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The impact of a 21-day ultra-endurance ride on the heart in young, adult and older adult recreational cyclists

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ABSTRACT

Background: This study assessed the acute effect of 21 days of challenging exercise on heart structure and function in recreationally active people across a range of age categories.
Methods: 15 recreationally active people completed a 21-day fundraising cycling ride (MADRIDE) over a distance of 3515 km. Twenty-four hour Holter electrocardiography and blood biochemistry analyses were performed before and after the MADRIDE.
Results: Incidence of cardiac arrhythmia was higher after MADRIDE (OR: 5.93; 95% CI: 5.68–6.19), with increases in both ventricular arrhythmias (OR: 9.90; 95% CI: 9.27–10.57) and supraventricular arrhythmias (OR: 3.09; 95% CI: 2.91–3.29). Adults (OR: 11.45; 95% CI: 7.41–17.69) and older adults (OR: 10.42 95% CI 9.83–11.05) were approximately 10 times more likely to experience arrhythmias after the MADRIDE. Whereas, young participants experienced 18% less cardiac arrhythmias after MADRIDE (OR: 0.82; 95% CI: 0.75–0.90). Aortic valve max velocity was reduced (MD: −0.12 m/s; 95% CI: −0.19–0.05 m/s) and mitral valve deceleration time was slower (MD: −28.91 m/s; 95% CI: −50.97–6.84 m/s) after MADRIDE. Other structural and functional characteristics along with heart rate variability were not different after MADRIDE.
Conclusions: Multi-day challenging exercise increased the incidence of both supraventricular and ventricular arrhythmias in active adults and older adults. Increases in arrhythmia rates after MADRIDE occurred without changes in cardiac structure and autonomic control. Further exploration is necessary to identify the causes of exercise-induced cardiac arrhythmia in adult and older adults.

1. Introduction

Exercise training promotes positive changes to the cardiovascular, musculoskeletal and metabolic systems, and collectively the benefits are indisputable across all ages [1,2]. Additional health benefits are seen with increasing exercise dose [3], such as regular endurance exercise training. Cycling is a popular form of endurance exercise that is experiencing growth in participation rates around the world [4]. Accordingly, participation in ultra-endurance cycling events (i.e., events that exceed 6 h [5]) has increased in individuals across the lifespan [6–9]. Examples include 'Bicycle Illinois', where participants cycle 137 km per day for six days [10] and the 'Great Victorian Bike Ride', where participants cycle between 50 and 100 km per day for up to nine days [11]. These events are open to participants of all ages, including children, and completing these events has become a personal goal for many entrants [9].

The chronic effects of cycling on the heart of professional athletes have been well documented [12–16]. In addition, the acute effects of multi-day ultra-endurance events, such as the Tour de France, have also been investigated [e.g., 17]. These effects are typically described under the umbrella term 'athlete's heart' [18] and include beneficial cardiac adaptations that occur as a result of chronic exercise training, such as bradyarrhythmia and cardiac enlargement, but with no signs of cardiovascular disease [19]. Further, athletes have a lower sudden cardiac

Abbreviations: HF, Power in the high frequency; LF, Power in the low frequency; LF/HF, ratio of LF to HF power; LV, Left ventricle; MADRIDE, make a difference, change our world bicycle ride; NN, Normal-to-normal intervals between QRS complexes; Norm, Normalised units; OR, Odds ratio; pNN50, Proportion derived by dividing NN50 by the total number of NN intervals; Poincaré SD1, Length of the transverse line of the Poincaré plot area; Poincaré SD2, Length of the longitudinal line of the Poincaré plot area; RMSSD, Square root of the mean squared difference of successive NN intervals; SDNN, SD of all NN intervals.

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death risk (e.g., only one sudden cardiac death has occurred during the Tour de France, an incidence rate of 0.007/100,000 participant years [20]). Regardless, cyclists are at elevated risk of adverse cardiovascular disease events [21] and sudden cardiac death is still reported in both professional [20] and recreational [22–24] cyclists. Although rare [26], sudden cardiac death has occurred in ultra-endurance cycling events around the world, and the real incidence is likely to be underestimated [25]. For example, a 23-year old professional cyclist died after suffering a double cardiac arrest in the 'Carpathian Couriers Race' [20], and fatalities attributed to myocardial infarction occurred during an endurance event in London (RideLondon) in 2014, 2016 and 2017, where these recreational cyclists were 36, 48 and 67 years of age, respectively.

