Original Article

Association between cardiorespiratory fitness and submaximal systolic blood pressure among young adult men: a reversed J-curve pattern relationship

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Objectives: Exercise blood pressure is a marker of future cardiovascular morbidity and mortality among individuals with or without high resting BP or any other cardiovascular disease (CVD) signs and symptoms at present. The purpose of this study was to evaluate the association between SBP during submaximal exercise and cardiorespiratory fitness (CRF) among young men. Further, we investigated the trend displayed by submaximal SBP (SSBP) across different levels of CRF.

Methods: Graded exercise test (GXT) using a Modified Bruce protocol was performed on 204 men; SSBP was recorded at each stage of the protocol. Quintiles of CRF were established on the basis of peak oxygen consumption (VO_2), with the first quintile (Q) being the lowest fit group and fifth Q the most fit.

Results: The mean VO_2 peaks in Q 1 through 5 were 32.3, 39.1, 43.4, 48.1 and 55.5 ml/kg per min, respectively. In a model adjusted for age, race, body fat percentage, resting SBP, alcohol intake and smoking, the largest difference in SSBP was observed between men in Q 1 and 2, with 7.6 mmHg ($P = 0.05$), 9.4 mmHg ($P = 0.02$) and 9.5 mmHg ($P = 0.04$) lower SSBP at minutes 6, 8 and 10 of GXT, respectively. SSBP plateaus at Q 3, followed by an increase in the higher Qs, although still lower than Q1.

Conclusion: There was a reverse J-curve pattern relationship between SSBP and CRF, with the lowest SSBP among men with fair or good CRF and highest among those with poor CRF.

Keywords: cardiorespiratory fitness, cardiovascular diseases, hypertension, submaximal exercise, SBP

Abbreviations: BP , blood pressure; CHD, coronary heart disease; CRF, cardiorespiratory fitness; CVDs, cardiovascular diseases; DXA, dual X-ray absorptiometry; EDV, endothelium-dependent vasodilation; GXT, graded exercise test; LVH, left ventricular hypertrophy; SSBP, submaximal SBP; VO_2, oxygen consumption

INTRODUCTION

Cardiovascular diseases (CVDs) are the leading cause of death globally, as more people die annually from CVDs than from any other causes [1]. CVD deaths are projected to increase to nearly 23.3 million annually by 2030 [1,2]. About 600 000 people die of CVD in the United States every year, thus representing nearly one in every four deaths [3]. Exercise blood pressure (BP) is an important marker of CVD events, such as incident hypertension [4–8], myocardial infarction [9,10], stroke [11] and CVD mortality [12,13] among individuals with or without high resting BP or overt CVD signs at present. A study has reported that among middle-aged men without a history of coronary heart disease (CHD), an exaggerated exercise BP response may account for 4.31 times higher risk for myocardial infarction [9]. SBP during submaximal exercise at and after 6 min of exercise has been investigated extensively, and generally higher submaximal SBP (SSBP) is an excellent predictor of left ventricular hypertrophy (LVH) [14–16], which is a major predictor of CVD mortality [17]. Exaggerated SBP during exercise among 426 normotensive individuals was associated with higher atherosclerotic markers, which signifies that despite no apparent symptoms or signs of CVD, an end-organ damage is occurring and this could potentially later lead to an increased risk of CVD events [18].

Low levels of cardiorespiratory fitness (CRF) are associated with a higher risk of CVD and hypertension [19–25]. It is also known that the risk of having metabolic syndrome is higher in those with lower levels of CRF [26,27]. Almost two decades ago, researchers reported that CRF was associated with lower SSBP after 7 years among middle-aged healthy men [28]. Moreover, Kokkinos *et al*. [29] observed that there was an association between low CRF and higher SSBP response after 6 min of exercise in a population of 1411 normotensive and hypertensive women. A recent study

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reported that lower SSBP was independently associated with higher CRF among older adults with untreated pre-hypertension or mild hypertension [30]. A previous study presented evidence suggesting that aerobic exercise training in African-Americans with severe systemic hypertension attenuates an exaggerated BP during exercise [31]. Other research shows that both aerobic training and regular vigorous exercise significantly reduces SSBP [32,33]. Clinical and experimental studies have linked the effect of CRF on all-cause mortality to improved vascular endothelial function [34–36].

