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Original research

Flow-mediated dilation and exercise blood pressure in healthy adolescents

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ABSTRACT

Objectives: Exercise blood pressure is a robust predictor of cardiovascular disease risk. Endothelial dysfunction occurs early in development of cardiovascular disease and is associated with greater exercise blood pressure in adults. However, it is not yet clear whether endothelial function is associated with exercise blood pressure in youth. The purpose of this study was to examine the relationship between endothelial function, indexed by brachial artery flow-mediated dilation, and submaximal exercise blood pressure in healthy adolescents.
Design: Cross-sectional study.
Methods: Adolescents ($N = 45$) completed a graded submaximal treadmill test. Blood pressure was measured during rest and each exercise stage. Ultrasound measurement of brachial artery flow-mediated dilation was completed on a separate visit. Pearson correlations and multiple regression were used to assess the unadjusted and multivariate adjusted associations between flow-mediated dilation and exercise blood pressure, respectively.
Results: Lower flow-mediated dilation was associated with lower diastolic blood pressure ($r = 0.37$, $p = 0.01$) and greater pulse pressure ($r = -0.38$, $p = 0.01$) during exercise. The significance did not change when adjusting for age, gender, fitness, or resting blood pressure. Exploratory analyses suggest that flow-mediated dilation was associated with exercise diastolic blood pressure primarily among adolescents with low resting diastolic blood pressure.
Conclusions: Studies in youth are important to understand the early pathogenesis of cardiovascular disease. Findings from this study suggest that endothelial function may play a role in regulating blood pressure responses during submaximal exercise in healthy adolescents.

1. Introduction

Altered blood pressure (BP) responses during acute exercise are associated with cardiovascular disease (CVD) morbidity and mortality in adults[1] and can add valuable information to the prediction of future CVD beyond that of resting BP.[2,3] Moreover, in clinical settings, exercise tests are commonly used to identify individuals with CVD. While the association between exercise BP and CVD in adults has been well-studied, less is known about the mechanisms whereby greater BP during acute exercise is associated with greater CVD risk. Additionally, little is known about the association between exercise BP and cardiovascular risk in youth. Studies investigating the early pathogenesis of CVD are of great public health importance because the initiation of the atherosclerotic process and the antecedents of CVD appear in youth.[4,5]

The endothelium plays an essential role in protecting against the initial stages of atherosclerotic progression.[6] Normal arterial function requires a balance between vasodilation and vasoconstriction, which is achieved in part by endothelial cell secretions of vasoactive substances (e.g. nitric oxide). This balance helps regulate blood flow and vascular tone during rest and exercise.[7,8] Alterations in endothelial function likely contribute to BP responses during acute exercise[9] and may be a potential mediator in the relationship between exercise BP and CVD risk. In adults, endothelial dysfunction is associated with greater exercise BP.[10–12] However, few studies have assessed the relationship between endothelial function and exercise BP in youth.

BP responses to maximal aerobic exercise are frequently assessed in CVD research; however, youth spend a very small percentage of time during conditions of maximal exertion in everyday life. BP responses to submaximal exercise intensities are more

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comparable to the intensities of activities that youth routinely experience. Examination of the association between endothelial function and submaximal exercise BP in healthy youth is important to understand how endothelial function may impact blood pressure during normal daily activities and may provide insight into the mechanisms whereby exercise BP is associated with greater CVD risk in youth.[13]

Flow-mediated dilation (FMD) of the brachial artery, assessed non-invasively via ultrasound, has been validated in youth as a marker of vascular endothelial function.[14] Thus, the purpose of this study was to examine the relationship between endothelial function, indexed by brachial artery FMD, and submaximal exercise BP in healthy, normal weight, adolescents. We hypothesized that lower FMD (e.g. worse endothelial function) would be associated with greater exercise BP. In exploratory fashion, we also examined whether the relationship between FMD and exercise BP varied by fitness level or resting BP given that these factors are associated with greater cardiovascular disease risk and exercise BP.[13,15]

2. Methods

Adolescents, aged 13–16, years were recruited for study through flyers and an existing database of families who had provided consent to be contacted for research studies. Exclusion criteria included history of CVD, smoking, body mass index (BMI) > 85th percentile, currently taking medications that could influence cardiovascular or endothelial functions (e.g. BP medication, depression medication), or any medical condition that would limit the ability to complete the exercise protocol (i.e. exercise-induced asthma, musculoskeletal conditions, insulin dependent diabetes). Additionally, adolescents were excluded if they had a resting SBP > 140 or resting DBP > 90. Parents provided written informed consent for their child's participation and the adolescent provided written assent before participating in the study. Ethical approval of the study was obtained from the Social and Behavioral Sciences Institutional Review Board at the University at Buffalo.

