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ORIGINAL RESEARCH

Clinical and Cardiovascular Magnetic Resonance Characteristics of Veteran Male Endurance Athletes With Atrial Fibrillation: VENTOUX-AF

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BACKGROUND: Older male endurance athletes exhibit an increased risk of atrial fibrillation (AF) of which the pathogenesis is unclear. We aimed to determine whether left atrial (LA) remodeling on cardiovascular magnetic resonance, blood pressure during exercise, and bradyarrhythmia on implantable loop recorder monitoring were associated with AF in athletes.

METHODS: VENTOUX-AF (Cardiac Magnetic Resonance Assessment of Left Atrial Fibrosis in Veteran Endurance Athletes) was a cross-sectional study comparing 39 male athletes with AF (27 symptomatic and 12 detected on implantable loop recorder) aged ≥50 years exercising ≥10 hour/week for ≥15 years with 94 exercise-matched male athletes in sinus rhythm and 33 sedentary male patients with AF. Participants underwent exercise testing and 3-dimensional late-gadolinium enhancement cardiovascular magnetic resonance with LA fibrosis quantification. A total of 106 asymptomatic athletes in sinus rhythm at recruitment received implantable loop recorder to detect incident AF and bradyarrhythmia.

RESULTS: Exercise systolic (208.5±29.9 versus 192.4±25.9 mm Hg, P=0.008) and exercise diastolic blood pressure (96.4±17.6 versus 88.3±9.7 mm Hg, P=0.02) were greater in athletes with AF than athletes in sinus rhythm. There was no difference in LA remodeling indices including LA fibrosis between these groups. During follow-up (median 730 days) of 106 athletes in sinus rhythm at baseline with implantable loop recorder, AF cumulative prevalence was 11.3% (12/106) and significantly associated with bradyarrhythmia (hazard ratio 5.89, 95% CI, 1.59–21.8, P=0.008). LA ejection fraction (52.5±11.6 versus 39.1±17.3%, P<0.001), LA fibrosis (7.6 [interquartile range, 4.7–9.2]) versus 2.9% [1.8–5.6], P=0.02) and exercise systolic blood pressure (208.5±29.9 versus 183.2±30.8 mm Hg, P<0.001) were greater in athletes with AF than sedentary patients with AF.

CONCLUSIONS: Hypertensive response to exercise was common in athletes with AF but LA remodeling and fibrosis were not. Further studies are required to determine whether these factors play a role in the pathogenesis of AF in athletes.

Key Words: AF in athletes ■ exercise-induced hypertension ■ sports cardiology

Moderate habitual exercise has been shown to protect against the development of atrial fibrillation (AF).[1,2] However, the prevalence of AF is believed to be greater in endurance athletes than the general population, particularly in older athletes.[3] Athletes who develop AF are reportedly highly symptomatic.[4] Importantly, they may have a risk of stroke that is not fully appreciated by conventional

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CLINICAL PERSPECTIVE

What Is New?

- Left atrial fibrosis and remodeling, although common among veteran male endurance athletes, are not associated with atrial fibrillation (AF) in contrast to exaggerated blood pressure response to exercise and bradyarrhythmia.

What Are the Clinical Implications?

- Athletes with AF may have normal resting blood pressure but an exaggerated blood pressure response to exercise. However, further studies are needed to investigate this potential association.
- Bradyarrhythmia was more common in veteran male athletes with incident AF and this may lead to challenges in effectively managing AF in athletes with rate-limiting medication. However, only 12 athletes developed incident AF and therefore the association of AF with bradyarrhythmia warrants further study.

Nonstandard Abbreviations and Acronyms

EIH	exercise-induced hypertension
ILR	implantable loop recorder
LAEF	left atrial ejection fraction

risk-stratification models.[5] The pathophysiology of AF in athletes is currently unknown and improved understanding is required to aid preventative strategies.

Structural left atrial (LA) remodeling is associated with AF and may also play a role in the development of AF in athletes.[6] LA dilatation is common among endurance athletes where it is proportional to physical fitness and the degree of left ventricular (LV) dilatation seen in athlete's heart.[7,8] Although LA dilatation is associated with an increased risk of developing AF in nonathletic populations, it is unclear whether this is also true in athletes.[9,10] LA fibrosis is considered a hallmark of LA remodeling and an electrophysiological substrate for the initiation and maintenance of AF.[11] Endurance athletes may develop LA fibrotic remodeling through repetitive increased stretch and raised circulating levels of profibrotic plasma biomarkers.[12–14] Data regarding LA fibrosis in athletes is limited due to the practically challenging advanced cardiovascular magnetic resonance (CMR) techniques required to visualize LA fibrosis. A small study demonstrated LA fibrosis on CMR was significantly greater in healthy veteran athletes compared with age- and sex-matched sedentary controls.[15] However, neither group were followed up for the incidence of AF and it is unknown whether LA fibrosis is associated with AF in endurance athletes.

