Exposure to secondhand smoke and risk of peripheral arterial disease in southern Chinese non-smokers: The Guangzhou Biobank Cohort Study-Cardiovascular Disease Subcohort

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Abstract

Objectives

We studied the association between secondhand smoke (SHS) exposure and peripheral arterial disease (PAD) in Chinese non-smokers.

Methods

We conducted a cross-sectional study using baseline data from the Guangzhou Biobank Cohort Study: Cardiovascular Disease Sub-cohort Study (GBCS-CVD). Guangzhou residents aged ≥50 years were recruited between 2003 and 2008. Baseline data included measurement of ankle brachial pressure index (ABPI) and self-reported smoking status and SHS exposure. Univariate and multivariate logistic regression analyses were used to analyse the association between SHS and PAD (defined as ABPI<0.9).

Results

Of the 1,507 non-smokers, 24 (1.6%) had PAD. Of these, 12 were men and 12 women. Exposure to SHS at home of ≥25 hours per week, was reported by 16.7% of PAD cases compared with 3.8% of those without PAD (χ^2 test, p=0.003). After adjustment for potential confounders, exposure to ≥25 hours per week at home was still associated with PAD (adjusted OR 7.86, 95% CI 2.00-30.95, p=0.003), with suggestion of a dose-response relationship.

Conclusion

Our results extend the US Surgeon General's 2006 report that SHS exposure is an independent risk factor for PAD. National smoke-free legislation is needed to protect all people from exposure.

Keywords

Peripheral arterial disease; Secondhand smoke; Tobacco smoke pollution; China

Introduction

China is the world's largest producer and consumer of tobacco. Forty-two percent of the world's cigarettes are produced by China and 30% of the world's cigarettes are consumed by 350 million Chinese smokers.[1] Smoking prevalence is decreasing in developed countries, such as Western Europe and North America. However, global prevalence is still increasing due to increasing prevalence in large, developing countries such as China.[2, 3] In the absence of new policies and changes in cessation rates, the global number of smokers is predicted to increase to 872 million by 2030.[4]

The US Surgeon's General's (USSG) report from 2010 has reported that the evidence supports that active smoking causes atherosclerotic diseases, including peripheral arterial disease (PAD).[5] Side-stream smoke, from burning cigarette tips, is particularly injurious to the vascular system. It contains higher concentrations of small, respirable particles (<2.5μm) and toxic gases than mainstream smoke inhaled by active smokers.[6-8] Thirty minutes of exposure can significantly reduce coronary flow velocity reserve in healthy non-smokers.[9]

The USSG 2006 report describing the health implications of secondhand smoke (SHS) also states that there is sufficient evidence to show that SHS exposure causes coronary heart disease (CHD).[10] However, although there is evidence to support increased risk of PAD in those exposed to SHS, [11-13] it remains inadequate to show SHS causes PAD.

Indeed, to date there have only been four published studies that have examined the association between SHS exposure and PAD [11-14] and only one of these was conducted in Asia.[11] Using UK data, we have previously shown an overall association between SHS

exposure and PAD,[12] and a dose relationship between cotinine concentration and risk of intermittent claudication in non-smokers with 9.2% of cases of intermittent claudication attributable to cotinine concentrations ≥0.7ng/mL.[13] The current study aimed to further assess the association between SHS and PAD in older Chinese.

Methods

Data source

The Guangzhou Biobank Cohort Study is an ongoing, general population cohort of older adults living in Guangzhou, south China. The methods have been reported in detail previously.[15] A community social and welfare association, The Guangzhou Health and Happiness Association for the Respectable Elders (GHHARE), was chosen as the sampling frame. The association, with around 100,000 members, has branches throughout Guangzhou and membership is open to individuals aged ≥50 years for a nominal fee. From 2003 to 2008, 30,519 eligible participants were randomly selected from the association's membership list and constituted the Guangzhou Biobank Cohort.[16] The Guangzhou Biobank Cohort Study was approved by the Guangzhou Medical Ethics Committee of the Chinese Medical Association. Written informed consent was collected from all participants.

