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The influence of aerobic fitness on electrocardiographic and heart rate variability parameters in young and older adults

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ABSTRACT

Long-term endurance training is associated with an increased risk of atrial arrhythmia in older adults (OA). We tested the hypothesis that Aerobically-Fit OA would have prolonged indices related to atrial arrhythmias (e.g. PR-intervals and P durations) compared to younger adults (YA) and Aerobically-Unfit OA. 10–minute stable supine electrocardiogram (ECG) recordings were collected at 1000 Hz in 15 YA (4F, 22 ± 2 years, 50.7 ± 8.5 ml/kg/min), 11 Aerobically-Unfit OA (6♀, 63 ± 7 years, 25.2 ± 2.3 ml/kg/min) and 10 Aerobically-Fit OA (4F, 64 ± 3 years, 45.5 ± 7.0 ml/kg/min) to assess ECG morphology and spectral indices of heart rate variability. In the pooled sample, age was a predictor of PR-interval ($r = 0.75$) and P wave duration ($r = 0.80$) (both, $p < 0.01$). Regardless of age, aerobic fitness was positively associated with PR interval duration ($r = 0.81$; $p < 0.01$). Aerobically-Fit OA had prolonged PR-intervals (187 ± 17 vs 161 ± 14 vs. 168 ± 20 ms) and P-wave durations (123 ± 9 vs. 97 ± 9 vs. 96 ± 9 ms) compared to YA and Aerobically-Unfit OA, respectively (all, $p < 0.05$). In addition, Aerobically-Fit OA had greater normalized high-frequency (HF) power compared to Aerobically-Unfit OA (40.7 ± 4.5nu vs. 30.1 ± 14.2 ± nu; $p = 0.03$) suggestive of enhance parasympathetic tone. These data highlight that the combination of age-related electrical remodeling and enhanced vagal tone in OA with higher aerobic fitness may contribute to prolongation of atrial-related ECG indices. This is further supported by the correlation between HF power and PR-interval duration ($r = 0.45$; $p = 0.02$). These findings may help identify older individuals at risk for atrial arrhythmias who are otherwise free of cardiovascular disease.

1. Introduction

It is widely accepted that regular aerobic exercise reduces the risk of early all-cause mortality associated with coronary artery disease and stroke (Kokkinos, 2012). However, there is growing evidence that long-term participation in endurance activities increases the risk of atrial arrhythmias in both young (Schnohr et al., 2015; Goodman et al., 2018) and middle-aged adults (Molina et al., 2008; Myrstad et al., 2014; Müssigbrodt et al., 2017). Furthermore, a systematic review suggests that the risk of atrial fibrillation (AF) is higher in endurance athletes compared with their sedentary counterparts (Abdulla and Nielsen, 2009). This is compounded by the fact that age has a direct association with AF risk (Mirza et al., 2012). As such, middle-aged and elderly athletes may be at a higher risk for atrial arrhythmogenesis (Myrstad et al., 2014). Masters athletes demonstrate increased left atrial volumes, prolonged P-wave and PR interval durations (> 200 ms), enhanced vagal tone, and frequent premature atrial contractions (Wilhelm et al., 2011). Importantly, longer P-wave (atrial depolarization) and PR interval (conduction through AV node) durations are clinical predictors for the development of AF (Park et al., 2014).

Peak oxygen consumption (VO_2peak) represents the gold standard measure of aerobic fitness and is widely used to predict disease risk and overall health status (Franklin and McCullough, 2009). Furthermore, middle-aged men (40–60 years of age) with high aerobic fitness have an increased risk of AF (Crump et al., 2018). The combination of ageing-related cardiac remodeling (i.e., enhanced atrial volume and fibrosis) and enhanced vagal tone in exercise trained individuals (Wilhelm et al., 2011) may reduce atrial refractoriness and provide a substrate for AF in older adults with higher aerobic fitness.