Traditional risk factors associated with AF such as diabetes, obesity, and resting hypertension are often not present in endurance athletes. Other less well-studied clinical characteristics including exercise-induced hypertension (EIH) and enhanced parasympathetic tone may play a role in the development of AF in athletes.[16] Endurance athletes, particularly men, may develop an exaggerated blood pressure (BP) response to exercise and are more likely to develop overt hypertension prospectively.[17–19] In nonathletic populations, hypertension is a well-established cause for AF but it is unknown whether EIH is associated with AF in athletes.[20]

Increased parasympathetic tone leading to resting bradycardia is common among trained athletes and may facilitate reentry arrhythmia and AF by shortening the atrial refractory period.[12,21] Vagally induced AF, which typically occurs at night, after a heavy meal or after intense exercise, occurs more frequently in athletes compared with sedentary patients.[22,23] However, it is not known whether recognition of profound bradyarrhythmia can help identify athletes at risk of developing AF.

We aimed to investigate whether EIH, bradyarrhythmia, and indices of LA remodeling on CMR including LA fibrosis quantification were specifically associated with athletes with AF using exercise testing, cardiac rhythm monitoring, and comprehensive CMR.

METHODS

Ethical Approval

This research was granted ethical approval by the South Yorkshire & Humber National Health Service Research Ethics Committee (21/YH/0231). Each participant provided written informed consent before participation at the University of Leeds Advanced Imaging Centre, Leeds General Infirmary, Leeds, UK. Data are available by request to the corresponding author.

Recruitment

This observational cross-sectional study included 3 cohorts: athletes with AF, athletes in sinus rhythm (SR), and sedentary patients with AF.

Athletic participants were either recruited de novo or included from VENTOUX (Ventricular Arrhythmia and Cardiac Fibrosis in Endurance Experienced Athletes), a previous study where asymptomatic athletes were followed up for the detection of arrhythmia on implantable loop recorders (ILRs) over 2 years.[24] VENTOUX participants were male cyclists or triathletes aged ≥50 years old currently undertaking ≥10 hours of formal exercise per week for ≥15 years and regularly competing at the local, national, or international level. Exclusion criteria consisted of preexisting cardiovascular disease

(including coronary artery disease, tachyarrhythmia such as AF, and arterial hypertension), significant medical condition, or symptoms suggestive of underlying cardiovascular disease (anginal chest pain, palpitations, exertional dyspnea, and syncope).

Athletes with AF were recruited de novo from sporting clubs/organizations within the United Kingdom via email invitation to their respective club/organization or included from VENTOUX from those who developed AF during follow-up. Athletes with AF were male, aged ≥50 years old, and currently undertaking ≥10 hours of formal exercise per week for ≥15 years. De novo recruited participants had a formal diagnosis of AF by a consultant cardiologist (P.S.).

Sedentary patients with AF were recruited de novo from arrhythmia clinics at Leeds Teaching Hospitals NHS Trust, Leeds, UK. Sedentary patients with AF were male, aged ≥50 years old, and undertook ≤3 hours of formal exercise per week with a confirmed diagnosis of AF by a consultant cardiologist (P.S.).

Athletes in SR were included from VENTOUX from those athletes who did not develop AF on ILR follow-up.

Exclusion criteria for all participants included known ischemic heart disease, diabetes, and contraindication to CMR.

Baseline Assessment

Participants underwent baseline assessment consisting of physical examination which included measurement of resting BP and heart rate. Self-reported sporting and social histories were documented and cardiovascular risk factors were recorded. In those with a diagnosis of AF, medical records were examined to confirm AF diagnosis along with AF status, date of AF diagnosis, and any treatment received.

CMR Protocol

Participants underwent CMR imaging on a 3.0T Magnetom Prisma Siemens system and consisted of (full protocol detailed in the Supplementary Material):

- Cine imaging in short-axis and multiple long-axis planes for volumetric analysis.
- Adenosine stress and rest quantitative myocardial perfusion to identify myocardial ischemia.
- Pre-and postcontrast T1 mapping to allow estimation of the myocardial extracellular volume fraction.
- T2 mapping to identify inflammation and edema.
- Motion-corrected bright and dark blood late gadolinium enhancement imaging in short-axis and multiple long-axis planes to identify and quantify LV fibrosis.
- High-resolution 3-dimensional late gadolinium enhancement LA imaging during end-systole using a 3-dimensional inversion recovery-prepared, prospectively ECG-gated, respiration-navigated pulse sequence to identify and quantify LA fibrosis.

CMR Analysis

CMR studies were analyzed using commercially available software (CVI42, Circle Cardiovascular Imaging Inc. Calgary, Canada). Volumetric data were calculated by semiautomated tracing of the LV (endocardial and epicardial borders excluding papillary muscles), right ventricle (endocardial borders), LA, and right atrium. LV/right ventricular volumes, LV mass, and LA volumes were indexed to body surface area (BSA). T1 and T2 mapping and quantitative myocardial perfusion analysis are detailed within the Supplementary Material.

