ESC European Society of Cardiology

European Heart Journal - Case Reports (2023) **7**, 1–5
https://doi.org/10.1093/ehjcr/ytad002

CASE REPORT
Cardiovascular imaging

Exercise-induced right ventricular cardiomyopathy in an endurance cyclist: a case report

James Clark [1]*, Yasir Bakhit[1], and Manish Motwani [2,3]

[1]Department of Cardiology, Betsi Cadwaladr University Health Board, Wrexham Maelor Hospital, Wrexham LL13 7TD, UK; [2]Division of Cardiovascular Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK; and [3]Manchester Heart Centre, Manchester University NHS Foundation Trust, Manchester, UK

Received 9 February 2022; first decision 12 April 2022; accepted 4 January 2023; online publish-ahead-of-print 10 January 2023

Background The wide-ranging benefits of frequent and moderate exercise are well recorded in the literature. Chronic deleterious remodelling in response to exercise is less well described. We describe an amateur endurance cyclist who, in addition to developing a heart failure syndrome and electrocardiographic evidence of arrhythmia, also developed severe functional tricuspid regurgitation.

Case summary After developing palpitations during long distance cycle rides as part of his fitness regimen, a 69-year-old male presented to emergency services but was discharged. While continuing to enjoy long-distance cycling, he began to develop peripheral swelling and presented for a second time to hospital. Subsequent investigation found he had a dilated right heart, exercise-induced arrhythmia, and mid-wall myocardial fibrosis. A diagnosis of exercise-induced cardiomyopathy was made. He was managed with diuretics and immediate cessation of exercise. His symptoms improved and he remains symptom free.

Discussion The volume of blood passing through the right heart increases during exercise. In vulnerable individuals undertaking frequent endurance exercise, this can promote structural remodelling and fibrotic change. It is unclear if cessation of exercise can reverse the remodelled heart. There are some early advances in predictive biomarkers and imaging techniques in categorizing those in the population who would be at risk of developing this cardiomyopathy, and those who can undergo intense exercise regimens without concern. If those at risk of developing an exercise-induced cardiomyopathy can be accurately identified, the next dilemma is how can their risk of heart failure or sudden death be acceptably minimized.

Keywords Exercise-induced cardiomyopathy • Right ventricle • Heart failure • Arrhythmia • Case report

ESC Curriculum 2.1 Imaging modalities • 2.3 Cardiac magnetic resonance • 4.5 Tricuspid regurgitation • 6.7 Right heart dysfunction

Learning points

- Frequent, sustained exercise in susceptible individuals can lead to persistent right ventricular overload and adverse remodelling.
- In previously well athletes, this accumulative damage can predispose to right-sided-heart failure, arrhythmia, and sudden death. In this case, functional tricuspid regurgitation was also seen.

* Corresponding author. Tel: +44 7528760525, Email: James.clark2@wales.nhs.uk
Handling Editor: Belinda Gray
Peer-reviewers: David Oxborough; Georgia Daniel
Compliance Editor: Nikolaos Spinthakis
Supplementary Material Editor: Niklas Schenker

Introduction

With multiple high-profile examples, sudden death during exercise is an important topic in society. Many are attributed to arrhythmogenicity from abnormal myocardium, and so it is important to consider the risk associated with exercise, especially in those with a pre-existing arrhythmogenic substrate.[1,2] Less studied are the processes by which an athlete's arrhythmia risk profile can be altered by undertaking strenuous exercise.

It has been proposed that repeatedly sustained haemodynamic strain from increased cardiac output associated with endurance exercise can cause right heart maladaptation. Sequelae may involve increased wall stress with chamber dilatation, as well as myocardial necrosis and fibrosis in susceptible individuals providing potential substrate for arrhythmia and sudden death.[2,3]

This case describes a 69-year-old male who is an amateur endurance athlete. He first complained of palpitations in 2014. Later in 2019, his palpitations returned, alongside lower limb swelling. Echocardiography and magnetic resonance demonstrated severe right ventricular (RV) dilatation with biventricular subendocardial scarring, but the RV function was normal. In addition, severe central tricuspid regurgitation (TR) was observed. We postulate that these structural changes were a response to repeated sustained endurance training.