At baseline, all participants completed a questionnaire to provide information on demographics (including age, sex, occupation and education), lifestyle (including smoking status, exposure to SHS, alcohol intake and physical activity) and personal and family medical history. Trained research staff measured height and weight and obtained blood samples for assays.[16]

A sub-group of 1,996 participants were randomly selected from subjects in the third phase of recruitment in the main cohort.[16] This subgroup took part in the Guangzhou Biobank Cohort Study-Cardiovascular Disease Sub-cohort Study (GBCS-CVD) which collected more detailed information relevant to cardiovascular disease. Additional measurements included brachial systolic and diastolic blood pressure, and ankle systolic blood pressure in the dorsalis pedis

and posterior tibial arteries in both legs. The present study used the baseline data from GBCS-CVD.

Inclusion criteria and definitions

Our study was restricted to participants who reported themselves as non-smokers; defined as either never or ex-smokers. The ankle brachial pressure index (ABPI) was calculated for each leg as the ratio of the highest measurement of ankle systolic blood pressure (either dorsalis pedis or posterior tibial artery) to the brachial systolic blood pressure. PAD was defined as an ABPI <0.9 in at least one leg.[17] The level of SHS exposure was self-reported. Participants reported their exposure as hours exposed per week at home and at work and the number of cohabitants who smoked. We classified their overall duration of exposure at home or at work as: none, <25 or ≥25 hours per week.[18] Occupation was categorized into official/manager, technician/seller/police, farmer/worker, other and non/housewife. Alcohol consumption was self-reported and classified as never/< once per month and ≥ once per month. Physically active was defined as self-report of moderate or vigorous activity on at least four days during the previous week. Body mass index (BMI) was categorized into normal weight (<25 kg/m^2), overweight (25-30 kg/m^2) and obese (≥30 kg/m^2). Dyslipidemia was defined as a total cholesterol concentration ≥5.2mmol/L and/or triglyceride concentration ≥1.7 mmol/L and/or high-density lipoprotein concentration <1.0 mmol/L and/or low-density lipoprotein concentration ≥3.3 mmol/L. Hypertension was defined as a blood pressure measurement of > 140/90 mmHg or self-reported history of medications. Personal history of diabetes and family history of coronary heart disease (CHD) and stroke were based on self-report of a physician diagnosis.

Statistical analyses

Categorical and ordinal data were summarized using frequencies and percentages. Chi-square tests for trend were applied to ordinal variables and Chi-square tests to categorical variables respectively. Univariate and multivariate logistic regression models were used to examine the association between levels of SHS exposure and PAD using no exposure as the referent category. Several hierarchical models with different level of statistical adjustment were developed: unadjusted, partially adjusted (age, sex and occupation) and fully adjusted (partially adjusted model plus alcohol intake, physical activity, BMI category, dyslipidemia, diabetes, hypertension and family history of CHD or stroke). All statistical analyses were undertaken using Stata v12.0 (Stata Corporation, College Station, Texas, USA).

Results

Of the 1,996 individuals who participated in the cardiovascular disease sub-cohort study (GBCS-CVD), 1,921 (96.2%) had a valid ABPI measurement. Among these, 1,507 (78.4%) were non-smokers and included in this study. Of these, 1,121 (74.4%) reported themselves as never smokers and 386 (25.6%) as ex-smokers. Of the latter, 369 (95.6%) had quit smoking for more than one year. Twenty four (1.6%) of the non-smokers had PAD. Participants with PAD were significantly more likely to be overweight or obese (Table 1). There were no significant differences between the participants with and without PAD in terms of age, sex, occupation, alcohol intake, physical activity, diabetes, dyslipidemia, hypertension and family history of CHD or stroke (Table 1).

