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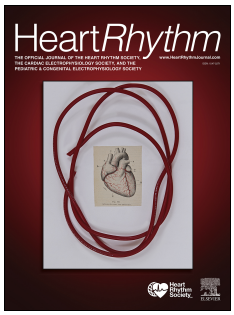

2024 HRS expert consensus statement on arrhythmias in the athlete: Evaluation, treatment, and return to play

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2024 HRS expert consensus statement on arrhythmias in the athlete: Evaluation, treatment, and return to play

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KEYWORDS Arrhythmogenic diseases, athletes, electrophysiology, emergency action plans, return to play, risk assessment, sports cardiology, sudden cardiac arrest, sudden cardiac death, shared decision-making

ABBREVIATIONS AAD = antiarrhythmic drug; AAOCA = anomalous aortic origin of coronary arteries; ABiMVP = arrhythmogenic bileaflet mitral valve prolapse; ACM = arrhythomogenic cardiomyopathy; AED = automated emergency defibrillator; AFL = atrial flutter; AN-SUD = autopsy-negative sudden unexplained death; AP = accessory pathway; APERP = accessory pathway effective refractory period; ARVC = arrhythmogenic right ventricular cardiomyopathy; ATP = antitachycardia pacing; AV = atrioventricular; AVRT = atrioventricular reciprocating tachycardia; CHD = congenital heart disease; CK = creatine kinase; CMR = cardiac magnetic resonance imaging; CPET = cardiopulmonary exercise testing; CPP = cardiac physiologic pacing; CPR = cardiopulmonary resuscitation; CRT = cardiac resynchronization therapy; CPVT = catecholaminergic polymorphic ventricular tachycardia; CT = computed tomography;

CTA = computed tomographic angiography; CTI = cavotricuspid isthmus; DCM = dilated cardiomyopathy; Dx = diagnosis; ECG = electrocardiogram; EICR = exercise-induced cardiac remodeling; EMS = emergency medical services; HCM = hypertrophic cardiomyopathy; AS = inherited arrhythmia syndrome; ICD = implantable cardioverter-defibrillator; LAAO = left atrial appendage occlusion; LCSD = left cardiac sympathetic denervation; LQTS = long QT syndrome; LTE = life-threatening events; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract; PAC = premature atrial contraction; PVC = premature ventricular contraction; PVI = pulmonary vein isolation; RVOT = right ventricular outflow tract; RWI = relationships with industry; SCA = sudden cardiac arrest; SCA/D = sudden cardiac arrest and death; SCD = sudden cardiac death; SCT = sickle cell trait; SPERRI = shortest preexcited R-R interval; SQTS = short QT syndrome; TTM = targeted temperature management; VF = ventricular fibrillation; WPW = Wolff-Parkinson-White

Developed in collaboration with the American College of Cardiology (ACC), the American Heart Association (AHA), the American Medical Society for Sports Medicine (AMSSM), the Asia Pacific Heart Rhythm Society (APHRS), the European Heart Rhythm Association (EHRA), the Latin American Heart Rhythm Society (LAHRS), and the Pediatric and Congenital Electrophysiology Society (PACES). Endorsed by AMSSM, APHRS, EHRA, LAHRS, and PACES.

Abstract

Youth and adult participation in sports continues to increase, and athletes may be diagnosed with potentially arrhythmogenic cardiac conditions. This international multidisciplinary document is intended to guide electrophysiologists, sports cardiologists, and associated health care team members in the diagnosis, treatment, and management of arrhythmic conditions in the athlete with the goal of facilitating return to sport and avoiding the harm caused by restriction. Expert, disease-specific risk assessment in the context of athlete symptoms and diagnoses is emphasized throughout the document. After appropriate risk assessment, management of arrhythmias geared toward return to play when possible is addressed. Other topics include shared decision-making and emergency action planning. The goal of this document is to provide evidence-based recommendations impacting all areas in the care of athletes with arrhythmic conditions. Areas in need of further study are also discussed.

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Top 10 Take-Home Messages

1. For many arrhythmogenic disease entities, current data in athletes, while often not large enough to be definitive, have not confirmed increased arrhythmic risk of continuing sports participation for athletes who are appropriately risk-assessed and treated, and thus the approach to return to play is one of individualized shared decision-making.
2. The overarching goal in caring for athletes should be facilitating the athlete's return to sport if this is the desired outcome, through appropriate risk assessment and athlete-focused management of their arrhythmic condition. Restriction from sport is not benign.
3. Both venue-based and individualized emergency action plans including plans for early defibrillation are critical to survival of athletes with sudden cardiac arrest.
4. Disease-specific and guideline-based risk assessment and treatment of arrhythmogenic conditions prior to return to play is critical.
5. For patients with underlying complex arrhythmias, appropriate strategies for sudden death prevention and arrhythmia suppression are needed prior to return to play, including confirmation of suppression of arrhythmia during exercise.
6. Treatment decisions—including those regarding antiarrhythmic medications, ablation, and devices—should take athletic performance and training into consideration.
7. Exercise stress testing in athletes for diagnostic purposes or defining therapeutic efficacy should mimic the athlete's sport where possible and be terminated based on maximal effort, symptoms, and/or documentation of arrhythmia.
8. Endurance exercise in particular may contribute to arrhythmogenic conditions such as atrial fibrillation and genotype-negative arrhythmogenic right ventricular cardiomyopathy; risks and benefits of continued participation in endurance sports should be carefully weighed in athletes with these conditions.
9. The choice of pacemaker or defibrillator form factor and programming parameters should take into consideration the type of sport and training required so as to minimize risk of damage to the system.
10. Athletes with a diagnosis of Wolff-Parkinson-White pattern or syndrome should be allowed to return to play pending timely expert evaluation and treatment, as there is lack of conclusive evidence of increased risk of life-threatening arrhythmias with athletic participation.

Section 1 Introduction

1.1 Preamble

The Heart Rhythm Society (HRS) has developed scientific and clinical documents guiding the management of cardiac arrhythmias since 1996. This HRS-led expert consensus statement was developed in collaboration with the American College of Cardiology (ACC), the American Heart Association (AHA), the American Medical Society for Sports Medicine (AMSSM), the Asia Pacific Heart

Rhythm Society (APHRS), the European Heart Rhythm Association (EHRA), the Latin American Heart Rhythm Society (LAHRS), and the Pediatric and Congenital Electrophysiology Society (PACES). This international expert consensus statement is intended to educate clinicians providing arrhythmia-related care to athletes, foster acceptance of the shared decision-making model for these populations, and promote research in best approaches for prevention, diagnosis, and management of arrhythmias in athletes.

1.2 Document scope and rationale

Sports cardiology is a rapidly evolving field. In the past decades, both youth sports, and adult individuals participating in organized sports such as marathons, have increased exponentially. Understanding cardiac care of the athlete requires specialized expertise, as sports participation in itself leads to changes that can be both adaptive and potentially maladaptive, such as the increased incidence of atrial fibrillation (AF) well documented in endurance athletes. Further, treatment decisions may be influenced by the desire to return to sports. To meet these needs, the field of sports cardiology is growing rapidly. As sports cardiology grows, attention to arrhythmic issues in the athlete needs to grow in parallel.

The overarching goal of this document is to provide evidence-based and expert consensus recommendations on the diagnosis, treatment, and management of arrythmias in athletes of all ages, with an emphasis on shared decision-making. Participation in sports has innumerable benefits, both physical and psychological. Restriction from sports is not benign, with significant deleterious impact on psychological well-being and quality of life. While not always achievable, the goal should be facilitating the athlete's return to sport if this is the desired outcome, through appropriate risk assessment and athlete-focused management of their arrhythmic condition, and concerted efforts to achieve equity of care for all athletes.

1.3 Editorial independence

This expert consensus statement is sponsored by the HRS and was developed without commercial support. All writing committee members volunteered their time to the writing and review efforts.

1.4 Organization of the writing committee

The writing committee consisted of internationally recognized experts from 5 countries in the fields of clinical electrophysiology (EP), cardiology, pediatric EP and cardiology, genetic cardiology, sports cardiology, sports medicine, and clinical research science. Each writing committee member served as a representative of either HRS or the collaborator society and was nominated according to each organization's processes. HRS strives to ensure that the writing committee contains both requisite expertise and diverse representation from the broader medical community. This is achieved by selecting participants from a wide range of backgrounds representing different geographic regions, genders, races, ethnicities, intellectual perspectives, and scopes of clinical practice and by inviting organizations and professional societies with related interests and expertise to participate as collaborators. In addition, a patient partner was included in the writing committee to ensure a focus on delivering optimal patient care that is in alignment with patients' wants, needs, and preferences.

HRS has rigorous policies and methods to ensure that documents are developed without bias or improper influence. The HRS policy on relationships with industry (RWI) and other entities can be found

in the *HRS Code of Ethics and Professionalism: Appendix C* and in the *HRS Clinical Document Development Methodology Manual and Policies*. A majority of the writing committee was free of relevant RWI throughout the development of the document, and sections with recommendations were written by the writing committee members who were free of relevant RWI. For full transparency, **Appendix 1** is a comprehensive list of RWI (both relevant and nonrelevant to the document topic) disclosed by the writing committee members. **Appendix 2** is a comprehensive list of RWI disclosed by the peer reviewers.

1.5 Evidence review and formulation of recommendations

This expert consensus statement was developed in accordance with the clinical practice methodology processes detailed in the *HRS Clinical Document Development Methodology Manual and Policies: Executive Summary,*[1] and with the standards issued in 2011 by the Institute of Medicine (now National Academy of Medicine).[2]

The writing committee reviewed evidence gathered by electronic literature searches (MEDLINE, PubMed, Embase, Cochrane Library, Ovid). No specific year was chosen for the oldest literature. Literature searches focused whenever possible on randomized controlled trials, but systematic reviews, nonrandomized and registry studies, cohort studies, and case series were included. Evidence tables are included in **Appendix 3** and summarize the evidence used by the writing committee to formulate recommendations. References are representative of the totality of data and are not meant to be all-inclusive. Limitations of the evidence base are discussed in individual sections.

To assess consensus after discussions, the writing committee members participated in surveys. A predefined threshold of 70% approval for each recommendation was required, with a minimum quorum of two-thirds of the writing committee. An initial failure to reach consensus was resolved by subsequent discussions, revisions as needed, and re-voting. Writing committee members with RWI did not vote on recommendations concerning relevant topics.

1.6 Class of recommendation and level of evidence

Recommendations in this expert consensus statement are designated with both a class of recommendation (COR) and a level of evidence (LOE). The COR denotes the strength of the recommendation based on the assessment of the magnitude and certainty of the benefits in proportion to the risks. The LOE reflects the quality of the evidence that supports the recommendation based on type, quantity, and consistency of data from clinical trials and other sources (**Table 1**).[3]

For clarity and usefulness, each recommendation is linked to the supportive evidence through the specific references from the literature used to justify the LOE rating, which are also summarized in their evidence tables (**Appendix 3**). Each recommendation is accompanied by explanatory text. Flow diagrams and appropriate tables provide a summary of the recommendations and are intended to assist clinicians at the point of care.

Table 1 ACC/AHA recommendation system: Applying class of recommendation and level of evidence to clinical strategies, interventions, treatments, and diagnostic testing in patient care (updated May 2019)*

CLASS (STRENGTH) OF RECOMMENDATION	
CLASS 1 (STRONG)	**Benefit >>> Risk**
Suggested phrases for writing recommendations: • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	
CLASS 2a (MODERATE)	**Benefit >> Risk**
Suggested phrases for writing recommendations: • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	
CLASS 2b (WEAK)	**Benefit ≥ Risk**
Suggested phrases for writing recommendations: • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	
CLASS 3: No Benefit (MODERATE) **(Generally, LOE A or B use only)**	**Benefit = Risk**
Suggested phrases for writing recommendations: • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	
CLASS 3: Harm (STRONG)	**Risk > Benefit**
Suggested phrases for writing recommendations: • Potentialy harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
• High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	**(Randomized)**
• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	**(Nonrandomized)**
• Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies	
LEVEL C-LD	**(Limited Data)**
• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects	
LEVEL C-EO	**(Expert Opinion)**
• Consensus of expert opinion based on clinical experience	

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Adapted with permission from the American College of Cardiology (ACC) and the American Heart Association (AHA).

1.7 Document review and approval

The HRS invites public and stakeholder involvement in document development. In addition to patient representation in the writing committee, draft recommendations were posted for public comment, and contribution was solicited from regulatory agencies and patient organizations.

This expert consensus statement was approved by the writing committee and underwent internal review by the HRS Scientific and Clinical Documents Committee. The document underwent external peer review by reviewers appointed by HRS and each of the collaborating societies, and revisions were made

by the chairs. A record of writing committee response to reviewer comments and rationale is maintained by the HRS.

1.8 Document updates

The HRS Scientific and Clinical Documents Committee reviews each clinical practice document for currency at least every 5 years, or earlier in the event of newly published data. The literature is routinely monitored to evaluate the continued validity of recommendations.

1.9 Relevant clinical practice documents

Clinical practice documents relevant to the topic of diagnosing, managing, and treating arrhythmias in athletes were used to inform the development of this consensus statement. **Table 2** lists the relevant clinical practice guidelines and consensus statements that the writing committee considered as fundamental to the development of this document.

Table 2 Relevant clinical practice documents

Title	Publication year
PACES/HRS Expert consensus statement on the management of the asymptomatic young patient with a Wolff-Parkinson-White (WPW, ventricular preexcitation) electrocardiographic pattern[4]	2012
AHA/ACC Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Preamble, principles, and general considerations[5]	2015
International criteria for electrocardiographic interpretation in athletes: Consensus statement[6]	2017
Sports cardiology: Core curriculum for providing cardiovascular care to competitive athletes and highly active people[7]	2017
AHA/ACC/HRS Guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death[8]	2017
ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease[9]	2020
AHA/ACC Guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy[10]	2020
APHRS/HRS expert consensus statement on the investigation of decedents with sudden unexplained death and patients with sudden cardiac arrest, and of their families[11]	2020
Recommendations for participation in leisure-time physical activity and competitive sports in patients with arrhythmias and potentially arrhythmogenic conditions. Part 1: Supraventricular arrhythmias[12]	2021
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[13]	2021
ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death[14]	2022
ESC Guidelines for the management of cardiomyopathies[15]	2023

ACC/AHA/ACCP/HRS Guideline for the diagnosis and management of atrial fibrillation[16]	2023
HRS/APHRS/LAHRS Guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure[17]	2023
2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy[18]	2024

Section 2 General concepts and principles

2.1 Definitions

The key terms related to athletes used in this consensus statement are defined in **Table 3**.

Table 3 Definitions

Term	Definition
Athletes	Individuals who are engaged in habitual and vigorous training for the purposes of obtaining a high level of fitness. This includes competitive athletes, high-level recreational exercise enthusiasts, and occupational (tactical) athletes.
Age domains in athletes	Given the complexity of the interaction between age and different arrhythmic diseases, rather than use arbitrary age cut points, athletes are considered in different age domains based on stages of development. **Young** = prepubertal and adolescent Prepubertal: < / ≈ 12 years old Adolescent ≈ 13-17 years old **Young adult** ≈ 18-24 years old **Adult** > / ≈ 25 years old **Master** > / ≈ 35 years old
Return to play/return to sport	These terms refer to returning to the desired level or intensity of recreational or competitive sport participation.

Definition of an athlete

Although there is no universal definition of "athlete" in the medical literature,[19] in this document, athletes are defined as individuals who are exposed to regular and high cardiovascular stress demands due to habitual vigorous exercise training for the purposes of obtaining a high level of fitness and for competition, occupation, or recreation. This definition of the athlete is broader than that used in other clinical practice documents on sports eligibility in athletes with cardiovascular diseases.[5,20-22] Specifically, the 2015 AHA/ACC scientific statement[5] defines a "competitive" athlete as "one who participates in an organized team or individual sport that requires regular competition against others as a central component, places a high premium on excellence and achievement, and requires some form of systematic (and usually intense) training." However, athletes may also be noncompetitive "exercise enthusiasts" or people who engage in regular, vigorous exercise training for purposes of recreation or other health benefits. Moreover, there is emerging recognition of the "tactical" athlete, such as members of law enforcement, military, or fire departments.[23] These individuals are also exposed to regular and high cardiovascular stress demands, not for competition or recreation, but for service and

occupation. As issues related to management of arrhythmias may be similar for these types of athletes, this document addresses all of these groups. Throughout this document, "return to play" and "return to sport" refer to a return to the desired level or intensity of recreational, occupational, or competitive sport participation.

This document applies to both adult and pediatric athletes. Age considerations in the context of the clinical management of many arrhythmias are complex and do not fit well using a binary adult versus pediatric age cut point (eg, 18 or 21 years old) or a consensus-based lower pediatric age cut point (prior consensus cardiovascular recommendations for sports eligibility[5] and guidelines for the interpretation of the athletic electrocardiogram [ECG][6] used 12 years of age as a lower pediatric age cut point). Additionally, emphasis on competitive youth sports beginning at younger ages is increasing and genetic heart conditions, especially those with high penetrance, can affect young children. In this document the management of athletes with arrhythmias is considered in terms of the age domains defined in **Table 3**. The term "Masters athlete" is often used to indicate either formally, an athlete over 35 years, or informally, an older athlete.[7,24] "Young" is used in this document to refer to prepubertal and adolescent athletes. In areas where no age-group is specified, recommendations do not vary by age.

2.2 Clinical considerations for athletes with arrhythmias

Recommendations for clinical considerations for athletes with arrhythmias		
COR	**LOE**	**Recommendations**
1	**C-EO**	**1. In athletes with symptoms of arrhythmias, clinical evaluation should include exercise history and history of performance-enhancing drugs.**
1	**C-EO**	**2. In athletes with symptoms of arrhythmias, differential diagnosis should include consideration of etiologies specific to their sport.**
1	**C-EO**	**3. In athletes with symptoms of arrhythmias, evaluation should be performed by clinicians with an understanding of unique electrical and structural adaptations specific to the athlete (ECG or cardiac structural) and of the differentiation of "grey zone" cardiac phenotypes.**
1	**C-EO**	**4. In athletes with symptoms of or concern for arrhythmias, exercise stress testing should be based on maximal effort and/or symptom reproduction rather than heart rate or protocol completion.**
1	**C-EO**	**5. In athletes with symptoms of or concern for arrhythmias, exercise stress testing should be performed based on sport type and situation where symptoms are elicited.**
1	**C-LD**	**6. In athletes with arrhythmogenic conditions returning to play, a stress test should be performed prior to return to play.[25,26]**
1	**C-EO**	**7. In athletes with arrhythmias, clinical management strategies should consider limitations on athletic performance caused by the arrhythmia or by the pharmacological treatments for the arrhythmia, to optimize return to play if desired.**

1	**C-EO**	**8. In athletes with arrhythmias, clinical management strategies should take into account athlete- and sport-specific considerations including impact of therapeutic options on timing of return to play and any sport-specific restrictions.**
1	**C-EO**	**9. In athletes with arrhythmias who are not returning to competitive sports, plans for other levels of exercise should be discussed.**

Synopsis

The clinical evaluation of arrhythmias that could be life-threatening when provoked during exercise is generally the same for all patients, whether they are considered an athlete or not. Similarly, "red flag" symptoms, such as unheralded syncope during exercise, lead to a similar differential diagnosis and high clinical concern for both athletes and nonathletes. However, compared with nonathletes, there are several reasons why athletes come with distinct considerations in the approach to and the evaluation of arrhythmias, as well as in the determination of treatment options.

Recommendation-specific supportive text

1. Some arrhythmias (eg, AF, ventricular tachycardia in the setting of arrhythmogenic cardiomyopathy [ACM]) have independent associations or direct causal links with exercise training habits.[27,28] As a result, a detailed exercise history, including both during and outside of organized sports, may provide clues to the diagnosis of different arrhythmia syndromes. Exercise history includes type of sport, frequency, and duration, and type of training and intensity of training and work demands for the tactical athlete. A history of performance-enhancing drug use is also important, as these can have arrhythmic effects (**Table 4**).[29-33] Thus, for athletes, differential diagnoses may be uniquely guided by exercise or training habits.

2. Unique sport-specific factors must be considered in determining the differential diagnosis for symptomatic athletes. For example, dietary habits within the culture of some sports (eg, eating disorders) can precipitate arrhythmic symptoms or lead to a high burden of ectopic beats and should be ascertained during the clinical evaluation. Also, performance-enhancing drugs can impact cardiac structure and electrical function (**Table 4**).[29-33] Additionally, exercise-associated collapse with prior prodromal symptoms immediately after finishing prolonged exercise such as a distance race is consistent with a benign presyncopal or syncopal event.

3. Interpretation of electrical and cardiac structural alterations in athletes can impact the consideration of the diagnosis of arrhythmias in athletes, and thus it is critical that clinicians evaluating athletes have appropriate training in how vigorous exercise influences cardiac structure and function and how these changes manifest on cardiac testing.[7,28] Overdiagnosis of cardiac abnormalities in the athlete is frequent due to lack of recognition of these changes. It is well understood that habitual and vigorous exercise training and the subsequent changes in autonomic tone and hemodynamic physiologic stresses can lead to cardiovascular adaptations.[28,34] These physiologic changes can lead to alterations on the surface 12-lead ECG[6] and also changes in cardiac phenotypes, termed exercise-induced cardiac remodeling (EICR) (**Table 5**) or, colloquially, the "athlete's heart,"[28] which can overlap with cardiac pathology, termed "grey zone" phenotypes. Exercise history, as above, is critical to understand expected adaptations (**Figure 1**).[7,28] High vagal tone may manifest on the 12-lead ECG as sinus bradycardia

or sinus arrhythmia or first-degree and Mobitz I second-degree atrioventricular (AV) block.[6] Vigorous exercise can lengthen repolarization, including to levels which may indicate risk.[35] EICR is a sport-specific phenomenon. All vigorous sports involve combinations of dynamic (endurance/isotonic) and static (strength/isometric) physiology in a continuum.[7] Dynamic exercise requires increases in oxygen delivery, and thus endurance training, dynamic exercise over long periods of time, represents a volume hemodynamic challenge to the heart, with resultant chamber dilatation. Static exercise increases afterload, and thus strength training presents a pressure challenge, in which, over time, cardiac hypertrophy occurs. In endurance or mixed endurance-strength sports, the pattern of hypertrophy is generally eccentric with concomitant biventricular and biatrial enlargement. Advanced imaging such as cardiac magnetic resonance imaging (CMR) can be helpful in differentiating EICR from pathology in "grey zone" athletes.[36,37]

Recognition of the consequences of these phenotypic alterations is important for several reasons. The first is diagnosis: arrhythmias in the context of EICR may have very different implications than those occurring in pathological states, and thus, recognition of "grey zone" phenotypic crossover between extreme forms of adaptive EICR versus mild forms of cardiomyopathy—hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), or ACM—is critical.[28,38] Next, changes in cardiac structure over time, in particular, left atrial dilatation in Masters athletes, may predispose an athlete to atrial arrhythmias (see **Section 5**). Finally, for some cardiovascular disease entities, specifically some of the arrhythmogenic cardiomyopathies (see **Section 8**), endurance exercise with its increased volume challenge may increase progression of disease and thus need to be discussed as part of the shared decision-making process.

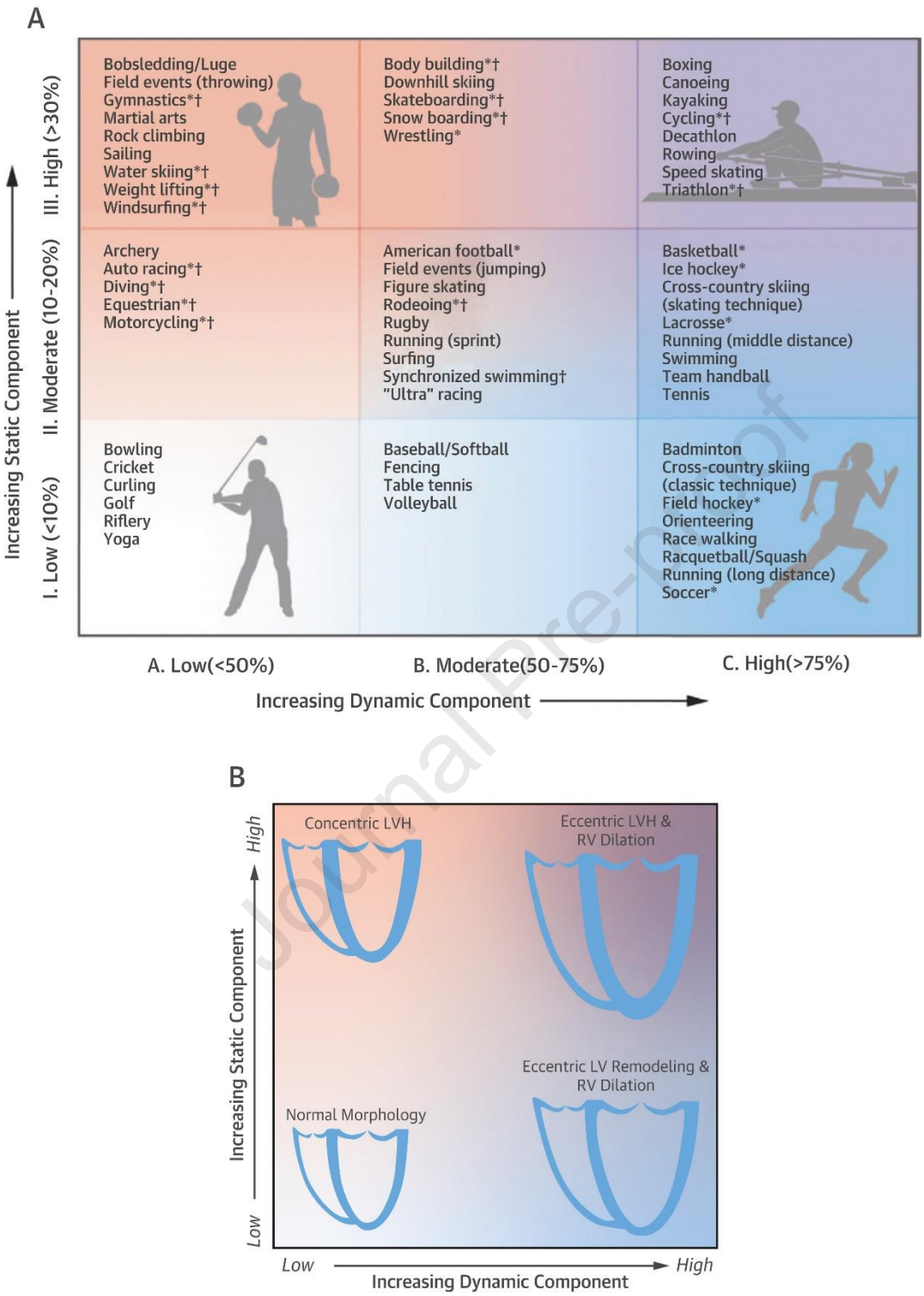

Figure 1

Expected ventricular adaptation from static and dynamic stressors on the heart. (A) Physiological classification of common sporting disciplines representing relative contributions of static and dynamic physiology. (B) Anticipated structural cardiac adaptations that develop as a function of the static and dynamic stressors. ∗Danger of bodily collision. †Increased risk if syncope occurs. LV = left ventricular; LVH = left ventricular hypertrophy; RV = right ventricular. Reprinted with permission from Baggish et al.[7]

4. Athletes may present with symptoms only at very high exercise intensities. As such, it is critical that in the clinical evaluation of the symptomatic athlete, exercise stress testing proceeds to maximal volitional effort (or symptoms) and is not terminated based on heart rate thresholds (eg, 85% maximum predicted heart rate). Maximal effort may be determined by the rating of perceived exertion (eg, Borg scale) or maximum heart rate achieved, although heart rate alone should not be considered a stopping point. Cardiopulmonary exercise testing (CPET) is also useful in adjudicating maximal effort through measured VO_{2max}, maximum exercise heart rate, surpassing the ventilatory threshold, and the respiratory exchange ratio. CPET that incorporates quantitative gas and metabolic analyses may enhance understanding of a patient's particular physiology and limitations. Exercise protocols may vary, but generally require a more accelerated ramp effort beyond standard protocols (eg, Bruce protocol).[39,40] In small studies, a "burst" protocol involving a sudden high workload has shown increased sensitivity for detecting abnormalities in catecholaminergic polymorphic ventricular tachycardia (CPVT)[41] and HCM.[42] Reported protocols include a first stress test, in which the treadmill speed/grade at maximum heart rate is determined, and then a second test, in which the treadmill exercise is started at this speed/grade. For athletes in whom stress testing does not invoke symptoms and/or symptoms are rare, external/internal monitoring during the athlete's usual training and competition situation may be a next step, as described in **Section 4** in more detail.

5. It is also important to test the athlete with the appropriate exercise modality based on the type of athlete and the environment in which symptoms are elicited. To appropriately assess the athlete, use a treadmill (sometimes with additional sprint intervals), cycle ergometry, and rowing ergometry (if available).

6. Using the stress test to determine arrhythmia suppression for athletes returning to play after diagnosis and treatment of an arrhythmic condition has been reported as part of return-to-play protocols for conditions including CPVT and other genetic heart diseases, with long-term results suggesting overall safety of the protocol.[26] It is used in the general population for determining beta blocker response,[25,43] and efficacy of surgery for anomalous aortic origin of coronary arteries (AAOCA). Discussion of the exercise stress test for guiding programming of implantable cardioverter-defibrillators (ICDs) and pacemakers appears in more detail in those sections. For some entities, such as Wolff-Parkinson-White (WPW), where an identifiable cure for arrhythmia exists, exercise stress testing prior to return to play is not needed, but for most arrhythmic entities, complete cure is difficult to determine and documentation of arrhythmia suppression is needed.

7. In addition to the accepted medical standards of care, consideration of limitations on athletic performance, related to symptomatology and/or potential treatments, become more relevant for athletes. For example, symptoms from an arrhythmia or subsequent pharmacotherapy choices (eg, beta blockers, antiarrhythmic drugs) can limit performance and thus may require procedural treatment strategies. Overall, clinical management options in all of these scenarios, particularly when taking into consideration return to play, can be complex, and therefore require an expert-guided and shared-decision-making approach.

8. For professional and high-level collegiate athletes, there will likely be heightened emphasis on the timing of return to play given the financial investment from the team/sponsors and/or

concomitant income concerns from the athlete. Prior to initiation of pharmacological treatments, it should be determined whether medications under consideration require disclosure to supervising bodies and/or influence eligibility. Data on performance-enhancing effects of beta blockers are minimal, with one study in marksmen showing improved shooting performance,[44] another no improvement in archers, with resulting prohibition of these agents by the World Anti-Doping Agency for sports requiring precision and accuracy such as archery and skiing.[45,46] Tactical athletes, such as divers, may face unique challenges due to demands of the job and environment.

9. For athletes who do not return to play and cease a competitive athletic career, regardless of the diagnosis or condition, an exercise prescription should be discussed and encouraged. Maintaining a healthy and high level of cardiorespiratory fitness improves overall health and reduces the risk of other forms of cardiovascular disease. Athletes not returning to competitive sports should not be discouraged from exercising. CPET can be used in determining an exercise prescription, and detailed discussions with the athlete on their specific exercise goals should be a part of this process. Transition away from competitive sports can be psychologically difficult for athletes, particularly if not voluntary, with loss of athletic identity leading to depression or other psychological distress. Career-ending injuries can impact athletes for 10 years after retirement. Working with the athlete's care network, including team physicians and sports psychologists with experience in these issues, is important for the athlete's well-being.[47]

Table 4 Potential arrhythmic effects of certain stimulants and performance-enhancing drugs[29-33]

Stimulant/PED	Potential arrhythmic effect
Cocaine	Ectopy, QT prolongation, early repolarization, myocardial fibrosis and infarction, Na^+, K^+, and Ca^{2+} channel dysfunction, atrial arrhythmias, ventricular arrhythmias, bradyarrhythmias, SCD
Amphetamines	Ectopy, QT prolongation, atrial arrhythmias, ventricular arrhythmias, K^+ and Ca^{2+} channel dysfunction. atrial arrhythmias, ventricular arrhythmias, SCD
Marijuana	Ectopy, QT prolongation, atrial arrhythmias, ventricular arrhythmias, myocardial infarction, cardiomyopathy, atrial arrhythmias, stroke
Ecstasy	Ectopy, atrial arrhythmias, ventricular arrhythmias, myocardial infarction, valvular heart disease, cardiomyopathy, myocardial infarction, SCD
Caffeine	Ectopy, sinus tachycardia
Anabolic steroids	Myocardial dysfunction, coronary artery disease, myocardial fibrosis, left ventricular hypertrophy, atrial fibrillation

Ectopy refers to premature atrial contractions (PACs) and/or premature ventricular contractions (PVCs). PED = performance-enhancing drug; SCD = sudden cardiac death.

Table 5 Exercise-induced cardiac remodeling (electrical and structural)[28]

High autonomic/vagal tone	Electrocardiographic findings
	• Sinus bradycardia • Sinus arrhythmia • Junctional rhythm • Ectopic atrial rhythm • Early repolarization

	• First-degree atrioventricular block • Mobitz I second-degree atrioventricular block
Hemodynamic challenge	**Cardiac structural findings**
Isotonic exercise	• Eccentric left ventricular hypertrophy • Symmetric right ventricular enlargement • Biatrial dilation • Low-normal/mildly reduced left ventricular systolic function • Enhanced left ventricular diastolic function
Isometric exercise	• Concentric left ventricular remodeling • Normal right ventricular dimensions • Normal biatrial dimensions • No changes in left ventricular function

2.3 Shared decision-making and clinical management determination

This document presents a shared decision-making approach to return to play, for decisions both around whether to return to play and around treatments tailored to facilitating that decision. Historically, return to play decisions have used algorithm-like approaches based on specific cutoffs for clinical variables and sport classifications. However, for many disease entities, current prospective data in athletes have not confirmed increased arrhythmic risk of continuing sports participation for athletes who are appropriately risk-assessed and treated, emphasizing the importance of individualized shared decision-making. Clinical characteristics indicating higher risk of sudden cardiac arrest (SCA), which then guide treatment such as ICD and other disease-specific therapies, have been described for most cardiovascular disease entities. Whether there are clinical characteristics that interact with vigorous exercise to increase arrhythmic risk has not yet been delineated for most entities. Thus, this document focuses on risk assessment and treatment using shared decision-making that should take into account well-described disease-specific risk factors for SCA as well as sport-specific factors as described in **Section 2.3**.

Participation in vigorous athletic activity has multiple benefits, both psychological and physical, which have been reviewed elsewhere.[48] Restriction from sports is not benign and is associated with significant impact on quality of life and psychological distress. Among athletes diagnosed through screening, loss of athletic identity is a large component of distress, and those disqualified from sports show the highest level of distress.[49,50] For adolescents receiving defibrillators, restriction from sports can be the most life-altering and distressing aspect of the device, and athletic adults with HCM experience lasting psychological difficulty adjusting to exercise restriction.[51,52]

Recommendations for shared decision-making and clinical management determination		
COR	**LOE**	**Recommendations**
1	**C-LD**	**1. In athletes with arrhythmogenic conditions, determination of clinical treatment options should be made through shared decision-making, prioritizing preferences, values, and goals of the athlete.[53]**
1	**C-EO**	**2. In athletes with arrhythmogenic conditions, the fundamentals of shared decision-making should be grounded in core principles of knowledge,**

		humility, respect and trust, teamwork with key stakeholders, and transparent communication.

Synopsis

The preferences and values of individual athletes are key factors when determining clinical management strategies. These values may differ from those of nonathletic patients and need to be elicited from shared risk discussions and as part of the shared decision-making process. Shared decision-making with patients is grounded in the core principles of knowledge, humility, respect and trust, and transparent communication with all parties involved, including 3rd party stakeholders that generally come with ascending levels of competitive sport.

Recommendation-specific supportive text

1. The clinical evaluation and treatment decisions for athletes are founded on shared principles and disclosed risks between the practitioner and patient. As such, shared decision-making is not just a core tenet that underlies the determination of sports eligibility for athletes with cardiovascular disease,[54,55] but it is also a core principle in considering all the various treatment options. In a shared decision-making paradigm, the clinician counsels the patient on the potential clinical management options. Then, in concert with the patient's personal preferences, morals, and values, treatment strategies are constructed. Shared decision-making is widely advocated throughout all medicine. Levine and Stray-Gundersen first introduced the concept of individual responsibility for athletes in 1994 in the context of determining sports eligibility.[56] In sports cardiology, the shift away from medical paternalism stemmed from several key factors that included the publication of data challenging assumptions of increased risk of sports for individuals with cardiovascular disease,[57,58] and the ethical imperative for patient-centered care as mandated by the Institute of Medicine, the American College of Cardiology, and others.[59] Moreover, other updated disease-specific guidelines, such as for HCM,[10] acknowledge ongoing clinical uncertainties and advocate for individualized shared decision-making. The lack of randomized controlled trials and robust data evaluating the safety of sports participation in various cardiovascular conditions emphasizes the need to include shared decision-making with the athlete in discussions involving their own medical care. Shared decision-making regarding exercise has been shown to decrease decisional conflict and decisional regret.[53] As described in more detail elsewhere, shared decision-making for return-to-play decision-making is consistent with legal precedents which have affirmed the "team physician" model.[55]

2. Medical treatment options for athletes diagnosed with arrhythmias are generally affected by a desire to return to play, return to regular vigorous exercise habits, or, for occupational athletes, an expedited return to a physically demanding occupation. As such, although evidence-based best shared decision-making practices with athletes remain uncertain,[60] inclusion of shared decision-making remains of paramount importance in the guidance and determination of treatment options and in ensuring equity of care for all athletes. The fundamentals of shared decision-making with athletes are grounded in several core principles: knowledge of the disease/condition and implications of potential interventions, both positive and negative; humility; respect for the athlete's values, goals, and preferences; and trust. Clear, transparent communication regarding risk, including when risk is unknown, is critical. The physician should

ensure that risk is understood by the athlete and family. Discussion of all treatment options with the athlete and other key parties throughout the shared decision-making process is critical.[55]

An additional and unique aspect of shared decision-making with athletes is the influence of key 3rd party stakeholders that come with ascending levels of competitive sport and in certain occupations. For all young athletes, schools, teams, and leagues are all involved in the decision to return to play. For higher-level athletes, elite collegiate and professional further stakeholders are involved (eg, athletic directors, general managers, owners, sponsors), and 3rd party influences play a key role in return-to-sports decision-making. Collaborative discussion with team physicians is paramount. However, the goal of the shared decision-making process between the practitioner and athlete and/or athlete's family is still a patient-centered focus, regardless of level of the athlete. The privacy of the athlete must also be maintained to the extent possible in communication with stakeholders. For tactical athletes, such as those in the military, governing bodies will determine eligibility.

Collaborative discussion among the athlete, family, treating physician, team physician, additional experts, and other institutional stakeholders (athletic departments and athletic trainers) is critical to balancing risk tolerances and institutional resources/responsibilities,[55] as shown in **Figure 2**. The shared decision-making model does not offer "clearance" (implying no risk) but rather outlines a decision-making process and documents understanding and acceptance of risk by athlete and physician. All counseling the athlete should also make clear their support for the athlete should they decide to not return to play. With clear communication and discussion and understanding of risk, athlete-centered outcomes can be achieved in most clinical management and, ultimately, return-to-play decisions.

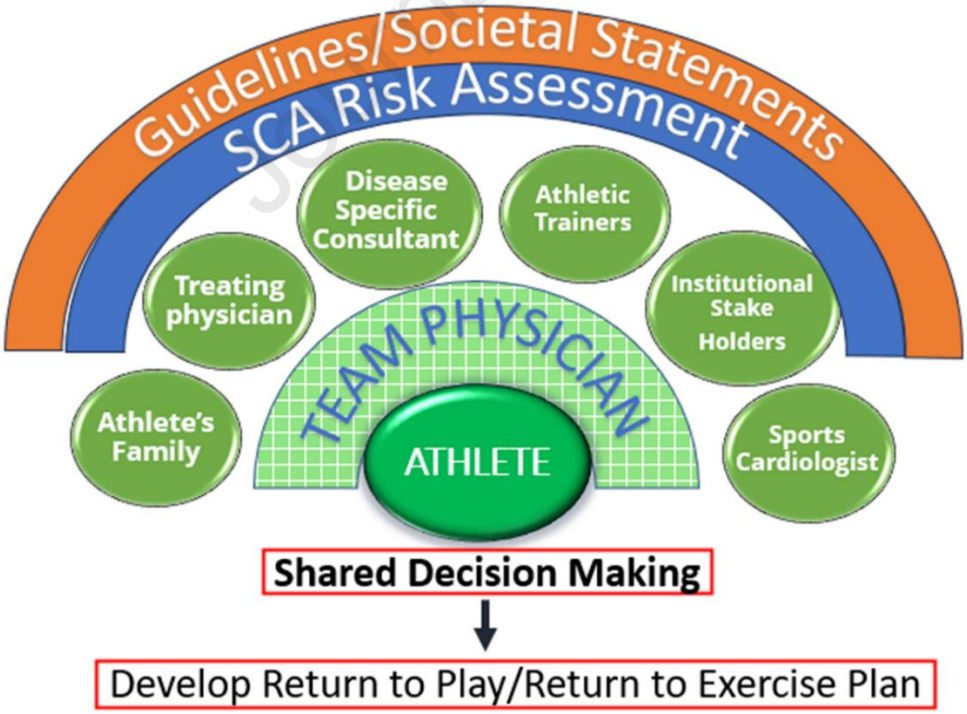

Figure 2
Model for shared decision-making for athletes with cardiovascular disease. In the team-physician-led decision-making process, physicians incorporate shared decision-making, guided by respect for patients' goals and preferences, while integrating

collaborative discussion among the athlete, family, treating physician, team physician, additional experts, and other institutional stakeholders (athletic departments and athletic trainers) in balancing risk-tolerances. SCA = sudden cardiac arrest. Reprinted with permission from Martinez et al.[55]

2.4 Emergency action planning for sudden cardiac arrest

Recommendations for emergency action planning		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. For athletes training or competing at schools, recreational facilities, or other athletic venues, an emergency action plan (EAP) should be in place to respond to acute medical and cardiac events to improve survival from SCA.[61-65]**
1	**B-NR**	**2. For athletes training or competing at schools, recreational facilities, or other athletic venues, steps for rapid and early cardiopulmonary resuscitation and defibrillation should be included in an EAP to improve survival from SCA.[61-65]**
1	**B-NR**	**3. For athletes competing at interscholastic levels or in other organized leagues, relevant governing bodies should put into place policies and direct resources toward increasing the effectiveness of EAPs.[61-65]**
1	**B-NR**	**4. For athletes training or competing at schools, recreational facilities, or other athletic venues, there should be medical support and infrastructure that enables all athletes and team-affiliated staff to learn cardiopulmonary resuscitation (CPR) and be familiar with automated emergency defibrillators (AEDs).[61-67]**

Synopsis

Effective emergency action planning, inclusive of immediate SCA recognition and CPR initiation and rapid defibrillation, is critical in all competitive sports participation and must be in place in venues in which athletes practice and compete. Legislative efforts that support EAP efforts must remain a point of emphasis. Key components of effective EAPs are listed in **Table 6**.

Recommendation-specific supportive text

1. EAPs to facilitate recognition and response to cardiac arrest in athletic venues are considered best practice, as time to defibrillation is the most important factor influencing survival.[61-65,68,69] As most young individuals suffering SCA do not have a prior diagnosis, venues need to be prepared for SCA in any athlete. The EAP is a written document, and regularly rehearsed. Specific individuals, including physicians, athletic trainers, and coaches, who are regularly present when athletes are training or competing, should be trained in rapid assessment for potential SCA and certified in CPR. An emergency communication system should be in place integrating plans for early defibrillation and communication with emergency medical services (EMS), as well as logistics for transfer to the closest appropriate medical center after SCA resuscitation. EAPs should be individualized to each sport and venue.[70]

2. Early CPR and defibrillation has been demonstrated to save lives in the general population.[61-65] Time to defibrillation is a critical factor in survival of SCA. In venues where SCA may occur such as schools and venues for training and sporting events, there should be an accessible AED within 3 minutes.[71-73] Among athletes, survival from cardiac arrest is significantly higher if an AED is

used.[69] Athletes at club-sponsored events have lower levels of resuscitation and survival compared with school-sponsored events.[61] AEDs should be placed near fields or courts where an arrest may occur.

3. Increasing the effectiveness of EAPs requires directed efforts and resources.[61-65] Ensuring EAPs are in place at the secondary school level generally requires statewide legislative policies. In addition, dedicated financial resources for schools are necessary to ensure standardized education and rehearsals of EAP processes, maintenance of EAP equipment, and regular updates of key EAP tenets.

4. As described in detail above, early CPR and early defibrillation save lives.[61-65] Training in CPR and AED use have been demonstrated to improve use of these.[66,67] In an analysis of the CARES (Cardiac Arrest Registry to Enhance Survival) dataset,[67] an EMS-based registry for out-of-hospital cardiac arrests, states with laws requiring CPR training have higher rates of CRP in out-of-hospital cardiac arrests. Survey data also show that active and more extensive training in CPR increases willingness to perform it.[66]

Table 6 Key components of emergency action plans

Components
✓ A written EAP for the recognition and treatment of SCA has been reviewed and rehearsed by key personnel at least annually.
✓ Those likely to be first responders in the event of SCA (teachers, administrators, coaches, strength and conditioning coaches, athletic trainers, team physicians, etc) have received training and are up to date in CPR and AED use.
✓ A communication system has been established for a rapid and coordinated response to cardiac arrest.
✓ AEDs are placed strategically to achieve < 3-minute retrieval time.
✓ EAPs are individualized to the sport (facility-based, running, water sports, etc).
✓ Signage indicating the location of AEDs is clear and visible.
✓ AEDs are accessible (never in locked cabinets or behind locked doors) and are regularly checked for proper battery charge and functional electrode pads.
✓ Emergency medical service entrance and exit to facilities is predetermined, accessible, and secure.
✓ Ideally, EAPs should be reviewed and practiced with local emergency medical services.

AED = automated external defibrillator; CPR = cardiopulmonary resuscitation; EAP = emergency action plan; SCA = sudden cardiac arrest.

Section 3 Sudden cardiac arrest in athletes

3.1 Epidemiology of sudden cardiac arrest and death in athletes

Sudden cardiac arrests (SCAs) are rare in the young athlete, with most series describing a rate of 1-2 per 100,000 person-years.[74,75] SCAs are more common as athletes age, predominantly due to the increased prevalence of coronary disease. Many states mandate AEDs and EAPs at schools, sporting events, and gymnasiums. Sporting activities may increase the odds of an arrest due to several factors, including direct effects of autonomic changes, increased heart rate, myocardial ischemia, and cardiac dilation.

SCA is an important cause of death in athletes of all ages. However, attempts to define both incidence and causes have been limited by methodological issues. Accurate estimation of incidence requires all cases of both SCA with survival and SCA with sudden cardiac death (SCD) (numerator) in a specific

cohort to be identified. Many studies on SCA are retrospective, do not include cases with survival, have estimated or inexact cohorts (denominators), and do not have the necessary granularity to accurately represent risk among different populations. For example, risk of SCA varies drastically by sex; therefore, inclusion of both sexes in risk calculations underrepresents risk in males and overrepresents risk in females.[74,76-82] Risk also appears to differ based on sport and reported race.[79-84] Further, the specific causes of SCA change with age.[85-88] Hereditary and congenital conditions are the predominant causes of SCA in younger athletes, and acquired causes, specifically coronary artery disease, are the principal causes in Masters athletes.[85,88,89] Estimates of SCA that include wide age ranges with different primary etiologies give imprecise representations of risk. Finally, many studies examining SCA in athletes include only sports- or exercise-related SCA, which is a subset of all SCA. While some studies suggest that up to 90% of deaths in young athletes occur during exercise,[90] others suggest that number is closer to 50%.[79,82,91,92] A tool designed to decrease bias in reporting and conduction of studies of SCA in athletes has recently been developed and should improve the quality of these data.[93]

Incidence

Two recent systematic reviews and meta-analyses reported the rate of sudden cardiac arrest and death (SCA/D) in young athletes as 1.7-1.9 deaths per 100,000 person-years (1 death per 52,000-58,000 person-years).[74,75] They included a heterogenous group of studies that included both sexes, had wide age ranges, and had both SCD occurring at any time and sports- or exercise-related SCD. Most did not include cases of SCA survivors. Incidence numbers must be interpreted in the context of the above limitations. **Table 7** includes the incidence of SCA/D in athletes aged 14-26 years and includes studies assessed at low or intermediate risk of bias.[93,94] When multiple reports of the same database appeared, the most recent or comprehensive study was included in the table. The overall incidence of SCA/D in this population is generally reported as 1 death in 50,000 person-years in college-age athletes with slightly lower rates in high school athletes (likely an artifact of less coverage in media reports in the high school age range) with higher rates in males and certain sports. **Table 8** includes the incidence of sports- and exercise-related SCA including information on how cases were identified (numerator) and how the population was defined (denominator). Rates of death in sports- and exercise-related SCA/D tend to be lower: around 1 death in 200,000 person-years. Many of these studies use population-based registries that accurately identify deaths; however, clearly defining and identifying athletes can be challenging. A more comprehensive list of all studies on the incidence of SCA/D in athletes that includes those with wider age ranges is in **Table 9**. This table highlights the wide range of estimates of incidence and the existence of groups that are potentially at much higher risk of SCA/D including males, Black athletes, and athletes playing men's basketball, men's soccer, and American football.

Commotio cordis (also discussed in **Section 4**) is SCA precipitated by a blunt, nonpenetrating blow to the anterior precordium at a specific point during the cardiac cycle in a structurally normal heart.[95] Commotio cordis is sometimes included in databases of SCA/D or sudden death but may be differentiated as a traumatic death, as there is no underlying cardiac condition. Commotio occurs most often in ball sports but can also occur with a blow to the chest in martial/fighting arts or other contact sports. In the Commotio Cordis Registry, there were 167 cases in athletes of all ages (68% died) over 42 years (1970-2012), or about 4 cases a year.[96] At a national cardiac pathology referral center in the United Kingdom, 6 cases of commotio cordis were reported in athletes over 28 years[92] and there were two cases of commotio cordis found over 20 years in National Collegiate Athletics Association (NCAA) athletes with an incidence of 1 in 4,553,258 athlete years.[79,82]

The incidence of SCA/D in older or Masters athletes is equally difficult to ascertain. Studies vary by the definition of an athlete, and it is often difficult to clearly define the population (denominator) of older exercising or competitive athletes. Most information on the incidence of SCA in those aged > 35 years is exercise-related SCA/D and comes from data at long distance races and other events. In a 2012 study of 10.9 million runners, there were 59 arrests, for an incidence rate of 0.54 per 100,000 participants with a 29% survival rate.[97] A recent study of deaths during 46 long distance races with over 1,000,000 participants reported a rate of 2.33 per 100,000 runners with major cardiovascular events with a 90% resuscitation rate.[98] While it is well established that cardiorespiratory fitness lowers overall mortality and other adverse health outcomes,[99] even among the most fit, the immediate risk of SCA/D is increased during and shortly after physical exertion.[100,101]

Causes of SCA

As with incidence rates, there are limitations of the currently available studies that report on causes of SCA. The United States has no coordinated system for postmortem evaluation, instead relying on a patchwork of medical examiners and coroners with variable expertise and often limited by poor funding in the testing performed. Specialized referral centers exist in some parts of the United States and other parts of the world, but studies from those centers may reflect ascertainment bias, with a larger proportion of undiagnosed or structurally normal cases being referred. Conversely, it has been suggested that less specialized centers are more likely to overdiagnose structural or myocardial disease.[92] Most studies reporting on the causes of SCA include only those athletes that died and therefore may be overrepresenting cardiac conditions that are more lethal; electrical abnormalities are rarely diagnosed after death because the heart is structurally normal. Those diagnosed with autopsy-negative sudden unexplained death (AN-SUD) represent a variety of pathologies including channelopathies such as long QT syndrome (LQTS), CPVT, Brugada syndrome, and conduction abnormalities like WPW. Genetic testing (molecular autopsy) has been shown to be helpful in these cases, with one study detecting pathogenic variants in 44% of young people with exertion-related sudden unexplained death.[102] In addition, our understanding of pathology is evolving. There is an increasing prevalence of left ventricular hypertrophy with or without fibrosis noted that may represent a cardiomyopathy not yet phenotypically expressed, or the fibrosis may be an underlying primary trigger for arrythmia. **Table 10** includes studies of the causes SCA/D in young people and the relative contributions of each entity in the study. AN-SUD appears to be the most frequent cause of SCA/D in young athletes, followed by cardiomyopathies and coronary artery abnormalities. In athletes aged > 30–35 years, coronary artery disease is the most common cause of SCA/D, with the incidence increasing with age (**Figure 3**).

Exertional death in athletes with sickle cell trait (SCT) occurs suddenly and is included in some registries of sudden death.[103] Although cardiac conditions may coexist in athletes with SCT, the primary mechanism of exertional death in athletes with SCT is thought to be most likely explosive rhabdomyolysis.[104] When differentiating SCD from death due to SCT, one must consider the presence of underlying cardiac pathology and contextual information regarding the collapse.[105] Collapse in SCA/D includes loss of consciousness, but the athlete with SCT typically experiences a conscious collapse. Death due to SCT should not be included as a cardiac cause.

Summary

The incidence of SCA/D is higher in males, Black athletes, and certain sports such as basketball, American football, and soccer. The causes of SCA/D death vary in younger and older athletes, with structural or electrical conditions the primary causes in younger athletes and coronary artery disease in older athletes (**Figure 3**). Future research should focus on inclusion of both SCA and SCD and should take into account age, sex, race, and sport.

Table 7 Incidence of sudden cardiac arrest and death in athletes in low or intermediate risk of bias studies with sex, race, and sport rates*

Study	SCD or SCA/D?	Age range (years), no. of cases	Overall incidence of SCA/D	Male SCA/D incidence	Female SCA/D incidence	Black SCA/D incidence	White SCA/D incidence	Sex and sport-specific incidence	Risk of bias
High school age (~14-18 years)									
Toresdahl et al, 2014[78]	SCA/D	14-18, N=44	1:88,000	1:58,000	1:323,000				Low
Drezner et al, 2014[106]	SCA/D	14-18, N=13	1:71,000					Male, basketball 1:21,000	Intermediate
Malhotra et al, 2018[84]	SCD	15-17, N=8						Male, soccer 1:14,794	Low
Harmon et al, 2016[80]	SCA/D	14-18, N=104	1:67.000	1:45,000				Male, basketball 1:37,000	Intermediate
Peterson et al, 2021[81]	SCA/D	14-18, N=204	1:66,000	1:44,000	1:204,000			Male, ice hockey 1:24,000 Male, basketball 1:40,000 White, football 1:20,000	Low
College/university age (~18-25 years)									
Peterson et al, 2021[81]	SCA/D	18-24, N=39	1:51,000	1:35,000	1:123,000	Black, male 1:18,000	White, male 1:39,000	Black, male, basketball 1:4800 White, male, basketball 1:15,000 Black, football 1:28,000 White, football 1:20,000	Low
Petek et al, 2023[82]	SCD	17-26, N=143	1:64,000	1:43,000	1:165,000	1:27,000	1:75,000	Football 1:32,000 Male, basketball 1: 12,000 Male, cross-country 1:38,000 Male, Div 1, White, basketball 1:6000 Male, Div 1, Black, basketball 1:8000	Low

*Includes studies assessed at low or intermediate risk of bias.[94] When multiple reports of the same database appeared, the most recent or comprehensive study was included in the table. Div 1 = National Collegiate Athletics Association Division 1; SCA = sudden cardiac arrest; SCA/D = sudden cardiac arrest and death; SCD = sudden cardiac death.

Table 8 Incidence of sudden sports-related SCD in population-based studies

Study	Study design and population	Case identification (numerator)	Population definition (denominator)	SCD or all SCA/D?	Study years	Age range (years), no. of cases	Annual incidence
Holst et al, 2010[107]	Retrospective cohort; athletes and general population in Denmark	Review of death certificates, Cause of Death Registry, and National Patient Registry in Denmark	Interview data of people aged 16-35 years from the National Danish Health and Morbidity Study	SCD	2000-2006	12-35, N=15 12-35, N=428	*Athletes* 1:83,000 *General population* 1:27,000
Marijon et al, 2011[108]	Prospective cohort; general population in France	Data from emergency medical system	General population statistics, data from the Minister of Health and Sport to estimate young competitive athlete population	SCA/D	2005-2010	10-75, N=820 10-35, N=50	*General population* 1:217,000 *Young competitive athlete* 1:102,000 *Young noncompetitive athlete* 1:455,000
Risgaard et al, 2014[109]	Retrospective cohort; competitive and noncompetitive athletes in Denmark	Review of death certificates and the Danish National Patient Registry	Competitive and noncompetitive athlete populations in Denmark estimated based on survey data from the Danish National Institute of Public Health	SCD	2007-2009	12-35, N=44	*Competitive athlete* 1:213,000 *Noncompetitive athlete* 1:233,000
Bohm et al, 2016[110]	Prospective cohort; sports-related SCD in all persons in Germany	Voluntary reporting to German National Registry, web-based media search, regional institutes	Physical activity estimated from the German Health Update study and extrapolated to population data from the German Federal Statistical Office	SCD	2012-2014	10-79, N=144	*Sports participants* 1:1,200,000
Grani et al, 2016[111]	Retrospective; sports-related SCD in all persons in German-speaking Switzerland	Forensic reports	Physical activity estimated from survey on sports participation by the Swiss Federal Office of Sports	SCD	1999-2010	10-39, N=69	*Sports participants* Competitive 1:90,000 Recreational 1:192,000
Weizman et al, 2023[112]	Retrospective; sports-related SCD in 3 European registries	Review of death certificates and medical records	Population areas of the 3 registries	SCA/D	2006-2014	19-96, N=760; Female N=56, Male N=704	*People with SCA during sports* Female 1:5,263,000 Male 1:380,000

SCA = sudden cardiac arrest; SCA/D = sudden cardiac arrest and death; SCD = sudden cardiac death.

Table 9 Incidence of sudden cardiac arrest and death in athletes

Study	Study design and population	Case identification (numerator)	Population definition (denominator)	Sports-related SCD or all SCD?	SCD or all SCA/D?	Study years	Age range (years), no. of cases	Annual incidence	Risk of bias
Van Camp et al, 1996[113]	Retrospective cohort; high school and college athletes	National Center for Catastrophic Sports Injury Research and media reports	Data from NCAA, NFHS, NAIA, and NJCAA, added together with conversion factor (1.9 for high school and 1.2 for college) used to account for multisport athletes "based on discussions with representatives from the national organizations"	Sports-related	SCD	1983-1993	13-24, N=160	*College and high school* Overall 1:188,000 Male 1:134,000 Female 1:752,000 *High school* Overall 1:213,000 Male 1:152,000 Female 1:861,000 *College* Overall 1:94,000 Male 1:69,000 Female 1:356,000	High
Corrado et al, 2003[114]	Prospective cohort; athletes and nonathletes in the Veneto Region of Italy	Mandatory reporting of sudden death	Registered athletes in the Sports Medicine Database of the Veneto Region of Italy and the Italian Census Bureau	All	SCD	1979-1999	12-35, N=51 12-35, N=208	*Athletes* Overall 1:47,000 Male 1:41,000 Female 1:93,000 *Nonathletes* Overall 1:143,000	Low
Drezner et al, 2005[115]	Retrospective survey; college athletes	Survey of NCAA Division 1 institutions (244/326 responded)	Reported number of athletes	All	SCD		N=5	*College* Overall 1:67,000	Intermediate
Maron et al, 2009[116]	Retrospective cohort; amateur and competitive athletes	Registry for Sudden Death in Athletes	An estimated 10.7 million participants per year ≤ 39 years of age in all organized amateur and competitive sports	All	SCA/D	1980-2006	8-39, N=1046	*Athletes* 1:164,000	High
Drezner et al, 2009[63]	Cross-sectional survey; high school athletes	Survey of 1710 high schools with AEDs	Reported number of student athletes	All cases occurring on campus	SCA/D	2006-2007	14-17, N=14	*High school* 1:23,000 (SCA/D) 1:64,000 (SCD)	Intermediate
Steinvil et al, 2011[117]	Retrospective cohort; athletes in Israel	Retrospective review of 2 Israeli newspapers	Competitive athletes registered in the Israel Sport Authority in 2009; extrapolated this data for prior 24 years based on the growth of the Israeli population (age 10-40 years) from the Central Bureau of Statistics; allowed for a presumed doubling of the sporting population over 24 years	All	SCD	1985-2009	12-44, N=24	*Athletes* 1:38,000	High

Study	Study design and population	Case identification (numerator)	Population definition (denominator)	Sports-related SCD or all SCD?	SCD or all SCA/D?	Study years	Age range (years), no. of cases	Annual incidence	Risk of bias
Maron et al, 2013[118]	Retrospective cohort; Minnesota high school athletes	Registry for Sudden Death in Athletes	Minnesota State High School League statistics (estimated using conversion factor of 2.3 to account for multisport athletes)	All	SCD	1986-2011	12-18, N=13	*High school* Overall 1:150,000 Male 1:83,000 Female 0	Intermediate
Toresdahl et al, 2014[78]	Prospective observational; high school students and student athletes	2149 high schools monitored for SCA events on school campus	Reported number of students and student-athletes	All cases occurring on school campus	SCA/D	2009-2011	14-18, N=44	*Student athlete* Overall 1:88,000 Male 1:58,000 Female 1:323,000 *Student nonathlete* Overall 1:326,000 Male 1:286,000 Female 1:357,000	Low
Drezner et al, 2014[106]	Retrospective cohort; Minnesota high school athletes	Public media reports	Minnesota State High School League statistics (sum of unduplicated athletes 2003-2004 through 2011-2012 school years)	All	SCA/D	2003-2012	14-18, N=13	*High school* Overall 1:71,000 Female 0 Male, basketball 1:21,000	Low
Harmon et al, 2015[79]	Retrospective cohort; college athletes	Parent Heart Watch database, NCAA Resolutions list, catastrophic insurance claims	Participation data from the NCAA	All	SCD	2003-2013	17-26, N=79	*College* Overall 1:53,000 Male 1:38,000 Female 1:122,000 Black 1:21,000 White 1:68,000 Football 1:36,000 Male, soccer 1:24,000 Male, black 1:16,000 Male, basketball 1:9,000 Male, black, basketball 1:5,300 Male, Div. 1 basketball 1:5,200	Low
Maron et al, 2016[119]	Retrospective cohort	Records of the Medical Examiner	Data from the Minnesota Department of Education, National Center for Education Statistics, and the Minnesota State High School League for Hennepin County, Minnesota	All	SCD	2000-2014	14-23, N=27	*Nonathlete* 1:39,000 *Athlete* 1:121,000	High
Harmon et al, 2016[80]	Retrospective cohort, United States high school athletes	Media reports	NFHS participation statistics	All	SCA/D	2007=2013	14-18, N=104	*High school* Overall 1:67,000 Male 1:45,000 Female 1:237,000	Intermediate

Study	Study design and population	Case identification (numerator)	Population definition (denominator)	Sports-related SCD or all SCD?	SCD or all SCA/D?	Study years	Age range (years), no. of cases	Annual incidence	Risk of bias
								Male, basketball 1:37,000	
Chatard et al, 2018[120]	Prospective, Pacific Island athletes who were screened	Prospectively followed	Defined cohort of 1450 athletes		SCD	2012-2015	10-40, N=3	*Pacific Island athletes* 1:2,416	High
Malhotra et al, 2018[84]	Prospective	Followed from time of screen to 2016	Defined cohort of 11,168 elite soccer athletes	All	SCD	1996-2016	15-17, N=8	*Elite male soccer athletes* 1:14,794	Low
Peterson et al, 2021[81]	Prospective	National Center for Catastrophic Sports Injury Research	Has defined cohort for high school and college athletes	All	SCA/D	2014-2018	14-18, N=204 18-24, N=39	*High school* Overall 1:66,000 Male 1:44,000 Female 1:204,000 Male, ice hockey 1:24,000 Male, basketball 1:40,000 *College* Overall 1:51,000 Male 1:35,000 Female 1:123,000 Black, male, basketball 1:4,800 White, male, basketball 1:15,000	Low
Petek et al, 2023[82]	Retrospective cohort study	National Collegiate Athletic Association resolutions list, Parent Heart Watch database and media reports, National Center for Catastrophic Sports Injury Research database, and insurance claims	Participation data from the NCAA	All	SCD	2002-2022	17-26 N=143	Overall 1:63,682 Male 1:43,348 Female 1:164,504 Football 1:32,000 Male, basketball 1:12,000 Male, cross-country 1:38,000 Male, Div 1, White, basketball 1:6,000 Male, Div 1, Black, basketball 1:8,000	Low

AED = automated emergency defibrillator; Div 1 = National Collegiate Athletics Association Division 1; NAIA = National Association of Intercollegiate Athletics; NCAA = National Collegiate Athletics Association; NFHS = National Federation of State High School Associations; NJCAA = National Junior College Athletic Association; SCA = sudden cardiac arrest; SCA/D = sudden cardiac arrest and death; SCD = sudden cardiac death.

Table 10 Studies of the causes of sudden cardiac arrest and death in athletes and young people*

Study	Years of study	Athletes or young people	Methods	Autopsy	Country	Sports-related or all deaths	Age range (years)	Cases	HCM	Idiopathic LVH/ fibrosis	Coronary artery anomalies	ACM/ARVC	DCM	AN-SUD**	CAD	Myocarditis related	Aortic dissection	Commotio cordis	Other
Corrado et al[121]	1979-1999	Athletes	Prospective, mandatory reporting, all deaths in Veneto region	Standard procedure at referral center	Italy	All	12-35	46	2%	0%	13%	26%	2%	2%	22%	11%	2%		17%
Maron et al[116]	1980-2006	Athletes	Retrospective, registry, media reports	Review of available autopsy	United States	All; includes SCA	8-39	1114	23%	5%	11%	3%	1%	35%	2%	4%	2%	6%	9%
Holst et al[107]	2000-2006	Young people	Retrospective, death certificates	Autopsy reports, hospital records	Denmark	Sports-related	12-35	14	0%	7%	7%	29%	0%	29%	14%	7%	0%		7%
Suarez-Mier et al[122]	1995-2010	Young people	SCD referred to National Institute of Forensic Sciences of Madrid	Standard procedure at referral center	Spain	Sports-related	9-35	81	10%	9%	6%	15%	0%	23%	14%	5%	0%		19%
Bohm et al[110]	2012-2014	Young People	Retrospective	Media reports, registry	Germany	Sports-related	10-34	29	7%	3%	10%	3%	3%	17%	21%	31%	0%		3%
Harmon et al[80]	2007-2013	Athletes	Retrospective, media reports	Autopsy reports	United States	All	14-18	50	14%	28%	8%	2%	0%	18%	6%	14%	0%		12%
Morentin et al[123]	2010-2017	Young people	Retrospective	Standard procedure at referral center	Spain	Sports-related	15-24	14	14%	21%	0%	36%	0%	0%	0%	21%	0%		7%
Thiene et al[124]	1980-2015	Athletes and young people	Prospective	Standard procedure at referral center	Italy	All	< 40	75	5%	0%	16%	27%	0%	11%	23%	4%	0%		15%
Wisten et al[125]	2000-2010	Young people	Retrospective	Death certificates, autopsy, and	Sweden	Exercise-related SCD	<35	62	16%	10%	0%	13%	6%	24%	11%	11%	0%		8%

				medical records															
Egger et al[126]	2014-2018	Athletes	Media reports, registry	Autopsy reports and interviews	Many	SCA/D	<35	104	11%	9%	13%	4%	1%		14%	13%	0%	7%	42%
Peterson et al[81]	2014-2018	Athletes	Media reports, reports to NCCSIR	Autopsy reports	United States	SCA/D	11-29	209	21%	13%	12%	6%	3%	10%	2%	4%	3%		16%
Bohm et al[127]	2012-2019	Young people	EMS and web-based screening	Autopsy reports	Germany, France	SCA/D	18-35	25 with autopsy	8%	4%			4%	24%	20%	16%			24%
Finocchiaro et al[92]	1994-2022	Athletes	All cases SCD referred to CRY	Standard procedure	United Kingdom	All	18-35	128	3%	12%	9%	8%	3%	52%	1%	0%	0%	5%	7%
Petek et al[82]	2002-2022	Athletes	NCAA database	Autopsy reports	United States	All	18-26	118	13%	17%	8%	5%	2%	19%	6%	7%	4%	2%	13%
Total								**2002**	**17%**	**8%**	**10%**	**6%**	**2%**	**29%**	**6%**	**5%**	**1%**	**4%**	**12%**

*If studies used same/similar or subsets of database most recent or complete included.

**Reported Wolff-Parkinson-White and long QT syndrome included in AN-SUD.

ACM = arrhythmogenic cardiomyopathy; AN-SUD = autopsy-negative sudden unexplained death; ARVC = arrhythmogenic right ventricular cardiomyopathy; CAD = coronary artery disease; CRY = Cardiac Risk in the Young; DCM = dilated cardiomyopathy; EMS = emergency medical services; HCM = hypertrophic cardiomyopathy; LVH = left ventricular hypertrophy; NCAA = National Collegiate Athletics Association; NCCSIR = National Center for Catastrophic Sport Injury Research; SCA = sudden cardiac arrest; SCA/D = sudden cardiac arrest and death; SCD = sudden cardiac death.

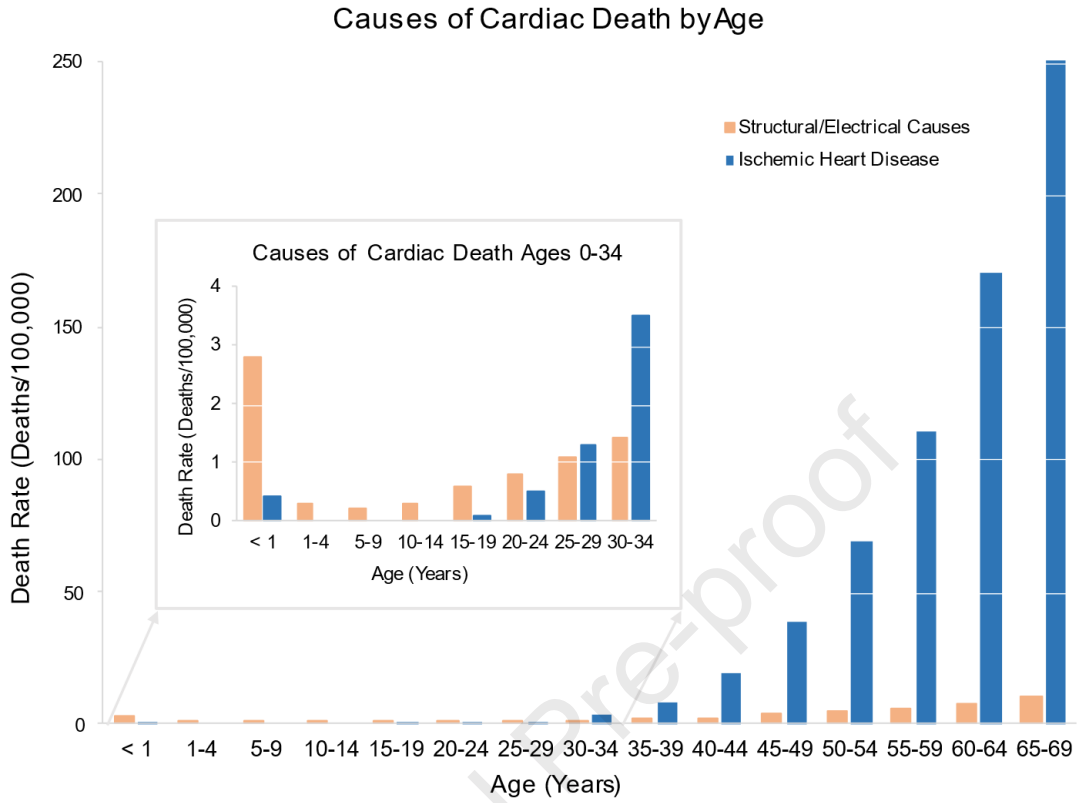

Figure 3

Coronary artery disease and other structural/electrical causes of cardiac death by age (1999-2020) from CDC Wonder.[88] ICD-10 codes for other structural/electrical causes include I40.0 (Infective myocarditis), I40.1 (Isolated myocarditis), I40.8 (Other acute myocarditis), I40.9 (Acute myocarditis, unspecified), I42.0 (Dilated cardiomyopathy), I42.1 (Obstructive hypertrophic cardiomyopathy), I42.2 (Other hypertrophic cardiomyopathy), I42.3 (Endomyocardial (eosinophilic) disease), I42.4 (Endocardial fibroelastosis), I42.5 (Other restrictive cardiomyopathy), I42.8 (Other cardiomyopathies), I42.9 (Cardiomyopathy, unspecified), I45.6 (Pre-excitation syndrome), I46.1 (Sudden cardiac death, so described), I46.9 (Cardiac arrest, unspecified), and Q24.5 (Malformation of coronary vessels).[88]

3.2 Sudden cardiac arrest prevention strategies

The prevention of SCA in athletes involves the detection of underlying cardiovascular conditions that may put a young athlete at risk including inherited cardiomyopathies, channelopathies, conduction abnormalities, and other congenital conditions. Approximately 1 in 300 young athletes will have an underlying cardiac condition that may predispose to SCA.[84,128-132] SCD is the leading medical cause of death in young athletes and the leading cause of death while exercising. In athletes aged > 30 to 35 years, coronary artery disease is the most likely entity to cause SCA. [85,88,89] Athletes aged > 25 years should have their coronary risk factors appropriately assessed.[133,134]

Recommendations for sudden cardiac arrest prevention strategies		
COR	**LOE**	**Recommendations**
1	**C-EO**	**1. In athletes, periodic preparticipation evaluations including screening for SCD risk is recommended.**

Synopsis

There is no generally agreed upon screening strategy, with the AHA/ACC recommending a preparticipation cardiovascular screen using a 14-point history and physical examination,[135-137] other professional societies recommending the addition of a 12-lead ECG,[138] and still others advocating performance of an ECG just for competitive athletes or based on available resources.[70,139-141] A full discussion of the nuances of preparticipation cardiovascular screening in young athletes is beyond the scope of this document; however, if preparticipation screening is performed, it is recommended that the evaluation include screening for SCD risk.

Recommendation-specific supportive text

1. Guidance for cardiovascular screening strategies varies but includes, at a minimum, a history and physical examination.[142-146] The ECG added to the history and physical examination has been shown to be complementary and to outperform history and physical alone in detecting some conditions leading to SCD,[129] and evolution of ECG screening criteria has significantly decreased false positive rates.[147] The need for experienced readers, the potential financial costs, and the limited utility in specific conditions and populations (eg, anomalous coronary arteries) are major limitations of ECG screening.[136,142-146] Many studies show increased diagnostic yield of ECG over history and physical exam.[90,129] ECG screening has not been clearly shown to improve mortality[90,117] in population studies. Whether history and physical improves mortality has not been tested. An in-depth review of the ECG screening debate is beyond the scope of this consensus document.

   As described in **Section 2**, athletic training leads to electrical and structural adaptation reflected in the ECG, and if a 12-lead screening ECG is performed, it should be evaluated by an individual with expertise in interpretation of young athletes' ECGs using modern criteria.[148]

   Athletes over 25 years of age need appropriate evaluation based on cardiovascular risk factors for atherosclerotic heart disease.[133,134]

   Echocardiography as a screening modality has been suggested[149] and is in use in some professional leagues. Very small studies show an increased yield of cardiac diagnoses compared with history and physical examination alone.[150] This modality is not widely recommended as a screening test.[151,152]

3.3 Diagnostic evaluation of sudden cardiac arrest

As shown in **Figure 4**, the initial diagnostic workup of an athlete with cardiac arrest begins in the emergency department, ideally in consultation with a cardiologist/electrophysiologist, with history (including prior diagnosis, medications, and family medical history), vital signs, physical examination, laboratory work, and ECG.[11] Although toxicology screen is less often positive in sports-related SCA than non-sports-related,[153] occasionally a positive test leading to diagnosis is found. Important steps to understand the event include obtaining AED strips, questioning any witnesses, and reviewing any available video of the event. A history of left chest impact immediately prior to the event can point to a commotio cordis event after other entities are evaluated and excluded. Exercise-related events are more common in the arrhythmogenic right ventricular cardiomyopathy (ARVC) form of ACM and in CPVT.[27,154-156] Patients with anomalous coronary arteries nearly exclusively die secondary to exercise-

induced triggering of arrhythmias,[82] quite likely mediated via acute coronary ischemia and resultant ventricular arrhythmias. If there is fever in the resuscitated athlete, hyperthermia-related collapse should be considered. Blood pressure could be low due to dehydration or high due to untreated hypertension. In the physical examination, stigmata of Marfan syndrome should be sought, as should murmurs that may be present in HCM and valvular disease.

The ECG is abnormal in approximately 90% of patients with HCM (left ventricular hypertrophy, T-wave abnormalities, pseudo–myocardial infarction patterns).[157-159] Similarly, patients with ARVC forms of ACM often, although not always, have abnormal ECGs with right bundle branch blocks, epsilon waves, and T-wave inversions in the anterior leads.[160] Patients with Brugada syndrome may present with the classic type I covered pattern with T wave abnormalities in V1-V2,[161,162] although the pattern can be intermittent. Patients with WPW have a delta wave, although the preexcitation can be subtle in young patients with fast AV nodes, particularly with left-sided pathways. For many conditions, the ECG abnormalities may be inconsistent, and it is important to obtain serial ECGs. Patients with early repolarization syndrome present with ventricular fibrillation (VF) and early repolarization on 12-lead ECGs.[163] Patients with genetic cardiomyopathies and myocarditis will often have nonspecific ST and T wave abnormalities. Patients with commotio cordis often have precordial ST elevation on their presenting ECG.[164] Short QT on ECG or short-coupled premature ventricular contractions (PVCs) on ECG or telemetry may also lead to a diagnosis.[165-167] ECGs are typically normal in CPVT, anomalous coronary arteries, and idiopathic VF. ECGs often show prolonged QTc in resuscitated patients,[168-170] so the initial ECGs should not automatically lead to a diagnosis of LQTS. In a small study with repeated ECGs, most had returned to normal within 3-5 days, although 20% remained abnormal at discharge.[168-170] After the initial workup in the emergency department, next steps could include the cardiac catheterization laboratory if there is ST elevation consistent with an acute infarct or targeted temperature management (TTM)[171] if they remain unconscious. Further workup can wait until TTM is completed. All patients should be admitted and placed on cardiac telemetry.

Hospitalization continues until the diagnostic workup is complete, and secondary preventive measures are implemented as directed by the diagnosis. Workup includes cardiac echocardiogram in all patients who survive a cardiac arrest. This can show abnormalities in athletes with HCM, ACM, and other cardiomyopathies as well as congenital heart disease (CHD). Bileaflet prolapse points to further evaluation for arrhythmic mitral valve prolapse with CMR.[172] Echocardiograms are typically normal in myocarditis, CPVT, LQTS, WPW (although some can have Ebstein anomaly of the tricuspid valve), early repolarization, and commotio cordis. Echocardiograms should be interpreted in the context of cardiac adaptation to exercise. If the diagnosis is still in doubt, patients should receive CMR, which is more sensitive in diagnosis of structural heart disease such as HCM, ACM, or arrhythmic mitral valve prolapse or noncompaction as well as myocarditis.

Exercise stress testing can be helpful in diagnosing CPVT if it induces ventricular arrhythmias. Burst exercise stress testing may increase sensitivity for CPVT.[41] Stress testing can also be helpful in LQTS, as the QT will often lengthen in recovery;[173] epinephrine can also bring out QT lengthening.[174] Ajmaline, procainamide, or flecainide administration can bring out the abnormalities of Brugada syndrome.

Genetic testing is increasingly useful in the workup of patients with cardiac arrest, especially in younger patients and those with idiopathic VF or idiopathic cardiomyopathies. A pathogenic or likely pathogenic variant can be found in approximately 65% of patients with HCM, 60% of patients with ARVC forms of

ACM, 75-80% of patients with LQTS,[175] 60% of patients with CPVT, 20%-30% of patients with Brugada,[176] and up to 30% of patients with genetic cardiomyopathies. Variants in RYR2, suggestive of calcium deficiency release syndrome, which is electrically silent, may be seen on genetic testing.[177] Variants of uncertain significance are of little use.[178-183] ECGs of family members should be obtained. The finding of a pathogenic variant will also impact family member cascade screening (see also **Section 8.3**).

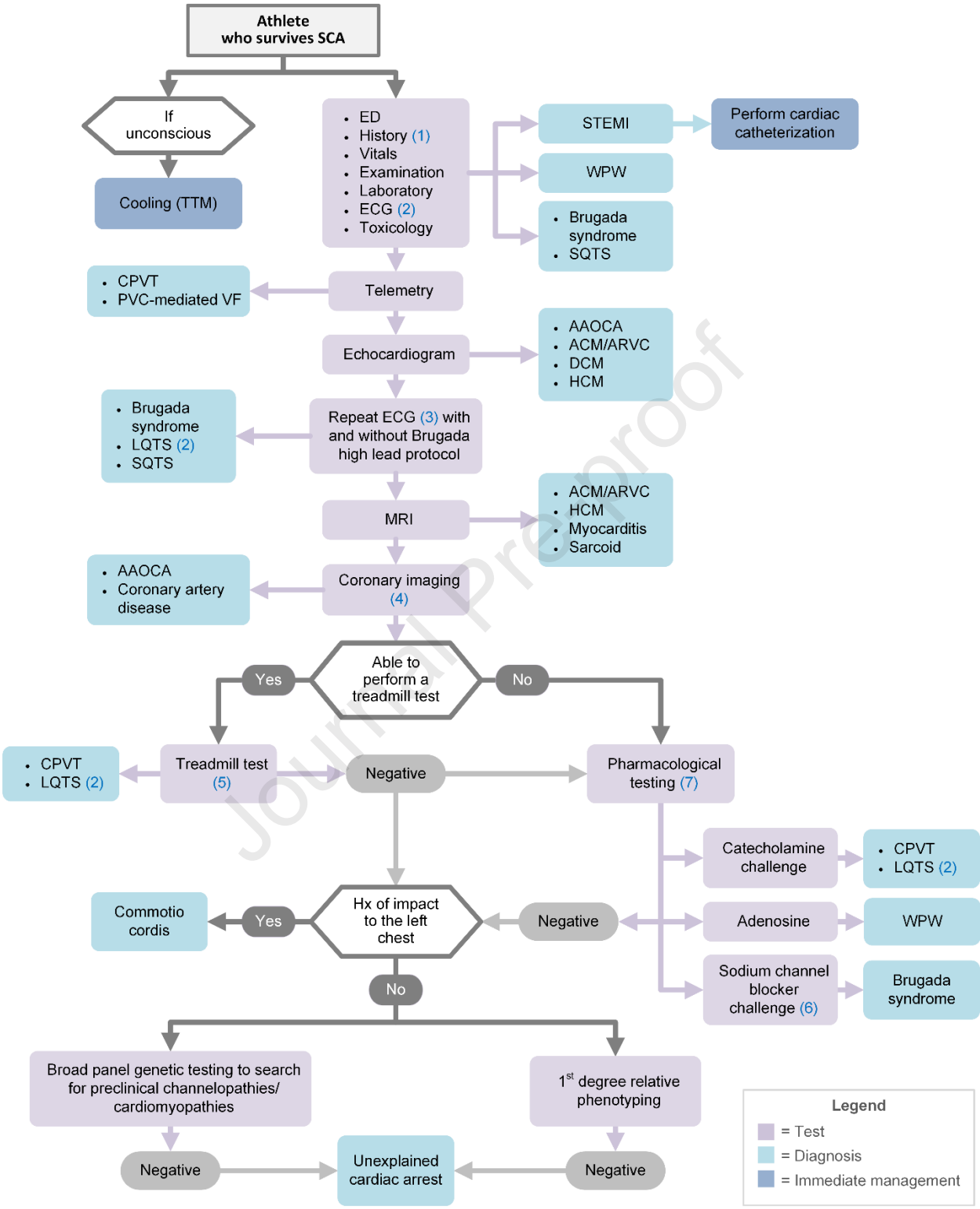

Figure 4

Diagnostic algorithm for the evaluation of sudden cardiac arrest (SCA) in athletes. (1) History should include circumstances of arrest, past medical history, and family medical history. The circumstances of the arrest may drive the clinical investigation. For example, if the patient was struck in the chest, commotio cordis is high in the differential. If the arrest is associated with a high adrenergic state or noise/startle/emotion, then adrenergic testing should be performed. If the arrest happened while the

patient is at rest or sleeping, then Brugada syndrome is in the differential, so high precordial lead ECG and sodium blocking pharmacologic testing should be performed.[162] Initial ECG may be diagnostic of Wolff-Parkinson-White (WPW) syndrome, Brugada syndrome, or ST elevation myocardial infarction (STEMI). (2) If the post-arrest electrocardiogram ECG (after 3-4 days) shows no persistent QT prolongation, use caution in interpreting catecholamine challenge or stress test results. (3) ECGs early after an arrest will often have long corrected QT intervals (QTc) as well as other transient abnormalities that include transient QT prolongation, transient T-wave inversions, or other repolarization abnormalities. (4) For the younger patient without risk factors for coronary artery disease, a computed tomography coronary angiogram protocol would identify those with anomalous coronary arteries. For those more likely to have coronary disease, a cardiac catheterization may be used. (5) In the evaluation of CPVT, a burst exercise stress test is more likely to bring on the arrhythmias of CPVT.[41] (6) Specific sodium channel blocker tests may include ajmaline, procainamide, and/or flecainide. Ajmaline has more false-positive test results. (7) Pharmacological testing based on clinical suspicion. AAOCA = anomalous aortic origin of coronary arteries; ACM = arrhythmogenic cardiomyopathy, ARVC = arrhythmogenic right ventricular cardiomyopathy, CPVT = catecholaminergic polymorphic ventricular tachycardia, DCM = dilated cardiomyopathy, Dx = diagnosis, ED = emergency department, HCM = hypertrophic cardiomyopathy, Hx = history, LQTS = long QT syndrome, MRI = magnetic resonance imaging, PVC = premature ventricular contraction, TTM = targeted temperature management.

3.4 Emergency action plan for and immediate treatment of sudden cardiac arrest

Prompt recognition of SCA, implementation of an EAP, and time to defibrillation are crucial to survival.[68] In addition to anecdotal examples of public resuscitation of athletes, data have also demonstrated the importance of execution and importance of EAPs in saving the life of athletes. In sports-related SCA in high school athletes, survival rates of 85% are reported when the arrest was witnessed and an AED was used.[64,69] EAPs have been widely recommended at all levels of sport,[70-73,140,184] although recreational sporting leagues may be less prepared.[185] EAPs also save lives in all attending the events—coaches, referees, and spectators. The first step to an efficient emergency response is prompt recognition of SCA. Any athlete who is collapsed and nonresponsive should be assumed to have SCA until proven otherwise. Treatment of SCA involves activation of the EMS, early cardiopulmonary resuscitation, and early defibrillation. AEDs should be placed strategically to achieve < 3-minute retrieval time. AEDs need to be accessible in an unlocked cabinet. Coaches and other potential first responders should be trained in CPR and AED use, and plans should be practiced at least annually. A system that requires regular checks to ensure proper operation of AEDs is critical. Organizations should coordinate plans with local EMS providers. When EAPs are practiced and rehearsed regularly, SCA can be survived[64,69] (see **Table 6**). In addition to general planning for venues, when athletes with known cardiovascular disease are returning to play, individualized EAPs should also be in place.

Recommendations for emergency action plan for and immediate treatment of sudden cardiac arrest sudden cardiac arrest		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In athletes who have collapsed and are nonresponsive, SCA should be presumed and acted upon until proven otherwise.[61,64]**
1	**C-EO**	**2. For athletes with a known SCA-predisposing heart condition who are returning to play, an individualized EAP should be in place.**

2b	**C-EO**	**3. In athletes with a known SCA-predisposing heart condition (and/or their families), obtaining and carrying a personal AED with their personal athletic equipment may be considered as part of their EAP made via shared decision-making.**

Synopsis

EAPs and early access to defibrillation are crucial to the survival of SCA. An acutely collapsed, unconscious athlete should be assumed to be in SCA until proven otherwise. AEDs should be available at all venues with reasonable risk of SCA occurring including recreational venues. Athletes with known cardiac conditions that may predispose them to SCA should have individualized EAPs with consideration for a personal AED.

Recommendation-specific supportive text

1. Because prompt resuscitation efforts improve survival in athletes,[61-65] immediate recognition is critical to implement life-saving interventions. Collapsed athletes often have tonic-clonic movements of arms and limbs, which can be mistaken for a seizure or other noncardiac cause of collapse, critically delaying treatment.[63,64] Likewise, agonal gasping can be mistaken for respirations and assessment of the presence or absence of pulse can be difficult in emergency situations, especially for lay responders. Therefore, any athlete with acute collapse who is unconscious should be assumed to have suffered a cardiac arrest and AED pads applied. Application of an AED is not dangerous, and a shock will not be discharged in the absence of an abnormal shockable rhythm. Delay in CPR due to efforts to prevent "tongue swallowing" and clear the airway have been described—this is not necessary and CPR should not be delayed.[186]

2. Athletes with a known condition predisposing for SCA or those returning to sport after SCA should have an individualized EAP that addresses ready access to an AED and any factors (equipment, location, potential responders) that may complicate resuscitation. The plan should be coordinated by medical staff and reviewed and practiced with potential responders.[71-73] AEDs should be placed near fields or courts where an arrest may occur. Sports that practice or compete outside a defined venue such as cross-country should consider how EMS will be activated and accessed. An EAP in this case may include running with a partner, carrying a phone, and awareness of location for directing EMS. EAPs in unique environments such as swimming facilities should be reviewed and practiced. Those with SCA should be removed from the pool, but most AEDs are self-grounded and safe to use on wet athletes, in wet environments (such as pool decks or on snow and ice), or on metal grates. Rowing provides particular challenges including extraction from a shell or boat that should be considered and practiced annually.[187] Equipment can present barriers to resuscitation. EAP rehearsals in sports with pads or other protective equipment should include instruction and practice on how to remove pads and quickly access the chest for compressions and electrode pad application.

3. A personal AED may benefit athletes with a known SCA-predisposing heart condition,[188] whose risk may not warrant an implantable device but is not zero. A personal AED has been recommended by PACES, based on the known imprecision of risk stratification, non-risk-free nature of the ICD, particularly in children, and effectiveness of AEDs.[188] The risks and benefits, including psychological burden, as well as the importance of upkeep of the AED, need to be

discussed with the patient and family as part of a shared decision-making process.[54] Avoidance of economic disparities requires coverage of personal AEDs when recommended.

3.5 Sudden cardiac arrest treatment and implantable cardioverter-defibrillator management in athletes

The treatment of an athlete who has had a SCA has many similarities to that for nonathletes, but there are some important differences in that management decisions take into consideration the impact of treatment (eg, choice of medication or type of ICD) on sports performance. Also, return to play after a cardiac arrest requires confirmation that the underlying arrhythmic vulnerability has been identified and treated appropriately.

Recommendations for sudden cardiac arrest treatment and implantable cardioverter-defibrillator management in athletes		
COR	**LOE**	**Recommendations**
1	C-EO	1. In athletes who have experienced SCA, a comprehensive evaluation and shared decision-making discussion of potential risks of sports participation with an expert provider is recommended.
1	C-EO	2. In athletes who have experienced SCA, further evaluation including addressing psychological readiness should be completed prior to return to play.
1	A	3. In athletes who have experienced SCA, an ICD should be implanted as indicated based on underlying disease entity.[189-191]
2a	B-NR	4. In athletes with an ICD, return to play is reasonable, in the context of shared decision-making that includes underlying disease entity, clinical characteristics, and sport type.[192-194]
2a	B-NR	5. In athletes who have experienced SCA and are undergoing ICD implant, it is reasonable to consider sport type and disease entity in the decision regarding ICD type and location.[192,195]
2a	C-EO	6. For athletes undergoing ICD implantation who will be returning to play, a waiting period of 4-6 weeks after a new implant or 2 weeks after generator replacement is reasonable.
1	B-NR	7. In athletes who have experienced SCA and have an ICD, ICD detection criteria should be programmed to long duration and a high rate cutoff to prevent unnecessary shocks.[192,193,196,197]
1	C-EO	8. In athletes who have experienced SCA, exercise stress testing at maximum effort should be performed to measure heart rate, assess for arrhythmias during exertion, and confirm appropriate sensing by the ICD (if applicable) prior to return to vigorous exercise.
1	C-EO	9. In athletes who have experienced SCA, an individualized EAP should be in place prior to return to play.
1	A	10. In athletes who have experienced SCA, regular EP follow-up is recommended, including remote monitoring of ICDs (if applicable).[198-200]
1	C-EO	11. In athletes with an ICD who experience an ICD shock, an evaluation of the cause, treatment of the underlying etiology, and confirmation of appropriate device function should be done prior to return to play.

