

Pre-participation Cardiovascular Evaluation for Athletic Participants to Prevent Sudden Death: Position Paper From the EHRA and the EACPR, Branches of the ESC. Endorsed by APHRS, HRS, and SOLAECE

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Abbreviations

AMI:	acute myocardial infarction
ARVC:	arrhythmogenic right ventricular cardiomyopathy
CACS:	coronary artery calcium score
CAD:	coronary artery disease
ChD:	Chagas heart disease
CMR:	cardiac magnetic resonance
CPVT:	catecholaminergic polymorphic ventricular tachycardia
CTCA:	computed tomography coronary angiography
CV:	cardiovascular
EACPR:	European Association for Cardiovascular Prevention and Rehabilitation
LGE:	late gadolinium enhancement
LQTS:	long QT syndrome
LV/RV:	left/right ventricle
PPE:	pre-participation evaluation
PVC:	premature ventricular contraction
SCD:	sudden cardiac death
TTE:	transthoracic echocardiography
VF:	ventricular fibrillation

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Introduction

- Sudden cardiac death (SCD) associated with athletic activity is rare
- Victims are typically young and apparently healthy, but many harbour underlying cardiovascular (CV) disease ^{1,2}
- Most cases of SCD are due to ventricular fibrillation (VF) or ventricular tachyarrhythmia (VT) degenerating into VF, in individuals with arrhythmogenic disorders
- Athletic activity may trigger these arrhythmic events ³

This position paper aims to review the evidence for the identification of at-risk individuals

1. Kim et al. *NEJM* 2010;**366**:130–40

2. Hammon et al. *Circulation* 2015;**132**:10–9

3. Corrado et al. *J Am Coll Cardiol* 2013;**42**:1959–63



Definition of sudden cardiac death in athletes

SCD = sudden and unexpected death occurring during, or shortly after, exercise (with varying time intervals up to 24 h used by different investigators), if witnessed by a bystander and/or happening in an individual who was otherwise known to be healthy.

Incidence of SCD in athletes

- Lack of rigorous studies
- Best estimate is 1–2/100,000 athletes aged 12–35 years ^{1–4}
- A robust Italian study suggested incidence 3x higher in athletes vs. non-athletes,² but a Danish study found decreased rates of SCD in athletes ⁵
- Incidence similar in competitive and recreational athletes ⁴
- 2–25x higher incidence in males than females ^{1–6}
- 5–10x higher incidence in age >35 years ^{1,4–6}
- High incidence in black athletes (5.5/100,000) and male basketball players (>10/100,000) ^{1,6}

1. Harmon et al. *Circulation* 2015;**132**:10–9

2. Corrado et al. *JACC* 2003;**42**:1959–63

3. Maron et al. *JACC* 2014;**63**:1636–43

4. Risgaard et al. *Heart Rhythm* 2014;**11**:1673–81

5. Holst et al. *Heart Rhythm* 2010;**7**:1365–71

6. Harmon et al. *Heart* 2014;**100**:1227–34



Causes of SCD in athletes

Hypertrophic cardiomyopathy (HCM)

- HCM is defined as left ventricular hypertrophy (LVH) that cannot be solely explained by abnormal loading conditions
- HCM prevalence is 1:500 in European, American, Asian and African populations ^{1,2}
- Clinical manifestations include heart failure (HF) and atrial fibrillation, although patients can be asymptomatic and SCD may be the first manifestation ²
- In most series, HCM is the most common cause of SCD in young people engaged in competitive sport ^{3,4}

1. Hammon et al. *Circulation* 2015;**132**:10–9

2. Elliot et al. *Eur Heart J* 2014;**35**:2733–79

3. Harmon et al. *Heart* 2014;**100**:1227–34

4. Maron et al. *JAMA* 1996;**276**:199–204

Causes of SCD in athletes

HCM diagnosis

- Generally carried out with 2D echocardiography or MRI ¹
- Otherwise unexplained LVH, wall thickness ≥ 13 mm in females, ≥ 15 mm in males or >3 SD from average ¹
- 'Grey zone' at 13–15 mm ²
- Cardiac magnetic resonance (CMR) imaging better in distal LV and lateral wall
- CMR with late gadolinium enhancement (LGE) can detect myocardial fibrosis
- Abnormal ECG patterns are common, but no single diagnostic pattern ³
- Exercise test, 24 h ECG and serial imaging tests may be useful
- Genetic testing may be useful in borderline patients ¹

1. Elliot et al. *Eur Heart J* 2014;**35**:2733–79 2. Caselli et al. *Am J Cardiol* 2014;**114**:1383–9 3. Ryan et al. *Am J Cardiol* 1995;**76**:689–94

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Causes of SCD in athletes

Factors supporting athlete's heart diagnosis in athletes with LVH in the 'grey zone'

- Clinical
 - Lack of HCM family history ¹
 - Absence of diffuse T-wave inversion in ECG ¹
- CMR imaging
 - Homogenous distribution of LVH
 - Lack of LGE areas in the LV (myocardial fibrosis)
- Echocardiography
 - Normal or enlarged LVEDD (≥ 55 mm)
 - Symmetric (IVS and PW, base to apex) LVH
 - Normal diastolic function (E/A ratio >1 ; e' peak velocity >11.5 cm/s)
- LVH regression after complete deconditioning
- Lack of known HCM-causing mutations in genetic testing

1. Caselli et al. *Am J Cardiol* 2014;**114**:1383–9



Causes of SCD in athletes

Arrhythmogenic right ventricular cardiomyopathy (ARVC)

