Workload-indexed blood pressure response is superior to peak systolic blood pressure in predicting all-cause mortality

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Abstract

Aims: The association between peak systolic blood pressure (SBP) during exercise testing and outcome remains controversial, possibly due to the confounding effect of external workload (metabolic equivalents of task (METs)) on peak SBP as well as on survival. Indexing the increase in SBP to the increase in workload (SBP/MET-slope) could provide a more clinically relevant measure of the SBP response to exercise. We aimed to characterize the SBP/MET-slope in a large cohort referred for clinical exercise testing and to determine its relation to all-cause mortality.

Methods and results: Survival status for male Veterans who underwent a maximal treadmill exercise test between the years 1987 and 2007 were retrieved in 2018. We defined a subgroup of non-smoking 10-year survivors with fewer risk factors as a lower-risk reference group. Survival analyses for all-cause mortality were performed using Kaplan–Meier curves and Cox proportional hazard ratios (HRs (95% confidence interval)) adjusted for baseline age, test year, cardiovascular risk factors, medications and comorbidities. A total of 7542 subjects were followed over 18.4 (interquartile range 16.3) years. In lower-risk subjects ($n = 709$), the median (95th percentile) of the SBP/MET-slope was 4.9 (10.0) mmHg/MET. Lower peak SBP (< 210 mmHg) and higher SBP/MET-slope (> 10 mmHg/MET) were both associated with 20% higher mortality (adjusted HRs 1.20 (1.08–1.32) and 1.20 (1.10–1.31), respectively). In subjects with high fitness, a SBP/MET-slope > 6.2 mmHg/MET was associated with a 27% higher risk of mortality (adjusted HR 1.27 (1.12–1.45)).

Conclusion: In contrast to peak SBP, having a higher SBP/MET-slope was associated with increased risk of mortality. This simple, novel metric can be considered in clinical exercise testing reports.

Keywords

Mortality, clinical exercise testing, external workload, epidemiology

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Introduction

Blood pressure (BP) is routinely assessed and reported as an integral part of clinical exercise testing.¹ Current scientific statements and guidelines by the American Heart Association¹ and the American College of Sports Medicine (ACSM)² define an exaggerated systolic BP (SBP) response to exercise as a peak SBP of ≥ 210 mmHg in males and ≥ 190 mmHg in females. These thresholds approximate the 90th percentile in young, healthy subjects,^{3–5} but are not consistently associated with outcome. In fact, systematic reviews and meta-analyses^{6–8} suggest a complex and somewhat ambiguous association between the SBP response to exercise and mortality. In some populations, a high

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peak SBP has been related to a lower-risk of future cardiovascular events and all-cause mortality.^{9–12}

Using absolute thresholds for SBP response to exercise is problematic due to the linear relationship between SBP (via cardiac output) and external workload,^{13–15} as higher achieved workloads implies higher level of fitness, which, in turn, is strongly associated with survival.^{16,17} Reporting SBP in relation to workload could account for this relationship and, therefore, provide a more robust and physiologically relevant measure than absolute peak SBP. Guidelines on exercise testing provide an estimated normative increase in SBP of ~ 10 mmHg/metabolic equivalent of task (MET),^{1,2} although this suggested value of the SBP/MET-slope was recently challenged.¹⁸ To our knowledge, the SBP/MET-slope has never been evaluated in a large clinical population, and its prognostic value is unknown.

The purpose of this study was to characterize the SBP/MET-slope, as a measure of workload-indexed SBP response to exercise, in a large clinical population of males referred for exercise testing and to determine its association with all-cause mortality.

Methods

Study design and sample

The Veterans Exercise Testing Study is an ongoing, prospective evaluation of US Veterans referred for exercise testing, designed to address exercise test, clinical and lifestyle factors and their associations to health outcomes. The study was approved by the Institutional Review Board at Stanford University, and all subjects gave written informed consent prior to undergoing the baseline examination. Male Veterans who underwent a treadmill exercise test at the Veterans Affairs Health Care System in Palo Alto, California between 1987 and 2007 were considered for inclusion ($n = 9079$). The exclusion criteria are detailed in Figure 1(a).

Demographic, clinical and medication information was obtained from each subject's computerized medical records just prior to the exercise test. This included information on previous cardiovascular and pulmonary disease, hypertension, hypercholesterolemia, diabetes mellitus, smoking status (current and past) and use of cardiac medications and family history of coronary disease. For details on the definitions used, see the online supplementary material (Methods 1.1. and Table S1).

