Original article:

Effect of Second hand Smoke on Arterial Stiffness among Healthy Women

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Abstract

Introduction*:* Arterial stiffness is recognised as a significant cardiovascular risk factor and an independent predictor of all causes of cardiovascular death. Women are the largest population exposed to cigarette smoke either at work or from their partner. The objectives of this study are to compare the arterial stiffness (augmentation index and pulse wave velocity) between second hand smoke (SHS) and non second hand smoke (non-SHS). ***Designs and method***: Comparative cross-sectional study was conducted among 118 healthy female subjects (64 SHS and 54 non-SHS). The women were in the SHS group if their spouse is a smoker and they had an exposure to cigarette smoke for at least three years, minimum of15 minutes two days a week. Pulse wave analysis and pulse wave velocity was used to study the arterial stiffness. Pulse wave analysis reported as percentage of augmentation index. Pulse wave velocity equal to carotid femoral distance (meter) divided by time (second) ***Results****:* The mean augmentation index (AIx) for SHS groups was 17.9 (SD7.06) and for non SHS groups was 20.7(SD6.11). The mean of Pulse wave velocity was 8.94 (SD1.36) in SHS groups and 9.02 (SD8.68) in non SHS groups. ANOVA and ANCOVA shown significance difference in crude mean (p = 0.047) and estimated marginal mean (p = 0.028) of augmentation index between SHS and non - SHS after controlling for age and BMI. However, there was no significant difference in crude mean (p = 0.795) and estimated marginal mean (p = 0.716) pulse wave velocity between SHS and non - SHS after controlling for age and BMI. ***Conclusion****:* An increase in augmentation index amongst non SHS in this study most probably due to exposure to environmental tobacco at work compared to exposure to spouse's smoke

Keywords: Second hand smoke; arterial stiffness; augmentation index

Bangladesh Journal of Medical Science Vol. 18 No. 02 April'19. Page : 340-346
DOI: https://doi.org/10.3329/bjms.v18i2.40706

Introduction

Second hand smoke(SHS) consists of approximately 85% side-stream smoke (from the burning ends of cigarettes or smoke that escapes from the tip of a cigarette, cigar or pipe) and approximately 15%mainstream smoke (smoke that is inhaled through a tobacco product and exhaled by a tobacco smoker).[1]Many toxic constituents, such as carbon monoxide and benzopyrene, are found in higher concentrations in side-stream smoke than in inhaled

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smoke.[2] Today, despite policiesnot to allow people to smoke in public, cigarette smoke still remains a major problem in almost all countries. This will expose many people as passive smokers or, as we refer to this exposure, ETS.

Second hand smoke exposure to nicotine is believed to be responsible for the cardiovascular impact in this population. The negative effect of second hand smoke on pathophysiological mediators[3]of coronary artery disease are nearly as similar in active smokers, including impaired platelet function,[4] damage to the vascular endothelium,[5] a rise in inflammatory molecules and dysfunctional lipid metabolism.[6]Many studies have shown evidence that smoking alters the physiology,[7]biochemistry[8] and immunology[9]ofnon-smokers.

In recent years, many studies have found that passive and active smokers had acute stiffening of the arterial wall that resulted in significantly increased arterial wave reflection.[10] Arterial stiffness is recognised as an important cardiovascular risk factor and an independent predictor of all causes of cardiovascular death.[11,12] The negative effect of tobacco on the endothelial function will involve either acute or chronic exposure.[13] The long-term effect of cigarette smoking on the endothelium is associated with endothelium-dependent coronary vasodilation regardless of the presence or absence of atherosclerotic wall thickening.[14-16] The effect will occur even in healthy young adults who are smokers.[15,16] As a result of endothelial dysfunction, thrombosis and vasospasm will cause atherosclerotic plaque to rupture and will cause decreased blood flow.[17] Therefore, an increase in arterial stiffness will increase the risk of hypertension and other cardiovascular disease. In acute exposure to ETS, the effect of endothelial dysfunction is usually transient,[18] yet, chronic exposure causes irreversible endothelial damage.[19] Two main compounds of cigarette smoke, nicotine and carbon monoxide, play an important role in causing endothelial dysfunction by impairing the endothelium vasodilator response.[20]

