Recommendations for participation in leisure-time physical activity and competitive sports of patients with arrhythmias   
and potentially arrhythmogenic conditions  
Part 2: Ventricular arrhythmias, channelopathies and implantable defibrillators

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# Introduction

Ventricular tachyarrhythmias obviously create a prognostic threat to the athlete since they may lead to sports-related sudden death. The prevalence of sports-related sudden cardiac death in athletes is 2.1/100000 athletes years.1 Moreover, ventricular arrhythmias may result in symptoms which may create hindrance to continue physical activity, and may even result in syncope or presyncope that could compromise the safety of the athlete or other participants. Ventricular arrhythmias may be the final common pathway of other cardiovascular conditions, like hypertension, ischemic and valvular heart disease, congenital malformations and dilated cardiomyopathy. These conditions formed the focus of other articles in the updated series on ‘Recommendations for Participation’.2-4 This text deals specifically with athletes in whom some form of ventricular rhythm disorder is documented, or when the patient is diagnosed to have inherited a genetic disorder (channelopathy) that may predispose to ventricular arrhythmias. Also, recommendations on sports participation in patients with a pacemaker or an implantable cardioverter defibrillator (ICD) are discussed in this text. A companion text on recommendations in athletes with supraventricular arrhythmias is published in the European Journal of Preventive Cardiology.5 Both texts update European recommendations from 2005 and 2006.6-8 The introductory chapters of that first part described the framework for evaluating eligibility to perform sports, based on three elements which are also dealt within this part, i.e. considering the prognostic risk of the arrhythmias when performing sports, the symptomatic impact during sports, and the potential that physical activity might promote progression of underlying structural problems. The same aspects will obviously also be addressed in the different chapters of this text.

As in the SVT article, the recommendations are formulated using ‘coloured hearts’. This grading does not include definitions of the ‘level of evidence’. A green heart indicates a ‘should do this’ recommendation or indicated treatment or procedure that is based on at least one randomized trial, or is supported by strong observational evidence that it is beneficial and effective. A yellow heart indicates general agreement and/or scientific evidence favouring a ‘may do this’ statement or the usefulness/efficacy of a treatment or procedure. A ‘yellow heart’ symbol may be supported by randomized trials based on a small number of patients or which is not widely applicable. Treatment strategies for which there is scientific evidence of potential harm and should not be used (‘do not do this’) are indicated by a red heart.

It is important to note that there remains a paucity of large-scale and/or prospective data on the safety of sports participation with the aforementioned conditions. Therefore, most recommendations represent expert consensus on what is considered appropriate participation in competitive or recreational sports activity. The recommendations mentioned in this paper may also apply to professional working environments demanding more than light physical activity. Clinicians dealing with athletes or patients have to consider these recommendations as guidance for individualized medical advice and shared decision making in many instances, not as rigid standards or protocols. Factors that have to be taken into account when tailoring recommendations are the type of sports (degree of isometric and isotonic work; low, moderate to high total cardiovascular demand; progressive demand or burst activity), patient motivation, ambient factors (temperature, humidity) and relevance of any incapacitating situation like dizziness or (pre)syncope (e.g. during sports like diving, driving, mountaineering etc.). It is also important to realize that often there is no clear distinction between competitive and leisure time activities, nor between competition and training (with the latter sometimes demanding more strenuous exercise than the competition itself). Patients often ask for quantitative limits of allowed activity (e.g. based on heart rate): however, there is no data to support such quantitative advice, except in the individual case where exercise testing has shown reproducible arrhythmia induction beyond a certain level and never below. Conventionally, exercise at >70% of individualised maximum oxygen uptake (dynamic) or >50% of maximum voluntary contraction (static) is considered “high intensity”.9 Several other factors have the potential to influence the impact of an effort on the organism, such as exercise duration, time of the day, weather, temperature, time between training sessions, (de)hydration, and nutrition. This can cause a similar exercise to be light to moderate on one day and intense on another day. As an adjunct, ratings of perceived exertion (RPE, such as the Borg scale) might be used to approximate the relative intensity of any activity.10, 11 An exercise with an RPE of ≥15 is considered high intensive. The use of such scales, however, has its own limitations, and moderate correlations with oxygen uptake variables have been reported.12

The physician should also discuss with the patient that systematic or progressive training cannot cure or prevent exercise-related arrhythmias, contrary to the belief of many. In general, patients should even be advised not to pursue progressive training effects in endurance programs like running or biking (even during non-competitive activity) since these may lead to an insidious increase in work load (with an increased risk for arrhythmia triggering) or a progression of the underlying disease process (e.g. arrhythmogenic cardiomyopathy (AC), see below). Structured training programs to achieve ever higher goals and competition should be considered high intensive.

# 1. Documented ventricular arrhythmias

Cardiovascular evaluation, performed during regular follow-up or triggered by symptoms, may reveal ventricular arrhythmias on a 12-lead ECG, exercise ECG or long-term ECG recording (Holter, event recorder). Many of these documented arrhythmias can be asymptomatic. We will discuss the prognostic significance of such arrhythmias, the need for further work-up, management options, and impact on sports eligibility.

## 1.1. Ventricular premature beats and nonsustained ventricular tachycardia

Most studies have shown that only a minority of athletes exhibit frequent or complex ventricular arrhythmias (VAs) with a prevalence that did not differ with that of their sedentary counterparts.13-21

*Characteristics of VPBs*

*Number and complexity*

Holter monitoring is a key test for the evaluation of the “arrhythmic burden”, i.e. the number of VPBs during 24 hours and their tendency to become more “complex” in the form of couplets, triplets or nonsustained ventricular tachycardia (nsVT). More than 500 VPBs per 24 hours is considered a minor diagnostic criterion of arrhythmogenic cardiomyopathy.22, 23 Biffi et al. demonstrated that elite athletes with frequent (>2000/24-hour) VPBs and nsVT had a higher probability of an underlying heart disease compared to athletes with rare and isolated VPBs (30% vs. 1.8%; p<0.001).20 However, a high number of VPBs in itself does not confer an increased risk of malignant events. Ectopic foci located in the right or left ventricular outflow tract (RVOT or LVOT) or in the fascicles of the left bundle branch may give rise to very frequent VPBs (>10,000/24-hour) that are usually isolated and occur in the absence of a pathological substrate.24, 25 Very frequent VPBs are associated with a benign prognosis if an underlying disease and tachycardia-mediated left ventricular (LV) dysfunction are excluded.24, 26-29 Therefore, follow-up of LV function is warranted. On the other hand, systematic investigation of SCD in athletes with retrospective evaluation of prior ECG tracings demonstrated that even rare VPBs may be a warning sign of an underlying heart disease in an otherwise asymptomatic individual, and, thus, should be dismissed as an insignificant finding.30

*Morphology*

The assessment of the morphology of the ectopic QRS complex on surface ECG helps to identify the anatomic origin of the VPBs and to recognize a distinctive category of “idiopathic” forms, which are characterized by the absence of an underlying structural heart disease and a favorable prognosis (Figure 1).31, 32 The most common form of idiopathic VPBs show an ECG pattern of “left bundle branch block (LBBB) + inferior QRS axis” (“infundibular” pattern): negative QRS-complex in lead V1, R/S transition beyond V3 and negative QRS complex in lead aVL. This morphology denotes the origin of VAs from RVOT. A similar morphology but with small R-waves in V1 and earlier precordial transition (R/S = 1 by V2 or V3) indicates the origin from the LVOT. On Holter monitoring, the arrhythmia manifests as frequent isolated VPBs and couplets, and even occasional triplets or runs of nsVT may occur. Typically, VAs are transiently suppressed by sinus tachycardia and decrease or disappear during stress testing while re-appearing during recovery.33 Another morphology of idiopathic VPBs shows an ECG pattern of “right bundle branch block (RBBB) + superior QRS axis (rarely inferior QRS axis)” morphology and narrow QRS (<130 ms). This “fascicular” pattern indicates origin from the specialized conduction system, usually the left posterior fascicle of the left bundle branch.34 Like the infundibular VPBs, fascicular forms often occur in the absence of underlying structural heart disease.33, 34 Another relatively common source of idiopathic VPBs is the mitral valve annulus: VPBs show “RBBB + inferior QRS axis” morphology with RS pattern in V1, monophasic R or Rs pattern in leads V2 to V6 and inferior axis in the limb leads.35 The majority of competitive athletes (from 68 to 73%) with VPBs in the absence of an underlying disease show VAs with infundibular pattern, followed by fascicular pattern in 15-21%, and 9% with a LVOT pattern. Other morphologies, such as LBBB/superior axis or RBBB/QRS>130 ms are rare.28, 36, 37 A study using 12-lead 24-hour Holter monitoring conducted in 288 athletes, found that only 6 athletes showed >500 VPBs/days 5 with outflow tract morphologic features and 1 with a fascicular pattern; in 4 this was associated with ≥1 complex VAs.18

Conversely, other morphologies of VPBs, such as LBBB+intermediate or superior axis or RBBB+intermediate or superior axis and wide QRS are uncommon in athletes and when present are usually less numerous, tend to be complex and/or exercise-induced and may be associated with an underlying myocardial disease. VPBs with a RBBB-like morphology and wide QRS more often predict the presence of myocardial lesions (particularly non-ischemic LV myocardial scar) compared with infundibular VPBs.18, 38-41

*Relation to exercise*

VPBs induced by exercise raise clinical warning because VAs associated with heart diseases are often worsened by adrenergic stimulation.1, 18, 39, 40, 42-45 A higher prevalence of myocardial substrates was found in a CMR study among athletes with exercise-induced VPBs compared to those with exercise-suppressed VAs (56% vs. 21%).40 Exercise-induced VAs with a RBBB morphology or complex VAs were the strongest predictors of pathological CMR (odds ratio=5.3). On the other hand, reduction or disappearance of VPBs with increasing exercise load is typical of idiopathic and benign VAs, particularly those showing an infundibular pattern.46, 47 Exercise-induced isolated or repetitive VPBs with multiple morphologies, especially with beat-to-beat alternating morphologies (so-called “bi-directional” pattern) are associated with a high risk of effort-related SCD and may be the expression of catecholaminergic polymorphic VT (CPVT), which predisposes to adrenergic-dependent VAs which can degenerate into ventricular fibrillation (see section below).44

*Response to detraining*

The available studies do not allow the establishment of the prognostic value of detraining in athletes with VPBs. The evidence is conflicting: some studies have demonstrated reduction or disappearance of VAs with detraining, without relapse on re-training,48, 49 while others have shown that the persistence or reduction of VAs did not differ in athletes who continued training vs. athletes who interrupted sport activity.50 Moreover, a regression to the mean phenomenon may explain (part of) these findings when those with the most pronounced arrhythmic expression are chosen for later evaluation. Therefore, the prognosis seems to depend on the presence of an underlying pathological substrate and detraining cannot be seen as a simple management strategy.

*Evaluation of athletes with VPBs*

According to the number, morphologic pattern, complexity, response to exercise and clinical manifestation, VPBs can be classified as common and likely benign vs. uncommon and potentially malignant because of underlying cardiac pathology (Table 1 and Figure 2).51 Any uncommon finding qualifies the VPB as ‘uncommon’, which may indicate underlying structural or electrical anomalies, and hence requires further evaluation. This approach has important implications for the cardiovascular evaluation, risk stratification, and management of the athlete with VPBs, although so far there is a paucity of prospective data on the proportion of athletes in whom potentially malignant underlying disease could be detected by using the approach described below.

*Electrocardiography*

The ECG is an essential part of the evaluation of athletes with VPBs because concomitant repolarization/depolarization abnormalities may provide important information on a possible underlying cardiomyopathy or channelopathy.52-54 Athletes with VPBs and concomitant repolarization/depolarization abnormalities require an in-depth cardiovascular evaluation. As described above, 12-lead ECG is extremely useful also for the identification of VPB morphology.

*Exercise testing*

Exercise testing allows to assess the behavior of VAs with increasing work-load and may also show other abnormal findings suggestive of an underlying cardiac disease such as ST-segment changes (ischemia), abnormal blood pressure response (HCM) or impaired exercise capacity (cardiomyopathy; possibly also based on respiratory gas analysis). Exercise testing should not be stopped at the 85% of theoretical maximal heart rate but continued until the athlete is exhausted in order to increase the test sensitivity.55

*Echocardiography*

Echocardiography represents the first imaging test for investigating the presence of a structural heart disease in athletes with VPBs. Echocardiography aims to assess the systolic and diastolic function, ventricular hypertrophy, wall motion abnormalities and valvular function. Moreover, echocardiography is recommended as the basal screening modality for identification of coronary artery origin anomalies which is a leading cause of ischemia-induced VAs and SCD in athletes.56-59 However, echocardiography has no ability to detect some life-threatening conditions such as myocardial bridging, coronary stenosis, or segmental subepicardial-mediomural myocardial fibrosis.

*Cardiac magnetic resonance*

Beyond the accurate evaluation of cardiac size, function and regional wall motion abnormalities, CMR has the unique power to identify and quantify myocardial tissue abnormalities such as edema, fatty infiltration, or replacement-type fibrosis.41 CMR identified the presence of non-ischemic LV scar in a sizeable proportion of athletes with apparently unexplained VPBs, complex VAs or repolarization abnormalities.18, 19, 38, 40, 41, 60 As a consequence, CMR has become a key test for the evaluation of athletes with VPBs even if the echocardiography is negative or inconclusive, particularly if the ectopic QRS is wide and shows a RBBB + superior axis pattern, suggesting the origin from the lateral LV wall, and VPBs are repetitive and/or exercise-induced.40

*Flow-chart for management of athletes with VPBs*

The International criteria for ECG interpretation in athletes suggest that further evaluation is warranted when ≥2 VPBs are recorded on a resting 12-lead ECG. Even a single VPB may deserve attention, especially in the presence of one or more of the following features: 1) high-level endurance athletes; 2) a positive family history of premature SCD or cardiomyopathy, 3) relevant symptoms, 4) associated ECG abnormalities, 5) uncommon VPB morphology (Table 1 and Figure 1) and 6) a short coupling interval.

Figure 2 reports a practical flow-chart for management of athletes with VPBs. While further tests in athletes with abnormal first-line examinations depend on the disease that is suspected, the work-up of athletes with negative results depends on the morphology of VPBs. Athletes with common VPB patterns can be considered eligible for competitive sports, unless the clinical suspicion of disease is high (e.g. serious arrhythmic symptoms and/or positive family history for SCD/cardiomyopathy). Athletes with an uncommon morphology of VPBs and/or complex or exercise-induced VPBs should undergo a contrast-enhanced CMR, regardless of symptoms or familial background, to rule out a concealed myocardial substrate at risk of malignant arrhythmic events during sports activity. Other examinations such as coronary computed tomography or coronary angiography may be considered in selected populations (e.g. athletes with high coronary risk score). Further diagnostic evaluation with sophisticated and costly imaging tests or molecular genetic testing is limited to the small subset of athletes with uncommon VPB characteristics. Furthermore, the arrhythmogenic effects of illicit drugs should be taken into account as a potential cause of arrhythmias in athletes.61

Benign and asymptomatic VPB do not require treatment if underlying cardiac disease is excluded. In symptomatic athletes, medical therapy with beta-blockers (if allowed) or class-1 drugs can be considered, although ablation of the ectopic focus may constitute a more definitive treatment option.

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| **Consensus statements – VPBs and nonsustained ventricular tachycardia** | **Symbol** |
| Athletes with ≥2 VPBs on a baseline ECG (or ≥1 VPB in case of high-endurance athletes, or positive family history of premature SCD or cardiomyopathy, relevant symptoms, associated ECG abnormalities, uncommon VPB morphology and/or short coupling interval) should undergo thorough evaluation to exclude underlying structural or arrhythmogenic conditions. This includes a detailed familial history taking.52 |  |
| Testing includes 12-lead ECG (morphology suggestive of common and likely benign, or uncommon and potentially malignant VPB forms), 24 hour Holter monitoring possibly with a 12-lead system and including a sports session (morphology, number and complexity of VBPs), exercise test (increase or decrease with exertion), and suitable imaging (echocardiography and CT and/or cardiac MRI). |  |
| If no indication of familial or structural underlying disease, all competitive and leisure-time sports activities are allowed. |  |
| Athletes with a high prevalence of asymptomatic VPBs (in absence of structural heart disease) should be re-evaluated annually (particularly in case of children and adolescents) in order to identify potential changes in the arrhythmic burden and in underlying cardiac condition. |  |
| In symptomatic athletes without structural heart disease, medical treatment for VPB may be an option. Transcatheter ablation may represent the most appropriate therapeutic approach in these subjects. |  |

## 1.2 Sustained ventricular tachycardia

Documentation of sustained VT requires stringent evaluation to distinguish idiopathic VT from potentially life threatening monomorphic VTs related to structural heart disease. Polymorphic VTs and VTs with alternating complexes (“bi-directional VT”) during exercise are often associated with structural disease or inherited electrophysiological disorder and carry a high risk of malignant events.62

Idiopathic, monomorphic sustained VTs are considered benign. However, symptoms (dizziness, (pre)syncope)) depend on VT cycle length (CL) and vascular tone.

Twelve-lead ECG QRS assessment of VT allows identification of the site of origin (see section 1.1). The majority of focal idiopathic VT are due to triggered activity and arise from the endocardial outflow tract region (RVOT>>LVOT) with a repetitive pattern at low levels of exercise and suppression at higher levels. Occasionally exercise-induced sustained VTs occur63. However, focal, idiopathic right and left ventricular non-outflow tract VTs have been recognized. Epicardial idiopathic VT arising from the crux of the heart are due to a focal, catecholamine sensitive mechanism and are often rapid under catecholaminergic stimulation, producing syncope64. Idiopathic verapamil-sensitive, left fascicular reentrant VT (left posterior >> left anterior>>upper septal type) are recognized by the typical ECG and often present as sustained VT65. Many of these are also catecholamine-dependent.

Identifying the specific VT mechanism (triggered activity, automaticity and reentry) has diagnostic and therapeutic implications. Although the mode of onset of VT documented on Holter recordings or during exercise testing can be helpful, differentiation often requires an invasive electrophysiology study.

*Evaluation of athletes with sustained VT*

For general assessment of athletes with ventricular arrhythmias, see section 1.1. Late contrast-enhanced CMR (CE-CMR) should be performed in particular for non-fascicular VT morphologies, even if echocardiography is negative. Distinguishing idiopathic RVOT-VT from early arrhythmogenic cardiomyopathy (AC) affecting the RVOT and exercise-induced arrhythmogenic remodeling (EI-AR) with isolated subepicardial RVOT scar can be particularly challenging66. Suspicion for the latter is high if ≥2 distinct VT morphologies with typically fast heart rates are observed in high-level endurance athletes.43, 66, 67

*Interventional treatment*

Catheter ablation of idiopathic VT is often effective68 but close follow-up is warranted, since some athletes may have underlying concealed cardiac disease which will only manifest itself over time.

Although ablation of scar-related VT can also be successfully performed with favorable long-term outcome, in particular in patients with EI-AR66, there are no data to indicate that resumption of athletic activity after successful ablation is safe, since the underlying substrate likely is still present. In addition, intensive endurance training may increase the penetrance and arrhythmic risk in arrhythmogenic cardiomyopathy and may cause or aggravate exercise-induced arrhythmogenic remodeling in the absence of mutations.66, 69 Accordingly, these athletes should not participate in most competitive and recreational sports.

Implantation of an automatic implantable defibrillator (ICD) in athletes with sustained VT and structural heart disease or channelopathies should follow current guidelines for secondary prevention of sudden cardiac death.70

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| **Consensus statement – Sustained ventricular tachycardia** | **Symbol** |
| Sustained VT disqualifies for competitive sports except for the particular case when all of the following apply: a) absence of familial sudden death, b) no indication of any underlying structural pathology or channelopathy, c) a typical presentation of focal or fascicular idiopathic VT and d) no symptoms of hemodynamic compromise during VT with/without exercise. |  |
| Catheter ablation of symptomatic focal idiopathic RVOT VT and idiopathic left fascicular re-entrant VT can be performed with high success rates (80-95%) and with low complication rates and is recommended in athletes to allow resumption of competitive sports.68 |  |
| Athletes with idiopathic, monomorphic VT, without hemodynamic compromise during exercise, can resume competitive or leisure-time athletic disciplines in which syncope does not lead to an enhanced risk for athlete or others (enhanced risk during e.g. driving, climbing, diving). |  |
| Athletes with idiopathic, monomorphic VT who have undergone successful VT ablation and are without any symptoms or other sign of recurrence (on Holter or exercise test) during a 3-month follow-up period, can resume full competitive or leisure-time athletic activity. |  |
| Symptomatic athletes with ≥2 distinct VT morphologies or VT highly suspicious for reentry as underlying mechanism with negative imaging studies, including CE-CMR, should undergo invasive EP study to assess inducibility of VT and confirm re-entry as underlying mechanism and electroanatomical unipolar and bipolar voltage mapping to identify concealed substrates. |  |
| Athletes with idiopathic, monomorphic VT who choose to undergo drug treatment for suppression and are without any symptoms during a 3-month follow-up period, including exercise testing or EP study, may resume full competitive or leisure-time athletic activity. |  |
| Ablation of idiopathic VT from non-fascicular and non-outflowtract locations, in particular epicardial sources may involve greater procedural complexity and procedural risks and lower success rates, but should be considered dependent on athletes’ preference. |  |
| Athletes with structural heart disease or channelopathies and sustained VT should not participate in intense recreational and competitive sports regardless of the acute therapeutic response to ablation/drug treatment. |  |

## 1.3 Ventricular fibrillation / resuscitated sudden death

Unless a reversible condition can be treated, athletes will qualify for implantation of an ICD. Identifiable and treatable, reversible causes encompass (1) atrial fibrillation with rapid conduction over an accessory pathway which is subsequently successfully ablated, (2) electrolyte imbalance due to a transient cause, (3) proarrythmic drug reactions (e.g. acquired QTc prolongation due to e.g. psychotropic medication), (4) transient ischemia without myocardial infarction (MI), which is followed by complete revascularization,71 (5) transient ischemia without MI due to coronary arterial vasoconstriction in response to cocaine, and (6) acute myocarditis, followed by normalization of cardiac function, serum markers of inflammation/myocardial injury and absence of frequent and complex ectopy. Whether absence of (post)myocarditis late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR) imaging should be required is a matter of discussion. After complete resolution of myocarditis sequellae is confirmed (including absence of any inducible arrhythmias during exercise or EP study in case of residual LGE), resumption of competitive sports can only be considered after a 3- to 6-month period.39, 72

It should be noted that patients may remain at higher risk for sudden death, even after resolution of the transient cause (especially when it is ischemic in origin)73. In addition, concealed forms of channelopathies need to be considered (see specific sections).

