The endurance athletes heart: acute stress and chronic adaptation

Keith George,1 Greg P Whyte,1 Danny J Green,1,2 David Oxborough,3 Rob E Shave,4 David Gaze,5 John Somauroo1,6

ABSTRACT
The impact of endurance exercise training on the heart has received significant research and clinical attention for well over a century. Despite this, many issues remain controversial and clinical interpretation can be complex of biomarkers of cardiomyocyte insult. This review assesses the current state of knowledge related to two areas of research where problems with clinical decision making may arise: (1) the impact of chronic endurance exercise training on cardiac structure, function and electrical activity to the point where the athletic heart phenotype may be similar to the expression of some cardiac pathologies (a diagnostic dilemma referred to as the 'grey-zone') and (2) the impact of acute bouts of prolonged exercise on cardiac function and the presentation of biomarkers and cardiomyocyte insult in the circulatory system. The combination of acute endurance exercise stress on the heart and prolonged periods of training are considered together in the final section.

INTRODUCTION
Endurance athletes perform significant volumes of exercise training. This training places a substantial demand on the heart that acts as a physiological and metabolic stimulus for adaptation in cardiac muscle. The clinical relevance of cardiac changes with endurance exercise can be reviewed in three broad areas: (1) how does heart structure, function or electrical activity adapt to endurance training? (2) Are there any consequences for cardiac function and cardiomyocyte integrity that arise from undertaking acute bouts of (ultra)endurance exercise? (3) What, if any, clinically relevant cardiac changes can be observed in endurance athletes if lifelong endurance exercise can be documented?

These questions are relevant and are reflected in recent case studies1 and case–control series2 as well as reviews.3–5 The following review seeks to summarise and clinically contextualise the historical database, emerging data, controversies and clinical quandaries as well as to direct future research.

CHRONIC ENDURANCE EXERCISE TRAINING AND THE HEART
The clinical value of data pertaining to cardiac adaptation to chronic endurance exercise training has largely been focused on two specific ideas: (1) cardiac adaptation to training is specific to the training stimulus and (2) knowledge of the 'upper limits' of physiological cardiac adaptation is vital to inform the differentiation of the athlete's heart from pathologies that may predispose the athletes to sudden cardiac death.6 Although a significant body of knowledge has been produced to address these issues, clinical uncertainty can still arise and new data are being produced.

The 'Morganroth Hypothesis' and left ventricular adaptations to endurance training
The major impetus in this field was provided by the first study to use echocardiography to image the athlete's heart.7 Morganroth and colleagues7 described an eccentric left ventricular (LV) hypertrophy in endurance athletes that reflected an increased LV internal dimension and mass, with minor changes in LV wall thickness. In a parallel group of resistance-trained athletes LV wall thickness and mass were increased but LV dimension was not, consequently the LV wall to chamber ratio was increased and Morganroth et al7 termed this concentric hypertrophy. A differential haemodynamic stimulus was proposed as the mechanism to explain this dichotomy and confirmatory cross-sectional8 and longitudinal evidence9 has prompted widespread adoption of these ideas.10 While most research has confirmed an eccentric LV hypertrophy in endurance athletes, the support for a concentric LV hypertrophy in resistance-trained athletes has been challenged by cross-sectional11 12 and longitudinal13 14 data sets.

The robust evidence supporting an eccentric LV hypertrophy in endurance athletes is exemplified by the outcome of two meta-analyses.15 16 The contention is that the LV adaptation to prolonged periods of training is important in the development of an enhanced cardio-respiratory capacity and endurance performance. Current knowledge of the upper limits of physiological adaptation of the LV is derived mainly from endurance athletes.17 18 Although more extreme LV dimensions have been reported in some endurance athletes,19 20 these data have not been replicated in more recent studies of similar athletes.21–25 Consequently, the current consensus is that the upper limit of physiological cardiac adaptation in endurance athletes is represented by an internal dimension of the LV of <65 mm and LV wall thickness of <14 mm (table 1). Concern for pathology and follow-up is needed when LV dimensions exceed these data.26