Little is known about the acute effect of ultra-endurance exercise on the heart in the general population who exercise recreationally. Existing data are limited to one cohort study that included before and after measurements on a group of 20 cardiologists aged 32 to 54 years who completed an eight day cycle covering 1580 km [27]. These authors reported no clinically important functional or biochemical changes to the heart [27]. Although reassuring, transthoracic echocardiograms were only obtained for seven adult cyclists, the volume of exercise was modest when compared to most ultra-endurance events, and the cyclists obtained professional cycling advice several months prior to the ride. In contrast, it is likely that many participants in public multi-day endurance events are of a broad age range and have a varied exercise training background with no specialist advice; consequently, such participants might be exposed to an increased risk of major cardiovascular disease events.

Considering that participation in challenging multi-day ultra-endurance events is increasing across the lifespan, there is a need to assess the acute effects of such events on the heart of non-athletic populations. Therefore, the aim of this study was to assess the acute effects of 21 days of challenging exercise on cardiovascular structure and function in recreationally active people across a range of age categories.

2. Methods

2.1. Participants and training history

Fourteen male and one female (mean ± SD: age, 34.7 ± 19.3 years; height, 1.79 ± 0.08 m; body mass, 78.3 ± 17.6 kg; BSA, 1.96 ± 0.25) volunteered to participate. The study protocol conformed to the ethical guidelines of the Declaration of Helsinki and was approved by the relevant human research ethics committee (reference number: HREC/17/BHCG/9). Adult participants provided written informed consent. Participants who were <18 years of age gave written assent and their parents/legal guardians provided written informed consent. Inclusion criteria were as follows: aged 10 years or older; cycle one or more times a week for at least an hour; and planning to participate in the 'make a difference, change our world' charity bicycle ride (MADRIDE; http://madcow.org.au/mad-ride-bunbury-bendigo-2017/).

Participants completed the AHA/ACSM Health/Fitness Facility Pre-participation Screening [28] and a training history questionnaire prior to participating. Participants reported riding recreationally for 8.4 ± 12.3 (young: 6.2 ± 3.6; adult: 6.6 ± 6.9; and older adult: 11.5 ± 19.2; $p = 0.420$) years. Six participants had ridden for less than two years and a single participant reported 50 years of experience. Participants completed 8.7 ± 4.1 (young: 10.5 ± 2.1; adult: 9.0 ± 4.2; and older adult: 7.3 ± 5.7; $p = 0.368$) months training for the ride with 3.6 ± 1.0 (young: 4.3 ± 1.0; adult: 3.3 ± 0.9; and older adult: 3.3 ± 0.9; $p = 0.441$) sessions per week. Each session typically lasted 2.9 ± 1.4 (young: 3.3 ± 1.6; adult: 3.5 ± 1.8; and older adult: 2.1 ± 0.4; $p = 0.529$) hours and covered 78 ± 26 (young: 85.0 ± 28.5; adult: 85.0 ± 27.4; and older adult: 67.5 ± 24.4; $p = 0.395$) km/session.

2.2. MADRIDE and testing protocol

The MADRIDE was a 21-day fundraising cycling ride over a distance of 3515 km, which is similar in duration and distance to the Tour de France [29]. However, participants cycled all 21 days at an altitude that did not exceed 300 m. Participants attended a single cardiology department for cardiovascular evaluation before and after completing the MADRIDE. All measurements were performed within two weeks of the start (9.2 ± 3.2 days) and completion (3.0 ± 1.8 days) of the MADRIDE and the timing of these measurements were not different between age groups ($p = 0.301$).