We ascertained vital status of the participants as of July 20, 2018. We verified dates of death using the VA Beneficiary Identification and Record Locator System File, which has been estimated to be 95% complete and accurate.¹⁹ Follow-up time was the time from the exercise test to death or to the date when a subject was last verified to be alive.

Exercise assessments

Each subject underwent a standardized treadmill exercise test, using an individualized ramp protocol. Standard criteria for termination were used, including signs of inducible cardiac ischemia or a sustained drop in SBP.^{1,2} A SBP > 250 mmHg or a diastolic BP > 115 mmHg were relative indications for test termination.^{1,2} Peak exercise capacity in METs was estimated automatically using standard ACSM equations.² Age-predicted peak METs were calculated using a population-specific equation, as follows: $18 - (0.15 \times \text{age})$.²⁰

BP was measured by auscultation, standing at rest before the exercise test (SBPrest) and just prior to test termination (SBPpeak). The Δ SBP was calculated as (SBPpeak – SBPrest) and indexed by the increase in METs from rest (Δ METs; (peak METs – 1)) to obtain the SBP/MET-slope. For details on the exercise test measurements and calculations, see the online supplementary material (Methods 1.2).

Subgroups and categories

Lower-risk group. To explore the effect of comorbidities and risk factors on the SBP/MET-slope and to obtain 50th, 90th and 95th percentiles, we defined a subgroup of patients with lower cardiovascular risk. This group included non-smoking subjects surviving at least 10 years following the exercise test, without a history of diabetes mellitus, hypertension or cardiovascular disease. A detailed description of the selection of lower-risk subjects is presented in the online supplementary material (Methods 1.3).

SBP/MET-slope versus peak MET categories. To determine the effect of the SBP/MET-slope on mortality in subjects with higher versus lower fitness, we defined four groups based on the median value of peak METs and of the SBP/MET-slope of the main sample: 1) higher MET/lower slope; 2) higher MET/higher slope; 3) lower MET/lower slope; and 4) lower MET/higher slope.

Hypotensive BP response group. Subjects with a Δ SBP ≤ 0 mmHg or an exercise test terminated due to a sustained drop in SBP were not included in the main sample, but analyzed separately in the outcome analysis.

Statistical analysis

SPSS software v25.0 (IBM Corp, Armonk, NY, USA) was used for database management and statistical analysis. Survival analyses were performed using R Studio v1.1.456 (R Studio Inc., Vienna, Austria)

Figure 1. Study flowchart (a) and comorbidities and cardiovascular risk factors over time. The 244 subjects with no increase or drop in SBP with exercise were only included in a separate survival analysis. In (b) and (c), the proportion (%) of subjects with prevalent comorbidities (b) and different risk factors (c) per year of inclusion are visualized.

CAD: coronary artery disease; HCM: hypertrophic cardiomyopathy; ICD: implantable cardiac defibrillator; MET: metabolic equivalent of task; RPE: rating of perceived exertion; SBP: systolic blood pressure.

with the survival (v2.38) and survminer (v0.4.3) packages. Continuous variables were presented as mean (standard deviation) or median (interquartile range (IQR)) based on their distribution. We compared means, medians and proportions using Student's t -tests, Mann–Whitney U-tests and χ^2 tests, respectively. Two-sided statistical significance was set at <0.05.

All outcome analyses were performed with 20-year all-cause mortality as the end-point. We applied the Kaplan–Meier method according to quartiles of the hemodynamic variables of interest, comparing survival over time using the log-rank (Mantel–Cox) test.

Unadjusted and adjusted Cox proportional hazard ratios (HRs) were calculated for quartiles of hemodynamic variables as well as for standardized continuous variables (Z-scores). Logistic regression was used to determine predicted probability of death within 20 years. The covariables included in the adjusted Cox models are detailed in the online supplementary material (Methods 1.4). Several sensitivity analyses were performed excluding subjects on cardiac medications and/or different combinations of cardiovascular diseases. A landmark analysis set to year 1997 was performed to explore the stability over time in survival based on SBP/MET-slope.

Table 1. Clinical characteristics.