To the best of our knowledge, there is no study demonstrating the relation and trend between SSBP and CRF among young healthy men. Therefore, the purpose of this study is to examine the association between SSBP and CRF after 6 min of exercise during graded exercise test (GXT) in young healthy men. Further, we assessed the trend displayed by SSBP across a broad spectrum of CRF.

MATERIALS AND METHODS

Participants and enrolment process

The participants in this investigation were drawn from the Energy Balance Study, a prospective observational study [37]. A sample of 204 normotensive (resting BP <140/90 mmHg) men aged 21–35 years with a BMI between 20 and 35 kg/m^2 was included in the analysis. Exclusion criteria included use of medications to lose weight, started or stopped smoking in the previous 6 months, or planned weight loss surgery. Further, men were excluded for resting BP exceeding 150 mmHg systolic and/or 90 mmHg diastolic, an ambulatory blood glucose level of greater than 145 mg/dl or those currently diagnosed with or taking medications for a major chronic health condition. Men with a history of anxiety, depression or panic were excluded, as were those taking selective serotonin inhibitors for any reason. Informed consent was obtained from every man prior to data collection.

Anthropometry

All anthropometric measurements were performed with the participant wearing surgical scrubs and in bare feet; BMI (kg/m^2) was calculated from the average of two height and weight measurements. Body fat was measured using a dual X-ray absorptiometry (DXA) scanner and used to calculate BF%.

Exercise testing procedure

A trained exercise physiologist prepared participants for the GXT, including a standard 12-lead ECG and BP measurement; BP cuff of a manual auscultatory sphygmomanometer was placed on the left arm of the individual followed by an examination of the pre-exercise BP, resting ECG and heart rate (HR). Once the participant is cleared for participation in terms of pre-exercise BP (≤150/80 mmHg) and ECG, the GXT is administered using a Modified Bruce protocol on a motorized treadmill. The first three stages (6 min) of the modified Bruce GXT were for warming up at a slow speed of 1.7 mph at 0, 5 and 10% grade, respectively. After 6 min of GXT, both the speed and grade increased every 2 min. Speed and grade at minutes 6, 8 and 10 were 1.7 mph, 10%; 2.5 mph, 12%; 3.4 mph, 14%, respectively. All individuals exercised to volitional fatigue and criteria for a maximal test included two of the following variables: a respiratory quotient at least 1.15, rate of perceived exertion at least 17 using the Borg scale of perceived exertion, achieved age predicted max HR and oxygen consumption (VO_2) or HR plateaued with increasing workload. A maximal test criterion was achieved by a majority of the men (89.1%). CRF was defined as the VO_2 peak during the GXT. SSBP was recorded after 90 s in each stage of the protocol by a trained staff member. The individual was instructed to rest their left arm on the shoulder of the staff at each stage of GXT to examine the SSBP. They were also instructed to keep their palm facing up to avoid gripping of the staff's shoulder and getting an external support, as it was examined while the individual was walking/running on the treadmill.

Smoking history was recorded by providing the individuals a medical history questionnaire and alcohol intake was calculated from multiple, telephone-administered 24-h dietary recall interviews. Resting SBP was calculated from an average of two measurements recorded using manual sphygmomanometer by trained technicians. A third measurement was taken if the difference in SBP was more than 10 mmHg for the first two measurements. All study protocols were approved by the University of South Carolina Institutional Review Board.

Statistical analysis

Quintiles (Qs) of CRF were established, with Q 1 representing the group of men with lowest CRF, whereas Q 5 represented those with the highest CRF. One-way analysis of variance (ANOVA) was used to determine the means across all the Q of CRF. Chi-square was used to calculate the number of men who were white and who ever smoked. Multivariate analyses including potential covariates (age, race, BF%, resting SBP, alcohol intake and smoking) were performed to determine the association between SSBP at various exercise stages and Q of CRF. Analyses were done using SPSS version 22 (IBM, Armonk, New York, USA) with P value less than 0.05 for statistical significance.

