former smokers	Current smokers	Cigarettes smoked (no./day)			Never smokers	Former smokers	Current smokers	Cigarettes smoked (no./day)	
				1-19	20-29	≥30				1-19	≥20
No. of subjects	312	845	436	160	178	98	2,372	177	122	90	32
Radial augmentation index (rAI)											
High rAI, no.	60	158	97	36	36	25	423	41	35	23	12
OR (95%CI)[a] of high rAI	1.0	0.9 (0.7-1.3)	1.4 (0.9-2.0)	1.3 (0.8-2.1)	1.2 (0.8-2.0)	1.9 (1.1-3.2)*	1.0	1.7 (1.2-2.5)†	2.5 (1.6-3.8)‡	2.2 (1.3-3.6)†	3.6 (1.7-7.6)‡
OR (95%CI)[b] of high rAI	1.0	1.0 (0.7-1.5)	1.4 (0.9-2.1)	1.3 (0.8-2.2)	1.2 (0.8-2.0)	1.9 (1.1-3.4)*	1.0	1.8 (1.2-2.7)†	2.5 (1.6-3.9)‡	2.2 (1.3-3.6)†	3.6 (1.7-7.6)‡
Central pulse pressure (cPP)											
High cPP, no.	63	176	83	31	37	15	498	32	16	12	4
OR (95%CI)[a] of high cPP	1.0	1.0 (0.7-1.4)	1.2 (0.8-1.8)	1.0 (0.6-1.7)	1.5 (0.9-2.4)	1.2 (0.6-2.2)	1.0	1.3 (0.9-2.0)	1.1 (0.6-1.9)	1.2 (0.6-2.2)	0.9 (0.3-2.8)
OR (95%CI)[b] of high cPP	1.0	1.1 (0.8-1.6)	1.3 (0.9-2.0)	1.2 (0.7-2.0)	1.6 (0.9-2.6)	1.3 (0.6-2.5)	1.0	1.2 (0.8-1.9)	1.1 (0.6-2.0)	1.2 (0.6-2.3)	1.0 (0.3-3.0)
Brachial pulse pressure (bPP)											
High bPP, no.	62	177	85	34	36	15	474	25	14	9	5
OR (95%CI)[a] of high bPP	1.0	1.0 (0.7-1.5)	1.3 (0.9-1.9)	1.2 (0.7-1.9)	1.5 (0.9-2.4)	1.2 (0.6-2.3)	1.0	1.0 (0.6-1.6)	1.0 (0.6-1.8)	0.9 (0.4-1.8)	1.4 (0.5-3.7)
OR (95%CI)[b] of high bPP	1.0	1.0 (0.7-1.5)	1.3 (0.9-1.9)	1.2 (0.7-2.0)	1.4 (0.9-2.3)	1.2 (0.6-2.3)	1.0	1.0 (0.6-1.6)	1.0 (0.6-1.9)	0.9 (0.4-1.9)	1.3 (0.5-3.5)

*P<0.05, †P<0.01, ‡P<0.001 compared with never smokers.

Abbreviations: OR, odds ratio; CI, confidence interval.

[a] adjusted for age.

[b] adjusted for age, height, weight, heart rate, serum non-HDL cholesterol and HDL cholesterol, alcohol intake (g/day), antihypertensive medication use and diabetes mellitus.

Table 3 Sex-specific, age- and multivariable ORs (95%CIs) of high values of radial augmentation index (rAI), central and brachial pulse pressure (cPP and bPP) according to smoking pack-years group.

	Men					Women				
	Non-current smokers	Pack-years of current smokers			P for trend	Non-current smokers	Pack-years of current smokers			P for trend
		<30	30-44	≥45			<12	12-23	≥24	
No. of subjects	1,157	145	139	152		2,549	38	42	42	
Radial augmentation index (rAI)										
High rAI, n	218	22	35	40		464	7	15	13	
OR (95%CI)[a] of high rAI	1.0	0.9 (0.6-1.5)	1.8 (1.2-2.8)†	1.6 (1.1-2.4)*	<0.01	1.0	1.4 (0.6-3.2)	3.5 (1.8-6.8)‡	2.4 (1.2-4.7)*	<0.001
OR (95%CI)[b] of high rAI	1.0	0.9 (0.5-1.4)	1.8 (1.2-2.8)†	1.6 (1.1-2.4)*	<0.01	1.0	1.4 (0.6-3.2)	3.3 (1.7-6.5)‡	2.3 (1.2-4.5)*	<0.001
Central pulse pressure (cPP)										
High cPP, n	239	22	29	32		530	4	7	5	
OR (95%CI)[a] of high cPP	1.0	0.9 (0.5-1.5)	1.7 (1.1-2.7)*	1.1 (0.7-1.8)	0.17	1.0	1.0 (0.3-2.9)	1.6 (0.7-3.9)	0.8 (0.3-2.0)	0.95
OR (95%CI)[b] of high cPP	1.0	1.0 (0.6-1.7)	1.7 (1.0-2.8)*	1.1 (0.7-1.8)	0.21	1.0	0.9 (0.3-2.8)	1.8 (0.7-4.3)	0.8 (0.3-2.1)	0.99
Brachial pulse pressure (bPP)										
High bPP, n	239	25	27	33		499	2	5	7	
OR (95%CI)[a] of high bPP	1.0	1.1 (0.7-1.7)	1.6 (1.0-2.5)	1.2 (0.8-1.8)	0.13	1.0	0.5 (0.1-2.2)	1.2 (0.4-3.2)	1.3 (0.5-3.0)	0.64
OR (95%CI)[b] of high bPP	1.0	1.1 (0.7-1.8)	1.5 (0.9-2.5)	1.2 (0.7-1.8)	0.19	1.0	0.5 (0.1-2.2)	1.2 (0.4-3.2)	1.3 (0.5-3.1)	0.63

*P<0.05, †P<0.01, ‡P<0.001 compared with non-current smokers.

Abbreviations: OR, odds ratio; CI, confidence interval.

The smoking pack-years was defined as the mean packs of cigarettes smoked per day multiplied by the years of smoking.

[a] adjusted for age.

[b] adjusted for age, height, weight, heart rate, serum non-HDL cholesterol and HDL cholesterol, alcohol intake (g/day), antihypertensive medication use and diabetes mellitus.