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ARTICLE

Blood pressure measurements during treadmill exercise testing and the risk for the future development of atrial fibrillation

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Abstract

Hypertension is a well-established risk factor for the onset and progression of atrial fibrillation (AF). Blood pressure (BP) measurements during routine exercise stress testing (EST) may identify subjects at increased risk for developing AF. We performed a retrospective analysis of treadmill EST carried out using the Bruce protocol in patients aged ≥40 years without a history of AF ($n = 17{,}617$; 42% women). BP was measured at rest, peak exercise, and 2-min recovery and analyzed for its association with the risk for developing AF. During a mean follow-up of 7 years, AF was documented in 4.5% of the patients. The incidence rate of AF per 1000 person-years increased with the rise in CHA_2DS_2VASc scores (3.26 for a Score=0 to 19.78 for scores ≥6). In a multivariate analysis, adjusting for risk score components and exercise capacity, systolic BP measurements taken at rest (≥130 vs. ≤110 mmHg), peak exercise (>170 vs. ≤150 mmHg), and recovery (>150 vs. ≤130 mmHg) were associated with an increased risk for AF: the hazard ratios (HRs) were 1.56 (95% CI, 1.30–1.87), 1.21 (1.01–1.45), and 1.33 (1.10–1.62), respectively. Similarly, diastolic BP measurements taken at rest (≥90 vs. <80 mmHg), peak exercise (≥100 vs. <90 mmHg), and recovery (>90 vs. ≤80 mmHg) were associated with an increased risk for AF: the HRs were 1.80 (1.36–2.38), 2.08 (1.28–3.37), and 1.56 (0.81–3.02), respectively. The association of exercise BP with AF was further observed when the BPs were analyzed as continuous variables and in subjects without a baseline diagnosis of hypertension. In conclusion, systolic and diastolic BP taken at the rest, peak exercise and recovery phases of EST may provide independent predictive information regarding future risk for developing AF.

Keywords Exercise stress testing · blood pressure · atrial fibrillation · cardiovascular disease

Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmia with potential adverse consequences when undiagnosed or untreated [1]. The incidence of AF is increasing due to the extended longevity of the population and more frequent identification of asymptomatic arrhythmia by wearable devices [2]. AF is associated with a significant increase in the incidence of stroke, congestive heart failure, impaired quality of life, and mortality [3]. CHA_2DS_2-VASc scoring is a well-validated method of risk stratification that is recommended for the risk assessment and prediction of stroke in patients with AF [4]. It constitutes a cornerstone in the therapeutic decision of whether to treat AF patients with anticoagulation therapy. However, it also has a noteworthy predictive value for the occurrence of AF itself in populations at risk [5, 6]. Hypertension is one of the components of the CHA_2DS_2-VASc risk score and itself is a well-established independent risk factor for developing AF [7]. Both AF and hypertension share common risk factors; the occurrence of both disorders is continuously increasing, and their coexistence is frequently reported [8]. In addition, hypertension has variable downstream effects on cardiovascular hemodynamics, myocardial structure, and renal function, which are recognized to increase the incidence of AF and promote its progression [9].

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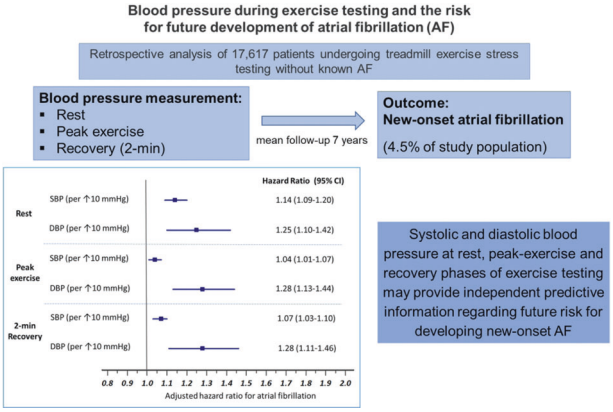
Graphical Abstract

Higher systolic and diastolic blood pressure measurements during rest, peak-exercise, and recovery phases of exercise stress testing were independently associated with future risk of developing new-onset atrial fibrillation. The predictive ability of blood pressure was retained after adjustment to measures of exercise capacity, CHA2DS2VASc score, and baseline diagnosis of hypertension.