Synopsis

As summarized in the recommendation algorithm in **Figure 5**, return to play requires shared decision-making, individual EAPs, and appropriate follow-up and care with a cardiologist with experience in athletes and ICDs. Physical and psychological readiness need to be confirmed. Decision-making around treatment after SCA is based on the underlying disease. Patients with most of the underlying diseases causing SCA benefit from medical therapy, ablation, and/or an ICD. Patients with LQTS respond well to beta blockers, and beta blockers are likely beneficial for patients with CPVT as well. Patients with genetic cardiomyopathies and a depressed ejection fraction are generally treated with guideline-directed medical therapy and an ICD. For those receiving an ICD, device type and programming should be personalized to the athlete. Patients with WPW who survived a cardiac arrest usually should undergo ablation (see **Section 7**). Efficacy of treatment, whether medical, procedural, or device-based, should be confirmed by exercise stress testing prior to return to play, as should an individual EAP via discussion with stakeholders.

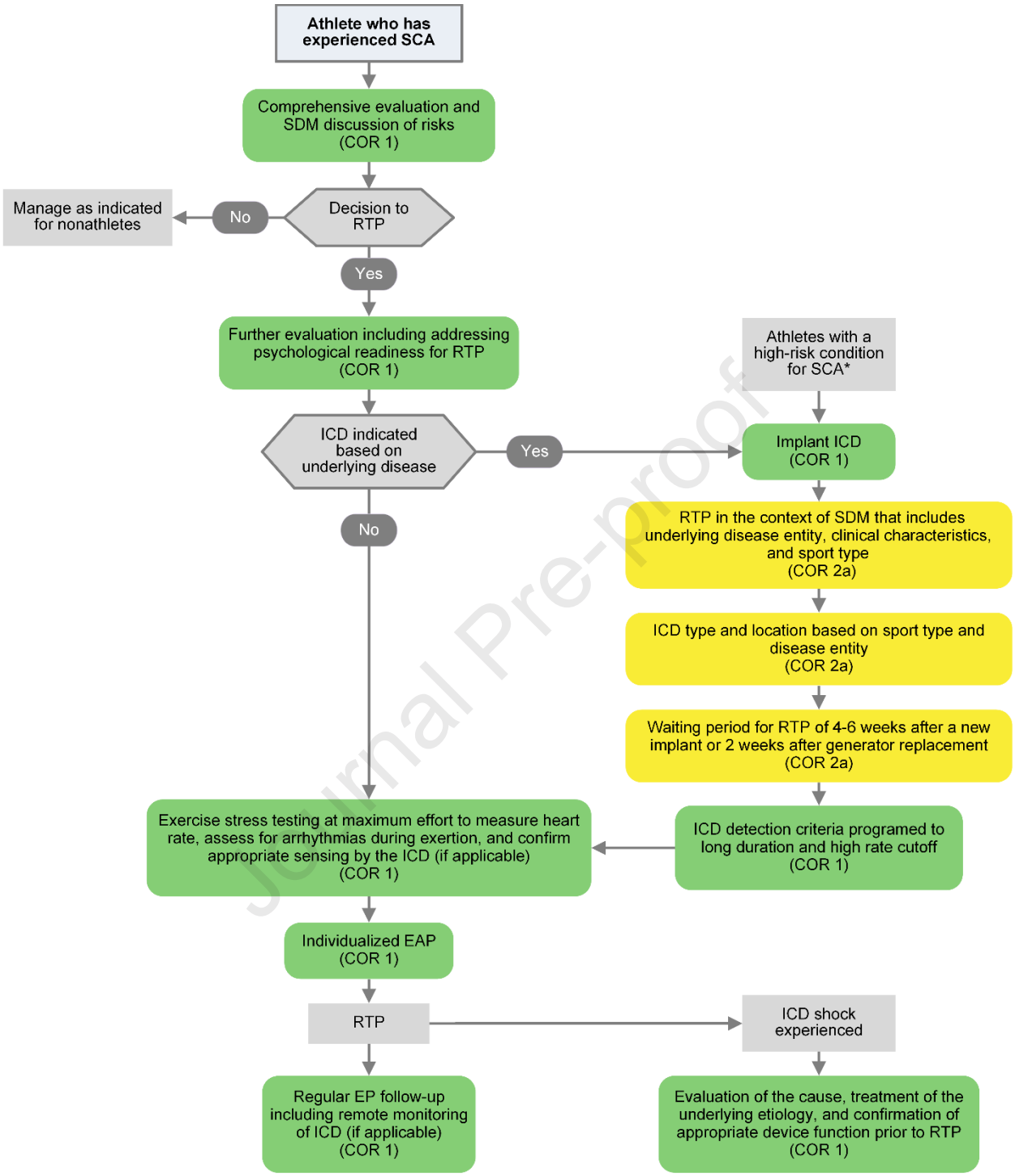

Figure 5

Algorithm for the management of sudden cardiac arrest (SCA) in athletes. Colors correspond to the class of recommendation (COR) in **Table 1**. *See **Section 8**. EAP = emergency action plan; EP = electrophysiology**;** ICD = implantable cardioverter-defibrillator; RTP = return to play; SDM = shared decision-making.

Recommendation-specific supportive text

1. Comprehensive evaluation to fully understand potential risks and benefits of return to play with a cardiologist who is not only an expert in the disease entity but also knowledgeable regarding the demands of sports settings is important.[54-56,201,202] The risk of recurrent SCA, underlying heart disease, type of sport, and wishes of the athlete are all important considerations. In addition, other stakeholders such as team physicians, parents, coaches, and institutions should be involved in the decision-making process.

2. Any athlete who has had SCA should have a full and complete evaluation, as discussed in detail in **Section 3.3** and **Figure 4**, to determine causation, if possible, and assess risk before return to play.[11] This workup should also include an assessment for psychological readiness. Survivors of SCA in general have high rates of subsequent psychological distress, including depression, anxiety, and post-traumatic stress.[203] Return to play even after less life-altering events can be psychologically difficult for athletes.[47] Cognitive, emotional, and behavioral responses to injury, such as resilience and optimism, vary in athletes, and these factors have been demonstrated to determine outcomes in athletes returning to sport after injury. Building confidence, providing support, and fostering autonomy have all been associated with improved outcomes with return to play after injury. How psychological factors impact return to sport after a cardiac event has not been studied, but these likely have a similar impact. Specific instruments to assess readiness are undergoing investigation in the sports medicine community.[204] Athletes returning to play after SCA need attention to both illness-related and sports-related emotional needs.

3. Medical decisions around treatment of the athlete surviving SCA, including device implantation, are based on the underlying disease and should be directed by an expert in that disease entity. As shown in **Figure 6**, most conditions leading to SCA in athletes are treated with an ICD, with the exception of those with reversible causes such as a ST elevation myocardial infarction, ablated WPW syndrome, commotio cordis, or surgically corrected anomalous coronary arteries.[8,205] Other electrical disorders can occasionally be treated medically or with ablation, without a device, under expert care. Decisions regarding ICDs in CPVT require an electrophysiologist experienced with this entity, as ICD shocks can be arrhythmogenic and there are some data suggesting medical therapies and/or sympathetic denervation are effective, as detailed in **Section 7.1**.[206] Other than these exceptions, randomized controlled trials in the general population have demonstrated that survivors of a ventricular tachycardia or VF SCA have improved long-term survival when randomized to an ICD compared with medical therapy.[189-191] These trials excluded those thought to have a reversible cause such as myocardial infarction, severe potassium disorders, commotio cordis, etc.

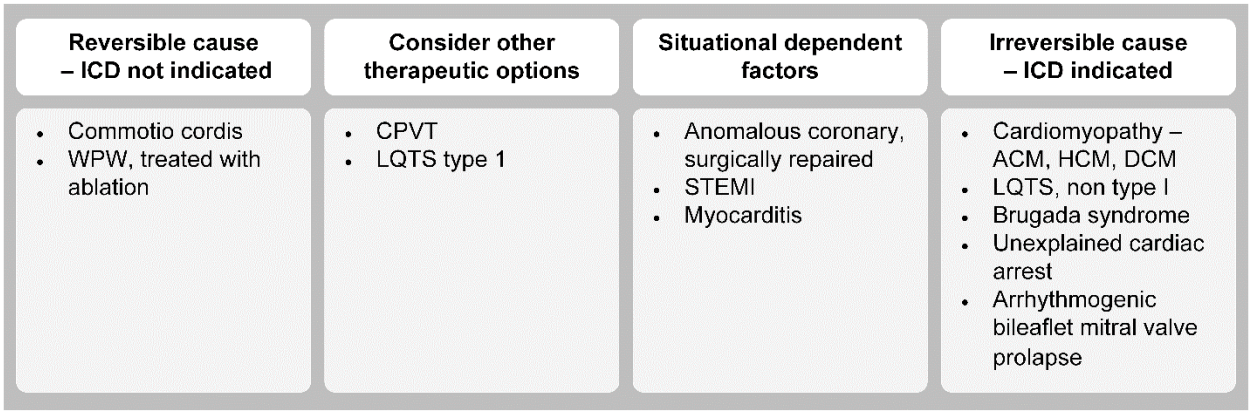

Figure 6 Treatment of sudden cardiac arrest based on disease entity. ACM = arrhythmogenic cardiomyopathy; CPVT = catecholaminergic polymorphic ventricular tachycardia; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter-defibrillator; LQTS = long QT syndrome; WPW = Wolff-Parkinson-White.

4. Several retrospective and prospective observational studies have demonstrated lack of high risk for adverse events in athletes continuing to participate with an ICD. The ICD sports registry[192,193] enrolled 440 athletes participating in competitive (N=393) or dangerous (N=47) sports, including 77 engaged in varsity/junior varsity/traveling team competition, and followed them for a median of 44 months. There were no tachyarrhythmic deaths or resuscitated SCAs during sports participation and no injuries related to arrhythmias during sports. Appropriate and inappropriate shocks occurred. More athletes experienced shocks during physical activity than rest, but there was no difference between competition/training and other physical activity. Most ventricular arrhythmias occurring during sports were converted with the first programmed shock, with multiple shocks occurring rarely.[192,193] A recent retrospective series of elite athletes included 8 with ICDs, with similar findings.[194]

5. For some sports, the subcutaneous implantable cardioverter-defibrillator may have advantages over the transvenous implantable cardioverter-defibrillator, although more research is needed. The main issue with transvenous ICDs is lead durability. In theory, sports involving significant arm/shoulder movement, such as rowing, swimming, or weightlifting, may create wear on the lead insulation and connections, potentially causing inappropriate shocks. The subcutaneous ICD lead is placed subcutaneously and outside the thorax, which is a potential advantage for athletes in sports with repetitive arm use. However, the lead being outside the thorax may be a disadvantage for athletes in contact or ball-based sports. A secondary analysis of the ICD Sports Registry data[207] found that sports with repetitive arm use and contact sports were not associated with lead malfunction. However, the sample size and follow-up time in this analysis were limited, and more research is needed to accurately assess this risk. To date, no studies have been published on the experience of athletes with subcutaneous ICDs, but research is ongoing. If choosing a subcutaneous ICD, sensing testing should be performed in different body positions. The newly approved extravascular ICD may offer other benefits, as the lead is implanted substernally.[208] **Figure 7** shows available ICD systems with advantages and disadvantages.

   When choosing a transvenous ICD for an athlete, other factors should be considered. Dual-chamber devices offer the ability to pace the atrium, but this is rarely necessary for athletes.

Better discrimination of supraventricular arrhythmias has not been proven in clinical trials.[209] In addition, dual-chamber devices have a higher rate of lead complications.[195] Therefore, unless atrial pacing is needed, athletes should receive a single-chamber device. For athletes participating in collision sports, who are not represented in the ICD Sports Registry, it is unknown whether system damage might be higher. One small series has described a minimally invasive epicardial device with the generator placed posterior to the anterior rectus muscle in the subcostal region. This system can be considered in high-collision-sport athletes, although data are not yet available in athletes.[210]

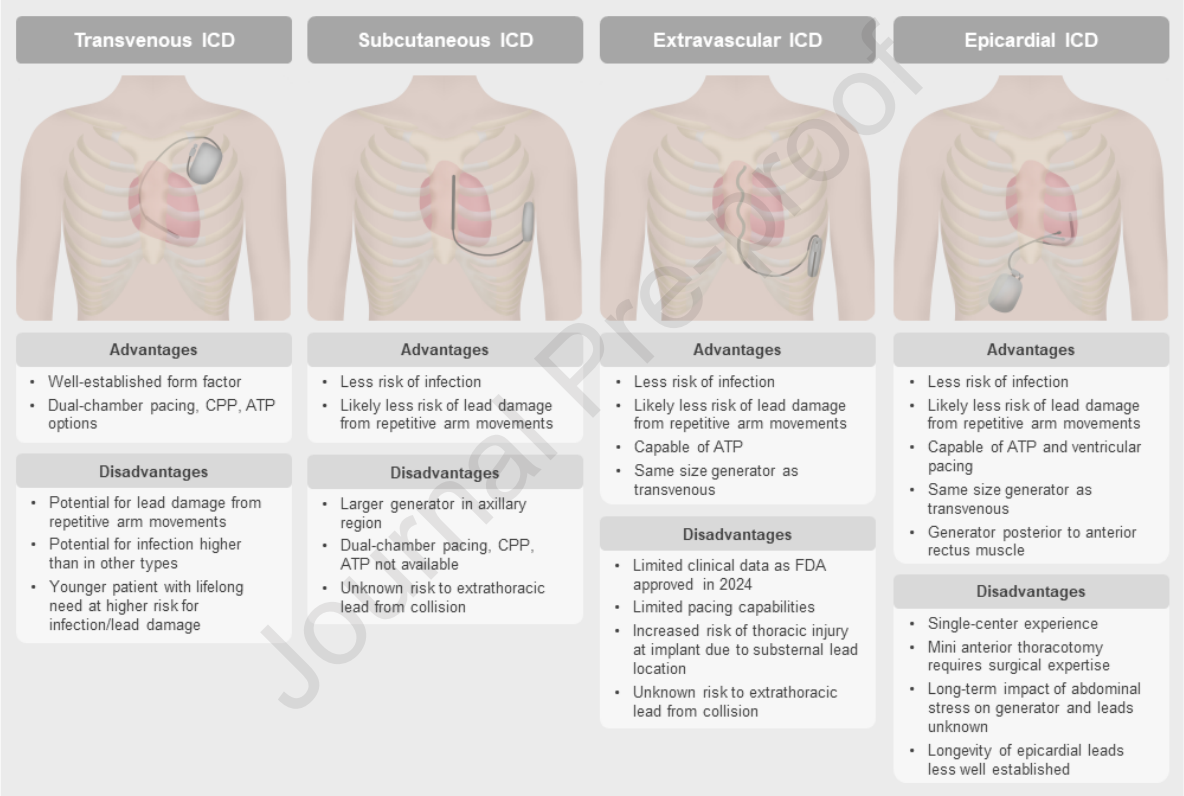

Figure 7
Athletespecific advantages and disadvantages of 4 different options for ICD form factors. ATP = antitachycardia pacing; CPP = cardiac physiologic pacing; FDA = Food and Drug Administration; ICD = implantable cardioverter defibrillator.

6. Avoidance of reaching or lifting for 4-6 weeks after implantation of transvenous leads has been traditionally recommended to avoid lead dislodgment before lead endothelization is complete. Several small studies of resistive range-of-motion exercise[211] and early removal of arm restriction[212,213] have not shown arm/shoulder movement to increase dislodgment or other complications, and an ongoing randomized trial of lenient versus strict arm restriction after device implant is ongoing.[214] However, at this time, as randomized data are not available and the published small studies did not investigate vigorous exercise/arm motion in athletes, continuation of the traditional advisory is recommended. Two weeks should be allowed for healing of the skin incision.

7. Young athletes can achieve very rapid heart rates (in general 220 – age). In the nonathlete, programming ventricular tachycardia detection rates > 200 bpm has been shown to reduce inappropriate shocks and increase longevity.[196] In the athlete, data have shown that high rate cutoffs and long duration programming decreased both appropriate and inappropriate shocks with no increase in syncope.[197]

8. Exercise stress testing that recreates the demands of an athlete's sport as closely as possible including maximal effort should be performed prior to return to sport to evaluate treatment efficacy and ICD programming. Protocols with exercise intensity targeting nonathletes may not be sufficient to recreate the training demands of an athlete. Stress testing of athletes is addressed in detail in **Section 2.3**.

9. EAPs that take into account the needs of the specific athlete, their sport, and their setting are important to consider and should be coordinated by medical staff. [73,215-217] These action plans could include a personal AED that is with the athlete at all times, particularly if ICD was not indicated, knowledge of the athlete's condition by the coach and medical staff, and surrounding personnel trained in CPR and AED use. In addition, special considerations related to settings where the athlete practices or competes (ie, outside of an arena or gymnasium) should be understood such as water sports (eg, swimming, rowing, canoeing) or sports in outdoor settings (cross-country or winter sports), including how to contact and provide timely access to an athlete by EMS. Individual EAPs are discussed in more detail in **Section 3.4**.

10. Most athletes with SCA have an underlying arrhythmia etiology requiring long-term follow-up, and most will have an ICD. Because athletes, particularly in college, may live far from their primary home, and from their primary EP team, maintaining continuity of care requires a purposeful care plan. Although there are no specific data in athletes, remote monitoring of ICDs improves outcomes and is recommended for all ICD patients.[218] Effective remote monitoring requires a defined physician or physician group that is responsible for this remote monitoring.[219] The primary EP team could include physicians where the athletes lives or where they go to school, but the athlete should at least have knowledge of a local care team with experience in ICDs. The monitor should follow the patient to the school and back during long breaks. The covering personnel should have the contact information of the patient.

11. Patients with ICD shocks and/or antitachycardia pacing therapy require an evaluation before returning to play to determine whether the therapy is appropriate or inappropriate. For inappropriate shocks, the leads and system should be evaluated and revised if indicated. If oversensing is the etiology, programming should be optimized. ICD therapy is increased by activity.[192,220] For athletes with appropriate shocks, ventricular arrhythmias should be treated as indicated with medications and/or ablation, and treatment efficacy should be confirmed prior to return to play.

Section 4 Commotio cordis

Commotio cordis—sudden death with relatively innocent chest wall impact—was described in the 19th century,[221] but only in the last 15 years has it become more widely known. Current estimates of incidence range from 10 to 20 events a year in the United States.[95,222] In some series, commotio cordis

was the second leading cause of sudden death in young athletes in the United States when it was included as a cause of athletic deaths,[223] although more recent data from the NCAA describe just 2 of the 127 SCAs over 20 years as being due to commotio cordis.[82] Commotio cordis is also increasingly described in European nations.[224,225] Commotio cordis has also been described in nearly every sport, and even in nonsport activity due to collision with body parts such as elbows, fists, and knees.

Based on human and experimental data, commotio cordis is likely due to immediate VF triggered by chest wall impact. A necessary confluence of patient characteristics (age, chest wall compliance, location of impact) and impact object variables (timing, hardness, shape) is what underlies the relatively rarity of commotio cordis.[226,227] Susceptible patients are young and typically male. There may also be a genetic predisposition or protection from commotio cordis.[228]

Successful resuscitation cases, originally thought rare in commotio cordis, are now routinely reported, likely due to increased recognition that VF is the cause of sudden collapse after chest wall impact and the increased prevalence of AEDs and knowledge of CPR in the community (see **Table 6**).[229,230] Prompt recognition and early defibrillation are paramount. The critical importance of emergency action planning for sporting venues is described in **Section 2.5**.

4.1 Commotio cordis prevention and diagnosis

Recommendations for commotio cordis prevention		
COR	**LOE**	**Recommendations**
1	**C-EO**	**1. In athletes who have experienced SCA with a history of blow to the chest, underlying heart disease should be excluded prior to diagnosing commotio cordis.**
1	**C-EO**	**2. For athletes participating in sports for which chest protectors are used, chest protectors should meet sports- and position-appropriate standards.**
2a	**C-EO**	**3. In athletes under age 13 years, the use of age-appropriate safety baseballs is reasonable to reduce the risk of commotio cordis.**

Synopsis

Athletes suffering SCA after a blow to the chest need full evaluation to exclude the possibility of underlying heart disease prior to making a diagnosis of commotio cordis. The risk of commotio cordis can likely be decreased. Coaching and rules should be amended to not allow blocking the ball with the chest in sports. Chest protectors were present in one-third of the individuals who suffered commotio cordis during competitive sports.[231,232] In some sports such as hockey, the arms were lifted, pulling the chest protector upward and thus exposing the chest.[232] However, in other sports such as lacrosse and baseball, the ball struck the chest protector, which was directly over the heart, and commotio cordis still resulted. Age-appropriate safety (ie, softer) baseballs will decrease the risk of VF with chest wall impact.[233]

Recommendation-specific supportive text

1. Commotio cordis is a rare cause of SCA in athletes. Athletes suffering SCA after a blow to the chest need full evaluation to exclude the possibility of underlying heart disease prior to making that diagnosis. Commotio cordis stems from a rare external event—a blow to the chest timed in

milliseconds to the cardiac cycle—and it does not carry risk of recurrence. It is critical to exclude other potential etiologies that may require secondary prevention of SCA with an ICD and/or arrhythmia suppression.

2. To facilitate the development of effective chest protectors and ensure their quality, based on data from the experimental model[233] and other data, a mechanical surrogate to assess the ability of chest wall protectors to decrease the risk of commotio cordis was developed.[234] This has been licensed to the National Operating Committee on Standards for Athletic Equipment (NOCSAE)[235] and is in use by such organizations as the National Federation of State High School Associations (NFHS),[236] the NCAA Baseball Rules Committee,[237] and USA Lacrosse.[238] Similar standardization should be implemented worldwide.

3. A reduction in the risk of commotio cordis is likely possible with age-appropriate safety baseballs. Commotio cordis is rarely seen with safety baseballs, and these balls have been tested in an experimental model and were found to lower the risk of VF with ball impact.[233] Similar modifications have not been attempted in other sports.

Section 5 Symptoms of arrhythmias in athletes

5.1 Syncope in athletes

Syncope is a transient loss of consciousness, associated with the inability to support postural tone, with rapid and spontaneous recovery, secondary to diffuse cerebral hypoperfusion.[239] This clinical symptom, with a spectrum of underlying mechanisms and etiologies, can be classified as cardiogenic, neurally mediated, or orthostatic syncope. Neurally mediated syncope occurs when neural reflexes modify heart and blood pressure inappropriately, which can occur in response to multiple vagal stimuli including strong emotion, micturition, defecation, swallowing, and coughing. Orthostatic syncope occurs with a loss of vascular tone resulting in cerebral hypoperfusion. In athletes this most often occurs after the abrupt cessation of strenuous exercise and pooling of blood in the extremities. Loss of consciousness in athletes can also be related to nonsyncopal causes including head trauma, heat illness, hyponatremia, and SCT.[240]

Loss of consciousness in both athletes and nonathletes can also be due to systemic causes such as diabetes, seizures, or intoxication or psychogenic causes, which should be included in the differential diagnosis.

Nontraumatic loss of consciousness while exercising needs to be considered cardiac until proven otherwise. As described in detail below, only a small fraction of those with exertional syncope will ultimately be diagnosed with cardiac disease but an appropriate workup is essential, as these entities can be life-threatening. Exertional syncope should be investigated to rule out cardiac substrates including cardiomyopathies such as HCM or ACM anomalous coronary artery origin, or electrical abnormalities leading to ventricular arrhythmia such as LQTS or CPVT, all of which are associated with sudden death.[240] An algorithm for the approach to syncope in the athlete is shown in **Figure 8**.

5.1.1 Etiologies (cardiac/electrophysiology differential)

There are many underlying cardiac causes, either structural or electrical, that can be responsible for syncope in athletes. The diagnostic approach for athletes with syncope should be focused to exclude

these cardiac substrates for ventricular tachyarrhythmia and SCD. Syncope in athletes that occurs during exercise is more likely to be associated with structural cardiac pathology potentially associated with SCD than syncope that occurs post-exercise or is not exercise-related, although this remains a rare cause.[241] Colivicchi et al[242] describe a cohort of 7568 athletes of whom 474 (6.2%) reported at least 1 syncopal episode. In the majority of athletes, syncope was unrelated to exercise (86.7%); syncope was post-exertional in 57 (12.0%) and exertional in 6 (1.3%). All episodes of nonexertional or post-exertional syncope had the typical features of neurally mediated fainting with a prodrome and were not related to cardiac disease. Of the 6 athletes with exertional syncope, 1 had HCM and 1 had right ventricular outflow tract (RVOT) ventricular tachycardia. Although this study showed a relatively high rate of cardiac causes, subsequent series have shown cardiac etiologies in 8-10% of exercise-related syncope.[242-247] **Table 11** shows series of studies in athletes that looked at the etiology of syncope during exercise. From a total of 6 studies, 82 athletes manifested syncope during exercise. Most of the episodes (75 of 82 [91.5%]) were not associated with structural heart disease. The remainder (8.5%) occurred in athletes diagnosed with cardiovascular disease, which included HCM in 1 of 7 (14.2%), RVOT ventricular tachycardia in 1 of 7 (14.2%), mitral valve prolapse in 3 of 7 (42.8%), angina in 1 of 7 (14.2%), and anomalous coronary artery in 1 of 7 (14.2%). The majority of these events did not occur in the setting of underlying structural or electrical disease; however, because these diseases can be life-threatening, workup is indicated.

Table 11 Series of athletes with syncope

Study	Study design (N)	Age	Syncope Timing	Syncope N (%)	Findings
Colivicchi et al, 2004[242]	Preparticipation screening N=7568 athletes, 474 reported prior syncope in the past 5 years	16 ± 3 years	During exertion	6 (1.3%)	1/6 (16.7%) HCM; 1/6 (16.7%) RVOT VT; 4/6 (66.7%) noncardiac
			Post-exertion	57 (12.0%)	100% noncardiac
			Non-exercise-related	411 (86.7%)	100% noncardiac
Colivicchi et al, 2002[243]	Cohort study N=33 athletes with recurrent exercise-related syncope	Mean age 21.4 ± 3.2 years	During exertion	33 (100%)	2/33 (6%) mitral valve prolapse; 4/33 (12.1%) hypotension during maximal exercise; 22/33 (66.6%) head-up tilt testing positive
			Post-exertion	NR	NR
			Non-exercise-related	NR	NR
Holtzhausen et al, 1994[245]	Prospective series in 56 km ultramarathoners N=111 athletes, 46 collapsed during or after the race	33 ± 8 years	During exertion	8	3/8 (37.5%) hypoglycemia; 3/8 (37.5%) gastroenteritis; 1/8 (12.5%) angina; 1/8 (12.5%) asthma
			Post-exertion	38	Diagnosed exercise-associated collapse
			Non-exercise related	NR	NR
Kaiser-Nielsen et al, 2017[246]	Retrospective series in athletes referred for any symptom N=201 athletes, 38 with syncope	Median age 27 years	During exertion	10 (26.3%)	Reported no cardiac syncope, specific diagnoses NR
			Post-exertion	13 (35.2%)	Reported no cardiac syncope, specific diagnoses NR
			Non-exercise-related	15 (39.5%)	Reported no cardiac syncope, specific diagnoses NR
McKinney et al, 2017[247]	Preparticipation screening N=1419 athletes, 16 reported prior exertional syncope	12–35 years	During exertion	16 (100%)	1/16 (6.3%) mitral valve prolapse
			Post-exertion	NR	NR
			Non-exercise-related	NR	NR
Gier et al, 2023[244]	Retrospective series in college athletes with syncope/presyncope N=55 athletes, 15 with syncope related to exercise	19.7 ± 1.5 years	During exertion	9 (25.0%)	1/9 (11.1%) anomalous aortic origin of coronary artery
			Post-exertion	6 (16.7%)	No underlying cardiac condition
			Non-exercise-related	NR	NR

HCM = hypertrophic cardiomyopathy; RVOT VT = right ventricular outflow tract ventricular tachycardia; NR = not related.

5.1.2 Etiologies (noncardiac differential)

Noncardiogenic causes of syncope can be broken down to orthostatic syncope and neurally mediated (reflex) syncope.[239,248] A thorough and complete history can suggest the cause of syncope and direct the workup. The most common cause of syncope in athletes is post-exertional syncope due to the abrupt decrease in venous return that occurs when activity is stopped and there is a relaxation of the "muscular pump," a form of orthostatic syncope.[249] With prolonged exertion there is significant vasodilation, and the sudden loss of pressure by skeletal muscle causes pooling of the blood in the extremities, which leads to loss of consciousness. Training-induced increases in vagal tone may increase likelihood of this occurrence. Post-exertional orthostatic syncope can be witnessed at any time; a common example occurs in long-distance running often as athletes cross the finish line, exiting "the chutes." Likewise, post-exertional orthostatic syncope is common in rowing, particularly when training on dry land on a rowing ergometer while doing set workouts or "pieces." Post-exertional syncope does not reflect underlying life-threatening disease, and it can be treated with attention to volume, electrolyte, and hydration status as well as a slow cool-down period. In some cases, compression stockings, either knee or thigh high, may be helpful. Inadequate nutrition may exacerbate this type of syncope, and eating regularly or consultation with a nutritionist can be helpful.[250] In athletes with heat-related post-exercise syncope who have not responded to nonpharmacological treatment, one small series has suggested an H1-receptor antagonist may be helpful.[251] Neurally mediated syncope occurs when neural reflexes modify heart and blood pressure inappropriately, which can occur in response to strong emotion, micturition, defecation, swallowing, and coughing in both athletes and nonathletes.

As shown in **Table 12**, loss of consciousness can occur from other athletic-related conditions such as head trauma, heat illness, hyponatremia, and exertional collapse related to SCT.[249] History and context should inform these diagnoses. For heat illness, treatment is emergent and includes rapid cooling, best accomplished in an ice bath with evaluation of rectal temperature. Cooling is critical and should occur before transport to emergency care. Hyponatremia should be suspected in situations where significant consumption of water has occurred. This is typical in a long-distance race or marathon in a participant with a slower pace and longer overall duration of exercise. Hyponatremia is associated with incoordination and altered mental status. One in 12 Black individuals are heterozygous for SCT, which is associated with an increased risk of sudden death.[103] This is distinct from sickle cell disease, which is generally incompatible with strenuous physical activity. The pathogenesis of exercise-associated collapse associated with SCT is sickling of red blood cells in the microvasculature leading to muscle death, massive release of potassium, and fatal arrhythmia. Exercise-associated collapse associated with SCT occurs only when athletes are unable to stop and recover and are pushed beyond their physical capacity, which is almost always when training. Any struggling and collapsing athlete should not be pushed and should be allowed to recover. If the athlete is known to have SCT, physical activity should be halted if the athlete is struggling. If they collapse, EMS should be activated and the emergency room informed of likely etiology. Finally, loss of consciousness in both athletes and nonathletes can be due to seizures, intoxication, and psychogenic causes and should be included in the differential diagnosis.

Table 12 Noncardiac causes of loss of consciousness

Cause	History	Pathogenesis	Treatment	Workup
Post-exertional/ orthostatic	Occurs after heavy exercise, usually after abrupt cessation of heavy exertion	With cessation of exercise, the muscle pump is lost and blood pools in extremities	• Supine position with legs lifted • Attention to hydration, electrolytes, and nutrition • Consider compression stockings	• With classic history, no workup is necessary • ECG may be considered
Neurally mediated	• Strong emotion • Micturition • Defecation • Swallowing • Coughing	Inappropriate heart and blood pressure response	None	• With classic history, no workup is necessary • ECG may be considered
Heat illness	• High wet-bulb globe index* or temperature/humidity • Altered mental status • Incoordination • Conscious with progressive collapse	Increased core body temperature	Immediate cooling	• Immediate rectal temperature • Comprehensive metabolic profile, LFTs, CK, and ECG if patient does not respond immediately to cooling
Hyponatremia	• Endurance race • Slower times • High water consumption • Conscious, progressive collapse • Altered mental status	Low sodium	Sodium administration, dependent on severity, should be done in the emergency room	Comprehensive metabolic panel

Exertional collapse associated with SCT	• Athlete with SCT (1 in 12 Black individuals)
	• Not all individuals with SCT are aware
	• Extreme exertion when athlete feels they cannot stop to recover, typically in settings of training, timed run, or not letting teammates down
		RBC sickle in peripheral vasculature "clogging" capillaries leading to muscle necrosis, massive potassium and myoglobin release, and arrythmia or renal failure	• Stop activity when athlete is struggling
			• If recovery is not immediate, consider:
			  ○ Oxygen therapy
			  ○ Transport to hospital
			  ○ Make emergency room aware that immediate electrolytes are needed
			  ○ Supportive care with attention to kidney function
				Comprehensive metabolic panel

*Measure of heat stress in direct sunlight, taking into account temperature, wind speed, humidity, sun angle, and cloud cover. CK = creatine kinase; ECG = electrocardiogram; LFT = liver function test; RBC = red blood cell; SCT = sickle cell trait.

5.1.3 Diagnostic and monitoring strategies for syncope in athletes

Recommendations for diagnostic and monitoring strategies for syncope in athletes		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In athletes with syncope, a detailed history and physical examination should be performed to guide further diagnostic evaluation.[129,131,252]**
1	**B-NR**	**2. In all athletes with syncope during exertion, an ECG, exercise stress test, and transthoracic echocardiogram should be performed.[129,131,253-262]**
1	**C-EO**	**3. In athletes with syncope during exertion with high-risk features, withholding from sports participation pending evaluation is indicated.**
1	**B-NR**	**4. In athletes with syncope during exertion with high-risk features and with negative primary evaluation, advanced imaging should be performed.[254,263,264]**
1	**C-EO**	**5. In athletes with syncope, tests should be interpreted in the context of EICR.**
1	**B-R**	**6. In athletes with unexplained syncope or when arrhythmic syncope is suspected, ambulatory ECG monitoring is beneficial.[265-267]**
2a	**B-NR**	**7. In athletes with a high suspicion of arrhythmic etiology, unexplained after initial testing, and/or whose symptoms are rare, loop recorder implantation can be useful.[268,269]**
2b	**C-LD**	**8. In athletes with syncope with high-risk features and negative initial evaluation, an EP study may be considered.[270,271]**
3: Harm	**C-LD**	**9. In athletes with syncope, tilt table testing is not recommended because of high prevalence of false positives leading to inappropriate interventions.[272-274]**
3: No benefit	**C-EO**	**10. In athletes with a history suggestive of noncardiac syncope, further evaluation is not indicated.**

Synopsis

Syncope in an athlete requires a thorough evaluation including history, physical, and advanced testing as appropriate. While the majority of syncope during exertion is noncardiac, cardiac workup is indicated to rule out life-threatening conditions. Identification of the cause enables appropriate treatment, shared decision-making, and return to play when appropriate. The characteristics of high risk as described below will determine appropriate workup as well as timing of return to play. Use of diagnostic specific modalities is described below.

Recommendation-specific supportive text

1. An algorithm for the evaluation of syncope with exercise is shown in **Figure 8**. Most important are the history and physical exam, which determine the etiology of syncope in the majority of cases.[239] The history should be obtained from the athlete, bystanders, athletic trainers, and a review of video evidence when available. For athletes, determining whether true loss of consciousness occurred, versus near syncope, and determining whether the event occurred

during or after exercise are the most important features determining likelihood of a life-threatening etiology, as described in **Section 5.1.1** and **Table 11**. Characteristics of higher-risk syncope appear in **Table 13** and include acute face plant or other manifestation of acute or abrupt loss of consciousness and postural tone without protective reflexes during exertion, abrupt palpitations, prior history of syncope, shortness of breath that limits their ability to exercise, and chest pain. Typical situational triggers and symptoms suggestive of vaso-vagal origin should be queried.[239] A social history related to the use of recreational drugs or performance-enhancing drugs should be obtained (see **Table 4**). Family history of sudden, young, or unusual death also indicates need for more extensive workup.

2. The ECG is the principal tool for the detection of cardiovascular abnormalities in athletes with syncope. There are a wide range of expected findings that occur as a result of physical conditioning that need to be taken into account when evaluating an athlete's ECG, as outlined in the International Criteria for Electrocardiographic Interpretation in Athletes consensus statement.[148] Many of these findings would be considered abnormal in nonathletes and if unrecognized may result in additional testing and unnecessary restriction from exercise.[148] Echocardiography for the assessment of structural heart disease is important, as the ECG does not have complete sensitivity for many of the conditions that may lead to syncope, including cardiomyopathy and anomalous origin of a coronary artery. Stress testing is critical for identifying exercise-induced arrhythmias, which may be diagnostic and/or indicate need for advanced imaging.[275,276] As described in detail in **Section 2.3**, exercise stress testing should mimic the activity during which syncope occurred. Standard exercise protocols that are intended to elicit ischemia are not appropriate for the assessment of syncope in the athlete.

3. Those athletes with syncope during exercise who present with high-risk features (**Table 13**) such as acute face plant during exertion, abrupt palpitations, prior history of syncope, shortness of breath that limits their ability to exercise, chest pain, and/or a family history of sudden death, require cessation of sports activity until the necessary testing can be obtained.

4. In athletes with an initial nondiagnostic evaluation, advanced imaging, such as CMR or cardiac computed tomographic angiography (CTA), provide increased sensitivity for coronary artery anomalies and cardiomyopathies. CMR has unique abilities to characterize tissue. Late gadolinium enhancement is a marker of fibrosis or extracellular protein deposition. T1 and T2 mapping allow further quantification of fibrosis or infiltration, as well as edema. These increase sensitivity for diagnosis of HCM, ACMs, and arrhythmogenic bileaflet mitral valve prolapse (ABiMVP), even when the echocardiogram or ECG does not demonstrate these.[277] Angelini et al[263] described a series of 5169 children aged 11 to 18 years undergoing screening including CMR, with probable high-risk cardiovascular conditions found in 76 (1.4%) of the participants, in whom ECG showed no abnormalities. CMR could be useful in athletes with syncope and suspected structural abnormalities, including AAOCA. Prevalence of AAOCA is reported in 1.5%-1.7% of CTAs done for a variety of indications; the most common AAOCA was an origin of the right coronary artery from the left coronary sinus, followed by an origin of the left circumflex artery arising from the right coronary sinus.[278,279] In one small study of patients with syncope,[264] CTA revealed AAOCA after prior workup was unrevealing. CTA is currently considered a "gold standard" for diagnosis of AAOCA, identifying both the ostia and course of the coronary arteries, and ongoing technical advancements have decreased acquisition time and radiation exposure.[280]

CMR is emerging as an alternative to CTA, particularly as data on tissue characteristics and cardiac structure can be obtained at the same time.[281] If AAOCA is found, invasive coronary angiography, flow measurements, and assessment of ischemia is generally needed to determine functional significance.

5. As discussed in detail in **Section 2**, normal EICR leads to structural and electrical changes that are not pathological. Understanding these changes is critical to interpretation of testing in athletes to avoid incorrect diagnosis of pathological entities.

6. Rhythm monitoring strategies are an important part of the assessment for syncope during exertion particularly in the instance where a cardiac condition is suspected or the activity that triggered the symptoms could not be reproduced on an exercise stress test. **Table 14** describes features of available systems to guide selection of the appropriate device depending on the frequency and duration of the symptoms, including the device configuration, advantages/limitations of the device, and sports-specific considerations. In the absence of prodrome, a device with autodetection such as a loop/event recorder or implantable loop recorder should be considered. In the SYNARR-Flash study of general patients with syncope,[265] 4-week external ECG monitoring had a diagnostic yield of 71.6%. Holter monitoring has a good diagnostic performance, especially in those patients with daily symptoms.[282] In one cohort of 654 athletes with symptoms or signs of arrhythmias, including syncope, or an abnormal ECG, Holter monitoring established a diagnosis of arrhythmia in a substantial proportion of the patients.

If immediate results are needed, a continuous ECG monitor is a better option than a Holter monitor or certain patch monitors that need to be returned for processing. Multiple channels are helpful if activity may create artifact on a single lead.

7. Implantable loop recorders have been found to be useful in several studies in the general population for establishing the etiology of syncope especially in cases where infrequent episodes fall outside the recording window of other modalities (eg, 2-week patch monitor).[268,269,283] In addition, the subcutaneous location allows continuous recordings for athletes during any sport, whether in the water or during periods of high perspiration.

8. There is no evidence about the usefulness of an EP study including arrhythmia induction, voltage mapping, and drug infusion in athletes with syncope. The 2017 AHA/ACC guidelines on syncope[239] recommend an EP study in the general population with syncope and suspected arrhythmic disease, although the yield in those with no structural heart disease is low (2%-9%).[270,271] The yield of an EP study in diagnosis in athletes when there is no obvious etiology after a thorough evaluation is unknown.

9. Specificity of the tilt test in athletes is low, with a positive test in 47% of patients with arrhythmic syncope, and presyncope with typical hemodynamic features can be induced on tilt even in patients without a syncopal history.[273] Studies of healthy athletes with no syncope history show rates of positive tilt testing in 20%-100% of asymptomatic endurance runners.[284-286] This high frequency of false positives can bias medical judgment and make true diagnosis more difficult[287] and may lead to unnecessary therapeutic interventions such as medications or procedures.

10. Neurally mediated or orthostatic syncope is common in athletes with noncardiogenic syncope. If the patient's clinical context is characteristic of a neurally mediated episode or orthostatic syncope, no further workup is necessary.

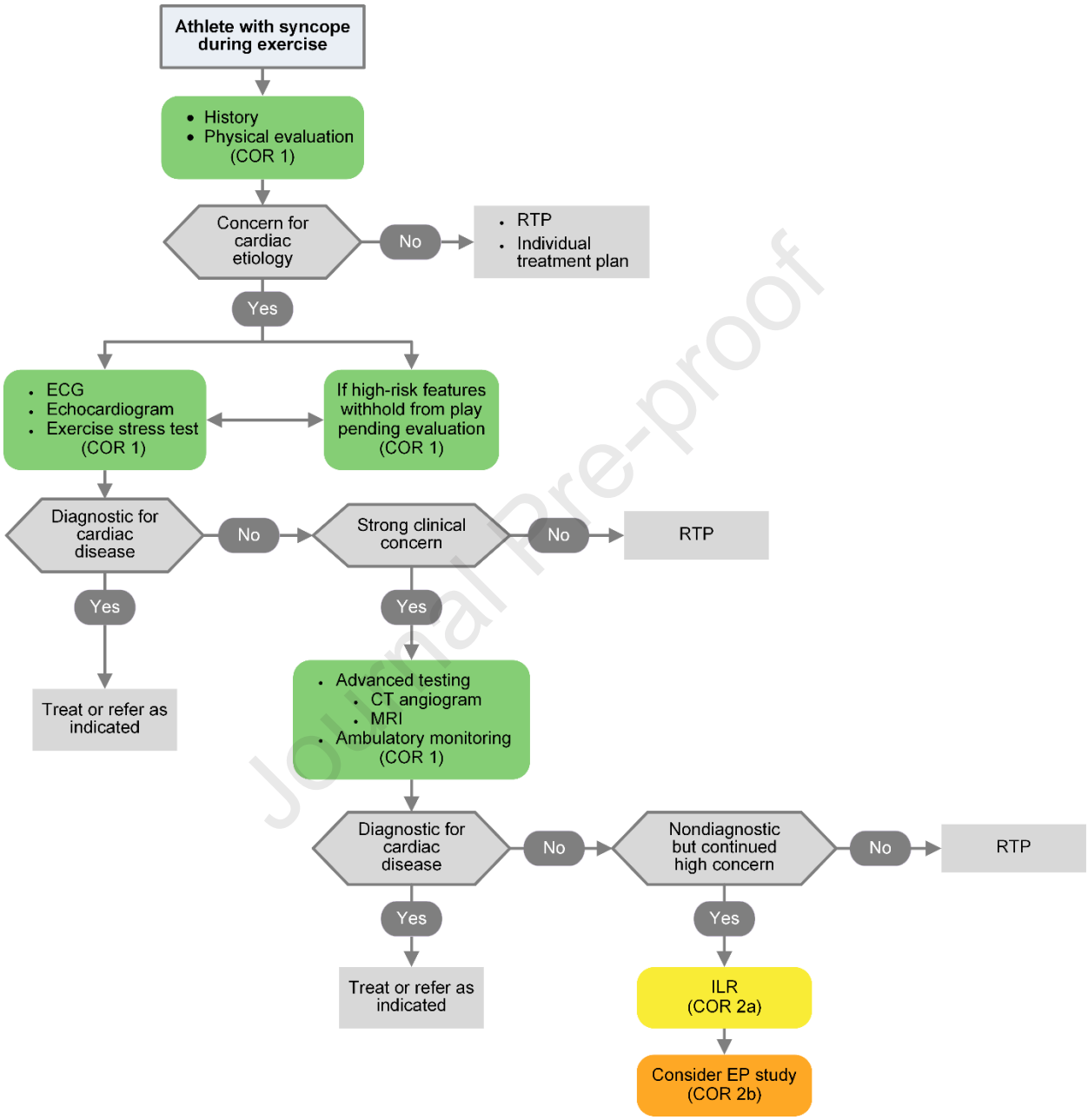

Figure 8

Algorithm for the evaluation of syncope during exercise. Colors correspond to the class of recommendation (COR) in **Table 1**. CT = computed tomography; ECG = electrocardiogram; EP = electrophysiology**;** MRI = magnetic resonance imaging; RTP = return to play.

Table 13 High-risk features for cardiac syncope

High-risk features
Absence of prodrome
Acute face plant during exertion
Abrupt palpitations
Shortness of breath that limits the ability to exercise
Chest pain

Table 14 Features of ambulatory monitors, including external and implantable recorders

Monitor type	Device configuration	Recording time	Advantage	Limitations	When to use	Sports-related considerations
Holter monitor (wire based)	Small, battery-operated recorder with 2 - 3 leads for recording	Continuous recording for 24-48 hours	Continuous recordings of multiple channels (2-3); inexpensive for clinics	Time-limited recording; device must be returned and processed creating delays	Frequent symptoms (daily)	Bulky and gets in the way of most activities; not waterproof and needs to be removed to shower or bathe; still useful for burden (eg, PVCs) assessment
External loop/event monitor	Small, battery-operated recorder with 1-3 leads for recording	Records up to 30 days of rhythm data before and after triggered event	May be worn continuously or applied during symptoms; some devices transmit real-time data to a monitoring center	Some require activation of recording and others are auto-triggered to record; some devices must be returned and processed creating delays	Less frequent symptoms (weekly to monthly)	Bulky and gets in the way of most activities; not waterproof and not useful without autodetection in syncope without prodrome
Patch continuous monitor	All-in-one adhesive device with continuous recording; no wires or battery packs; some have Bluetooth capability	Similar to Holter, records up to 30 days of patient-triggered events along with auto-triggered events	All-in-one adhesive device without wires	Typically, only a single lead, which can suffer from signal distortion; can cause skin irritation	Daily, near daily, or weekly	Smaller profile and less obtrusive than Holter or loop/event monitor; some are waterproof
Implantable loop recorder	Small, subcutaneously implanted monitoring device; Bluetooth or smartphone app communication	Long-term monitor that lasts up to 3-4 years	Records rhythm when activated and has autodetection algorithms that can be programmed; continuously recording useful in infrequent syncope without prodrome	MRI conditional (safe under specific MRI environments); can impact MRI image quality; false or noisy signals can be an issue; requires procedure to remove	Less frequent symptoms (monthly to yearly) that may lead to syncope	Subcutaneous and generally unaffected by activity (including swimming) or perspiration

Monitor type	Device configuration	Recording time	Advantage	Limitations	When to use	Sports-related considerations
Mobile cardiac telemetry	Patch or lead-based sensor transmits continuous ECG information to monitoring center via cellphone technology	Can be worn up to 30 days; transmits real-time rhythm data to a monitoring center for immediate review	Auto-trigger algorithms that detect abnormal rhythms and transmit data to the monitoring center; records all cardiac activity so useful in frequent syncope without prodrome	Generally, more expensive; not readily available	Less frequent palpitations (weekly to monthly)	Nonpatch versions are bulky and not waterproof; requires cell tower connection so limited in some areas
Commercially available wearables	Fitness trackers, smartwatches, handheld electrodes, chest strap	ECG displayed and stored directly on device and can be sent wirelessly and shared with care team	Commercially available (does not require a prescription); algorithms available for autodetection of arrhythmias, easy to use	Ability to integrate into electronic health record still a challenge	Palpitations lasting long enough to manually record	Challenging to record mid-exercise and not usable in all conditions; more data needed on effect of sports on quality of tracings and alerts; cost prohibitive for some

ECG = electrocardiogram; MRI = magnetic resonance imaging; PVC = premature ventricular contraction.

5.1.4 Treatment of neurally mediated or orthostatic syncope in athletes

Neurally mediated syncope and orthostatic syncope are common in athletes. Treatment plans can be similar to those for nonathletes. The management of neurally mediated syncope or orthostatic syncope begins with nonpharmacological treatment and education of both the athlete and the athletic personnel on recognizing the triggers of syncopal episodes as well as the implementation of physiological measures to reduce the likelihood of syncope. Special attention is required in the athlete to reduce the risk of injury based on the sport and/or the circumstances.

Recommendations for treatment of neurally mediated or orthostatic syncope in athletes		
COR	**LOE**	**Recommendations**
1	**C-EO**	**1. In athletes with neurally mediated or orthostatic syncope, providing education on the diagnosis, nonpharmacological treatment, prognosis, and triggers of syncope is recommended.**
1	**C-EO**	**2. In athletes with neurally mediated or orthostatic syncope, communication among the medical and athletic teams for preparation to manage a syncopal event is recommended.**

Synopsis

Most of the pharmacological and nonpharmacologic measures for the athlete are similar to those for the nonathlete, with athlete-specific considerations as noted below.

Recommendation-specific supportive text

1. The identification of triggers and application of the countermeasures can reduce the rate of recurrence. Athletes should be trained to recognize their prodromal symptoms and stop physical activity and execute physical counterpressure maneuvers (sitting down, bending the head forward, leg crossing)[288] in an attempt to abort the episode. A cool-down period after intense exercise, rather than stopping abruptly, is critical. The National Athletic Trainers´ Association recommends[289] that athletes should maintain hydration (+1% to –1% of body mass) for best exercise performance and should not lose more than 2% of body mass after exercise. It is possible to have oral prehydration of no more than 2% of body mass and to consume sodium chloride supplements during exercise to keep an adequate plasma volume and vascular tone.[289] Knee-high compression socks attenuated the drop in cardiac stroke volume and cerebral blood flow velocity, suggesting that these may be an effective countermeasure to reduce the incidence of post-exercise syncope.[290] Reassurance that these are not life-threatening conditions and can most often be managed with conservative measures may reduce anxiety in athletes with these symptoms. Cardioneuroablation is emerging as a promising therapy for vagal syncope but is not yet standard of care.[291]

2. All athletes with neurally mediated syncope or orthostatic syncope require close medical monitoring to reduce the rate of syncopal episodes that impact quality of life and sports performance of the athlete. Measures should be put in place to reduce the risk of syncopal episode in environments such as a high dives, skating rinks, and cycling paths or in other similar high-risk scenarios where loss of consciousness could endanger the life of the athlete.

5.2 Palpitations in athletes

Palpitations are the perception of rapid heartbeats, extra beats, or skipped beats. They may be related or unrelated to exercise in athletes and can be associated with cardiac pathology, systemic pathology, or normal physiological processes. Athletes are often in tune with their body, and anything out of the ordinary, such as palpitations, can cause significant distress. Palpitations in an athlete thus require further evaluation.

5.2.1 Etiology of palpitations

Similar to nonathletes, the most common causes of palpitations in athletes are sinus tachycardia or premature atrial and/or premature ventricular beats. Arrhythmic conditions such as supraventricular tachycardia (SVT), AF/atrial flutter, and ventricular tachycardia are less common (**Table 15**).[282,292-295] In a retrospective cohort of 6579 elite athletes,[282] 659 underwent Holter monitoring, of whom 162 reported symptoms (palpitations, syncope, dizziness, chest pain). The most common arrhythmic findings in this group of athletes were premature atrial contractions (62%), PVCs (39%), nonsustained ventricular tachycardia (1.5%), and AF/atrial flutter (< 1%).[282] Importantly, the vast majority of symptomatic palpitations were not associated with structural cardiac abnormalities.

5.2.2 Diagnostic strategies in athletes with palpitations

Diagnostic strategies in athletes with palpitations		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In athletes with palpitations, a history, physical examination, and resting 12-lead ECG are recommended.[129]**
1	**B-NR**	**2. In athletes with palpitations associated with exercise, exercise stress testing should be performed to mimic the athlete's sport, or monitoring during exercise should be performed.[282]**
2a	**B-NR**	**3. For athletes in a team setting, supplying athletic trainers with smartphone-based ECGs for onsite assessment of palpitations can be useful.[294]**
2b	**C-LD**	**4. In athletes with palpitations, a personal (portable or wearable) ECG may be considered as a diagnostic tool.[293]**

Synopsis

When evaluating an athlete with palpitations, it is important to obtain a detailed history along with a physical examination and 12-lead ECG. It is critically important to know the frequency of palpitations, the relation with exercise, and if there are associated symptoms such as chest pain or lightheadedness. When considering a monitoring strategy for athletes, it is important to take the sport into consideration and select a monitor that has adequate data recording but doesn't impede the athletes' ability to participate in the sport.

Recommendation-specific supportive text

1. Athletes with palpitations should have a comprehensive evaluation including history, physical examination, and 12-lead ECG.[7,129,296] Description of symptoms such as heart racing with abrupt onset/offset, versus gradual ramp up and ramp down, favor sustained arrhythmia including

supraventricular or ventricular tachycardia. Irregularity suggests ectopic beats or AF. The association with exercise and any associated symptoms of lightheadedness, chest pain, or syncope are important. A family history of cardiovascular disease increases the likelihood of underlying heart disease. During the physical examination, it is important to assess the pulse for the presence of ectopic beats or irregularity. The ECG may reveal ectopy or evidence of potential underlying cardiac conditions.[7,129,296] When evaluating the athlete's ECG, it is important to recognize that the changes that may be considered abnormal in nonathletes can occur commonly in athletes due to physical adaptation.[148] The routine use of echocardiography in evaluation of palpitations, in the absence of documented arrhythmia or other concerning personal or family history, is not supported by data, and recommendations regarding this use vary,[297] with use in unselected populations felt not appropriate, although some have recommended its use in the athlete with exertional symptoms.[36]

2. In athletes with palpitations occurring during exercise, it is important to identify the rhythm associated with symptoms. The standard exercise stress test has the benefit of availability, a controlled environment, and recording of the rhythm with 12-lead ECGs but often doesn't mimic the activity that triggered the symptoms such as swimming, jumping, or climbing. Stress testing in athletes is discussed in more detail in **Section 2.3**. In circumstances where the trigger is hard to reproduce in the typical exercise laboratory or stress testing does not invoke the symptoms, then a monitoring strategy that enables rhythm determination during the activity can be useful. **Table 14** describes features of available systems to guide selection of monitoring strategy. When selecting a monitor for an athlete, the frequency and the duration of the palpitations should be considered.[298] There are also sport-specific considerations such as whether the recording device is waterproof (swimming) or gets in the way of the athletic activity (eg, Holter monitor in rowing and climbing). If monitoring with the selected device captures the symptom and demonstrates a normal rhythm, then reassurance is indicated to allay the concerns of the athlete.[7,296]

3. Athletic trainers are often present at sporting events, and if provided with a smartwatch or handheld ECG recording devices, they can record the athlete's heart rhythm at the time they are symptomatic. This strategy has been shown to decrease need for cardiology evaluation, as most often the rhythm during symptoms is sinus.[294]

4. In athletes who have palpitations that are infrequent or difficult to capture with standard recording devices, commercially available wearable devices that allow rhythm recordings, such as a smartwatch or handheld electrodes, can be helpful. These devices also have limitations, including accuracy and the requirement that the user have the device always available.[293,294,298,299]

Table 15 Series of athletes with palpitations, arrhythmias, and cardiomyopathies documented

Study	Study design/population	Age	No. patients with palpitations	Arrhythmic findings	Structural conditions	Monitoring strategy
Boraita et al, 2022[282]	A retrospective cohort of elite athletes; 654/6579 (9,9%) had any sign/symptom related to arrhythmia or abnormal resting/exercise ECG, and they were evaluated with Holter including at least one hard training session	Median age 24 years (interquartile age range 19–28)	162/654 reported symptoms (palpitations, syncope, dizziness, chest pain)	Sinus bradycardia (96% of cases), Premature atrial and ventricular beats (61.9% and 39.4%, respectively), sinus pauses ≥3 s, high-grade atrioventricular blocks, and AF/atrial flutter were rare (<1%). Polymorphic PVCs (1.4%) and idioventricular rhythm (0.005%). PVC couplets (10.7%) (PVC triplets 1.8%; sustained ventricular tachycardia 0.0%; and NSVT 1.5%)	HCM (6), DCM (2), ACM (2), LV noncompaction (8), ICM (1)	Most underwent single Holter evaluation, 19% underwent 2 or more evaluations
Jewson et al, 2022[293]	Case series; 6 athletes with symptoms related to exercise; 4/6 palpitations	Ages 16-28 years	4/6	Athletes with palpitations (2 patients with SVT, 1 patient with AF, and 1 patient with normal ECG). Athletes without palpitations (1 with atrial flutter, 1 with normal traces)	None found	6 leads, Smartphone ECG AliveCor Kardia device
Peritz et al, 2015[294]	Case series; 6 college athletes	Ages 18-21 years	6	No arrhythmias detected	None found	Single-lead ECG by AliveCor Heart monitor
Sciarra et al, 2022[295]	Athletes with palpitations and unknown origin with external loop recorder/cohort study; 61 athletes/61 sedentary controls with palpitations at least once monthly	Median age 24 years (age range 18-37 years)	61	7 (sustained SVT), 2 (NSVT), 4 (PVCs), 3 (PACs), 28 (no arrhythmic findings during palpitations), 11 (negative symptoms and findings)	None found	The median duration of ECG monitoring was 12 days
Biffi et al, 2002[292]	Observational study (Long-Term Clinical Significance of Frequent and Complex Ventricular Tachyarrhythmias in Trained Athletes); 355 athletes with palpitations or 3 or more PVCs in resting ECG; they were evaluated with 24-hour ambulatory Holter	Group A ages 24 ± 10 years; group B ages 24 ± 10 years; group C ages 25 ± 11 years	18/355	8/18 (≥ 2000 PVCs and ≥ 1 NSVT) for group A; 10/18 (≥ 100 to < 2000 PVCs) for group B	Group A (≥ 2,000 PVCs and ≥ 1 NSVT) (7 ARVC, 6 mitral valve prolapse, 4 myocarditis, 4 DCM); group B (≥ 100 to < 2,000 PVCs) (5 mitral valve prolapse); group C (< 100 PVCs) nonstructural condition	24-hour ambulatory (Holter) ECG

ACM = arrhythmogenic cardiomyopathy; AF = atrial fibrillation; DCM = dilated cardiomyopathy; ECG = electrocardiogram; HCM = hypertrophic cardiomyopathy; IC = ischemic cardiomyopathy; LV = left ventricular, NSVT = nonsustained supraventricular tachycardia, PAC = premature atrial contraction, PVC = premature ventricular contraction; SVT = supraventricular tachycardia.

Section 6 Ventricular arrhythmias

Ventricular arrhythmias are similarly prevalent in athletes and nonathletes[282,300-302] and are 5- to 10-fold less common in women athletes as compared with men.[262,302,303] There is no clear correlation between the amount and type of exercise and ventricular arrhythmias.[282,300,301] PVCs or other ventricular arrhythmias may be identified when an athlete presents with palpitations, or asymptomatic PVCs may be identified during an ECG obtained for preparticipation screening[6,70] or for other purposes. Typical PVCs are those of an outflow tract or fascicular morphology. Complex ventricular arrhythmias include PVCs of atypical morphology and/or that are multifocal, have a short-coupling interval, or occur as multiples, including couplets, triplets, or nonsustained ventricular tachycardia. High-risk ventricular arrhythmias are defined as those with morphological as well as clinical features including nonsuppression with exercise suggestive of higher risk of malignant prognosis, as shown in detail in **Table 16**. Benign PVCs and benign idiopathic ventricular tachycardia are defined as those occurring in the absence of structural heart disease, identified electrical disease, or high-risk electrical features, as noted above.

Inherited cardiomyopathies (HCM, ACM, and DCM), ABiMVP, inherited channelopathies (LQTS, Brugada, and CPVT), and acquired pathologies (coronary artery disease, myocarditis, and sarcoid) are all heart diseases associated with ventricular arrhythmias. Identifying whether one of these pathologies is present is critical, as the presence of underlying heart disease is the primary determinant of prognosis and outcomes in ventricular arrhythmias.

6.1 Evaluation of ventricular arrhythmias in athletes

The primary initial objective in the assessment of an athlete with PVCs is to determine whether these are benign focal premature beats or the potential sign of structural or electrical heart disease, which can be associated with SCA. In addition to underlying heart disease, a syndrome of acquired heart disease has been described in highly trained endurance athletes who develop ventricular arrhythmias in the absence of inherited heart disease. Heidbuchel et al[304] reported that ventricular arrhythmias in endurance athletes (predominantly professional cyclists) most frequently arose from the right ventricle, were often associated with mild structural or functional abnormalities, and could be life-threatening despite an absence of clinical or genetic evidence of inherited heart disease.[304,305] This entity was initially termed “exercise-induced ARVC,” and validation of the observation of an “ARVC-like” syndrome in endurance athletes without evidence of inheritance has also been referred to as genotype negative ARVC.[306] More recently, Venlet et al[307] provided an invasive electrophysiological description of this syndrome, noting that endurance athletes often had epicardial-based scar originating around the RVOT that was associated with very rapid, potentially life-threatening ventricular tachycardia. There have also been descriptions of arrhythmogenic subepicardial scar in the left ventricle of endurance athletes, again in the absence of inherited heart disease.[308,309]

Thus, in the athlete presenting with ventricular arrhythmias, the clinician must consider the possibility of 3 main categories, each with different prognostic and therapeutic implications. Two of these entities, benign ventricular ectopy in the absence of structural heart disease and ventricular arrhythmias associated with structural heart disease (inherited or acquired), have features that are similar to nonathletic populations, with the caveat that it can be difficult to distinguish between the structural and

functional changes of “athlete’s heart” and subtle pathology. The third entity, exercise-induced ACM, is unique to endurance athletes.

Recommendations for the evaluation of ventricular arrhythmias in athletes		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In athletes with symptoms suspicious for ventricular arrhythmias, a resting 12-lead ECG and ambulatory ECG monitor are recommended to assess ventricular arrhythmia burden and complexity.**[310,311]
2a	**B-NR**	**2. In athletes with symptoms suspicious for suspected ventricular arrhythmias, exercise stress testing is reasonable to assess ventricular arrhythmia occurrence, characteristics, and morphology.**[255,312]
1	**C-EO**	**3. In athletes with ventricular arrhythmias, taking a history of supplements and performance-enhancing drug use is recommended to identify potential triggers for ventricular arrhythmias.**
1	**C-LD**	**4. In athletes with 2 or more asymptomatic typical PVCs, or 1 atypical PVC, on a 12-lead ECG, further evaluation with ambulatory monitoring and cardiac imaging is recommended.**[292]
2b	**C-EO**	**5. In athletes with 1 asymptomatic typical PVC (single outflow tract or fascicular morphology) on a 12-lead ECG, further evaluation may be considered.**
1	**C-EO**	**6. In athletes with PVCs of a single outflow tract or fascicular morphology, assessment of cardiac structure and function with echocardiography is recommended to exclude underlying pathology.**
1	**B-NR**	**7. In athletes with higher-risk ventricular arrhythmias and/or abnormal primary testing, comprehensive cardiac imaging including CMR and exercise stress testing is recommended to assess for underlying structural heart disease and behavior of PVCs with exercise.**[88,313,314]
2b	**C-LD**	**8. In adult athletes with ventricular arrhythmias with higher-risk but nondiagnostic features after comprehensive examination, EP study with voltage mapping may be useful in defining the extent and location of the arrhythmogenic substrate.**[307,315]
1	**C-EO**	**9. In athletes with ventricular arrhythmias with higher-risk features, withholding from sports participation pending evaluation is recommended.**

Synopsis

Ventricular arrhythmias, including PVCs and ventricular tachycardia, can be diagnosed in athletes with a range of presentations from asymptomatic benign ectopy to SCD. For the athlete with PVCs, the challenge is to accurately differentiate between the healthy heart (inclusive of the spectrum of physiological changes associated with athletic training) as opposed to underlying structural heart disease that constitutes a risk for malignant arrhythmias.

Accurate diagnosis requires an assessment of clinical history and cardiac imaging in a facility sufficiently experienced with the range of EICR that can be observed in the well-trained athlete. **Table 16** provides a

hierarchical flow from simpler, less expensive, noninvasive tests through increasingly specialized examinations. Low-risk features are compared with higher-risk features that can assist in discriminating between the normal athlete and the athlete who may have prognostically significant structural or electrical heart disease. Higher-risk features will direct the extent and timing of evaluation. An algorithm of the recommendations for evaluating ventricular arrhythmias in athletes is shown in **Figure 9**.

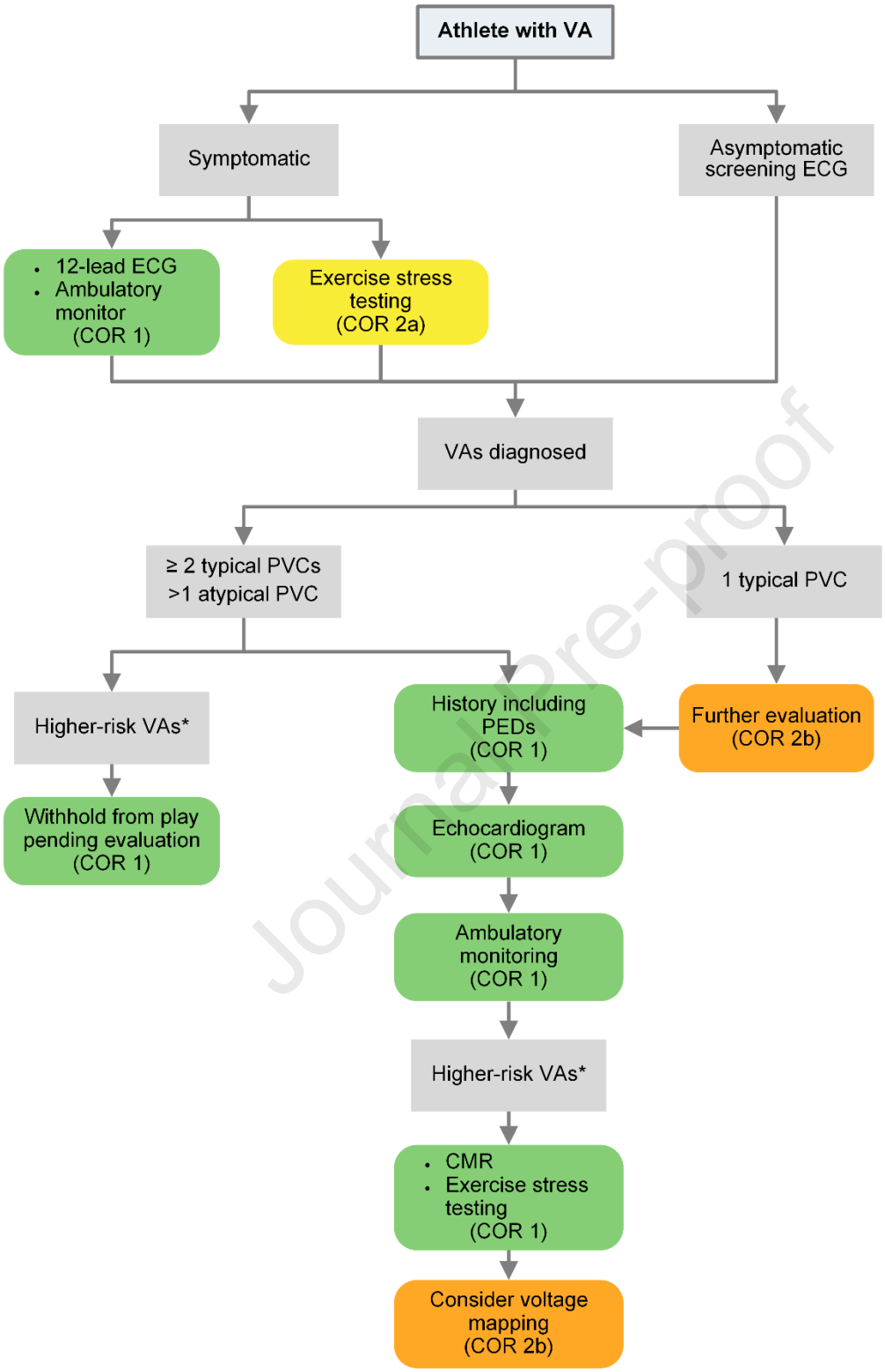

Figure 9
Evaluation of athletes with ventricular arrhythmias (VAs). Colors correspond to the class of recommendation (COR) in **Table 1**. *See text and **Table 16** for definition of higher risk.; CMR = cardiac magnetic resonance imaging; ECG = electrocardiogram; PED = performance-enhancing drug; PVC = premature ventricular contraction; RVOT = right ventricular outflow tract.

Recommendation-specific supportive text

1. A 12-lead ECG is a critical initial assessment tool, as it provides information on the characteristics of the ventricular arrhythmia.[292,316-318] The morphology of the PVC enables the clinician to determine whether it is from a common and benign site (outflow tract or fascicular morphology) as opposed to complex PVCs of uncommon (non-outflow-tract) or multiple sites, that have a short-coupling interval (< 300 ms), or occur in multiples (couplets, triplets, or nonsustained ventricular tachycardia).[319] High-risk PVCs are defined as those with morphological as well as clinical features suggestive of higher risk of malignant prognosis (**Table 16**).

   The suspicion of underlying cardiac pathology is increased in athletes in whom there are multiple consecutive ventricular beats (couplets, triplets, or nonsustained ventricular tachycardia) and/or multifocal PVCs.[282,292,300-302]

   Although there are no studies specific to athletic populations, ambulatory ECG monitoring is important to determine the burden of PVCs given the association between very high burden ectopy (10% burden) and left ventricular dysfunction.[311,316] Longer-term monitoring may be needed if symptoms are less frequent. Features of available monitors are shown in **Table 14**.

2. Exercise stress testing is a valuable means of attempting to reproduce an athlete's symptoms and evaluate for the presence, location, and complexity of ventricular arrhythmias. There is some evidence to suggest that exercise stress tests of greater intensity and duration may be more sensitive in identifying ventricular arrhythmias[262] and that the disappearance of PVCs during exercise is less likely associated with structural heart disease,[312] whereas the appearance of PVCs during recovery may be a marker of poorer outcomes.[320] These observations are derived from general populations, and the specificity of these findings in athletic populations is unclear. Details of exercise stress testing in athletes appears in **Section 2.3**.

3. Performance-enhancing drugs and supplements have the potential to trigger ventricular arrhythmias in athletes (see **Table 4**).[321] Evidence supporting this assertion is largely limited to case studies and anecdotes in part because of the illicit nature of many substances used by athletes.[322] However, it is widely accepted that androgenic agents, stimulants including agents treating attention-deficit/hyperactivity disorder, agents interfering in hemoglobin synthesis or oxygen transit, and many other experimental agents can have arrhythmogenic effects. It is critical that the use of supplements and drugs be identified so that the athlete can be counseled as to the potential health effects.

4. Atypical or complex PVCs refer to ventricular ectopic beats that are not of RVOT or fascicular origin or are multifocal, have a short-coupling interval, or occur as multiples (couplets, triplets, or nonsustained ventricular tachycardia). Typical PVCs are those arising from the RVOT (left bundle branch block pattern with inferior axis) or fascicles (right bundle branch block pattern and QRS duration < 130 ms). Higher burden is associated with a higher likelihood of underlying heart disease.[292]

   Complex ventricular arrhythmias can be a marker of underlying structural heart disease. In some cases, abnormalities may be identified with echocardiography, but it is important to recognize that CMR may be necessary to identify subtle pathology. In particular, tissue characterization with delayed enhancement imaging can be used to identify myocardial scar even in the absence

of overt wall-thinning of segmental functional abnormalities. In athletes, the identification of some scar patterns (particularly mid-wall or subepicardial left ventricular scar) have been associated with potentially life-threatening ventricular arrhythmias.[308,309,313] CMR is also critical in the setting of PVCs and mitral valve regurgitation on echocardiography to evaluate for ABiMVP.[172,323]

5. The evaluation of athletes with a single typical PVC is controversial because PVCs arising from the RVOT or fascicles are common and rarely associated with structural heart disease. However, the RVOT is also the most frequent site of origin of PVCs in ACM and can be the only manifestation of underlying disease.[324] Consideration should be given to the poor specificity of typical PVCs in identifying structural heart disease. When accompanied by other ECG abnormalities or any suspicion of symptoms, further investigation is warranted.

6. It is recognized that PVCs commonly originate from some cardiac sites of which the RVOT is most common. Although RVOT arrhythmias can be associated with pathologies such as ACM, in almost all settings this will be associated with other risk markers such as symptoms, family history, multiple ectopic morphologies, or abnormalities on ECG or echocardiography. Thus, it is reasonable that evaluation be restricted to a more limited evaluation in athletes with echocardiography alone in whom none of these red flags are present.

7. **Table 16** describes higher-risk features that may indicate the need for more extensive evaluation to identify or rule out underlying structural heart disease.

   There have been few studies that have quantified the additional diagnostic yield of CMR as compared with echocardiography in athletes with ventricular arrhythmias, mostly because CMR has assumed the clinical standard of care in most settings. It may be reasonable to extrapolate from studies of ECG abnormalities in athletes in which echocardiography identified an underlying cardiomyopathy in 37 of 118 (31%) athletes with abnormal T-wave inversion and CMR identified a further 24 cardiomyopathies in the remaining 94 (26%) athletes in which the echocardiogram was considered normal.[325] If the echocardiogram suggests ABiMVP, CMR is needed to evaluate for features of ABiMVP including mitral annular dysjunction and late gadolinium enhancement indicative of scar.[172] In athletes in whom there is suspicion of cardiac sarcoid, positron emission tomography may aid in diagnosis.[326] In those with higher suspicion of coronary anomaly, computed tomography angiography can be indicated.[280]

8. Cardiac imaging has been combined with high-intensity exercise to increase the diagnostic sensitivity in the differentiation between healthy athletes and athletes with complex right ventricular arrhythmias. In athletes with right ventricular pathology, exercise imaging testing using echocardiography[327] and CMR[328] have been shown to unmask right ventricular dysfunction that was subtle or absent at rest. These observations are limited to a single-center experience and require specialist exercise imaging equipment and expertise. However, where available, exercise cardiac imaging could be considered as part of the thorough diagnostic workup of athletes in whom pathology is suspected.

   Stress testing is critical to evaluate for the presence of CPVT, as both resting ECG and structural imaging are normal. Stress testing protocols for athletes are described in detail in **Section 2.3**.

Also, some data suggest that suppression of PVCs with exercise may portend a better prognosis,[316] while emergence of or increasing PVCs during recovery can raise concern.[312]

Evidence supporting the use of myocardial biopsy in the evaluation of athletes with ventricular arrhythmias is confined to case reports or small observational studies.[292,315] Data on the clinical utility of signal-averaged ECGs are inconclusive, and thus this modality is rarely used in clinical practice.[8]

9. The extent and location of myocardium with abnormal EP (arrhythmogenic foci or low-voltage regions) can assist in diagnosis, risk stratification, and planning of therapy. Corrado et al[315] used electroanatomical mapping to identify low-voltage regions in the RVOT that were then used to guide endocardial biopsies for the confirmation of ACM in cases (inclusive of athletes) in which other disease features were absent or subtle. Venlet et al[307] described electrophysiological characteristics that appeared unique to highly trained endurance athletes. In a cohort of consecutive patients with right ventricular tachycardia, athletes were observed to have RVOT scar from which very rapid ventricular tachycardia could be readily induced. Furthermore, these arrhythmias could be successfully treated with epicardial ablation.[307] Heidbuchel et al[304] included an invasive EP study in their evaluation of athletes presenting with right ventricular arrhythmias and determined that ventricular tachycardia inducibility was the only test that was predictive of a subsequent major arrhythmic event. In a study by Dello Russo et al,[329] electroanatomic mapping and endomyocardial biopsy increased diagnostic yield in athletes with complex ectopy and nondefinitive noninvasive evaluation.

A high-dose isoproterenol challenge may be a useful adjunct during an EP study, as demonstrated in a single-center experience of patients presenting with PVCs or suspected ACM.[330,331] The induction of polymorphic PVCs with ≥ 1 couplet or non-RVOT ventricular tachycardia following isoproterenol infusion accurately identified patients with ACM. Although this procedure has not been specifically studied in athletic populations, it would seem a reasonable addition to a standard EP study in athletes with right ventricular arrhythmias, especially if there are any additional features raising the possibility of ACM.

10. As above, these higher-risk features indicate a higher likelihood of underlying structural or electrical disease that may be life-threatening. For athletes with many of these entities, appropriate treatment can decrease risk of death. Informed shared decision-making around treatments and return to play for athletes with these entities requires diagnosis, and thus return to play should be delayed to allow for this informed process.

Table 16 Risk features from history and tests used to identify structural or electrical heart disease

Low-risk features	Higher-risk features
Clinical	
Asymptomatic	Presyncope, syncope, dyspnea, or sudden-onset exercise intolerance
Palpitations suggestive of simple PVCs	Sustained rapid palpitations
No history suggestive of inherited heart disease	Family history of collapse, syncope, sudden death, or cardiomyopathy
Electrocardiographic	
Monomorphic PVCs with outflow tract or fascicular morphology (“typical morphology”)	Polymorphic PVCs or with non-outflow-tract or fascicular morphology (“atypical morphology”)

Normal 12-lead ECG (other than PVCs)	Abnormal ECG (in addition to PVCs), eg, low voltage
Normal PVC coupling interval	Short PVC coupling interval
Single PVCs	Couplets, triplets, or nonsustained ventricular tachycardia
Low burden of PVCs on Holter ECG	High-burden PVCs (> 10% burden)
Exercise stress testing	
Suppression of PVCs with exercise	Nonsuppression or emergence of PVCs with exercise or emergence of PVCs during recovery
No symptoms and normal hemodynamics	Symptoms of sudden-onset exercise intolerance associated with emergence of arrhythmias
Echocardiography/stress echocardiography	
Normal cardiac structure and function for an athlete (ie, inclusive of athlete's heart changes)	Increased wall thickness or excessive ventricular dilation, reduced systolic function, or segmental abnormalities
Clear augmentation of biventricular function with exercise	Reduced contractile reserve during exercise (of the left or right ventricle)
Cardiac magnetic resonance imaging	
Normal structure and function	Increased wall thickness or excessive ventricular dilation, reduced systolic function, or segmental abnormalities
No evidence of post-contrast enhancement	Delayed gadolinium enhancement, particularly mid-wall or epicardial enhancement
Invasive electrophysiology	
Focal arrhythmogenic site	Multiple inducible arrhythmias
Catecholamine triggering of focal site	Catecholamine triggering of rapid polymorphic arrhythmias
Normal electroanatomical mapping	Low-voltage regions (noting a tendency to epicardial pathology in endurance athletes)

ECG = electrocardiogram; PVC = premature ventricular contraction; RVOT = right ventricular outflow tract.

6.2 Treatment of ventricular arrhythmias in the athlete

6.2.1 Treatment of benign ventricular arrhythmias in the athlete

Benign PVCs and benign idiopathic ventricular tachycardia are defined as those occurring in the absence of structural heart disease, identified electrical disease, or high-risk electrical features, as noted above. As described in **Section 6.1**, in athletes with ventricular arrhythmias, a comprehensive approach is required to evaluate for an underlying etiology and to appropriately risk stratify into benign or high-risk types. Treatment of benign ectopy, once benign nature is confirmed, is determined by symptoms and burden.

Recommendations for treatment of benign ventricular arrhythmias in the athlete		
COR	**LOE**	**Recommendations**
1	**B-R (caffeine, sleep apnea)**	**1. In athletes with symptomatic benign ventricular arrhythmias, risk factor management, including avoidance of performance-enhancing or illicit drugs, weight loss, treatment of obstructive sleep apnea, smoking cessation, alcohol and caffeine avoidance, and hypertension management, as well as reassurance is recommended.**[332-335]

	C-EO (other risk factors)	
1	C-EO	**2. In the asymptomatic athlete with benign ventricular arrhythmias, observation is recommended.**
1	C-LD	**3. In the asymptomatic athlete with a high burden of benign PVCs (> 10% burden) in the absence of structural heart disease, active monitoring for PVC-induced cardiomyopathy with serial imaging and ambulatory monitoring is recommended.[336]**
1	B-R	**4. In athletes with symptomatic benign ventricular arrhythmias desiring treatment, catheter ablation is useful as first-line therapy, or if antiarrhythmic drugs are contraindicated or poorly tolerated.[337-344]**
2a	B-R	**5. In athletes with symptomatic benign ventricular arrhythmias, a trial of medical therapy with beta blockers or calcium channel blockers is reasonable.[345-347]**
2a	B-R	**6. In athletes with symptomatic benign ventricular arrhythmias, antiarrhythmic drug therapy with class IC agents is reasonable.[348,349]**
2a	C-EO	**7. In athletes with benign ventricular arrhythmias, stress testing after treatment with either ablation or medications can be useful to determine arrhythmia suppression.**

Synopsis

Management of ventricular arrhythmias in the athlete is largely similar to that in the nonathlete population. In those considered low risk with benign ventricular arrhythmias, close follow-up and reassurance with treatment or change in exercise regimen may be pursued, as spontaneous reduction may occur. In those who require treatment for benign PVCs or benign idiopathic ventricular tachycardia due to ongoing symptoms, medical therapy may be poorly tolerated due to detrimental impact on exercise performance; therefore, there may be a lower threshold to consider catheter ablation as first-line therapy in athletes. An algorithm of the recommendations for treating benign ventricular arrhythmias in athletes is shown in **Figure 10**.

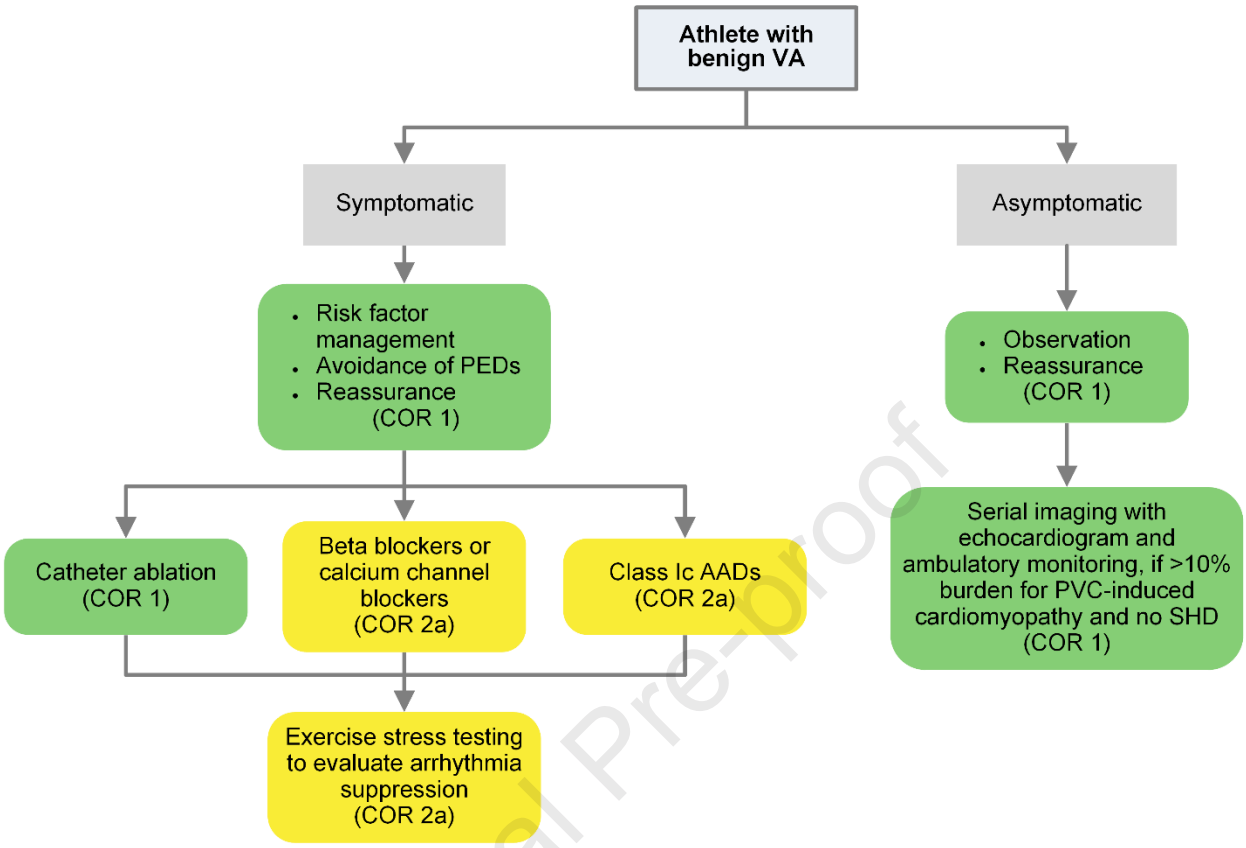

Figure 10
Algorithm for the treatment of athletes with benign ventricular arrhythmias (VAs). Colors correspond to the class of recommendation (COR) in **Table 1**. AAD = antiarrhythmic drug; PED = performance-enhancing drug; PVC = premature ventricular contraction; SHD = structural heart disease.

Recommendation-specific supportive text

1. Modifiable factors include common risk factors observed in the nonathlete population, such as hypertension, smoking, and sleep apnea, while specific risk factors likely more relevant to the athlete include use of performance-enhancing drugs and stress from poor recovery and sleep deprivation.[318,321,332,333,350,351] The use of cannabis and association with PVCs has not been described, although it is reasonable to recommend cessation to evaluate response. For caffeine and sleep apnea, data suggest that modifying these risk factors decreases PVCs. For other factors, trials of discontinuation of known predisposing factors are warranted, although data on intervention are sparse.[332,335] Reassurance on the benign nature with favorable prognosis should be provided, along with education on symptoms that may be attributed to ventricular arrhythmias that would warrant future evaluation. Reassurance of the benign nature may decrease anxiety as well as perceived symptoms.

2. In athletes who are found to have benign ventricular arrhythmias after evaluation and are asymptomatic, treatment is not indicated and should not be given.

3. Although there is no single threshold burden cutoff, observational studies have suggested that highest risk of PVC-induced cardiomyopathy is at a burden of ≥ 20%, although it may occur with

a burden of > 10%.[311,336,337] Serial monitoring with an echocardiogram will evaluate for left ventricular dysfunction or dilation for evaluation of PVC-induced cardiomyopathy and ambulatory monitoring for changes in PVC burden. There is no accepted timeframe for monitoring, as it will depend on ongoing burden of ventricular arrythmias and clinical symptoms; a repeat at 6 months and then every 1-2 years may be reasonable.

4. In a meta-analysis including 5 studies with only 1 randomized controlled trial including 1113 patients, those that underwent catheter ablation had a lower burden of PVCs in follow-up as compared with antiarrhythmic drug therapy.[340] The study highlighted the high heterogeneity in PVC morphologies included, mapping and ablation technology utilized, and follow-up evaluation of PVC burden. Complication rates from ablation ranged from of 0% to 5.6%, while adverse effects from antiarrhythmic drugs ranged from 9.5% to 21%.

The location of idiopathic ventricular arrhythmias impacts the success rate. Those with ventricular arrhythmias originating from the RVOT have reported success rates approaching 80% to 95% with limited complication rates.[338,344,352] Ablation of ventricular arrhythmias originating from the left ventricular outflow tract (LVOT) are more complex, as these may require ablation in adjacent structures, such as epicardial ablation in the coronary venous vasculature.[341] Less common locations include right ventricular and left ventricular papillary muscles, with repeat procedures required in approximately 30% of cases.[343] Locations involving the fascicular system or parahisian locations can also be successfully ablated in 70%-90%; however, the risk of AV block needs to be carefully considered.

5. Beta blockers and calcium channels blockers are effective at reducing symptoms attributed to ventricular arrhythmias and may reduce burden in approximately one-third of patients.[348] Antiarrhythmic drugs, specifically the class IC agent flecainide, have shown superior efficacy in reducing PVC burden as compared with the beta blockers.[349] Verapamil has shown to be effective in fascicular ventricular tachycardia.[353] When considering this option, it is important to discuss with the athlete that beta blockers and nondihydropyridine calcium channel blockers may lead to fatigue[354] or impact exercise performance, although a low or moderate dose may be tolerated in some athletes. For those choosing this option, follow-up to determine any adverse effects is needed. Importantly, beta blockers are prohibited by the World Anti-Doping Agency only in sports that rely on stability of the upper extremities, such as archery, golf, or shooting.[46]

6. Antiarrhythmic drugs, specifically the class IC agent flecainide, have shown superior efficacy in reducing PVC burden as compared with beta blockers. In a study including 103 participants with outflow tract PVCs (burden ≥ 5%) randomized to carvedilol versus flecainide, overall PVC burden decreased in both groups with superior efficacy in flecainide (20.3% to 14.6% with carvedilol versus 17.1% to 6.6% with flecainide, $p < 0.0001$).[349] In an observational prospective study including 120 patients with frequent PVCs (≥ 5%), the median relative reduction of PVCs was 32.7%, 30.5%, and 81.3%, in the conservative therapy, beta blockers/calcium channel blockers, and antiarrhythmic groups, respectively.[348] Only one-third achieved complete cessation of PVCs in the antiarrhythmic drug group. Taken together, antiarrhythmic drug therapy results in a greater reduction of PVC burden often without complete cessation. Exercise stress test should be performed after initiation of class IC agents to monitor for use-dependent QRS widening. Confirmation of no over inducible ischemia is also important prior to initiation. In a study of

serial testing, when an initial stress test did not preclude use of flecainide, later development of QRS widening was not found.[355]

7. As these arrhythmias are benign, symptoms, rather than exercise results, will guide return to play. However, as benign PVCs can be exercise-induced as above, stress testing as part of evaluation of efficacy of treatment may be helpful.

6.2.2 Treatment of complex ventricular arrhythmias in the athlete

Recommendations for complex ventricular arrhythmias		
COR	**LOE**	**Recommendations**
1	**C-EO**	**1. In the athlete with complex ventricular arrhythmias, management based on underlying pathology is recommended, with consideration of treatment impact on exercise performance, and shared decision-making to individualize treatment strategy.**
1	**A**	**2. In athletes who have survived sustained ventricular tachycardia in the absence of a reversible cause, an ICD is recommended, based on underlying pathology.[189,356]**
1	**B-NR**	**3. In athletes with monomorphic ventricular arrhythmias with underlying structural heart disease including inherited entities and coronary artery disease, catheter ablation for arrhythmia suppression is useful as first-line therapy or when antiarrhythmic drug therapy is contraindicated or has failed.[357-361]**
1	**B-NR**	**4. In athletes with VF triggered by monomorphic PVCs, catheter ablation is recommended.[362-366]**
1	**C-EO**	**5. In athletes with complex ventricular arrhythmias, documentation of suppression of arrhythmias with a maximal exercise stress test is recommended prior to return to play.**
1	**B-NR**	**6. In athletes with suspected PVC-induced cardiomyopathy, catheter ablation is useful as first-line therapy or when antiarrhythmic drug therapy is contraindicated or has failed regardless of symptoms.[337,344,367-369]**
2a	**B-NR**	**7. In athletes with suspected PVC-induced cardiomyopathy, medical therapy (antiarrhythmic drug therapy, as well as guideline-directed medical therapy for decreased ejection fraction) is reasonable to improve left ventricular function regardless of symptoms.[370]**
2a	**C-LD**	**8. In athletes with ventricular arrhythmias and nonfamilial and/or genotype-negative phenotype-positive ARVC (presumed exercised induced), catheter ablation and/or ICD is reasonable after appropriate risk stratification.[307]**
3: Harm	**B-NR**	**9. In athletes with ventricular arrhythmias and nonfamilial and/or genotype-negative phenotype-positive ARVC (presumed exercised induced), continuation of vigorous endurance sports is harmful.[304,305,307]**

Synopsis

Athletes with complex ventricular arrhythmias, such as those with polymorphic or sustained patterns or those with underlying pathology such as cardiomyopathies, myocarditis, and inherited arrhythmia disorders, require appropriate risk assessment and directed treatment approaches; these entities have important implications on exercise recommendations. Medical therapy with beta blockers, calcium channel blockers, and antiarrhythmic drugs may be considered, although catheter ablation has been shown to be more effective than medical therapy in most cases. Device therapy recommendations, including transvenous and subcutaneous ICDs, follow recommendations similar to those for nonathletes for primary and secondary prevention. For all entities underlying complex arrhythmias, both sudden death prevention and arrhythmia suppression are critical prior to return to play, including confirmation of suppression of arrhythmia during exercise. Understanding of the impact of exercise on ventricular arrhythmias continues to evolve. An algorithm of the recommendations for the management of athletes with complex ventricular arrhythmias is shown in **Figure 11**.