	Main sample (n = 7298)	Lower-risk (n = 709)	Higher risk (n = 6589)	P*	Drop or no increase in SBP with exercise (n = 244)
Age (yrs)	58.6 ± 11.0	53.4 ± 12.2	59.2 ± 10.7	<0.001	64.4 ± 10.2 [†]
Height (cm)	176.3 ± 7.9	176.7 ± 7.9	176.3 ± 7.9	0.24	175.1 ± 7.8 [†]
Body mass index (kg/m ²)	28.5 ± 5.1	27.6 ± 4.5	28.6 ± 5.2	<0.001	27.4 ± 4.6 [†]
Body surface area (m ²)	2.05 ± 0.20	2.03 ± 0.19	2.05 ± 0.20	0.005	1.99 ± 0.17 [†]
Risk factors (n, %)					
Smoking	3636 (49.8)	0	3636 (55.2)	–	107 (43.9)
Hypertension	4291 (58.8)	0	4291 (65.1)	–	167 (68.4) [†]
Diabetes mellitus	1023 (14.0)	0	1023 (15.5)	–	44 (18.0)
Hypercholesterolemia	2803 (38.4)	211 (29.8)	2592 (39.3)	<0.001	82 (33.6)
Family history CAD	1716 (23.5)	156 (22.0)	1560 (23.7)	0.33	38 (15.6) [†]
Previous heart disease and comorbidities (n, %)					
CAD	1643 (22.5)	0	1643 (24.9)	–	116 (47.5) [†]
Stroke	204 (2.8)	0	204 (3.1)	–	8 (3.3)
Claudication	273 (3.7)	0	273 (4.1)	–	16 (6.6) [†]
Atrial fibrillation	110 (1.5)	0	110 (1.7)	–	13 (5.3) [†]
COPD	329 (4.5)	0	329 (5.0)	–	10 (4.1)
Current medication (n, %)					
Anti-hypertensive	3205 (44.0)	0	3205 (48.6)	–	140 (57.4) [†]
Beta-blocker	1494 (20.4)	0	1488 (22.6)	–	94 (38.5) [†]
Aspirin	1717 (23.5)	79 (11.0)	1638 (24.9)	<0.001	56 (23.0)
Statin	659 (9.0)	38 (5.4)	620 (9.4)	0.001	22 (9.0)

*P-value for difference between higher and lower cardiovascular risk groups.

[†]p < 0.05 for comparison with main sample.

For details on the definitions used for each risk factor and comorbidity, readers are referred to the online supplementary methods.

SBP: systolic blood pressure; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease.

Results

Study population characteristics

A total of 7298 males (mean age 58.6 ± 11.0 years; 5th–95th percentiles 40.6–76.3 years) were included in the main sample, of which 709 subjects were defined as having lower cardiovascular risk (Table 1). In addition, 244 subjects with a drop or no increase in SBP during exercise (Δ SBP ≤ 0 mmHg) were included for separate analysis. This group presented with a considerably higher prevalence of previous coronary artery disease (CAD) (47.5% vs 22.5%, $p < 0.001$) than other subjects. The risk factor profile and prevalence of comorbidities at the time of inclusion changed over the study enrollment period (Figure 1(b) and (c)). The unadjusted and adjusted relative risks of mortality associated with comorbidities, risk factors and use of medication are presented in the online supplementary material (Table S2).

Hemodynamic data

In total, 1152 (15.8%) subjects had an exaggerated SBP response to exercise as defined by the guidelines

(i.e. peak SBP ≥ 210 mmHg). This group achieved higher absolute peak METs (as absolute and percentage of age-predicted), a higher rate of perceived exertion and a higher peak heart rate than those with peak SBP < 210 mmHg (online supplementary material, Table S3). In addition, these subjects presented with higher systolic and diastolic BP at rest (148 ± 19 vs 129 ± 17 and 88 ± 11 vs 80 ± 11 mmHg, both $p < 0.001$) and lower prevalence of previous CAD than subjects with peak SBP < 210 mmHg.

Peak METs correlated weakly with SBP at rest ($r = -0.12$, $p < 0.001$) and with peak SBP ($r = 0.16$, $p < 0.001$) and slightly stronger with Δ SBP ($r = 0.29$, $p < 0.001$). The SBP/MET-slope showed a moderate negative correlation with peak METs ($r = -0.50$, $p < 0.001$), but this association was weaker in subjects within the middle two quartiles of fitness (i.e. 6.2–10.9 METs; online supplementary material, Table S4 and Figure S1).