- ARVC is a progressive inherited heart muscle disease causing ventricular electrical instability that may lead to arrhythmic SCD
- Prevalence 1:1,000 to 1:5,000 ¹
- Characterised by progressive loss of myocardium, myocyte death and fibro-fatty scar, which predispose to ventricular arrhythmia ^{1,2}
- Competitive sports confer 5x increased risk of SCD in young people with ARVC ³
- Exercise may accelerate disease progression ^{4,5}

1. Priori et al. *Europace* 2013;**15**:1389–406

2. Corrado et al. *Heart* 2000;**83**:588–95

3. Corrado et al. *JACC* 2003;**42**:1959–63

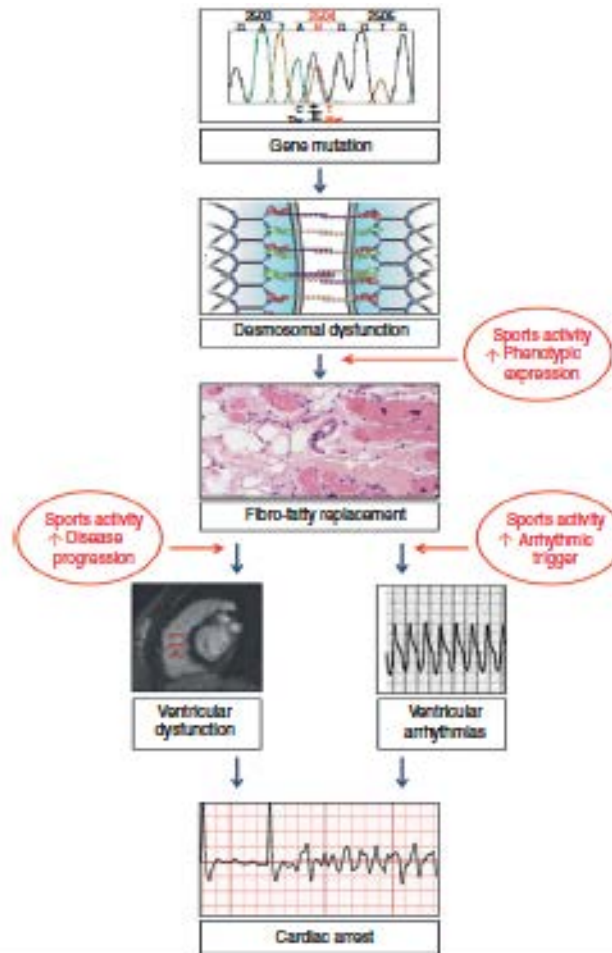
4. James et al. *JACC* 2013;**62**:1290–7

5. Ruwald et al. *Eur Heart J* 2015;**36**:1735–43



Causes of SCD in athletes

ARVC progression:



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Causes of SCD in athletes

Diagnosis of ARVC

- Taskforce criteria: combination of genetic, ECG, arrhythmia, morpho-functional and histopathological findings ¹
- ECG abnormalities in up to 80%; most common are prolonged QRS duration ≥ 110 ms, inverted T waves in right precordial leads (V1–V3) or beyond in absence of complete right bundle branch block in individuals aged >14 years, or late potentials by signal-averaged ECG ^{1,2}
- Ventricular arrhythmias (PVCs or NSVT) are common, often with left bundle branch block pattern and either superior or inferior axis ²
- Echocardiography, right ventricular angiography and CMR are useful ^{1,3}
- Genetic diagnosis useful for family screening ⁴

1. Marcus FI et al. *Eur Heart J* 2010;**31**:806–14

3. Marra MP et al. *Circ Arrhythm Electrophysiol* 2012;**5**:91–100
2013.124

2. Corrado et al. *Heart* 2000;**83**:588–95

4. Te Rijdt WP et al. *Eur J Hum Genet* 2014;**22**:doi:10.1038/ejhg



Causes of SCD in athletes

Representative ECG from a patient with ARVC



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Causes of SCD in athletes

Coronary congenital abnormalities

- Most common are coronary arteries arising from anomalous sinus in aortic root
- Affects 0.5–1.0% of individuals ¹
- Most are clinically silent, but some develop ventricular ischaemia, and SCD is the first manifestation in a minority of cases ¹
- Higher risk of SCD in patients with left coronary artery originating in right coronary sinus or coronaries coursing between aorta and pulmonary artery ¹
- Exercise may trigger ventricular ischaemia, electrical instability and VF
- Some studies suggest this is the 2nd most common cause of SCD in athletes ^{2,3}
- Nearly half of athletes who suffer SCD from coronary arteries with anomalous origin were previously asymptomatic ⁴

1. Angelini P. *Circulation* 2007;**115**:1296–305

3. Harmon KG et al. *Circulation* 2015;**132**:10–9

2. Maron BJ et al. *JAMA* 1996;**296**:199–204

4. Basso C et al. *JACC* 2000;**35**:1493–501



Causes of SCD in athletes

Coronary congenital abnormalities: diagnosis

- Rest ECG is usually normal unless previous MI ¹
- Exercise test has low sensitivity ¹
- Expert sonographers can localise origin of both coronary arteries in most individuals ²
- For definite diagnosis, invasive coronary or computed tomography angiography is required

1. Basso C et al. *JACC* 2000;**35**:1493–501

2. Wyman et al. *J Am Soc Echocardiogr* 2008;**21**:786–8

Causes of SCD in athletes

Ventricular pre-excitation

- Atrioventricular (AV) bypass tracts cause early, anomalous ventricular activation before normal activation through the AV node
- Estimated prevalence 1:1,000 ¹
- Can be asymptomatic or present with paroxysmal supraventricular tachycardia symptoms – palpitations, syncope
- Symptomatic patients at high risk of SCD ($\approx 0.15\%/yr$)
- Ventricular pre-excitation seen in $\approx 1\%$ of athletes with SCD

