

Myocardial fibrosis and its relationship with ventricular arrhythmias and reduced ventricular systolic function in young and veteran endurance athletes

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Aims

The prevalence of ventricular fibrosis and its association with ventricular arrhythmias (VAs) and reduced ventricular systolic function in endurance athletes remains unclear.

Methods and results

We evaluated 296 young [median age 19 (17–22)] and 138 middle-aged [56 (50–60)] male endurance athletes, alongside 66 middle-aged non-athletic controls [54 (49–60)], all without known cardiac disease. Cardiac magnetic resonance imaging assessed myocardial fibrosis and biventricular function. Twenty-four-hour Holter monitoring was used to quantify VAs. Non-hinge-point fibrosis was more prevalent in middle-aged athletes compared with young athletes (20 vs. 3%, $P < 0.001$) and middle-aged controls (20 vs. 9%, $P = 0.045$), while hinge-point fibrosis did not differ. Reduced left ventricular ejection fraction and/or right ventricular ejection fraction was more frequent in middle-aged athletes than controls (23 vs. 8%, $P = 0.009$), but similar to young athletes (23 vs. 22%, $P = 0.906$). Middle-aged athletes had a higher prevalence of non-sustained ventricular tachycardia (8 vs. 2%, $P = 0.006$), >100 premature ventricular complexes/24 h (13 vs. 5%, $P = 0.004$), multifocal ventricular ectopy (11 vs. 4%, $P = 0.003$), and complex ventricular ectopy (25 vs. 10%, $P < 0.001$) compared with young athletes, with

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no significant differences compared with controls. Non-hinge-point fibrosis increased the odds of a higher burden of unifocal and multifocal ventricular ectopy, but not of reduced systolic function.

Conclusion

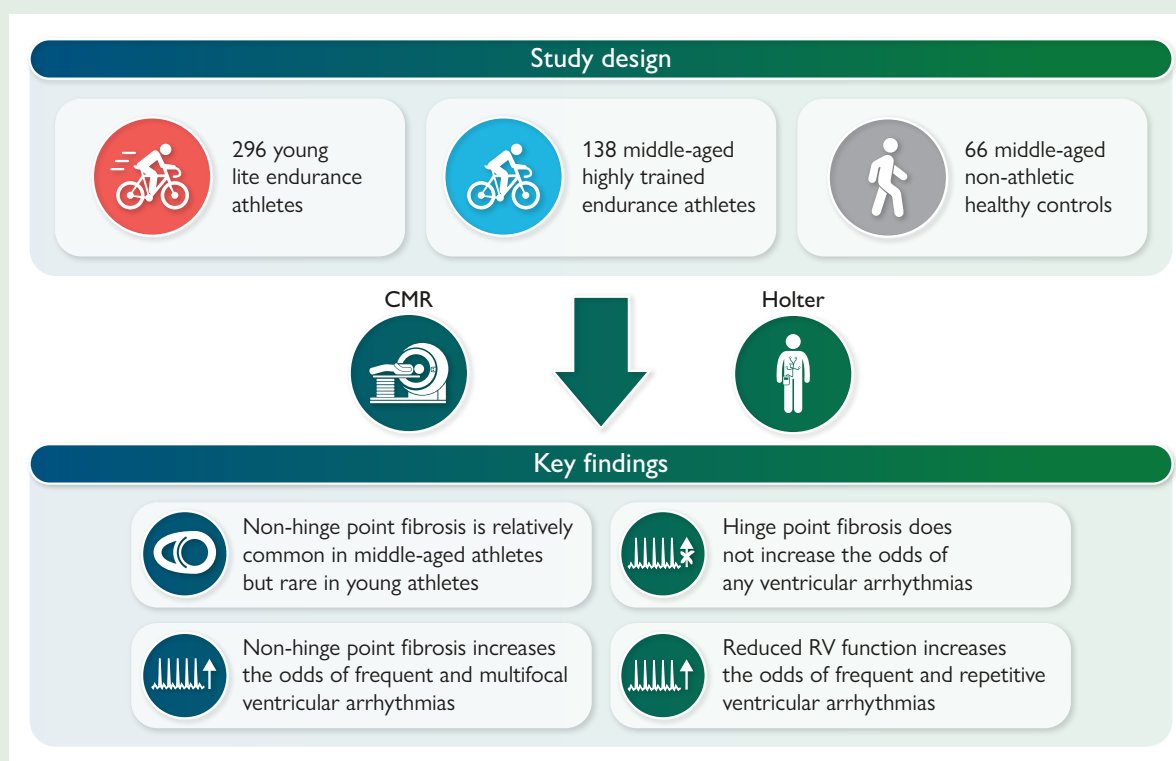
Middle-aged athletes more frequently exhibit myocardial fibrosis than young athletes and middle-aged non-athletes. Non-hinge-point fibrosis is present in up to one-fifth of middle-aged athletes and predictive of a higher burden of both unifocal and multifocal ventricular ectopy. Reduced systolic function is more prevalent in athletes and not predicted by fibrosis.

Lay summary

We studied young and middle-aged male endurance athletes and non-athletes using heart magnetic resonance imaging scans and 24 h heart rhythm monitoring to evaluate scarring of the heart muscle, pumping function, and abnormal heart rhythms.

- Scarring of the heart muscle is relatively common in middle-aged athletes, but rare in the young. About one in five middle-aged athletes showed a particular ‘non-hinge-point’ pattern of scar tissue, which was rare in young athletes and also less frequent in middle-aged non-athletic individuals.
- Non-hinge-point scar was linked with more frequent abnormal heart rhythms. Athletes with this pattern of scar more frequently had premature ventricular beats (extra beats originating from the heart’s lower chambers).

Graphical Abstract



Keywords

Athlete's heart • Endurance exercise • Myocardial fibrosis • Ejection fraction • Ventricular arrhythmias • Premature ventricular complexes

Introduction

Despite the well-described cardiovascular benefits of exercise,¹ chronic exposure to high-intensity endurance training may lead to adverse cardiac adaptations in a subset of athletes. Myocardial fibrosis, in particular, has been the subject of intense investigation, as it is considered a relatively unambiguous marker of adverse remodelling and appears to occur more frequently in endurance athletes than in the general population.^{2–7}

Several distinct patterns of myocardial fibrosis have been described, including non-ischaemic mid-myocardial or epicardial striae in the

lateral left ventricular (LV) wall, as well as ischaemic patterns such as endocardial or transmural scarring. These scar patterns have all been associated with ventricular arrhythmias (VAs) and with impaired ventricular function at rest or during exercise.^{1–3,8–10} In contrast, hinge-point fibrosis, a pattern more commonly observed in endurance athletes, has not been linked to VAs or sudden cardiac death (SCD),^{11–13} although it has been associated with reduced right ventricular (RV) systolic function.¹³

Despite this interest in myocardial fibrosis among athletes, existing data on its prevalence and potential association with VAs largely derive from smaller studies and remain to be confirmed in a broader athletic

cohort. Furthermore, evidence on myocardial fibrosis in a younger athletic population remains scarce.