The median (IQR) SBP/MET-slope in the lower-risk group was 4.9 (2.8) mmHg/MET, with a 95th and 97.5th percentile of 10.0 and 11.1 mmHg/MET, respectively (Figure 2(a); online supplementary material, Table S5). In the main sample, the median SBP/MET-slope

Figure 2. Peak SBP and SBP/MET-slope in the main sample (in gold) and in the subset of lower-risk subjects (in blue). The distribution of the SBP/MET-slope (calculated as $\Delta\text{SBP}/\Delta\text{MET}$) and peak SBP in each group are illustrated in (a) and (c), where arrows denote the 50th, 90th and 95th percentiles in the lower-risk group. In (b), the mean value of the SBP/MET-slope (95% CI) as well as the 90th percentiles across age groups are presented. The red horizontal line represents the suggested average, normative value of 10 mmHg/MET (as per American Heart Association guidelines). As only 18 subjects were > 75 years in the lower-risk group, no data are presented for this group. In (d), the SBP/MET-slope as a quadratic function of peak SBP is shown. In (a) and (d), 18 outliers (0.2%) in the main sample with a slope of >30 are not included.

was 6.2 (4.7) mmHg/MET (95th percentile: 16.0 mmHg/MET). The SBP/MET-slope increased with age in both groups (Figure 2(b)).

All-cause mortality and exercise hemodynamics

In our cohort ($n=7542$), the median (IQR) follow-up time was 18.4 years (16.3). During 138,546 person-years of observation, 3678 participants died (26.5 deaths per 1000 person-years).

SBP at rest and peak exercise and mortality. There was an increased risk of mortality for subjects in the two upper quartiles of SBP at rest (i.e. > 130 mmHg) in unadjusted

analysis, but no difference between quartiles in fully adjusted analysis (online supplementary material, Figure S2). For peak SBP, subjects with lower peak SBP had greater risk of 20-year mortality during follow-up in both unadjusted and adjusted analyses (Figure 3). The HRs for each hemodynamic variable standardized as Z-score are presented in the online supplementary material (Table S6).

An excessive SBP response to exercise as defined by the guidelines (i.e. peak SBP ≥ 210 mmHg) was not related to increased mortality in unadjusted analysis (HR 0.92, 95% confidence interval (CI) 0.83–1.01, $p=0.07$). When considering other risk factors, subjects *without* an excessive SBP response to exercise (i.e. peak

SBP < 210 mmHg) had 20% higher relative risk of mortality (fully adjusted HR 1.20, 95% CI 1.08–1.32, $p < 0.001$) versus subjects with peak SBP ≥ 210 mmHg. After excluding subjects with atrial fibrillation or previous CAD, stroke, claudication in a sensitivity analysis, the fully adjusted HR associated with a peak SBP < 210 mmHg was 1.17 (95% CI 1.04–1.32, $p = 0.010$).

Subjects with a drop or no increase in SBP with exercise had a 88% (HR 1.88, 95% CI 1.61–2.20, $p < 0.001$) higher unadjusted risk of all-cause mortality as compared with those with Δ SBP > 0 mmHg. After adjusting for comorbidities, risk factors and beta-blockers, there was a statistically non-significant 12% increase in risk associated with a drop or no increase in SBP (HR 1.12, 95% CI 0.95–1.32, $p = 0.17$).

SBP/MET-slope and mortality. Subjects with higher SBP/MET-slope had greater cumulative risk of mortality during follow-up (Figure 3). In the highest quartile of the SBP/MET-slope (i.e. > 9 mmHg/MET), 1028 subjects (57%) died during 20 years of follow-up, compared with 703 subjects (37%) in the lowest quartile (i.e. ≤ 4.3 mmHg/MET). After adjusting for age, test year, body mass index and cardiovascular risk factors, medications and comorbidities, subjects with an SBP/MET-slope in the highest quartile had a 23% (HR 1.23, 95% CI 1.12–1.36) higher risk of mortality than subjects in the lowest quartile. Excluding subjects with beta-blockers, anti-hypertensive medication, previous cardiovascular comorbidities or atrial fibrillation did not substantially alter these findings (sensitivity analyses; online supplementary material, Tables S7 and S8). Subjects with an SBP/MET-slope > 10 mmHg/MET (95th percentile in lower-risk group and by guidelines suggested normal, average increase) had a 69% (HR 1.69, 95% CI 1.56–1.84) and 20% (HR 1.20, 95% CI 1.10–1.31) higher risk of all-cause mortality versus those with ≤ 10 mmHg/MET in the unadjusted and fully adjusted model, respectively. The relationship between SBP/MET-slope and mortality had a J-shape, with the lowest mortality for those with a slope around 4 mmHg/MET (online supplementary material, Figure S3). In a landmark analysis, overall survival increased by two years from the first to the second period of inclusion (landmark year 1997), but the prognostic pattern of SBP/MET-slope persisted (online supplementary material, Figure S4).