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| **Consensus statement – Ventricular fibrillation / resuscitated sudden death** | **Symbol** |
| In athletes with a resucitated sudden death reversible conditions should be defined and treated. |  |
| In athletes without definitive guarantee that a resolved transient cause of resusciated sudden death will never recur, competitive sports are contra-indicated. |  |

# 2. Arrhythmias in the context of known ischemic heart disease

Ventricular arrhythmias are a marker of worse prognosis and in IHD are evaluated by resting and Holter ECG or if necessary by wearable or implantable loop recorder. If dizziness or syncope occurs, physical activity should be restricted until medical assessment. In case of documented non-sustained VTs (≥3 VPBs), exercise should be limited to non-competitive sports.4 Presence of myocardial ischemia has to be localized and quantified by appropriate methods (e.g. ergometry, stress echocardiography, exercise stress myocardial perfusion scintigraphy and/or perfusion MRI) to guide strategies of revascularization and to step-up medication with the aim to eliminate ischemia.71

IHD patients without ischemia, non-sustained or sustained arrhythmias, who are considered low-risk for cardiac events, can perform competitive sports without restrictions but with close follow-up.4 In case of ischemia and/or arrhythmia despite optimal medication and revascularization, patients are considered high-risk. Nonetheless, exercise training at a non-competitive level is still recommended, since it has been shown to slow progression of coronary atherosclerosis,74-76 and improve morbidity and mortality.77 Recommendations for individually tailored exercise prescription as well as participation in leisure time or competitive sports in IHD have been published by the European Society of Cardiology.4, 78

Once ischemia and arrhythmias have been treated successfully, annual follow-up is sufficient and should include as a minimum patient history, physical examination, risk factor analysis, resting ECG, and diagnostic procedures to identify or rule out ischemia and/or arrhythmia, i.e. exercise-testing, stress echocardiography, stress scintigraphy and/or perfusion cardiac magnetic resonance imaging (CMR) as chosen appropriate.

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| **Consensus statement – Arrhythmias in the context of known ischemic heart disease** | **Symbol** |
| In case of ischemia with or without VT, despite optimal medication and revascularization, only non-competitive sports are allowed. |  |
| Without ischemia and without VT, i.e. low-risk patients, there are no restrictions for competitive sports. |  |
| Annual follow-up is recommended in any athlete with known ischemic heart disease. |  |

# 3. Arrhythmias in the context of inherited arrhythmogenic conditions

A number of familial arrhythmogenic conditions have been characterized over the last decades as underlying causes for arrhythmias and sudden death in athletes,79, 80 and in the near future this number will grow.

## 3.1 Contemporary approach to phenotyping, cascade screening and genotyping

It is well established that high-level physical exertion in patients with inherited arrhythmogenic diseases may aggravate the underlying condition and precipitate cardiac arrhythmias and sudden cardiac death.81-83 The diagnosis of most inherited arrhythmogenic conditions is based on clinical evaluation, personal and family history. Due to variable clinical expression such conditions may remain undetected leaving many unaware and exposed to the exertion-associated elevated risk.

Cardiovascular pre-participation evaluation (PPE) as advocated by the ESC encompasses medical history, physical examination as well as a 12-lead electrocardiogram (ECG) to detect pre-existing cardiac conditions.53 Upon positive findings, additional testing such as echocardiography, stress testing, cardiovascular magnetic resonance (CMR) imaging and 24h Holter monitoring may be indicated.

When the presence of inherited arrhythmogenic disease is suspected, the athlete and his family should be referred to a dedicated inherited cardiovascular disease clinic where structured phenotyping, risk stratification and management is provided to all consenting relatives.84-90 A detailed pedigree is assembled with all available data on the phenotype and genotype of each relative. In line with known/observed inheritance patterns, a cascade screening approach is initiated, starting with the athlete and his first-degree relatives (FDR), cascading further down to their next of kin.

Next to risk stratification, the screening of first-degree relatives may be useful to further define the familial phenotype and observe its heterogeneity. However, in the perspective of complex variable expressivity and often incomplete penetrance the timing and decision to investigate FDRs must always be weighed carefully against potential harm that may be inflicted as it may have grave impact on life-style, anxiety levels and psychological burden.91

Genotyping to identify the underlying molecular defect is useful as it may provide confirmation of the clinical diagnosis in the athlete and allows the identification of affected family members in a pre-symptomatic state.92-94 The yield of genetic testing as well as the diagnostic, therapeutic and prognostic significance in each of the inherited diseases will be discussed in the following sections.

Genetic screening in healthy individuals without (family) history and normal PPE is not recommended since variants of unknown significance (VUS) may be revealed that reflect evolutionary genetic diversity. Incorrect interpretation of VUS can lead to medical overconsumption and erroneously affect eligibility for sport participation.91 Therefore, with the exception of Sudden Unexplained Death Syndrome where genetic screening has become the cornerstone of the molecular autopsy, the decision to genotype should primarily be driven by the phenotype that was established previously in the athlete or in a first-degree relative as part of cascade screening.92, 95-100

With the advent of next generation sequencing techniques pre-selected gene panels and whole exome/genome sequencing are available with high sensitivity and specificity and with reasonable turnaround times. There is recent evidence that copy number variations (CNV’s) play a role in the pathogenesis of inherited arrhythmogenic conditions. Additional techniques to detect CNV’s should be included in routine genetic testing.101

Sequence analysis and interpretation should be performed in compliance with proposed standards for variant interpretation, adopting 5 classes of pathogenicity: 1/ benign, 2/ likely benign, 3/ uncertain significance, 4/ likely pathogenic and 5/ pathogenic.102

It should be noted that acquired factors, non-penetrance, variable and late manifestation of the phenotype as well as oligogenic rather than monogenic disease architecture may further complicate linkage analysis. Although clear guidelines exist, intense scrutiny should be upheld when classifying variants and assigning potentially life-changing clinical consequences to molecular data.103, 104 This requires experienced multidisplinary units specialised in variant interpretation and classification, based on all gathered genetic and phenotypical data. Classification is a continuous process open to revision and re-classification based on newly emerging genotype-phenotype correlation data from further cascade screening.105

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| **Consensus statement – Approach to phenotyping, cascade screening and genotyping** | **Symbol** |
| Suspected inherited arrhythmogenic disease should be assessed in a dedicated cardiogenetics clinic, including cascade screening. |  |
| Genotyping to identify the underlying molecular defect is useful to confirm clinical diagnosis in the proband and allows pre-symptomatic identification of affected family members. |  |
| Sequence analysis and interpretation should be performed in compliance with proposed standards for variant interpretation, adopting 5 classes of pathogenicity. |  |
| Cardiac screening of first-degree relatives may be useful for risk stratification and to further define the familial phenotype. |  |
| Genetic screening in healthy individuals without (family) history and normal pre-participation evaluation is not recommended |  |

## 3.2 Long QT Syndrome

Long QT syndrome can be suspected on a routine ECG if the corrected QTc interval according to Bazett’s formula is ≥470 or ≥480 ms in asymptomatic male or female athletes respectively.52, 106 The diagnosis can be corroborated based on clinical criteria (Table 2).107, 108 A QTc of ≥500 ms is diagnostic.109 Details on how to measure the corrected QTc interval in athletes and the upper normal values were published in the 2018 “International recommendations for electrocardiographic interpretation in athletes”.52 Congenital long QT syndrome should be distinguished from acquired forms, i.e. due to circumstances, which can be reversed and prevented. Once acquired LQTS is established, sports activity should be prohibited until factors, such as QT-prolonging drugs have been stopped and potential electrolyte disturbance have been corrected.

Whenever LQTS is suspected, the following should be done: a careful clinical history of proband and family, a baseline ECG, an exercise stress test (focusing on T wave changes during recovery and the QTc interval after 4 min of recovery which, if ≥30 ms longer than at baseline, suggests LQTS),110 and a 24-hour Holter recording (preferably a 12-lead type since diagnostic patterns are often seen only in precordial leads).

Genetics have become essential for management. Therefore, genetic testing should be performed when available in all athletes with suspicion of LQTS. A large proportion of LQTS gene carriers, especially with LQT1, may have a borderline QT prolongation.111 The risk of cardiac events during sport activities is largely gene-specific. LQT1 patients, with a reduction in the IKs current which impairs the normal QT shortening during heart rate increases, are at highest risk during stressful exercise.112 Moreover, a *de novo* disease-causing mutation carries a more uncertain arrhythmic risk (no family history).

Sudden death is often the sentinel event and >60% of cardiac arrests occur in previously asymptomatic subjects. This has two implications: 1) being asymptomatic until age 18-20 years is no guarantee of low risk; 2) once LQTS has been diagnosed, therapy should start without hesitation.107 General precautions include avoidance of QT-prolonging drugs, dehydration and electrolyte imbalance. Beta-blocker therapy is extremely effective, although the basal heart rate in athletes may limit the dose. There is a preference for nadolol or propranolol which are more effective than other beta-blockers.107

LQTS patients who already had a cardiac arrest should receive an ICD.62 For patients with a LQTS-related syncopal episode while on beta-blocker therapy, either an ICD or left cardiac sympathetic denervation should be considered.113 If ICD is contraindicated or refused, left cardiac sympathetic denervation should be considered.62

Athletes with LQTS and prior cardiac arrest or arrhythmic syncope should not be allowed to practice competitive sports. ICD implantation does not constitute a clearance for intensive or competitive sports. Continued sports participation with an ICD is possible, but specific recommendations apply (see below section 5.5.6).

Electrocardiographically manifest LQTS patients, even when asymptomatic and on treatment with beta-blockers and other precautionary measures should not be considered eligible to practice in more than light- to moderate intensity recreational sport disciplines. American guidelines are more lenient in this respect (except for LQT1), provided that precautions include the presence of an automatic external defibrillator (AED) ‘as part of the athlete’s personal sports safety gear’.114 We consider such obligation impractical to impossible (e.g. winter sports; water sports), and it puts responsibilities on clubs or other bystanders which cannot be justified by a medical recommendation for an individual athlete. Moreover, although LQTS-related cardiac arrest is uncommon during competitive sports,115 AED efficacy is not 100% in such cases.116 On the other hand, the presence of AED may be considered by the athlete when choosing a sport facility/gym/arena to participate in leisure time sports.

In asymptomatic LQTS mutation carriers without a prolonged QT interval, i.e. <470/480 ms in men/women (“genotype positive / phenotype negative”) shared decision-making is required, balancing the risk for arrhythmias (mainly based on the known genotype) vs. psychological well-being. A negative exercise stress test has no predictive value because arrhythmias are usually triggered by the combination of physical exercise and emotional stress. Team sports are more dangerous for LQTS patients than solo sports, in which the athlete can decide if and when to slow down. Moreover, there can be more psychological stress in a team environment, acting as an arrhythmia-triggering factor. Low-intensity competitive sports are preferred over high-intensity sports, certainly for LQT1 patients. The risk of cardiac events during physical activity is relatively modest for LQT2 and LQT3 patients, allowing more flexibility in allowing them to practice sports. In other, more rare, forms of LQTS, close discussion with cardiogenetics experts is required to evaluate the relationship of the subform with arrhythmias from available literature data. LQT1 patients should swim in a supervised pool and avoid diving before being acquainted to the temperature of the water. Sudden unexpected auditory stimuli may trigger polymorphic VT in patients with the LQT2 subtype.112

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| **Consensus statement – Congenital long QT Syndrome** | **Symbol** |
| All LQTS athletes should avoid QT prolonging drugs (www.crediblemeds.org) and electrolyte imbalance like hypokalemia and hypomagnesemia (potassium supplementation is recommended before taking part to sports activity). |  |
| All LQTS athletes with prior symptoms or prolonged QTc should be on therapy with beta-blockers at target dose. |  |
| Athletes with LQTS and prior cardiac arrest or arrhythmic syncope should not be allowed to practice competitive sports (with or without ICD). |  |
| Athletes with a QTc >500 ms, a de novo disease-causing mutation (especially if LQT1), or genetically confirmed LQTS with a QTc ≥470 ms in men or ≥480 ms in women should not practice more than light- to moderate intensity recreational sports, even when on beta-blockers. |  |
| Recommendations to sports participation require open discussion with the athlete and their entourage, finding a balance between life protection and quality of life during shared decision making. |  |
| It is reasonable to allow individual sports at low to moderate intensity for asymptomatic athletes with a LQT1 mutation but QTc <470/480 ms and who are on prophylactic beta-blocker therapy, but team sports and high-intensity sports are discouraged. |  |
| It is reasonable to allow all types of sports participation for asymptomatic athletes with a LQT2 or LQT3 mutation but QTc <470/480 ms, and who are on prophylactic beta-blocker therapy. |  |
| For asymptomatic athletes with other LQTS mutations and QTc <470/480 ms, cardiogenetics consult and shared-decision making are required. |  |

## 3.3 Short-QT syndrome

The Short QT syndrome (SQTS) is a very rare disease described just 20 years ago.117 So far, only slightly more than 100 patients have been described worldwide. The clinical presentation tends to be quite severe, with a high incidence of cardiac arrest and sudden death.118 The diagnostic criteria are not yet firm and require either a QTc ≤340 ms or a QTc between 341 and 360 but with an associated history of life-threatening arrhythmias or a family history for SQTS or for sudden death before age 40, as well as atrial fibrillation.119-121 Moreover, the diagnosis based on the QTc interval is dependent on the QTc correction formula, the prediction accuracy of which requires further assessment.122 There is an overwhelming predominance of male patients. While no specific triggers for arrhythmic episodes have been identified in the European Short QT Registry,119 one report indicated that most episodes of cardiac arrest occurred at rest/sleep and just 15% during emotions or exercise.121 Current therapy is based on either quinidine or ICD, both burdened by significant limitations118 The protective effect of quinidine during exercise is unknown. Thus, it should be clear that there is no ground for solid recommendations regarding sports activity. Given the clinical severity and the (rare) occurrence of events during exercise, it may be desirable that patients with SQTS should not practice sports activity with the possible exception of some leisure activity.

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| **Consensus statements – Congenital short QT Syndrome** | **Symbol** |
| It is recommended to restrict all athletes with SQTS, diagnosed or suspected, from all competitive sports. |  |
| It is reasonable to allow light to moderate leisure sport activity to asymptomatic SQTS patients without family history of sudden cardiac death. |  |

## 3.4 Brugada Syndrome

The Brugada syndrome (BrS) is an inherited condition associated with an elevated risk of ventricular fibrillation (VF) and sudden cardiac death (SCD) in young individuals with a structurally normal heart.123, 124 This disease presents with an autosomal dominant pattern of inheritance with incomplete penetrance and variable expressivity.124 More than 500 pathogenic genetic variants have been described, mostly located in the SCN5A gene.125 Unfortunately, a pathogenic variant is only found in 25-30% of individuals.126-128 Although BrS was initially described as a purely electrical disease, minor structural abnormalities may sometimes be observed.129-132

The true prevalence of BrS is unknown due to the dynamic nature of the ECG pattern, which is frequently inapparent.133 It shows a male predominance.134-136 BrS typically manifests in adulthood, but it can also occur in children and the elderly.137-140 Most patients are asymptomatic at the time of evaluation and remain so throughout their lives. In symptomatic patients, the majority of events occur during sleep or rest, during febrile states or, occasionally, from heat stroke.141-148 The conduction defects explain why some may develop ventricular arrhythmias during exercise.149 Also, exercise may unmask the typical type 1 Brugada pattern in patients with non-diagnostic ECGs150-154 and, during/immediately after exercise, ST-segment augmentation may be observed (Figure 3).150-161

Diagnosis is made when a type 1 Brugada pattern is observed (coved-type ST-segment elevation ≥2 mm followed by a negative T-wave in ≥1 of the right precordial leads positioned in the 4th, 3rd or 2nd intercostal space), either spontaneously or during a sodium-channel blocker test, once all other known causes of ST-segment elevation have been ruled out, including acute myocardial ischemia or infarction, acute myocarditis, Prinzmetal angina, dissecting aortic aneurysm, acute pulmonary thromboemboli, Duchenne muscular dystrophy, Friedreich ataxia, mediastinal tumor compressing the right ventricular outflow tract, arrhythmogenic right ventricular cardiomyopathy, etc. (Figure 4).162-164 In some cases, it may be difficult to distinguish the BrS ECG from the non-pathological electrical remodelling in athletes, which can include the presence of incomplete right bundle branch block, ST segment elevation/early repolarisation, and T-wave inversion in right precordial leads, mimicking the Brugada pattern.165, 166 For the differential diagnosis, it is useful to analyse the ST-T waveform. Athletes show an upsloping ST-segment with a mean STJ/ST80 ratio ≤1, whereas BrS patients show a downsloping ST-segment with a STJ/ST80 ratio >1167. When in doubt, it is sometimes useful to perform a drug challenge with a sodium channel blocker. Other unspecific ECG findings in BrS which are also common after long-term sport training include sinus node dysfunction168-170, P-wave, PR and QRS prolongation149, 171, 172 and supraventricular arrhythmias (mainly atrial fibrillation).149, 173-176

Symptomatic patients (SD and/or syncope, particularly in the presence of spontaneous type 1 Brugada pattern) should undergo ICD implantation.62, 177 Quinidine or catheter ablation is recommended in patients with recurrent ventricular arrhythmias or when ICD implantation is not an option.62, 177 In asymptomatic patients with only inducible type 1 Brugada ECG pattern, only preventive measures are recommended, like avoidance of triggering drugs (www.brugadadrugs.org), electrolyte unbalance, and increases in core temperature >39°C (e.g by minimizing immersion in hot tubs, saunas and steam rooms; by avoiding sporting in warm/humid conditions; or by abstaining from prolonged endurance events such as triathlon and marathons). During febrile illness, fever should be treated aggressively.62, 177 Risk stratification in the asymptomatic population with spontaneous type 1 ECG pattern is more challenging. In this group of patients, electrophysiological study with programmed ventricular stimulation may be considered for risk stratification.62, 177

Theoretically, an enhanced vagal tone at rest178 might increase the susceptibility of high-level athletes to die at rest but there is no data to support such association. In general, there is a scarcity of large prospective studies evaluating the effect of exercise and sport in BrS and no reports are available directly associating physical activity to cardiac events. Therefore, asymptomatic BS patients, phenotypically-negative BrS mutation carriers or those with only an inducible ECG pattern can compete in all sports that are not associated with an increase in core temperature >39°C (which should be checked during training sessions).

For symptomatic BrS patients (syncope and/or aborted SCD), ICD implantation is recommended. After ICD implantation, if asymptomatic for ≥3 months and when paying attention to precautionary measures (i.e. avoidance of drugs, fever or heat stroke), all sports (also competitive) can be considered after shared-decision making, considering the findings from the Sports ICD Safety Registry (see below).

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| **Consensus statement – Brugada Syndrome** | **Symbol** |
| In BrS patients with episodes of suspected arrhythmic syncope and/or aborted SCD, ICD implantation is recommended. |  |
| In all patients with overt BrS and in all phenotypically-negative mutation carriers, avoidance of drugs that may aggravate the BrS (www.brugadadrugs.org), of electrolyte imbalance, and of increases in core temperature are recommended. In case of febrile illness, fever should be treated aggressively. |  |
| If there is no recurrent event during 3 months in symptomatic BrS patients after ICD implantation, leisure or competitive sports may be resumed based on shared-decision making.\* |  |
| Asymptomatic BrS patients, asymptomatic mutation carriers, and asymptomatic athletes with only an inducible ECG pattern, may participate in all sports that are not associated with an increase in core temperature >39°C (e.g. endurance events under extremely hot and/or humid conditions). |  |
| *\*Avoid contact sports in case of ICD implanted.* | |

## 3.5 Catecholaminergic polymorphic ventricular tachycardia (CPVT)

Catecholaminergic ventricular tachycardia (CPVT) is a highly lethal primary cardiac electrical disease (typically before age 20-30y), characterised by complex ventricular arrhythmias (classically, bidirectional VT) triggered by adrenergic stimuli (typically, emotional stress or exercise), leading to syncope or SCD (Figure 5).179, 180 This clinical entity may comprise 5 to 10% of patients with familial arrhythmias but without QTc prolongation or Brugada-type ECG abnormalities.181Currently, the genetic cause is identified in 65% of patients with a clinical diagnosis.182 Most cases are secondary to autosomal dominant mutations in the RyR2 gene (the calcium release channel of the sarcoplasmic reticulum) or, less frequently, to autosomal recessive mutation in CASQ2 (another protein involved in intracellular calcium handling).182-187 Mutations in either gene lead to abnormal calcium release from the sarcoplasmic reticulum that is more pronounced in high beta-adrenergic states.185, 188 Other genes, including TRDN, ANK2 (also referred to as LQT4-syndrome), TRD and KCNJ2 are involved in a minority of cases.