However, it is still unclear how aerobic fitness in older adults (OA)

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Table 1
Participant characteristics.

	YA	Aerobically-Unfit OA	Aerobically-Fit OA
No. of participants (F)	15 (4)	11 (6)	10 (4)
Age (years)	22 ± 2	63 ± 7*	64 ± 3*
Height (cm)	177.3 ± 6.5	163.9 ± 9.1*	172.4 ± 8.3†
Weight (kg)	76.1 ± 9.3	68.9 ± 12.0	74.5 ± 11.0
BMI (kg/m^2)	24.2 ± 2.7	25.6 ± 4.5	25.0 ± 3.2
VO_{2peak} (ml/kg/min)	50.7 ± 8.5	25.2 ± 2.3*	45.5 ± 7.0†

Values are means ± SD. BMI; body mass index, OA; older adult, VO_{2peak}; peak O_2 consumption, YA; young adult.
* $p < 0.05$ vs YA.
† $p < 0.05$ vs. Aerobically Unfit OA.

influences the atrial-related components of the electrocardiogram (ECG) and cardiac vagal tone. As such, the present study assessed how alterations in resting ECG morphology relate to aerobic fitness and cardiac vagal tone in young adults (YA), Aerobically Fit (VO_2peak > 30 ml/kg/min) and unfit (VO_2peak < 30 ml/kg/min) older adults (OA). We expect that individuals with higher aerobic fitness and cardiac vagal tone, independent of age, will exhibit prolonged ECG parameters specific to atrial activation (i.e., PR interval and P-wave duration), compared to those with lower aerobic fitness. Additionally, we expect this to be more pronounced in Aerobically Fit OA compared to both YA and Aerobically Unfit OA.

2. Methods

2.1. Participants

This study complied with the Declaration of Helsinki and was approved by the Health Science Research Ethics Board at Dalhousie University. Secondary data analyses were performed on de-identified participants with complete aerobic fitness and ECG data sets (Table 1). Younger ($n = 15$, 4F; 18–30 years) and older ($n = 21$, 10F; 55–80 years) adults were included if they had a body mass index (BMI) < 30 kg/m^2, no history of cardiovascular disease, and were not on any medication. To help assess the impact of age and aerobic fitness we stratified older participants into two groups based on the Canadian Society for Exercise Physiology (CSEP, 2013) aerobic fitness guidelines. OA who had a VO_2peak < 30 ml/kg/min were classified as "Aerobically-Unfit" while OA with VO_2peak > 30 ml/kg/min were classified as "Aerobically-Fit". Aerobic fitness was similar between YA (50.7 ± 8.5 ml/kg/min) and Aerobically-Fit OA (45.5 ± 7.0 ml/kg/min, Table 1). Both YA and Aerobically-Fit OA had higher ($p < 0.05$) aerobic fitness than the Aerobically-Unfit OA (25.2 ± 2.3 ml/kg/min).

2.2. Experimental measurements

2.2.1. Aerobic fitness

A graded cycle ergometer protocol was used to determine VO_2peak, which involved a 5-minute warm-up (30-50 W) followed by a 20 W/min increase in workload until voluntary exhaustion. The workload was then immediately reduced to the warm-up level for a 5-minute cool-down period. Participants wore a facemask surrounding their mouth and nose connected in series with a metabolic system (TrueOne 2400®, Parvomedics Inc., Sandy, UT). VO_2peak was determined as the highest 30-second average obtained during the test.

2.2.2. Electrocardiogram

A 3-lead ECG examination was performed during supine rest in a quiet thermo-neutral room a minimum of 2 days after the exercise test. ECG data were sampled continuously from Lead II at 1000 Hz using PowerLab (PL3508 PowerLab 8/53, ADInstruments, Sydney, Australia) data acquisition system. Data were displayed in real-time during testing and stored on LabChart data analysis software (ADInstruments, Sydney, Australia) for subsequent analysis.