Timeline

Date	Setting	Investigation	Result
29 August 2014	A and E	Electrocardiogram (ECG)	Occasional ventricular ectopic beats.
17 December 2014	Outpatient	Holter monitor	Ventricular bigeminy, short runs of atrial tachycardia, and atrial ectopic beats.
28 April 2019	A and E	ECG	Normal sinus rhythm.
17 May 2019	Outpatient	5-day Holter	Atrial tachyarrhythmia and ectopy. Non-sustained ventricular tachycardia. Sinus pauses up to 5.2 s.
31 July 2019	Outpatient	ETT	Ventricular bigeminy worsening on exercise (Right ventriular outflow origin).
	Outpatient	Transthoracic echocardiography	Moderately dilated RV with moderately dilated atrium. Moderate-to-severe TR.
30 September 2019	Outpatient	Cardiac magnetic resonance (CMR) in local centre	Left ventricle mildly dilated. RV and atrium dilated with late gadolinium enhancement in focal mid wall, epicardial pattern with pericardial involvement in basal inferolateral segments in a non-ischaemic pattern.
25 November 2019	Outpatient	Transoesophageal echocardiography	Severely dilated right atrium, RV moderately dilated, moderate central TR and dilated tricuspid annulus. No septal defects.
16 August 2020	Outpatient	CMR arrhythmogenic RV cardiomyopathy (ARVC) protocol	Further RV and right atrial dilatation compared with previous. Septal flattening. Left atrium newly enlarged. The myocardial enhancement was unchanged. No ARVC.
17 December 2020	Outpatient	Computed tomography	No venous or arterial abnormalities

Case presentation

Our patient first sought medical help in 2014 for palpitations. At this point, he was an otherwise fit, 61-year-old man who enjoyed cycling 40–60 miles continuously several times per week for many years. He was presented to accident and emergency after experiencing palpitations at the end of a bout of cycling, but no significant shortness of breath or chest pain were reported. An outpatient ambulatory ECG monitor related to this attendance demonstrated short runs of focal atrial tachycardia and unifocal ectopy. As his palpitations had abated, no further investigation was initiated. However, the patient returned to emergency services 5 years later with a resurgence of palpitations related temporally to his exercise. On this attendance, he was referred to the cardiology outpatient clinic in a secondary care centre.

He had now suffered worsening palpitations for 5 years, with associated mild lower limb swelling. His palpitations came in bursts, felt subjectively regular, and would come on during or shortly after exercise. He had no presyncope, and his ability to exercise was not limited. There was no family history of sudden death or heart disease. He had previously been a healthy man, suffering no chronic disease. At this stage, his resting ECG showed sinus rhythm, with frequent unifocal ventricular ectopy with a left bundle appearance and an inferior axis. An example is given in *Figure 1A*. As his symptoms had worsened, an ambulatory ECG monitor was repeated in an effort to correlate ECG findings with his palpitations. This had shown non-sustained ventricular tachycardia, sinus pauses of up to 5.2 s and runs of narrow complex tachycardias. However, he reported no symptoms while wearing the monitor. To better understand the relationship between his palpitations and exercise, he undertook an exercise tolerance test (ETT), achieving 94% of his heart rate target, completing 10.03 min of the Bruce protocol. During Stage 2, he went into ventricular bigeminy (RV outflow tract morphology), and this improved, but did not abate in Stage 3, and became more frequent in Stage 4 and during recovery. This is shown in *Figure 1B*.

He was advised to curtail exercise in the light of its probable causative association with the arrhythmia and then began investigations for a presumed cardiomyopathy. Firstly, transthoracic echocardiography demonstrated a dilated right heart with moderate, central TR, and annular dilatation. The tricuspid valve structure was normal. Transoesophageal echocardiography was sought to investigate intra atrial shunting. The atrium was severely dilated, with a moderately dilated and normally functioning RV. No intra-atrial abnormality explained the structural changes. There was moderate, central TR. A CMR study was then requested to better understand myocardial wall abnormalities of the RV but it was inconclusive. The MR was repeated with an ARVC protocol in August 2020. ARVC taskforce criteria were not met. The report concluded that there had been advancement in the atrial enlargement, with myocardial scarring in the basal inferolateral wall. His RV was volume overloaded.