Cardiac dimensions in endurance athletes are subject to significant between-subject variability, but most subjects present with values below the normative limits reported in table 1. There are, however, a small number of endurance athletes who express cardiac dimensions above these upper normal limits and this overlaps with lower levels of disease penetration in pathologies such as dilated cardiomyopathy and hypertrophic cardiomyopathy (HCM). This overlap between physiology and...
pathology has been termed the ‘grey-zone’\(^\text{28}\) and reflects an area of diagnostic uncertainty. Approximately 80% of non-traumatic sudden deaths in young athletes are caused by inherited or congenital cardiac defects of which HCM is the most common pathology associated with sudden cardiac death.\(^\text{29}\) Superior athletic performance can co-exist with a hereditary cardiac disease; however, athlete deaths where HCM is implicated predominantly occur in intermittent power/speed sports such as soccer, American football and basketball.\(^\text{30}\) The observation of HCM in endurance athletes is rare,\(^\text{30,31}\) likely because of the low prevalence in the population, the RV in the athletic population is generally larger than in the normal healthy population, the RV outflow wall thickness at end-diastole; RVOT, RV outflow tract dimension; LAD, left atrial diameter; LAVol, LA volume; LAVolI, LAVol index; M, males; F, females; LV, left ventricle; RV, right ventricle; LA, left atrium.

### Emerging evidence: the RV and left atria in the endurance athlete

Understanding RV adaptation to endurance exercise will inform the diagnostician in the process of differentiating physiological adaptation from inherited cardiomyopathies such as ARVC, which accounts for approximately 4% of cardiac sudden death in the athletic population.\(^\text{29}\) Similar to the LV, eccentric RV hypertrophy has been documented in endurance athletes.\(^\text{44,45}\) In support of cardiac magnetic resonance studies, recent echocardiographic studies have provided a more comprehensive evaluation of RV structure\(^\text{24-26}\) and some normative data are presented in table 1. D’Andrea et al\(^\text{26}\) and Oxborough et al\(^\text{25}\) demonstrated larger RV diameters at both the RV inflow and outflow in endurance athletes compared to published normal ranges, sedentary controls and strength-trained athletes.\(^\text{26}\) Furthermore, Oxborough et al\(^\text{25}\) demonstrated an increased RV: LV ratio, suggesting that the degree of remodelling maybe unequal in endurance athletes. This could be explained by a disproportionate wall stress being applied to the thin-walled RV.\(^\text{46}\)

### Table 1: Normative athlete data for key LV, RV and left atrium dimensions including selected references since Pluim et al’s meta-analysis in 2000

<table>
<thead>
<tr>
<th>Citation</th>
<th>Athletes (n)</th>
<th>LVM (g)</th>
<th>IVSd (mm)</th>
<th>LVDd (mm)</th>
<th>LVPWd (mm)</th>
<th>RVI (mm)</th>
<th>RVOT (mm)</th>
<th>LAD (mm)</th>
<th>LAVol (ml)</th>
<th>LAVol (ml/m²)</th>
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</thead>
<tbody>
<tr>
<td>La Gerche(^\text{24})</td>
<td>Cyclists/runners (n=40)</td>
<td>11.0±1.5</td>
<td>56±5</td>
<td>11.0±1.6</td>
<td>44±5</td>
<td>34±5</td>
<td>40±4</td>
<td>65±17</td>
<td>32±8</td>
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<tr>
<td>Oxborough(^\text{25})</td>
<td>Cyclists/runners (n=102)</td>
<td>220±52 (118–377)</td>
<td>53±5 (42–62)</td>
<td>11.0±1.3 (8.0–13.0)</td>
<td>44±5 (30–55)</td>
<td>34±5 (26–49)</td>
<td>40±4 (29–54)</td>
<td>65±17 (37–111)</td>
<td>32±8 (20–58)</td>
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<tr>
<td></td>
<td>(89–186)</td>
<td>(8.0–14.0)</td>
<td>(6.0–12.0)</td>
<td>(6.0–10.0)</td>
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<tr>
<td>D’Andrea(^\text{26})</td>
<td>Mixed (395)</td>
<td>9.7±3.1</td>
<td>9.2±2.1</td>
<td>38±5 (32–45)</td>
<td>31±6 (25–38)</td>
<td>29±9</td>
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<tr>
<td>Wilhelm(^\text{27})</td>
<td>Runners (M=60, F=61)</td>
<td>M: 11.2±1.1</td>
<td>M: 10.7±1.0</td>
<td>M: 10.0±1.0</td>
<td>M: 11.0±1.5</td>
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<td></td>
<td>F: 9.2±1.1</td>
<td>F: 9.2±1.3</td>
<td>F: 11.0±1.6</td>
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<tr>
<td>Abergel(^\text{23})</td>
<td>Cyclists (286)</td>
<td>11±1.3</td>
<td>60±4</td>
<td>10.0±1.0</td>
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<td>Nagashima(^\text{19})</td>
<td>Ultramarathoners (291)</td>
<td>10.2±1.9 (5.0–19.0)</td>
<td>62±7 (42–75)</td>
<td>10.0±1.4 (5.0–15.0)</td>
<td>40±5 (26–49)</td>
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<tr>
<td>Pluim(^\text{15})</td>
<td>Mixed meta-analysis (413)</td>
<td>249±15 (233–264)</td>
<td>10.5±0.4 (10.1–10.9)</td>
<td>54±9 (53–55)</td>
<td>10.3±0.3 (10.0–10.6)</td>
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Data are mean±SD and (range) where applicable. LV, left ventricular mass; IVSd, interventricular septal thickness at end-diastole; LVDd, LV internal dimension at end-diastole; LVPWd, RV posterior wall thickness at end-diastole; RVI, right ventricular inflow dimension; RVOT, RV outflow tract dimension; LAD, left atrial diameter; LAVol, LA volume; LAVolI, LA volume index; M, males; F, females; LV, left ventricle; RV, right ventricle; LA, left atrium.
more representative of physiological conditioning in this setting.