1. Hiss RG, Lamb LE. *Circulation* 1962;**25**:947–61

2. Maron BJ et al. *Circulation* 2009;**119**:1085–92

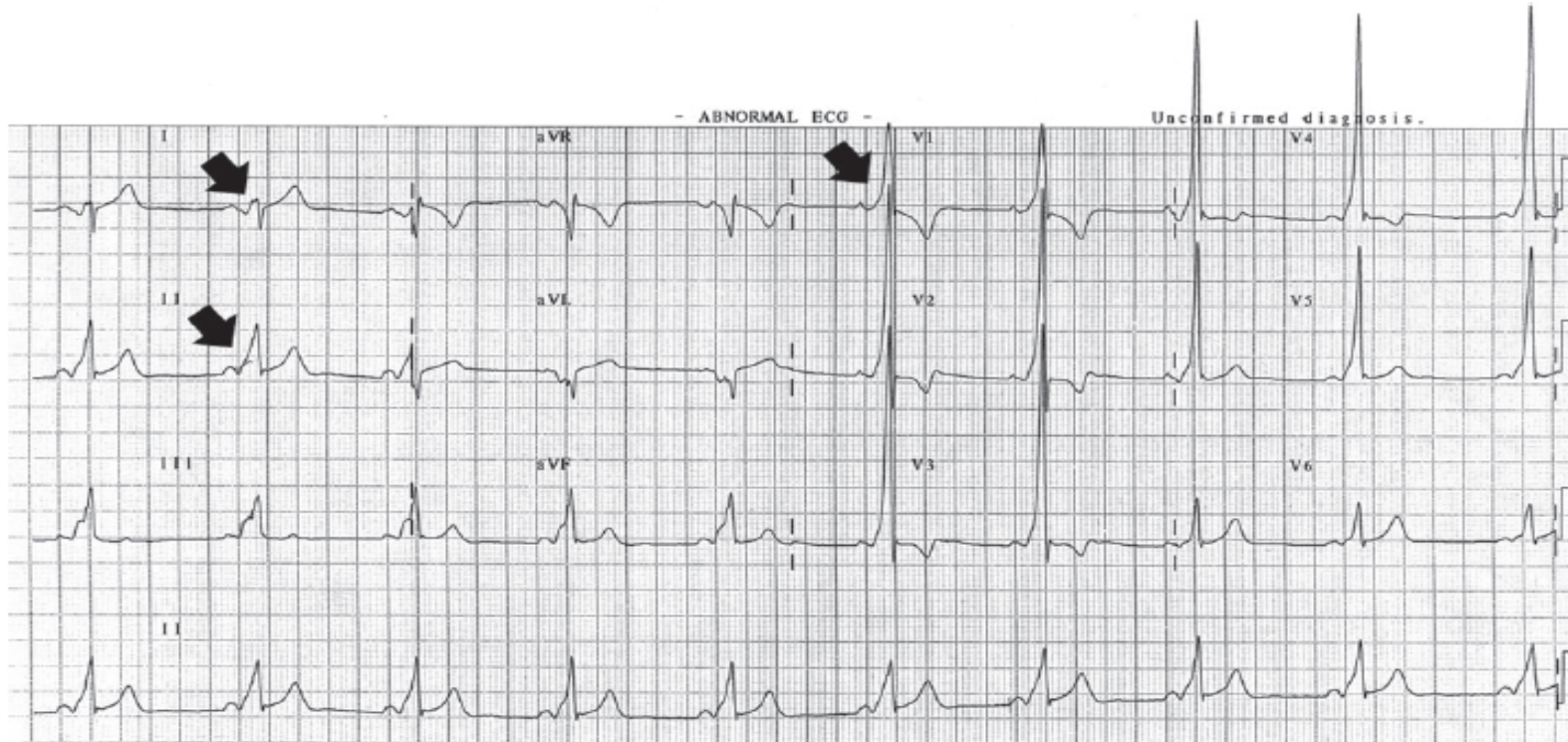
Causes of SCD in athletes

Ventricular pre-excitation: diagnosis

- ECG with characteristic delta-wave pattern
- Delta waves have slurred upstroke QRS complexes and short PR intervals (<120 ms)
- Pre-excitation may be masked in adrenergic settings when AV node conduction is fast

Causes of SCD in athletes

Representative ECG from a patient with a pre-excitation syndrome



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Causes of SCD in athletes

Left ventricle non-compaction (LVNC)

- Recently identified cardiomyopathy characterised by abnormal, prominent LV wall trabeculations and deep intertrabecular recesses, often associated with thin, compacted epicardial myocardial layer ¹
- Seen in <0.5% of all echocardiographic studies ²
- Subtypes include dilated, hypertrophic, biventricular, restrictive and benign LV hypertrabeculation forms ³
- Asymptomatic or symptoms of progressive LV systolic dysfunction, potentially lethal arrhythmias or thromboembolic events
- To date, not reported as a significant cause of SCD in athletes

1. Priori SG et al. *Europace* 2015;**17**:1601–87

2. Aras D et al. *J Card Fail* 2006;**12**:726–33

3. Brescia ST et al. *Circulation* 2013;**127**:2202–8



Causes of SCD in athletes

LVNC: diagnosis

- Generally non-specific ECG findings ¹
- Non-compaction to compaction ratio >2:1 on echocardiogram ¹
- Increased left ventricular trabeculation detected in highly trained athletes, fulfilling LVNC criteria in up to 8% ²
- Benign outcomes associated with normal systolic function, absence of ECG abnormalities, absence of complex ventricular arrhythmias, and a negative family history ³