RESULTS

Table 1 summarizes the descriptive statistics for men in various Qs of CRF; Mean VO_2 peak ± SD in Q 1 through Q 5 were 32.3 ± 3.5, 39.1 ± 1.8, 43.4 ± 1.0, 48.1 ± 1.5, 55.5 ± 3.0, respectively. Categorizing the mean VO_2 peak according to the American College of Sports Medicine Guidelines for Exercise Testing and Prescription [38] displayed a broad spectrum of CRFs, which appeared to skew towards the higher end of CRF distribution; Q 1 was more likely to represent poor CRF, Q 2 fair CRF, Q 3 good CRF, Q 4 excellent CRF and Q 5 superior CRF levels. However, there was no quintile that represented a very poor CRF level. Age, resting SBP, alcohol intake and smoking history did not differ significantly across the Q of CRF, but there were significant differences in CRF, weight, BF%, BMI and race ($P < 0.01$).

A significant quadratic trend was displayed by SBP during SE across the Qs of CRF at minutes 6, 8 and 10 of the GXT (P value for quadratic trend ≤0.02) (Table 2).

TABLE 1. Means ± SD of descriptive variables across the quintiles of cardiorespiratory fitness

	Quintile 1 ($N=40$)	Quintile 2 ($N=42$)	Quintile 3 ($N=40$)	Quintile 4 ($N=41$)	Quintile 5 ($N=41$)	P^a
Age (years)	28.7 ± 3.7	27.3 ± 3.8	27.6 ± 3.7	27.6 ± 4.1	26.3 ± 3.7	0.11
VO_2 peak	32.3 ± 3.5	39.1 ± 1.8	43.4 ± 1.0	48.1 ± 1.5	55.5 ± 3.0	<0.01
Weight (kg)	90.2 ± 15.8	83.0 ± 12.7	79.5 ± 11.9	79.9 ± 8.8	75.0 ± 6.7	<0.01
Body fat %	30.6 ± 5.6	24.4 ± 7.1	21.9 ± 5.4	20.2 ± 5.5	16.5 ± 4.8	<0.01
BMI ($kg/m^{2)}$	28.5 ± 3.8	25.9 ± 3.3	24.5 ± 2.8	25.4 ± 2.1	23.5 ± 2.0	<0.01
Resting SBP (mmHg)	128.0 ± 10.3	126.6 ± 11.6	123.8 ± 12.1	129.0 ± 10.0	126.6 ± 11.8	0.29
Alcohol (g/day)	9.1 ± 29.5	8.4 ± 14.3	13.9 ± 23.6	17.8 ± 21.0	15.6 ± 25.9	0.29
Race (whites) %	52.5	59.5	62.5	75.6	87.8	<0.01
Ever smoked (N)	30.0	23.8	30.0	36.6	21.9	0.89

VO_2, oxygen consumption.
[a]P value is for quadratic trend.

TABLE 2. Means of submaximal SBP across various quintiles of cardiorespiratory fitness (Crude model)

	Quintile 1 ($N=36$)	Quintile 2 ($N=41$)	Quintile 3 ($N=39$)	Quintile 4 ($N=39$)	Quintile 5 ($N=40$)	P^a
Minute 6	158.6 (153.0–164.2)	148.6 (143.4–153.9)	147.3 (141.9–152.7)	153.3 (147.9–158.7)	153.0 (147.7–158.3)	0.01
Minute 8	170.7 (165.0–176.3)	158.7 (153.4–164)	157.9 (152.5–163.3)	164.5 (159.0–169.9)	163.4 (158.0–168.7)	<0.01
Minute 10	183.7 (177.1–190.2)	171.7 (165.5–177.8)	165.5 (159.2–171.8)	178.0 (171.7–184.3)	176.1 (169.9–182.3)	<0.01

[a]P value is for quadratic trend.

TABLE 3. Means of submaximal SBP across various quintiles of cardiorespiratory fitness (adjusted model)

	Quintile 1 ($N=35$)	Quintile 2 ($N=41$)	Quintile 3 ($N=39$)	Quintile 4 ($N=38$)	Quintile 5 ($N=40$)	*P
Minute 6	156.0 (149.8–162.2)	148.4 (143.4–153.3)	149.2 (144.2–154.2)	152.9 (147.7–158.1)	154.5 (148.9–160.1)	0.03
Minute 8	167.9 (161.6–174.3)	158.5 (153.4–163.5)	159.5 (154.3–164.7)	164.1 (158.8–169.4)	165.3 (159.6–171.0)	0.01
Minute 10	180.6 (173.2–188.0)	171.1 (165.1–177.0)	167.4 (161.3–173.4)	177.6 (171.4–183.9)	178.5 (171.7–185.2)	<0.01

Adjusted for age, race, body fat percentage, SBP, alcohol intake and smoking history.
*P value is for quadratic trend.