The prevalence of CPVT is roughly estimated to be 1/10000,189 but there is no systematic population study to confirm it. When untreated, up to 60% of patients will have experienced syncope and 30% SCD by the age of 40.190, 191

CPVT patients have a normal resting ECG and no structural anomalies; therefore, the disease can only be detected if the athlete undergoes exercise testing. Diagnosis is made when catecholamine-induced bidirectional or polymorphic VT is observed in individuals <40 years of age.164 Family members with a pathogenic mutation or showing complex premature ventricular contractions or bidirectional/polymorphic VT induced by exercise are also considered to have CPVT.164 The presence of a positive family history of SCD <40 years and the presence of exercise-induced ventricular ectopy should raise suspicion.164

Long-term management strategies in CPVT have the objective of reducing adrenergic stimulation. Lifestyle modifications include avoiding emotional stress and restricting sports activity not exceeding current recommendations for the general population (i.e. moderate intensity physical activity of 30-60min/d on 3-7 days per week).62, 177, 192 Ventricular arrhythmias may also occur at intermediate heart rates (100-130 bpm) during moderate intensity activity, such as playing at school or in recreational sports. However, preliminary retrospective analyses suggest that, with appropriate treatment, sport practice may be possible when avoiding sudden bursts of exercise.193 Therefore, intensive or strenuous but not moderate physical exercise is discouraged unless exercise testing or Holter recording has demonstrated persistent arrhythmias despite treatment during moderate activity.62 Based on prior exercise testing, individualised maximal heart rate limits may be specified.

Initial medical therapy includes beta-blocker treatment without intrinsic sympathomimetic activity.62, 177, 192 Flecainide, which is a direct RYR2-channel blocker, can be used in association with beta-blockers in case of recurrence despite standard therapy.62, 177, 189, 192, 194-198 Left cardiac sympathetic denervation is an alternative in patients who are not appropriately controlled with medical therapy.62, 189, 197 Finally, ICD implantation is recommended for patients who remain symptomatic despite treatment (pharmacological with/without sympathetic cardiac denervation) or who have experienced an aborted SCD.62, 189 In CPVT patients with an ICD, the high risk of an arrhythmic storm is particularly high199

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| **Consensus statement – Catecholaminergic polymorphic ventricular tachycardia** | **Symbol** |
| In CPVT patients, competitive and intensive leisure-time sports are NOT recommended. |  |
| Under appropriate treatment, if stress-test shows absence of any type of ventricular ectopy/arrhythmia and if the patient is asymptomatic for a minimum of 3 months, low-intensity to moderate leisure-time sports may be considered, including those with an ICD\* |  |
| Gene carriers of a pathogenic CPVT mutation without an overt phenotype should be managed as patients with manifest CPVT (i.e. only allowing low-intensity sports). A beta-blocker should be considered. |  |
| Follow-up should include stress tests and/or continuous ECG monitoring (Holter) during leisure-time low-intensity sports activities to ensure control of exercise-induced ventricular arrhythmias |  |
| Avoidance of stressful/emotional situations, dehydration, electrolyte disturbances, or hyperthermia is recommended |  |
| *\*Avoid contact sports in case of ICD implanted.* | |

## 3.6 Arrhythmogenic Cardiomyopathy

Arrhythmogenic cardiomyopathy (AC) is a heritable cardiac disorder histologically characterized by fibrofatty replacement of the right and/or left ventricular myocardium.200 Clinically, it is characterized by life-threatening ventricular arrhythmias and high risk of sudden cardiac death (SCD) which are often triggered by exercise or adrenergic stress.201, 202 Although its prevalence is relatively low (1 out of 2,500-5,000),200, 203 it is an important cause of SCD in young individuals and athletes.201, 203

Its diagnosis is based on the 2010 Task Force Criteria,23 which combine electrophysiological and anatomical features with genetic testing and clinical features of the disease. The genetic testing reveals mutations in approximately 50% of patients, and the most common mutated genes encode cardiac desmosome proteins.204 In some families, mutations in the ryanodine-receptor gene have been detected, indicating that there may be overlap forms between AC and catecholaminergic VT.205 ECG is a central element of the diagnosis: it is abnormal in most athletes, and electrical abnormalities usually precede structural changes. 200 Common ECG changes include repolarization abnormalities (inverted T-waves), conduction and depolarization disturbances.206 In advanced stages of the disease, 2D-echocardiography and cardiac magnetic resonance (CMR) may exhibit a dilated right ventricular (RV) cavity and RV motion abnormalities. However, in early stages and also in the left-dominant variant, morphological AC-related changes may be mild and undetectable by standard 2D-echocardiography. CMR and echocardiographic deformation imaging provide a precise evaluation of motion abnormalities,207, 208 and CMR gives information on tissue characterization facilitating AC diagnosis in these early stages.209

AC is characterized by reduced penetrance and variable expressivity making risk stratification even more essential.200 Established risk factors for life-threating ventricular arrhythmias include: prior aborted SCD, unexplained syncope, sustained ventricular tachycardia and right and/or left ventricular dysfunction.210 Exercise has also emerged as a consistent risk factor for accelerating the disease phenotype and promoting fatal arrhythmias.69, 211 In murine models of desmosomal cardiac mutations, high-intense exercise accelerated disease development,212, 213 arrhythmic presentation214 and AC morphological changes. Similar results have been confirmed in genotype-positive phenotype-negative AC patients in which high-intense exercise was related with an increased penetrance,69, 215 an increased risk for ventricular tachyarrythmias,69 an accelerated myocardial dysfunction and heart failure development.69, 215 Additionally, exercise load reduction resulted in lower ventricular arrhythmias burden,69 and restricting exercise to the AHA minimum upper bound (i.e. </=650 MET-hours/year) substantially reduced the expression of disease phenotype.211 Among athletes with definite AC diagnosis, participating in competitive sports was associated with premature disease presentation,209 and an increased risk of ventricular tachyarrhythmias and SCD.216 Furthermore, exercise load (intensity + duration) demonstrated to be the best predictor of ventricular dysfunction while exercise intensity alone was an independent predictor of ventricular arrhythmias.217 Similar to AC mutations carriers, the reduction of exercise load in AC patients decreased the risk of ventricular arrhythmias and SCD.218 On the other hand, there is also emerging evidence of an athlete’s cohort that fulfilled AC criteria but in which no known AC mutations could been found (‘gene-elusive AC’ or ‘exercise-induced AC’ patients), suggesting that intense exercise alone can result in disease development.43, 219, 220

All these data support a restrictive approach regarding sports competition and high intensity exercise training in athletes with positive genotype and/or positive phenotype for AC, but they support low intensity exercise training for a healthy lifestyle. AC athletes should be informed about the current evidence of the whole spectrum AC exercise-related risks in the context of their particular case. Given that AC usually affects young adults and that it demonstrates high risk of SCD, a main clinical decision in AC patients is the placement of an implantable cardioverter defibrillator (ICD).221 This decision should be made based on current risk stratification criteria and not for the sole intention of maintaining athletic activity.222

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| **Consensus statement – Arrhythmogenic cardiomyopathy** | **Symbol** |
| Individuals diagnosed with definite or borderline AC\* should not participate in competitive sports and should avoid leisure-time activities of moderate to high intensity. |  |
| Individuals diagnosed with possible AC\* based on one major criterium should not participate in competitive sports and should avoid leisure-time activities of moderate to high intensity. |  |
| In individuals diagnosed with possible AC\* based on two minor criteria, sports eligibility should be considered on an individual basis after a comprehensive evaluation of the potential diagnosis. Specifically, for the following combination of minor criteria, intensive and competitive exercise restriction is reasonable:  - Familiy history and any additional minor criterium from a different category  - Tissue characterization and any additional minor criteria from a different category |  |
| The recommendations to avoid leisure-time activities of moderate to high intensity apply also for genotype-positive phenotype-negative individuals and gene-elusive AC patients. |  |
| The need for ICD should be evaluated based on risk stratification criteria and not for the sole purpose of continuing athletic activity. |  |

\* Diagnostic terminology for current Task Force criteria:23   
- definite diagnosis: 2 major, or 1 major and 2 minor criteria, or 4 minor criteria from different categories   
- borderline: 1 major and 1 minor, or 3 minor criteria from different categories;   
- possible: 1 major, or 2 minor criteria from different categories

## 3.7 Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) is a primary myocardial disease characterized by a dilated and hypokinetic left ventricle with or without associated right ventricular dysfunction. Supraventricular and ventricular arrhythmias are present in almost 40% of cases.223 Although infrequent, DCM is a recognized cause of SCD in athletes. In addition, the physiological response to endurance exercise may result in an enlarged LV cavity with mildly reduced systolic function, causing diagnostic confusion with a mild form of DCM.224

Evaluation of athletes with a suspected or confirmed diagnosis of DCM should include a baseline 12-lead ECG, a transthoracic echocardiogram, a cardiopulmonary exercise test, and an ECG monitor which should include monitoring during training or competition. Additional investigations may be required for diagnosis and risk stratification including cardiovascular magnetic resonance imaging, exercise imaging studies, genetic testing, familial evaluation and repeat assessment after a period of detraining.

For detailed exercise recommendations for athletes with DCM we refer to the recently published document by the Sport Cardiology Section of the European Association of Preventive Cardiology (EAPC).2 The document allows for a more individualized approach where well-informed athletes, with a low risk profile (asymptomatic status, EF ≥40%, absence of frequent, complex or exercise-induced arrhythmias) may participate in all competitive sports, depending on existing medicolegal practices. Annual follow-up is recommended but may be more frequent (6-monthly) in adolescent and young adult athletes who are more vulnerable to exercise related SCD.

Athletes with a pathogenic variant capable of causing DCM but who do not have phenotypic evidence of DCM after comprehensive evaluation, should be allowed to compete in all sports but remain under periodic surveillance to monitor the potential progression to a DCM phenotype.

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| **Consensus statement – Dilated cardiomyopathy** | **Symbol** |
| The presence of LV cavity dilatation with preserved LV function, in the absence of a family history of DCM, abnormal ECG patterns, and atrial/ventricular tachyarrhythmias should be considered to represent expression of physiological  cardiac remodeling rather than DCM. Therefore, no restriction to competitive sports is applicable to this cohort of athletes. |  |
| It seems reasonable that athletes with an unequivocal diagnosis of DCM, but mildly reduced LV systolic function (EF ≥40%) may selectively be allowed to participate in all competitive sports (with the exception of those in whom occurrence of syncope may be associated with serious harm or death), provided that they are:  (1) Asymptomatic,  (2) Without prior history of unexplained syncope, and  (3) Without frequent/complex ventricular tachyarrhythmias on ambulatory ECG monitoring and exercise testing. |  |
| Athletes with a diagnosis of DCM who are:  (1) symptomatic, or have  (2) LV ejection fraction <40%, or  (3) extensive LGE (i.e. >20%) on CMR and/or  (4) frequent/complex ventricular tachyarrhythmias on ambulatory ECG monitoring and exercise testing, or  (5) history of unexplained syncope.  should be advised not to engage in competitive sports. These patients should be advised to limit their exercise programs to leisure-time activities and undergo regular clinical surveillance, consistent with current recommendations  for the management of DCM. |  |
| Adapted from Pelliccia et al, Eur Heart J 20192 | |

## 3.8 Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is an inherited myocardial disease characterized by a hypertrophied left ventricle in the absence of cardiac or systemic disease capable of inducing the same magnitude of left ventricular (LV) hypertrophy.225 Its prevalence in the general population is estimated at 1 in 500 individuals and it has consistently been implicated in exercise-related sudden cardiac death.201, 226 The majority of athletes with HCM are asymptomatic and are identified following the investigation of an abnormal ECG. Occasionally, athletes are evaluated as a result of familial disease or symptoms.

Evaluation of athletes is similar as described above for DCM.

Detailed exercise recommendations on athletes with HCM have been published by the Sport Cardiology Section of the European Association of Preventive Cardiology (EAPC).2 The document allows for a more individualized approach where well-informed athletes, with low risk profile (asymptomatic status, absence of frequent, complex or exercise-induced arrhythmias, no significant left ventricular outflow gradient at rest or on exercise, low 5-year ESC risk score), may be able to participate in all competitive sports, depending on existing medicolegal practices. Annual follow-up is recommended but may be more frequent (6-monthly) in adolescent and young adult athletes who are more vulnerable to exercise related SCD.

Available evidence from relatively small studies suggests that gene carriers for HCM do not incur excess risk.227, 228 Athletes without phenotypic evidence of the disease after comprehensive evaluation, should be allowed to compete in all sports but remain under periodic surveillance to monitor the potential development of an overt HCM phenotype.

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| **Consensus statement – Hypertrophic cardiomyopathy** | **Symbol** |
| Participation in intensive exercise programs and competitive sport should be considered on an individual basis, after full evaluation of the disease characteristics and risk determinants, and with agreement between the athlete and the physician.  It seems reasonable that adult athletes may selectively be allowed to participate in all competitive sports (with exception of those where occurrence of syncope may be associated with harm or death) if:  (1) Mild clinical expressions of HCM  (2) Low ESC risk score225  (3) Adult age  Such athletes should be reviewed annually to assess symptoms and changes in risk proﬁle. |  |
| Conditions that reasonably represent absolute contraindications for sport participation include:  (1) History of aborted SCD/CA;  (2) Symptoms, particularly unheralded syncope;  (3) Exercise-induced ventricular tachycardia;  (4) High ESC 5-year risk score;225  (5) Signiﬁcant increase in LV outﬂow gradient (>50 mmHg)  (6) Abnormal blood pressure response to exercise (<25 mmHg systolic pressure increase during exercise)229. |  |
| Adapted from Pelliccia et al, Eur Heart J 20192 | |

## 3.9 Familial disease of unknown origin

A familial pattern of clinical events may be present without structural heart disease or electrocardiographic patterns that fall under a defined condition. Clinical events may include documented arrhythmias, unexplained presyncope or syncope and sudden death. In some cases, monitoring family members over time may uncover a clear phenotype. In others, pooling of clinical and genetic data, may result in the discovery of novel conditions. Three recent representative examples include: 1. The “early repolarisation syndrome”, where the presence of J-point elevation ≥1mm in ≥2 contiguous inferior and/or lateral leads of a 12-lead ECG has been associated with increased risk of malignant arrhythmias.230 Early repolarisation, however, is frequently present on the ECG of athletes and outside the context of symptoms or concerning family history is considered a normal variant.231 2. “multifocal ectopic Purkinje-related premature contractions (MEPPC)” is characterized by atrial and ventricular arrhythmias and conduction defects which may progress to dilated cardiomyopathy.232 The condition has been attributed to pathogenic variants in the SCN5A gene and may specifically benefit from Class-1 antiarrhythmic drugs or amiodarone; 3. “familial cardiac arrhythmia syndrome with widespread ST-segment depression” is an autosomal dominant cardiac syndrome characterized by marked, persistent, non-ischemic ST-segment depression, the development of atrial fibrillation and ventricular arrhythmias and some degree of left ventricular dysfunction.233 The genetics of this condition remain elusive. It is likely that the future will reveal more familial arrhythmogenic disorders, of which some can create particular vulnerability during exercise.

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| **Consensus statement – Familial disease of unknown origin** | **Symbol** |
| Athletes with antecedents of undefined familial history of arrhythmias and/or sudden cardiac death, require referral to an expert cardiogenetics center, since rare forms of inherited familial syndromes are being described. |  |
| In the absence of definitive risk stratification algorithms, exercise recommendations in these athletes should be governed by symptoms, family history, frequency and complexity of arrhythmias and the presence of a concomitant cardiomyopathy. |  |

# 4. Device therapy

## 4.1 Pacemakers and resynchronisation therapy

Although there are no available data, pacemaker (PM) carriers are rare among those who practice sports. Recommendations are important for 1) those practicing regular sports activity but who are in need of a PM and want to know if they can continue after implantation, and 2) for PM patients with an underlying heart disease (ischemic cardiomyopathy, heart failure) in whom rehabilitation and regular sport practice are considered important to improve outcome.234 Usually, PM patients have less severe disease and co-morbidities than implantable defibrillator (ICD) carriers. Moreover, there is less risk of malfunction for a PM than for an ICD.235 For all these reasons, it seems that one could be more permissive for sports practice in patients with a PM.

In the absence of structural heart disease, competitive or recreational sports participation is allowed. In patients with a PM and underlying heart disease, recommendations to these underlying diseases apply. E.g. in patients implanted with a cardiac resynchronization device for heart failure treatment (CRT), mild to moderate sport practice is beneficial and possible.236.

For all implanted patients (PM, CRT and ICD), sport activities with a risk of chest trauma or violent contacts (e.g. rugby, boxing, martial arts) should be avoided.237-240 Other sports (like soccer, basketball, baseball) can be allowed while wearing appropriate padding. In addition, sports with pronounced arm movements (like volleyball, basketball, tennis, climbing) may also increase the risk for late lead damage due to subclavian crush (with insulation or conductor failure).238, 241, 242 Because there is no concern on lead fracture, leadless pacemakers could be potentially more adapted for some sports or athletes.

Precautionary implantation measures, like the use of bipolar leads,243 implantation on the contralateral side of the dominant arm (e.g. at the left side in a right handed tennis player), extrathoracic access of the subclavian vein,244 fixation within the pocket or submuscular placement, and avoidance of full arm movements until complete healing and fixation of the leads (at least 4 weeks) should be particularly considered in these patients.

After implantation, individual programming of the upper sensor and the tracking rate guided by exercise testing and/or Holter ECG (and excluding inappropriate rate acceleration in other circumstances, e.g. horse-back riding)245 is required. Follow-up should be regularly scheduled (usually every 6 months, or telemonitoring with regular transmissions).

Electromagnetic interference is unlikely with modern devices and no cases have been reported, but should always be suspected and closely evaluated in specific athletic environments with electronic equipment. Also myopotential sensing may result in inhitibion of pacing, a problem that is more common with unipolar electrodes, although it usually can be corrected with appropriate reprogramming of the device.243, 246 Bipolar leads are less sensitive to this problem.

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| **Consensus statement – Pacemakers and resynchronisation therapy** | **Symbol** |
| Athletes with pacemakers with/without resynchronisation and underlying disease need to follow the recommendations pertaining to the underlying disease. |  |
| Without evidence for structural heart disease or inherited arrhythmogenic condition, all sports are allowed. |  |
| Direct impact to the device should be prevented by adapting the site of lead and/or device implantation, by padding or restricting direct impact sports. |  |
| Holter recordings and device interrogation allow appropriate tailoring of rate-responsive pacing parameters, exclusion of myopotential or electromagnetic inhibition, and detection of ventricular arrhythmias. |  |
| A 6 monthly follow-up or remote monitoring should be instituted in pacemaker carriers with moderate to intense sports participation. |  |

## 4.2 Implantable cardioverter defibrillators

Although receiving an ICD per se does not necessarily impair overall quality of life,247 ICD recipients do perceive restrictions for physical activity after ICD implantation as limiting, and express fear for receiving shocks.248 Staying active is important for its proven benefits, both mentally and physically,249 also in ICD patients.250 In this context, physical exercise should be encouraged.

Previous recommendations concerning sports participation in ICD recipients were restrictive,6, 8 primarily based on theoretical considerations, due to the lack of scientific data.251

Recently, follow-up data on 440 athletes in the Sports ICD Safety Registry (393 participating in organized competitive sports, 47 in high-risk sports) have been reported.252, 253 Also the outcomes of 80 additional recreational athletes are available.254 These data are important as they can serve to counsel competitive and leisure time athletes, leading to a process of shared decision making. Over a median follow-up of 44 months no resuscitated sudden cardiac death, no significant injury related to arrhythmia or shock and no generator malfunctions occurred. Lead survival was 94% at 5 years and 85% at 10 years.252, 253 Shocks were common: 10% of patients received an appropriate shock during competition or practice. Shocks did occur more frequently during exercise than at rest (20% vs. 10%), but, contrary to common belief, no difference was found between competition/practice and other activities. Recreational athletes, however, experienced fewer appropriate and inappropriate shocks during physical activity than participants in competitive sports.254 This highlights the issues with the definition of “sports intensity”. Moreover, of those athletes who received shocks, about 30% stopped sports at least temporarily,252, 254 indicating a psychological impact that may be relevant in the long-term if patients would start to fear therapy from their life-saving device.

In the discussion about whether or not to perform sports with an ICD, we propose attention for “four Ds” to structure management: danger, disease, device and dysrhythmias.

### Danger:

This includes considerations about the safety of the athlete and his/her environment. Conceivably every human has the right to decide on his own life and the risks taken in this context but the safety of others should be respected. This implies that situations where loss of focus or loss of consciousness could cause harm to a third party (like in motor sports, diving, mountain climbing) should be avoided.

### Disease:

The underlying heart disease plays an important role in the decision about sports participation, where exercise might aggravate the disease or cause or provoke arrhythmias. As such, the disease specific considerations as described above should be taken into account.

### Device

Exercise can affect the device in various ways. The same risks for the lead and device and the same implantation related considerations as for pacemakers exist for ICDs (see above). Additionally, the type of device (single chamber, dual chamber, subcutaneous (S-ICD)) must be considered although no firm data in this regard are available in athletes. After implantation, return to sports can be allowed after a 6 week period of (relative) rest, preferably after performing an exercise test. If sport with a high risk of collision is performed, shielding and padding need to be discussed, although its effectiveness has never been proven.

Next, device programming needs attention: the athlete must be aware of the programmed detection rate cut-offs to be able to avoid reaching those during exercise. Conversely, detection zones, tracking- and sensor driven rates, need to be programmed sufficiently high to allow for high (enough) heart rates during exercise. A detection rate cut-off of ≥200 bpm proved safe and reduced the occurrence of shocks in the ICD Sports Safety Registry.255 Prior exercise- and long-term ECG recordings will be important for assessment of sinus tachycardia: when inappropriate device triggering due to sinus tachycardia is anticipated, clear instructions to the patient concerning activity limitation and/or institution of bradycardic therapy (with beta-blockers if possible) are mandatory.