2.3. Data analysis

The ECG waveforms were analyzed using the ECG Analysis software in LabChart® (Hosseini and Jamshir, 2015). 10-minute stationary traces void of movement artifacts were selected for each recording to assess ECG morphology and heart rate variability (HRV). ECG complexes were averaged over the duration of the recording to determine RR interval, PR interval, P-wave duration, QRS duration, and QT interval. QT intervals were corrected for heart rate (QT_c) using Framingham's formula (Vandenberk et al., 2016).

Spectral analysis of the RR time series was performed using the HRV Module in LabChart® to assess cardiac autonomic modulation. Normalized low frequency (LF) power (0.04 to 0.15 Hz), high frequency (HF) power (0.15 to 0.45 Hz) and the LF/HF ratio were assessed for each participant. LF power reflects a combination of both sympathetic and parasympathetic modulation of heart rate (HR). Conversely, HF power is primarily representative of vagal HR control. Finally, LF/HF power represents sympathovagal balance (Piccirillo et al., 2009).

2.4. Statistical analysis

All statistics were conducted using SPSS version 25.0 (IBM). Because of the potential interactions between age, aerobic fitness, ECG parameters, and HRV indices; multiple linear regression analyses were conducted with age and aerobic fitness as covariates when comparing ECG and HRV data in the pooled population. Where appropriate, one-way ANOVA or ANCOVA with Tukey post-hoc testing was performed to determine group differences. Body height is a well-established correlate of atrial arrhythmia (Rosenberg et al., 2012) and our Unfit OA participants were significantly shorter than both the YA and Fit OA (Table 1). As such, we included height as a covariate when assessing atrial ECG parameters. Normality was determined via the Shapiro-Wilk test. The LF/HF ratio failed the normality test. However, when log transformation was applied to the LF/HF ratio data set normality was achieved. Statistical analysis was then performed on the log transformed LF/HF data prior to being transformed back for presentation. The assumption of sphericity was tested using Mauchly's test and the Greenhouse-Geisser correction factor to the degrees of freedom was used for all positive tests. All data are presented as means ± SD. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Relationship between age versus ECG and HRV parameters

The following results were based on the pooled sample. Age was positively associated with prolonged PR interval ($r = 0.75$; $p < 0.01$) and P wave duration ($r = 0.8$; $p < 0.01$; Table 2) when controlling for the influence of VO_2peak and height. Age was also directly associated with longer QT interval duration (Table 2). However, there was no association between age and QRS interval, or rate corrected QTc (all, $p > 0.58$; Table 2). Additionally, VO_2peak was negatively correlated with age, demonstrating a decline in aerobic fitness in older individuals ($r = -0.57$; $p < 0.001$). There was no interaction between age and any HRV parameters when controlling for aerobic fitness (all, $p > 0.21$). Furthermore, body height was not independently associated with any of the dependent variables in the pooled sample of participants (all, $p > 0.09$; Table 2).

3.2. Relationship between aerobic fitness versus ECG and HRV parameters

VO_2peak was correlated with HR ($r = -0.43$; $p < 0.05$), PR

Table 2
Standardized correlation coefficients for age, VO_2peak, and body height versus ECG and HRV parameters.

Parameter	Age	VO_2peak	Body height
Heart rate	−0.04	−0.43*	−0.075
PR interval	0.75**	0.81**	−0.161
P duration	0.80**	0.21	0.154
QRS interval	−0.03	0.29	0.232
QT interval	0.37*	0.65**	−0.354
QTc	−0.03	−0.16	−0.343
HF power	−0.22	0.56**	−0.249
LF power	0.17	−0.67**	0.201
LF/HF ratio	0.01	−0.52**	0.231

* $p < 0.05$.
** $p < 0.01$.

