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Research Article

Exercise systolic blood pressure variability is associated with increased risk for new-onset hypertension among normotensive adults

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Abstract

Both resting blood pressure (BP) variability and exercise BP previously showed association with incident hypertension. The aim of the present study was to examine whether visit-to-visit variability in exercise systolic blood pressure (SBP) can predict the risk for new-onset hypertension among normotensive adults. We investigated 6546 normotensive men and women who were annually screened in a tertiary medical center and completed treadmill exercise tests at each visit. Based on the initial three baseline annual visits, long-term intervisit variability of exercise SBP among the three tests was measured using standard deviation (SD) and coefficient of variation for each participant. The rate of newly diagnosed hypertension was measured in different variability levels during 6 ± 3 years of follow-up. Multivariate analysis adjusted for various clinical factors, including resting BP, showed that each 5 mm Hg rise in the SD of exercise SBP resulted in a significant 5% increase in the risk for the development of future hypertension ($P = .015$). Subjects in the upper exercise SBP SD variability tertile had a 28% ($P = .007$) increased risk for hypertension during follow-up, as compared with those in the lowest tertile. Similar results were achieved for the assessment of coefficient of variation of exercise SBP. In conclusion, visit-to-visit variability in exercise SBP can predict the development of future hypertension among normotensive individuals. J Am Soc Hypertens 2016;10(6):527–535.

Keywords: Exercise; hypertension; systolic blood pressure; variability.

Introduction

Essential hypertension is a widespread condition in the adult population and a well-known risk factor for the development of atherosclerosis, as well as morbidity and mortality from cardiovascular diseases (CVDs). Because of its significant burden on public health, attempts have been taken to improve the detection of patients at risk for development of future hypertension and associated CVD.[1]

Several studies have focused on blood pressure (BP) variability as a potential risk factor. Personal BP variability can be considered as short term, such as circadian changes, or long term, such as changes between annual office visits.[2] Data from a recent study suggested that long-term visit-to-visit variability in resting systolic blood pressure (SBP) values may have prognostic significance that is similar or even stronger than average BP.[3] Moreover, it was shown that children with visit-to-visit variability in resting SBP

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and diastolic BP (DBP) were more likely to develop future hypertension as adults.[4] Another risk factor to be considered is exercise BP, which has been found to be associated with the development of incident hypertension and CVD. Both exaggerated SBP and DBP during exercise tests (exercise stress test [EST]) were linked to increased risk for future hypertension among healthy individuals.[5–10]

To our knowledge, the association between visit-to-visit variability in BP responses to exercise and the development of new-onset hypertension has not been studied yet. Accordingly, the primary objective of the present study was to examine whether exercise BP variability is a predictor of future hypertension among normotensive individuals.

Methods

Study Population

The study population was described previously.[7,11] Briefly, the Institute for Medical Screening of the Chaim Sheba Medical Center performs nearly 9000 examinations annually. Data for the present study were retrieved from a computerized database established in the year 2000. All participants were asymptomatic men and women attending periodic health screening examinations as private individuals or as part of health executive programs. Each annual examination includes a standard questionnaire regarding their demographic characteristics, medical history, lifestyle, and health-related habits, as well as any unusual medical event since the previous visit. The questionnaire includes a dichotomous evaluation of self-reported physical activity and smoking status, in the form of yes/no questions. At each encounter, the height and weight of all participants are measured, together with a physical examination, BP measurement using a standard sphygmomanometer, and laboratory blood tests that are analyzed at the center's laboratory. The Institutional Review Board of the Sheba medical center approved this study on the basis of strict maintenance of participants' anonymity during database analyses (approval number 8995-11-SMC). Data from subjects were recorded anonymously. No individual consent was obtained.

Inclusion and Exclusion Criteria

The complete database included 25,890 subjects. Inclusion criteria for the study included at least four annual consecutive visits to the center with exercise BP documented (three baseline visits and at least one additional visit to evaluate outcome). Subjects were excluded if: (1) they had fewer than four visits (n = 14,441); (2) had a diagnosis of hypertension in any of the three baseline visits, were using antihypertensive medications, or had a history of CVD, as defined by their primary care physicians (n = 2508); and (3) had no three consecutive and complete EST documentations (n = 452) or had longer than a 2-year gap between two consecutive visits (n = 1407). To focus on subjects with a truly normal-range BP, without abnormal or extreme baseline characteristics, we excluded subjects with a 3-year average resting SBP $\geq$ 140 or DBP $\geq$ 90, based on measurements from the initial three visits (n = 536). The final study sample comprised 6546 individuals.

Resting and Exercise BP Assessment

Over 3 years and at each annual examination, office resting BP was obtained, after 5 minutes of rest, in the left arm in the seated position by an examining nurse using a mercury column sphygmomanometer, according to recent guidlines.[12] A maximal EST according to the Bruce protocol was taken under the supervision of and interpreted by a board certified cardiologist at each annual visit.[13] Participants were encouraged to achieve their maximal age-specific target heart rate, and the test was terminated due to exhaustion or due to angina or other medical reasons. Participants who did not complete the entire EST for any reason were excluded from the study. During exercise, BP was recorded at the end of each 3-minute stage, at peak exercise, and during recovery. Exercise SBP and DBP were defined according to their absolute values at peak exercise. Measurements from the three baseline visits were used to calculate the average resting and exercise DBP and SBP. EST duration time was used to calculate metabolic equivalents (METS) based on well-characterized regression equations.[14]

Exercise BP Variability Analysis

Exercise BP visit-to-visit variability was determined by the standard deviation (SD) and coefficient of variation (CV) of SBP peak exercise values among the first three exercise tests. Study population was divided into tertiles based on exercise BP variability. SD of exercise SBP tertiles cutoff values was: $\leq$10 mm Hg, 10–15.3 mm, Hg and $\geq$15.3 mm Hg. CV of exercise SBP was similarly divided into tertiles ($\leq$6.0%, 6.0%–9.8%, and $\geq$9.8%). The risk for new-onset hypertension in each tertile was compared to the lowest tertile. In a secondary analysis, exercise DBP variability was also assessed. SD of exercise DBP tertiles cutoff values was: $\leq$ 2.9 mm Hg, 2.9–5.8 mm Hg, and $\geq$5.8 mm Hg; and CV of exercise DBP tertiles was $\leq$6.9%, 6.9%–7.9%, and $\geq$7.9%. To further validate the consistency of the tertile analyses, both SD and CV of SBP and DBP exercise values were also assessed as continuous measures.

For all participants, the following parameters from the initial baseline visit were recorded: Age, sex, body mass index (BMI), low-density lipoprotein, high-density lipoprotein, total cholesterol, triglycerides (TGs), and glucose levels. Estimated glomerular filtration rate was estimated according to the Modification of Diet in Renal Disease Study equation.[15] Smoking status was determined by the