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FULL RESEARCH PAPER
Exercise physiology & testing

Blood pressure response to graded bicycle exercise in males and females across the age and fitness spectrum

Kristel Janssens [1,2]*, Stephen J. Foulkes [2,3], Amy M. Mitchell [2], Christophe Dausin [4], Sofie Van Soest [5], Luke Spencer [2,6], Stephanie J. Rowe [2,6,7], Paolo D'Ambrosio [2,6], Adrian D. Elliott [8], Tim Van Puyvelde [2,5], Evelyn B. Parr [1], Rik Willems [5,9], Hein Heidbuchel [10,11], Guido Claessen [9,12], and Andre La Gerche [2,6,7,13]

[1]Exercise and Nutrition Research Program, The Mary MacKillop Institute for Health Research, ACU, Level 5, 215 Spring Street, Melbourne, VIC 3000, Australia; [2]Heart, Exercise and Research Trials (HEART) Lab, St. Vincent's Institute of Medical Research, 9 Princes Street, Fitzroy, Melbourne, VIC 3065, Australia; [3]Integrated Cardiovascular Exercise Physiology and Rehabilitation Lab, Faculty of Nursing, University of Alberta, Edmonton, Canada; [4]Department of Movement Sciences, Exercise Physiology Research Group, KU Leuven, Leuven, Belgium; [5]Department of Cardiology, UZ Leuven, Leuven, Belgium; [6]Department of Medicine, The University of Melbourne, Melbourne, Australia; [7]Department of Cardiology, St. Vincent's Hospital Melbourne, Melbourne, Australia; [8]Centre for Heart Rhythm Disorders, University of Adelaide and Royal Adelaide Hospital, Adelaide, Australia; [9]Department of Cardiovascular diseases, KU Leuven, Leuven, Belgium; [10]Department of Cardiovascular Sciences, University of Antwerp, Antwerp, Belgium; [11]Department of Cardiology, University Hospital Antwerp, Antwerp, Belgium; [12]Faculty of Medicine and Life Sciences, UHasselt, Biomedical Research Institute, Hasselt, Belgium; and [13]HEART Lab, Victor Chang Cardiovascular Research Institute, Sydney, Australia

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Aims

Blood pressure (BP) responses to exercise are frequently measured, with the concern that greater increases are a marker of disease. We sought to characterize the normal exercise BP response in healthy adults and its relationships with age, sex, and fitness.

Methods and results

Five hundred and eighty-nine participants [median age 46 (interquartile range 24–56) years, 81% male] underwent cardiopulmonary exercise testing with repeated, automated BP measures. An exaggerated maximal systolic BP (SBP_{max}) was defined from current guidelines as ≥210 mmHg in males and ≥190 mmHg in females. Individual linear regression analyses defined the relationship between BP and workload (W; SBP/W-slope and DBP/W-slope). Participants with or without an exaggerated SBP_{max} and above- or below-median SBP/W-slope were compared. An exaggerated SBP_{max} was found in 51% of males and 64% of females and was more prevalent in endurance-trained athletes (males 58%, females 72%, $P < 0.001$). The mean SBP/W-slope was lower in males (0.24 ± 0.10 mmHg/W) than females (0.27 ± 0.12 mmHg/W, $P = 0.031$). In both sexes, peak oxygen uptake (VO_{2peak}) was inversely correlated with SBP/W-slope ($P < 0.01$). Those with an exaggerated SBP_{max} and below-median SBP/W-slope were 10 years younger and had a 20% higher VO_{2peak}, on average ($P < 0.001$). A non-exaggerated SBP_{max} and above-median SBP/W-slope was observed in older individuals with the lowest VO_{2peak}.

Conclusion

In a large cohort of healthy individuals, an exaggerated SBP_{max} was common and associated with higher fitness. In contrast, higher SBP indexed to W was associated with older age, lower fitness, and female sex. Thus, sex, age, and fitness should be considered when evaluating BP response to exercise.

Registration

Pro@Heart: NCT05164328, ACTRN12618000716268; ProAFHeart: ACTRN12618000711213; Master@Heart: NCT03711539