interval ($r = 0.81$; $p < 0.01$), and QT interval ($r = 0.65$; $p < 0.01$) in the pooled sample when controlling for the effects of age and body height (Table 2). HF power was positively associated with higher VO_2peak ($r = 0.57$, $p < 0.01$), consistent with the negative relationship observed between resting HR and aerobic fitness ($r = -0.43$; Table 2). YA demonstrated the largest HF power (both, $p < 0.05$; Fig. 1A) and Aerobically-Fit OA had greater HF power than Aerobically-Unfit OA ($p = 0.03$; Fig. 1A). Among pooled participants, HF power was associated with prolongation of the PR interval ($r = 0.45$, $p = 0.03$) but was not related to P-wave duration ($r = 0.26$, $p = 0.13$). Both LF power and the LF/HF ratio were greatest in Aerobically-Unfit OA (all, $p < 0.05$; Fig. 1B and C). However, no differences in LF power ($p = 0.11$) or LF/HF ratio ($p = 0.15$) were found between Aerobically-Fit OA and YA (Fig. 1C).

3.3. Between group comparisons on ECG morphology

With the inclusion of height as a covariate, we found there was no difference between the YA and Aerobically-Unfit OA groups (all, $p > 0.26$) in resting HR, PR interval, P-wave duration, QRS interval, QT interval, and QTc (Table 3). Interestingly, the Aerobically-Fit OA group had longer PR intervals and P-wave durations compared to both YA ($p < 0.001$) and Aerobically-Unfit OA ($p = 0.01$) (Table 3; Fig. 2B and C). However, there were no differences in PR interval ($p = 0.28$) or P-wave duration ($p = 0.31$) between YA and Aerobically-Unfit OA (Table 3; Fig. 2B and C).

4. Discussion

We found that Aerobically Fit OA have prolonged PR intervals and P-wave durations compared to both YA and their Aerobically Unfit counterparts due, in part, to enhanced vagal tone. To our knowledge, this is the first study to demonstrate the combined effects of aerobic fitness, age, and cardiac vagal tone on PR interval and P-wave prolongation. Consistent with previous research (Havmoller et al., 2007), age was a predictor of PR interval and P-wave duration. The multiple regression model, with age and VO_2peak as predictors, produced a significant model for heart rate, PR Interval, P wave duration, HF power, LF power, and LF/HF ratio. Age had significant positive regression weights with PR-interval and P-wave duration after controlling for VO_2peak. VO_2peak was a better predictor of PR interval than age most likely due to increased vagal tone in those with higher levels of fitness (Table 2; Fig. 1). Strikingly, we found that OA with higher aerobic fitness levels demonstrated an exaggerated prolongation in PR interval and P-wave duration compared to both younger and less fit OA (Fig. 2). Both PR interval and P-wave duration are associated with increased atrial chamber volume, remodeling, and risk for atrial arrhythmias (Park et al., 2014; Nielsen et al., 2015). The combination of age-related atrial remodeling and enhanced vagal tone may combine to contribute to prolongation of both of these intervals in Aerobically Fit