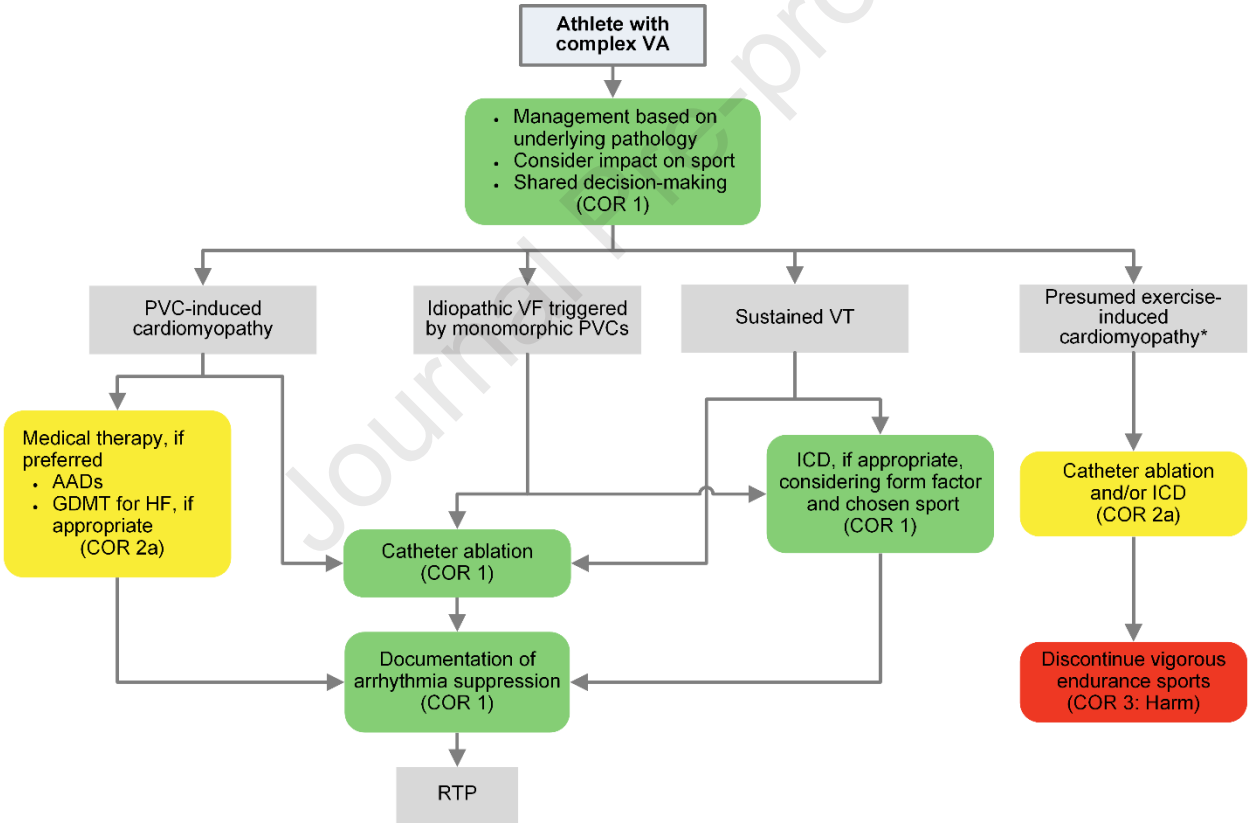

Figure 11
Algorithm for the treatment of athletes with complex ventricular arrhythmias (VAs). Colors correspond to the class of recommendation (COR) in **Table 1**. *Genotype-negative phenotype-positive arrhythmogenic right ventricular cardiomyopathy. AAD = antiarrhythmic drug; AVN = atrioventricular node; GDMT = guideline-directed medical therapy; HF = heart failure; ICD = implantable cardioverter-defibrillator; PVC = premature ventricular contraction; RTP = return to play; VF = ventricular fibrillation; VT = ventricular tachycardia.

Recommendation-specific supportive text

1. While most athletes with ventricular arrhythmias will have no underlying cardiac pathology, the management of those with structural or electrical heart disease depends on the specific etiology. Ventricular arrhythmias associated with ARVC forms of ACM, HCM, myocarditis, or genetic arrhythmias including Brugada or CPVT may localize to the right ventricular free wall or left ventricular endocardium, have a polymorphic or repetitive pattern, may exacerbate with exercise, and put the athlete at higher risk of SCD. The role of PVC burden as a predictor of risk varies based on underlying disease. For example, even > 500 PVCs/hour is considered a minor criterion for ARVC.[371] Thorough evaluation and shared decision-making involving the potential utility of EP study, catheter ablation, medical therapy, device therapy, and change in exercise regimen are needed on an individual basis.

2. The decision process for implantation of an ICD follows that for nonathletes.[8] For most underlying etiologies of sustained ventricular tachycardia (after excluding benign idiopathic ventricular tachycardia; see **Table 16**), clinical trial data have demonstrated a reduction in the risk of death driven by reduction in arrhythmic death in those with an ICD. In most cases, only a single lead device is required, and decision to proceed with a transvenous versus subcutaneous ICD relies on multiple factors, including patient body size, age, athlete's sport, and need for pacing or antitachycardia pacing in the setting of sustained monomorphic ventricular tachycardia. Implanting transvenous leads at a young age portends a higher risk of lead damage over the lifetime and complexity and morbidity with extraction. Sports with extreme ipsilateral arm movements (golf, tennis, swimming) may increase the risk of transvenous lead damage or dislodgement and may favor subcutaneous ICD. Detailed discussion regarding device choice and return to play with an ICD appears in **Section 3.5**.

3. In addition to prevention of sudden death with an ICD, athletes with ventricular tachyarrhythmias may need arrhythmia suppression. In the general population, ablation has been demonstrated as superior to alternative strategies for suppression of ventricular arrhythmias.[358,372] The outcomes of ventricular arrhythmia ablation depend on the underlying substrate. Those with ARVC forms of ACM or myocarditis have observed lower risk of ventricular tachycardia recurrence following ablation than those with HCM or sarcoidosis.[357] Superior outcomes have also been observed with a combined endocardial and epicardial ablation approach, such as in those with ARVC/ACM and HCM, and this approach should be performed in centers with appropriate expertise.[359] Ablation alone does not improve survival in those with underlying structural or electrical heart disease but is useful for suppression of arrhythmia.[360,361] Arrhythmia suppression is one factor to be considered prior to return to play. For some entities, such as ACMs, other considerations also need to be addressed, as discussed in detail in **Section 7**.

4. VF can be caused by short-coupled PVCs from fascicular system, outflow tracts, moderator band, papillary muscles, or, less commonly, the ventricular myocardium, in the absence of structural heart disease or genetic arrhythmia syndromes.[362,363] Ablation can be highly successful for arrhythmia suppression in those with monomorphic and frequent PVCs, although recurrence may occur requiring repeat ablation. ICD is also generally considered for SCA prevention.[364-366,373] In those with unsuccessful ablation, polymorphic PVCs, or patient preference to avoid invasive

procedures, antiarrhythmic drug therapy with quinidine may be considered, as it has demonstrated high short-term success rates based on observational studies.[366,374]

5. For athletes in whom a comprehensive shared decision-making approach has led to a decision to return to play, arrhythmia suppression should be documented prior to their return. Athletes with complex ventricular arrhythmias suppressed with either medical therapy or ablation should undergo evaluation to document suppression during exercise with an exercise stress test. Details on stress testing in athletes appear in **Section 2.3**. Underlying specific heart conditions also influence the decision to return to play and must be considered on an individual basis. In cases of myocarditis, it is reasonable to return to competitive sport at a minimum of 3 months after repeat imaging to demonstrate resolution along with demonstration of suppression of ventricular arrhythmias.[375,376]

6. Left ventricular dysfunction has been associated with high PVC burden (generally > 10% and usually > 20%). In prospective studies of patients with high-burden idiopathic PVCs, left ventricular function normalized in approximately 80% of patients with catheter ablation.[344,367] In some cases, such as those with an epicardial origin, recovery of ventricular function may be delayed over a year.[368]

7. In those for whom ablation is not preferred or ineffective, adequate pharmacological suppression of PVCs in those with suspected PVC-induced cardiomyopathy can lead to recovery. In a retrospective study of 20 patients with PVC-induced cardiomyopathy treated with class IC antiarrhythmic drugs, PVC burden decreased from an average 36% to 10% and mean left ventricular ejection fraction (LVEF) increased from 36% to 49% over nearly 4 years of treatment with no adverse effects.[370] As PVC-induced cardiomyopathy is often a diagnosis of exclusion, guideline-directed medical therapy for heart failure with reduced ejection must also be included in the medical regimen.

8. Athletes with high volumes of high-intensity exercise with predominately right ventricular enlargement and dysfunction with no desmosomal variant presenting with symptomatic ventricular arrhythmias are candidates for an EP study and cardiac ablation with high likelihood of success.[305] Although most arrhythmias originate in the right ventricle, epicardial ablation may be required.[307] In those with sustained ventricular tachycardia that is not treated effectively with ablation and/or those with sustained cardiac arrest, an ICD should be placed in accordance with evidence-based criteria for secondary prevention of SCD.[189,356]

9. For those diagnosed with exercise-induced ARVC or genotype negative ARVC,[306] as described above, observational data have suggested that detraining may result in resolution of ventricular arrhythmias and structural changes.[377] As studies are still limited on this diagnostic entity, shared decision-making discussions regarding management decisions for ongoing evaluation of ventricular arrhythmias, further risk assessment of SCD, and serial imaging should be pursued.

Section 7 Inherited arrhythmias and cardiomyopathies

7.1 Athletes with inherited arrhythmia syndromes

IAS, including LQTS, Brugada syndrome, CPVT, and short QT syndrome (SQTS), have been identified in series of sudden deaths in athletes.[79,91] Previously, this resulted in disqualification for most IAS-positive athletes from most sports, even in those with only a positive genetic test result and no phenotypic expression.[9,378] However, in 2015, the AHA/ACC sports participation guidelines acknowledged and enabled return to play with a model of shared decision-making for IAS-positive athletes.[5,58] This was catalyzed by observational data demonstrating very low rates of IAS-associated breakthrough cardiac events after diagnosis and institution of guideline-directed and genotype/patient-tailored therapies for athletes with LQTS[26,194,379-384] and athletes with CPVT.[26,383,385] Accordingly, after expert evaluation and treatment, athletes with IAS are increasingly returning to play in a shared decision-making model under the guidance of their genetic cardiologist or sports cardiologist who has direct expertise with their specific IAS. These recommendations aim to assist physicians with treatment and management of athletes with IAS, before and after return to play.

Recommendations for athletes with inherited arrhythmia syndromes		
COR	**LOE**	**Recommendations**
1	**C-LD**	**1. In athletes with IAS, an assessment by an expert in genetic cardiology and a shared decision-making model of care is recommended.[194,381]**
1	**B-NR**	**2. In athletes with a positive genetic test for IAS, comprehensive assessment and cardiac testing are recommended to determine the risk category.[41,386-388]**
2a	**B-NR**	**3. In athletes with LQTS or CPVT in whom beta blocker therapy leads to decreased performance in their sport and/or subsequent quality-of-life issues, left cardiac sympathetic denervation (LCSD) can be effective.[389-391]**
2a	**B-NR**	**4. In athletes with IAS who have received a clinically indicated ICD, sports participation is reasonable.[192,193,392,393]**
3: Harm	**C-LD**	**5. In athletes with IAS, ICD implantation for the sole purpose of return to play is potentially harmful and should not be done.[394]**

Synopsis

Prior to return to play, it is critical that athletes undergo assessment by an expert in genetic cardiology, with appropriate cardiac testing to guide treatment and risk assessment and inform shared decision-making, as shown in **Figure 12**. The desire to return to play without loss of athletic performance may be a factor in treatment decisions. For athletes with IAS in whom ICDs are clinically indicated, return to play after appropriate treatment is reasonable, but as ICDs are not without risks, they should not be implanted for the sole purpose of return to play.

Recommendation-specific supportive text

1. IAS are complex conditions and can vary widely in their clinical manifestations and potential risks. Given the intricate nature of these syndromes, a thorough evaluation by a specialist in

genetic cardiology is crucial to accurately diagnose the specific syndrome and determine its implications for an athlete's health. While exercise training can lengthen repolarization,[35] a prolonged QT requires evaluation. This assessment involves evaluating both genetic and clinical features including personal and family history and test findings. By conducting a comprehensive risk assessment, the expert can guide appropriate risk management strategies, to allow informed decision-making around lifestyle modifications, medication, or even restrictions on certain physical activities. As described in detail in **Section 2.3**, a shared decision-making model empowers the athlete to actively participate in decisions about their health care, ensuring that the chosen interventions align with their personal values, preferences, and goals. Athletes often have unique goals and aspirations related to their sport. Balancing these aspirations with the potential health risks associated with IAS requires careful consideration. A shared decision-making model allows the athlete to collaborate with the health care provider in making informed choices that optimize both their athletic pursuits and their long-term well-being.[9,194,395]

2. Athletes who have been identified as having a positive genetic test for an IAS require comprehensive clinical evaluation, with a minimum of ECG and maximum capacity stress testing (LQT/CPVT) with or without high-lead ECG (Brugada syndrome) and Holter monitoring to determine their phenotypic disease expression and guide treatment and for risk assessment before they return to play. Various clinical parameters are known to confer differing levels of risk, including specific genotype, QTc duration, disease expression, symptoms, and documentation of arrhythmias.[41,386-388,396]

3. Beta blockers can lead to side effects including fatigue and reported decreased athletic performance in some athletes.[354] In athletes with LQTS or CPVT, LCSD monotherapy has been shown to be a safe and effective therapeutic option when performed in experienced centers,[389] with the largest cohort of 64 patients demonstrating a low nonlethal recurrent event rate of 5% with no surgical complications at 2.7 years mean follow-up.[391] LCSD performed in high-volume centers has demonstrated effective reduction of arrhythmias and a lower risk of adverse events. A recent study reviewed long-term follow-up for 125 patients (mean follow-up of 12.9 ± 10.3 years) and demonstrated an overall 86% decrease in mean yearly event rate with no major complications and a low minor complication rate.[390] While rates of significant complications are low, and quality of life not adversely impacted by LCSD,[391,397] impact on athletic performance has not been reported.

4. Data from the ICD multinational sports registry show that competitive and recreational sports participation for athletes with ICDs can be safe, including for those who participate in vigorous and competitive sports; however, they should be informed they are at risk of both appropriate and inappropriate shocks.[192,392,393] In athletes with IAS with clinical evidence of high risk for SCD and benefit from ICD based on standard clinical criteria, the programming of the ICD should include consideration for the individual's age, sport, and specific disease phenotype (see **Section 3**).

5. Although lifesaving in those at significant risk of SCA, ICDs are not without risk. A meta-analysis[394] of 4916 young patients with IAS and ICDs showed a 20% rate of inappropriate shocks (annual rate of 4.7% per year) as well as a 22% rate of ICD-related complications (4.4% per year) and a 0.5% ICD-related mortality (0.08% per year).

7.1.1 Athletes with long QT syndrome

Recommendations for athletes with long QT syndrome		
COR	**LOE**	**Recommendations**
2a	B-NR	1. In athletes with LQTS under expert assessment and supervision, return to play is reasonable in a shared decision-making model after risk assessment, education, and initiation of appropriate therapies.[26,194,379-382,398]
1	B-NR	2. In athletes with LQTS, review and/or cessation of medications known to prolong the QT interval is recommended, and whenever possible, prevention and correction of electrolyte disturbances are recommended.[399,400]
1	B-NR	3. In athletes with asymptomatic LQTS and a normal corrected QT interval (concealed variant-positive LQTS), initiation of QT-related preventative measures is recommended prior to return to play.[399,400]
2a	B-NR	4. In athletes with asymptomatic LQTS and a corrected QT interval < 470 ms, therapy with beta blockers can be useful.[387]
1	B-NR	5. In athletes with LQTS with symptoms and/or a corrected QT interval > 470 ms, guideline-directed and genotype/patient-tailored therapy with medications, LCSD, and/or device therapy should be optimized fully before return to play.[26,387,390,401]
1	B-NR	6. In athletes with LQTS on beta blocker therapy, nonselective beta blockers (especially nadolol and propranolol) are recommended, with dosing tailored to the patient's risk profile and response to therapy.[387]
2a	B-NR	7. For athletes with LQTS and severe bradycardia, other treatment configurations besides beta blockers (eg, alternative medical therapy, LCSD, and device therapy) are reasonable.[26,389-391]
2a	B-NR	8. In athletes with LQTS (including type 1), participation in swimming/diving is reasonable with appropriate precautions.[402]
1	B-NR	9. In athletes with LQTS who are unable to tolerate beta blockers or who have ongoing events on beta blockers, treatment intensification with medication, LCSD, and/or device therapy should be done and reoptimized fully prior to return to play.[26,390,401,403]

Synopsis

Despite a paucity of scientific data, athletes with LQTS have historically been recommended to avoid competitive sports. In more recent iterations of guidelines, such as the AHA/ACC sports participation guidelines, as observational data has emerged showing a low rate of events for athletes with LQTS, there has increasingly been an acceptance that in a shared decision-making model, return to play for athletes with LQTS can be enabled. The current recommendations incorporate recent observational studies demonstrating low rates of breakthrough cardiac events for athletes who are managed in a specialized clinic. **Figure 12** highlights the recommended approach for athletes with LQTS. Athletes

should be assessed at a specialized center and managed as part of a shared decision-making model where their personalized risk and management decisions are optimized. Athletes with LQTS breakthrough events require reassessment and optimization of therapies, which may include medications, LCSD, and devices before considering return to play.

Recommendation-specific supportive text

1. Athletes with LQTS who are managed in a specialized center may return to play as part of a shared decision-making model following an expert assessment and discussion of risk. Prior to return to play, a plan should be in place including access to an AED and consideration for purchasing their own personal AED and having an individualized EAP. The largest cohort to date, from Mayo clinic, including 494 athletes with LQTS returning to play after risk assessment and personalized treatment plans from a specialized genetic heart disease team, showed no deaths and a low event rate of 1.16 nonlethal events per 100 athlete-years follow-up.[26] In a recent French cohort, they also showed no deaths and a low event rate of 0.0007/year after diagnosis, with no events in any competitive athlete, and no events in patients treated with beta blockers.[380] Smaller series have shown similar findings.[379,398]

2. It is important that athletes with LQTS minimize risk through a thorough physician-led review for known triggers for QT prolongation and torsade de pointes, including QT-prolonging medications (www.crediblemeds.org) and electrolyte disturbances (particularly hypokalemia and hypomagnesemia). They should avoid training-related heat exhaustion and heat stroke (particularly LQT2), take caution with regard to over-the-counter medications (including supplements), and receive counseling around avoidance of illicit substances.[396,399,400]

3. There are no current data to support exercise restrictions in athletes with LQTS who have no symptoms and a normal corrected QT interval (concealed variant-positive LQT athletes). A single-center study[383] demonstrated a low event rate of 0.3 nonlethal events per 100 patient-years for low-risk patients. Intentional nontherapy is a valid option in this lower-risk cohort, with a study of 55 asymptomatic low-risk patients with LQTS with a mean QTc 448 ms and managed with conservative preventative measures only, including avoidance of QT-prolonging medications and potential electrolyte disturbance, demonstrating no events at mean follow-up of 7.5 years.[404]

4. In athletes with QTc < 470ms, data from a large Italian cohort[387] show that the risk of life-threatening arrhythmias is very low in all genotypes for QTc < 460 ms (< 1% 5-year risk off therapy) and low for QTc 460-470 ms (< 3% for LQT1 and LQT2 and 3%-6% for LQT3 5-year risk off therapy). In these individuals, conservative preventive measures with intentional nontherapy can be considered in an individualized shared decision-making discussion.[399,400,404] The initiation of beta blockers in those with indication of [387] higher risk of arrhythmia such as LQT2/3 genotypes or those at the upper end of the QTc range (< 460-470 ms) can confer further arrhythmic protection.

5. In athletes with symptomatic LQTS or QTc prolongation > 470 ms, treatment with nonselective beta blockers, particularly nadolol or propranolol, has been shown to reduce the risk of ventricular arrhythmias.[387,405] The dose of beta blockers can be titrated according to exercise stress testing performed 3 months after commencement of therapy, with an aim to reduce

mean heart rate by 15%-20%, or aiming for 0.8-1.5 mg/kg nadolol.[25,43] In patients who are confirmed genotype LQT3 (and selected individuals with LQT2), there is evidence to support the use of mexiletine either in conjunction with beta blockers or as monotherapy in athletes unable to tolerate beta blockers.[401,403] In some higher-risk athletes—based on genotype, QTc interval, and clinical history[396] or those with documented arrhythmias requiring escalation of therapies—LCSD and ICD are further adjunctive therapies. LCSD has been shown to be a safe and effective therapeutic option in a large LQT cohort of 125 patients, with an overall 86% decrease in mean yearly event rate with no major complications and a low minor complication rate of ptosis of 2.4%.[390] Slow beta blocker dose titration may help achieve appropriate dosage with fewer side effects. Individuals should be stable on therapy for a duration of 3 months with no breakthrough arrhythmias to ensure adequacy of current therapy prior to returning to play.

6. In athletes with LQTS on beta blockers, data from a large Italian cohort including 1710 LQTS patients followed for median 7.1 years demonstrated that treatment with nonselective beta blockers, particularly nadolol, is superior to other beta blockers in preventing arrhythmias across all LQT genotypes (HR0.38).[387,405] When nadolol is not available, propranolol would be an appropriate substitute beta blocker.

7. Athletes with LQTS may be unable to tolerate beta blockers due to severe bradycardia-associated symptoms. In these athletes, therapeutic options include active nontherapy (in very-low-risk individuals), alternative medical therapy (QT-preventive therapies, or mexilitene for LQT2/3), LCSD monotherapy, device implantation, or a combination of these options. LCSD has been shown to be a safe and effective option for monotherapy.[389] The largest published LCSD monotherapy cohort of 64 patients demonstrated a low nonlethal recurrent event rate of 5% with no surgical complications at 2.7 years mean follow-up.[391] Device implantation may be considered in this cohort, with studies demonstrating some benefit from intentional atrial pacing particularly for higher-risk individuals with LQT2 (reduction in event rate from 1.01 breakthrough cardiac events per year to 0.02 breakthrough cardiac events per year),[406] while ICD implantation for higher-risk individuals unable to tolerate beta blockers, particularly those with symptomatic LQT2, can be considered.[26,383] While most LQT patients receiving a device will benefit from both pacing and defibrillation capability, rarely, pacing alone may provide sufficient protection. [406]

8. Swimming/diving in athletes with LQT1 has historically required careful consideration due to prior data describing swimming as a genotype-specific trigger with increased risk of ventricular arrhythmias and SCD.[402,407] However, the swimming-LQT1 connection is most established in those individuals who are previously undiagnosed and therefore untreated. For LQT1 athletes whose competitive sport of choice is swimming, development of a personalized management plan including purchase of a personal AED to be in the area of the athlete while swimming, avoidance of swimming alone, and a preference for swimming in pools rather than in open water are considerations for the athlete in a shared decision-making model of care.

9. LCSD has been shown to be an effective additional therapy at reducing further breakthrough cardiac events for those who have recurrent ICD shocks or cardiac events on beta blocker therapy. For athletes unable to tolerate beta blockers despite a gradual loading phase, LCSD has been effective as monotherapy in selected LQTS populations as above. In a large international

cohort, patients with a QTc > 500 ms have a 50% chance of QT reduction by 60 ms, and 86% reduction in mean yearly event rate after LCSD.[390] Mexiletine has been shown to reduce the QT interval by a mean of 63 ms and reduce annual event rate to 0.7% per year in a small cohort of 34 patients with LQT3 and is an appropriate adjunctive therapy or monotherapy for athletes with LQT3. There are also limited data showing that mexiletine can shorten the QT interval for patients with LQT2.[403]

7.1.2 Catecholaminergic polymorphic ventricular tachycardia

Recommendations for athletes with catecholaminergic polymorphic ventricular tachycardia		
COR	**LOE**	**Recommendations**
1	**C-LD**	**1. In athletes with asymptomatic CPVT and a negative exercise stress test (genotype-positive phenotype-negative), return to play is recommended with discussion of prophylactic CPVT-directed medical therapy.[26,383,385,408]**
1	**B-NR**	**2. In athletes with asymptomatic CPVT and a positive exercise stress test, a CPVT-directed medical treatment program guided by normalization of the stress test is recommended before considering return to play.[26,41,383,385]**
2b	**C-LD**	**3. In athletes with previously symptomatic CPVT while not on therapy, return to play may be considered after establishing and confirming appropriate therapy.[383]**
1	**C-LD**	**4. In athletes with previously symptomatic CPVT for whom return to play is being considered, combination therapy with beta blocker and flecainide, and consideration of triple therapy with LCSD, is recommended before return to play, with a goal of optimizing therapy to normalize the exercise stress test.[41,383]**
3: Harm	**C-EO**	**5. In athletes with ongoing symptomatic CPVT despite establishment of dual or triple therapy, return to play is potentially harmful.**

Synopsis

Exercise restrictions have historically been a mainstay of management for individuals with CPVT due to the adrenergic basis of the ventricular arrhythmias that are the hallmark of the condition. There are very limited data reviewing the safety of athletes with CPVT competing in high-intensity sports. Most data come from a single center, demonstrating no deaths for CPVT athletes who are managed in a specialized clinic; however, the nonfatal event rates are higher than for other IAS from the same center. For athletes with CPVT considering return to play, the absence of ventricular arrhythmias and normalization of the stress test is critical prior to considering return to play. Some athletes may require escalation with multiple therapies before this can be considered, as demonstrated in **Figure 12**.

Recommendation-specific supportive text

1. For athletes who have been diagnosed with CPVT on predictive (cascade) familial genetic testing but have normal exercise stress testing (no clinical evidence of exercise-induced arrhythmias, complete absence of PVCs including burst protocol to unmask those with incomplete penetrance), return to play is reasonable with consideration for commencement of medical

therapy with beta blocker and/or flecainide as part of a shared decision-making model. Data show that repeatability for ventricular arrhythmias can be variable, and therefore repeat exercise stress tests should be performed in these patients annually.[26,41,383,385,408]

2. Data for ongoing sports participation in overt CPVT are very limited. A single-center retrospective study of 63 individuals with CPVT is the largest published cohort and demonstrated the same event rate of 1.41/100 years for athletes and nonathletes with CPVT being managed in a specialized center, with no deaths in either group.[26,383,385]

3. Athletes who have CPVT and have had symptoms including syncope or cardiac arrest prior to commencing therapy should undergo a thorough clinical assessment, risk stratification, genotype and be established on dual or triple medical therapy before considering return to play.[383]

4. When titrating dual or triple therapies in athletes with CPVT, complete normalization of the stress test is the goal (complete absence of PVCs). Bigeminal PVCs may be acceptable, but couplets or more extensive nonsustained SVTs require continued treatment intensification. There are limited data for athletes with symptomatic CPVT who wish to return to play; however, the expert consensus is that this can only be considered in individuals who are established on dual or triple therapy (beta blocker ± flecainide ± LCSD) in a shared decision-making model. LCSD is best performed by an experienced high-volume center. The individuals need to be closely monitored with regular (6-12 month) burst exercise stress testing).[41,383]

5. For athletes who demonstrate a severe CPVT phenotype that is unable to be suppressed with optimization of medical therapy, high-intensity exercise with increased heart rate and adrenergic response is not safe.[14]

7.1.3 Brugada syndrome

Recommendations for athletes with Brugada syndrome		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In athletes with Brugada syndrome, avoidance of arrhythmia triggers including sodium-channel blocking drugs, alcohol, and heavy meals is recommended.[409]**
1	**C-LD (Fever)**	**2. In athletes with Brugada syndrome, aggressive treatment of fever (C-LD)[410] and avoidance of hyperthermia (C-EO) are recommended, including taking precautions to prevent overheating particularly for prolonged endurance exercise in warm climates.**
	C-EO (hyperthermia)	

Synopsis

There are limited data in athletes with Brugada syndrome. As there are no data showing that exercise increases risk in these individuals, there is no evidence to support exercise restrictions for these individuals. Athletes with Brugada syndrome may be at risk with increased core body temperature, due

to the known association of fever and arrhythmia, and therefore this is an important consideration for endurance athletes, particularly in warm climates. The recommendations for athletes with Brugada appear in **Figure 12**.

Recommendation-specific supportive text

1. Athletes who are diagnosed with Brugada syndrome need to avoid known triggers for arrhythmia including the sodium-channel blocking medications listed at www.brugadadrugs.org.[396,411] It is also recommended that athletes with Brugada syndrome avoid heavy meals,[409] marijuana,[409,412] and excessive alcohol consumption[412] due to limited case reports suggesting increased risk of arrhythmia.

2. In athletes with Brugada syndrome, fever or raised core body temperature is known to be a trigger for arrhythmia; therefore, aggressive treatment of fever and avoidance of training-related heat exhaustion and heat stroke is recommended, with particular attention for heat management in prolonged endurance exercise, particularly when being performed in warm climates. Case series as well as case report describe individuals demonstrating a spontaneous type 1 Brugada pattern when febrile and subsequently suffering arrhythmic events. In a cellular model of Brugada syndrome, the phenotype was exacerbated with increased temperatures of the cell culture from 37 to 40 degrees.[410,413-415] As arrhythmias in individuals with Brugada syndrome are not adrenergically driven, should an athlete with Brugada suffer an arrhythmia, treatments will not specifically impact sports participation.[162]

7.1.4 Short QT syndrome

Recommendations for athletes with short QT syndrome		
COR	**LOE**	**Recommendations**
1	**C-EO**	**1. In athletes with SQTS, patient education about the importance of fluid and electrolyte balance during endurance exercise is recommended.[400]**
2a	**C-LD**	**2. In athletes with symptomatic SQTS and/or a QTc < 320 ms, treatment with quinidine can be beneficial.[416,417]**

Synopsis

There are no athlete specific data for SQTS, which is a very rare condition. These recommendations are based on limited data in nonathletic SQTS cohorts and are shown in **Figure 12**.

Recommendation-specific supportive text

1. SQTS is very rare, and therefore there are no data for safety or risk of exercise in athletes with this condition. Avoidance of electrolyte disturbances is recommended to reduce the risk of ventricular arrhythmias.[400]

2. There are limited data in small cohorts demonstrating that quinidine may be a useful therapy in athletes with SQTS, particularly in those with symptoms, those with SQT1, or those who demonstrate a short QT interval (QTc < 320 ms).[416,417] ICDs have also been used in this population, although data are insufficient to define indications.

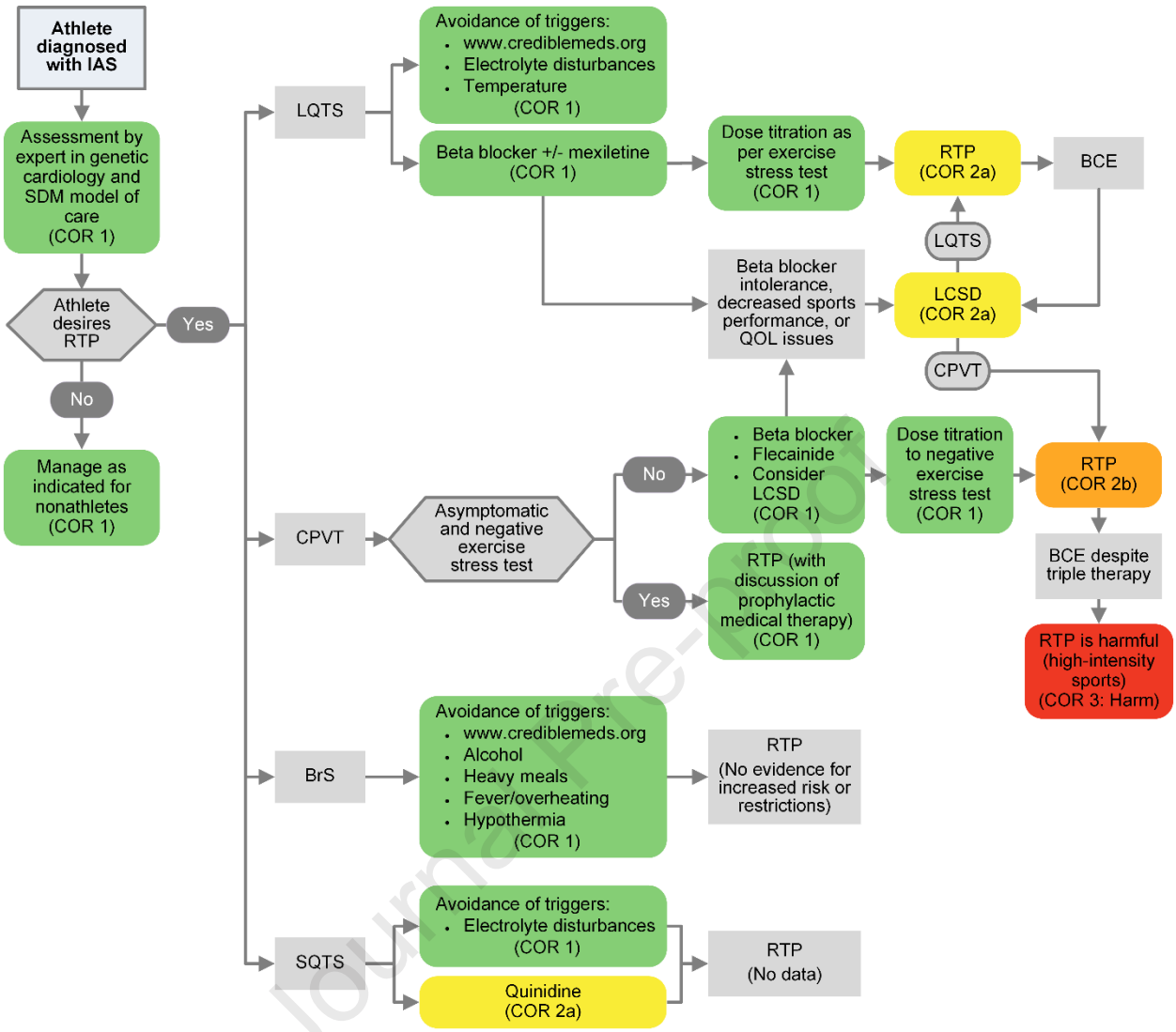

Figure 12
Algorithm for the management and treatment of inherited arrhythmias. Colors correspond to the class of recommendation (COR) in **Table 1**. BCE = breakthrough cardiac event; BrS = Brugada syndrome; CPVT = catecholaminergic polymorphic ventricular tachycardia; IAS = inherited arrhythmia syndrome; LCSD = left cardiac sympathetic denervation; LQTS = long QT syndrome; RTP = return to play; SQTS = short QT syndrome; QOL = quality of life.

7.2 Athletes with inherited cardiomyopathies

Inherited cardiomyopathies including HCM, ACM (of which one form is ARVC), and DCM have been identified in series of SCD in athletic cohorts.[82,84,91] Due to a perception of elevated risk, guidelines have historically led to blanket restrictions for athletes with inherited cardiomyopathies from participating in sports despite limited evidence of risk in athletes who have been diagnosed with these entities, risk-assessed, and appropriately treated.[418-420] More recently, guidelines have begun to acknowledge that some athletes with cardiomyopathies can return to play in a shared decision-making model.[10] Recent studies in athletes with HCM who have been appropriately risk-assessed and treated have not shown evidence of risk with return to play. The recent international multicenter LIVE-HCM study[421] demonstrated no increased cardiac event rate in vigorous exercisers compared with nonvigorous

exercisers with HCM, without findings demonstrating risk in multiple retrospective studies.[26,194,422,423] However, in athletes with some ACMs, studies have demonstrated that participation in sports involving high-intensity endurance training may increase risk of ventricular arrhythmias, heart failure, and SCD, particularly in *PKP2*-mediated or exercise-induced ACM/ARVC.[27,154,155,424] Studies in individuals with DCM have demonstrated certain genotypes such as *LMNA* to pose higher risk to athletes than other genotypes such as *TTN*.[425,426] For an athlete with potential DCM, careful evaluation including advanced imaging such as stress echocardiogram and CMR, is important to differentiate EICR, which can include mildly decreased ejection fraction, from DCM.

7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after return to play

Recommendations for the treatment and management of athletes with inherited cardiomyopathies before and after return to play		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In athletes with inherited cardiomyopathies, expert assessment by clinician(s) with genetic and sports cardiology experience and a shared decision-making model of care is recommended.[26]**
1	**B-NR**	**2. In athletes with inherited cardiomyopathies, genetic testing is recommended.[27,425-429]**
1	**C-LD**	**3. In athletes with inherited cardiomyopathies considering return to play, or returning to play after arrhythmia treatment, a maximal stress test is recommended to identify exercise-induced ventricular arrhythmias.[430,431]**
3: Harm	**B-NR**	**4. In athletes with inherited cardiomyopathies, an ICD should not be implanted solely to facilitate return to play.[192,193,383]**

Synopsis

Athletes with inherited cardiomyopathies require careful assessment, risk stratification, and management in expert genetic heart disease or sports cardiology centers. These recommendations aim to assist physicians with treatment and management of athletes with inherited cardiomyopathies before and after return to play. Nonfamilial cardiomyopathies are not discussed in this section of the document. The overall recommendations are summarized in **Figure 13**.

Recommendation-specific supportive text

1. Athletes with inherited cardiomyopathies require specialized expertise in genetic heart disease and/or sports cardiology in order for the athlete, their family, and other stakeholders to be fully informed with regard to participation in their particular sport for an athlete with their phenotype and/or genotype. The discussion should center around any potential risks (or lack thereof) of their ongoing sports participation, as part of a shared decision-making model.[10,26,395,432]

2. In athletes who fulfill diagnostic criteria for inherited cardiomyopathies, genetic testing can guide personalized therapeutic decision-making and risk stratification. The identification of a genetic result can be used for predictive testing in family members.[433] Genetic testing can be

helpful to clarify diagnosis in athletes who have borderline phenotypes, as the identification of a genetic result can assist in providing the athlete with a personalized assessment.[27,425-429,434]

3. As described above, a key component of all series of athletes with cardiomyopathies who have returned to play, is expert assessment and treatment.[10] Stress testing in HCM is important in initial assessment, for evaluation of both LVOT obstruction and possible unrecognized symptoms of dyspnea on exertion as well as increases in ventricular arrhythmia. Nonsustained ventricular tachycardia is an important marker of risk for young and young adult individuals with HCM and for those with ACMs.[430,431] As for all athletes returning to play after arrhythmia treatment, stress test evaluates efficacy of arrhythmia suppression interventions.

4. Athletes with cardiomyopathies should receive an ICD based on standard clinical risk assessment. Data from both the ICD sports multinational registry and the Mayo Clinic show that competitive and recreational sports participation for athletes with inherited cardiomyopathies and ICDs can be safe, with no deaths, device malfunctions, or damage associated with participation in competitive athletes. However, athletes need to be informed of the risk of both inappropriate and appropriate shocks, although the risk of shocks has not been shown to be greater during competition than in leisure activities.[192,193,383,393] ICDs have risks and should never be implanted solely to facilitate return to play (see **Section 7.2.1**).

7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy

Recommendations for the treatment and management specific to athletes with hypertrophic cardiomyopathy		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In athletes with genotype-positive phenotype-negative HCM, return to play in conjunction with expert assessment is recommended.[421]**
1	**B-NR**	**2. In young athletes with HCM who return to play, close follow-up with regular reassessment and ongoing risk stratification is recommended due to risk of evolution of their phenotype, including in those who are genotype-positive phenotype-negative.[435]**
2a	**B-NR**	**3. In athletes with phenotype-positive HCM, participation in competitive sports is reasonable with appropriate therapy and EAP including access to an AED.[194,384,421-423]**
1	**B-NR**	**4. In athletes with symptomatic obstructive HCM, intentional measures to attenuate the left ventricular obstruction are recommended before return to play.[436-438]**

Synopsis

Until recently, athletes with a diagnosis of HCM were restricted from participating in sports, due to perceived increased risk of sudden death with sports despite limited evidence in this area.[418-420] More recently, guidelines have begun to acknowledge that some athletes with cardiomyopathies, including those with HCM, can return to play in a shared decision-making model of care.[10] There have been a number of recent publications that have begun to provide increased evidence for recommendations for

physicians managing patients with HCM. The recent international multicenter LIVE-HCM study demonstrated no increased cardiac event rate in vigorous exercisers compared with nonvigorous exercisers with HCM,[421] which was also demonstrated in multiple retrospective series of athletes.[26,194,422,423] **Figure 13** presents the summary of the recommendations for assessment and management of athletes with HCM.

Recommendation-specific supportive text

1. In athletes with genotype-positive phenotype-negative HCM, there are no data to support exercise restrictions. The LIVE-HCM study[421] included 126 genotype-positive phenotype-negative HCM individuals with no events reported in this group. Expert assessment to ensure full evaluation of current phenotypic expression and appropriate serial testing in follow-up should be facilitated in a timely fashion.

2. There are less data assessing the safety of high-intensity exercise in young (children/adolescent) athletes with HCM compared with adult cohorts. In addition, there is known age-related penetrance of disease, and therefore some young athletes may still be evolving their full disease phenotype at their initial assessment and require serial reassessment.[10,435] Close follow-up (at least once per year) for young (children and adolescent) athletes with HCM is important for ongoing assessment and risk stratification.

3. Recent data support a shared decision-making model of guided return to play for athletes with HCM after expert assessment, with multiple studies showing lack of harm,[26,194,421-423] and only a case series of 2 athletes suggesting harm.[84] The most important aspect of expert assessment is evaluation for risk for SCA, with ICD implantation for those meeting standard criteria indicating elevated SCA risk. Risk assessment includes evaluation of personal and family history, presence of nonsustained ventricular tachycardia, and evaluation for CMR markers of elevated risk.[10]

   The LIVE-HCM study[421] examined the impact of vigorous exercise on arrhythmic events in 1660 individuals with HCM. Among the participants who continued to exercise, there was no increased risk of arrhythmic outcomes—including death, cardiac arrest, appropriate ICD shock, or arrhythmic syncope—in the vigorous exercisers compared with those who were sedentary (event rate 4.7% vs 4.6%, respectively). In the LIVE-HCM study,[421] a post hoc analysis of a small group of younger athletes (aged 14-22 years) identified 42 athletes competing in varsity-level sports in whom there was 1 event of a resuscitated cardiac arrest (event rate 5.7/1000 person-years), 50 athletes participating in other vigorous exercise with no events (event rate 0), and 97 athletes participating in nonvigorous sports with 6 events (event rate 20.7/1000 person-years). Multiple small single-center studies of athletes with HCM who elected to continue to participate in sports have shown no evidence of increased harm in low-risk HCM athletes who continue to participate compared with those from the same center who elect to discontinue.[26,194,422,423] A recent series of elite athletes with genetic cardiovascular disease (HCM, n=40)[194] showed no adverse events, as did a series of 40 athletes with nonobstructive HCM who continued to play,[422] including 28 professional athletes with no life-threatening arrhythmias or change in structural or functional phenotype. There are limited data to support liberal adoption of high-intensity exercise in athletes with phenotype-positive HCM who are identified to have high-risk features (eg, high HCM risk score, exercise-induced syncope, documented ventricular arrhythmias). A screening cohort study reported 2 athletes diagnosed with HCM who continued

to play despite advice and died suddenly,[84] leading to concern that higher-risk HCM athletes may be at higher risk of ventricular arrhythmias if they continue to participate in high-intensity sports, but clinical details of these individuals were not described. Most patients with HCM, including athletes, at high risk for sudden death will receive an ICD. Data from the ICD sports registry, which included 65 athletes with HCM, showed no ICD failures or injury.[192,193] Athletes require careful counseling and personalized risk assessment with appropriate protection from SCA as indicated, in a specialized center with a shared decision-making model, an EAP, and access to an AED. For athletes with HCM whose evaluation does not indicate ICD, consideration can be given to purchasing a personal AED. Data on risks of exercise in individuals with HCM who have undergone septal reduction therapy (myectomy or alcohol ablation) are not yet available.

The latest guidelines from the European Society of Cardiology (ESC)[15] and the AHA/ACC,[18] drawing on similar data, emphasize the importance of expert assessment (including appropriate treatment for athletes with elevated SCA risk) and shared decision-making (addressing potential and not fully understood risks) in consideration of return to play for athletes with HCM. The writing committee concurs with shifting away from universal exercise restrictions for those with HCM, with similar emphasis on expert assessment and shared decision-making. The writing committee reached consensus that with expert assessment, shared decision-making, and the implementation of appropriate therapy and EAPs, returning to play for athletes with HCM is reasonable (2a classification), whereas the ESC and AHA/ACC guidelines state it may be considered (2b classification). This decision was based on weighing the increasing evidence of low risk against the minimal evidence of high risk and the harm of restriction, as was done with other conditions discussed in this consensus statement for which evidence is similar and were given a 2a classification. While reaching consensus, the writing committee decision was not unanimous, with concerns raised that a 2a recommendation might deemphasize the mandatory need for expert assessment and long-term follow-up of these athletes, which is critical for ensuring equity of risk assessment and care for all athletes with HCM. However, the consensus of the group was that by emphasizing the need for expert assessment, this evidence-based recommendation will foster a model of process for return to play.

4. Athletes with HCM and symptoms attributed to LVOT obstruction (> 30 mmHg) have been successfully managed with therapies including medical therapy, alcohol septal ablation, and surgical myectomy to reduce the obstruction and improve symptoms to facilitate return to play.[10] In a single-center retrospective study of 58 HCM athletes,[436] 22 (38%) were found to have LVOT obstruction, of whom 5 underwent myectomy; however, only 4 (7%) reported exertional symptoms. There were no deaths; however, 1 patient with severe hypertrophy and myectomy had recurrent ICD shocks and no longer continued participating in sports. In this cohort, reduced peak VO2 did not correlate with outcomes.[436] Increased exercise LVOT gradients in asymptomatic HCM patients have been shown to be associated with decreased exercise performance.[437] Increasing data show that use of sarcomere inhibitors can improve symptoms in LVOT obstruction and reduce need for myectomy; however, there are no specific data reviewing these new medications in athletic individuals.[438]

7.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies

Recommendations for management specific to athletes with arrhythmogenic and dilated cardiomyopathies		
COR	**LOE**	**Recommendations**
1	B-NR	1. In athletes with genotype-positive phenotype-negative ACM, genotype-informed discussion with the athlete around the potential associations between high-intensity endurance exercise and increased likelihood of developing overt ACM phenotype and ventricular arrhythmias is recommended.[27]
1	B-NR	2. In athletes with genotype-positive but phenotype-negative ACM, sports participation should be tailored to patient's genotype and the intensity and duration of sport.[27,425-429]
1	B-NR	3. In athletes with phenotype-positive ACM, sports participation should be tailored to patient's genotype and the intensity and duration of sport.[27,425-429]
2b	C-LD	4. In athletes with phenotype-positive ACM and a lower-risk genotype, participation in vigorous endurance sports may be considered.[439]
3: Harm	B-NR	5. In athletes with phenotype-positive ACM and higher-risk genotypes, participation in vigorous endurance sports is potentially harmful.[27]
3: Harm	B-NR	6. In athletes with nonfamilial and/or genotype-negative phenotype-positive ARVC (presumed exercised induced), continuation of vigorous endurance sports is harmful.[305,328]
2a	B-NR	7. In athletes with DCM who are asymptomatic with LVEF > 45% and no high-risk clinical features, return to play following expert assessment and commencement of medical therapy is reasonable.[440-442]
2b	C-LD	8. In athletes with DCM who are asymptomatic with LVEF < 45% who have been appropriately risk assessed and risk treated, return to play may be considered.[440-442]

Synopsis

There is established evidence that exercise, particularly endurance exercise (see **Section 2** and **Figure 1**), requires careful consideration for individuals with ACM and DCM. There is increasing evidence demonstrating that the underlying genotype is important when reviewing exercise-related risk stratification, management, and return to play. These recommendations present the current data, with **Table 17** showing the gene-specific evidence currently available. **Figure 13** presents the summary of the recommendations for assessment and management of athletes with ACM and DCM. Informed discussion with shared decision-making for exercise is the preferred and evidence-based approach.[53,54,432]

Recommendation-specific supportive text

1. In athletes with *PKP2* variants associated with ACM/ARVC (genotype-positive phenotype-negative), studies have shown ongoing participation in vigorous-endurance exercise to lead to

more rapid progression to overt disease, increased risk of ventricular arrhythmias, and increased risk of heart failure.[27,443] In athletes with a positive genetic test for ACM pathogenic variants in genes besides *PKP2* and normal imaging and stress testing, there are limited data assessing the risks of endurance or high-intensity exercise. Therefore, the risk of ongoing participation in endurance sports for these athletes incorporating genotype and type of exercise can be approached with athlete counseling and shared decision-making. **Table 17** shows the role of exercise in increasing penetrance in specific ACM genotypes.

2. There are limited data to support blanket exercise restrictions for nonendurance exercise in genotype-positive phenotype-negative ACM athletes. Regular surveillance (at least once per year) assessing cardiac imaging, stress testing, and monitoring ensures that any development of an overt phenotype is identified, risk stratified, and managed appropriately.[444] **Table 17** shows the role of exercise in increasing penetrance in specific ACM genotypes. Evidence of the association of participation in frequent, high-intensity exercise with disease onset (eg, penetrance) is most compelling for *PKP2*, in which such exercise is associated with higher likelihood of disease expression and worse clinical presentation.[27,154,443]

3. In athletes with clinical evidence of ACM, participation in competitive/recreational sports involving low to moderate intensity is reasonable; however, participation in high-intensity or frequent endurance exercise is not recommended, particularly for patients with *PKP2*-related ARVC, due to an association with increased risk of ventricular arrhythmias and sudden death.[27,154] In one study of these patients,[154] competitive sport was associated with two-fold increased risk of ventricular arrhythmias, death, and symptoms compared with patients who were inactive or who participated in recreational sports. In this cohort, recreational sports were not associated with increased symptoms, ventricular arrhythmias, or death. In a large postmortem ACM SCD cohort of 202 cases,[424] athletes were 16 times more likely to die during exertion than nonathletes. In this cohort, a small proportion (25%) underwent genetic testing, with pathogenic variants identified in *PKP2*, *DSP*, and *TMEM43*. In the largest cohort of patients with genetic heart disease who have returned to play, athletes with ACM had an event rate of 8.16/100 patient-years, which trended higher than seen in other genetic heart diseases at the same institution.[26] **Table 17** summarizes the data on the impact of exercise on risk of sustained ventricular arrhythmias and structural progression that differs based on specific ACM genotypes. Data are most robust for patients with *PKP2* variants and for patients with nonfamilial gene-negative ARVC.

4. As demonstrated in **Table 17**, studies in some genotypes such as *PLN* demonstrate no signal for increased risk of progression or penetrance with endurance exercise, and therefore blanket restrictions cannot be supported.[439] Nonetheless, in a retrospective study of 185 *PLN* carriers,[429] the majority (74%) of malignant ventricular arrhythmia events occurred during exercise (2/3 during low-intensity exercise and 1/3 during moderate to high intensity exercise) as did 13/19 (68%) SCDs, highlighting the importance of nuanced discussions and shared decision-making. Disease-specific risk assessment, with ICD implantation if indicated, as well as disease-specific treatment, is critical prior to consideration of return to play.

5. In athletes with *PKP2*-mediated ACM/ARVC with evidence of disease on imaging or stress testing, participation in high-intensity or endurance exercise is not recommended due to an

association with increased risk of ventricular arrhythmias and sudden death.[27,154] This has also been demonstrated in mouse models of ARVC across desmosomal genotypes.[443,445-447] Other higher-risk genotypes include *DSP*, *LMNA*, and *TMEM43*, as mentioned previously (see **Table 17**).[424-426,448,449]

6. Studies have shown endurance athletes with genotype-negative exercise-induced right ventricular remodeling to be associated with higher rates of ventricular arrhythmias with persistent endurance exercise[305,328] and greater clinical benefit from exercise modification.[306] While studies comparing continuation versus discontinuation are lacking, since the phenotype develops due to endurance exercise, a pillar of treatment is removal of the underlying cause (see **Section 5**).

7. There are no data demonstrating benefit for exercise restriction in athletes with DCM who do not have symptoms or higher-risk clinical features (LVEF < 45%, documented ventricular arrhythmias on Holter or EST, significant late gadolinium enhancement on CMR, high-risk genotypes, failure of LVEF to augment by > 10% with stress).[439-442,450,451] With borderline LVEF, it is important to differentiate DCM from EICR.[450,451]

8. There are limited data reviewing the safety of ongoing exercise for athletes with DCM with no symptoms but impaired ventricular function. Assessment of risk for SCA, with ICD implantation for those meeting standard criteria indicating elevated SCA risk, is critical. Risk assessment includes evaluation of personal and family history, presence of nonsustained ventricular tachycardia, and CMR markers of elevated risk. There are data demonstrating the presence of late gadolinium enhancement to be a predictor of SCD risk in DCM cohorts; it is therefore an important factor in risk stratification and shared decision-making.[440-442]

Table 17 Association of vigorous (> 6 METs) endurance exercise with clinical outcomes in ACMs

Genotype of ACM	Arrhythmias/SCD	Progression	Penetrance
PKP2	+++	+++	+++
Nonfamilial/gene-negative ARVC	+++	++	Not applicable
LMNA	+	++	++
TMEM43	++	+	+
DSP	++	+/-	+/-
DSG2	+	+	+
DSC2	+	+	?
PLN	+	-	-
FLNC	+	?	?
JUP/Naxos disease	?	?	?
RBM20	?	?	?
DES	?	?	?

+++ Replication across multiple clinical studies from different cohorts and supported by understanding of pathophysiology and experimental data.
++ Replication across multiple clinical studies from different cohorts OR quality clinical study plus support from experimental data.
+ Single clinical study or clear pathophysiology.
+ / - Mixed findings from studies.
? No strong clinical evidence or clear pathophysiology.
- Evidence does not support deleterious effect of endurance exercise.
ACM = arrhythmogenic cardiomyopathy; SCD = sudden cardiac death.

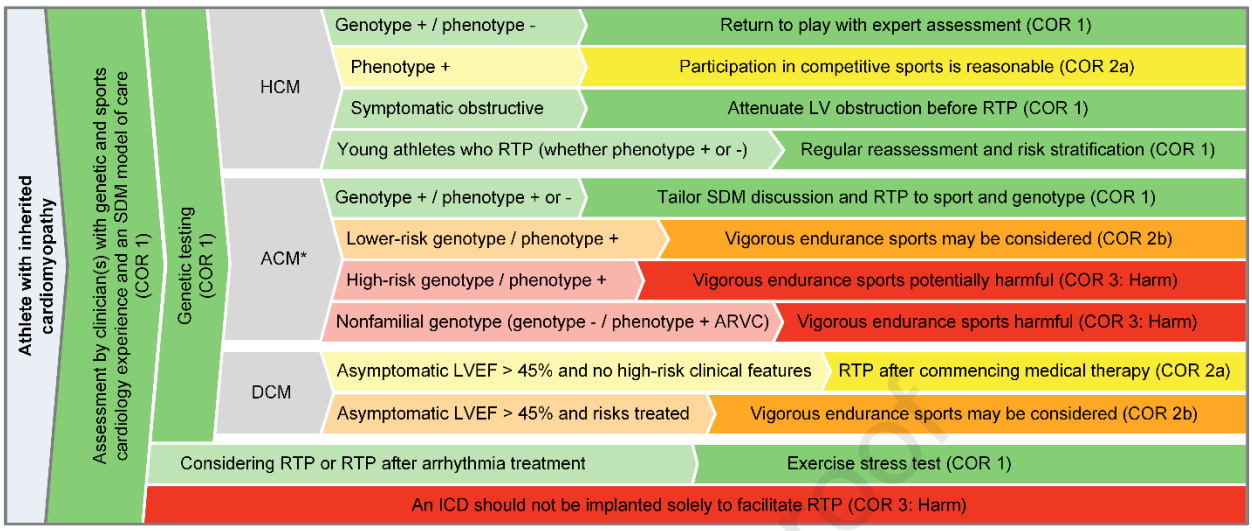

Figure 13

Recommendations for athletes with inherited cardiomyopathies returning to play. Colors correspond to the class of recommendation (COR) in **Table 1**. *Tailor management to genotype. ACM = arrhythmogenic cardiomyopathy; ARVC = arrhythmogenic right ventricular cardiomyopathy; DCM = dilated cardiomyopathy; GDMT = guideline-directed medical therapy; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter-defibrillator; LV = left ventricular; LVEF = left ventricular ejection fraction; RTP = return to play.

7.3 Moving from athlete to family: Implications of a genetic diagnosis

Most genetic heart diseases are inherited in an autosomal dominant manner with incomplete penetrance and variable expressivity.[178,433] This means family members have a 50% chance of inheriting the same cardiac condition. An athlete may represent the initial patient found with inherited disease, (proband) whether due to presentation with symptoms or to preparticipation screening. For the physician treating the athlete diagnosed with an inherited condition, appropriate medical care also involves addressing the athlete's family. As availability for genetic testing has expanded exponentially, with many more individuals undergoing genetic testing, understanding the nuances of cardiac genetic testing is important. Genetic counseling is an important adjunct to genetic testing.[452,453]

Recommendations for moving from athlete to family: Implications of a genetic diagnosis		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In athletes with suspected genetic heart disease, family history including 3 generations on both sides of the family is recommended.[454,455]**
1	**B-NR**	**2. In athletes with suspected genetic heart disease based on family history and/or phenotype, consultation with (or referral to) a multidisciplinary team with expertise in genetic heart disease is recommended.[456-458]**
1	**B-NR**	**3. In athletes with genetic heart disease who have a positive genetic test, variant-specific, predictive cascade testing in the appropriate family members is recommended in conjunction with genetic counseling.[459-466]**
1	**B-NR**	**4. In the absence of genetic testing or when the athlete has a negative test result for a genetic heart disease, first-degree relatives should undergo clinical**

		screening including ECG and echocardiogram as minimum baseline investigations.[464,465,467-470]
1	**B-NR**	**5. In athletes with a genetic variant but without phenotypic expression of the disease, counseling about return to play should be disease- and variant-specific.**[456-466]
3: Harm	**B-NR**	**6. Athletes with a genetic variant for arrhythmogenic conditions should not be restricted from play by governing bodies based on genetic results alone.**[49-52]

Synopsis

Genetic testing can assist with diagnosis, risk stratification, and management decisions in an athlete.[434,471] Most genetic heart diseases are inherited in an autosomal dominant manner, which carries important implications for the extended family.[178,433] A detailed family history is important when establishing the genetic basis to disease. The yield of genetic testing for genetic heart diseases ranges from 20%-30% (Brugada syndrome) up to 75%-80% (LQTS).[175,176,178,179,181-183] The yield also increases in the presence of a family history of disease or sudden death.[452] If an athlete is positive for a pathogenic or likely pathogenic variant, predictive testing of family members and relatives can identify those who are at risk and require ongoing screening. **Figure 14** summarizes the approach to athletes' families following a diagnosis of an inherited cardiac condition.

Recommendation-specific supportive text

1. Documenting a careful family history in athletes who have or are suspected to have a genetic heart disease (including IAS and cardiomyopathies), extending to 3 generations of relatedness, may identify any high-risk family history (eg, family history of SCD) to aid in risk assessment of the athlete as well as in identifying individuals who are at 50% risk of having the same condition due to the autosomal dominant inherited pattern of most of these conditions, to aid in family cascade screening.[178,433,453,454]

2. Multidisciplinary teams should include both genetic counselors and clinicians with experience in the clinical evaluation and risk assessment of genetic cardiovascular disease. In athletes and their families undergoing genetic testing, there are important ethical and legal considerations, including potential insurance implications or sport restrictions imposed by governing bodies. Genetic counseling in conjunction with genetic testing ensures that the athlete and family fully understand the implications of the testing being performed.[456-458]

3. Athletes who have undergone genetic testing may have an actionable variant identified (class 4 or 5 variants, ie, likely pathogenic or pathogenic), and their first-degree family members are at a 50% chance of carrying the same variant.[452] Family members who test positive will need clinical evaluation to determine presence and severity of phenotype. Ongoing clinical screening is not necessary for family members who test negative for the family's disease-causative variant.[433,471] Genetic counseling guides the process for athlete and family.[459-466]

4. In athletes with inherited cardiac conditions, if no variant has been identified, clinical screening in first-degree relatives (parents, siblings, and children), with a minimum of ECG and echocardiogram (and including Holter monitoring, exercise stress testing, or CMR depending on

the underlying condition in the family), has been shown to increase the diagnostic yield in family members who may have the same genetic heart disease.[464,465,467-470]

5. As described in **Section 7.2.3** and shown in **Table 17**, there is significant variation among genotypes regarding the role of vigorous exertion in increasing penetrance of disease. Individuals in whom a genetic variant is found based on family cascade screening after the diagnosis in a proband, with subsequent determination of absence of phenotype, should be similarly counseled.[456-466]

6. Genetic testing in medicine has the ability to improve recognition and treatment of disease. However, the conflict between the potential of genetic testing to improve health and the potential ethical issues it raises for privacy and autonomy are increasingly recognized, in general,[472,473] and in the context of sports.[474] Particularly as the penetrance of cardiomyopathy as well as the clinical course of carriers of genetic variants for electrical disease is highly variable and the factors poorly understood, genetic results should not be used to guide decisions by governing bodies to determine eligibility. As described in **Section 2.4**, restriction from sports can lead to significant harm.[51,52]

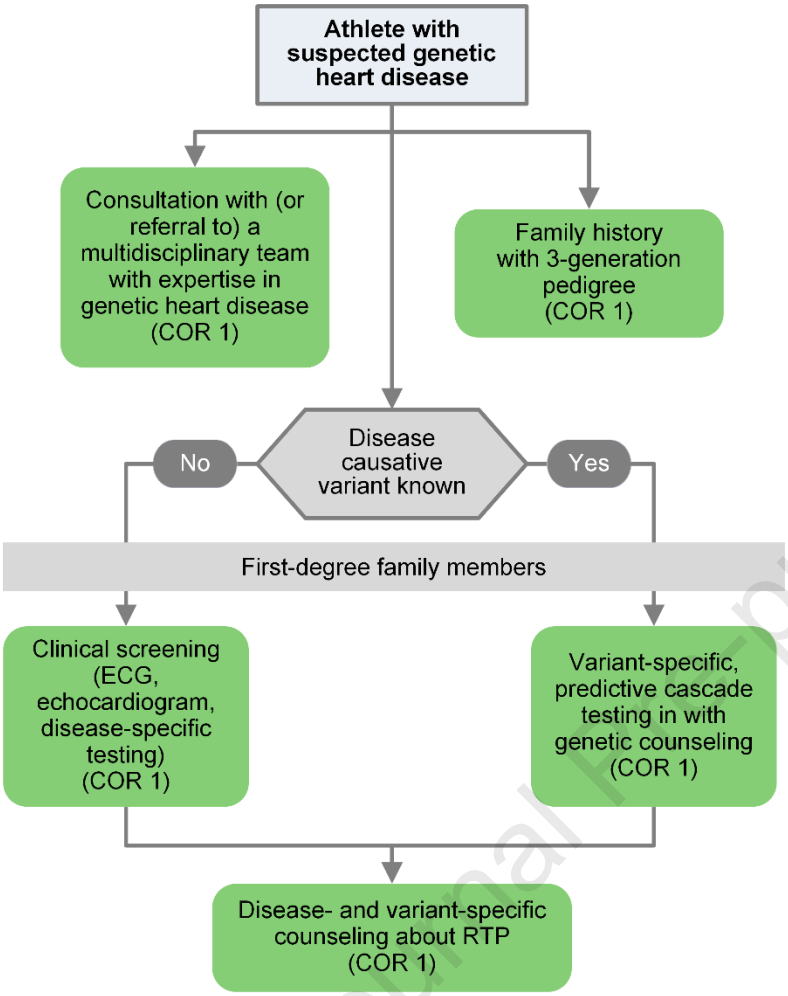

Figure 14
Flow chart demonstrating approach to families of athletes with genetic heart disease. Colors correspond to the class of recommendation (COR) in **Table 1**. ECG = electrocardiogram; RTP = return to play.

Section 8 Atrial fibrillation

Managing athletes with AF is complex because they perceive themselves as healthy individuals and often want to continue sports. AF in athletes can occur in several situations. First, AF can occur in the setting of a previously undetected genetic electrical or structural disease, such as Brugada syndrome or HCM. Acquired conditions may also lead to AF, such as hypertension or myocarditis. Finally, it may be the consequence of long-term endurance training or a combination of the previous factors. Evaluation and establishing a diagnosis, prognosis, and specific treatment are mandatory.

Long-term high-intensity endurance training is a risk factor for AF with a cumulative effect. Therefore, AF is uncommon in young athletes in the absence of underlying abnormality. However, as a causative factor for AF, endurance training often goes unrecognized because the incidence of AF starts to rise when athletes are in their 50s and 60s and have already significantly declined endurance practice. AF related to endurance training is much more prevalent among men, but the reasons are not yet fully

understood. This may be due to lower cumulative training in women or to differences in the presence of concomitant factors for AF between men and women, such as height or autonomic tone.

In patients involved in endurance sports, such as cycling or running, a careful discussion regarding the potential contribution of their practice to recurrences is probably necessary. To date, data on the reversibility of AF upon endurance practice cessation are based only on clinical observations and experimental models. Current management of the athlete with AF is similar to that for the nonathlete, with additional considerations detailed below.

In summary, athletes with AF should undergo a careful evaluation to uncover preexisting conditions. A detailed analysis of their lifetime and present sport practice is also necessary to establish the appropriate management.

8.1 Epidemiology and pathophysiology of atrial fibrillation in athletes

There are many putative mechanisms underpinning the risk of AF in endurance athletes, although few have current implications in the assessment and management of the athlete with AF.

8.1.1 Epidemiology of atrial fibrillation

In athletes, the prevalence and risk of AF varies based on sex, age, and type of sports participation. Although the prevalence of AF increases with age, the relative risk for athletes compared with nonathletes is greater in younger athletes.[475,476,477,478] Strong evidence from multiple studies demonstrates a relationship between AF prevalence and participation in endurance sports. While initial studies showed this association in males, recent studies suggest that AF may also be more prevalent among female endurance athletes.[475,479,480] Overall, although the prevalence of AF increases with age, the relative risk of AF associated with athletic training is greater in younger individuals. In Scandinavian cross-country skiers of mean age 37 years,[478] 1.2% developed AF in 8 years of follow-up and AF was significantly more common in the fastest athletes and those who had completed the most races. In older skiers,[476] AF was nearly twice as common among 505 athletes of median age 68 years as compared with 1867 nonathletes (prevalence 29% versus 18%; relative risk 1.9 [1.5-2.4]). This is comparable to the findings of a recent meta-analysis of 13 studies[477] over the past 2 decades including nearly 64,000 athletes that concluded that athletes were 2.46 times more likely to have prevalent AF (95% CI 1.73 to 3.51). The odds ratio increased to 3.6 when athletes aged < 55 years were considered.[477] A potential exception to the almost universal observation of increased AF risk among athletes was a study by Boraita et al[481] in which a low prevalence of AF (0.3%) was reported among 6813 Spanish athletes. However, it should be noted that the cohort comprised very young athletes (mean age 22 years) of which 65% were male and only 28% were endurance athletes. Male gender, increasing age, endurance sport participation, and years of sports training were all associated with AF, thereby confirming a likely association between athleticism and AF even in a cohort with lowest expected prevalence.[481] Although less studied, atrial flutter is also more common among endurance athletes than among nonathletic individuals.[475]

While endurance sports alone may increase vulnerability to AF, factors underlying AF in the general population can also affect athletes. Conditions that are associated with AF in nonathletes include hypertension, valvular heart disease, and hyperthyroidism.[16] It is reasonable to assume that these conditions would also increase the prevalence of AF in athletes, although this has not been specifically

investigated in athlete populations. There is speculation about a link between an exaggerated blood pressure response during exercise stress testing and AF, but the evidence supporting this association is currently limited.

There is a clear association between several cardiomyopathies and AF that is particularly relevant to younger athletes with AF. The strongest associations are with HCM, DCM, and ACM (where AF is found in 10%-25% of patients in each subtype). Similarly, AF is more common in patients with LQTS and Brugada syndrome.[482] There are no studies that have assessed the prevalence of underlying cardiac disorders in athletic populations. As described above, athletic training is associated with AF and the relative risk is greatest in young athletes. It is unclear to what extent the excess risk of AF in young athletes is due to environmental factors (athletic training) or genetic predisposition.

For young and young adult athletes, AF might be the first manifestation of an inherited cardiac condition. Three genes (*TTN*, *SCN5A*, and *KCNA5*) have been strongly associated with AF, while a further 9 genes (including *LMNA* and *KCNQ1*) have been associated with AF to a lesser extent. Studies in early-onset AF cohorts have returned a yield of pathogenic variants (predominantly in *TTN*) in approximately 1%-3% of early-onset AF patients.[483-487] The prevalence of rare variants among athletic populations with AF has not been specifically investigated. Discussions regarding the utility of clinical genetic testing in patients with AF should highlight the low expected yield.

Mechanisms underlying the increase in AF incidence in endurance athletes are hypothesized. Atrial dilation is known to be a risk factor for AF in nonathletes and is also associated with more advanced atrial disease in which reversion to and maintenance of sinus rhythm may be less likely. In athletes, atrial dilation is common and can be profound. Whereas there has been a consistent observation of greater atrial volumes in patients with AF than in patients without a history of AF, this is not as clear in athletes. In a matched cohort of athletes with and without AF, Trivedi et al[488] found no difference in atrial volumes. Similarly, Sorensen et al[489] observed considerable overlap in atrial volumes between nonathletes with AF and athletes with no history of AF. Thus, the association between atrial enlargement and AF, and the resulting prognostic implications, should be considered with care in endurance athlete populations.

The use of performance-enhancing drugs (stimulants, etc) may be an additional factor that predisposes athletes to AF. There is limited evidence linking the use of performance-enhancing drugs to AF, but this may be due to the fact that it is an extremely elusive cohort for study. In the general population, stimulants taken recreationally increase AF (see **Table 4**).

8.1.2 Pathophysiology of atrial fibrillation in the athlete

There are several putative mechanisms to explain the increase in AF observed in endurance athletes. Some knowledge of these concepts may assist the clinician when discussing management with an athlete with AF but are not yet sufficiently established to influence therapeutic options.

Some theories on the causation of AF in athletes have been extensively discussed elsewhere[490,491] and include structural remodeling of the atrium in response to repeated exposure to increased volume and pressure loads during exercise. There is some evidence in murine models that this remodeling includes changes to the sino-atrial node with downregulation of HCN channels that may contribute to more profound bradycardia and AF.[492] There is also evidence that exercise-induced AF may be mediated through increased vagal stimulation[493] and increases in proinflammatory substrate and fibrosis.[493,494]

8.2. Atrial fibrillation evaluation in athletes

Recommendations for the atrial fibrillation evaluation in athletes		
COR	**LOE**	**Recommendations**
1	**C-LD**	**1. In athletes with symptoms or personal ECG (portable wearable) findings concerning for AF, electrocardiographic documentation is recommended to establish a diagnosis of AF.**[495-497]
1	**C-LD**	**2. In athletes with AF, a detailed history and physical examination focused on identifying reversible or modifiable factors as well as exercise history should be performed.**[475,498-505]
1	**C-LD**	**3. In athletes with AF, initial evaluation should include 12-lead ECG, transthoracic echocardiogram, and laboratory evaluation.**[506-509]
2a	**C-LD**	**4. In athletes with AF, rhythm monitoring can be useful to evaluate burden, rate of ventricular response during an episode, relationship to symptoms, and documentation of other arrhythmias.**[510,511]
2a	**C-LD**	**5. In young and young adult athletes with AF, advanced imaging such as CMR is reasonable.**[507,512]
2a	**B-NR**	**6. In young and young adult athletes with AF and clinical suspicion of channelopathy or cardiomyopathy, genetic testing is reasonable.**[483-486,506,507]
2b	**B-NR**	**7. In young and young adult athletes with AF, genetic testing may be considered.**[483-486,506,507,513]
1	**C-EO**	**8. In young and young adult athletes with AF, withholding from sports participation pending evaluation of malignant etiologies is recommended.**
1	**C-EO**	**9. In athletes with AF, recommendations regarding intensive endurance sports participation while evaluation is ongoing should take into consideration symptoms, heart rate, and pattern of AF.**
2a	**C-EO**	**10. In athletes with AF, it is reasonable for patient counseling to clarify that sports-related AF is not life-threatening and sports participation is guided by symptoms.**
1	**B-NR**	**11. Athletes with AF should be managed in a center with expertise in both AF and the care of athletes.**[514,515]

Synopsis

The athlete with AF requires a comprehensive evaluation largely similar to that for nonathletes. Lone AF, or AF in patients with a structurally normal heart, should be a diagnosis of exclusion after thorough evaluation. Age may influence underlying etiological factors. Young athletes may have a higher incidence of underlying inherited arrhythmia syndromes (IAS) or cardiomyopathies, or SVT.[507,512] Despite otherwise excellent health status, Masters athletes may have typical risk factors, such as hypertension, obesity, and obstructive sleep apnea.[498,499,502] The relationship between exercise and the AF is well documented: moderate amounts of exercise carry benefit, while a sedentary lifestyle increases risk. A J-shaped curve has been demonstrated, with high-intensity endurance training also associated with increased risk of AF.[475,503,504] The role of exercise in promoting AF applies to athletes typically

participating in greater than 10 or more hours per week of high-intensity endurance activity over many years. While the impact of detraining on AF recurrence is unknown, moderation of exercise and avoidance of sedentary behavior should be encouraged while evaluation is performed. An algorithm of the recommendations for the evaluation of athletes with possible AF is shown in **Figure 15**.

Recommendation-specific supportive text

1. Confirmation of AF can be obtained by 12-lead ECG during symptoms. If long-term monitoring is needed to establish a diagnosis, ambulatory rhythm monitoring, a smartwatch with ECG sensors, or implanted loop recorders can be utilized. Although smartwatches are evolving to detect AF with high sensitivity, it is recommended that rhythm strips are thoroughly reviewed to confirm AF diagnosis.[495-497] Further confirmation with an ECG or ambulatory patch monitor, particularly in those with low burden, should be pursued. Features of available monitor types appear in **Table 14**. In those with palpitations during exercise, an exercise stress test may aid in diagnosis.

2. The initial evaluation of a patient with AF involves classifying AF (paroxysmal, persistent, longstanding persistent, or permanent) and associated symptoms, determining its cause, reversible or inciting factors, and comorbidities, and obtaining exercise capacity and exercise history. Risk factors, many of which are potentially modifiable, are the largely same for athletes as for the general population and include obstructive sleep apnea, use of stimulants, alcohol, obesity, hypertension, and coronary artery disease, particularly in older athletes.[498-502] The use of performance-enhancing drugs may be considered specifically in the athlete, although studies have not evaluated an association with AF.[321,516] Exercise history should focus on current and lifetime exercise volume. While moderate levels of physical activity are associated with AF risk reduction, high-intensity endurance training has been associated with increased risk of AF.[475,503-505] The physical exam may disclose resting bradycardia, irregular pulse in the presence of AF or a rapid, regular pulse in atrial flutter, elevated jugular venous pressure in setting of heart failure, or murmurs suggestive of valvular disease.

3. All patients with documented AF should have an ECG during AF episode and in sinus rhythm to evaluate for potential underlying etiologies including supraventricular arrhythmias such as typical atrial flutter and presence of delta wave suggestive of an accessory pathway (AP). Moreover, an ECG may suggest an IAS, including Brugada pattern or LQTS, as both have been associated with AF, particularly in children and young adults.[506,507] An echocardiogram will evaluate for structural heart disease including CHD and cardiomyopathy, cardiac function, and atrial size.[509] It is important to take into consideration the athlete's sport and training history to distinguish the athlete's heart from pathological remodeling on imaging, as athletes have been shown to have an increased incidence of left atrial enlargement.[508,517] Initial laboratory evaluation should include complete blood count, serum electrolytes, renal and hepatic function, and thyroid function.

4. For those with frequent symptoms, ambulatory monitors with a single patch electrode can diagnose and quantify arrhythmia burden for up to 30 days. Extended monitoring (> 30 days) with an implantable cardiac monitor can be used for long-term monitoring of AF burden in those with infrequent episodes.[510,511] The use of smartwatches for detection of AF and monitoring of AF may be a long-term monitoring option if rhythm strips can be reliably obtained by the user

and reviewed by the provider.[495-497] See **Table 14**, which describes features of some available monitoring systems.

5. AF is rare in general in the young and is also rare in young and young adult athletes. Young athletes may have a higher incidence of underlying IAS or cardiomyopathies, or SVT, than older athletes.[507,512] Thus, advanced imaging with CMR, computed cardiac tomography, and/or positron emission tomography is reasonable for evaluation of underlying structural cardiac abnormalities. CMR is discussed in further detail in **Section 5**.

6. Young adult athletes with AF who have a strong family history or imaging or electrocardiographic findings concerning for a cardiomyopathy or channelopathies should undergo genetic testing.[506,507] Several genes associated with cardiomyopathies and channelopathies associated with familial AF have been identified in the general AF population.[513,518,519] Three genes (*TTN*, *SCN5A*, and *KCNA5*) have been strongly associated with AF, while a further 9 genes (including *LMNA* and *KCNQ1*) have been associated with AF to a lesser extent. Studies in early-onset AF cohorts have returned a yield of pathogenic variants (predominantly in *TTN*) in approximately 1%-3% of early-onset AF patients.[483-486 518,519] As these entities may be associated with SCA, if there is clinical suspicion for cardiomyopathy or channelopathy, referral for genetic counseling and testing, as discussed in more detail in **Section 7**, is useful.

7. Whether all young and young adult athletes should be referred for genetic counseling, even in the absence of other clinically suspicious findings, is less clear-cut. As above, data suggest a small prevalence of genes associated with cardiomyopathies and channelopathies, which may be associated with SCA; some of these have preventive measures to decrease that risk, others have potential increase in penetrance with exercise (see **Section 7**). Studies are ongoing to determine clinical utility of genetic testing in all early-onset AF.

8. As some underlying etiologies of AF may carry risk of SCA,[506,507] exclusion of underlying cardiomyopathy, myocarditis, or electrolyte or thyroid abnormalities should be evaluated and managed prior to intensive sport participation, particularly in the young or young adult athlete.

9. For adult athletes with AF in whom episodes are frequent with rapid ventricular rates and causing severe symptoms, intensive sports participation should be discontinued until AF is managed effectively. For athletes without high suspicion of an underlying life-threatening etiology, and whose symptoms are not life-threatening, restriction while evaluation is undergoing is not indicated.

10. With AF that occurs during exercise that is asymptomatic to minimally symptomatic with controlled ventricular rates and without preexcitation, exercise may continue if tolerated. If symptoms are severe or worsen with exercise, AF conducts with rapid ventricular rate, or if there is preexcitation, then it is recommended to stop exercise until rate and/or rhythm is controlled. For tactical athletes such as military pilots, who are required to maintain physical fitness similar to that of athletes, governing bodies will determine participation, balancing potential risks with individualized approaches. In one small series of 27 active-duty pilots,[520] of whom 44% completed deployments flying low-performance aircraft, half of these were treated with ablation. Long-term follow-up is not described.

11. Patients with AF have better outcomes including decreased stroke and death when managed by specialists.[515] A recent study from a single center[514] has shown reduced readmission rates, as well as reduced initial length of stay and costs, when AF patients were managed as part of a dedicated AF center. Poor outcomes associated with variations in care are well documented.[521] Similarly, specialists in the care of athletes provide additional expertise.[7] Not all centers may have access to all specialists, and geographic and insurance considerations may not always allow consultations with individual/s with these expertise, but when possible, such consultations should be sought.

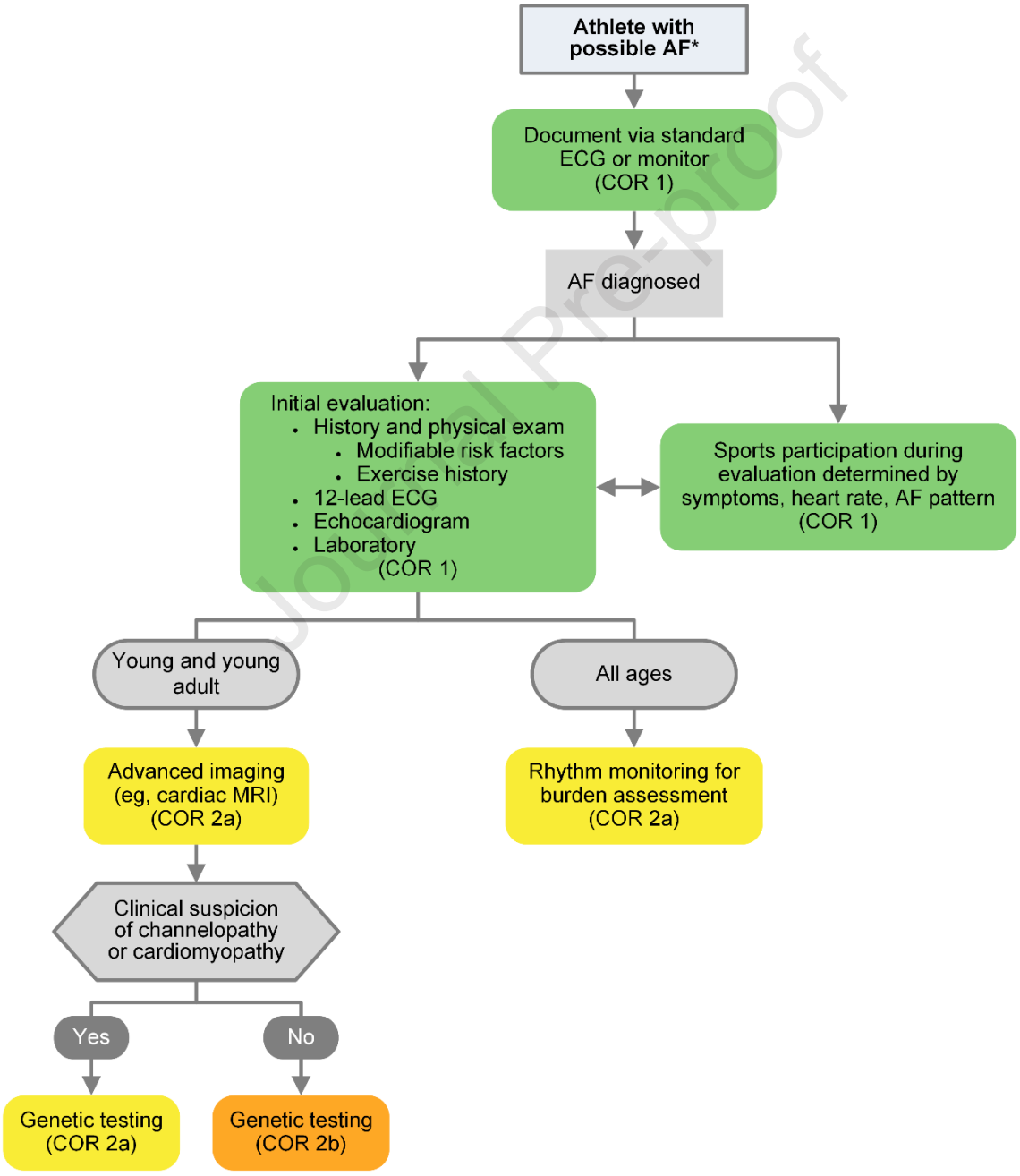

Figure 15
Algorithm for the evaluation of athletes suspected of having AF. Colors correspond to the class of recommendation (COR) in **Table 1**. *Based on symptoms or wearable device data. AF = atrial fibrillation; ECG = electrocardiogram; MRI = magnetic resonance imaging; SMD = shared decision-making;

8.3. Treatment of atrial fibrillation in athletes

8.3.1 Risk factor modification in athletes with atrial fibrillation

Recommendations for risk factor modification in athletes with atrial fibrillation		
COR	**LOE**	**Recommendations**
1	**B-R**	**1. In athletes with AF, risk factor management, including weight loss, treatment of obstructive sleep apnea, alcohol avoidance, and hypertension management is recommended.[522,523]**
2b	**C-LD**	**2. In athletes with AF who engage in long-term, high-intensity endurance training, exercise detraining with modification to low to moderate levels of exercise may be considered.[477,524-528]**

Synopsis

Management of AF in the athlete is largely based on extrapolation of clinical trial data from nonathletes, observational studies, and expert opinion. Standard risk factors should be discussed and modified, as in nonathletes. Data on detraining are sparse but may be effective in some and can be discussed as an option. An algorithm of the recommendations for treatment of AF in athletes including risk factor management, prevention of thromboembolism, and rhythm control in athletes with AF is shown in **Figure 15**.

Recommendation-specific supportive text

1. Modifiable risk factors that are commonly observed in the nonathlete population should not be overlooked in the athlete population. These include hypertension, obesity, obstructive sleep apnea, smoking, and use of alcohol and, for some individuals, caffeine.[522,523,529] These also include use of performance-enhancing drugs. While the association of performance-enhancing drugs with AF risk remains unclear,[321] anabolic steroids have been associated with atrial electrical mechanical delay in bodybuilders, and testosterone replacement in nonathletic populations is associated with an increase in AF.[516,530]

2. The association between volume of exercise and development of AF is well established as a U-shaped relationship based on observational data, particularly in middle-aged men, in which both low and high volumes of exercise, specifically endurance exercise, increases the risk of AF.[477,526-528] This relationship has not been demonstrated in nonendurance sports. The increased risk of AF with endurance exercise applies to a select group of athletes participating in high levels of endurance exercise, such as greater than 10 or more hours per week of high-intensity exercise.[491]

   While the association of long duration of vigorous endurance athletics with the development of AF is well established, whether decrease in exercise once AF develops will decrease AF

recurrence has not yet been demonstrated. Although studies are ongoing, there currently are no published randomized controlled data evaluating the impact of exercise detraining on AF burden in endurance athletes. Complete cessation of exercise may not be necessary given the protective benefits of moderate exercise on AF and the detrimental effects of exercise cessation on psychological mindset and quality of life.[525] Not all athletes may wish to pursue exercise cessation, but discussion of this option will inform shared decision-making.

8.3.2 Prevention of thromboembolism in athletes with atrial fibrillation

Recommendations for prevention of thromboembolism in athletes with atrial fibrillation		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. For athletes with nonvalvular AF, stroke risk assessment using a validated risk score, such as CHA_2DS_2-VASc, or other disease-specific factors is recommended.[531-533]**
1	**A**	**2. For athletes with nonvalvular AF with an estimated annual thromboembolic risk of ≥ 2% per year (CHA_2DS_2-VASc score of ≥ 2 in men or ≥ 3 in women, or other disease-specific factors), oral anticoagulation is recommended [534-538]**
1	**C-EO**	**3. In athletes with AF on anticoagulation who are participating in sports with a risk of trauma, a shared decision-making discussion about continued participation is recommended.**
2b	**B-NR**	**4. In athletes with AF, left atrial appendage occlusion (LAAO) may be considered based on anticoagulation indication and bleeding risk, taking into account patient preference to avoid long-term anticoagulation, in a shared decision-making context.[539,540]**
2b	**C-EO**	**5. In athletes meeting anticoagulation criteria who wish to temporarily participate in sports with a high risk of bleeding, temporarily withholding anticoagulation may be considered with a shared decision-making discussion.**

Synopsis

The risk of stroke is lower in athletes with AF than in nonathletes with AF, based on 2 observational cohort studies that have made similar observations regarding the risk of stroke in athletes with and without AF as compared with matched nonathlete populations.[476,478] The risk of stroke in athletes with AF was 27%-40% lower than in nonathletes with AF.[476,478] Whether these data can support differing anticoagulation regimens has not been tested. For athletes participating in collision sports and other sports with risk of bleeding, anticoagulation may increase risk, and shared decision-making about continued participation and form of stroke prevention is needed. An algorithm of the recommendations for treatment of AF in athletes including risk factor management, prevention of thromboembolism, and rhythm control in athletes with AF is shown in **Figure 15**.

Recommendation-specific supportive text

1. Similar to the approach in the nonathlete population, consideration of anticoagulant therapy should be based on risk of thromboembolism assessed by the CHA_2DS_2-VASc score (or other emerging scores, not yet equally validated in most populations), as available data suggest that athletes with risk factors remain at risk of stroke.[16,531-533] While some studies suggest athletes

are at lower risk than nonathletes with AF,[476,478,534] data are not sufficient to support different anticoagulation regimens. For athletes with AF in the setting of underlying specific disease entities, anticoagulation decisions should follow recommendations for that entity. For example, athletes with AF in the setting of HCM should receive anticoagulation regardless of CHA_2DS_2-VASc score.[10]

2. In those with elevated stroke risk, direct oral anticoagulation is preferred over warfarin based on large, randomized trials.[536-538] Although the CHA_2DS_2-VASc score has not been validated in the athletic population, stroke risk is still considered to be elevated in small studies even in those with low CHA_2DS_2-VASc score.[534] Furthermore, female sex is considered a risk modifier and age dependent; female sex is added to the score for age > 65 years or ≥ 2 non-sex-related stroke risk factors. Recommendations should not be influenced by whether AF pattern is paroxysmal, persistent, or permanent, although there remain insufficient data for anticoagulation for those with overall low burden or short episodes of AF, such as those with < 6 hours of AF.[541-543] As above, for those with AF in the setting of specific disease entities with distinct risk assessment, anticoagulation should follow those guidelines.

Targeting intermittent anticoagulation around an episode of AF, termed "pill-in-the-pocket" oral anticoagulation, has shown feasibility in pilot studies in those with a low risk of stroke and has been suggested as an alternative approach by some.[544,545] However, the small sample sizes were not powered to evaluate long-term stroke outcomes, and thus data do not support or refute this approach.[544,546] Therefore, pill-in-the-pocket strategy should be based on a shared decision-making process with consideration of overall stroke risk based on comorbidities and need for long-term AF monitoring, especially in those who are asymptomatic. As above, athletes with underlying disease-entities should follow disease-specific anticoagulation recommendations.

3. with AF at high risk of stroke on anticoagulation participating in contact sports (such as football, rugby, wrestling, martial arts, or boxing) and sports with low but potential risk of injury (such as bicycling or skiing) should counseled on the risk of major bleeding while on anticoagulation with continued participation. No data exist on withholding anticoagulation to allow participation in those at high risk of stroke, and in most cases, anticoagulation should not be withheld to allow participation. Data are also lacking on to what degree anticoagulation increases risk of serious bleeding in the setting of injury. A shared decision-making process considering patient preferences and values, overall stroke risk, and type of sport should guide the decision on sport and anticoagulation management.