### Dysrhythmias

Both atrial and ventricular arrhythmias need consideration: occurrence of a ventricular tachyarrhythmia can cause both shocks and hemodynamic compromise. This requires an aggressive management with a low threshold for VT ablation. After an ICD intervention or VT ablation, 6 weeks of sports restriction must be respected.

The most common cause of inappropriate shocks in transvenous ICD is the occurrence of sinus tachycardia and supraventricular arrhythmias.256, 257 In several heart diseases (e.g. AC, BS, SQTS)258 atrial arrhythmias are more prevalent than in control populations. Also the practice of endurance sports itself carries a higher risk for developing AF.259, 260 As antiarrhythmic drugs potentially interfere with chronotropy and inotropy, ablative therapy should be considered early. Implantation of a dual chamber ICD for the sole reason of atrial arrhythmia detection and discrimination is generally not warranted since usually not effective.255, 261-264 Given the fact that many of these athletes are young, there is a higher risk for long-term lead complications when more leads are implanted. Therefore, restraint is needed concerning the implantation of more complex ICD systems, and their indication should be weighed in every patient.

Remote monitoring has shown to reduce mortality in the ICD population.265, 266 It also has the potential for early detection of both arrhythmias and device failure. Hence, routine inclusion of athletes in remote monitoring programs is highly recommended.

In conclusion, athletes with ICDs need to be carefully evaluated and counseled concerning the potential impact of their activity on the ICD and vice versa. A process of shared decision making, taking into account the underlying heart disease, the athlete’s ambitions, the intensity of the exercise and common sense is the fundament of giving a sound advice. Careful follow-up, including remote follow-up, with prompt intervention when novel symptoms or worsening of the underlying heart disease occurs, is mandatory.

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| --- | --- |
| **Consensus statement – Implantable cardioverter defibrillators** | **Symbol** |
| When counseling ICD recipients for sports participation, the underlying disease should be taken into consideration first. |  |
| If not contra-indicated for the underlying heart disease, physical activity should be encouraged in ICD recipients. |  |
| Dangerous situations in the context of loss of focus or consciousness should be avoided, both regarding safety for the athlete as for third parties. |  |
| All athletes with devices should be remotely monitored. |  |
| Shared decision-making should be considered to decide about continuation of intensive or competitive sports participation in ICD patients, taking into account the effect of sports on the underlying substrate, the fact that intensive sports will trigger more appropriate and inappropriate shocks, the psychological impact of shocks on the athlete/patient, and the potential risk for third parties. |  |
| Device implantation and settings should be carefully considered in function of sports participation (e.g. side of implantation, detection times, rate response). Holter recordings and device interrogation allow appropriate tailoring of rate-responsive pacing parameters, exclusion of myopotential or electromagnetic inhibition, and detection of ventricular arrhythmias. |  |
| Atrial and ventricular arrhythmias need to be treated promptly with low thresholds for ablation to minimize the risk of (inappropriate) therapy |  |
| An ICD is not a substitute for disease-related recommendations when these mandate sports restriction. |  |
| Implantation of a dual chamber system for the sole reason of arrhythmia discrimination is not recommended. |  |

# References

1. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? J Am Coll Cardiol 2003;**42**(11):1959-63.

2. Pelliccia A, Solberg EE, Papadakis M, Adami PE, Biffi A, Caselli S, La Gerche A, Niebauer J, Pressler A, Schmied CM, Serratosa L, Halle M, Van Buuren F, Borjesson M, Carre F, Panhuyzen-Goedkoop NM, Heidbuchel H, Olivotto I, Corrado D, Sinagra G, Sharma S. Recommendations for participation in competitive and leisure time sport in athletes with cardiomyopathies, myocarditis, and pericarditis: position statement of the Sport Cardiology Section of the European Association of Preventive Cardiology (EAPC). Eur Heart J 2019;**40**(1):19-33.

3. Niebauer J, Borjesson M, Carre F, Caselli S, Palatini P, Quattrini F, Serratosa L, Adami PE, Biffi A, Pressler A, Schmied C, van Buuren F, Panhuyzen-Goedkoop N, Solberg E, Halle M, La Gerche A, Papadakis M, Sharma S, Pelliccia A. Recommendations for participation in competitive sports of athletes with arterial hypertension: a position statement from the sports cardiology section of the European Association of Preventive Cardiology (EAPC). Eur Heart J 2018;**39**(40):3664-3671.

4. Borjesson M, Dellborg M, Niebauer J, LaGerche A, Schmied C, Solberg EE, Halle M, Adami E, Biffi A, Carre F, Caselli S, Papadakis M, Pressler A, Rasmusen H, Serratosa L, Sharma S, van Buuren F, Pelliccia A. Recommendations for participation in leisure time or competitive sports in athletes-patients with coronary artery disease: a position statement from the Sports Cardiology Section of the European Association of Preventive Cardiology (EAPC). Eur Heart J 2019;**40**(1):13-18.

5. Heidbuchel H, Adami PE, Antz M, Braunschweig F, Delise P, Scherr D, Solberg E, Wilhelm EN, Pelliccia A. Recommendations for participation in leisure-time physical activity and competitive sports in patients with arrhythmias and potentially arrhythmogenic conditions

Part 1: Supraventricular arrhythmias. A position statement of the Section of Sports Cardiology and Exercise from the European Association of Preventive Cardiology (EAPC) and the European Heart Rhythm Association (EHRA), both associations of the European Society of Cardiology

. Eur J Prevent Cardiol 2020: (submitted).

6. Pelliccia A, Fagard R, Bjornstad HH, Anastassakis A, Arbustini E, Assanelli D, Biffi A, Borjesson M, Carre F, Corrado D, Delise P, Dorwarth U, Hirth A, Heidbuchel H, Hoffmann E, Mellwig KP, Panhuyzen-Goedkoop N, Pisani A, Solberg EE, van-Buuren F, Vanhees L, Blomstrom-Lundqvist C, Deligiannis A, Dugmore D, Glikson M, Hoff PI, Hoffmann A, Hoffmann E, Horstkotte D, Nordrehaug JE, Oudhof J, McKenna WJ, Penco M, Priori S, Reybrouck T, Senden J, Spataro A, Thiene G, Study Group of Sports Cardiology of the Working Group of Cardiac R, Exercise P, Working Group of M, Pericardial Diseases of the European Society of C. Recommendations for competitive sports participation in athletes with cardiovascular disease: a consensus document from the Study Group of Sports Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. Eur Heart J 2005;**26**(14):1422-45.

7. Heidbuchel H, Panhuyzen-Goedkoop N, Corrado D, Hoffmann E, Biffi A, Delise P, Blomstrom-Lundqvist C, Vanhees L, Ivarhoff P, Dorwarth U, Pelliccia A, Study Group on Sports Cardiology of the European Association for Cardiovascular P, Rehabilitation. Recommendations for participation in leisure-time physical activity and competitive sports in patients with arrhythmias and potentially arrhythmogenic conditions Part I: Supraventricular arrhythmias and pacemakers. Eur J Cardiovasc Prev Rehabil 2006;**13**(4):475-84.

8. Heidbuchel H, Corrado D, Biffi A, Hoffmann E, Panhuyzen-Goedkoop N, Hoogsteen J, Delise P, Hoff PI, Pelliccia A, Study Group on Sports Cardiology of the European Association for Cardiovascular P, Rehabilitation. Recommendations for participation in leisure-time physical activity and competitive sports of patients with arrhythmias and potentially arrhythmogenic conditions. Part II: ventricular arrhythmias, channelopathies and implantable defibrillators. Eur J Cardiovasc Prev Rehabil 2006;**13**(5):676-86.

9. Mitchell JH, Haskell W, Snell P, Van Camp SP. Task Force 8: classification of sports. J Am Coll Cardiol 2005;**45**(8):1364-7.

10. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;**14**(5):377-81.

11. Scherr J, Wolfarth B, Christle JW, Pressler A, Wagenpfeil S, Halle M. Associations between Borg's rating of perceived exertion and physiological measures of exercise intensity. Eur J Appl Physiol 2013;**113**(1):147-55.

12. Chen MJ, Fan X, Moe ST. Criterion-related validity of the Borg ratings of perceived exertion scale in healthy individuals: a meta-analysis. J Sports Sci 2002;**20**(11):873-99.

13. Bjornstad H, Storstein L, Meen HD, Hals O. Ambulatory electrocardiographic findings in top athletes, athletic students and control subjects. Cardiology 1994;**84**(1):42-50.

14. Pilcher GF, Cook AJ, Johnston BL, Fletcher GF. Twenty-four-hour continuous electrocardiography during exercise and free activity in 80 apparently healthy runners. Am J Cardiol 1983;**52**(7):859-61.

15. Talan DA, Bauernfeind RA, Ashley WW, Kanakis C, Jr., Rosen KM. Twenty-four hour continuous ECG recordings in long-distance runners. Chest 1982;**82**(1):19-24.

16. Viitasalo MT, Kala R, Eisalo A. Ambulatory electrocardiographic recording in endurance athletes. Br Heart J 1982;**47**(3):213-20.

17. Viitasalo MT, Kala R, Eisalo A. Ambulatory electrocardiographic findings in young athletes between 14 and 16 years of age. Eur Heart J 1984;**5**(1):2-6.

18. Zorzi A, De Lazzari M, Mastella G, Niero A, Trovato D, Cipriani A, Peruzza F, Portolan L, Berton G, Sciacca F, Tollot S, Palermo C, Bellu R, D'Ascenzi F, Muraru D, Badano LP, Iliceto S, Schiavon M, Perazzolo Marra M, Corrado D. Ventricular Arrhythmias in Young Competitive Athletes: Prevalence, Determinants, and Underlying Substrate. J Am Heart Assoc 2018;**7**(12).

19. Zorzi A, Mastella G, Cipriani A, Berton G, Del Monte A, Gusella B, Nese A, Portolan L, Sciacca F, Tikvina S, Tollot S, Trovato D, Iliceto S, Schiavon M, Corrado D. Burden of ventricular arrhythmias at 12-lead 24-hour ambulatory ECG monitoring in middle-aged endurance athletes versus sedentary controls. Eur J Prev Cardiol 2018;**25**(18):2003-2011.

20. Biffi A, Pelliccia A, Verdile L, Fernando F, Spataro A, Caselli S, Santini M, Maron BJ. Long-term clinical significance of frequent and complex ventricular tachyarrhythmias in trained athletes. J Am Coll Cardiol 2002;**40**(3):446-52.

21. Palatini P, Maraglino G, Sperti G, Calzavara A, Libardoni M, Pessina AC, Dal Palu C. Prevalence and possible mechanisms of ventricular arrhythmias in athletes. Am Heart J 1985;**110**(3):560-7.

22. Novak J, Zorzi A, Castelletti S, Pantasis A, Rigato I, Corrado D, McKenna W, Lambiase PD. Electrocardiographic differentiation of idiopathic right ventricular outflow tract ectopy from early arrhythmogenic right ventricular cardiomyopathy. Europace 2017;**19**(4):622-628.

23. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA, Calkins H, Corrado D, Cox MG, Daubert JP, Fontaine G, Gear K, Hauer R, Nava A, Picard MH, Protonotarios N, Saffitz JE, Sanborn DM, Steinberg JS, Tandri H, Thiene G, Towbin JA, Tsatsopoulou A, Wichter T, Zareba W. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the Task Force Criteria. Eur Heart J 2010;**31**(7):806-14.

24. Niwano S, Wakisaka Y, Niwano H, Fukaya H, Kurokawa S, Kiryu M, Hatakeyama Y, Izumi T. Prognostic significance of frequent premature ventricular contractions originating from the ventricular outflow tract in patients with normal left ventricular function. Heart 2009;**95**(15):1230-7.

25. Ventura R, Steven D, Klemm HU, Lutomsky B, Mullerleile K, Rostock T, Servatius H, Risius T, Meinertz T, Kuck KH, Willems S. Decennial follow-up in patients with recurrent tachycardia originating from the right ventricular outflow tract: electrophysiologic characteristics and response to treatment. Eur Heart J 2007;**28**(19):2338-45.

26. Califf RM, McKinnis RA, Burks J, Lee KL, Harrell FE, Jr., Behar VS, Pryor DB, Wagner GS, Rosati RA. Prognostic implications of ventricular arrhythmias during 24 hour ambulatory monitoring in patients undergoing cardiac catheterization for coronary artery disease. Am J Cardiol 1982;**50**(1):23-31.

27. Kennedy HL, Whitlock JA, Sprague MK, Kennedy LJ, Buckingham TA, Goldberg RJ. Long-term follow-up of asymptomatic healthy subjects with frequent and complex ventricular ectopy. N Engl J Med 1985;**312**(4):193-7.

28. Delise P, Sitta N, Lanari E, Berton G, Centa M, Allocca G, Cati A, Biffi A. Long-term effect of continuing sports activity in competitive athletes with frequent ventricular premature complexes and apparently normal heart. Am J Cardiol 2013;**112**(9):1396-402.

29. Gaita F, Giustetto C, Di Donna P, Richiardi E, Libero L, Brusin MC, Molinari G, Trevi G. Long-term follow-up of right ventricular monomorphic extrasystoles. J Am Coll Cardiol 2001;**38**(2):364-70.

30. Corrado D, Basso C, Schiavon M, Thiene G. Screening for hypertrophic cardiomyopathy in young athletes. N Engl J Med 1998;**339**(6):364-9.

31. Yamada T. Idiopathic ventricular arrhythmias: Relevance to the anatomy, diagnosis and treatment. J Cardiol 2016;**68**(6):463-471.

32. Luebbert J, Auberson D, Marchlinski F. Premature Ventricular Complexes in Apparently Normal Hearts. Card Electrophysiol Clin 2016;**8**(3):503-14.

33. John RM, Stevenson WG. Outflow Tract Premature Ventricular Contractions and Ventricular Tachycardia: The Typical and the Challenging. Card Electrophysiol Clin 2016;**8**(3):545-54.

34. Sung R, Scheinman M. Spectrum of Fascicular Arrhythmias. Card Electrophysiol Clin 2016;**8**(3):567-80.

35. Al'Aref SJ, Ip JE, Markowitz SM, Liu CF, Thomas G, Frenkel D, Panda NC, Weinsaft JW, Lerman BB, Cheung JW. Differentiation of papillary muscle from fascicular and mitral annular ventricular arrhythmias in patients with and without structural heart disease. Circ Arrhythm Electrophysiol 2015;**8**(3):616-24.

36. Verdile L, Maron BJ, Pelliccia A, Spataro A, Santini M, Biffi A. Clinical significance of exercise-induced ventricular tachyarrhythmias in trained athletes without cardiovascular abnormalities. Heart Rhythm 2015;**12**(1):78-85.

37. Steriotis AK, Nava A, Rigato I, Mazzotti E, Daliento L, Thiene G, Basso C, Corrado D, Bauce B. Noninvasive cardiac screening in young athletes with ventricular arrhythmias. Am J Cardiol 2013;**111**(4):557-62.

38. Schnell F, Claessen G, La Gerche A, Bogaert J, Lentz PA, Claus P, Mabo P, Carre F, Heidbuchel H. Subepicardial delayed gadolinium enhancement in asymptomatic athletes: let sleeping dogs lie? Br J Sports Med 2016;**50**(2):111-7.

39. Zorzi A, Perazzolo Marra M, Rigato I, De Lazzari M, Susana A, Niero A, Pilichou K, Migliore F, Rizzo S, Giorgi B, De Conti G, Sarto P, Serratosa L, Patrizi G, De Maria E, Pelliccia A, Basso C, Schiavon M, Bauce B, Iliceto S, Thiene G, Corrado D. Nonischemic Left Ventricular Scar as a Substrate of Life-Threatening Ventricular Arrhythmias and Sudden Cardiac Death in Competitive Athletes. Circ Arrhythm Electrophysiol 2016;**9**(7).

40. Cipriani A, Zorzi A, Sarto P, Donini M, Rigato I, Bariani R, De Lazzari M, Pilichou K, Thiene G, Iliceto S, Basso C, Corrado D, Perazzolo Marra M, Bauce B. Predictive value of exercise testing in athletes with ventricular ectopy evaluated by cardiac magnetic resonance. Heart Rhythm 2019;**16**(2):239-248.

41. Nucifora G, Muser D, Masci PG, Barison A, Rebellato L, Piccoli G, Daleffe E, Toniolo M, Zanuttini D, Facchin D, Lombardi M, Proclemer A. Prevalence and prognostic value of concealed structural abnormalities in patients with apparently idiopathic ventricular arrhythmias of left versus right ventricular origin: a magnetic resonance imaging study. Circ Arrhythm Electrophysiol 2014;**7**(3):456-62.

42. Gimeno JR, Tome-Esteban M, Lofiego C, Hurtado J, Pantazis A, Mist B, Lambiase P, McKenna WJ, Elliott PM. Exercise-induced ventricular arrhythmias and risk of sudden cardiac death in patients with hypertrophic cardiomyopathy. Eur Heart J 2009;**30**(21):2599-605.

43. Heidbuchel H, Hoogsteen J, Fagard R, Vanhees L, Ector H, Willems R, Van Lierde J. 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**(16):1473-80.

44. Priori SG, Napolitano C, Memmi M, Colombi B, Drago F, Gasparini M, DeSimone L, Coltorti F, Bloise R, Keegan R, Cruz Filho FE, Vignati G, Benatar A, DeLogu A. Clinical and molecular characterization of patients with catecholaminergic polymorphic ventricular tachycardia. Circulation 2002;**106**(1):69-74.

45. Sofi F, Capalbo A, Pucci N, Giuliattini J, Condino F, Alessandri F, Abbate R, Gensini GF, Califano S. Cardiovascular evaluation, including resting and exercise electrocardiography, before participation in competitive sports: cross sectional study. BMJ 2008;**337**:a346.

46. Morshedi-Meibodi A, Evans JC, Levy D, Larson MG, Vasan RS. Clinical correlates and prognostic significance of exercise-induced ventricular premature beats in the community: the Framingham Heart Study. Circulation 2004;**109**(20):2417-22.

47. Selzman KA, Gettes LS. Exercise-induced premature ventricular beats: should we do anything differently? Circulation 2004;**109**(20):2374-5.

48. Biffi A, Maron BJ, Verdile L, Fernando F, Spataro A, Marcello G, Ciardo R, Ammirati F, Colivicchi F, Pelliccia A. Impact of physical deconditioning on ventricular tachyarrhythmias in trained athletes. J Am Coll Cardiol 2004;**44**(5):1053-8.

49. Biffi A, Maron BJ, Culasso F, Verdile L, Fernando F, Di Giacinto B, Di Paolo FM, Spataro A, Delise P, Pelliccia A. Patterns of ventricular tachyarrhythmias associated with training, deconditioning and retraining in elite athletes without cardiovascular abnormalities. Am J Cardiol 2011;**107**(5):697-703.

50. Delise P, Lanari E, Sitta N, Centa M, Allocca G, Biffi A. Influence of training on the number and complexity of frequent VPBs in healthy athletes. J Cardiovasc Med (Hagerstown) 2011;**12**(3):157-61.

51. D'Ascenzi F, Zorzi A, Alvino F, Bonifazi M, Corrado D, Mondillo S. The prevalence and clinical significance of premature ventricular beats in the athlete. Scand J Med Sci Sports 2017;**27**(2):140-151.

52. Sharma S, Drezner JA, Baggish A, Papadakis M, Wilson MG, Prutkin JM, La Gerche A, Ackerman MJ, Borjesson M, Salerno JC, Asif IM, Owens DS, Chung EH, Emery MS, Froelicher VF, Heidbuchel H, Adamuz C, Asplund CA, Cohen G, Harmon KG, Marek JC, Molossi S, Niebauer J, Pelto HF, Perez MV, Riding NR, Saarel T, Schmied CM, Shipon DM, Stein R, Vetter VL, Pelliccia A, Corrado D. International recommendations for electrocardiographic interpretation in athletes. Eur Heart J 2018;**39**(16):1466-1480.

53. Mont L, Pelliccia A, Sharma S, Biffi A, Borjesson M, Brugada Terradellas J, Carre F, Guasch E, Heidbuchel H, La Gerche A, Lampert R, McKenna W, Papadakis M, Priori SG, Scanavacca M, Thompson P, Sticherling C, Viskin S, Wilson M, Corrado D, Reviewers, Lip GY, Gorenek B, Blomstrom Lundqvist C, Merkely B, Hindricks G, Hernandez-Madrid A, Lane D, Boriani G, Narasimhan C, Marquez MF, Haines D, Mackall J, Manuel Marques-Vidal P, Corra U, Halle M, Tiberi M, Niebauer J, Piepoli M. 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. Eur J Prev Cardiol 2017;**24**(1):41-69.

54. Corrado D, Pelliccia A, Heidbuchel H, Sharma S, Link M, Basso C, Biffi A, Buja G, Delise P, Gussac I, Anastasakis A, Borjesson M, Bjornstad HH, Carre F, Deligiannis A, Dugmore D, Fagard R, Hoogsteen J, Mellwig KP, Panhuyzen-Goedkoop N, Solberg E, Vanhees L, Drezner J, Estes NA, 3rd, Iliceto S, Maron BJ, Peidro R, Schwartz PJ, Stein R, Thiene G, Zeppilli P, McKenna WJ. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. Eur Heart J 2010;**31**(2):243-59.

55. Sirico F, Fernando F, Di Paolo F, Adami PE, Signorello MG, Sannino G, Bianco A, Cerrone A, Baioccato V, Filippi N, Ferrari U, Tuzi M, Nurzynska D, Di Meglio F, Castaldo C, D'Ascenzi F, Montagnani S, Biffi A. Exercise stress test in apparently healthy individuals - where to place the finish line? The Ferrari corporate wellness programme experience. Eur J Prev Cardiol 2019;**26**(7):731-738.