LA volumes were produced by semi-automated tracing of the LA endocardial border in the 4- and 2-chamber cine views to calculate mean minimum and maximum volumes. Maximum LA volume was defined as the volume at end-systole before the opening of the mitral valve. The LA volume at end-diastole immediately post closure of the mitral valve was used to define minimum LA volume. LA ejection fraction (LAEF) was calculated by using the following formula:

$$\text{LAEF} = \frac{(\text{LAV}_{\text{max}} - \text{LAV}_{\text{min}})}{\text{LAV}_{\text{max}}}$$

Segmental LA fibrosis quantification was performed using commercially available software (ADAS, Galgo Medical, Barcelona, Spain). Transaxial stack late gadolinium enhancement images underwent quality control to assess for proper myocardial nulling and the presence of artifact and images deemed of insufficient quality were excluded. LA midmyocardial walls were semiautomatically contoured using segmented LA images where the pulmonary veins and the mitral valve annulus were manually excluded. A 3-dimensional LA model was automatically reconstructed by the software with manual adjustment using corresponding CMR images to ensure exclusion of the pulmonary valve and mitral valve. LA fibrosis was quantified using an image intensity ratio method that compared the LA wall pixel intensity with blood pool signal. An image intensity ratio of >1.2 was defined as enhanced tissue and thus fibrosis.[25,26] Total LA and enhanced LA areas were derived and used to automatically calculate relative LA fibrosis percentage. LA fibrosis quantification was performed by the same level CMR 3 reporter who was blinded to the arrhythmia status of the participant. Participants with a history of AF ablation were excluded from fibrosis analysis due to the possibility of overestimating iatrogenic fibrosis.

Exercise Test

Participants underwent an exercise cycling test on a stationary exercise bicycle (Wattbike Pro, Wattbike, UK) after abstaining from caffeine and strenuous exercise for 24 hours prior (Table S1 in the Supplementary

Material). During exercise testing, maximum heart rate, and maximum power were recorded. BP was recorded at rest, at the end of the 5-minute warmup period, at peak exertion, and in recovery. Exercise BP was indexed to workload for standardization of BP values according to individual fitness levels.[27,28]

Implantable Loop Recorder Follow-Up

During a previous study (VENTOUX), 106 asymptomatic athletes in SR at recruitment underwent implantation of ILRs.[24] During this study, they were followed up for the incidence of AF and bradyarrhythmia. AF was defined as ≥6 minutes of AF and athletes without ≥6 minutes of AF on monitoring were classified as athletes in SR.[29] Bradyarrhythmia was defined as per consensus guidelines which consider profound sinus bradycardia <30 beats per minute, asystolic pause ≥3 seconds, or third-degree atrioventricular block to be abnormal ECG findings in athletes.[30] All arrhythmias were confirmed by a consultant cardiologist.

Statistical Analysis

Statistical analyses were undertaken using SPSS statistics 29 (IBM SPSS, Armonk, NY, USA). Normality of data was assessed using Shapiro–Wilk test. Continuous data were presented as mean±SD or median (interquartile range) depending on the normality of the data. Categorical data were presented as frequency (%). Categorical variables were compared using chi-square test. Depending on normality of data, continuous variables were compared with either 1-way ANOVA with post hoc Tukey correction or Kruskal–Wallis test with post hoc Bonferroni correction. Cox proportional hazard regression analysis was used to compare the probability of developing AF. A *P* value of <0.05 was considered statistically significant in all analyses.

RESULTS

The final analysis included 166 participants: 39 athletes with AF, 33 sedentary patients with AF, and 94 athletes in SR (Figure 1).

Athletes With AF Versus Athletes in SR

Athletes with AF were significantly older than athletes in SR (63.0±6.2 versus 58.7±5.4 years, *P*=0.002) (Table). Exercise systolic BP (208.5±29.9 versus 192.4±25.9 mm Hg, *P*=0.008) and exercise diastolic BP (96.4±17.6 versus 88.3±9.7 mm Hg, *P*=0.02) were both greater in athletes with AF than athletes in SR despite no significant difference in resting BP values (Figure 2).

There were no significant differences in LAEF (52.5±11.6 versus 57.2±7.8%, *P*=0.07), LA volume indexed to BSA (54.7±17.8 versus 53.0±12.1 mL/m^2, *P*=1.00), or LA fibrosis (7.6 (4.7–9.2) versus 7.6 (3.8–11.4)%, *P*=1.00) in athletes with and without AF.

In the VENTOUX subgroup of 106 asymptomatic athletes in SR at baseline who were prospectively followed up on ILR monitoring, 12 athletes developed AF with a cumulative prevalence of 11.3% (median follow-up 720 days) and an AF incidence rate per person-year of 0.06%. Athletes who developed AF on ILR were significantly older than those who did not (63.4±5.9 versus 58.7±5.4 years, *P*=0.02) with no other significant differences in baseline or CMR characteristics (Table S2 in the Supplementary Material).