The tests for trend across increasing exposure, measured by number of smoking cohabitants, hours of SHS exposure at home and at work were all non-significant (Table 2). However, a direct comparison between the high exposure and no exposure groups achieved significance using all three measures: ≥2 cohabitants (χ^2 test, p=0.017); ≥25 hours per week at home (χ^2 test, p=0.003); ≥25 hours of exposure per week at work (χ^2 test, p=0.039). Similarly, on univariate logistic regression analyses, participants with PAD were significantly more likely to report cohabitation with two or more smokers and SHS exposure of at least 25 hours at home and work (Table 3). After adjustment for age, sex and occupation, the association with two or more smoking cohabitants remained statistically significant (OR 4.72, 95% CI 1.40-15.88, p=0.012), as did the association with exposure in the home of at least 25 hours per week (OR 7.96, 95% CI 2.09-30.34, p=0.002) (Table 3). Further adjustment for other potential confounders barely changed the odds ratios and they remained statistically significant (Table 3). In relation to exposure at home, there was also evidence of a possible

dose response relationship (p=0.013) (Table 3). There were no significant interactions with any of the covariates included in the models; for example p=0.824 for age and p=0.264 for sex.

Discussion

We found a statistically significant association between SHS exposure at home and PAD, independent of potential confounding factors, with evidence of a dose response relationship.

The USSG states that active smoking is a causal determinant of PAD.[5] Likewise stated that SHS causes CHD.[10] However, currently, only four published studies have examined the association between SHS exposure and PAD and thus evidence is lacking to infer causality.[11-14] The first study to show this association was a cross-sectional study conducted in Beijing, North China among 1,209 women aged ≥60 years who had never smoked. Overall, 22% of the women had PAD and 40% reported exposure to SHS. Women with PAD (22.4%) were more likely to report SHS exposure (adjusted OR 1.67, 95% CI 1.23-2.16, p<0.001). They also demonstrated evidence of a dose response relationship with the number of cigarettes exposed per day for intermittent claudication (IC), ABPI<0.9 or either (p values for trend=0.009, 0.002 and 0.002 respectively) and with daily duration of exposure (p values for trend=0.003, 0.048 and 0.001 respectively).[10] The second cross-sectional study on 5,653 non-smokers in the USA found no significant association between overall SHS exposure (defined as cotinine 0.05-10 ng/mL) and PAD (defined as ABPI<0.9). However, a significantly increased risk of PAD was found in the highest decile of cotinine levels (>155 ng/mL), a more reliable indicator of SHS exposure.[11] Our recent cross-sectional study examined 5,686 never smokers in Scotland, of whom 31.1% reported ever exposed to SHS. Individuals with ABPI<0.9 were significantly more likely to report high SHS exposure at work and a high overall duration of exposure (adjusted ORs: 3.82, 95%CI 1.11-13.12, p=0.034; 5.56, 95%CI 1.82-17.06, p=0.003 respectively).[12] In another cross-sectional study using the Scottish Health Survey, a pan-Scotland study with salivary cotinine measurements, we studied 4,231

non-smokers aged >45 years and showed similar findings. Individuals with a cotinine ≥2.7 ng/mL were significantly more likely to have IC (adjusted OR 1.76, 95%CI 1.04-3.00, p=0.036) compared with those with cotinine <0.7 ng/mL. Overall, 9.2% of IC cases in this study were attributable to raised cotinine concentrations. The dose-response relationship was stronger among those aged <60 years (adjusted p values for trend <0.001).[13] In this present study, we also observed a dose response relationship across different exposure levels and the association was statistically significant for ≥25 hours of SHS exposure per week.

The present study used data from the GBCS-CVD. In order to maximize statistical power, we analyzed never and ex-smokers together as non-smokers. The majority (95.6%) of ex-smokers had quit smoking for at least 1 year before the recruitment. This is the first study including men and women so far to examine SHS and PAD in Chinese and the first to examine SHS and PAD in southern Chinese. In our study, exposure to SHS was based on self-report, as it was in two previously published papers using this cohort.[19,20] We were not able to corroborate self-report using objective measurements such as cotinine concentration. Also in common with the previous studies, we had to analyze exposure to home and exposure at work separately. We were unable to analyze overall exposure for two reasons. Firstly, participants were not asked to report exposure in other locations. Secondly, 8.2% of participants had missing data on exposure at home and 8.4% on exposure at work, but 13.9% had missing data on one or other reducing statistical power in an already small study.