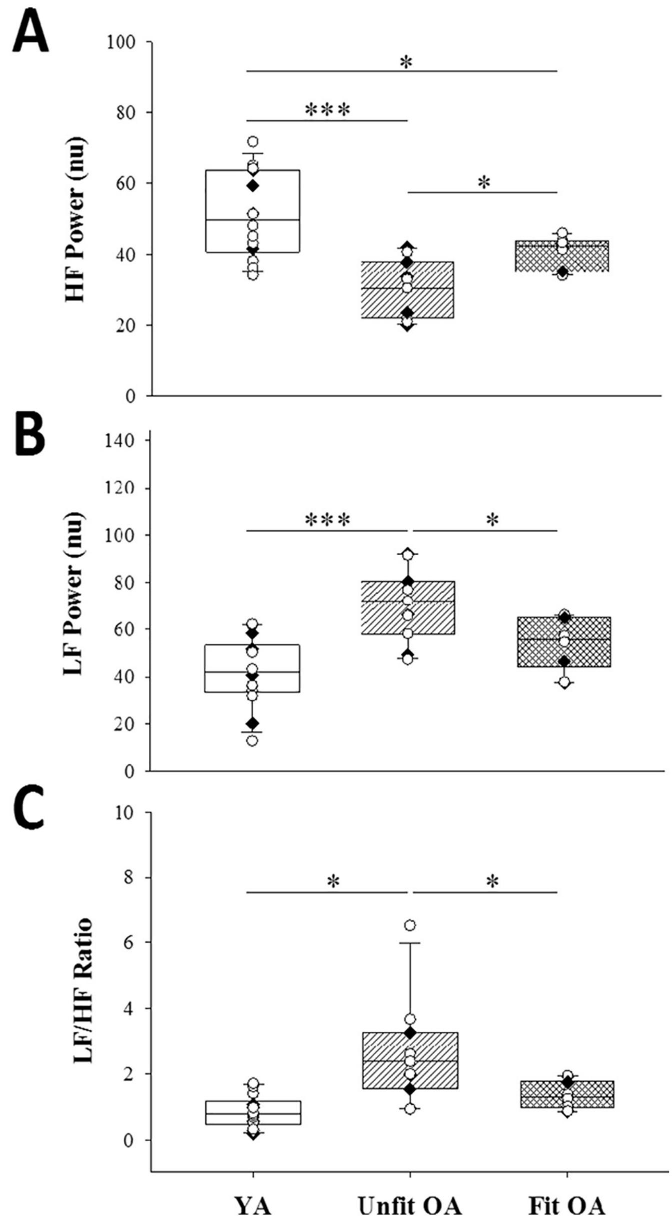

Fig. 1. Normalized frequency domain measurements of HRV in younger, Aerobically Fit older, and Aerobically Unfit older adults. Summary data illustrating the effects of aerobic fitness in younger and older adults on (A) normalized HF power (B) LF power and (C) LF/HF ratio. White circles indicate males, black diamonds indicate females *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$; $n = 15$ for YA, 11 for Aerobically Unfit OA, and 10 for Aerobically Fit OA.

Table 3
ECG parameters in younger adults, Aerobically Fit and Unfit older adults.

ECG parameter	YA	Aerobically Unfit OA	Aerobically Fit OA
Heart rate (bpm)	62 ± 12	67 ± 7	57 ± 7†
PR interval (ms)	160.6 ± 14.5	168.3 ± 20.4	187.3 ± 17.2*†
P duration (ms)	97.4 ± 9.1	96.4 ± 9.6	123.2 ± 8.9*†
QRS interval (ms)	83.6 ± 18.9	73.8 ± 8.9	80.6 ± 17.3
QT interval (ms)	376.8 ± 21.8	360.5 ± 22.0	388.6 ± 40.0
QTc (ms)	378.2 ± 18.5	379.2 ± 13.6	376.3 ± 30.6

Values are means ± SD. OA; older adult, YA; young adult.
* $p < 0.05$ vs YA.
† $p < 0.05$ vs. Aerobically Unfit OA.