In terms of predefined bradyarrhythmia, 32 athletes (30.2%) developed sinus bradycardia <30 beats per minute, 19 (17.9%) experienced an asystolic pause ≥3 seconds and third-degree atrioventricular block was present in 4 (3.8%) athletes during follow-up. Fourteen of these athletes developed a combination of >1 bradyarrhythmia subtype leading to a total of 39 (36.8%) who experienced ≥1 bradyarrhythmia. All bradyarrhythmia was detected asymptomatically. Twelve athletes who developed AF had a greater incidence of bradyarrhythmia than athletes who were free of AF during follow-up (9 [75.0%] versus 30 [31.9%], *P*=0.004) (Table S3 in the Supplementary Material). By Cox regression, athletes who experienced bradyarrhythmia had a higher risk of developing AF compared with athletes who did not (hazard ratio [HR], 5.89 [95% CI, 1.59–21.79], *P*=0.008) (Figure S1 in the Supplementary Material).

Athletes With AF Versus Sedentary Patients With AF

Athletes with AF had lower body mass index (25.2±2.6 versus 28.6±4.2 kg/m^2, *P*<0.001) and resting heart rate (55.6±11.1 versus 67.6±14.2 beats per minute, *P*<0.001) along with a lower prevalence of hypertension (4 [10.3%] versus 10 [30.3%], *P*=0.03) and hyperlipidemia (4 [10.3%] versus 15 [45.5%], *P*<0.001) than sedentary patients with AF. Athletes with AF exhibited typical features of athletic cardiac remodeling with increased LV size indexed to BSA (103.7±21.1 versus 81.6±16.0 mL/m^2, *P*<0.001), right ventricle size indexed to BSA (108.3±24.9 versus 83.1±17.5 mL/m^2, *P*<0.001), and greater LV mass indexed to BSA (67.3±13.1 versus 53.9±7.9 g/m^2, *P*<0.001) compared with sedentary patients with AF (Table).

Despite no significant difference in LA volume indexed to BSA (54.7±17.8 versus 49.9±14.9 mL/m^2, *P*=0.34), LAEF was significantly greater in athletes with AF compared with sedentary patients with AF (52.5±11.6 versus 39.1±17.3%, *P*<0.001). LA fibrosis (interquartile range, 7.6 [4.7–9.2] versus 2.9 [1.8–5.6]%, *P*=0.02) and exercise systolic BP (208.5±29.9 versus 183.2±30.8 mm Hg, *P*<0.001) were also significantly

