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<sup>1</sup> Boehmer JP, Hariharan R, Devecchi FG, et al. A Multisensor algorithm predicts heart failure events in patients with implanted devices: results from the MultiSENSE study. JACC Heart Fail. 2017 Mar;5(3):216-26. CRM-572611-AA

**S-ICD is effective in preventing sudden death in Arrhythmogenic Cardiomyopathy athletes during exercise**

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**Running Title:** S-ICD in ACM athletes

**Total number of tables:** 1

**Total number of figures:** 1

**Financial support:** none.

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**Disclosures.** Prof. Claudio Tondo serves as member of EU Medtronic Advisory Board and Boston Scientific Advisory Board. The other authors declare no relationships with industry.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/pace.13702](#).

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## Abstract

Here we describe the cases of two elite athletes, with a diagnosis of Arrhythmogenic Cardiomyopathy (ACM), in which a Subcutaneous Implantable Cardioverter Defibrillator (S-ICD) has been implanted. Both patients experienced a ventricular tachycardia during exercise and received effective S-ICD shocks that interrupted arrhythmias. This report reveals for the first time that the S-ICD is effective in reverting arrhythmias in ACM patients, even during exercise. Moreover, these cases **may** confirm that competition/physical activity is associated with ICD shocks.

**Keywords:** subcutaneous ICD, arrhythmogenic cardiomyopathy, elite athletes, efficacy, ventricular tachycardia.

## Introduction

Arrhythmogenic Cardiomyopathy (ACM) is a genetic disease characterized by ventricular arrhythmias that may lead to sudden cardiac death.

Diagnosis is reached when different major or minor criteria, established by the 2010 Task Force<sup>1</sup>, are met, which include imaging criteria, bioptic tissue results, electrocardiographic (ECG) features, arrhythmia presence and characteristics, and family history.

Intense physical exercise is recognized as a trigger of life-threatening arrhythmic events. Indeed, athletes have an increased risk of sudden cardiac death<sup>2</sup>. The most used therapy to prevent such events is the implantation of an Implantable Cardioverter Defibrillator (ICD). Indeed, ICD is widely used and effectively protects the athlete population during competition and exercise<sup>3,4</sup>. In ACM patients, endurance and dynamic exercise may be strictly related to the phenotype severity, both as cardiac function deterioration and as precocity of major ventricular arrhythmic events<sup>5</sup>.

Current guidelines<sup>6,7</sup> recommend an ICD implantation for ACM patients with a history of aborted sudden cardiac death and hemodynamically poorly tolerated ventricular tachycardia (VT; recommendation class I level C), as well as in primary prevention for ACM patients with hemodynamically-tolerated sustained VT (recommendation class IIa level B).

Despite its life-saving potential, ICD implantation is associated with a high rate of complications and significant impact on quality of life. Among complications, during implantation, pneumothorax, hemothorax, and cardiac tamponade could occur, while in the long term, lead dislodgement, fracture or defect can cause the loss of

effectiveness of the ICD system, or inappropriate shocks<sup>8</sup>. When indicated, lead extraction is a complex procedure, associated with important comorbidity and mortality. In recent years, the Subcutaneous ICD (S-ICD) has been developed to treat ventricular arrhythmias, without the need for the lead placement within or on the heart<sup>9</sup>. However, S-ICD efficacy has been evaluated only partially respect to all the possible applications where it could substitute transvenous ICD. In particular, its efficacy in ACM patients undergoing intense physical exercise has never been tested. This report describes the cases of two elite athletes diagnosed with ACM, in which S-ICD has demonstrated life-saving by defibrillating high frequency VT during sport activities.

### **Case Reports**

**Case 1:** A 21-years old male elite basketball player was admitted to our Center after a cardiac arrest caused by ventricular fibrillation (VF) during a competition. He was immediately treated with cardiopulmonary resuscitation and seven external defibrillation shocks, allowing the successful conversion to sinus rhythm. After stabilization, the patient underwent non-invasive and invasive evaluations: electrocardiogram was normal; cardiac magnetic resonance (CMR) showed a biventricular dilatation compatible with training and a dubious delayed enhancement area near tricuspid valve; coronary angiography resulted normal; electroanatomical mapping (CARTO System, Biosense Webster) of both ventricles did not detect low-voltage areas and late potentials; the histological examination of endomyocardial byoptic samples did not show pathological findings. An S-ICD (Boston Scientific) was proposed for secondary prevention. The S-ICD had two therapy zones programmed: 220-250 beats/min (conditional zone) and >250 beats/min (shock zone) with sensing selected in the primary vector (1x gain).