Compared with men in CRF Q 1, those in Q 2 and Q 3 had significantly lower SSBP, whereas there was no significant difference among those in CRF Qs 4 and 5. However, the mean values in Qs 4 and 5 were lower than Q 1. The quadratic trend remained significant across all the time points after adjustment of potential confounders, including resting SBP, body fat percentage, age, race, smoking and alcohol intake. In an adjusted model (Table 3), the largest difference in SSBP was observed between men in Q 1 and Q 2, those achieving a VO_2 peak of 39.1 ± 1.8 ml/kg per min versus those achieving 32.3 ± 3.5 ml/kg per min, with 7.6 mmHg ($P=0.05$), 9.4 mmHg ($P=0.02$) and 9.5 mmHg ($P=0.04$) lower SSBP at minutes 6, 8 and 10, respectively. SSBP plateaus at Q 3, among those achieving a VO_2 peak of 43.4 ± 1.0 ml/kg per min, followed by an increase in the higher Qs, with VO_2 peaks of 48.1 ± 1.5 and 55.5 ± 3.0 ml/kg per min. Figure 1 displays a quadratic trend between SSBP and CRF adjusted for the covariates at minutes 6, 8 and 10 of the GXT, showing a decrease in SSBP, followed by plateauing and then, finally, an increase.

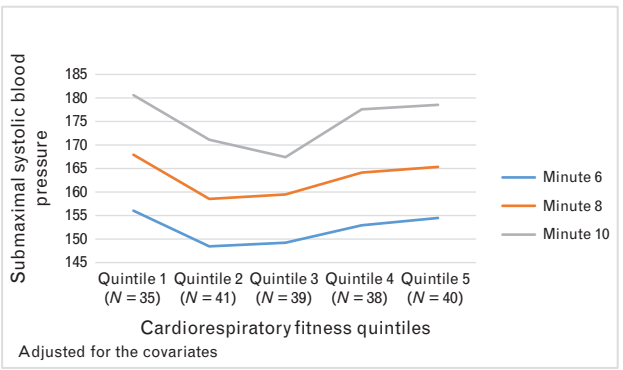

FIGURE 1 Trend displayed between submaximal SBP and cardiorespiratory fitness.

Results were similar when an association between delta SBP (calculated for minutes 6, 8 and 10 by subtracting resting SBP from SSBP at each time point) and CRF was examined with quadratic P values 0.03, 0.01, 0.004, respectively. There was a reverse J-curve pattern with lowest delta SBP in Qs 2 and 3 and the highest in quintile 1. Delta SBP in Qs 4 and 5 was higher than Qs 2 and 3 but lower than Q 1.

DISCUSSION

There was no significant association between resting SBP and CRF; however, a significant quadratic relationship was noted between SSBP and CRF; resting SBP did not differ significantly between the CRF quintiles. The results demonstrate a reverse J-curve pattern relationship between SSBP and CRF. Fair CRF (Q 2) when compared with poor CRF (Q 1) was associated with a significantly lower SSBP at minutes 6, 8 and 10 of GXT. SSBP plateaued with a further increase in CRF among men with good CRF (Q 3). Moreover, a slightly higher SSBP among men with excellent and superior CRF (Q 4 and Q 5) than fair and good (Q 2 and Q 3) indicated a reversed J-curve pattern. Metabolic demands at and after 6 min of exercise on GXT are similar to the

demand of most routine daily activities; it is likely that the cardiac workload during such activities is relatively low in men with fair and good CRF compared with poor and extremely fit men.