It is important to consider RV function in the presence of significant RV remodelling, in that ARVC often results in an impairment to RV function. The development of strain imaging (figure 1) has provided scope for quantitative evaluation of regional and global RV function and highlighted lower RV global strain values in elite endurance athletes, owing to a reduction in basal function. This finding has been reproduced in endurance athletes at rest yet with augmented apical function that may suggest that global RV strain is likely to be a useful indicator of physiological adaptation. In order to provide a sensible approach to the differentiation of ARVC from endurance athletic conditioning the presence of RV inflow dilatation, normal RV function during exercise (demonstrated using standard or quantitative echocardiography) and the lack of saccular outpouching in the RV outflow are consistent with physiological adaptation. Finally, the presence of a prominent RV moderator band has been evidenced in both ARVC and the endurance athlete and therefore should not be used as diagnostic criteria.

The left atrium (LA) of the endurance athlete has received even less attention than the RV. Oxborough et al observed a large indexed LA volume, with 88% of the 102 endurance athletes having values above the American Society of Echocardiography’s normal range (figure 2 and table 1). This is also of importance when differentiating physiology from pathology and should be considered a normal finding in endurance athletes. It is difficult to fully ascertain the prognostic implications of LA remodeling; however, there is some evidence to suggest the endurance athlete has an increased risk of atrial fibrillation/flutter which correlates well with LA size. The LA is known to dilate in a non-uniform manner and therefore the use of LA volume and LA area is recommended over and above standard linear LA dimension and therefore may provide additional prognostic / diagnostic value. There is evidence of superior LA function in elite athletes when compared with patients with hypertensive LV hypertrophy; however, there are no data specifically in the endurance athlete population.

In summary, the heart of an endurance athlete is more than likely to demonstrate changes in morphology, function and electrical activity. This may place some endurance athletes in the diagnostic ‘grey-zone’ and it is crucial that an accurate determination of physiology or pathology is made. New research, with developing tools, is providing more insight into the phenotype of the athlete heart by detailing morphological adaptation in the RV and LA as well as documenting multiple facets of global and regional function. More data are required in heterogeneous groups of endurance athletes and in testing the utility of new imaging tools in helping diagnostic decision making.

**CARDIAC RESPONSES TO ACUTE (ULTRA)ENDURANCE EXERCISE**

The endurance athlete’s heart is viewed as healthy, highly responsive to acute exercise and resistant to fatigue and damage. This pervasive view has been challenged by recent reports of an acute reduction in cardiac function and the release...
of cardiac biomarkers, which are highly specific for cardiomyocyte stress or damage, in response to acute bouts of (ultra) endurance exercise.

(Ultra)Endurance exercise and cardiac function

During (ultra)endurance exercise, the total cardiac work is considerable and the heart must also cope with an elevation in core temperature, increased levels of catecholamines, increased mechanical work, altered pH and exposure to reactive oxygen species. Whether the heart can maintain performance in the face of such challenges has been the focus of recent debate. Since Saltin and Stenberg suggested that prolonged exercise could impair intrinsic cardiac contractile function, a number of studies have addressed the phenomenon of 'exercise-induced cardiac fatigue'. In an attempt to provide consensus our group and others have reviewed the literature and Middleton et al performed a meta-analysis, collating data related to the effect of prolonged exercise on ejection fraction (global LV contractility) and the ratio of early to atrial peak diastolic filling velocities (global LV diastolic filling). A significant overall effect of exercise was noted for both parameters. The post-exercise reduction in ejection fraction was small (c.2%), was mediated by increasing exercise duration and poor training status and was related to changes in ventricular dimension (an index of preload). This latter point suggests that the reduction may be attributed, in part, to altered cardiac loading and not intrinsic cardiac function per se. The post-exercise decline in diastolic filling was more consistent between studies and was independent of loading and heart rate, suggesting a direct effect of exercise upon lusitropic function.