2.3. Echocardiography and blood pressure

Two-dimensional Doppler transthoracic echocardiogram examinations were performed using a cardiovascular ultrasound machine (Vivid E9; GE Healthcare, Horten, Norway). Data were analysed by a single experienced cardiac sonographer according to the recommendations of the American Society of Echocardiography [30], with the average of three measurements used for analyses. Blood pressure was measured in the supine position using a portable Vital Signs Monitor (Welch Allyn, Skaneateles Falls, NY) after the transthoracic echocardiogram data were collected. The following structural parameters were determined: end-diastolic aortic root diameter, inferior vena cava diameter, interventricular septum diameter in diastole, left ventricular (LV) mass (calculated according to the cube formula [30]), LV internal diameter in diastole, LV internal diameter in systole, LV outflow tract diameter, and posterior wall thickness in diastole. Volume parameters: left atrial volume, LV end diastolic volume, LV end systolic volume, right atrial volume, and stroke volume. Left atrial volume, LV end diastolic volume and LV end systolic volume were calculated using the biplane, and right atrial volume using the single plane method of disks summation (modified Simpson's rule). Measurements are presented as relative values indexed to body surface area (BSA; i.e., mm/m^2, g/m^2, ml/m^2, etc.) using the Mosteller formula [31]. The following functional parameters were determined: aortic valve maximum velocity, diastolic blood pressure, systolic blood pressure, mitral valve deceleration time, LV ejection fraction, heart rate, early diastolic lateral mitral annular velocity, pulmonary artery acceleration time, peak transmitral flow velocity in early diastole, peak transmitral flow velocity in late diastole, ratio of transmitral flow in early to late diastole, pulmonary valve maximum velocity, early diastolic septal mitral annular velocity, tricuspid annular plane systolic excursion, and tricuspid regurgitation velocity. In addition, valvular regurgitation severity was assessed and classified into none, mild, moderate and severe according to the recommendations of the American Society of Echocardiography [32].

2.4. Electrocardiography and 24-hour Holter monitoring

A 12-lead electrocardiogram test was performed to screen patients for cardiovascular abnormalities prior to the ride (Philips PageWriter TC70 Series; Philips, Amsterdam, The Netherlands) with participants lying in a reclined supine position.

A 5-lead Holter monitor (SEER Light; GE Healthcare, Horten, Norway) was then fitted to all participants and worn for 24 h prior to the MADRIDE and repeated following completion of the ride. Data were processed according to the manufacturer's software (MARS Holter Analysis System version 8; GE Healthcare, Horten, Norway) to calculate QRS complexes, ventricular and supraventricular beats (isolated, couplets and bigeminal cycles). Both electrocardiogram and Holter monitor data were analysed by a blinded experienced cardiac technician and verified by a cardiologist. In addition, R-R intervals were exported using QRSDK software (MARS Holter Analysis System version 8; GE Healthcare, Horten, Norway) and non-sinus intervals were excluded. N—N intervals and time co-ordinates (time at the beginning of each N—N) were imported into custom-designed software (LabVIEW 2016; National Instruments, UK). For frequency domain analysis, N—N intervals were resampled (linear interpolation at 4 Hz), detrended and windowed (Hanning; 256 samples with 50% overlap) before Fast Fourier Transformation to determine the power spectral density in LF bandwidth (0.04–0.15 Hz) and HF bandwidth (0.15–0.40 Hz) to calculate cardiac autonomic activity assessed through markers of heart rate variability as described previously [33]. Specifically, time (NN mean and SD, pNN50, RMSSD) and frequency (Total power, LF, HF, LF/HF, Poincaré SD1 and SD2, and SD1/SD2) domain parameters were calculated according to recommendations by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [34].

2.5. Biochemical analyses

Damage to the heart was assessed using serum creatine kinase and highly sensitive Troponin I analyses undertaken at a commercial pathology laboratory (Clinical Laboratories, Australia). Cardiac damage was pre-defined as a highly sensitive Troponin I value exceeding 25 ng/L (male) and 16 ng/L (female), and muscle damage was pre-defined as a creatine kinase value exceeding 200 U (male) or 161 U (female).

2.6. Data and statistical analyses

Data were grouped by age with participants categorised according to coronary artery disease risk [35] as follows: young <18 years; adults 18–44 years, and; older adults ≥45 years. Statistical analyses were performed using SPSS for Windows (version 25; IBM Corporation, Armonk, NY, USA). Shapiro-Wilks tests confirmed that these data did not breach the assumptions of normality; therefore, group data were expressed as mean and 95% confidence intervals (95% CI). Statistical significance was set at $p < 0.05$. To assess the effect of the MADRIDE on cardiovascular structure and function, mixed model ANOVAs (within factor: measurement time; between factor: participant age) were performed. Significant interaction effects (age × time) or main effects (age) were followed up using simple main effect analyses with pairwise comparisons and Bonferroni correction. To investigate the incidence rate of arrhythmias by time (before versus after), odds ratios (OR) with 95% confidence intervals were calculated as described previously [36]. Specifically, data were grouped and analysed for all arrhythmias, and split into total ventricular and supraventricular arrhythmias as well as sub-groupings of isolated, couplets and bigeminal cycles.

3. Results

All 15 participants completed the MADRIDE covering a distance of 3515 km, averaging 167 ± 72 km per day at 26.3 ± 2.4 km/h. The MADRIDE did not cause a change in body mass (95% CI: −0.4 to 1.2).

