Cardiac Issues in Football

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Epidemiology

Incidence of Sudden Cardiac Death

Sudden cardiac death (SCD) in athletes is tragic, affecting not only the victim and their families but also teammates, schools, and entire communities. It is often portrayed as a rare, but tragic event; however, SCD is the most common medical cause of death in athletes, including football athletes.

The reported incidence of SCD varies widely depending on study methodology. In order to calculate a precise incidence of SCD, an accurate numerator (number of cases) and denominator (the population at risk) are needed. There is no mandatory reporting of SCD in the United States and deaths are often identified via media report or insurance claim information. Media reports will miss SCDs, particularly those in "lower profile" athletes or those that occur away from the field. In NCAA athletes, media reports identified only 70% of SCDs, with deaths that occurred in lower divisions less likely to be reported [1]. In competitive Danish athletes, media reports identified only 4–20% of the sports-related deaths [2, 3]. Likewise, insurance claims do not identify the vast majority of SCDs in athletes. In a study of Minnesota high school athletes, insurance claims identified only 14% of the SCDs and in National Collegiate Athletic Association (NCAA) athletes, insurance claims identified only 10% [4].

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K. W. Farmer (ed.), *Football Injuries*,
https://doi.org/10.1007/978-3-030-54875-9_15

Denominators are often estimated based on generalized sport participation numbers or activity surveys, which are then extrapolated to the population, leading to compounded error. Populations of similar risk should be grouped together. For incidence calculations, populations where the sex, race/ethnicity and sport played are known provide the most precise estimation, however this level of detail is rare. Risk of cardiovascular disease varies significantly with age, especially after the age of 25 where coronary artery disease (CAD) becomes a more common cause of death; thus, inclusion of wide age ranges decreases accuracy. Only age groups of similar risk should be pooled. Inaccuracy in numerator, denominator, or both can lead to wildly varied estimates. Methodology must be carefully scrutinized when considering estimates of SCD.

Another source of inaccuracy is reporting only SCD cases occurring with exertion, sometimes referred to as "exertional death" or "sports-related SCD," or those occurring only during official team activities. This approach will miss many deaths and underrepresent the true burden of SCD. In one study of NCAA athletes, 42% of deaths did not occur during exertion [1]. Sports-related SCD *is not the same* as SCD in athletes and is a critical distinction. The incidence of SCD in athletes, occurring at any time, is important when considering primary prevention. Sports-related SCD numbers may be useful when creating an emergency action plan for an event or venue.

Sudden cardiac arrest (SCA) is also an important endpoint to consider. SCA is SCD prevented; most often because the athlete had a witnessed SCA with bystander access to a defibrillator. There is no mandatory reporting for SCA in the United States, and many cases of SCA are not reported in the media, making incidence numbers extremely difficult to ascertain. Reporting and tracking systems for SCA need to be improved to truly understand how often SCA occurs in athletes.

Football-Specific Incidence

There are groups of athletes that are at higher risk for SCA/D including male athletes, black athletes, football athletes, and male basketball athletes [1]. In studies that have reported on the incidence of SCD, football athletes have been consistently demonstrated as higher risk including studies in college and high school [1, 5–8] (Table 15.1).

Like other sports, SCD is the most common medical cause of death in football athletes, accounting for 12% of all deaths, 45% of medical deaths, and 42% of the deaths that occurred during exertion [9]. In studies not reporting incidence numbers but reporting the proportion of deaths attributable to football, football consistently represents a large proportion of the SCD, usually just behind male basketball athlete SCD [8, 10].

Table 15.1 Incidence of sudden cardiac death in athletes with a focus on football athletes

Study	Year	SCA/D or SCD?	Population	Incidence of SCD (in athlete-years)
Harmon	2015	SCD	NCAA athlete	1 in 53,703
			NCAA male athletes	1 in 37,790
			NCAA black athlete	1 in 21,491
			NCAA football athlete	1 in 35,951
			Black football athlete	1 in 21,987
			White football athlete	1 in 47,031
			NCAA male basketball athlete	1 in 8,978
Harmon	2016	SCA/D	High school athlete	1 in 67,064
			High school male athlete	1 in 44,832
			High school football athlete	1 in 86,494
Maron	2014		NCAA football athlete	1 in 39,060

Etiology of Sudden Cardiac Death

The etiology of SCD is important to consider, particularly when developing screening strategies. Initial studies of the causes of SCD suggested hypertrophic cardiomyopathy (HCM) occurred most commonly, accounting for 37% of cases; however, this data was likely skewed due to ascertainment bias (cases were collected through a HCM center), and cases which would be considered as autopsy-negative sudden unexplained death (AN-SUD) were not included in the cohort [11]. Later studies in NCAA athletes and athletes in Europe suggested the most common cause of death in athletes was AN-SUD [1, 12]. AN-SUD is thought to be secondary to arrhythmias or electrical disease.