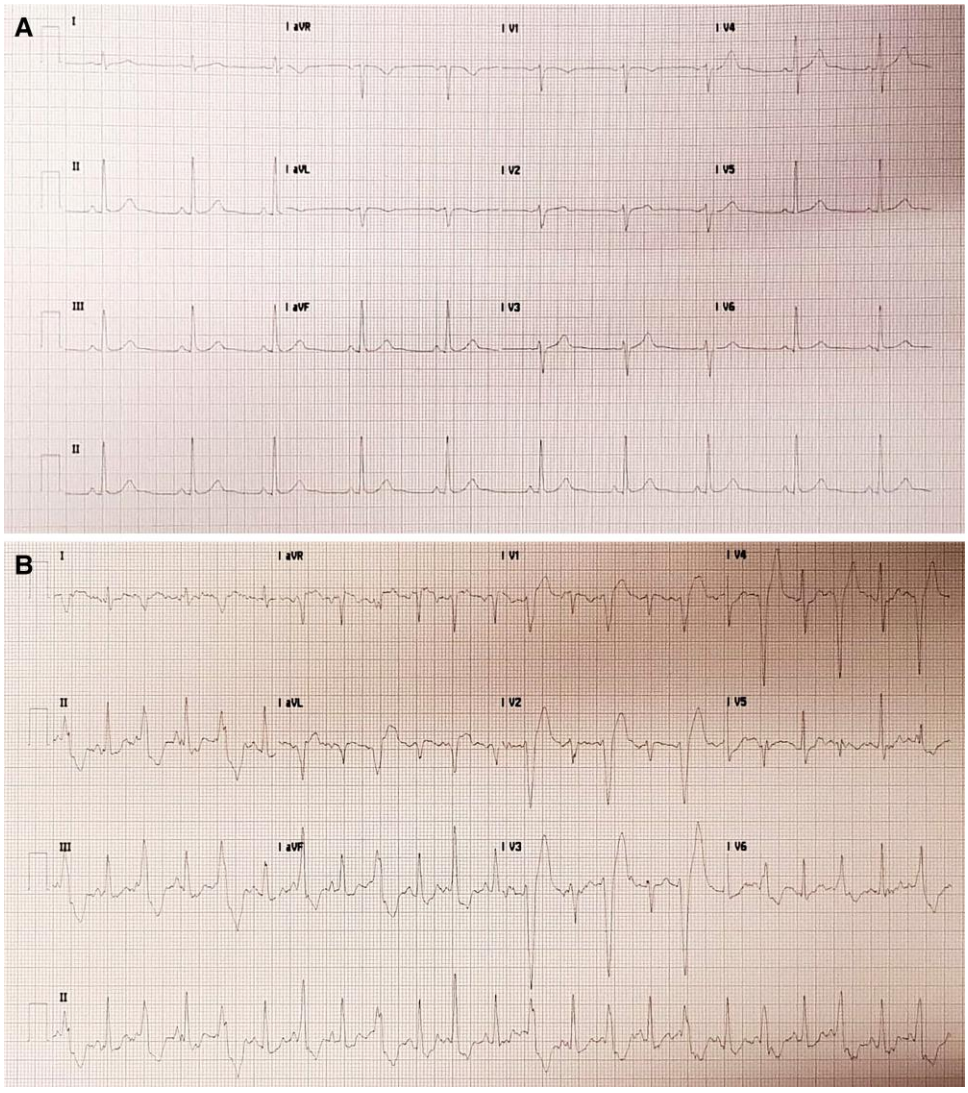

Figure 1 Electrocardiograms showing normal sinus rhythm and exercise provoked ectopy. (*A*) Baseline electrocardiogram. (*B*) Ventricular bigeminy of right ventricular origin during Stage 4 of the Bruce protocol.

After computed tomography was conducted of both his coronary and pulmonary circulation, it was certain there were no obstructive coronary disease, shunts, or anomalous venous drainage.

To reduce his mild pitting oedema, furosemide 40 mg daily was prescribed orally, which effectively reduced his symptoms. He had previously been advised to limit his exercise but continued to cycle cycling for several hours a day.