We were able to define PAD on the basis of ABPI measurement rather than self-reported symptoms.[13] Clairotte et al. have suggested that the sensitivity of PAD could be increased by changing the definition to ABPI<1.0. [21] However, the subsequent report by the American Heart Association concluded that ABI≤0.9 remains the “most common and consensual

threshold." [22] Similarly, in our recent review of published studies on active smoking and PAD [23], ABPI<0.9 was the most commonly used definition. Participants were randomly selected from an association with branches throughout Guangzhou and should be reasonably representative of the relatively healthy general population in Guangzhou. We were able to adjust for many potential confounders including age, sex, occupation, diabetes, hypertension and dyslipidemia. The results reached statistically significance. However, because of small numbers of PAD cases, some confidence intervals were wide and, therefore, the precision of our estimates of effect size was low. Because of the small size of the study, the results should be interpreted accordingly and should be corroborated in future larger studies or meta-analyses. Like all previous studies, our study was cross-sectional. Therefore, a temporal relationship could not be established but reverse causation is unlikely.

The World Health Organization's Framework Convention on Tobacco Control (FCTC) has emphasized the need for effective legislation to protect against exposure to SHS in indoor public places.[24] In China, public awareness of the health risks associated with SHS exposure is low.[25-27] A Chinese nationally representative household survey reported that, among non-smokers aged ≥15 years, 556 million (72.4%) were exposed to SHS, and 50% were exposed daily. Exposure in public places, households and indoor workplaces was 72.7%, 67.3% and 63.3% respectively.[1] The FCTC came into force in China in 2006.[28] Initially, smoke-free legislation, prohibiting smoking in public places, was adopted by only seven cities.[29] Subsequently, Beijing, Shanghai and Guangzhou have also enacted local regulations prohibiting smoking in public places.[30] The USSG states that evidence is sufficient to state that smoking causes cardiovascular diseases[5] and that SHS exposure causes CHD.[10] Our study adds to the limited published evidence supporting an association between SHS exposure and PAD. National smoke-free legislation is needed to protect all people from SHS

exposure.

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Declaration of conflicting interest

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Table 1. Characteristics of non-smokers by presence or absence of peripheral arterial disease

	PAD N=24 N (%)	No PAD N=1,483 N (%)	P value*
Age (years)			
<60	14 (58.3)	931 (62.8)	0.665
≥60	10 (41.7)	552 (37.2)	
Missing	0	0	
Sex			
Male	12 (50.0)	567 (38.2)	0.240
Female	12 (50.0)	916 (61.8)	
Missing	0	0	
Occupation			
Official/manager	10 (41.7)	549 (37.0)	0.730
Technician/seller/police	5 (20.8)	204 (13.8)	
Farmer/worker	1 (4.2)	157 (10.6)	
Other	5 (20.8)	272 (18.3)	
None/housewife	3 (12.5)	288 (19.4)	
Missing	0	13	
Alcohol intake in last year			
Never - <1/month	15 (62.5)	935 (64.3)	0.731
≥1/month	5 (20.8)	228 (15.4)	
Missing	4	302	
Physical activity in last week			
≥4 days	11 (45.8)	598 (40.3)	0.773
≤3 days	13 (54.2)	869 (58.6)	
Missing	0	16	
Body mass index			
Normal	11 (45.8)	1,007 (67.9)	0.009
Overweight	11 (45.8)	439 (29.6)	
Obese	2 (8.3)	35 (2.4)	
Missing	0	2	
Diabetes			
No	23 (95.8)	1,434 (96.7)	0.920
Yes	1 (4.2)	45 (3.0)	
Missing	0	4 (0.3)	
Total cholesterol (mmol/L)			
≤5.2	6 (25.0)	397 (26.8)	0.965
>5.2	18 (75.0)	1,084 (73.1)	
Missing	0	2	
Triglyceride (mmol/L)			
<1.7	13 (54.2)	936 (63.1)	0.658

