Effect of Aerobic Exercise on Arterial Stiffness in Individuals with Different Smoking Statuses

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ABSTRACT
This study aimed to investigate the immediate effects of acute bout of aerobic exercise on arterial stiffness in individuals with different smoking statuses. A total of 940 male individuals (mean age of 36.82 ± 7.76 years) in the Kailuan study cohort were selected to participate in the fifth National Physical Fitness Monitoring. All participants completed measurements of brachial–ankle pulse wave velocity (baPWV) before and after twice-quantitative cycle ergometer exercise. Four groups were defined: (1) non-smokers (n = 231), (2) former smokers (n = 165), (3) light smokers (1–10 cigarettes/day, n = 254), (4) heavy smokers (> 10 cigarettes/day, n = 290). Generalized linear models were established to analyze between-group differences in the change in baPWV before and after acute aerobic exercise in individuals with different smoking statuses. Overall, after acute aerobic exercise, baPWV was immediately decreased significantly (−33.55 cm/s [95% CI, −39.69 to −27.42]). Compared with non-smokers, former smokers, light smokers, and heavy smokers showed a greater decrease in baPWV (−12.17 cm/s [95% CI, −30.08 to 5.75], −18.43 cm/s [95% CI, −34.69 to −2.16], and −22.46 cm/s [95% CI, −38.39 to −6.54]) respectively. There is a transient decrease in baPWV in individuals with different smoking statuses. Compared with non-smokers, baPWV decreased more significantly in light and heavy smokers.

# These authors have contributed equally to this work
Introduction

Arterial stiffness is not only a sign of vascular aging, but is also an independent risk factor for cardiovascular diseases, renal failure, cognitive dysfunction, and all-cause mortality [1–4]. Observational and longitudinal cohort studies have shown that age and blood pressure (BP) are the main risk factors for arterial stiffness [5, 6]. However, traditional risk factors, such as diabetes, smoking, and chronic inflammation, are also risk factors for arterial stiffness [7–9]. Arterial stiffness is significantly increased after smoking compared with before smoking in healthy young people [10]. Additionally, Tomiyama et al. (2010) found that the progression of arterial stiffness was significantly faster in smokers than in non-smokers of the same age [11].

In 2010, the American Heart Association suggested that an ideal healthy lifestyle, such as being a non-smoker, moderate exercise, and a healthy diet, can reduce the risk of cardiovascular disease and all-cause mortality [12]. In particular, long-term regular aerobic exercise is an effective lifestyle intervention that reduces the damage to blood vessels caused by risk factors, such as smoking, hypertension, and diabetes [13–15]. However, the results of research on the immediate effect of acute bout of aerobic exercise on arterial stiffness in individuals with different smoking statuses are inconsistent [16, 17]. Doonan et al. (2011) studied 24 smokers and found that arterial stiffness increased immediately after aerobic exercise [16]. A study of 50 healthy non-smokers showed that arterial stiffness decreased immediately after aerobic exercise [17]. These studies were small-sample studies on a Caucasian population.

To the best of our knowledge, few studies have investigated and compared the effect of acute aerobic exercise-induced changes on arterial stiffness in Asian men with different smoking statuses. Therefore, we used data from the Kailuan Study to evaluate short-term changes in arterial stiffness following an acute aerobic exercise test in men with different smoking statuses.

Materials and Methods

Study design and participants

The data of this study were derived from the subjects in the Kailuan Study population who were selected to participate in the fifth National Fitness Monitoring. The Kailuan Study began in 2006 and participants were followed up every 2 years thereafter in 2008–2009, 2010–2011, 2012–2013, 2014–2015, 2016–2017, and 2018–2019 [18, 19]. To systematically assess the nationwide physical fitness of individuals, the State Sports General Administration initiated the fifth National Physique Monitoring in 2020. In addition to the general population, special monitoring also had been carried out on the public security, finance, construction and coal industries of typical workers [20].