3.1. Echocardiography

The pattern between measurement time and participant age was significant for inferior vena cava diameter ($F_{(2, 12)} = 8.387$, $p = 0.005$; Table 1). Compared to before, adult participants' inferior vena cava diameter was significantly higher (mean difference [MD]: 1.65 mm/BSA; 95% CI: 0.17–3.13 mm/BSA, $p = 0.039$) and older adult participants were significantly lower (MD: −1.23 mm/BSA; 95% CI: −2.18–−2.84 mm/BSA, $p = 0.016$) after the MADRIDE. However, there were no before to after differences for young participants (MD: −0.34 mm/BSA; 95% CI: −2.07–1.39 mm/BSA, $p = 0.520$).

There was a difference before to after the MADRIDE in aortic valve maximum velocity ($F_{(1, 12)} = 14.670$, $p = 0.002$; Table 1), with aortic valve maximum velocity after MADRIDE significantly lower (MD: 0.12 m/s; 95% CI: −0.19–−0.05 m/s, $p = 0.002$). There was also a difference before to after in mitral valve deceleration time ($F_{(1, 12)} = 8.149$, $p = 0.014$), with mitral valve deceleration time after MADRIDE significantly slower (MD: −28.91 ms; 95% CI: −50.97–−6.84 ms, $p = 0.014$).

Mild regurgitation of the aortic valve ($n = 2$), mitral ($n = 1$) and tricuspid ($n = 1$) were identified before the MADRIDE (all other participants displayed nil to trivial regurgitation; $n = 11$). After the MADRIDE mild regurgitation was found in the aortic valve ($n = 1$) and mitral valve ($n = 1$) only, all other participants displayed nil or trivial signs of regurgitation ($n = 13$).

3.2. Twenty-four hour Holter monitoring

The pattern between measurement time and participant age was not significant for total arrhythmia number ($F_{(2, 12)} = 1.358$, $p > 0.05$). Similarly, there were no main effects for time ($F_{(1, 12)} = 1.259$, $p > 0.05$) or age ($F_{(2, 12)} = 1.076$, $p > 0.05$). Of the 1,323,709 (23.7 ± 1.1 h before) and 1,359,904 (24.0 ± 0.0 h after) cardiac cycles analysed, the incidence of arrhythmia was higher after MADRIDE (OR: 5.93; 95% CI: 5.68 to 6.19; Table 2). The increase in arrhythmia after MADRIDE was evident in both ventricular arrhythmias (OR: 9.90; 95% CI: 9.27 to 10.57) and supraventricular arrhythmias (OR: 3.09; 95% CI: 2.91 to 3.29). Before the MADRIDE, two participants displayed no arrhythmias, six displayed rare (1−20), five displayed infrequent (>20–100), one displayed occasional (>100–1000) and one displayed frequent arrhythmias (>1000). After the MADRIDE none of the participants displayed no arrhythmias, rare and infrequent arrhythmias were the same as baseline, two participants displayed occasional and two displayed frequent arrhythmias.

After the MADRIDE, both adults and older adults experienced more than a 10-fold increase in arrhythmia rates (adults OR: 11.45; 95% CI: 7.41 to 17.69 and older adults OR: 10.42 95% CI 9.83 to 11.05). Whereas cardiac arrhythmias were 18% less likely in young participants (OR: 0.82; 95% CI: 0.75 to 0.90) after the MADRIDE (Table 2). Ten participants reported a larger number of arrhythmias after the MADRIDE. In the five that displayed a reduced number of arrhythmias, the largest before to after difference was 7 instances of arrhythmia. There were no

Table 1
CV structural and functional characteristics before and after the MADRIDE ($n = 15$).