The diagnosis yet undetermined; a third CMR was conducted in a tertiary centre, concluding: Severely dilated right heart—both right atrium and RV are disproportionately dilated. Although RV is dilated, no major imaging-based Task Force Criteria for ARVC were satisfied as there is no regional or global RV dysfunction, nor were there any soft features of ARVC such as fatty infiltration, microaneurysms, etc. Both ventricles currently have had a normal systolic function. However, there is non-ischaemic-type mid-wall focal fibrosis in basal-to-mid inferolateral LV as well as diffuse fibrosis throughout the right atrial wall. These

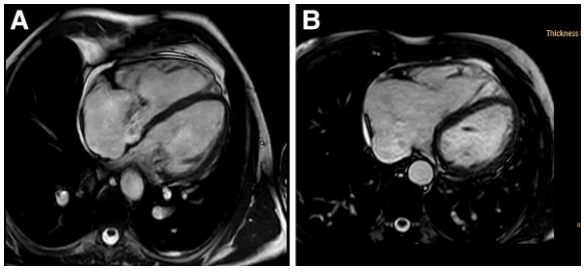

Figure 2 Cardiac magnetic resonance cine images showing severely dilated right atrium and right ventricle. (*A*) Four-chamber plane. (*B*) Right ventricular trans-axial plane.

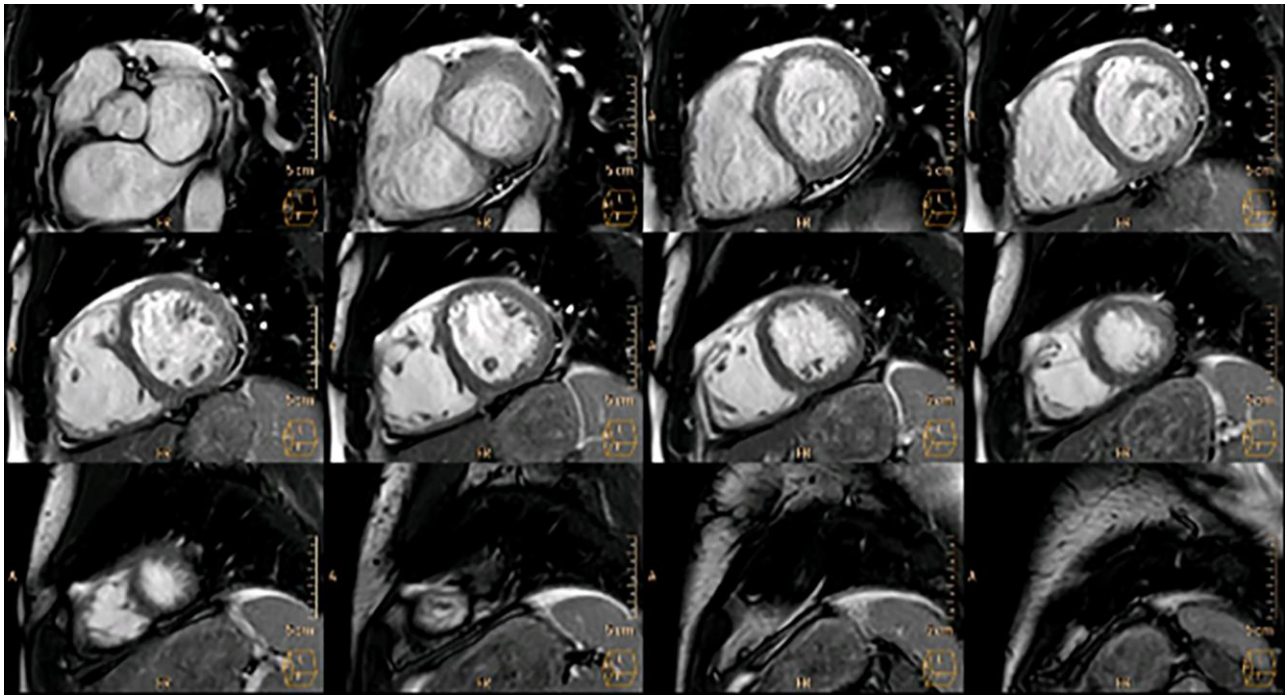

Figure 3 Cardiac magnetic resonance cine images in short-axis plane (base-to-apex) showing severely dilated right ventricle and basal-to-mid septal flattening in diastole consistent with right ventricular-volume-loading.

features in the context of clinical history are most consistent with exercise-induced RV cardiomyopathy, which typically results from repeated high-intensity endurance exercise (classically repeated endurance cycling). The patient cycles 40–60 miles daily, once or twice a week. The LV non-ischaemic scar is also a feature of a veteran's athletic/endurance heart, and that which seems more likely than a separate clinically silent episode of myocarditis here. Severe TR is secondary to annular dilatation but now adds to a vicious cycle of RV-volume-loading, RA/RV dilatation, TR, and RV-volume-loading. Holter findings also seem consistent with exercise-induced physiology (asymptomatic bradycardia and ectopy). Additional differentials include isolated atrial amyloid, ARVD, or idiopathic isolated fibrotic atrial cardiomyopathy. Still, these all would be expected to have additional clinical features or family history, rather than high functioning asymptomatic status.