4. Clinical trials have demonstrated that percutaneous LAAO provides stroke risk reduction similar to that of warfarin, although there remains an upfront procedural risk.[540,547] LAAO has not been studied in the athlete population. Given the potentially lower stroke risk based on a low CHA_2DS_2-VASc score, oral anticoagulation will remain the preferred strategy for stroke prevention in most athletes. In patients with an elevated stroke risk who are poor candidates for long-term anticoagulation, LAAO may be considered after documentation of shared decision-making.[548]

5. There are minimal data addressing the safety of brief periods of withholding anticoagulation. In one study of perioperative direct oral anticoagulation management, withholding anticoagulation 1-2 days prior to surgery was associated with an arterial thromboembolism rate of 0.16%-

0.6%.[549] Intermittent withholding of anticoagulation in athletes participating in contact/collision sports with risk of bleeding in the context of drug pharmacokinetics has been suggested in the setting of venous thromboembolic disease. However, data are not available to support the safety of this approach.[550]

8.3.3 Rate and rhythm control in athletes with atrial fibrillation

Recommendations for rate and rhythm control in athletes with atrial fibrillation		
COR	**LOE**	**Recommendations**
1	**A (QoL)** **B-NR (Exec. perf.)**	**1. For symptomatic athletes, maintenance of sinus rhythm is recommended to improve quality of life (A) and exercise performance (B-NR).[551-553]**
1	**B-R**	**2. In athletes with symptomatic AF, catheter ablation is recommended as first-line therapy, or if antiarrhythmic drugs are contraindicated or poorly tolerated.[552,554-562]**
1	**A**	**3. In athletes undergoing catheter ablation for AF, in whom typical atrial flutter has been previously documented or induced during an EP study, cavotricuspid isthmus ablation is recommended.[563-567]**
1	**C-EO**	**4. In athletes with AF and rapid ventricular rate, control of ventricular rate using a beta blocker or nondihydropyridine calcium channel blocker is recommended after consideration of impact on exercise performance and resting heart rate.**
1	**B-R**	**5. In athletes with symptomatic paroxysmal AF undergoing ablation without a documented arrhythmia trigger, a pulmonary vein isolation (PVI)-only approach is recommended.[568-570]**
2a	**A**	**6. In athletes with infrequent, symptomatic paroxysmal AF, antiarrhythmic drug therapy (with flecainide or propafenone with the addition of a beta blocker or nondihydropyridine calcium channel blocker) is reasonable as a "pill-in-the-pocket" approach if drug therapy is preferred.[571-573]**
2a	**B-NR**	**7. In young and young adult athletes with AF, an EP study is reasonable to evaluate an AP or predisposing arrhythmias such as atrial flutter or paroxysmal SVT, for ablation either as a stand-alone procedure or as part of a planned PVI.[512,574-576]**
2b	**C-LD**	**8. In athletes with AF, antiarrhythmic drug therapy with flecainide or propafenone with the addition of a beta blocker or nondihydropyridine calcium channel blocker may be considered as a daily medication if drug therapy is preferred.[571,577]**

3: Harm	**B-R**	**9. In athletes with AF, catheter ablation to restore sinus rhythm with the sole intent of eliminating the need for long-term anticoagulation should not be performed.[578,579]**

Synopsis

Rate and rhythm control strategies should be individualized based on a shared decision-making after discussion of symptoms and risks of medications and catheter ablation and consideration of the athlete's sport and preference. Detraining has limited data in its role in AF treatment and may be challenging to implement over extended periods of time in the athlete. Rhythm control is the preferred strategy in athletes with symptomatic AF. Given the superiority of catheter ablation as compared with antiarrhythmic drug therapy in reducing AF recurrence in the nonathlete population and the likely higher intolerance to medical therapy in the athletic population, as well as data showing equivalent efficacy in athletes, catheter ablation can be recommended as first-line therapy. An algorithm of the recommendations for treatment of AF in athletes including risk factor management, prevention of thromboembolism, and rhythm control in athletes with AF is shown in **Figure 16**.

Recommendation-specific supportive text

1. AF has been shown to negatively impact quality of life and exercise performance in the general population. Although no studies have specifically evaluated these outcomes in athletes, this remains particularly relevant to the athlete with AF. Rhythm control, primarily with catheter ablation, has shown to improve quality of life and exercise performance as evaluated by CPET in the nonathlete population.[551-553]

2. Clinical trial data have demonstrated the superiority of catheter ablation with PVI as compared with antiarrhythmic drug therapy in prevention of AF recurrence and improvement in quality of life with low risk of adverse events.[552-557] Several observational studies have shown no difference in AF recurrence after ablation in athletes as compared with nonathletes.[558-561] In one small series,[580] quality of life and training time increased after ablation. An early rhythm control strategy with ablation is useful as first-line therapy[581] or if the athlete does not tolerate antiarrhythmic drugs. The 2023 ACC/AHA/ACCP/HRS guideline on AF[16] describes that catheter ablation as a first-line therapy for all patients with AF who prefer this approach is useful (class I), and for athletes specifically, as reasonable (2a). Given that AF ablation is shown to be as effective in athletes as nonathletes, this writing committee has determined that catheter ablation is recommended in athletes.

   Based on consensus, intensive exercise should be restricted for at least 2 weeks post-procedure to avoid vascular complications at line insertion sites in the groin. Resumption of exercise should begin with moderate levels of activity and increased over the following weeks to regular intense activity, assuming no post-procedural complications or symptomatic AF recurrence. While post-ablation inflammation may increase the risk of AF for the 2-3 months after the procedure,[582] whether vigorous exercise during this period increases the short- or long-term risk of recurrence after ablation has not been evaluated.

3. Empiric cavotricuspid isthmus (CTI) ablation at the time of PVI has not been shown to improve freedom from long-term atrial arrhythmia recurrence,[563-565] and thus empiric CTI ablation without documentation of typical atrial flutter is not recommended.[567,583] However, if typical

atrial flutter has been documented or induced, CTI ablation is recommended, as atrial flutter may precede and induce AF. In those with only typical atrial flutter without AF, CTI ablation is recommended as first-line therapy.[564,584,585]

4. In athletes with rapid ventricular rate during AF, rate control is recommended with or without a rhythm control strategy. Beta blockers and nondihydropyridine calcium channel blockers may lead to fatigue or impact exercise performance,[354] although a low or moderate dose may be tolerated in some athletes. Importantly, beta blockers are prohibited by the World Anti-Doping Agency only in sports that rely on stability of the upper extremities, such as archery, golf, or shooting.[46]

5. Given the unclear benefit of empiric adjunctive lesions beyond PVI particularly in paroxysmal AF, such as left atrial linear ablation, posterior wall isolation, left atrial appendage isolation, superior vena cava isolation, or complex fractionated electrogram ablation, further empiric ablation does not provide benefit beyond PVI alone and should be avoided given the possible excess risk of the procedure.[569,570,586] In addition to procedural complications, extensive catheter ablation may result in stiff left atrial syndrome impacting exercise performance.[568,587]

6. In the absence of structural heart disease or coronary artery disease, class IC agents may be the preferred antiarrhythmic drugs in the athlete with AF due to minimal side effects and when used as the pill-in-the-pocket approach. Although serious adverse events are rare, initiation of pill-in-the-pocket strategy should be performed in a monitored setting.[572] Importantly, class IC agents should be coadministered with an AV nodal blocker. While data are lacking in athletes, based on the potential for proarrhythmias with class IC agents (see the supportive text for recommendation 8 below), the general absence of stress test to evaluate for QRS widening with exercise in pill-in-the-pocket users, and the drug pharmacokinetics, sport participation should be avoided for 48 hours to allow drug clearance, to minimize the risk of 1:1 atrial flutter and ventricular proarrhythmia.

7. Rapid atrial activation during an SVT may trigger AF particularly in young patients. Inducible SVT during an EP study, such as AV nodal reentrant tachycardia or AV reentrant tachycardia, has been observed in up to 39% of young patients with AF with ablation resulting in decreased AF recurrence.[512,574-576] The 2023 ACC/AHA/ACCP/HRS guideline on AF[16] states that in patients with early-onset AF, an EP study and targeted ablation of any SVTs found “may be reasonable” (2b). This writing group has determined that given the high prevalence of other supraventricular arrhythmias, and the high rate of arrhythmia-free success with a targeted ablation in the young and young adults, this approach is reasonable (2a) either as a stand-alone procedure or as part of planned PVI.

8. Like the general population, athletes who have frequent episodes of AF who prefer antiarrhythmic drug therapy will require daily medication as compared with a pill-in-the-pocket approach. In the absence of structural or coronary heart disease, flecainide or propafenone along with an AV nodal blocker may be considered an initial strategy, although these may be poorly tolerated due to the negative impact on exercise performance and should be used with care in athletes in light of their use-dependence and risks of proarrhythmia and development of atrial flutter with 1:1 conduction.[588,589] Exercise stress test should be performed after initiation of class IC agents to monitor for use-dependent QRS widening. If palpitations occur, activity

should be stopped and rhythm diagnosis made. Dronedarone is another option, although efficacy may be less.[590,591] Class III agents such as sotalol or dofetilide may be considered; however, these should be used with care in athletes at risk of dehydration due to transient renal failure leading to drug accumulation and proarrhythmic drug effects.[16] Sotalol may be poorly tolerated due to the beta blocker effect of decreased exercise performance. Disopyramide may be considered in athletes with vagal-mediated AF given the anticholinergic effect of the medication. Amiodarone should be considered as relatively contraindicated or used as last resort due to the significant toxicities.

9. AF catheter ablation to restore sinus rhythm should not be performed with the sole intent of eliminating the need for anticoagulation. The indication for anticoagulation should be based on the stroke risk assessment by the CHA_2DS_2-VASc score. There are currently no data supporting the use of a rhythm control strategy with catheter ablation to remove the need for anticoagulation.[583] As most studies have not shown ablation to reduce stroke risk, and given the increased stroke risk in those who discontinue anticoagulation after ablation,[578,579] current guidelines[16] recommend continuation of anticoagulation after ablation if CHA_2DS_2-VASc score is ≥ 2. A shared decision-making discussion based on competing risks of stroke along with consideration for long-term monitoring of AF is needed to guide anticoagulation strategies. A low threshold for anticoagulation continuation should remain in those at high risk of stroke.

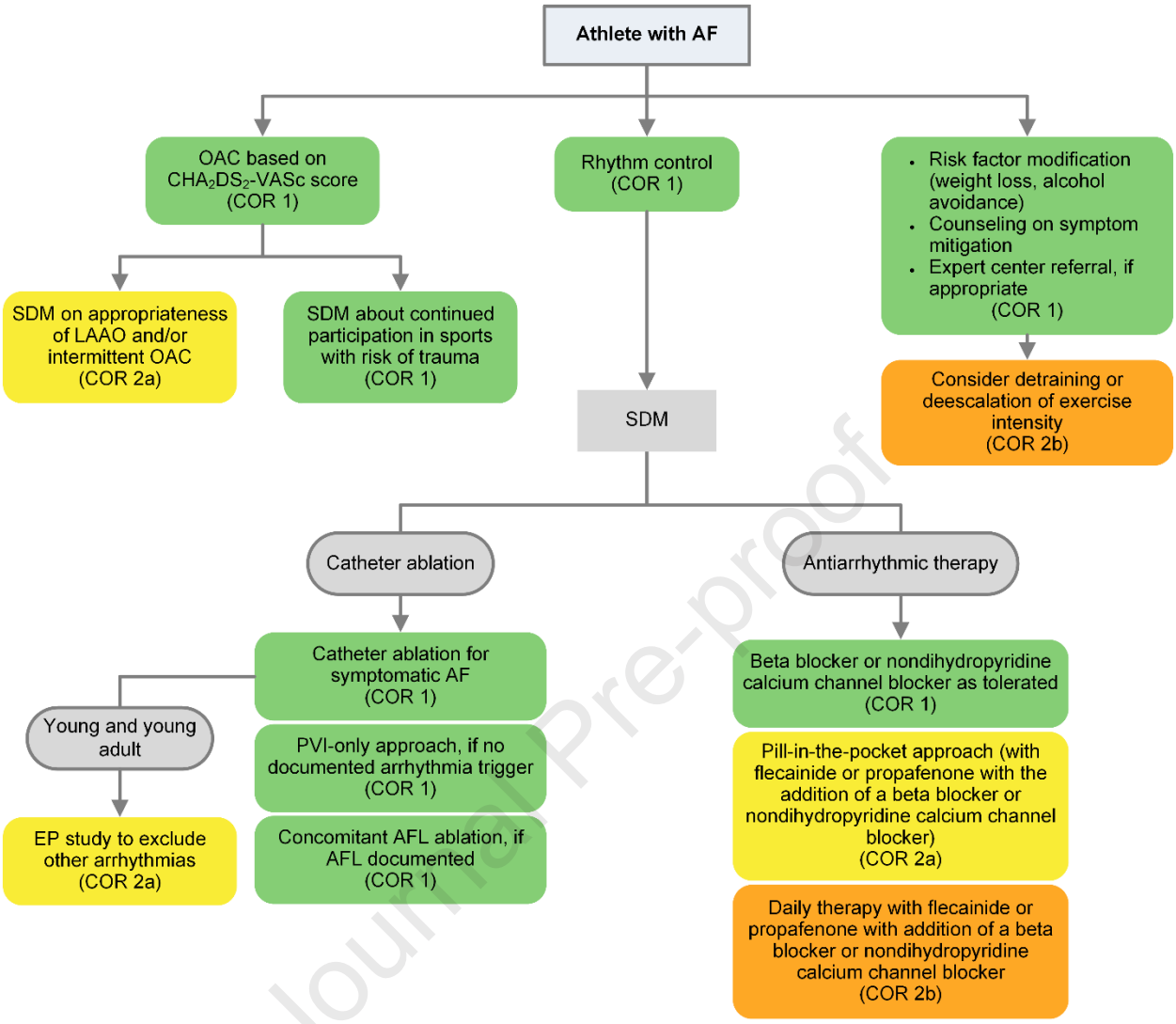

Figure 16
Algorithm for the evaluation and management of athletes suspected of having atrial fibrillation (AF). Colors correspond to the class of recommendation (COR) in **Table 1**. AF = atrial fibrillation; AFL = atrial flutter; ECG = electrocardiogram; EP = electrophysiology; LAAO = left atrial appendage occlusion; OAC = oral anticoagulation; MRI = magnetic resonance imaging; PVI = pulmonary vein isolation; SDM = shared decision-making.

Section 9 Wolff-Parkinson-White pattern and syndrome

The following terms are used to differentiate between WPW pattern and syndrome in this document:

- **WPW pattern:** The term "WPW pattern" refers to patients with preexcitation manifest on an ECG in the absence of symptoms.
- **WPW syndrome:** The term "WPW syndrome" refers to patients with both preexcitation manifest on an ECG and symptomatic arrhythmias involving the AP.

As described in **Section 2**, the use of ECG screening in preparticipation evaluation of athletes is controversial, with some professional societies in favor, and others less so. Regardless, the use of ECG screening is increasing, with one survey of NCAA team physicians describing use of ECG screening in 38%

of schools and in 50% of Division 1 programs.[592] Some regions in the United States and in other countries have mandated ECG screening for the preparticipation exam in high school sports. These ECGs detect potentially lethal conditions in 0.3% of athletes, with the most common finding, WPW pattern, representing almost half of the abnormalities found.[129] WPW syndrome accounts for 1% of SCD in the athletic population based on a long-term registry,[116] but the exact incidence is not known because the autopsy detail necessary to diagnose WPW syndrome as a cause of sudden death is difficult. It is likely that a proportion of sudden death secondary to WPW syndrome is attributed to "autopsy negative" SCD, which is recognized as a common etiology of SCD in contemporary studies in young and athletic individuals.[82,92,593] As described in detail below, incidence of WPW pattern, and death due to WPW syndrome, does not differ in athletes and nonathletes. However, as athletes represent the population of young, asymptomatic individuals most likely to undergo ECG and thus be found with WPW pattern, management of WPW pattern is uniquely relevant to this group.

9.1 Epidemiology and natural history

The prevalence of WPW pattern is 0.1%, as documented in the Copenhagen Baby Heart Study looking at ECGs for over 17,000 neonates.[594] It is usually an isolated abnormality in an otherwise normal heart in a healthy person. In a minority it occurs as part of structural, congenital, or genetic cardiac conditions, notably Ebstein malformation of the tricuspid valve, cardiac rhabdomyomas, and HCM often associated with glycogen storage and regulation disorders.[595-599]

Both epidemiological and EP study–based data have demonstrated that the incidence of life-threatening events (LTEs) is higher in individuals with a WPW pattern on ECG and symptoms (ie, WPW syndrome). The clinical presentation and natural history of individuals with the WPW pattern on ECG (ie, without symptoms) is highly variable and may differ with age, AP location, and AP conduction properties.[595,600-603] Most individuals with preexcitation (the WPW pattern) never experience an arrhythmia and are found to harbor the abnormality incidentally, for instance, on an ECG performed during preparticipation athletic screening. Rarely, patients with WPW syndrome present with a cardiomyopathy due to the dyssynchronous ventricular contraction associated with a preexcited sinus rhythm; this is most often seen in children.[604-606] Finally, syncope or aborted SCD may be the first manifestation of WPW syndrome.[596,607] Although most patients with WPW syndrome resuscitated from SCD have had prior symptoms, a cardiac arrest may be the sentinel event, particularly in children and adolescents.[607] The overall incidence of SCD in WPW syndrome is most often quoted as 1 event per 1000 person-years, but risk has been observed to be higher in children, with one meta-analysis reporting a rate of 1.93 events per 1000 person-years in asymptomatic children compared with 0.86 events per 1000 person-years in asymptomatic adults.[608] Of note, geographical differences have been cited in the reported risk of WPW syndrome–related SCD.[608] In Italian studies,[609-613] the risk is estimated at 2.16 per 1000 person-years, which is higher than the 0.36 per 1000 person-years (95% CI, 0.05–0.94) reported in non-Italian studies.[614]

Previous guidelines have advocated a more aggressive approach to the management of WPW pattern in competitive athletes and patients with high-risk occupations.[9,615] Theoretically, during exercise, fluctuations in autonomic tone and exercise-related adrenergic stimulation may increase vulnerability to atrioventricular reciprocating tachycardia (AVRT), which in turn may increase the risk of AVRT disorganizing to AF, or even preexcited AF independent of AVRT, culminating in VF and SCD. Studies have shown that exercise-induced adrenergic activation increases AP conduction.[616,617]

However, while WPW pattern may be found more commonly in athletes due to ECG screening in this population, epidemiological studies do not suggest that SCD from just having the WPW pattern is more common in the athlete versus the nonathlete, and training does not alter the conduction properties of the AP.[618] In a series of children with WPW syndrome who had experienced an LTE,[607] this event occurred most often at rest or with noncompetitive activity. Activities of daily life may also precipitate an arrhythmia, and therefore SCD is not limited to the athlete and LTEs are not limited to athletic activities.[607,619]

Given the lack of evidence showing a difference in the risk of WPW-related SCD in athletes versus nonathletes, while the recommendations in **Sections 9.1 and 9.2** refer to the athlete population, they may be considered for all patients with WPW pattern and a structurally normal heart, irrespective of athletic participation.

Based on data showing that the risks of pediatric patients and adults differ, with the incidence of LTEs in children with a WPW pattern being much higher than in adults, the strengths of recommendations in this section have been adjusted for individuals < 18 years (prepubertal and adolescent) and ≥ 18 years of age (young adult and adult).[4,608,614,620]

9.2 Evaluation of athletes with Wolff-Parkinson-White pattern or syndrome

Recommendations for the evaluation of athletes with Wolff-Parkinson-White pattern or syndrome		
COR	**LOE**	**Recommendations**
1	**C-LD**	**1. In athletes with a WPW pattern on ECG, cardiac evaluation including physical examination, family history, and echocardiography at diagnosis is recommended whether symptoms are present or absent.[595,621]**
1	**C-LD**	**2. In athletes with a WPW pattern and no symptoms, return to play during evaluation and pending treatment is recommended.[607]**
1	**C-EO**	**3. In athletes with a WPW pattern, regardless of symptoms, shared decision-making among patients, families, and their electrophysiologist is recommended regarding catheter ablation and/or EP studies, which includes a discussion of procedural risks, benefits, AP recurrences after ablation, and limitations of risk stratification tools.**
1	**C-LD**	**4. In athletes with a right anteroseptal WPW pattern on ECG, pharmacologic testing with intravenous adenosine and/or an EP study should be performed to rule out a fasciculoventricular pathway before attempting catheter ablation, as fasciculoventricular pathways do not participate in the AVRT circuit and are not associated with rapid antegrade conduction.[622,623]**
1	**C-LD**	**5. In athletes with a WPW pattern who either choose not to have an ablation or have an unsuccessful ablation, periodic cardiology follow-up is recommended regardless of symptoms.[624]**
1	**C-LD**	**6. In athletes with WPW pattern or syndrome who have had a catheter ablation, periodic cardiology follow-up is recommended for at least 1 year post-procedure to evaluate for AP recurrence.[625]**

Synopsis

The lifetime risk of mortality related to WPW pattern appears to be numerically low. However, the risk seems to be "front loaded" in the earlier decades of life,[4,607,608,620] and SCD can be the sentinel event in a child with WPW pattern. Several decades of research has shown that risk stratification in WPW pattern is imperfect. The greatest concern is the ability of the AP to conduct rapidly to the ventricles, which has been traditionally measured by noninvasive parameters such as persistent preexcitation or intermittent loss of preexcitation on ambulatory monitoring, serial ECGs, and exercise stress testing, and invasively with EP studies to assess the shortest and average intervals between preexcited beats during AF (shortest preexcited R-R interval [SPERRI]) and accessory pathway effective refractory period (APERP) (**Table 18**). Recent data have shown that the noninvasive and even invasive parameters previously thought to reassure the clinician that an AP had a "low" or "high" risk for rapid ventricular conduction may not accurately risk stratify all WPW pattern patients.[607,626,627] **Table 18** describes the evolution of recommendations for evaluation and treatment of WPW pattern in prior documents based on the evolving data as above.

Recommendation-specific supportive text

1. WPW has been associated with CHD, most commonly Ebstein malformation of the tricuspid valve and congenitally corrected transposition of the great arteries,[595] hypertrophic and infiltrative cardiomyopathy typically associated with *PRKAG2* gene variants,[598] cardiac rhabdomyomas,[599] tachycardia-induced cardiomyopathy, and dyssynchrony-related cardiomyopathy.[604] Thus, a complete evaluation and an echocardiogram are indicated in every patient with WPW pattern.

2. As above, in series of WPW patients experiencing LTEs,[607] these events occurred most often at rest or with noncompetitive activity.[607,619] Thus, there is no evidence that return to play during evaluation would increase risk.

3. Although the reported risk of SCD in WPW is numerically low, data suggest that the incidence of LTEs in children with asymptomatic WPW pattern may be much higher than in adults and is higher than in children without.[4,607,608,614,620] Given the limitations of current risk stratification strategies, it may be difficult to identify who is at risk for SCD. Therefore, the pediatric EP community has adopted a low threshold for offering catheter ablation as a treatment strategy to all children with a WPW pattern.[628] This may result in overtreatment of asymptomatic patients who are actually not at risk for SCD. Although ECG algorithms have improved over time,[629] localization of APs is imperfect, and the EP study can clarify both anatomic location and arrhythmia risk. Contemporary studies have shown high efficacy and low complications with catheter ablation,[624,630-634] and to date there have been no reported cases of permanent AV block with cryoablation of APs near the conduction system. However, no invasive procedure is without risk. In addition, studies have shown that 5%-12% of APs recur during follow-up.[624,630,631,634] The patient and family should be engaged in a shared decision-making process in which both conservative and more aggressive options are presented and discussed on a case-by-case basis.[202,635] Specifically, they should be informed of the small risk of life-threatening arrhythmias developing in the absence of treatment, along with the success rate and complications associated with catheter ablation of the AP as well as the infrequent risks associated with a stand-alone EP study.

4. Fasciculoventricular APs are rare variants of preexcitation. These pathways demonstrate minimum preexcitation on the ECG and are uncommon but may also be underrecognized. Fasciculoventricular ECGs may be misinterpreted as WPW pattern with right anteroseptal APs; therefore, it is important to differentiate the two entities. Typically, fasciculoventricular pathway ECG characteristics are (1) a shorter QRS duration (< 130 ms), (2) a not-so-short PR interval (110–120 ms), (3) a flat or negative delta wave in V1, (4) a narrow delta/R wave in V2, (5) S wave amplitude < 20 mm in V1, and (6) notching in the descending limb of the S wave in V1.[636,637] These pathways are completely infranodal structures, so there is no risk of rapid antegrade conduction during atrial tachyarrhythmias. However, fasciculoventricular pathways may be associated with other tachycardia circuits as a bystander, and recognizing their bystander role is crucial in order not to attempt unnecessary, and potentially harmful, ablation close to the His bundle region. This diagnosis during an EP study can be made by (1) multisite atrial pacing that results in no effect on the preexcitation degree in a fasciculoventricular pathway, (2) constant and positive HV interval with incremental and programmed atrial stimulation, (3) preexcited junctional beats, and 4) AV block or increase in PR interval without change in QRS morphology in response to intravenous adenosine.[622,623,638] Patients with a fasciculoventricular pathway associated with a *PRKAG2* variant have distinct clinical, ECG, echocardiographic, and electrophysiologic profiles and should be correctly identified because of their ominous long-term prognosis. Patients without a variant have an excellent arrhythmia-free prognosis.[639]

5. If after a shared decision-making discussion, the patient with WPW pattern and/or their family/caregiver elect not to proceed with an EP study and/or ablation, or if there is failure to eliminate the AP with ablation, routine cardiology follow-up is indicated to monitor for the development of symptoms.[624] Whether alternative treatment is needed after a failed ablation will depend on clinical and electrophysiological characteristics.

6. In patients with WPW pattern who have had a catheter ablation, periodic cardiology follow-up is recommended for at least 1 year after the ablation procedure to evaluate for AP recurrence. Follow-up is recommended for symptoms suggestive of SVT and to monitor the ECG for reappearance of WPW pattern.[624] Recurrence of anterograde and/or retrograde AP conduction after catheter ablation occurs in 5%-12% of cases.[624,630,631,634] Although this recurrence is more likely within the first 36 hours of the ablation procedure,[625] it can occur ≥ 1 year after the ablation procedure.

Table 18 WPW pattern on ECG: Differences in the class of recommendation between 4 previously published expert consensus statements and this 2024 expert consensus statement

Recommendation	2003 ACC* (adults)	2015 ACC† (adults)	2012 PACES‡	2019 ESC§	2020 ESC^	2024 HRS¶
Exercise stress test for risk stratification of asymptomatic patients with WPW pattern on ECG	n/a	1, B-NR	2a, B/C	2b, B	n/a	n/a
EP study for risk stratification in asymptomatic patients with WPW pattern on ECG	n/a	2a, B-NR	2a, B/C	1, B	1, B	1, B-NR

Catheter ablation in patients with WPW pattern on ECG with symptoms and /or arrhythmias	1, B	1, B-NR	n/a	1, B	1, C	1, B-NR
Catheter ablation in asymptomatic patients with WPW pattern on ECG and high-risk markers	2a, B	2a, B-NR	2a, B/C	1, B	n/a	1, B-NR
Catheter ablation in asymptomatic patients with WPW pattern on ECG without high-risk markers	2a, B	2a, B-NR	2b, C	2b, C	n/a	2a, C-LD
Catheter ablation in asymptomatic patients with WPW pattern on ECG and ventricular dysfunction secondary to LV dyssynchrony	n/a	n/a	2b, C	2b, C	n/a	1, C-LD

*2003 ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmia—executive summary[640]
†2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular arrhythmia[641]
‡2012 PACES/HRS expert consensus statement on the management of the asymptomatic young patient with a Wolff-Parkinson-White (WPW, ventricular preexcitation) electrocardiographic pattern[4]
§2019 ESC guidelines for the management of patients with supraventricular tachycardia[642]
^2020 ESC guidelines on sport cardiology and exercise in patients with cardiovascular disease[9]
¶2024 HRS expert consensus statement on the management of arrhythmias in the athlete: Evaluation, treatment, and return to play
ECG = electrocardiogram; EP = electrophysiology; LV = left ventricular; n/a = not applicable (there is no equivalent recommendation); WPW = Wolff-Parkinson-White.

9.3 Treatment of athletes with Wolff-Parkinson-White

Recommendations for the treatment of athletes with Wolff-Parkinson-White		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. In athletes with a WPW pattern on ECG and symptomatic or documented arrhythmias, catheter ablation of AP(s) is recommended to manage the symptoms caused by the arrhythmia and reduce the risk of LTEs.[600,611,625,630,631]**
1	**C-LD**	**2. In athletes with a WPW pattern on ECG and left ventricular dysfunction attributed to left ventricular dyssynchrony, catheter ablation of AP(s) is recommended to improve left ventricular remodeling and left ventricular function regardless of anterograde characteristics of the AP(s).[604,606,621]**
1	**B-NR**	**3. In young athletes (aged < 18 years) with a persistent WPW pattern on the ECG, an EP study is recommended to identify high-risk* AP(s) properties.[607,611,628]**
2a	**C-LD**	**4. In young athletes (aged < 18 years) with an intermittent WPW pattern on the ECG, an EP study is reasonable to identify high-risk* AP(s) properties.[627,628]**
2a	**B-NR**	**5. In young adult and adult athletes (aged ≥ 18 years) with a persistent WPW pattern on the ECG, an EP study is reasonable to identify high-risk* AP(s) properties.[611,613]**
2b	**B-NR**	**6. In young adult and adult athletes (aged ≥ 18 years) with an intermittent WPW pattern on the ECG, an EP study may be considered to identify high-risk* AP(s) properties.[611,613,643]**

1	B-NR	7. In athletes with a WPW pattern on ECG and ≥ 1 high-risk properties* present during the EP study, catheter ablation of AP(s) is recommended to prevent LTEs.[607,628,644]
2a	C-LD	8. In athletes with a WPW pattern on ECG and without high-risk properties* identified on EP testing, catheter ablation of AP(s) is reasonable.[628,645]
2a	C-LD	9. In athletes with a WPW pattern on ECG undergoing ablation, cryoablation is reasonable in those with anteroseptal and midseptal AP(s) to reduce the risk of permanent injury to the conduction system.[634,646-649]
3: Harm	C-LD	10. In athletes with a WPW pattern on ECG found to be due to fasciculoventricular pathway, catheter ablation should not be performed due to potential harm to the conduction system.[622,623]

*High-risk markers: spontaneous or inducible SVT, APERP ≤ 250 ms, SPERRI ≤ 250 ms, multiple APs.

Synopsis

Catheter ablation of an AP, when performed by an experienced operator, is associated with a high cure rate (>90%) and low risk (<1%) of major complications.[624,630-632,634,650,651] Significant complications associated with catheter ablation of APs include but are not limited to AV block, cardiac perforation, stroke, and coronary artery injury.[624,630-634] With the use of cryoablation, there are currently no reported cases of permanent AV node injury requiring a pacemaker.[647-649] In the last 15 years, catheter ablation of APs is routinely performed with zero or minimal fluoroscopy.[652,653] Given that both noninvasive and even invasive testing do not confer absolute certainty about risk, the threshold for catheter ablation in WPW as a strategy for preventing SCD is lower in children including those with a "low-risk" AP (**Figure 16**). AP recurrences occur despite accurate mapping and initially successful elimination of APs. Although the complication rate is low, an ablation procedure cannot be guaranteed to be without risk. Specific recommendations, even when supported by substantial data, do not replace the need for clinical judgment and patient-specific decision-making, which should involve shared decision-making among the patient, their family, and the electrophysiologist performing the procedure. An algorithm of the recommendations for the treatment of athletes with WPW is shown in **Figure 17**.

Recommendation-specific supportive text

1. Children and young adults with WPW syndrome typically present with arrhythmia symptoms, but the prevalence of documented SVT may be lower and is age related.[4,600] Both epidemiological and EP study–based data demonstrate that symptoms are a predictor of higher risk for LTEs. In the pivotal study by Klein et al,[596] VF during AF with rapid conduction over the AP occurred with a higher prevalence in patients with a prior history of documented arrhythmias (AVRT and/or AF compared with those who were asymptomatic and without documented arrhythmias). In a 5-year prospective study,[610] malignant presentation with rapid preexcited AF was reported in 7% and cardiac arrest in 1.4% of previously symptomatic patients with WPW syndrome, suggesting that a subset of symptomatic patients may eventually experience more catastrophic arrhythmic events, including syncope, hemodynamic collapse, and/or cardiac arrest. In a prospective study of 2169 patients,[611] VF occurred in 1.5% of 1001 patients with WPW syndrome who did not undergo catheter ablation, whereas no patients with a successful catheter ablation developed malignant arrhythmias over an 8-year follow-up period, making a

strong case for catheter ablation as a beneficial treatment to prevent AVRT and SCD in WPW syndrome. In accordance with prior scientific guidelines,[640-642,654] a class 1 indication for catheter ablation in patients with WPW syndrome remains unchanged in this document. Studies have established that AVRT triggering AF is an independent predictor of the risk for SCD in WPW syndrome.[596,609,610] The majority of initially symptomatic patients with WPW syndrome may remain asymptomatic after the first episode of AVRT or experience an SVT recurrence without SCD, but it is not possible to predict the natural history of each individual patient. In the current era, the established efficacy and safety of catheter ablation in permanently eliminating APs with a low risk of serious complications and ability to perform procedures with zero or minimum radiation exposure[630,631,633,634] justifies catheter ablation as the first-line therapy for reducing risk of SCD as well as AVRT in patients with WPW. While data are lacking, following ablation, a waiting period of 1-2 weeks to allow healing of incision sites is generally observed.

2. Ventricular preexcitation-associated cardiomyopathy is defined as left ventricular dysfunction in the absence of sustained tachyarrhythmias and is different from tachycardia-induced cardiomyopathy, as left ventricular dysfunction is attributed to chronic electromechanical dyssynchrony from alterations in cardiac contraction.[655] Preexcitation-induced cardiomyopathy occurs predominantly in the setting of right-sided pathways.[621] Abnormal early activation of the right ventricle from right-sided pathways leads to late activation of the interventricular septum and left ventricular myocardium.[656] Although the "typical" age of presentation is unknown, preexcitation-induced dysfunction can occur in infancy,[657] may be severe enough to necessitate mechanical support,[658] and affects those with intermittent as well as persistent preexcitation.[659] In children this usually responds favorably to loss of preexcitation by spontaneous resolution or catheter ablation, which allows for mechanical resynchronization, reverse remodeling, and improvements in ventricular function.[606]

3. Increasingly, children (aged < 18 years) with WPW pattern are identified when preexcitation is incidentally detected on ECG performed for sports screening, medication administration, or other noncardiac reasons. The lifetime risk of SCD in those with WPW pattern is low, yet it is "front loaded" in the young.[660] A meta-analysis[608] evaluating sudden death among patients with an asymptomatic WPW pattern identified an LTE rate of 1.93 per 1000 person-years in children and 0.85 per 1000 patient-years (< 0.1% per year) in adults. In the prospective WPW registry study,[611] among the 15 patients who had VF over the 8-year follow-up period, 13 (86%) were children (median age 11 years). Determining which patients with a WPW pattern are at highest risk for LTEs by history alone remains a challenge. Very young children are less reliable communicators of symptoms than adults. Even older children may not report or recognize symptoms and can have symptoms that are not typical of an arrhythmia.[612] Present data confirm that asymptomatic WPW pattern is not without risk, and malignant arrhythmias correlate better with EP study–derived risk stratification than the presence or absence of symptoms.[607,610] In a contemporary study of pediatric WPW syndrome,[607] the LTE was the sentinel symptom in 65%. Given the potential for a more malignant course of WPW in children irrespective of symptoms, benefit of directly proceeding to an EP study regardless of the outcome of noninvasive testing likely outweighs the risk. This is a change that has occurred since the published recommendations from the 2012 consensus document[4] based on contemporary data.[607,608,626,627,661] Data affirm that SPERRI < 250 ms, anterograde APERP ≤ 240 ms, and the

presence of multiple AP and Ebstein malformation of the tricuspid valve are useful markers of high-risk APs[607,610,612] but remain imperfect predictors, and young patients may experience LTEs from WPW syndrome without prior symptoms or markers of high risk on EP study.

4. It has been postulated that patients with intermittent preexcitation generally have poor antegrade conduction characteristics and therefore a lower risk of SCD.[4] However, there are no large studies regarding intermittently conducting APs with regard to long-term risk of developing VF. There are recent reports of intermittent preexcitation in patients with fast anterograde AP conduction during an EP study and also presentation with an LTE.[662-666] Orczykowski et al[667] investigated 1007 patients with APs and reported that 7% of the 56 patients who experienced SCA had intermittent preexcitation on resting ECG. Other studies[643,664,665] found that APs with intermittent conduction were capable of very fast anterograde conduction, especially when tested during isoproterenol infusion at an EP study. It is possible that fast anterograde conduction observed in cases of intermittent preexcitation mostly reflects the high catecholamine sensitivity of some APs. Aside from catecholamine sensitivity, repetitive retrograde penetration of the AP (linking) can contribute to the presence of intermittent preexcitation despite short AP anterograde refractory period, and this mechanism might act synergistically with catecholamine sensitivity.[668] Therefore, in patients with intermittent WPW pattern on the ECG, an EP study with isoproterenol is reasonable to identify high-risk APs properties.

5. As outlined above, the prognosis and risk of the WPW pattern is lower in adults compared with children, which is presumably driven by survival bias with a lower residual risk. Moderate-quality data support a differential risk, with the greatest risk in symptomatic patients with persistent WPW pattern, followed by asymptomatic WPW pattern, followed by intermittent preexcitation.[596,614,643] The lifetime risk of sudden death in WPW is low, emphasizing the importance of shared decision-making given the competing risks of undergoing diagnostic EP studies, that frequently lead to ablation, compared to the natural history rate of approximate 0.86 events per 1000 person-years.[608] Age plays a role in risk and shared decision-making, with male sex, previous syncope, and age < 30 years representing risk factors for adverse outcomes.[596,607,669-671] If an EP study is pursued, consideration should be given to the fact that EP study–derived risk stratification is imperfect, and a low threshold for ablation should be considered.

6. As outlined above, clear evidence of abrupt loss of preexcitation with exercise stress testing or during ambulatory monitoring predicts a longer AP refractory period and a longer SPERRI.[661] This associates with lower risk of rapidly conducted AF and associated degeneration to VF. The residual risk is undoubtedly very low but not zero, based largely on case reports and more robust data in pediatric series.[626,627,664] Though generally a reason to convey low risk and not proceed with an EP study and ablation, shared decision-making is important, and proceeding with invasive risk stratification and possible ablation is reasonable.

7. For patients with a WPW pattern on ECG, high-risk APs are associated with younger age, the presence of multiple APs, CHD, SPERRI ≤ 250 ms, anterograde APERP ≤ 240 ms, or AVRT precipitating preexcited AF or atrial flutter.[4,596,610,641,644,654,672] Based on the seminal study by Klein et al,[596] SPERRI ≤ 250 ms during an EP study has become the “gold standard” for invasive

risk assessment in patients with a WPW pattern on the ECG. Studies have shown SPERRI ≤ 250 ms to be more sensitive at detecting high-risk AP than the antegrade AP effective refractory period in children and adults.[596,673] Bromberg et al[669] evaluated symptomatic children with WPW ≤18 years of age and found that all patients with clinical VF in whom AF was inducible at EP study had a SPERRI ≤ 220 ms (sensitivity 100%) and concluded that SPERRI ≤ 220 ms was more sensitive than clinical history for identifying those at risk for SCD. The sensitivity of SPERRI in AF is 88%–100% for identifying adult patients with WPW at risk for VF, but because of the low incidence of cardiac arrest in these patients, the positive predictive value of a SPERRI in adults is low.[596,608,674] The negative predictive value of the SPERRI ≥ 250 ms is well established.[608,675] Studies have shown that catheter ablation of APs markedly reduces the frequency of arrhythmic events and may prevent SCD in patients with ≥ 1 high-risk markers.[610,612,644] It is important to note that the use of isoproterenol markedly increases the prevalence of positive assignment of patients to a high-risk category.[611,673,676,677] Conversely, the effects of anesthetic agents may have similar capacity to affect the AP properties that are used to determine indications for catheter ablation.[607,645] It appears logical that sympathetic stimulation in a patient with AF and manifest preexcitation may enhance AP conduction to become more rapid and degenerate to VF and enhance AV nodal and retrograde AP conduction rendering baseline noninducible AVRT to become inducible. Isoproterenol use in the EP laboratory may therefore be considered a means to counterbalance the effects of sedation and anesthesia, but to what extent it represents physiologic stress or exertion is unknown.[673,674,678]

8. Studies have shown that while the direct measurement of AP characteristics are a better measure of risk than symptoms or noninvasive testing, these measures are imperfect, especially in children.[607,645] In a large international multicenter case-control registry study of 912 children,[607] although survivors of an LTE had significantly shorter APERP, SPERRI, and shortest preexcited paced cycle length (SPPCL) values than WPW syndrome controls without LTEs, over one-third had a SPERRI ≥ 250 ms and would have been classified as low risk even though they had experienced a high-risk clinical event. One explanation for this may be that most pediatric EP studies are performed under general anesthesia, which may hinder the ability to measure pathway conduction accurately.[645] Considering the concerns with accurate invasive risk stratification, the majority of pediatric electrophysiologists surveyed ablate most APs, even in patients with asymptomatic WPW pattern, regardless of risk assessment measures. An exception to this may be the low-risk septal pathways, where risk of heart block is low but not zero, potentially modifying the risk-benefit ratio.[628]

9. Radiofrequency ablation in the septal arrhythmia substrates has low but irreversible risk of AV block leading to permanent pacemaker implantation. However, with the advent of transcatheter cryoablation, anteroseptal and midseptal APs can be ablated without permanent damage to the conduction system. Currently, there are no reports in the literature of high-grade AV requiring a permanent pacemaker after cryoablation of an AP. Several studies have previously reported a lower acute success rate and a higher recurrence rate with cryoablation of septal APs when compared with radiofrequency ablation.[646] The higher recurrence rate may be attributed to the limitations in achieving effective lesions associated with the tip size of the cryoablation catheter as well as defining the cryothermal application time and temperature profile[647,648] for successful AP elimination. With over 15 years of worldwide experience in cryoablation of arrhythmias in

children, techniques continue to be refined so that the success rate of cryoablation of anteroseptal and midseptal pathways is comparable to radiofrequency ablation (85%-95% success rate, 12%-18% recurrence rate)[647,648] and the safety profile significantly superior to radiofrequency ablation.[631,634,679,680]

10. Fasciculoventricular APs arise from the His bundle and the fascicles and usually connect to the right ventricle, in which case the ECG features mimic a right anteroseptal AP. They have only anterograde conduction with decremental properties and are not substrates for reentrant tachycardia or sudden death and should not be ablated. If SVT is present, it is important to recognize that the fasciculoventricular pathway is a bystander and not integral to the SVT circuit. The diagnosis is critical to avoid unnecessary and potentially harmful ablation to the AV node and His bundle region.[637,638]

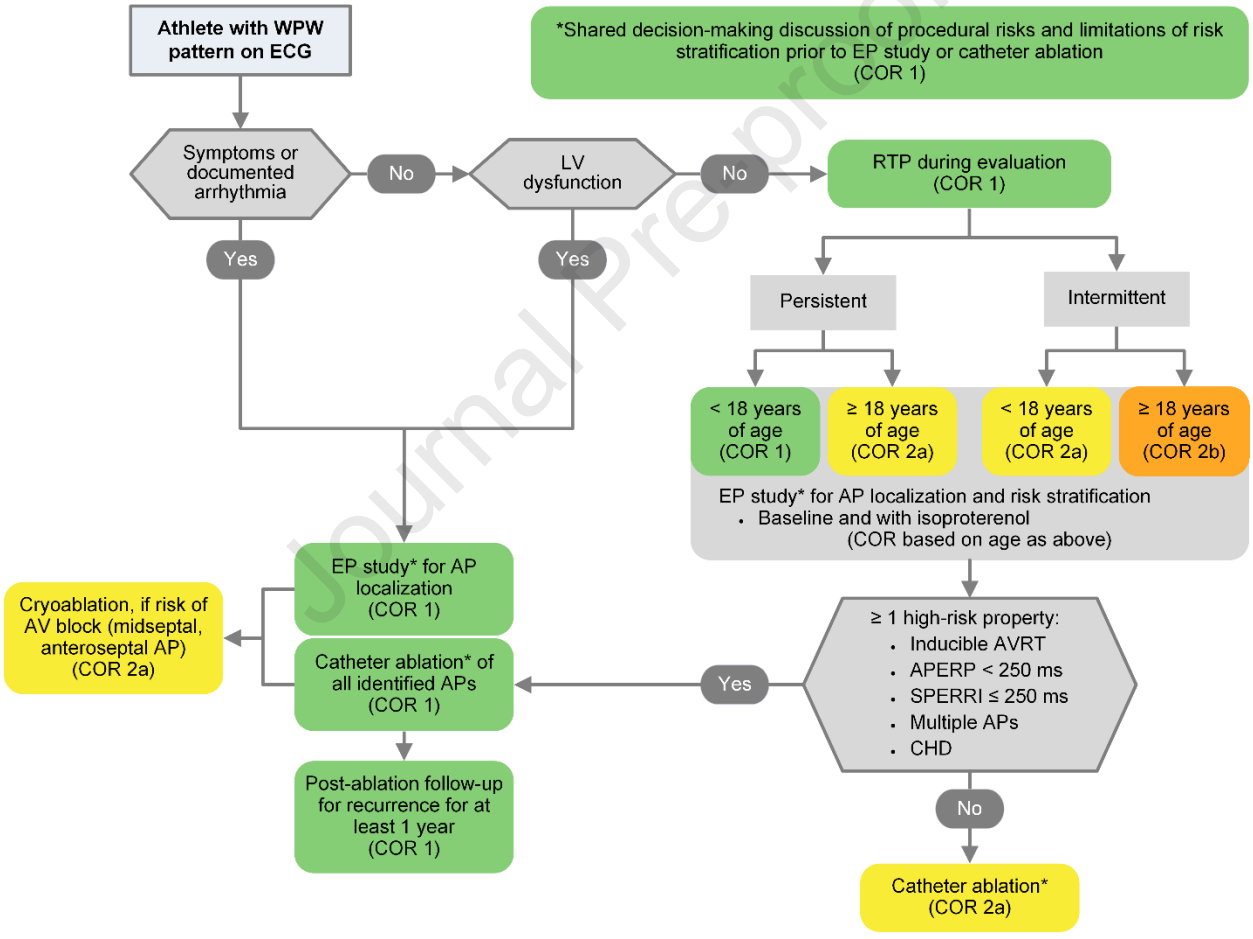

Figure 17
Algorithm for the treatment of Wolff-Parkinson-White (WPW) pattern in athletes. Colors correspond to the class of recommendation (COR) in **Table 1**. AP = accessory pathway; APERP = accessory pathway effective refractory period; AV = atrioventricular; AVRT = atrioventricular reciprocating tachycardia; CHD = congenital heart disease; ECG = electrocardiogram; EP = electrophysiology; LV = left ventricular; SPERRI = shortest preexcited R-R interval.

Section 10 Bradycardia and pacemakers

10.1 Athletes with bradycardia

Sinus and AV nodal slowing are expected adaptations to athletic training, particularly in high vagal states such as sleep or at rest. These changes are dose dependent, with one study showing a significant difference in sinus bradycardia (< 3 hours/week vs 3-6 hours/week) and first-degree AV-block (< 3 hours/week vs > 10 hours/week) based on current sport exposure and, similarly, a significant difference in sinus bradycardia (0-1000 hours vs 2001-3000 hours) and first-degree AV-block (0-1000 hours vs > 4000 hours) in lifetime sport exposure.[681] These adaptations are likely due to both changes in autonomic balance and ion-channel effects on the sinus and AV nodes.[682,683]

Recommendations for athletes with bradycardia		
COR	**LOE**	**Recommendations**
1	**B-NR**	**1. For athletes with significant distal conduction disease, including left bundle branch block, bifascicular block, or complete heart block at any level, evaluation prior to return to play is recommended.[684,685]**
2a	**C-EO**	**2. In athletes with significant sinus and/or AV node disease that does not correct with light exercise, further evaluation during return to play is reasonable.**
3: No benefit	**B-NR**	**3. In athletes with asymptomatic sinus node slowing or first-degree heart block/second-degree Mobitz type I AV block (Wenckebach) at rest, further evaluation is not recommended because these are expected adaptations to training.[686-688]**

Synopsis

More profound bradycardias should first be evaluated with response to light exercise, and, if they persist, with ambulatory monitoring and/or exercise stress testing. If they remain persistent, further testing to exclude the possibility of cardiomyopathy may be indicated. Mild distal abnormalities including isolated right bundle branch block or left anterior fascicular block can be seen in athletes, but more significant distal disease, or heart block at any level, requires further evaluation. Findings should be correlated with history to ensure that the patient is asymptomatic and that there is no family history of cardiomyopathy or conduction system disease. Cardioneuroablation, first described as a means of targeting ganglionated plexi for vasovagal syncope, has gained recent interest as a treatment for hypervagotonic sinus node dysfunction.[689,690] However, much more study is needed to understand this procedure's role in the treatment of symptomatic bradycardia.

Recommendation-specific supportive text

1. Mild distal abnormalities including left anterior fascicular block and right bundle branch block in isolation (eg, no symptoms or underlying structural heart disease) can be seen in athletes.[6,691] More significant distal abnormalities including left bundle branch block (present in < 1:1000 athletes), bifascicular block, or Mobitz II second-degree AV block or complete heart block often reflect underlying myocardial and/or electrical pathology.[684,685] These include cardiomyopathies, infiltrative disease such as sarcoidosis, amyloidosis, or Chagas disease, or channelopathies including LQTS with functional 2:1 AV block. Congenital complete heart block can be due to genetic heart disease including genes coding for transcription factors such as TBX, NKX2.5, and

GATA4,[692,693] and family history should include presence of AV block or pacemakers in other family members. Evaluation includes imaging, cardiac monitoring, and exercise stress testing.

2. Profound sinus bradycardia (heart rates < 30 bpm while awake) or AV nodal slowing with PR interval > 400 ms that does not correct with light exercise may require evaluation with ambulatory monitoring and/or stress test. If it remains persistent, the abnormality can reflect underlying pathology including myocardial or electrical disease (including Lyme), and evaluation with imaging and cardiac monitoring are reasonable. Clinical sick sinus syndrome has been reported as more common in adult current and prior competitive endurance skiiers[527] and cyclists,[694] in dose-dependent fashion based on numbers of races and finishing times.

3. Bradycardias are an expected adaptation to intense exercise, due to changes in sympathovagal balance[682,683] and to modulation of ion channels in the SN.[682,683] Thus, sinus bradycardia, nonsinus atrial rhythms, junctional isorhythmic or escape rhythms, first-degree AV block, and second-degree AV block type 1 (Wenckebach) are all expected findings in a trained athlete. These findings are most evident during sleep and can also be seen at rest.

10.2 Athletes with a pacemaker

Recommendations for athletes with a pacemaker		
COR	**LOE**	**Recommendations**
1	**C-LD**	**1. In athletes with a pacemaker and without exercise-limiting underlying conditions, return to play is recommended.[192,193,207,393]**
2b	**C-EO**	**2. For athletes who are completely pacemaker-dependent, collision sports may be considered after a shared decision-making discussion of the potential risks and the absence of data on safety.**
1	**C-LD**	**3. For athletes undergoing permanent pacemaker implantation, consideration for cardiac physiological pacing to reduce symptoms from right ventricular pacing and the risk of pacing-induced cardiomyopathy should be based on characteristics including ejection fraction, pacing burden, and QRS morphology.[695-702]**
2a	**C-EO**	**4. For athletes undergoing pacemaker implantation who will be returning to play, a waiting period of 4-6 weeks after a new transvenous implant, or 2 weeks after leadless implant or generator replacement, is reasonable.**
1	**C-LD**	**5. For athletes with a pacemaker and AV block, programming rate-adaptive AV delay and post-ventricular atrial refractory period shortening should be performed to prevent pacemaker Wenckebach or 2:1 conduction at high sinus rates.[703]**
1	**B-NR**	**6. For athletes with a pacemaker and sinus node dysfunction, programming should be optimized to avoid right ventricular pacing.[704,705]**
1	**C-EO**	**7. For a young or young adult athlete undergoing pacemaker implant, it should be confirmed that the device programming options allow age-appropriate heart rates.**

1	**C-LD**	**8. For athletes with sinus node dysfunction and a permanent pacemaker, an exercise stress test with the appropriate modality based on the type of sport and the environment in which symptoms are elicited should be performed for programming of rate-response and other exercise-related parameters.[706]**

Synopsis

For athletes who have received a pacemaker, return to play should be based on the presence of other exercise-limiting conditions. For a pacemaker-dependent athlete who wishes to return to collision sports, data on safety are lacking. Cardiac physiologic pacing (CPP), which includes cardiac resynchronization therapy (CRT), His bundle pacing, and left bundle branch area pacing, may be particularly important for athletes and should be the chosen mode as indicated for the general population. Choice of device and programming to maximize heart rate as needed for sport performance should address rate-responsive parameters, and these should be maximized using exercise stress testing, along with selecting ventricular pacing avoidance algorithms to minimize ventricular pacing burden. **Figure 18** is a summary of the recommendations for athletes with permanent pacemakers. The role for a leadless pacemaker is not yet well defined. Lead issues are obviated with this device, but neither the ability to perform adequate pacing to meet the needs of an athlete nor lifelong management for a young person with this device has been demonstrated.[707,708] For those with heart block, maintaining 1:1 AV synchrony is critical to maintain heart rate and cardiac output. Reports of currently available dual-chamber leadless pacemakers do not describe complete AV synchrony.[709,710]

Recommendation-specific supportive text

1. There are no prospective studies of athletes with permanent pacemakers. Data can be extrapolated from studies of sports participation for athletes with ICDs, which have not shown levels of lead malfunction higher than that in unselected populations.[192,193,207,393] The decision should be made in shared-decision-making fashion, taking into account underlying diagnosis and physiology.

2. While studies of athletes with ICDs have not shown higher-than-expected levels of lead malfunction, few athletes participated in collision sports. Lead malfunction rates in collision sports are not known.[192,193,207,393] Trauma-induced lead fracture and pacemaker failure are rare events and have been reported with blunt trauma to the chest, weightlifting, hyperextension injuries to the lead-bearing upper extremity, clavicular crush, clavicular fractures, and sudden deceleration, suggesting that similar sports-related injuries may result in lead and pacemaker malfunction.[711-719]

3. Although no studies have specifically assessed right ventricular pacing versus CPP in athletes who require a pacemaker, the importance of minimizing pacing to prevent pacing-induced cardiomyopathy is well established in the general pacing population.[17,695,697,698,700,701,720] A recent meta-analysis showed that His bundle pacing and biventricular pacing, compared with right ventricular pacing, were superior to right ventricular pacing in patients with normal or mildly reduced left ventricular function in terms of heart failure and all cause death.[696] Multiple small studies also showed that the various CPP approaches can preserve left ventricular function in those who need significant pacing.[17,696,699]

The benefit of CPP (CRT, His, or left bundle branch area pacing) has so far been mainly studied in CRT candidates with ejection fraction ≤ 35%.[721-724] The Biventricular Versus Right Ventricular Pacing in Heart Failure Patients With Atrioventricular Block (BLOCK HF) trial[724] was one of the few studies with patients with reduced left ventricular function (≤ 50%) and expected high amount of ventricular pacing. This study showed that those randomized to CRT had improved outcomes. More recently, left bundle branch area pacing has been shown to reduce QRS duration and improve ventricular function, which might preserve ventricular function or improve those with mild dysfunction.[702]

While there are no athlete-specific data, maintaining cardiac output is likely to be of importance to maximize exercise performance. In the absence of data specific to athletes, the management of athletes requiring pacing, including those who are expected to have < 40% pacing burden, should adhere to the latest pacing guidelines as appropriate.[17]

4. Avoidance of reaching or lifting for 4-6 weeks after implantation of transvenous leads has been traditionally recommended to avoid lead dislodgment before lead endothelization is complete. Several small studies of resistive range-of-motion exercise[211] and early removal of arm restriction[212,213] have not shown arm/shoulder movement to increase dislodgment or other complications, and an ongoing randomized trial of lenient versus strict arm restriction after device implant is ongoing.[214] However, at this time, as randomized data are not available, and the published small studies did not investigate vigorous exercise/arm motion in athletes, continuation of the traditional advisory is recommended. Two weeks should be allowed for healing of the skin incision.

5. At sinus rates beyond the maximum tracking rate, standard upper rate behavior leads to pacemaker Wenckebach and 2:1 conduction, which decreases maximal cardiorespiratory performance in the young, when it occurs.[703] Rate-adaptive AV delay and post-ventricular atrial refractory period shortening prevent this undesirable upper rate behavior.[725] These issues can be corrected in athletes by the programming of these parameters guided by exercise stress testing.[726]

6. Deleterious effects of right ventricular pacing include adverse remodeling, increased heart failure, and AF.[727,728] Programming of algorithms designed to decrease the frequency of right ventricular pacing have been shown to decrease incidence of heart failure and AF.[704,705] Particularly if physiological pacing is not employed, these algorithms should be utilized.[729] Data on these programming options are not available in athletes. However, it is likely that the findings would be similar.

7. Pacemakers vary in available programmable options. For an athlete to achieve maximal performance, maximizing cardiac output requires that heart rate needs to reach age-predicted maximum, with appropriate AV synchrony. To achieve this, for the young/young adult athlete with sinus node dysfunction, the maximum sensor rate programable must exceed age-predicted maximum heart rate. For the athlete with AV block, refractory periods and rate-adaptive AV delay must allow 1:1 conduction at age-predicted maximum heart rate.

8. Chronotropic incompetence may be the result of natural aging, medications for treatment of tachyarrhythmias or other heart disease, or congenital anomalies or surgery to repair these

defects. All current pacemakers include sensors to detect a signal indicating the need for a faster heart rate to meet metabolic demand. Sensors can be based on parameters resulting from exercise (tertiary sensors) such as accelerometers, the least physiological type. Secondary sensors detect metabolic demand, such as minute ventilation. Primary sensors detect parameters underlying cardiac function with exercise, such as closed-loop stimulation. Sensed stimuli can be mechanical (accelerometer or piezoelectric) or intrathoracic impedance-based (for minute ventilation). Other sensors in the lead itself measure intracardiac impedance reflecting contractility. Advantages and disadvantages of these systems have been outlined,[730,731] but few data have addressed the relative efficacy in the general population and there are no data in athletes. For athletes, there are hypothesized pros and cons of each type of sensor. Accelerometers underestimate the degree of activity in many activities, particularly those in which the shoulder has little movement such as biking. Minute ventilation is proportional to effort, but onset is delayed. Blended sensors may be better in the general population.[732] Closed-loop systems have theoretical advantages but have not been tested in chronotropic incompetence or in athletes.[733] Given the absence of data in athletes, it is not currently possible to make athlete-specific recommendations regarding choice of sensor. However, regardless of sensor choice, programming should be individualized. While data in athletes are not available, in the general population, one randomized study has shown that use of exercise stress testing to program rate-response settings individually improved maximal heart and exercise capacity.[706] Patients with a pacemaker who report decreased endurance, exercise stress testing, and particularly CPET may help clarify both the components of those symptoms and their overall aerobic capacity. Principles for exercise stress testing in athletes appears in detail in **Section 2**.

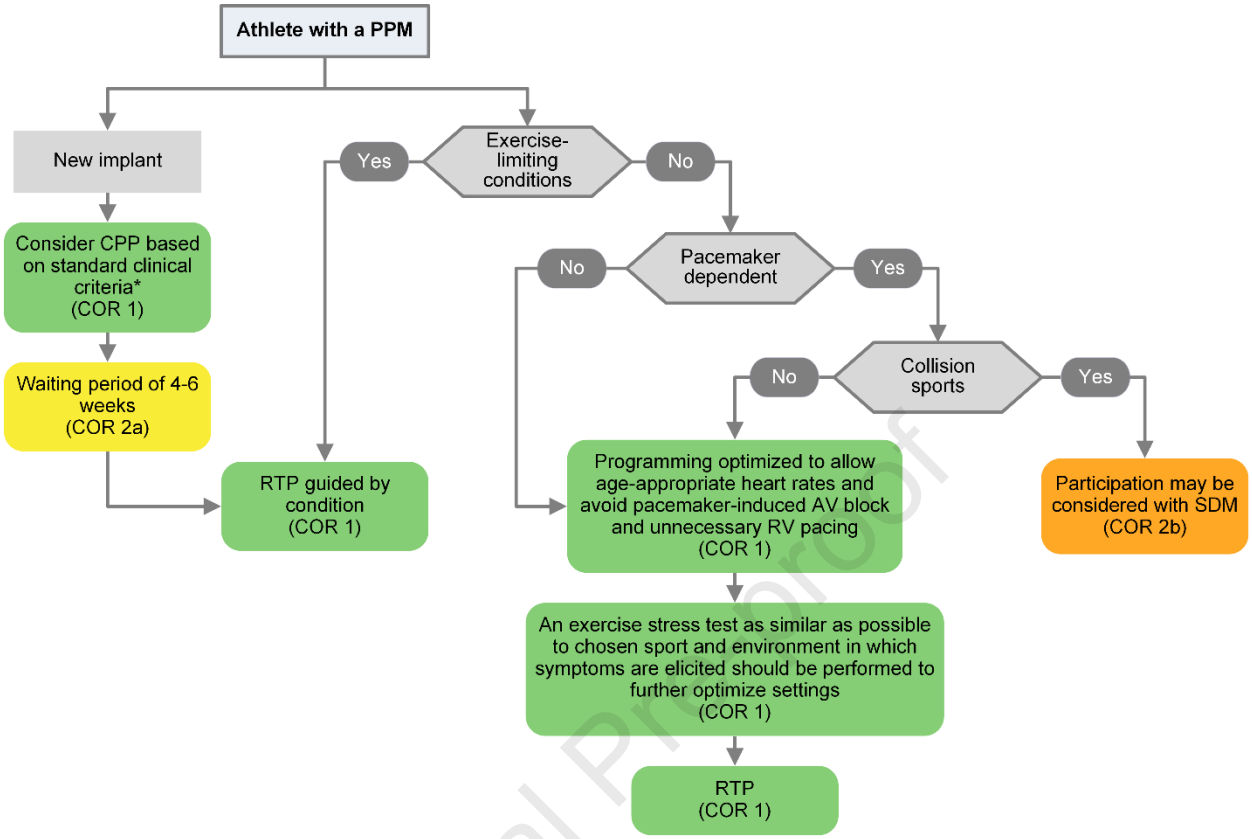

Figure 18
Algorithm for return to play in athletes with permanent pacemakers. Colors correspond to the class of recommendation (COR) in **Table 1**. **See 2023 HRS/APHRS/LAHRS guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure.*[17] AV = atrioventricular; CPP = cardiac physiological pacing; PPM = permanent pacemaker; RTP = return to play; RV = right ventricular; SDM = shared decision-making.

Section 11 Gaps and future directions

The care of an athlete with arrhythmia integrates multiple aspects of cardiology and sports medicine and should incorporate relevant considerations regarding impacts of type and sport and intensity of exercise. The writing committee in this first Arrhythmias in the Athlete document has made recommendations based on data in the athlete when available, data in nonathletes where relevant, and expert consensus, unanimous or nearly for all recommendations, in areas where guidance is clearly needed but data are lacking. Identified gaps and important avenues for future research to further inform shared decision-making around management of arrhythmias in the athlete are listed in **Table 19**.

Table 19 Identified gaps and needs for future studies

Knowledge gap	Future needs and directions
Impact of race and ethnicity on arrhythmias in the athlete	Recognizing populations at risk, but also recognizing the dangers of categorizing findings based on race (such as the "Black athlete ECG"), is critical to providing care to all athletes equitably.

Knowledge gap	Future needs and directions
Women athletes	The majority of studies of athletes with arrhythmias have analyzed primarily male athletes. Improved inclusion and access for women in studies is needed.
Role of performance-enhancing drugs	More data are needed on the role of performance-enhancing drugs in exacerbating arrhythmias.
Role of wearables and artificial intelligence	The roles of wearables and artificial intelligence in medicine are growing exponentially, but their roles in monitoring different aspects of health and screening for future cardiovascular disease need further study.
Post-procedure management	Data are lacking on optimal waiting periods to return to play after procedures, to allow incisional healing and avoid lead dislodgment.
SCA prevention	Understanding the epidemiology of and how to best screen athletes for underlying cardiac disease that may predispose to SCA are areas of ongoing research.
SCA treatment: EAP	Continued advocacy work for EAP and access to AEDs is needed, recognizing that EAPs may be defined differently depending on local resources and socioeconomics.
SCA treatment: Home/personal AEDs	There are many cardiac conditions in which the risk of SCA is not high enough to warrant implantation of an ICD, but the risk is not zero. While obtaining a home AED is recommended, data are needed on the medical and psychological outcomes of this intervention for children living at home and young adults on their own.
SCA treatment: ICDs	Data in moderate-sized studies have demonstrated low risk in patients participating in sports with transvenous ICDs performing most sports. Safety of sports, particularly related to system malfunction, for other modalities such as subcutaneous, extravascular, and epicardial/abdominal ICDs is not yet defined. Data are lacking on risk of collision sports to the lead, in any system.
Syncope workup	While cardiac causes of syncope are rare, they can be life-threatening. Defining the appropriate workup that eliminates nonuseful testing without losing sensitivity for-life-threatening entities is an important avenue of future research.
AF anticoagulation overall strategy	Some data suggest that athletes with AF may have lower stroke risk than nonathletes with similar CHA_2DS_2-VASc scores. However, data are not currently sufficient to support different anticoagulation strategies in athletes. Data on the impact of anticoagulation on rates of serious bleeding in the setting of

Knowledge gap	Future needs and directions
	injury in sports with low but potential risk of injury, such as bicycling and skiing, are also lacking.
AF safety of brief cessation of anticoagulation for activities with high risk of trauma	Data suggest thromboembolic risk in anticoagulation cessation in other circumstances, such as perioperative, is low but not zero. Safety of brief cessation in generally healthy athletes has not been investigated
AF rhythm management: Medications	While anecdotally and theoretically antiarrhythmic medications could increase proarrhythmia in athletes, the safety and tolerability of antiarrhythmic medications in athletes has not been described.
AF rhythm management: Ablation	Whether athletes would benefit from ablation strategies beyond PVI is unknown. Anecdotal reports suggest that overablation could be harmful by causing pulmonary vein stenosis or stiff left atrial syndrome and/or by affecting pulmonary vein function.
AF rhythm management: The ideal time to refrain from vigorous exercise after ablation	While inflammation at the time of AF ablation creates an immediate increased risk of recurrence during the 2-3 months post-ablation, whether vigorous exercise would alter the immediate or long-term risk of recurrence is not known.
Ventricular arrhythmia management	While documentation of arrhythmia suppression after pharmacological or ablative therapy on a stress test prior to return to play seems clinically relevant, data are needed to evaluate the predictive value of stress testing in this context.
HCM	Data are emerging that show arrhythmic risk is lower than hypothesized for patients with HCM. Data are lacking on how vigorous exercise may impact long-term progression of the underlying myopathy, with theoretical considerations supporting both beneficial and deleterious effects.
ACM	For many cardiomyopathies, data are few at best, or completely lacking on both the arrhythmic risk of exercise and the impact of exercise on penetrance and progression of disease. Even for those entities in which excessive exercise has been shown to be detrimental, safe thresholds have not been defined.
Channelopathies	Whether there is a role for extended monitoring (such as implantable loop recorders or wearable devices) has not been defined.
Rhythm monitoring for inherited cardiomyopathies and channelopathies	Whether there is a role for extended monitoring (such as implantable loop recorders or wearable devices) has not been defined.
Channelopathies: Left cardiac sympathetic denervation	While complication rate is not high and quality of life is not adversely impacted by left cardiac sympathetic

Knowledge gap	Future needs and directions
	denervation,[391,397] whether sympathetic denervation impacts athletic performance has not been reported.
PVCs	While prior data show that frequent PVCs in the absence of underlying heart disease do not carry risk with sports, studies restricted athletes with highest burden from return to play. More data are needed on return to play with very frequent PVCs.
Myocarditis	Data are lacking on how myocarditis may impact future arrhythmia risk. Outcomes in athletes who return to play with residual scar on CMR, or residual PVCs or premature atrial contractions, is needed.
WPW risk assessment for young adults	As described in detail above, data have emerged that show that for those with WPW who are under 18 years of age, noninvasive and even invasive risk stratification lack sensitivity and thus ablation is recommended. For those above age 30 years, risk is low and can likely be estimated noninvasively. However, data are few on individuals in the young adult range, 18-25 years old, a group of importance since WPW may be identified during preparticipation screening as entering college.
Education/training	Formal education and training in the care of arrhythmias in athletes needs to be regularly available at national scientific meetings, in board review content, and during fellowship training, if possible.
Pacemakers	Role of leadless pacing, both single and dual chamber, has not yet been studied, especially with regard to form factor, programming, and battery life.

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Appendix 1 Writing committee member disclosure of relationships with industry and other entities

Writing committee member	Employment	Honoraria/speaking/ consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ partnership/ principal/majority stockholder	Stock or stock options	Intellectual property/ royalties	Other
Rachel Lampert, MD, FHRS (Chair)	Yale University School of Medicine, New Haven, Connecticut	1: Medtronic†	None	0: Boston Scientific 0: MediLynx 0: Medtronic	None	None	None	None	None
Eugene H. Chung, MD, MPH, MSci, FHRS (Vice-Chair)	Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts	None	None	None	None	None	None	None	None
Michael J. Ackerman, MD, PhD	Mayo Clinic, Rochester, Minnesota	0: Abbott 3: ARMGO Pharma 1: BioMarin 0: Boston Scientific 2: Bristol-Myers Squibb 0: Daiichi Sankyo 1: Illumina 0: InVitae 0: Medtronic 2: Tenaya Therapeutics 1: UpToDate	None	None	None	0: AliveCor 0: Anumana	None	5: Pfizer 0: Thryv Therapeutics	None
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Writing committee member	Employment	Honoraria/speaking/ consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ partnership/ principal/majority stockholder	Stock or stock options	Intellectual property/ royalties	Other
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Writing committee member	Employment	Honoraria/speaking/ consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ partnership/ principal/majority stockholder	Stock or stock options	Intellectual property/ royalties	Other
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Lluis Mont, MD, PhD, FEHRA	Hospital Clínic, Universitat de Barcelona., Barcelona, Spain	1: Abbott Medical 1: Biosense Webster 1: Boston Scientific 1: Medtronic	None	2: Abbott Medical 2: Biosense Webster 2: Boston Scientific 1: Medtronic	1: Abbott 1: Biosense Webster 1: Boston Scientific 1: Medtronic	None	1: ADAS 3D 1: Corify Health Care S.L.	None	None
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Maully J. Shah, MBBS, FHRS, CCDS, CEPS-P	Childrens Hospital of Philadelphia,	0: IBHRE 1: Medtronic 0: Tenaya Therapeutics	None	0: Medtronic	None	None	None	None	1: JACC

Writing committee member	Employment	Honoraria/speaking/ consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ partnership/ principal/majority stockholder	Stock or stock options	Intellectual property/ royalties	Other
	Philadelphia, Pennsylvania								

Number value: **0** = $0; **1** = ≤ $10,000; **2** = > $10,000 to ≤ $25,000; **3** = > $25,000 to ≤ $50,000; **4** = > $50,000 to ≤ $100,000; **5** = > $100,000.
This table is a comprehensive list of the relationships with industry and other entities (RWI)—regardless of relevance to the document topic—disclosed by each writing committee member for the 12 months prior to the initial meeting of the writing committee and up through the completion of the document. The table does not necessarily reflect the RWI of the writing committee members at the time of publication. Please refer to the *HRS Code of Ethics and Professionalism* for definitions of disclosure categories or additional information about the HRS policy on the disclosure of relationships with industry and other entities. To mitigate potential bias and conflict of interest, the recommendations and supportive text were written by writing committee members who were free of relevant RWI.

*Research and fellowship support are classed as programmatic support. Sources of programmatic support are disclosed but are not regarded as a relevant relationship with industry for writing group members or reviewers.

†This RWI was ended in March 2022, 8 months prior to writing committee selection and 10 months prior to the start of document development.

AMSSM = American Medical Society for Sports Medicine; IBHRE = International Board of Heart Rhythm Examiners; JACC = Journal of the American College or Cardiology; NIH = ; NHLBI = ; NSGC = National Society of Genetic Counselors

Appendix 2 Reviewer disclosure of relationships with industry and other entities

Peer Reviewer	Employment	Honoraria/ speaking/ consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ partnership/ principal/majority stockholder	Stock or stock options	Intellectual property/ royalties	Other
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Tee Joo Yeo, MBBS	National University Heart Centre Singapore, Singapore	None	None	None	None	None	None	None	None
Miguel A. Leal, MD, FHRS	Emory School of Medicine, Atlanta, Georgia	1: Sanofi	None	1: Medtronic	None	None	None	None	None

Peer Reviewer	Employment	Honoraria/ speaking/ consulting	Speakers' bureau	Research*	Fellowship support*	Ownership/ partnership/ principal/majority stockholder	Stock or stock options	Intellectual property/ royalties	Other
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Kristen K. Patton, MD, FHRS	University of Washington, Seattle, Washington	1: Great Wall International Congress of Cardiology	None	None	None	None	None	None	0: ACGME RC Internal Medicine 0: AHA Clinical Cardiology Council 0: JAMA Cardiology (Associate Editor) 0: U.S. Food & Drug Administration
Jordan M. Prutkin, MD, MHS, FHRS	University of Washington, Seattle, Washington	None	None	None	None	None	None	4: UpToDate	None
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Number value: **0** = $0; **1** = ≤ $10,000; **2** = > $10,000 to ≤ $25,000; **3** = > $25,000 to ≤ $50,000; **4** = > $50,000 to ≤ $100,000; **5** = > $100,000.

This table is a comprehensive list of the relationships with industry and other entities (RWI)—regardless of relevance to the document topic—disclosed by the reviewers at the time the document was under review. The table does not necessarily reflect the RWI of the reviewers at the time of publication. Please refer to the *HRS Code of Ethics and Professionalism* for definitions of disclosure categories or additional information about the HRS policy on the disclosure of relationships with industry and other entities.

*Research and fellowship support are classed as programmatic support. Sources of programmatic support are disclosed but are not regarded as a relevant relationship with industry for writing group members or reviewers.

ACC = American College of Cardiology; ACGME = Accreditation Council for Graduate Medical Education; ADFM = Association of Departments of Family Medicine; AHA = American Heart Association; AMSSM = American Medical Society for Sports Medicine; HRCRS = Heart Rhythm Clinical Research Solutions; HRSA = Health Resources and Services Administration; JAMA = Journal of the American Medical Association; MLS = Major League Soccer; NBA = National Basketball Association; NCRD = National Cardiovascular Data Registry; NIH = National Institutes of Health.

Subsection	Rec #	First Author	Year	DOI	Article Title	Aim	Study type	Size	Endpoints	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Comparator(s)	Outcomes (Results and P values)	Other Relevant Findings or Adverse Events	Conclusions	Limitations
2.2 Clinical considerations for athletes with arrhythmias	6	Anys	2021	https://doi.org/10.1016/j.hrthm.2021.04.021	Dose response to nadolol in congenital long QT syndrome	Explore dose response to nadolol on exercise test in LQTS patients in order to propose a more personalized therapeutic approach	Retrospective cohort study	95 patients included, 337 stress tests under nadolol	Importance of personalized treatment in LQTS; proposes a method for predicting the effect of titration improving the care of patients with LQTS.	LQTS patients with at least 1 exercise test under nadolol were included retrospectively between 1993 and 2017, and diagnosis could be made based on ECG, personal or family history, or familial screening.	Patients who did not have at least 1 stress test under nadolol; patients with insufficient information to validate the diagnosis; patients who did not have a confirmed diagnosis through pathogenic mutation identification.	Patients underwent gradual cycle exercise tests. Doses adjusted to weight and response to treatment were recorded and evaluated by the percentage of age-predicted maximum heart rate reached on exercise test.	Overresponders and underresponders, mainly based on LQTS1 and LQTS2 genotypes, to evaluate the dose response	Negative correlation between dose change and percentage of age-predicted maximum heart rate change (P<.0001).	Side effects related to nadolol included asthenia, orthostatic hypotension, erectile dysfunction, and bradycardia. Adverse effects led to treatment discontinuation or decrease in 12% of patients. Additionally, 7% of patients had problems with adherence.	Major variability in the dose response to nadolol in LQTS patients, highlighting the need for personalized dosages. Intraindividual analysis showed a relatively constant dose-response relationship, allowing for guided dose adaptation after the first exercise test.	Missing data due to the retrospective nature of the study, especially regarding the physical activity of patients, which could impact the response to treatment. Practical performance and interpretation of exercise tests in children are difficult.
2.2 Clinical considerations for athletes with arrhythmias	6	Tobert	2021	https://doi.org/10.1016/j.jacc.2021.04.026	Return-to-Play for Athletes With Long QT Syndrome or Genetic Heart Diseases Predisposing to Sudden Death	The prevalence and outcomes of athletes with sudden cardiac death predisposing GHDs, particularly LQTS after their return to play	Retrospective cohort study	672 athletes, including 494 with LQTS (231 female), mean age 14.8, mean follow up 4.1 years,	BCE	Athletes with genetic heart disease wishing to return to play	Athletes with GHD no longer wishing to play	n/a	BCE in those outside of RTP period	No deaths, overall event rate 5.9% of whom event rate of 3% in athletes during RTP period and 2.8% outside of RTP period, of these 0.6% and 0.4% were sports related BCE respectively. Overall event rate 1.16 nonletal events per 100 athletes-years follow up	Includes 130 athletes from above study	Low event rate overall, particularly in LQTS	Single centre, retrospective cohort, referral biase
2.3 Shared decision-making and clinical management determination	1	Sweeney	2023	https://doi.org/10.1161/CIRCGEN.123.004133	Characterizing Decision-Making Surrounding Exercise in ARVC: Analysis of Decisional Conflict, Decisional Regret, and Shared Decision-Making	Evaluate the extent and implications of SDM for exercise, decisional conflict, and decisional regret in patients with ARVC and at-risk relatives.	Cross-sectional study	205 patinents with ARVC, mean age 43.9, M/F equally represented	Decisional conflict scale (DCS) scores, Decisional regret scale (DRS) scores, Shared decision-making (SDM) scores, Association between SDM and decisional conflict/regret, Impact of SDM on exercise levels	Adults diagnosed with arrhythmogenic right ventricular cardiomyopathy (ARVC) or with positive genetic testing who were enrolled in the Johns Hopkins ARVC Registry.	Not an adult, diagnosed with something other than ARVC	Questionnaire that included exercise history and current exercise, SDM (SDM-Q-9), decisional conflict, and decisional regret.	Levels of decisional conflict, extent of SDM for exercise, age at diagnosis, genotype (specifically DSP variants), and levels of decisional regret.	Response rate was 64.8%; 68.0%, n=121 reported clinically significant decisional conflict regarding exercise at diagnosis/genetic testing (DCS ≥ 25), and half (55.1%, n=98) in the past year; prevalence of decisional regret was also high with 55.3% (n=99) reporting moderate to severe decisional regret (DRS ≥ 25); extent of SDM was highly variable ranging from no (0) to perfect (100) SDM (mean, 59.6±25.0). diagnosis during adolescence (≤ age 21) reported significantly more SDM (P=0.013); SDM was associated with less decisional conflict (ß=−0.66, R2=0.567, P P<0.001); no difference in vigorous intensity aerobic exercise in the 6 months after diagnosis/genetic testing or the past year (P=0.56; P=0.34, respectively)	Significant levels of decisional conflict and decisional regret experienced by participants regarding exercise decision-making, which can have psychosocial implications and impact the quality of life of individuals with ARVC.	SDM is associated with lower decisional conflict and decisional regret; and no difference in postdiagnosis exercise.	Complexity and uncertainty surrounding exercise decisions for patients with ARVC; lack of studies on the extent and consequences of shared decision-making for exercise; retrospective nature of the study affecting participant recall; need for prospective studies to reduce bias.
2.4 Emergency action planning for sudden cardiac arrest	1, 2, 3	Austin	2022	https://doi.org/10.1161/CIRCOUTCOMES.121.008640	Differences in Survival Outcomes in Adolescent Male Basketball Players at School-Sponsored Versus Select Club-Sponsored Events and Implications for Racial Disparities	Examine and compare survival outcomes in adolescent male basketball players with SCA during school-sponsored versus select club-sponsored events.	Obersvational, retrospective cohort study	60 cases; mean age 15.4 years, range 12-19; 45% Black, 38% White, 17% other	Survival to hospital discharge; comparison of survival outcomes in adolescent male basketball players with SCA between school-sponsored and select club-sponsored events.	Adolescent male basketball players, ages 12-19 in the NCCSIR database who experienced sudden cardiac arrest	Those outside of the age range	n/a	School-sponsored events versus select club-sponsored events in terms of survival outcomes and emergency response (use of CPR or AED)	Overall survival for cases occurring at select club events versus middle/high school events was 39% and 67%, respectively (P=0.05); survival was lower in athletes of Black (37%) and other race (50%) versus White athletes (74%; P=0.02); the unadjusted/adjusted risk ratios for Black versus White athlete survival were 0.50 (95% CI, 0.29–0.87; P=0.01) and 0.61 (95% CI, 0.35–1.07; P=0.09); among only high school athletes, survival (71% vs 39%; P=0.04), reported bystander CPR (91% vs 54%; P=0.004), and reported AED use (79% vs 31%; P=0.002) were higher in cases occurring during school versus select club events. Provision of CPR in 90% of school cases vs. 56% at club events. AED use 64% of school events vs. 22% at club events.	Black male basketball players represent the highest risk athlete group for SCA.	Adolescent male basketball players with exercise-related SCA had higher survival rates in school-sponsored events compared to select club events, with better emergency response measures in school settings. Racial disparities in survival outcomes were noted, with higher survival rates in White athletes than Black athletes.	Potential for missed cases of SCA; missing data due to low follow-up and response rates; lack of investigation into the causes of higher SCA incidence in Black athletes; potential underpowering of the sample size to detect effects when adjusting for other variables; presence of unexamined factors that could impact racial disparities in survival outcomes.
2.4 Emergency action planning for sudden cardiac arrest	1, 2, 3	Blom	2014	https://doi.org/10.1161/circulationaha.114.010905	Improved survival after out-of-hospital cardiac arrest and use of automated external defibrillators	Determine if survival with favorable neurologic outcome after out-of-hospital cardiac arrest has increased in The Netherlands between 2006 and 2012, with a focus on the impact of automated external defibrillator (AED) use on survival rates.	Population-based, restrospective cohort study	6133 cases	Rates of survival with favorable neurologic outcome after out-of-hospital cardiac arrest, which increased significantly between 2006 and 2012, particularly in patients presenting with a shockable initial rhythm.	Patients with out-of-hospital cardiac arrest from cardiac causes between 2006 and 2012.	Emergency medical service-witnessed arrests, arrests with unequivocal noncardiac causes documented, aborted resuscitation efforts in individuals with a do-not resuscitate status, and patients with signs of prolonged death	n/a	Survival rates with favorable neurologic outcome after OHCA between 2006 and 2012 and AED use rates during the study period.	Rates of survival with favorable neurologic outcome after out-of-hospital cardiac arrest increased significantly (N=6133, 16.2% to 19.7%; P for trend=0.021), although solely in patients presenting with a shockable initial rhythm (N=2823; 29.1% to 41.4%; P for trend<0.001). In this group, survival increased at each stage but was strongest in the prehospital phase (odds ratio, 1.11 [95% CI, 1.06–1.16]). Rates of AED use almost tripled during the study period (21.4% to 59.3%; P for trend <0.001), thereby decreasing time from emergency call to defibrillation-device connection (median, 9.9 to 8.0 minutes; P<0.001).	Survival analysis at each consecutive stage of resuscitation care showed that the largest increase was found in the prehospital phase, indicating that the large investments in improvement of prehospital care had the desired effects	Increased AED use is associated with improved survival rates in patients with a shockable initial rhythm after out-of-hospital cardiac arrest.	Observational nature of the data; lack of detailed covariates in the resuscitation process; acceptance of missing data; primary focus on prehospital parameters over in-hospital care
2.4 Emergency action planning for sudden cardiac arrest	1, 2, 3	Drezner	2009	https://doi.org/10.1161/CIRCULATIONAHA.109.855890	Effectiveness of emergency response planning for sudden cardiac arrest in United States high schools with automated external defibrillators	Analyze effectiveness of emergency response planning for SCA in US high schools with onsite AED programs	Cross-sectional survey	1710 schools; mean athletes/school = 371	Survival rates of SCA; victims to hospital discharge; provision of bystander CPR; receipt of a shock; initial rhythm observed after collapse	High schools with at least one AED	High schools with no AED	n/a	High schools with AED programs and those without such programs, focusing on the presence of EAPs for SCA; occurrence of SCA events within a specific timeframe	High schools with onsite AED programs and established emergency response plans have a high survival rate for SCA victims, including student athletes and older nonstudents.Of the 36 SCA cases, 35 (97%) were witnessed, 34 (94%) received bystander cardiopulmonary resuscitation, and 30 (83%) received an AED shock; 23 SCA victims (64%) survived to hospital discharge	The annual incidence of SCA in a high school student athlete estimated from this study is 4.4 in 100,000. 9/14 students survivied.	School-based AED programs provide a high survival rate for both student athletes and older nonstudents who suffer SCA on school grounds.	Responder bias; self-reported data; possible misreporting of resuscitation details; lack of a standardized monitoring system for SCA in schools or young athletes; absence of a comparison group without AEDs.
2.4 Emergency action planning for sudden cardiac arrest	1, 2, 3	Drezner	2013	https://doi.org/10.1136/bjsports-2013-092786	Outcomes from sudden cardiac arrest in US high schools: a 2-year prospective study from the National Registry for AED Use in Sports	Monitor large cohort of US high schools to determine outcomes of SCA; potential effectiveness of school-based AED programs.	Prospective observational study	2149 high schools	Survival to hospital discharge	Cases of SCA that occurred on school campuses - non-traumatic and of primary cardiac origin; victims confirmed unconscious w/ absent pulse and respirations.	Events that did not occur on the school campus, were traumatic in nature, were not of primary cardiac origin, did not involve a victim confirmed unconscious with absent pulse and respirations; cases that occurred outside the study time period	n/a	Source of the AED used in resuscitation (school supply vs. offsite EMS); presence of a EAP for SCA	AED programs present in 87% of participating schools; 59 cases of SCA were confirmed during the study period including 44% cases in students and 56% in adults; 66% cases occurred at an athletic facility during training or competition; 55 93% cases were witnessed and 92% received prompt cardiopulmonary resuscitation; AED applied in 85% cases and a shock delivered onsite in 66%; 71% of SCA victims survived to hospital discharge, including 85% students, 61% adults.	Cases in which the school had AED but it was not used in the resuscitation (ie, responding EMS provided the defibrillator) also had a reasonably high survival rate	High school AED programs show high survival rate for individuals experiencing SCA on school campuses	Cross-sectional design; lack of a control group of SCA cases in schools w/o AED program; unknown long-term neurological outcomes of SCA victims; potential for unreported cases of SCA.
2.4 Emergency action planning for sudden cardiac arrest	1, 2, 3	Valenzuela	2000	https://doi.org/10.1056/nejm200010263431701	Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos	Investigate the effectiveness of training casino security officers in AED and CPR to increase the rate of survival to discharge from the hospital after cardiac arrest	Observational study	148 individuals with witnessed cardiac arrest due to ventricular fibrillation; mean age 65±11 years; predominantly male	Survival to discharge from the hospital	Unconscious and unresponsive, having no palpable carotid pulse, and no spontaneous respiration	Subjects less than nine years of age or weighing 36 kg or less	n/a	Survival rates/time intervals for defibrillation in different scenarios: within 3-min after collapse vs > 3-min; comparison with traditional emergency-response systems in other locations.	The survival rate for patients with ventricular fibrillation who received their first defibrillation within three minutes was 74 percent, compared to 49 percent for those who received it later.	Survival rates may not significantly differ between study sites with inconsistent collapse-to-defib intervals of 3-4 min and those with the best traditional ems systems; however, the outcomes from the former may represent an advancement over ems systems with prolonged response times.	Rapid defib by nonmed personnel using AED can improve survival after out-of-hospital cardiac arrest due to vfib, with intervals of no more than three minutes from collapse to defib necessary to achieve the highest survival rates.	Lack of access to data on cardiac arrests in casinos other than the participating ones; legal liability concerns affecting the willingness of casinos to participate; absence of formal neurologic testing in survivors

Subsection	Rec #	First Author	Year	DOI	Article Title	Aim	Study type	Size	Endpoints	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Comparator(s)	Outcomes (Results and P values)	Other Relevant Findings or Adverse Events	Conclusions	Limitations
2.4 Emergency action planning for sudden cardiac arrest	1, 2, 3, 4	Son	2017	https://doi.org/10.15441/ceem.16.160	Association between public cardiopulmonary resuscitation education and the willingness to perform bystander cardiopulmonary resuscitation: a metropolitan citywide survey	Determine how factors related to CPR education influence bystander CPR willingness.	Observational, cross-sectional survey study	Male: 480, Female: 520	CPR willingness	Subjects aged 19 years or above, with prior experience in CPR education, who had undergone CPR education sessions at least once, willing to perform CPR, selected by quota sampling, and part of the metropolitan city of Daegu in 2012.	Aged 18 or younger with no prior CPR education	n/a	Male vs. Female; Age GroupsE; ducation Levels	Multivariate analyses revealed several factors significantly associated with CPR willingness: didactic plus practice group (adjusted odds ratio [AOR], 3.38; 95% confidence interval [CI], 2.3 to 5.0), group with more than four CPR education session (AOR, 7.68; 95% CI, 3.21 to 18.35), interval of less than 6 months from the last CPR education (AOR, 4.47; 95% CI 1.29 to 15.52), and education with automated external defibrillator (AOR, 5.98; 95% CI 2.30 to 15.53).	Willingness to perform CPR greatest when most recent training was between 6 months to 1 year	Practice sessions and automated electrical defibrillator training in public CPR education, more frequent CPR training, and shorter time period from the most recent CPR education sessions associated with increased willingness to perform CPR	Potential recall bias in self-reported timing and frequency of previous education sessions; uncertainty in predicting actual CPR performance based on survey responses; necessity for systematic planning of CPR reeducation for first-aid responders
2.4 Emergency action planning for sudden cardiac arrest	1, 2, 3, 4	Vetter	2022	https://doi.org/10.1016/j.jacc.2022.03.359	Impact of State Laws: CPR Education in High Schools	Evaluate the association b/t state laws requiring CPR education in high schools and bystander CPR rates following out-of-hospital cardiac arrest.	Observational, retrospectie cohort study	291,388 OHCA cases from 20 states using CARES dataset	Rates of bystander CPR (BCPR) following out-of-hospital cardiac arrest; OHCA in states with laws requiring CPR education in high schools.	Nontraumatic OHCAs in HS from states with at least 50% population catchment submitted to CARES during the study period;	Arrests in medical facilities, nursing homes, or witnessed by 911 responders; additional 1,676 arrests (0.6%) were excluded because of missing values on any variables of interest	n/a	States with laws enacted that require CPR training in high schools compared to states without such laws.	OHCAs occurring in states with laws enacted had higher odds of BCPR compared with OHCAs in states without a law: OR: 1.12; 95% CI: 1.08-1.15; marginal probability: 42.4%; 95% CI: 37.8-46.9 vs 39.9%; 95% CI: 35.4-44.4.	CPR/AED education in low socioeconomic minority communities has the potential for the greatest benefit	States with laws enacted that require CPR training in high schools have higher rates of BCPR following OHCA.	Recent implementation of laws; limited data availability for state-specific characteristics; generalizability issues due to incomplete data collection

Subsection	Rec #	First Author	Year	DOI	Article Title	Aim	Study type	Size	Endpoints	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Comparator(s)	Outcomes (Results and P values)	Other Relevant Findings or Adverse Events	Conclusions	Limitations
3.4 Emergency action plans forand immediate treatment of sudden cardiac arrest	1	Austin	2022	https://doi.org/10.1161/CIRCOUTCOMES.121.008640	Differences in Survival Outcomes in Adolescent Male Basketball Players at School-Sponsored Versus Select Club-Sponsored Events and Implications for Racial Disparities	Examine and compare survival outcomes in adolescent male basketball players with SCA during school-sponsored versus select club-sponsored events, focusing on differences in emergency response and survival rates between the two settings, as well as racial disparities in survival outcomes.	Obersvational, retrospective cohort study	60 cases; mean age 15.4 years, range 12-19; 45% Black, 38% White, 17% other	Survival to hospital discharge; comparison of survival outcomes in adolescent male basketball players with SCA between school-sponsored and select club-sponsored events.	Adolescent male basketball players, ages 12-19 in the NCCSIR database who experienced sudden cardiac arrest	Those outside of the age range	n/a	School-sponsored events versus select club-sponsored events in terms of survival outcomes and emergency response (use of CPR or AED)	Overall survival for cases occurring at select club events versus middle/high school events was 39% and 67%, respectively (P=0.05); survival was lower in athletes of Black (37%) and other race (50%) versus White athletes (74%; P=0.02); the unadjusted/adjusted risk ratios for Black versus White athlete survival were 0.50 (95% CI, 0.29–0.87; P=0.01) and 0.61 (95% CI, 0.35–1.07; P=0.09); among only high school athletes, survival (71% vs 39%; P=0.04), reported bystander CPR (91% vs 54%; P=0.004), and reported AED use (79% vs 31%; P=0.002) were higher in cases occurring during school versus select club events. Provision of CPR in 90% of school cases vs. 56% at club events. AED use 64% of school events vs. 22% at club events.	Black male basketball players represent the highest risk athlete group for SCA.	Adolescent male basketball players with exercise-related SCA had higher survival rates in school-sponsored events compared to select club events, with better emergency response measures in school settings. Racial disparities in survival outcomes were noted, with higher survival rates in White athletes than Black athletes.	Potential for missed cases of SCA; missing data due to low follow-up and response rates; lack of investigation into the causes of higher SCA incidence in Black athletes; potential underpowering of the sample size to detect effects when adjusting for other variables; presence of unexamined factors that could impact racial disparities in survival outcomes.
3.4 Emergency action plans forand immediate treatment of sudden cardiac arrest	1	Drezner	2013	https://doi.org/10.1136/bjsports-2013-092786	Outcomes from sudden cardiac arrest in US high schools: a 2-year prospective study from the National Registry for AED Use in Sports	Monitor large cohort of US high schools to determine outcomes of SCA; potential effectiveness of school-based AED programs.	Prospective observational study	2149 high schools	Survival to hospital discharge	Cases of SCA that occurred on school campuses - non-traumatic and of primary cardiac origin; victims confirmed unconscious w/ absent pulse and respirations.	Events that did not occur on the school campus, were traumatic in nature, were not of primary cardiac origin, did not involve a victim confirmed unconscious with absent pulse and respirations; cases that occurred outside the study time period	n/a	Source of the AED used in resuscitation (school supply vs. offsite EMS); presence of a EAP for SCA	AED programs present in 87% of participating schools; 59 cases of SCA were confirmed during the study period including 44% cases in students and 56% in adults; 66% cases occurred at an athletic facility during training or competition; 55 93% cases were witnessed and 92% received prompt cardiopulmonary resuscitation; AED applied in 85% cases and a shock delivered onsite in 66%; 71% of SCA victims survived to hospital discharge, including 85% students, 61% adults.	Cases in which the school had AED but it was not used in the resuscitation (ie, responding EMS provided the defibrillator) also had a reasonably high survival rate	High school AED programs show high survival rate for individuals experiencing SCA on school campuses	Cross-sectional design; lack of a control group of SCA cases in schools w/o AED program; unknown long-term neurological outcomes of SCA victims; potential for unreported cases of SCA.
3.5 Sudden cardiac arrest treatment and ICD management	3	Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators	1997	https://doi.org/10.1056/NEJM199711273372202	A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias	To examine the effect on overall survival of initial therapy with an ICD as compared with amiodarone or sotalol in patients resuscitated from VF or symptomatic, sustained VT with hemodynamic compromise.	RCT, multicenter	1016 patients	Mortality	Patients who were resuscitated from near-fatal VF; sustained VT with syncope; or sustained VT with an LVEF ≤0.40 and symptoms suggesting severe hemodynamic compromise.	Arrhythmia that was judged to have a transient or correctable cause, excessively high risk (life expectancy <1 y, class IV HF, awaiting a heart transplant, or requiring a balloon pump, other mechanical means, or inotropic drug administration for hemodynamic support) or excessively low risk (event occurring within 5 d of cardiac surgery or angioplasty, or occurring in-hospital <5 d after MI), previous ICD implant (or attempted implant), chronic serious bacterial infection, or were unable to give verbal consent due to neurologic impairment, or a contraindication to amiodarone.	ICD	Amiodarone	Overall survival was greater with the ICD, with unadjusted estimates of 89.3% as compared with 82.3% in the antiarrhythmic-drug group at 1 y, 81.6% vs. 74.7% at 2 y, and 75.4% vs. 64.1% at 3 y (p<0.02). The corresponding reductions in mortality (with 95% CI) with the ICD were 39±20%, 27±21%, and 31±21%	Study terminated early after 1016 of 1200 patients enrolled. 81% had CAD.	Among survivors of VF or sustained VT causing severe symptoms, ICD is superior to AAD therapy for reducing overall mortality.	Amiodarone dose and ICD therapies were not standardized, no control group.
3.5 Sudden cardiac arrest treatment and ICD management	3	Kuck	2000	https://doi.org/10.1161/01.CIR.102.7.748	Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: the Cardiac Arrest Study Hamburg (CASH)	To compare patients surviving SCA randomized to ICD vs. antiarrhythmic drug therapy (antiamiodarone, propafenone or metoprolol).	RCT, multicenter	288 patients after exclusion of propafenone group	Primary endpoint: all-cause mortality. Secondary endpoints: sudden death and recurrence of cardiac arrest.	Pts resuscitated from SCA of ventricular arrhythmia.	Patients were excluded from the study if cardiac arrest occurred within 72 hours of an acute myocardial infarction, cardiac surgery, electrolyte abnormalities, or proarrhythmic drug effect.	ICD implantation or antiarrhythmic drug therapy (amiodarone, propafenone, or metoprolol).	ICD group compared to amiodarone or metoprolol groups.	Propafenone arm dropped early b/c of a 61% higher mortality rate than in 61 ICD patients. Over a mean follow-up of 57±34 months, the crude death rates were 36.4% (95% CI 26.9% to 46.6%) in the ICD and 44.4%(95% CI 37.2% to 51.8%) in the amiodarone/metoprolol arm. Overall survival was higher, though not significantly, in patients assigned to ICD than in those assigned to drug therapy (1-sided P=0.081, hazard ratio 0.766, [97.5% CI upperbound 1.112]). In ICD patients, the percent reductions in all-cause mortality were 41.9%, 39.3%, 28.4%, 27.7%, 22.8%,11.4%, 9.1%, 10.6%, and 24.7% at years 1 to 9 of follow-up.	During the trial, 6.1% of patients in the ICD arm and 11 (5.8%) in the drug arm crossed over or added the other therapy by 24 months. Three patients assigned to ICD and none of those assigned to amiodarone received beta-blockers during follow-up. Perioperative mortality was 4% in the first 15 patients receiving an endocardial ICD.	Long-term follow-up suggests that ICD therapy is associated with a lower rate of all-cause mortality and sudden death compared to amiodarone or metoprolol therapy in cardiac arrest survivors.	Small number of patients and participating centers, underpowered, selection bias for patients with well-preserved LVEF, and changes in treatment standards over the long recruitment period.
3.5 Sudden cardiac arrest treatment and ICD management	3	Connolly	2000	https://doi.org/10.1161/01.CIR.101.11.1297	Canadian implantable defibrillator study (CIDS); A randomized trial of the implantable cardioverter defibrillator against amiodarone	Compare the effectiveness of implantable cardioverter defibrillators (ICDs) versus amiodarone in preventing death in patients at high risk of arrhythmic events due to previous ventricular fibrillation or sustained ventricular tachycardia.	RCT	659 patients with resuscitated ventricular fibrillation (VF) or sustained ventricular tachycardia (VT), or with unmonitored syncope.	Primary: all-cause mortality. Secondary: arrhythmic death.	Patients with documented VF, out-of-hospital cardiac arrest requiring defibrillation or cardioversion, documented sustained VT, or unmonitored syncope with documented VT. Exclusion of recent acute myocardial infarction or electrolyte imbalance.	(1) ICD or amiodarone not considered appropriate as a treatment for the tachyarrhythmia, (2) excessive perioperative risk for ICD implanta-tion; (3) previous amiodarone therapy for6 weeks; (4) nonarrhythmic medical condition making 1-year survival unlikely, and (5) long-QT syndrome	ICD or amiodarone	ICD group compared to amiodarone group	A nonsignificant reduction in the risk of death was observed with the ICD, from 10.2% per year to 8.3% per year (19.7% relative risk reduction; 95% confidence interval, 27.7% to 40%; P=0.142).	28.1% of ICD patients received amiodarone during the study. 21.4% of amiodarone patients received an ICD.	A 20% relative risk reduction occurred in all-cause mortality and a 33% reduction occurred in arrhythmicmortality with ICD therapy compared with amiodarone; this reduction did not reach statistical significance	Trial stopped early because of benefit of ICD, so did not reach statistical significance. Relatively high rate of amiodarone use in pts with ICDs (21.7%). Non-blinding of the External Validation Committee to treatment allocation, potential biases in cause-specific mortality determination, and crossover treatments might have affected the results.