ACM diagnosis was confirmed by genetic analysis and by CMR at follow-up (delayed enhancement in right ventricle (RV)), both major criteria<sup>1</sup>.

The patient was disqualified from competitive sport activities.

One year after S-ICD implantation, the patient was admitted to our emergency unit for an S-ICD shock occurred during non-competitive exercise (basketball playing; sinus rhythm frequency preceding VT: 150 beats/min). The S-ICD interrogation documented a 250 beats/min VT induced by exercise. The VT was interrupted after 16 sec with a shock of 65 J (**Figure 1 A**).

**Case 2:** A 20-years old male elite cyclist was admitted to our center for palpitations, pre-syncope, non-sustained VT and ventricular premature complexes (left bundle branch block and superior axis) during a competition. ECG showed mild ST-segment elevation in V2-V4 and negative T waves in DII, DIII, aVF. CMR documented right and left ventricle dilatation with RV dyskinesia, end-diastolic volume to BSA 138ml/m<sup>2</sup> and a delayed enhancement area in the posterolateral wall of left ventricle, suggestive of fatty tissue infiltration.

RV electroanatomical mapping (EnSite NAVX System, Abbott) showed a small low-voltage area in the RV outflow tract. The electrophysiological study induced a monomorphic hemodynamically tolerated sustained VT. The histological examination of endomyocardial biopsies revealed increased cardiomyocyte size with irregular nuclei, signs of necrosis and fibro-fatty substitution, compatible with ACM.

The diagnosis of ACM was therefore reached<sup>1</sup>. The genetic analysis did not reveal any ACM associated mutation.

A primary prevention S-ICD implantation was proposed. The S-ICD had two therapy zones programmed: 220-240 beats/min (conditional zone) and >240 beats/min (shock zone) with sensing selected in the primary vector (1x gain).

The patient was disqualified from competitive sport activities and  $\beta$ -blocker therapy was recommended.

Tre months after S-ICD implantation, the remote system latitude allowed the detection of four episodes of 240 beats/min VT, preceded by a sinus tachycardia of 150 beats/min. All VTs were interrupted after 14-20 sec with 65 J shocks (**Figure 1 B**). The patient was immediately contacted and confirmed having perceived shocks during exercise (cycling).

Characteristics of both patients are summarized in **Table 1**.

## **Discussion**

The described patients represent emblematic cases demonstrating the efficacy of the S-ICD, implanted either in primary or secondary prevention in elite athletes diagnosed with ACM. A very recent paper, indeed, reported S-ICD efficacy to treat ventricular arrhythmias in ACM patients<sup>10</sup>, though no attention was devoted to the subcategory of athletes.

Despite competitive sport disqualification for the diagnosis of ACM, as recommended by the 2017 VA/SCD Guidelines<sup>7</sup>, the two described athletes underwent non-competitive intense exercise, which triggered VT,

requiring S-ICD interventions. Even if there is a general consensus that exercise training, in patients with an ICD, seems to be safe and not associated with increased risk of shocks<sup>11</sup>, it might not be the case for specific diseases such as ACM. In this case, the genetic predisposition may increment the effect of intense physical exercise, both from the point of view of heart muscle stretching, and for the augmented adrenergic stimulation adverse effect. The two phenomena may result in a greater arrhythmic burden in ACM patients during physical activity. Moreover, sympathetic activation may, in some cases, determine a defibrillation threshold increase and ineffective shocks<sup>12</sup>. However, in our cases, we observed a fast recognition and treatment of arrhythmias by the S-ICD during exercise. This supports the fact that S-ICD is protective even in patient practicing intense physical activity.

The decision of implanting an S-ICD was taken in view of the young age of the patients: indeed the lack of transvenous access avoids the risks of catheter damage and infections during the long life expectancy with the ICD. Moreover, the S-ICD device easily allows CMR follow-up, particularly important for ACM disease progression monitoring<sup>13</sup>.

To the best of our knowledge, to date no reports described S-ICD use in ACM athletes nor the S-ICD efficacy in discriminating high frequency heart rhythm (due to intense exercise) from VT, and in interrupting life-threatening VT. Indeed, S-ICD are susceptible to T-wave oversensing caused by high rate-dependent ECG changes during exercise, leading to inappropriate shocks as highlighted for ACM by a previous work<sup>14</sup>. However, preimplantation screening methods (i.e. Automatic Screening Tool), algorithm updates (i.e. SMART PASS Filter) and experience have evolved<sup>15</sup>, reducing inappropriate shock rate, as demonstrated by the Effortless study<sup>16</sup>.