The chamber dilatation and RV-volume-loading are shown in *Figures 2* and *3*.

Conclusion

Immediate curtailment was advised once exercise was implicated as a basis for his cardiomyopathy. Diuresis was the mainstay of managing his lower limb swelling, and he was started on 40 mg of furosemide orally, which was reduced to 20 mg daily as maintenance. As the history and radiological findings supported an exercise-induced cardiomyopathy, no genetic testing was offered. The implant of a cardiac defibrillator (ICD) was later discussed with the patient on the basis that his heart was structurally abnormal with evidence of arrhythmia. Additionally, device therapy for primary prevention purposes in related conditions such as ARVC is supported by the evidence base, so it was offered pragmatically.[4] Our patient declined.

Discussion

The deleterious effects of chronic right heart adaptation in endurance have been mostly gleaned from marathon runners. Meta-analyses of right heart trials support the notion that haemodynamic strain during exercise causes biomarker change, myocardial dysfunction; and there is further evidence that this correlates with the duration of exercise. Cellular necrosis from wall stress and subsequent impaired function lead to heart failure.[5,6] Fibrotic myocardium, which acts as an arrhythmogenic substrate, is a proposed mechanism for sudden cardiac death (SCD), and perhaps there is an overlap with ARVC.[1]

Our patient has a grossly dilated right heart with severe functional TR. The studies described above support a longstanding change with little potential for reversal once fibrosis is established. The risk of SCD is of concern concerns to patients and physicians alike and management options should be directed towards this. Non-sustained ventricular tachycardias and atrial tachyarrhythmias seen on continuous monitoring are of particular concern, as this indicates a volatile substrate for sustained arrhythmia.

This begs the question of risk stratification and identification of predicators for persisting dynamic changes in RV dilatation, and of SCD. Magnetic resonance imaging of ischaemic damage in athletes with normal coronary arteries could quantify a causative marker of risk, and exercise testing can elicit silent ischaemic episodes, raising the potential as another tool for establishing risk.[7] Importantly, it is unclear how RV dysfunction occurs in some, and not others and as a transient phenomenon in some and permanent in others but appears to associate with exercise volume.[3]

Concerning immediate change with exercise, La Gerche et al.'s cohort study[8] found correlation between RV impairment and high sensitivity troponin release directly after endurance events. Research into separate cardiomyopathic diseases may offer useful biomarkers in established disease, which could potentially be manipulated. Galactin-3

is one such example which is already a marker of SCD in hypertrophic cardiomyopathy and could be helpful in those unable to undergo magnetic resonance imaging or in primary prevention defibrillation where the decision for implantation in athletes is complex.[9] Another, desmosomal gene expression, well studied in ARVC has found interesting correlation in exercise induced cardiomyopathy. Those who exercise the most intensely and have cardiomyopathic RV changes tend to have the lowest desmosomal mutations, suggesting a non-genetic basis resulting in injury patterns similar to ARVC.[10,11] Additionally (as exercise correlates with lower desmosomal gene expression), this suggests that independent of inherited risk, exercise can compound the otherwise subphenotypic genetic risk.[12]

Positioning of scar tissue also appears to be important in its arrhythmogenic potential and is already used prognostically in ARVC.[1] This also acts as a causative mechanism to explain chronic adverse remodelling.[3,13] While scar burden and positioning could form the basis for screening tools assessing risk of RV remodelling or SCD, ICD implantation remains a cornerstone preventative strategy of SCD.