In this study, we aimed to assess the prevalence of myocardial fibrosis and its relationship with VAs and reduced ventricular systolic function in both young and middle-aged endurance athletes as well as in middle-aged non-athletic controls. In addition, we sought to explore potential links between myocardial fibrosis, VAs, and reduced systolic function across different age groups and fitness levels. These insights may help refine future risk stratification strategies in athletic populations.

Methods

Study participants

Our study cohort consisted of young elite competitive endurance athletes from the Pro@Heart study, and both middle-aged highly trained endurance athletes and healthy non-athletic controls from the Master@Heart study. The respective study protocols have previously been defined.^{14,15} In Pro@Heart male athletes aged between 14 and 23 years were recruited through their sports federation or team and were eligible if they were (i) competing in an endurance sport in which aerobic conditioning is a principal component of performance (e.g. triathlon, cycling, rowing/canoeing, cross-country skiing, distance running ≥ 1500 m, and swimming ≥ 400 m), (ii) competing at a national or international level, and (iii) non-smokers. Athletes with a known pre-existing cardiac or respiratory conditions or with contra-indications to cardiac magnetic resonance (CMR) imaging were excluded. Participants of the Pro@Heart study were examined at one of five medical facilities: University Hospitals Leuven (Leuven, Belgium), University Hospital Antwerp (Antwerp, Belgium), Jessa Ziekenhuis (Hasselt, Belgium), Baker Heart and Diabetes Institute (Melbourne, Australia), and St Vincent's Hospital (Melbourne, Australia).

In the Master@Heart study, participants were informed about the study through a dedicated web portal (www.masteratheart.be), and an online screening questionnaire was used to assess the eligibility of study candidates. The web portal was advertised to both the athletic and wider community through media advertisements (e.g. traditional broadcasting and social media). Promotional material aimed at non-athletes omitted reference to exercise or sports to mitigate the risk of selection bias. Male participants aged between 45 and 70 years were included. Athletes were defined as those engaging in ≥ 6 –8 h per week of high-intensity endurance exercise and non-athletic controls as those engaging in < 3 h per week of physical activity without a prior history of exposure to high-intensity endurance exercise. Participants were excluded from Master@Heart if they (i) had a background of any cardiovascular disease, (ii) were current or past smokers, (iii) were taking any anti-diabetic, statins, or anti-hypertensive medication, (iv) had a body mass index (BMI) > 27.2 kg/m², and (v) had a known allergy to iodine contrast agents. Participants of the Master@Heart study underwent investigations at one of three medical centres: University Hospitals Leuven, University Hospital Antwerp, and Jessa Ziekenhuis.

Both studies conformed to the Declaration of Helsinki and were approved by local Ethics Committees (Pro@Heart trial registration number: S57241; Master@Heart trial registration number: S61336). All participants provided written informed consent.

Cardiac magnetic resonance imaging

CMR was performed using a 1.5 or 3.0 T magnetic resonance imaging (MRI) scanner (Magnetom Aera and Sigma 1.5 T—Siemens Healthineers, Erlangen, Germany; Ingenia, Achieva, or Ambition 1.5 T—Philips Medical Systems, Best, The Netherlands—Prisma 3.0 T, Siemens Healthineers). A steady-state free precession dynamic echo-gradient sequence was used to obtain cine-loops during breath-hold in short axis and four chamber views. Left ventricular mass (LVM) and biventricular volumes, LV ejection fraction (LVEF) and RV ejection fraction (RVEF) were quantified using the commercially available software ‘Suiteheart’ (Neosoft, Pewaukee, USA), or

‘Rightvol’ (Leuven, Belgium), a customized analysis software package. Measurements were indexed to body surface area (BSA) to derive indexed left (LVEDVi) and right (RVEDVi) ventricular end-diastolic volumes, left (LVESVi) and right (RVESVi) ventricular end-systolic volumes, and LVM (LVMi). Reduced ventricular systolic function was defined as an LVEF $< 50\%$ and/or RVEF $< 45\%$.¹⁶ Sensitivity analyses were conducted using alternative more liberal thresholds for reduced systolic function (LVEF $\leq 52\%$, RVEF $\leq 45\%$) in line with the current ESC position statement for athletic populations.¹⁷ Myocardial fibrosis was assessed by late gadolinium enhancement (LGE) imaging on breath-hold phase-sensitive inversion recovery sequences 10 min after administration of gadolinium-diethylenetriamine penta-acetic acid. Hinge-point LGE (H-LGE) was defined as LGE located at the interventricular septum where the right ventricle attaches to the septum (hinge points). Late gadolinium enhancement in other locations was considered non-hinge-point LGE (NH-LGE).

To assess the reproducibility of LGE assessment, an intra-observer analysis was performed by a radiologist with specialty in CMR for University Hospitals Leuven (J.B.) and Jessa Hospital Hasselt (O.G.).

Holter monitoring

All participants underwent 24 h Holter monitoring to determine heart rate (HR) boundaries and to detect arrhythmias. At Belgian centres, either a Spiderview Holter device (Microport, Clamart, France), analysed offline with SyneScope software (ELA Medical, Paris, France), or a RootiRx patch monitoring device (Rooti Labs, Taipei, Taiwan) were used. Australian centres used a PocketECG Holter device (MEDICalgorithmics, Warsaw, Poland). Traditional Holter devices recorded using either two or three leads, depending on the device configuration, whereas RootiRX is a single lead patch monitoring device. Bradycardia was defined as HR < 50 /min. Non-sustained ventricular tachycardia (NSVT) was defined as ≥ 3 consecutive ventricular beats at > 100 /min lasting < 30 s. Multifocal VAs were defined as a total premature ventricular complex (PVC) burden $> 100/24$ h with at least one PVC of a different non-dominant morphology. Complex VAs were defined as ≥ 1 PVC couplet and/or NSVT.

