

Association of Blood Pressure and Fitness With Levels of Atherosclerotic Risk Markers Pre-Exercise and Post-exercise

Roland von Känel, Suzi Hong, Meredith A. Pung, and Paul J. Mills

Background: Physical fitness may attenuate the increased atherosclerotic risk in patients with systemic hypertension. We investigated the association of screening blood pressure (BP) and cardiorespiratory fitness with baseline levels and exercise-induced changes in levels of soluble atherosclerotic risk markers.

Methods: Twenty-six otherwise healthy and unmedicated subjects with elevated BP (systolic BP and/or diastolic BP $\geq 130/85$ mm Hg) and 40 subjects with normal BP underwent 20-min treadmill exercise at 65% to 70% of predetermined peak oxygen consumption (VO_{2peak}). Interleukin (IL)-6, soluble intercellular adhesion molecule (sICAM)-1, von Willebrand factor (VWF) antigen, and plasminogen activator inhibitor (PAI)-1 antigen were measured at baseline (ie, pre-exercise), early postexercise, and late postexercise (ie, 25 min after exercise).

Results: At baseline, higher screening mean arterial BP (MAP) independently predicted higher sICAM-1 levels ($P = .031$), and lower VO_{2peak} independently predicted

higher IL-6 ($P = .016$) and PAI-1 ($P < .001$) levels. Early and late postexercise lower VO_{2peak} was associated with higher mean PAI-1 ($P \leq .072$) and IL-6 ($P \leq .026$) levels, and higher screening MAP was associated with higher mean sICAM-1 levels ($P \leq .035$). Higher VO_{2peak} was associated with a greater PAI-1 increase from baseline to early postexercise in subjects with elevated BP ($P = .045$) but not in those with normal BP.

Conclusions: Circulating levels of some atherosclerotic risk markers at baseline and with exercise were higher with elevated BP and lower with better fitness. Greater fitness did not particularly protect subjects with elevated BP from potentially harmful responses of atherosclerotic risk markers to acute physical exercise. Am J Hypertens 2007;20:670–675 © 2007 American Journal of Hypertension, Ltd.

Key Words: Cellular adhesion, exercise, fitness, hemostasis, hypertension, inflammation.

Elevated plasma levels of proinflammatory and prothrombotic markers contribute to the increased risk of atherosclerosis and atherothrombotic events in individuals with elevated systemic blood pressure (BP).^{1,2} Increased cardiorespiratory fitness attenuates the risk of atherosclerotic cardiovascular diseases.³ Among hypertensive men, physical fitness was inversely associated with plasma levels of C-reactive protein and soluble intercellular adhesion molecule (sICAM)-1.⁴ Atherosclerotic risk increases linearly with higher BP and moreover is predicted by both systolic and diastolic BP.⁵ We therefore hypothesized that in a sample of subjects with and without elevated BP, higher mean arterial BP (MAP) and poorer fitness would show associations with higher plasma baseline levels of atherosclerotic markers of inflammation and

thrombogenicity. We further hypothesized that the positive relationship between MAP and atherosclerotic markers would be attenuated by good fitness.

In patients with coronary heart disease and hypertension, short-term strenuous physical activity is a triggering factor for an acute coronary event commonly initiated by the rupture of an atherosclerotic plaque.^{6,7} Subsequently, an exercise-induced prothrombotic and proinflammatory milieu may contribute to the rapid growth of a coronary thrombus.⁸ Whether fitness affects the exercise-induced acute change in proatherogenic factors in hypertension has not been studied. We hypothesized that increases in proinflammatory and prothrombotic activity with exercise are associated with a higher screening MAP and lower fitness level. We further hypothesized that the positive associa-

Received September 22, 2006. First decision October 19, 2006. Accepted January 1, 2007.

From the Division of General Internal Medicine and Cardiovascular Prevention and Rehabilitation (RvK), Swiss Cardiovascular Center Berne, Department of Cardiology, University Hospital Berne, Berne, Switzerland; and Behavioral Medicine Program (RvK, SH, MAP, PJM), Department of

Psychiatry, University of California at San Diego, San Diego, California.

Supported by Grants M01-RR-00827-25 and R01 HL-57265-05 from the National Institutes of Health, Bethesda, Maryland.

Address correspondence and reprint requests to Dr. Paul J. Mills, University of California at San Diego Medical Center, 200 W. Arbor Dr., San Diego, CA 92103-0804; e-mail: pmills@ucsd.edu

tion between MAP and the exercise-induced increase in levels of inflammation and thrombogenesis is less pronounced in fit individuals.