Fitness, SBP/MET-slope and mortality. Fitness was positively associated with survival in unadjusted and adjusted analyses (online supplementary material, Figure S2). When stratified by fitness, higher SBP/MET-slope (i.e. > 6.2 mmHg/MET) was associated with worse unadjusted survival in subjects with higher fitness (> 7.3 Δ MET, $p < 0.001$), but not in unfit subjects

(≤ 7.3 Δ MET, $p = 0.73$; online supplementary material, Figure S5). When adjusting for peak METs in continuous analysis of hemodynamic variables based on Z-scores, most HRs were statistically non-significant (online supplementary material, Table S6).

Discussion

This study demonstrated in a large cohort of male Veterans that higher workload-indexed SBP response to exercise rather than higher peak SBP was predictive of all-cause mortality. We also observed that in a subset of lower-risk subjects, a 10 mmHg increase in SBP per MET corresponded to the upper 95th percentile rather than an average value as proposed by current exercise testing guidelines.

Reappraisal of the normal SBP response to exercise

During lower- or whole-body exercise, external workload is closely related to cardiac output and SBP, confirmed by early invasive studies.^{13,15,21} Accordingly, in male athletes reaching maximal effort,²² upper limits of normality in peak exercise SBP have been reported to be higher than in the general population.^{3,5} However, the normal workload-indexed response in SBP with exercise is not well defined.¹⁸ Although current guidelines on exercise testing suggest that SBP increases, on average, by 10 mmHg/MET during graded exercise,^{1,2} the underlying evidence is equivocal, and was recently questioned.¹⁸ In a subgroup of 709 subjects with lower cardiovascular risk and surviving at least 10 years from baseline, we observed 5 mmHg/MET and 10 mmHg/MET to represent the 50th and 95th percentile, respectively. Notably, we also observed a median SBP/MET-slope of 6.4 mmHg/MET in the remaining 6589 subjects with higher baseline risk. Our data suggest that the proposed normal increase in SBP per MET of 10 mmHg/MET^{1,2} represent an upper limit rather than an average expected increase.

Peak SBP and mortality

The definition and consequence of an exaggerated BP response with exercise remain controversial,^{4,18,23} and is more consistently reported as predictive of future development of hypertension^{7,24–27} than of cardiovascular risk and future mortality.^{6,11,28} Comparison across studies is challenging, considering the inconsistencies that exist in definitions and terminology for BP response to exercise.^{1,29–31} In addition, SBP determined at a sub-maximal^{24,28} or at peak external workload^{11,25,26} have been used to define thresholds. We found the adjusted relative risk of all-cause mortality to be 20% greater in subjects who did *not* reach a peak SBP ≥ 210 mmHg

Figure 3. Cumulative survival and relative risk of death over 20 years per quartile of peak SBP and SBP/MET-slope. Kaplan–Meier curves (with 95% CIs shaded) and Cox proportional HRs illustrating higher mortality in lower quartiles of peak SBP (left side) and in higher quartiles of the SBP/MET-slope (right side). HRs adjusted for test year, age, body mass index, cardiovascular risk factors, medications and comorbidities, as noted in methods. MET, metabolic equivalent of task.

during exercise. This risk was still 16% higher after excluding subjects with known baseline cardiovascular disease. However, it is possible that a significant proportion of subjects had undiagnosed, subclinical cardiovascular disease, which could manifest itself as an inability to adequately increase SBP during exercise. Nevertheless, our data suggest that in a clinical referral sample, reaching the threshold defined as an exaggerated SBP response per current guidelines is not necessarily associated with increased risk of mortality in males.