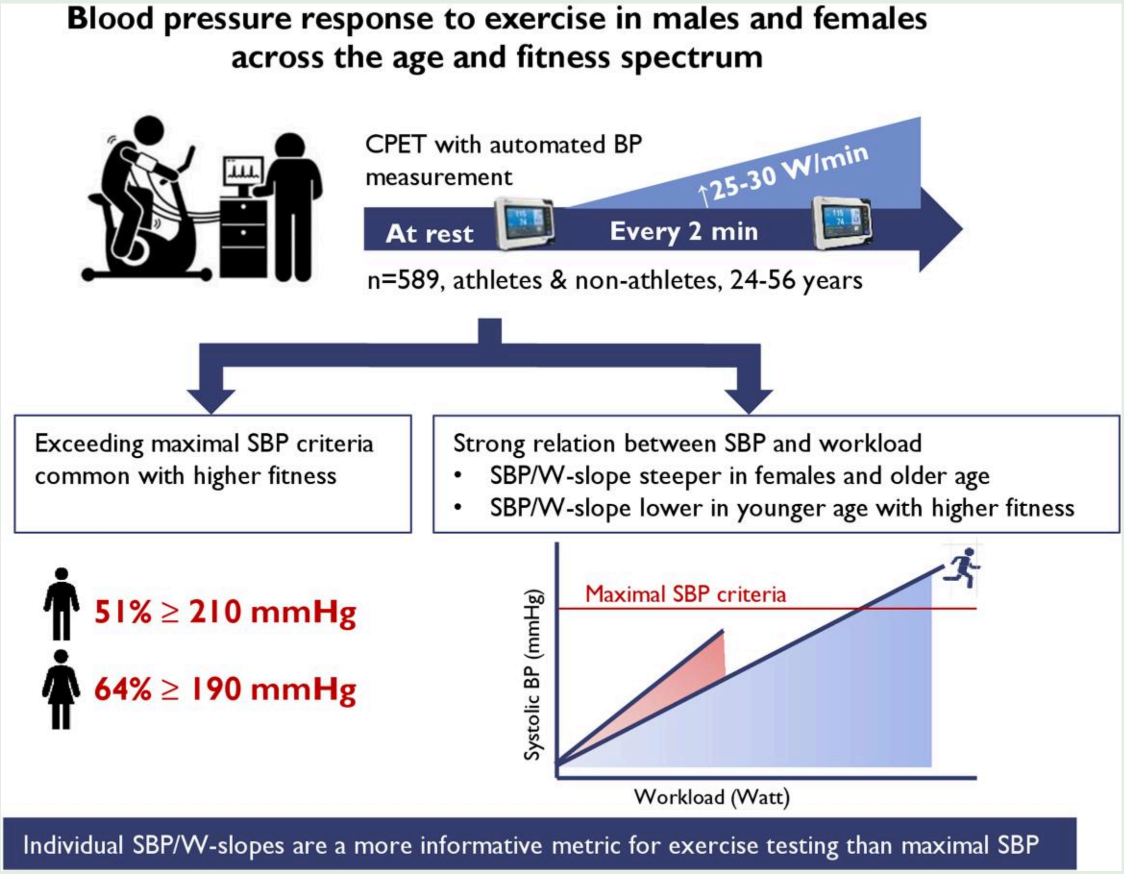
Lay summary

We evaluated the predictors of blood pressure (BP) responses to exercise in 589 healthy individuals. We showed that there is a strong, positive relationship between the increase in systolic BP (SBP) during exercise with cardiorespiratory fitness and exercise workload (W).

- During intensive exercise, high maximal SBPs are more prevalent in young fit individuals than older, less-fit individuals. Systolic blood pressure measures are higher in females than males when indexed to W.
- Previous diagnostic cut-offs for peak exercise BP are frequently exceeded in healthy individuals and are likely to have poor disease specificity. Workload-indexed exercise BP is therefore a more informative metric than peak exercise BP.

* Corresponding author. Tel: +61 3 9231 2480, Email: kristel.janssens@svi.edu.au

Graphical Abstract



CPET, cardiopulmonary exercise testing; SBP, systolic blood pressure; SBP/W-slope, SBP indexed to workload

Keywords Athlete • Exercise • Hypertension • Sex differences • Workload-indexed

Introduction

Hypertension is the strongest modifiable risk factor for cardiovascular disease (CVD), being responsible for over half of CVD deaths related to stroke and coronary artery disease.[1] A phenomenon known as 'masked hypertension' occurs in 10–15% of adults when resting office blood pressure (BP) measurements fail to identify individuals with hypertension that is evident during routine daily activities.[2–4] It has been suggested that an exaggerated BP response during graded exercise testing could predict latent[5–7] and masked hypertension irrespective of resting BP.[8–10]

The normal limits and clinical significance of an exaggerated BP response during exercise have not been clearly defined,[11] and there are differing recommendations for the diagnosis of masked hypertension.[12,13] Until recently, an exaggerated BP response was defined as a maximal systolic BP (SBP_{max}) during exercise of ≥210 mmHg in males and ≥190 mmHg in females.[14] However, SBP_{max} is directly related to aerobic fitness,[15–17] with higher SBP_{max} in fitter individuals, potentially secondary to heightened cardiac output during intensive exercise and not pathological hypertension. As a result, there has been increasing recognition that indexing SBP to exercise workload (W; a metric that is highly co-linear with cardiac output) may provide a greater insight into physiologic systemic vascular function and load.[11,18] Current studies that provide reference values for SBP indexed to W primarily involve individuals referred for clinical exercise testing[19] or small cohorts of athletic individuals.[20–22]

We aimed to validate previous findings relating to SBP indexed to exercise W in a large cohort of males and females across the age and fitness spectrum and assess associations with age, sex, and fitness. Furthermore, we extend this to include changes in diastolic BP (DBP) during exercise using a validated automated BP monitor.

In contrast to the doctrine that higher SBP at maximal exertion is associated with markers of adverse vascular health (defined by associations with older age and lower fitness), we hypothesized that higher SBP measured at peak exercise would paradoxically be associated with younger age and greater fitness. Systolic blood pressure indexed to W has the potential to address this paradox related to flow-associated pressure increases, and thus, we hypothesized that steeper SBP/W-slopes would be associated with markers of adverse vascular health.

Methods

This study includes data from three multicentre international prospective studies, specifically designed to determine the impact of high-volume endurance training on cardiovascular structure and function. The following studies shared the same protocol of incremental exercise to volitional fatigue with the same automated BP measurements: the Pro@Heart study, 'the prospective athlete heart study—elucidating genetic determinants of cardiac remodelling using exercise as an environmental stress' (trial registration number NCT05164328, ACTRN12618000716268); the ProAFHeart study, 'atrial remodelling and the risk of arrhythmias in endurance athletes' (ACTRN12618000711213); and the Master@Heart study (trial registration number NCT03711539). The full protocols for the Pro@Heart and Master@Heart study have been described elsewhere.[23,24] Research protocols received approval from the Human Research Ethics Committees at the various enrolment locations, the Alfred Hospital Ethics Committee, Melbourne, Australia (333/15, 484/16), and the UZ/KU Leuven Research Ethics Committee, Belgium (S57241, S61336). All participants gave written informed consent.