All the participants in this study are workers engaged in the coal industry. According to the Labor Law, few female employees were underground coal miners or workers in dangerous occupation [21]. Therefore, 1,200 male coal miners aged 20–49 years were selected by random methods as subjects of the fifth National Physique Monitoring, using the employee information database reported and established by the four affiliated companies of the Kailuan Group. All participants were asked to perform these tests, including body morphology, physical function, and physical fitness. We also measured brachial–ankle pulse wave velocity (baPWV) before and immediately after acute aerobic exercise.

This study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Kailuan General Hospital. All participants provided written informed consent.

Inclusion and exclusion criteria

In this study, a total of 1,200 employees of the Kailuan Group participated in the fifth National Physique Monitoring, of whom 1,138 participated in the 2018–2019 follow-up of the Kailuan Study. Those who did not have baPWV measured twice before and after exercise (n = 185) and those without a twice-quantitative cycle ergometer exercise (n = 13) were excluded. Finally, 940 individuals were included for analysis (Fig. 1).

Exercise protocol

The procedure of performing cycling exercises complies with the Exercise Standards for Testing and Training released by the American Heart Association (AHA) and is briefly described below [22]. All participants and measurements were performed in a quiet, temperature-controlled room (22–25 °C). Before cycling exercise, the participants had avoided alcohol, tobacco, ingest caffeine or perform vigorous activities within 12 hours. After a preliminary pe-
period of 15 minutes of supine rest, pre-exercise measurements of baPWV were made in the supine position. Cycling exercise was then performed with individually tailored ramp protocols via upright cycle ergometry (GMCS-GLC3, Beijing, China). Following a brief warm-up by cycling against unloaded exercise (0 watts) for 30 seconds, according to individual’s fitness conditions, participants started to cycle at a moderate intensity (50 watts–80 watts) for 3 minutes so that the heart rate reached 60% ~ 80% of their estimated maximum heart (calculated as 220 minus age in years), and the resistance was increased by 25 watts in next 3 minutes. Throughout the exercise, participants were instructed to maintain a pedaling cadence of 60 revolutions per minute (rpm). The cycling exercise finished with 30 seconds of unloaded (0 watts). HR was monitored and recorded continuously. Maximum oxygen consumption (VO2max) was indirectly estimated based on the cycling exercise and calculated by the ergometry according to a previously described equation [23].

BaPWV measurement

All participants underwent baPWV measurement after 12 h abstinence from smoking and fasting. We used the BP-203 RPE III networked arterial stiffness detection device (Omron Health Medical [China] Co., Ltd.) automation to measure baPWV. We used the BP-203 RPE III networked arterial stiffness detection device (Omron Health Medical [China] Co., Ltd.) automation to measure baPWV. BaPWV is determined by measuring the pulse waves of the brachial artery and ankle, and dividing the distance between the upper arm and ankle (DAB), which is calculated using linear regression of body height, by the time difference between the two pulses (TAB) [24]. Briefly, the calculation formula is expressed as baPWV = DAB/TAB. BaPWV was recorded before and immediately (or as soon as possible) after cycling exercise, which simultaneously records BP, HR following standard operation procedures [25]. For the first measurement, participants in light clothes had not been smoking and were seated for at least 15 minutes in a room with the temperature controlled between 22°C and 25°C. The participants were asked to lie down on an examination couch in the supine position and remain quiet during the measurement. Cuffs were wrapped on both arms and ankles. The lower edges of the arm cuffs were positioned 2–3 cm above the transverse striation of the cubital fossa, while the lower edges of the ankle cuffs were positioned 1–2 cm above the superior aspect of the medial malleolus. One heart sound detector was placed at the left and right edges of the sternum. Measurements were repeated twice for each subject, and the result of the second time was used as the final result.

The maximum of the left and right sides of baPWV was used for analysis.

Smoking status

The smoking status of the subjects (i.e., non-smokers, former smokers, and current smokers) was assessed with a questionnaire. We ensured the accuracy of smoking information through a telephone follow-up survey. Non-smokers were defined as having no history of smoking, former smokers [26] as not smoking for at least 6 months, and current smokers [27] as any who had smoked at least one cigarette per day for 1 year. Additionally, to calculate pack-years in current smokers, data on the average number of cigarettes smoked per day and the years of cigarette smoking were collected. Pack-years of smoking were defined as the average number of packs of cigarettes smoked per day multiplied by the duration of smoking in years [28]. On the basis of the number of cigarettes smoked per day, current smokers were classified into the two following groups: light smokers (1–10 cigarettes/day) and heavy smokers (>10 cigarettes/day) [29]. To further confirm our findings, we divided the smokers into light smokers (<4 pack-years) and heavy smokers (>4 pack-years) in accordance with the pack-years as described in Celermajer et al.’s (1993) [30] study as well.