In one cohort of endurance cyclists who had sought medical aid for palpitations or presyncope, almost all had evidence of ventricular dysrhythmia to some degree, with the majority of that being RV in origin. Nine of 46 of these individuals had ICD implants, with 6 having appropriate shocks with 18 of the cohort having sustained arrhythmia.[14] This cohort most closely represents the risks associated with the case presented, describing a significant lifetime risk of arrhythmia, and the implicit benefit of ICD implantation. Impact of performance, adverse events related to lead damage, and inappropriate shocks are of particular concern in the intensive exerciser.

Endurance exercise is enjoyed by many, but some may have a predisposition to poor tolerance of RV loading, leading to potentially irreversible heart adaptation. This can lead to heart failure syndromes, secondary valvular disease, and arrhythmia.

The patient has provided written consent for their anonymized information to be used in publication for educational purposes in compliance with COPE guidelines.

Lead author biography

James Clark is a cardiology specialist registrar working in south Wales. He have an interest in heart failure and devices.

Supplementary material

Supplementary material is available at *European Heart Journal—Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for the submission and publication of this case, including images, has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

References

1. Goff ZD, Calkins H. Sudden death related cardiomyopathies - arrhythmogenic right ventricular cardiomyopathy, arrhythmogenic cardiomyopathy, and exercise-induced cardiomyopathy. *Prog Cardiovasc Dis* 2019;**62**:217–226.
2. Westrol MS, Kapitanyan R, Marques-Baptista A, Merlin MA. Causes of sudden cardiac arrest in young athletes. *Postgrad Med* 2010;**122**:144–157.
3. La Gerche A, Burns AT, Mooney DJ, Inder WJ, Taylor AJ, Bogaert J, *et al.* Exercise-induced right ventricular dysfunction and structural remodelling in endurance athletes. *Eur Heart J* 2012;**33**:998–1006.
4. Barakat AF, Saad M, Elgendy AY, Mentias A, Abuzaid A, Mahmoud AN, *et al.* Primary prevention implantable cardioverter defibrillator in patients with non-ischaemic cardiomyopathy: a meta-analysis of randomised controlled trials. *BMJ Open* 2017;**7**:e016352.
5. Elliott AD, La Gerche A. The right ventricle following prolonged endurance exercise: are we overlooking the more important side of the heart? A meta-analysis. *Br J Sports Med* 2015;**49**:724–729.
6. La Gerche A, Claessen G. Increased flow, dam walls, and upstream pressure: the physiological challenges and atrial consequences of intense exercise. *JACC Cardiovasc Imaging* 2016; **9**:1389–1391.
7. Pancholy SB, Schalet B, Kuhlmeier V, Cave V, Heo J, Iskandrian AS. Prognostic significance of silent ischemia. *J Nucl Cardiol* 1994;**1**:434–440.
8. La Gerche A, Connelly KA, Mooney DJ, MacIsaac AI, Prior DL. Biochemical and functional abnormalities of left and right ventricular function after ultra-endurance exercise. *Heart* 2008;**94**:860–866.
9. Emet S, Dadashov M, Sonsoz MR, Cakir MO, Yilmaz M, Elitok A, *et al.* Galectin-3: A novel biomarker predicts sudden cardiac death in hypertrophic cardiomyopathy. *Am J Med Sci* 2018;**356**:537–543.
10. La Gerche A, Robberecht C, Kuiperi C, Nuyens D, Willems R, de Ravel T, *et al.* Lower than expected desmosomal gene mutation prevalence in endurance athletes with complex ventricular arrhythmias of right ventricular origin. *Heart* 2010;**96**:1268–1274.
11. James CA. Nature and nurture in arrhythmogenic right ventricular cardiomyopathy—A clinical perspective. *Arrhythm Electrophysiol Rev* 2015;**4**:156–162.
12. Heidbüchel H, La Gerche A. The right heart in athletes. Evidence for exercise-induced arrhythmogenic right ventricular cardiomyopathy. *Herzschrittmacherther Elektrophysiol* 2012;**23**:82–86.
13. Heidbuchel H, La Gerche A. The impact of long-term endurance sports on the right ventricle: evidence for exercise-induced arrhythmogenic RV cardiomyopathy. In Gaine S, Naeije R, Peacock A (eds.), *The Right Heart*. London: Springer; 2014.
14. Heidbüchel H, Hoogsteen J, Fagard R, Vanhees L, Ector H, Willems R, *et al.* High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias. Role of an electrophysiologic study in risk stratification. *Eur Heart J* 2003;**24**:1473–1480.