Although these studies showed a lower incidence of strictly pathologically defined HCM, there is an increasing recognition of athletes dying with left ventricular hypertrophy (LVH) with fibrosis or cardiomyopathy that does not meet pathologic criteria for HCM [1, 12]. It is unclear if this is on the HCM continuum or is acquired from intense physical activity. If cases of LVH and possible cardiomyopathy are included with HCM, the incidence increases to around 25% [1, 12]. In a recent study including athletes 11–29 years old in the United States, HCM was the leading cause of death representing 16% of the cases, but when combined with LVH/possible cardiomyopathy represented 30% of all SCDs [10].

The etiology of SCD in football, specifically, is less often described. For the most part, the causes of death in NCAA football athletes paralleled the larger cohort of all NCAA athletes [1]. AN-SUD was the most common cause of death; however, there was a higher incidence of myocarditis (19%) and coronary artery disease (CAD) (13%) in football players compared to other NCAA athletes [1]. The increased incidence of CAD in football players may be related to the large body (and fat) masses of some of the players. HCM was responsible for 13% of SCD in football athletes; however when combined with LVH/possible cardiomyopathy represented 25% of

the group. Interestingly, in men's basketball and men's soccer, HCM/LVH/possible cardiomyopathy caused 50% and 57% of SCDs, respectively. The reason for this differential is unclear. In the only other study looking at SCD in football, HCM represented 25% of SCD cases, which was similar to the proportion of HCM in male basketball players [10].

Screening

Since the 1960's when the American Medical Association (AMA) first called for screening young athletes prior to participation, the pre-participation evaluation (PPE) has been customary. In 1996, the American Heart Association (AHA) published cardiovascular screening recommendations stating that "some form of pre-participation cardiovascular screening for high school and collegiate athletes is justifiable and compelling, based on ethical, legal, and medical grounds" [13]. One in 300–400 athletes will have a cardiovascular condition that predisposes to SCD [14]. Primary prevention consists of screening for those conditions with the intent to manage and mitigate risk, while secondary prevention is treating an SCA once it has occurred. Both are important. The AHA and American College of Cardiology (ACC) state the purpose of the PPE is "to prospectively identify or raise suspicion of previously unrecognized and largely genetic congenital cardiovascular diseases known to cause SCA and sudden death in young people" [15]. Other organizations creating guidelines agree that the primary objective of the PPE is to detect potentially life-threatening conditions in athletes [16]. The benefits and drawbacks of various screening strategies are outlined below.

History of Physical Examination

History and physical examination has long been the mainstay of pre-participation screening. The AHA and the ACC have endorsed a screen which includes a personal and family history along with blood pressure measurement, cardiac auscultation, femoral artery pulse check, and examination for physical stigmata of Marfan syndrome as the "best available and most practical" strategy since their initial statement in 1996, affirming this position in both 2007 and 2014 while acknowledging "the standard history and physical examination intrinsically lack the capability to reliably identify many potentially lethal cardiovascular abnormalities" [13, 15, 17].

The recently published *Preparticipation Physical Evaluation Monograph, fifth Edition*, also endorses this recommendation [16]. However, recent statements from the NCAA and the American Medical Society for Sports Medicine (AMSSM) acknowledge that while the history and physical examination is pragmatic and widely practiced, it has limited ability to identify athletes at risk for SCA/D [18, 19].

Drawbacks of the history and physical as a detection strategy for underlying cardiovascular disease include a low sensitivity and a high false-positive rate. In an early study looking at 115 cases of SCD in athletes, only four athletes (3%) were

suspected of having a cardiovascular condition and only one athlete (<1%) was correctly identified [20]. In a recent meta-analysis including almost 50,000 athletes, the sensitivity of history for cardiovascular conditions predisposing to SCD was 20% and physical exam was 9% [21]. It is not surprising that relying on a symptom-based questionnaire results in low sensitivity, as SCD is the presenting manifestation of underlying cardiovascular conditions in up to 80% of athletes SCDs. Low sensitivity is not the only concern; the recommended screening questions include symptoms which are fairly common in those without disease, with up to 67% of high school athletes and 33% of NCAA athletes answering affirmatively to at least one question, resulting in a high false-positive rate [14, 22].