One important factor to consider when reviewing previous literature on the SBP response to exercise and its association with outcomes is the baseline risk

factor profile of the population being studied. In a study on 4907 males free from known heart disease and with a negative exercise electrocardiogram, Filipovský et al.³² found an increased relative risk of all-cause and cardiovascular mortality with higher Δ SBP during bicycle exercise testing. Similarly, in a highly selected sample of 300 normotensive, asymptomatic subjects undergoing clinical treadmill testing at the Mayo Clinic, the adjusted odds ratio for a major cardiovascular event within 7.7 ± 2.9 years of testing was 3.62 ($p = 0.03$) in subjects with a peak exercise SBP of ≥ 214 mmHg ($n = 150$), compared with those with a peak SBP of 170–192 mmHg ($n = 150$).³⁰ In contrast, studies including subjects with verified or high risk of

CAD have shown better⁹ or similar¹² survival in subjects reaching a peak SBP ≥ 210 mmHg than in subjects with lower peak SBP. Moreover, Hedberg et al.¹⁰ showed that in 372 community-dwelling 75-year-old subjects, those with the highest Δ SBP at the baseline exercise test (≥ 55 mmHg) had the lowest risk of all-cause and cardiovascular mortality during an average follow-up time of 10.6 years. In the current study, 23% of the sample had a history of CAD, while 2.8% and 3.7% had a previous diagnosis of stroke or claudication, respectively. Notably, the proportion of subjects with known CAD referred for exercise testing declined from $\sim 40\%$ during the early years of study inclusion (1987–1988) to $\sim 10\%$ around the year 2000 (Figure 1). However, after excluding subjects with previous cardiovascular disease, the relationships between low Δ SBP or a high SBP/MET-slope and mortality persisted.

The impact and rationale of considering external workload for risk prediction

In contrast to the lower mortality associated with a higher peak SBP or Δ SBP in our subjects, indexing the increase in SBP to external workload revealed an inverse relationship as a greater SBP/MET-slope was associated with higher mortality. Having an SBP/MET-slope over 10 mmHg/MET was associated with 69% and 20% higher risk of 20-year all-cause mortality in unadjusted and adjusted analyses, respectively. Given the strong association between fitness and survival,^{1,16,17} and the near-linear relationship between external workload and SBP,^{13–15} this is somewhat expected. In fact, studies measuring SBP at a defined submaximal workload have shown an association between submaximal SBP measures and mortality,^{28,33} as well as with incident myocardial infarction³⁴ and stroke.³⁵ Using a meta-analytic approach, Schultz et al.⁶ showed that SBP at a submaximal intensity significantly increased the risk of experiencing a composite of cardiovascular event and/or death by 4% per 10 mmHg, while SBP at peak exercise was not associated with higher risk. Thus, relating exercise SBP to workload, either as SBP measured at a defined submaximal workload or as the SBP/MET-slope as in our study, seems superior in terms of prognostic capability. The SBP/MET-slope offers a method more applicable to ramp protocols, where precise measures at a specified submaximal workload may be difficult to accurately obtain.

The current study also underscores the strong relationship between fitness and survival,^{1,16,17} as peak METs was a strong determinant of survival, and adjusting for peak METs in the continuous analysis of Z-scores rendered most HRs non-significant. However, the SBP/MET-slope added precision in terms of

predicting survival in subjects with higher fitness. Specifically, in subjects achieving a peak METs value ≥ 8.2 (the median in the main sample), having an SBP/MET-slope ≥ 6.2 was associated with 27% higher adjusted risk of all-cause mortality.

Limitations

First, our subjects were recruited as a clinically referred cohort and were all male; thus, these results are not necessarily representative of a general population or females. Second, measures of cardiac output and oxygen uptake were unavailable, and we relied on estimated external workload (METs) from standard, validated ACSM formulas.² Third, submaximal measures of SBP were unavailable, and could have provided additional insight to the SBP response to exercise. Finally, we only had data on all-cause mortality, and our results call for studies exploring the association between SBP/MET-slope and cardiovascular end-points.

Conclusions

Subjects exceeding the threshold defined as an exaggerated SBP response to exercise had better survival, while higher SBP/MET-slope was associated with worse survival. The SBP/MET-slope may add prognostic precision, at least among subjects with higher fitness, and could be considered for integration into clinical exercise testing reports.

Author contribution

FH and JM both contributed equally as senior authors in this work. KH, FH and JM contributed to the conception or design of the study. JM acquired the data and managed the database. KH, NC, TK, JWC, FH and JM contributed to the interpretation of data for the work. KH drafted the manuscript. All authors critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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