Cardiopulmonary exercise testing

Maximal oxygen uptake ($\text{VO}_{2\text{max}}$) was determined in a sports-specific manner when possible. In the Pro@Heart study, cyclists and triathletes performed a continuous bicycle stress test on their racing bike or Excalibur Sport ergometer (Lode, Groningen, Netherlands), whilst runners performed a treadmill exercise test. Rowers and cross-country skiers performed the test on a standard bike. In the Master@Heart study, continuous bicycle stress test until exhaustion was performed for all participants, including non-athletic controls. Respiratory gas exchange was analysed using a breath-by-breath open circuit spirometry system (Vyntus™ CPX Metabolic Cart; Vyaire Medical, Höchberg, Germany or Cortex Metalyzer 3b; Cortex, Leipzig, Germany). $\text{VO}_{2\text{max}}$ was determined as the highest 30 s average oxygen uptake. Predicted $\text{VO}_{2\text{max}}$ was calculated according to Wasserman as $\text{VO}_{2\text{max}} = \text{weight (kg)} \times [50.72 - (0.372 \times \text{age})]$.¹⁸

Statistical analysis

Data were analysed using SPSS Statistics version 29 (IBM Corporation, Armonk, NY, USA) and R version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria). Data are presented as mean $\pm$ standard deviation (SD)] (normal), median (25th–75th percentiles) (non-normal), or n (%) (categorical). Normality was tested using the Shapiro–Wilk test. Comparisons used t-tests/analysis of variance or Mann–Whitney U/Kruskal–Wallis (continuous), and χ^2 /Fisher's exact test (categorical), as appropriate. Binary logistic regression (enter method) was used for pre-specified outcomes (NSVT, > 100 PVC/24 h, multifocal VA, complex VA, LVEF $< 50\%$, and RVEF $< 45\%$), selected for clinical relevance based on the existing literature. Models were adjusted for age, BMI, and systolic and diastolic blood pressure (BP), chosen for their known associations with PVC burden and ventricular remodelling.^{19,20} For rare outcomes, Firth's penalized logistic regression was applied. Left ventricular ejection fraction and RVEF were additionally analysed as continuous

variables using linear regression. Collinearity diagnostics confirmed tolerance >0.5 and variance inflation factor <5.

To assess predictors of PVC burden (PVC/24 h) as a count outcome, zero-inflated negative binomial regression was applied. To achieve model convergence, patients with extreme PVC burdens (>1000 PVC/24 h; *n* = 8) were excluded, and systolic and diastolic BP were omitted as covariates. The final model included NH-LGE, H-LGE, LVEF <50%, and RVEF <45%, with age and BMI as confounders.

Sensitivity analyses included: (i) restricting analyses to middle-aged athletes and middle-aged non-athletes to reduce age-related confounding given the absence of a young non-athlete control group, and (ii) repeating systolic function models using European Society of Cardiology (ESC)-recommended cut-offs (LVEF ≤52%, RVEF ≤45%) to test robustness of findings.

Analyses used a complete-case approach, as the cohort was defined *a priori* to include only participants with both CMR and Holter data. Population characteristics had no missing data. Self-reported exercise data were only available for middle-aged athletes and non-athletes, and cardiopulmonary exercise testing (CPET) data were missing in 72 young athletes (*n* = 296) but complete in all other subgroups. Given the subgroup-specific nature of these missing data, multiple imputations were not performed.

A two-tailed *P*-value <0.05 was considered statistically significant.

Results

Population characteristics—middle-aged athletes compared with young athletes

Median age of the middle-aged athletes was 56 (50–61) years, compared with 19 (17–22) years for the young athletes, *P* < 0.001.

Middle-aged athletes had a higher BMI and resting diastolic BP than the young athletic group. Resting systolic BP was comparable between the groups. Relative VO₂max was lower, while the percentage of predicted VO₂max was higher in middle-aged athletes compared with young athletes. The majority of both middle-aged athletes and young athletes were cyclists (59 and 80%, respectively), with a higher proportion of runners among middle-aged athletes (Table 1).

Population characteristics—middle-aged athletes compared with middle-aged controls

Median age was similar for middle-aged athletes at 56 (50–61) years compared with 54 (49–60) years in the middle-aged non-athletic control group (*P* = 0.321). The middle-aged athletes had a lower median body weight and BMI compared with the non-athletes, while resting BP did not differ significantly (Table 1). Both relative VO₂max and the percentage of predicted VO₂max were higher in the middle-aged athletes than in the non-athletic controls. Approximately 52% of controls were recreational joggers and 24% did not participate in regular endurance exercise. Middle-aged athletes reported significantly more weekly hours of exercise and years of endurance exercise compared with middle-aged controls.

Cardiac imaging—middle-aged athletes compared with young athletes

Indexed LV and RV volumes, as well as LV mass, were lower in middle-aged athletes compared with young athletes (Table 2, Figure 1). Although average LVEF was lower in middle-aged athletes,

Table 1 Population characteristics

	Young athletes (<i>n</i> = 296)	Middle-aged athletes (<i>n</i> = 138)	Middle-aged controls (<i>n</i> = 66)	<i>P</i> -value MA vs. YA	<i>P</i> -value MA vs. MC
Age (years)	19 (17–22)	56 (50–61)	54 (49–60)	<0.001	0.321
Weight (kg)	69 (64–74)	73 (68–79)	77 (72–84)	<0.001	<0.001
Height (cm)	180 ± 6	178 ± 6	179 ± 6	0.001	0.517
BMI (kg/m ²)	21.3 (20.0–22.6)	23.3 (21.9–24.4)	24.2 (22.8–25.7)	<0.001	<0.001
BSA (m ²)	1.89 (1.80–1.97)	1.90 (1.83–2.00)	1.95 (1.87–2.06)	0.044	0.005
Systolic BP (mmHg)	126 (119–133)	123 (116–131)	122 (114–134)	0.111	0.946
Diastolic BP (mmHg)	67 ± 9	75 ± 9	76 ± 9	<0.001	0.761
Hours exercise per week ^a	—	11 (10–14)	1 (0–3)	—	<0.001
Years of endurance exercise ^a	—	27 (15–39)	6 (0–33)	—	<0.001
Lifetime exercise hours ^a	—	13 994 (8307–23 500)	624 (0–2896)	—	<0.001
Sport— <i>n</i> (%)				<0.001	<0.001
Cycling	238 (80)	82 (59)	1 (2)		
Running	23 (8)	19 (14)	34 (52)		
Cycling and running	0 (0)	23 (17)	2 (3)		
Other	35 (12)	14 (10)	29 (44)		
None	0 (0)	0 (0)	16 (24)		
VO ₂ max (mL/min/kg) ^b	65.5 ± 7.2	47.2 ± 6.9	35.9 ± 6.4	<0.001	<0.001
Percentage of predicted VO ₂ max (%) ^b	149 [140–162]	157 [144–175]	119 [102–133]	<0.001	<0.001

Data presented as mean ± SD, median (25th–75th percentile) or number (%). *P*-values for pairwise comparisons (MA vs. YA and MA vs. MC); Bonferroni-corrected significance threshold: *P* < 0.025; Bold values denote a statistically significant difference.
BMI, body mass index; BSA, body surface area; BP, blood pressure; VO₂max, maximal amount of oxygen the body can utilise per kg/min; MA, middle-aged athletes; YA, young athletes; MC, middle-aged controls.
^aSelf-reported exercise amounts available for middle-aged athletes and controls.
^bCardio-pulmonary exercise data were available and is reported for all middle-aged athletes and controls, and for 76% of young athletes (224 of 296).