An abnormal blood pressure (BP) result during exercise stress testing (EST) could represent a valuable indicator for the early recognition of patients at higher risk of developing AF. Studies have found a positive correlation between an exaggerated BP response during exercise stress testing (EST) and an increased incidence of major adverse cardiovascular events and the future development of hypertension, thereby emphasizing the importance and predictive value of repeated BP measurements during EST [10, 11]. In addition, an abnormal BP response to exercise may be associated with autonomic dysfunction, which has also been related to an increased incidence of AF [12, 13]. Nevertheless, few data exist regarding the ability of BP measurements during EST to predict the development of AF [14]. The purpose of the present study was to investigate the association between BP measurements taken at the rest, peak exercise, and recovery phases of EST and future risk for developing AF.

Methods

Study population

The study was a retrospective analysis of treadmill EST performed in the Cardiology Department at Carmel Medical Center, Haifa, Israel, between January 2005 and December 2019. Subjects aged 40 years or older undergoing EST using the Bruce protocol were included in the study. Patients with a history of AF as well as patients with a hypotensive response to exercise, defined as a failure of the systolic BP (SBP) to rise during exercise, and those for whom the exercise duration was <3 min, were excluded from the study population. Only the first exercise test performed by each patient during the study period was included in the analysis. The primary study endpoint was the occurrence of new-onset AF during long-term follow-up. Data on AF were retrieved from the Clalit Health Services (CHS) Health Maintenance Organization chronic disease registry, in which an AF diagnosis is based on ICD-9 codes (427.31 and 427.32) from a discharge diagnosis, a primary care physician, and community clinic visits. The diagnosis of AF has a high validity with a sensitivity of 85.4%, specificity of 95.0%, positive predictive value of 81.4%, and negative predictive value of 96.2% [15]. Data on vital status were retrieved from the Ministry of Interior. Cohort participants were followed-up until the first occurrence of the study outcome (AF), death, or the end of follow-up on 30 April 2021 was reached. Demographic data, risk factors, and comorbidities at the timepoint of exercise testing were retrieved from the computerized database of the CHS. At study entry, a CHA_2DS_2-VASc risk stratification score, ranging from 0 to 9 depending on the number and weight of the score's risk components, was calculated for each participant. The CHA_2DS_2-VASc score is calculated as follows: Congestive heart failure (1 point); Hypertension (1 point); Aged 65–74.9 years (1 point); Aged ≥75 years (2 points); Diabetes mellitus (1 point); Stroke (2 points); vascular disease (1 point); and Female sex (1 point) [4].

A study population outline is presented in Fig. 1. The study database was approved by the Carmel Medical Center Ethics Committee, which waived the need for individual patient consent due to the retrospective nature of the study.

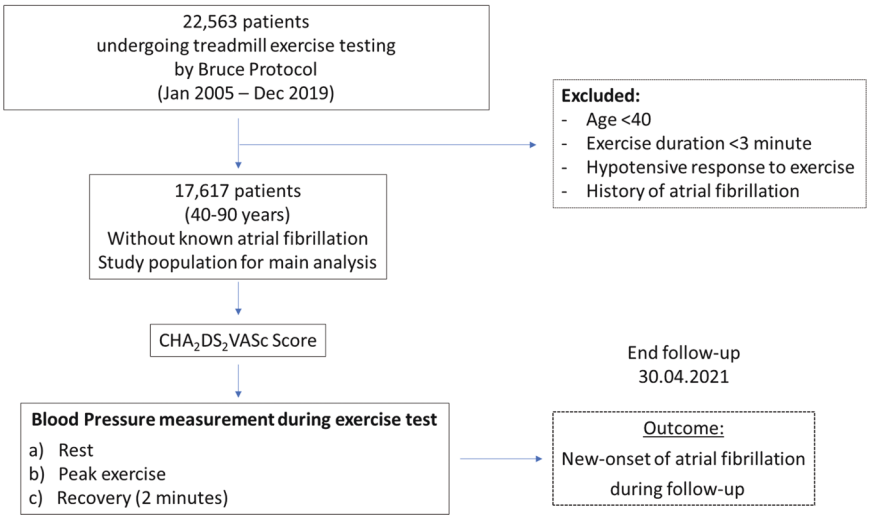


Fig. 1 Study outline

Table 1 Clinical characteristics of patients with vs. without atrial fibrillation during follow-up