Ongoing developments with non-invasive imaging (tissue-Doppler imaging, strain/strain rate assessment), has extended our knowledge in this area. For example, speckle-tracking assessment of myocardial deformation has allowed strain and strain rate to be assessed in longitudinal, radial and circumferential planes and at basal, mid- and apical wall levels of the LV and in the longitudinal plane for the RV and LA. Using these approaches recent work has described a negative effect of prolonged exercise on RV function and LA function. Recent work by La Gerche et al suggests that exercise-induced changes in function may occur in the RV but not the LV. A post-exercise drop in RV function was linked to cardiac biomarker appearance and increased race duration. While RV ejection fraction had returned to baseline one week after exercise, the link between a lower RV ejection fraction and chronic structural changes (evidence of cardiac fibrosis) would suggest that the clinical implications are worthy of ongoing study.

The determination of mechanism(s) underpinning changes in cardiac function following prolonged exercise is challenging, especially when dealing with human subjects using non-invasive imaging techniques. Although altered loading and heart rate may account for a proportion of the change in cardiac function, there is some evidence that supports other mechanisms. A downregulation of β-adrenoreceptors, related to reduced contractile state, has been shown previously in humans, although there are conflicting data in an animal model. Recently, Chan-Dewar and colleagues reported an increase in the electromechanical delay in the heart after prolonged exercise that was related to a decline in peak systolic tissue velocity. This suggests that the site of cardiac fatigue is beyond the electrical activation process and thus intrinsic to the myocytes. Whether this reflects changes in energy metabolism (substrate availability) or alterations in calcium handling cannot be deduced from human studies at this point in time. Another mechanism, which has received much attention, is a direct link between cardiomyocyte damage and reduced...
function. Data related to this specific theory are presented in the next subsection.

The concept of exercise-induced cardiac fatigue remains controversial and the clinical relevance of postexercise changes in cardiac function is not fully evaluated. Most descriptive data detail a rapid recovery of LV and/or RV dysfunction. There are, however, occasional reports of more persistent changes in function. La Gerche et al. observed a postexercise reduction in RV tissue velocities that remained depressed at 1 week in one athlete, while Neilan et al. reported reduced diastolic function 3–4 weeks following completion of the Boston Marathon. Further, a suggested link between increased RV end-systolic wall stress with exercise, RV dysfunction, RV remodelling and clinically relevant RV arrhythmias, in some endurance athletes, requires further study.

(Ultra)Endurance exercise and cardiac biomarker release

The potential that prolonged exercise can induce cardiomyocyte damage, which may underpin changes in heart function, has received significant attention recently. Multiple studies have reported significant elevations in cardiac troponin I or T (cTnI, cTnT), which are highly cardio-specific markers of cellular damage. These data have been reviewed and subjected to meta-analysis. In this meta-analysis, the overall event rate (positive serum sample for cTnT after prolonged exercise) was 47%. Continuing studies have attempted to attribute cTn release following prolonged activity to exercise characteristics (eg, duration or intensity) or subject-related parameters (eg, age or training status). To date, these data lack consistency and generally explains only a small proportion of the variance in data. Individual studies generally assess a single blood draw postexercise. We caution against this limited analysis as this will likely underestimate the true rate of cTn appearance during or following ultraendurance events. A unique laboratory-based marathon with blood draws every 30 min during the race and at frequent intervals during recovery observed elevated cTn in all runners.

The clinical relevance of cTn release with exercise, and whether an elevated cTn explains changes in LV and RV function, is controversial. Following exercise the concentrations of cTn released are typically very small with very rapid appearance and removal. This is in contrast to cTn kinetics following myocardial infarction. Exercise is possibly the only documented cardiovascular consequence in a small proportion of athletes. Specific interest has been directed towards the concept of adverse cardiac remodelling and fibrosis as well as arrhythmias and ECG abnormalities.