Table 2 Cardiac magnetic resonance imaging

	Young athletes (n = 296)	Middle-aged athletes (n = 138)	Middle-aged controls (n = 66)	P-value MA vs. YA	P-value MA vs. MC
LVEDVi (mL/m ²)	140 ± 18	116 ± 17	97 ± 17	<0.001	<0.001
LVESVi (mL/m ²)	63 (55–70)	54 (47–62)	42 (35–50)	<0.001	<0.001
LVSVi (mL/m ²)	77 ± 11	61 ± 9	54 ± 9	<0.001	<0.001
LVEF (%)	55 (53–58)	53 (50–56)	56 (53–59)	<0.001	<0.001
LVEF < 50%—n (%)	42 (14)	28 (20)	5 (8)	0.108	0.021
LVMi (g/m ²)	84 (76–94)	68 (62–74)	53 (49–59)	<0.001	<0.001
RVEDVi (mL/m ²)	151 (136–164)	120 (108–133)	101 (89–116)	<0.001	<0.001
RVESVi (mL/m ²)	74 (64–82)	57 (50–66)	48 (40–56)	<0.001	<0.001
RVSVi (mL/m ²)	77 (69–86)	62 (56–68)	53 (48–61)	<0.001	<0.001
RVEF (%)	52 (49–55)	51 (48–55)	53 (50–57)	0.939	0.045
RVEF < 45%—n (%)	32 (11)	12 (9)	2 (3)	0.497	0.234
LVEF < 50% and/or RVEF < 45%—n (%)	65 (22)	31 (23)	5 (8)	0.906	0.009
Total LGE—n (%)	67 (23)	52 (38)	13 (23)	0.001	0.033
H- LGE—n (%)	56 (19)	30 (22)	11 (17)	0.492	0.398
NH-LGE—n (%)	10 (3)	28 (20)	6 (9)	<0.001	0.045
Burden of LVM (%)	1 (1–2)	1 (1–2)	4 (2–6)	0.413	0.033
Non-ischaemic—n (%)	10 (100)	21 (75)	4 (67)	0.156	0.644
Ischaemic—n (%)	0 (0)	7 (25)	2 (33)		

Data presented as mean ± SD, median (25th–75th percentile) or number. P-values for pairwise comparisons (MA vs. YA and MA vs. MC); Bonferroni-corrected significance threshold: $P < 0.025$; Bold values denote a statistically significant difference.

LVEDVi, left ventricular end-diastolic volume indexed to BSA; LVESVi, left ventricular end-systolic volume indexed to BSA; LVSVi, left ventricular stroke volume indexed to BSA; LVEF, left ventricular ejection fraction; LVMi, left ventricular mass indexed to BSA; RVEDVi, right ventricular end-diastolic volume indexed to BSA; RVESVi, right ventricular end-systolic volume indexed to BSA; RVSVi, right ventricular stroke volume indexed to BSA; RVEF, right ventricular ejection fraction; LGE, late gadolinium enhancement; H-LGE, hinge-point LGE; NH-LGE, non-hinge-point LGE; MA, middle-aged athletes; YA, young athletes; MC, middle-aged controls.

the prevalence of LVEF < 50% did not differ significantly between middle-aged and young athletes. Right ventricular ejection fraction and the prevalence of reduced RV systolic function did not differ between middle-aged and young athletes. Sensitivity analyses applying alternative thresholds (LVEF ≤ 52% and RVEF ≤ 45%) are presented in [Supplementary material online, Table S1](#). Prevalence of reduced LV systolic function increased across all groups, with the difference between young and middle-aged athletes now statistically significant. Prevalence of reduced RV systolic function was minimally affected.

Overall, myocardial LGE was more common in middle-aged athletes compared with young athletes. Non-hinge -LGE, in particular, was significantly more prevalent in middle-aged athletes compared with young athletes. The majority of NH-LGE cases in athletes was characterized as non-ischaemic (i.e. with a mid-myocardial or epicardial pattern), with only a minority of NH-LGE in the middle-aged athletes classified as ischaemic (25%). The burden of NH-LGE, if present, was low and comparable between the two groups. The prevalence of H-LGE was similar between the two athletic groups.

Cardiac imaging—middle-aged athletes compared with middle-aged controls

Compared with middle-aged non-athletes, the middle-aged athletes had significantly larger indexed LV and RV volumes and LV mass ([Table 2, Figure 1](#)). Left ventricular ejection fraction was lower, and LVEF < 50% was more prevalent in the middle-aged athletes compared with the non-athletic controls. Right ventricular ejection fraction and the prevalence of reduced RV systolic function showed no significant difference between middle-aged athletes and non-athletes. Sensitivity

analyses applying ESC-recommended thresholds (LVEF ≤ 52% and RVEF ≤ 45%) yielded similar results (see [Supplementary material online, Table S1](#)).

Although overall LGE and NH-LGE were more prevalent in middle-aged athletes compared with middle-aged non-athletes, these differences did not reach statistical significance after correction for multiple comparisons (Bonferroni-adjusted threshold $P < 0.025$; observed P-values: 0.033 and 0.045, respectively). Similar to the middle-aged athletes, the majority of NH-LGE cases in non-athletes were classified as non-ischaemic, with a minority classified as ischaemic (33%). Non-hinge -LGE was also low and comparable between the two groups. The prevalence of H-LGE was also similar between middle-aged athletes and non-athletes.

In the intra-observer analysis, the studies of 27 subjects were blindly re-analysed at University Hospitals Leuven. Similarly, at Jessa Hospital Hasselt, the studies of 50 subjects underwent blinded re-analysis. For NH-LGE, intra-observer agreement was 93% with Cohen's kappa 0.83 and 96% with Cohen's kappa 0.85 in Leuven and Hasselt, respectively. For H-LGE, intra-observer agreement was 78% with Cohen's kappa 0.56 and 84% with Cohen's kappa 0.68 in Leuven and Hasselt, respectively.