Variables	Overall $n = 17617$	No AF $n = 16822$ (95%)	AF $n = 795$ (4.5%)	P value
Age (years)	59.6 ± 9.6	59.3 ± 9.6	64.5 ± 8.6	<0.001
Sex (female)	7318 (41.5%)	7083 (42.1%)	235 (29.6%)	<0.001
Hypertension	8049 (45.7%)	7521 (44.7%)	528 (66.4%)	<0.001
Hyperlipidemia	12077 (68.6%)	11483 (68.3%)	594 (74.7%)	<0.001
Diabetes mellitus	3727 (21.2%)	3495 (20.8%)	232 (29.2%)	<0.001
Obesity	4764 (27.4%)	4510 (27.2%)	254 (32.1%)	0.003
BMI (kg/m^2)	27.8 ± 4.5	27.8 ± 4.5	28.5 ± 4.4	<0.001
Smoking	8349 (47.4%)	7926 (47.1%)	423 (53.2%)	0.001
COPD	498 (2.8%)	464 (2.8%)	34 (4.3%)	0.013
Chronic kidney disease	577 (3.3%)	528 (3.1%)	49 (6.2%)	<0.001
Ischemic heart disease	3715 (21.1%)	3454 (20.5%)	261 (32.8%)	<0.001
Prior myocardial infarction	2262 (12.8%)	2084 (12.4%)	178 (22.4%)	<0.001
Prior stroke/TIA	669 (3.8%)	630 (3.7%)	39 (4.9%)	0.101
Peripheral artery disease	294 (1.7%)	270 (1.6%)	24 (3%)	0.006
Heart failure	241 (1.4%)	219 (1.3%)	22 (2.8%)	0.002
CHA_2DS_2Vasc score	1.68 ± 1.3	1.66 ± 1.30	2.23 ± 1.40	<0.001
Positive exercise test	1701 (9.7%)	1584 (9.4%)	117 (14.7%)	<0.001

AF atrial fibrillation, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *TIA* transient ischemic attack

Exercise stress testing

Treadmill EST was performed using the Bruce protocol for all patients [16]. EST was performed mainly as a diagnostic test, either as a screening tool for asymptomatic subjects or as part of the evaluation of ischemia in symptomatic patients. Participants were generally instructed not to take beta-blockers the morning of the test and to perform maximal effort during a graded incremental exercise test. Exercise capacity was assessed according to the metabolic equivalents (METs) achieved at peak exercise. Exercise termination was conducted in a standard fashion by a rapid reduction in the treadmill rate and incline followed by 10–20 s of walking at the level. Heart rate and BP were measured at rest and at the second minute of each Bruce stage during exercise and recovery. BP was measured by an exercise technician using a manual stationary device [767-Series Mobile Sphygmomanometer device (Welch Allyn)] with an appropriately sized arm cuff. BP at rest was measured in the standing position before initiating exercise. In the current analysis, SBP and diastolic BP (DBP) were analyzed at three time points during EST: (a) pre-exercise at rest, (b) peak exercise, and (c) in the recovery phase, at the second minute after the cessation of exercise. A positive result for EST was defined as symptoms suggestive of angina and/or electrocardiographic ST-segment changes >1 mm.