1. Towbin JA et al. *Lancet* 2015;**386**:813–25

2. Gati S et al. *Heart* 2013;**99**:401–8

3. Caselli S et al. *Am J Cardiol* 2015;**116**:801–8

Causes of SCD in athletes

Dilated cardiomyopathy (DCM)

- Characterised by LV or biventricular dilatation and systolic dysfunction in the absence of abnormal loading conditions or CAD sufficient to cause global systolic impairment ¹
- Patients may be asymptomatic for many years and occasionally present with life-threatening VT and/or supraventricular tachyarrhythmia
- Ventricular arrhythmias can be triggered by exercise, but is a relatively uncommon cause of SCD in athletes ²
- Diagnosis: imaging shows dilated (usually spherical) LV cavity, systolic dysfunction (ejection fraction <50%, with blunted increase during exercise) and occasionally wall motion abnormalities. ECG show non-specific findings

1. Pinto YM et al. *Eur Heart J* 2016;**37**:1850–8

2. Maron BJ et al. *Circulation* 2009;**119**:1085–92



Causes of SCD in athletes

Valvulopathies

- Bicuspid aortic valves are found in $\approx 1\%$ of the general population¹ and confer risk of aortic stenosis or regurgitation, ascending aorta dilation and dissection
- Mitral valve prolapse is the most common cause of primary mitral regurgitation in young to middle-aged individuals
- Both may lead to LV dysfunction and ventricular arrhythmias during exercise
- No evidence that exercise accelerates valvulopathy progression, but valvulopathies are sometimes a cause of SCD in athletes
- Diagnosis by physical examination (cardiac murmur) and cardiac imaging test

1. Siu SC, Silversides CK. *JACC* 2010;**55**:2789–800

Causes of SCD in athletes

Inherited primary arrhythmia syndromes

Genetically determined, primary arrhythmic disorders in absence of clinically determined structural heart disease.¹ These include:

- Long QT syndrome
- Short QT syndrome
- Catecholaminergic polymorphic ventricular tachycardia
- Brugada syndrome

1. Priori SG et al. *Europace* 2015;**17**:1601–87

Causes of SCD in athletes

Long QT syndrome (LQTS)

- Group of disorders characterised by prolonged QT interval on ECG and predisposition to develop life-threatening arrhythmias such as *torsades de pointes* during exercise or stress
- Prevalence of 1:2,000 newborns ¹
- Disease-causing mutation can be identified in 75% of patients by genetic screening²
- Emotional stress and exercise, particularly swimming, are important triggers for ventricular arrhythmias and SCD in LQT1, but significant overlap exists between genotypes

1. Schwartz PJ et al. *Circulation* 2009;**120**:1761–7 2. Ackerman MJ et al. *Europace* 2011;**13**:1077–109

Causes of SCD in athletes

LQTS: diagnosis

- Measurement of QTc using Bazett's formula on repeated 12-lead ECG at stable heart rates (60–100 bpm). Consider LQTS if unexplained syncope and QTc >460 ms or asymptomatic and QTc \geq 480 ms ¹
- When QTc prolongation not obvious, use risk score (age, clinical/family history, QTc duration, T-wave morphology, previous history of *torsades de pointes*);² LQTS risk score >3 is diagnostic
- Exercise test can demonstrate maladaptation of QT interval to rapidly increasing heart rate ³
- QT adapts poorly to sinus tachycardia after standing up quickly in LQTS ⁴
- 12-lead ambulatory ECG recommended to evaluate QT interval at different times in a day
- Additional ECG features include excessive bradycardia for age, visible T-wave alternans or notches on T-wave (LQT2) and long sinus pauses (LQT3)
- A LQTS diagnosis should always be confirmed by a specialised cardiologist

1. Priori SG et al. *Europace* 2015;**17**:1601–87

3. Vincent GM et al. *Am J Cardiol* 1991;**68**:498–503

2. Schwartz PJ et al. *Circulation* 1993;**88**:782–4

4. Viskin S et al. *JACC* 2010;**55**:1955–61



Causes of SCD in athletes

Long QT syndrome



ECG from a patient with LQTS. Note the prolonged QT interval (510 ms)

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Causes of SCD in athletes

Short QT syndrome (SQTS)

- Mutations in five genes have been linked to SQTS, but in 80% of cases no genetic cause has been identified
- Prevalence of 1:2,000 in children, but 1:1,000 in adults, predominantly men¹
- No specific triggers identified for arrhythmia
- Diagnosis:
 - ESC guidelines state QTc ≤ 340 ms²
 - consider if QTc ≤ 360 ms or family history of SCD in patients with known mutation
 - eliminate secondary causes of short QT (e.g. high K⁺, Ca²⁺, acidosis, hyperthermia)

1. Dhutia H et al. *Br J Sports Med* 2016;**50**:124–9

2. Priori SG et al. *Europace* 2015;**17**:1601–87

Causes of SCD in athletes

Short QT syndrome



ECG from a patient with SQTs. Note the shortened QT interval (260 ms)

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Causes of SCD in athletes

Catecholaminergic polymorphic ventricular tachycardia (CPVT)