56. Prakken NH, Cramer MJ, Olimulder MA, Agostoni P, Mali WP, Velthuis BK. Screening for proximal coronary artery anomalies with 3-dimensional MR coronary angiography. Int J Cardiovasc Imaging 2010;**26**(6):701-10.

57. Zeppilli P, dello Russo A, Santini C, Palmieri V, Natale L, Giordano A, Frustaci A. In vivo detection of coronary artery anomalies in asymptomatic athletes by echocardiographic screening. Chest 1998;**114**(1):89-93.

58. Pelliccia A, Spataro A, Granata M, Biffi A, Caselli G, Alabiso A. Coronary arteries in physiological hypertrophy: echocardiographic evidence of increased proximal size in elite athletes. Int J Sports Med 1990;**11**(2):120-6.

59. Pelliccia A, Spataro A, Maron BJ. Prospective echocardiographic screening for coronary artery anomalies in 1,360 elite competitive athletes. Am J Cardiol 1993;**72**(12):978-9.

60. Muser D, Piccoli G, Puppato M, Proclemer A, Nucifora G. Incremental value of cardiac magnetic resonance imaging in the diagnostic work-up of patients with apparently idiopathic ventricular arrhythmias of left ventricular origin. Int J Cardiol 2015;**180**:142-4.

61. Furlanello F, Serdoz LV, Cappato R, De Ambroggi L. Illicit drugs and cardiac arrhythmias in athletes. Eur J Cardiovasc Prev Rehabil 2007;**14**(4):487-94.

62. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck K-H, Hernandez-Madrid A, Nikolaou N, Norekvål TM, Spaulding C, Van Veldhuisen DJ, Kolh P, Lip GYH, Agewall S, Barón-Esquivias G, Boriani G, Budts W, Bueno H, Capodanno D, Carerj S, Crespo-Leiro MG, Czerny M, Deaton C, Dobrev D, Erol Ç, Galderisi M, Gorenek B, Kriebel T, Lambiase P, Lancellotti P, Lane DA, Lang I, Manolis AJ, Morais J, Moreno J, Piepoli MF, Rutten FH, Sredniawa B, Zamorano JL, Zannad F. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC) Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). European Heart Journal 2015;**36**(41):2793-2867.

63. Lerman BB, Cheung JW, Ip JE, Liu CF, Thomas G, Markowitz SM. Mechanistic subtypes of focal right ventricular tachycardia. J Cardiovasc Electrophysiol 2018;**29**(8):1181-1188.

64. Doppalapudi H, Yamada T, Ramaswamy K, Ahn J, Kay GN. Idiopathic focal epicardial ventricular tachycardia originating from the crux of the heart. Heart Rhythm 2009;**6**(1):44-50.

65. Prystowsky EN, Padanilam BJ, Joshi S, Fogel RI. Ventricular arrhythmias in the absence of structural heart disease. J Am Coll Cardiol 2012;**59**(20):1733-44.

66. Venlet J, Piers SRD, Jongbloed JDH, Androulakis AFA, Naruse Y, den Uijl DW, Kapel GFL, de Riva M, van Tintelen JP, Barge-Schaapveld DQCM, Schalij MJ, Zeppenfeld K. Isolated Subepicardial Right Ventricular Outflow Tract Scar in Athletes With Ventricular Tachycardia. Journal of the American College of Cardiology 2017;**69**(5):497-507.

67. Dello Russo A, Pieroni M, Santangeli P, Bartoletti S, Casella M, Pelargonio G, Smaldone C, Bianco M, Di Biase L, Bellocci F, Zeppilli P, Fiorentini C, Natale A, Tondo C. Concealed cardiomyopathies in competitive athletes with ventricular arrhythmias and an apparently normal heart: role of cardiac electroanatomical mapping and biopsy. Heart Rhythm 2011;**8**(12):1915-22.

68. Liu Y, Fang Z, Yang B, Kojodjojo P, Chen H, Ju W, Cao K, Chen M, Zhang F. Catheter Ablation of Fascicular Ventricular Tachycardia: Long-Term Clinical Outcomes and Mechanisms of Recurrence. Circ Arrhythm Electrophysiol 2015;**8**(6):1443-51.

69. James CA, Bhonsale A, Tichnell C, Murray B, Russell SD, Tandri H, Tedford RJ, Judge DP, Calkins H. Exercise increases age-related penetrance and arrhythmic risk in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated desmosomal mutation carriers. J Am Coll Cardiol 2013;**62**(14):1290-1297.

70. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck KH, Hernandez-Madrid A, Nikolaou N, Norekval TM, Spaulding C, Van Veldhuisen DJ. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J 2015;**36**(41):2793-2867.

71. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Juni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO, Group ESCSD. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;**40**(2):87-165.

72. Grun S, Schumm J, Greulich S, Wagner A, Schneider S, Bruder O, Kispert EM, Hill S, Ong P, Klingel K, Kandolf R, Sechtem U, Mahrholdt H. Long-term follow-up of biopsy-proven viral myocarditis: predictors of mortality and incomplete recovery. J Am Coll Cardiol 2012;**59**(18):1604-15.

73. Wyse DG, Friedman PL, Brodsky MA, Beckman KJ, Carlson MD, Curtis AB, Hallstrom AP, Raitt MH, Wilkoff BL, Greene HL. Life-threatening ventricular arrhythmias due to transient or correctable causes: high risk for death in follow-up. J Am Coll Cardiol 2001;**38**(6):1718-24.

74. Niebauer J, Hambrecht R, Velich T, Hauer K, Marburger C, Kalberer B, Weiss C, von Hodenberg E, Schlierf G, Schuler G, Zimmermann R, Kubler W. Attenuated progression of coronary artery disease after 6 years of multifactorial risk intervention: role of physical exercise. Circulation 1997;**96**(8):2534-41.

75. Niebauer J, Maxwell AJ, Lin PS, Wang D, Tsao PS, Cooke JP. NOS inhibition accelerates atherogenesis: reversal by exercise. Am J Physiol Heart Circ Physiol 2003;**285**(2):H535-40.

76. Adams V, Reich B, Uhlemann M, Niebauer J. Molecular effects of exercise training in patients with cardiovascular disease: focus on skeletal muscle, endothelium, and myocardium. Am J Physiol Heart Circ Physiol 2017;**313**(1):H72-H88.

77. Fletcher GF, Landolfo C, Niebauer J, Ozemek C, Arena R, Lavie CJ. Promoting Physical Activity and Exercise: JACC Health Promotion Series. J Am Coll Cardiol 2018;**72**(14):1622-1639.

78. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corra U, Cosyns B, Deaton C, Graham I, Hall MS, Hobbs FDR, Lochen ML, Lollgen H, Marques-Vidal P, Perk J, Prescott E, Redon J, Richter DJ, Sattar N, Smulders Y, Tiberi M, van der Worp HB, van Dis I, Verschuren WMM, Binno S, Group ESCSD. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2016;**37**(29):2315-2381.

79. Corrado D, Thiene G, Nava A, Rossi L, Pennelli N. Sudden death in young competitive athletes: clinicopathologic correlations in 22 cases. Am J Med 1990;**89**(5):588-96.

80. Maron BJ, Haas TS, Murphy CJ, Ahluwalia A, Rutten-Ramos S. Incidence and causes of sudden death in U.S. college athletes. J Am Coll Cardiol 2014;**63**(16):1636-43.

81. Maron BJ, Chaitman BR, Ackerman MJ, Bayes de Luna A, Corrado D, Crosson JE, Deal BJ, Driscoll DJ, Estes NA, 3rd, Araujo CG, Liang DH, Mitten MJ, Myerburg RJ, Pelliccia A, Thompson PD, Towbin JA, Van Camp SP. Recommendations for physical activity and recreational sports participation for young patients with genetic cardiovascular diseases. Circulation 2004;**109**(22):2807-16.

82. Pelliccia A, Zipes DP, Maron BJ. Bethesda Conference #36 and the European Society of Cardiology Consensus Recommendations revisited a comparison of U.S. and European criteria for eligibility and disqualification of competitive athletes with cardiovascular abnormalities. J Am Coll Cardiol 2008;**52**(24):1990-6.

83. Borjesson M, Urhausen A, Kouidi E, Dugmore D, Sharma S, Halle M, Heidbuchel H, Bjornstad HH, Gielen S, Mezzani A, Corrado D, Pelliccia A, Vanhees L. Cardiovascular evaluation of middle-aged/ senior individuals engaged in leisure-time sport activities: position stand from the sections of exercise physiology and sports cardiology of the European Association of Cardiovascular Prevention and Rehabilitation. Eur J Cardiovasc Prev Rehabil 2011;**18**(3):446-58.

84. Bai R, Napolitano C, Bloise R, Monteforte N, Priori SG. Yield of genetic screening in inherited cardiac channelopathies: how to prioritize access to genetic testing. Circ Arrhythm Electrophysiol 2009;**2**(1):6-15.

85. Behr ER, Dalageorgou C, Christiansen M, Syrris P, Hughes S, Tome Esteban MT, Rowland E, Jeffery S, McKenna WJ. Sudden arrhythmic death syndrome: familial evaluation identifies inheritable heart disease in the majority of families. Eur Heart J 2008;**29**(13):1670-80.

86. Priori SG, Napolitano C. Role of genetic analyses in cardiology: part I: mendelian diseases: cardiac channelopathies. Circulation 2006;**113**(8):1130-5.

87. Hofman N, Tan HL, Alders M, van Langen IM, Wilde AA. Active cascade screening in primary inherited arrhythmia syndromes: does it lead to prophylactic treatment? J Am Coll Cardiol 2010;**55**(23):2570-6.

88. Nunn LM, Lambiase PD. Genetics and cardiovascular disease--causes and prevention of unexpected sudden adult death: the role of the SADS clinic. Heart 2011;**97**(14):1122-7.

89. Ingles J, Yeates L, Semsarian C. The emerging role of the cardiac genetic counselor. Heart Rhythm 2011;**8**(12):1958-62.

90. van Langen IM, Birnie E, Leschot NJ, Bonsel GJ, Wilde AA. Genetic knowledge and counselling skills of Dutch cardiologists: sufficient for the genomics era? Eur Heart J 2003;**24**(6):560-6.

91. Manrai AK, Funke BH, Rehm HL, Olesen MS, Maron BA, Szolovits P, Margulies DM, Loscalzo J, Kohane IS. Genetic Misdiagnoses and the Potential for Health Disparities. N Engl J Med 2016;**375**(7):655-65.

92. van der Werf C, Hofman N, Tan HL, van Dessel PF, Alders M, van der Wal AC, van Langen IM, Wilde AA. Diagnostic yield in sudden unexplained death and aborted cardiac arrest in the young: the experience of a tertiary referral center in The Netherlands. Heart Rhythm 2010;**7**(10):1383-9.

93. Tiziano FD, Palmieri V, Genuardi M, Zeppilli P. The Role of Genetic Testing in the Identification of Young Athletes with Inherited Primitive Cardiac Disorders at Risk of Exercise Sudden Death. Front Cardiovasc Med 2016;**3**:28.

94. Thiene G, Carturan E, Corrado D, Basso C. Prevention of sudden cardiac death in the young and in athletes: dream or reality? Cardiovasc Pathol 2010;**19**(4):207-17.

95. Anderson JH, Tester DJ, Will ML, Ackerman MJ. Whole-Exome Molecular Autopsy After Exertion-Related Sudden Unexplained Death in the Young. Circ Cardiovasc Genet 2016;**9**(3):259-65.

96. Tester DJ, Medeiros-Domingo A, Will ML, Ackerman MJ. Unexplained drownings and the cardiac channelopathies: a molecular autopsy series. Mayo Clin Proc 2011;**86**(10):941-7.

97. Semsarian C, Ingles J, Wilde AA. Sudden cardiac death in the young: the molecular autopsy and a practical approach to surviving relatives. Eur Heart J 2015;**36**(21):1290-6.

98. Tester DJ, Medeiros-Domingo A, Will ML, Haglund CM, Ackerman MJ. Cardiac channel molecular autopsy: insights from 173 consecutive cases of autopsy-negative sudden unexplained death referred for postmortem genetic testing. Mayo Clin Proc 2012;**87**(6):524-39.

99. Bagnall RD, Das KJ, Duflou J, Semsarian C. Exome analysis-based molecular autopsy in cases of sudden unexplained death in the young. Heart Rhythm 2014;**11**(4):655-62.

100. Semsarian C, Ingles J. Molecular autopsy in victims of inherited arrhythmias. J Arrhythm 2016;**32**(5):359-365.

101. Mates J, Mademont-Soler I, Del Olmo B, Ferrer-Costa C, Coll M, Perez-Serra A, Pico F, Allegue C, Fernandez-Falgueras A, Alvarez P, Yotti R, Espinosa MA, Sarquella-Brugada G, Cesar S, Carro E, Brugada J, Arbelo E, Garcia-Pavia P, Borregan M, Tizzano E, Lopez-Granados A, Mazuelos F, Diaz de Bustamante A, Darnaude MT, Gonzalez-Hevia JI, Diaz-Flores F, Trujillo F, Iglesias A, Fernandez-Aviles F, Campuzano O, Brugada R. Role of copy number variants in sudden cardiac death and related diseases: genetic analysis and translation into clinical practice. Eur J Hum Genet 2018;**26**(7):1014-1025.

102. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, Grody WW, Hegde M, Lyon E, Spector E, Voelkerding K, Rehm HL. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med 2015;**17**(5):405-24.

103. Richard P, Denjoy I, Fressart V, Wilson MG, Carre F, Charron P. Advising a cardiac disease gene positive yet phenotype negative or borderline abnormal athlete: is sporting disqualification really necessary? Br J Sports Med 2012;**46 Suppl 1**:i59-68.

104. Hosseini SM, Kim R, Udupa S, Costain G, Jobling R, Liston E, Jamal SM, Szybowska M, Morel CF, Bowdin S, Garcia J, Care M, Sturm AC, Novelli V, Ackerman MJ, Ware JS, Hershberger RE, Wilde AAM, Gollob MH. Reappraisal of Reported Genes for Sudden Arrhythmic Death. Circulation 2018;**138**(12):1195-1205.

105. Lopes LR, Brito D, Belo A, Cardim N. Genetic characterization and genotype-phenotype associations in a large cohort of patients with hypertrophic cardiomyopathy - An ancillary study of the Portuguese registry of hypertrophic cardiomyopathy. Int J Cardiol 2018.

106. Chandra N, Bastiaenen R, Papadakis M, Panoulas VF, Ghani S, Duschl J, Foldes D, Raju H, Osborne R, Sharma S. Prevalence of electrocardiographic anomalies in young individuals: relevance to a nationwide cardiac screening program. J Am Coll Cardiol 2014;**63**(19):2028-34.

107. Schwartz PJ, Ackerman MJ. The long QT syndrome: a transatlantic clinical approach to diagnosis and therapy. Eur Heart J 2013;**34**(40):3109-16.

108. Schwartz PJ, Crotti L. QTc behavior during exercise and genetic testing for the long-QT syndrome. Circulation 2011;**124**(20):2181-4.

109. Basavarajaiah S, Wilson M, Whyte G, Shah A, Behr E, Sharma S. Prevalence and significance of an isolated long QT interval in elite athletes. Eur Heart J 2007;**28**(23):2944-9.

110. Horner JM, Horner MM, Ackerman MJ. The diagnostic utility of recovery phase QTc during treadmill exercise stress testing in the evaluation of long QT syndrome. Heart Rhythm 2011;**8**(11):1698-704.

111. Priori SG, Napolitano C, Schwartz PJ. Low penetrance in the long-QT syndrome: clinical impact. Circulation 1999;**99**(4):529-33.

112. Schwartz PJ, Priori SG, Spazzolini C, Moss AJ, Vincent GM, Napolitano C, Denjoy I, Guicheney P, Breithardt G, Keating MT, Towbin JA, Beggs AH, Brink P, Wilde AA, Toivonen L, Zareba W, Robinson JL, Timothy KW, Corfield V, Wattanasirichaigoon D, Corbett C, Haverkamp W, Schulze-Bahr E, Lehmann MH, Schwartz K, Coumel P, Bloise R. Genotype-phenotype correlation in the long-QT syndrome: gene-specific triggers for life-threatening arrhythmias. Circulation 2001;**103**(1):89-95.

113. Vincent GM, Schwartz PJ, Denjoy I, Swan H, Bithell C, Spazzolini C, Crotti L, Piippo K, Lupoglazoff JM, Villain E, Priori SG, Napolitano C, Zhang L. High efficacy of beta-blockers in long-QT syndrome type 1: contribution of noncompliance and QT-prolonging drugs to the occurrence of beta-blocker treatment "failures". Circulation 2009;**119**(2):215-21.

114. Ackerman MJ, Zipes DP, Kovacs RJ, Maron BJ, American Heart Association E, Arrhythmias Committee of Council on Clinical Cardiology CoCDiYCoC, Stroke Nursing CoFG, Translational B, American College of C. Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 10: The Cardiac Channelopathies: A Scientific Statement From the American Heart Association and American College of Cardiology. Circulation 2015;**132**(22):e326-9.

115. Johnson JN, Ackerman MJ. Return to play? Athletes with congenital long QT syndrome. Br J Sports Med 2013;**47**(1):28-33.

116. Drezner JA, Rogers KJ. Sudden cardiac arrest in intercollegiate athletes: detailed analysis and outcomes of resuscitation in nine cases. Heart Rhythm 2006;**3**(7):755-9.

117. Gussak I, Brugada P, Brugada J, Wright RS, Kopecky SL, Chaitman BR, Bjerregaard P. Idiopathic short QT interval: a new clinical syndrome? Cardiology 2000;**94**(2):99-102.

118. Schwartz PJ, Crotti L. Long QT and short QT syndromes. In: cardiac electrophysiology: from cell to bedside, 7th Edition. (Zipes DP and Jalife J, Eds.) Elsevier/Saunders, Philadelphia, PA, ISBN: 9780323447331, pp. 893-904, 2018.

119. Giustetto C, Schimpf R, Mazzanti A, Scrocco C, Maury P, Anttonen O, Probst V, Blanc JJ, Sbragia P, Dalmasso P, Borggrefe M, Gaita F. Long-term follow-up of patients with short QT syndrome. J Am Coll Cardiol 2011;**58**(6):587-95.

120. Gollob MH, Redpath CJ, Roberts JD. The short QT syndrome: proposed diagnostic criteria. J Am Coll Cardiol 2011;**57**(7):802-12.

121. Mazzanti A, Kanthan A, Monteforte N, Memmi M, Bloise R, Novelli V, Miceli C, O'Rourke S, Borio G, Zienciuk-Krajka A, Curcio A, Surducan AE, Colombo M, Napolitano C, Priori SG. Novel insight into the natural history of short QT syndrome. J Am Coll Cardiol 2014;**63**(13):1300-1308.

122. Providencia R, Karim N, Srinivasan N, Honarbakhsh S, Vidigal Ferreira MJ, Goncalves L, Marijon E, Lambiase PD. Impact of QTc formulae in the prevalence of short corrected QT interval and impact on probability and diagnosis of short QT syndrome. Heart 2018;**104**(6):502-508.

123. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report. J Am Coll Cardiol 1992;**20**(6):1391-6.

124. Brugada J, Campuzano O, Arbelo E, Sarquella-Brugada G, Brugada R. Present Status of Brugada Syndrome: JACC State-of-the-Art Review. Journal of the American College of Cardiology 2018;**72**(9):1046-1059.

125. Sarquella-Brugada G, Campuzano O, Arbelo E, Brugada J, Brugada R. Brugada syndrome: clinical and genetic findings. Genet Med 2016;**18**(1):3-12.

126. Schulze-Bahr E, Eckardt L, Breithardt G, Seidl K, Wichter T, Wolpert C, Borggrefe M, Haverkamp W. Sodium channel gene (SCN5A) mutations in 44 index patients with Brugada syndrome: Different incidences in familial and sporadic disease. Human Mutation 2003;**21**(6):651-652.

127. Rudic B, Schimpf R, Veltmann C, Doesch C, Tülümen E, Schoenberg SO, Borggrefe M, Papavassiliu T. Brugada syndrome: clinical presentation and genotype—correlation with magnetic resonance imaging parameters. EP Europace 2016;**18**(9):1411-1419.

128. Kapplinger JD, Tester DJ, Alders M, Benito B, Berthet M, Brugada J, Brugada P, Fressart V, Guerchicoff A, Harris-Kerr C, Kamakura S, Kyndt F, Koopmann TT, Miyamoto Y, Pfeiffer R, Pollevick GD, Probst V, Zumhagen S, Vatta M, Towbin JA, Shimizu W, Schulze-Bahr E, Antzelevitch C, Salisbury BA, Guicheney P, Wilde AAM, Brugada R, Schott J-J, Ackerman MJ. An international compendium of mutations in the SCN5A-encoded cardiac sodium channel in patients referred for Brugada syndrome genetic testing. Heart Rhythm 2010;**7**(1):33-46.

129. Frustaci A, Priori SG, Pieroni M, Chimenti C, Napolitano C, Rivolta I, Sanna T, Bellocci F, Russo MA. Cardiac Histological Substrate in Patients With Clinical Phenotype of Brugada Syndrome. Circulation 2005;**112**(24):3680-3687.

130. Frustaci A, Russo MA, Chimenti C. Structural myocardial abnormalities in asymptomatic family members with Brugada syndrome and SCN5A gene mutation. European Heart Journal 2009;**30**(14):11763.

131. Catalano O, Antonaci S, Moro G, Mussida M, Frascaroli M, Baldi M, Cobelli F, Baiardi P, Nastoli J, Bloise R, Monteforte N, Napolitano C, Priori SG. Magnetic resonance investigations in Brugada syndrome reveal unexpectedly high rate of structural abnormalities. European Heart Journal 2009;**30**(18):2241-2248.