Ambulatory rhythm monitoring—middle-aged athletes compared with young athletes

Middle-aged athletes had a higher 24 h burden of premature atrial complexes (PACs) and higher prevalence of >100PAC/24 h compared with young athletes ([Table 3, Figure 1](#)). Middle-aged athletes also

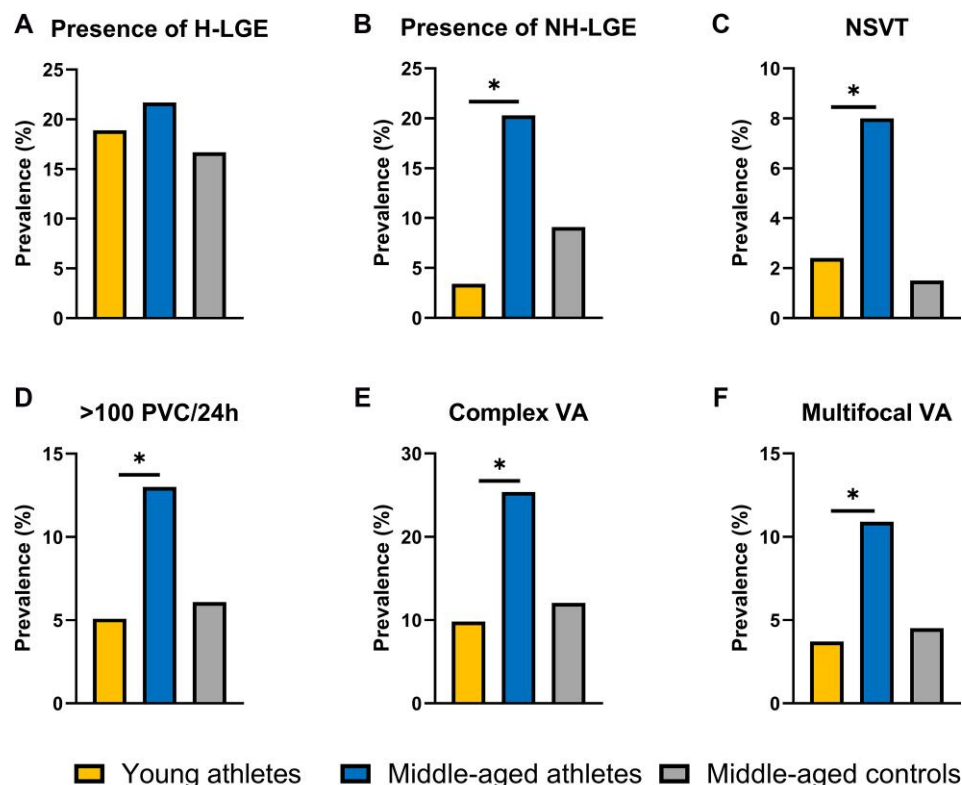


Figure 1 Prevalence of hinge-point late gadolinium enhancement (A), non-hinge-point late gadolinium enhancement (B), non-sustained ventricular tachycardia (C), >100 premature ventricular complexes per 24 h (D), complex ventricular arrhythmia (E), and multifocal ventricular arrhythmia (F) in young athletes, middle-aged athletes, and middle-aged non-athletic controls. Asterisk (*) indicates significance (Bonferroni-corrected significance threshold: $P < 0.025$) using χ^2 or Fisher's exact test as appropriate.

demonstrated a higher 24 h PVC burden, and a greater prevalence of >100PVC/24 h. NSVT, complex VAs, and multifocal VAs were all more prevalent in middle-aged athletes than in young athletes. All observed NSVT episodes were monomorphic.

Ambulatory rhythm monitoring—middle-aged athletes compared with middle-aged controls

Middle-aged athletes showed a similar 24 h burden of PACs and prevalence of >100PAC/24 h compared with middle-aged non-athletes (Table 3, Figure 1). While the 24 h PVC burden and prevalence of >100PVC were numerically higher in middle-aged athletes, these differences were not statistically significant. NSVT, complex VAs, and multifocal VAs were also more frequently observed in middle-aged athletes compared with non-athletes, without reaching statistical significance. NSVT episodes in middle-aged controls were also monomorphic.

None of the participants in the cohort were on negatively chronotropic or anti-arrhythmic medications or had implanted cardiac devices.

The relationship between fibrosis, reduced systolic function, and arrhythmias

The results of logistic regression analyses for LVEF < 50% and RVEF < 45% are presented in Table 4, with corresponding complete univariable

analyses shown in [Supplementary material online, Table S2](#). Neither NH-LGE nor H-LGE significantly altered the odds of LVEF < 50% and/or RVEF < 45%. This remained the case in a multivariable model adjusted for age, BMI, systolic BP, and diastolic BP as independent variables. However, in additional multivariable linear regression analyses (see [Supplementary material online, Table S3](#)), the presence of NH-LGE was associated with a 1.81% lower LVEF. No significant associations were found between H-LGE and LVEF. Similarly, neither NH-LGE nor H-LGE was associated with RVEF.

Table 5 shows the results of logistic regression for NSVT, >100PVC/24 h, multifocal VAs, and complex VAs, with corresponding complete univariable analyses shown in [Supplementary material online, Table S2](#). Neither H-LGE, NH-LGE, LVEF < 50% nor RVEF < 45% increased the odds of NSVT in the adjusted multivariable model. Both NH-LGE and RVEF < 45% increased the odds of >100 PVC/24 h, whilst RVEF < 45% doubled the odds of complex VAs. Non-hinge -LGE increased the odds of multifocal VAs by four- to five-fold, whilst H-LGE, LVEF < 50%, and RVEF < 45% did not. Results of zero-inflated negative binomial regression for 24 h PVC burden are presented in Table 6. Consistent with the logistic regression analyses, the presence of NH-LGE and RVEF < 45% was associated with higher PVC burden. In addition, LVEF < 50% was independently associated with increased PVC burden.

Sensitivity analyses restricted to the sub-cohort of middle-aged athletes and non-athletes are presented in [Supplementary material online,](#)

Table 3 Twenty-four-hour Holter monitoring

	Young athletes (n = 296)	Middle-aged athletes (n = 138)	Middle-aged controls (n = 66)	P-value MA vs. YA	P-value MA vs. MC
Minimum HR (b.p.m.)	36 (32–40)	41 (36–45)	46 (40–50)	<0.001	<0.001
PAC/24 h	7 (3–18)	30 (15–64)	26 (9–66)	<0.001	0.231
>500 PAC/24 h—n (%)	6 (2)	7 (5)	2 (3)	0.126	0.721
>100 PAC/24 h—n (%)	20 (7)	24 (17)	12 (18)	0.001	1.000
PVC/24 h	1 (0–4)	6 (2–26)	5 (2–11)	<0.001	0.365
>500 PVC/24 h—n (%)	4 (1)	7 (5)	1 (2)	0.042	0.441
>100 PVC/24 h—n (%)	15 (5)	18 (13)	4 (6)	0.004	0.154
NSVT—n (%)	7 (2)	11 (8)	1 (2)	0.006	0.108
Complex VA—n (%)	29 (10)	35 (25)	8 (12)	<0.001	0.030
Multifocal VA—n (%)	11 (4)	15 (11)	3 (5)	0.003	0.136

Data presented as mean $\pm$ SD, median (25th–75th percentile) or number (%). P-values for pairwise comparisons (MA vs. YA and MA vs. MC); Bonferroni-corrected significance threshold: $P < 0.025$; Bold values denote a statistically significant difference.