The AHA/ACC recommendations for pre-participation cardiovascular screening in athletes do provide a standardized framework for evaluation and are considered the standard of care. Despite these recommendations being in place for over 20 years, they have not been widely implemented, with one study showing less than 6% of primary care physicians compliant with recommendations [23]. The benefits of the history and physical include wide accessibility. While cost is often cited as a benefit of history and physical compared to other screening strategies, this is typically in comparison to a pre-participation screen done at a school with volunteer workforce. Exams done in an office setting represent a significant cost. These volunteer screens may be widely accessible; however, they lack the ability to meet many of the other objectives of a PPE which are better accomplished within the medical home [16]. In the end, one must balance the low sensitivity and the high false-positive rate of history and physical examination with its wide accessibility and relatively low prevalence of SCD in many populations. It should not, however, be viewed as an effective screen for cardiovascular disorders.

Electro Cardiogram (ECG)

In 2005, the European Society of Cardiology recommended the addition of an ECG to the PPE based largely on the experience of the Italians who demonstrated an 89% reduction in athlete SCD after the implementation of a screening program including ECG [24, 25]. This has caused heated debate between proponents of ECG screening and those who oppose it. Recent statements from the NCAA and AMSSM recognize the statistical superiority of a screening strategy, which includes ECG while acknowledging barriers that include lack of infrastructure to adequately interpret the ECGs and access to appropriate follow-up cardiovascular care.

There has been an evolution in the criteria used to interpret ECG in athletes. Many findings which would be concerning in other settings should be considered normal in athletes and the result of physiological response to exercise. The false-positive rate using the latest criteria for interpretation of ECG in athletes, the International Criteria, is around 2% [26]. ECG can reliably detect the majority of conditions associated with SCD including hypertrophic cardiomyopathy (HCM) and electrical diseases such as long QT syndrome (LQTS) and Wolff-Parkinson-White (WPW) syndrome. ECG does not reliably detect coronary artery anomalies,

atherosclerotic coronary artery disease, or aortic pathology, which accounted for 20% of the deaths in the NCAA cohort [1]. It is estimated that ECG identifies about two-thirds to three-fourths of cardiovascular conditions associated with SCD in most studies. In a recent study of elite English soccer players, ECG identified 86% of the cardiovascular conditions discovered [27]. In a meta-analysis comparing the sensitivity of history and physical examination and ECG in almost 50,000 athletes, ECG was 94% sensitive for the cardiovascular conditions identified [21].

ECG is superior to history and physical alone for the detection of cardiovascular conditions associated with SCD; however, it is unknown if this affects outcomes. Arguments against ECG include the low prevalence of cardiovascular disease in this population. Football players are at higher risk than other populations with an SCD risk of 1 in 36,000 athlete-years. Sixty-two percent of "Power 5" autonomy conferences include ECG as part of their cardiovascular screen; however, this may be impractical in other settings with fewer resources [28]. In a more recent 2019 survey [29] of head athletic trainers and team physicians at Autonomy Five schools, 72% (34/47) reported including ECG as part of their cardiovascular screen with 97% (33/34) of those screening all athletes from all sports. Ultimately, the decision to include ECG or not should depend on the physician's assessment of the risk-benefit ratio based on the resources available to them.

Echocardiogram

Echocardiogram (echo) is used in some settings as an adjunct to history and physical examination and ECG in cardiovascular screening. The type of echo varies from a full echo done on a hospital-grade ultrasound machine by a licensed cardiac sonographer to cardiac screening protocols administered by a sports physician using point-of-care ultrasound. Echocardiogram has the advantage of being able to visualize structural pathology including cardiomyopathies, aortic pathology, and some congenital artery abnormalities. Although echocardiography may identify serious disease in the absence of an abnormal ECG, the diagnostic yield from asymptomatic athletes with a normal history and physical examination and ECG is low [30]. Echocardiograms can identify congenital or structural conditions not associated with SCD, which may benefit from routine surveillance. The 2019 survey of Autonomy Five schools reported only 29.8% (14/47) obtain routine screening echo with 64% (9/14) of those screening all athletes from all sports [29].

The added value of echocardiogram compared to ECG to diagnose cardiomyopathy specifically has been questioned as the morphological alterations of exercise training can paradoxically cause changes in the cardiac structure that are difficult to differentiate from pathological changes, especially for non-experts [30]. Some have suggested that screening point-of-care echocardiograms could decrease the rate of referrals for further evaluations after a positive history and physical examination or ECG; however, this hypothesis remains unproven [31].