Previous studies have provided evidence that improving CRF from poor to fair to good is one of the cornerstones of therapeutic behavioural changes for better CVD prognosis and overall survival [19,20,39,40]. Among middle-aged men and women, the health benefits due to improvements in the CRF plateau at the VO_2 of 35.0 and 31.5, respectively, with no further survival benefit compiling from higher CRF levels [19,41]. Studies have shown that the maximum difference in mortality is between CRF Q1 and Q2 or lowest CRF and the next lowest CRF categories [19,41], with a further decline accruing from an increase in CRF followed by a plateau [19,41,42]. Moreover, recent studies have also shown that there could be a loss of cardiovascular health benefits, to some extent, with extreme levels of CRF and exercise producing a J-curve pattern between CRF and cardiovascular prognosis [42–45]. Data have shown that despite the extraordinary CRF, cardiovascular abnormalities in marathon runners are reported each year [46]. Our data include men with a broad CRF distribution consisting of extremely higher levels, which could be the potential factor that is resulting in a J-curve pattern association.

Although our study design does not allow us to determine the specific mechanisms responsible, the findings generate some speculation. Exercise or physical conditioning helps in reducing the work of the heart during submaximal workloads, leading to lower HR at a given cardiac output [47], which could be partially explained by the mechanism of the Frank Starling law (increased left ventricular ejection resulted from improved diastolic function) [48], and by reduced afterload due to lower total peripheral resistance [47]. Increased CRF is associated with lower arterial stiffness among healthy adults [49]. Studies have suggested a positive relation of CRF and exercise with vasodilator nitric oxide formation and its bioactivity among healthy individuals [50,51]. Moreover, another study among individuals with chronic heart failure has reported that exercise training improves both vascular endothelial nitric oxide formation and agonist-mediated endothelial-dependent vasodilation (EDV) of the skeletal muscle vasculature that could lead to correction of endothelial dysfunction [34]. Exaggerated SSBP could be attributed to endothelial dysfunction defined as reduced EDV and pro-inflammatory condition in the vasculature [52]. Primary cause for endothelial dysfunction is decrease in production and bioactivity of nitric oxide and increase in vasoconstrictor endothelin, which potentially leads to arterial stiffness and reduced EDV [53] followed by reduced ability to buffer the increase in SBP during exercise [54].

At the other end of CRF spectrum, cardiac overuse could potentially be the cause for increasingly common consequence of overdosing of exercise [45,55], which may be associated with adverse outcomes, including accelerated coronary calcification, early ageing of the heart, LVH and cardiac muscle fibrosis [43,56]. Extreme exercise may also amplify oxidant stress and transiently stiffen blood vessels [57,58]. LVH may lead to an increase in SSBP during submaximal workload due to a higher force of systolic contraction, while arterial stiffening weakens the ability of the arteries to buffer the rise in SSBP generated by left ventricular ejection [54].

To the best of our knowledge, this is the first study demonstrating the association between SSBP and CRF among men aged 21–35 years. Our data represent men with a broad range of CRF, which is useful in displaying the trend at both ends of CRF spectrum; however, it should be noted that the overall CRF trend was skewed towards higher CRF levels with no quintile having very poor CRF. Furthermore, our data consist of SSBP at various time points of GXT, with similar trends evident at various stages after 6 min. Manual auscultatory sphygmomanometer and not the automated sphygmomanometer was used to measure resting, pre-exercise and exercise BP, which is considered to be more accurate [59].

Several study limitations should be emphasized. A majority of the participants enrolled in the study were non-Hispanic whites and with moderate to high socioeconomic status. In addition, a large percentage of this population was from the university campus, including students and staff, so future research must determine whether these results are generalizable to other populations. A small percentage of data (5.4%) was lost due to missing SSBP and a covariate, alcohol intake history. Failure in measurement of SSBP during the GXT was mainly due to staff being unable to hear the Korotkoff sound during BP measurement; however, the characteristics of men who were lost in the analysis were similar to those present in the analysis. Finally, as with any other cross-sectional study, causality between the dependent variable (SSBP) and independent variable (CRF) cannot be established.

In conclusion, there was a reverse J-curve pattern relationship between SSBP and CRF, suggesting that men with poor CRF had the highest SSBP, whereas the lowest SSBP was noted in men with fair and/or good CRF. It is comforting to know that fair to good levels of CRF, which is easily obtainable in most with poor CRF by simply obtaining modest amounts of PA, are associated with lower SSBP, which could translate into favourable cardiovascular prognosis.

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Conflicts of interest

There are no conflicts of interest.

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