- Characterised by adrenergic-induced bidirectional or polymorphic ventricular tachycardia
- Prevalence around 1:10,000
- Two-thirds of cases due to known genetic mutations ¹
- Silent mutations in 20% ²
- If undiagnosed, mortality rates are 30–50% by age 40 ^{1,2}
- Physical activity is a common trigger of ventricular arrhythmias in patients with CPVT
- Diagnosis – structurally normal heart, normal ECG. Effort or emotion trigger ventricular premature beats that increase in complexity with heart rate

1. Priori SG et al. *Europace* 2013;**15**:1389–406

2. Priori SG et al. *Circulation* 2002;**106**:69–74

Causes of SCD in athletes

Brugada syndrome

- Characterised by right bundle branch block, persistent ST segment elevation and sudden death due to polymorphic ventricular tachycardia (PVT) and/or VF in absence of other cardiomyopathies.¹ May be accompanied by mild RV abnormalities
- Inherited disease, but may be sporadic in up to 60% of cases ²
- Prevalence of 1:1,000 in Asia, but <1:10,000 in Europe and America ³
- Ventricular arrhythmias generally occur at rest. Chronic athletic conditioning or raised body temperature during exercise may exacerbate the condition

1. Brugada P, Brugada J. *JACC* 1992;**20**:1391–6

2. Rudic B et al. *Europace* 2016;**18**:1411–9

3. Mizusawa Y, Wilde AA. *Circ Arrhythm Electrophysiol* 2012;**5**:606–16

Causes of SCD in athletes

Brugada syndrome: diagnosis

- Brugada syndrome is diagnosed in the presence of type 1 ST elevation either spontaneously or after intravenous administration of a sodium channel blocker in at least one right precordial lead (V1 and V2), placed in a standard or superior position (up to the second intercostal space)
- Other signs might also be present:
 - Attenuation of ST elevation during exercise with reappearance during recovery ¹
 - First-degree AV block and left axis deviation
 - Atrial fibrillation
 - Late potentials in high resolution ECG
 - QRS fragmentation
 - Ventricular refractory period <200 ms and HV interval >60 ms in electrophysiological study
 - Absence of diagnosis of alternative cardiomyopathy

1. Amin AS et al. *Circ Arrhythm Electrophysiol* 2009;2:531–9



Causes of SCD in athletes

Brugada syndrome



ECG showing characteristic findings from Brugada syndrome (arrows)

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Causes of SCD in athletes

Acquired cardiac abnormalities

These become proportionally more important in older athletes and include:

- Coronary artery disease
- Chagas disease
- Myocarditis
- Exercise-induced cardiac injury

Causes of SCD in athletes

Coronary artery disease (CAD)

- Atherosclerotic CAD is the predominant cause of SCD in the general population. The risk of a myocardial infarction and SCD is increased with vigorous physical activity, particularly in sedentary individuals ¹
- Around 10% of AMIs may be triggered by physical activity ²
- Around 30% of SCD cases after exercise experienced symptoms of ischaemia in the previous week ³
- Most due to acute plaque rupture or erosion/acute thrombosis, but one study found no acute thrombosis in five cases with SCD and CAD ⁴
- Diagnosis – rest ECG has a limited sensitivity and diagnostic accuracy

1. Thompson PD et al. *Circulation* 2007;**115**:2358–68

3. Marijon E et al. *Circulation* 2015;**131**:1384–91

2. Giri S et al. *JAMA* 1999;**282**:1731–6

4. Kim JH et al. *NEJM* 2012;**366**:130–40

Causes of SCD in athletes

Coronary artery disease

- European Association for Cardiovascular Prevention and Rehabilitation (EACPR) recommendation:
 - Assessing CV risk profile (by a validated risk score form) of the candidate and the type and intensity of physical activity
- Athletes aged ≥ 35 years and/or participating in vigorous physical or sport activity should:
 - Understand the nature of cardiac prodromal symptoms and the need for prompt medical attention
 - Undergo exercise stress testing if symptoms of possible CAD are present
 - Exercise stress test might be considered in senior athletes at a high CV risk, although conflicting data exists on the use of this approach

1. Borjesson M et al. *Eur J Cardiovasc Prev Rehabil* 2011;**18**:446–58

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Causes of SCD in athletes

Chagas disease

- Chagas heart disease is the most important cause of non-ischaemic cardiomyopathy in Latin America and may become a global health problem due to emigration ¹
- Occurs in 20–30% of infected individuals and symptoms appear 10–30 years after initial infection ²
- Cardiac arrhythmia and SCD (primarily due to scar related sustained VT) are common,² although there is limited evidence that this is exacerbated by exercise³
- Sinus node dysfunction, AV and intra-ventricular conduction disturbances commonly seen on ECGs of asymptomatic patients can progress to sinus node standstill and complete AV block, causing syncope and SCD ²
- Diagnosis: epidemiological enquiry and serological tests

1. Guerri-Guttenberg RA et al. *Eur Heart J* 2008;**29**:2587–91 2. Rassi A et al. *Lancet* 2010;**375**:1388–402 3. Matos LD et al. *Arq Bras Cardiol* 2011;**96**:e3–6

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Causes of SCD in athletes

Myocarditis

- Characterised by inflammation of myocardium
- Symptoms range from minor regional wall motion abnormalities or pericardial effusion to severe LV systolic dysfunction and potentially lethal ventricular arrhythmias
- Commonly found in SCD in athletes; vigorous physical activity may also worsen disease

Causes of SCD in athletes

Myocarditis

Diagnosis:

- Systemic viral symptoms, including upper respiratory tract or gastrointestinal manifestations, with development of cardiac-related symptoms such as HF, arrhythmias or chest pain
- Myocardial necrosis markers are often increased in plasma in early stages
- ECG may show ST-segment and T-wave abnormalities, or ventricular arrhythmias
- Cardiac imaging techniques may show global or regional wall motion abnormalities and pericardial effusion. Cardiac MRI may identify myocardial oedema and LGE patches in early stages
- Myocardial biopsy gives a definitive diagnosis, but usually is not required