132. van Hoorn F, Campian ME, Spijkerboer A, Blom MT, Planken RN, van Rossum AC, de Bakker JMT, Wilde AAM, Groenink M, Tan HL. SCN5A Mutations in Brugada Syndrome Are Associated with Increased Cardiac Dimensions and Reduced Contractility. PLoS One 2012;**7**(8):e42037.

133. Veltmann C, Schimpf R, Echternach C, Eckardt L, Kuschyk J, Streitner F, Spehl S, Borggrefe M, Wolpert C. A prospective study on spontaneous fluctuations between diagnostic and non-diagnostic ECGs in Brugada syndrome: implications for correct phenotyping and risk stratification. European Heart Journal 2006;**27**(21):2544-2552.

134. Letsas KP, Gavrielatos G, Efremidis M, Kounas SP, Filippatos GS, Sideris A, Kardaras F. Prevalence of Brugada sign in a Greek tertiary hospital population. Europace 2007;**9**(11):1077-80.

135. Pecini R, Cedergreen P, Theilade S, Haunso S, Theilade J, Jensen GB. The prevalence and relevance of the Brugada-type electrocardiogram in the Danish general population: data from the Copenhagen City Heart Study. Europace 2010;**12**(7):982-6.

136. Benito B, Sarkozy A, Mont L, Henkens S, Berruezo A, Tamborero D, Arzamendi D, Berne P, Brugada R, Brugada P, Brugada J. Gender Differences in Clinical Manifestations of Brugada Syndrome. Journal of the American College of Cardiology 2008;**52**(19):1567-1573.

137. Brugada J, Brugada R, Antzelevitch C, Towbin J, Nademanee K, Brugada P. Long-Term Follow-Up of Individuals With the Electrocardiographic Pattern of Right Bundle-Branch Block and ST-Segment Elevation in Precordial Leads V1 to V3. Circulation 2002;**105**(1):73-78.

138. Priori SG, Napolitano C, Gasparini M, Pappone C, Bella PD, Giordano U, Bloise R, Giustetto C, De Nardis R, Grillo M, Ronchetti E, Faggiano G, Nastoli J. Natural History of Brugada Syndrome: Insights for Risk Stratification and Management. Circulation 2002;**105**(11):1342-1347.

139. Brugada J, Brugada R, Brugada P. Determinants of Sudden Cardiac Death in Individuals With the Electrocardiographic Pattern of Brugada Syndrome and No Previous Cardiac Arrest. Circulation 2003;**108**(25):3092-3096.

140. Milman A, Andorin A, Gourraud JB, Sacher F, Mabo P, Kim SH, Maeda S, Takahashi Y, Kamakura T, Aiba T, Conte G, Juang JJM, Leshem E, Rahkovich M, Hochstadt A, Mizusawa Y, Postema PG, Arbelo E, Huang Z, Denjoy I, Giustetto C, Wijeyeratne YD, Napolitano C, Michowitz Y, Brugada R, Casado-Arroyo R, Champagne J, Calo L, Sarquella-Brugada G, Tfelt-Hansen J, Priori SG, Takagi M, Veltmann C, Delise P, Corrado D, Behr ER, Gaita F, Yan GX, Brugada J, Leenhardt A, Wilde AAM, Brugada P, Kusano KF, Hirao K, Nam GB, Probst V, Belhassen B. Age of First Arrhythmic Event in Brugada Syndrome: Data From the SABRUS (Survey on Arrhythmic Events in Brugada Syndrome) in 678 Patients. Circ Arrhythm Electrophysiol 2017;**10**(12).

141. Miyazaki T, Mitamura H, Miyoshi S, Soejima K, Aizawa Y, Ogawa S. Autonomic and antiarrhythmic drug modulation of ST segment elevation in patients with Brugada syndrome. Journal of the American College of Cardiology 1996;**27**:1061-1070.

142. Kasanuki H, Ohnishi S, Ohtuka M, Matsuda N, Nirei T, Isogai R, Shoda M, Toyoshima Y, Hosoda S. Idiopathic ventricular fibrillation induced with vagal activity in patients without obvious heart disease. Circulation 1997;**95**(9):2277-85.

143. Matsuo K, Kurita T, Inagaki M, Kakishita M, Aihara N, Shimizu W, Taguchi A, Suyama K, Kamakura S, Shimomura K. The circadian pattern of the development of ventricular fibrillation in patients with Brugada syndrome. Eur Heart J 1999;**20**(6):465-70.

144. Mizumaki K, Fujiki A, Tsuneda T, Sakabe M, Nishida K, Sugao M, Inoue H. Vagal Activity Modulates Spontaneous Augmentation of ST Elevation in the Daily Life of Patients with Brugada Syndrome. Journal of Cardiovascular Electrophysiology 2004;**15**(6):667-673.

145. Probst V, Denjoy I, Meregalli PG, Amirault J-C, Sacher F, Mansourati J, Babuty D, Villain E, Victor J, Schott J-J, Lupoglazoff J-M, Mabo P, Veltmann C, Jesel L, Chevalier P, Clur S-AB, Haissaguerre M, Wolpert C, Le Marec H, Wilde AAM. Clinical Aspects and Prognosis of Brugada Syndrome in Children. Circulation 2007;**115**(15):2042-2048.

146. Takigawa M, Noda T, Shimizu W, Miyamoto K, Okamura H, Satomi K, Suyama K, Aihara N, Kamakura S, Kurita T. Seasonal and circadian distributions of ventricular fibrillation in patients with Brugada syndrome. Heart Rhythm 2008;**5**(11):1523-1527.

147. Chockalingam P, Rammeloo LA, Postema PG, Hruda J, Clur S-AB, Blom NA, Wilde AA. Fever-Induced Life-Threatening Arrhythmias in Children Harboring an SCN5A Mutation. Pediatrics 2011;**127**(1):e239-e244.

148. Michowitz Y, Milman A, Sarquella-Brugada G, Andorin A, Champagne J, Postema PG, Casado-Arroyo R, Leshem E, Juang JJM, Giustetto C, Tfelt-Hansen J, Wijeyeratne YD, Veltmann C, Corrado D, Kim SH, Delise P, Maeda S, Gourraud JB, Sacher F, Mabo P, Takahashi Y, Kamakura T, Aiba T, Conte G, Hochstadt A, Mizusawa Y, Rahkovich M, Arbelo E, Huang Z, Denjoy I, Napolitano C, Brugada R, Calo L, Priori SG, Takagi M, Behr ER, Gaita F, Yan GX, Brugada J, Leenhardt A, Wilde AAM, Brugada P, Kusano KF, Hirao K, Nam GB, Probst V, Belhassen B. Fever-related arrhythmic events in the multicenter Survey on Arrhythmic Events in Brugada Syndrome. Heart Rhythm 2018;**15**(9):1394-1401.

149. Rossenbacker T, Carroll SJ, Liu H, Kuiperi C, de Ravel TJ, Devriendt K, Carmeliet P, Kass RS, Heidbuchel H. Novel pore mutation in SCN5A manifests as a spectrum of phenotypes ranging from atrial flutter, conduction disease, and Brugada syndrome to sudden cardiac death. Heart Rhythm 2004;**1**(5):610-5.

150. Furuhashi M, Uno K, Tsuchihashi K, Nagahara D, Hyakukoku M, Ohtomo T, Satoh S, Nishimiya T, Shimamoto K. Prevalence of asymptomatic ST segment elevation in right precordial leads with right bundle branch block (Brugada-type ST shift) among the general Japanese population. Heart 2001;**86**(2):161-166.

151. Grimster A, Segal OR, Behr ER. Type I Brugada electrocardiogram pattern during the recovery phase of exercise testing. Europace 2008;**10**(7):897-898.

152. Papadakis M, Petzer E, Sharma S. Unmasking of the Brugada phenotype during exercise testing and its association with ventricular arrhythmia on the recovery phase. Heart 2009;**95**(24):2022.

153. Ozeke O, Cagli KE, Aras D, Ilkay E. Exercise-induced ventricular tachycardia associated with asymptomatic Brugada syndrome in a patient with urinary bladder stone. Turk Kardiyol Dern Ars 2009;**37**(2):128-131.

154. Jayasuriya C, Whitman M. Exercise-induced Brugada sign. Europace 2011;**13**(3):446-447.

155. Boersma LVA, Jaarsma W, Jessurun ER, Van Hemel NHM, Wever EFD. Brugada Syndrome: A Case Report of Monomorphic Ventricular Tachycardia. Pacing and Clinical Electrophysiology 2001;**24**(1):112-115.

156. García-Borbolla M, García-Borbolla R, Valenzuela LF, Trujillo F. Ventricular Tachycardia Induced by Exercise Testing in a Patient With Brugada Syndrome. Revista Española de Cardiología (English Version) 2007;**60**(09):993-994.

157. Esperer HD, Hoos O, Hottenrott K. Syncope due to Brugada syndrome in a young athlete. British Journal of Sports Medicine 2007;**41**(3):180-181.

158. Amin AS, de Groot EAA, Ruijter JM, Wilde AAM, Tan HL. Exercise-Induced ECG Changes in Brugada Syndrome. Circulation: Arrhythmia and Electrophysiology 2009;**2**(5):531-539.

159. Makimoto H, Nakagawa E, Takaki H, Yamada Y, Okamura H, Noda T, Satomi K, Suyama K, Aihara N, Kurita T, Kamakura S, Shimizu W. Augmented ST-Segment Elevation During Recovery From Exercise Predicts Cardiac Events in Patients With Brugada Syndrome. Journal of the American College of Cardiology 2010;**56**(19):1576-1584.

160. Subramanian M, Prabhu MA, Harikrishnan MS, Shekhar SS, Pai PG, Natarajan K. The Utility of Exercise Testing in Risk Stratification of Asymptomatic Patients With Type 1 Brugada Pattern. Journal of Cardiovascular Electrophysiology 2017;**28**(6):677-683.

161. Masrur S, Memon S, Thompson PD. Brugada Syndrome, Exercise, and Exercise Testing. Clinical Cardiology 2015;**38**(5):323-326.

162. Baranchuk A, Nguyen T, Ryu MH, Femenía F, Zareba W, Wilde AAM, Shimizu W, Brugada P, Pérez-Riera AR. Brugada Phenocopy: New Terminology and Proposed Classification. Annals of Noninvasive Electrocardiology 2012;**17**(4):299-314.

163. Bayés de Luna A, Brugada J, Baranchuk A, Borggrefe M, Breithardt G, Goldwasser D, Lambiase P, Riera AP, Garcia-Niebla J, Pastore C, Oreto G, McKenna W, Zareba W, Brugada R, Brugada P. Current electrocardiographic criteria for diagnosis of Brugada pattern: a consensus report. Journal of Electrocardiology 2012;**45**(5):433-442.

164. Priori SG, Wilde AA, Horie M, Cho Y, Behr ER, Berul C, Blom N, Brugada J, Chiang C-E, Huikuri H, Kannankeril P, Krahn A, Leenhardt A, Moss A, Schwartz PJ, Shimizu W, Tomaselli G, Tracy C. HRS/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of Patients with Inherited Primary Arrhythmia Syndromes: Document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. Heart Rhythm 2013;**10**(12):1932-1963.

165. Chung EH, McNeely DE, III, Gehi AK, Brickner T, Evans S, Pryski E, Waicus K, Stafford H, Mounsey JP, Schwartz JD, Huang S, Pursell I, Ciocca M. Brugada-type patterns are easily observed in high precordial lead ECGs in collegiate athletes. Journal of Electrocardiology 2014;**47**(1):1-6.

166. Sharma S, Drezner JA, Baggish A, Papadakis M, Wilson MG, Prutkin JM, La Gerche A, Ackerman MJ, Borjesson M, Salerno JC, Asif IM, Owens DS, Chung EH, Emery MS, Froelicher VF, Heidbuchel H, Adamuz C, Asplund CA, Cohen G, Harmon KG, Marek JC, Molossi S, Niebauer J, Pelto HF, Perez MV, Riding NR, Saarel T, Schmied CM, Shipon DM, Stein R, Vetter VL, Pelliccia A, Corrado D. International recommendations for electrocardiographic interpretation in athletes. European Heart Journal 2018;**39**(16):1466-1480.

167. Corrado D, Pelliccia A, Heidbuchel H, Sharma S, Link M, Basso C, Biffi A, Buja G, Delise P, Gussac I, Anastasakis A, Borjesson M, BjÃ¸rnstad HH, CarrÃ¨ F, Deligiannis A, Dugmore D, Fagard R, Hoogsteen J, Mellwig KP, Panhuyzen-Goedkoop N, Solberg E, Vanhees L, Drezner J, Estes NAM, Iliceto S, Maron BJ, Peidro R, Schwartz PJ, Stein R, Thiene G, Zeppilli P, McKenna WJ. Recommendations for interpretation of 12-lead electrocardiogram in the athlete. European Heart Journal 2010;**31**(2):243-259.

168. Letsas KP, Korantzopoulos P, Efremidis M, Weber R, Lioni L, Bakosis G, Vassilikos VP, Deftereos S, Sideris A, Arentz T. Sinus node disease in subjects with type 1 ECG pattern of Brugada syndrome. Journal of Cardiology 2013;**61**(3):227-231.

169. Morita H, Fukushima-Kusano K, Nagase S, Miyaji K, Hiramatsu S, Banba K, Nishii N, Watanabe A, Kakishita M, Takenaka-Morita S, Nakamura K, Saito H, Emori T, Ohe T. Sinus Node Function in Patients With Brugada-Type ECG. Circulation Journal 2004;**68**(5):473-476.

170. Bordachar P, Reuter S, Garrigue S, Caï X, Hocini M, Jaïs P, Haïssaguerre M, Clementy J. Incidence, clinical implications and prognosis of atrial arrhythmias in brugada syndrome. European Heart Journal 2004;**25**(10):879-884.

171. Alings M, Wilde A. "Brugada" syndrome: clinical data and suggested pathophysiological mechanism. Circulation 1999;**99**(5):666-73.

172. Maury P, Rollin A, Sacher F, Gourraud J-B, Raczka F, Pasquié J-L, Duparc A, Mondoly P, Cardin C, Delay M, Derval N, Chatel S, Bongard V, Sadron M, Denis A, Davy J-M, Hocini M, Jaïs P, Jesel L, Haïssaguerre M, Probst V. Prevalence and Prognostic Role of Various Conduction Disturbances in Patients With the Brugada Syndrome. American Journal of Cardiology 2013;**112**(9):1384-1389.

173. Morita H, Kusano-Fukushima K, Nagase S, Fujimoto Y, Hisamatsu K, Fujio H, Haraoka K, Kobayashi M, Morita ST, Nakamura K, Emori T, Matsubara H, Hina K, Kita T, Fukatani M, Ohe T. Atrial fibrillation and atrial vulnerability in patients with Brugada syndrome. Journal of the American College of Cardiology 2002;**40**(8):1437-1444.

174. Kusano KF, Taniyama M, Nakamura K, Miura D, Banba K, Nagase S, Morita H, Nishii N, Watanabe A, Tada T, Murakami M, Miyaji K, Hiramatsu S, Nakagawa K, Tanaka M, Miura A, Kimura H, Fuke S, Sumita W, Sakuragi S, Urakawa S, Iwasaki J, Ohe T. Atrial Fibrillation in Patients With Brugada Syndrome: Relationships of Gene Mutation, Electrophysiology, and Clinical Backgrounds. Journal of the American College of Cardiology 2008;**51**(12):1169-1175.

175. Schimpf R, Giustetto C, Eckardt L, Veltmann C, Wolpert C, Gaita F, Breithardt G, Borggrefe M. Prevalence of Supraventricular Tachyarrhythmias in a Cohort of 115 Patients with Brugada Syndrome. Annals of Noninvasive Electrocardiology 2008;**13**(3):266-269.

176. Pappone C, Radinovic A, Manguso F, Vicedomini G, Sala S, Sacco FM, Ciconte G, Saviano M, Ferrari M, Sommariva E, Sacchi S, Ciaccio C, Kallergis EM, Santinelli V. New-onset atrial fibrillation as first clinical manifestation of latent Brugada syndrome: prevalence and clinical significance. European Heart Journal 2009;**30**(24):2985-2992.

177. Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, Deal BJ, Dickfeld T, Field ME, Fonarow GC, Gillis AM, Granger CB, Hammill SC, Hlatky MA, Joglar JA, Kay GN, Matlock DD, Myerburg RJ, Page RL. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology 2018;**72**(14):e91-e220.

178. Smith ML, Hudson DL, Graitzer HM, Raven PB. Exercise training bradycardia: the role of autonomic balance. Medicine & Science in Sports & Exercise 1989;**21**(1):40-44.

179. Leenhardt A, Lucet V, Denjoy I, Grau F, Ngoc DD, Coumel P. Catecholaminergic polymorphic ventricular tachycardia in children. A 7-year follow-up of 21 patients. Circulation 1995;**91**(5):1512-9.

180. Leenhardt A, Denjoy I, Guicheney P. Catecholaminergic Polymorphic Ventricular Tachycardia. Circulation: Arrhythmia and Electrophysiology 2012;**5**(5):1044-1052.

181. Tester DJ, Kopplin LJ, Will ML, Ackerman MJ. Spectrum and prevalence of cardiac ryanodine receptor (RyR2) mutations in a cohort of unrelated patients referred explicitly for long QT syndrome genetic testing. Heart Rhythm 2005;**2**(10):1099-105.

182. Ackerman MJ, Priori SG, Willems S, Berul C, Brugada R, Calkins H, Camm AJ, Ellinor PT, Gollob M, Hamilton R, Hershberger RE, Judge DP, Le Marec H, McKenna WJ, Schulze-Bahr E, Semsarian C, Towbin JA, Watkins H, Wilde A, Wolpert C, Zipes DP. HRS/EHRA Expert Consensus Statement on the State of Genetic Testing for the Channelopathies and Cardiomyopathies: This document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). Europace 2011;**13**(8):1077-1109.

183. Roston TM, Yuchi Z, Kannankeril PJ, Hathaway J, Vinocur JM, Etheridge SP, Potts JE, Maginot KR, Salerno JC, Cohen MI, Hamilton RM, Pflaumer A, Mohammed S, Kimlicka L, Kanter RJ, LaPage MJ, Collins KK, Gebauer RA, Temple JD, Batra AS, Erickson C, Miszczak-Knecht M, Kubuš P, Bar-Cohen Y, Kantoch M, Thomas VC, Hessling G, Anderson C, Young M-L, Choi SHJ, Cabrera Ortega M, Lau YR, Johnsrude CL, Fournier A, Van Petegem F, Sanatani S. The clinical and genetic spectrum of catecholaminergic polymorphic ventricular tachycardia: findings from an international multicentre registry. EP Europace 2018;**20**(3):541-547.

184. Laitinen PJ, Brown KM, Piippo K, Swan H, Devaney JM, Brahmbhatt B, Donarum EA, Marino M, Tiso N, Viitasalo M, Toivonen L, Stephan DA, Kontula K. Mutations of the Cardiac Ryanodine Receptor (RyR2) Gene in Familial Polymorphic Ventricular Tachycardia. Circulation 2001;**103**(4):485-490.

185. Priori SG, Napolitano C, Tiso N, Memmi M, Vignati G, Bloise R, Sorrentino V, Danieli GA. Mutations in the cardiac ryanodine receptor gene (hRyR2) underlie catecholaminergic polymorphic ventricular tachycardia. Circulation 2001;**103**(2):196-200.

186. Lahat H, Pras E, Olender T, Avidan N, Ben-Asher E, Man O, Levy-Nissenbaum E, Khoury A, Lorber A, Goldman B, Lancet D, Eldar M. A Missense Mutation in a Highly Conserved Region of CASQ2 Is Associated with Autosomal Recessive Catecholamine-Induced Polymorphic Ventricular Tachycardia in Bedouin Families from Israel. The American Journal of Human Genetics 2001;**69**(6):1378-1384.

187. Lahat H, Eldar M, Levy-Nissenbaum E, Bahan T, Friedman E, Khoury A, Lorber A, Kastner DL, Goldman B, Pras E. Autosomal Recessive Catecholamine- or Exercise-Induced Polymorphic Ventricular Tachycardia: Clinical Features and Assignment of the Disease Gene to Chromosome 1p13-21. Circulation 2001;**103**(23):2822-2827.

188. Mohamed U, Napolitano C, Priori SG. Molecular and Electrophysiological Bases of Catecholaminergic Polymorphic Ventricular Tachycardia. Journal of Cardiovascular Electrophysiology 2007;**18**(7):791-797.

189. Priori SG, Wilde AA, Horie M, Cho Y, Behr ER, Berul C, Blom N, Brugada J, Chiang C-E, Huikuri H, Kannankeril P, Krahn A, Leenhardt A, Moss A, Schwartz PJ, Shimizu W, Tomaselli G, Tracy C, Reviewers D, Ackerman M, Belhassen B, Estes NAM, Fatkin D, Kalman J, Kaufman E, Kirchhof P, Schulze-Bahr E, Wolpert C, Vohra J, Refaat M, Etheridge SP, Campbell RM, Martin ET, Quek SC. Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes. Europace 2013;**15**:1389-1406.

190. Priori SG, Napolitano C, Memmi M, Colombi B, Drago F, Gasparini M, DeSimone L, Coltorti F, Bloise R, Keegan R, Cruz Filho FES, Vignati G, Benatar A, DeLogu A. Clinical and Molecular Characterization of Patients With Catecholaminergic Polymorphic Ventricular Tachycardia. Circulation 2002;**106**(1):69-74.