3.5 Sudden cardiac arrest treatment and ICD management	4, 5, 7	Lampert	2013	https://doi.org/10.1161/CIRCULATIONAHA.112.000447	Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry	Evaluate the safety of sports participation for athletes with implantable cardioverter-defibrillators (ICDs).	Prospective, multinational registry	372 athletes with ICDs aged 10 to 60 years participating in organized or high-risk sports.	Primary: serious adverse events (tachyarrhythmic death or resuscitated tachyarrhythmia) during or up to 2 hours after sports, or severe injury from arrhythmia-related syncope or shock during sports.	Athletes aged 10 to 60 years with ICDs who were actively participating in organized sports or high-risk sports.	Athletes not participating in sports, or those who did not meet the specific criteria for organized or high-risk sports participation.	Monitoring and data collection through a secure web-based daabase, phone interviews, and medical record reviews.	n/a	No primary endpoint events occurred. There were 49 shocks during competition/practice, 39 during other physical activity, and 33 at rest. 10% shocks during sports, 8% during other physical acitivy 6% at rest.	The ICDs effectively terminated all arrhythmia episodes. Lead malfunction rates were low, with 97% at 5 years and 90% at 10 years.	The study concluded that many athletes with ICDs can engage in vigorous and competitive sports without experiencing physical injury or failure of the device to terminate arrhythmias. These findings support more informed decision-making regarding sports participation for athletes with ICDs.	Self-selection bias of participants, most with normal LV Efs; potential underreporting of ICD shocks because of self reporting; not enough data on contact or collision sport athletes.
3.5 Sudden cardiac arrest treatment and ICD management	4, 7	Lampert	2017	https://doi.org/10.1161/CIRCULATIONAHA.117.027828	Safety of Sports for Athletes With Implantable Cardioverter-Defibrillators: Long-Term Results of a Prospective Multinational Registry	Evaluate the long-term safety of sports participation for athletes with ICDs (long-term outcomes of Lampert 2013 study).	Prospective, multinational registry	440 participants (n=393 in organized sports, n = 47 in high-risk sports)	Primary: tachyarrhythmic death, resuscitated tachyarrhythmia, or injury related to arrhythmia or shock during sports. Secondary: incidence of appropriate and inappropriate shocks, and ICD lead/system damage.	Athletes with ICDs participating in organized or high-risk sports.	Athletes not participating in organized or high risk sports or no completing enrollment interview.	Monitoring and data collection through a secure web-based daabase, phone interviews, and medical record reviews.	n/a	No tachyarrhythmic deaths or injuries related to arrhythmia during sports were reported. Small proportions of participants experienced appropriate shocks during sports without severe consequences.	10% shocks during sports (3/100 person years), more recieved shocks with physical activity (20%) compared to rest (10%) p<0.0001. Presence of ARVC associated with shocks in sports.	Athletes with ICDs engaged in vigorous acitivity with no signal for harm, underlying disease is important particularly ARVC. Engaging in sports is generally safe for athletes with ICDs, supporting more inclusive guidelines for these athletes.	Self-selection bias of participants, most with normal LV Efs; potential underreporting of ICD shocks because of self reporting; not enough data on contact or collision sport athletes.
3.5 Sudden cardiac arrest treatment and ICD management	4	Martinez	2023	https://doi.org/10.1016/j.jacc.2023.05.059	Return-to-Play for Elite Athletes With Genetic Heart Diseases Predisposing to Sudden Cardiac Death	To evaluate if patients with genetic heart diseases associated with SCD could safely return to competitive sports	Multicenter retrospective study	76 elite athletes (66% Division I, 34% professional; 28% women; average age 19.9 ± 5 years) diagnosed with GHDs.	Incidence of cardiac events related to genetic heart disease during follow-up.	Elite athletes diagnosed with sudden death predisposing GHDs (including hypertrophic cardiomyopathy, long QT syndrome, and others) allowed for RTP after comprehensive clinical evaluation and shared decision-making.	n/a	Comprehensive clinical evaluation, risk stratification, and tailored therapy for GHD followed by RTP.	n/a	During a mean follow-up of 7 ± 6 years, there was only one exercise-related (1.3%) and two non-exercise-related GHD-associated adverse cardiac events among the athletes, with no fatalities reported.	A large proportion of athletes who were initially disqualified were able to return to sports without significant adverse outcomes	RTP for elite athletes with GHDs, following appropriate clinical management and shared decision-making, is associated with low rates of non-fatal events, challenging the traditional restrictive guidelines on sports participation.	Retrospective study design, small number of patients, and selection bias.
3.5 Sudden cardiac arrest treatment and ICD management	5	Hu	2016	https://doi.org/10.1016/j.hlc.2015.07.008	Efficiencies and Complications of Dual Chamber versus Single Chamber Implantable Cardioverter Defibrillators in Secondary Sudden Cardiac Death Prevention: A Meta-analysis	To compare complications of dual chamber vs single chamber ICDs in secondary SCA	Meta-analysis	9 trials, 2594 patients	Efficacy endpoints were mortality, appropriate therapy, inappropriate detection of SVT, inappropriate therapy. Safety endpoints were lead-related complication and all complications.	Randomized controlled trials and retrospective studies comparing clinical outcomes between DC-ICDs and SC-ICDs for secondary SCD prevention.	Studies focused only on pediatric populations or those not designed for secondary SCD prevention.	Dual chamber ICDs	Single chamber ID	Compared with DC-ICDs, SC-ICDs were associated with a significant reduction in lead complications (RR:3.30; 95% CI: 1.17-9.30; p=0.02). However, both groups had similar rates of mortality (OR: 0.91; 95%CI: 0.91-1.51; p=0.73), appropriate therapy (RR: 0.90; 95%CI: 0.73-1.11; p=0.32), inappropriate detection of SVT (RR: 1.82; 95%CI: 0.71-4.62; p=0.21), inappropriate therapy (RR: 2.08; 95%CI: -0.22-0.19; p=0.86) and all complications (OR: 1.27; 95%CI: 0.19-8.67; p=0.81)	The ORs for lead-related complication in these studies ranged from 1.17 to 9.30. Lead-related complications were significantly more common in DC-ICDs, but there were no significant differences in overall complications between the two device types.	Besides more lead-related complications, DC-ICDs had similar efficacy and all complications as SC-ICDs in secondary sudden cardiac death prevention.	Potential biases due to the retrospective nature of some included studies and the variability in study designs and populations.
3.5 Sudden cardiac arrest treatment and ICD management	7	Moss	2012	https://doi.org/10.1056/NEJMoa1211107	Reduction in inappropriate therapy and mortality through ICD programming	Determine whether higher rate and delayed ICD therapy settings reduce inappropriate therapies and mortality compared to conventional ICD programming.	RCT, multicenter, international	1500 patients with primary-prevention indications for an ICD, across multiple international centers.	Primary: first occurrence of inappropriate therapy (ie, therapy delivered for nonventricular tachyarrhythmias), either antitachycardia pacing or shock. Secondary: death from any cause and the first episode of syncope.	Patients aged ≥21 with indications for primary prevention with an ICD or CRT-D, in sinus rhythm, meeting specific cardiovascular conditions.	Implanted pacemaker, ICD, or resynchronization device; had a history of permanent atrial fibrillation; had undergone coronary-artery bypass grafting or percutaneous coronary intervention or had an enzyme-positive myocardial infarction within 3 months before enrollment.	ICD programmed to conventional therapy, high-rate therapy, or delayed therapy.	Comparison between high-rate therapy, delayed therapy, and conventional therapy groups.	High-rate therapy and delayed ICD therapy, as compared with conventional device programming, were associated with reductions in a first occurrence of inappropriate therapy (hazard ratio with high-rate therapy vs. conventional therapy, 0.21; 95% confidence interval [CI], 0.13 to 0.34; P<0.001; hazard ratio with delayed therapy vs. conventional therapy, 0.24; 95% CI, 0.15 to 0.40; P<0.001) and reductions in all-cause mortality (hazard ratio with high-rate therapy vs. conventional therapy, 0.45; 95% CI, 0.24 to 0.85; P=0.01; hazard ratio with delayed therapy vs. conventional therapy, 0.56; 95% CI, 0.30 to 1.02; P=0.06)	No significant differences in procedure-related adverse events among treatment groups.	High-rate and delayed ICD programming settings reduced the occurrence of inappropriate therapies and all-cause mortality compared to conventional settings, supporting programming changes in clinical practice for primary prevention ICDs.	Follow-up period may not have been long enough to observe all potential outcomes; device programming complexity and potential for device-related complications were not fully explored.
3.5 Sudden cardiac arrest treatment and ICD management	7	Olshansky	2019	https://doi.org/10.1016/j.hrthm.2018.10.032	Competitive athletes with implantable cardioverter-defibrillators-How to program? Data from the Implantable Cardioverter-Defibrillator Sports Registry	To assess the association of tachycardia programming characteristics of ICDs with occurrence of shocks, transient loss-of-consciousness, and death among athletes.	Subanalysis of a prospective, multinational registry (Lampert 2013).	440 athletes with ICDs followed for a median of 44 months.	Occurrence of shocks (appropriate and inappropraite), transient loss-of-consciousness, and death.	Athletes with ICDs participating in sports with an ICD.	n/a	Analysis of ICD programming characteristics divided into groups for rate cutoff (very high, high, or low) and detection (long-detection interval [.nominal] or nominal).	Comparison of different ICD programming settings within the athlete cohort.	ICD shocks were received by 98 athletes (64 appropriate, 32 inappropriate); 2 patients received both. Programming a high-rate cutoff was associated with decreased risk of total (P = .01) and inappropriate (P = .04) shocks overall and during competition or practice. Programming long-detection intervals was associated with fewer total shocks (P = .02).	No athlete died of an arrhythmia (related or unrelated) to ICD shocks. 3 patients had sustained ventricular tachycardia below programmed detection rate, presenting as palpations and/or dizziness.	High-rate cutoff and long-detection duration programming of ICDs in athletes at risk for sudden death can reduce total and inappropriate ICD shocks without affecting survival or the incidence of transient loss-of-consciousness.	Duration data not available for all patients, reducing the power to detec significant differences; impact of medications on arrhythmia/ICD programming not addressed; long-term follow up data needed.
3.5 Sudden cardiac arrest treatment and ICD management	10	Crossley	2011	https://doi.org/10.1016/j.jacc.2010.12.012	The CONNECT (Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision) trial: the value of wireless remote monitoring with automatic clinician alerts	Evaluate if wireless remote monitoring with automatic clinician alerts reduces the time to clinical decision following a cardiac event, compared to standard in-office care.	RCT, multicenter	1997 patients with implantable cardioverter-defibrillators across 136 clinical sites	Primary: time from a clinical event to a clinical decision. Secondary: cardiovascular healthcare utilization	1) being able and willing to replace regularly scheduled in-office follow-ups with remote followups; and 2) being able to attend all required follow-up visits	1) permanent AF (constant AF for which there were no plans to attempt to restore sinus rhythm); 2) chronic warfarin therapy; 3) having had a previous ICD, CRT device, or pacemaker; 4) being 18 years of age; and 5) having a life expectancy 15 months	Wireless remote monitoring with automatic clinician alerts.	Standard in-office follow-up care.	The median time from clinical event to clinical decision per patient was reduced from 22 days in the in-office arm to 4.6 days in the remote arm (P < 0.001). The mean length of stay per cardiovascular hospitalization decreased from 4.0 to 3.3 days in the remote arm (P = 0.002).	n/a	Wireless remote monitoring with automatic clinician alerts significantly reduced the time to clinical decision and hospital stay compared to in-office follow-up, and was associated with a significant reduction in mean length of CV hospital stay.	Non-adjudication of events related to specific disease states, reliance on adverse events that resulted in healthcare utilization, and use of cost estimations due to lack of detailed cost data.
3.5 Sudden cardiac arrest treatment and ICD management	10	Hindricks	2014	https://doi.org/10.1093/eurheartj/eht207	Quarterly vs. yearly clinical follow-up of remotely monitored recipients of prophylactic implantable cardioverter-defibrillators: results of the REFORM trial	This study investigated the possibility of longer in-office follow-up intervals in primary prevention ICD patients under remote monitoring with automatic daily data transmissions from the implant memory.	RCT, non-blinded, parallel-design non-inferiority trial	155 ICD recipients (mean age 63 ± 10 years, 85.8% males)	Rate of scheduled and unscheduled ICD follow-up visits, quality of life (SF-36), and clinical outcomes.	Primary prevention ICD patients under remote monitoring who met the MADIT II trial enrollement criteria (survivors of a myocardial infarction and to have a LVEF < 30%).	Myocardial infarction within 30 days before enrolment, NYHA class IV, a secondary prevention indication for ICD therapy, or living in an area lacking the GSM mobile phone coverage needed for remote monitoring transmission.	3 month FU visits (Q-group = 78 patients)	12 month FU visits (Y-group = 77)	Compared with the 3-month follow-up interval, the 12-month interval resulted in a minor increase in the number of unscheduled follow-ups (0.64 vs. 0.27 per patient-year; P = 0.03) and in a major reduction in the total number of in-office ICD follow-ups (1.60 vs. 3.85 per patient-year; P < 0.001). No significant difference was found in mortality, hospitalization rate, or hospitalization length during the 2-year observation period. The SF-36 scores favored the 12-month intervals in the domains ‘social functioning’ and ‘mental health’	Loss to follow-up was higher in the 12-month group (10 vs. 3; p = 0.04).	In prophylactic ICD recipients under automatic daily remote monitoring, the extension of the 3-month in-office follow-up interval to 12 months appears to be save and reduce the burden of ICD follow-up visits without affecting patient outcomes.	Potential bias due to non-blinding of group assignments, QoL results may have been affected by patient's knowledge of group assignment, potential recall bias in Y-group due to longer FU time, and more than 1/3 of patients did not complete the study.

3.5 Sudden cardiac arrest treatment and ICD management	10	Mabo	2012	https://doi.org/10.1093/eurheartj/ehr419	A randomized trial of long-term remote monitoring of pacemaker recipients (the COMPAS trial)	Examine the safety and efficacy of long-term remote monitoring of pacemakers.	RCT, multicenter, non-inferiority trial	538 pacemaker recipients (mean age 76±9 years, 65% males)	Primary: proportion of patients experiencing at least one major adverse event (MAE). Secondary: hospitalizations for atrial arrhythmias and strokes, and quality of life assessments.	Pacemaker recipients capable of undergoing long-term follow-up, with devices capable of remote monitoring.	Patients with spontaneous ventricular rates <30 bpm, those unable to comply with the study protocol, or without signed informed consent.	Remote monitoring group (n=269) followed with telecardiology systems transmitting data automatically; control group (n=269) followed with standard in-office visits.	Comparison between remote monitoring follow-up and standard in-office care.	Over a follow-up of 18.3 months, 17.3% of patients in the active and 19.1% in the control group experienced at least one MAE ($P < 0.01$ for non-inferiority). Hospitalizations for atrial arrhythmias (6 vs. 18) and strokes (2 vs. 8) were fewer ($P < 0.05$), and the number of interim ambulatory visits was 56% lower ($P < 0.001$) in the active than the control group. Changes in pacemaker programming or drug regimens were made in 62% of visits in the active vs. 29% in the control group ($P < 0.001$).	Reduction in interim ambulatory visits by 56% in the active group compared to the control group. Quality of life remained unchanged in both groups.	Remote monitoring was a safe alternative to conventional care and significantly lowered the number of ambulatory visits during long-term follow-up of permanently paced patients.	Non-inferiority sstudy design, potential biases from non-blinding and from reliance on device and patient compliance for effective remote monitoring.

Subsection	Rec #	First Author	Year	DOI	Article Title	Aim	Study type	Size	Endpoints	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Comparator(s)	Outcomes (Results and P values)	Other Relevant Findings or Adverse Events	Conclusions	Limitations
5.1.3 Diagnostic and monitoring strategies for syncope	1, 2	Harmon	2015	https://doi.org/10.1016/j.jelectrocard.2015.02.001	The effectiveness of screening history, physical exam, and ECG to detect potentially lethal cardiac disorders in athletes: A systematic review/meta-analysis	To perform a systematic review/meta-analysis of evidence comparing screening strategies	meta analysis	47,137 athletes	examining the efficacy of screening with history and physicalexam (PE) based on the American Heart Association (AHA) or similar recommendations andelectrocardiogram (ECG)	(1) the studyreported on the outcomes of cardiovascular screening inathletes using history, physical exam, and ECG; (2) thehistory questions and physical exam were based on the AHArecommendations or similar guidelines; and (3) ECGs wereinterpreted using modern standards defined as criteriaattempting to account for the physiologic changes of trainingin the athletic heart.	Non-English language reports, confe-rence abstracts, and review or clinical commentary articleswere excluded.	The Preferred Reporting Items for Systematic Reviewsand Meta-Analyses (PRIMSA) guidelines were followed con-ducting and reporting this review	NA	the sensitivityand specificity of ECG was 94%/93%, history 20%/94%, and PE 9%/97%. The overall false positive rateof ECG (6%) was less than that of history (8%), or physical exam (10%). Positive likelihood ratios wereECG 14.8, history 3.22 and PE 2.93 and negative likelihood ratios were ECG 0.055, history 0.85, and PE0.93	There were a total of 160 potentially lethal cardiovascular conditions detected for a rate of 0.3% or 1in 294. The most common pathology was Wolff-Parkinson-White (67, 42%), Long QT Syndrome(18, 11%), hypertrophic cardiomyopathy (18, 11%), dilated cardiomyopathy (11, 7%), coronary arterydisease or myocardial ischemia (9, 6%) and arrhythmogenic right ventricular cardiomyopathy (4, 3%)	The most effective strategy for screening for cardiovascular disease in athletes is ECG. It is5 times more sensitive than history, 10 times more sensitive than physical exam, has higher positivelikelihood ratio, lower negative likelihood ratio and a lower false positive rate	The meta-analysis did not have the level of data to investigatethe interaction of several factors on the outcome. the criteria used toevaluate ECG results. There was a moderate degree of heterogeneity among theestimates for specificity and sensitivity.
5.1.3 Diagnostic and monitoring strategies for syncope	1, 2	Williams	2019	https://doi.org/10.1161/JAHA.119.012235	Performance of the American Heart Association (AHA) 14-Point Evaluation Versus Electrocardiography for the Cardiovascular Screening of High School Athletes: A Prospective Study	Comparison of AHA 14 points evaluation vs ECG in young athletes	prospective study	3620 high school athletes(median age, 16 years; range 13–19	The primary outcome measure was identificationof a cardiovascular disorder associated with sudden cardiac death	NA	NA	HA 14-pointevaluation and ECG	NA	The most common history responses included chest pain(8.1%), family history of inheritable conditions (7.3%), and shortness of breath (6.4%). Abnormal physical examination was presentin 356 (9.8%) athletes, and 103 (2.8%) athletes had an abnormal ECG. Sixteen (0.4%) athletes had conditions associated withsudden cardiac death. The sensitivity (18.8%), specificity (68.0%), and positive predictive value (0.3%) of the AHA 14-pointevaluation was substantially lower than the sensitivity (87.5%), specificity (97.5%), and positive predictive value (13.6%) of ECG	NA	The AHA 14-point evaluation performs poorly compared with ECG for cardiovascular screening of high schoolathletes	This study involved ECG interpretation by physiciansexperienced in ECG screening and familiar with modern standards for ECG interpretation in athletes. Thus, ECGinterpretation accuracy may not be reproducible in othersettings or with clinicians with less experience. ECGinterpretation was not blinded and occurred concurrentlywith review of the history and physical examination forms.
5.1.3 Diagnostic and monitoring strategies for syncope	1	Alboni	2001	https://doi.org/10.1016/s0735-1097(01)01241-4	Diagnostic Value of History in PatientsWith Syncope With or Without Heart Disease	To establish what historical findings are predictive of the cause of syncope	porspective study	341 no atheletes patients were analyzed. The mean age of the patients was61620 years; 184 were men	To define the cause of syncope through the historical findings	syncopal episode in the previous two months (defined as a brief, self-limited loss of consciousness with the inability to maintain postural tone) and were ≥18 years	incomplete evaluation or protocol violation	Each patientwas interviewed using a standard questionnaire.	NA	In patients with certain orsuspected heart disease, the most specific predictors of a cardiac cause were syncope in thesupine position or during effort, blurred vision and convulsive syncope. Significant andspecific predictors of a neurally mediated cause were time between the first and last syncopalepisode.4 years, abdominal discomfort before the loss of consciousness and nausea anddiaphoresis during the recovery phase. In the patients without heart disease, palpitation wasthe only significant predictor of a cardiac cause	NA	The presence of suspected or certain heart disease after the initial evaluation is a strong predictor of a cardiac cause of syncope. A few historical findings are useful to predict cardiac and neurally mediated syncope in patients with and without heart disease.	In syncope, there is no diagnostic "gold"standard against which other diagnostic tests may be mea-sured;
5.1.3 Diagnostic and monitoring strategies for syncope	2	Ajam	2022	https://doi.org/10.1186/s44156-022-00012-7	Cardiac imaging findings in anomalous origin of the coronary arteries from the pulmonary artery; narrative review of the literature	Utility of echocardiography in evaluation of ARCAPA	Narrative review	27 cases	Diagnosis of ARCAPA by echocardiography	case reports which described cases aged above 18 with the confirmed origin of the right coronary artery (RCA) from the pulmonary artery without other congenital cardiac anomalies	NA	NA	NA	Echocardiography found RCA origin in PA in 4 (14.3%) of patients	NA	echocardiography can be a convenient and noninvasive method whenever ARCAPA is suspected	echocardiographic findings are highly operator dependent. only included published ARCAPA cases.
5.1.3 Diagnostic and monitoring strategies for syncope	2, 4	Basso	2000	https://doi.org/10.1016/s0735-1097(00)00566-0	Clinical Profile of Congenital CoronaryArtery Anomalies With Origin From theWrong Aortic Sinus Leading toSudden Death in Young Competitive Athletes	clinical profile of athletes with SCD and congenital coronary anomalies	retrospective	27	characterizing the clinical profile	1. <35yo, 2. autopsy with coronary artery anomalies, 3. no history of alcohol or toxic abuse. 4. Competitive athlete at the time of death.	NA	Evaluation	NA	10/27 w symptoms, 4/10 with syncope. Resting/exercise ECG is not enough to define congenital coronary artery anomalies in athletes.	NA	a history of exertional syncope or chest pain requiresexclusion of this anomal	retrospective study, small group.
5.1.3 Diagnostic and monitoring strategies for syncope	2	Brunetti	2023	https://doi.org/10.1093/eurjpc/zwac224	Reproducibility of ventricular arrhythmias at exercise testing for prediction of non-ischaemic left ventricular scar in athletes	tested the diagnostic value of VA reproducibility at repeated exercise testing (ET)	Observational cohort study	75 athletes	VA reproducibility in repeated ET as a marker of non ischemic left ventricular scar in cCMR.	Athletes were included if (i) they showed ≥3 PVBs or ≥1 repetitive VA (couplets or non-sustained VT) on screening ET; (ii) underwent CMR for exclusion of an underlying substrate; (iii) had undergone a second ET within 12 months, off-therapy and with the same modality (25–50 W/min ramp protocol on cycle-ergometer)	Exclusion criteria were the following: (i) isolated, monomorphic PVBs with a left bundle branch block (LBBB)/inferior QRS axis (infundibular) or right bundle branch block (RBBB) and QRS duration <130 ms (fascicular) that were suppressed by exercise, because they carry a low risk of an underlying pathological substrate; (ii) previous cardiac arrest or sustained ventricular tachycardia, positive family history for cardiomyopathy or sudden premature death, suspicious symptoms (particularly pre-syncope or syncope), abnormal ECG changes or echocardiography because they are reasons for CMR prescription regardless of VA characteristics.	Repeated stress testing	cCMR	At first ET, athletes with NILVS showed a higher prevalence of exercise-induced VA (93% vs. 53%, P < 0.001), while other VA characteristics did not differ between groups. At repeated ET, reproducibility was observed in 97% of athletes with vs. 13% without NILVS (P < 0.001). The remaining 87% of athletes with normal CMR either did not show any VA at repeated ET (59%) or showed arrhythmias with different patterns, mostly infundibular. Reproducibility yielded a positive predictive value for NILVS of 83% and a negative predictive value of 98%.	NA	VA reproducibility at repeated ET predicted an underlying NILVS in athletes with VA and otherwise normal clinical work-up	single-centre observational study on a relatively small sample of predominantly male Caucasian athletes who were referred to our third-level centre and who needed to meet several inclusion criteria.

5.1.3 Diagnostic and monitoring strategies for syncope	2	Calkins	1995	https://doi.org/10.1016/0002-8703(95)90398-4	Clinical presentation and long-term follow-up of athletes with exercise-induced vasodepressor syncope	The purpose of this study is to report on a series of patients who were referred for evaluation of syncope that occurred during or immediately after exercise and in whom a diagnosis of vasodepressor syncope was established	Case series	9 women and 8 men; mean age of 28 ± 17 years	to determine the frequency and type of recurrent symptoms	NA	NA	NA	NA	The mean age at onset of symptoms was 23 ± 16 years. In 10 patients syncope occurred only in association with exercise. Pharmacologic therapy was successful in normalizing the patients' response to upright tilt in each of the 10 patients in whom it was attempted. During a mean follow-up period of 35 ± 9 months, none of the patients placed on pharmacologic therapy has had recurrent syncope. Seventeen (88%) of 19 patients have resumed participation in athletics	NA	vasodepressor syncope is a cause of syncope in athletes and that patients with exercise-related vasodepressor syncope can safely continue to participate in athletics.	NA
5.1.3 Diagnostic and monitoring strategies for syncope	2	Cantinotti	2021	https://doi.org/10.3390/healthcare9020231	Echocardiographic Screening of Anomalous Origin of Coronary Arteries in Athletes with a Focus on High Take-Off	to analyze the feasibility and the detection rate of AAOCA by echocardiography in children and adults	Systematic review	33,592 children and adults (age range: 12-49 years)	to diagnose the high take-off of coronary arteries	NA	NA	ECHO	NA	Echocardiographic evaluation of the origins of coronary arteries by transthoracic echocar-diography is feasible and accurate.	NA	screening of AAOCA by echocardiography is feasible and accurate when appropriate examinations are performed; however, specific acoustic windows and definitions of defects other than AAOCA need to be standardized to improve sensitivity and specificity	TE ECHO and 3D ECHO were not used.
5.1.3 Diagnostic and monitoring strategies for syncope	2	Davis	2001	https://doi.org/10.1016/s0735-1097(00)01136-0	Major coronary artery anomalies in a pediatric population: incidence and clinical importance	To determine the incidence and clinical significance of major coronary artery anomalies in asymptomatic children using transthoracic two-dimensional echocardiography	prospective	2,388 children and adolescents	anomalous origin of their coronary arteries identified by ECHO	This includes patients referred for evaluation of innocent murmurs as well as for functional assessments	NA	ECHO	NA	Four (0.17%) were identified with anomalous origin of their coronary arteries: two with ALMCA and two with ARCA. The two patients with ALMCA were 15 and 18 years of age, and the two with ARCA were 2½ weeks and 12 years of age. All patients were male and three of the four were athletes, with one being a highly competitive swimmer. The reasons for referral to a cardiologist were irregular rhythm (two patients), evaluation of a murmur (one patient) and to rule out Marfan syndrome (one patient). None of the four patients had a family history for any unexplained sudden cardiac death; one patient had a family history of mitral valve prolapse.	NA	Although directed echocardiography can generally confirm the diagnosis of anomalous origin of coronary arteries, this exam's sensitivity has not been fully established. Negative findings with regard to coronary artery abnormalities in a patient referred for cardiovascular symptoms do not preclude the performance of further evaluation	Prospective evaluation. No comparator.
5.1.3 Diagnostic and monitoring strategies for syncope	2	Hayashi	2012	https://doi.org/10.1093/europace/eus031	The role of stress test for predicting genetic mutations and future cardiac events in asymptomatic relatives of catecholaminergic polymorphic ventricular tachycardia probands	to elucidate the value of exercise-stress test (EST) for predicting mutations and future cardiac events in CPVT-family relatives.	prospective study	67	EST as a diagnostic tool in asymptomatic relatives of CPVT	asymptomatic relatives of 17 CPVT probands	NA	EST and genetic testing	positive vs negative stress testing	Exercise-stress test, which was considered positive with the induction of ventricular tachycardia or premature ventricular contractions consisting of bigeminy or couplets, was positive in 17 relatives (25%). Genetic analysis disclosed mutations in 16 of these 17 relatives (94%) and in 16 of the 50 relatives (32%) with negative exercise-stress test; the sensitivity and specificity for a positive genotype were 50 and 97%, respectively (P< 0.001).	Among 32 mutation carriers, cardiac events occurred in 7 of the 16 relatives with positive and 2 of the 16 relatives with negative exercise-stress test during the follow-up period of 9.6 ± 3.8 years, and four with positive and two with negative stress test were not on regular beta-blocker treatment at these events. In the 16 relatives with positive stress test, those on beta-blocker treatment demonstrated a trend of lower cardiac event rate (Log-rank P= 0.054).	In asymptomatic relatives of CPVT probands, exercise-stress test can be used as a simple diagnostic tool	As exercise-stress tests were repeated in a limited number of the patients, we cannot confirm the usefulness of the repeated stress tests categorically. Small sample size.
5.1.3 Diagnostic and monitoring strategies for syncope	2	Horner	2008	https://doi.org/10.1016/j.hrthm.2008.08.038	Ventricular ectopy during treadmill exercise stress testing in the evaluation of long QT syndrome	to determine the diagnostic importance of exercise-induced ventricular ectopy in the evaluation of LQTS.	prospective study	381	Association of Ventricular ectopy induced in a treadmil exercise stress test with LQTS vs CPVT.	From 1998 to 2006, 381 patients with a referral diagnosis of LQTS underwent a treadmill exercise stress test	NA	Stress test	NA	exercise-induced ventricular ectopy beyond single PVCs was far more common among patients with CPVT (14/16 [88%]; P <.0001) and included PVCs in bigeminy in 13 (81%), couplets in 7 (47%), and nonsustained ventricular tachycardia in 3 (19%). Of note, bidirectional VT was not present in any of the 16 patients diagnosed with CPVT, including the 10 with genetically proven, RYR2-mediated CPVT.	NA	Exercise-induced ventricular ectopy exceeding single PVCs was observed in less than 10% of patients referred for LQTS evaluation, including 2% of patients ultimately dismissed as normal. Exercise-induced bigeminy is strongly associated with the presence of significant cardiovascular disease but is far more likely to indicate CPVT than LQTS.	Prospective study. Small sample size.
5.1.3 Diagnostic and monitoring strategies for syncope	2	Leren	2017	https://doi.org/10.1016/j.jcmg.2016.06.011	Combination of ECG and Echocardiography for Identification of Arrhythmic Events in Early ARVC	to investigate early markers of arrhythmic events (AEs) and improve risk stratification in early arrhythmogenic right ventricular cardiomyopathy (ARVC).	cross-sectional study	162 included subjects with ARVC	Risk stratification of arrhythmias and SCD in subjects with ARVC	ARVC index patients AND mutation-positive family members	NA	2D-ECHO, ECG, CMR and genetic testing.	NA	Of 162 included subjects with ARVC (41 ± 16 years of age, 47% female), 73 had early ARVC, including mutation positive family members not fulfilling definite ARVC diagnosis. AEs occurred in 15 (21%) subjects with early ARVC. Those with AEs in early disease had larger RV diameter (40 ± 4 mm vs. 37 ± 5 mm), more pronounced RVMD (39 ± 15 ms vs. 26 ± 11 ms), and more pathological signal averaged ECGs compared with those without AEs (all p ≤ 0.05)	Adding measurements of RV diameter and RVMD to electrical parameters improved identification of subjects with AEs compared with electrical parameters alone (p = 0.05).	The addition of early structural changes increased the ability to detect subjects with arrhythmic events compared with electrical parameters alone	This study was cross-sectional in design with the inherent limitations. The limited number of patients with early ARVC makes the model for identifying subjects with arrhythmic events vulnerable to overfitting
5.1.3 Diagnostic and monitoring strategies for syncope	2	Quinto	2023	https://doi.org/10.1080/15438627.2021.1937162	Can exercise test intensity and modality affect the prevalence of arrhythmic events in young athletes?	to compare submaximal Harvard Step Test (HST) with incremental Maximal Exercise Test (MET) on treadmill to induce and detect arrhythmias in younger athletes	Cohort study	1000 athletes	Incidence of arrhythmias	NA	NA	HST vs MET	NA	Incidence of arrhythmias remained higher for MET also considering separately exercise phase (0.8% vs. 5.2%; p < 0.001) and recovery phase (2.0% vs. 6.0%; p < 0.01)	NA	Higher test intensity and longer exercise duration might influence test outcomes, making MET more arrhythmogenic.	No randomization.

5.1.3 Diagnostic and monitoring strategies for syncope	4	Angelini	2018	https://doi.org/10.14503/THIJ-18-6645	High-Risk Cardiovascular Conditions in Sports-Related Sudden Death: Prevalence in 5,169 Schoolchildren Screened via Cardiac Magnetic Resonance	prevalence of high-risk cardiovascular conditions (hr-CVC) that predispose young people to sudden cardiac death (SCD)	prospective screening	5169 school children	prevalence of hr-CVC	informed consent AND Enrollment in middle or high school .	history of cardiac disease was an exclusion criterion.	CMR	NA	CMR results revealed 76 previously undiagnosed cases of hr-CVC (1.47% of the total cohort)	NA	our estimate is accurate, only 1.47% of our partici- pants will need specialized secondary evaluations. The remaining 98.53% can probably be reassured about their cardiac health on the basis of a single 30-minute screening study	creening study was voluntary, so our f indings are potentially subject to psychological, so-cial, and economic pre-testing biases
5.1.3 Diagnostic and monitoring strategies for syncope	4	Gao Y	2022	https://doi.org/10.3389/fped.2022.879753	Congenital Anomalous Origin of Coronary Artery Disease in Children With Syncope: A Case Series	to analyze the characteristics of congenital anomalous origin of coronary artery in pediatric patients with syncope.	restrospective	eight patients were included in the study with a median age of 12.5 ± 2.7 (8-16) years	relation of syncope and congenital coronary artery disease.	NA	NA	coronary artery computed tomography angiography (CTA)	NA	ECG and echocardiography are the common methods for investigating cardiac syncope, they have limited ability to find coronary artery anomalies	NA	When coronary artery anomalies are suspected, coronary CTA should be considered.	restrospective, small sample size.
5.1.3 Diagnostic and monitoring strategies for syncope	6	Locati	2016	https://doi.org/10.1093/europace/euv311	External prolonged electrocardiogram monitoring in unexplained syncope and palpitations: results of the SYNARR-Flash study	linical work-up of unexplained syncope and/or sustained palpitations of suspected arrhythmic origin.	prospective	395 patients (57.7% females, 56.9+18.7 years, 28.1%	arrhythmic cause identification	both the following inclusion criteria: (i) recent (within 1month) episode of syncope or sustained palpitations (index event), afterbeing discharged from emergency room or hospitalization without aconclusive diagnosis, and (ii) suspected arrhythmic origin according tothe clinical features defined in the 2009 Syncope Guidelines,	NA	External prolonged ECG	NA	the 4-week diagnostic yield was 71.6% and predictors of diagnostic events were history of recurrentpalpitations (P,0.001) and early start of recording (P%0.001)	NA	The 4-week external ECG monitoring can be considered as first-line tool in the diagnostic work-up of syncope andpalpitation.	prospective trial
5.1.3 Diagnostic and monitoring strategies for syncope	6	Reed	2018	https://doi.org/10.1136/emermed-2018-207570	Diagnostic yield of an ambulatory patch monitor in patients with unexplained syncope after initial evaluation in the emergency department: the PATCH-ED study	Benefit of patch monitor in unexplained syncope	Prospective pilot study	16 years or over (86 patients)	Diagnosing underlying arrhythmia in ED syncope	Patients aged 16 years or over who presented between 17 November 2015 and 16 June 2017 within 6 hours of an episode of syncope and whose syncope remained unexplained after ED assessment	obvious underlying cause after ED assessment	patch monitor	single-centre, prospective pilot study with a historical unmatched comparator group	90-day diagnostic yield for symptomatic significant arrhythmia was 10.5% (95% CI 4.0 to 16.9; 9 of 86) versus 2.0% (95% CI 0.9 to 3.1; 12 of 603) in the comparator group	NA	early ambulatory ECG monitoring in ED patients with unexplained syncope is probably warranted	prospective
5.1.3 Diagnostic and monitoring strategies for syncope	6	Solbiati	2016	https://doi.org/10.1002/14651858.CD011637.pub2	Implantable loop recorder versus conventional diagnostic workup for unexplained recurrent syncope	To assess the incidence of mortality, quality of life, adverse events and costs of ILRs versus conventional diagnostic workup in people with unexplained syncope	systematic review	579 participants	Mortality	randomised controlled trials of adult participants (i.e. ≥ 18 years old) with a diagnosis of unexplained syncope comparing ILR with standard diagnostic workup	NA	NA	NA	the meta-analysis showed no evidence of a difference in the risk of long-term mortality between participants who received ILR and those who were managed conventionally at follow-up (RR 0.97, 95% CI 0.41 to 2.30; participants = 255; studies = 2; very low quality evidence) with no evidence of heterogeneity.	NA	there is no evidence that an ILR-based diagnostic strategy reduces long-term mortality as compared to a standard diagnostic assessment (very low quality evidence). No data were available for short-term all-cause mortality. Moderate quality evidence shows that an ILR-based diagnostic strategy increases the rate of aetiologic diagnosis as compared to a standard diagnostic pathway. No conclusive data were available on the other end-points analysed.	only two studies reported data on mortality and none of them had considered death as a primary endpoint
5.1.3 Diagnostic and monitoring strategies for syncope	7	Krahn	1999	https://doi.org/10.1161/01.cir.99.3.406	Use of an extended monitoring strategy in patients with problematic syncope. Reveal Investigators	to determine the cause of syncope	Prospective Observational	85	NA	recurrent undiagnosed syncope	NA	implantable loop recorder	NA	An arrhythmia was detected in 42% of patients who recorded a rhythm during recurrent symptoms, with bradycardia present in 18 and tachycardia in 3. Five of the 18 bradycardic patients and 2 additional sinus rhythm patients received a clinical diagnosis of neurally mediated syncope. Patients who experienced presyncope were much less likely to record an arrhythmia during symptoms compared with recurrence of syncope (24% versus 70%, *P*=0.0005)	No	The strategy of prolonged monitoring is effective and safe in patients with problematic syncope	a small proportion of patients were unable to activate the device after a spontaneous event
5.1.3 Diagnostic and monitoring strategies for syncope	7	Radovanović	2021	https://doi.org/10.1111/anec.12864	Diagnostic value of implantable loop recorders ILR) in patients with unexplained syncope or palpitations	to determine ILR diagnostic value in patients with unexplained syncope, presyncope, or palpitations suggesting cardiac arrhythmias.	retrospective, observational, single-center study.	181	arrhythmia as the cause of syncope or palpitations.	patients with unexplained syncope, presyncope, or recurrent palpitations suggesting cardiac arrhythmia	NA	ILR	NA	ILR was diagnostic in 98 patients (54.1%). There was no significant difference in diagnostic value of ILR in regard to the baseline patients' characteristics	The mean time to occurrence of the diagnostic event was 11.1 ± 9.6 months. The time to occurrence of a diagnostic event did not differ significantly between patients who underwent basic as compared to extended diagnostics before ILR implantation.	ILR was able to achieve an etiological diagnosis in 54.1% of patients with unexplained syncope, presyncope, or palpitations suggesting cardiac arrhythmias. In a subgroup of patients with recurrent palpitations, ILR was significantly less diagnostic than in patients with syncope or presyncope	A small size population. No comparator.

5.1.3 Diagnostic and monitoring strategies for syncope	8	Gatzoulis	2009	https://doi.org/10.1111/j.1542-474X.2009.00286.x	Correlation of noninvasive electrocardiography with invasive electrophysiology in syncope of unknown origin: implications from a large syncope database	utility of noninvasive electrocardiographic evaluation (12-lead ECG and 24-hour ambulatory electrocardiographic recordings) to predict electrophysiology study results in patients with undiagnosed syncope	Observational study	421 patients	to predict electrophysiology testing outcomes	patients with undiagnosed syncope who had an electrocardiogram (ECG), an electrophysiology study, and 24-hour ambulatory monitoring	NA	electrocardiogram (ECG), an electrophysiology study, and 24-hour ambulatory monitoring	NA	Patients were divided into four groups: group 1, abnormal ECG and ambulatory monitor; group 2, abnormal ECG only; group 3, abnormal ambulatory monitor; and group 4, normal ECG and ambulatory monitor. The likelihood of finding at least one abnormality during electrophysiologic testing among the four groups was highest in group 1 (82.2%) and lower in groups 2 and 3 (68.1% and 33.7%, respectively). In group 4, any electrophysiology study abnormality was low (9.1%). Odds ratios (OR) were 35.9 (P < 0.001), 17.8 (P < 0.001), and 3.5 (P = 0.064) for abnormal findings on electrophysiology study, respectively (first three groups vs the fourth one).	NA	Abnormal ECG findings on noninvasive testing are well correlated with potential brady- or/and tachyarrhythmic causes of syncope, in electrophysiology study of patients with undiagnosed syncope.	Limitations of Electrophysiology Test (sensibility, espicificity)
5.1.3 Diagnostic and monitoring strategies for syncope	8	Sagrista-Sauleda	2001	https://doi.org/10.1053/euhj.2000.2398	Variations in diagnostic yield of head-up tilt test and electrophysiology in groups of patients with syncope of unknown origin	To assess the diagnostic yield of the head-up tilt test and electrophysiology in patients with syncope of unknown origin	Observational study	600	abnormal findings	clinical suspect of syncope of unknown origin.	NA	Tilt test	NA	The diagnostic yield from electrophysiology was higher in patients with an abnormal ECG than in those with a normal ECG (22% vs 3·7%,P <0·0005, OR 7·1), and it was especially low in patients with a normal ECG and without organic heart disease (2·6%).	NA	The diagnostic yield of the tilt test and electrophysiology differs in groups of patients with syncope of unknown origin, established according to simple clinical criteria	Simple selection of patients based in simple clinical criteria.
5.1.3 Diagnostic and monitoring strategies for syncope	9	Brignole	1993	https://doi.org/10.1016/0735-1097(93)90426-2	Role of autonomic reflexes in syncope associated with paroxysmal atrial fibrillation	to evaluate the role of autonomic reflexes in the genesis of syncope associated with the onset of paroxysmal atrial fibrillation.	cohort study	56	syncope or atrial fibrillation induction	unexpected syncope preceded and followed of palpitations. Documentations of atrial fibrillation. Abscense of AV conduction alterations or accesory bypass tracts.	Other causes of syncope. Severe heart failure. Recent acute illness.	Carotid sinus massage and head-up tilt testing	Patients with syncope and AF vs AF without syncope.	Results of carotid sinus massage were positive in 15 (37%) of 40 patients but in no control subjects (p = 0.002). Head-up tilt test findings were positive in 25 (66%) of 38 patients and in 2 (12%) of 16 control subjects (p = 0.0004). The induction of atrial fibrillation in the upright position elicited syncope in 16 (42%) of 38 patients but in none of 16 control subjects (p = 0.001). At the beginning of atrial fibrillation, systolic blood pressure was lower in patients than in control subjects (88 ± 32 vs. 127 ± 32 mm Hg), whereas mean heart rate was similar (142 ± 35 vs. 134 ± 25 beats/min). The correlation between heart rate and systolic blood pressure was weak (r = 0.35), and in five patients syncope occurred at a heart rate ≤130 beats/min. At the time of syncope, heart rate decreased (–12 ± 21 beats/min) in patients with induced syncope, whereas it remained unchanged in patients without induced syncope (+1 ± 17 beats/min, p = 0.04) or slightly increased in control subjects (+9 ± 21 beats/min, p = 0.009)	NA	Patients with syncope associated with paroxysmal atrial fibrillation are predisposed to an abnormal neural response during both sinus rhythm and arrhythmia	Small sample size
5.1.3 Diagnostic and monitoring strategies for syncope	9	Fu	2012	https://doi.org/10.1113/jphysiol.2011.224998	Cardiac output and sympathetic vasoconstrictor responses during upright tilt to presyncope in healthy humans	Patients with syncope associated with paroxysmal atrial fibrillation are predisposed to an abnormal neural response during both sinus rhythm and arrhythmia	Retrospective analisys	25	haemodynamic responses and baroreflex sensitivity	subjects who developed presyncope during a tilt-table test with microneurographic recordings were included	Women taking oral contraceptives were excluded or recurrent syncope.	upright tilt test	NA	muscle sympathetic nerve activity, haemodynamic responses and baroreflex sensitivity during early tilting were not different between presyncopal subjects and controls.	Hypotension was mediated by a drop in cardiac output in all presyncopal subjects, accompanied by a decrease in total peripheral resistance in 16 of them (64%, group A). In the other 9 subjects, total peripheral resistance was well maintained even at presyncope (36%, group B). Cardiac output was smaller (3.26 ± 0.34 (SEM) vs. 5.02 ± 0.40 l min−1, P = 0.01), while total peripheral resistance was greater (1327 ± 117 vs. 903 ± 80 dyn s cm−5, P < 0.01) in group B than group A at presyncope	An intrinsic impairment of vasomotor responsiveness and sympathetic baroreflex function is not the cause of neurally mediated (pre)syncope in this population	beat-to-beat haemodynamics were derived from the Modelflow method (NO GOLD STANDARD). none of our subjects had a history of recurrent syncope, and these subjects may be different from clinical patients with recurrent syncope. upright tilt was terminated at presyncope but not syncope.
5.1.3 Diagnostic and monitoring strategies for syncope	9	Leitch	1992	https://doi.org/10.1161/01.cir.85.3.1064	Syncope associated with supraventricular tachycardia. An expression of tachycardia rate or vasomotor response?	To explore the mechanism of syncope during supraventricular tachycardia	Observational study	22	syncope induction	Patient with syncope and SVT	NA	Tilst test and E. Study.	NA	The cycle length of tachycardia when upright was shorter than when supine (297±9 compared with 357± 10 msec, p<0.001), and mean blood pressure fell to a greater extent after the onset of tachycardia (fall in mean blood pressure, 53±6 compared with 24±3 mm Hg, p<0.001). Mean blood pressure correlated significantly with tachycardia cycle length when supine (r=0.58, p=0.005) but not when tilted upright (r=0.18, p=0.45). Syncope occurred in seven patients during upright tachycardia. These seven patients had a greater fall in mean blood pressure with upright tachycardia than the 15 patients without syncope (fall in mean blood pressure, 70+4 compared with 45±5 mm Hg,p=0.01), but there was no difference in the tachycardia cycle length (311+ 10 compared with 290+ 11 msec,p=0.29). Six of the seven patients with tachycardia-induced syncope also had syncope with tilt testing in sinus rhythm compared with four of the 15 patients without tachycardia-induced syncope (p =0.02).	NA	syncope during supraventricular tachycardia is related to vasomotor factors and does not predict a more rapid tachycardia rate	the mechanism of spontaneous syncope could not be determined because of technical limitations in monitoring and because of the low frequency of spontaneous syncopal episodes.

5.2.2 Diagnostic strategies in athletes with palpitations	1	Harmon	2015	https://doi.org/10.1016/j.jelectrocard.2015.02.001	The effectiveness of screening history, physical exam, and ECG to detect potentially lethal cardiac disorders in athletes: A systematic review/meta-analysis	To perform a systematic review/meta-analysis of evidence comparing screening strategies	meta analysis	47,137 athletes	examining the efficacy of screening with history and physicalexam (PE) based on the American Heart Association (AHA) or similar recommendations andelectrocardiogram (ECG)	(1) the studyreported on the outcomes of cardiovascular screening inathletes using history, physical exam, and ECG; (2) thehistory questions and physical exam were based on the AHArecommendations or similar guidelines; and (3) ECGs wereinterpreted using modern standards defined as criteriaattempting to account for the physiologic changes of trainingin the athletic heart.	Non-English language reports, confe-rence abstracts, and review or clinical commentary articleswere excluded.	The Preferred Reporting Items for Systematic Reviewsand Meta-Analyses (PRIMSA) guidelines were followed con-ducting and reporting this review	NA	the sensitivityand specificity of ECG was 94%/93%, history 20%/94%, and PE 9%/97%. The overall false positive rateof ECG (6%) was less than that of history (8%), or physical exam (10%). Positive likelihood ratios wereECG 14.8, history 3.22 and PE 2.93 and negative likelihood ratios were ECG 0.055, history 0.85, and PE0.93	There were a total of 160 potentially lethal cardiovascular conditions detected for a rate of 0.3% or 1in 294. The most common pathology was Wolff-Parkinson-White (67, 42%), Long QT Syndrome(18, 11%), hypertrophic cardiomyopathy (18, 11%), dilated cardiomyopathy (11, 7%), coronary arterydisease or myocardial ischemia (9, 6%) and arrhythmogenic right ventricular cardiomyopathy (4, 3%)	The most effective strategy for screening for cardiovascular disease in athletes is ECG. It is5 times more sensitive than history, 10 times more sensitive than physical exam, has higher positivelikelihood ratio, lower negative likelihood ratio and a lower false positive rate	The meta-analysis did not have the level of data to investigatethe interaction of several factors on the outcome. the criteria used toevaluate ECG results. There was a moderate degree of heterogeneity among theestimates for specificity and sensitivity.
5.2.2 Diagnostic strategies in athletes with palpitations	2	Boraita	2022	https://doi.org/10.3389/fcvm.2022.896148	Holter-determined arrhythmias in young elite athletes with suspected risk: Insights from a 20-year experience	We assessedthe occurrence of cardiac rhythm alterations, as well as the associationbetween echocardiography-determined conditions and rhythm alterations	restrospective	6579	prevalence of dangerous" ventriculararrhythmias associated with underlying serious cardiac structural pathologies.	NA	NA	underwent in-depth cardiological examination (including echocardiographicevaluation, and resting and exercise electrocardiogram [ECG]) between01/02/1998 and 12/31/2018. Holter monitoring was performed in thosereporting cardiovascular symptoms, with suspicion of cardiac structuralabnormalities potentially associated with dangerous arrhythmias, or withresting/exercise ECG features prompting a closer examination	NA	inus bradycardia was themost common finding (present in 96% of cases), yet with a relatively lowproportion of severe (<30 bpm) bradycardia (12% of endurance athletes duringnight-time). Premature atrial and ventricular beats were alsocommon (61.9and 39.4%, respectively) but sinus pauses≥3s, high-grade atrioventricularblocks, and atrial fibrillation/flutter were rare (<1%). Polymorphic prematureventricular contractions (PVC, 1.4%) and idioventricular rhythm (0.005%)were also rare. PVC couplets were relatively prevalent (10.7%),but complexventricular arrhythmias were not frequent (PVC triplets: 1.8%; sustainedventricular tachycardia: 0.0%; and nonsustained ventricular tachycardia: 1.5%).	no associations were found between arrhythmias And major cardiac structural alterations (includingmitral prolapse)	Irrespective of the sports discipline, "dangerous" ventriculararrhythmias are overall infrequent even among young elite athletes whorequire Holter monitoring due to the presence of symptoms or abnormalechocardiographic/ECG findings, and do not seem to be associated withunderlying serious cardiac structural pathologies	retrospective design with no subsequent follow-up, theyoung age of most elite athletes (<30 years on average,albeit with a mean 10-year competition experience). Holter analysis of only part (~10%) of the total sample
5.2.2 Diagnostic strategies in athletes with palpitations	3	Peritz	2015	https://doi.org/10.1016/j.jelectrocard.2015.07.010	Smartphone ECG aids real time diagnosis of palpitations in the competitive college athlete	To detect common arrhythmias using Smartphone heart rate monitors	Case series	6	Identifications of arrhythmias.	NA	NA	AliveCor Monitor	NA	NA	NA	A smartphone ECG is neither a substitute for a 12-lead ECG nor a replacement for a thorough history and physical examination	Small sample size, no comparator.
5.2.2 Diagnostic strategies in athletes with palpitations	4	Jewson	2022	https://doi.org/10.1093/ehjcr/ytac126	Use of a smartphone electrocardiogram to diagnose arrhythmias during exercise in athletes: a case series	To identify arrhythmias in athletes using Smartphone electrocardiograms (ECGs)	Case series	6	Identifications of arrhythmias.	NA	NA	Alivecor Kardia device	NA	NA	NA	The utility of detecting no arrhythmia during symptoms let reassurance and confidence across all cases is perhaps the most valuable aspect of this device	Small sample size, no comparator.

Subsection	Rec #	First Author	Year	DOI	Article Title	Aim	Study type	Size	Endpoints	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Comparator(s)	Outcomes (Results and P values)	Other Relevant Findings or Adverse Events	Conclusions	Limitations
6.1 Evaluation of ventricular arrhythmias in athletes	1	Dukes	2015	https://doi.org/10.1016/j.jacc.2015.04.062	Ventricular Ectopy as a Predictor of Heart Failure and Death		Prospective cohort study										
6.1 Evaluation of ventricular arrhythmias in athletes	1	Baman	2010	https://doi.org/10.1016/j.hrthm.2010.03.036	Relationship between burden of premature ventricular complexes and left ventricular function		Retrospective cohort study										
6.1 Evaluation of ventricular arrhythmias in athletes	2	Brunetti	2023	https://doi.org/10.1093/eurjpc/zwac224	Reproducibility of ventricular arrhythmias at exercise testing for prediction of non-ischaemic left ventricular scar in athletes	tested the diagnostic value of VA reproducibility at repeated exercise testing (ET)	Prospective cohort study										
6.1 Evaluation of ventricular arrhythmias in athletes	2	Jacobsen	1978	https://doi.org/10.1016/s0022-3476(78)80066-3	Premature ventricular contractions in normal children		Prospective cohort study										
6.1 Evaluation of ventricular arrhythmias in athletes	4	Biffi	2002	https://doi.org/10.1016/S0735-1097(02)01977-0	Long-term clinical significance of frequent and complex ventricular tachyarrhythmias in trained athletes	Clarify the clinical relevance of ventricular tachyarrhythmias assessed by 24-h ambulatory electrocardiograms (ECG) in a large, unique, and prospectively evaluated athletic population.	Prospective cohort study	355	Cardiovascular events				Group A with > or = 2,000 PVDs/24 h (n = 71); Group B with > or = 100 <2,000 PVDs/24 h (n = 153); and Group C with only <100 PVDs/24 h (n = 131).	Cardiac abnormalities were detected in 26 of the 355 study subjects (7%) and were significantly more common in Group A (21/71, 30%) than in Group B (5/153, 3%) or Group C athletes (0/131, 0% p < 0.001). Only the 71 athletes in Group A were excluded from competition. During follow-up (mean, 8 years), 70 of 71 athletes in Group A and each of the 284 athletes in Groups B and C have survived without cardiovascular events.		Frequent and complex ventricular tachyarrhythmias are common in trained athletes and are usually unassociated with underlying cardiovascular abnormalities.	
6.1 Evaluation of ventricular arrhythmias in athletes	7	Crescenzi	2021	https://doi.org/10.1161/JAHA.120.018206	Predictors of Left Ventricular Scar Using Cardiac Magnetic Resonance in Athletes With Apparently Idiopathic Ventricular Arrhythmias		Prospective cohort study, multicenter										
6.1 Evaluation of ventricular arrhythmias in athletes	7	Dello Russo	2011	https://doi.org/10.1016/j.hrthm.2011.07.021	Concealed cardiomyopathies in competitive athletes with ventricular arrhythmias and an apparently normal heart: role of cardiac electroanatomical mapping and biopsy		Prospective cohort study										
6.1 Evaluation of ventricular arrhythmias in athletes	8	Venlet	2017	https://doi.org/10.1016/j.jacc.2016.11.041	Isolated Subepicardial Right Ventricular Outflow Tract Scar in Athletes With Ventricular Tachycardia		Retrospective cohort study										
6.1 Evaluation of ventricular arrhythmias in athletes	8	Corrado	2008	https://doi.org/10.1016/j.jacc.2007.11.027	Three-dimensional electroanatomical voltage mapping and histologic evaluation of myocardial substrate in right ventricular outflow tract tachycardia		Prospective cohort study										
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	1	Marcus	2023	https://doi.org/10.1056/NEJMoa2204737	Acute Effects of Coffee Consumption on Health among Ambulatory Adults	Evaluate the effects of caffeine on ectopy.	Prospective, randomized, crossover.	100 adults	14 days, ectopy as read by ambulatory patch monitor	>18 yo, consumed coffee at least once per year	CIEDs, AVN blockade or AAD	Caffeine	No caffeine	58 PACs vs 53 PACs and 154 PVCs vs 102 PVCs (rate ratio 1.51; 95% CI 1.18 to 1.94).	N/A	Small sample size of young and healthy participants, unblinded.	Low number of patients and ectopy
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	1	von Rotz	2017	https://doi.org/10.1136/heartjnl-2016-309632	Risk factors for premature ventricular contractions in young and healthy adults	To assess risk factors for PVCs in the young.	Observational	2048 patients.	N/A	Patients aged between 25 and 41 years were asked to par- ticipate in the "Genetic and phenotypic determi- nants of blood pressure and other cardiovascular risk factors" (GAPP) study.	Main exclusion criteria were an established cardiovascular disease, known obstructive sleep apnoea, renal failure, current intake of antidiabetic drugs, other severe comorbidities or a body mass index (BMI) >35kg/m2.	N/A	NA	N/A	In multivariable regression analyses, we found 17 significant risk factors for PVC frequency. Low educational status (risk ratio (RR) 3.33; 95% CI 1.98 to 5.60), body height>median (1.58, 95% CI 1.11 to 2.24) and increasing levels of waist:hip ratio (2.15, 95% CI 1.77 to 2.61), N-terminal pro brain natriuretic peptide (1.52, 95% CI 1.30 to 1.76) and Sokolow-Lyon Index (1.38, 95% CI 1.15 to 1.66) (all ps≤0.01) were associated with a higher PVC frequency. Physical activity (RR fourth vs first quartile 0.51, 95% CI 0.34 to 0.76) and increasing levels of haemoglobin (0.58, 95% CI 0.47 to 0.70) and glucagon-like peptide-1 (0.72, 95% CI 0.64 to 0.82) (all	PVC occurrence is common even in healthy low-risk individuals, and its frequency is associated with several covariates mainly related to cardiovascular risk factors, markers of cardiac structure and function and socioeconomic status.	Select cohort, limited generalizability. Cross-sectional.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	1	Kerola	2018	https://doi.org/10.1161/JAHA.118.010078	Modifiable Predictors of Ventricular Ectopy in the Community	Predictors/risk factors of PVCs	Propsective.	1424	N/A	CHS participatants	None stated	N/A	N/A	5-year increase in PVCs	Predictors on increased PVCs included increased blood pressure, no or low-intensity exercise, and smoking.	Enhancing physical activity, smoking cessation, and aggressive control of blood pressure may represent fruitful strategies to mitigate PVC frequency and PVC-associated adverse outcomes.	Participants only ≥ 65 years, observational.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	1	DeBacker	1979	https://doi.org/10.1161/01.cir.59.4.762	Ventricular premature contractions: a randomized non-drug intervention trial in normal men	To evaluate medication suppression effect on PVCs.	Randomized controlled trial.	81 healthy men.	PVC burden.	Healthy men aged 35-57 years of age with no cardiac history, willingess to participate, and PVCs.	Those with cardiac issues.	Group B) lifestyle changes, Group C) Exercise	Group A: control.	Moderate changes in VPC rates occurred in both experimental and control groups but no significant group differences were found at rest or during any induction test.Only 24 hour PVC monitor.	No change in PVC burden.	N?A	Outsdated. Small study.

6.2.1 Treatment of benign ventricular arrhythmias in the athlete	4	Zhong	2014	https://doi.org/10.1016/j.hrthm.2013.10.033	Relative efficacy of catheter ablation vs antiarrhythmic drugs in treating premature ventricular contractions: a single-center retrospective study	Determine efficacy of radiofrequency ablation vs antiarrhythmic drug therapy on PVC burden	Observational	510 patients	PVC burden and LVEF	Patients with PVCs treated with ablation or AAD	N/A	Ablation, AAD	Ablation vs AAD	Redduction in PVC frequency was greater by RFA than with AADs (-21,799/24 h vs -8,376/24 h; P < .001). The left ventricular ejection fraction (LVEF) was increased significantly after RFA (53%-56%; P < .001) but not after AAD (52%- 52%; P = .6) therapy.	PVC coupling interval less than 450 ms, less impaired left ventricular function, and RFA were independent predictors of LVEF normalization performed by using multivariate analysis.	RFA appears to be more effective than AADs in PVC reduction and LVEF normalization.	Observational, restrospective, therefore subject to patient selection bias.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	4	Ling	2014	https://doi.org/10.1161/CIRCEP.113.000805	Radiofrequency ablation versus antiarrhythmic medication for treatment of ventricular premature beats from the right ventricular outflow tract: prospective randomized study	RFA vs AAD on outflow tract PVC	Randomized controlled trial.	330	PVC burden at 1st, 3rd, 6th, and 12th months and LVEF at baseline, 3 and 6 months.	Outflow tract PVCs	Structural heart disease, ARVC, hyperthyroidism, electrolyte disturbance, drug poisoning, refusal to participate, AAD prescriptions.	Ablation	AAD	.During the 1-year follow-up period, VPB recurrence was significantly lower in patients randomized to RFCA group (32 patients, 19.4%) versus AADs group (146 patients, 88.6%; P<0.001, log-rank test)	n a liner GEE model, the left ventricular eject fraction had a tendency to increase after the treatment in both groups (coefficient, 0.584; 95% confidence intervals [0.467-0.702]; P<0.001).	Catheter ablation is more efficacious than AADs for preventing VPB recurrence in patients with frequent VPBs originating from the RVOT.	Holter monitors instead of continuous monitors may lead to inaccurate follow-up PVC burden, only 1 - year follow-up.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	4	Latchamsetty	2015	https://doi.org/10.1016/j.jacep.2015.04.005	Multicenter Outcomes for Catheter Ablation of Idiopathic Premature Ventricular Complexes	Report multicenter outcomes of ablation of PVCs	Observational	1185	complication rates, clinical outcomes	Patients with decreased LVEF or LV dilation without a known cause other than PVCs	Prior infarct or delayed enhancement identified on CMR.	PVC ablation	N/A	Acute procedural success was achieved in 84% of patients. In 245 patients (21%) with PVC-induced cardiomyopathy, the mean ejection fraction improved from 38% to 50% (p < 0.01) after ablation.	The overall complication rate was 5.2% (2.4% major complications and 2.8% minor complications), and complications were most commonly related to vascular access (2.8%). There was no procedure-related mortality.	Catheter ablation of frequent PVCs is a low-risk and often effective treatment strategy to eliminate PVCs and associated symptoms. In patients with PVC-induced cardiomyopathy, cardiac function is frequently restored after successful ablation.	Patients were primiarly from tertiary referral centers, procedures performed by experienced operators, Holter-monitoring not available for all patients in follow-up.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	4	De Silva	2023	https://doi.org/10.1016/j.jacep.2023.01.035	Catheter Ablation vs Antiarrhythmic Drug Therapy for Treatment of Premature Ventricular Complexes: A Systematic Review	This study reviewed evidence comparing CA vs AADs for the treatment of PVCs.	Systematic review	Five studies (1 randomized controlled trial) enrolling 1,113 patients (57.9% female) were analyzed.	PVC burden in follow-up.	Key words including variations of "PVC" and "ablation" were searched through Medline, Embase, and Cochrane Libarary databases.	Reviews, no comparison arms, same dataset, case reports, pediatrics.	Ablation	AAD	CA seemed superior to AADs for PVC recurrence, frequency, and burden. One study reported long-term symptoms (CA superior).	Quality of life or cost-effectiveness was not reported. Complication and adverse event rates were 0% to 5.6% for CA and 9.5% to 21% for AADs.	In conclusion, CA seems to reduce recurrence, burden, and frequency of PVCs compared with AADs. There is a lack of data on patient- and health care–specific outcomes such as symptoms, quality of life, and cost-effectiveness. Several upcoming trials will offer important insights for management of PVCs.	N/A
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	4	Yamada	2010	https://doi.org/10.1161/CIRCEP.110.939744	Idiopathic ventricular arrhythmias originating from the left ventricular summit: anatomic concepts relevant to ablation	Describe characteristics and procedural details of patients undergoing ablation from the LV summit.	Single center observational	27 patients	Ablation outcomes.	Among 221 consecutive patients with LV Idiopathic VAs, 27 patients had VAs mapped and ablated on the Summit of the LV	N/A	Ablation	N/A	Successful ablation from the Great Cardiac Vein in 14 patients and on the epicardial surface of the LV in 4. In 5 patients ablation abandoned because of origin in the inaccessible region. In 4 patients ablation abandoned due to close proximity to epicardial coronary artery.	A right bundle-branch block, transition zone, R-wave amplitude ratio in leads III to II, Q-wave amplitude ratio in leads aVL to aVR, and S waves in lead V6 accurately predicted the site of origin.	LV summit VAs may be ablated within the GCV or inferior to the GCV on the epicardial surface, though sites superior to the GCV are often inaccessible to ablation.	Small sample size, single center.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	4	Liao	2021	https://doi.org/10.1016/j.hrthm.2020.07.021	Left ventricular summit arrhythmias with an abrupt V	Report outcomes of V3 transition PVCs	Observational	78 patients	PVC burden	ATV3 ablation	Non-ATV3	PVC ablation	N/A	ATV3 is a simple and distinct ECG pattern indicative of a site of origin from the septal margin of the LV summit. The right-left aortic interleaflet triangle vantage point was effective to eliminate OTVA with ATV3 that overwhelmingly exhibited the earliest activation from the epicardium or mid-myocardium. Test characteristics for ATV3 were superior to ECG patterns validated for the anterior LV ostium. At 12±11 months, freedom from ventricular arrhythmia recurrence was 89% and 82% in the ATV3 and control groups, respectively.	ATV3 is a simple and distinct ECG pattern indicative of a site of origin from the septal margin of the LV summit. The right-left aortic interleaflet triangle vantage point was effective to eliminate OTVA with ATV3 that overwhelmingly exhibited the earliest activation from the epicardium or mid-myocardium. Test characteristics for ATV3 were superior to ECG patterns validated for the anterior LV ostium.	ATV3 is a simple and distinct ECG pattern indicative of a site of origin from the septal margin of the LV summit. The right-left aortic interleaflet triangle vantage point was effective to eliminate OTVA with ATV3 that overwhelmingly exhibited the earliest activation from the epicardium or mid-myocardium. Test characteristics for ATV3 were superior to ECG patterns validated for the anterior LV ostium.	Referral bias given tertiary center.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	4	Yokokawa	2010	https://doi.org/10.1016/j.hrthm.2010.07.013	Predictors of successful catheter ablation of ventricular arrhythmias arising from the papillary muscles	To assess the predictors of successful catheter ablation in patients with ventricular arrhythmias arising from the PAPs.	Single Center Observational	40 patients.	Successful PVC ablation	Patients with PVCs originating from papillary muscles undergoing ablation.	Non-papillarly muscle PVCs.	Ablation.	N/A	40 consecutive patients referred for ablation of symptomatic premature ventricular complexes (PVCs) (N=19) or VT (VT) (N=21) originating from a Papillary muscle in the LV (N=32) or RV (N=8). Antiarrhythmic drugs failed to control the VAs in 24 patients. 20 of 40 patients (50%) had SHD: prior MI in 10 patients, dilated cardiomyopathy in 9, and VHD in 1 pt. Catheter ablation was acutely successful in 33 of 40 patients (83%).	Pleomorphic QRS morphologies observed in 31/40 patients.By MRI, the mass of the arrhythmogenic PM was greater in patients with failed than successful ablations.In follow-up, the PVC burden was reduced from 15%+11% to 3%+3%; p<0.01) after successful ablation.	VAs may originate in the papillary muscles of both the LV and the RV. PVCs from the papillary muscles are often pleomorphic. Catheter ablation is successful in approximately 80% of cases, with greater mass of the papillary muscle predicting lower efficacy of ablation.	Small sample size, observational, no definite reason for ablation failure.

6.2.1 Treatment of benign ventricular arrhythmias in the athlete	4	Bogun	2007	https://doi.org/10.1016/j.hrthm.2007.03.003	Radiofrequency ablation of frequent, idiopathic premature ventricular complexes: comparison with a control group without intervention	Ablation vs none, idiopathic PVCs	Single Center Observational	60	PVC burden , LVEF	60 consecutive patients with idiopathic, frequent PVCs (>10/h), a reduced LV EF (EF; mean 34%±13%) was present in 22 (37%) patients	Structural heart disease	Ablation	none	Ablation was completely successful in 48 (80%) patients. In patients with an abnormal EF before ablation, LV function normalized in 18 (82%) of 22 patients from a baseline of 34% to 59% +/- 7% (P <.0001) within 6 months.	In the four patients in whom ablation was ineffective, the EF further declined from 34% +/- 10% to 25% +/- 7% (P = .06) during follow-up. In a control group of 11 patients with a similar PVC burden (30% +/- 8%) and a reduced EF (28% +/- 13%) who did not undergo ablation, the EF remained unchanged in 10/11 patients over 19 +/- 17 months of follow-up and one patient underwent heart transplantation.	LV dysfunction in the setting of frequent, idiopathic PVCs may represent a form of cardiomyopathy that can be reversed by catheter ablation of the PVCs.	Observational, small sample size. Heterogenous PVCs.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	5	Gill	1993	https://doi.org/10.1016/0002-8703(93)90664-u	Verapamil for the suppression of idiopathic ventricular tachycardia of left bundle branch block-like morphology	To examine the efficacy of verapamil for the suppression of idiopathic ventricular tachycardia (VT) of left bundle branch block LBBB-like morphology.	Observational.	42 patients.	Ventricular arrhythmia recurrence.	Structurally normal heart with VT.	Coronary disease or reduced ventricular function.	Verapamil.	N/A	After baseline testing, patients were treated with verapamil 120 mg thrice daily for at least 5 half-lives for the drug to load before evaluation. With Holter monitoring, 74% of patients with evidence of VT at baseline testing demonstrated a change of status from nonsustained VT to no VT or from sustained VT to nonsustained VT. Four patients had nonsustained VT during verapamil treatment but no VT at baseline. There was a significant reduction in the number of ventricular ectopic beats over 24 hours (baseline: 15541 ± 17599 vs verapamil treatment: 8892 ± 15582, p < 0.01). Exercise-induced VT was suppressed in 56% of patients with VT during baseline testing, but no effect of verapamil on the tachycardia was observed in 26%. The remaining patients demonstrated a partial response to verapamil; the rate of VT was unchanged, although the duration of the runs was reduced. Sustained monomorphic VT was inducible in only 5 patients, of whom 4 were rendered noninducible; 1 patient remained inducible. However, of the 13 patients with nonsustained VT inducible at baseline, 4 became sustained, of which 2 were hemodynamically unstable. There was no obvious difference in the age or sex distribution of the patients, axis of VT, presence of abnormal cardiac histology, or late potentials among patients responding to verapamil during Holter monitoring or exercise testing. VT of an inferior axis was more likely to respond to verapamil, whereas VT of a superior axis did not respond to verapamil during Holter monitoring.	N/A	Idiopathic VT of LBBB-like morphology can be suppressed in approximately two thirds of the patients by verapamil. In patients with a partial response, the rate of VT is unaffected. Some patients exhibit exacerbation of the arrhythmia and verapamil should be avoided in these cases.	Small cohort.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	5	Krittayaphong	2002	https://doi.org/10.1067/mhj.2002.125516	Effect of atenolol on symptomatic ventricular arrhythmia without structural heart disease: a randomized placebo-controlled study	To determine the efficacy of atenolol in the treatment of symptomatic VAs	RCT	52 patients	PVC burden	VA with LBBB, inferior axis morphology. Symptomatic.	Structural heart disease.	Atenolol	Placebo	Atenolol significantly decreased PVC count (p=0.001) and average heart rate (p<0.001) compared to placebo. Both placebo and atenolol decreased symptom frequency.	Atenolol improves symptoms and decreases PVC count from ambulatory monitoring. Placebo improved symptoms to the same extent as atenolol but had no effect on severity of VA. This might be the so-called placebo effect, which is a concern when treating patients or doing research on the effects of a drug.	Atenolol improves symptoms and decreases PVC count from ambulatory monitoring. Placebo improved symptoms to the same extent as atenolol but had no effect on severity of VA. This might be the so-called placebo effect, which is a concern when treating patients or doing research on the effects of a drug.	Small trial. Only 1 month follow-up.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	5	Gill	1992	https://doi.org/10.1111/j.1540-8159.1992.tb03033.x	Comparison of verapamil and diltiazem in the suppression of idiopathic ventricular tachycardia	To examine the efficacy of verapamil and diltiazem in the suppression of idiopathic VT.	Clinical trial, cross-over.	8 patients.	VT recurrence.	VA with LBBB, inferior axis morphology. Symptomatic.	Structural heart disease.	Verapamil.	Diltiazem.	Eight patients (mean age 29.8 ± 12.3 years, two males and six females) with VT, without any underlying cardiac abnormaJity on clinical examination and noninvasive investigation, were studied. The inducibiJity of the clinical VT was examined by treadmill exercise testing and programmed ventricular stimulation fPVSJ. In six patients, VT was inducible by exercise testing and in the remaining two by PVS. Following baseline testing, verapamil {120-mg thrice daily] and diltiazem (60-mg thrice daily) were administered in random order, allowing 5 half-lives for the drug to load before evaluation. Two patients had complete suppression of the VT and the remaining six patients demon- strated a partial response to both calcium antagonists. In the patients with a partial response, the duration of the longest run ofVT was reduced (baseline 96.0, 34.2 SEMJ; verapamil 19.2 (7.5); diltiazem 45.3 (21.4 beatsj, whereas, there was no change in the rate of VT (baseline 199.7 (8.0); verapamiJ 184.5 (11.4); diltiazem 201.0 (9.5 beat/min).	No adverse events.	We conclude that idiopathic VT of LBBB-like morphology can be suppressed in approximately two thirds of the patients by verapamil. In patients with a partial response, the rate of VT is unaffected. Some patients exhibit exacerbation of the arrhythmia and verapamil should be avoided in these cases.	Small study.
6.2.1 Treatment of benign ventricular arrhythmias in the athlete	6	Tang	2021	https://doi.org/10.1111/jce.15150	Effectiveness of medical therapy for treatment of idiopathic frequent premature ventricular complexes	Evaluated the effectiveness of medical versus conservative therapy for frequent PVCs.	Observational	120 patients.	PVC burden and LVEF	Idiopathic PVCs ≥5% burden and no structural heart disease	Structural heart disease	Medical therapy	conservative	Median initial PVC burden ranged from 15.5% to 20.6%. The median relative reduction of PVCs was 32.7%, 30.5%, and 81.3%, in the conservative therapy, BBs/CCBs, and AADs cohorts, respectively. AADs had greater PVC reduction compared with BBs/CCBs (p = 0.017) and conservative therapy (p = 0.045). PVC reduction to <1% was comparable across groups at 35.0%, 17.0%, 33.3%, respectively.	Four patients (4/120, 3.3%) developed left ventricular dysfunction. Rates of adverse drug reactions and medication discontinuation were similar between groups, with no serious adverse events noted.	In patients with idiopathic frequent PVCs, BB, and CCB have limited effectiveness in PVC reduction. Class I and III AADs have superior effectiveness for medical therapy in symptomatic patients, but only achieved complete PVC resolution suppression in one-third of patients.	Observational, small size, lack of long-term monitoring.

6.2.1 Treatment of benign ventricular arrhythmias in the athlete	6	Hwang	2023	https://doi.org/10.3390/jcm12082887	Comparing the Efficacy of Carvedilol and Flecainide on the Treatment of Idiopathic Premature Ventricular Complexes from Ventricular Outflow Tract: A Multicenter, Randomized, Open-Label Pilot Study	To determine the efficacy of coreg versus flecainide on outflow tract PVCs.	Multicenter, RCT	103 patients.	PVC burden at 12 weeks.	24 h Holter recording a PVC burden ≥ 5%, which showed positive R waves in leads II, III, and aVF, and without structural heart disease	Structural heart disease, PVC burden <5%.	Flecainide	Carvedilol	After 12 weeks of treatment, the mean PVC burden significantly decreased in both groups: 20.3 ± 11.5 to 14.6 ± 10.8% with carvedilol ($p < 0.0001$) and 17.1 ± 9.9 to 6.6 ± 9.9% with flecainide ($p < 0.0001$).	The degree of symptom improvement did not differ between the two groups ($p = 0.685$).	Both carvedilol and flecainide effectively suppressed OT PVCs in patients without structural heart disease, with flecainide showing a superior efficacy compared to carvedilol.	Lack of prolonged ECG monitoring, dosing was not controlled, small sample size, although pilot study.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	2	Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators	1997	https://doi.org/10.1056/NEJM199711273372202	A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias	To examine the effect on overall survival of initial therapy with an ICD as compared with amiodarone or sotalol in patients resuscitated from VF or symptomatic, sustained VT with hemodynamic compromise.	Multicenter, RCT	1016 patients.	Mortality	Patients who were resuscitated from near-fatal VF; sustained VT with syncope; or sustained VT with an LVEF ≤0.40 and symptoms suggesting severe hemodynamic compromise.	Arrhythmia that was judged to have a transient or correctable cause, excessively high risk (life expectancy <1 y, class IV HF, awaiting a heart transplant, or requiring a balloon pump, other mechanical means, or inotropic drug administration for hemodynamic support) or excessively low risk (event occurring within 5 d of cardiac surgery or angioplasty, or occurring in-hospital <5 d after MI), previous ICD implant (or attempted implant), chronic serious bacterial infection, or were unable to give verbal consent due to neurologic impairment, or a contraindication to amiodarone.	ICD	Amiodarone	Overall survival was greater with the ICD, with unadjusted estimates of 89.3% as compared with 82.3% in the antiarrhythmic-drug group at 1 y, 81.6% vs. 74.7% at 2 y, and 75.4% vs. 64.1% at 3 y ($p<0.02$). The corresponding reductions in mortality (with 95% CI) with the ICD were 39±20%, 27±21%, and 31±21%	Study terminated early after 1016 of 1200 patients enrolled. 81% had CAD.	Among survivors of VF or sustained VT causing severe symptoms, ICD is superior to AAD therapy for reducing overall mortality.	Amiodarone dose and ICD therapies were not standardized, no control group.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	2	Connolly	2000	https://doi.org/10.1053/euhj.2000.2476	Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials. AVID, CASH and CIDS studies. Antiarrhythmics vs Implantable Defibrillator study. Cardiac Arrest Study Hamburg. Canadian Implantable Defibrillator Study	To obtain the most precise estimate of the efficacy of the ICD, compared to amiodarone, for survival in patients with malignant VA.	Meta-anaylsis	3 RCTS	934 patients (ICD) and 932 patients (amiodarone)	RCTs evaluating the ICD vs. AAD therapy in patients with sustained VA or SCD	N/A	ICD	Amiodarone	Reduction in death from any cause with the ICD, HR 0.72; 95% CI 0.60-0.87; p=0.0006).	Arrhythmic death, HR 0.50 (95% CI 0.37-0.67; p<0.0001). P heterogeneity=0.306 Patients with LVEF ≤35% derived more benefit from ICD therapy than those with more preserved left ventricular function. Survival was extended by a mean of 4.4 mo by the ICD over a followup period of 6 y.	Results from the three trials of the ICD vs amiodarone are consistent with each other. There is a 28% reduction in the relative risk of death with the ICD that is due almost entirely to a 50% reduction in arrhythmic death.	Only three trials included.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	3	Vaseghi	2018	https://doi.org/10.1016/j.jacep.2018.05.007	Outcomes of Catheter Ablation of Ventricular Tachycardia Based on Etiology in Nonischemic Heart Disease: An International Ventricular Tachycardia Ablation Center Collaborative Study	Ventricular tachycardia (VT) ablation outcomes across nonischemic cardiomyopathy (NICM) etiologies and adjust these outcomes by patient-related comorbidities that could explain differences in arrhythmia recurrence rates.	Observational	2,075	VT recurrence, heart transplant, death		Ischemic VT	Ablation	N/A	One-year freedom from VT was 69%, and freedom from VT, heart transplantation, and death was 62%. On unadjusted competing risk analysis, VT ablation in ARVC demonstrated superior VT-free survival (82%) versus DICM ($p \leq 0.01$). Valvular cardiomyopathy had the poorest unadjusted VT-free survival, at 47% ($p < 0.01$).	After adjusting for comorbidities, including age, heart failure severity, ejection fraction, prior ablation, and antiarrhythmic medication use, myocarditis, ARVC, and DICM demonstrated similar outcomes, whereas hypertrophic cardiomyopathy, valvular cardiomyopathy, and sarcoidosis had the highest risk of VT recurrence.	Catheter ablation of VT in NICM is effective. Etiology of NICM is a significant predictor of outcomes, with ARVC, myocarditis, and DICM having similar but superior outcomes to hypertrophic cardiomyopathy, valvular cardiomyopathy, and sarcoidosis, after adjusting for potential covariates.	Retrospective, referral bias based on VT ablation centers.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	3	Mahida	2019	https://doi.org/10.1016/j.hrthm.2018.10.016	Ablation compared with drug therapy for recurrent ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy: Results from a multicenter study	To compare outcomes of AAD and/or β-blocker (BB) therapy with those of VT ablation (with AAD/BB) in patients with ARVC who had recurrent VT.	Observational, multicenter	110 patients.	Freedom from VT, survival or transplantation.	Those with ARVC and An additional inclusion criterion was that all 14 patients experienced either 1) ≥3 episodes of sustained VT (requiring either external 15 DC cardioversion, ATP, ICD shock, or acute chemical cardioversion) resulting in 16 separate presentations at distinct time points or, 2) ≥3 cumulative appropriate shocks 17 for VT (either 3 consecutive shocks on the same presentation, i.e. VT storm, or 3 18 cumulative shocks over 2 separate presentations).	N/A	Ablation	Medical therapy	When comparing initial AAD/BB therapy (n = 77) and VT ablation (n = 32) after ≥3 VT episodes, a single ablation procedure rendered 35% of patients free of VT at 3 years compared with 28% of AAD/BB-only–treated patients (P = .46). Of the 77 AAD/BB-only–treated patients, 43 subsequently underwent ablation. For all 75 patients who underwent ablation, 56% were VT-free at 3 years after the last ablation procedure. Epicardial ablation was used in 40/75 (53%) and was associated with lower VT recurrence after the last ablation procedure (endocardial/epicardial vs endocardial-only; 71% vs 47% 3-year VT-free survival; P = .05). Importantly, there was no difference in survival free of death or transplantation between the ablation- and AAD/BB-only–treated patients (P = .61).	Procedural complications occurred in 3 (4%) of patients. No procedure-related deaths.	In patients with ARVC and a high VT burden, mortality and transplantation-free survival are not significantly different between drug- and ablation-treated patients. These patients have a high risk of recurrent VT despite drug therapy. Combined endocardial/epicardial ablation is associated with reduced VT recurrence as compared with endocardial-only ablation.	No standardized approaches to medical therapy, ablation, and ICD programming.