Outcome	Before MADRIDE	After MADRIDE	*p*-Values		
			Interaction	Time	Age
Structural and volume characteristics					
Ao R (mm/m^2)	16.7 [15.3–18.2]	16.9 [15.7–18.1]	NS	NS	0.021
IVS_d (mm/m^2)	4.64 [4.29–4.98]	4.64 [4.26–5.03]	NS	NS	NS
IVC (mm/m^2)	10.9 [9.0–12.7]	11.5 [9.6–13.4]	0.005		
$LVID_d$ (mm/m^2)	26.5 [25.0–28.0]	26.8 [25.1–28.4]	NS	NS	NS
$LVID_s$ (mm/m^2)	17.1 [16.0–18.3]	16.4 [15.0–17.8]	NS	NS	NS
LV Mass (g/m^2)	89.0 [82.8–95.3]	88.4 [80.8–96.1]	NS	NS	NS
LVOT (mm/m^2)	12.2 [11.1–13.3]	12.5 [11.2–13.8]	NS	NS	NS
PWT (mm/m^2)	4.73 [4.40–5.06]	4.57 [4.19–4.95]	NS	NS	NS
LV EDV (ml/m^2)	71.2 [66.0–76.4]	73.2 [68.7–77.7]	NS	NS	NS
LV ESV (ml/m^2)	28.3 [24.0–32.6]	29.7 [26.8–32.7]	NS	NS	NS
LAV (ml/m^2)	34.9 [31.0–38.8]	37.1 [31.9–42.3]	NS	NS	NS
RAV (ml/m^2)	32.6 [27.9–37.3]	34.3 [29.8–38.9]	NS	NS	NS
SV (ml/m^2)	53.2 [48.2–58.2]	54.1 [46.3–61.9]	NS	NS	NS
Functional characteristics					
AoV V_{max} (m/s)	1.29 [1.11–1.47]	1.43 [1.27–1.59]	NS	0.002	NS
BP_d (mm Hg)	72.5 [66.2–78.8]	69.3 [63.9–74.7]	NS	NS	0.005
BP_s (mm Hg)	122.9 [114.6–131.2]	119.7 [111.0–128.3]	NS	NS	NS
DT (ms)	189.8 [154.0–228.6]	209.4 [176.8–242.0]	NS	0.014	NS
EF (%)	60.8 [58.2–63.4]	59.5 [56.1–62.9]	NS	NS	0.006
E/A ratio	1.75 [1.39–2.12]	1.61 [1.32–1.89]	NS	NS	0.027
HR (bpm)	57.2 [52.1–62.3]	58.8 [53.5–64.1]	NS	NS	NS
Lateral E′ (cm/s)	15.0 [10.5–19.5]	14.2 [9.5–18.9]	NS	NS	0.005
PAAT (ms)	158.4 [141.6–175.2]	157.7 [142.4–173.0]	NS	NS	NS
Peak E (m/s)	0.76 [0.67–0.85]	0.72 [0.64–0.81]	NS	NS	NS
Peak A (m/s)	0.47 [0.39–0.56]	0.48 [0.40–0.56]	NS	NS	NS
PV V_{max} (m/s)	1.05 [0.95–1.15]	1.14 [1.03–1.25]	NS	NS	NS
RV S′ (cm/s)	13.1 [11.1–15.2]	14.1 [12.7–15.4]	NS	NS	NS
Septal E′ (cm/s)	10.2 [6.8–13.4]	10.7 [8.2–13.1]	NS	NS	0.018
TAPSE (mm/m^2)	11.0 [10.1–11.9]	11.3 [10.1–12.5]	NS	NS	NS

Data are presented as mean [95% CI]. '*p* value' represents the repeated measures two-way mixed model ANOVA (within factor: time [pre vs post]; between factor: age [young vs adult vs older adult]). NS = $p > 0.05$. Ao R = End-diastolic aortic root diameter; AoV V_{max} = Aortic valve maximum velocity; BP_d = Blood pressure in diastole; BP_s = Blood pressure in systole; CV = Cardiovascular; DT = mitral valve deceleration time; EF = ejection fraction; E/A ratio = Ratio of trans mitral flow in early (Peak E) to late (Peak A) diastole; g = Gram; HR = Heart rate; IVC = Inferior vena cava diameter; IVS_d = End-diastolic interventricular septal diameter; Lateral E' = Early diastolic lateral mitral annular relaxation velocity; LAV = Left atrial volume; LV = Left ventricle; EDV = End diastolic volume; ESV = End systolic volume; $LVID_d$ = Left ventricular internal diameter at end-diastole; $LVID_s$ = Left ventricular internal diameter at end-systole; LV Mass = Left ventricular mass; LVOT = Left ventricular outflow tract; ml = mill; mm = millimetre; m^2 = metre squared; PAAT = Pulmonary artery acceleration time; Peak E_d = Peak transmitral flow velocity in early diastole; Peak A_d = Peak transmitral flow velocity in late diastole; PWT_d = End-diastolic posterior wall thickness; PV V_{max} = Pulmonary valve maximum velocity; RAV = Right atrial volume; RV S′ = Tricuspid annular systolic velocity; Septal E' = Early diastolic septal mitral annular relaxation velocity; SV = Stroke volume; TAPSE = Tricuspid annular plane systolic excursion.