Study participants

Enrolled participants were current or former endurance-trained athletes or non-athlete control participants (<3 h of endurance exercise per week). Participants were included in the current analysis if they underwent a cardiopulmonary exercise test with concurrent BP assessment between February 2018 and December 2023 at either the Baker Heart and Diabetes Institute, Melbourne, Australia, or UZ Leuven, Belgium. Participants were excluded if they had (i) diagnosed hypertension and were on antihypertensive treatment, (ii) an implanted cardiac device, (iii) permanent atrial fibrillation (AF) or in AF at the time of exercise testing, (iv) clinically diagnosed cardiomyopathy, or (v) missing BP measurement at maximal exertion.

Study protocol

Clinical information and anthropometry

A health and lifestyle questionnaire was administered to participants to establish cardiovascular risk factors, comorbidities, and medication use. Height and weight were measured to calculate body mass index.

Resting blood pressure measurement

Resting BP was assessed in the supine position after 5–10 min of rest, using a correctly sized cuff and digital automatic BP machine (Omron HEM-907XL Pro BP Monitor or Omron model M6W, Omron Healthcare, Kyoto, Japan).

Bicycle exercise test

The exercise test was conducted on an electronically braked bicycle ergometer (LODE Excalibur Sport, Groningen, The Netherlands, or the Avantronic Cyclus 2, Leipzig, Germany). Two minutes of passive resting data were obtained prior to commencing exercise. Following a 1 min warm-up at an initial resistance of 30–60 W, the W increased progressively until volitional fatigue, with the power output at volitional fatigue defined as maximal W (W_{max}). Peak heart rate (HR_{peak}) achieved during exercise was obtained from continuous 12-lead ECG monitoring (Vyntus^{TM} ECG 12-lead PC-ECG, Vyaire Medical, GmbH, Germany).

Blood pressure during exercise

The BP response during exercise was measured with an automated auscultatory BP device that incorporates R-wave gating from QRS complexes derived from a 3-lead ECG and a microphone for K-sound detection (Tango® M2 ECG-gated Automated BP Monitor, Suntech Medical Inc, NC, USA) which has been previously validated during exercise.[25] Measurements were performed seated on the ergometer prior to commencing exercise, at 2 min intervals throughout the test, at maximal exertion, and during recovery. Maximal SBP (SBP_{max}) was determined as the highest SBP achieved during exercise. Based on the prevailing definition,[14] a $SBP_{max} \geq 210$ mmHg for males and ≥190 mmHg for females was defined as an exaggerated SBP_{max}. A non-exaggerated SBP_{max} was characterized as a 'normal' SBP_{max}. For each BP measurement, the corresponding W was recorded. The SBP or DBP W-slopes were derived from individual linear regression analyses of SBP and DBP against W with SBP/DBP as the dependent variable (see Supplementary material online, *Figure S1*).

Cardiorespiratory fitness

Gas exchange data were collected continuously throughout the test using a calibrated metabolic cart (Vyntus^{TM} CPX, Metabolic Cart, Vyaire Medical GmbH, or Cortex Metalyzer 3b, Leipzig, Germany) for the measurement of peak oxygen uptake (VO_{2peak}), calculated as the highest value from a 30 s rolling average using 5 s averaged breath-by-breath values.

Statistical analysis

Variables were assessed for normality using the Shapiro–Wilk test. Continuous data are presented as mean (± standard deviation; parametric) or median (interquartile range; non-parametric), and categorical variables as number and frequency or percentage. Where relevant, percentages (%) are reported within each cohort. A $P < 0.05$ (two-tailed) was considered statistically significant. The independent *t*- or Mann–Whitney *U*-tests were used to compare continuous variables and Pearson's χ^2 test to compare categorical variables between sexes. Given the sexual dimorphism of BP,[26] we stratified all analyses by sex to account for potential sex-specific BP responses to exercise.

A linear regression was performed on multiple measures for each participant to determine the equation SBP $= m \times$ Watt $+ c$ and the correlation coefficient (*r*). A generalized linear mixed model analysis was used to determine the group regression for males and females, with individuals considered as a random effect, thereby accounting for inter-individual variability in baseline ($W = 0$) SBP values. The mean correlation coefficient was determined as the mean of all individual values.

Univariable linear regression analysis was used to assess the potential associations of clinical, demographic, and exercise testing variables with the SBP- and DBP/W-slope. To avoid violating the assumption of independence, SBP_{max} and W_{max} were excluded from the linear regression analysis. Variables from the univariable analysis were included in a multivariable linear forward stepwise regression model to determine the primary predictors of the SBP- and DBP/W-slope. Due to the representation of weight and BMI in $VO_{2peak,}$ these variables were excluded for violating the assumption of independence. We tested for multicollinearity among predictor variables in the multivariable model using a variance inflation factor (VIF) analysis.

To determine the associations of age and sex (and their interaction) with SBP/W-slope, we used univariate linear regression with age as a co-variate and sex as a fixed factor with an interaction for age and sex on SBP/W-slope as the dependent variable. We explored the potential relevance of SBP_{max} and SBP/W-slope by dividing the cohort into four subgroups based on sex-specific cut-offs for an exaggerated SBP_{max} and SBP-slope values below or above the median. This resulted in the following groups: Group 1, normal SBP_{max} and below-median SBP/W-slope; Group 2, normal SBP_{max} and above-median SBP/W-slope; Group 3, exaggerated SBP_{max} and below-median SBP/W-slope; Group 4, exaggerated SBP_{max} and above-median SBP/W-slope. Demographics were compared across the four subgroups using a one-way ANOVA with a Bonferroni *post hoc* test. All data were analysed using SPSS for windows software version 26.0 (SPSS Inc., Chicago, IL, USA).