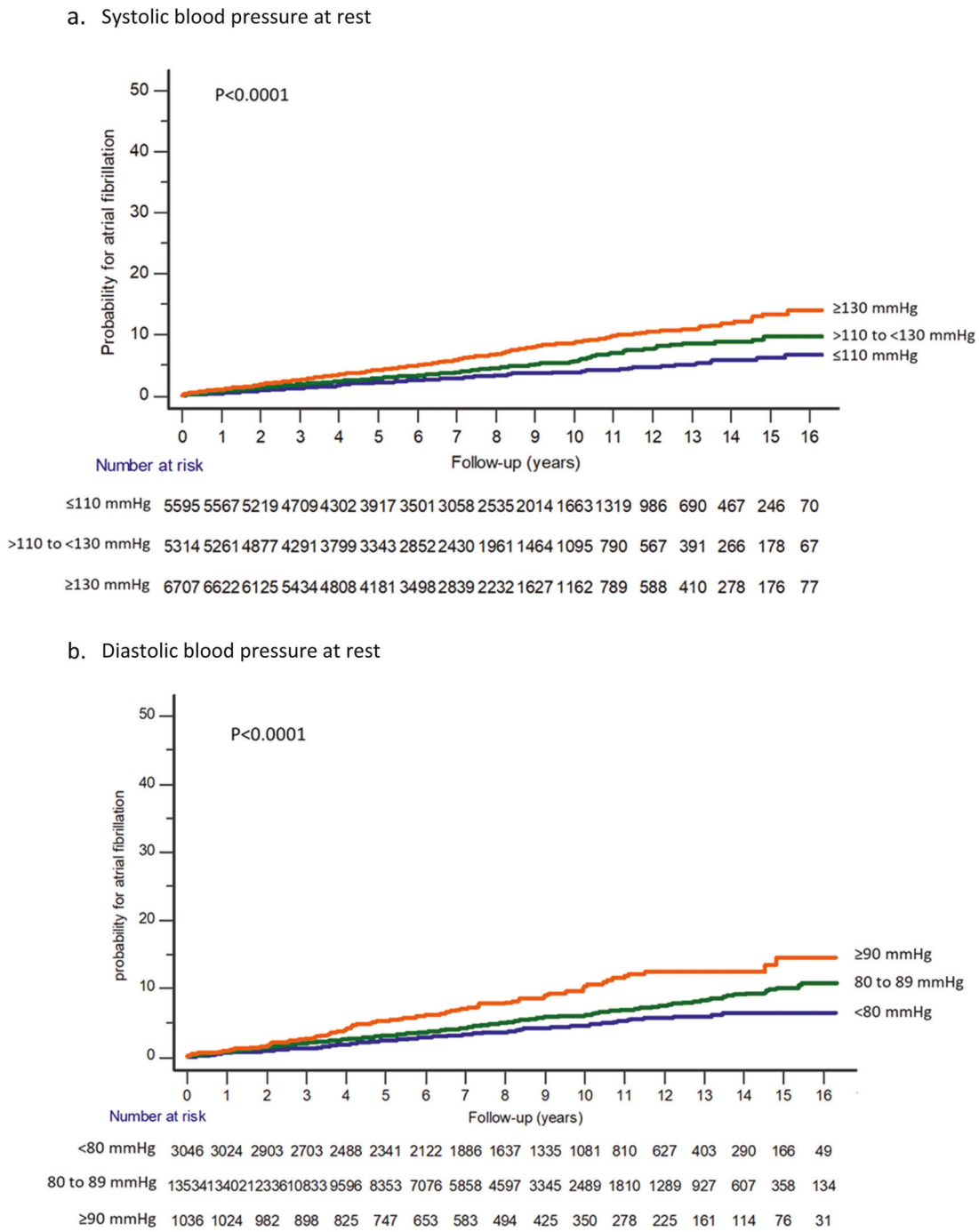


Fig. 2 Kaplan–Meier curves presenting the cumulative probability of developing atrial fibrillation, according to systolic and diastolic blood pressures taken at rest. DBP diastolic blood pressure, SBP systolic blood pressure

Data analysis

Continuous data are reported as the means and standard deviations or medians and interquartile ranges (IQRs), and categorical variables are reported as numbers and percentages. Normality of the distribution was assessed using the Kolmogorov–Smirnov test. Differences between normally distributed continuous variables were evaluated using the independent-samples T test, and differences between non-normally distributed variables were evaluated by the Mann–Whitney U test. The chi-square test was used to compare categorical variables. Demographics and comorbidities are presented according to the occurrence of AF during follow-up. Graphically, the incidence rate of AF per

Table 2 Occurrence and hazard ratio of atrial fibrillation during follow-up, according to blood pressure measurements during exercise testing

