HHS Public Access

Author manuscript

J Am Coll Cardiol. Author manuscript; available in PMC 2018 October 10.

Published in final edited form as:

J Am Coll Cardiol. 2017 October 10; 70(15): 1941–1943. doi:10.1016/j.jacc.2017.08.011.

Submaximal blood pressure responses to exercise in young adulthood and long-term cardiovascular health

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Hypertension is a leading cause of cardiovascular disease (CVD). Although resting BP is accessible and predicts CVD, dynamic BP changes during normal living are also important. Relationships between exercise-based measures of altered vascular reserve (e.g., exercise BP) in young adults and future CVD are underexplored and may offer mechanistic insights into CVD development across the life course. Accordingly, we measured association of submaximal exercise BP with risk factors, vascular calcium, and CVD in the Coronary Artery Risk Development in Young Adults (CARDIA) study participants without resting hypertension who underwent treadmill exercise testing. Individuals who withdrew consent (N=1), had missing pre-exercise systolic or diastolic BP or heart rate (N=202), hypertension (N=826), significant resting tachycardia (rate>120 beats/min; N=21), or missing BP or heart rate during submaximal exercise (N=209) were excluded.

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[†]With special acknowledgement to Dr. James Gregory Terry (Vanderbilt University, Nashville, TN), Dr. Samuel Gidding (Nemours Cardiac Center, Wilmington, DE), Dr. Mercedes Carnethon (Northwestern University, Chicago, IL)

Conflict of Interest: Dr. Shah is a consultant for MyoKardia, which had no role in this research.

Exercise testing was performed according to a modified Balke protocol(1). BP was measured with a mercury sphymomanometer by a study technician at rest and at 1:30 of each stage. For this analysis, we used submaximal measurements (stage 2; second 2 minutes of exercise protocol, 6.4 METs) to standardize workload. Outcomes included coronary arterial and abdominal aortic calcification (CAC, AAC, respectively)(2) and incident CVD events. CVD events were comprised of non-fatal myocardial infarction or stroke; coronary revascularization or hospitalization for non-MI acute coronary syndrome; hospitalization for congestive heart failure, or transient ischemic attack; revascularization for angiographically or ultrasound-demonstrated obstruction of carotid arteries or peripheral arterial disease; fatal atherosclerotic coronary heart disease, fatal stroke, fatal atherosclerotic disease other than coronary or stroke, and fatal non-atherosclerotic cardiac disease. Participants free of CVD events were censored first occurrence of non-CVD death, last contact, or August 31, 2014.

Logistic regression estimated the association of submaximal BP with calcification metrics, adjusted for age, sex, race, resting systolic or diastolic BP and CVD risk factors. Cox regression estimated submaximal BP relationship with CVD over 28 years, adjusted for age, race, sex, parental history of myocardial infarction (at younger than 60 years), exercise test duration, body mass index, diabetes, cigarette smoking (cigarettes/day), total cholesterol, high-density lipoprotein, and baseline BP, collected at baseline study visit. We performed a sensitivity analysis adjusting each regression for time-dependent development of hypertension over follow-up. SAS 9.3/9.4 (SAS Institute, Cary, NC) was used for all analyses. A two-tailed $P<0.05$ was statistically significant.

Our sample consisted of 3,856 participants (median age 25 years; interquartile range IQR 22–28 years), 43% male, 49% African American, with a median body mass index (BMI) 23 kg/m^2. Resting systolic and diastolic BP were normal (median resting systolic BP [SBP] 114 mmHg; diastolic BP [DBP] 76 mmHg). When stratified by tertiles of stage 2 (submaximal) SBP, the highest tertile of BP response had a greater proportion of African-Americans and males with greater cardiometabolic risk (by dyslipidemia, glucose, waist circumference, and BMI). At the Year 25 examination in CARDIA, 638 individuals (26%) had CAC>0, and 1231 (51%) had AAC. After adjustment (including for resting BP), mean arterial pressure [MAP] and DBP were both associated with CAC, but not AAC (Table). At a median 27.8 years (interquartile range 27.7–28.0 years), each 10-mmHg higher submaximal SBP, DBP, and MAP were associated with an increased multivariable-adjusted hazard of long-term clinical CVD (Table). There was no effect modification of submaximal BP measures by race or sex on CVD (interaction $P>0.05$). The association between submaximal MAP during exercise and CVD persisted after adjustment for time-dependent hypertension development (Table).

In conclusion, increase in BP with submaximal exercise in young adults is linked to vascular calcification and CVD over 25 years. These results suggest a complex interplay between components of exercise responses in downstream CVD: while exercise time (a marker of fitness) impacts myocardial (but not necessarily vascular calcification) phenotypes(3), BP responses early during exercise in young adults may mark future vascular risk. Ultimately, the observation that distinct components of exercise response at a very early stage in CVD may impact the heart and vascular system differently suggests that exercise may provide

prognostic, therapeutically relevant information, even in young adults without resting hypertension.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table

Regression models for incident vascular calcification, hypertension, and CVD. Time-dependent hypertension adjustment was performed for incident CVD. Details of adjustment are included in the manuscript's text.

Outcome	Number of Cases/Total Participants	Submaximal Systolic BP (per 10 mmHg)		Submaximal Mean Arterial Pressure (per 10 mmHg)		Submaximal Diastolic BP (per 10 mmHg)	
		Odds (or Hazard) Ratio (95% CI)	P	Odds (or Hazard) Ratio (95% CI)	P	Odds (or Hazard) Ratio (95% CI)	P
Coronary artery calcification							
Presence at Y25	626/2407	1.03 (0.97–1.10)	0.32	1.17 (1.03–1.32)	0.01	1.13 (1.02–1.26)	0.03
>100 at Y25	197/2407	1.07 (0.97–1.18)	0.18	1.29 (1.07–1.56)	0.008	1.20 (1.02–1.42)	0.03
Abdominal aortic calcification							
Presence at Y25	1202/2359	1.06 (1.00–1.12)	0.06	1.03 (0.93–1.15)	0.54	0.96 (0.87–1.05)	0.36
Incident CVD	135/3782	1.12 (1.01–1.24)	0.03	1.35 (1.12–1.64)	0.002	1.22 (1.01–1.46)	0.04
With time-dependent hypertension adjustment		1.10 (0.99–1.21)	0.06	1.32 (1.09–1.60)	0.004	1.21 (1.00–1.45)	0.05