While endurance training can result in significant cardiac remodelling some interest has been given to whether these changes are reversible and/or can eventually lead to pathological events. It has long been known that short-term deconditioning is associated with some regression in cardiac dimensions but two recent studies from Italy have made significant progress in this area. Pelliccia et al. studied 114 young Olympic endur-ance athletes free of cardiovascular disease over a mean of 8.6 years (range of follow-up 4–17 years). Over this period, no cardiac events or pathological diagnoses occurred and they concluded that up to 17 years of intense, uninterrupted endurance training was not associated with the development of any abnormal cardiac dimensions, any deterioration in LV function and no cardiovascular symptoms. In a different study, Pelliccia and colleagues prospectively followed 40 elite male athletes (mostly endurance based) with large cardiac dimensions (LVIDd>60 mm, wall thickness >13 mm), over a 5.6 years deconditioning period (range 1–15 years). The withdrawal from high volumes of intense training led to a reduction in cardiac dimensions at the group level. While all athletes demonstrated a reduction in wall thickness to below 13 mm, nine athletes still had an LVIDd above 60 mm. The authors suggested that in some athletes the resolution of cavity enlargement was incomplete and could not rule out future clinical implications. Further research tracking elite endurance athletes over longer periods of time, postretirement, seem necessary to illuminate these initial findings.

A different element of structural cardiac remodelling has been the focus of recent research in endurance athletes. The presence of myocardial fibrosis in the heart of trained subjects has been observed in case studies of endurance athletes, animals undergoing high volumes of endurance training and three case series in endurance athletes. The study of fibrosis may be important as it could provide a substrate for the increased prevalence of arrhythmias, particularly in veteran athletes. Fibrosis in the RV was recently reported in an animal model of overtraining and was associated with diastolic

controls. In a recent study, Claessen detected and treated cardiovascular effects of lifelong endurance exercise in a very small number of endurance athletes. Heidbuchel 91 reported that a significant proportion of patients presenting for atrial flutter/ablation surgery were regular athletes and concluded that a history of endurance sports and subsequent LA remodelling may be a risk factor for the development of atrial flutter. This latter point is supported by Molina et al. 95 Ventricular arrhythmias have also been reported in trained athletes 94 but are normally benign, reduce with detraining, 95 are independent of cardiac remodelling 95 96 and appear to be suppressed after retraining. 94

More complex cardiac arrhythmias have also been reported in small numbers of endurance athletes. Heidbuchel et al. 73 reported on a case series of 46 endurance athletes (mainly cyclists) with symptomatic arrhythmias that were largely of RV origin. Over a 5-year follow-up, nine sudden cardiac deaths were reported. In the absence of cardiovascular disease the authors speculated that for some athletes endurance training may contribute to the development and/or progression of an underlying arrhythmogenic substrate. In a follow-up study from the same group, Ector et al. 74 noted a significantly reduced RV ejection fraction in endurance athletes with ventricular arrhythmias. They concluded that endurance exercise could act as a trigger for arrhythmias as well as contributing to changes in RV function. This group has speculated that there may be a link between the acute effects of prolonged exercise on RV function and long-term clinical complications in some endurance athletes, coined the term ‘exercise-induced right ventricular cardiomyopathy’.

In summary, it is very likely that in the vast majority of endurance athletes a lifelong habit of training will improve cardiovascular morbidity and mortality. Further research is required, however, to determine the potential for detrimental cardiovascular effects of lifelong endurance exercise in a very small proportion of athletes and how these individuals may be detected and treated.

CONCLUSIONS

The heart of the endurance athlete is placed under great stress during training and competition. Cardiac adaptation to exercise training encompasses morphological, functional and electrical changes that are referred to as the ‘athletic or athletes’ heart’. For the most part, the endurance athletic heart is easily differentiated from normal hearts that may present with similar phenotypic characteristics. For those athletes that do present in the diagnostically challenging ‘grey zone’, on-going study will likely further refine the definitions. Acute (ultra) endurance exercise bouts represent a significant stress to the heart and there is now substantive evidence of ‘cardiac fatigue’ and/or biomarker release associated with prolonged activity. It is, however, entirely likely that for the vast majority of endurance athletes, the stress of acute exercise will lead to healthy, physiological adaptation in the heart. For a very small minority, though, there is emerging evidence that endurance exercise may be part of a patho-physiological cascade that clinicians must be aware of and respond appropriately too.

What this review adds

- The endurance athlete will develop morphological, functional and electrical characteristics of the athletic heart and for a small minority this will place them in a diagnostic ‘grey-zone’.
- Developing techniques, such as 3D and speckle-tracking echo-cardiography as well as cardiac magnetic resonance, that accurately assess cardiac structure and function at a global and regional level will likely impact upon any diagnostic dilemmas.
- The cardiac work performed during endurance exercise can be profound to the point that ‘cardiac fatigue’ and biomarkers of cardiac damage have been reported in endurance athletes after acute exercise.
- In the vast majority of endurance athletes, the chronic accumulation of acute exercise stress will produce a healthy, physiological adaptation. In a small number, endurance exercise may be implicated in various pathological cascades that are of relevance to the athlete and their medical support team.

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REFERENCES

37. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–63.
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