6.2.2 Treatment of complex ventricular arrhythmias in the athlete	3	Dukkipati	2011	https://doi.org/10.1161/CIRCEP.110.957290	Long-term outcomes of combined epicardial and endocardial ablation of monomorphic ventricular tachycardia related to hypertrophic cardiomyopathy	To detail a series of case reports from multiple centers where combined epicardial-endocardial ablation was performed in a highly selected group of patients with HCM-related MMVT.	Observational, multicenter.	10 patients	Procedural outcomes and freedom from ICD shocks.	Those with monomorphic VT and hypertrophic cardiomyopathy undergoing ablation.	N/A	Ablation	N/A	Electrophysiological-identified epicardial scar was present in 8 (80%) patients, endocardial scar in 6 (60%), and no scar in 1 (10%). In the 5 patients with inducible, stable MMVT, 3 cases were successfully terminated with ablation from the epicardium and 1 from the endocardium. The case that failed catheter ablation required surgical cryoablation to abolish the incessant VT. In the remaining 5 patients, 4 underwent Epicardial and endocardial ablation of sites with good pace maps and late/fractionated potentials. No ablation was performed in the remaining patient because of noninducibility and lack of identifiable scar. After 37±17 months (limits, 2 to 62 months; median, 37 months), the freedom from recurrent implantable cardioverter-defibrillator shocks was 78% (7/9 patients) in those who underwent ablation.	No major complications.	In highly selected patients with HCM, combined epicardial and endocardial mapping and ablation is a feasible and reasonably efficacious option for MMVT if refractory to aggressive trials of antiarrhythmic drugs and antitachycardia pacing.	Highly select patient population, tertiary centers.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	3	Nademanee	2023	https://doi.org/10.1161/CIRCULATIONAHA.122.063367	Long-Term Outcomes of Brugada Substrate Ablation: A Report from BRAVO (Brugada Ablation of VF Substrate Ongoing Multicenter Registry)	To report the results of the multicenter, international BRAVO (Brugada Ablation of VF Substrate Ongoing Registry) for treatment of high-risk symptomatic BrS.	Observational, multicenter.	159 patients.	VF recurrence.	the patient must have had coved type ST-segment elevation >2 mm (type 1) pattern over the right precordial leads (leads V1, V2, or V3,), either spontaneously or after sodium channel blocker administration, and must have had an epicardial Brugada-substrate ablation for symptomatic BrS.	Structural heart disease	Ablation	N/A	After a single ablation procedure, 128 of 159 (81%) patients remained free of VF recurrence; this number increased to 153 (96%) after a repeated procedure (mean 1.2±0.5 procedures; median=1), with a mean follow-up period of 48±29 months from the last ablation. VF burden and frequency of shocks decreased significantly from 1.1±2.1 per month before ablation to 0.003±0.14 per month after the last ablation (P<0.0001). The Kaplan-Meier VF-free survival beyond 5 years after the last ablation was 95%.	The only variable associated with a VF-free outcome in multivariable analysis was normalization of the type 1 Brugada ECG, both with and without sodium-channel blockade, after the ablation (hazard ratio, 0.078 [95% CI, 0.008 to 0.753]; P=0.0274). There were no arrhythmic or cardiac deaths. Complications included hemopericardium in 4 (2.5%) patients.	Ablation treatment is safe and highly effective in preventing VF recurrence in high-risk BrS. Prospective studies are needed to determine whether it can be an alternative treatment to implantable cardioverter-defibrillator implantation for selected patients with BrS.	No control group, no standardized VT ablation techniques, referral bias.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	3	Enriquez	2019	https://doi.org/10.1111/jce.13900	Papillary muscle ventricular arrhythmias in patients with arrhythmic mitral valve prolapse: Electrophysiologic substrate and catheter ablation outcomes	To characterize the electrophysiological substrate and outcomes of catheter ablation in patients with MVP and PM PVCs.	Single center observational	25 patients.	PVC elimination.	Mitral valve prolapse and PVCs mapped to the papillary muscles.	N/A	Ablation	N/A	PVC-triggered VF was the presentation in 4 patients and a fifth patient died suddenly during follow-up. The left ventricle ejection fraction (LVEF) was 50.5% ± 11.8% and PVC burden was 24.4% ± 13.1%. A cardiac magnetic resonance imaging was performed in nine cases and areas of late gadolinium enhancement were found in four of them. A detailed LV voltage map was performed in 11 patients, three of which exhibited bipolar voltage abnormalities. Complete PVC elimination was achieved in 19 (76%) patients and a significant reduction in PVC burden was observed in two (8%). In patients in which the ablation was successful, the PVC burden decreased from 20.4% ± 10.8% to 6.3% ± 9.5% (P = 0.001). In 5/6 patients with depressed LVEF and successful ablation, the LV function improved postablation. No significant differences were identified between patients with and without VF.	N/A	PM PVCs are a source of VF in patients with MVP and can induce PVC-mediated cardiomyopathy that reverses after PVC suppression. Catheter ablation is highly successful with more than 80% PVC elimination or burden reduction.	Small sample size, observational, single center.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	4	Noda	2005	https://doi.org/10.1016/j.jacc.2005.05.077	Malignant entity of idiopathic ventricular fibrillation and polymorphic ventricular tachycardia initiated by premature extrasystoles originating from the right ventricular outflow tract	To assess the clinical characteristics and the efficacy of radiofrequency catheter ablation (RFCA) for idiopathic ventricular fibrillation (VF) and/or polymorphic ventricular tachycardia initiated by ventricular extrasystoles originating from the right ventricular outflow tract (RVOT).	Single center observational	16 patients	Syncope, VF, and cardiac arrest in follow up	Those undergoing RFCA for idiopathic ventricular tachyarrhythmias from the RVOT with spontaneous VF and/or polymorphic VT	N/A	Catheter ablation	N/A	Radiofrequency catheter ablation by targeting the initiating ventricular extrasystoles eliminated episodes of syncope, VF, and cardiac arrest in all patients during follow-up periods of 54 +/- 39 months.	Holter recordings showed frequent isolated ventricular extrasystoles with the same morphology as that of initiating ventricular extrasystoles, and non-sustained polymorphic ventricular tachycardia with short cycle length (mean of 245 +/- 28 ms) in all 16 patients.	The malignant entity of idiopathic VF and/or polymorphic ventricular tachycardia was occasionally present in patients with idiopathic ventricular arrhythmias arising from the RVOT. Radiofrequency catheter ablation was effective as a treatment option for this entity.	Small sample size, observational, single center.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	4	Sadek	2015	https://doi.org/10.1016/j.hrthm.2014.08.029	Idiopathic ventricular arrhythmias originating from the moderator band: Electrocardiographic characteristics and treatment by catheter ablation	To define the electrocardiographic (ECG) characteristics and procedural techniques to successfully identify and ablate MB PVCs/VT	Observational, single center.	10	Freedom from sustained VAs.	Those with moderator band PVCs undergoing ablation	N/A	Ablation	None	Six patients required a repeat procedure. After mean follow-up of 21.5 ± 11.6 months, all patients were free of sustained VAs, with only 1 patient requiring antiarrhythmic drug therapy and 1 patient having isolated PVCs no longer inducing VF.	There were no procedural complications.	VAs originating from the MB have a distinctive morphology and often are associated with PVC-induced ventricular fibrillation. Catheter ablation can be safely performed and is facilitated by ICE imaging.	Single center, small sample size, no standardized follow-up for monitoring.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	4	Knecht	2009	https://doi.org/10.1016/j.jacc.2009.03.065	Long-term follow-up of idiopathic ventricular fibrillation ablation: a multicenter study	This multicenter study sought to evaluate the long-term follow-up of patients ablated for idiopathic ventricular fibrillation (VF).	Observational, single center.	38 patients.	VF recurrence	Those undergoing ablation of primary idiopathic VF initated by short coupled PVC.	N/A	Ablation	None	During a median post-procedural follow-up of 63 months, 7 (18%) of 38 patients experienced VF recurrence at a median of 4 months. Five of these 7 patients underwent repeat ablation without VF recurrence. Survival free of VF was predicted only by transient bundle-branch block in the originating ventricle during the electrophysiological study (p < 0.0001). The number of significant events (confirmed VF or aborted sudden death) was reduced from 4 (interquartile range 3 to 9) before to 0 (interquartile range 0 to 4) after ablation (p = 0.01).	N/A	Ablation for idiopathic VF that targets short coupled VPB triggers is associated with a long-term freedom from VF recurrence.	Observational, follow-up not standardized.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	4	Van Herendael	2014	https://doi.org/10.1016/j.hrthm.2013.12.030	Catheter ablation of ventricular fibrillation: importance of left ventricular outflow tract and papillary muscle triggers	To characterize sites of origin of VPDs triggering VF and PMVT.	Single center observational	30 patients	VF/PMVT in follow-up.	30 patients among 1132 consecutive patients undergoing catheter ablation of VAs of all types	N/A	Ablation	None	Acute VPD elimination was achieved in 26 patients (87%), with a decrease in VPDs in another 3 patients (97%). During median follow-up of 418 days (interquartile range [IQR] 144–866), 5 patients developed a VF/PMVT recurrence after a median of 34 days (IQR 1–259). Rare recurrence was noted in patients with and without structural disease and from each distinct anatomic origin. The total burden of VF/PMVT episodes/shocks was reduced from a median of 9 (IQR 2.5–22.5) in the 3 months before ablation to 0 (IQR 0–0, total range 0–2) during follow-up (P <.0001).	In 21 patients, VF/PMVT occurred in the setting of cardiomyopathy; in 9 patients, VF/PMVT was idiopathic. The origin of VPD trigger was from the Purkinje network in 9, papillary muscles in 8, left ventricular outflow tract in 9, and other low-voltage areas unrelated to Purkinje activity in 4. Each distinct anatomic area of origin was associated with VF/PMVT triggers in patients with and without heart disease.	Catheter ablation of VPD-triggered VF/PMVT is highly successful. Left ventricular outflow tract and papillary muscles are common and are previously unrecognized sites of origin of these triggers in patients with and without structural heart disease.	Single center, small sample size, no standardized follow-up for monitoring.

6.2.2 Treatment of complex ventricular arrhythmias in the athlete	4	Belhassen	2022	https://doi.org/10.1016/j.jacep.2022.04.013	Short-Coupled Idiopathic Ventricular Fibrillation: A Literature Review With Extended Follow-Up	To review case reports of the main clinical and electrocardiogram (ECG) characteristics of patients with SC-IVF as well as their management.	Observational, review of case reports	86 patients.	Outcomes during follow-up.	Short-coupled malignant vetnricular arrhythmias.	N/A	N/A	None	In 75% of the 81 cases published during the last 40 years, extended information and follow-up (from 2.63 ± 4.5 years to 10.67 ± 7.8 years; P < 0.001, between the original publication to the latest update) could be obtained from the authors. The review shows that short-coupled malignant ventricular arrhythmias occurred almost equally in males and females, at the mean age of 40 years. A tendency for later occurrence of the arrhythmia by 4 years was observed in females. A prior history of syncope was noted in 45.3% of the patients, whereas arrhythmic storm occurred in 42% at presentation. The most common mode of revelation of short-coupled malignant ventricular arrhythmias was syncope (53.5%), followed by aborted cardiac arrest (26.7%) and recurrent arrhythmic event after prior implantable-cardioverter defibrillator implantation for idiopathic ventricular fibrillation (17.4%). For the first time, short-coupled malignant arrhythmias exhibiting "not-so-short" coupling intervals (≥350 milliseconds) were found in a significant proportion of patients (17.4%). During long-term follow-up, quinidine yielded a slightly higher success rate in arrhythmia control than ablation. Larger studies are necessary to assess the best strategy for the management of this potentially lethal arrhythmia.	N/A	Short-coupled PVCs exhibiting coupling intervals ≥350 were found in a significant proportion of patients. Quinidine yielded highest success rates as compared to ablation.	Heterogeneity in the diagnosis of structural heart disease over the years taking into account that the patients included in this review were collected during more than 7 decades.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	6	Zhong	2014	https://doi.org/10.1016/j.hrthm.2013.10.033	Relative efficacy of catheter ablation vs antiarrhythmic drugs in treating premature ventricular contractions: a single-center retrospective study	Determine efficacy of radiofrequency ablation vs antiarrhythmic drug therapy on PVC burden	Observational	510 patients	PVC burden and LVEF	Patients with PVCs treated with ablation or AAD	N/A	Ablation, AAD	Ablation vs AAD	Redduction in PVC frequency was greater by RFA than with AADs (-21,799/24 h vs -8,376/24 h; P < .001). The left ventricular ejection fraction (LVEF) was increased significantly after RFA (53%-56%; P < .001) but not after AAD (52%- 52%; P = .6) therapy.	PVC coupling interval less than 450 ms, less impaired left ventricular function, and RFA were independent predictors of LVEF normalization performed by using multivariate analysis.	RFA appears to be more effective than AADs in PVC reduction and LVEF normalization.	Observational, restrospective, therefore subject to patient selection bias.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	6	Bogun	2007	https://doi.org/10.1016/j.hrthm.2007.03.003	Radiofrequency ablation of frequent, idiopathic premature ventricular complexes: comparison with a control group without intervention	Ablation vs none, idiopathic PVCs	Single Center Observational	60	PVC burden , LVEF	60 consecutive patients with idiopathic, frequent PVCs (>10/h), a reduced LV EF (EF; mean 34%±13%) was present in 22 (37%) patients	Structural heart disease	Ablation	none	Ablation was completely successful in 48 (80%) patients. In patients with an abnormal EF before ablation, LV function normalized in 18 (82%) of 22 patients from a baseline of 34% to 59% +/- 7% (P <.0001) within 6 months.	In the four patients in whom ablation was ineffective, the EF further declined from 34% +/- 10% to 25% +/- 7% (P = .06) during follow-up. In a control group of 11 patients with a similar PVC burden (30% +/- 8%) and a reduced EF (28% +/- 13%) who did not undergo ablation, the EF remained unchanged in 10/11 patients over 19 +/- 17 months of follow-up and one patient underwent heart transplantation.	LV dysfunction in the setting of frequent, idiopathic PVCs may represent a form of cardiomyopathy that can be reversed by catheter ablation of the PVCs.	Observational, small sample size. Heterogenous PVCs.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	6	Yarlagadda	2005	https://doi.org/10.1161/CIRCULATIONAHA.105.546432	Reversal of cardiomyopathy in patients with repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract	To examine a potential causal relationship between repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract and cardiomyopathy and the role of ablation in reversing this process.	Single center observational	27 patients	LVEF in follow-up.	Idiopathic RVOT PVCs with depressed LVEF (≤45%)	N/A	Ablation	N/A	Successful ablation was performed in 23 patients (85%), including 7 of 8 patients with depressed ventricular function. In this latter group, ventricular function improved in all patients (from 39±6% to 62±6%; P=0.017).	Patients with depressed ventricular function were more likely to be older than patients with normal function (58±14 versus 42±18 years; P=0.013). However, the burden of ventricular ectopy was similar in patients with (17 859±13 488 ectopic beats per 24 hours) and without (17 541±11 479 ectopic beats per 24 hours; P=0.800) preserved ventricular function.	Successful ablation of the focal source of ventricular ectopy results in normalization of left ventricular function. Patients with ectopy-induced cardiomyopathy are significantly older than patients with preserved ventricular function, which suggests either that older patients are more susceptible to the development of a cardiomyopathy or that the cardiomyopathy has had a longer period of time in which to evolve.	Single center, small sample size, no standardized follow-up for monitoring.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	6	Yokokawa	2013	https://doi.org/10.1016/j.hrthm.2012.10.011	Recovery from left ventricular dysfunction after ablation of frequent premature ventricular complexes	To evaluate the positive predictors of idiopathic PVCs-induced cardiomyopathy.	Single center observational	264 patients.	LVEF in follow-up.	Frequent idiopathic PVCs	Structural heart disease	Ablation	N/A	The ejection fraction normalized at a mean of 5±6 months postablation. The majority of patients (51 of 75, 68%) with PVC-induced LV dysfunction had a recovery of LV function within 4 months. In 24 (32%) patients, recovery of LV function took more than 4 months (mean 12±9 months; range 5–45 months).	An epicardial origin of PVCs was more often present (13 of 24, 54%) in patients with delayed recovery of LV function than in patients with early recovery of LV function (2 of 51, 4%; P<.0001). The PVC-QRS width was significantly longer in patients with delayed recovery than in patients with recovery within 4 months (170±21 ms vs 159±16 ms; P = .02). In multivariate analysis, only an epicardial PVC origin was predictive of delayed recovery of LV function in patients with PVC-induced cardiomyopathy.	PVC-induced cardiomyopathy resolves within 4 months of successful ablation in most patients. In about one-third of the patients, recovery is delayed and can take up to 45 months. An epicardial origin predicts delayed recovery of LV function.	Single center, small sample size, no standardized follow-up for monitoring.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	6	Huntrakul	2023	https://doi.org/10.1016/j.jacep.2022.09.016	Left and Right PVC-Induced Ventricular Dysfunction	To assess whether frequent PVCs have an impact on right ventricular (RV) function.	Observational, single center.	47 patients.	RV function assessed by CMR.	Those with PVCs >500 per 24 hours.	Structural heart disease, including ischemic heart disease; if late gadolinium enhancement was present on the LV or RV myocardium; or if they met major criteria for ARVC.	Ablation.	N/A	A total of 19 patients (40%) had RV dysfunction, and 4 of the patients with RV dysfunction (9%) had isolated RV dysfunction. Cardiac magnetic resonance was repeated 1.9 ± 1.3 years after ablation. In patients with successful ablation, RV function improved, and in patients without successful ablation, RV function did not significantly change (before and after ablation RVEF 0.45 ± 0.09 and 0.52 ± 0.09; P < 0.001 vs. 0.46 ± 0.07 and 0.48 ± 0.04; P = 0.14, respectively).	N/A	Frequent PVCs can cause RV cardiomyopathy that parallels LV cardiomyopathy and is reversible with successful ablation.	Retrospective, small sample size, referral bias.

6.2.2 Treatment of complex ventricular arrhythmias in the athlete	7	Hyman	2018	https://doi.org/10.1016/j.hrthm.2017.12.018	Class IC antiarrhythmic drugs for suspected premature ventricular contraction-induced cardiomyopathy	To determine the safety and efficacy of IC-AADs in patients suspected of having PVC-CM.	Observational, single center.	20 patients.	PVC suppression, LVEF in follow-up.	Those with suspected PVC-induced cardiomyopathy.	Structural heart disease.	Class IC-AAD	N/A	Patients had undergone an average of 1.3 ± 0.2 previous unsuccessful ablations. Six had an implantable or wearable defibrillator. With IC-AAD treatment, mean PVC burden decreased from 36.2% ± 3.5% to 10.0% ± 2.4% (P <.001). Mean left ventricular ejection fraction (LVEF) increased from 37.4% ± 2.0% to 49.0% ± 1.9% (P <.001). Seven patients with myocardial delayed enhancement on cardiac magnetic resonance imaging (all <5% of the total myocardium) experienced similar improvement in LVEF (from 36.8% ± 4.3% before IC-AAD to 51.7% ± 3.7% afterward; P <.01). Over an average 3.8 ± 0.9 treatment-years, no sustained ventricular arrhythmias or sudden cardiac deaths occurred.	No adverse events.	In patients suspected of having PVC-CM, IC-AADs effectively suppressed PVCs, leading to LVEF recovery in the majority.	Heterogeneity in treatment effects, observational, single-center, small sample size.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	8, 9	Venlet	2017	https://doi.org/10.1016/j.jacc.2016.11.041	Isolated Subepicardial Right Ventricular Outflow Tract Scar in Athletes With Ventricular Tachycardia	To evalaute the arrhythmogenic substrate for VT in athletes.	Observational	57 patients.	N/A	Consecutive patients with VT undergoing ablation.	Those with idiopathic VA (n = 229), ischemic cardiomyopathy (n = 15), congenital heart disease (n = 65), and dominant left ventricular (LV) cardiomyopathy (normal RV and abnormal LV dimensions and function) (n = 5).	Group A - all VT non-athletes	Goup B - all endurance atheltes with VT	Definite ARVC or post-inflammatory cardiomyopathy was diagnosed in 40 (87%) of 46 group A patients but was not diagnosed in any patients in group B. All group B patients underwent intensive endurance training for a median of 15 h/week (interquartile range [IQR]: 10 to 20 h/week) for a median of 13 years (IQR: 10 to 18 years). The cycle lengths of scar-related VTs were significantly faster in group B patients (257 ± 34 ms vs. 328 ± 72 ms in group A; p = 0.003). Catheter ablation resulted in complete procedural success in 10 (91%) of 11 group B patients compared with 26 (57%) of 46 group A patients (p = 0.034). During a median follow-up of 27 months (IQR: 6 to 62 months), 50% of group A patients but none of the group B patients had a VT recurrence.	N/A	This study describes a novel clinical entity of an isolated subepicardial right ventricular outflow tract scar serving as a substrate for fast VT in high-level endurance athletes that can be successfully treated by ablation. This scar pattern may allow distinguishing exercise-induced arrhythmogenic remodeling from ARVC and post-inflammatory cardiomyopathy.	Small study, referral bias.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	9	Heidbuchel	2003	https://doi.org/10.1016/s0195-668x(03)00282-3	High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias	To report outcomes of high-level endurance athletes with ventricular arrhythmias.	Observational, multicenter.	46 patients.	Major arrhythmic event.	Only athletes participating regularly in intense endurance sports (i.e. ≥3×2h/week for ≥5 years) were included. A total of 36 athletes presented with symptoms of lightheadedness, fatigue or (pre)syncope that were attributable to ventricular arrhythmias	N/A	N/A	N/A	Eighteen athletes developed a major arrhythmic event (sudden death in nine, all cyclists). They were significantly younger than those without event (median 23 years vs 38 years; P=0.01). Outcome could not be predicted by presenting symptoms, non-invasive arrhythmia evaluation or morphological findings at baseline. Only the induction of sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) during invasive electrophysiological testing was significantly related to outcome (RR 3.4; P=0.02). Focal arrhythmias were associated with a better prognosis than those due to reentry (P=0.02) but the mechanism could be determined in only 22 (48%).	N/A	Complex ventricular arrhythmias do not necessarily represent a benign finding in endurance athletes. An electrophysiological study is indicated for risk evaluation, both by defining inducibility and identifying the arrhythmogenic mechanism. Endurance athletes with arrhythmias have a high prevalence of right ventricular structural and/or arrhythmic involvement. Endurance sports seems to be related to the development and/or progression of the underlying arrhythmogenic substrate.	Retrospective, observational. Heterogeneniety in follow-up.
6.2.2 Treatment of complex ventricular arrhythmias in the athlete	9	La Gerche	2010	https://doi.org/10.1136/hrt.2009.189621	Lower than expected desmosomal gene mutation prevalence in endurance athletes with complex ventricular arrhythmias of right ventricular origin	To determine the yield of genetic testing in athletes with RV structual abnormalities and RV arrhythmias	Observational, multicenter.	47 athletes.	N/A	Athletes with complex VA or RV morphology perfoming 14 hours per week of moderate to intense sports for 19 years.	N/A	Clinical evaluation (detailed sports history, multi-modality imaging, electrophysiological study) and sequencing of five candidate desmosomal genes.	N/A	A clinical diagnosis of definite or suspected ARVC by task force criteria (TFC) was met in 24 (51%) and 17 (36%), respectively. ARVC classification was not related to the rate of major arrhythmic events (p=0.28). Pathogenic mutations (four novel) were identified in six athletes (12.8%), which is below published rates for familial ARVC (27–52%). Moreover, only two athletes had a suggestive family history. Severe RV dysfunction was more frequent in mutation carriers (33% vs 2%, p=0.04), but otherwise TFC features were similar to those without mutations. No mutations were found in the 20 athletes performing more than average weekly exercise, yet all met the criteria for definite or suspected ARVC.	In this athletic cohort, there was a lower than expected rates of desmosomal gene mutations, particularly among those performing the most exercise. This adds further weight to the hypothesis that an ARVC-like phenotype may be acquired through intense exercise without an identifiable genetic predisposition.	arvc phenotype may be associated with intense exercise without a genetic predisposition.	Small cohort.

Subsection	Rec #	First Author	Year	DOI	Article Title	Aim	Study type	Size	Endpoints	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Comparator(s)	Outcomes (Results and P values)	Other Relevant Findings or Adverse Events	Conclusions	Limitations
7.1 Athletes with inherited arrhythmia syndromes	1	Martinez	2023	https://doi.org/10.1016/j.jacc.2023.05.059	Return-to-Play for Elite Athletes With Genetic Heart Diseases Predisposing to Sudden Cardiac Death	To evaluate outcomes among high level athletes diagnosed with genetic heart disease	Retrospective cohort study	76 patients, 40 with HCM	Breakthrough cardiac events- arrhythmic syncope, symptomatic NSVT, appropriate VT or VF ICD shock, sustained VT, cardiac arrest with AED rescue or SCD	Elite level athlete: NCAA Division 1, Olympic, professional. Mean age 20 years.	n/a	Continuation of sports	n/a	No events during exercise. 1 HCM athlete with arrest, non-exertional, 1 HCM athlete, non-arrhythmic syncope	Athletes with GHD can RTP when comprehensively clinically evaluation and in SDM model, with low incidence of events	No adverse events related to RTP	Retrospective design, limited sample size, no comparator
7.1 Athletes with inherited arrhythmia syndromes	1	Johnson	2012	https://doi.org/10.1001/jama.2012.9334	Competitive sports participation in athletes with congenital long QT syndrome	To determine the outcomes of patients with LQTS who chose to remain athletes against guidelines recommendations	retrospective review	130	BCE in sports	competitive athletes diagnosed with LQTS age 6-40 years				overall event rate was 0.003/athlete-year		low event rate in those with LQTS returning to play in expert centre	small size, limited follow up
7.1 Athletes with inherited arrhythmia syndromes	2	Roston	2021	https://doi.org/10.1016/j.jacep.2021.02.013	Burst Exercise Testing Can Unmask Arrhythmias in Patients With Incompletely Penetrant Catecholaminergic Polymorphic Ventricular Tachycardia	To use a new protocol of burst exercise testing to unmaks incompletely penetrant CPVT phenotypes	pilot study	6	>/= 3 beats NSVT	consensus criteria for CPVT	no diagnosis of CPVT		standard EST (bruce protocol or equivalent)	new atrial or ventricular arrhythmias in 5/6 patients (83%)	no complications with new protocol	new protocol better identifies those with incompletely penetrant CPVT compared to standard testint	single centre, pilot study, small numbers, retrospective
7.1 Athletes with inherited arrhythmia syndromes	2	Gray	2017	https://doi.org/10.1016/j.hrthm.2017.02.026	Twelve-lead ambulatory electrocardiographic monitoring in Brugada syndrome: Potential diagnostic and prognostic implications	prospecitvely assess overall burden of type 1 Brugada ECG changes and association with cardiac events	cohort study	54 patients	frequency, temporal and spatial burden of type 1 Brugad ECG pattern on 12 lead holter monitoring and association with cardiac events	adult patient with BrS				34% of "drug-induced" brugada patients actually demonstrated a spontaneous pattern over the 24 hour period. Cardiac events were associated with higher temporal burden of type 1 pattern, most pronounced in evening		ambulatory 12 lead monitoring has diagnosis and prognostic utility in BrS	small size, single centre, manual data anlaysis
7.1 Athletes with inherited arrhythmia syndromes	2	Mazzanti	2018	https://doi.org/10.1016/j.jacc.2018.01.078	Interplay Between Genetic Substrate, QTc Duration, and Arrhythmia Risk in Patients With Long QT Syndrome		prospective cohort study										
7.1 Athletes with inherited arrhythmia syndromes	2	Sy	2011	https://doi.org/10.1161/CIRCULATIONAHA.111.028258	Derivation and validation of a simple exercise-based algorithm for prediction of genetic testing in relatives of LQTS probands		prospective cohort study										
7.1 Athletes with inherited arrhythmia syndromes	3	Collura	2009	https://doi.org/10.1016/j.hrthm.2009.03.024	Left cardiac sympathetic denervation for the treatment of long QT syndrome and catecholaminergic polymorphic ventricular tachycardia using video-assisted thoracic surgery		Case series										
7.1 Athletes with inherited arrhythmia syndromes	3	Dusi	2022	https://doi.org/10.1016/j.jacep.2021.09.002	Left Cardiac Sympathetic Denervation for Long QT Syndrome: 50 Years' Experience Provides Guidance for Management	single-centre report of results of LCSD for LQTS	cohort study	125	BCE	LCSD performed for LQTS mostly symptomatic patients, n-31 for primary prevention		LCSD		overall 86% decreased in mean yearly cardiac event rate (p<0.0001), those with QTc>500ms have 50% chance of shortening this by 60ms with LCSD	no major surgical complications, , 2.4% ptosis rate, no difference in outcomes according to genotype		
7.1 Athletes with inherited arrhythmia syndromes	3	Niaz	2020	https://doi.org/10.1161/CIRCEP.120.008830	Left Cardiac Sympathetic Denervation Monotherapy in Patients With Congenital Long QT Syndrome	cohort review of LQTS patients selected to have LCSD as monotherapy	cohort study	204	breakthrough cardiac events	Single centre, LCSD as stand alone monotherapy		LCSD		mean follow up 2.7 years, 3 pateitns with nonlethal post LCSD breakthrough cardaic event	no significant surgical complications,	Safe alternative for patients who do not tolerate BB	single centre
7.1 Athletes with inherited arrhythmia syndromes	4	Lampert	2013	https://doi.org/10.1161/CIRCULATIONAHA.112.000447	Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry	Evaluate the safety of sports participation for athletes with implantable cardioverter-defibrillators (ICDs).	Prospective, multinational registry	372 athletes with ICDs aged 10 to 60 years participating in organized or high-risk sports.	Primary: serious adverse events (tachyarrhythmic death or resuscitated tachyarrhythmia) during or up to 2 hours after sports, or severe injury from arrhythmia-related syncope or shock during sports.	Athletes aged 10 to 60 years with ICDs who were actively participating in organized sports or high-risk sports.	Athletes not participating in sports, or those who did not meet the specific criteria for organized or high-risk sports participation.	Monitoring and data collection through a secure web-based daabase, phone interviews, and medical record reviews.	n/a	No primary endpoint events occurred. There were 49 shocks during competition/practice, 39 during other physical activity, and 33 at rest.	The ICDs effectively terminated all arrhythmia episodes. Lead malfunction rates were low, with 97% at 5 years and 90% at 10 years. 10% shocks during sports, 8% during other physical acitivy 6% at rest.	The study concluded that many athletes with ICDs can engage in vigorous and competitive sports without experiencing physical injury or failure of the device to terminate arrhythmias. These findings support more informed decision-making regarding sports participation for athletes with ICDs.	Self-selection bias of participants, most with normal LV Efs; potential underreporting of ICD shocks because of self reporting; not enough data on contact or collision sport athletes.
7.1 Athletes with inherited arrhythmia syndromes	4	Lampert	2017	https://doi.org/10.1161/CIRCULATIONAHA.117.027828	Safety of Sports for Athletes With Implantable Cardioverter-Defibrillators: Long-Term Results of a Prospective Multinational Registry	long term outcomes of above study	prospective national registry	440	death, arrest, significant injury	athletes with ICDS participating in organised or high risk sports				no tachyarrhythmic deaths or externally resusciated arrhythmias during or after sports and no sports related inuries from syncope or shock during sports	10% shocks during sports (3/100 person years), more recieved shocks with physical activity (20%) compared to rest (10%) p<0.0001. presence of ARVC associated with shocks in sports	athletes with ICDs engaged in vigorous acitivity with no signal for harm, underlying disease is important particularly ARVC	
7.1 Athletes with inherited arrhythmia syndromes	4	Heidbuchel	2019	https://doi.org/10.1177/2047487319834852	Intensive recreational athletes in the prospective multinational ICD Sports Safety Registry: Results from the European cohort		prospective registry study										
7.1 Athletes with inherited arrhythmia syndromes	4	Saarel	2018	https://doi.org/10.1161/circep.118.006305	Safety of Sports for Young Patients With Implantable Cardioverter-Defibrillators: Long-Term Results of the Multinational ICD Sports Registry	to determine the incidence of serious adverse events due to sports particiation in young patients with icds	prospective national registry	129 athletes, mean age 16, 40% female, 92% white	primary: SAE during or <2hours after sports (either tachyarrhythmic death, externally resuscitated tachyarrhythmia or severe injury from syncope or shock. Secondary: shocks or system damage (eg lead/device malfunction)	athlet age 1-21 with ICD who were already participating in organised sports		nil		no events in primary outcome, secondary- 25% rate of 1 shock of which most were appropriate. Rate 1.5 appropriate shocks during sports per 100 years, 2 athletes had shocks which did not occur during competition or practice.	Lead malfunciton rate 20.4% at 10 years, no athletes with SICD in this study	shocks do occur, butno serious adverse events, lead malfucionт similar to those in unselected paediatric populations	self-reporting of shocks, few patients in study playing contact sports

7.1 Athletes with inherited arrhythmia syndromes	5	Olde Nordkamp	2016	https://doi.org/10.1016/j.hrthm.2015.09.010	Implantable cardioverter-defibrillator harm in young patients with inherited arrhythmia syndromes: A systematic review and meta-analysis of inappropriate shocks and complications		Systematic review and meta-analysis									
7.1.1 Athletes with long QT syndrome	1, 5, 7, 9	Tobert	2021	https://doi.org/10.1016/j.jacc.2021.04.026	Return-to-Play for Athletes With Long QT Syndrome or Genetic Heart Diseases Predisposing to Sudden Death	The prevalence and outcomes of athletes with sudden cardiac death predisposing GHDs, particularly LQTS after their return to play	retrospective cohort study	672 athletes, including 494 with LQTS (231 female), mean age 14.8, mean follow up 4.1 years,	BCE	athletes with genetic heart disease wishing to return to play	athletes with GHD no longer wishing to play	nil	BCE in those outside of RTP period	no deaths, overall event rate 5.9% of whom event rate of 3% in athletes during RTP period and 2.8% outside of RTP period, of these 0.6% and 0.4% were sports related BCE respectively. Overall event rate 1.16 nonletal events per 100 athletes-years follow up	includes 130 athletes from above study	low event rate overall, particularly in LQTS	single centre, retrospective cohort, referral biase
7.1.1 Athletes with long QT syndrome	1	Martinez	2023	https://doi.org/10.1016/j.jacc.2023.05.059	Return-to-Play for Elite Athletes With Genetic Heart Diseases Predisposing to Sudden Cardiac Death	To evaluate outcomes among high level athletes diagnosed with genetic heart disease	Retrospective cohort study	76 patients, 40 with HCM	Breakthrough cardiac events- arrhythmic syncope, symptomatic NSVT, appropriate VT or VF ICD shock, sustained VT, cardiac arrest with AED rescue or SCD	Elite level athlete: NCAA Division 1, Olympic, professional. Mean age 20 years.	n/a	Continuation of sports	n/a	No events during exercise. 1 HCM athlete with arrest, non-exertional, 1 HCM athlete, non-arrhythmic syncope	Athletes with GHD can RTP when comprehensively clinically evaluation and in SDM model, with low incidence of events	No adverse events related to RTP	Retrospective design, limited sample size, no comparator
7.1.1 Athletes with long QT syndrome	1	Aziz	2015	https://doi.org/10.1016/j.jacep.2015.03.006	Sports Participation in Genotype Positive Children With Long QT Syndrome	To examine the prevalence and outcomes of sports participation (competitive and recreational) in single-centre LQTS paediatric population	Retrospecitve cohort study	103 LQTS patients participated in sports, 49% female, follow up 7.1 years, avg QTc 468ms	SAE during or up to 2 hours post sports (death, externally resuscitated, syncope, severe injury secondary to syncope or arrhythmia)	children (4-21yrs) with genotype positive LQTS participating in sports	patients with assumed LQTS but genotype negative, incomplete medical records or inconsistent follow up, age <4yrs			no patients had symptoms during participation, no deaths,	5 appropraite ICD shocks in 2 patients which occurred outside of sports participation	low event rate	retrospective review, single centre, selection bias, high proportion LQT1 on BB,
7.1.1 Athletes with long QT syndrome	1	Davydoff	2022	https://doi.org/10.1093/europace/euac047	Does sports participation increase risk in patients with long QT syndrome? Results from a large French cohort	To evaluate incidence of cardiac arrhythmias during sports practice in LQTS patients	retrospective cohort study	246 patients, >18 years, 57% females, median age 43, median QTc 457ms	CAE after diagnosis of LQTS	all LQTS patients in french registry	nil	nil	CAE prior to diagnosis or LQTS	Event rate 0.003/year prior to diagnosis, event rate 0.0007/year after diagnosis, overall rate of 0.002/year prior and after LQTS diagnosis	no events were seen in any competitive athlete, all events were in leisure sport athletes. No events in patients on BB	low event rate for CAE for patients who participate in sports after LQTS diagnosis, even competitively. No events in patients on BB	retrospective, may underestimate events, by definition deceased patients were not included, recall basis, 1/3 of patients who received study questionaire did not reply
7.1.1 Athletes with long QT syndrome	1	Johnson	2012	https://doi.org/10.1001/jama.2012.9334	Competitive sports participation in athletes with congenital long QT syndrome	To determine the outcomes of patients with LQTS who chose to remain athletes against guidelines recommendations	retrospective review	130	BCE in sports	competitive athletes diagnosed with LQTS age 6-40 years				overall event rate was 0.003/athlete-year		low event rate in those with LQTS returning to play in expert centre	small size, limited follow up
7.1.1 Athletes with long QT syndrome	1	Johnson	2013	https://doi.org/10.1136/bjsports-2012-091751	Return to play? Athletes with congenital long QT syndrome	To determine the prevalence and outcomes of patients with LQTS who chose to remain athletes following their diagnosis	cohort study	overall cohort 353 patients aged 6-40yrs, avg age 17 years, 56% female, 52% LQT1, 37% LQT2, 10% LQT3, avg QTc 472, 130 remained competitive athletes	arrhythmic cardiac event	athlete with LQTS choosing to participate in SDM model	nil	nil	athletes with LQTS who chose not to continue sports	low event rate <0.8% of 1 appropriate shock in 650 athlete-years of follow up, no deaths		guidelines for athlets with LQTS excluding them from competition may be overly aggressive and restrictive	data isolated to LQTS and athltes, some sports classifications (IIIb and IIIc) had low numbers, age restricted 6-40 years
7.1.1 Athletes with long QT syndrome	1	Chambers	2017	https://doi.org/10.1161/JAHA.116.005445	Cardiac Events During Competitive, Recreational, and Daily Activities in Children and Adolescents With Long QT Syndrome	to assess cardiac event rates during competitive and recreational sports and daily activities among treated LQTS children	cohort study	172 children, mean age9, 55% female QTc 474ms	cardiac events	LQTS children on treatment (83% BB alone)	not participating in competitive or recreational activities, genotype positive phenotype negative, other conditisn (eg ATS)	nil		combined 1203 years follow up 13 events in 9 patients. 4 during recreational exercise and 9 during ADL, no deaths	prior symptoms and QTc duration were significantly associated with CE during ADL or recreational sports	low event rate among appropriately managed children with LQTS	single centre, observiation retrospective study, recall bias, some patients had self-excluded by not participating in sports
7.1.1 Athletes with long QT syndrome	2, 3	Amin	2008	https://doi.org/10.1172/JCI35337	Fever-induced QTc prolongation and ventricular arrhythmias in individuals with type 2 congenital long QT syndrome		Case series									
7.1.1 Athletes with long QT syndrome	2, 3	Scherr	2012	https://doi.org/10.1249/MSS.0b013e318258aaf4	Repolarization perturbation and hypomagnesemia after extreme exercise		prospective cohort study									
7.1.1 Athletes with long QT syndrome	4, 5, 6	Mazzanti	2018	https://doi.org/10.1016/j.jacc.2018.01.078	Interplay Between Genetic Substrate, QTc Duration, and Arrhythmia Risk in Patients With Long QT Syndrome		prospective cohort study									
7.1.1 Athletes with long QT syndrome	5, 7, 9	Dusi	2022	https://doi.org/10.1016/j.jacep.2021.09.002	Left Cardiac Sympathetic Denervation for Long QT Syndrome: 50 Years' Experience Provides Guidance for Management	single-centre report of results of LCSD for LQTS	cohort study	125	BCE	LCSD performed for LQTS mostly symptomatic patients, n-31 for primary prevention		LCSD		overall 86% decreased in mean yearly cardiac event rate (p<0.0001), those with QTc>500ms have 50% chance of shortening this by 60ms with LCSD	no major surgical complications, , 2.4% ptosis rate, no difference in outcomes according to genotype		
7.1.1 Athletes with long QT syndrome	5, 9	Mazzanti	2016	https://doi.org/10.1016/j.jacc.2015.12.033	Gene-Specific Therapy With Mexiletine Reduces Arrhythmic Events in Patients With Long QT Syndrome Type 3		Retrospective cohort study									
7.1.1 Athletes with long QT syndrome	7	Collura	2009	https://doi.org/10.1016/j.hrthm.2009.03.024	Left cardiac sympathetic denervation for the treatment of long QT syndrome and catecholaminergic polymorphic ventricular tachycardia using video-assisted thoracic surgery		Case series									
7.1.1 Athletes with long QT syndrome	7	Niaz	2020	https://doi.org/10.1161/CIRCEP.120.008830	Left Cardiac Sympathetic Denervation Monotherapy in Patients With Congenital Long QT Syndrome	cohort review of LQTS patients selected to have LCSD as monotherapy	cohort study	204	breakthrough cardiac events	Single centre, LCSD as stand alone monotherapy		LCSD		mean follow up 2.7 years, 3 pateitns with nonlethal post LCSD breakthrough cardaic event	no significant surgical complications,	Safe alternative for patients who do not tolerate BB	single centre
7.1.1 Athletes with long QT syndrome	8	Ackerman	1999	https://doi.org/10.4065/74.11.1088	Swimming, a gene-specific arrhythmogenic trigger for inherited long QT syndrome	determine the genetic basis for LQTS in patients with history of swimming-triggered events	case cohort report	35						9/35 cases of personal or extended family hsitory of drowning or near-drowning		swimming is gene-specific trigger for LQTS1	small cohort, single centre

7.1.1 Athletes with long QT syndrome	9	Bos	2019	https://doi.org/10.1161/CIRCEP.118.007280	Mexiletine Shortens the QT Interval in Patients With Potassium Channel-Mediated Type 2 Long QT Syndrome		retrospective chart review									
7.1.2 Catecholaminergic polymorphic ventricular tachycardia	1, 2	Tobert	2021	https://doi.org/10.1016/j.jacc.2021.04.026	Return-to-Play for Athletes With Long QT Syndrome or Genetic Heart Diseases Predisposing to Sudden Death	The prevalence and outcomes of athletes with sudden cardiac death predisposing GHDs, particularly LQTS after their return to play	retrospective cohort study	672 athletes, including 494 with LQTS (231 female), mean age 14.8, mean follow up 4.1 years,	BCE	athletes with genetic heart disease wishing to return to play	athletes with GHD no longer wishing to play	nil	BCE in those outside of RTP period	no deaths, overall event rate 5.9% of whom event rate of 3% in athletes during RTP period and 2.8% outside of RTP period, of these 0.6% and 0.4% were sports related BCE respectively. Overall event rate 1.16 nonletal events per 100 athletes-years follow up	includes 130 athletes from above study	low event rate overall, particularly in LQTS	single centre, retrospective cohort, referral biase
7.1.2 Catecholaminergic polymorphic ventricular tachycardia	1, 2, 3, 4	Tobert	2022	https://doi.org/10.1016/j.mayocp.2022.03.024	Outcomes of Athletes With Genetic Heart Diseases and Implantable Cardioverter-Defibrillators Who Chose to Return to Play	to review outcomes for GHD patients who had RTP with ICD	cohort study	125	BCEs, ICD complications, inappropriate shocks	GHD patients with ICD who had RTP from single centre				overall 18% of athletes recieved an appropriate shock. athletes with ICD likely to have BCE than those without ICD BCE event rate 6.3/100 athletes years	1.34/100 athlete years inappropriate shock rate, 5.01/100 athlete years rate of other ICD complications. No complications during sports	no sports related SCD or sports related ICD damage reported	single centre
7.1.2 Catecholaminergic polymorphic ventricular tachycardia	1, 2	Ostby	2016	https://doi.org/10.1016/j.jacep.2016.01.020	Competitive Sports Participation in Patients With Catecholaminergic Polymorphic Ventricular Tachycardia: A Single Center's Early Experience	outcomes of continued sports partcipation in cpvt	retrospective review/cohort	cohort of 63 of whom 31 were "ever" athletic	cpvt events	cpvt diagnosis, ever an athlete, age >6yo			non athletes from same institution	event rate 1.41 per 100 athlete-years, no difference in outcome between athletes and non athletes p=0.43, no deaths in either group		higher event rate than seen in LQTS however no difference between CPVT athletes and CPVT non athletes	single centre, retrospective, small cohort
7.1.2 Catecholaminergic polymorphic ventricular tachycardia	1	Peltenburg	2023	https://doi.org/10.1093/europace/euac177	Repeatability of ventricular arrhythmia characteristics on the exercise-stress test in RYR2-mediated catecholaminergic polymorphic ventricular tachycardia		retrospective cohort study									
7.1.2 Catecholaminergic polymorphic ventricular tachycardia	2, 4	Roston	2021	https://doi.org/10.1016/j.jacep.2021.02.013	Burst Exercise Testing Can Unmask Arrhythmias in Patients With Incompletely Penetrant Catecholaminergic Polymorphic Ventricular Tachycardia	To use a new protocol of burst exercise testing to unmaks incompletely penetrant CPVT phenotypes	pilot study	6	>/= 3 beats NSVT	consensus criteria for CPVT	no diagnosis of CPVT		standard EST (bruce protocol or equivalent)	new atrial or ventricular arrhythmias in 5/6 patients (83%)	no complications with new protocol	new protocol better identifies those with incompletely penetrant CPVT compared to standard testint	single centre, pilot study, small numbers, retrospective
7.1.3 Brugada syndrome	1	Nishizaki	2008	https://doi.org/10.1111/j.1540-8167.2007.00972.x	Influence of meals on variations of ST segment elevation in patients with Brugada syndrome		prospective cohort study									
7.1.3 Brugada syndrome	2	Rattanawong	2016	https://doi.org/10.1111/anec.12288	Fever-induced Brugada Syndrome is more common than previously suspected: A cross-sectional study from an endemic area	To determine the prevalence of fever-induced Brugada Syndrome in a febrile population compared to a non-febrile control group.	Cross-sectional study	401 patients from a hospital in Thailand, including 152 febrile and 249 nonfebrile patients.	Prevalence of Brugada Syndrome in febrile versus nonfebrile patients	Adults presenting with a body temperature ≥38 °C (febrile) or <38 °C (nonfebrile), without structural heart disease or myocardial infarction.	Patients unwilling to participate, with structural heart disease, myocardial infarction, or those without an ECG during the nonfebrile state.	Standard and high-lead electrocardiography performed on febrile and nonfebrile patients.	Febrile group compared to nonfebrile control group for the presence of Brugada pattern.	Brugada Syndrome was found in 4.0% of febrile patients and 0.8% of nonfebrile patients (P = 0.037).	No ventricular arrhythmias observed; prevalence of type-2 Brugada pattern and early repolarization pattern did not differ significantly between groups.	The prevalence of fever-induced Brugada Syndrome may be higher than previously reported, particularly in endemic areas.	Study limited to one hospital, may not represent general population; high prevalence findings might not generalize beyond the study setting.
7.1.4 Short QT syndrome (SQTS)	1	Scherr	2012	https://doi.org/10.1249/MSS.0b013e318258aaf4	Repolarization perturbation and hypomagnesemia after extreme exercise		prospective cohort study									
7.1.4 Short QT syndrome (SQTS)	2	Giustetto	2011	https://doi.org/10.1016/j.jacc.2011.03.038	Long-term follow-up of patients with short QT syndrome		prospective cohort stsudy									
7.1.4 Short QT syndrome (SQTS)	2	Mazzanti	2017	https://doi.org/10.1016/j.jacc.2017.10.025	Hydroquinidine Prevents Life-Threatening Arrhythmic Events in Patients With Short QT Syndrome		prospective cohort stsudy									
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	1	Tobert	2021	https://doi.org/10.1016/j.jacc.2021.04.026	Return-to-Play for Athletes With Long QT Syndrome or Genetic Heart Diseases Predisposing to Sudden Death	The prevalence and outcomes of athletes with sudden cardiac death predisposing GHDs, particularly LQTS after their return to play	retrospective cohort study	672 athletes, including 494 with LQTS (231 female), mean age 14.8, mean follow up 4.1 years,	BCE	athletes with genetic heart disease wishing to return to play	athletes with GHD no longer wishing to play	nil	BCE in those outside of RTP period	no deaths, overall event rate 5.9% of whom event rate of 3% in athletes during RTP period and 2.8% outside of RTP period, of these 0.6% and 0.4% were sports related BCE respectively. Overall event rate 1.16 nonletal events per 100 athletes-years follow up	includes 130 athletes from above study	low event rate overall, particularly in LQTS	single centre, retrospective cohort, referral biase
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	2	James	2013	https://doi.org/10.1016/j.jacc.2013.06.033	Exercise increases age-related penetrance and arrhythmic risk in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated desmosomal mutation carriers	To assess how exercise influences penetrance of ARVC amongst patients with desmosomal mutations	cohort study	87	sustained VT/VF, heart failure and diagnostic criteria	gene carriers of ARVC with normal phenotype		interview of regular physical activiy from age 10		endurance athletes more likely to meet TFC (82% vs 35%), develop symptoms at a younger age (30 vs 40, p=0.05) and have lower lifetime survivial free of VT/VF (p=0.013)and heart failure (p=0.004)	survival from first VT/VF event was lowest in those who exercise most both before and after clinical presentation. In those who reduced exercise, decreased VT/VF risk	endurance exercise and frequent exercise increase risk of VT/VF, HF and ARVC in carriers	
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	2	Pasotti	2008	https://doi.org/10.1016/j.jacc.2008.06.044	Long-term outcome and risk stratification in dilated cardiolaminopathies	review of large database of LMNAC families	registry	164 individuals of whom 94 carry LMNA variant				cardiac events; vents were death from any cause, death from heart failure (HF), heart transplantation, and SCD, including appropriate implantable cardioverter-defibrillator (ICD) interventions.		competiive sport associated with 3.38 higher chance of events on multivariate analysis			
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	2	Skjolsvik	2020	https://doi.org/10.1161/JAHA.119.012937	Exercise is Associated With Impaired Left Ventricular Systolic Function in Patients With Lamin A/C Genotype	explore associations between exercise exposure and disease severity in patients with lamin a/c	cohort study	69 patients	LVEF	patients with confimred Lamin ac mutations		exercise hours >3 mets and calculated cumulative lifetime exericse	patients were groupd in active or sedate based on lifetime exercise hours above or below median	decrease in LVEF per tertile increment in lifetime exericse of 4%, LVEF <45% was observed at younger age in active patients (p=0.007)		aciteve lamin a/c patients had worse systolic function compared to sedentary individuals which occured at younger age	
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	2	Ortiz-Genga	2016	https://doi.org/10.1016/j.jacc.2016.09.927	Truncating FLNC Mutations Are Associated With High-Risk Dilated and Arrhythmogenic Cardiomyopathies	demonstrate the assocation with truncating FLNC variants and high risk cardiomyopathies	retrospective cohort study	28 probands	LV dysfunction, death, ICD shock					truncating mutations in FLNC cause a left dominant arrhythmogenic cardiomuyopathy with a high risk for ventricular arrhythmias and SCD			

7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	2	Sawant	2016	https://doi.org/10.1016/j.hrthm.2015.08.035	Safety of American Heart Association-recommended minimum exercise for desmosomal mutation carriers	To ascertain howexercise intensity is associated with outcomes among at risk members of families with PKP2 mutations	retrospective cohort study with patients drawn from the Johns Hopkins ARVD/C Registry; participants recruited from 10 families segregating heterozygous radical PKP2 mutations	Participants recruited from 10 extended families segregating heterozygous radical PKP2 mutations; 37 individuals (9 probands; 28 family members)		PKP2 mutations identified through either research or commercially available testing; 13 years or older; cognitively intact	Mutationsin other desmosomal genes (DSP, DSG2, DSC2, JUP) and non-desmosomal genes (PLN and TMEM43) were excluded	Structured interviews to ascertain exercise history since age 10		After adjustment for age, sex, family membership, participation in endurance athletics (p=0.03) and higher intensity exercise (p=0.004) were associated with diagnosis. Endurance athletes were also significantly more likely to develop VT/VF (p=0.02). Family members who restricted exercise were significantly less likely to be diagnosed and had no VT/VF.		Data suggests restricting unaffected desmosomal mutation carriers from endurance and high intensity athletics but potentially not from AHA recommended minimum levels of exercise	
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	2	van Rijsingen	2014	https://doi.org/10.1161/CIRCGENETICS.113.000374	Outcome in phospholamban R14del carriers: results of a large multicentre cohort study	To evaluate the mortality, cardiac disease outcome and possible risk factors for malignant ventricular arrhythmias in individuals carrying PLN R14del.	retrospective cohort study	403	First occurrence of malignant ventricular arrhythmias, end stage heart failure or call cause mortality	Phospholamban R14del mutation carriers				No premature death or major cardiac event occurred below age 15 years. LVEF<45% and sustained or nonsustained VT were highly significant risk factors (p<0.001). Sustained or nonsustained VT is an independent predictor for malignant ventricular arrhythmias (HR 4 and 2.6 respectively)		PLN R14del mutation carriers are at high risk for malignant ventricular arrhythmias and end stage heart failure with LVEF < 45% and sustained or nonsustained ventricular tachycardia as independent risk factors	
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	3	Monserrat	2003	https://doi.org/10.1016/s0735-1097(03)00827-1	Non-sustained ventricular tachycardia in hypertrophic cardiomyopathy: an independent marker of sudden death risk in young patients	To study the realtionship between the characteristics of NSVT during Holter monitoring and prognosis in hypertrophic caridomyopathy	cohort study	531		patients with confirmed hypertrophic cardiomyopathy; Age14 - 75 years; follow-up for more than one day; successful completion of Holter monitoring	Age <14 or > 75 years; absent follow-up data; insufficient Holter data to faciliate analysis	Ambulatory ECG monitoring		42 (9.8%) of 427 patients without NSVT and 26 (25%) of the 104 patients with NSVT died (0=0.0001). Of the 32 patients that died suddenly, 13 had NSVT (P=0.005). The relative risk of sudden death in patients with NSVT was highest in those less than or equal to 30 years		Non-sustained VT is associated with an increased risk of sudden death in young patients with HCM	Small sample size
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	3	Wang	2017	https://doi.org/10.1161/CIRCEP.116.004604	Prognostic Implications of Nonsustained Ventricular Tachycardia in High-Risk Patients With Hypertrophic Cardiomyopathy	To evaluate the prevanelnce of nsvt as well as rate, length and frequency of runs in HCM patients judged at potentially increased risk of sudden death	retrospective cohort study	160	ICD treated ventricular tachyarrhythmias including ATP and ICD shocks; survival	Adult patients (>18 years) implanted with an ICD and followed for at least 6 months with a diagnosis of HCM		Ambulatory ECG monitoring; ICD interrogation		160 patients (60% male) with HCM and ICDs were followed for median of 4 years after ICD implanation. NSVT > 200/minu was significantly associated with ICD treated VT/VF (p,).0001). Slower NSVT was not. NSVT with runs of >7 beats was significantly associated with ICD treated VT/VF (p.0028). Shorter bursts were not. Repetitive NSVT (>1) was significantly associated with ICD treated VT/VF (p=0.0017). Single runs were not.		Non-sustained VT was independently associated with ICD treated ventricular arrhythmias. Faster rate (> 200 per minute), longer (>7 beats) and repetitive runs was more highly predictive of ICD treated VT/VF.	
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	4	Lampert	2013	https://doi.org/10.1161/CIRCULATIONAHA.112.000447	Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry	to review the risks of ongoing sports participation with ICDs	prospective national registry	372		athletes with ICDS participating in organised or high risk sports		phone interview and medical records		death, RCA or arrhythmia or shock-related injury during sports	ICD terminated all episodes, no significant damage to devices	10% shocks during sports, 8% during other physical acitivy 6% at rest	
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	4	Lampert	2017	https://doi.org/10.1161/CIRCULATIONAHA.117.027828	Safety of Sports for Athletes With Implantable Cardioverter-Defibrillators: Long-Term Results of a Prospective Multinational Registry	long term outcomes of above study	prospective national registry	440	death, arrest, significant injury	athletes with ICDS participating in organised or high risk sports				no tachyarrhythmic deaths or externally resusciated arrhythmias during or after sports and no sports related inuries from syncope or shock during sports	10% shocks during sports (3/100 person years), more recieved shocks with physical activity (20%) compared to rest (10%) p<0.0001. presence of ARVC associated with shocks in sports	athletes with ICDs engaged in vigorous acitivity with no signal for harm, underlying disease is important particularly ARVC	
7.2.1 Treatment and management of athletes with inherited cardiomyopathies before and after RTP	4	Tobert	2022	https://doi.org/10.1016/j.mayocp.2022.03.024	Outcomes of Athletes With Genetic Heart Diseases and Implantable Cardioverter-Defibrillators Who Chose to Return to Play	to review outcomes for GHD patients who had RTP with ICD	cohort study	125	BCEs, ICD complications, inappropriate shocks	GHD patients with ICD who had RTP from single centre				overall 18% of athletes recieved an appropriate shock. athletes with ICD likely to have BCE than those without ICD BCE event rate 6.3/100 athletes years	1.34/100 athlete years inappropriate shock rate, 5.01/100 athlete years rate of other ICD complications. No complications during sports	no sports related SCD or sports related ICD damage reported	single centre
7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy	1, 3	Lampert	2023	https://doi.org/10.1001/jamacardio.2023.1042	Vigorous Exercise in Patients With Hypertrophic Cardiomyopathy	To determine whether engagement in vigorous exercise is associated with increased risk of ventricular arrhythmias or death in individuals with HCM	Prospective comparative cohort study, non-inferiority analysis	1660 total, 709 vigorous exercisers, 259 competitive. Subgroup 14-22 years old, total N= 203, 42 phenotype positive highest-level (interscholastic varsity/traveling team)	composite of death, resuscitated cardiac arrest, arrhythmic syncope and appropriate shock from ICD	patients with HCM (or those who are G+P- , total 8%), age 8-60 years	unable to participate in vigorous exercise, class III or IV heart failure excluded	self-reported levels of physical activity: sedentary, moderate or vigorous-intensity	Vigorous compared to non-vigorous. Subgroup comparisons competitive, vs non. Subgroup analysis age 14-22 comparing varsity/etc versus other vigorous versus non-vigorous	total of 4.6% of nonvigorous and 4.7% of vigorous exercisers reached compositive end point. Rates of 15.3 and 15.9 per 1000 persons-years. HR 1.01, below pre-specified UCL for non-inferiority. Similar findings in subgroup 14-22 years old for varsity/etc athletes.	multivariate anlaysis, no higher event rate in vigorous exercisers vs nonvigorous exercisers. G+P- individuals- no events.	no increased rate of death or life-threatening arrhythmias than those exerciseing moderately or those who were sedentary	nonrandomised
7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy	2	Gray	2011	https://doi.org/10.1016/j.jacard.2011.07.095	Natural history of genotype positive-phenotype negative patients with hypertrophic cardiomyopathy	To investigate the natural history of genotype positive, phenotype negative HCM patients presenting at all ages	retrospective cohort study	32		Individuals attending a single clinic who tested positive for a pathogenic gene mutation and without any evidence of hypertrophy on 2D echo (G+P-) at their first visit; followed for a minimum of 12 months				During the mean followup period of 4.1 +/-2.8 years, no patients developed new symptoms. Seriual echo showed a small increase in LV thickness in those aged <= 18 years consistent with normal growth. No increase was observed in those > 18 (p=0.50). Only one patient developed clinical HCM.		Genetic testing in HCM has led to the identification of a subgroup of HCM patients who are G+P-. These patients are usually asymptomatic, have no signs of HCM phenotype and can present at all ages. The G+P- state may represent a more benign form of HCM particularly if a patient remains phenotype negative in adulthood.	
7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy	3	Martinez	2023	https://doi.org/10.1016/j.jacc.2023.05.059	Return-to-Play for Elite Athletes With Genetic Heart Diseases Predisposing to Sudden Cardiac Death	To evaluate outcomes among high level athletes diagnosed with genetic heart disease	Retrospective cohort study	76 patients, 40 with HCM	Breakthrough cardiac events- arrhythmic syncope, symptomatic NSVT, appropriate VT or VF ICD shock, sustained VT, cardiac arrest with AED rescue or SCD	Elite level athlete: NCAA Division 1, Olympic, professional. Mean age 20 years.	n/a	Continuation of sports	n/a	No events during exercise. 1 HCM athlete with arrest, non-exertional, 1 HCM athlete, non-arrhythmic syncope	Athletes with GHD can RTP when comprehensively clinically evaluation and in SDM model, with low incidence of events	No adverse events related to RTP	Retrospective design, limited sample size, no comparator

7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy	3	Turkowski	2018	https://doi.org/10.1161/CIRCULATIONAHA.117.031306	Return-to-Play for Athletes With Genetic Heart Diseases	The prevalence and outcomes of athletes with sudden cardiac death predisposing GHDs, after their return to play	retrospective cohort study	Total 366, 23 with HCM	BCE	athletes with genetic heart disease participating in competitive sports at initial evaluation. Mean age 15	NA	continuation sports	those who continued to participate versus those who stopped ("former athletes")	Higher event rate in those who stopped (p 0.03)	NA	return to play was not associated with increase in event rates	HCM not large percent of group, not analyzed separately
7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy	3	Basu	2022	https://doi.org/10.1016/j.jacc.2022.08.715	Impact of Exercise on Outcomes and Phenotypic Expression in Athletes With Nonobstructive Hypertrophic Cardiomyopathy	outcomes in athletes with hcm who continued sports	retrosepctive review	53 total, 28 professional athlete	arrhythmic events, changes in echo parameters	athlete with HCM continuing to train. age range 19-65	NA	continuation sports	baseline assessment compared to last clinical followup	mean follow up 4.5 years, no symptoms, no deaths, no sustained VT or syncope, 4 had new NSVT	all athletes had low ESC SCD risk score, no athlete had hx of syncope mild phenotype (avg wall thickness 14.6mm), no LVOTO, 41% with LGE	in a low risk cohort with mild HCM, continuation of intense sport was not associated with significant arrhythmias nor did it have a negative impact on the cardiac phenotype.	Study population age range 19-65 years
7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy	3	Pelliccia	2020	https://doi.org/10.1136/bjsports-2019-100890	Clinical outcomes in adult athletes with hypertrophic cardiomyopathy: a 7-year follow-up study	incidence of cardiovascular events in a cohort of patients with HCM engaged in long-term exercise programmes and competitive sport	retrospective cohort study	88	death/ACA	adults with HCM participating in competitive sports at initial evaluation. age range 19-44	n/a	continuation sports	those who stopped training (n=61) compared to those who continued training (n=27)	2 patients suffered SCA or death, both outside of sport participation. 22% reported symptoms. Kaplan meier analysis showed no difference between those who continued sports versus discontinued	3 syncope, 10 palps, 4 chest pain 2 dyspnoea, 2 SCA/death. Major event Rate 0.3% per year	voluntary continued participation in sports was not associated with increased major cardaic events or clinical worsening in a cohort of low risk hcm patients	Study population age range 19-44 years
7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy	4	Newman	2023	https://doi.org/10.1016/j.amjcard.2022.11.008	Cardiopulmonary Exercise Testing in Athletes With Hypertrophic Cardiomyopathy	to investigate CPET in athletes with HCM and clinical characteristics associated with objective measures of aerobic capacity	single centre retrospective cohort study	n=58 athletes with HCM	VO2 max,clinical outcomes	adult athlete with hcm				mild reduction in VO2 max 37.9mL/m2- more likely in those on BB or with LVOTO	9% underwent myectomy and 14% received ICD for primary prevention, nod eaths	prognostic role of CPET is unclear in athletes with HCM, reduced peak VO2 max did not corrlate with symptom status or clinical outcomes	
7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy	4	Nistri	2010	https://doi.org/10.1016/j.amjcard.2010.06.057	Timing and significance of exercise-induced left ventricular outflow tract pressure gradients in hypertrophic cardiomyopathy	To assess the patterns of onset of physiologicall provoked LVOTO and exercise performance in individuals with HCM and no baseline obstruction	cohort study	74 patients						16 patient developed LVOTO at low exercise levels. The timing of the gradient onset was not predictable from baseline clinical or echo or symptoms		supportive of value of exercise echocardiography in HCM	
7.2.2 Treatment and management for athletes with hypertrophic cardiomyopathy	4	Olivotto	2020	https://doi.org/10.1016/S0140-6736(20)31792-X	Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial	To assess the efficacy and safety of mavacamten for targeted medical treatment of obstructive hypertrophic cardiomyopathy	multicentre randomized double blined, placebo controlled parallel group trial	251	Primary endpoint was a composite to assess clinical response at week 30 compared with baseline (pVO2 and NYHA class). Secondary endpoints were change from baseline to week 30 in post exercise LVOT gradient, pVO2, NYHA class improvement, patient reported outcomes	Age 18 or greater with obstructive hypertrophic cardiomyopathy, peak LVOT gradient at least 50 mmHg at rest, after valsalva or exercise, LVEF 55% or above, NYHA II-III symptoms. Patients had to be able to perform upright CPET.	History of syncope or sustained ventricular tachyarrhythmia with exercise within 6 months before screening; QTc (Fridericia) more than 500 ms; paroxysmal or intermittent atrial fibrillation on screening ECG; persistent or permanent AF not on OAC for 4 weeks or more or not adequately rate controlled within 6 months; septal reduction therapy less than six months prior	1:1 randomization to once daily oral mavacamten or placebo for 30 weeks with dose titration at weeks 8 and 14		patients on mevacamten had greater reductions than those on placebo in post exercise LVOT gradient (P<0.0001), greater increase in pVO2 (p=0.0006) and improved symptom scores (p<0.0001).	7 patients on mevacamten and 2 on placebo had a transient decrease in LVEF to less than 50%	Treatment with mevacamten improved exercise capacity, LVOT obstruction, NYHA functional class, and health status in patients with obstructive HCM.	
7.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	1, 2, 3, 5	James	2013	https://doi.org/10.1016/j.jacc.2013.06.033	Exercise increases age-related penetrance and arrhythmic risk in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated desmosomal mutation carriers	To assess how exercise influences penetrance of ARVC amongst patients with desmosomal mutations	cohort study	87	sustained VT/VF, heart failure and diagnostic criteria	gene carriers of ARVC with normal phenotype		interview of regular physical activiy from age 10		endurance athletes more likely to meet TFC (82% vs 35%), develop symptoms at a younger age (30 vs 40, p=0.05) and have lower lifetime survivial free of VT/VF (p=0.013)and heart failure (p=0.004)	survival from first VT/VF event was lowest in those who exercise most both before and after clinical presentation. In those who reduced exercise, decreased VT/VF risk	endurance exercise and frequent exercise increase risk of VT/VF, HF and ARVC in carriers	
7.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	2, 3	Pasotti	2008	https://doi.org/10.1016/j.jacc.2008.06.044	Long-term outcome and risk stratification in dilated cardiolaminopathies	review of large database of LMNAC families	registry	164 individuals of whom 94 carry LMNA variant				cardiac events; vents were death from any cause, death from heart failure (HF), heart transplantation, and SCD, including appropriate implantable cardioverter-defibrillator (ICD) interventions.		competiive sport associated with 3.38 higher chance of events on multivariate analysis			
7.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	2, 3	Skjolsvik	2020	https://doi.org/10.1161/JAHA.119.012937	Exercise is Associated With Impaired Left Ventricular Systolic Function in Patients With Lamin A/C Genotype	explore associations between exercise exposure and disease severity in patients with lamin a/c	cohort study	69 patients	LVEF	patients with confimred Lamin ac mutations		exercise hours >3 mets and calculated cumulative lifetime exericse	patients were groupd in active or sedate based on lifetime exercise hours above or below median	decrease in LVEF per tertile increment in lifetime exericse of 4%, LVEF <45% was observed at younger age in active patients (p=0.007)		aciteve lamin a/c patients had worse systolic function compared to sedentary individuals which occured at younger age	
7.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	2, 3	Ortiz-Genga	2016	https://doi.org/10.1016/j.jacc.2016.09.927	Truncating FLNC Mutations Are Associated With High-Risk Dilated and Arrhythmogenic Cardiomyopathies	demonstrate the assocation with truncating FLNC variants and high risk cardiomyopathies	retrospective cohort study	28 probands	LV dysfunction, death, ICD shock					truncating mutations in FLNC cause a left dominant arrhythmogenic cardiomuyopathy with a high risk for ventricular arrhythmias and SCD			
7.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	2, 3	Sawant	2016	https://doi.org/10.1016/j.hrthm.2015.08.035	Safety of American Heart Association-recommended minimum exercise for desmosomal mutation carriers	To ascertain howexercise intensity is associated with outcomes among at risk members of families with PKP2 mutations	retrospective cohort study with patients drawn from the Johns Hopkins ARVD/C Registry; participants recruited from 10 families segregating heterozygous radical PKP2 mutations	Participants recruited from 10 extended families segregating heterozygous radical PKP2 mutations; 37 individuals (9 probands; 28 family members)		PKP2 mutations identified through either research or commercially available testing; 13 years or older; cognitively intact	Mutationsin other desmosomal genes (DSP, DSG2, DSC2, JUP) and non-desmosomal genes (PLN and TMEM43) were excluded	Structured interviews to ascertain exercise history since age 10		After adjustment for age, sex, family membership, participation in endurance athletics (p=0.03) and higher intensity exercise (p=0.004) were associated with diagnosis. Endurance athletes were also significantly more likely to develop VT/VF (p=0.02). Family members who restricted exercise were significantly less likely to be diagnosed and had no VT/VF.		Data suggests restricting unaffected desmosomal mutation carriers from endurance and high intensity athletics but potentially not from AHA recommended minimum levels of exercise	

7.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	2, 3	van Rijsingen	2014	https://doi.org/10.1161/CIRCGENETICS.113.000374	Outcome in phospholamban R14del carriers: results of a large multicentre cohort study	To evaluate the mortality, cardiac disease outcome and possible risk factors for malignant ventricular arrhythmias in individuals carrying PLN R14del.	retrospective cohort study	403	First occurrence of malignant ventricular arrhythmias, end stage heart failure or call cause mortality	Phospholamban R14del mutation carriers			No premature death or major cardiac event occurred below age 15 years. LVEF<45% and sustained or nonsustained VT were highly significant risk factors (p<0.001). Sustained or nonsustained VT is an independent predictor for malignant ventricular arrhythmias (HR 4 and 2.6 respectively)		PLN R14del mutation carriers are at high risk for malignant ventricular arrhythmias and end stage heart failure with LVEF < 45% and sustained or nonsustained ventricular tachycardia as independent risk factors	
7.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	4	van Lint	2023	https://doi.org/10.1007/s12471-023-01800-4	Exercise does not influence development of phenotype in PLN p.(Arg14del) cardiomyopathy	To evaluate the impact of exercise on the development of phenotype in carriers of the PLN p.(Arg14del) mutation, particularly looking at arrhythmic risk and progression to heart failure.	Observational cohort study	207 adult carriers of PLN p.(Arg14del) from three Dutch university medical centers	Clinical diagnosis of ARVC or DCM, sustained VA and hospitalization for heart failure	Adult carriers of PLN p.(Arg14del) mutation aged 18 years and older, willing to participate in the study and provide exercise history.	n/a	Structured interviews to document exercise history and clinical follow-up to determine phenotype and clinical outcomes.	n/a	No significant association was found between exercise history and the development of cardiomyopathy phenotypes or survival free from VA and HF.	Exercise history did not predict development of ventricular arrhythmias or heart failure; no reason to limit mild-moderate exercise in asymptomatic carriers without signs or symptoms.	There was no association between the amount of exercise and the susceptibility to develop ARVC, DCM, VA or HF in PLN p.(Arg14del) carriers suggesting unaffected PLN carriers can safely perform mild-moderate exercise	Recall bias as exercise history assessed retrospectively; voluntary response bias; small study population that was not particularly active; single country and predominantly Caucasian population
8.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	6	La Gerche	2010	https://doi.org/10.1136/hrt.2009.189621	Lower than expected desmosomal gene mutation prevalence in endurance athletes with complex ventricular arrhythmias of right ventricular origin	to determine the yield of genetic testing in athletes with RV structual abnormalities and RV arrhythmias	cohort study	47 athletes		complex VA or RV morphology perfoming 14 hrous per week of moderate to intense sports for 19 years			rate of genetic result was 12.8% in this cohort,severe RV dysfunction more frequent in those who were genotype positive (33% vs 2%, p=0.04)		arvc phenotype may be associated with intense exercise without a genetic predisposition.	
8.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	6	La Gerche	2015	https://doi.org/10.1093/eurheartj/ehv202	Exercise-induced right ventricular dysfunction is associated with ventricular arrhythmias in endurance athletes	To review predictors of arrhythmias in athletes	cohort study	17 athletes with RV ventricular arrhythmias	ventricular arrhythmia compared to those without				Exericse indued increases in RV geometry were attenuated in endurance athletes with ventricular arrhythmias compared to healthy endurance athletes and nonathletes	During exercise CMR decreases in RVESV and augmentation of RV function were less in the arrhythmic group compared to the 2 other groups. ROC curve analysis shows RV exercise meausres can differentate these athletes from those without arrhythmia (AUC 0.96)	exercise testing reveals RV contractive dysfunction in those who are knows to have RV arrhythmias	
8.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	7, 8	Halliday	2019	https://doi.org/10.1016/j.jcmg.2018.07.015	Outcome in Dilated Cardiomyopathy Related to the Extent, Location, and Pattern of Late Gadolinium Enhancement	to investigate the association between extent, location and pattern of LGE in a large nonischaemic DCM cohort	cohort study	874 patients	all cause mortality and SCD				HR for all cause mortaltiy 1.56 to 2.31 (for 0->5.1% of DGE) and HR for SCD up to 4.87 (>5.1% DGE)	marked non linear relationship between LGE extent and outcomes. Presence of septal LGE associated with mortality, combination of septal and free wall LGE was most associated with SCD		presentce of DGE associated with increased risk of SCD and death even with small extent of DGE
8.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	7, 8	Halliday	2017	https://doi.org/10.1161/CIRCULATIONAHA.116.026910	Association Between Midwall Late Gadolinium Enhancement and Sudden Cardiac Death in Patients With Dilated Cardiomyopathy and Mild and Moderate Left Ventricular Systolic Dysfunction	Whether LGE on CMR identifeid patients with DCM without severe LV dysfunction at high risk of SCD	prospective cohort	399 patients	prespecifed primary composite of SCD or aborted SCD	DCM with LVEF >40%			HR of LGE 9.3 p<0.0001	estimated HRS for primary end point for patients with LGE extent up to 11.8% for those with >5% LGE	midwall LGE identifies DCM patients who may be at incrased risk of SCD	median age is 50 in this cohort, not athletic
8.2.3 Management specific to athletes with arrhythmogenic and dilated cardiomyopathies	7, 8	Perazzolo Marra	2014	https://doi.org/10.1016/j.hrthm.2014.01.014	Impact of the presence and amount of myocardial fibrosis by cardiac magnetic resonance on arrhythmic outcome and sudden cardiac death in nonischemic dilated cardiomyopathy	To assess the value of the presence and extent of myocardial fibrosis as evidenced by contrast-enhanced cardiac MRI for predicting major arrhythmic events and sudden cardiac death in patients with non ischemic dilated cardiomyopathy	prospective cohort	137 patients (median age 49 years; 108 men)	index combined end point of major arrhythmic eents such as SCD, cardiac arrest due to VF, sustained VT or appropriate ICD intervention	depressed LV systolic function (EF<50%) on non-CMR study; angiographic study showing the absence of flow limiting CAD (greater than or equal to 50% luminal stenosis); absence of either valvular or hypertensive heart disease and congenital heart abnormalities	Recent onset of heart failure (<1 month); diagnosis of hypertrophic cardiomyopathy, restrictive cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, suspected infiltrative heart disease or other specific cardiomyopathy; hemodynamic unstable conditions; contraindication to CMR (claustrophobia, pacemaker, ICD, metallic clips, atrial fibrillation, severe obesity preventing entering the scanner bore, pregnancy); chronic renal failure with eGFR <30 ml/min	Detailed clinical evaluation including 12 lead ECG, 2 D eho, contrast enhanced MRI, coronary angiography		LV-LGE was identified in 76 (55.5%); median extent of LGE was 9%; The presence of LV-LGE was unrelated to sex, age, NYHA functional class, LVEF or other clinical baseline characteristic. Over a median followup of 3 years, 69 (50.3%) underwent ICD implantation (primary in 62; secondary in 7). The primary arrhythmic end point occurred in 22 (16.1%). Patients who experienced arrhythmic events significantly more often showed LBBB (p=0.02) and the presence of LV LGE on CE-CMR p=0.04. The annual event rate was 7% in patients with LV LGE vs 3.3% in those without LGE (p=0.002). The prevalence of major arrhythmic events was not associated with a specific LGE pattern.		The presence of LV LGE is an independent predictor of arrhythmic outcome; the absence of LGE characterizes a low arrhythmic subgroup of patients with no SCD events during followup	Infiltrative disease could not be excluded definitively; quantification of hyperenhanced signals of nonischemic myocardial scar is not yet standardized
7.3 Moving from athlete to family: Implications of a genetic diagnosis	1	Ingles	2013	https://doi.org/10.1038/gim.2013.44	Clinical predictors of genetic testing outcomes in hypertrophic cardiomyopathy	Identify clinical variables that can predict probands with hypertrophic cardiomyopathy in whom a pathogenic mutation will be identified	Retrospective cohort study; national registry	265 unrelated individuals diagnosed with hypertrophic cardiomyopathy	Detection of a mutation (pathogenic variant)	Patients with a clinical diagnosis of HCM who had undergone genetic testing between 2002-2011 that included the following genes: MYBPC3, MYH7, TPM1, TNNT2, TNNI3, ACTC1, MYL2, MYL3, ACTN2, TCAP	Probands not meeting clinical diagnostic criteria for HCM were not included (i.e., physiologic hypertrophy in response to athletic training or hypertension).	Genetic testing for hypertrophic cardiomyopathy.	n/a	38 (52%) had at least one mutation. Pathogenic variants were more likely to be detected in probands with hypertrophic cardiomyopathy with an established family history of disease (72 vs. 29%, P<0.0001), and a positive family history of sudden cardiac death further increased the detection rate (89 vs. 59%, P<0.0001). Multivariate analysis identified female gender, increased left-ventricular wall thickness, family history of hypertrophic cardiomyopathy, and family history of sudden cardiac death as being associated with greatest chance of identifying a gene mutation. Multiple mutation carriers (n = 16, 6%) were more likely to have suffered an out-of-hospital cardiac arrest or sudden cardiac death (31 vs. 7%, P = 0.012).	n/a	Family history is a key clinical predictor of a positive genetic diagnosis.	Retrospective design; potential for selection bias as participants were from specialized clinics; the method of genetic testing employed for each case was dependent on the best available technology at the time and so incorporates a number of different genetic testing approaches, all of which are now dated.

7.3 Moving from athlete to family: Implications of a genetic diagnosis	1	Waddell-Smith	2016	https://doi.org/10.1136/openhrt-2015-000329	Inpatient detection of cardiac-inherited disease: the impact of improving family history taking	Compare diagnostic value of family histories recorded by inpatient cardiology teams with a multigenerational family tree obtained by specially trained allied professionals.	Observational, prospective implementation study	37 patients; 2 experienced cardiac nurses trained in Family history taking.	1. Extent of family history documentation; 2. detection rate of potentially heritable cardiovascular condition.	hospital inpatients who were definitely or potentially affected by cardiac-inherited disease at two 2 tertiary adult cardiac units in New Zealand.	n/a	Family history documentation of experienced cardiology nburses trained in cardiac inherited diseases and family history taking (and established as regional coordinators for a National Cardiac Inherited Disease Registry).	Family history documentation of inpatient adult cardiovascular care team.	Inpatient team: 20 (54%) had no documentation of FHx during their admission. Of the 17 with some FHx, 14 were insufficient. In the 3 cases where a familial condition was documented the patients knew their diagnosis and informed the team. In contrast, when pedigrees were obtained by the coordinators, 29 (78%) patients were able to provide three full generations of FHx. Twelve of the 29 pedigrees (41%) were strongly consistent with a heritable pathology for the patient's condition.	n/a	Appropriately trained staff taking pedigrees in the inpatient unit increase detection of heritable conditions.	Small sample size and potential selection bias.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	2, 5	Earle	2019	https://doi.org/10.1016/j.ahj.2018.11.013	Development of a cardiac inherited disease service and clinical registry: A 15-year perspective	Desribe timeline, components, and growth of a national inherited heart disease and sudden death registry and the associated service.	Observational, descriptive study of a registry development	2,746 registrants covering seven forms of cardiac inherited disease; 941 probands enrolled	n/a	Probands with suspected cardiac inherited disease and their families as of 10/2017.	n/a	n/a	n/a	22% registered due to SCD/SCA. Taking a multidisciplinary approach has been a key features for the success of the registry.	The registry facilitated the development of the world's first national, fully funded molecular genetic autopsy service.	Multidisciplinary team needs to include pathologists and genetics expertise.	Study does not detail specific clinical outcomes or comparative data but focuses on the structural and procedural development of the registry and service.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	2, 5	Ingles	2008	https://doi.org/10.1097/GIM.0b013e3181612cc7	Psychosocial impact of specialized cardiac genetic clinics for hypertrophic cardiomyopathy	Describe the psychosocial factors associated with attending a specialty cardiac genetic clinic, and to determine whether these may be predictors of comorbid anxiety and depression in this population.	Cross-sectional questionnaire study	109 participants from a specialized hypertrophic cardiomyopathy clinic	the Hospital Anxiety and Depression Scale, Patient Experience Scales, and Patient Satisfaction Scales scores	Individuals attending the HCM Clinic, RPAH, Sydney, Australia from September 2003 to September 2006 (77% HCM patients; 23% at-risk relatives).	Pateints < age 17 years	Psychological assessments using standardized scales.	Follow-up via this multidisciplinary specialized cardiac genetic service vs. community cardiology care.	24% of patients were well adjusted to their diagnosis; HADS scores showed prevalance of anxiety and depression of 45% and 18%. logistic regression models adjusting for age, gender, and educational attainment show that those HCM patients who reported seeing other cardiologists on a regular basis were significantly more likely to have a higher HADS depression score, compared with those who attended regular follow-up at the RPAH HCM Clinic.	n/a	HCM patients who attend specialized cardiac genetic clinics are better adjusted and worry less.	Cross-sectional design limits causality inference and may reflect selection bias; Very wide confidence interval.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	2, 5	Zentner	2015	https://doi.org/10.5694/mja14.01674	The Cardiac Genetics Clinic: a model for multidisciplinary genomic medicine	Database exploration of referral diagnoses, sex, number of clinic visits and incidence of genetic testing in a population of individuals attending.	Retrospective database exploration of cohort data	1170 patients attending the Cardiac Genetics Clinic at the Royal Melbourne Hospital from 2007 to 2013	Classification of patients into diagnostic categories, number of probands and at-risk relatives assessed, incidence and outcomes of genetic testing.	All individuals initially attending the multidisciplinary Cardiac Genetics Clinic (CGC) at the Royal Melbourne Hospital between July 2007-July 2013, either as the proband or as an at-risk family member.	n/a	Assessment and genetic testing at the Cardiac Genetics Clinic	n/a	Genetic testing (mutation detection or predictive testing) was undertaken in 381 individuals (32.6%), and a pathogenic mutation was identified in 47.6% of tests, representing 15.3% of the total population.	The majority of patients (57.5%) made only one clinic visit. Median age was 39 years.	The Cardiac Genetics Clinic plays a role in managing genetic cardiac diseases, with a shift towards more comprehensive gene panel-based testing improving mutation detection rates.	Retrospective design
7.3 Moving from athlete to family: Implications of a genetic diagnosis	3, 5	Christian	2022	https://doi.org/10.1136/openhrt-2021-001815	Diagnostic validity and clinical utility of genetic testing for hypertrophic cardiomyopathy: a systematic review and meta-analysis	Define the diagnostic validity and clinical utility of genetic testing for patients with hypertrophic cardiomyopathy (HCM) and their at-risk relatives.	Systematic review and meta-analysis	132 articles, 24897 patients from predominantly adult and pediatric cohorts undergoing genetic testing for HCM.	Detection of a mutation (pathogenic variant); Diagnostic rates, genotype-phenotype correlations, disease penetrance.	Studies that assessed the diagnostic validity and clinical utility of genetic testing in HCM using predefined PICOTS.	Non-English publications, studies not addressing the predefined PICOTS directly.	Genetic testing for hypertrophic cardiomyopathy across multiple gene panels, incorporating ACMG/AMP standards for variant classification.	Comparison of detection rates and clinical outcomes between different genetic testing standards (e.g., ACMG/AMP), and between pediatric and adult cohorts.	The detection rate based on pathogenic and likely pathogenic variants was significantly higher in paediatric cohorts compared with adults (56% vs 42%; p=0.01) and in adults with a family history compared with sporadic cases (59% vs 33%; p=0.005). Overall, disease penetrance in adult cohorts was 62%. Penetrance was 55% in gene positive family member only cohorts. There was a significant difference in penetrance depending on if probands were included or excluded (73% vs 55%; p=0.003) as expected.	No specific adverse events related to genetic testing were reported.	Genetic testing for HCM provides significant diagnostic validity, particularly with refined genetic testing standards and in pediatric cohorts. It also has substantial clinical utility in managing and predicting disease outcomes based on genotype-phenotype correlations.	Heterogeneity of variant classification; heterogeneity of panel size used; retrospective nature of many included studies. The impact of genetic testing standards on long-term clinical outcomes remains unclear due to the heterogeneity of data and lack of standardized reporting across studies.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	3, 5	Cirino	2022	https://doi.org/10.1002/jgc4.1604	The uptake and utility of genetic testing and genetic counseling for hypertrophic cardiomyopathy-A systematic review and meta-analysis	Summarize the uptake and utility of genetic counseling and genetic testing for patients with HCM and their at-risk family members, as well as the impact of genetic counseling/testing on patient-reported outcomes (PROs).	Systematic review and meta-analysis	48 studies published through 3/12/2021, with variable sample sizes that included patients with HCM and their at-risk relatives.	Uptake of genetic testing and counseling, impact on patient-reported outcomes (PROs), and effectiveness of cascade screening.	Studies involving genetic testing and counseling in patients with HCM and their relatives, examining outcomes related to diagnostic utility and patient impact.	Non-English studies, studies not addressing the systematic review's predefined research questions directly.	Genetic testing and genetic counseling interventions in HCM.	Comparisons were made between different patient groups within the HCM population regarding the uptake of genetic testing and counseling.	Uptake of cascade screening for HCM at-risk relatives was 61% for cascade genetic testing (95% CI: 45, 75), 58% for cardiac screening (e.g. echocardiography) (95% CI: 40, 73), and 69% for either/both approaches (95% CI: 43, 87). Relatives of probands with a positive genetic test result were significantly more likely to undergo cascade screening compared to relatives of probands with a negative result (odds ratio = 3.17, 95% CI: 2.12, 4.76). Genetic counseling was associated with high satisfaction, increased perceived personal control and empowerment, and decreased anxiety. PROs after genetic testing varied and genetic counseling was associated with high satisfaction and improved PROs.	Multiple studies found little difference in PROs between individuals receiving positive versus negative genetic test results; however, other studies found that individuals with positive genetic test results experienced worse psychological outcomes.	The uptake of genetic counseling and testing is variable in HCM families, but associated with high satisfaction and improved patient-reported outcomes.	Limited by the heterogeneity of included studies and variability in genetic testing methodologies across studies.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	3, 5	Davey	2005	https://doi.org/10.1007/s10897-005-0519-6	Evaluating genetic counseling: client expectations, psychological adjustment and satisfaction with service	Evaluate the genetic counseling services provided by Genetic Services of Western Australia (GSWA) to determine the impact of counseling on client expectations, satisfaction with the service, and psychological adjustment, defined as wellbeing and perceived personal control (PPC).	Observatiponal, pre/post intervention (questionnaire) study	122 clients who received genetic counseling at Genetic Services of Western Australia	Perceived personal control (PPC Questionnaire by Berkenstadt et al 1999; satisfaction (GC Satisfaction Scale - Shiloh, 1990): Well Being (v 28 General Health Questionnaire);	Clients who attended genetic counseling from 11/2002 to 10/2023 3 non-cardiology clinics were included: familial cancer, general genetics, pediatric clinic or their parents if the patient was <16 years old.	Attendees of emergency appointments; non-English speakers.	Provision of genetic counseling services including information delivery, psychological support, and decision-making assistance.	n/a	41% response rate. The mean general GHQ score decreased from 49 (44%) pre-counseling, to 46(41%) post-counseling, (p=.010). Each component of the GHQ also decreased, but the change was only statistically significant somatic symptoms (z=−1.957,p<.050), and the anxiety and insomnia (z=−2.761,p<.060) dimensions. Perceived personal control also increased overall (z=−3.751,p≤.001)and in the cognitive (z=−5.496,p≤.001) and be-havioral (z=−2.778,p=.005) dimensions.	n/a	Client expectations of the service as a means of providing information were met Genetic counseling ounseling maintained and enhance psychological wellbeing. The role of counseling in facilitating perceived personal cotrol was a key contributor to a high sense of satisfaction in clients	Small sample size; potential selection bias due to specific inclusion criteria; reliance on self-reported measures which may affect the accuracy of psychological assessments.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	3, 5	Hofman	2010	https://doi.org/10.1016/j.jacc.2009.12.063	Active cascade screening in primary inherited arrhythmia syndromes: does it lead to prophylactic treatment?	To describe medical follow-up including cardiovascular evaluation and treatment following identification of pathogenic channelopathy variants through cascade genetic screening.	Retrospective chart review	509 relatives tested positive for disease-causing familial mutations from 1996 to 2008	Cardiac evaluation and therapy subsequent to detection of carrier status through cascade screening.	Gene positive relatives in families with CPVT, Brugada Syndrome, and LQTS ascertained through a cardiogenetics service in Amsterdam.	Relatives without identified mutations or those not undergoing cascade screening.	Cascade screening followed by appropriate prophylactic treatments (medications, devices) based on mutation and clinical evaluation.	n/a	After a mean follow-up of 69 ± 31 months (LQTS), 60 ± 19 months (CPVT), and 56 ± 21 months (BrS), treatment was initiated and ongoing in 65% (199 of 308), 71% (85 of 120), and 6% (5 of 81) of the relatives in the LQTS, CPVT, and BrS families, respectively. Eight carriers were lost to follow-up. Treatment included drug treatment (n = 249) or implantation of pacemakers (n = 26) or cardioverter-defibrillators (n = 14). All mutation carriers received lifestyle instructions and a list of drugs to be avoided.	All mutation carriers received lifestyle instructions and a list of drugs to be avoided.	Cascade screening in families with LQTS, BrS, or CPVT, which was based on DNA mutation carrying and subsequent cardiologic investigation, resulted in immediate prophylactic treatment in a substantial proportion of carriers	Retrospective design, variability in treatment initiation based on clinical judgment, and lack of a control group.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	3, 5	Ison	2019	https://doi.org/10.1002/jgc4.1050	The impact of cardiovascular genetic counseling on patient empowerment	To assess how cardiovascular genetic counseling impacts patient empowerment and awareness/ communication of surveillance recommendations with family members.	Observational, pre/post intervention (questionnaire) study	42 adult patients attending a CVGC appointment	Change in pateint empowerment (Genetic Counseling Outcome Scale); knowledge of cardiac surveillance recommendations	Adults attending an in-person genetic counseling appointment at a certified genetic counselor at medical center in Indiana.	Individuals with cardiovascular indications secondary to a syndrome (e.g., Marfan syndrome, William syndrome.) were excluded.	Patients completed the GCOS survey and a 5-item survey about knowledge of cardiac surveillance recommendations before and after their CVGC appointment.	Comparison of pre- and post-GC survey results	The mean difference between pre- and post-GC empowerment scores was 17.5 points (mean pre-GC score = 118.5, mean post-GC score = 136, p < 0.0001; effect size, d = 0.94). Forty percent of individuals (17/42) were aware of surveillance recommendations for at-risk family members prior to GC; this increased to 76% of individuals (32/42) post-GC (p < 0.01).	n/a	There is a significant increase in empowerment and awareness of recommendations for at-risk relatives as a result of CVGC demonstrating the utility of cardiovascular genetic counseling.	No control group, small sample size, possible selection and self-reporting bias.