Results

Participants characteristics

Five hundred and eighty-nine participants (81% male) were included in the analysis (*Figure 1*). Participants were predominantly endurance-trained athletes (77%) with cycling (46%) being the most popular sport, followed by rowing (24%). *Table 1* presents the characteristics

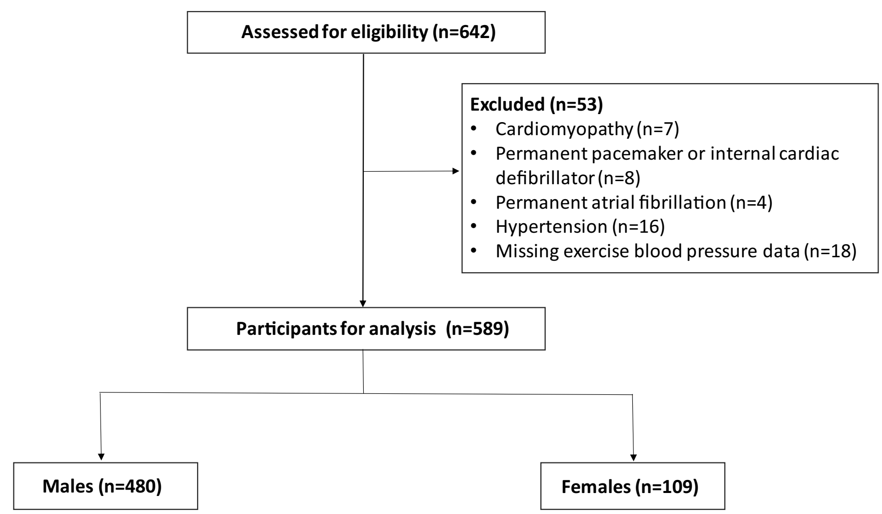


Figure 1 CONSORT diagram: number of participants assessed and excluded and final study sample for analysis stratified for sex.

Table 1 Baseline participant characteristics for the full cohort and sex comparison

Variable	All ($n = 589$)	Male ($n = 480$)	Female ($n = 109$)	P-value
Demographics and clinical characteristics				
Age (years)	46 (24–56)	48 (25–57)	29 (22–47)	<0.001
Height (cm)	178 ± 8	180 ± 7	171 ± 7	<0.001
Weight (kg)	74 (67–81)	76 (69–83)	66 (60–72)	<0.001
BMI (kg/m^2)	23.4 (21.7–25.1)	23.6 (21.9–25.3)	22.9 (21.1–24.1)	<0.001
Resting SBP (mmHg)	124 (115–132)	125 (117–134)	116 (108–125)	<0.001
Resting DBP (mmHg)	71 (65–78)	72 (66–79)	66 (61–73)	<0.001
Resting HR (b.p.m.)	54 (47–60)	54 (47–59)	53 (46–61)	0.748
Endurance athlete, *n* (%)	455 (77)	366 (76)	89 (82)	
Running, *n* (%)	70 (15)	56 (15)	14 (16)	0.920
Cycling, *n* (%)	211 (46)	199 (54)	12 (13)	<0.001
Rowing, *n* (%)	107 (24)	61 (17)	46 (52)	<0.001
Triathlon, *n* (%)	46 (10)	36 (10)	10 (11)	0.694
Other, *n* (%)	21 (5)	14 (4)	7 (8)	0.103
Non-athlete, *n* (%)	134 (23)	114 (24)	20 (18)	
Medications				
Beta-blocker, *n* (%)	6 (1)	5 (1)	1 (1)	0.907
Lipid-lowering drug, *n* (%)	8 (1)	7 (1)	1 (1)	0.660
Exercise testing and blood pressure response to exercise				
Maximal HR (b.p.m.)	176 (166–188)	176 (164–187)	181 (169–190)	0.041
Maximal workload (Watt)	333 (282–407)	360 (300–420)	293 (229–349)	<0.001
VO_{2peak} (mL/kg/min)	47.9 (39.5–56.2)	48.0 (40.7–57.1)	44.8 (34.9–51.7)	<0.001
Exercise SBP_{max} (mmHg)	208 (188–228)	210 (190–230)	199 (183–212)	<0.001
Exaggerated SBP, *n* (%)	316 (54)	246 (51)	70 (64)	0.014
SBP/W-slope (mmHg/W)	0.25 ± 0.11	0.24 ± 0.10	0.27 ± 0.12	0.031
DBP/W-slope (mmHg/W)	0.000 (−0.026 to 0.029)	−0.005 (−0.030 to 0.023)	0.010 (−0.010 to 0.050)	<0.001

Values are median (IQR), mean ± SD, or *n* numbers (%). The *P*-value is for comparison between sexes.
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate, VO_{2peak}, peak oxygen uptake, SBP_{max}, maximal SBP; W, workload.