191. Hayashi M, Denjoy I, Extramiana F, Maltret A, Buisson NR, Lupoglazoff J-M, Klug D, Hayashi M, Takatsuki S, Villain E, Kamblock J, Messali A, Guicheney P, Lunardi J, Leenhardt A. Incidence and Risk Factors of Arrhythmic Events in Catecholaminergic Polymorphic Ventricular Tachycardia. Circulation 2009;**119**(18):2426-2434.

192. Roston TM, Vinocur JM, Maginot KR, Mohammed S, Salerno JC, Etheridge SP, Cohen M, Hamilton RM, Pflaumer A, Kanter RJ, Potts JE, LaPage MJ, Collins KK, Gebauer RA, Temple JD, Batra AS, Erickson C, Miszczak-Knecht M, Kubuš P, Bar-Cohen Y, Kantoch M, Thomas VC, Hessling G, Anderson C, Young M-L, Cabrera Ortega M, Lau YR, Johnsrude CL, Fournier A, Kannankeril PJ, Sanatani S. Catecholaminergic Polymorphic Ventricular Tachycardia in Children: Analysis of Therapeutic Strategies and Outcomes From an International Multicenter Registry. Circulation: Arrhythmia and Electrophysiology 2015;**8**(3):633-642.

193. Ostby SA, Bos JM, Owen HJ, Wackel PL, Cannon BC, Ackerman MJ. Competitive Sports Participation in Patients With Catecholaminergic Polymorphic Ventricular Tachycardia: A Single Center’s Early Experience. JACC: Clinical Electrophysiology 2016;**2**(3):253-262.

194. van der Werf C, Kannankeril PJ, Sacher F, Krahn AD, Viskin S, Leenhardt A, Shimizu W, Sumitomo N, Fish FA, Bhuiyan ZA, Willems AR, van der Veen MJ, Watanabe H, Laborderie J, Haïssaguerre M, Knollmann BC, Wilde AAM. Flecainide Therapy Reduces Exercise-Induced Ventricular Arrhythmias in Patients With Catecholaminergic Polymorphic Ventricular Tachycardia. Journal of the American College of Cardiology 2011;**57**(22):2244-2254.

195. Khoury A, Marai I, Suleiman M, Blich M, Lorber A, Gepstein L, Boulos M. Flecainide therapy suppresses exercise-induced ventricular arrhythmias in patients with CASQ2-associated catecholaminergic polymorphic ventricular tachycardia. Heart Rhythm 2013;**10**(11):1671-1675.

196. Watanabe H, van der Werf C, Roses-Noguer F, Adler A, Sumitomo N, Veltmann C, Rosso R, Bhuiyan ZA, Bikker H, Kannankeril PJ, Horie M, Minamino T, Viskin S, Knollmann BC, Till J, Wilde AAM. Effects of flecainide on exercise-induced ventricular arrhythmias and recurrences in genotype-negative patients with catecholaminergic polymorphic ventricular tachycardia. Heart Rhythm 2013;**10**(4):542-547.

197. De Ferrari GM, Dusi V, Spazzolini C, Bos JM, Abrams DJ, Berul CI, Crotti L, Davis AM, Eldar M, Kharlap M, Khoury A, Krahn AD, Leenhardt A, Moir CR, Odero A, Olde Nordkamp L, Paul T, Rosés i Noguer F, Shkolnikova M, Till J, Wilde AAM, Ackerman MJ, Schwartz PJ. Clinical Management of Catecholaminergic Polymorphic Ventricular Tachycardia: The Role of Left Cardiac Sympathetic Denervation. Circulation 2015;**131**(25):2185-2193.

198. Kannankeril PJ, Moore JP, Cerrone M, et al. Efficacy of flecainide in the treatment of catecholaminergic polymorphic ventricular tachycardia: A randomized clinical trial. JAMA Cardiology 2017;**2**(7):759-766.

199. Lampert R, Olshansky B, Heidbuchel H, Lawless C, Saarel E, Ackerman M, Calkins H, Estes NAM, Link MS, Maron BJ, Marcus F, Scheinman M, Wilkoff BL, Zipes DP, Berul CI, Cheng A, Law I, Loomis M, Barth C, Brandt C, Dziura J, Li F, Cannom D. Safety of Sports for Athletes With Implantable Cardioverter-Defibrillators: Results of a Prospective, Multinational Registry. Circulation 2013;**127**(20):2021-2030.

200. Corrado D, Link MS, Calkins H. Arrhythmogenic Right Ventricular Cardiomyopathy. N Engl J Med 2017;**376**(15):1489-90.

201. Finocchiaro G, Papadakis M, Robertus JL, Dhutia H, Steriotis AK, Tome M, Mellor G, Merghani A, Malhotra A, Behr E, Sharma S, Sheppard MN. Etiology of Sudden Death in Sports: Insights From a United Kingdom Regional Registry. J Am Coll Cardiol 2016;**67**(18):2108-2115.

202. Denis A, Sacher F, Derval N, Lim HS, Cochet H, Shah AJ, Daly M, Pillois X, Ramoul K, Komatsu Y, Zemmoura A, Amraoui S, Ritter P, Ploux S, Bordachar P, Hocini M, Jais P, Haissaguerre M. Diagnostic value of isoproterenol testing in arrhythmogenic right ventricular cardiomyopathy. Circ Arrhythm Electrophysiol 2014;**7**(4):590-7.

203. Peters S, Trummel M, Meyners W. Prevalence of right ventricular dysplasia-cardiomyopathy in a non-referral hospital. Int J Cardiol 2004;**97**(3):499-501.

204. Hoorntje ET, Te Rijdt WP, James CA, Pilichou K, Basso C, Judge DP, Bezzina CR, van Tintelen JP. Arrhythmogenic cardiomyopathy: pathology, genetics, and concepts in pathogenesis. Cardiovasc Res 2017;**113**(12):1521-1531.

205. d'Amati G, Bagattin A, Bauce B, Rampazzo A, Autore C, Basso C, King K, Romeo MD, Gallo P, Thiene G, Danieli GA, Nava A. Juvenile sudden death in a family with polymorphic ventricular arrhythmias caused by a novel RyR2 gene mutation: evidence of specific morphological substrates. Hum Pathol 2005;**36**(7):761-7.

206. Nasir K, Bomma C, Tandri H, Roguin A, Dalal D, Prakasa K, Tichnell C, James C, Spevak PJ, Marcus F, Calkins H. Electrocardiographic features of arrhythmogenic right ventricular dysplasia/cardiomyopathy according to disease severity: a need to broaden diagnostic criteria. Circulation 2004;**110**(12):1527-34.

207. Aquaro GD, Barison A, Todiere G, Grigoratos C, Ait Ali L, Di Bella G, Emdin M, Festa P. Usefulness of Combined Functional Assessment by Cardiac Magnetic Resonance and Tissue Characterization Versus Task Force Criteria for Diagnosis of Arrhythmogenic Right Ventricular Cardiomyopathy. Am J Cardiol 2016;**118**(11):1730-1736.

208. Mast TP, Taha K, Cramer MJ, Lumens J, van der Heijden JF, Bouma BJ, van den Berg MP, Asselbergs FW, Doevendans PA, Teske AJ. The Prognostic Value of Right Ventricular Deformation Imaging in Early Arrhythmogenic Right Ventricular Cardiomyopathy. JACC Cardiovasc Imaging 2018.

209. Te Riele A, James CA, Sawant AC, Bhonsale A, Groeneweg JA, Mast TP, Murray B, Tichnell C, Dooijes D, van Tintelen JP, Judge DP, van der Heijden JF, Crosson J, Hauer RNW, Calkins H, Tandri H. Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy in the Pediatric Population: Clinical Characterization and Comparison With Adult-Onset Disease. JACC Clin Electrophysiol 2015;**1**(6):551-560.

210. Corrado D, Wichter T, Link MS, Hauer R, Marchlinski F, Anastasakis A, Bauce B, Basso C, Brunckhorst C, Tsatsopoulou A, Tandri H, Paul M, Schmied C, Pelliccia A, Duru F, Protonotarios N, Estes NA, 3rd, McKenna WJ, Thiene G, Marcus FI, Calkins H. Treatment of arrhythmogenic right ventricular cardiomyopathy/dysplasia: an international task force consensus statement. Eur Heart J 2015;**36**(46):3227-37.

211. Sawant AC, Te Riele AS, Tichnell C, Murray B, Bhonsale A, Tandri H, Judge DP, Calkins H, James CA. Safety of American Heart Association-recommended minimum exercise for desmosomal mutation carriers. Heart Rhythm 2016;**13**(1):199-207.

212. Martherus R, Jain R, Takagi K, Mendsaikhan U, Turdi S, Osinska H, James JF, Kramer K, Purevjav E, Towbin JA. Accelerated cardiac remodeling in desmoplakin transgenic mice in response to endurance exercise is associated with perturbed Wnt/beta-catenin signaling. Am J Physiol Heart Circ Physiol 2016;**310**(2):H174-87.

213. Moncayo-Arlandi J, Guasch E, Sanz-de la Garza M, Casado M, Garcia NA, Mont L, Sitges M, Knoll R, Buyandelger B, Campuzano O, Diez-Juan A, Brugada R. Molecular disturbance underlies to arrhythmogenic cardiomyopathy induced by transgene content, age and exercise in a truncated PKP2 mouse model. Hum Mol Genet 2016;**25**(17):3676-3688.

214. Kirchhof P, Fabritz L, Zwiener M, Witt H, Schafers M, Zellerhoff S, Paul M, Athai T, Hiller KH, Baba HA, Breithardt G, Ruiz P, Wichter T, Levkau B. Age- and training-dependent development of arrhythmogenic right ventricular cardiomyopathy in heterozygous plakoglobin-deficient mice. Circulation 2006;**114**(17):1799-806.

215. Saberniak J, Hasselberg NE, Borgquist R, Platonov PG, Sarvari SI, Smith HJ, Ribe M, Holst AG, Edvardsen T, Haugaa KH. Vigorous physical activity impairs myocardial function in patients with arrhythmogenic right ventricular cardiomyopathy and in mutation positive family members. Eur J Heart Fail 2014;**16**(12):1337-44.

216. Mazzanti A, Ng K, Faragli A, Maragna R, Chiodaroli E, Orphanou N, Monteforte N, Memmi M, Gambelli P, Novelli V, Bloise R, Catalano O, Moro G, Tibollo V, Morini M, Bellazzi R, Napolitano C, Bagnardi V, Priori SG. Arrhythmogenic Right Ventricular Cardiomyopathy: Clinical Course and Predictors of Arrhythmic Risk. J Am Coll Cardiol 2016;**68**(23):2540-2550.

217. Lie OH, Rootwelt-Norberg C, Dejgaard LA, Leren IS, Stokke MK, Edvardsen T, Haugaa KH. Prediction of Life-Threatening Ventricular Arrhythmia in Patients With Arrhythmogenic Cardiomyopathy: A Primary Prevention Cohort Study. JACC Cardiovasc Imaging 2018;**11**(10):1377-1386.

218. Wang W, Orgeron G, Tichnell C, Murray B, Crosson J, Monfredi O, Cadrin-Tourigny J, Tandri H, Calkins H, James CA. Impact of Exercise Restriction on Arrhythmic Risk Among Patients With Arrhythmogenic Right Ventricular Cardiomyopathy. J Am Heart Assoc 2018;**7**(12).

219. La Gerche A, Robberecht C, Kuiperi C, Nuyens D, Willems R, de Ravel T, Matthijs G, Heidbuchel H. Lower than expected desmosomal gene mutation prevalence in endurance athletes with complex ventricular arrhythmias of right ventricular origin. Heart 2010;**96**(16):1268-74.

220. Sawant AC, Bhonsale A, te Riele AS, Tichnell C, Murray B, Russell SD, Tandri H, Tedford RJ, Judge DP, Calkins H, James CA. Exercise has a disproportionate role in the pathogenesis of arrhythmogenic right ventricular dysplasia/cardiomyopathy in patients without desmosomal mutations. J Am Heart Assoc 2014;**3**(6):e001471.

221. James CA, Calkins H. Arrhythmogenic Right Ventricular Cardiomyopathy: Progress Toward Personalized Management. Annu Rev Med 2018.

222. Cadrin-Tourigny J, Bosman LP, Nozza A, Wang W, Tadros R, Bhonsale A, Bourfiss M, Fortier A, Lie OH, Saguner AM, Svensson A, Andorin A, Tichnell C, Murray B, Zeppenfeld K, van den Berg MP, Asselbergs FW, Wilde AAM, Krahn AD, Talajic M, Rivard L, Chelko S, Zimmerman SL, Kamel IR, Crosson JE, Judge DP, Yap SC, van der Heijden JF, Tandri H, Jongbloed JDH, Guertin MC, van Tintelen JP, Platonov PG, Duru F, Haugaa KH, Khairy P, Hauer RNW, Calkins H, Te Riele A, James CA. A new prediction model for ventricular arrhythmias in arrhythmogenic right ventricular cardiomyopathy. Eur Heart J 2019;**40**(23):1850-1858.

223. Pinto YM, Elliott PM, Arbustini E, Adler Y, Anastasakis A, Bohm M, Duboc D, Gimeno J, de Groote P, Imazio M, Heymans S, Klingel K, Komajda M, Limongelli G, Linhart A, Mogensen J, Moon J, Pieper PG, Seferovic PM, Schueler S, Zamorano JL, Caforio AL, Charron P. Proposal for a revised definition of dilated cardiomyopathy, hypokinetic non-dilated cardiomyopathy, and its implications for clinical practice: a position statement of the ESC working group on myocardial and pericardial diseases. Eur Heart J 2016;**37**(23):1850-8.

224. Quarta G, Papadakis M, Donna PD, Maurizi N, Iacovoni A, Gavazzi A, Senni M, Olivotto I. Grey zones in cardiomyopathies: defining boundaries between genetic and iatrogenic disease. Nat Rev Cardiol 2017;**14**(2):102-112.

225. Authors/Task Force m, Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, Hagege AA, Lafont A, Limongelli G, Mahrholdt H, McKenna WJ, Mogensen J, Nihoyannopoulos P, Nistri S, Pieper PG, Pieske B, Rapezzi C, Rutten FH, Tillmanns C, Watkins H. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J 2014;**35**(39):2733-79.

226. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980-2006. Circulation 2009;**119**(8):1085-92.

227. Jensen MK, Havndrup O, Christiansen M, Andersen PS, Diness B, Axelsson A, Skovby F, Kober L, Bundgaard H. Penetrance of hypertrophic cardiomyopathy in children and adolescents: a 12-year follow-up study of clinical screening and predictive genetic testing. Circulation 2013;**127**(1):48-54.

228. Gray B, Ingles J, Semsarian C. Natural history of genotype positive-phenotype negative patients with hypertrophic cardiomyopathy. Int J Cardiol 2011;**152**(2):258-9.

229. McKenna WJ, Behr ER. Hypertrophic cardiomyopathy: management, risk stratification, and prevention of sudden death. Heart 2002;**87**(2):169-76.

230. Haissaguerre M, Derval N, Sacher F, Jesel L, Deisenhofer I, de Roy L, Pasquie JL, Nogami A, Babuty D, Yli-Mayry S, De Chillou C, Scanu P, Mabo P, Matsuo S, Probst V, Le Scouarnec S, Defaye P, Schlaepfer J, Rostock T, Lacroix D, Lamaison D, Lavergne T, Aizawa Y, Englund A, Anselme F, O'Neill M, Hocini M, Lim KT, Knecht S, Veenhuyzen GD, Bordachar P, Chauvin M, Jais P, Coureau G, Chene G, Klein GJ, Clementy J. Sudden cardiac arrest associated with early repolarization. N Engl J Med 2008;**358**(19):2016-23.

231. Noseworthy PA, Weiner R, Kim J, Keelara V, Wang F, Berkstresser B, Wood MJ, Wang TJ, Picard MH, Hutter AM, Jr., Newton-Cheh C, Baggish AL. Early repolarization pattern in competitive athletes: clinical correlates and the effects of exercise training. Circ Arrhythm Electrophysiol 2011;**4**(4):432-40.

232. Calloe K, Broendberg AK, Christensen AH, Pedersen LN, Olesen MS, de Los Angeles Tejada M, Friis S, Thomsen MB, Bundgaard H, Jensen HK. Multifocal atrial and ventricular premature contractions with an increased risk of dilated cardiomyopathy caused by a Nav1.5 gain-of-function mutation (G213D). Int J Cardiol 2018;**257**:160-167.

233. Bundgaard H, Jons C, Lodder EM, Izarzugaza JMG, Romero Herrera JA, Pehrson S, Tfelt-Hansen J, Ahlberg G, Olesen MS, Holst AG, Wellens H, de Villiers C, Hastings R, Stuart G, Brunak S, Wilde AAM, Watkins H, Christensen AH. A Novel Familial Cardiac Arrhythmia Syndrome with Widespread ST-Segment Depression. N Engl J Med 2018;**379**(18):1780-1781.

234. Senden PJ, Sabelis LW, Zonderland ML, van de Kolk R, Meiss L, de Vries WR, Bol E, Mosterd WL. Determinants of maximal exercise performance in chronic heart failure. Eur J Cardiovasc Prev Rehabil 2004;**11**(1):41-7.

235. Deharo JC, Bongiorni MG, Rozkovec A, Bracke F, Defaye P, Fernandez-Lozano I, Golzio PG, Hansky B, Kennergren C, Manolis AS, Mitkowski P, Platou ES, European Heart Rhythm A. Pathways for training and accreditation for transvenous lead extraction: a European Heart Rhythm Association position paper. Europace 2012;**14**(1):124-34.

236. Conraads VM, Vanderheyden M, Paelinck B, Verstreken S, Blankoff I, Miljoen H, De Sutter J, Beckers P. The effect of endurance training on exercise capacity following cardiac resynchronization therapy in chronic heart failure patients: a pilot trial. Eur J Cardiovasc Prev Rehabil 2007;**14**(1):99-106.

237. Schuger CD, Mittleman R, Habbal B, Wagshal A, Huang SK. Ventricular lead transection and atrial lead damage in a young softball player shortly after the insertion of a permanent pacemaker. Pacing Clin Electrophysiol 1992;**15**(9):1236-9.

238. Deering JA, Pederson DN. Pacemaker lead fracture associated with weightlifting: a report of two cases. Mil Med 1993;**158**(12):833-4.

239. Gould L, Betzu R, Taddeo M, Judge JD, Lee J. Pulse generator failure due to blunt trauma. Clin Cardiol 1988;**11**(8):581-2.

240. Grieco JG, Scanlon PJ, Pifarre R. Pacing lead fracture after a deceleration injury. Ann Thorac Surg 1989;**47**(3):453-4.

241. Altun A, Erdogan O. Pacemaker lead failure suggestive of crush injury. Cardiol Rev 2003;**11**(5):256.

242. Noble SL, Burri H, Sunthorn H. Complete section of pacemaker lead due to subclavian crush. Med J Aust 2005;**182**(12):643.

243. Jain P, Kaul U, Wasir HS. Myopotential inhibition of unipolar demand pacemakers: utility of provocative manoeuvres in assessment and management. Int J Cardiol 1992;**34**(1):33-9.

244. Chan NY, Kwong NP, Cheong AP. Venous access and long-term pacemaker lead failure: comparing contrast-guided axillary vein puncture with subclavian puncture and cephalic cutdown. Europace 2017;**19**(7):1193-1197.

245. Lamas GA, Keefe JM. The effects of equitation (horseback riding) on a motion responsive DDDR pacemaker. Pacing Clin Electrophysiol 1990;**13**(11 Pt 1):1371-3.

246. Exner DV, Rothschild JM, Heal S, Gillis AM. Unipolar sensing in contemporary pacemakers: using myopotential testing to define optimal sensitivity settings. J Interv Card Electrophysiol 1998;**2**(1):33-40.

247. Tomzik J, Koltermann KC, Zabel M, Willich SN, Reinhold T. Quality of Life in Patients with an Implantable Cardioverter Defibrillator: A Systematic Review. Front Cardiovasc Med 2015;**2**:34.

248. Rahman B, Macciocca I, Sahhar M, Kamberi S, Connell V, Duncan RE. Adolescents with implantable cardioverter defibrillators: a patient and parent perspective. Pacing Clin Electrophysiol 2012;**35**(1):62-72.

249. Vanhees L, Geladas N, Hansen D, Kouidi E, Niebauer J, Reiner Z, Cornelissen V, Adamopoulos S, Prescott E, Borjesson M, Bjarnason-Wehrens B, Bjornstad HH, Cohen-Solal A, Conraads V, Corrado D, De Sutter J, Doherty P, Doyle F, Dugmore D, Ellingsen O, Fagard R, Giada F, Gielen S, Hager A, Halle M, Heidbuchel H, Jegier A, Mazic S, McGee H, Mellwig KP, Mendes M, Mezzani A, Pattyn N, Pelliccia A, Piepoli M, Rauch B, Schmidt-Trucksass A, Takken T, van Buuren F, Vanuzzo D. Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular risk factors: recommendations from the EACPR. Part II. European journal of preventive cardiology 2012;**19**(5):1005-33.

250. Isaksen K, Morken IM, Munk PS, Larsen AI. Exercise training and cardiac rehabilitation in patients with implantable cardioverter defibrillators: a review of current literature focusing on safety, effects of exercise training, and the psychological impact of programme participation. Eur J Prev Cardiol 2012;**19**(4):804-12.

251. Heidbuchel H, Carre F. Exercise and competitive sports in patients with an implantable cardioverter-defibrillator. Eur Heart J 2014;**35**(44):3097-102.

252. Lampert R, Olshansky B, Heidbuchel H, Lawless C, Saarel E, Ackerman M, Calkins H, Estes NA, Link MS, Maron BJ, Marcus F, Scheinman M, Wilkoff BL, Zipes DP, Berul CI, Cheng A, Law I, Loomis M, Barth C, Brandt C, Dziura J, Li F, Cannom D. Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry. Circulation 2013;**127**(20):2021-30.