Blood pressure during exercise testing	Proportion with event	Rate per 1000 person-years	Unadjusted hazard ratio	CHA_2DS_2Vasc adjusted hazard ratio	Multivariable adjusted[a] hazard ratio
Rest BP (mmHg)					
>140/90	551/14022 (3.9%)	5.56	Ref.	Ref.	Ref.
≥140/90	244/3595 (6.8%)	9.95	1.79 (1.54–2.08) $P<0.001$	1.50 (1.29–1.75) $P<0.001$	1.41 (1.21–1.65) $P<0.001$
SBP (mmHg)					
≤110	179/5595 (3.2%)	4.15	Ref.	Ref.	Ref.
>110 to <130	221/5315 (4.2%)	6.09	1.48 (1.21–1.80) $P<0.001$	1.33 (1.09–1.63) $P=0.004$	1.24 (1.02–1.52) $P=0.032$
≥130	395/6707 (5.9%)	8.94	2.18 (1.82–2.60) $P<0.001$	1.75 (1.46–2.10) $P<0.001$	1.56 (1.30–1.87) $P<0.001$
DBP (mmHg)					
<80	120/3046 (3.9%)	4.72	Ref.	Ref.	Ref.
80–89	588/13535 (4.3%)	6.55	1.40 (1.15–1.70) $P=0.001$	1.25 (1.03–1.52) $P=0.027$	1.18 (0.97–1.44) $P=0.102$
≥90	87/1036 (8.4%)	10.39	2.20 (1.67–2.90) $P<0.001$	1.89 (1.43–2.49) $P<0.001$	1.80 (1.36–2.38) $P<0.001$
Per 10 mmHg SBP increase			1.25 (1.20–1.30) $P<0.001$	1.18 (1.12–1.23) $P<0.01$	1.14 (1.09–1.20) $P<0.001$
Per 10 mmHg DBP increase			1.37 (1.21–1.54) $P<0.001$	1.28 (1.13–1.24) $P<0.001$	1.25 (1.10–1.42) $P<0.001$
Peak exercise BP (mmHg)					
SBP (mmHg)					
≤150	223/5923 (3.8%)	5.24	Ref.	Ref.	Ref.
>150 to ≤170	299/6714 (4.5%)	6.68	1.28 (1.08–1.53) $P=0.005$	1.21 (1.01–1.44) $P=0.035$	1.15 (0.97–1.37) $P=0.016$
>170	273/4980 (5.5%)	7.54	1.45 (1.21–1.73) $P<0.001$	1.37 (1.15–1.64) $P<0.001$	1.21 (1.01–1.45) $P=0.032$
DBP (mmHg)					
<90	644/15661 (4.1%)	6.00	Ref.	Ref.	Ref.
90–99	134/1811 (7.4%)	8.84	1.47 (1.22–1.77) $P<0.001$	1.34 (1.11–1.62) $P=0.002$	1.39 (1.15–1.68) $P=0.001$
≥100	17/145 (11.7%)	14.82	2.47 (1.53–4.00) $P<0.001$	2.43 (1.50–3.93) $P<0.001$	2.08 (1.28–3.37) $P=0.003$
Per 10 mmHg SBP increase			1.08 (1.04–1.11) $P<0.001$	1.06 (1.03–1.10) $P<0.001$	1.04 (1.01–1.07) $P=0.022$
Per 10 mmHg DBP increase			1.38 (1.22–1.55) $P<0.001$	1.30 (1.15–1.47) $P<0.001$	1.28 (1.13–1.44) $P<0.001$
Recovery BP (mmHg) (2 min)					
SBP (mmHg) (n = 17337)					
≤130	219/5872 (3.7%)	4.84	Ref.	Ref.	Ref.
>130 to ≤150	338/7588 (4.5%)	6.65	1.39 (1.17–1.65) $P=0.011$	1.25 (1.05–1.48) $P=0.011$	1.16 (0.97–1.37) $P=0.101$
>150	231/3877 (6%)	8.86	1.85 (1.54–2.23) $P<0.001$	1.58 (1.31–1.91) $P<0.001$	1.33 (1.10–1.62) $P=0.003$
DBP (mmHg) (n = 17281)					
≤80	682/16037 (4.3%)	6.07	Ref.	Ref.	Ref.
<80 to 90	91/1141 (8%)	10.56	1.74 (1.40–2.16) $P<0.001$	1.56 (1.25–1.95) $P<0.001$	1.52 (1.22–1.90) $P<0.001$
>90	9/103 (8.7%)	12	1.98 (1.03–3.82) $P=0.042$	1.97 (1.02–3.80) $P=0.043$	1.56 (0.81–3.02) $P=0.197$
Per 10 mmHg SBP increase			1.14 (1.10–1.17) $P<0.001$	1.10 (1.07–1.14) $P<0.001$	1.07 (1.03–1.10) $P>0.001$
Per 10 mmHg DBP increase			1.44 (1.26–1.65) $P<0.001$	1.35 (1.17–1.55) $P<0.001$	1.28 (1.11–1.46) $P=0.001$

DBP diastolic blood pressure, *SBP* systolic blood pressure

[a]Adjusted for age, gender, hypertension, hyperlipidemia, diabetes mellitus, obesity, smoking, chronic kidney disease, vascular disease, prior stroke, heart failure, metabolic equivalents (METs) achieved and positive exercise test

1000 person-years and hazard ratios were plotted according to age decades and CHA_2DS_2VASc scores.