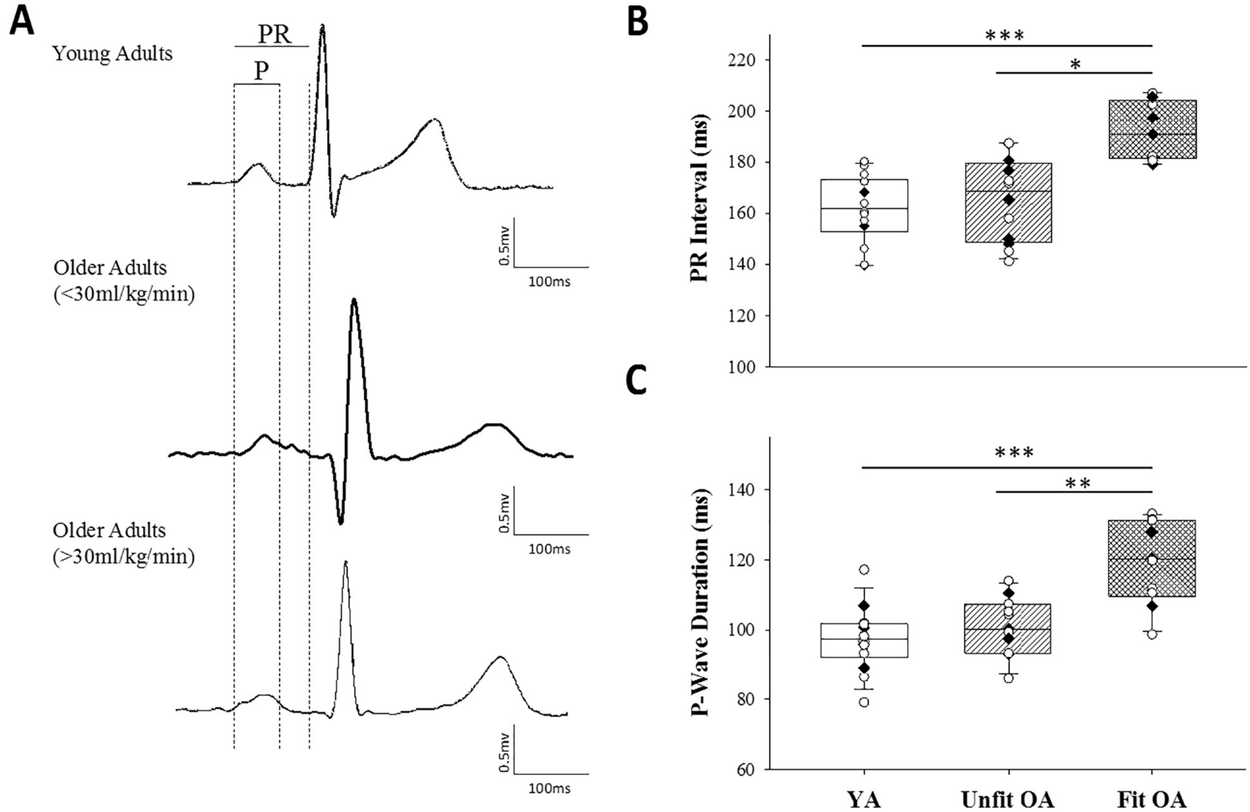

Fig. 2. Stratification of PR interval and P wave duration based on aerobic fitness in older adults. (A) Representative ECG tracings from young adults, Aerobically Fit older adults, and Aerobically Unfit older adults. Summary of PR Interval duration (B) and P wave duration (C) in young adults, Aerobically Fit older adults, and Aerobically Unfit older adults. White circles indicate males, black diamonds indicate females. $*p < 0.05$, $**p < 0.01$, $***p < 0.001$; $n = 15$ for YA, 11 for Aerobically Unfit OA, and 10 for Aerobically Fit OA.

OA. As such, clinicians should be mindful that high aerobic fitness in older individuals might distract from the possibility that this population could have pro-arrhythmic prolonged PR-intervals upon examination of their ECG.

Previous arrhythmia studies support this theory demonstrating that middle-aged men with the highest aerobic fitness levels had the greatest risk of developing AF (Crump et al., 2018). Additionally, a recent study showed that masters athletes (40–60 years old) have longer filtered P-wave durations compared to age-matched controls supporting the theory that these changes are, at least in part, related to larger atrial volumes and remodeling associated with higher VO_2peak (Opondo et al., 2018). Surprisingly, we did not find any differences in atrial electrical activity between Aerobically Unfit OA and YA. However, Aerobically Unfit older individuals had a relatively higher level of cardiac sympathetic modulation (i.e., higher LF/HR ratio), potentially shortening PR interval and P-wave duration despite well documented age-related structural remodeling (Havmoller et al., 2007).