HR, heart rate; PAC, premature atrial complex; PVC, premature ventricular complex; NSVT, non-sustained ventricular tachycardia; complex VA, ≥ 1 PVC couplet, triplet and/or NSVT; multifocal VA, >100 PVC/24 h with ≥ 1 PVC of different morphology.

Table 4 Univariable and multivariable logistic regression for reduced systolic function

	Univariable model		Multivariable model ^a		
	OR (95% CI)	P-value	OR (95% CI)	P-value	Model AUC
LVEF < 50%					
Presence of NH-LGE	1.77 (0.83–3.75)	0.137	1.88 (0.84–4.19)	0.123	0.583
Presence of H-LGE	1.05 (0.57–1.93)	0.887	1.07 (0.57–1.99)	0.833	
RVEF < 45%					
Presence of NH-LGE	0.70 (0.21–2.37)	0.569	0.75 (0.21–2.63)	0.651	0.593
Presence of H-LGE	1.01 (0.47–2.17)	0.976	1.00 (0.46–2.16)	0.994	

^aConfounders included as independent variables in multivariable models: BMI, systolic BP, diastolic BP and age.

OR, log odds ratio; CI, confidence interval; AUC, area under the curve; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction.

Tables S4 and S5. The association between NH-LGE and arrhythmic burden remained consistent, while the predictive value of RVEF < 45% for arrhythmia outcomes no longer reached statistical significance, even in univariable analysis.

Additional sensitivity analyses applying alternative thresholds for reduced systolic function (LVEF $\leq 52\%$ and RVEF $\leq 45\%$) yielded similar results across logistic regression models for reduced systolic function and arrhythmic outcomes (see [Supplementary material online, Tables S6 and S7](#)).

Further logistic regression analyses were performed in the subgroup with available self-reported exercise data (middle-aged athletes and middle-aged non-athletes). Due to the smaller sample size and limited number of events in this subgroup, models were restricted to lifetime exercise hours and age as covariates.

In univariable logistic regression, lifetime hours of exercise (expressed per 1000 lifetime hours) predicted the presence of NH-LGE [odds ratio (OR) 1.04 (1.01–1.07), $P = 0.017$]; this association remained significant in a multivariable model adjusted for age [OR 1.03 (1.00–1.07), $P = 0.048$]. In contrast, lifetime hours of exercise did not predict the presence of H-LGE.

Lifetime hours of exercise also predicted the presence of NSVT [OR 1.07 (1.02–1.12), $P = 0.004$], and this association remained significant after adjustment for age [OR 1.06 (1.02–1.11), $P = 0.009$]. Lifetime

hours of exercise were not associated with >100 PVCs/24 h, multifocal VA, or complex VA.

Finally, lifetime exercise hours predicted the presence of RVEF < 45% in both univariable analysis [OR 1.06 (1.01–1.10), $P = 0.007$] and after adjustment for age [OR 1.06 (1.01–1.10), $P = 0.012$].

Discussion

We present the largest study to date to systematically assess myocardial fibrosis, ventricular function, and VAs in athletes using cardiac MRI and ambulatory rhythm monitoring. Importantly, our cohort includes not only middle-aged athletes and non-athletes, but also a large group of young athletes, a population largely under-represented in prior research.

Our findings confirm a higher prevalence of non-hinge-point myocardial fibrosis in middle-aged athletes, extending previous findings from smaller or more selectively recruited cohorts to a broader athletic population. In contrast, both non-hinge-point fibrosis and VAs were rare among young athletes, highlighting that data from older athletes cannot be directly extrapolated to younger populations. These findings also caution against considering myocardial fibrosis a benign or expected feature in young endurance athletes.

While the prognostic significance of non-hinge-point myocardial fibrosis remains uncertain, we demonstrate an association between

Table 5 Univariable and multivariable Firth's penalized logistic regression for ventricular arrhythmia

	Univariable model		Multivariable model ^a		
	OR (95% CI)	P-value	OR (95% CI)	P-value	Model AUC
NSVT					
Presence of NH-LGE	2.25 (0.57–6.73)	0.219	1.30 (0.32–4.16)	0.688	0.728
Presence of H-LGE	1.21 (0.36–3.28)	0.736	1.08 (0.32–3.00)	0.889	
LVEF < 50%	2.21 (0.73–5.81)	0.147	1.47 (0.40–4.61)	0.539	
RVEF < 45%	4.03 (1.32–10.78)	0.017	3.34 (0.94–10.86)	0.062	
>100PVC/24 h					
Presence of NH-LGE	4.75 (2.08–10.27)	< 0.001	3.64 (1.46–8.76)	0.006	0.755
Presence of H-LGE	1.64 (0.75–3.38)	0.208	1.61 (0.70–3.49)	0.250	
LVEF < 50%	1.99 (0.87–4.21)	0.099	1.52 (0.57–3.73)	0.393	
RVEF < 45%	3.79 (1.62–8.27)	0.003	3.27 (1.21–8.52)	0.020	
Multifocal VA					
Presence of NH-LGE	5.70 (2.37–12.97)	<0.001	3.99 (1.53–10.06)	0.006	0.743
Presence of H-LGE	1.69 (0.70–3.74)	0.230	1.63 (0.65–3.77)	0.284	
LVEF < 50%	1.96 (0.78–4.48)	0.146	1.77 (0.61–4.70)	0.281	
RVEF < 45%	2.33 (0.79–5.81)	0.116	1.84 (0.55–5.48)	0.308	
Complex VA					
Presence of NH-LGE	1.92 (0.88–3.91)	0.099	1.35 (0.59–2.90)	0.466	0.678
Presence of H-LGE	1.77 (0.99–3.08)	0.055	1.72 (0.95–3.03)	0.073	
LVEF < 50%	1.64 (0.86–3.00)	0.131	1.22 (0.58–2.44)	0.589	
RVEF < 45%	2.36 (1.13–4.66)	0.023	2.33 (1.02–5.14)	0.046	

^aConfounders included as independent variables in multivariable models: BMI, systolic BP, diastolic BP and age. Bold values denote statistical significance.

OR, log odds ratio; CI, confidence interval; AUC, area under the curve; NSVT, non-sustained ventricular tachycardia; NH-LGE, non-hinge-point late gadolinium enhancement; H-LGE, hinge-point late gadolinium enhancement; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction; PVC, premature ventricular complex; multifocal VA, >100PVC/24 h with ≥1 PVC of different morphology; complex VA, ≥1 PVC couplet, triplet and/or NSVT.