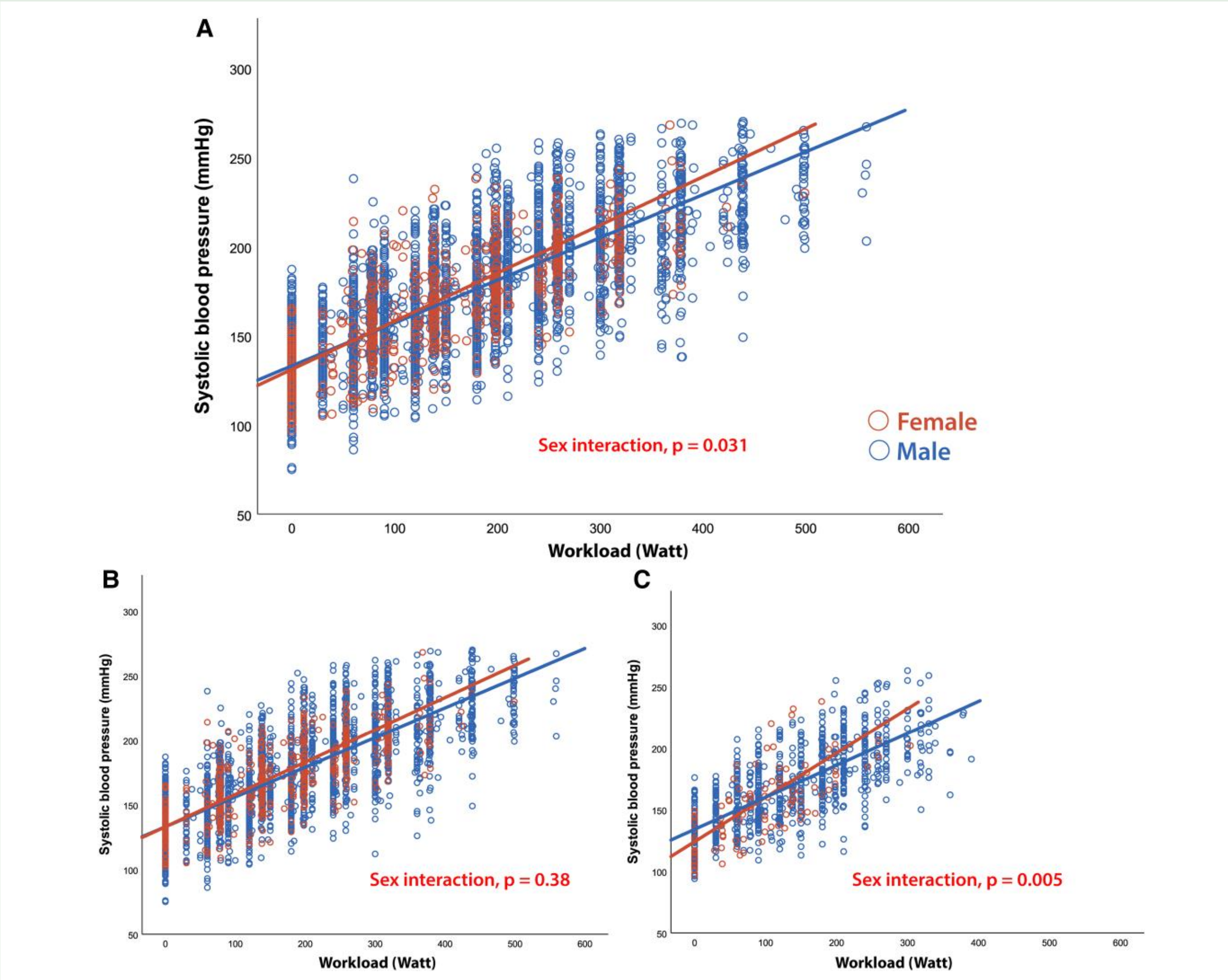


Figure 2 Scatterplot of multiple individual systolic blood pressure measurements during graded bicycle exercise testing with linear regression lines for systolic blood pressure indexed to workload in males ($n = 480$; blue colour) and females ($n = 190$; red colour) in *A*) the full cohort, *B*) athletes, and *C*) non-athletes. Overall, females have a steeper mean systolic blood pressure/workload-slope compared with males, 0.27 ± 0.12 mmHg/W vs. 0.24 ± 0.10 mmHg/W, respectively ($P = 0.031$). This was primarily due to sex differences in non-athletes (sex interaction, $P = 0.005$), whereas this difference was not apparent in athletes (sex interaction, $P = 0.38$).

and sex comparisons of the entire cohort. Median resting SBP was higher in males than females [125 (117–134) mmHg vs. 116 (108–125) mmHg, $P < 0.001$]. Males had higher VO_{2peak} [48.0 (40.7–57.1) mL/kg/min vs. 44.8 (34.9–51.7) mL/kg/min, $P < 0.001$] and attained a higher W_{max} than females [360 (300–420) W vs. 293 (229–349) W, $P < 0.001$].

Maximal blood pressure response

The median SBP_{max} for males and females approximated the cut-offs[14] for an exaggerated SBP response [210 (190–230) mmHg in males and 199 (183–212) mmHg in females, $P < 0.001$, for comparison]. Amongst the entire cohort, 51% of male and 64% of female participants had an exaggerated SBP_{max} ($P = 0.014$). This sex difference in SBP_{max} prevalence was primarily driven by the athlete subgroup, whereby an exaggerated SBP_{max} was more prevalent in female (72%) compared with male endurance athletes (58%, $P = 0.014$). In contrast, for non-athletes, the prevalence of an exaggerated SBP_{max} was similar between females (30%) and males (31%, $P = 0.950$).

Blood pressure responses indexed to workload

A strong association between SBP and W was observed with a mean $R^2 = 0.85 \pm 0.18$ ($P < 0.05$). *Figure 2* shows the SBP indexed to W response (SBP/W-slope) for males and females in the full cohort and within the athlete and non-athlete subgroups. In the full cohort, the mean SBP/W-slope was lower in males compared with females (0.24 ± 0.10 mmHg/W vs. 0.27 ± 0.12 mmHg/W, $P = 0.031$). Subgroup analyses revealed that the sex differences in the SBP/W relationship may have been driven by the non-athlete participants (0.26 ± 0.13 mmHg/W in males vs. 0.36 ± 0.20 mmHg/W in females, $P = 0.005$). In contrast, there was no sex difference for the mean SBP/W-slope in the athlete subgroup (0.24 ± 0.10 mmHg/W vs. 0.25 ± 0.09 mmHg/W, $P = 0.378$) for