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Causes of SCD in athletes

Exercise-induced SCD

Exercise may:

- Accelerate an inherited predisposition to an arrhythmogenic RV cardiomyopathy¹
- Cause arrhythmogenic remodelling on the basis of recent works, although controversial:
 - Especially of the RV, based on observation that professional cyclists presenting with RV arrhythmias rarely show clinical or genetic evidence of inherited disease²
 - Evidence that intense exercise puts disproportionate strain on RV³
- Exacerbate the severity of cardiac damage due to concurrent illness
 - Haemodynamic overload of intense exercise may impair healing/exacerbate myocardial inflammation⁴

1. Saberniak J et al. *Eur J Heart Fail* 2014;**16**:1337–44

3. La Gerche A, Heidbuchel H. *Circulation* 2014;**130**:992–1002

2. Heidbuchel H et al. *Eur Heart J* 2003;**24**:1473–80

4. Kiel RJ et al. *Eur J Epidemiol* 1989;**5**:348–50



Causes of SCD in athletes

Implications of exercise-induced SCD

Need to consider serial pre-participation cardiac evaluation, especially in at-risk groups:

- Individuals undertaking intense exercise (cyclists, rowers, marathon runners etc.)
- After an overt viral illness

Role of screening techniques in SCD

ECG

- Addition of 12-lead ECG to pre-participation screening allows early detection of cardiomyopathies or channelopathies which usually manifest with ECG abnormalities
- Improves sensitivity from <25% for clinical history/exam to >90% for ECG¹
- Meta-analysis concluded that ECG is the most effective strategy for detecting underlying cardiac conditions predisposing to SCD, in comparison to clinical history and physical examination¹
- Limitations include sensitivity and specificity
 - Low sensitivity for congenital coronary artery abnormalities and stable ischaemic heart disease
 - False-positive rate 5–10%
- Diagnostic accuracy may be improved with standardised ECG interpretation criteria

1. Harmon KG et al. *J Electrocardiol* 2015;**48**:329–38



Role of screening techniques in SCD

ECG

In favour of ECG	Against ECG
<ul style="list-style-type: none"> • Non-expensive, readily available • More sensitive than history/physical examination¹ • Abnormal in >80% cardiomyopathies, myocarditis, pre-excitation syndromes and ion channel disorders, which account for $\frac{2}{3}$ of cardiac arrest in young athletes^{2,3} • Modern diagnostic criteria allow potential to standardise and simplify interpretation, increasing diagnostic accuracy⁴ • Notable decline ($\approx 90\%$) in SCD over 25 years in young athletes after implementation of Italian ECG screening programme⁵ 	<ul style="list-style-type: none"> • Evidence for survival benefit limited to single observational study • Highly trained athletes may develop ECG anomalies that mimic cardiomyopathies⁶ • Commonly misinterpreted leading to expensive diagnostic workup or unnecessary disqualification of athletes, or potentially lethal condition misinterpreted as normal variant⁷ • Some CV disorders responsible for SCD are not associated with ECG changes⁸ • False positives jeopardise effectiveness⁹ • Abnormal ECG findings lead to disqualification of up to 2% of athletes⁵

1. Heidbuchel H et al. *Br J Sports Med* 2012;**46**:i44–50

4. Corrado D et al. *NEJM* 1998;**339**:364–9

7. Rowin EJ et al. *Am J Cardiol* 2012;**110**:1027–32

2. Ryan MP et al. *Am J Cardiol* 1995;**76**:689–94

5. Corrado D et al. *JAMA* 2006;**296**:1593–601

8. Angelini P. *Circulation* 2007;**115**:1296–305

3. Sheikh N et al. *Circulation* 2014;**129**:1637–49

6. Pelliccia A et al. *Circulation* 2000;**102**:278–84

9. Maron BJ et al. *JACC* 2015;**66**:2356–61

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Role of screening techniques in SCD

ECG: European Society of Cardiology (ESC) recommendations

Physiological adaptation

Do not require further reevaluation

- Sinus bradycardia ($>30\text{bpm}$) -51% to 68%-
- Sinus arrhythmia -20% to 23%-
- Ectopic atrial rhythm -1%-
- Junctional escape rhythm -0.4%-
- 1st degree AV block ($PR\ interval > 200\ ms$) -7%-
- Mobitz Type I (Wenckebach) 2nd degree AV block – 0.1%-
- Incomplete RBBB -24% to 27%-
- Isolated QRS voltage criteria for LVH -23% to 36%-
- Early repolarization ($ST\ elevation$, $J\text{-point elevation}$, $J\text{-waves}$ or $terminal\ QRS\ slurring$) -37% to 72%-
- Convex ('domed') ST segment elevation combined with T-wave inversion in leads V1–V4 in black/African athletes