Table 2
Odds of CV arrhythmias overall and split for age before and after the MADRIDE ($n = 15$).

Age group (y)	Abnormality	Incidence of arrhythmia		Odds ratio (95% CI)
		Before	After	
Overall	Overall	2358	14,362	5.93 (5.68 to 6.19)
	Ventricular (all)	983	9995	9.90 (9.27 to 10.57)
	-Isolated	966	7522	7.58 (7.09 to 8.11)
	-Couplets	1	13	12.65 (1.66 to 96.73)
	-Bigeminal cycles	16	2460	149.66 (91.54 to 244.68)
	Supraventricular (all)	1375	4367	3.09 (2.91 to 3.29)
	-Isolated	1362	4082	2.92 (2.74 to 3.10)
	-Couplets	7	206	28.65 (13.49 to 60.84)
	-Bigeminal cycles	6	79	12.82 (5.59 to 29.39)
<18 ($n = 5$)	Overall (total)	1104	922	0.82 (0.75 to 0.90)
	Ventricular (all)	9	5	0.55 (0.18 to 1.63)
	-Isolated	9	5	0.55 (0.18 to 1.63)
	-Couplets	0	0	NA
	-Bigeminal cycles	0	0	NA
	Supraventricular (all)	1095	917	0.82 (0.76 to 0.90)
	-Isolated	1095	912	0.82 (0.75 to 0.90)
	-Couplets	0	2	NA
	-Bigeminal cycles	0	3	NA
18–44 ($n = 4$)	Overall (total)	22	263	11.45 (7.41 to 17.69)
	Ventricular (all)	7	173	23.68 (11.12 to 50.41)
	-Isolated	7	173	23.68 (11.12 to 50.41)
	-Couplets	0	0	NA
	-Bigeminal cycles	0	0	NA
	Supraventricular (all)	15	90	5.75 (3.33 to 9.93)
	-Isolated	15	89	5.68 (3.29 to 9.82)
	-Couplets	0	1	NA
	-Bigeminal cycles	0	0	NA
≥45 ($n = 6$)	Overall (total)	1232	13,177	10.42 (9.83 to 11.05)
	Ventricular (all)	967	9817	9.89 (9.26 to 10.57)
	-Isolated	950	7344	7.53 (7.04 to 8.06)
	-Couplets	1	13	12.67 (1.66 to 96.83)
	-Bigeminal cycles	16	2460	149.81 (91.63 to 244.93)
	Supraventricular (all)	265	3360	12.35 (10.90 to 14.00)
	-Isolated	252	3081	11.91 (10.48 to 13.55)
	-Couplets	7	203	28.26 (13.30 to 60.03)
	-Bigeminal cycles	6	76	12.34 (5.38 to 28.34)

Odds ratio data are presented as mean (95% CI). CV = Cardiovascular; n = number; NA = not available.

differences in heart rate variability metrics before or after the MADRIDE (Table 3; $p > 0.05$).

3.3. Biochemical analyses

Creatine kinase activity was elevated in three (before) and four (after) of the nine participants tested, where values ranged from 15 to 407 U before and 24–480 U after the MADRIDE. Highly sensitive troponin I was below 10 ng/L for all participants before and after the MADRIDE.

4. Discussion

To our knowledge, this was the first study to assess the acute effects of challenging cycling on cardiovascular structure and function in recreationally active people across the lifespan. The main finding was a six-fold higher incidence of cardiac arrhythmias without concurrent changes in autonomic function. The increase in arrhythmia after multi-day challenging exercise was evident in both ventricular and supraventricular rhythms. Although the incidence of arrhythmias in adult and older adults was at least 10-fold higher after MADRIDE, participants aged <18 years experienced reduced arrhythmia incidence after MADRIDE. These findings demonstrate that when performing multi-day challenging exercise, recreationally active adults can experience acute changes in cardiac rhythm without evidence of structural changes to the heart.

Table 3
Frequency and time domain HRV calculated before and after the MADRIDE ($n = 15$).