Table 2 Simple linear regression analysis of systolic blood pressure/workload-slope (mmHg/W) with clinical, demographic, and exercise variables in males and females

Variable	R^2	Unstandardized β	Unstandardized β 95% CI	Standardized β	*P*-value
Males					
Age (years)	0.106	0.002	0.001 to 0.003	0.325	<0.001
Height (cm)	0.035	−0.003	−0.004 to −0.001	−0.186	<0.001
Weight (kg)	0.003	−0.001	−0.001 to 0.000	−0.052	0.251
BMI (kg/m^2)	0.005	0.003	−0.001 to 0.006	0.073	0.110
Resting SBP (mmHg)	0.002	0.000	0.000 to 0.001	0.046	0.319
Resting DBP (mmHg)	0.030	0.002	0.001 to 0.003	0.173	<0.001
VO_{2peak} (mL/kg/min)	0.088	−0.003	−0.003 to −0.002	−0.297	<0.001
HR_{peak} (bpm)	0.072	−0.002	−0.002 to −0.001	−0.268	<0.001
Females					
Age (years)	0.005	0.001	−0.001 to 0.002	0.074	0.445
Height (cm)	0.055	−0.004	−0.008 to −0.001	−0.234	0.015
Weight (kg)	0.011	−0.001	−0.004 to 0.001	−0.103	0.284
BMI (kg/m^2)	0.000	0.001	−0.009 to 0.011	0.019	0.848
Resting SBP (mmHg)	0.004	−0.001	−0.002 to 0.001	−0.062	0.527
Resting DBP (mmHg)	0.001	0.000	−0.002 to 0.003	0.034	0.728
VO_{2peak} (mL/kg/min)	0.084	−0.003	−0.005 to −0.001	−0.290	0.002
HR_{peak} (b.p.m.)	0.007	−0.001	−0.003 to 0.001	−0.082	0.396

CI, confidence interval; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; W, workload; VO_{2peak}, peak oxygen uptake; HR_{peak}, peak heart rate.

males and females, respectively. The effect of sex on SBP/W-slope was significantly different according to athletic status (sex × athlete interaction, $P = 0.02$). The median DBP/W-slope was also lower in males vs. females [−0.005 (−0.030 to 0.023) mmHg/W vs. 0.010 (−0.010 to 0.050) mmHg/W, respectively, $P < 0.001$].

Univariable and multivariable predictors of workload-indexed exercise blood pressure responses

There was a weak positive association between SBP/W-slope and both age ($R^2 = 0.106$, $P < 0.001$) and resting DBP ($R^2 = 0.030$, $P < 0.001$) for males but not females (*Table 2*). Weak negative associations were also observed between SBP/W-slope and height ($R^2 = 0.035$, $P < 0.001$), VO_{2peak} ($R^2 = 0.088$, $P < 0.001$), and HR_{peak} ($R^2 = 0.072$, $P < 0.001$) in males. Similarly, females had weak negative associations between SBP/W-slope and height ($R^2 = 0.055$, $P = 0.015$) and VO_{2peak} ($R^2 = 0.084$, $P = 0.002$), but no significant association was seen with HR_{peak}. Weight and resting SBP were not significantly associated with the SBP/W-slope in males or females.

Weaker associations were seen for the above-mentioned variables and DBP/W-slope in males. For females, the DBP/W-slope did not reveal significant associations with any of the evaluated variables (see Supplementary material online, *Table S1*).

Univariable predictors were added into separate forward stepwise multivariable regression models (stratified for sex) to predict SBP/W-slope (*Table 3*). Age, height, and VO_{2peak} were significant predictors in males and explained 14% of the variance in SBP/W-slope. In females, VO_{2peak} and height were identified as significant predictors of the SBP/W-slope, explaining 10% of the variance. For the DBP/W-slope in males, the significant predictors were height, VO_{2peak}, and HR_{peak} (adjusted $R^2 = 0.072$, $P < 0.001$; *Table 3*). For females, the model did not retain any variables.

Impact of age and sex on systolic blood pressure/workload-slope

When including age and sex (and their interaction) into a multivariable model, the overall model predicted 9% of the variance in SBP/W-slope ($P < 0.001$). Age ($P < 0.001$), sex ($P = 0.001$), and their interaction ($P = 0.047$) significantly influenced the SBP/W-slope (i.e. sex impacted the effect of age on SBP/W-slope and vice versa). For males, the SBP/W-slope showed a significant increase with age [β = 0.002, 95%CI (0.001–0.003), $P < 0.001$] although in females, there was no significant association ($P = 0.363$). When comparing the SBP/W-slope between sexes, males had a lower SBP/W-slope compared with females [β= −0.093, 95% CI (−0.147 to −0.039), $P = 0.001$].

Subgroup analysis based on maximal systolic blood pressure and systolic blood pressure- or diastolic blood pressure/workload-slope

Four subgroups consisting of normal and exaggerated SBP_{max} and those below- and above-median SBP/W-slope (0.23 mmHg/W for males and 0.25 mmHg/W for females) are characterized in *Table 4*. Individuals with an exaggerated SBP_{max} and low SBP/W-slope were younger with a higher VO_{2peak} compared with the other groups. Conversely, a normal SBP_{max} and high SBP/W-slope were associated with the lowest VO_{2peak} and older age. The two groups with a normal SBP_{max} had a lower resting SBP compared with the two groups with an exaggerated SBP_{max} (118 ± 13 mmHg and 121 ± 12 mmHg for a normal SBP_{max} and above- or below-median SBP/W-slope, respectively, vs. 127 ± 15 mmHg and 128 ± 12 mmHg for an exaggerated SBP_{max} and above- or below-median SBP/W-slope, respectively, $P < 0.001$). When comparing individuals with values below or above the median DBP/W-slope, a lower DBP/W-slope was associated with younger age