Table 6 Zero-inflated negative binomial regression for 24 h premature ventricular complex burden

24 h PVC burden	IRR (95% CI)	P-value
Presence of NH-LGE	3.37 (1.84–6.19)	<0.001
Presence of H-LGE	1.26 (0.80–1.98)	0.311
LVEF < 50%	2.21 (1.31–3.71)	0.003
RVEF < 45%	2.85 (1.53–5.30)	0.001

Incidence rate ratios (IRR) with 95% confidence intervals (CIs) and P-values obtained from zero-inflated negative binomial regression. Model adjusted for age and BMI. Patients with PVC burden >1000/24 h (n=8) excluded to achieve model convergence. Bold values denote statistical significance.

NH-LGE, non-hinge-point late gadolinium enhancement; H-LGE, hinge-point late gadolinium enhancement; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction; PVC, premature ventricular complex.

this type of fibrosis and a higher burden of multifocal and frequent VAs. In addition, we confirm the association between reduced RV ejection fraction and increased ventricular ectopic burden, further supporting a potential mechanistic link between RV dysfunction and VAs in the context of long-term endurance training.

Does exercise promote the occurrence of myocardial fibrosis?

A key finding of this study is the 20% prevalence of NH-LGE in middle-aged, highly trained endurance athletes. To our knowledge,

this is the first study to systematically assess myocardial fibrosis using cardiac MRI in a cohort of this size, encompassing both athletes across a broad age range and a non-athletic control group. The observed prevalence aligns with findings from smaller studies involving elite runners and triathletes, and extends these findings to a broader endurance athlete population.^{2,21–23} Further supporting this association, cumulative lifetime endurance exercise hours were a modest but significant predictor of NH-LGE in a multivariable model adjusted for age, including both middle-aged athletes and non-athletic controls.

These findings strengthen the association between long-term high-volume endurance exercise and myocardial fibrosis. However, the cross-section design limits causal inference. Moreover, although the cardiovascular risk profile of middle-aged athletes was generally low, the potential for residual confounding cannot be excluded.

While a lower prevalence of NH-LGE was observed in middle-aged non-athletes (9%) compared with middle-aged endurance athletes (20%), this difference did not reach statistical significance. Although a combined influence of both ageing and long-term endurance exercise on the development of myocardial fibrosis is plausible, the limited number of non-athletic controls likely reduced statistical power to detect between-group differences.

In contrast, NH-LGE was relatively rare in young athletes, with a prevalence of just 3%. Whereas previous studies have predominantly focused on middle-aged athletic populations, data on younger athletic populations remain scarce (2). Our findings suggest that non-hinge-point myocardial fibrosis is uncommon in young athletes, and that caution is warranted when extrapolating findings from older cohorts to younger individuals. Importantly, the presence of fibrosis

in a young athlete should not be dismissed as a benign or physiological adaptation and may warrant further clinical evaluation.

Interestingly, although H-LGE has been reported as relatively common in endurance athletes and has been linked to cumulative exercise exposure,^{7,13,23} we observed no significant difference in the prevalence of H-LGE across the three study groups, despite a trend towards higher prevalence in the athletic cohorts. These findings should be interpreted with caution, as intra-observer agreement for H-LGE detection in our study was only moderate.

Is myocardial fibrosis a risk factor for ventricular arrhythmias in athletes?

Sudden cardiac death is a rare but devastating event in athletes. Cardiomyopathies, including dilated, hypertrophic, and arrhythmogenic sub-types, as well as myocardial fibrosis in isolation, are among the potential causes of SCD and/or clinically significant VAs in this population.^{24,25} Among these, non-hinge-point fibrosis patterns have been associated with potentially life-threatening arrhythmias in several smaller studies.^{8,9,22} However, the prognostic significance of NH-LGE remains debated: some studies report that up to one in five athletes with NH-LGE experience malignant VAs,⁹ whilst others have observed no such events in athletes with similar scar patterns.²⁶

In our cohort, systematic ambulatory rhythm monitoring was used to explore the relationship between myocardial fibrosis and VAs. Although neither NH-LGE nor reduced resting ejection fraction predicted NSVT, the overall prevalence of NSVT was low (4%), limiting statistical power. In contrast, NH-LGE was significantly associated with a higher burden of both unifocal and multifocal PVCs. Moreover, middle-aged athletes had significantly higher rates of VAs, particularly multifocal and complex VA, compared with young athletes. These findings are clinically relevant given the evolving emphasis on VA morphology and complexity, rather than burden alone, in arrhythmic risk stratification.^{27–29} Although higher PVC burden has previously been associated with increased SCD risk,³⁰ multifocal PVC's have been linked to myocardial abnormalities and adverse outcomes in non-athletic populations.²⁸

It is important to acknowledge that 24 h rhythm monitoring has limited sensitivity, and only subclinical VAs were detected in our cohort. As such, definite conclusions regarding the association between myocardial fibrosis and clinically significant arrhythmias cannot be drawn. Whether the observed association between myocardial fibrosis and subclinical arrhythmias reflects an increased risk of clinically significant arrhythmias or SCD in athletes remains unclear. Prospective, longitudinal studies are needed to clarify the long-term arrhythmic risk associated with myocardial fibrosis in this population.

No statistically significant difference in VA prevalence was found between middle-aged athletes and non-athletic controls. Although previous studies have reported similar rates of frequent or complex VAs between athletes and non-athletes,^{31–33} our control group size was limited, and findings should be interpreted with caution.

Hinge-point LGE, often considered a benign physiological adaptation to chronic RV pressure overload in endurance athletes,^{11–13} showed no association with VAs in our cohort. However, given only moderate intra-observer agreement for H-LGE detection, these results should also be interpreted cautiously. Importantly, robust prospective data on the prognostic relevance of H-LGE are still lacking.

Another important observation is the relatively limited extent of LGE in our cohort, especially in comparison with previous studies on the arrhythmogenic and prognostic implications of myocardial scar in

athletes.^{8,9} Across all groups, mean NH-LGE burden remained below 4% of LVM, with only five individuals exceeding an LGE burden of 5% and none exceeding 10%. In contrast, Schnell *et al.*⁸ reported an LGE burden of $12.0 \pm 4.8\%$ of LVM in a cohort of asymptomatic athletes with isolated sub-epicardial fibrosis detected during workup of abnormalities on their regular screening examination. Our observations suggest that even small amounts of myocardial fibrosis may carry arrhythmogenic potential. Supporting this, studies in non-athletic populations with dilated cardiomyopathy (DCM) have demonstrated that LGE burdens $<5\%$ of LVM are associated with significantly increased risk of death or SCD.³⁴ Similarly, in hypertrophic cardiomyopathy, LGE averaging $5.9 \pm 7.3\%$ of LV mass has been linked to elevated SCD risk.³⁵

Is myocardial fibrosis associated with impaired ventricular systolic function in athletes?