BP was documented at rest, peak exercise, and 2-min recovery. SBP was categorized into 3 subgroups according to values closest to the tertile cutoffs. The narrow range of DBP values did not enable tertile categorization; therefore, DBP was classified into three groups according to the sequential distribution of the values and clinical discretion. In addition, both SBP and DBP were analyzed as continuous variables per 10 mmHg increase in BP. The proportion of events and event rates per 1000 person-years were calculated according to the categorical distribution of the three BP measures (at rest, peak exercise, and recovery). The unadjusted and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for developing new-onset AF during follow-up were calculated for each BP measurement. An adjustment was made for the CHA_2DS_2VASc score. In an additional multivariable model, adjustments were made for the CHA_2DS_2-VASc score individual components as well as variables not incorporated in the risk score, including the presence of hyperlipidemia, obesity, smoking, chronic kidney disease, chronic obstructive pulmonary disease, METs achieved, and positive EST results. Kaplan–Meier curves were used to estimate the cumulative incidence of AF over time according to the different BP measurements, with comparisons between categories performed using the log-rank test.

Sensitivity analysis with calculation of p-for-interaction was performed to investigate the differential effect of a baseline diagnosis of hypertension (yes/no) on the prognostic impact of BP measurements. The results were considered statistically significant when the two-sided p value was <0.05. SPSS statistical software version 25.0 and MEDCALC version 16.8.4 were used to perform all statistical analyses.

Results

EST was performed using the Bruce protocol in 17,617 patients aged ≥40 years without known AF. The mean age was 59.6 ± 9.6 years, and 42% of the patients were women. A history of ischemic heart disease was evident in 3715 patients (21.1%). During a median follow-up period of 6.7 years (IQR 3.8–9.5 years), 795 patients (4.5% of the study population) experienced their first AF event. The clinical characteristics according to the occurrence of AF are presented in Table 1. The incidence of AF increased with age, with a hazard ratio of 8.67 for developing AF in patients in their ninth decade of life compared with those in their fifth decade of life (Supplementary Fig 1a). In addition, the incidence rate of AF during follow-up increased with the increase in CHA_2DS_2VASc risk scores, ranging from 3.26 per 1000 patient-years in patients with a score of 0–19.78 in patients with scores ≥6 (Supplementary Fig. 1b). The univariable and multivariable associations of the clinical and risk score variables with new-onset AF are presented in Supplementary Table 1. Older age, male sex, and hypertension were strong independent predictors of AF; the risk for AF was lower with increased baseline exercise capacity.

Blood pressure during EST and the future occurrence of AF

Kaplan–Meier plots displaying the distribution of the time to new-onset AF stratified by categories of SBP and DBP at rest are displayed in Fig. 2, and those during peak exercise and recovery are displayed in Supplementary Fig. 2. Event rates and unadjusted and adjusted HRs for AF according to the different BP measures are presented in Table 2. The multivariable adjusted HRs (95% CIs) for AF were significantly higher in patients in the third tertile vs. those in the first tertile of SBP at rest (≥130 vs. ≤110 mmHg), peak exercise (>170 vs. ≤150 mmHg), and recovery (>150 vs. ≤130 mmHg), with HRs of 1.56 (1.30–1.87), 1.21 (1.01–1.45), and 1.33 (1.10–1.62), respectively. The adjusted HRs for AF in the highest vs. lowest subgroups for DBP at rest (≥90 vs. <80 mmHg), peak exercise (≥100 vs. <90 mmHg) and recovery (>90 vs. ≤80 mmHg) were 1.80 (1.36–2.38), 2.08 (1.28–3.37) and 1.56 (0.81–3.02), respectively. A dichotomous cutoff for resting hypertension (≥140/90 vs. <140/90 mmHg) also displayed a significant association with the future development of AF [adjusted HR (95% CI) 1.41 (1.21–1.65), $p < 0.001$]. In addition, for each 10 mmHg increase in SBP or 10 mmHg increase in DBP, there was an associated increased risk for AF when measurements were taken at rest, peak exercise, and recovery (Table 2).