In conclusion, from these cases we could draw the following messages: I) S-ICD is effective in reverting life-threatening arrhythmias in ACM patients, even during exercise; II) strenuous activity **may** induce ICD shocks in ACM patients, and possibly disease progression, therefore sport restriction should be recommended.

#### **Authorship contributions**

**VC** and **MAD**: [1] data acquisition, analysis and interpretation; [2] drafting the paper; [3] manuscript approval.

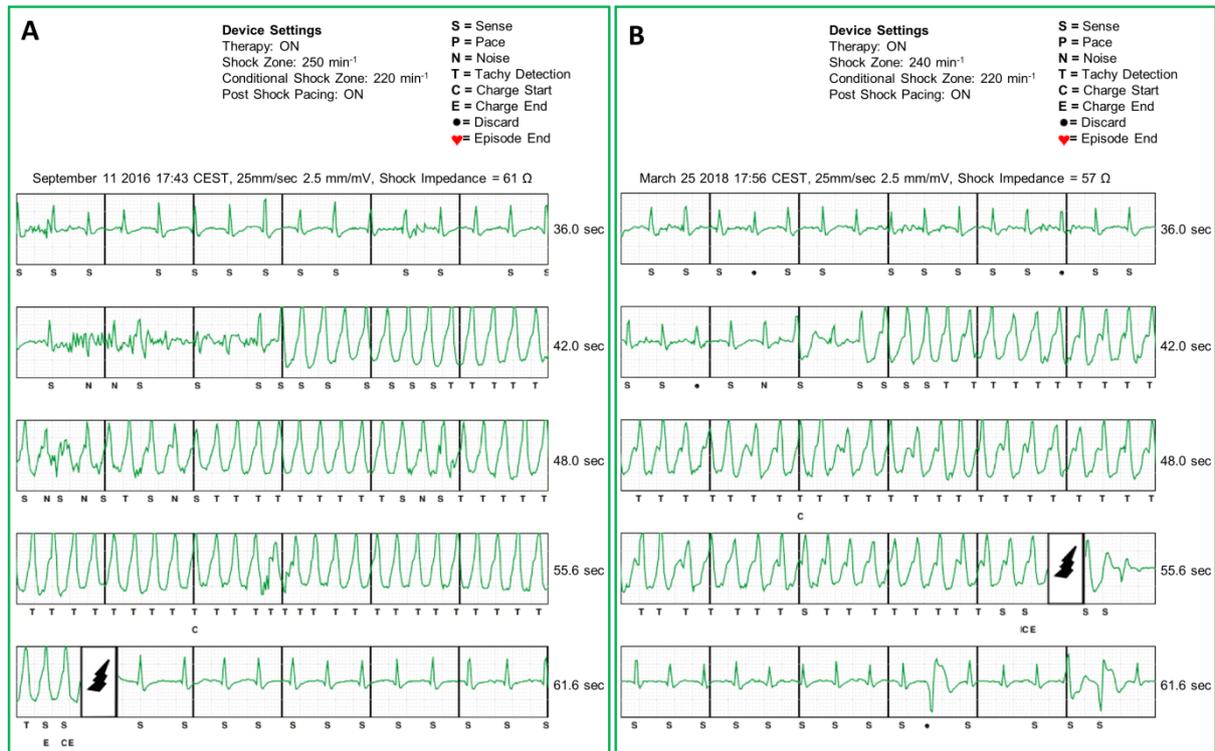
**ES**: [1] data interpretation; [2] drafting the paper; [3] manuscript approval. **CT** and **ADR**: [1] research design; [2] revising the paper critically; [3] manuscript approval.

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## Figure Legend



**Figure 1.** S-ICD registrations of the described events induced by exercise. **A)** Case 1: S-ICD shock after 16 sec of 250 beats/min VT. **B)** Case 2: S-ICD shock after 14 sec of 240 beats/min VT.

**Table 1.** Patients' characteristics.

Case n.	Age/sex	Type of sport	Type of spontaneous arrhythmias	Symptoms	Previous cardiac arrest	ACM criteria	Genetics	s-ICD implantation for
1	21 / Male	Basket	Ventricular fibrillation	-	Yes	2 major	<i>PKP2</i> : c.2009delC (pathogenic)  <i>RYR2</i> : c.10355T>C (variant of unknown significance)	secondary prevention
2	20 / Male	Cycling	NSVT and PVC (LBBB and superior axis)	Palpitation, pre-syncope	No	3 major	Negative	primary prevention

NSVT: Non-sustained ventricular tachycardia; PVC: premature ventricular contractions; LBBB: left bundle branch block.