An increase in arterial stiffness is associated with factors such as age, smoking, hypertension, diabetes, hypercholesterolemia and atherosclerosis.[21] When the vessel stiffen, the pulse wave velocity(PWV) and the amplitude of the reflected wave arrive earlier and augment the central systolic pressure. The increase in the PWV is due to the increase in aortic stiffness, whereas the augmentation index may be due to the impact of the increase in the PWV and the vascular smooth muscle tone of the peripheral muscular arteries.[18] The stiffer the artery, the faster a pressure wave travels through it and the extent to which the arterial wave is reflected from the periphery.[12] Therefore, early wave reflection elevates systolic and pulse pressure and impedes coronary perfusion.[18,21]

The arterial stiffness can be assessed non-invasively by measuring the augmentation index (AIx) and the PWV.[12] The augmentation index represents the reflected wave of the aorta expressed as a percentage of the pulse pressure. The higher value of the AIx indicates an earlier return of the reflected wave to the aorta and may be due to either decreased aortic compliance or increased peripheral resistance. The PWV is the most clinically relevant measurement because the aorta and its first branches are responsible for most of the pathophysiological effects of arterial stiffness.[22] In measuring the PWV, the quantitative information on large arteries can be obtained.

This study set out to describe the arterial stiffness (augmentation index and PWV) in SHS and non-SHS and to compare the arterial stiffness between these two groups.

Materials and methods

We conducted a comparative cross sectional study at the outpatient department of the Hospital Universiti Sains Malaysia from May 2011 to May 2012. The sample size calculated based on a sample size calculation using Power and Sample Size Calculation software for comparing two means. After considering 10% of non-response rate total for both groups were 128 participants. Participants were recruited using convenience sampling following screening by inclusion and exclusion criteria. The women ages 25-45 were included in the SHS group if their spouse was a smoker and had an exposure to tobacco smoke at least three years, minimum of15 minutes two days a week. However, we excluded those with established cardiovascular disease or who had any cardiovascular risk factors, such as hypertension, diabetes and dyslipidemia. We also excluded those with a body mass index (BMI) $\geq$ 30 kg/m^2.Consented patients then had face to face interviews with the investigator. The sociodemographic data section was filled up by

the investigator. Weight and height were obtained on the day of the interview. The respondent was given an appointment date for assessment of arterial stiffness. During the appointment day, respondent were asked to lying down on the bed with her right arm supported by pillow. The assessment of arterial stiffness was performed using applanation tonometry. The tonometer was placed on the radial artery till the radial waveform appeared on the monitor. When the required wave identified, it will be freeze. Then, the researcher PROCEEDS with PWV measurement. The Electrocardiography (ECG) probe was attached to participants' chest wall and the rhythm will appeared on the monitor. The tape was used to measure the distance from the carotid artery to femoral artery. The applanation tonometry will placed on the carotid artery and the required waveform identified. The same procedure will applied for femoral wave. This procedure took around 30 minutes.

Analysis was done using SPSS Version 20.0. Descriptive analysis was done for all numerical variables and was expressed as mean and standard deviation while all categorical data as frequencies and percentage. ANOVA and ANCOVA was used to compare the arterial stiffness between SHS and non – SHS.

Assessment of arterial stiffness using applanation tonometry

Arterial stiffness was measured using the Syphgmo Cor system. This device was certified by the Australian Register of Therapeutic Goods (ARTG) and has been assigned the listing number AUST L 64615. It contains a tonometer and an electronic module. The tonometer (SPT-301B) was used for non-invasive assessment of arterial stiffness using central aortic pressure. The arterial pressure waveform consists of two components. The first waveform is the forward travelling wave when the left ventricles contract and the second reflected wave is that returning from the bifurcation. The backward pressure occurs as a result of a wave reflection. It is created primarily by impedance mismatch at the branch points of the arterial system with very small resistance from the arterioles.