A diagnosis of hypertension was present at baseline in 8049 patients (46%). AF occurred during follow-up in 6.6% of patients with known hypertension compared with 2.8% of those without known hypertension.

In general, the prognostic impact of each 10-mmHg increase in BP during EST tended to be more prominent in patients without known hypertension but reached statistical significance only for DBP at rest (P for interaction = 0.030) and SBP at recovery (P for interaction = 0.043) and reached borderline significance for SBP at rest (P for interaction = 0.052) (Fig. 3).

Discussion

Repeated BP measurements during EST provide prognostic information regarding the risk for developing AF. Higher SBP and DBP levels during the rest, peak exercise, and recovery phases of EST were independently associated with an increased risk of AF during long-term follow-up.

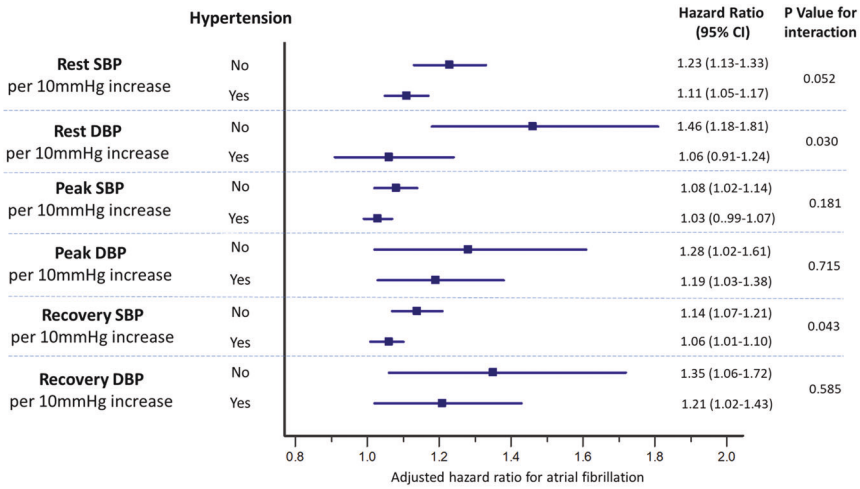


Fig. 3 The effect of a baseline diagnosis of hypertension on the risk for developing atrial fibrillation, according to blood pressure measurements during exercise stress testing. CI confidence interval, DBP diastolic blood pressure, SBP systolic blood pressure. Adjusted for CHA_2DS_2Vasc risk scores, hyperlipidemia, obesity, smoking, chronic kidney disease, chronic obstructive pulmonary disease, metabolic equivalents achieved, and positive exercise test

The predictive ability of BP was retained after adjustment for measures of exercise capacity, CHA_2DS_2VASc scores, and a baseline diagnosis of hypertension.

Several studies have previously reported worse outcomes in patients with an abnormal BP response to exercise during EST (hypotensive or hypertensive), with an increased risk of cardiovascular morbidity and mortality [10, 17]. Moreover, a hypertensive response to exercise was shown to be a marker of increased risk for the future diagnosis of new-onset hypertension in patients without known hypertension [11]. This may be related to endothelial dysfunction in younger individuals and decreased proximal aortic compliance with large arterial stiffness in the older population [18, 19]. Despite the well-established epidemiological relationship between hypertension and AF, involving both genetic and environmental factors, the pathophysiological basis explaining the higher propensity for AF among hypertensive patients is not known. The mechanisms are likely complex, and many mechanisms have been proposed [20]. Structural and functional abnormalities of the left atrium, including hypertrophy, fibrosis, and inflammation, are considered potential triggers contributing to the progression of remodeling and the onset of AF [7]. Moreover, the renin-angiotensin-aldosterone system (RAAS) has been implicated in the pathogenesis of AF in hypertensive patients through several mechanisms [7, 21]. Higher circulating levels of angiotensin II, angiotensin converting enzyme (ACE) and aldosterone with an overexpression of cardiac mineralocorticoid receptors are observed in patients with AF [22–24]. Hence, it has been reported that RAAS antagonists, when used as antihypertensive therapy in patients with hypertension, may reduce the likelihood of developing AF, although the evidence is not conclusive [25]. These mechanisms support the findings in our analysis of higher AF occurrence among patients with preexisting hypertension.