7.3 Moving from athlete to family: Implications of a genetic diagnosis	3, 4, 5	Knight	2020	https://doi.org/10.1016/j.hrthm.2019.06.015	Genetic testing and cascade screening in pediatric long QT syndrome and hypertrophic cardiomyopathy	Examine the use of genetic testing and yield of cascade screening for children across diverse regions in the United States and identify obstacles.	Retrospective chart review	Cascade screening: 315 index patients (mean age 9.0 ± 5.8 years) from six US pediatric centers Relative screening: 601 relatives from the 315 index patients	Acceptance of cascade screening; documented reason for non-acceptance; documentation of whether family ws informed of heritability and recurrence risk; cardiovascular screening performed; genetic testing performed.	Index case age < 21 years and a clinical diagnosis of and/or gene-positive status for LQTS or HCM established from 2008 - 2014.	Adults and second opinion diagnoses to prevent duplication of subjects.	Genetic testing and cascade screening for LQTS and HCM.	n/a	Families had a 75% (254) acceptance of cascade screening. The yield of relative screening was 39% (232/601), an average of 0.91 detected per family. Genetic testing was less utilized in HCM index patients and relatives. Screening participation was greater in families of gene-positive index patients (88%) (P <.001) compared to gene-negative patients (53%).	Cascade method utilization: Cardiology-only 45%, combined genetic and cardiology 39%, and genetic only 16%. Screening yield by method: combined 57%, genetic-only 29%, and cardiology-only 20%. Family decisions were the leading barriers to cascade screening (26% lack of followthrough and 26% declined), whereas insurance (6%) was the least cited barrier.	Family participation in cascade screening is high, but the greatest barriers are family mediated (declined, lack of followthrough). Positive proband genetic testing led to greater participation.	Retrospective nature, reliance on self-reported data, and limited ability to generalize beyond the participating centers.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	3, 4, 5	Ko	2018	https://doi.org/10.1038/gim.2017.79	Genetic testing impacts the utility of prospective familial screening in hypertrophic cardiomyopathy through identification of a nonfamilial subgroup	Determine the yield of family scteening for HCM and how it is impacted by a probands genetic test result.	Restrospective cohort study, questionnaire	120 survey respondents reporting outcome of cardiac screning of 267 family members.	Reported testing and clinical diagnoses of relatives.	Adults diagnosed with HCM 2008-2014 participating in the UMichigan HCM Registry.	Individuals with left ventricular hypertrophy from systemic, syndromic, or metabolic conditions were excluded.	Genetic testing and subsequent familial screening based on genetic test results.	Comparison between HCM patients with positive vs. negative genetic testing results.	Response rate 37%. Subjects with positive genetic test or family history (n=74, 62%) reported an HCM diagnosis in 34 of 203 first-degree relatives who were screened (17%). Affected family members were diagnosed at a mean age of 30–39 years, and 22 of 34 experienced HCM-related adverse events (65%). Gene test–negative subjects with no prior family history of HCM (n=46, 38%) reported an HCM diagnosis in only 2 of 64 first-degree relatives who were screened (3%, p<0.001).	Positive genetic test was a strong predictor of a new diagnosis of HCM in relatives (p=0.004). Negative genetic testing suggested a non-Mendelian inheritance.	Genetic testing can differentiate between familial and nonfamilial HCM, influencing screening strategies and reducing unnecessary screening in some families.	Retrospective design; Self-reported data from an online survey; Outcomes of relatives reported by the index cases who may not have the relevant information.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	3, 5	Murray	2022	https://doi.org/10.1002/jgc4.1499	Strength of the genetic counselor: patient relationship is associated with extent of increased empowerment in patients with arrhythmogenic cardiomyopathy	To examine the impact of the genetic counselor-patient relationship on patient empowerment in individuals with arrhythmogenic cardiomyopathy (ACM), and how this relationship affects outcomes regardless of whether genetic testing was previously ordered.	Prospective, cross-sectional survey-based (questionnaire pre-post genetic counseling) study	120 patients referred for first-time genetic counseling at the Johns Hopkins Arrhythmogenic Cardiomyopathy center	Empowerment - Genetic counseling outcome scale (GCOS); Cardiac anxiety - Cardiac anxiety scale (CAQ); GC:client therapeutic alliance - Working alliance inventory (WAI-SR).	Adults age 18+; who spoke English; scheduled for a first in-person outpatient GC from 1/2017 to 8/2018 through the Johns Hopkins ARVC Center with either (a) a clinical diagnosis of ACM or possible ACM (70%) or (b) at risk for ACM based on genotype and/or family history (30%).	Individuals who did not complete both pre- and post-visit surveys. Post-GC questionnaire administered before test results returned.	Genetic counseling session with surveys conducted pre- and post-visit.	Comparison of outcomes between patients with and without prior genetic testing ordered.	Response rate 59%. There was a significant increase in GCOS score (mean 15.7 points) within 4 weeks post-GC session (p<.0001) with no significant difference in GCOS change between patients who had genetic testing ordered previously and those attending pre-test counseling (17.4 ± 18.2 versus. 14.1 ± 16 [p=.35]). Average CAQ score was high at baseline (1.67 ± 0.68), and there was a significant inverse relationship between pre-GC CAQ score and extent of increase in GCOS score (p=.008) post-GC. Controlling for baseline anxiety, there was a strong positive relationship between the WAI-SR score and GCOS change (B = 0.80, 95% CI: 0.43, 1.17, p<.001).	No significant difference in GCOS change between patients who had genetic testing ordered previously and those attending pre-test counseling (17.4 ± 18.2 versus. 14.1 ± 16 [p=.35]).	there is an increase in empowerment from pre- to post-genetic counseling session, which is influenced positively by the strength of the working alliance with the genetic counselor, and is negatively influenced by pre-visit anxiety.	Single-center design, self-reported measures, low response rate.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	4	Ingles	2017	https://doi.org/10.1161/CIRCGENETICS.116.001620	Nonfamilial Hypertrophic Cardiomyopathy: Prevalence, Natural History, and Clinical Implications	To determine the prevalence, natural history, and potential clinical implications of a nonfamilial subgroup of HCM (negative genetic testing; no known HCM family history).	Retrospective cohort study	413 unrelated probands with HCM seen at a specialized HCM center (166 with neither a positive genetic test nor a positive family history)	Clinical outcomes and genetic testing results	Unrelated probands with HCM seen in a specialized HCM center between 2002 and 2015 and genetic testing performed.	Patients with phenocopies or those without a confirmed genetic diagnosis.	Genetic testing and clinical follow-up.	Nonfamilial HCM patients (no causative variants and no family history) vs. familial HCM patients.	Adjusted predictors of nonfamilial status were older age (odds ratio, 1.04; 95% confidence interval, 1.02–1.06; P=0.0001), male sex (odds ratio, 1.96; 95% confidence interval, 1.11–3.45; P=0.02), hypertension (odds ratio, 2.80; 95% confidence interval, 1.57–5.00; P=0.0005), and nonasymmetric septal morphology (odds ratio, 3.41; 95% confidence interval, 1.64–7.08; P=0.001). They had a less severe clinical course with greater event-free survival from major cardiac events (P=0.04) compared with sarcomere-positive HCM probands.	Genotype prediction scores showed good performance in identifying genotype-positive patients (area under the curve, 0.71–0.75) and, in combination with pedigree characteristics, were further improved.	Approximately 40% of HCM probands have a nonfamilial subtype, with later onset and less severe clinical course. A revised clinical pathway for management for them and refined clinical surveillance recommendations for family members may be warranted. This highlightsthe role of genetic testing, a detailed pedigree in management of families.	Retrospective study design; Potential underestimation of genetic variants not covered by the testing panels used.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	4	Muller	2023	https://doi.org/10.1016/j.jacc.2023.05.005	Individualized Family Screening for Arrhythmogenic Right Ventricular Cardiomyopathy	Determine the predictors and probability of ARVC development over time among at-risk relatives.	Observational cohort study (Registry)	136 relatives from the Netherlands Arrhythmogenic Cardiomyopathy Registry without definite ARVC 49 external replication/validation cohort from Italy with similar characteristics	ARVC diagnosis; fulfillment of additional Task Force Criteria	Relatives of ARVC probands > age 14 managed at 3 Dutch centers who did not fulfill definite 2010 ARVC task force criteria at time of first clinical evaluation and who underwent complete ARVC evaluation at baseline (ECG, Holter, imaging)	< age 14	Longitudinal follow-up with clinical assessments including electrocardiography, Holter monitoring, and cardiac imaging.	Comparison between subjects with possible ARVC and those with borderline ARVC.	In 8.1 years (IQR: 4.2-11.4 years) of follow-up, 41 (33%) had developed definite ARVC. Independent of baseline phenotype, symptomatic subjects (P = 0.014) and those 20 to 30 years of age (P = 0.002) had a higher hazard of developing definite ARVC. Furthermore, patients with borderline ARVC had a higher probability of developing definite ARVC compared with those with possible ARVC (1-year probability 13% vs 0.6%, 3-year probability 35% vs 5%; P < 0.01). External replication showed comparable results (P > 0.05).	n/a	Symptomatic relatives and those aged 20-30, particularly those with borderline ARVC, have a higher probability of developing definite ARVC and may benefit from more frequent follow-up. Less frequent monitoring may be appropriate for others. These data suggest a refined screening algorithm for at-risk ARVC family members based on age, symptoms, and results of baseline testing.	Potential selection bias, the retrospective nature of registry data, and small smaple size.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	4	Sharma	2022	https://doi.org/10.1161/CIRCGEN.121.003530	Arrhythmogenic Right Ventricular Cardiomyopathy Prevalence and Arrhythmic Outcomes in At-Risk Family Members: A Systematic Review and Meta-Analysis	Estimate the prevalence of ARVC and arrhythmia in family members and define whether family genotype was a significant predictor of diagnosis and ventricular arrhythmias in family members across studies	Systematic review and meta-analysis	41 studies; meta-analysis of 1359 family members from 13 unique cohorts	Prevalence of ARVC diagnosis and ventricular arrhythmias according to 2010 Task Force Criteria	Studies reporting on the prevalence of ARVC and VA in at least 10 family members of ARVC patients	Studies not using 2010 Task Force Criteria or not focused on family members	Meta-analysis of existing data	Comparison between gene-positive and gene-elusive family members	Meta-analysis of 1359 family members, from 13 unique cohorts showed an average prevalence estimate of 25% for diagnosis as per Task Force Criteria (95% CI, 0.15–0.35, I2=96.44%). Overall prevalence of sustained vantricular arrhythmia among gene-positive family members was 18% (95% CI, 0.13–0.23, I2=33.25%) in 7 independent studies (n=597). Family genotype was a significant risk factor for diagnosis of both ARVC (odds ratio, 6.91 [95% CI, 1.27–37.70]; P=0.0005) and sustained vantricular arrhythmia (odds ratio, 13.62 [95% CI, 0.91–204.13]; P=0.06).	Male gender was not associated with disease prevalence in relatives (odds ratio, 1.18 [95% CI, 0.72–1.95]; P=0.42) or VA (odds ratio, 0.81 [95% CI, 0.51–1.29]; P=0.91).	The prevalence of ARVC and VA in at-risk family members differs significantly based on family genotype. These data suggest relaxed longitudinal screening for relatives of gene negative (gene elusive) probands "as long as they are asymptomatic and not athletes".	Variability in study designs, definitions of outcomes, and potential publication bias.
7.3 Moving from athlete to family: Implications of a genetic diagnosis	4	te Riele	2016	https://doi.org/10.1093/eurheartj/ehv387	Approach to family screening in arrhythmogenic right ventricular dysplasia/cardiomyopathy	Determine predictors of ARVD/C diagnosis and optimize arrhythmic risk stratification among first-degree relatives of ARVD/C patients.	Retrospective cohort study (Registry)	274 first-degree relatives of 138 ARVD/C probands	Diagnosis of ARVC per fullfillment of 2010 Task Force Criteria. Sustained Ventricular arrhythmia defined as sustained VA; VF, sudden cardiac death; appropriate ICD therapy for sustained VA or VF.	First-degree relatives of an ARVC patient and had undergone full clinical evaluation for ARVC.	Relatives who had not undergone full clinical evaluation.	Evaluation based on 2010 Task Force Criteria	Comparison among different family members (siblings, parents, children)	At the time of their initial evaluation, 78 (28%) relatives had definite ARVC. Ninety-six (35%) relatives were diagnosed by last follow up (6.7 ± 3.8 years). Siblings had a three-fold-increased risk of ARVC diagnosis compared with parents and children (odds ratio 3.11, P < 0.001). Multivariable logistic regression identified symptoms (P < 0.001), being a sibling (P < 0.001), the presence of a pathogenic mutation (P < 0.001), and female sex (P = 0.010) as predictors of ARVC diagnosis. During follow-up, 21 (8%) relatives experienced a sustained ventricular arrhythmia.	Task Force Criteria independent of family history had higher prognostic value for arrhythmic events compared to conventional criteria.	One-third of first-degree relatives develop manifest ARVD/C. Siblings have highest risk of disease, even after correcting for age and sex.	Retrospective design and potential for selection bias.

7.3 Moving from athlete to family: Implications of a genetic diagnosis	6	Asif	2015	https://doi.org/10.1016/j.jelectrocard.2014.12.018	Stages of psychological impact after diagnosis with serious or potentially lethal cardiac disease in young competitive athletes: a new model	to determine the psychological impact of being diagnosed with cardaic disease in young competitive athletes	qualitative research semi-structured interview	25	qualitative research to identify domains, categories and core ideas	young cometitive athletes (age 14-35yrs) with a cardiac diagnosis that required medical surveillance, evaluation or treatment		30-60 minute semi-structured interview	experience during and after diagnosis	athletest progressed through 4 stages of pyschological impact. Risk factors fo increased psychological morbidity included higher level of competitiion, permanent disqualification from sports, persistent reminders and unanticipated outcomes	limited support mechanisms provided by treating team/medical programs	athletes with cardiac disease are emotionally vulnerable and experience 4 stages of psychological adjustent.	qualitative study
7.3 Moving from athlete to family: Implications of a genetic diagnosis	6	Asif	2016	https://doi.org/10.1136/bjsports-2015-095560	The impact of diagnosis: measuring the psychological response to being diagnosed with serious or potentially lethal cardiac disease in young competitive athletes	to determine the psychological impact of athletes diagnosed with cardiac disease	cohort study	30	Impact of event scale-revised (IES-R)	age 14-35, diagnosed with serious cardiovascular disorder, engaged in competitive sports, at least 6 months post disagnosis		IES-R		overall mean score 16.6 (normal <12, significant stress = >33), highest subscale is avoidance then intrusion then hyperarousal. Higher risk athletes= permanently disqualified, regular meidcaiton, genetic conditions.	athletes with cardiomyopathy and channelopathy reported highest results, no gender differences	athletes diagnosed with cardiac disease are at risk of psychological distress	small cohort,heterogeneous cardiac conditions
7.3 Moving from athlete to family: Implications of a genetic diagnosis	6	Luiten	2016	https://doi.org/10.1136/openhrt-2016-000488	Exercise restrictions trigger psychological difficulty in active and athletic adults with hypertrophic cardiomyopathy	to identify key features os psychological distress associated with exercise restrictions for active/athletic adults with HCM	survey followed by qualitative research semi-structured interview	54 (survey) then 16 of those proceeded to interview	survey - Likert cale rating agreement. interview transcripts were analysed using adapted grounded theory methodology whereby initial codes and themes were generated from a reivew of a subset of 4 interviews	>16 years individuals with HCM from stanford ICC clinic				high prevalence of psychological difficulty (54% of responders). Psychological disgress is not limited to young or eleive athletes though there is an association with high level athletic competitiveness and greater psychological difficulty.	drop in athleticiism after diagnosis, lack of understanding from family or friends and avoiding exercise completely were detrimental to coping	adults with HCM experience psycholgical effects (which are long lasting) and difficulty adjusting when subject to exericse restrictions	small single cetre, semi-qualitative study
7.3 Moving from athlete to family: Implications of a genetic diagnosis	6	Rahman	2012	https://doi.org/10.1111/j.1540-8159.2011.03229.x	Adolescents with implantable cardioverter defibrillators: a patient and parent perspective	to explore the experiences of adolescents living with ICD and their care givers	qualitative research semi-structured interview	6 adolescents and 6 parents		adolescents age 12-17 from royal children's hospital Melbourne Australia with presumed or diagnosed cardiac genetic condition	not fluent in english, or if neurological impairments that precluded interviewing			both adolescents and parents were able to adjust to life after ICD and dscribed benefits to having the device	adolescents sometimes self-impose limitations on what they percieve they can do themselves after ICD impant. Ongoing medical appointments are disruptive	adolescents with ICDs and their parents cope well	small size, single centre

Subsection	Rec #	First Author	Year	DOI	Article Title	Aim	Study type	Size	Endpoints	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Comparator(s)	Outcomes (Results and P values)	Other Relevant Findings or Adverse Events	Conclusions	Limitations
8.2. Atrial fibrillation evaluation in athletes	1	Perez	2019	https://doi.org/10.1056/NEJMoa1901183	Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation	To assess the feasibility and accuracy of AF detection using a smart watch	Observational	419297	AF detection and confirmation	People without known AF		Apple watch and iphone		2161 participants (0.52%) received notifications of irregular pulse		The probability of receiving an irregular pulse notification was low. Among participants who received notification of an irregular pulse, 34% had atrial fibrillation on subsequent ECG patch readings and 84% of notifications were concordant with atrial fibrillation.	
8.2. Atrial fibrillation evaluation in athletes	1	Wasserlauf	2019	https://doi.org/10.1161/CIRCEP.118.006834	Smartwatch Performance for the Detection and Quantification of Atrial Fibrillation	To compare the accuracy of an AF-sensing watch (AFSW; Apple Watch with KardiaBand) with simultaneous recordings from an insertable cardiac monitor (ICM; Reveal LINQ).	Observational	24 patients	Sensitivity in detecting AF	Pateints with paroxysmal AF				98% sensitivity for episodes and 98% sensitive for duration.		Devices may represent an inexpensive, noninvasive approach to long-term AF surveillance and management.	
8.2. Atrial fibrillation evaluation in athletes	1	Gao	2022	https://doi.org/10.1016/j.jacasi.2022.07.006	Consumer-Led Screening for Atrial Fibrillation: A Report From the mAFA-II Trial Long-Term Extension Cohort	Report the trends on prevalent AF detection over time and risk factors, with a consumer-led photoplethysmography screening approach.	Observational	3,499,461	Detection and confirmation of AF	People with Huawei smartphones >18 yrs age				AF detected in 0.43%. 5227 subjects with AF detected were followed up and AF confirmed in 94%		Photoplethysmography-based smart devices can facilitate screening for AF with >93% confirmation of detected AF episodes even for the low-risk general population	
8.2. Atrial fibrillation evaluation in athletes	2	Claessen	2011	https://doi.org/10.1136/hrt.2010.216150	Long-term endurance sport is a risk factor for development of lone atrial flutter	Determine whether those with lone AF were more likely endurance athletes	Case control	58 vs 58	Prevalence of athleticism	Flutter ablation				The proportion of regular sportsmen (≥3 h of sports practice per week) among patients with lone atrial flutter was significantly higher than that observed in the general population (50% vs 17%; p<0.0001).		A history of endurance sports and subsequent left atrial remodelling may be a risk factor for the development of atrial flutter.	
8.2. Atrial fibrillation evaluation in athletes	2	Gami	2007	https://doi.org/10.1016/j.jacc.2006.08.060	Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation	Determine if OSA and obesity predict AF/AFL.	Observational.	3,542 patients, mean age 49	Incident AF	Patients referred for sleep study	Diagnosis of AF	N/A	N/A	Univariate predictors of AF were age, male gender, hypertension, coronary artery disease, heart failure, smoking, body mass index, OSA (hazard ratio 2.18, 95% CI 1.34 to 3.54) and multiple measures of OSA severity. In subjects <65 years old, independent predictors of incident AF were age, male gender, coronary artery disease, body mass index (per 1 kg/m2, hazard ratio 1.07, 95% CI 1.05 to 1.10), and the decrease in nocturnal oxygen saturation (per 0.5 U log change, hazard ratio 3.29, 95% CI 1.35 to 8.04). Heart failure, but neither obesity nor OSA, predicted incident AF in subjects ≥65 years of age.		Obesity and the magnitude of nocturnal oxygen desaturation, which is an important pathophysiological consequence of OSA, are independent risk factors for incident AF in individuals <65 years of age.	Non-athletes; selection bias as patients were referred for suspect sleep apnea; AF likely underdiagnosed given follow up heterogeniety
8.2. Atrial fibrillation evaluation in athletes	2	Schmidt	2014	https://doi.org/10.1016/j.amjcard.2013.11.037	Comparison of the frequency of atrial fibrillation in young obese versus young nonobese men undergoing examination for fitness for military service	Determine if obesity in young adulthood predicts AF	Observational.	12,850 men, median age 19	Follow up time median 29 years, incident AF		None listed	N/A	N/A	The incidence of AF per 100,000 person-years was 53 for men of normal weight (BMI: 18.5 to 24.9 kg/ m2), 54 for underweight men (BMI <18.5 kg/m2), 106 for overweight men (BMI: 25.0 to 24.9 kg/m2), and 144 for obese men (BMI ‡30 kg/m2). With normal weight as the reference group, the adjusted HR for AF was 0.99 (95% CI 0.52 to 1.87) for underweight men, 2.08 (95% CI 1.48 to 2.92) for overweight men, and 2.87 (95% CI 1.46 to 5.62) for obese men. The adjusted HR associating 1 unit increase in BMI with AF was 1.12 (95% CI 1.07 to 1.16).	N/A	Overweight and obese young men had more than twice the risk of AF.	Observational, non-athletes.
8.2. Atrial fibrillation evaluation in athletes	2	Mukamal	2005	https://doi.org/10.1161/CIRCULATIONAHA.105.547844	Alcohol consumption and risk of atrial fibrillation in men and women: the Copenhagen City Heart Study	Evaluate association of alcohol consumption on incident atrial fibrillation.	Prospective cohort study, observational.	16,415 enrolled in Copenhagen City Heart Study	Incident AF via hospitalization records or ECG at follow up.	All included who were enrolled in Copenhagen City Heart Study.	Diagnosis of AF, history or coronary artery disease and use of cardiac medication, missing information.	N/A	N/A	Among both women and men, alcohol consumption throughout the moderate range was not associated with risk of atrial fibrillation. However, consumption of 35 or more drinks per week among men was associated with a hazard ratio of 1.45 (95% CI 1.02 to 2.04); few women consumed this amount of alcohol. Approximately 5% of cases of atrial fibrillation among men were attributable to heavy alcohol use.	N/A	Heavy alcohol consumption was associated with higher risk of AF, at least in men.	Observational, non-athletes, AF diagnosis in follow up likely under diagnosed.
8.2. Atrial fibrillation evaluation in athletes	2	Marcus	2021	https://doi.org/10.1016/j.jacep.2020.11.026	A Randomized, Double-Blind, Placebo-Controlled Trial of Intravenous Alcohol to Assess Changes in Atrial Electrophysiology	Identify acute changes in human atrial electrophysiology during alcohol exposure.	Placebo controlled	100(50 in each group)	pulmonary vein atrial effective refractory periods (AERPs)	Patients undergoing AF ablation		Infusion of ETOH to blood alchol conc of 0.08%	Placebo	Pulmonary vein atrial effective refractory periods (AERPs) reduced by 12ms (P=0.026) and not in placebo.		Acute exposure to alcohol reduces AERP, particularly in the pulmonary veins. These data demonstrate a direct mechanistic link between alcohol and AF.	
8.2. Atrial fibrillation evaluation in athletes	2	Shapero	2016	https://doi.org/10.1186/s40798-016-0053-0	Cardiovascular Risk and Disease Among Masters Endurance Athletes: Insights from the Boston MASTER (Masters Athletes Survey To Evaluate Risk) Initiative	To develop a comprehensive clinical CV profile of masters athletes	Questionnaire	591		Masters athletes						AF is associated with prior exercise exposure whereas CAD is associated with typical risk factors including dyslipidemia and prior tobacco use.	
8.2. Atrial fibrillation evaluation in athletes	2	Elosua	2006	https://doi.org/10.1016/j.ijcard.2005.05.020	Sport practice and the risk of lone atrial fibrillation: a case-control study	To determine the association between sport practice and the prevalence of AF in men.	Case-control	160 (51 with AF)						Current practice of sport was associated with a higher prevalence of LAF (OR=3.13; 95% CI: 1.39–7.05). The practice of more than 1500 lifetime hours of sport appears to be the threshold for the observed association. Current practice of sport with a lifetime practice greater than 1500 h was associated with LAF (OR=2.87; 95% CI: 1.20–6.91).		In men, the combination of current and prolonged lifetime sport practice is associated with higher risk of AF.	
8.2. Atrial fibrillation evaluation in athletes	2	Grimsmo	2010	https://doi.org/10.1097/HJR.0b013e32833226be	High prevalence of atrial fibrillation in long-term endurance cross-country skiers: echocardiographic findings and possible predictors--a 28-30 years follow-up study	To determine the prevalence of LAF in long-term endurance cross-country skiers and to examine possible predictors.	Observational	149		Long-term cross country skiiers				A high prevalence (12.8%) of AF was found. The only predictor from both 1976 and 1981 associated with AF was a long PQ time (r = 0.38, P = 0.001 and r = 0.27, P = 0.02, respectively), whereas bradycardia was another predictor (r = 0.29, P = 0.012). At follow-up, left atrial enlargement was a marker associated with AF (P < 0.001).		Long PQ time, bradycardia and left atrial enlargement seem to be important risk factors for LAF among long-term endurance cross-country skiers.	

8.2. Atrial fibrillation evaluation in athletes	2	Molina	2008	https://doi.org/10.1093/europace/eun071	Long-term endurance sport practice increases the incidence of lone atrial fibrillation in men: a follow-up study	To determine the incidence of lone atrial fibrillation (LAF) in males according to sport practice and to identify possible clinical markers related to LAF among marathon runners.	Retrospective case-control	555		Marathon runners vs sedentary men			The annual incidence rate of LAF among marathon runners and sedentary men was 0.43/100 and 0.11/100, respectively.		Long-term endurance sport practice is associated with a higher risk of symptomatic LAF in men.		
8.2. Atrial fibrillation evaluation in athletes	3	Giustetto	2014	https://doi.org/10.1016/j.hrthm.2013.10.043	Atrial fibrillation in a large population with Brugada electrocardiographic pattern: prevalence, management, and correlation with prognosis	To analyze the prevalence of AF/Afl in Brugada patients	Observational	560		Type 1 Brugada ECG			Among 560 patients with Brugada type 1 ECG (BrECG), 48 (9%) had AF/AFI.		Prevalence of AF/AFl in Brugada patients is higher than in the general population of the same age.		
8.2. Atrial fibrillation evaluation in athletes	3	Johnson	2008	https://doi.org/10.1016/j.hrthm.2008.02.007	Prevalence of early-onset atrial fibrillation in congenital long QT syndrome	Prevalence of AF in patients with congenital LQTS.	Observational	457		Familial LQTS			Compared to the background prevalence of 0.1%, early-onset AF was observed in almost 2% of patients with genetically proven LQTS		AF more comon in LQTS		
8.2. Atrial fibrillation evaluation in athletes	3	McClean	2015	https://doi.org/10.1093/ehjci/jeu215	Chronic adaptation of atrial structure and function in elite male athletes	Establish the degree of structural and functional adaptations in the left (LA) and right atria (RA) in elite male athletes	Case-control	36 athletes and 20 controls					Enlarged atria in endurance athletes				
8.2. Atrial fibrillation evaluation in athletes	3	Olivotto	2001	https://doi.org/10.1161/hc4601.097997	Impact of atrial fibrillation on the clinical course of hypertrophic cardiomyopathy	prognostic implications of AF in HCM	Observational	480		HCM patients			AF occurred in 107 patients (22%; incidence, 2%/y) and was independently predicted by advancing age, congestive symptoms, and increased LA size at diagnosis. Patients with AF had increased risk for HCM-related death (OR, 3.7; P<0.002) because of excess heart failure–related mortality but not sudden, unexpected death.		In a community-based HCM population, AF (1) was common, with 22% prevalence over 9 years; (2) was associated with substantial risk for heart failure–related mortality, stroke, and severe functional disability, particularly in patients with outflow obstruction, those ≤50 years of age, or those developing chronic AF; and (3) was nevertheless compatible with benign outcome in 35% of patients.		
8.2. Atrial fibrillation evaluation in athletes	4	Goodyer	2018	https://doi.org/10.1001/jamacardio.2018.1176	Association of Burden of Atrial Fibrillation With Risk of Ischemic Stroke in Adults With Paroxysmal Atrial Fibrillation: The KP-RHYTHM Study	Is the burden of atrial fibrillation associated with the risk of ischemic stroke and other thromboembolism in paroxysmal atrial fibrillation?	Observational	1965		Paroxysmal AF			A greater burden of atrial fibrillation (≥11%) on 14-day noninvasive, continuous electrocardiographic monitoring was associated with a significantly higher rate of thromboembolism while not taking anticoagulation vs a lower burden.		Greater atrial fibrillation burden is associated with a higher risk of ischemic stroke independent of known risk factors		
8.2. Atrial fibrillation evaluation in athletes	4	Jansson	2021	https://doi.org/10.1016/j.ijcha.2021.100791	Atrial fibrillation burden, episode duration and frequency in relation to quality of life in patients with implantable cardiac monitor	To assess the relation between atrial fibrillation (AF) characteristics and health-related quality of life (QoL)	Observational analysis from RCT	150		Paroxysmal AF			Greater AF burden (p = 0.003) and longer AF episodes (p = 0.013) were associated with impaired QoL		AF burden is an important endpoint		
8.2. Atrial fibrillation evaluation in athletes	5	El Assaad	2021	https://doi.org/10.1016/j.hrthm.2021.07.066	Management and outcomes of atrial fibrillation in 241 healthy children and young adults: Revisiting "lone" atrial fibrillation-A multi-institutional PACES collaborative study	To assess recurrence patterns and treatment efficacy in AF.	Observational, retrospective.	241 subjects (83% male; mean age at onset 16 years	AF recurrence during 2.1 ± 2.6 years of follow-up.	Patients ≤ 21 years of age	Contributory diseases	N/A	AF recurred in 94 patients (39%) during 2.1 ± 2.6 years of follow-up. In multivariable analysis, predictors of AF recurrence were family history in a first-degree relative <50 years of age (odds ratio [OR] 1.9; P = .047) and longer PR interval in sinus rhythm (OR 1.1 per 10 ms; P = .037). AF recurrence was similar whether patients began no treatment (39/125 [31%]), began daily antiarrhythmic therapy (24/63 [38%]), or had an ablation at any time (14/53 [26%]; P = .39).	Ablating non-AF substrate with supraventricular tachycardia improved freedom from AF recurrence (P = .013).	Recurrence of AF in the pediatric population is common, and the incidence of recurrence was not impacted by "no treatment," "medication only," or "ablation" treatment strategy. Ablation of pathways and other reentrant targets was the only intervention that decreased AF recurrence in children and young adults.	Observational, non-athletes, AF diagnosis in follow up likely under diagnosed.
8.2. Atrial fibrillation evaluation in athletes	6, 7	Chalazan	2023	https://doi.org/10.1038/s41431-023-01383-z	Genetic testing in monogenic early-onset atrial fibrillation	Rare variant search in 12 AF associated genes	Cohort	200 <60 years including 94 <45 years					3% yield of rare variants in 12 AF associated genes				
8.2. Atrial fibrillation evaluation in athletes	6, 7	Choi	2020	https://doi.org/10.1161/CIRCRESAHA.119.315686	Monogenic and Polygenic Contributions to Atrial Fibrillation Risk: Results From a National Biobank	LOF rare variants vs AF PRS	Large data observational	500000					.44% yield of LOF variants explained o.2% of variance in AF vs PRS explaining 5%				
8.2. Atrial fibrillation evaluation in athletes	6, 7	Lazarte	2021	https://doi.org/10.1093/europace/euaa421	Enrichment of loss-of-function and copy number variants in ventricular cardiomyopathy genes in 'lone' atrial fibrillation	LOF variants in 195 young (<60 yrs) 'lone' AF	Cohort	195					3.1% yield of LOF variants (all in titin)				
8.2. Atrial fibrillation evaluation in athletes	6, 7	Yoneda	2021	https://doi.org/10.1001/jamacardio.2021.3370	Early-Onset Atrial Fibrillation and the Prevalence of Rare Variants in Cardiomyopathy and Arrhythmia Genes	Define the prevalence of disease-associated variants in susceptibility genes for inherited cardiomyopathy and arrhythmia syndromes	Cohort	1293	Rare variant prevalence	AF < 66 years of age			10% with disease associated variants (mostly in DCM genes), 17% if restricted to AF<30 years		Genetic testing in patients with early-onset atrial fibrillation identifies pathogenic variants associated with more serious inherited cardiomyopathy and arrhythmia syndromes.		
8.2. Atrial fibrillation evaluation in athletes	6, 7	Giustetto	2014	https://doi.org/10.1016/j.hrthm.2013.10.043	Atrial fibrillation in a large population with Brugada electrocardiographic pattern: prevalence, management, and correlation with prognosis	To analyze the prevalence of AF/Afl in Brugada patients	Observational	560		Type 1 Brugada ECG			Among 560 patients with Brugada type 1 ECG (BrECG), 48 (9%) had AF/AFI.		Prevalence of AF/AFl in Brugada patients is higher than in the general population of the same age.		

8.2. Atrial fibrillation evaluation in athletes	6, 7	Johnson	2008	https://doi.org/10.1016/j.hrthm.2008.02.007	Prevalence of early-onset atrial fibrillation in congenital long QT syndrome	To analyze, in a large population of Brugada patients, the prevalence of AF/AFl, its correlation with prognosis, and the efficacy of hydroquinidine (HQ) treatment.	Observational, comparative study.	252 patients with LQTS; 205 patients with positive FAMILION genetic test for LQTS.	Incident AF	N/A		N/A	Population-based prevalence (non-LQTS)	Early-onset AF was documented in 8 (1.7%) of 457 patients, including 6 (2.4%) of 252 patients seen at Mayo and 2 (1%) of 205 patients with a positive FAMILION test. Five (2.4%) of 211 patients with LQT1-susceptibility mutations had documented AF, compared to 0 of 174 patients with LQT2, 1 of 59 patients with LQT3, 1 of 1 patient with Andersen-Tawil syndrome, and 1 of 34 patients with multiple mutations. The average age at diagnosis of AF of the six patients evaluated at Mayo was 24.3 years (range 4-46 years). Early-onset AF (age <50 years) was significantly more common in patients with LQTS compared to population-based prevalence statistics (P <.001, relative risk 17.5).		Compared to the background prevalence of 0.1%, early-onset AF was observed in almost 2% of patients with genetically proven LQTS and should be viewed as an uncommon but possible LQT-related dysrhythmia.	Observational, underreporting of AF possible, non-athletes.
8.2. Atrial fibrillation evaluation in athletes	7	Goodyer	2019	https://doi.org/10.1161/CIRCGEN.119.002713	Broad Genetic Testing in a Clinical Setting Uncovers a High Prevalence of Titin Loss-of-Function Variants in Very Early Onset Atrial Fibrillation	Assess prevalence of rare variants in very early onset AF	Observational	25		AF <45 years				6 of the 25 patients (24%) had actionable variants deemed likely pathogenic or pathogenic. Four of these 6 patients had likely pathogenic, loss-of-function variants in the sarcomeric gene Titin		Clinical genetic evaluations revealed not only a high rate of familial vEAF but also cardiomyopathy within the pedigrees	
8.2. Atrial fibrillation evaluation in athletes	11	Medhekar	2023	https://doi.org/10.1002/clc.23974	Impact of a dedicated center for atrial fibrillation on resource utilization and costs	To determine whether a dedicated Center for AF from the ED would reduce costs of care.	Case-control	96 vs 96		96 patients referred to a specialist AF centre with new-onset AF vs 96 control				After 30 days of follow-up, patients referred to the center for AF had a lower average cost ($619 vs. $1252, p < 0.001) compared to controls		Directing patients with AF that present to the ED to follow-up at a dedicated Center for AF significantly reduced overall costs	
8.2. Atrial fibrillation evaluation in athletes	11	Perino	2017	https://doi.org/10.1016/j.jacc.2017.04.054	Treating Specialty and Outcomes in Newly Diagnosed Atrial Fibrillation: From the TREAT-AF Study	To evaluate the association between treating specialty and AF outcomes among patients newly diagnosed with AF.	Observational	184161						40% received cardiology care and 60% received primary care only. After adjustment for covariates, cardiology care was associated with reductions in stroke (hazard ratio [HR]: 0.91; 95% confidence interval [CI]: 0.86 to 0.96; p < 0.001) and death (HR: 0.89; 95% CI: 0.88 to 0.91; p < 0.0001) and increases in hospitalizations for AF/supraventricular tachycardia (HR: 1.38; 95% CI: 1.35 to 1.42; p < 0.0001) and myocardial infarction (HR: 1.03; 95% CI: 1.00 to 1.05; p < 0.04).		In patients with newly diagnosed AF, cardiology care was associated with improved outcomes, potentially mediated by early prescription of oral anticoagulation therapy.	
8.3.1 Risk factor modification	1	Huxley	2011	https://doi.org/10.1161/CIRCULATIONAHA.110.009035	Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: the Atherosclerosis Risk in Communities (ARIC) study	To determine what proportion of the burden of AF in blacks and whites could theoretically be avoided by the maintenance of an optimal risk profile.	Observational.	14,598 patients.	Atrial fibrillation.	ARIC participants.	N/A	AF incidence	No AF	The population-attributable fraction of AF resulting from having a nonoptimal risk profile was estimated separately for black and white men and women. During a mean follow-up of 17.1 years, 1520 cases of incident AF were identified. The age-adjusted incidence rates were highest in white men and lowest in black women (7.45 and 3.67 per 1000 person-years, respectively). The overall prevalence of an optimal risk profile was 5.4% but varied according to race and gender: 10% in white women versus 1.6% in black men. Overall, 56.5% of AF cases could be explained by having ≥1 borderline or elevated risk factors, of which elevated blood pressure was the most important contributor.	N/A	As with other forms of cardiovascular disease, more than half of the AF burden is potentially avoidable through the optimization of cardiovascular risk factors levels.	AF diagnosis relies on hospital discharge codes, unable to differentiate AF type, unknown serial changes in risk factors.
8.3.1 Risk factor modification	1	Middledorp	2018	https://doi.org/10.1093/europace/euy117	PREVEntion and regReSsive Effect of weight-loss and risk factor modification on Atrial Fibrillation: the REVERSE-AF study	To evaluate the impact of weight and risk factor management (RFM) on progression of the AF.	Propsective observational study, sub-analysis.	355 patients.	Progression of AF	Consecutive AF patients	Those who had a history of myocardial infarction or cardiac surgery in the previous 12 months, significant cardiac valvulopathy or ventricular dysfunction, active malignancy, auto-immune or systemic inflammatory diseases, severe renal or hepatic failure, and <24 months of follow-up and/or from other states.	Weight loss and risk factor management.	Usual care	Weight loss was categorized as: Group 1 (<3%), Group 2 (3–9%), and Group 3 (≥10%). Change in AF type was determined by clinical review and 7-day Holter yearly. Atrial fibrillation type was categorized as per the Heart Rhythm Society consensus. There were no differences in baseline characteristic or follow-up duration between groups (P = NS). In Group 1, 41% progressed from paroxysmal to persistent and 26% from persistent to paroxysmal or no AF. In Group 2, 32% progressed from paroxysmal to persistent and 49% reversed from persistent to paroxysmal or no AF. In Group 3, 3% progressed to persistent and 88% reversed from persistent to paroxysmal or no AF (P < 0.001). Increased weight loss was significantly associated with greater AF freedom: 45 (39%) in Group 1, 69 (67%) in Group 2, and 116 (86%) in Group 3 (P ≤ 0.001).	N/A	Obesity is associated with progression of the AF disease. This study demonstrates the dynamic relationship between weight/risk factors and AF. Weight-loss management and RFM reverses the type and natural progression of AF.	Not randomized, performance bias. No continous AF monitoring.
8.3.1 Risk factor modification	2	Newman	2021	https://doi.org/10.1136/bjsports-2021-103994	Risk of atrial fibrillation in athletes: a systematic review and meta-analysis	To evaluate the risk of AF in athletes.	Meta-analyses of non-randomized studies	70478 patients.	Atrial fibrillation	Athletes >18 years who performed regular exercise for a 2-year period	Studies without a control group.	Athletes	Non-athletes	The risk of developing AF was significantly higher in athletes than in non-athlete controls (OR: 2.46; 95% CI 1.73 to 3.51; p<0.001, Z=4.97).	Mode of exercise and risk of AF were moderately correlated (B=0.1259, p=0.0193), with mixed sport conferring a greater risk of AF than endurance sport (B=−0.5476, p=0.0204). Younger (<55 years) athletes were significantly more likely to develop AF compared with older (≥55 years) athletes (B=−0.02293, p<0.001).	Athletes have a significantly greater likelihood of developing AF compared with non-athlete controls, with those participating in mixed sport and younger athletes at the greatest risk. Future studies of AF prevalence in athletes according to specific exercise dose parameters, including training and competition history, may aid further in delineating those at risk.	Residual confounding, mostly males.
8.3.1 Risk factor modification	2	Khurshid	2023	https://doi.org/10.1001/jama.2023.10875	Accelerometer-Derived "Weekend Warrior" Physical Activity and Incident Cardiovascular Disease	To examine associations between an accelerometer-derived "weekend warrior" pattern (ie, most MVPA achieved over 1-2 days) vs MVPA spread more evenly with risk of incident cardiovascular events.	Retrospective, observational.	89,573 patients.	Associations between activity pattern and incident atrial fibrillation, myocardial infarction, heart failure, and stroke were assessed using Cox proportional hazards regression, adjusted for age, sex, racial and ethnic background, tobacco use, alcohol intake, Townsend Deprivation Index, employment status, self-reported health, and diet quality.	Participants in the UK Biobank cohort providing a full week of accelerometer-based physical activity data between June 8, 2013, and December 30, 2015.	N/A	Active weekend warrior.	Active regular exercise and inactive.	hen stratified at the threshold of 150 minutes or more of MVPA per week, a total of 37 872 were in the active WW group (42.2%), 21 473 were in the active regular group (24.0%), and 30 228 were in the inactive group (33.7%). In multivariable-adjusted models, both activity patterns were associated with similarly lower risks of incident atrial fibrillation (active WW: hazard ratio [HR], 0.78 [95% CI, 0.74-0.83]; active regular: 0.81 [95% CI, 0.74-0.88; inactive: HR, 1.00 [95% CI, 0.94-1.07]), myocardial infarction (active WW: 0.73 [95% CI, 0.67-0.80]; active regular: 0.65 [95% CI, 0.57-0.74]; and inactive: 1.00 [95% CI, 0.91-1.10]), heart failure (active WW: 0.62 [95% CI, 0.56-0.68]; active regular: 0.64 [95% CI, 0.56-0.73]; and inactive: 1.00 [95% CI, 0.92-1.09]), and stroke (active WW: 0.79 [95% CI, 0.71-0.88]; active regular: 0.83 [95% CI, 0.72-0.97]; and inactive: 1.00 [95% CI, 0.90-1.11]).	Findings were consistent at the median threshold of 230.4 minutes or more of MVPA per week, although associations with stroke were no longer significant (active WW: 0.89 [95% CI, 0.79-1.02]; active regular: 0.87 [95% CI, 0.74-1.02]; and inactive: 1.00 [95% CI, 0.90-1.11]).	Physical activity concentrated within 1 to 2 days was associated with similarly lower risk of cardiovascular outcomes to more evenly distributed activity.	Activity only measrured for one week, limited generalizability.

8.3.1 Risk factor modification	2	Elliott	2022	https://doi.org/10.1016/j.jacep.2022.12.002	An Exercise and Physical Activity Program in Patients With Atrial Fibrillation: The ACTIVE-AF Randomized Controlled Trial	To determine the efficacy of an exercise and physical activity intervention on AF burden and symptoms among patients with symptomatic AF.	Randomized controlled trial.	120 patients	AF recurrence, off antiarrhythmic medications and without catheter ablation and symptom severity.	Symptomatic paroxysmal or persistent AF, aged 18 to 80 years, and referred for rhythm management and consideration for AF ablation	The absence of AF lasting >30 seconds in the past 3 months documented by 12-lead electrocardiogram (ECG) or Holter monitoring, AF ablation within the past 12 months, permanent AF, myocardial infarction or cardiac surgery within the past 12 months, autoimmune or systemic inflammatory disease, left ventricular ejection fraction <45%, moderate to severe valvular disease, and inability to participate in a structured exercise program due to a musculoskeletal condition.	Structured exercise program	Usual care	By 12 months, freedom from AF was achieved in 24 (40%) of 60 patients in the exercise group and 12 (20%) of 60 patients in the control group (HR: 0.50: 95% CI: 0.33 to 0.78). At 6 months, AF symptom severity was lower in the exercise group compared with the control group (mean difference –2.3; 95% CI: –4.3 to –0.2; P = 0.033). This difference persisted at 12 months (–2.3; 95% CI: –4.5 to –0.1; P = 0.041). Total symptom burden was lower at 6 months in the exercise group but not at 12 months.	Peak oxygen consumption was increased in the exercise group at both 6 and 12 months. There were no between-group differences in cardiac structure or function, body mass index, or blood pressure.	Participation in an exercise-based intervention over 6 months reduced arrhythmia recurrence and improved symptom severity among patients with AF.	Two-thirds of those screened were excluded, performance bias. Only 1-year follow-up.
8.3.1 Risk factor modification	2	Aizer	2009	https://doi.org/10.1016/j.amjcard.2009.01.374	Relation of vigorous exercise to risk of atrial fibrillation	To describe a large prospective assessment of the relation between vigorous exercise and AF.	Observational	16921 participants	Atrial fibrillation risk.	Healthy men in the Physicians' Health Study.	N/A	No AF	AF	uring 12 years of follow-up, 1,661 men reported developing AF. With increasing frequency of vigorous exercise (0, 1, 1 to 2, 3 to 4, 5 to 7 days/week), multivariate relative risks for the full cohort were 1.0 (referent), 0.90, 1.09, 1.04, and 1.20 (p = 0.04). This risk was not significantly increased when exercise habits were updated or in models excluding variables that may be in the biological pathway through which exercise influences AF risk.	In subgroup analyses, this increased risk was observed only in men <50 years of age (1.0, 0.94, 1.20, 1.05, 1.74, p <0.01) and joggers (1.0, 0.91, 1.03, 1.30, 1.53, p <0.01), where risks remained increased in all analyses.	Frequency of vigorous exercise was associated with an increased risk of developing AF in young men and joggers. This risk decreased as the population aged and was offset by known beneficial effects of vigorous exercise on other AF risk factors.	Observational, recall bias, generalizability.
8.3.1 Risk factor modification	2	Andersen	2013	https://doi.org/10.1093/eurheartj/eht188	Risk of arrhythmias in 52 755 long-distance cross-country skiers: a cohort study	To investigate the association of number of completed races and finishing time with risk of arrhythmias among participants of Vasaloppet, a 90 km cross-country skiing event.	Observational	527448 participants	Risk of arrhythmia.	Participants in the 90km skiing event Vasaloppet who completed the race during the period 1989–98, without prior CV disease.	Individuals with prior CVD.	Number of races.	1 completed race.	Among 52 755 participants, 919 experienced arrhythmia during follow-up. Adjusting for age, education, and occupational status, those who completed the highest number of races during the period had higher risk of any arrhythmias [hazard ratio (HR)1.30; 95% CI 1.08–1.58; for ≥5 vs. 1 completed race], AF (HR 1.29; 95% CI 1.04–1.61), and bradyarrhythmias (HR 2.10; 95% CI 1.28–3.47).	Those who had the fastest relative finishing time also had higher risk of any arrhythmias (HR 1.30; 95% CI 1.04–1.62; for 100–160% vs. >240% of winning time), AF (1.20; 95% CI 0.93–1.55), and bradyarrhythmias (HR 1.85; 95% CI 0.97–3.54). SVT or VT/VF/CA was not associated with finishing time or number of completed races.	Among male participants of a 90 km cross-country skiing event, a faster finishing time and a high number of completed races were associated with higher risk of arrhythmias. This was mainly driven by a higher incidence of AF and bradyarrhythmias. No association with SVT or VT/VF/CA was found.	Observational, confounding.
8.3.1 Risk factor modification	2	Morseth	2016	https://doi.org/10.1093/eurheartj/ehw059	Physical activity, resting heart rate, and atrial fibrillation: the Tromsø Study	To examine the association of physical activity and resting heart rate (RHR) with hospital-diagnosed atrial fibrillation (AF) in a Norwegian cohort.	Observational	20,484 participants	Atrial fibrillation risk.	Participants in the Tromso Study survey 1987-1987	N/A	Physical activity	Low Physical Activty	During a mean follow-up period of 20 years (409 045 person-years), 750 participants (70.5% men) were diagnosed with AF. Compared with the low physical activity group, moderately active individuals had a 19% lower risk of any AF [adjusted hazard ratio (HR) 0.81, 95% confidence interval (CI) 0.68–0.97], whereas highly active had similar risk of AF. Vigorously active individuals showed a non-significantly higher risk of AF (adjusted HR 1.37, 95% CI 0.77–2.43). Risk of AF increased with decreasing RHR (adjusted HR 0.92, 95% CI 0.86–0.98 for each 10 b.p.m. increase in RHR), and RHR < 50 b.p.m. was a risk factor for AF (P < 0.05).	N/A	Leisure time physical activity was associated with AF in a J-shaped pattern. Moderate physical activity was associated with a reduced risk of AF, whereas higher activity levels attenuated the benefits of moderate activity. Low RHR was a risk factor for AF. Moderate and vigorous physical activity may affect AF risk via different pathophysiological mechanisms.	Observational, confouding, recall bias.
8.3.2 Prevention of thromboembolism in athletes with AF	1	Fox	2017	https://doi.org/10.1136/bmjopen-2017-017157	Improved risk stratification of patients with atrial fibrillation: an integrated GARFIELD-AF tool for the prediction of mortality, stroke and bleed in patients with and without anticoagulation	To provide an accurate, web-based tool for stratifying patients with atrial fibrillation to facilitate decisions on the potential benefits/risks of anticoagulation, based on mortality, stroke and bleeding risks.	Observational.	39,898 participants.	Risk of stroke and bleeding.	Participants in the GARFIELD-AF registry	Patients with a transient reversible cause of AF and those for whom follow-up was not envisaged or possible were excluded.	N/A	N/A	The discriminatory value of the GARFIELD-AF risk model was superior to CHA2DS2-VASc for patients with or without anticoagulation. C-statistics (95% CI) for all-cause mortality, ischaemic stroke/systemic embolism and haemorrhagic stroke/major bleeding (treated patients) were: 0.77 (0.76 to 0.78), 0.69 (0.67 to 0.71) and 0.66 (0.62 to 0.69), respectively, for the GARFIELD-AF risk models, and 0.66 (0.64–0.67), 0.64 (0.61–0.66) and 0.64 (0.61–0.68), respectively, for CHA2DS2-VASc (or HAS-BLED for bleeding). In very low to low risk patients (CHA2DS2-VASc 0 or 1 (men) and 1 or 2 (women)), the CHA2DS2-VASc and HAS-BLED (for bleeding) scores offered weak discriminatory value for mortality, stroke/systemic embolism and major bleeding. C-statistics for the GARFIELD-AF risk tool were 0.69 (0.64 to 0.75), 0.65 (0.56 to 0.73) and 0.60 (0.47 to 0.73) for each end point, respectively, versus 0.50 (0.45 to 0.55), 0.59 (0.50 to 0.67) and 0.55 (0.53 to 0.56) for CHA2DS2-VASc (or HAS-BLED for bleeding).	Upon validation in the ORBIT-AF population, C-statistics showed that the GARFIELD-AF risk tool was effective for predicting 1-year all-cause mortality using the full and simplified model for all-cause mortality: C-statistics 0.75 (0.73 to 0.77) and 0.75 (0.73 to 0.77), respectively, and for predicting for any stroke or systemic embolism over 1 year, C-statistics 0.68 (0.62 to 0.74).	Performance of the GARFIELD-AF risk tool was superior to CHA2DS2-VASc in predicting stroke and mortality and superior to HAS-BLED for bleeding, overall and in lower risk patients. The GARFIELD-AF tool has the potential for incorporation in routine electronic systems, and for the first time, permits simultaneous evaluation of ischaemic stroke, mortality and bleeding risks.	Validity of risk factors, no adjudication.

8.3.2 Prevention of thromboembolism in athletes with AF	1	Lip	2010	https://doi.org/10.1378/chest.09-1584	Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation	To refine stroke risk in patients with AF.	Observational.	1,084 patients.	Thromboembolic events.	Patients in the Euro Heart Survey were enrolled if they were 18 years old and if they had an ECG or Holter recording showing AF during the qualifying admission/consultation or in the preceding 12 months.	Mitral stenosis or previous heart valve surgery.	N/A	N/A	The classic CHADS2 (Congestive heart failure, Hypertension, Age.75, Diabetes, prior Stroke/transient ischemic attack) schema categorized the largest proportion (61.9%) into the intermediate-risk strata, whereas the Birmingham 2009 schema classified 15.1% into this category. The Birmingham 2009 schema classified only 9.2% as low risk, whereas the Framingham scheme categorized 48.3% as low risk. Calculated C-statistics suggested modest predictive value of all schema for TE. The Birmingham 2009 schema fared marginally better (C-statistic, 0.606) than CHADS2. However, those classified as low risk by the Birmingham 2009 and NICE schema were truly low risk with no TE events recorded, whereas TE events occurred in 1.4% of low-risk CHADS2 subjects. When expressed as a scoring system, the Birmingham 2009 schema (CHA2DS2-VASc acronym) showed an increase in TE rate with increasing scores (P value for trend5.003).	N/A	Our novel, simple stroke risk stratification schema, based on a risk factor approach, provides some improvement in predictive value for TE over the CHADS2 schema, with low event rates in low-risk subjects and the classification of only a small proportion of subjects into the intermediate-risk category. This schema could improve our approach to stroke risk stratification in patients with AF.	Survey database.
8.3.2 Prevention of thromboembolism in athletes with AF	1	Singer	2013	https://doi.org/10.1161/JAHA.113.000250	A new risk scheme to predict ischemic stroke and other thromboembolism in atrial fibrillation: the ATRIA study stroke risk score	To develop a new AF stroke prediction model using the original Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) AF cohort and externally validated the score in a separate, contemporary, community-based inception AF cohort, ATRIA–Cardiovascular Research Network (CVRN) cohort	Observational	10,927 patients.	Thromboembolic events.	Those ≥18 years old in the ATRIA-Cardiovascular Research Network cohort with either 2 or more outpatient AF diagnoses (ICD-9 code 427.31) or 1 outpatient AF diagnosis with ECG validation.	N/A	N/A	N/A	Derivation ATRIA cohort consisted of 10 927 patients with nonvalvular AF contributing 32 609 person-years off warfarin and 685 thromboembolic events (TEs). The external validation ATRIA-CVRN cohort included 25 306 AF patients contributing 26 263 person-years off warfarin and 496 TEs. Cox models identified 8 variables, age, prior stroke, female sex, diabetes mellitus, heart failure, hypertension, proteinuria, and eGFR<45 mL/min per 1.73 m2 or end-stage renal disease, plus an age×prior stroke interaction term for the final model. Point scores were assigned proportional to model coefficients. The c-index in the ATRIA cohort was 0.73 (95% CI, 0.71 to 0.75), increasing to 0.76 (95% CI, 0.74 to 0.79) when only severe events were considered. In the ATRIA-CVRN, c-indexes were 0.70 (95% CI, 0.67 to 0.72) and 0.75 (95% CI, 0.72 to 0.78) for all events and severe events, respectively. The C-index was greater and net reclassification improvement positive comparing the ATRIA score with the CHADS2 or CHA2DS2-VASc scores.	N/A	The ATRIA stroke risk score performed better than existing risk scores, was validated successfully, and showed improvement in predicting severe events, which is of greatest concern. The ATRIA score should improve the antithrombotic decision for patients with AF and should provide a secure foundation for the addition of biomarkers in future prognostic models.	Complicated score.
8.3.2 Prevention of thromboembolism in athletes with AF	2	Pallikadavath	2023	https://doi.org/10.1097/JSM.0000000000001115	The AFLETES Study: Atrial Fibrillation in Veteran Athletes and the Risk of Stroke	To evaluate the risk of stroke in athletes with AF.	Observational.	1,002 participants through an international survey.	Stroke.	Individuals that had competed in ≥1 competitive events and were ≥40 years old were included.	N/A	N/A	N/A	he average age was 52.4 ± 8.5 years, and 84% were male. The most common sports were cycling (n = 677, 72%), running (n = 558, 59%), and triathlon (n = 245, 26%). There were 190 (20%) individuals who reported AF and 26 individuals (3%) who reported stroke; of which, 14 (54%) had AF. Lifetime exercise dose [odds ratio (OR), 1.02, 95% confidence interval (95% CI),1.00-1.03, P = 0.02] and swimming (OR, 1.56, 95% CI, 1.02-2.39, P = 0.04) were associated with AF in multivariable analysis, independent of other risk factors. Atrial fibrillation was associated with stroke (OR, 4.18, 95% CI, 1.80-9.72, P < 0.01), even in individuals with a low (0/1) CHA2DS2-VASc score (OR, 4.20, 95% CI, 1.83-9.66, P < 0.01).	N/A	This survey provides early evidence that veteran endurance athletes who develop AF may be at an increased risk of developing stroke, even in those deemed to be at low risk by CHA2DS2-VASc score.	Surveys are subject to sampling, response, and volunteer bias. Self-reported outcomes. Confounding.
8.3.2 Prevention of thromboembolism in athletes with AF	2	Connolly	2009	https://doi.org/10.1056/NEJMoa0905561	Dabigatran versus warfarin in patients with atrial fibrillation	To evaluate the safety and effectiveness of dabigatran as compared to warfarin in stroke prevention in patients with AF.	Randomized controlled trial.	18,113 patients.	Stroke or systemic embolism.	Patients were eligible if they had atrial fibrillation documented on electrocardiography performed at screening or within 6 months beforehand and at least one of the following characteristics: previous stroke or transient ischemic attack, a left ventricular ejection fraction of less than 40%, New York Heart Association class II or higher heart-failure symptoms within 6 months before screening, and an age of at least 75 years or an age of 65 to 74 years plus diabetes mellitus, hypertension, or coronary artery disease.	Presence of a severe heart valve disorder, stroke within 14 days or severe stroke within 6 months before screening, a condition that increased the risk of hemorrhage, a creatinine clearance of less than 30 ml per minute, active liver disease, and pregnancy.	Dabigatran	Warfarin	Rates of the primary outcome were 1.69% per year in the warfarin group, as compared with 1.53% per year in the group that received 110 mg of dabigatran (relative risk with dabigatran, 0.91; 95% confidence interval [CI], 0.74 to 1.11; P<0.001 for noninferiority) and 1.11% per year in the group that received 150 mg of dabigatran (relative risk, 0.66; 95% CI, 0.53 to 0.82; P<0.001 for superiority).	Rate of major bleeding was 3.36%/year in warfarin group, compared with 2.71% /year in group receiving 110 mg of dabigatran (P=0.003) and 3.11%/year in group receiving 150 mg of dabigatran (P=0.31). The rate of hemorrhagic stroke was 0.38%/year in the warfarin group, as compared with 0.12%/year with 110 mg of dabigatran (P<0.001) and 0.10% per year with 150 mg of dabigatran (P<0.001). The mortality rate was 4.13%/year in the warfarin group, as compared with 3.75%/year with 110 mg of dabigatran (P=0.13) and 3.64%/year with 150 mg of dabigatran (P=0.051).	In patients with atrial fibrillation, dabigatran given at a dose of 110 mg was associated with rates of stroke and systemic embolism that were similar to those associated with warfarin, as well as lower rates of major hemorrhage. Dabigatran administered at a dose of 150 mg, as compared with warfarin, was associated with lower rates of stroke and systemic embolism but similar rates of major hemorrhage.	Therapeutic INR reached only 64% of the time. RE-LY reported a higher rate of major bleeding in warfarin-treated patients compared to prior studies.

8.3.2 Prevention of thromboembolism in athletes with AF	2	Granger	2011	https://doi.org/10.1056/NEJMoa1107039	Apixaban versus warfarin in patients with atrial fibrillation	To evaluate the safety and effectiveness of apixaban as compared to warfarin in stroke prevention in patients with AF.	Randomized controlled trial.	18,201 patients	Ischemic or hemorrhagic stroke or systemic embolism	Eligible patients had AF or flutter at enrollment or 2 or more episodes of AF or flutter, as documented by electrocardiography, at least 2 weeks apart in the 12 months before enrollment. Plus at least 1 of the following risk factors for stroke : an age of at least 75 years; previous stroke, transient ischemic attack, or systemic embolism; symptomatic heart failure within the previous 3 months or left ventricular ejection fraction of no more than 40%; diabetes mellitus; or hypertension requiring pharmacologic treatment.	Key exclusion criteria were atrial fibrillation due to a reversible cause, moderate or severe mitral stenosis, conditions other than atrial fibrillation that required anticoagulation (e.g., a prosthetic heart valve), stroke within the previous 7 days, a need for aspirin at a dose of >165 mg a day or for both aspirin and clopidogrel, and severe renal insufficiency (serum creatinine level of >2.5 mg per deciliter [221 µmol per liter] or calculated creatinine clearance of <25 ml per minute).	Apixaban	Warfarin	The median duration of follow-up was 1.8 years. The rate of the primary outcome was 1.27% per year in the apixaban group, as compared with 1.60% per year in the warfarin group (hazard ratio with apixaban, 0.79; 95% confidence interval [CI], 0.66 to 0.95; P<0.001 for noninferiority; P=0.01 for superiority).	Rate of major bleeding was 2.13%/year in the apixaban group, as compared with 3.09%/year in the warfarin group (hazard ratio, 0.69; P<0.001), and the rates of death from any cause were 3.52% and 3.94%, respectively (hazard ratio, 0.89; P=0.047). The rate of hemorrhagic stroke was 0.24% per year in the apixaban group, as compared with 0.47% per year in the warfarin group (hazard ratio, 0.51; P<0.001), and the rate of ischemic or uncertain type of stroke was 0.97% per year in the apixaban group and 1.05% per year in the warfarin group (hazard ratio, 0.92; P=0.42).	In patients with atrial fibrillation, apixaban was superior to warfarin in preventing stroke or systemic embolism, caused less bleeding, and resulted in lower mortality.	Therapeutic INR reached only 62% of the time.
8.3.2 Prevention of thromboembolism in athletes with AF	2	Giugliano	2013	https://doi.org/10.1056/NEJMoa1310907	Edoxaban versus warfarin in patients with atrial fibrillation	To evaluate the safety and effectiveness of edoxaban compared to warfarin in stroke prevention in patients with AF.	Randomized controlled trial.	21,105 patients	Stroke or systemic embolism.	Eligible patients were 21 years of age or older and had atrial fibrillation documented by means of an electrical tracing within the 12 months preceding randomization, a score of 2 or higher on the CHADS2 risk assessment, and anticoagulation therapy planned for the duration of the trial.	Atrial fibrillation due to a reversible disorder; an estimated creatinine clearance of less than 30 ml per minute; a high risk of bleeding; use of dual antiplatelet therapy; moderate-to-severe mitral stenosis; other indications for anticoagulation therapy; acute coronary syndromes, coronary revascularization, or stroke within 30 days before randomization; and an inability to adhere to study procedures.	Edoxaban	Warfarin	The annualized rate of the primary end point during treatment was 1.50% with warfarin (median time in the therapeutic range, 68.4%), as compared with 1.18% with high-dose edoxaban (hazard ratio, 0.79; 97.5% confidence interval [CI], 0.63 to 0.99; P<0.001 for noninferiority) and 1.61% with low-dose edoxaban (hazard ratio, 1.07; 97.5% CI, 0.87 to 1.31; P=0.005 for noninferiority). In the intention-to-treat analysis, there was a trend favoring high-dose edoxaban versus warfarin (hazard ratio, 0.87; 97.5% CI, 0.73 to 1.04; P=0.08) and an unfavorable trend with low-dose edoxaban versus warfarin (hazard ratio, 1.13; 97.5% CI, 0.96 to 1.34; P=0.10)	The annualized rate of major bleeding was 3.43% with warfarin versus 2.75% with high-dose edoxaban (hazard ratio, 0.80; P<0.001) and 1.61% with low-dose edoxaban (hazard ratio, 0.47; P<0.001). The corresponding annualized rates of death from cardiovascular causes were 3.17% versus 2.74% (hazard ratio, 0.86; P=0.01), and 2.71% (hazard ratio, 0.85; P=0.008), and the corresponding rates of the key secondary end point were 4.43% versus 3.85% (hazard ratio, 0.87; P=0.005), and 4.23% (hazard ratio, 0.95; P=0.32).	Both once-daily regimens of edoxaban were noninferior to warfarin with respect to the prevention of stroke or systemic embolism and were associated with significantly lower rates of bleeding and death from cardiovascular causes.	Treatment interruptions more frequent in warfarin group as compared to edoxaban group.
8.3.2 Prevention of thromboembolism in athletes with AF	2	Patel	2011	https://doi.org/10.1056/NEJMoa1009638	Rivaroxaban versus warfarin in nonvalvular atrial fibrillation	To evaluate the safety and effectiveness of rivaroxaban compared to warfarin in stroke prevention in patients with AF.	Randomized controlled trial.	14,264 patients	Stroke or systemic embolism.	Nonvalvular atrial fibrillation, as documented on electrocardiography, who were at moderate-to-high risk for stroke	Valvular AF, reversible AF, and significant comorbitidies such as active bleeding, endocarditis, thrombocytopenia, severe stroke, etc.	Rivaroxaban	Warfarin	In the primary analysis, the primary end point occurred in 188 patients in the rivaroxaban group (1.7% per year) and in 241 in the warfarin group (2.2% per year) (hazard ratio in the rivaroxaban group, 0.79; 95% confidence interval [CI], 0.66 to 0.96; P<0.001 for noninferiority). In the intention-to-treat analysis, the primary end point occurred in 269 patients in the rivaroxaban group (2.1% per year) and in 306 patients in the warfarin group (2.4% per year) (hazard ratio, 0.88; 95% CI, 0.74 to 1.03; P<0.001 for noninferiority; P=0.12 for superiority).	Major and nonmajor clinically relevant bleeding occurred in 1475 patients in the rivaroxaban group (14.9% per year) and in 1449 in the warfarin group (14.5% per year) (hazard ratio, 1.03; 95% CI, 0.96 to 1.11; P=0.44), with significant reductions in intracranial hemorrhage (0.5% vs. 0.7%, P=0.02) and fatal bleeding (0.2% vs. 0.5%, P=0.003) in the rivaroxaban group.	In patients with atrial fibrillation, rivaroxaban was noninferior to warfarin for the prevention of stroke or systemic embolism. There was no significant between-group difference in the risk of major bleeding, although intracranial and fatal bleeding occurred less frequently in the rivaroxaban group.	Unclear if differences in as-treated and intention-to-treat analyses represent significant differences in underlying efficacy. Warfarin group only therapeutic 55% of the time.
8.3.2 Prevention of thromboembolism in athletes with AF	4	Holmes	2014	https://doi.org/10.1016/j.jacc.2014.04.029	Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial	To assess the safety and efficacy of LAA occlusion for stroke prevention in patients with NVAF compared with long-term warfarin therapy.	Randomized controlled trial.	407 patients.	1. Composite of stroke, systemic embolism, cardiovascular/unexplained death; 2. Composite of ischemic stroke or systemic embolism >7 days after randomization; 3. Composite of all-cause death, ischemic stroke, systemic embolism, or device/procedure-related events requiring major intervention within 7 days of the procedure	CHADS2 score of 1 if they also had any of the following higher-risk characteristics: female age ≥75 years, baseline ejection fraction ≥30% but <35%, age 65 to 74 years and either diabetes or coronary disease, and age ≥65 years with congestive heart failure.	Exclusion criteria included requirement for long-term anticoagulation therapy for reasons other than AF, contraindication to warfarin or aspirin, previous stroke/transient ischemic attack within 90 days of enrollment, symptomatic carotid disease, or a patent foramen ovale or atrial septal defect requiring treatment	Percutaneous left atrial appendage occlusion.	Warfarin.	At 18 months, the rate of the first coprimary efficacy endpoint (composite of stroke, systemic embolism [SE], and cardiovascular/unexplained death) was 0.064 in the device group versus 0.063 in the control group (rate ratio 1.07 [95% credible interval (CrI): 0.57 to 1.89]) and did not achieve the prespecified criteria noninferiority (upper boundary of 95% CrI ≥1.75). The rate for the second coprimary efficacy endpoint (stroke or SE >7 days' postrandomization) was 0.0253 versus 0.0200 (risk difference 0.0053 [95% CrI: −0.0190 to 0.0273]), achieving noninferiority.	Early safety events occurred in 2.2% of the Watchman arm, significantly lower than in PROTECT AF, satisfying the pre-specified safety performance goal.	LAA occlusion is a reasonable alternative to warfarin therapy for stroke prevention in patients with NVAF who do not have an absolute contraindication to short-term warfarin therapy.	Low event rates with limited power to establish noninferiority.

8.3.2 Prevention of thromboembolism in athletes with AF	4	Reddy	2014	https://doi.org/10.1001/jama.2014.15192	Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial	To determine whether a local strategy of mechanical left atrial appendage (LAA) closure was noninferior to warfarin.	Randomized controlled trial.	707 patients.	A composite efficacy end point including stroke, systemic embolism, and cardiovascular/unexplained death, analyzed by intention-to-treat.	Age 18 years or older; paroxysmal, persistent, or permanent nonvalvular AF; 1 or more CHADS2 risk factors (age ≥75 years, hypertension, diabetes, heart failure or left ventricular [LV] systolic dysfunction, prior transient ischemic attack [TIA] or stroke); and eligibility for long-term anticoagulation with warfarin.	Major exclusion criteria were patent foramen ovale with atrial septal aneurysm, an atrial septal defect, mechanical valve prosthesis, LV ejection fraction less than 30%, mobile aortic atheromata, and symptomatic carotid disease. Eligible patients underwent neurological examination by a neurologist, and those with a history of prior thromboembolism underwent baseline magnetic resonance imaging or computed tomography (CT) neuroimaging.	Percutaneous left atrial appendage occlusion.	Warfarin.	A mean (SD) follow-up of 3.8 (1.7) years (2621 patient-years), there were 39 events among 463 patients (8.4%) in the device group for a primary event rate of 2.3 events per 100 patient-years, compared with 34 events among 244 patients (13.9%) for a primary event rate of 3.8 events per 100 patient-years with warfarin (rate ratio, 0.60; 95% credible interval, 0.41-1.05), meeting prespecified criteria for both noninferiority (posterior probability, >99.9%) and superiority (posterior probability, 96.0%). Patients in the device group demonstrated lower rates of both cardiovascular mortality (1.0 events per 100 patient-years for the device group [17/463 patients, 3.7%] vs 2.4 events per 100 patient-years with warfarin [22/244 patients, 9.0%]; hazard ratio [HR], 0.40; 95% CI, 0.21-0.75; P = .005) and all-cause mortality (3.2 events per 100 patient-years for the device group [57/466 patients, 12.3%] vs 4.8 events per 100 patient-years with warfarin [44/244 patients, 18.0%]; HR, 0.66; 95% CI, 0.45-0.98; P = .04).	N/A	After 3.8 years of follow-up among patients with nonvalvular AF at elevated risk for stroke, percutaneous LAA closure met criteria for both noninferiority and superiority, compared with warfarin, for preventing the combined outcome of stroke, systemic embolism, and cardiovascular death, as well as superiority for cardiovascular and all-cause mortality.	Cannot generalize to those on direct oral anticoagulants.
8.3.3 Rate and rhythm control	1	Mujović	2021	https://doi.org/10.1161/JAHA.120.017445	Improvement of Maximal Exercise Performance After Catheter-Ablation of Atrial Fibrillation and Its Prognostic Significance for Long-Term Rhythm Outcome	To assess long-term exercise tolerance improvement and its prognostic implications following catheter-ablation (CA) of paroxysmal and nonparoxysmal AF	Observational, prospective, single-center	110 patients.	Cardiopulmonary exercise testing parameters.	Consecutive patients (n=170) who underwent CA for symptomatic AF refractory to at least 1 Class IC or III AAD	Those excluded were those in which baseline cardiopulmonary exercise testing (CPET) was contraindicated or inconclusive in 21 patients because of uncontrolled atrial tachyarrhythmia (n=12), known severe coronary artery disease (n=3), previous syncope (n=2), orthopedic diagnosis limiting physical performance (n=2), or patient's inability to cooperate during the test (n=2).	Catheter ablation	N/A	Of 110 patients (mean age 57.5±10.6 years, 77.2% males) with paroxysmal AF (n=66) or nonparoxysmal AF (n=44), the 12-month exercise tolerance improved significantly in those who maintained sinus rhythm during the first 12 months post-CA (n=96), but not in patients with AF recurrence (n=14). After CA, the 12-month respiratory exchange ratio at maximal workload significantly increased in patients with paroxysmal AF, whereas those with nonparoxysmal AF significantly reduced their heart rate during the 12-month cardiopulmonary exercise testing (all P≤0.001). During the follow-up of 42.8±7.8 months, a total of 29 patients (26.3%) experienced recurrent AF.	On multivariate analysis including patients without recurrent AF at 12 months after CA, the extent of work time improvement at follow-up cardiopulmonary exercise testing was independently associated with the rhythm outcome beyond 12 months postprocedure (hazard ratio of 0.936 [95% CI, 0.894–0.979] for each 10 seconds increase in the work time following ablation, P=0.004).	CA of AF was associated with recovery of exercise intolerance in patients with paroxysmal AF or nonparoxysmal AF. Inability to improve exercise capacity at 12 months post-CA was an independent risk factor for later AF recurrence.	Small cohort, no control, no continuous AF monitoring after ablation.
8.3.3 Rate and rhythm control	1, 2	Mark	2019	https://doi.org/10.1001/jama.2019.0692	Effect of Catheter Ablation vs Medical Therapy on Quality of Life Among Patients With Atrial Fibrillation: The CABANA Randomized Clinical Trial	To determine whether catheter ablation is more beneficial than conventional drug therapy for improving QOL in patients with AF.	Randomized controlled trial.	2204 patients.	Quality of life as assessed by questionaires at 12 months.	Aged 65 years and older or younger than 65 years with 1 or more risk factors for stroke (hypertension, heart failure, history of stroke, diabetes, or other heart problems), had 2 or more episodes of paroxysmal AF or 1 episode of persistent AF in the prior 6 months, and were suitable for catheter-based treatment or rhythm and/or rate control drug therapy.	Prior left atrial catheter ablation for AF or had failed 2 or more antiarrhythmic drugs	Ablation	Drug therapy	The mean AFEQT summary score was more favorable in the catheter ablation group than the drug therapy group at 12 months (86.4 points vs 80.9 points) (adjusted difference, 5.3 points [95% CI, 3.7-6.9]; P < .001). The mean MAFSI frequency score was more favorable for the catheter ablation group than the drug therapy group at 12 months (6.4 points vs 8.1 points) (adjusted difference, −1.7 points [95% CI, −2.3 to −1.2]; P < .001) and the mean MAFSI severity score was more favorable for the catheter ablation group than the drug therapy group at 12 months (5.0 points vs 6.5 points) (adjusted difference, −1.5 points [95% CI, −2.0 to −1.1]; P < .001).	N/A	Among patients with symptomatic atrial fibrillation, catheter ablation, compared with medical therapy, led to clinically important and significant improvements in quality of life at 12 months. These findings can help guide decisions regarding management of atrial fibrillation.	High crossover. Treatment group not masked.
8.3.3 Rate and rhythm control	1	Johnson	2023	https://doi.org/10.1161/CIRCEP.122.011565	Atrial Fibrillation Ablation in Young Adults: Measuring Quality of Life Using Patient-Reported Outcomes Over 5 Years	To investigate AF ablation outcomes and QoL benefits in young adults undergoing AF ablation using a large prospectively maintained registry and automated patient-reported outcomes (PRO).	Observational, prospective, single-center	241 young adults.	Quality of life as assessed by questionnaires at 12 months.	Patients aged 50 years or younger undergoing AF ablation	N/A	Ablation	N/A	sing PROs, 90% of patients reported improvement in QoL throughout all survey time points up to 5 years postablation (P<0.0001). The baseline median AF severity score was 14 and improved to between 2 and 4 on all follow-up after ablation (P<0.0001). Patients also reported fewer and shorter AF episodes, fewer emergency room visits secondary to AF, and fewer hospitalizations (P<0.0001).	N/A	Ablation remains an effective rhythm-control strategy in young adults with AF. Young adults also experience significant improvement in QoL with reduction of the frequency and duration of AF episodes and AF-related healthcare utilization.	The study population was predominantly composed of obese, white, non-Hispanic males, limiting the generalizability of the results.
8.3.3 Rate and rhythm control	2	Wazni	2021	https://doi.org/10.1056/NEJMoa2029554	Cryoballoon Ablation as Initial Therapy for Atrial Fibrillation	To assess safety and efficacy of cryoballoon ablation as initial first-line therapy	Randomized controlled trial.	203 participants.	Treatment success (defined as freedom from initial failure of the procedure or atrial arrhythmia recurrence after a 90-day blanking period to allow recovery from the procedure or drug dose adjustment, evaluated in a Kaplan–Meier analysis)	18 to 80 years of age and had recurrent symptomatic paroxysmal atrial fibrillation	Previous treatment with an antiarrhythmic drug (class I or III) for 7 or more days, an enlarged left atrial diameter (>5 cm), or a previous left atrial ablation or left atrial surgical procedure	AF ablation.	Medical therapy.	In the ablation group, initial success of the procedure was achieved in 97% of patients. The Kaplan–Meier estimate of the percentage of patients with treatment success at 12 months was 74.6% (95% confidence interval [CI], 65.0 to 82.0) in the ablation group and 45.0% (95% CI, 34.6 to 54.7) in the drug-therapy group (P<0.001 by log-rank test).	Two primary safety end-point events occurred in the ablation group (Kaplan–Meier estimate of the percentage of patients with an event within 12 months, 1.9%; 95% CI, 0.5 to 7.5). Overall, 31 of 104 in the ablation group and 43 of 99 in the drug-therapy group reported at least 1 cardiovascular-related health care utilization event.	Cryoballoon ablation as initial therapy was superior to drug therapy for the prevention of atrial arrhythmia recurrence in patients with paroxysmal atrial fibrillation. Serious procedure-related adverse events were uncommon	f/u short, selected patients, monitoring not continuous

8.3.3 Rate and rhythm control	2	Andrade	2021	https://doi.org/10.1056/NEJMoa2029980	Cryoablation or Drug Therapy for Initial Treatment of Atrial Fibrillation	Comparing radiofrequency catheter ablation with antiarrhythmic drug therapy as first-line treatment in patients with paroxysmal atrial fibrillation.	Randomized controlled trial.	303 patients.	The primary end point was the first documented recurrence of any atrial tachyarrhythmia (atrial fibrillation, atrial flutter, or atrial tachycardia) between 91 and 365 days after catheter ablation or the initiation of an antiarrhythmic drug. The secondary end points included freedom from symptomatic arrhythmia, the atrial fibrillation burden, and quality of life.	Adults (>18 years of age) who had symptomatic atrial fibrillation and at least one episode of atrial fibrillation detected on electrocardiography within 24 months before randomization.	History of regular (daily) use of a class I or class III antiarrhythmic drug at therapeutic doses	Ablation	Drug therapy	At 1 year, a recurrence of atrial tachyarrhythmia had occurred in 66 of 154 patients (42.9%) assigned to undergo ablation and in 101 of 149 patients (67.8%) assigned to receive antiarrhythmic drugs (hazard ratio, 0.48; 95% confidence interval [CI], 0.35 to 0.66; P<0.001).	Symptomatic atrial tachyarrhythmia had recurred in 11.0% of the patients who underwent ablation and in 26.2% of those who received antiarrhythmic drugs (hazard ratio, 0.39; 95% CI, 0.22 to 0.68). The median percentage of time in atrial fibrillation was 0% (interquartile range, 0 to 0.08) with ablation and 0.13% (interquartile range, 0 to 1.60) with antiarrhythmic drugs. Serious adverse events occurred in 5 patients (3.2%) who underwent ablation and in 6 patients (4.0%) who received antiarrhythmic drugs.	Among patients receiving initial treatment for symptomatic, paroxysmal atrial fibrillation, there was a significantly lower rate of atrial fibrillation recurrence with catheter cryoballoon ablation than with antiarrhythmic drug therapy, as assessed by continuous cardiac rhythm monitoring.	No CV outcomes, selected patients
8.3.3 Rate and rhythm control	2	Packer	2019	https://doi.org/10.1001/jama.2019.0693	Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation: The CABANA Randomized Clinical Trial	To determine whether catheter ablation is more effective than conventional medical therapy for improving outcomes in AF.	Randomized controlled trial.	2204 patients.	The primary end point was a composite of death, disabling stroke, serious bleeding, or cardiac arrest.	Aged 65 years and older or younger than 65 years with 1 or more risk factors for stroke (hypertension, heart failure, history of stroke, diabetes, or other heart problems), had 2 or more episodes of paroxysmal AF or 1 episode of persistent AF in the prior 6 months, and were suitable for catheter-based treatment or rhythm and/or rate control drug therapy.	Prior left atrial catheter ablation for AF or had failed 2 or more antiarrhythmic drugs	Ablation	Drug therapy	Of the patients assigned to catheter ablation, 1006 (90.8%) underwent the procedure. Of the patients assigned to drug therapy, 301 (27.5%) ultimately received catheter ablation. In the intention-to-treat analysis, over a median follow-up of 48.5 months, the primary end point occurred in 8.0% (n = 89) of patients in the ablation group vs 9.2% (n = 101) of patients in the drug therapy group (hazard ratio [HR], 0.86 [95% CI, 0.65-1.15]; P = .30).	Among the secondary end points, outcomes in the ablation group vs the drug therapy group, respectively, were 5.2% vs 6.1% for all-cause mortality (HR, 0.85 [95% CI, 0.60-1.21]; P = .38), 51.7% vs 58.1% for death or cardiovascular hospitalization (HR, 0.83 [95% CI, 0.74-0.93]; P = .001), and 49.9% vs 69.5% for AF recurrence (HR, 0.52 [95% CI, 0.45-0.60]; P < .001).	Among patients with AF, the strategy of catheter ablation, compared with medical therapy, did not significantly reduce the primary composite end point of death, disabling stroke, serious bleeding, or cardiac arrest. However, the estimated treatment effect of catheter ablation was affected by lower-than-expected event rates and treatment crossovers, which should be considered in interpreting the results of the trial.	High crossover
8.3.3 Rate and rhythm control	2	Hsu	2023	https://doi.org/10.1016/j.jacc.2022.11.060	Initial Findings From the National Cardiovascular Data Registry of Atrial Fibrillation Ablation Procedures	To characterize the patient, hospital, and physician characteristics and in-hospital outcomes related to AF ablation in the first 5 years of the registry.	Observational.	76,219 patients.	AF ablation procedural complications.	All patients included in NCDR AF Ablation Registry.	N/A	AF ablation.	N/A	The prevalence of any complication during procedural admission was 2.50% and major complication was 0.9%, including significant bradycardia in 0.47%, heart failure in 0.47%, and pericardial effusion requiring intervention in 0.44%. Hospitalization >1 day occurred in 11.8% of patients, and in-hospital death was rare (n = 41 [0.05%]).	Successful isolation of all pulmonary veins was achieved in 92.4% of patients	The NCDR AFib Ablation Registry is the largest multicenter, prospective cohort study of patients undergoing catheter ablation worldwide. Results in the first 5 years showed that successful pulmonary vein isolation is achieved in the majority of patients, with a low rate of complications.	Relies on voluntary participation, lacks granularity with some procedural characteristics and outcomes.
8.3.3 Rate and rhythm control	2	Koopman	2011	https://doi.org/10.1093/europace/eur142	Efficacy of radiofrequency catheter ablation in athletes with atrial fibrillation	To analyze the efficacy of AF ablation in athletes.	Observational, cohort.	135 athletes.	AF recurrence at 3 years.	Inclusion required (i) symptomatic AF, (ii) paroxysmal, or persistent for <1 year, (iii) refractory to at least one anti-arrhythmic drug, and (iv) focally induced as documented on Holter monitoring by showing frequent atrial pre-mature beats or runs of atrial tachycardia inducing bouts of AF.	Missing sports questionnaire, missing data, or ablation procedures performed in other centres. Patients with important underlying atrial structural changes [i.e. left atrial (LA) diameter ≥55 mm] or permanent AF.	Athletes undergoing ablation.	Controls undergoing ablation.	Survival analysis showed similar AF recurrence rate after a first ablation for controls and endurance athletes, though non-endurance athletes had a significantly higher AF recurrence rate (48 vs. 46 vs. 34% freedom from AF at 3 year follow-up after a single ablation, P= 0.04). Final outcome after all ablations was similar (87 vs. 84 vs. 85% freedom from AF at 3-year follow-up, P = 0.88). No other independent predictor for AF recurrence was identified.	N/A	In patients with documented focal induction of non-permanent AF and absence of structural heart disease, PVI is as effective in endurance athletes as in other patients.	Non-randomized, small sample size, no continuous monitoring.
8.3.3 Rate and rhythm control	2	Calvo	2010	https://doi.org/10.1093/europace/eup320	Efficacy of circumferential pulmonary vein ablation of atrial fibrillation in endurance athletes	To evaluate the efficacy of CPVA in AF secondary to endurance sport practice.	Observational, cohort.	182 patients.	Freedom from arrhythmia.	Consecutive patients with drug-refractory AF undergoing ablation.	N/A	Athletes undergoing ablation.	Controls undergoing ablation.	Freedom from arrhythmia after a single CPVA was similar in the lone AF sport group compared with the remaining patients (P = 0.446).	Left atrial size and long-standing AF were the only independent predictors for arrhythmia recurrence after ablation.	Circumferential pulmonary vein ablation was as effective in AF secondary to endurance sport practice as in other etiologies of AF.	Non-randomized, small sample size, no continuous monitoring.
8.3.3 Rate and rhythm control	2	Mandsager	2020	https://doi.org/10.1016/j.jacep.2020.05.009	Outcomes of Pulmonary Vein Isolation in Athlete	To assess outcomes of pulmonary vein isolation (PVI) performed on athletes at a tertiary care center and to characterize its efficacy and physiological effects.	Observational, cohort.	144 patients.	AF recurrence.	Patients with atrial fibrillation who were athletes and who underwent pulmonary vein isolation.	Patients who were not athletes.	Ablation.	Non-athlete controls.	Freedom from AF at 3 years was up to 75% in athletes with paroxysmal AF. This increased to 86% with multiple procedures. Compared to a matched cohort of non-athletes, the success rates were similar (p =0.23).	Maximum metabolic equivalents on exercise treadmill testing were unchanged after ablation (13.1 vs. 12.7, p=0.44).	Pulmonary vein isolation was found to be effective in athletes and did not result in a significant change in exercise capacity.	Non-randomized, small sample size, no continuous monitoring.
8.3.3 Rate and rhythm control	2	Furlanello	2008	https://doi.org/10.1111/j.1540-8167.2007.01077.x	Radiofrequency catheter ablation of atrial fibrillation in athletes referred for disabling symptoms preventing usual training schedule and sport competition	To investigate the effectiveness of CA of idiopathic AF in athletes with palpitations impairing physical performance and compromising eligibility for competitive activities.	Observational, cohort.	20	AF recurrence, maximal exercise capacity, quality of life.	Consecutive athletes with AF undergoing ablation.	N/A	Ablation	N/A	Preablation, effort-induced AF could be documented in 13 patients (65%) during stress ECG and significantly reduced maximal effort capacity (176 ± 21 W), as compared with patients with no AF during effort (207 ± 43 W, P < 0.05). At the end of CA protocol, which also included ablation of atrial flutter (AFL) in 7 patients, 18 (90.0%) patients were free of AF and two (10.0%) reported short-lasting (minutes) episodes of palpitations during 36.1 ± 12.7 months follow-up. Compared with preablation, postablation maximal exercise capacity significantly improved (from 183 ± 32 to 218 ± 20 W, P < 0.02). All baseline quality of life (QoL) parameters pertinent to physical activity significantly improved (P < 0.05) at the end of CA protocol. All athletes obtained reeligibility and could effectively reinitiate sport activity.	N/A	AF, alone or in combination with AFL, may significantly impair maximal effort capacity thereby limiting competitive performance. Multiple PV isolation proved very effective in these patients to restore full competitive activity and allow reeligibility.	Small sample size, no comparison.