253. Lampert R, Olshansky B, Heidbuchel H, Lawless C, Saarel E, Ackerman M, Calkins H, Estes NAM, Link MS, Maron BJ, Marcus F, Scheinman M, Wilkoff BL, Zipes DP, Berul CI, Cheng A, Jordaens L, Law I, Loomis M, Willems R, Barth C, Broos K, Brandt C, Dziura J, Li F, Simone L, Vandenberghe K, Cannom D. Safety of Sports for Athletes With Implantable Cardioverter-Defibrillators: Long-Term Results of a Prospective Multinational Registry. Circulation 2017;**135**(23):2310-2312.

254. Heidbuchel H, Willems R, Jordaens L, Olshansky B, Carre F, Lozano IF, Wilhelm M, Mussigbrodt A, Huybrechts W, Morgan J, Anfinsen OG, Prior D, Mont L, Mairesse GH, Boveda S, Duru F, Kautzner J, Viskin S, Geelen P, Cygankiewicz I, Hoffmann E, Vandenberghe K, Cannom D, Lampert R. Intensive recreational athletes in the prospective multinational ICD Sports Safety Registry: Results from the European cohort. Eur J Prev Cardiol 2019;**26**(7):764-775.

255. Olshansky B, Atteya G, Cannom D, Heidbuchel H, Saarel E, Anfinsen OG, Cheng A, Gold MR, Mussigbrodt A, Patton KK, Saxon L, Wilkoff B, Willems R, Dziura J, Li F, Brandt C, Simone L, Matthias W, Lampert R. Competitive athletes with implantable cardioverter-defibrillators-How to program? Data from the Implantable Cardioverter-Defibrillator Sports Registry. Heart Rhythm 2018.

256. Theuns D, Brouwer TF, Jones PW, Allavatam V, Donnelley S, Auricchio A, Knops RE, Burke MC. Prospective blinded evaluation of a novel sensing methodology designed to reduce inappropriate shocks by the subcutaneous implantable cardioverter-defibrillator. Heart Rhythm 2018;**15**(10):1515-1522.

257. Auricchio A, Schloss EJ, Kurita T, Meijer A, Gerritse B, Zweibel S, AlSmadi FM, Leng CT, Sterns LD, PainFree SSTI. Low inappropriate shock rates in patients with single- and dual/triple-chamber implantable cardioverter-defibrillators using a novel suite of detection algorithms: PainFree SST trial primary results. Heart Rhythm 2015;**12**(5):926-36.

258. Camm CF, James CA, Tichnell C, Murray B, Bhonsale A, te Riele AS, Judge DP, Tandri H, Calkins H. Prevalence of atrial arrhythmias in arrhythmogenic right ventricular dysplasia/cardiomyopathy. Heart Rhythm 2013;**10**(11):1661-8.

259. Heidbuchel H, Anne W, Willems R, Adriaenssens B, Van de Werf F, Ector H. Endurance sports is a risk factor for atrial fibrillation after ablation for atrial flutter. Int J Cardiol 2006;**107**(1):67-72.

260. Andersen K, Farahmand B, Ahlbom A, Held C, Ljunghall S, Michaelsson K, Sundstrom J. Risk of arrhythmias in 52 755 long-distance cross-country skiers: a cohort study. Eur Heart J 2013;**34**(47):3624-31.

261. Zeitler EP, Sanders GD, Singh K, Greenfield RA, Gillis AM, Wilkoff BL, Piccini JP, Al-Khatib SM. Single vs. dual chamber implantable cardioverter-defibrillators or programming of implantable cardioverter-defibrillators in patients without a bradycardia pacing indication: systematic review and meta-analysis. Europace 2018;**20**(10):1621-1629.

262. Wilkoff BL, Fauchier L, Stiles MK, Morillo CA, Al-Khatib SM, Almendral J, Aguinaga L, Berger RD, Cuesta A, Daubert JP, Dubner S, Ellenbogen KA, Estes NA, 3rd, Fenelon G, Garcia FC, Gasparini M, Haines DE, Healey JS, Hurtwitz JL, Keegan R, Kolb C, Kuck KH, Marinskis G, Martinelli M, McGuire M, Molina LG, Okumura K, Proclemer A, Russo AM, Singh JP, Swerdlow CD, Teo WS, Uribe W, Viskin S, Wang CC, Zhang S, Document R. 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. Europace 2016;**18**(2):159-83.

263. Deisenhofer I, Kolb C, Ndrepepa G, Schreieck J, Karch M, Schmieder S, Zrenner B, Schmitt C. Do current dual chamber cardioverter defibrillators have advantages over conventional single chamber cardioverter defibrillators in reducing inappropriate therapies? A randomized, prospective study. J Cardiovasc Electrophysiol 2001;**12**(2):134-42.

264. Sinha AM, Stellbrink C, Schuchert A, Mox B, Jordaens L, Lamaison D, Gill J, Kaplan A, Merkely B. Clinical experience with a new detection algorithm for differentiation of supraventricular from ventricular tachycardia in a dual-chamber defibrillator. J Cardiovasc Electrophysiol 2004;**15**(6):646-52.

265. Akar JG, Bao H, Jones PW, Wang Y, Varosy PD, Masoudi FA, Stein KM, Saxon LA, Normand SL, Curtis JP. Use of Remote Monitoring Is Associated With Lower Risk of Adverse Outcomes Among Patients With Implanted Cardiac Defibrillators. Circ Arrhythm Electrophysiol 2015;**8**(5):1173-80.

266. Varma N, Piccini JP, Snell J, Fischer A, Dalal N, Mittal S. The Relationship Between Level of Adherence to Automatic Wireless Remote Monitoring and Survival in Pacemaker and Defibrillator Patients. J Am Coll Cardiol 2015;**65**(24):2601-2610.

**Table 1. Classification of premature ventricular beats in athletes****Any uncommon finding qualifies the VPB as ‘uncommon’**

|  |  |  |
| --- | --- | --- |
|  | **COMMON**  **Likely benign** | **UNCOMMON**  **Potentially malignant** |
| **VPBs characteristics** |  |  |
| Morphology | LBBB/inferior axis;  RBBB and narrow QRS | LBBB/intermediate or superior axis;  RBBB and wide QRS |
| Response to exercise | Decrease/suppression | Persistence/increase |
| Complexity | Isolated, monomorphic | Repetitive, polymorphic |
| Short coupling interval (R on T) | No | Yes |
| **Clinical findings** |  |  |
| Symptoms | No | Yes |
| Family history of premature SCD\* or cardiomyopathy | No | Yes |
| ECG abnormalities | No | Yes |
| Imaging abnormalities | No | Yes |

\*premature sudden cardiac death (SCD) or cardiomyopathy is defined as that occurring before 40 year-old in males and before 50 year-old in females

LBBB=left bundle branch block; VPBs=premature ventricular beats; RBBB=right bundle branch block; SCD=sudden cardiac death

Adapted from D’Ascenzi F, et al. Scand J Med Sci Sports 201751

**Table 2. Diagnostic criteria for Long QT Syndrome**

|  |  |  |  |
| --- | --- | --- | --- |
|  | | | **POINTS** |
| **ELECTROCARDIOGRAPHIC FINDINGS#** | | |  |
| A | QTc^ | ≥ 480 ms | 3 |
| 460 – 479 ms | 2 |
| 450 – 459 (male) ms | 1 |
| B | QTc^ 4th minute of recovery from exercise stress test ≥ 480 ms | | 1 |
| C | TORSADE DE POINTES \* | | 2 |
| D | T WAVE ALTERNANS | | 1 |
| E | NOTCHED T WAVE IN 3 LEADS | | 1 |
| F | LOW HEART RATE FOR AGE @ | | 0.5 |
| **CLINICAL HISTORY** | | |  |
| A | SYNCOPE \* | WITH STRESS | 2 |
| WITHOUT STRESS | 1 |
| B | CONGENITAL DEAFNESS | | 0.5 |
| **FAMILY HISTORY** | | |  |
| A | FAMILY MEMBERS WITH DEFINITE LQTS $ | | 1 |
| B | UNEXPLAINED SUDDEN CARDIAC DEATH BELOW AGE 30 AMONG IMMEDIATE FAMILY MEMBERS $ | | 0.5 |

SCORE: ≤ 1 point: low probability of LQTS   
 1.5 to 3 points: intermediate probability of LQTS   
 ≥ 3.5 points high probability of LQTS

# In the absence of medications or disorders known to affect these electrocardiographic features

^ QTc calculated by Bazett's formula where QTc = QT/√RR

\* Mutually exclusive

@ Resting heart rate below the 2nd percentile for age

$ The same family member cannot be counted in A and B

Adapted with permission from Schwartz & Crotti, Circulation (2011)108

# Figure legends

Figure 1

Examples of common (A and B) and uncommon (C and D) morphologies of premature ventricular beats (VPBs). A) VPB with LBBB morphology and inferior axis originating from right ventricular outflow tract; B) VPB with RBBB and narrow configuration with superior axis originating from the fasciculum; C) VPB with LBBB morphology and superior axis, originating from right ventricular apex; D) VPB with RBBB and wide QRS configuration with superior axis, originating from the left ventricle.   
Adapted from D’Ascenzi F, et al. Scand J Med Sci Sports 201751

Figure 2

A practical flow-chart for clinical evaluation of VPBs in the athlete.

VPB: ventricular premature beats; P/E: physical exam; CE: contrast-enhanced; POS: positive; NEG: negative.   
Adapted from D’Ascenzi F, et al. Scand J Med Sci Sports 201751

Figure 3

Stress test in a patient with Brugada syndrome. At baseline, a normal ECG is observed, with no precordial ST-segment elevation. During exercise, the right precordial leads show a mild ST-segment elevation and gradual T-wave negativation. During recovery, the Brugada type 1 pattern becomes evident and ventricular premature contractions occur. After 5 minutes of observation, the Brugada pattern and the ventricular ectopy disappears.

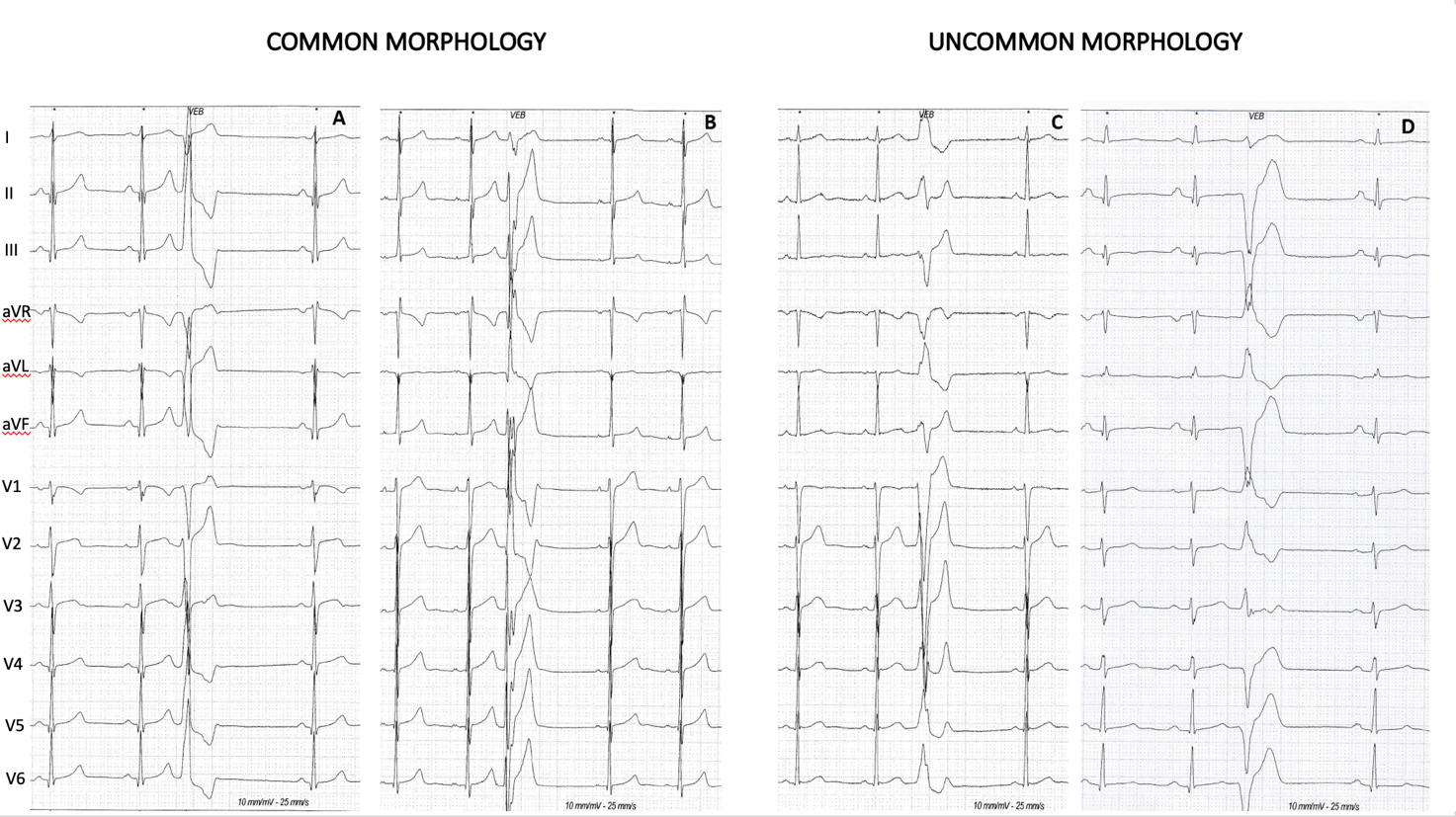
Figure 4

Diagnostic Brugada type 1 pattern showing ST segment elevation ≥2 mm followed by a negative T-wave in ≥1 of the right precordial leads.

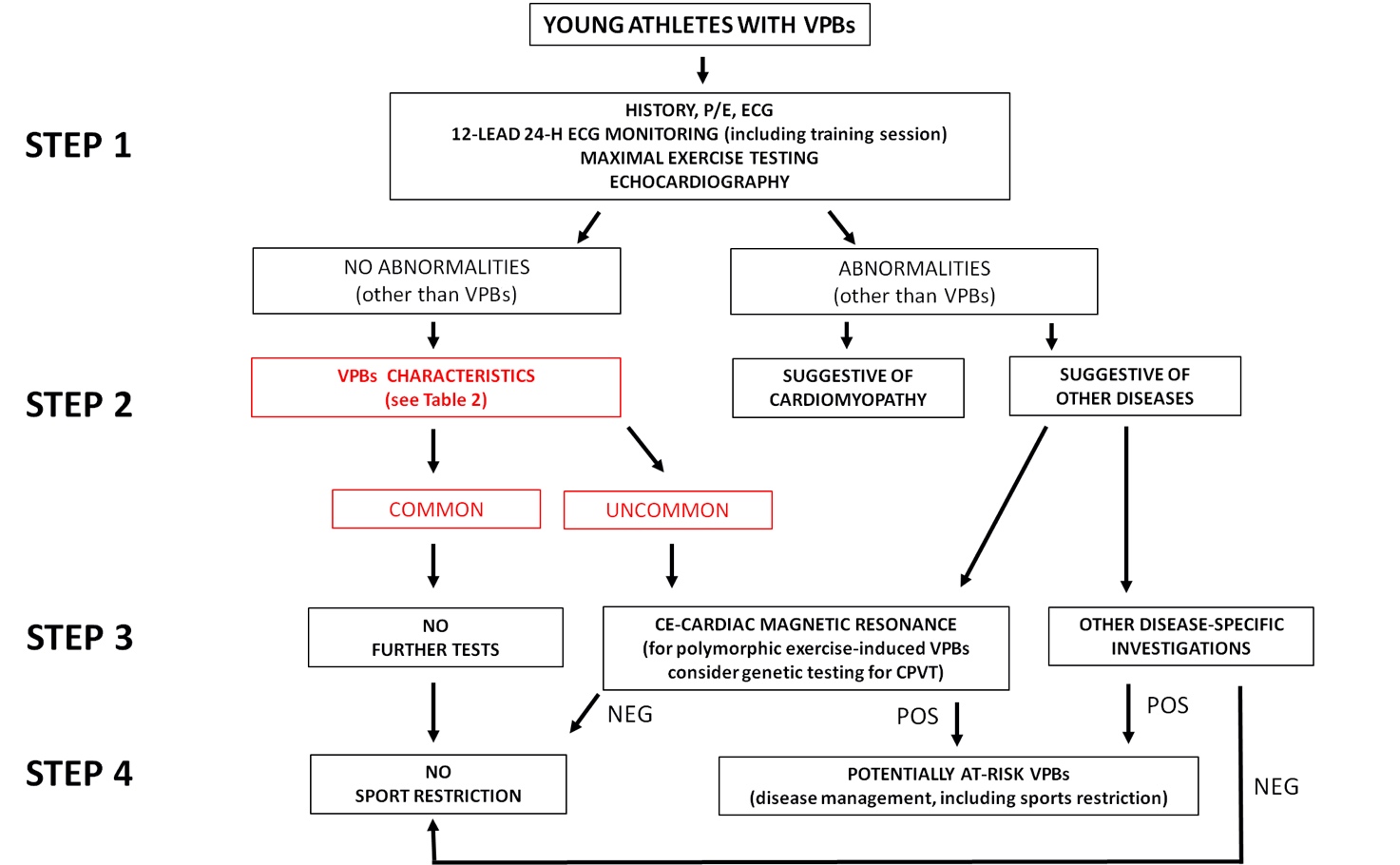
Figure 5

Stress test in a patient with catecholaminergic polymorphic ventricular tachycardia. At baseline, there is normal sinus rhythm with no ventricular ectopy. During exercise, as the heart rate increases there are progressively more complex ventricular arrhythmias. During early recovery, the ventricular ectopic activity ceases.

**Figure 1**



**Figure 2**

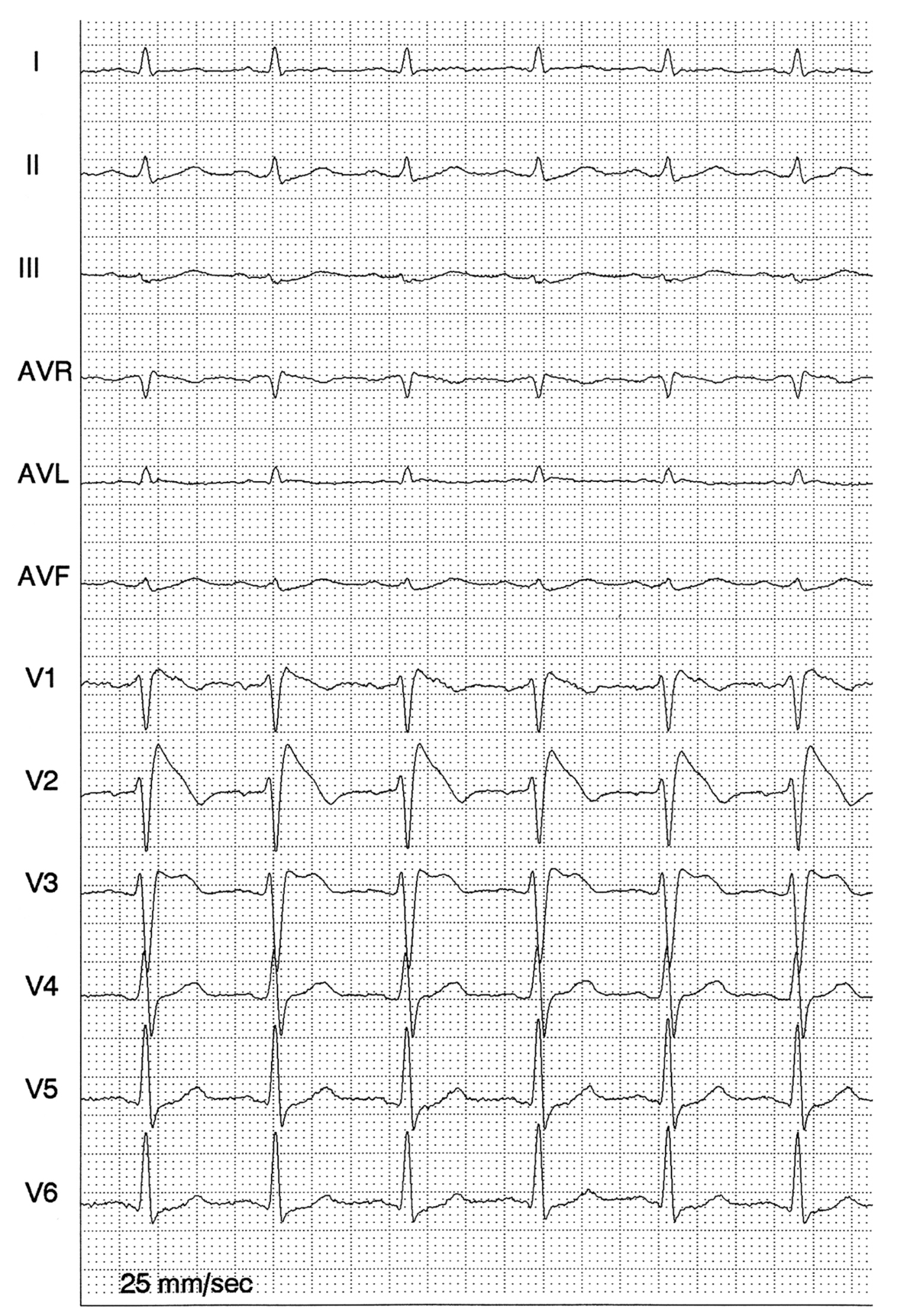


**Figure 3**

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**Figure 4**



**Figure 5**