Adolescents were tested on 2 days: an exercise day and an ultrasound day to assess FMD. Prior to each meeting, adolescents were instructed not to eat anything at least 3 h prior to the visit and not to participate in any intense physical activity or to consume any caffeine the day of or the day before the visit. The ultrasound appointment was completed at least 24 h after the exercise appointment, so that the exercise protocol would not affect the FMD measurement.

On the exercise day, height, weight and pubertal maturation were measured at the beginning of the appointment. Body weight was measured to the nearest 0.01 kg with the subjects wearing shorts and a t-shirt. Height was measured with a stadiometer. BMI was calculated according to the following formula: ($BMI = kg/m^2$). BMI percentile was determined according to age and sex using the Center for Disease Control and Prevention growth charts.[16] To assess maturation, adolescents were given the gender-appropriate set of standardized line drawings of pubertal development[17] and classified their development based upon maturation of the secondary sex characteristics.[18] Adolescents were fitted with a Polar heart rate (HR) monitor (Port Washington, NY) and an appropriate size BP cuff. BP was measured with a Suntech Tango monitor (Morrisville, NC). The Suntech Tango uses the auscultatory method aided by electrocardiographic R-wave gating and an oscillometric transducer and is a valid and reliable measure of BP during rest and exercise.[19] Measurement of BP followed standard guidelines regarding cuff length and width, placement of the cuff around the arm 2.5 cm above the antecubital space, and seating of the cuff on the arm by inflating and deflating the cuff before taking any measurements. Adolescents were also fitted with a face mask attached to a metabolic cart (Vmax Encore Metabolic Cart, Sensormedics) via a sampling line to measure oxygen (O_2) consumption. The metabolic cart was calibrated according to manufacturer instructions prior to each subject appointment.

Adolescents rested for 10 min to collect resting HR, BP, and O_2 consumption. Adolescents then completed 5, 4-min stages of increasing intensity on a treadmill. Four minute stages were used to ensure the subject reached a steady state. The exercise protocol was used to determine submaximal exercise BP's and to determine the O_2 consumption, or physical working capacity (PWC), at a HR of 170 bpm as a measure of aerobic fitness. PWC measures are used widely to assess aerobic fitness and are validated for use in youth.[20] The first stage of the exercise protocol was 2.7 METS. The velocity and % grade of the treadmill was progressively increased (approximately 1 MET increase each stage) until a HR of 170 bpm was attained or the subject completed 5 stages. Before beginning the protocol, subjects were given time to learn to walk comfortably on the treadmill. HR and O_2 consumption were measured continuously during baseline and each exercise stage. BP was measured twice during the last 2 min of baseline and twice during the last 2 min of each exercise stage. After the test, adolescents were provided with rest and water.

FMD measures were performed by sonographers who were trained and certified at Wake Forest University School of Medicine. Brachial artery ultrasound scans were performed using a high resolution B-mode ultrasound imaging machine (Biosound Esaote, Inc., Indianapolis, IN) with a 10-MHz transducer. Prior to the test adolescents rested in the supine position for 15 min in a quiet temperature-controlled room with minimal lighting. A BP cuff was placed on the upper left arm to record BP at baseline and at the end of the test. The adolescent's right arm was extended at the level of the heart with a beanbag placed in the right hand to prevent movement. Another BP cuff (pediatric size) was applied to the right forearm, 2 in. below the antecubital fossa. The sonographer positioned the transducer to longitudinally visualize both the near and far walls of the brachial artery. A continuous scanning procedure was used which maintained the transducer at this same location and angle of interrogation throughout the entire 8 min scan (1 min baseline, 4 min occlusion, 3 min deflation). During the occlusion period, the forearm BP cuff was inflated to 50 mmHg above the baseline SBP (but did not exceed 200 mmHg). De-identified images of the brachial artery were recorded on videotape using a super VHS recorder. Ultrasound scans were analyzed on-site using ImagePro Plus software (Media Cybernetics Inc., Bethesda, MD) by sonographers blinded to the adolescent's exercise test results. FMD was calculated as the maximal diameter measured during the 3 min deflation period and is reported as a percent change from baseline diameter. Detailed descriptions of the image acquisition/analysis methods and reproducibility of the FMD protocol have been reported elsewhere.[21] Notably, this protocol has been used to assess FMD in numerous studies including the Cardiovascular Health Study.[22]

Variables were examined for normality. FMD was square-root transformed for analyses in order to normalize the distribution. The average BP obtained during the last exercise stage (6.5 MET intensity) was used in all analyses to represent exercise BP. Although not presented here, analyses including the other exercise stages showed similar results. Pulse pressure (PP) was calculated by subtracting DBP from SBP. Sex differences in participant characteristics were assessed via independent *t*-tests. Unadjusted correlations between FMD, exercise BP, and covariates were examined with Pearson correlations.

Multiple linear regression was used to determine if FMD was associated with exercise BP (SBP, DBP, PP) after multivariate adjustment. We tested the association of FMD and exercise BP when adjusting for age, gender, fitness, and resting BP. We also considered