Data collection

Information on demographic data and lifestyle factors (e.g., age, sex, alcohol consumption) and medical history (e.g., diabetes, hypertension) were collected using a self-reported questionnaire. Anthropometric indicators, including height, weight were derived from the fifth National Physique Monitoring data. BMI was calculated as weight (kg) divided by height squared (m²). The physical exercise was defined as taking exercise ≥ 3 times/week with at least 30 mins each time [31]. All participants underwent blood tests after 12 h fasting at each physical examination. The blood samples were analyzed using an auto-analyzer (Hitachi 747, Hitachi, Tokyo, Japan) on the day of the blood draw. The biochemical indicators tested included fasting blood glucose (FBG), triglycerides (TG) levels. Hypertension was defined as (i) systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or (ii) formerly diagnosed hypertension or using antihypertensive drugs [32]. Diabetes was defined as either a fasting blood glucose (FBG) level ≥ 7.0 mmol/L, self-reporting of a physician’s diagnosis, or self-reported use of antidiabetic medication [33].

Statistical analysis

Continuous variables that conformed to a normal distribution are presented as the mean ± standard deviation (X ± s). Data with a non-normal distribution are expressed as the median (interquartile range). Categorical variables are expressed as the number of samples (percentage). Demographic factors and hemodynamic parameters were compared between the groups using the one-way analysis of variance or the Wilcoxon rank sum test, as appropriate. Categorical variables were assessed using the χ² test for independence. The paired-sample t test was used to compare baPWV, HR, and BP values in each group post-exercise and pre-exercise.

Linear regression models were established to evaluate group changes in baPWV, HR and BP post-exercise and pre-exercise. In the linear regression models, we adjusted for age (continuous variable), the pre-exercise value of BMI (continuous variable), and TG level (continuous variable), education level (categorical variable), alcohol consumption (categorical variable), physical activity (categorical variable) and the timing of post-exercise measurements (continuous variable).

Generalized linear models were used to analyze differences in the change in baPWV between the groups. In generalized linear models, we adjusted for age and the pre-exercise values of baPWV in model 1. In model 2, we further adjusted for the pre-exercise values of BMI, HR, MAP, and TG level, the timing of post-exercise measurements, education level, alcohol consumption, physical activity.
In model 3, we further adjusted for the change in MAP and HR. Between-group differences are described by \( \beta \)-value and 95% confidence interval (CI).

Stratified analyses were performed based on the different physical activity levels among participants. To test the robustness of our findings, the following sensitivity analyses were performed: 1) We repeated the above-mentioned generalized linear model for sensitivity analysis of smokers classified by pack-years. 2) We excluded participants with diabetes mellitus, which is associated with a high baPWV and is a potential risk factor for arterial stiffness. 3) We also excluded participants with hypertension, which is associated with a high baPWV and is a potential risk factor for arterial stiffness.

4) To reduce the effect of the timing of post-exercise measurements, we also conducted another sensitivity analysis by excluding participants with the timing of post-exercise measurements exceeding 95% percent (26.7 minutes).

A \( P \) value < 0.05 was considered statistically significant with a two-sided test. SAS 9.4 (Version 9.4; SAS Institute, Cary, NC) was used for data analysis.