Athletic cardiac remodelling is characterized by balanced dilation of all four cardiac chambers in response to the volume and pressure loads of intensive training. The most profound changes are observed in endurance athletes, where a reduced ventricular EF at rest is often considered a physiological adaptation within the spectrum of exercise-induced remodelling.³⁶ Indeed, reduced EF has been observed in apparently healthy elite athletes, including Tour de France cyclists.³⁷ However, recent work from our group demonstrated that reduced EF in athletes is associated with a higher polygenic risk score for DCM, suggesting that subclinical cardiomyopathic processes may underlie this phenotype in a subset of athletes.³⁸

In line with these prior findings,³⁸ we observed that a reduced ventricular systolic function at rest (LVEF $<50\%$ and/or RVEF $<45\%$) was more prevalent in athletes than non-athletes, with no significant difference between young and middle-aged athlete subgroups. In earlier studies, reduced ventricular function has been linked to myocardial fibrosis.^{8,10} Moreover, even small areas of LGE in athletes with preserved EF have been associated with impaired myocardial deformation, particularly reduced radial strain, as assessed by CMR feature tracking.³⁹

In contrast, in our cohort, neither NH-LGE nor H-LGE predicted an LVEF $<50\%$ or RVEF $<45\%$ with similar findings when applying more liberal cut-offs of ≤ 52 and $\leq 45\%$, respectively. However, linear regression analysis revealed that NH-LGE was associated with a modest reduction in LVEF (-1.8%). These findings may reflect the relatively low scar burden in our cohort compared with previous reports. Nonetheless, this is a noteworthy finding (particularly among our younger athletes, who were predominantly elite cyclists) suggesting that reduced EF in this population may occur independently of detectable myocardial fibrosis.

Is reduced ventricular systolic function a risk factor for ventricular arrhythmia in athletes?

Reduced LVEF at rest was not associated with an increased risk of any type of VA in logistic regression, including $>100\text{PVC}/24\text{ h}$. Whilst continuous analysis revealed that LVEF $<50\%$ was associated with a higher 24 h PVC burden, the clinical significance of this finding is uncertain.

In contrast, an RVEF $<45\%$ significantly increased the odds of $>100\text{PVC}/24\text{ h}$ and of complex VAs. Although RVEF $<45\%$ was not associated with NSVT in the multivariable model, the overall rarity of NSVT in our cohort limited statistical power to detect such an

association. Consistently, RVEF <45% was an independent predictor of higher PVC burden in continuous analysis.

The combination of reduced RV systolic function and frequent or complex VAs may raise suspicion of arrhythmogenic RV cardiomyopathy (ARVC) or the phenocopy described in athletes as 'exercise-induced' or 'gene-elusive' ARVC.^{40,41} Heidbuchel and colleagues were the first to describe a link between VAs and RV dysfunction, observed both at rest and during exercise.^{42–45} Their work also highlighted that desmosomal gene mutations were rarely identified in these athletes, underscoring the potential role of chronic high-volume, high-intensity endurance exercise in the development of an ARVC-like phenotype.^{46,47}

Although no athletes in our cohort were formally diagnosed with ARVC, all participants in the Pro@Heart and Master@Heart studies will be followed up at regular intervals to detect any latent disease over time.

Future directions

In this cross-sectional study, we demonstrate an elevated prevalence of non-hinge-point myocardial fibrosis in middle-aged athletes. Both non-hinge-point fibrosis and reduced resting RV systolic function were associated with an increased burden of subclinical arrhythmias on 24 h rhythm monitoring. However, it remains uncertain whether these findings translate into a heightened risk of clinically significant arrhythmias or SCD.

Future research should prioritize prospective, longitudinal follow-up with extended and possibly more sensitive rhythm monitoring to evaluate the progression of myocardial fibrosis, changes in arrhythmia burden and complexity, and their long-term clinical implications in athletes. Both Master@Heart¹⁴ and Pro@Heart⁴⁸ are ongoing prospective studies, and participants will continue to undergo regular evaluations, providing a unique opportunity to address these critical knowledge gaps over time.

Limitations

Several limitations should be acknowledged. First, the study reports on an exclusively male Caucasian cohort, which may limit generalizability to female athletes and individuals of other ethnic backgrounds. Future studies involving more diverse populations are warranted to evaluate whether our findings hold across sex and ethnic groups.

Second, due to the cross-sectional nature of this study, causal relationships between myocardial fibrosis, reduced ventricular function, and VAs cannot be established. While our findings suggest associations between endurance training-related adaptations and subclinical arrhythmogenic markers, longitudinal data will be necessary to determine whether these features precede or predict adverse outcomes. The ongoing Pro@Heart and Master@Heart studies, both prospective by design, will enable follow-up of all participants to assess long-term clinical implications.

Third, the relatively small and unequal sample size of the middle-aged control group limited statistical power to detect group differences, particularly in fibrosis and arrhythmia prevalence. In addition, the absence of a young non-athletic control group precludes fully separating the effects of long-term endurance exercise and ageing. Nonetheless, the inclusion of a large cohort of young and middle-aged athletes alongside a control group is a key strength, offering unique age-stratified insights that have been largely lacking in the existing literature.

Exercise exposure was classified based on self-reported weekly training hours, which, although corroborated by VO₂max testing, may be prone to recall bias or reporting inaccuracies. Based on their VO₂max, it should be noted that the middle-aged non-athletic cohort was relatively fit and may therefore not be fully representative of the general middle-aged population, but rather of a fairly active

subpopulation. We also acknowledge that, despite adjusting for age in our multivariable analyses, residual confounding due to the absence of young controls cannot be completely excluded.

The presence of LGE was visually evaluated based on LGE and post-contrast T1 mapping. Although no universally accepted threshold for semi-quantitative assessment of non-ischaemic LGE exists, intra-observer reproducibility for NH-LGE was strong. However, agreement for H-LGE was only moderate, highlighting interpretative variability that should be considered when comparing results across studies.

Finally, rhythm monitoring was limited to 24 h Holter recordings, which may underestimate arrhythmic burden due to their limited sensitivity. In addition, variation in rhythm monitoring equipment across study centres constrained our ability to fully characterize PVC morphology beyond unifocal or multifocal patterns.

Conclusions

In a male Caucasian population, LGE was more prevalent in middle-aged compared with young endurance athletes and non-athletic controls, suggesting the development of myocardial substrate related to long-term intensive endurance training. Non-hinge-point LGE, even when focal and limited, was associated with a greater burden of multifocal ventricular ectopy, highlighting the potential prognostic relevance of even minor myocardial fibrosis in athletes. Similarly, reduced RV ejection fraction was linked to a greater burden of ventricular ectopy. Although neither myocardial fibrosis nor reduced RV function showed a statistically significant association with NSVT, the overall occurrence of NSVT was rare in this medium-sized cohort. These findings highlight the need for prospective studies to determine the clinical implications of myocardial fibrosis and RV dysfunction in endurance athletes.

Pro@Heart Consortium

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Supplementary material

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

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Data availability

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

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