Abnormal ECG findings

Require further evaluation

- T-wave inversion ($>1\ mm\ V2\text{-}V6$, II and aVF , I and aVL)
- ST segment depression ($>0,5\ mm$)
- Pathologic Q waves ($>3\ mm\ depth/>40\ ms\ duration$)
- Complete LBBB
- Intraventricular conduction delay ($\geq 140\ ms$)
- Left axis deviation (-30° to -90°)
- Left atrial enlargement ($P > 120\ ms$ in I or II ; negative portion of $P \geq 1\ mm$ and $\geq 40\ ms$ in $V1$)
- Right ventricular hypertrophy ($R\text{-}V1 + S\text{-}V5 > 10,5\ mm$ AND right axis deviation)
- Ventricular pre-excitation
- Long QT interval ($QTc \geq 470$ in male; $\geq 480\ ms$ in female)
- Short QT interval ($QTc \leq 320\ ms$)
- Brugada-like ECG pattern
- Profound sinus bradycardia ($< 30\text{bpm}$ or $pauses \geq 3\ s.$)
- Atrial tachyarrhythmias
- Premature ventricular contractions ($\geq 2\ PVCs/10s$)
- Ventricular arrhythmias (couplets, triplets and NSVT)

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Role of screening techniques in SCD

ECG: other concerns

- Need for improved expertise in interpretation – sports cardiology qualification ¹
- Psychological impact – most athletes undergoing ECG screening feel more confident and would recommend to others ^{2,3}
- Ethical concerns of only screening a subset of population – conflicting data about risk of SCD ^{4,5}
- All the above concerns also apply to medical history and physical examination

1. Heidbuchel H et al. *Eur J Prev Cardiol* 2013;**20**:889–903

2. Solberg EE et al. *Eur J Prev Cardiol*

3. Asif M et al. *Br J Sports Med* 2014;**48**:116–6

4. Corrado D et al. *JACC* 2003;**42**:1959–63

5. Kim JH et al. *NEJM* 2012;**366**:130–40

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Role of screening techniques in SCD

ECG exercise test

- Diagnostic yield depends on pre-test risk. In individuals at low-CAD risk, most positive tests are false positives
- In low- to moderate-risk individuals, number of deaths prevented by exercise testing is less than number of additional deaths from angiography ¹
- Limited sensitivity (68%) and specificity (<80%) ²
- Should be reserved for symptomatic or high-risk athletes

Ambulatory ECG monitoring

- Various options: short, 24 h or 7-day ECG Holter recordings, implantable devices, smartphone or wearable apps
- Most common indications are unexplained syncope and palpitations
- Low sensitivity for infrequent symptoms; therefore, better as 2nd-line test

1. Lahav D et al. *J Gen Intern Med* 2009;**24**:934–8

2. Gianrossi R et al. *Circulation* 1989;**80**:87–98



Role of imaging modalities in screening

Echocardiography

- Transthoracic echocardiography (TTE) identifies cardiomyopathy, is widely available, portable, free of ionising radiation and relatively inexpensive
- Various study protocols, from 1 min targeted parasternal image to 20 min
- Studies with first-line TTE have only identified minor/trivial congenital valvular abnormalities ^{1,2}
- Addition of TTE to ECG screening in children and young athletes did not increase diagnosis of cardiomyopathies ³
- Elite athletes have cavity dilatation and LVH that may lead to false-positive diagnosis of cardiomyopathy ^{4,5}
- May be useful in second line screening: onsite TTE reduces referral rates by 40–60%, but not cost-effective as 1st-line therapy ³

1. Feinstein RA et al. *Clin J Sport Med* 1993;**3**:149–52

2. Weidenbener EJ et al. *Clin J Sport Med* 1995;**5**:86–9

3. Anderson JB et al. *Am J Cardiol* 2014;**114**:1763–7

4. Gati S et al. *Heart* 2013;**99**:401–8

5. Pelliccia et al. *Ann Intern Med* 1999;**130**:23–31



Role of imaging modalities in screening

Cardiac Magnetic Resonance Imaging

- Better assessment of morphology and function of all cardiac chambers (particularly LV apex and RV) as well as acute oedema and myocardial fibrosis versus TTE ¹
- Is feasible to use during exercise ²
- Cardiac MRI can identify pathology in athletes when the ECG and echocardiography appear to be normal ³
- Expensive and limited availability
- Significance of LGE not fully established – has been reported in healthy athletes,^{4,5} but in others it is associated with serious pathology ⁶
- Not recommended for 1st-line screening

1. Jellis C et al. *JACC* 2010;**56**:89–97

2. La Gerche A et al. *Eur Heart J* 2015;**36**:1998–2101

3. Rowin EJ et al. *Am J Cardiol* 2012;**110**:1027–32

4. La Gerche A et al. *Eur Heart J* 2012;**33**:998–1006

5. Wilson M et al. *J Appl Physiol* 2011;**110**:1622–6

6. Schnell F et al. *Br J Sports Med* 2016;**50**:111–7



Role of imaging modalities in screening

Computed tomography coronary angiography (CTCA)

- CTCA useful for diagnosing congenital anomalies in coronary circulation or ischaemic heart disease, but should be reserved for those with abnormalities in first-line test or symptoms on pre-participation evaluation (PPE)

Coronary artery calcium scoring (CACS)

- CACS is an established marker of CV risk
- CACS may be considered in middle-aged and older athletes with at least moderate coronary risk and clinical suspicion

Current screening programmes, rationale and limitations

- PPE increasingly integrated into sporting competitions
- Aim: to identify pre-existing cardiac abnormalities, ensuring optimal management, and thereby reducing the potential for adverse events and loss of life
- The American Heart Association/American College of Cardiology (AHA/ACC) ¹ and ESC ² recommend CV pre-participation screening on medical, ethical and legal grounds
- The ESC recommend minimum personal history, physical examination and a resting 12-lead ECG, whereas AHA/ACC do not include ECG in their recommendations
- Some sporting associations also have their own protocols; cardiac screening is mandatory for Fédération Internationale de Football Association (FIFA) and the Union of European Football Associations (UEFA), whereas the International Olympic Committee (IOC) simply recommends it as best practice