Aerobically-Fit OA demonstrated an intermediate level of vagal tone (i.e., HF Power) compared to YA and Aerobically Unfit OA. Enhanced vagal tone, characteristic of individuals with higher VO_2peak, has been shown to prolong PR interval and reduce atrial refractoriness, consequently predisposing otherwise healthy hearts to AF (van den Berg et al., 2003). This is consistent with our observation of elevated vagal tone and prolonged PR interval in older adults with higher aerobic fitness.

While the participants in this study were not endurance athletes, nor did any participants have clinically abnormal ECG findings, our study demonstrates that the interplay between chronic vagal tone associated with higher fitness and age-related electrical remodeling may provide a substrate for maladaptive ECG alterations that could eventually predispose them to atrial arrhythmias. However, this is not to imply that older adults should curtail their exercise programs. There is still overwhelming evidence that exercise is beneficial and may outweigh the risks associated with sedentary behaviour (Kokkinos, 2012). While there is both basic and clinical evidence that long-term endurance training may increase the risk for the development of certain cardiac arrhythmias, there is still debate as to how this translates into long term mortality. Our lab and others have documented that VO_2peak is associated with improved vascular function (O'Brien et al., 2018) and reduced all-cause mortality (Laukkanen et al., 2004) in OA. Furthermore, a recent cohort study suggests that individuals with extreme cardiorespiratory fitness are associated with the lowest risk of all-cause mortality in comparison to less fit individuals (Mandsager et al., 2018).

We acknowledge that resting, supine HRV is inherently limited in the ability to assess a wide range of steady-state autonomic influences on the modulation of heart rate. It would be valuable for future studies to assess HRV in multiple physiological states (e.g. head-up tilt) in order to quantify both sympathetic and parasympathetic dominant states. Furthermore, measuring autonomic cardiac modulation in response to steady-state exercise may provide important information on the effects of changing autonomics on atrial electrophysiology and should be further investigated. Additionally, the present study did not measure atrial size in any of our participants. However, P wave and PR-interval duration have been shown to be an effective surrogate marker for atrial volume in both healthy (Kasser and Kennedy, 1969) and diseased states (Ariyarajah et al., 2005). Additionally, the cross-sectional nature of this study limits the possibility to investigate the causal associations between improvements in aerobic fitness and alterations in atrial electrophysiology. Recent studies (Opondo et al., 2018) have attempted to assess the causal relationship between endurance exercise training and atrial arrhythmogenesis but due to low training volumes, participant dropout, and small samples sizes, more rigorous studies are required to confirm these effects. As such, future studies should aim to assess the frequency and severity of atrial adaptations to endurance training in older adults and how age and aerobic fitness related changes in atrial structure and electrophysiology translate to increased risk of arrhythmias in this population.

Our findings advance the current literature by demonstrating a trend towards longer PR intervals and P-wave durations in more Aerobically Fit older adults due to a combination of age-related atrial electrical alterations and enhanced vagal tone. This may provide important insights into the pathophysiology related to the enhanced risk of AF described in older endurance athletes (Myrstad et al., 2014; Crump et al., 2018). Full understanding regarding the mechanisms of atrial electrical remodeling in ageing endurance athletes requires future studies to examine the interplay between atrial inflammation and fibrosis, atrial enlargement, and increased vagal tone.

In conclusion, we demonstrate that older adults with higher aerobic fitness have prolonged PR interval and P-wave duration compared to their younger and less fit older counterparts. Identifying the relationship between aerobic fitness and the propensity for changes in ECG morphology corresponding to atrial activation, may allow healthcare providers to more accurately predict those individuals at risk for the development of atrial arrhythmias.

Disclosures

The authors declare that there is no conflict of interest.

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