HRV variable	Before MADRIDE	After MADRIDE	p-Value		
			Interaction	Time	Age
NN mean (ms)	906 [852–960]	933 [867–998]	NS	NS	0.03
SDNN (ms)	73 [62–84]	76 [65–87]	NS	NS	NS
RMSSD (ms)	64 [49–79]	64 [50–78]	NS	NS	NS
pNN50 (%)	28.0 [20.1–36.0]	27.7 [19.5–36.0]	NS	NS	NS
Total power (ms^2)	5516 [3896–7136]	5540 [4049–7030]	NS	NS	NS
LF norm (%)	67.9 [62.1–73.7]	67.6 [62.1–73.2]	NS	NS	NS
HF norm (%)	28.7 [23.2–34.1]	29.1 [23.9–34.3]	NS	NS	NS
LF/HF	2.77 [2.03–3.50]	2.68 [1.99–3.37]	NS	NS	NS
Poincaré SD1 (ms)	45 [35–56]	45 [35–55]	NS	NS	NS
Poincaré SD2 (ms)	272 [237–307]	254 [225–282]	NS	NS	NS
SD1/SD2	0.16 [0.14–0.19]	0.17 [0.15–0.20]	NS	NS	NS

HRV = Heart Rate Variability. Data are presented as mean [95% CI]. 'p-Value' represents the repeated measures two-way mixed model ANOVA (within factor: time [pre vs post]; between factor: age [young vs adult vs older adult]). NS = $p > 0.05$. NN = normal-to-normal intervals between QRS complexes; SD = standard deviation; SDNN = SD of all NN intervals; RMSSD = square root of the mean squared difference of successive NN intervals; pNN50 = proportion derived by dividing NN50 by the total number of NN intervals; LF norm = normalised power in the low frequency; HF = normalised power in the high frequency; LF/HF = ratio of LF to HF power; Poincaré SD1 = length of the transverse line of the Poincaré plot area; Poincaré SD2 = length of the longitudinal line of the Poincaré plot area.

We report a six-fold higher incidence in cardiac arrhythmia in people without history of challenging exercise training (Table 2). Previous work has shown that regular participation in challenging exercise is associated with an increased rate of cardiac arrhythmias in trained athletes [e.g., 37,38], where post-training arrhythmia rates parallel those found in populations with cardiomyopathy [39]. Specifically, 70% of arrhythmias found in athletes do not appear to be related to any underlying structural heart disease [40] and, therefore, some authors advise that arrhythmias should be considered as a component of the athlete's heart spectrum [40,41]. However, participants in the current study had heart dimensions that were within normal ranges [42]; they were not highly trained athletes with cardiac enlargement from years of athletic training. Consequently, our results extend previous work to suggest that cardiac arrhythmias are not just an acute response to challenging exercise in highly trained athletes, but also in adult and older adult recreationally active individuals. In addition, participants in the current study were measured at a single time-point before and after the MADRIDE. Although this aspect of the study design has been routinely employed [e.g., 37,38,48], the time course of exercise-induced change in arrhythmia incidence rates is not known. Therefore, it is possible that the measurements taken after MADRIDE were taken at a time when the arrhythmia rates had not peaked or were recovering towards baseline values; both scenarios would underestimate the reported effect size. Future work should consider performing multiple follow-up measurements to identify the temporal pattern of how cardiac arrhythmia incidence changes after multi-day challenging exercise.

The increase in acute exercise-induced atypical cardiac cycles was not associated with major changes in cardiovascular structure or function; therefore, the mechanism(s) responsible for the arrhythmias are not clear. It is also likely that the dose of challenging exercise performed in this study resulted in increases in core temperature, fluid loss, catecholamine concentrations, acidosis [43], and reactive oxygen species production [44] as well as ionic perturbations [45], which can lead to cardiac arrhythmias. As no clinically significant cardiovascular disease adverse events were reported during or after the MADRIDE, the consequences of increased rates in arrhythmia are unclear. Nevertheless, cardiac arrhythmias can lead to adverse cardiovascular disease events and in rare cases of sudden cardiac death in highly-trained athletes [26]. With this in mind, it has been proposed that challenging exercise might trigger cardiovascular disease events when pre-existing undetected genetic defect or

acquired cardiovascular disease exists [46]. Without further exploration of the mechanism(s) that contribute to the acute and long-term effects of challenging exercise on cardiac arrhythmias, the cause of this association and the potential risks remain uncertain.