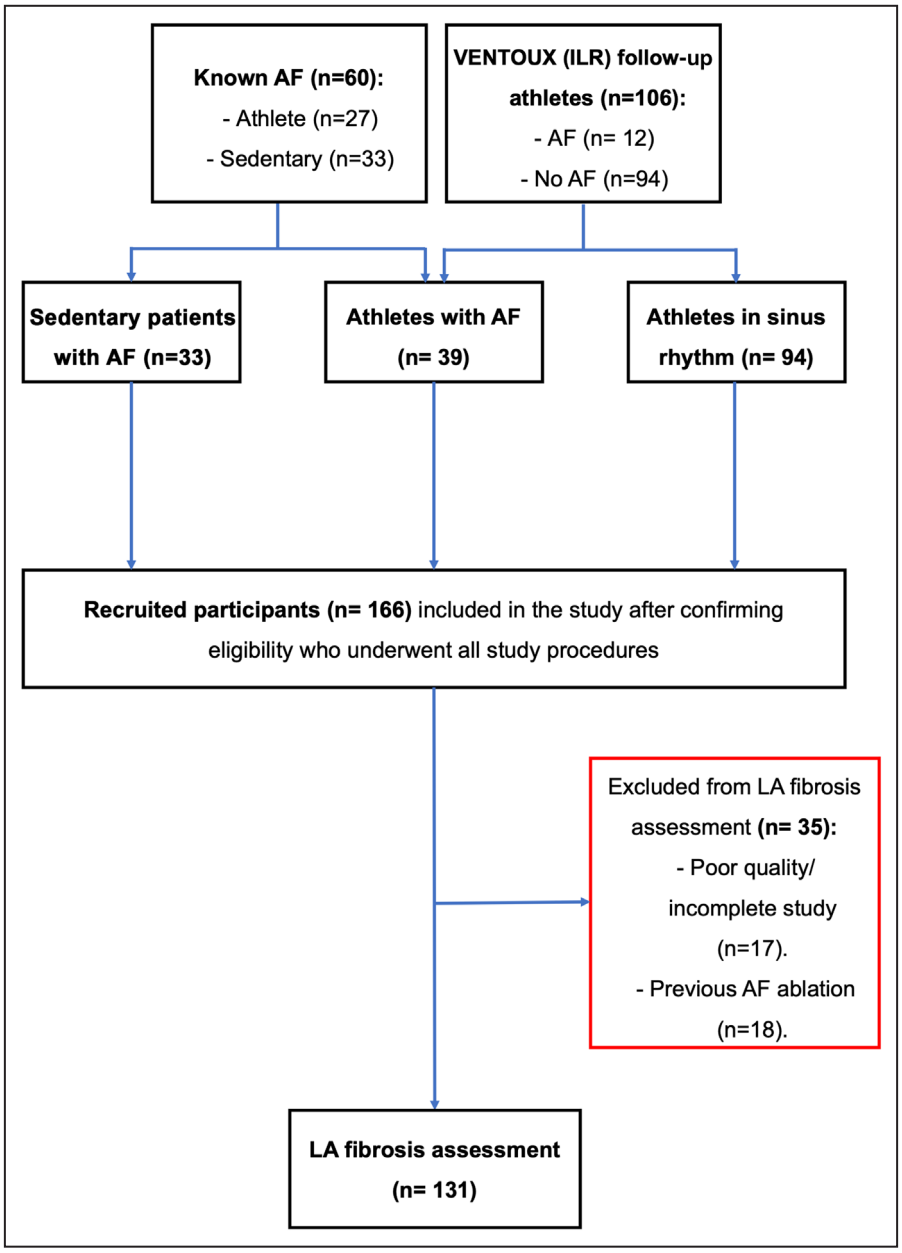

Figure 1. Consolidated Standards of Reporting Trials diagram: flow chart of recruited participants, excluded participants, and those who underwent LA fibrosis assessment.
AF indicates arial fibrillation; ILR, implantable loop recorder; LA, left atrial; and VENTOUX; Ventricular Arrhythmia and Cardiac Fibrosis in Veteran Endurance Athletes.

greater in athletes with AF compared with sedentary patients with AF with no difference in resting systolic BP (123.0±13.9 versus 125.3±16.0 mm Hg, *P*=0.72).

DISCUSSION

Our results indicate that an exaggerated BP response to exercise and bradyarrhythmia were distinct features in athletes with AF that require further study to determine whether they may play a role in the pathogenesis of AF in athletes. Although features of LA remodeling including LA fibrosis were prevalent among athletes with AF, they were not specific to this group.

Blood Pressure During Exercise

Exercise systolic and diastolic BP were both greater in athletes with AF compared with athletes in SR. This remained true when BP was indexed to hemodynamic

Table. Comparison of Athletes With AF Versus Athletes in SR Versus Sedentary Patients With AF