Although hypertension and AF often coexist, it is unclear whether there are BP thresholds for which the values above are associated with an increased burden of AF [26, 27]. In addition, there is a lack of data in the literature regarding the association between BP measurements during exercise and the risk for the future development of AF. In fact, to the best of our knowledge, the only direct analysis exploring the association between BP response during EST and AF has suggested that individuals with exercise-induced hypotension had the highest risk for developing AF [14]. This result was partially explained by preexisting coronary artery disease, impaired left ventricular dysfunction, and peripheral vasodilatation. Of note, subjects with a hypotensive response to exercise were excluded from the current analysis, as a hypotensive response to exercise is often associated with worse outcomes that are secondary to structural heart or valvular disease. Our findings shed light on the interplay between BP and AF, displaying an increased incidence of AF in patients with higher SBP and DBP measurements during the rest, peak exercise, and recovery phases of EST. The increase in the risk for developing AF was independent of exercise capacity and CHA_2DS_2VASc scores, variables that were both demonstrated in previous studies to be linked to the risk of AF, emphasizing the central role of BP in the epidemiology of AF [5, 6, 28].

The increased risk of AF observed in the current analysis was significant for BP levels that are not considered hypertensive. These findings are consistent with reports suggesting that the risk of AF is elevated in subjects with prehypertension or BP in the high-normal range [29–31]. Moreover, the significant association between BP at exercise and recovery with AF was retained in patients without known hypertension. It is possible that BP measurements during exercise better integrate the pathophysiological mechanisms that predispose an individual to AF. Subjects with a hypertensive response to exercise may be exposed more often to high pressure loads of the left ventricle, leading to hypertrophy, diastolic dysfunction, and increased filling pressures as well as retrograde atrial stretching and

structural remodeling. This results in an increased hemodynamic burden on the left atrium and the development of AF [9, 18, 32]. In this context, it should be noted that the relationship between leisure-time physical activity and AF risk is complex, with a suggested J-shaped pattern [33]. In addition, it was suggested that the development of AF in athletes appears to be independent of risk factors such as hypertension and diabetes [34].

AF is becoming a growing burden on health care systems, impacting morbidity and mortality. Hypertension is probably the most important modifiable risk factor for the development of AF [7]. SBP and DBP measurements during EST may help refine the individual risk prediction of AF and highlight the need for BP control before structural remodeling occurs to prevent future hypertension-related AF [9]. However, studies evaluating the impact of BP control on the future occurrence of AF have displayed conflicting results [27]. In addition, the treatment of individuals who show a hypertensive response to exercise without a baseline diagnosis of hypertension is controversial [35].

Several limitations of this study should be noted. As EST is often performed in patients for whom ischemic heart disease or arrhythmia is suspected, a selection bias may exist. We could also not exclude cases of AF occurring in contingency to an acute illness or periprocedural AF, where the exact pathophysiological role might not be related to the BP response to exercise. Moreover, BP changes over time were not assessed and may have an impact on the development of AF. In addition, although multivariable adjustment was performed, including many comorbidities with an impact on the incidence of AF, the potential effect of competing risks and residual unmeasured confounders, such as obstructive sleep apnea, may be possible. Finally, although closely related, the association between BP during EST and AF does not prove causation. The strengths of the present study include the large number of participants undergoing EST, the availability of outcome data with high validity regarding the occurrence of new-onset AF [15], and the analysis of repeated systolic and diastolic BP measurements during the rest, peak exercise, and recovery phases of EST. In addition, the adjustment of the risk models for exercise capacity and CHA_2DS_2VASc scores, which are well-established predictors of AF, and the performance of a sensitivity analysis in patients with and without baseline hypertension strengthen the significance of the results.

Conclusions

Repeated BP measurements during EST provide prognostic information regarding the risk for developing AF. A continuous and graded increase in systolic and diastolic BP during the rest, peak exercise, and recovery phases of EST was associated with higher rates of AF during long-term follow-up. The predictive ability of BP measurements was retained independent of exercise capacity and CHA_2DS_2-VASc scores. BP measurements during EST may help identify patients at a higher risk for developing AF, leading to intensified screening and targeted preventive measures, thus aiming to reduce the burden of AF and its associated health care expenses.

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Compliance with ethical standards

Conflict of interest The authors declare no competing interest.

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