This procedure is performed by applying a tonometer to the skin overlying the radial artery in order to record the radial wave form. The pressure waveform from the radial artery is preferred because the radial artery is supported by bone, and therefore, it allows an optimal pressure waveform to be recorded. The radial waveform is calibrated to the brachial blood pressure. This calibration allows the radial waveform to be transformed into a pressure waveform. The pulse wave analysis was reported as a percentage of the augmentation index. The augmentation index was calculated from the pressure difference between the peak systolic pressure and early inflection point that indicates the beginning upstroke of the reflected pressure wave divided by the pulse pressure. The data were fed directly into a computer. The aortic pressure waveform was generated using the generalised transfer function (SphygmoCor, Atecor Medical, and Version 6.2).

PWV was derived from the formula PWV equals distance divided by time. The unit used is in metres/seconds. The electrocardiogram ECG probe was attached on the participant's chest wall and the ECG rhythm appeared on the monitor. Carotid femoral distance was measured from the right carotid artery to the femoral artery. The distance was measured to the nearest centimetre using a measuring tape. All PWV measurements were performed with the patient in a comfortable supine position.

Ethical Clearance: The study protocol was approved by the Research Ethics Committee, USM on 7 January 2009(USMKK/PPP/JEPeM(221.3(07)).

Results

A total of 118 participants were involved in this study; 64 respondents were enrolled in the SHS group and only 54 respondents were in the non-SHS group. The response rate in non-ETS group was 84% as 10 of participants did not turn up for arterial stiffness measurement.

Demographic data

Table 1 shows the socio-demographic and medical characteristics of the study respondents. The mean (SD) age was 33.9 (6.73) years among the SHS group and 33.9 (7.74) years among the non-SHS group. Majority of the participants were Malay. A total of 52 (81.2 %) received a primary and secondary education in SHS group, while 25 (46.3%) had a primary and secondary education in non-ETS group. Most of the respondents were employed.

The mean (SD) BMI of the SHS and non-SHS respondents was 24.8 (4.83) kg/m^2 and 23.7 (4.04) kg/m^2, respectively.

Table 1: Socio-demographic and medical characteristics of SHS and non-SHS groups

Variables	SHS (n = 64)		Non-SHS (n = 54)	
	Mean (SD)	**N (%)**	**Mean** (SD)	**N (%)**
Age (years)	33.9 (6.73)		33.9 (7.74)	
Race				
Malay		62 (96.9)		42 (7.74)
Non-Malay		2 (3.1)		12 (22.2)
Education level				
Primary and secondary		52 (81.2)		25(46.3)
Tertiary		12 (18.8)		29(53.9)
Occupation				
Working		48 (75.0)		40(74.1)
Not working		16 (25.0)		14 (25.9)
BMI (kg/m2)	24.8 (4.83)		23.7 (4.04)	

Table 2 shows a comparison of the augmentation index and the PWV between the SHS and non-SHS patients. The mean augmentation index (AIx) for SHS groups was 17.9 (SD7.06) and for Non SHS groups was 20.7(SD6.11). The mean of Pulse wave velocity was 8.94 (SD1.36) in SHS groups and 9.02 (SD8.68) in non SHS groups. ANOVA and ANCOVA shown significance difference in crude mean (p = 0.047) and estimated marginal mean (p = 0.028) of augmentation index between SHS and non - SHS after controlling for age and BMI. However, there was no significant difference in crude mean (p = 0.795) and estimated marginal mean (p = 0.716) pulse wave velocity between SHS and non - SHS after controlling for age and BMI (Table 2).

Table 2: Comparison of augmentation index and pulse wave velocity between SHS and non-SHS of 118 patients

	SHS (n = 64)		Non-SHS (n = 54)			
	Mean (SD)	**EMM (95% CI)[a]**	**Mean (SD)**	**EMM (95% CI)[a]**	**F (df)**	***P* value**
Augmentation index (AIx)	17.9 (7.06)	17.9 (16.20,19.58)	20.7 (6.11)	20.7 (18.88,22.56)	4.95	0.028[a]
Pulse wave velocity	8.94 (1.36)	8.93 (8.62,9.24)	9.01 (1.38)	9.02 (8.68,9.35)	0.13	0.716[a]