	Athlete with AF (n=39)	Athlete in SR (n=94)	Sedentary patient with AF (n=33)	Athlete with AF vs athlete in SR *P* value	Athlete with AF vs sedentary patient with AF *P* value
Baseline characteristics					
Age, y	63.0±6.2	58.7±5.4	65.5±8.8	0.002*	0.21
Body mass index, kg/m^2	25.2±2.6	24.8±2.7	28.6±4.2	0.81	<0.001*
Resting heart rate, bpm	55.6±11.1	53.8±7.2	67.6±14.2	0.44	<0.001*
Systolic BP, mm Hg	123.0±13.9	119.3±10.3	125.3±16.0	0.28	0.72
Diastolic BP, mm Hg	76.0±8.1	74.1±7.0	75.4±9.5	0.39	0.95
Hyperlipidemia (n)	4 (10.3%)	3 (3.2%)	10 (30.3%)	0.10	0.03*
Hypertension (n)	4 (10.3%)	0	15 (45.5%)	0.002*	<0.001*
Beta blocker (n)	7 (18.0%)	0	20 (60.6%)	<0.001*	<0.001*
Calcium channel blocker (n)	2 (5.1%)	0	10 (30.3%)	0.03*	0.004*
Angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker (n)	2 (5.1%)	0	9 (27.3%)	0.03*	0.01*
Flecainide (n)	4 (10.3%)	0	6 (18.2%)	0.002*	0.33
Oral anticoagulant (n)	13 (33.3%)	0	28 (84.9%)	<0.001*	<0.001*
Previous AF ablation (n)	10 (25.6%)	N/A	8 (24.2%)	N/A	0.89
AF duration, d	1248 (0.0–2044)	N/A	989 (199–2683)	N/A	0.17
Paroxysmal AF (n)	33 (84.6%)	N/A	23 (69.7%)	N/A	0.13
Current smoker (n)	0	2 (2.1%)	4 (12.1%)	0.36	0.03*
Ex-smoker (n)	7 (18.0%)	15 (16.0%)	9 (27.3%)	0.78	0.34
Alcohol, units/wk	10.0 (2.0–16.0)	5 (1.0–14.5)	10.0 (1.4–21.5)	1.00	1.00
Training history					
Pure cyclist (n)	27 (69.2%)	75 (79.8%)	N/A	0.28	N/A
Training years, >10 h/wk	29.3±15.4	21.2±12.0	N/A	0.006*	N/A
Current exercise, h/wk	10.6±3.2	11.7±3.1	N/A	0.08	N/A
Exercise test					
Max power, W	278.8±55.0	323.2±41.5	121.4±55.9	<0.001*	<0.001*
Exercise SBP, mm Hg	208.5±29.9	192.4±25.9	183.2±30.8	0.008*	<0.001*
Exercise DBP, mm Hg	96.4±17.6	88.3±9.7	90.0±25.0	0.02*	0.21
Relative exercise SBP to workload, SBP/W	0.72±0.22	0.52±0.11	2.0±1.8	<0.001*	<0.001*
Relative exercise DBP to workload, DBP/W	0.37±0.16	0.25±0.05	1.01±0.92	<0.001*	<0.001*
Cardiac magnetic resonance					
LV EDVi, mL/m^2	103.7±21.1	108.4±15.1	81.6±16.0	0.31	<0.001*
LV EF, %	54.6±5.1	56.0±4.1	53.9±10.4	0.86	0.86
LV mass indexed, g/m^2	67.3±13.1	70.4±9.9	53.9±7.9	0.26	<0.001*
RV EDVi, mL/m^2	108.3±24.9	109.8±16.5	83.1±17.5	0.91	<0.001*
RV EF, %	52.5±11.6	53.1±5.1	51.9±7.6	0.51	1.00
LA volumeindexed, mL/m^2	54.7±17.8	53.0±12.1	49.9±14.9	1.00	0.34
LA EF, %	52.5±11.6	57.2±7.8	39.1±17.3	0.07	<0.001*
Right atrial volume, mL	116.9±48.7	97.3±27.6	95.8±36.4	0.005*	0.03*
Stress MBF, mL/g per min	2.2±0.6	2.2±0.7	2.2±0.6	0.95	0.97
Rest MBF, mL/g per min	0.7±0.2	0.6±0.2	0.8±0.4	0.50	0.08
Myocardial perfusion reserve	3.5±1.3	3.8±1.2	3.2±1.1	0.33	0.59
Inducible ischemia (n)	0	0	2 (6.1%)		0.12
Native T1, ms	1240.9±67.4	1242.6±40.9	1217.0±90.3	0.86	0.22
Extracellular volume, %	21.8±2.6	21.0±2.0	20.7±3.1	0.16	0.12
T2, ms	41.5±2.4	40.5±1.9	42.2±2.6	0.04*	0.32
Nonischemic LV fibrosis (n)	17 (43.6%)	42 (44.7%)	8 (24.2%)	0.91	0.09
LA fibrosis, %	7.6 (4.7–9.2)	7.6 (3.8–11.4)	2.9 (1.8–5.6)	1.00	0.02*

Values are mean±SD or frequency (%) or median (interquartile range). N=131 for left atrial fibrosis: athletes with AF=28, athletes in sinus rhythm=80, and sedentary patients with AF=23. ACE-I; AF indicates atrial fibrillation; BP, blood pressure; DBP, diastolic blood pressure; EDVi, end-diastolic volume indexed; EF, ejection fraction; LA, left atrial; LV, left ventricular; MBF, myocardial blood flow; RV, right ventricular; and SBP, systolic blood pressure.

*P<0.05.