Table 3 Predictors of systolic blood pressure/workload-slope (mmHg/W) and diastolic blood pressure/workload-slope (mmHg/W) from stepwise forward multivariable regression

Sex	Predictor	Adjusted R^2	Unstandardized ß	Unstandardized β 95%CI	Standardized ß	*P*-value
SBP/W-slope (mmHg/W)						
Male	Age (years)	0.138	0.001	0.001–0.002	0.195	<0.001
	VO_{2peak} (mL/kg/min)		−0.002	−0.002 to −0.001	−0.180	0.001
	Height (cm)		−0.002	−0.003 to −0.001	−0.142	0.001
Female	VO_{2peak} (mL/kg/min)	0.101	−0.003	−0.005 to −0.001	−0.256	0.007
	Height (cm)		−0.003	−0.007 to 0.000	−0.187	0.047
DBP/W-slope (mmHg/W)						
Male	Height (cm)	0.072	−0.001	−0.002 to −0.001	−0.191	<0.001
	VO_{2peak} (mL/kg/min)		−0.001	−0.001 to 0.000	−0.126	0.010
	HR_{peak} (b.p.m.)		0.000	−0.001 to 0.000	−0.098	0.045

SBP, systolic blood pressure; DBP, diastolic blood pressure; W, workload; CI, confidence interval; VO_{2peak}, peak oxygen uptake; HR_{peak}, peak heart rate.

Table 4 Participant characteristics stratified by sex-specific subgroups based on an exaggerated maximal systolic blood pressure response to exercise and above/below-median for systolic blood pressure/workload-slope (0.23 mmHg/W and 0.25 mmHg/W for males and females, respectively)

Variables	Normal SBP_{max}		Exaggerated SBP_{max}		*P*-value
	Low SBP/W-slope (*n* = 160)	High SBP/W-slope (*n* = 113)	Low SBP/W-slope (*n* = 137)	High SBP/W-slope (*n* = 179)	
Age (years)	41 ± 16	48 ± 16*	34 ± 15*	46 ± 16*	<0.001
Height (cm)	179 ± 8	177 ± 8	180 ± 8	177 ± 7	0.003
Resting SBP (mmHg)	121 ± 12	118 ± 13	128 ± 12*	127 ± 15*	<0.001
Resting DBP (mmHg)	71 ± 10	72 ± 9	69 ± 11	73 ± 10	0.004
Exercise testing					
Maximal HR (b.p.m.)	177 ± 17	172 ± 16	182 ± 14*	173 ± 15	<0.001
Maximal HR (% predicted)[a]	98 ± 7	98 ± 7	99 ± 6	99 ± 6	0.930
VO_{2peak} (mL/kg/min)	47.3 ± 9.9	42.1 ± 9.4*	55.4 ± 11.2*	47.0 ± 12.2	<0.001
VO_{2peak} (% predicted)[b]	118 ± 22	111 ± 24	133 ± 18*	125 ± 22*	<0.001

Values are mean ± SD.
SBP, systolic blood pressure; DBP, diastolic blood pressure; W, workload; HR, heart rate; VO_{2peak}, peak oxygen uptake.
[a]Predicted values based on the equation: 208 − 0.7 × age.[27]
[b]Predicted values based on the FRIEND VO_2 regression equation.[28]
Post hoc Bonferroni comparison: *$P < 0.05$ relative to normal SBP_{max} and low SBP/W-slope.

($P = 0.001$) and higher VO_{2peak} ($P = 0.003$; see Supplementary material online, *Table S2*).

Discussion

The prevailing clinical paradigm is that an exaggerated SBP_{max} during exercise is indicative of vascular dysfunction and masked hypertension. However, in our large sample of apparently healthy males and females of varied age and fitness, over 50% of participants had an exaggerated BP response to exercise that was paradoxically associated with higher cardiorespiratory fitness (CRF). In contrast, when SBP was expressed relative to exercise intensity, a higher SBP/W-slope was associated with older individuals with lower levels of fitness. The inverse association between SBP_{max}, age, and CRF suggests that SBP_{max} should not always be considered a valid indicator of vascular pathology. Rather, expressing SBP relative to W or measures of CRF may provide clinical insight into physiological vascular aging. When indexing the SBP during exercise to W, a higher SBP/W-slope was also observed in females compared with males, highlighting the importance of providing sex-specific reference values even for exercise BP responses.

We clearly demonstrate that healthy individuals frequently exceed conventional guidelines for exercise BP (peak SBP ≥ 210 mmHg in males and ≥190 mmHg in females). Thus, the specificity of absolute exercise BP cut-offs for possible identification of masked hypertension and vascular dysfunction needs to be questioned. Our data suggests that relying upon a single measure of SBP at peak exertion may be misleading if one seeks to identify vascular pathology. In ostensibly healthy individuals, we described a consistent linear relationship between SBP and W during incremental exercise, implying that if an individual is capable of exercising to a sufficient W, then a high SBP_{max} is virtually assured. This is illustrated by the fact that those with the highest SBP_{max} have the greatest CRF. Such findings are consistent with prior data suggesting that higher observed SBP_{max} recordings in athletes should lead to a reappraisal of what is considered the upper limits of normal.[17,29]