8.3.3 Rate and rhythm control	2	Morillo	2014	https://doi.org/10.1001/jama.2014.467	Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (RAAFT-2): a randomized trial	To compare radiofrequency ablation with antiarrhythmic drugs (standard therapy) in treating patients with paroxysmal AF as a first-line therapy.	Randomized controlled trial.	127 patients.	The time to the first documented atrial tachyarrhythmia of more than 30 seconds (symptomatic or asymptomatic AF, atrial flutter, or atrial tachycardia)	Older than 18 and no older than 75 years; were symptomatic with recurrent paroxysmal AF lasting more than 30 seconds (≤4 episodes within the prior 6 months); experienced at least 1 episode that was documented by surface ECG, 6 months before randomization; and had no previous antiarrhythmic drug treatment.	Patients were excluded if they had documented left ventricular ejection fraction of less than 40%; had left atrial diameter larger than 5.5 cm; had moderate to severe left ventricular hypertrophy (wall thickness >1.5 cm), valvular disease, coronary artery disease, or postcardiac surgery within 6 months; had undergone a left heart ablation procedure, either by surgery or by radiofrequency catheter ablation for AF; or had a complete contraindication for the use of heparin, warfarin, or both	Ablation	Medical therapy.	Forty-four patients (72.1%) in the antiarrhythmic group and in 36 patients (54.5%) in the ablation group experienced the primary efficacy outcome (hazard ratio [HR], 0.56 [95% CI, 0.35-0.90]; P = .02).	For the secondary outcomes, 59% in the drug group and 47% in the ablation group experienced the first recurrence of symptomatic AF, atrial flutter, atrial tachycardia (HR, 0.56 [95% CI, 0.33-0.95]; P = .03). No deaths or strokes were reported in either group; 4 cases of cardiac tamponade in the ablation group. In the standard treatment group, 26 patients (43%) underwent ablation after 1-year. QOL was moderately impaired at baseline in both groups and improved at the 1 year follow-up. However, improvement was not significantly different among groups.	Among patients with paroxysmal AF without previous antiarrhythmic drug treatment, radiofrequency ablation compared with antiarrhythmic drugs resulted in a lower rate of recurrent atrial tachyarrhythmias at 2 years. However, recurrence was frequent in both groups.	Small sample size, limited generalizability, lack of continuous monitoring.
8.3.3 Rate and rhythm control	3	Natale	2000	https://doi.org/10.1016/s0735-1097(00)00635-5	Prospective randomized comparison of antiarrhythmic therapy versus first-line radiofrequency ablation in patients with atrial flutter	To prospectively compare the outcome at follow-up of patients with atrial flutter randomly assigned to drug therapy or RF ablation.	Randomized controlled trial.	61 patients.	Recurrence of atrial flutter, rehospitalization and quality of life.	Consecutive patients referred to each institution if they had at least 2 symptomatic episodes of atrial flutter in the last f4our months.	Exclusion criteria included the following; 1) prior evidence of atrial fibrillation (AF); 2) the presence of significant left atrial enlargement (≥4.5 cm); and 3) previous treatment with antiarrhythmic medications.	Ablation	Medical therapy.	After a mean follow-up of 21 ± 11 months, 11 of 30 (36%) patients receiving drugs were in sinus rhythm, versus 25 of 31 (80%) patients who underwent RF ablation ($p < 0.01$). Of the patients receiving drugs, 63% required one or more rehospitalizations, whereas post-RF ablation, only 22% of patients were rehospitalized ($p < 0.01$). Following RF ablation, 29% of patients developed atrial fibrillation which was seen in 53% of patients receiving medications ($p < 0.05$). Sense of well being (pre-RF 2.0 ± 0.3 vs. post-RF 3.8 ± 0.5, $p < 0.01$) and function in daily life (pre-RF 2.3 ± 0.4 vs. post-RF 3.6 ± 0.6, $p < 0.01$) improved after ablation, but did not change significantly in patients treated with drugs.	N/A	In a selected group of patients with atrial flutter, RF ablation could be considered a first-line therapy due to the better success rate and impact on quality of life, the lower occurrence of atrial fibrillation and the lower need for rehospitalization at follow-up.	Lack of continuous monitoring, outdated.
8.3.3 Rate and rhythm control	3	Wazni	2003	https://doi.org/10.1161/01.CIR.0000101684.88679.AB	Randomized study comparing combined pulmonary vein-left atrial junction disconnection and cavotricuspid isthmus ablation versus pulmonary vein-left atrial junction disconnection alone in patients presenting with typical atrial flutter and atrial fibrillation	To evaluate if pulmonary vein–left atrial junction (PV-LAJ) disconnection may eliminate both AF and AFL.	Randomized controlled trial.	108 patients.	Atrial arryhthmia recurrence.	Patients had to have at least 1 documented episode of typical AFL while not taking antiarrhythmic medications.	N/A	PVI + CTI	PVI alone	Within the first 8 weeks after ablation, 32 of the group 2 patients had typical AFL documented, whereas none was seen in group 1. Twenty of these 32 converted to sinus rhythm after initiating antiarrhythmic drugs (AADs). Twelve were cardioverted, and AADs were started. After 8 weeks, all AADS were stopped, and only 3 patients continued to have recurrent sustained typical AFL that was eliminated by CTI ablation. Beyond 8 weeks of follow-up, 7 patients in group 1 and 6 patients in group 2 (14% and 11%, respectively) continued to have AF. Ten of these 13 patients underwent a repeat PV-LAJ disconnection procedure and were cured. The remaining 3 remained in normal sinus rhythm while taking AADs.	N/A	In patients with both AFL and AF, PV-LAJ disconnection alone may be sufficient to control both arrhythmias. CTI block reduced early postablation recurrence of arrhythmias, which in the majority of patients reflects a short-term clinical problem.	Outdated.
8.3.3 Rate and rhythm control	3	Mohanty	2013	https://doi.org/10.1161/CIRCULATIONAHA.113.001855	Results from a single-blind, randomized study comparing the impact of different ablation approaches on long-term procedure outcome in coexistent atrial fibrillation and flutter (APPROVAL)	To examine the impact of different ablation strategies on atrial fibrillation (AF) recurrence and quality of life in coexistent AF and atrial flutter (AFL).	Randomized controlled trial.	360 patients.	AF recurrence and quality of life.	Inclusion criteria were history of paroxysmal AF with failed treatment with at least 1 antiarrhythmic drug (AAD) and preablation evidence of typical AFL documented by 12-lead surface ECG.	Patients were excluded from the study if they were <18 or >85 years old, if they had had previous ablation, if they had left atrium size ≥ 5 cm, or if they had a contraindication to oral anticoagulation.	AF±AFL ablation	AFL ablation only	At 21±9 months of follow-up, 117 in group 1 (64%) and 34 in group 2 (19%) were arrhythmia free (P<0.001).	In group 1, scores on most quality-of-life subscales showed significant improvement at follow-up, whereas group 2 patients derived relatively minor benefit.	In coexistent AF and AFL, lower recurrence rate and better quality of life are associated with AF ablation only or AF+AFL ablation than with lone AFL ablation. Furthermore, quality of life directly correlates with freedom from arrhythmia, as shown in this study for the first time in patients blinded to the procedure.	Generic questionnaires.
8.3.3 Rate and rhythm control	3	Pontoppidan	2009	https://doi.org/10.1136/hrt.2008.153965	Prophylactic cavotricuspid isthmus block during atrial fibrillation ablation in patients without atrial flutter: a randomised controlled trial	To evaluate if patients with atrial fibrillation (AF) and no history of atrial flutter (AFL) had any benefit of prophylactic cavotricuspid isthmus block (CTIB) in addition to circumferential pulmonary vein ablation (CPVA).	Randomized controlled trial.	149 patients.	Recurrence at 3, 6 and 12 months.	Symptomatic paroxysmal or persistent AF.	Documentation of typical atrial flutter, previous CTIB or CPVA, patient refusal.	PVI	PVI+CTI	Six patients (4%) had cardiac tamponade, and one patient had a stroke. No difference was found in the cumulative AFL-free rate between the two treatment groups (CTIB+: 88% vs CTIB2: 84%, hazard ratio (HR) 0.80, 95% CI (0.34 to 1.90), p = 0.61). There was no difference in the cumulative AF-free rate between the groups (CTIB+: 34% vs CTIB2: 32%, HR 0.93, 95% CI (0.63 to 1.38), p = 0.71). Overall, 33% of the patients were free of AF after a single procedure. Including reprocedures, a complete or partial beneficial effect was noted in 62% of the patients at 12 months. At 12-month follow-up, 24 (50%) patients with documented AF or AFL in the Holter recordings were asymptomatic.	N/A	It was not possible to demonstrate any beneficial effect of CTIB in addition to CPVA with regard to AFL or AF recurrences during follow-up. Repetitive long- term Holter monitoring demonstrated a 33% rate of freedom from AF during a 1-year follow-up. Including additional CPVA procedures, a clinical effect was noted in 62% of the patients at 12 months. Patients with AF or AFL recurrences were often asymptomatic.	No continuious monitoring. Small sample size. Limited follow up period.
8.3.3 Rate and rhythm control	3	Romero	2020	https://doi.org/10.1111/jce.14614	Cavotricuspid isthmus line in patients undergoing catheter ablation of atrial fibrillation with or without history of typical atrial flutter: A meta-analysis	To examine whether CTI ablation for AF is associated with improvement in recurrence of all-atrial arrhythmias, compared with PVI alone in patients with and without typical atrial flutter (AFL).	Meta-analyses of non-randomized studies	Five studies of 1400 patients.	AF recurrence.	A) included patients underwent CA for AF; (B) included patients underwent CTI+PVI ablation, and controls underwent PVI alone; (C) reported all-atrial arrhythmia rate as an outcome.	N/A	PVI + CTI	PVI alone	fter a mean follow-up of 14.4□4.8 months, CTI+PVI was not associated withimprovement in recurrence of all-atrial arrhythmias when compared to PVI alone (Risk Ratio [RR]: 1.29, 95% Confidence Interval [CI]: 0.93-1.79, p=0.13). In the subgroup analysis, there were no differences between both groups in patients with AF without AFL (RR: 1.55, 95% CI: 0.96-2.48, p=0.07), and in patients with AF and AFL (RR: 0.91, 95% CI: 0.6-1.39, p=0.68).	N/A	In AF patients, irrespective of the presence of typical AFL, additional CTI ablation is not associated with improvement in recurrence of all-atrial arrhythmias, compared to PVI alone.	Limited trials. No long term monitoring.

8.3.3 Rate and rhythm control	5	Gibson	2011	https://doi.org/10.1016/j.hrthm.2011.02.026	Stiff left atrial syndrome after catheter ablation for atrial fibrillation: clinical characterization, prevalence, and predictors	The purpose of this study was to prospectively quantify the incidence of patients developing PH associated with diastolic hemodynamic abnormalities of the LA after radiofrequency ablation of AF and to identify the possible predictors.	Observation, prospective.	19 patients.	Stiff left atrial atrial syndrome.	Presence of new or worsening PH, dyspnea, and LA diastolic pressure abnormalities, unexplained dysnea.	At least mild mitral regurgitation.	Ablation.	N/A	New or worsening PH with associated LA diastolic abnormalities was detected in 19 (1.4%) patients after ablation. The prevalence of PH did not differ between AF types (P = .612). Compared with patients who did not develop PH, LA scarring (P <.001), diabetes (P = .026), and obstructive sleep apnea (OSA; P = .006) were more frequently observed among those who developed PH. In a multivariable logistic model, preprocedure LA size ≤45 mm (odds ratio [OR] = 6.13; P = .033), mean LA pressure (OR 1.14; P = .025), severe LA scarring (OR = 4.4; P = .046), diabetes mellitus (OR = 9.5; P = .004), and OSA (OR = 6.2; P = .009) were independently associated with the development of PH postablation.	N/A	After radiofrequency catheter ablation of atrial fibrillation (RFCAF), PH with LA diastolic dysfunction or the so-called stiff LA syndrome is a rare but potentially significant complication of AF ablation. Severe LA scarring, LA ≤45 mm, diabetes mellitus, OSA, and high LA pressure are clinical variables that predict the development of this syndrome. The main clinical findings include dyspnea, congestive heart failure, PH, and large V waves on pulmonary capillary wedge pressure (PCWP) or LA pressure tracings in the absence of mitral regurgitation.	Only identified based on symptoms and echocardiographic assessment of pulmonary arterial pressures.
8.3.3 Rate and rhythm control	5	Verma	2015	https://doi.org/10.1056/NEJMoa1408288	Approaches to catheter ablation for persistent atrial fibrillation	To evalaute adjuvant substrate modification in addition to pulmonary-vein isolation in patients with persistent atrial fibrillation.	Randomized controlled trial.	489 patients	Freeedom from any documented recurrence of atrial fibrillation lasting longer than 30 seconds after a single ablation procedure.	Patients were eligible if they were 18 years of age or older, had symptomatic persistent atrial fibrillation (i.e., a sustained episode lasting more than 7 days) refractory to at least one antiarrhythmic agent, and were undergoing ablation for the first time.	Exclusion criteria included paroxysmal atrial fibrillation, sustained atrial fibrillation lasting more than 3 years, and a left atrial diameter of 60 mm or greater.	PVI+CFAE ablation vs PVI plus additional linear	PVI only	There were also no significant differences among the three groups for the secondary end points, including freedom from atrial fibrillation after two ablation procedures and freedom from any atrial arrhythmia.	Complications included tamponade (three patients), stroke or transient ischemic attack (three patients), and atrioesophageal fistula (one patient).	Among patients with persistent atrial fibrillation, we found no reduction in the rate of recurrent atrial fibrillation when either linear ablation or ablation of complex fractionated electrograms was performed in addition to pulmonary-vein isolation.	Did not include a group of PVI+linear+CFAE. Did not evalaute impact of other adjunctive lesions. Underpowered for some subanaylses given 1:4:4 randomization.
8.3.3 Rate and rhythm control	5	Darden	2023	https://doi.org/10.1093/europace/euad124	In-hospital complications associated with pulmonary vein isolation with adjunctive lesions: the NCDR AFib Ablation Registry	To evaluate characteristics and in-hospital complications among patients undergoing PVI with and without adjunctive lesions.	Observational	50,937 patients	Any complication and major complication.	All patients included in NCDR AF Ablation Registry with lesion set information available.	Prior surgical or percutaneous catheter ablation (n = 15 101), left atrial appendage thrombus (n = 227), atrioventricular node ablation with pacemaker implantation (n = 429), those labelled as permanent AF (n = 101), and those with missing values on AF type or adjunctive lesions (n = 1175).	PVI+CTI vs PVI + adjunctive lesions	PVI only	. Adjusted odds of adverse events were calculated using multivariable logistic regression. A total of 50 937 patients [PAF: 30 551 (60%), persistent AF: 20 386 (40%)] were included. Among those with PAF, there were no differences in the adjusted odds of complications between PVI + CTI or PVI + adjunctive when compared with PVI only. Among persistent AF, PVI + adjunctive was associated with a higher risk of any complication [3.0 vs. 4.5%, odds ratio (OR) 1.30, 95% confidence interval (CI) 1.07–1.58] and major complication (0.8 vs. 1.4%, OR 1.56, 95% CI 1.10–2.21), while no differences were observed in PVI + CTI compared with PVI only.	Overall, there was high heterogeneity in adjunctive lesion type, and those receiving adjunctive lesions had a higher comorbidity burden.	Additional CTI ablation was common without an increased risk of complications. Adjunctive lesions other than CTI are commonly performed in those with more comorbidities and were associated with an increased risk of complications in persistent AF, although the current analysis is limited by high heterogeneity in adjunctive lesion set type.	Observational, confounding, lack of granularity with adjunctive lesion type.
8.3.3 Rate and rhythm control	6, 8	Alboni	2004	https://doi.org/10.1056/NEJMoa041233	Outpatient treatment of recent-onset atrial fibrillation with the "pill-in-the-pocket" approach	To evaluate the feasibility and the safety of self-administered oral loading of flecainide and propafenone in terminating atrial fibrillation of recent onset outside the hospital.	Observational, cohort.	210 patients.	Successful cardioversion of atrial fibrillation.	18 to 75 years, emergency room intervention for an episode of electrocardiographically documented AF of recent onset (<48 hours earlier), a mean heart rate > 70 BPM, and a systolic pressure of 100 mm Hg or more; a history of palpitations with abrupt onset hemodynamically well tolerated, at least 1 but fewer than 12 episodes of AF (excluding the target episode) in the previous year, and no cardiac symptoms apart from the episodes of arrhythmia.	Electrocardiographic evidence of ventricular pre-excitation or bundle branch block (QRS interval, >120 msec), a previous episode of AF lasting 7+ days , ischemic heart disease, dilated or HCM, history of heart failure, severe valvular heart disease, chronic cor pulmonale, left ventricular dysfunction (ejection fraction, <50 percent), long QT interval or the Brugada syndrome, the bradycardia–tachycardia syndrome, documentation of previous episodes of 2nd or 3rd-degree AVB, previous thromboembolic episodes, acute disease, very severe chronic diseases, renal or hepatic insufficiency, previous hypokalemia (potassium level, <3 mmol	Flecainide pill-in-the-pocket	N/A	Treatment was successful in 534 episodes (94 percent); the time to resolution of symptoms was 113±84 minutes. Among the 165 patients with recurrences, the drug was effective during all the arrhythmic episodes in 139 patients (84 percent).	Adverse effects were reported during one or more arrhythmic episodes by 12 patients (7 percent), including atrial flutter at a rapid ventricular rate in 1 patient and noncardiac side effects in 11 patients. The numbers of monthly visits to the emergency room and hospitalizations were significantly lower during follow-up than during the year before the target episode (P<0.001 for both comparisons).	In a selected, risk-stratified population of patients with recurrent atrial fibrillation, pill-in-the-pocket treatment is feasible and safe, with a high rate of compliance by patients, a low rate of adverse events, and a marked reduction in emergency room visits and hospital admissions.	Non-randomized.
8.3.3 Rate and rhythm control	6	Markman	2022	https://doi.org/10.1016/j.jacep.2022.07.010	Safety of Pill-in-the-Pocket Class 1C Antiarrhythmic Drugs for Atrial Fibrillation	This study sought to characterize real-world, contemporary use of the PIP approach, including the setting of initiation and incidence of adverse events.	Observational	273 patients.	Adverse events.	Patients receiving pill-in-the-pocket class IC antiarrhythmic drug.	N/A	Patients receiving pill-in-the-pocket class IC antiarrhythmic drug.	N/A	The first dose of PIP AAD was taken in a monitored setting in 167 (62%). Significant adverse events occurred in 7 patients (3%), 2 of whom had taken the dose in a monitored setting. Significant adverse events included unexplained syncope (1 of 7), symptomatic bradycardia/hypotension (4 of 7), and 1:1 atrial flutter (2 of 7). All occurred in patients taking 300 mg of flecainide (n = 4) or 600 mg of propafenone (n = 3). Electrical cardioversion was performed in 29 (11%) patients because of failure of the AAD to terminate AF. One patient required intravenous fluids and vasopressors for 2 hours because of persistent hypotension and bradycardia. Two patients required permanent pacemakers for bradycardia. The remaining patients required no intervention.	N/A	Our data support the current recommendation to initiate PIP AAD in a monitored setting because of rare significant adverse reactions that can require urgent intervention.	Single center, 39% were unmonitored.

8.3.3 Rate and rhythm control	6	Khan	2001	https://doi.org/10.1016/s0735-1097(00)01116-5	Single oral loading dose of propafenone for pharmacological cardioversion of recent-onset atrial fibrillation	To assess the efficacy and safety of the single dose oral loading regimen of propafenone for pharmacological cardioversion of recent-onset atrial fibrillation.	Review of clinical trials.	12 clinical trials.	Successful cardioversion of atrial fibrillation.	All patients with AF receiving propafenone for pharmacologic cardioversion.	N/A	Propafenone.	Varied.	Most of the trials used a single dose of 600 mg for oral loading. The success rates ranged from 56% to 83%, depending on the duration of AFib and follow-up after drug administration. The conversion time ranged from 110 ± 59 to 287 ± 352 min, depending on the duration of observation after drug administration. The single dose oral loading regimen of propafenone was significantly more efficacious than placebo in the first 8 h after administration but not at 24 h. Compared with the intravenous regimen, the oral regimen resulted in fewer conversions in the first 2 h, but both regimens were equally efficacious afterward. The oral propafenone regimen was as efficacious as the single dose oral loading regimen of flecainide but was superior to those of quinidine and amiodarone	The adverse effects reported were transient arrhythmia, reversible QRS-complex widening, transient hypotension and mild noncardiac side effects. The transient arrhythmias were chiefly at the time of conversion and included appearance of atrial flutter, bradycardia, pauses and junctional rhythm. No life-threatening proarrhythmic adverse effects were reported.	The single oral loading dose of propafenone appears to be highly effective for conversion of recent-onset AFib, with a relatively rapid effect within 2 to 3 h and freedom from serious adverse effects.	Outdated.
8.3.3 Rate and rhythm control	7	El Assaad	2021	https://doi.org/10.1016/j.hrthm.2021.07.066	Management and outcomes of atrial fibrillation in 241 healthy children and young adults: Revisiting "lone" atrial fibrillation-A multi-institutional PACES collaborative study	To assess recurrence patterns and treatment efficacy in AF.	Observational, retrospective.	241 subjects (83% male; mean age at onset 16 years	AF recurrence during 2.1 ± 2.6 years of follow-up.	Patients ≤ 21 years of age	Contributory diseases	N/A	N/A	AF recurred in 94 patients (39%) during 2.1 ± 2.6 years of follow-up. In multivariable analysis, predictors of AF recurrence were family history in a first-degree relative <50 years of age (odds ratio [OR] 1.9; P = .047) and longer PR interval in sinus rhythm (OR 1.1 per 10 ms; P = .037). AF recurrence was similar whether patients began no treatment (39/125 [31%]), began daily antiarrhythmic therapy (24/63 [38%]), or had an ablation at any time (14/53 [26%]; P = .39).	Ablating non-AF substrate with supraventricular tachycardia improved freedom from AF recurrence (P = .013).	Recurrence of AF in the pediatric population is common, and the incidence of recurrence was not impacted by "no treatment," "medication only," or "ablation" treatment strategy. Ablation of pathways and other reentrant targets was the only intervention that decreased AF recurrence in children and young adults.	Observational, non-athletes, AF diagnosis in follow up likely under diagnosed.
8.3.3 Rate and rhythm control	7	Sciarra	2010	https://doi.org/10.1093/europace/euq327	How many atrial fibrillation ablation candidates have an underlying supraventricular tachycardia previously unknown? Efficacy of isolated triggering arrhythmia ablation	To evaluate the prevalence of supraventricular tachycardia (SVT) inducibility in patients referred for AF ablation and to evaluate the effects of SVT ablation on AF recurrences.	Observation, prospective.	257 patients (185 males; mean age: 53.4 ± 14.6 years).	SVT and AF recurrence at 21 ± 11 months	All comers for AF ablation referral.	N/A	SVT ablation at time of AF ablation.	N/A	Twenty-six patients (10.1%; mean age: 43.4 ± 13.3 years; 17 males) had inducible SVT during electrophysiological study and underwent an ablation targeted only at SVT suppression. Ablation was successful in all 26 patients. The ablative procedures are: 12 slow-pathway ablations for atrioventricular nodal re-entrant tachycardia; 9 concealed accessory pathway ablations for atrioventricular re-entrant tachycardia; and 5 focal ectopic atrial tachycardia ablations. No recurrences of SVT were observed during the follow-up (21 ± 11 months). Two patients (7.7%) showed recurrence of at least one episode of AF. Patients with inducible SVT had less structural heart disease and were younger than those without inducible SVT (interventricular septum thickness: 8.4 ± 1.6 vs. 11.0 ± 1.4 mm, P < 0.01; left atrial diameter: 37.0 ± 3.0 vs. 44.0 ± 2.2 mm, P < 0.01; age: 43.4 ± 13.3 vs. 57.3 ± 11.2 years, P < 0.01).	Prevalence of paroxysmal AF was higher in patients with inducible SVT when compared with those with only AF (84.6 vs. 24.6%, P < 0.01).	A significant proportion of candidates to AF ablation are inducible for a SVT. SVT ablation showed a preventive effect on AF recurrences. Those patients should be selected for simpler ablation procedures tailored only on the triggering arrhythmia suppression.	Non-athletes, non-randomized, AF follow-up limited.
8.3.3 Rate and rhythm control	7	Strieper	2010	https://doi.org/10.1111/j.1747-0803.2009.00368.x	Catheter ablation of primary supraventricular tachycardia substrate presenting as atrial fibrillation in adolescents	To describe our findings in four adolescent patients presenting with recurrent atrial fibrillation.	Observational	Four patients.	Recurrence of atrial arrhyhtmia.	Adolescents with AF.	N/A	EPS	N/A	Each of the four underwent electrophysiologic study that revealed a primary reentry or automatic supraventricular tachycardia (SVT) substrate, which was able to be treated with radiofrequency ablation. In three of the four cases, elimination of the primary substrate prevented subsequent recurrence of SVT symptoms or documented SVT and/or atrial fibrillation.	N/A	Children and adolescents presenting with atrial fibrillation warrant an exhaustive search for a treatable primary cause of myocardial or electrical disease. If present, a primary SVT substrate may be successfully ablated to prevent recurrence of atrial fibrillation and any associated complications. Pulmonary vein isolation is rarely indicated in adolescents and should be avoided.	Small size.
8.3.3 Rate and rhythm control	7	Furst	2018	https://doi.org/10.1016/j.jacep.2018.02.014	Medical and Interventional Outcomes in Pediatric Lone Atrial Fibrillation	To describe the clinical characteristics of pediatric patients with lone atrial fibrillation (LAF) and their treatment outcomes.	Observational	62 patients.	AF recurrence.	≤21 years of age diagnosed with lone AF from 2004 to 2015	Patients with hemodynamically significant congenital heart disease requiring surgery, cardiomyopathy, history of renal or pulmonary disease, or known thyroid disease were excluded from the cohort. We also excluded patients with Wolff-Parkinson-White syndrome because these patients have a higher rate of AF than the general population	N/A	N/A	Sixty-two patients were identified with LAF; 88% were male, and 63% were athletes. Of the 33 patients taking antiarrhythmic medication, 20 (61%) experienced recurrence. Overall, 16 patients (26%) underwent ablation: PVI in 10 (62.5%), ablation of an accessory pathway in 3 (19%), and modification of the slow atrioventricular nodal pathway in 3 (19%). One-half of patients who underwent PVI experienced documented recurrence. Of those who solely underwent supraventricular tachycardia substrate ablation, one-half also had symptomatic or documented recurrence.	N/A	Ablation recurrence within this pediatric cohort was higher than expected. These recurrence rates may be demonstrative of the technical challenge of pediatric ablation compared with adult counterparts, characteristics of these patients such as athletic conditioning, or inherent differences in their atrial tissue, rendering it more refractory to substrate modification.	Observational, retrospective. Small sample size. Lack of continuous monitoring.
8.3.3 Rate and rhythm control	8	Karlson	1988	https://doi.org/10.1093/oxfordjournals.eurheartj.a062498	Disopyramide in the maintenance of sinus rhythm after electroconversion of atrial fibrillation. A placebo-controlled one-year follow-up study	To evaluate the efficacy of disopyramide on cardioversion of AF.	Randomized controlled trial.	90 patients	AF recurrence.	Atrial fibrillation of at least 6 weeks.	Paroxysmal AF, longstanding persistent AF, recent myocardial infarction, previous intolerance to disopyramide or at risk of anticholinergic side effects, treatment with antiarrhythmic drug, renal disease	Disopyramide	Placebo	After 1 month there was already a significant difference (P<0.01) between the two groups (disopyramide 70%, placebo 39%), a difference that was still remaining after 12 months (disopyramide 54%, placebo 30%). Twenty-four patients, all relapsing to atrial fibrillation before six months on placebo, were converted to sinus rhythm once again. They were then treated with disopyramide in an open manner and after 12 months 37% were still in sinus rhythm.	N/A	Disopyramide seems to be a useful drug in maintaining sinus rhythm after electroconversion of atrial fibrillation.	Outdated, small sample size. Lack of continuous monitoring.

8.3.3 Rate and rhythm control	9	Marrouche	2018	https://doi.org/10.1056/NEJMoa1707855	Catheter Ablation for Atrial Fibrillation with Heart Failure	To evaluate the efficacy of AF ablation in those with heart failure.	Randomized controlled trial.	363	Composite of death from any cause or hospitalization for worsening heart failure.	Patients had to have paroxysmal or persistent atrial fibrillation; an absence of response to, unacceptable side effects from, or unwillingness to take antiarrhythmic drugs; and NYHA class II, III, or IV heart failure and a LVEF of 35% or less. In addition, to facilitate detection of recurrence of atrial fibrillation, all the patients were required to have had implantation of a Biotronik-manufactured ICD or a CRT-D with automatic daily remote-monitoring capabilities.	Candidacy for heart transplantation or planned cardiovascular intervention.	Ablation	Medical therapy.	After a median follow-up of 37.8 months, the primary composite end point occurred in significantly fewer patients in the ablation group than in the medical-therapy group (51 patients [28.5%] vs. 82 patients [44.6%]; hazard ratio, 0.62; 95% confidence interval [CI], 0.43 to 0.87; P=0.007).	Significantly fewer patients in the ablation group died from any cause (24 [13.4%] vs. 46 [25.0%]; hazard ratio, 0.53; 95% CI, 0.32 to 0.86; P=0.01), were hospitalized for worsening heart failure (37 [20.7%] vs. 66 [35.9%]; hazard ratio, 0.56; 95% CI, 0.37 to 0.83; P=0.004), or died from cardiovascular causes (20 [11.2%] vs. 41 [22.3%]; hazard ratio, 0.49; 95% CI, 0.29 to 0.84; P=0.009).	Catheter ablation for atrial fibrillation in patients with heart failure was associated with a significantly lower rate of a composite end point of death from any cause or hospitalization for worsening heart failure than was medical therapy.	Unblinded, high crossover, all patients had a CIED.
8.3.3 Rate and rhythm control	9	Noseworthy	2015	https://doi.org/10.1161/JAHA.115.002597	Patterns of Anticoagulation Use and Cardioembolic Risk After Catheter Ablation for Atrial Fibrillation	To evaluate whether the risk of cardioembolism increases after discontinuation of OAC following catheter ablation.	Observational.	6886	Stroke.	All patients who underwent a catheter ablation for AF between January 1, 2005, and September 30, 2014, and were enrolled in health plan coverage at the time of and for at least 12 months before ablation. We required all patients to have at least 1 prescription for OAC filled.	secondary diagnosis codes for WPW syndrome, nonparoxysmal atrioventricular nodal tachycardia, paroxysmal supraventricular tachycardia, paroxysmal ventricular tachycardia, and ventricular premature beats. Patients with diagnostic or procedural codes indicating implantation of a pacemaker or a cardioverter-defibrillator in the 12 months before or during the index procedure were also excluded to avoid inclusion of patients undergoing atrioventricular nodal ablation and pacemaker implantation for AF.	Ablation	N/A	There was an increase in the use of non–vitamin K OAC after ablation from 0% in 2005 to 69.8% in 2014. OAC discontinuation was high, with only 60.5% and 31.3% of patients remaining on OAC at 3 and 12 months, respectively. The rate of discontinuation was higher in low-risk patients (82% versus 62.5% at 12 months for CHA2DS2-VASc 0–1 versus ≥2, respectively; P<0.001). Stroke occurred in 1.4% of patients with CHA2DS2-VASc ≥2 and 0.3% of those with CHA2DS2-VASc 0 or 1 over the study follow-up. The risk of cardioembolism in the first 3 months after ablation was increased among those with any time off OAC (hazard ratio 8.06 [95% CI 1.53–42.3], P<0.05). The risk of cardioembolism beyond 3 months was increased with OAC discontinuation among high-risk patients (hazard ratio 2.48 [95% CI 1.11–5.52], P<0.05) but not low-risk patients.	N/A	The overall risk of stroke in postablation patients is low; however, OAC discontinuation after ablation is common and is associated with increased risk of cardioembolism for all patients within the first 3 months and for high-risk patients in the long term. Continuing OAC for at least 3 months in all patients and indefinitely in high-risk patients appears to be the safest strategy.	Administrative data.

Subsection	Rec #	First Author	Year	DOI	Article Title	Aim	Study type	Size	Endpoints	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Comparator(s)	Outcomes (Results and P values)	Other Relevant Findings or Adverse Events	Conclusions	Limitations
9.2 Evaluation of athletes with WPW pattern or syndrome	1	Deal	1985	https://doi.org/10.1016/s0735-1097(85)80095-4	Wolff-Parkinson-White syndrome and supraventricular tachycardia during infancy: management and follow-up	Evaluate prognostic factors and the outcome of various treatment regimens	Retrospective cohort study, 2 centers	90	Persistent WPW pattern, associated CHD, death and recurrent SVT	WPW with SVTpresenting in first 4 months of life	> 4 months of age	Anti-arrhythmic or DC cardioversion	None	Outcomes of efficacy of interventions and mortality. 5 deaths (5.5%), 64% had persistence of WPW pattern at mean of 6.4 years, 30 (33%) had recurrrent SVT after one year of age , More recurrences of SVT in Type B compared to Type A and Type C (P <0.05)	High mortality associated with digoxin therapy 2%-5%.	Overall mortality related to arrhythmias in WPW was 5% and recurrence of SVT after 1 year in one third of patients	Small study , prior era
9.2 Evaluation of athletes with WPW pattern or syndrome	1	Dai	2018	https://doi.org/10.1093/europace/eux242	The effect of ventricular pre-excitation on ventricular wall motion and left ventricular systolic function	To evaluate the accuracy of exercise testing for predicting WPW characteristics in children	Comparative, retrospective	60 patients	Abnormal ventricular wall motion and LV dysfunction	Patients with WPW > 5 years and no congenital heart disease and control group with no WPW	< 5 years of age, congenital heart disease, tachycardiomyopathy, atrial conduction to ventricle via an accessory pathway while in atrial fibrillation, endless supraventricular tachycardia (SVT), intermittent ventricular pre-excitation, hyperthyroidism, electrolyte disturbance, liver or kidney dysfunction, or acute infection were excluded	Catheter ablation	Comparison between 3 groups (right manifest AP, left manifest AP and no manifest AP)	Right-sided accessory pathways were associated with abnormal motion of the interventricular septum, LV dyssynchrony, decreased LV systolic function, and increased LV diameter. Eighteen of 60 cases (30.0%) with right-sided accessory pathways had LV dyssynchrony, and these patients had lower LV ejection fraction and higher LV end-diastolic diameter	A right-sided free-wall accessory pathway may have more detrimental effects than a septal accessory pathway. Left ventricular dyssynchrony and abnormal interventricular septal motion appeared to be responsible for the pathogenesis of LV dysfunction and remodelling.	Right-sided accessory pathways may impair ventricular wall motion and LV systolic function, resulting in decreased LV ejection fraction and increased LV end-diastolic diameter. These effects occurred in patients with LV dyssynchrony. These effects, including LV dyssynchrony, resolved after radiofrequency ablation.	Small studyLVEF was calculated using the biplane Simpson's method which was the most reliable by 2D echo. However, the abnormal ventricular wall motion may affect the measurement of LVEF. Cardiac MRI not done due to cost
9.2 Evaluation of athletes with WPW pattern or syndrome	2	Etheridge	2018	https://doi.org/10.1016/j.jacep.2017.10.009	Life-Threatening Event Risk in Children With Wolff-Parkinson-White Syndrome: A Multicenter International Study	To characterize risk in children with WPW by comparing those who had experienced a life-threatening event (LTE) with a control population with WPW without a LTE but with EPS data available.	Retrospective cohort, mulitcenter, international	Case subjects with a LTE (n = 96) and 4:1 age matched controls (n = 816) with WPW and EPS data but without a LTE	LTE	Children age 21 years or younger with WPW. Cases had experienced a LTE and controls had EPS data available	> 22 years of age, outside study period of January 1990 through June 2016	None	Cases with a LTE (sudden death with an ECG with WPW, aborted sudden death, rapidly conducting AF) were age matched to controls without a LTE but in whom EPS data were available	Case subjects with LTE were older and less likely than controls to have symptoms or documented tachycardia. Mean age at LTE was 14.1 ± 3.9 years. The LTE was the sentinel symptom in 65%, consisting of rapidly conducted pre-excited AF (49%), aborted sudden death (45%), and SCD (6%). Three risk components were considered at EPS: SPERRI, APERP, and shortest paced cycle length with pre-excitation during atrial pacing (SPPCL), and all were shorter in cases than in control subjects. In multivariate analysis, risk factors for LTE included male sex, Ebsteins, rapid anterograde conduction (APERP, SPERRI, or SPPCL ≤250 ms), multiple pathways, and inducible AF. Of case subjects, 60 of 86 (69%) had ≥2 EPS risk stratification components performed; 22 of 60 (37%) did not have EPS-determined high-risk characteristics, and 15 of 60 (25%) had neither concerning pathway characteristics nor inducible atrioventricular reciprocating tachycardia.	LTE can be the initial symptom of WPW. Most LTE occurred during rest or routine activities	Young patients may experience LTE from WPW syndrome without prior symptoms or markers of high-risk on EPS.	Retrospective and enriched for patients with LTE
9.2 Evaluation of athletes with WPW pattern or syndrome	4	Gormel	2018	https://doi.org/10.1111/anec.12913	Fasciculoventricular pathways-A rare and innocent variant: A Retrospective study focusing on clinical and electrophysiologic characteristics	Clinical and electrophysiological properties of FVP	Single center, retrospective cohort study	26	Diagnosis of fasciculoventricular pathway by EP study	Patients who underwent electrophysiological study (EPS) for FVP between January 1998 and June 2020	Patients outside the study period and those who declined consent to procedure	EP study	n/a	All the 26 patients (100%) were males, with a mean age of 22.15 ± 3.50 years (range, 20–34 years). In the baseline electrocardiograms of the patients with FVP, pre-excitation and transitional zone were seen in leads V2–V4. During EPS procedures, normal AH interval and shortened HV interval were detected. All the patients had AH prolongation after atrial pacing due to atrioventricular (AV) nodal delay without change in pre-excitation degree. Five of the FVP patients (19.2%) had extra accessory pathways, all of which were ablated successfully while the FVPs were followed clinically.	The electrocardiographic findings of FVP patients were as follows: Mean PR interval was 112.46 ± 10.17 ms (range 90–130 ms), mean QRS complex width was 95.80 ± 15.15 ms (range 80–118 ms), QRS transition (R/S>1) occurred between V2 and V4 precordial leads, the polarity of delta waves were flat in 65.39% of patients and negative in 34.61% of patients in V1 lead, mean amplitude of S wave was 9.35 ± 2.59 ms (range 5–13 msn), and 42.3% of patients had notching in the descending limb of S waves in V1 lead	EPS is gold standard procedure facilitating the diagnosis of FVP which allows for adequate risk stratification. FVP patients with PRKAG2 gene mutations should be evaluated for high-risk clinical outcomes.	This study is a single-center retrospective study in which the epidemiological characteristics of the patients and findings of electrophysiological procedures were retrieved from institutional archive. Majority of our study group included male military staff referred for medical evaluation, inconsistent with the general population.
9.2 Evaluation of athletes with WPW pattern or syndrome	4	Sulu	2022	https://doi.org/10.1111/pace.14568	Electrocardiographic and electrophysiological characteristics of fasciculoventricular fibers in children	Clinical and electrophysiological features of our pediatric patients with fasciculoventricular fiber.	Single center, retrospective cohort study	27	Diagnosis of fasciculoventricular pathway by EP study	October 2013 and September 2021, 565 patients who underwent electrophysiological studies due to ventricular preexcitation	Patients outside the study period and those who declined consent to procedure	EP study	ECG features of preexcitation due to WPW	Two patients had hypertrophic cardiomyopathy and 1 patient had ccTGA. In the electrophysiological study, additional manifest WPW was found in 9 (33%) patients (3 patients with high risk, 6 patients with orthodromic supraventricular tachycardia), focal atrial tachycardia in a patient, and atrioventricular nodal reentry tachycardia in a patient. While the delta wave amplitude was found to be 2.56 ± 1.38(1-5.5) mm in the first 40 ms in surface electrocardiography in 9 patients with additional accessory pathway, it was found to be 1.64 ± 0.67(0.5-3) mm in the FVF group. There was no statistically significant difference between the 2 groups (p = .398). Delta wave amplitude > 3.5 mm was not detected in any patient with isolated FVF. Interestingly, delta wave amplitude was < 3.5 mm in 7 (78%) of 9 patients who were identified and ablated with an additional accessory pathway. Total 19 of the patients (59.3%) were adenosine-responsive (18 isolated FVF, 1 manifest AP+FVF adenosine-responsive. 8 patients with other manifest AP + FVF had no pre-procedural adenosine-asystole response, and all of them QRS were expanded).	Other tachyarrhythmia substrate frequency accompanying these FVP are quite high (approximately 40%) in EPS. Study highlights the important point that the use of adenosine alone is controversial, since adenosine response may also be in WPW patients. ECG alone may not be sufficient to distinguish FVP from WPW.	Delta wave characteristics similar to WPW. performing EPS in patients with suspected FVF based on surface ECG features seems to be important for the detection of additional tachyarrhythmias and risky accessory pathways	Sinlge center study, small cohort, response to adenosine may depend on escalating doses, unclear as to how many observers there were no assess delta waves and if there was signiciant interobserver variability. Also, unclear if the ECG measurements were made by blinded observers.
9.2 Evaluation of athletes with WPW pattern or syndrome	5	Van Hare	2004	https://doi.org/10.1046/j.1540-8167.2004.03645.x	Prospective assessment after pediatric cardiac ablation: demographics, medical profiles, and initial outcomes	Assess the short- and longer-term results and risks associated with radiofrequency (RF) ablation in children.	Multicenter prospective study	3 groups: the prospective cohort (n = 481), cohort-eligible registry participants (n = 504), and not cohort eligible registry participants (n = 1,776)	Success rates and complications of ablation	Children 0-16 years with SVT in the prospective arm and 0-21 in the registry arm	Significant CHD	Ablation	Prospectivley enrolled vs registry patients	Ablation success and complications	n/a	The study demonstrates high success rates and low complication rates, which are comparable to prior single-center retrospective studies	Study does not include era of cryoablation or consistent 3D mapping

9.2 Evaluation of athletes with WPW pattern or syndrome	6	Fujino	2020	https://doi.org/10.1016/j.jicc.2020.05.003	Clinical characteristics of challenging catheter ablation procedures in patients with WPW syndrome: A 10 year single-center experience	Evaluate the clinical factors associated with an unsuccessful ablation outcome or repeated sessions	Retrospective cohort study, single center	475 consecutive patients, age 38.2±16.2 years	Successful catheter ablation	WPW undergoing catheter ablation	Outside study period of August 2005 and December 2015	Catheter ablation	n/a	439 (92.4%) were cured by ablation, but it failed in 36 (7.6%) after the first procedure	17 recurrences in 26 hours, 4 after one year, 98.5% successfully ablated at mean follow-up of 8.3±3.0 years, 0.6% complications (2 TIA, 1 pericardial effusion needing no drainage), no AV block	Symptomatic WPW patients with multiple, parahisian, and broad APs had a significantly higher risk of recurrence. In half of the recurrence patients, AP recurrences were confirmed during the acute phase, but were rarely recorded in the very late phase	Single center study, retrospective, older population, RF only
9.3 Treatment of athletes with WPW	1	Cain	2013	https://doi.org/10.1016/j.amjcard.2013.05.035	Natural history of Wolff-Parkinson-White syndrome diagnosed in childhood	Examine the natural history of patients with WPW diagnosed in childhood followed longitudinally in a single institution	Retrospective cohort study, single center	446 children with WPW	None	children with WPW in the institution	None stated	None	None	The median age at diagnosis was 7 years, 61% were male, and 38% had SVT and 64% were symptomatic at presentation and 20% developed symptoms during f/u. . There were 6 sudden deaths with an overall incidence of 1.1/1000 patient years in children without CHD and 27/1000 patients years in children with CHD	n/a	Sudden death is more common in children wth WPW who have CHD	Small single center study, no control
9.3 Treatment of athletes with WPW	1, 3, 5, 6	Pappone	2014	https://doi.org/10.1161/CIRCULATIONAHA.114.011154	Wolff-Parkinson-White syndrome in the era of catheter ablation: insights from a registry study of 2169 patients	Evaluate long term outcomes and predictors of malignant arrhythmias in a large cohort of symptomatic or asymptomatic WPW patients undergoing electrophysiological testing (EPT) using a prospective patient registry.	Prospective registry study	2169 patients (symptomatic and asymptomatic) referred for evaluation or ablation of WPW syndrome	Occurrence of ventricular fibrillation (VF) or potentially malignant arrhythmias, and identification of risk factors	Patients with documented WPW syndrome undergoing baseline electrophysiological testing (EPT) with or without radiofrequency catheter ablation	Declined consent to undergo a baseline EPT	Radiofrequency catheter ablation (RFA)	RFA vs no-RFA	There were no differences in clinical and electrophysiological characteristics between the 2 groups except for symptoms. In no-RFA group, VF occurred in 1.5% and primarily in children (13 of 15; median age 11 years), and was associated with a short accessory pathway antegrade refractory period (P<0.001) and atrioventricular reentrant tachycardia initiating atrial fibrillation (P<0.001) but not symptoms. In the RFA group, ablation was successful in 98.5%, and after RFA, no patients developed malignant arrhythmias or VF over the 8-year follow-up. Untreated patients were more likely to experience malignant arrhythmias and VF (log-rank P<0.001). Time-dependent receiver-operating characteristic curves for predicting VF identified an optimal anterograde effective refractory period of the accessory pathway cutoff of 240 milliseconds.	13/15 (86%) had posteroseptal AP, 13 /15 (86%) were males , 2 patients with VF were adults (32 years of age) so VF was not only in pediatric patients.	The prognosis of the Wolff-Parkinson-White syndrome essentially depends on intrinsic electrophysiological properties of AP rather than on symptoms. RFA performed during the same procedure after electrophysiological testing is of benefit in improving the long-term outcomes.	Single-center, non-randomized, non-controlled study, and that a natural history study of patients with WPW syndrome requires a randomized trial to establish the role of RFA. Documented VFs/cardiac arrests numbers are relatively low, limiting multivariable models and time-dependent receiver-operating curve analysis. The possibility of fluctuations in autonomic tone could be another potential limitation.
9.3 Treatment of athletes with WPW	1	Fujino	2020	https://doi.org/10.1016/j.jicc.2020.05.003	Clinical characteristics of challenging catheter ablation procedures in patients with WPW syndrome: A 10 year single-center experience	Evaluate the clinical factors associated with an unsuccessful ablation outcome or repeated sessions	Retrospective cohort study, single center	475 consecutive patients, age 38.2±16.2 years	Successful catheter ablation	WPW undergoing catheter ablation	Patients outside study period of August 2005 and December 2015, patients who did not undergo catheter ablation	Catheter ablation	n/a	439 (92.4%) were cured by ablation, but it failed in 36 (7.6%) after the first procedure	17 recurrences in 26 hours, 4 after one year, 98.5% successfully ablated at mean follow-up of 8.3±3.0 years, 0.6% complications (2 TIA, 1 pericardial effusion needing no drainage), no AV block	Symptomatic WPW patients with multiple, parahisian, and broad APs had a significantly higher risk of recurrence. In half of the recurrence patients, AP recurrences were confirmed during the acute phase, but were rarely recorded in the very late phase	Single center study, retrospective, older population, RF only
9.3 Treatment of athletes with WPW	1	Dubin	2019	https://doi.org/10.1016/j.hrthm.2018.08.013	What have we learned in the last 20 years? A comparison of a modern era pediatric and congenital catheter ablation registry to previous pediatric ablation registries	To describe initial findings from the MAP-IT pilot registry and to compare these findings to earlier registries	Modern national registry data compard with older ablation registries	1417 procedures	Ablation outcomes and complications	All children < 21 undergoing an ablation without CHD and patients of all ages with CHD	Patients without an invasive EPS	Ablation	None	Acute success rates have improved from the initial PCAR registry for both accessory and slow pathway substrates. Both fluoroscopy and procedural times have significantly decreased across the time periods (fluoroscopy time 47.6 ± 40 minutes to 7.0 ± 9.2 minutes; P <.001; procedural time 257 ± 157 minutes to 166 ± 84 minutes; P <.001).	Both fluoroscopy and procedural times have significantly decreased across the time periods and there is no difference in success rates or complications in smaller children as compared to older children	Acute success rates and fluoroscopy and procedural times in pediatric ablation all have improved over the last 25 years.	Database assessment subject to errors associatrd with databases
9.3 Treatment of athletes with WPW	1	Krause	2021	https://doi.org/10.1093/europace/euaa325	Pediatric catheter ablation at the beginning of the 21st century: results from the European Multicenter Pediatric Catheter Ablation Registry 'EUROPA'	Contemporary data from prospective multicentre registries on catheter ablation in pediatric patients	Multicenter registry	Total = 684 (WPW- 380)	Catheter ablation	≤18 years if age with one year follow up	> 18 years of age	Catheter ablation	n/a	94% success rate, 12% (n = 44) had asymptomatic WPW. No AV block, 2 coronary injury, 1 cardiac perforation, no death, 1 AV fistula	No persistent AV block	Cryo: n=21, In subjects with right anteroseptal accessory pathways, cryoenergy failed in n = 1/5 patients (20%) and in subjects with right midseptal accessory pathways, cryoenergy failed in n = 1/3 individuals (33%).overall recurrence 6.8%	Retrospective, registry study. All patients did not have Cor angiography. Designed as a pilot study with 5 experienced tertiary pediatric EP centres including patients., results may not truly reflect the current state of pediatric catheter ablation globally. Follow up limited to 12 months. all AVRT lumped together (concelaed +manifest)
9.3 Treatment of athletes with WPW	2	Kwon	2010	https://doi.org/10.1111/j.1540-8167.2009.01612.x	Septal dyskinesia and global left ventricular dysfunction in pediatric Wolff-Parkinson-White syndrome with septal accessory pathway	Determine the extent to which the AP contributes to global left ventricular (LV) dysfunction	Retrospective cohort study, single center	62	EF%, Increased LV end diastolic dimensions	Children with WPW and echocardiogram	Adults excluded	Radiofrequency ablation	Patients with and without septal dyskinesia and increased LVEDD	The left ventricular ejection fraction (LVEF) of patients with septal APs (53 ± 11%) was significantly lower than that of patients with right (62 ± 5%) or left (61 ± 4%) APs (P = 0.001). Compared to patients with normal septal motion (n = 56), patients with septal dyskinesia (n = 6) had a reduced LVEF (61 ± 4% and 42 ± 5%, respectively) and an increased LV end diastolic dimension (P < 0.001 for both comparisons). Multivariate analysis identified septal dyskinesia as the only significant risk factor for reduced LVEF. All 6 patients with septal dyskinesia had right septal APs, and a preexcited QRS duration that was longer than that of patients with normal septal motion (140 ± 18 ms and 113 ± 32 ms, respectively; P = 0.045). After RFA there were improvements in both intraventricular dyssynchrony (septal-to-posterior wall motion delay, from 154 ± 91 ms to 33 ± 17 ms) and interventricular septal thinning (from 3.0 ± 0.5 mm to 5.3 ± 2.6 mm), and a significant increase in LVEF (from 42 ± 5% to 67 ± 8%; P = 0.001)	n/a	The dyskinetic segment activated by a right septal AP in WPW syndrome may lead to ventricular dilation and dysfunction. RFA produced mechanical resynchronization, reverse remodeling, and improvements in LV function	Small cohort, single center study, unblinded

9.3 Treatment of athletes with WPW	2	Seo	2011	https://doi.org/10.1016/j.jcmg.2010.11.020	Synchronicity of LV contraction as a determinant of LV twist mechanics: serial speckle-tracking analyses in WPW syndrome before and after radiofrequency catheter ablation	To investigate the isolated impact of synchronous patterns of left ventricular (LV) contraction (i.e., LV synchronicity) on LV twist behavior	Retrospective cohort study, single center	34	LV dysfunction before catheter ablation of AP	WPW ECG pattern	CHD, non sinus rhythm, arrhythmia < 1 week of evaluation, inadequate echo images	Echo	Before and after catheter ablation of AP	Overall, no significant changes were demonstrated in LV volumes, systolic and diastolic function, and end-systolic wall stress before versus after RFCA. After RFCA, median value of LVdys was attenuated from 33.5 (interquartile range [IQR]: 14.0 to 84.3) to 14.0 (IQR: 11.5 to 21.8) (p = 0.002), which was accompanied by a reduction in apical-basal rotation delay from 9.7% (IQR: 3.5 to 23.7) to 3.3% (IQR: 1.3 to 8.0) (p = 0.004). In contrast, LV twist increased from 14.2° (IQR: 9.1° to 18.4°) before to 19.7° (IQR: 15.0° to 22.6°) after RFCA (p = 0.002). Delta LV twist pre- to post-RFCA displayed a significant inverse correlation with changes in apical-basal rotation delay (r = −0.42, p = 0.01) and Delta LVdys (r = −0.39, p = 0.02).	LV dyysfunction and dyssynchrony is significantly related to LV twist	Improvement in LV dysfunction and LV twist after catheter ablation	The number of subjects enrolled was relatively small. Nevertheless, the study was sufficiently powered to reveal LV twist differences between pre- and post-RFCA. Second, it was assumed that the only change in the study population from pre- to post-RFCA was the loss of pre-excitation. No clinical correlations (e.g. NYHA class) was obtained
9.3 Treatment of athletes with WPW	3, 4, 7, 8	Chubb	2019	https://doi.org/10.1016/j.jpeds.2019.05.058	Management of Asymptomatic Wolff-Parkinson-White Pattern by Pediatric Electrophysiologists	Evaluate clinical management of asymptomatic WPW	Multicenter survey	113 responses	None	< 25 years of age with asymptomatic WPW	Symptomatic WPW	EPS	2003 survey	Only 12 (11%) believed that intermittent pre-excitation and 37 (33%) that sudden loss of pre-excitation on exercise test were sufficient evidence of accessory pathway safety to avoid an invasive electrophysiology study.	Optimal weight for electrophysiology study was 20 kg (IQR 18-22.5 kg), and 61% and 58% would then ablate all right-sided or left-sided accessory pathways, respectively, regardless of electrophysiological properties, whereas only 23% would ablate all septal accessory pathways (P < .001). Compared with 2003, respondents were more likely to consider inducible arrhythmia (77% vs 26%, P < .001) as sufficient indication alone for ablation	Operators are now performing electrophysiology study for asymptomatic Wolff-Parkinson-White regardless of noninvasive findings.	Survey study limited by the scope and precision of the questions and responses
9.3 Treatment of athletes with WPW	4	Escudero	2020	https://doi.org/10.1016/j.hrthm.2020.05.035	Loss of ventricular preexcitation during noninvasive testing does not exclude high-risk accessory pathways: A multicenter study of WPW in children	To compare accessory pathway (AP) characteristics and occurrences of sudden cardiac arrest (SCA) and rapidly conducted preexcited atrial fibrillation (RC-AF) in patients with nonpersistent and persistent preexcitation.	Retrospective cohort study combining 2 databases, multicenter and international	1589 children with WPW age <21 years	EPS data in intermittent and presisitent PX patients	Patients 21 years or younger with WPW and invasive electrophysiology study (EPS) data, SCA, or rapidly conducted AF in 2 multicenter databases.	Age > 21 years	None	Those with peristent preexcitation compared to those with loss of pre-excitation on Holter, ECG, Exercise test	Of 1589 patients, 244 (15%) had nonpersistent preexcitation and 1345 (85%) had persistent preexcitation. There were no differences in sex (58% vs 60% male; P=.49) or age (13.3±3.6 years vs 13.1±3.9 years; P=.43) between groups. Although APERP (344±76 ms vs 312±61 ms; P<.001) and SPPCL (394±123 ms vs 317±82 ms; P<.001) were longer in nonpersistent vs persistent preexcitation, there was no difference in SPERRI at EPS (331±71 ms vs 316±73 ms; P=.15). Nonpersistent preexcitation was associated with fewer high-risk APs (13% vs 23%; P<.001) than persistent preexcitation. Of 61 patients with SCA or RC-AF, 6 (10%) had nonpersistent preexcitation (3 SCA, 3 RC-AF).	n/a	Nonpersistent preexcitation was associated with fewer high-risk APs, though it did not exclude the risk of SCA or RC-AF in children with WPW.	Retrospective, database study
9.3 Treatment of athletes with WPW	5	Santinelli	2009	https://doi.org/10.1016/j.jacc.2008.09.037	The natural history of asymptomatic ventricular pre-excitation a long-term prospective follow-up study of 184 asymptomatic children	To describe the natural history of asymptomatic WPW in children and to determine the predictors of a potential LTE	Prospective follow-up study	184 children, 66% male, median age 10 years	The occurrence of the first arrhythmic event	Children (5-18 years) without symptoms with pre-excitation on ECG who underwent EPS and were followed for at least 24 months	Refused consent to participate, age < 5 or >18 or in another investigational study	All patients underwent an EPS but not an ablation	None	Over a median f/u of 57 months, 52 children had an arrhythmic event and it was a LTE in 19 children. Independent predictors of of a LTE were APERP and multiple AP	Some of the LTE arrhythmias were associated with atypical or minimal symptoms	Children with asymptomatic WPW and a short APERP or multiple AP are at risk for LTE and are candidates for "prophylactic" ablation	No control group, small study, not controlled, unblinded, possible seletion bias
9.3 Treatment of athletes with WPW	6	Klein	1983	https://doi.org/10.1016/0002-9149(83)90125-x	Intermittent preexcitation in the Wolff-Parkinson-White syndrome	To estimate the prevalence of intermittent preexcitation and test the hypothesis that intermittent preexcitation correlates with a moderate ventricular response during AF	Single center; enrolment of conesecutive patients in a prospective fashion	52 consecutive patients (37 +- 13 constant; 40+/- 15 intermittent	EP Study to depermne AP refractory period; AF induction was attempted in all patients if not documented spontaneously	Intermittent preexcitation using review of serial electrocardiograms, ambulatory monitoring, and treadmill testing and EPS	Not specified	Stress Test, ECG, EP study	n/a	50% of patients had intermittent preexcitation; As a group, patients with intermittent preexcitation demonstrated a longer anterograde ERP of the AP at comparable cylcle lengths and a longer minimum cycle length maintaining 1:1 conduction over the ap; 50% of patients with constant preexcitation had very rapid rates during AF versus 4/26 with intermittent preexcitation	n/a	Intermittent preexcitation suggests a benign prognosis in the event of AF	Small cohort, no comparator, older era study
9.3 Treatment of athletes with WPW	7	Pappone	2003	https://doi.org/10.1056/NEJMoa035345	A randomized study of prophylactic catheter ablation in asymptomatic patients with the Wolff-Parkinson-White syndrome	To determine if prophylactic catheter ablation of accessory pathways would provide meaningful and durable benefits as compared with no treatment in such patients.	Single center, randomized prospective study	224	Occurrence of arrhythmic events over a five-year follow-up period	72 high risk WPW patients	Low risk WPW patients	Treatment with catheter ablation	Treatment vs no treatment	Patients assigned to ablation had base-line characteristics that were similar to those of the controls. Two patients in the ablation group (5 percent) and 21 in the control group (60 percent) had arrhythmic events. One control patient had ventricular fibrillation as the presenting arrhythmia. The five-year Kaplan–Meier estimates of the incidence of arrhythmic events were 7 percent among patients who underwent ablation and 77 percent among the controls (P<0.001 by the log-rank test); the risk reduction with ablation was 92 percent (relative risk, 0.08; 95 percent confidence interval, 0.02 to 0.33; P<0.001).	Symptoms of supraventricular tachycardia developed in six patients of 146 asymptomatic patients. All but 1 of the 148 had single accessory pathways. Twenty patients stopped having ventricular preexcitation during follow-up.	Prophylactic accessory-pathway ablation markedly reduces the frequency of arrhythmic events in asymptomatic patients with the Wolff–Parkinson–White syndrome who are at high risk for such events.	Single center study
9.3 Treatment of athletes with WPW	8	Shwayder	2020	https://doi.org/10.1016/j.hrthm.2019.09.011	Difficulties with invasive risk stratification performed under anesthesia in pediatric Wolff-Parkinson-White Syndrome	To determine how closely measurements made in the electrophysiology laboratory in patients with WPW compared to SPERRI obtained during an episode of clinical pre-excited atrial fibrillation (Clinical-SPERRI)	Retrospective, multicenter study	49 children with WPW and a clinical SPERRI and EPS data, a subgroup of a larger WPW database, multicenter and international	EPS date where the APERP, SCL11, and SPERRI were compred to the clinical SPERRI	Children < 21 with EPS data and a clinical SPERRI available	Patients > age 21 years or without a clinical SPERRI	EPS	Comparison the EPS data APERP, SCL11 and SPERRI to a clinical SPERRI in WPW children	70% of EP measurements were made with patients under general anesthesia. Clinical-SPERRI moderately correlated with EP-SPERRI (r = 0.495; P = .012). However, 24% of patients with Clinical-SPERRI ≤250 ms would have been misclassified as having a low-risk pathway based on EP-SPERRI >250 ms. Clinical-SPERRI did not correlate with APERP or SPPCL (r < 0.3; P >.1). Mean EP-SPERRI, APERP, and SPPCL all were greater than Clinical-SPERRI.	n/a	EPS measurements of pathway characteristics made with patients under general anesthesia do not correlate well with Clinical-SPERRI. Of APERP, SPPCL, and EP-SPERRI, only EP-SPERRI had moderate correlation with Clinical-SPERRI. This study questions the predictive ability of invasive risk stratification with patients under general anesthesia, given that 24% of patients with high-risk Clinical-SPERRI (≤250 ms) had EP-SPERRI that may be considered low risk (>250 ms).	Limited number and retrospective

9.3 Treatment of athletes with WPW	9	Walsh	2021	https://doi.org/10.1016/j.jacep.2021.03.012	Outcomes From Pediatric Ablation: A Review of 20 Years of National Data	To examine success rates and repeat ablations over time and to evaluate whether modalities such as 3-dimensional (3D) mapping, contact force, and cryotherapy have improved outcomes.	Multicenter NICOR registry from U.K and ireland, retrospective	N=7069 (cryoablation in 286 or 4%, mixed RF and cryo in 2.7%)	1) successful elimination of pathway, 2) complication	Age < 18 years at first ablation , 1999-2018	> 18 years of age at time of ablation	Catheter ablation	None	Cryoablation was associated with needing a repeat procedure (OR: 2.9; 95% CI: 1.9 to 4.4),No permanent AV block or pacemaker implanation	55% of 3D mapping cases used <5 min of fluoroscopy	Overall success rates from pediatric ablations are excellent and compare favorably to other registries	This is a retrospective study and has many of the limitations associated with retrospective studies. It is not permissible under NICOR regulations to compare outcomes between centers when accessing the data for research purposes. Late complications not recorded
9.3 Treatment of athletes with WPW	9	Bravo	2018	https://doi.org/10.1093/europace/eux269	Safety and efficacy of cryoablation vs. radiofrequency ablation of septal accessory pathways: systematic review of the literature and meta-analyses	To compare the efficacy and safety of cryoablation and radiofrequency ablation (RFA) for treating septal accessory pathways (APs).	Systematic review and meta-analysis	Sixty-four articles were included: 38 articles reporting RFA and 27 articles reporting cryoablation procedures. 4244 septal APs : 3495 in the RFA cohort and 749 in the cryoablation cohort	1) successful elimination of pathway, 2) complication	Abstracts were selected if they made specific reference to RFA or cryoablation of accessory pathways. Articles retained from first abstract screening underwent full-text review to determine eligibility for data extraction based on the following inclusion criteria: original data in humans reported; study design consisting of a case series, case–control study, cohort study, or controlled trial; and absolute numbers for study endpoints available.	Case reports, letters, or editorial comments and studies without extractable outcome data referring septal location of accessory pathways were excluded	Cryoablation and radiofrequency ablation	Cryoablation vs. radiofrequency ablation	Acute procedural success rate of cryoablation was 86.0% (95% CI 81.6-89.4%) and RFA 89.0% (95% CI 86.8-91.0%). Recurrence rate of cryoablation was 18.1% (95% CI 14.8-21.8%) and RFA 9.9% (95% CI 8.2-12.0%). Long-term success rate after multiple ablation procedures of cryoablation was 75.9% (95% CI 68.2-82.3%) and RFA88.4% (95% CI 84.7-91.3%). There were no reported cases of persistent atrioventricular block (AVB) with cryoablation and 2.7% (95% CI 2.2-3.4%) with RFA.	n/a	RFA for treatment of septal APs report higher efficacy rates than do studies using cryoablation, but a significantly higher rate of AVB	Meta-analysis study with inherent limitations. No access to the primary data of the studies. Variations in study methodologies, patient and procedural characteristics and follow-up duration limit direct comparisons of the various studies. No large, randomized trials comparing the two methods directly. Potential publication bias due to selective study inclusion.
9.3 Treatment of athletes with WPW	9	Kaltman	2008	https://doi.org/10.1111/j.1540-8167.2007.01048.x	Time and temperature profile of catheter cryoablation of right septal and free wall accessory pathways in children	To evaluate the time and temperature profile at which loss of AP conduction occurs during cryoablation.	Single center, retrospective cohort study	25 patients, mean age 13.3 years	1) successful elimination of pathway, 2) complication Time delay: Interval from onset of cryoablation to catheter adherence; Temperature response time: Interval from onset of cryoablation to steady state of minimal catheter temperature	Children and adolescents with right sided AP undergoing cryoablation at study center	n/a	Cryoablation	None	Cryoablation was successful in 24/25 (96%) patients, no complications Temperature at loss of AP conduction was -66.2 +/--16.7 degrees C (range +32 to -84 degrees C).	Critical time to success (interval from cryoadherence to loss of AP conduction) was significantly shorter for permanently successful cryolesions, compared with transiently successful lesions (6.3 +/- 4.1 vs. 11.2 +/- 2.2 sec; P < 0.001	"Time to success" strategy may improve outcome of cryoablation for right-sided APs in children without compromising safety	Retrospective, single center study, not randomized, small number of patients, may not be generalizable to all septal Aps
9.3 Treatment of athletes with WPW	9	Karadeniz	2014	https://doi.org/10.1111/pace.12442	Cryoablation of septal accessory pathways in children: midterm results	To assess the efficacy and safety of cryoablation of right septal APs	Single center, retrospective cohort study	N=43	1) successful elimination of pathway, 2) complication	Patients with septal accessory pathways undergoing ablation at study center	n/a	Cryoablation	none	Acute success was achieved in 40 of 43 patients (93%). No complications were noted. During a mean follow-up of 8.8 ± 4.8 months, five patients (12.5%) experienced recurrence.	No fluoroscopy was used in 90% of patients (39/43). The mean fluoroscopy time in the remaining four patients was 3.7 ± 0.7 minutes	Cryoablation of septal APs can be performed safely with comparable efficacy to the reported RF ablation results using a limited fluoroscopy approach	retrospective, single center study, not randomized, small number of patients
9.3 Treatment of athletes with WPW	9	Kovach	2020	https://doi.org/10.1016/j.hrthm.2019.12.008	Outcomes of catheter ablation of anteroseptal and midseptal accessory pathways in pediatric patients	To evaluate the efficacy of different catheter approaches and ablation energy modalities used for catheter ablation at these sites	Single center, retrospective cohort study	N=223, 69% WPW	1) successful elimination of pathway, 2) complication	Patients with AS or MS undergoing ablation at study center from 2001-2017	1 patient with an AS pathway was excluded. This patient had undergone ablation previously at an outside institution, with residual pathway conduction but permanent AV node block	Catheter ablation	As vs MS	Acute success in 87% (AS 89%, MS 83%), There was no resultant permanent complete AV block and/or pacemaker. recurrence rate was 18%. There was no difference in success when comparing energy modalities, though the overall recurrence rate was higher for cryoablation. Recurrence rate was 18% ((AS 18%, MS 19%).	No difference in success rate between RF and Cryo	Both ablation energy modalities were equally successful, cryoablation may be associated with a higher chance of recurrence. Recurrences and repeat procedures may be anticipated to minimize risk to normal atrioventricular conduction during ablation in these regions	Retrospective, single center study, not randomized
9.3 Treatment of athletes with WPW	10	Gormel	2018	https://doi.org/10.1111/anec.12913	Fasciculoventricular pathways-A rare and innocent variant: A Retrospective study focusing on clinical and electrophysiologic characteristics	To examine the clinical and electrophysiological characteristics of	Single center, retrospective cohort study	n=26 patients diagnosed with FVP; N=1437 patients studied for accessory pathways	Diagnosis of fasciculoventricular pathway by EP study	Patients who underwent electrophysiological study (EPS) for FVP between January 1998 and June 2020	Patients outside the study period and those who declined consent to procedure	EP study	n/a	All 26 patients with FVP (100%) were males, with a mean age of 22.15 ± 3.50 years (range, 20–34 years). In the baseline electrocardiograms of the patients with FVP, pre-excitation and transitional zone were seen in leads V2–V4. During EPS procedures, normal AH interval and shortened HV interval were detected. All the patients had AH prolongation after atrial pacing due to atrioventricular (AV) nodal delay without change in pre-excitation degree. Five of the FVP patients (19.2%) had extra accessory pathways, all of which were ablated successfully while the FVPs were followed clinically.	The electrocardiographic findings of FVP patients were as follows: Mean PR interval was 112.46 ± 10.17 ms (range 90–130 ms), mean QRS complex width was 95.80 ± 15.15 ms (range 80–118 ms), QRS transition (R/S>1) occurred between V2 and V4 precordial leads, the polarity of delta waves were flat in 65.39% of patients and negative in 34.61% of patients in V1 lead, mean amplitude of S wave was 9.35 ± 2.59 ms (range 5–13 msn), and 42.3% of patients had notching in the descending limb of S waves in V1 lead	EPS is gold standard procedure facilitating the diagnosis of FVP which allows for adequate risk stratification. FVP patients with PRKAG2 gene mutations should be evaluated for high-risk clinical outcomes.	Single-center retrospective study limited to male military personnel referred for medical evaluation, which may not be generalizable to the general population.

9.3 Treatment of athletes with WPW	10	Sulu	2022	https://doi.org/10.1111/pace.14568	Electrocardiographic and electrophysiological characteristics of fasciculoventricular fibers in children	To examine the clinical and electrophysiological features of pediatric patients with fasciculoventricular fiber	Single center, retrospective cohort study	n=27 patients with fasciculoventricular fiber; N = 565 patients screened for ventrcular preexcitation Mean age 11.47 ± 4.25 years	Diagnosis of fasciculoventricular pathway by EP study	October 2013 and September 2021, 565 patients who underwent electrophysiological studies due to ventricular preexcitation	Patients outside the study period and those who declined consent to procedure	EP study	ECG features of preexcitation due to WPW	In the electrophysiological study, additional manifest WPW was found in 9 (33%) patients (3 patients with high risk, 6 patients with orthodromic supraventricular tachycardia), focal atrial tachycardia in a patient, and atrioventricular nodal reentry tachycardia in a patient. No statistically significant difference in Delta wave between the 2 groups (p = .398). Delta wave amplitude > 3.5 mm was not detected in any patient with isolated FVF. Interestingly, delta wave amplitude was < 3.5 mm in 7 (78%) of 9 patients who were identified and ablated with an additional accessory pathway. Total 19 of the patients (59.3%) were adenosine-responsive (18 isolated FVF, 1 manifest AP+FVF adenosine-responsive. 8 patients with other manifest AP + FVF had no pre-procedural adenosine-asystole response, and all of them QRS were expanded).	Two patients had HCM and 1 patient had ccTGA. Other tachyarrhythmia substrate frequency accompanying these FVP are quite high (approximately 40%) in EPS. Study highlights the important point that the use of adenosine alone is controversial, since adenosine response may also be in WPW patients. ECG alone may not be sufficient to distinguish FVP from WPW.	FVF is not a cause of tachyarrhythmia but the accessory pathway and other tachyarrhythmia substrate frequency accompanying FVF cases is ~40% in EPS. EPS is important for detecting additional tachyarrhythmias in patients with suspected FVF.	Sinlge center study, small cohort, response to adenosine may depend on escalating doses, unclear as to how many observers there were no assess delta waves and if there was signiciant interobserver variability. Also, unclear if the ECG measurements were made by blinded observers.

Subsection	Rec #	First Author	Year	DOI	Article Title	Aim	Study type	Size	Endpoints	Inclusion Criteria	Exclusion Criteria	Intervention(s)	Comparator(s)	Outcomes (Results and P values)	Other Relevant Findings or Adverse Events	Conclusions	Limitations
10.1 Athletes with bradycardia	1	Marek	2011	https://doi.org/10.1016/j.hrthm.2011.04.024	Feasibility and findings of large-scale electrocardiographic screening in young adults: data from 32,561 subjects	Observe findings in screened athletes	observational	32561	ECG abn	YH4L HS ECG program at 24 high schools, athletes and non athletes	n/a	none	Italian National Registry	none with LBBB, CHB	2.5% abnormal ECGs using 2005 ECG Criteria	ECG screening feasible, low cost with low prevalence of abnormalities	primarily Caucasian cohort, limited clinical follow up information
10.1 Athletes with bradycardia	1	Bent	2015	https://dx.doi.org/10.1016/j.jacc.2015.03.559	Systematic Comparison of Digital Electrocardiograms From Healthy Athletes and Patients With Hypertrophic Cardiomyopathy	Develop criteria to distinguish athlete's heart from HCM on ECG	cross sectional comparative	1124 athletes vs 255 HCM pts	ECG abn	Stanford sports medicine progrm and Stanford Center for Inherited Cardiovascular Diseases	n/a	none	sports medicine cohort compared to HCM cohort	6% HCM vs 0 athletes with LBBB	T wave inversions deeper than 0.5 mV, ST segment depressions deeper than 0.1 mV, and LBBB are major criteria for differentiation	Stanford criteria can distinguish HCM from athletes heart with low false positive	single center cohort
10.1 Athletes with bradycardia	3	Viitasalo	1982	https://doi.org/10.1136/hrt.47.3.213	Ambulatory electrocardiographic recording in endurance athletes	Observe findings on ambulatory ECG recording in highly trained endurance athletes	cross sectional comparative	35 male endurance athletes, 35 nonathlete controls	ambulatory ECG abn	at least 5 years intensive training, no CV disease, no medications; controls were medical students and army conscripts with no intensive exercise history	anyone not meeting inclusion criteria	none	endurance athletes compared to non athletes	significantly more bradycardia and sinus pauses in athletes	form of AV block form common in athletes, ventricular extrasystoles imilar between groups	sinus bradycardia and AV block common in athletes	predominalty male; mixed exercsie/training background as endurance group included basketball players, control group included army recruits
10.1 Athletes with bradycardia	3	Sharma	1999	https://doi.org/10.1136/bjsm.33.5.319	Electrocardiographic changes in 1000 highly trained junior elite athletes	Evaluate ECG changes in junior elite athletes	cross sectional comparative	1000 junior elite athletes, 300 non athletic controls	ECG abn	United Kingdom athlete screening program, sedentary secondary school volunteers as controls	n/a	none	athletes compared to controls	significantly more bradycardia in athletes	Mobitz I AV block present in 5% of athletes; findinlind significantly higher in athletes included prolonged PR, incomplete RBBB, voltage criteria for LVH, and prolonged QT interval	junior (<18 years old) elite athletes have wide range of ECG abnormalities compared to sedentary controls	mostly Caucasian male athletes, heterogeneous sample of sports
10.1 Athletes with bradycardia	3	Stein	2002	https://doi.org/10.1016/S0735-1097(02)01722-9	Intrinsic sinus and atrioventricular node electrophysiologic adaptations in endurance athletes	Evaluate sinus and AV node properties in endurance athletes before and after pharmacologic autonomic modulation	cross sectional comparative	6 endurance athletes and 6 volunteers	EP laboratory measurments of sinus node and AV node function	6 male runners running >50km per week and 6 healthu male non athletes	n/a	atropine and propanolol during EP study	athletes compared to controls	sinsu cycle length, Wenckebach cycle length, and effective refractory period of the AVN node were all longer at baseline, after atropine, and after propanolol in athletes		sinus automaticity and AV node conduction changes were due to intrinsic physiology and not autonomic influences	small study of only male athletes and controls; cannot rule out inherited characteristics; invasive study
10.2 Athletes with a pacemaker	1	Lampert	2013	https://doi.org/10.1161/CIRCULATIONAHA.112.000447	Safety of sports for athletes with implantable cardioverter-defibrillators: results of a prospective, multinational registry	Evaluate the safety of sports participation for athletes with implantable cardioverter-defibrillators (ICDs).	Prospective, multinational registry	372 athletes with ICDs aged 10 to 60 years participating in organized or high-risk sports.	Primary: serious adverse events (tachyarrhythmic death or resuscitated tachyarrhythmia) during or up to 2 hours after sports, or severe injury from arrhythmia-related syncope or shock during sports.	Athletes aged 10 to 60 years with ICDs who were actively participating in organized sports or high-risk sports.	Athletes not participating in sports, or those who did not meet the specific criteria for organized or high-risk sports participation.	Monitoring and data collection through a secure web-based daabase, phone interviews, and medical record reviews.	n/a	No primary endpoint events occurred. There were 49 shocks during competition/practice, 39 during other physical activity, and 33 at rest.	The ICDs effectively terminated all arrhythmia episodes. Lead malfunction rates were low, with 97% at 5 years and 90% at 10 years. 10% shocks during sports, 8% during other physical acitivy 6% at rest.	The study concluded that many athletes with ICDs can engage in vigorous and competitive sports without experiencing physical injury or failure of the device to terminate arrhythmias. These findings support more informed decision-making regarding sports participation for athletes with ICDs.	Self-selection bias of participants, most with normal LV Efs; potential underreporting of ICD shocks because of self reporting; not enough data on contact or collision sport athletes.
10.2 Athletes with a pacemaker	1	Lampert	2017	https://doi.org/10.1161/CIRCULATIONAHA.117.027828	Safety of Sports for Athletes With Implantable Cardioverter-Defibrillators: Long-Term Results of a Prospective Multinational Registry	Evaluate the long-term safety of sports participation for athletes with ICDs (long-term outcomes of Lampert 2013 study).	Prospective, multinational registry	440 participants (n=393 in organized sports, n = 47 in high-risk sports)	Primary: tachyarrhythmic death, resuscitated tachyarrhythmia, or injury related to arrhythmia or shock during sports. Secondary: incidence of appropriate and inappropriate shocks, and ICD lead/system damage.	Athletes with ICDs participating in organized or high-risk sports.	Athletes not participating in organized or high risk sports or no completing enrollment interview.	Monitoring and data collection through a secure web-based daabase, phone interviews, and medical record reviews.	n/a	No tachyarrhythmic deaths or injuries related to arrhythmia during sports were reported. Small proportions of participants experienced appropriate shocks during sports without severe consequences.	10% shocks during sports (3/100 person years), more recieved shocks with physical activity (20%) compared to rest (10%) p<0.0001. Presence of ARVC associated with shocks in sports.	Athletes with ICDs engaged in vigorous acitivity with no signal for harm, underlying disease is important particularly ARVC. Engaging in sports is generally safe for athletes with ICDs, supporting more inclusive guidelines for these athletes.	Self-selection bias of participants, most with normal LV Efs; potential underreporting of ICD shocks because of self reporting; not enough data on contact or collision sport athletes.
10.2 Athletes with a pacemaker	1	Link	2021	https://doi.org/10.1161/CIRCEP.120.009344	mplantable Cardioverter Defibrillator Lead Survival in Athletic Patients	Investigate the risk of ICD lead malfunction in athletes, particularly examining the impact of sports with varying degrees of arm movement and physical contact on lead survival.	Secondary analysis of data from a prospective, multinational registry study (Lampert 2013 and 2017)	440 athletes with ICDs, including those participating in organized sports, recreational sports, and high-risk sports with a significant range of physical activity levels.	Incidence of lead malfunction.	Athletes with ICDS participating in sports activities more vigorous than golf or bowling, and categorized based on the intensity of arm movement and contact level in their sports.	Athletes not participating in organized or high risk sports or no completing enrollment interview.	Monitoring data and medical record reviews.	Comparison of lead malfunction rates across different types of sports based on the degree of arm movement and contact level.	Lead malfunction occurred in 31 cases with an estimated lead survival free of malfunction of 95% at 5 years and 89% at 10 years. Risk factors for malfunction included younger age at implant, use of specific lead models, and higher annual hours of weight-lifting. Minimal collision sports.	No significant associations were found between lead malfunction and the type of sport based on arm usage or contact level.	Athletic activity, with the exception of frequent weight-lifting, does not significantly increase the risk of ICD lead malfunction. The study supports continued participation of athletes with ICDs in sports, underlining the importance of individual risk assessment.	Self-selection bias of participants, most with normal LV Efs; potential underreporting of ICD shocks because of self reporting; not enough data on contact or collision sport athletes. Categorization of sports may not fully capture the specific movements and impacts associated with each sport.
10.2 Athletes with a pacemaker	1	Saarel	2018	https://doi.org/10.1161/circep.118.006305	Safety of Sports for Young Patients With Implantable Cardioverter-Defibrillators	perform posthoc subanalysis of Lampert 2013 study on safety of sports for patients<=21 years with ICDs	propsective national registry	129	serious adverse even during or up to 2 hours after sports	athletes with ICDS participating in organised or high risk sports and 21 years old or younger	not participating in organized or high risk sports or no completing enrollment interview	phone interview and medical records	n/a	no tachyarrhythmic deaths or externally resusciated arrhythmias during or after sports and no sports related inuries from syncope or shock during sports	27% received at least 1 shock, all appropriate shocks were successful; 35% received inappropriate shocks	some young athletes with ICDs experienced shocks but no adverse events occurred; rates of shocks and lead malfunction were similar to previously reported nonathlete data	shocks self reported, few patients played contact or collision sports, no participants had a subcutaneous ICD
10.2 Athletes with a pacemaker	3	Abdelrahman	2018	https://doi.org/10.1016/j.jacc.2018.02.048	Clinical Outcomes of His Bundle Pacing Compared to Right Ventricular Pacing	compare clinical outcomes between his bundle pacing and RV pacing	single center observational	765; 332 had attempted his bundle pacing	combined endpoint of death, heart failure hospitalization (HFH), or upgrade to BIV pacing	patients referred for pacing and over 18 yr old	<18years old, already had CRT device, or exisiting pacemaker or ICD	His bundle pacing at one insitution, RV pacing at second institution	His pacing vs RV pacing	His bundle pacing successful in 92% of 332; combined primary endpoint was significantly reduced in His bundle pacing group (p=0.02); incidence of HFH also significantly reduced in His bundle pacing group (p=0.02)	difference in primary endpoint observed primarily in patients with >20% ventricular pacing (p=0.02); trend toward reduced mortality in His bundle pacing group (p=0.06)	His bundle pacing is feasible and reduces HFH and death compared to RV pacing	single center cohort
10.2 Athletes with a pacemaker	3	Fernandes	2020	https://doi.org/10.1111/jce.14490	Network meta-analysis of His bundle, biventricular, or right ventricular pacing as a primary strategy for advanced atrioventricular conduction disease with normal or mildly reduced ejection fraction	compare His bundle pacing, BIV pacing, and RV pacing for advanced AV block in patients normal or mildly reduced EF	meta analysis	6 studies compared BIV (704 patients) and RV pacing (614); 4 compared His (463 patients) and RV (568) pating	all-cause death, heart failure hospitalizations (HFH), EF, left ventricular volumes, 6-minute walk test, and QRS duration	studies comparing His bundle pacing or BIV pacing to RV pacing	studies not meeting aim	n/a	His bundle pacing or BIV pacing vs RV pacing	significantly lower mortality (p=0.002), HFH (p<0.001), increase in EF (p<0.001) and decrease in QRS duration (p<0.001) with HBP or BiVP as compared with RVP.	In network meta-analysis, HBP and BiVP were associated with significantly improved survival compared to RVP	His bundle pacing and BIV pacing were superior to RV pacing in patients with advanced AV block and mildly reduced to normal EF	meta analysis

10.2 Athletes with a pacemaker	3	Khurshid	2014	https://doi.org/10.1016/j.hrthm.2014.05.040	Incidence and predictors of right ventricular pacing-induced cardiomyopathy	identify incidence and predictors of RV pacing induced cardiomyopathy (PICM)	single center retrospective review	257	PICM was defined as ≥10% decrease in LVEF, resulting in LVEF <50%	normal baseline LV EF, single-chamber ventricular or dual-chamber pacemaker (but not ICD or BIV pacemaker), frequent (≥20%) RV pacing was present, and repeat echocardiogram available ≥1 year after implantation	alternative causes of cardiomyopathy	n/a	n/a	19.5% developed PICM, LV EF decrased by mean of 62.1% to 36.2% over 3.3 years; male gender (p=0.01) and wider baseline QRS (p<0.001) were independently associated with PICM; lower baseline EF also associated with developing PICM (p=0.3)	baseline QRS >115msec was 90% specific for developing PICM	men with wider baseline QRS are at increased risk of developing PICM, even if RV pacing burden <40%	single center, retrospective design
10.2 Athletes with a pacemaker	3	Kronborg	2014	https://doi.org/10.1093/europace/euu011	His or para-His pacing preserves left ventricular function in atrioventricular block: a double-blind, randomized, crossover study	compare LV function in response to long term His or para-His pacing to RV septal pacing	prospective randomized double blinded single center crossover study	38, 19 randomized to each group	LV function, NYHA class, quality of life scores, time to peak systolic velocity	primary pacemaker indication, AV block and QRS<120ms, EF>40%	sinus node disease, AF and bradycardia, AVB and QRS>120ms, urgent implant, EF<40%	His or para His pacing or RV septal pacing	His or para His pacing vs RV septal pacing	LVEF was significantly lower in RVSP group (50%+/-11%) than His pacing group (55%+/-10%; p=0.0005); time to peak velocity in two-chamber and apical long axis view were significantly longer with RVSP (p=0.02 and p=0.03, respectively)	no differences in NYHA, 6 min walk test, QOL assessments, or device related complications	His or para-His pacing preserves LV EF and mechanical synchrony compared to RV pacing in patients with AV block	single center
10.2 Athletes with a pacemaker	3	Sharma	2022	https://doi.org/10.1016/j.hrthm.2021.08.033	Clinical outcomes of left bundle branch area pacing compared to right ventricular pacing: Results from the Geisinger-Rush Conduction System Pacing Registry	compare clinical outcomes between left bundle branch area pacing (LBBAP) and RV pacing	two center, observational registry	703	all cause mortality, heart failure hospitalization (HFH), upgrade to BIV pacing	patients undergoing His bundle pacing, LBBAP, or conventional right ventricular (RV) lead implantation (RV apex or septum) based on operator preference; age 18 years or older	<18 years of age, had undergone cardiac resynchronization therapy, had existing cardiac implantable electronic device, left ventricular ejection fraction (LVEF)<35%, underwent HBP or leadless pacemaker implantation during the study period or without complete 6-month follow survey	LBBAP or RV pacing	321 LBBAP vs 382 RV pacing	QRS duration during LBBAP was similar to baseline and was narrower compared to RVP (p <.001); primary composite outcome was significantly lower with LBBAP compared to RVP (p<.001); among patients with ventricular pacing burden .20%, LBBAP was associated with significant reduction in the primary outcome compared to RVP (p<.001)	LBBAP associated with significant reduction in mortality (p=0.03) and HFH (p=0.004)	LBBAP was associated with a significant reduction in the composite outcome of all-cause mortality, HFH, or upgrade to BVP compared to conventional RVP, primarily driven by patients who needed over 20% ventricular pacing	observational, non radomized intervention, variable follow up
10.2 Athletes with a pacemaker	3	Somma	2023	https://doi.org/10.1016/j.hrthm.2022.09.019	Pacing-induced cardiomyopathy: A systematic review and meta-analysis of definition, prevalence, risk factors, and management	to characterize definition, prevalence, risk factors, and treatment strategies of pacing-induced cardiomyopathy (PiCM)	systematic review and meta analysis	26 studies, 57993 patients	prevalence, risks factors, and management strategies for PICM	studies in humans, reported definition, prevalence, risk factors, prognosis, or management of PiCM; over 50 patients; English language, and fully published status; data collected included study design, baseline patient demo graphic characteristics, procedural characteristics, follow-up duration, implant success rate, prevalence rate, management strategies, and prognosis	articles that did not have original data or studies were performed in animals or in vitro	n/a	n/a	Fifteen unique definitions of PiCM reported; pooled prevalence of PiCM was 12%; in meta-analysis, risk factors included male sex, history of myocardial infarction, chronic kidney disease, atrial fibrillation, baseline left ventricular ejection fraction, native QRS duration, right ventricular pacing percentage, and paced QRS duration; treatment strategies identified included biventricular cardiac resynchronization therapy (6 studies) and His-bundle pacing (3 studies); more than 1 in 10 patients with chronic right ventricular pacing developed PiCM	n/a	definitions of PiCM varies considerably; bbout 12% of patients with chronic RV pacing develop PiCM; risk factors include male sex, history of AF and MI, baseline LVEF, native QRS duration, RV pacing percentage, and paced QRS duration; current management strategies include biventricular CRT or HBP, and both are associated with improved clinical outcomes	meta analysis, most studies retrospective observational data
10.2 Athletes with a pacemaker	3	Vijayaraman	2019	https://doi.org/10.1016/j.hrthm.2019.03.026	Outcomes of His-bundle pacing upgrade after long-term right ventricular pacing and/or pacing-induced cardiomyopathy: Insights into disease progression	to assess the feasibility of HBP in patients with chronic RVP and longstanding AVB and to evaluate its efficacy in reversing the adverse remodeling induced by RVP	retrospective observational multicenter (6 studies) study	85	clinical outcomes with HBP	PICM; right ventricular (RV) lead failure; or pacing system infection requiring explantation and subsequent reimplantation of a new ventricular pacing lead	Patients with alternative causes of left ventricular (LV) dysfunction, including myocardial infarction, valvular heart disease, frequent (>15%) ventricular premature depolarizations, and uncontrolled hypertension (>160/100 mm Hg), were not considered to have PICM	n/a	n/a	HBP was successful 93%. QRS duration increased from 123 ± 31 ms at baseline to 177 ± 17 ms (p <.001) during RVP and decreased to 115 ± 20 ms with HBP (p <.001); in 60 patients with PICM in whom left ventricular ejection fraction decreased from 54% ± 7.7% at baseline to 34.3% ± 9.6% (*p* <.001), ejection fraction improved to 48.2% ± 9.8% (p <.001) after HBP.	HBP threshold was 1.47 ± 0.9 V @ 1 ms at implant and 1.9 ± 1.3 V @ 1 ms at last follow-up (25 ± 24 months)	despite a long duration of AVB and chronic RVP, HBP normalized QRS complexes with stable thresholds; structural changes induced by chronic RVP were reversed with HBP	retrospective design
10.2 Athletes with a pacemaker	3	Wang	2022	https://doi.org/10.1016/j.jacc.2022.07.019	Randomized Trial of Left Bundle Branch vs Biventricular Pacing for Cardiac Resynchronization Therapy	compare efficacy of left bundle branch pacing (LBBP)-CRT with BIV pacing CRT in patients with heart failure and reduced LVEF	prospective randomized trial	40; 20 in LBBP-CRT, 20 in BIV-CRT	change of LVEF; changes in echocardiographic measurements, N-terminal pro–B-type natriuretic peptide (NT-proBNP) concentration, NYHA functional class and 6-minute walk distance (6MWD), paced QRSd, and echocardiographic response to CRT	age 18 to 80 years, sinus rhythm, complete LBBB, LVEF ≤40 %, and NYHA functional class II to IV; at least 3-month guideline-directed medical therapy	ischemic cardiomyopathy; non-LBBB QRS morphology including right bundle branch block (RBBB) or intraventricular conduction delay; persistent atrial fibrillation; pregnancy	LBBP or BIV pacing	LBBP or BIV pacing	Intention-to-treat analysis showed significantly higher LVEF improvement at 6 months after LBBP-CRT than BiVP-CRT (p = 0.039)	LBBP-CRT appeared to have greater reductions in left ventricular end-systolic volume, changes in NYHA functional class, 6-minute walk distance, QRS duration, and rates of CRT response compared with BiVP-CRT	LBBP-CRT improved LVEF more than BIV pacing CRT in patients with nonischemic cardiomyyopathy and LBBB	small sample size, 6 month follow up, two centers only, nonischemic patients only
10.2 Athletes with a pacemaker	5	Mathony	2005	https://doi.org/10.1111/j.1540-8159.2005.09330.x	Optimal maximum tracking rate of dual-chamber pacemakers required by children and young adults for a maximal cardiorespiratory performance	Determine impact of max track rate n cardiorespiratory fitness	Prospective cohort study	15 patients aged 7–24 years with atrioventricular block and normal sinus-node chronotropic function	Peak oxygen uptake	AVB, normal sinus function. Age range 7-24 years	n/a	treadmill exercise test	NA	Those with wenckebach at max heart rate had decreased mVO2. Significant increases in maximal heart rate (P < 0.001), peak cardiorespiratory capacity (P < 0.001), peak oxygen uptake (P < 0.005), and oxygen uptake at the anaerobic threshold (P < 0.02) with higher MTR.	No heart rhythm disturbances observed with higher MTR settings.	AVB is detrimental to maximum performance, 1:1 tracking is critical	Small sample size and lack of a control group
10.2 Athletes with a pacemaker	6	Sweeney	2007	https://doi.org/10.1056/NEJMoa071880	Minimizing ventricular pacing to reduce atrial fibrillation in sinus-node disease	assess if programming to minimize ventricular pacing reduces atrial fibrillation (AF) onset	RCT	1065	time to persistent AF	pacemaker patients with sinus node dysfunction	persistent atrial fibrillation, two or more cardioversions for atrial fibrillation within a 6-month period, second- or third-degree atrioventricular block, or a life expectancy of less than 2 years.	programming of algorithm that minimizes pacing (530 patients)	standard DDD programming (535 patients)	persistent AF developed in 110 patients, 68 (12.7%) with conventional dual-chamber pacing and 42 (7.9%) with dual-chamber minimal ventricular pacing resulting in 40% reduction in relative risk; absolute reduction in risk was 4.8%; mortality rate was similar in the two groups (p=0.54)	median percentage of ventricular beats that were paced was lower in dual-chamber minimal ventricular pacing than in conventional dual-chamber pacing (9.1% vs. 99.0%, P<0.001)	dual-chamber minimal ventricular pacing moderately reduces risk of persistent AF in patients with sinus-node dysfunction	low heart failure risk population, industry sponsored
10.2 Athletes with a pacemaker	6	Arnold	2023	https://doi.org/10.1093/europace/euad065	Avoiding unnecessary ventricular pacing is associated with reduced incidence of heart failure hospitalizations and persistent atrial fibrillation in pacemaker patients	evaluate whether AV delay management (hysteresis) compared with standard pacing reduces unnecessary ventricular pacing and improved clinical outcomes	Prospective, observational	2592	AF, CHF	Pacemaker patients, all indications	life expectancy <1 year and current or planned pregnancy; change in the status of this feature during the study period	the AV hysteresis (AVH)	AVH vs standard programming	Decrease in AF and HF with VP-avoidance; no difference in mortality	AVH reduced ventricular pacing also in high grade AV block	AVH is associated with reduced HF hospitalization and persistent AF at 1 year	observational, approximately 2900 patients excluded due to incomplete data

10.2 Athletes with a pacemaker	8	Erol-Yilmaz	2005	https://doi.org/10.1111/j.1540-8159.2005.09382.x	Individual optimization of pacing sensors improves exercise capacity without influencing quality of life	assess sensor optimization on exercise capcity and quality of life	RCT, single-blind	54	chrontropic assessment and quality of life survery	>75% paced	<75% pacing	Optimized sensor settings (OSS)	Out of box settings	Maximum heart rate improved with OSS, exercise capacity improved, no change in quality of life	Accessible, rather than automatic slope sensor algorithms, were more effective	individual optimization of rate response settings improves exercise capacity and maximum HR but not quality of life	short follow up