1. Maron BJ et al. *JACC* 2015;**66**:2356–61

2. Pelliccia A et al. *Eur Heart J* 2005;**26**:1422–45



Current screening programmes, rationale and limitations

Evidence supporting PPE programmes: impact on cardiovascular mortality

- Italian experience (1979–2004, mandatory SCD reporting): rate of SCD in athletes decreased by 89% (3.6/100,000 person-years in pre-screening period to 0.4/100,000 person-years in the screening period), while SCD rate in a non-screened population did not change ¹
 - Limitations include a high mortality rate at baseline and not considering improvements in resuscitation
- Israel experience: yearly incidence of athletic field deaths did not change between 1985–1996 (2.54/100,000 persons) and 1997–2009 (2.66/100,000 persons) despite introduction of a screening programme including 12-lead ECG ²
 - Limitations include possible SCD under-reporting and a rough estimation of athletes at risk
- One study (1993–2004) compared young athletes from Veneto screened with ECG versus athletes from Minnesota screened by history and physical examination. The two regions did not differ significantly (0.87 versus 0.93, respectively; $P=0.88$) ³

Limitations of all studies have been identified

1. Corrado D et al. *JAMA* 2006;**296**:1593–60

2. Steinvil A et al. *JACC* 2011;**57**:1291–6

3. Maron BJ et al. *Am J Cardiol* 2009;**104**:276–80

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Current screening programmes, rationale and limitations

Cost effectiveness of PPE

Cost-effectiveness analysis¹ based on data from Italian experience: ²

- For every 10,000 athletes screened, estimated that 7% (n=700) undergo additional tests including 700 TTE, 133 (19%) exercise tests, 35 (5%) Holter, and 7 (1%) cardiac catheterisation, electrophysiological and/or CMR studies, eventually returning to competition. In addition, 200 athletes undergo more tests and are disqualified from sport participation
- Number of tests needed to save one life include 41,000 ECGs, 3,700 TTEs, 1,200 exercise stress tests, 54 Holter, 71 cardiac catheterisation, electrophysiological studies and/or CMR
- The cost of saving one life varies according to country; in the US this could be >\$10 million ¹
- Cost-effectiveness heavily relies on a *a priori* assumption. Other authors concluded that adding a single ECG to history/physical exam at participation entry would save 2.06 life-years/1,000 young athletes screened at a cost of \$42,000 per life-year saved

1. Halkin A et al. *JACC* 2012;**60**:2271–6

2. Corrado D et al. *JAMA* 2006;**296**:1593–60

Current screening programmes, rationale and limitations

Study	Target population	Cost/life-year	Cost/life saved	Comments
Fuller (2000) ¹	High School Athletes	H&P \$84 000 ECG: \$44 000	N/R	Screened once at study entry
Maron <i>et al.</i> (2007) ²	High school and middle school athletes	N/R	\$3 400 000	Approximate estimation in a non-dedicated paper
Wheeler <i>et al.</i> (2010) ³	High school and college athletes (14–22 years)	H&P: 199 000\$ H&P&ECG: \$76 100	N/R	Screened once at study entry
Halkin <i>et al.</i> (2012) ⁴	Registered high school, college, and professional participants	N/R	\$10 600 000–\$14 400 000	Annual screening
Leslie <i>et al.</i> (2012) ⁵	High school (≥14 years) freshmen participating in organized sports.	\$91 000	N/R	Screened once at study entry
Schoenbaum <i>et al.</i> (2012) ⁶	Athletes ≥14 years	Adding ECG to H&P: +\$68 000	\$900 000	
Corrado <i>et al.</i> (2013) ⁷	Young (12–35 yo) athletes	~\$67 000	~\$1 350 000	Approximate estimation in a non-dedicated paper
Assanelli <i>et al.</i> (2015) ⁸	European and Algerian athletes seeking a sports medical certificate	Europe: 4071 \$PPP Algeria: 582 \$PPP	N/R	Estimation on prospectively collected data

1. Fuller CM. *Med Sci Sports Exerc* 2000;**32**:887–90
3. Wheeler MT *et al.* *Ann Intern Med* 2010;**152**:276–86
5. Leslie LK *et al.* *Circulation* 2012;**125**:2621–9
7. Corrado D *et al.* *Heart* 2013;**99**:1365–73

2. Maron BJ *et al.* *Circulation* 2007;**115**:1643–55
4. Halkin A *et al.* *JACC* 2012;**60**:2271–6
6. Schoenbaum M *et al.* *Pediatrics* 2012;**130**:e380–9
8. Assanelli D *et al.* *Intern Emerg Med* 2015;**10**:143–50

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Consensus statement

- The major limitation of the present document is the limited scientific evidence inherent to most of the debated issues
- The aim of the PPE is not only to prevent SCD, but also for primary prevention of CVD and to identify and manage CV conditions that may worsen because of intensive athletic training
- Evidence suggests that the 12-lead ECG substantially improves the diagnostic power of PPE when using standardised interpretation criteria. Routine echocardiography and other imaging techniques do not appear to be cost effective
- PPE should be considered for individuals performing regular, intense exercise after providing information on both its benefits and limitations. Sporting organisations such as the IOC and national and international federations share the responsibility to advise elite and professional athletes of the benefits and limitations of PPE on the basis of perceived responsibility and public scrutiny
- There is a need for better characterisation of SCD and identification of individuals at risk. This will require improved non-invasive techniques to detect conditions that are not detected by current methods (e.g. coronary artery abnormalities and subclinical CAD)
- Further developments will reduce costs and improve the efficiency of PPE

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