To test the above hypotheses, we measured interleukin (IL)-6, sICAM-1, von Willebrand factor (VWF), and plasminogen activator inhibitor (PAI)-1 in plasma. We selected these molecules because they were previously shown to be increased with elevated BP;^{9–11} were predictive of first-time myocardial infarction;^{12–15} and, except for PAI-1, were responsive to physical exercise.^{16–19} Also, they all define paramount processes in atherosclerosis initiation and progression. Although also having anti-inflammatory properties, IL-6 is a potent initiator of the acute-phase response with sympathetic activation.²⁰ Soluble ICAM-1 reflects the endothelial expression of ICAM-1 that facilitates leukocyte transmigration and thereby vascular inflammation.²¹ The VWF mediates platelet adhesion to endothelial lesions; elevated VWF levels reflect a procoagulant state and endothelial activation or damage.²² High levels of antifibrinolytic PAI-1 give rise to intravascular fibrin accumulation.²³

Materials and Methods

Study Participants and Screening BP Assessments

This study was approved by the Institutional Review Board of the University of California at San Diego (UCSD). We recruited 66 healthy volunteers from the community who responded to a newspaper advertisement, other printed material (flyers and pamphlets), or word-of-mouth referral. All participants provided written, informed consent to participate in a study on the effects of fitness and exercise on cardiovascular risk in hypertension. Exclusion criteria included history of heart, liver, or renal disease; diabetes; severe asthma; psychosis; and current use of prescribed medication. These were questioned by self-report during the initial screening visit and verified by a history and physical examination performed by a licensed physician. Current pregnancy was verified by human chorionic gonadotropin screening, and obesity was determined by $>150\%$ ideal body weight.²⁴ Signs of heart disease were examined by electrocardiogram (ECG), and signs of liver or renal disease and diabetes were examined by laboratory liver, metabolic, and thyroid panels before a subject's eligibility was determined. If subjects were taking antihypertensive medication, this was tapered, followed by a 3-week washout period, under close monitoring of BP throughout the duration of the study to ensure safety.

Screening BP was measured three times on two separate days, using a Dinamap vital signs monitor (model 845XT; Critikon, Inc., Tampa, FL), and the mean was computed. We applied an appropriately sized cuff and typically allowed 1 min between readings after subject sat resting for approximately 10 min. We used either screening systolic and/or diastolic BP $\geq 130/85$ mm Hg as the

partition for the designation of hypertension, corresponding to recently published criteria for the definition of "high normal BP levels."²⁵ We selected this cutoff because it yielded two reasonably sized groups of subjects with either "normal BP" ($n = 40$) or "elevated BP" ($n = 26$), allowing us to meaningfully illustrate continuous associations between MAP and outcome variables.

Exercise Test Procedure

Exercise tests were performed at the UCSD Clinical Trials Center and Pulmonary Function Laboratory by a certified cardiopulmonary technician supervised by a physician. To determine the peak oxygen consumption ($\text{VO}_{2\text{peak}}$ [mL/kg/min]), subjects underwent a $\text{VO}_{2\text{peak}}$ test on a treadmill. Termination of the test was based on subjects' indication that they had reached their maximum capacity. The guidelines for verifying obtaining $\text{VO}_{2\text{peak}}$, such as perceived exertion, respiratory exchange ratio >1.0 , or peak heart rate (HR) similar to an age-predicted maximum ($220 \text{ bpm} - \text{age in years}$), were used to confirm that $\text{VO}_{2\text{peak}}$ had been obtained. We applied the standard Bruce protocol, where the speed and grade of the treadmill are increased by 1.7 mph and 10%, respectively, every 3 min. Expired gas was analyzed by use of a Sensormedics metabolic cart (Viasys Healthcare Inc., Conshohocken, PA) equipped with Vmax software (version 6-2A; Viasys Healthcare Inc., Conshohocken, PA), and ECG leads were recorded with Marquette CardioSoft version 3 (GE Medical Systems, Milwaukee, WI). Oxyhemoglobin saturation was monitored with pulse oximetry (Ohmeda; Datex, Louisville, CO). During exercise, BP was assessed by a trained nurse practitioner using a hand sphygmomanometer.

Approximately 1 week after the $\text{VO}_{2\text{peak}}$ test, subjects returned to the laboratory after having abstained from caffeine, vigorous exercise, alcohol, and smoking for 24 h. A 19-gauge venous forearm catheter was inserted, followed by a supine rest period to establish baseline values for the ECG and BP. After a warm-up period, 20 min of exercise were performed on the treadmill at a calculated (ie, 65–70% $\text{VO}_{2\text{peak}}$ assessed) steady-state/submaximal intensity. The VO_2 was monitored throughout the steady-state exercise, to maintain the predetermined intensity, and the subjective exertion was also monitored by Borg's 6–20 scale ratings of perceived exertion (RPE). The BP and RPE were recorded every 3 min during exercise. After the 20-min treadmill test, there was a 2-min cool-down phase, during which subjects walked slowly. Blood samples to assess atherosclerotic markers were obtained with the subject in supine position at "baseline" (ie, pre-exercise), "early postexercise" (ie, levels immediately after the 20-min exercise bout), and "late postexercise" (ie, levels 25 min after termination of the exercise bout).

Measurement of Atherosclerotic Markers

Whole blood was drawn into Vacutainer tubes (Becton Dickinson, Franklin Lakes, NJ) containing either EDTA

Download English Version:

<https://daneshyari.com/en/article/2862703>

Download Persian Version:

<https://daneshyari.com/article/2862703>

[Daneshyari.com](https://daneshyari.com)