Evaluating SBP relative to exercise W via SBP/W-slope, has been proposed[11,16] as a method to account for CRF, and may be a better differentiator of physiological vs. pathological vascular function. Several studies have highlighted that all-cause mortality is better predicted when SBP is indexed to W.[18,30] However, there is significant variability in the normal ranges of the relationship between SBP and W. Hedman *et al.*[19] evaluated age- and sex-specific reference values from 3839 adults undergoing clinical exercise testing and identified a mean SBP/W-slope of 0.41 ± 0.15 mmHg/W in males and 0.52 ± 0.21 mmHg/W in females. These values appear significantly higher compared with the mean SBP/W-slope observed in our cohort, a difference that may result from the fact that the cohort of Hedman *et al.*[19] was referred for clinical exercise testing and were less fit compared with our healthy, mostly athletic, population. However, our observed SBP/W-slopes were also lower than those reported in a study of young professional male handball and female soccer players.[20] In particular, our mean SBP/W-slope for females was approximately half of that derived from the small cohort ($n = 25$) of young females studied by Bauer *et al.*[20] (0.27 mmHg/W vs. 0.53 mmHg/W). On the other hand, our values are similar to those reported in two recent studies of young healthy endurance athletes.[21,22]

Consistent with our hypothesis, sub-divisions of our healthy cohort provided additional insights. We found that younger and aerobically fitter individuals had a higher SBP_{max} but lower SBP/W-slope and older, less-fit individuals had a lower SBP_{max} but steeper SBP/W-slope. The aforementioned findings support the superiority of exercise BP indexed to W as compared with SBP_{max} for the evaluation of vascular health. Our data provide sex-specific reference values for SBP- and DBP/W-slope across the age and fitness spectrum, facilitating the clinical assessment of BP response during graded exercise testing on a bicycle ergometer.

Sex differences

Despite females having a lower resting BP and SBP_{max} compared with males, we found that females have a higher SBP-slope relative to W, a finding similar to other studies.[20,22] Given that the increase in SBP during exercise is derived from a combination of changes in cardiac output and vascular resistance, this could indicate that females are generating a higher cardiac output for a certain power output compared with males. Another possibility may be that females have less peripheral vasodilation compared with males during exercise. Nayor *et al.*[31] demonstrated that a higher SBP/W-slope was associated with greater arterial stiffness measured by carotid pulse wave velocity in both sexes, but that this relative stiffness was greater in females. A similar response has been observed in females with heart failure with preserved ejection fraction.[32] During exercise, for a similar stroke volume, female heart failure patients have increased arterial stiffness.[32] We were unable to determine the contribution of vascular stiffness to differential exercise BP responses seen in this study, but our data support the need for sex-specific diagnostic thresholds for BP response to exercise.

When evaluating sex differences in the SBP/W-slope within the athlete subgroup, no significant difference was observed. This finding could generate the hypothesis that exercise training minimizes the sex difference in the SBP/W-slope. It is important to note the issue of sample size, particularly the small number of female non-athletes, means that the results of the larger combined cohort can be considered more robust. Additionally, the term 'athlete' is not binary. Therefore, we propose that the effect of athletic conditioning on the SBP/W-slope can be more reliably assessed using CRF, as measured by VO_{2peak}, rather than athletic status. Nonetheless, the continuous and categorical athletic assessments proved complimentary in our data with greater VO_{2peak} and athletic status being associated with a lower SBP/W relationship.

Sex-specific nomograms

The group regressions for the relationship between SBP and exercise W, derived from a generalized linear mixed model that accounts for individual differences as a random effect, can be interpolated to provide some limits of normality. For example, we derived the following equation for healthy males: exercise SBP = 0.221 [95% CI (0.217–0.226)] × W + 135 [95% CI (133–137)]. Thus, at 200 W, less than 5% of the male population would be expected to have a SBP ≥ 180 mmHg. For females, the equation—exercise SBP = 0.237 [95% CI (0.228–0.247)] × W + 133 [95% CI (129–136)]—predicts a slightly higher upper limit value of 182 mmHg at 200 W. Similarly, SBP cut-offs can be derived for lesser exercise Ws.

Limitations

We did not assess BP using gold standard 24 h ambulatory BP monitoring to confirm or exclude masked hypertension. Additionally, despite having a female cohort of endurance athletes comparably larger than prior studies, few were aged ≥50 years, limiting our ability to explore the effect of menopause on the SBP/W-slope. Lastly, the study population was primarily white; therefore, future research is needed across more ethnically diverse populations.

One of the strengths of this research is our methodology. Previous studies have relied upon a single measure of SBP obtained at peak exercise intensity or utilized auscultatory measures of BP during exercise, a technique that has seldom been validated against invasive standards. Accurate identification of the K-sounds at peak exercise can be extremely challenging, and it is impossible to blind the observer to context. We used an automated device that measures BP blind to the individuals age, sex, exercise intensity, and previous measures. We found that there was a high correlation for the individual relationships between SBP and W (mean $r = 0.92$), thereby providing a degree of internal validation.

Conclusions

To our knowledge, this is the largest study providing BP reference values for bicycle ergometer exercise across the age and fitness spectrum using an automated auscultatory BP device. We demonstrate that an exaggerated SBP_{max} is common and is associated with greater fitness. Indexing SBP to exercise W is a more informative metric than SBP_{max}; with higher slopes being associated with older, less-fit individuals and lower slopes with younger, fitter individuals. Sex, age, exercise intensity, and cardiorespiratory fitness must be considered when evaluating BP response to exercise.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

Author contribution

K.J., S.J.F., A.L.G., G.C., R.W., and H.H.: conceptualization. K.J., S.J.F., and A.L.G.: formal analysis. K.J., A.M.M., C.D., and S.V.S.: investigation. K.J., S.J.F., and A.L.G.: methodology. K.J., A.M.M., C.D., and S.V.S.: project administration. E.P., S.J.F., and A.L.G.: supervision. K.J., S.J.F., A.L.G.: writing—

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Data availability

The data underlying this article will be shared on reasonable request with the corresponding author.

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