Results

Baseline characteristics of the study population

The study population had a mean age of 36.82 ± 7.76 years (► Table 1). On the basis of smoking status, the study population was divided into non-smokers (n = 231), former smokers (n = 165), light smokers (n = 254), and heavy smokers (n = 290). Participants with heavy smoke had higher pre-exercise SBP, pre-exercise DBP, pre-exercise MAP, pre-exercise baPWV, TG level, and rate of alcohol consumption, lower education level than those in the other three groups (all \( P \) < 0.05). The heavy smoker group had higher rate of taking exercise than those in the other three groups, but there were no statistical difference among groups (\( P \) = 0.64). After the cycling exercise, baPWV of all participants significantly decreased (1375.08 ± 209.09 cm/s vs. 1341.53 ± 208.04 cm/s, \( P \) < 0.05), and their HR increased (80.24 ± 12.54 bpm vs. 85.73 ± 13.56 bpm, \( P \) < 0.05). There were no significant changes in SBP, DBP, or MAP before and after exercise (► Table 1).

Comparison of changes in BP, HR, and baPWV between the groups

In adjusted analyses, the changes in baPWV of all participants post-exercise were \(-33.55\) cm/s (95% CI, \(-39.69\) to \(-27.42\)), and the change in the heavy smoking group was more significantly than other three groups. The changes in HR of all participants were 5.59 bpm (95% CI, 4.94 to 6.24). The changes in MAP of all participants post-exercise were 0.33 mmHg (95% CI, \(-0.19\) to 0.85) (► Table 2).

Generalized linear model estimation of between-group differences in the change in baPWV

We used the generalized linear model to compare between-group differences in the change in baPWV. In Model 3, with the non-smokers as the control, the \( \beta \)-values and 95% CI of former smokers, light smoking smokers, and heavy smoking smokers were \(-12.17\) cm/s (95% CI, \(-30.08\) to 5.75), \(-18.43\) cm/s (95% CI, \(-34.69\) to \(-2.16\)), and \(-22.46\) cm/s (95% CI, \(-38.39\) to \(-6.54\)), respectively (► Table 3). For every increase in one standard deviation (6.26 cigarettes/day) in the number of cigarettes smoked, the \( \beta \)-value and 95% CI were \(-18.11\) cm/s (95% CI, \(-114.16\) to 77.95) (► Table 3).

Stratified analysis

In the stratified analysis, after adjustment for covariates, the result was consistent with the main analysis among participants without regular exercise habit. But for those with regular exercise habit, there were no significant difference in the change of baPWV in former smoker, light smoker, and heavy smoker, compared with non-smokers (Table S1).

Sensitivity analysis

The results of the sensitivity analysis were consistent with those of the main analysis, which indicated that the main results were robust (Table S2).

Discussion

Using a functional community population, this study showed that aerobic exercise immediately improved arterial stiffness in individuals with different smoking statuses. Remarkably, the beneficial effects of exercise on arterial stiffness appeared to be more evident in light and heavy smoker than in non-smoker.

Following a 7-minute bout of exercise, we observed a significant reduction in baPWV of 33.55 cm/s from resting values in young and middle-aged (36.82 ± 7.76 years) subjects. This finding is similar to that by Yamato et al. (2016) [34]. They found that baPWV in non-smoking healthy men (n = 26, age: 21.0 ± 1.0 years) was decreased by 33.5 cm/s after 15 minutes of aerobic exercise for 40 minutes. However, Doonan et al.’s (2011) [16] study of 24 healthy young smoking men and 53 non-smokers showed that carotid-femoral pulse wave velocity in smokers and non-smokers increased by 80 cm/s and 60 cm/s, respectively, after 5 minutes of exhausting exercise. There are several possible reasons for this discrepancy between our study and Doonan et al.’s (2011) study. The sample size of Doonan et al.’s study was small, the population was relatively young (26.06 ± 6.70 years), and the exercise style was more intense compared with our study. Additionally, the difference in the type of pulse wave velocity could be the reason for the inconsistent conclusion between the studies. A meta-analysis suggested that aerobic exercise had different effects on arterial stiffness of different segments. In this meta-analysis, after aerobic exercise, arterial stiffness in the peripheral segments was significantly improved, but it did not significantly improve arterial stiffness in the central segment [35].