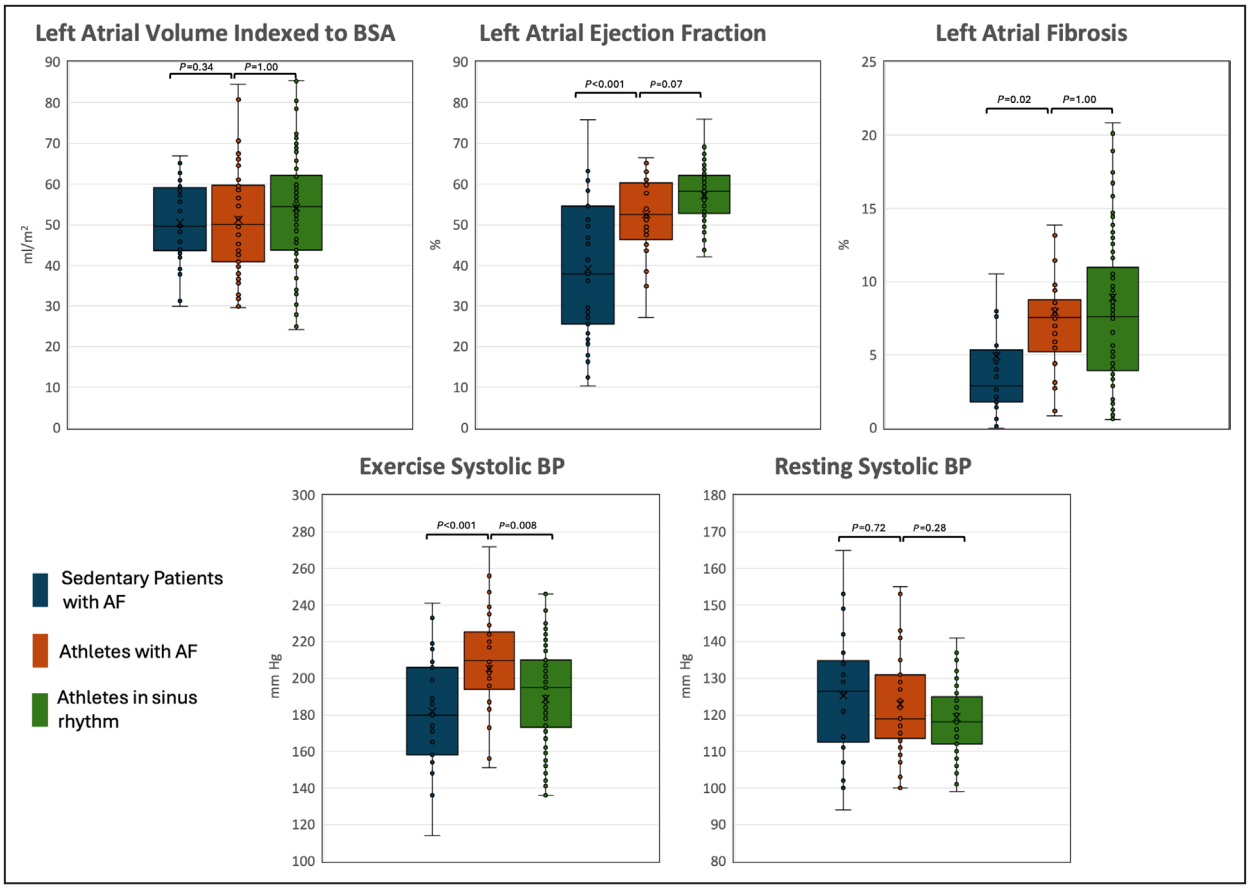

Figure 2. Comparison of LA remodeling indices and BP differences; box plot illustrations comparing LA volume (top left), LA ejection fraction (top middle), LA fibrosis (top right), exercise systolic BP (bottom left) and resting systolic BP (bottom right) in sedentary patients with AF (blue), athletes with AF (orange), and athletes in SR (green).
Black vertical lines represent range, colored boxes represent lower and upper quartiles with horizontal black line (median) and X (mean). AF indicates atrial fibrillation; BP, blood pressure; BSA, body surface area; LA, left atrial; and SR, sinus rhythm.

workload suggesting higher BP values were not due to an increased workload in athletes with AF. Although there are no consensus guidelines defining EIH, a systolic value of >210 mm Hg is commonly used whereas the 2013 American Heart Association Exercise Standards for Testing and Training guidelines classify >250 mm Hg as an exaggerated BP response.[31,32] In our study, the mean exercise systolic BP of athletes with AF was 208.5±29.9 mm Hg. Athletes who experience sustained bouts of hypertension of this magnitude during exercise for several years may have a greater risk of AF, particularly as athletes in this study were training >10 hours per week for >15 years. We therefore propose that an exaggerated hypertensive response to exercise may be a novel and potentially modifiable risk factor in the pathogenesis of AF in veteran athletes.

The mechanism of EIH in athletes is unproven but may include arterial stiffness, endothelin dysfunction, or renin-angiotensin-aldosterone system dysregulation.[33] Previous data suggest LV hypertrophy may also be associated with EIH.[34] However, this was not replicated in our study as there were no significant difference in LV mass between athletes with and without AF.[35] Increased LV mass and LA dilatation relate to fitness in addition to BP in athletes, and therefore it is possible that older athletes with less compliant vasculature have increased afterload, particularly during exercise that leads to AF but without further remodeling.

Increased Parasympathetic Tone

The overall incidence of bradyarrhythmia was 36.8% over 2 years. A previous study of 20 veteran runners demonstrated 8 (40%) to have sinus bradycardia <35 beats per minute, 8 (40%) had asystolic pauses >1.5 seconds, and 3 (15%) had third-degree atrioventricular block on 48-hour ambulatory ECG.[36] Furthermore, several studies have indicated that a significant proportion of veteran athletes require pacemaker insertion for bradyarrhythmia with implantation rates of up to 11%.[37,38] However, these findings are in contrast with younger athletes in whom bradyarrhythmia outside athletic physiological adaptation is rare.[39,40] Furthermore, Andersen et al.

found cumulative race exposure was associated with an increased risk of bradyarrhythmia and hospitalization due to bradyarrhythmia in male endurance athletes but not in female athletes.[41] Therefore, the high incidence of bradyarrhythmia in our study may have been related to the inclusion of older male endurance athletes.