In this study we found age had no significant effect on the total number of cardiac arrhythmias recorded. However, the incidence of cardiac arrhythmias in adult and older adult participants was at least 10-fold higher after completion of multi-day challenging exercise, whereas in participants aged <18 years, the incidence of cardiac arrhythmias was reduced (Table 2). Although the current study was completed with a focus on a single multi-day endurance event, the influence of age on arrhythmia incidence was in line with previous screening studies in competitive athletes who have a history of challenging exercise training [37,38,48]. For example, Andersen et al. [37] reported that cardiac arrhythmia incidence was lowest in those aged 15–24 years (4.6; 95% CI 3.2 to 6.6) and increased to be highest in those aged 65 years or more (130.4; 95% CI 110.7 to 153.7). Similarly, Zorzi et al. [38,48] reported that young (15–35 years [38]) and adult (35–60 years [48]) athletes with >10 isolated premature ventricular beats or ≥1 complex ventricular arrhythmias were significantly older than athletes who did not achieve this threshold. Older participants would likely have had more challenging exercise training experience and cumulative training experience is associated with a gradual increased risk of arrhythmias [49]. Furthermore, the cardiovascular system deteriorates in function with increasing age, making older age a primary risk factor for cardiac arrhythmias [45]. However, it is difficult to identify an exact mechanism for why young participants in the current study had a reduced arrhythmia incidence without completing further study. As participants older than 18 years of age experienced an increased arrhythmia incidence, and this might increase risk of cardiovascular disease events and even sudden cardiac death, electrocardiograph screening via 24 h Holter monitor analysis might be considered for adults who plan to compete in multi-day challenging exercise events. It is possible that physical fitness is a confounder that contributed to the age group-related difference in arrhythmia rates found in this study. It might be that the adult and older participants were less physically fit than the younger age group and that increased arrhythmia rates could have resulted from a disproportionate load on the right ventricle due to increased pulmonary pressure [47]. However, the potential influence of physical fitness on rates of arrhythmia is speculative because physical fitness was not measured prior to the MADRIDE.

The acute exercise-induced increase in arrhythmia rate was not associated with changes in heart rate variability (Table 3), and these values were favourable compared to threshold values considered unhealthy [e.g., 50] and tended to reflect values typical of the normal healthy range (e.g., Total Power, LF and HF normalised, RMSSD and pNN50; Table 3) before and after the MADRIDE. These data confirm that sympathovagal balance during Holter recordings was similar at both time points. This finding suggests that acute changes in arrhythmia incidence after challenging exercise were not caused by a systematic change in autonomic balance. This is important because stress has been shown to inhibit autonomic control [51] and lower autonomic control is associated with poor clinical outcomes, including increased cardiovascular disease morbidity and mortality [52]. In our participants, age did not significantly influence heart rate variability even though normal aging has been consistently associated with a persistent decrease in heart rate variability variables [53]. Given that participants trained for approximately eight months prior to the MADRIDE, and autonomic control is improved in trained athletes when compared to non-athletes [e.g., 51], it is likely that exercise training attenuated the effect of age on heart rate variability in this group.

The MADRIDE had little effect on cardiovascular structure or function (Table 1). In terms of cardiac structure, the change in inferior vena cava diameter might reflect an altered hydration status of the participants after the MADRIDE, as inferior vena cava diameter can be used to estimate central venous pressure [54]. Similarly, heart function was predominantly unchanged except for increases in aortic valve max velocity and mitral valve deceleration time after MADRIDE. These functional differences imply that 21 days of challenging exercise improved left ventricle compliance; however, stroke volume and all other volume characteristics were not changed. Although not significant, mean values for left ventricle end diastolic volume, and left and right atrial volumes were higher after the MADRIDE. This could indicate that minor cardiac remodelling occurred in some participants, contributing to a higher burden of arrhythmias. Although tricuspid annular systolic velocity and tricuspid annular plane systolic excursion were not significantly higher after MADRIDE, it has been suggested that challenging cycling contributes to proarrhythmogenic remodelling of the right ventricle [e.g., 6]. However, a limitation of this study was measurement of the right ventricle via two-dimensional echocardiography, which is technically challenging [42]. Future work should include right ventricle size metrics, such as right ventricle outflow tract diameter, derived from three-dimensional imaging techniques. It should also be acknowledged that a limitation of the study was that only a single female participant was recruited and as a result the findings are mostly generalisable to men.

5. Conclusions

Multi-day challenging exercise resulted in an increased rate of cardiac arrhythmias in adult and older adult recreational athletes, but not in young. There was little difference in cardiovascular function and no difference in cardiac structure and autonomic control. Further work is needed to identify the physiological mechanisms responsible for increased arrhythmias in adult and older adult recreational athletes following high levels of prolonged endurance exercise.

Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.03.016.

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