≥1.7	11 (45.8)	546 (36.8)	
Missing	0	1	
HDL cholesterol (mmol/L)			
≥1.0	23 (95.8)	1,438 (97.0)	0.936
<1.0	1 (4.2)	44 (3.0)	
Missing	0	1	
LDL cholesterol (mmol/L)			
<3.3	10 (41.7)	715 (48.2)	0.808
≥3.3	14 (58.3)	767 (51.7)	
Missing	0	1	
Hypertension			
No	17 (70.7%)	969 (65.3%)	0.835
Yes	7 (29.2%)	510 (34.4%)	
Missing	0	4	
Family history of CHD or stroke			
No	19 (79.2)	1,263 (85.2)	0.413
Yes	5 (20.8)	220 (14.8)	
Missing	0	0	

PAD peripheral arterial disease; N number; HDL high-density lipoprotein; LDL low-density lipoprotein; CHD coronary heart disease

* χ^2 tests for age, sex, occupation, alcohol intake in last year, physical activity in last week, diabetes, total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, hypertension, family history of CHD or stroke; χ^2 tests for trend for body mass index

Table 2. Self-reported secondhand smoke exposure among non-smokers by presence or absence of peripheral arterial disease

	PAD N=24 N (%)	No PAD N=1,483 N (%)	P value *
Number of cohabitants who smoke			
None	11 (45.8)	758 (51.1)	0.162
1	9 (37.5)	651 (43.9)	
≥2	4 (16.7)	73 (4.9)	
Missing	0	1	
Hours of exposure / week at home			
None	11 (45.8)	756 (51.0)	0.115
<25	7 (29.2)	547 (36.9)	
≥25	4 (16.7)	56 (3.8)	
Missing	2	124	
Hours of exposure / week at work			
None	10 (41.7)	585 (39.5)	0.222
<25	7 (29.2)	652 (44.0)	
≥25	6 (25.0)	124 (8.4)	
Missing	1	122	

*χ^2 tests for trend

Table 3. Logistic regression analyses of the association between self-reported secondhand smoke exposure and peripheral arterial disease among non-smokers

	Univariate			Partially adjusted*			Fully adjusted**		
	OR (95% CI)	P value	P value for trend	OR (95% CI)	P value	P value for trend	OR (95% CI)	P value	P value for trend
Number of cohabitants who smoke									
None	1.00		0.164	1.00		0.040	1.00		0.054
1	0.95 (0.39-2.31)	0.915		1.31 (0.48-3.53)	0.598		1.23 (0.45-3.35)	0.689	
≥2	3.78 (1.17-12.16)	0.026		4.72 (1.40-15.88)	0.012		4.52 (1.32-15.52)	0.017	
Hours of exposure / week at home									
None	1.00		0.118	1.00		0.009	1.00		0.013
<25	0.88 (0.34-2.28)	0.792		1.30 (0.45-3.74)	0.630		1.23 (0.42-3.59)	0.704	
≥25	4.91 (1.51-15.91)	0.008		7.96 (2.09-30.34)	0.002		7.86 (2.00-30.95)	0.003	
Hours of exposure / week at work									
None	1.00		0.224	1.00		0.549	1.00		0.623
<25	0.63 (0.24-1.66)	0.348		0.47 (0.17-1.31)	0.150		0.48 (0.17-1.35)	0.164	
≥25	2.83 (1.01-7.93)	0.048		2.00 (0.66-6.05)	0.217		1.93 (0.61-6.07)	0.261	

OR odds ratio; CI confidence interval
*adjusted for age, sex and occupation
**adjusted for age, sex, occupation, alcohol intake, physical activity, BMI category, total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, hypertension, diabetes, family history of CHD or stroke