Bradyarrhythmia was the strongest predictor of AF risk in our study conferring a 6-fold increased risk of developing AF. However, the total number of athletes (n=12) who developed AF during follow-up was low and therefore this finding should be interpreted cautiously. Whether increased vagal stimulation itself is causative of AF in athletes or is merely an incidental coexisting finding is unknown. It is also possible that bradyarrhythmia in veteran athletes is indicative of underlying sinus node dysfunction thus predisposing them to atrial arrhythmia.[42] Targeting the ganglionated plexi with radio-frequency cardioneuroablation may be of potential therapeutic benefit in those with vagally induced AF whereas detraining has been shown to normalize parasympathetic tone in animal models; therefore, further exploration of this hypothesis is needed.[4344]

LA Remodeling

We found LA fibrosis was prevalent among athletes but there was no difference in LA fibrosis between athletes with AF that was predominantly paroxysmal and athletes in SR. Endurance athletes are known to exhibit significant LA remodeling and it is therefore possible that LA fibrosis is simply a marker of this process.[45] However, the link between LA remodeling and AF risk in athletes is unclear as young athletes who exhibit marked cardiac remodeling are not believed to be at an increased risk of AF.[46]

LA fibrosis was significantly greater in athletes compared with sedentary patients with AF suggesting that factors related to prolonged, intense exercise may cause LA fibrosis. As our cohort exclusively consisted of high-intensity cyclists and triathletes, it is possible that the majority of our athletic cohort had high levels of LA fibrosis making the effect LA fibrosis indistinguishable, particularly as a small study demonstrated cyclists are believed to have the greatest extent of LA fibrosis.[47]

LAEF was significantly lower in sedentary patients with AF compared with athletes with AF and athletes in SR. Previous data regarding LA function in athletes is conflicting as certain studies suggest athletic training is associated with reduced LAEF whereas others have shown LAEF is maintained in older athletes.[8,48] In our study, athletes in SR trended toward the greatest LAEF suggesting athletic training was not associated with reduced LAEF. However, it is possible that LAEF was greater in this group due to being in SR as a previous study found LAEF was lower in patients depending on whether they were in SR or AF at the time of echocardiography assessment.[49] In our study, athletes with AF had a significantly greater LAEF than sedentary patients with AF suggesting that atrial myopathy is not associated with athletic training. This is supported by a study of symptomatic patients with AF undergoing catheter ablation in which those with increased cardiorespiratory fitness (VO_2max > 2.0 mL/kg/min) had reduced LA pressure and greater LA compliance compared with those with reduced cardiorespiratory fitness.[50]

LA size was similar between all groups but the underlying mechanism of LA dilatation likely differs between sedentary patients and athletes. In athletes, LA dilatation is believed to correspond with greater aerobic fitness capacity and therefore may be related to the exponential increase in cardiac output during exercise.[8] In sedentary patients, LA dilatation is related to the presence of comorbidities such as hypertension and obesity, which are associated with diastolic dysfunction and increased filling pressures.[51] Increased LA volume on CMR in patients suspected to have heart failure correlates with greater pulmonary capillary wedge pressure on right heart catheterization indicative of raised LA filling pressures.[52] In certain athletes, it is also possible that occult hypertension may also contribute to LA dilatation by causing LA pressure overload.

Although overall we did not find indices of LA remodeling were specific to athletes with AF, it is plausible that athletes who exhibit LA remodeling in combination with other extrinsic factors such as EIH and bradyarrhythmia are then more likely to develop AF.

Limitations

The main limitation of our study was the relatively small sample size, which exclusively consisted of White European veteran men and therefore limits translation to other groups. Older male athletes were chosen to best characterize the features of AF in athletes in the group believed to be at the greatest risk increased AF. However, emerging data suggest female athletes may also be at risk of AF and therefore similar studies are required in female athletes.[53] Athletes were recruited via self-referral, which may have led to a referral bias potentially leading to recruitment of athletes with AF who were more symptomatic. Alternatively, we recruited only current athletes and therefore this may have led to a selection bias excluding athletes with AF whose symptoms had led to a reduction in exercise training. Likewise, the results pertaining to asymptomatic athletes cannot be automatically extrapolated to symptomatic athletes. The use of cardiopulmonary testing would have enabled better assessment of cardiovascular fitness and also physiological adaptation

to allow proportionally assessment of BP and LA remodeling relative to fitness. Rate-limiting medication on the day of exercising in those with AF may have also influenced exercise BP data. The number of athletes who developed AF during follow-up was low, limiting the results of this subgroup. Furthermore, the use of ADAS software to identify LA fibrosis has not been histologically validated in athletes. Finally, our cross-sectional study demonstrates correlation and thus may be used for hypothesis-generating but our findings do not equate to causation.

CONCLUSIONS

Hypertensive response to exercise was associated with AF in veteran male athletes whereas LA fibrosis was not. Hypertensive response to exercise may therefore play a role in AF-pathogenesis but requires further study in longitudinal and interventional studies, particularly as it is potentially modifiable if proven to be a risk factor. CMR-indices of LA remodeling were distinct in athletes but this did not translate to AF risk.

ARTICLE INFORMATION

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Disclosures

We declare no disclosures or competing interests.

Supplemental Material

Data S1
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