[a]ANCOVA after adjusting for age and BMI

Discussion and conclusion

Socio-demographic characteristic

This cross-sectional study demonstrated both group had similar mean age of 33.9 years old. This age was considered relatively young in which they are not in cardiovascular risk by definition. Most of the study on cardiovascular risk assessment were focus on age more than 40 years to calculate the cardiovascular risk.[23,24] However, Framingham risk score can be counted as early as age of 30 years.[25] Since atherosclerosis starts in early adolescence and it progresses throughout a woman's lifetime based on individual risk factors. The mean BMI in the SHS group was slightly higher (24.8 [4.83] kg/

m^2 compared to the control group (23.7 [4.04] kg/ $m^{2)}$. Both groups of participants belong to the pre-obese group. So in this study, mean age of 33, second hand smoke women are considered to have some atherosclerotic changes that would affect their arterial stiffness and with exposure to passive smoker, will further increase their cardiovascular risk

Effect of passive smoking on arterial stiffness

Endothelial dysfunctions are important in early features of the artherogenic process, which may occur in systemic arteries of healthy teenagers and young adults.[16,21] The effect of cigarette smoke alters endothelial function and, thus, induces coronary vasoconstriction.[8] In acute exposure to SHS will lead to a short-term increase in arterial wall stiffness.[26] Mahmud and Feely demonstrate that even a single cigarette exposure will produce an acute increase in arterial stiffness in non-smokers.[21] Interestingly, they found an increase in the augmentation index in male, but not female, subjects after acute tobacco exposure.[21] The female subjects in this study were young healthy premenopausal, which may suggest the sensitivity of the arterial wall to smoking may be attenuated to the mechanism that involves circulating estrogen.[21]In Zhang *et al.* (2005) who did large population based study, found prevalence of stroke among Chinese women nonsmokers was significantly associated with husband's current smoke. They stated that the association was independent of socioeconomic and lifestyle factors as well as established risk factors for stroke. The longer duration and number of cigarettes will contribute to the higher prevalence of stroke among women. Women never smokers living with a husband who was a current heavy smoker (≥20 cigarettes per day) had a 62 percent greater probability of suffering a stroke than women never smokers living with a husband who never smoked.[27] The finding is similar to a study by Rehill *et al* who found an increase in systemic arterial stiffness following acute smoke exposure in healthy smokers compared to non-smokers.[13]

In the present study, we found that the augmentation index was significantly lower among the SHS group compared to non-SHS group but there was no difference in the PWV between the two groups. Our result findings was contrast to previous study findings. This probably most of the study population was based on the acute effect of smoke exposure. They found a significant increase in arterial stiffness among acute exposure SHS.[13,21] Adamopoulos *et al.* Also found that nicotine enhanced arterial wave reflection to the aorta and increased in carotid femoral pulse wave velocity in passive smokers.[28]

In this study, the exposure of 15 minutes, two days a week for three years duration might not be sufficient to demonstrate any effect on endothelial function. A study by Holay *et al.* comparing the chronic effect of tobacco exposure between active smokers, passive smoker and a control group for at least one hour daily, found no significant correlation between the severity of tobacco exposure and endothelial dysfunction.[16]

In this study, some methodological limitations need to be highlighted when interpreting these study results. Detailed information on the exposure to tobacco needs to be evaluated further to evaluate as second hand smoke, such asthe intensity of the exposure to smoke, the exact number of hours of exposure, the number of active smokers at home not only presence of husband who smoked. Size of the ventilation room where second hand smokers are involved is also important. We could not solely rely on exposure at home by husband's cigarette smoke as most husband usually smoke outside the house. Result of increase augmentation index among non SHS probably due to exposure to tobacco at work which was not detail in the questionnaire of this study. Further study on second hand smoke need to properly assess or defined second hand smoke not only rely on husband who are smokers. A cardiovascular risk are generally smaller among passive smokers with home exposure compared to work exposure.[29]

Conflict of interest

There is no commercial association that may create a conflict of interest in connection with this submitted manuscript. All authors are affiliated with the Universiti Sains Malaysia and receive no financial benefit from this study.

Acknowledgements

This study was supported and funded by research university grant Universiti Sains Malaysia 1001/ PPSP/812088.

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