Our study showed that there was a difference in the decrease in baPWV after aerobic exercise in individuals with different smoking statuses. After adjusting for related confounding factors, baPWV was more significantly immediately decreased in low-intensity and high-intensity smokers than in never smokers (by 18.43 and 22.46 cm/s, respectively). A more likely explanation is that short-term aerobic exercise may have ameliorated the adverse effects of oxidative chemicals contained in cigarette smoke on vascular endothelial function and sympathetic nervous system activity [36]. Oxidative chemicals in cigarette smoke can affect vascular endothelial function through inflammatory response [37] and oxidative stress [38], which reduce the activity of endothelial nitric oxide syn-
The production of nitric oxide [39]. Because aerobic exercise can stimulate the expression of antioxidant enzymes [40] and vasodilatory substances [41]. We speculate that the augmented antioxidant defense mechanism in current smokers is the reason why baPWV improvement is more significant than that in non-smokers after exercise.

Although we found that there was a difference in the decrease in baPWV after aerobic exercise in individuals with different smoking statuses, and this decrease in heavy smokers was more obvious, we did not examine the specific mechanism(s). Previous studies have shown that arterial stiffness is mainly determined by two factors. One factor is that the structure of arteries affects arterial...
A decrease in elastin in the middle layer of the arterial wall and an increase in fibrin cause changes in vascular structure, which increases arterial stiffness [42–45]. The other factor is that the functional status of arteries also affects arterial stiffness. Vascular endothelial dysfunction and nervous system activity disorders can affect vascular function, resulting in increased arterial stiffness [46, 47]. Short-term aerobic exercise increases blood flow by stimulating the production of endothelial nitric oxide, prostaglandin, and other vasodilator factors, and decreases vasoconstrictors (e.g., endothelin) [41, 48–50], or vascular modifications [51]. These processes can improve vascular endothelial function and arterial stiffness. In addition, an improvement in arterial stiffness after aerobic exercise may also be related to changes in the levels of circulatory metabolites. The Framingham study showed a significant reduction in circulating blood metabolites after aerobic exercise, which resulted in insulin resistance, body inflammation, and oxidative stress. Metabolites related to cardio-cerebral vascular protection were significantly increased [52].

Improving lifestyles and preventing and controlling multiple risk factors are still primary prevention measures for cardiovascular disease, which can effectively reduce the probability of adverse cardiovascular events [53]. Hamdy et al. (2005) found that long-term regular aerobic exercise delayed and reversed the process of vascular aging [54]. Our study showed that arterial stiffness in individuals with different smoking statuses were significantly immediately decreased after exercise compared with before exercise. However, this might not be a continuous change. If the exercise time is prolonged and the exercise frequency is increased, arterial stiffness may be maintained. Therefore, smokers can adopt a healthy lifestyle such as aerobic exercise to improve arterial stiffness, delay vascular aging, and reduce the damage to blood vessels caused by smoking.

This study has some limitations: (1) This was a cross-sectional study that was performed to examine the causal relationships between various factors and the difference in baPWV before and after exercise. (2) We did not find a dose–response relationship of the change in baPWV after aerobic exercise, possibly because we had difficulty in determining the specific number of cigarettes smoked per day. The number of cigarettes smoked was treated as a classification variable (1–10, 11–20, 21–30, 31–40, and > 40 cigarettes/day). Therefore, it is difficult to observe a dose–response relationship. (3) We used baPWV as a measurement of arterial stiffness instead of carotid–femoral pulse wave velocity, which is the gold standard. The validity and accuracy of baPWV against carotid–femoral pulse wave velocity have been demonstrated in previous studies [55], and the American Heart Association has also recommended baPWV as a common indicator for arterial stiffness [56]. (4) The study was conducted only in men, and findings could not be readily generalizable to female working populations or to workers in other settings or other countries. (5) Because of space and personnel constraints, the timing of baPWV measurement after aerobic exercise could not be unified. But baPWV was measured immediately (or as soon as possible) after aerobic exercise. In addition, when evaluating the short-term effect of acute aerobic exercise on arterial stiffness, we adjusted for the timing of baPWV measurement.

In summary, this study shows that a single aerobic exercise can immediately decrease baPWV in individuals with different smoking statuses.
ing statuses. Additionally, compared with non-smokers, baPWV decreased more significantly in light and heavy smokers.

Conflict of Interest

The authors declare that they have no conflict of interest.

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