Two recent studies of collegiate football players have suggested that differentiating normal from abnormal echocardiographic findings can be challenging and

indexing the interventricular septal diameter (IVSD) and left ventricular end-diastolic diameter (LVEDD) to body surface area (BSA) may provide a more specific measurement and limit false-positive findings [32] but does not appear to be applicable to the aortic root diameter (ARD) in these athletes [33].

Prevention

Even the best screening program will not identify all athletes with underlying cardiovascular disorders. Every school or institution that sponsors athletic activities should have a written and structured EAP (Chap. 14). Access to early cardiopulmonary resuscitation (CPR) and early defibrillation is the key to survival of SCA [34]. The EAP should be developed in conjunction with local emergency medical services, school or venue safety officials, likely first responders, and administrators. The EAP should be specific to each venue or field where football players practice or play and provide plans for a communication system, targeted first responders, the location of on-site automatic external defibrillators (AEDs), and transportation routes for arriving EMS. The EAP should be practiced at least annually by potential responders to SCA.

An identified team of targeted first responders (i.e., coaches, school health officials) should receive training in the recognition of SCA, CPR, and AED use. First responders in many situations are coaches. Recognition of SCA is the first step to response. Anyone who collapses and is unresponsive should be presumed to have had an SCA. Over 50% of athletes with SCA will have tonic-clonic movement of the limbs, which is often mistaken for a seizure causing critical delay. Agonal breaths or gasps should not be confused with respiration. Once SCA is recognized, CPR should be started and emergency medical services (EMS) should be activated. If there is a defibrillator on-site, it should be retrieved and placed on the athlete. On-site AED programs are ideal and the best means of achieving early defibrillation. Automated external defibrillators will not deliver a shock unless indicated. The target time from collapse to first shock should be less than 3 minutes.

Implantable Cardioverter-Defibrillators

Those deemed at high risk of future life-threatening ventricular arrhythmias sometimes have an implantable cardioverter-defibrillator (ICD) surgically implanted. This is a device that senses the rhythm and rate of the heart and will fire if life-threatening rhythms such as ventricular tachycardia or ventricular fibrillation are noted. Some athletes have returned to play after being diagnosed with a cardiac condition and receiving an ICD but only after achieving a thorough understanding of the risks and benefits being reviewed in a shared decision-making process [35]. Recent guidelines have recognized an evolving standard regarding return to play with an ICD; however, most experts consider it inadvisable to play football, a

collision sport, with an ICD [36]. Damage to the device or the leads could cause malfunction. There is also a risk of inappropriate shock or failure of the device to abort lethal arrhythmias.

Potential Specific Causes of Cardiac Issues in American Football

Covered in this section are some of the most commonly encountered cardiac conditions in American football. Be aware that there are other relatively rare conditions not included and if concerned for these, cardiac specialist consultation and reference to the most recent consensus guidelines is recommended.

Structural

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is an inherited heterogeneous heart disease characterized most commonly by left ventricular hypertrophy (LVH) and is an important cause of arrhythmogenic sudden death and heart failure [37–39]. Best estimates conclude that the combination of HCM/idiopathic LVH/possible cardiomyopathy accounts for 24–36% of sudden cardiac deaths (SCD) in athletes [1, 10, 17].

HCM is diagnosed by a hypertrophied but nondilated LV chamber in the absence of another cardiac or systemic disease, such as hypertension (HTN), capable of causing the magnitude of hypertrophy seen [40]. LV wall thicknesses can range from mildly enlarged (13–15 mm) to massive with a thickness of up to 60 mm [40]. LVH is typically asymmetric with the anterior septum usually predominant [40]. When outflow tract obstruction occurs, it is usually from systolic anterior motion of the mitral valve [40].

Myocardial fibrosis is common [38] in HCM and, together with disorganized cellular architecture and expanded interstitial collagen, serves as life-threatening arrhythmogenic substrates [40]. The estimated phenotypic prevalence is 1 in 500 [37–39] with a possible genotypic prevalence of 1 in 200 [39]. Pathogenic mutations are transmitted in an autosomal dominant pattern, and more than 1500 different mutations have been identified within more than 11 different sarcomere- and myofilament-related genes, with more than 70% of mutations in just two genes, ß-myosin heavy chain (*ß-MYH7*) and myosin-binding protein C (*MYBPC3*) [37, 41, 42].

With genetic testing, an increasing amount of HCM family members are recognized with pathogenic mutations (genotype positive) but in the absence of a clinical phenotype (phenotype-negative) [42]. When spontaneous conversion to phenotype-positive occurs, it is usually between 12 and 20 years of age [42] at the time of substantial LV remodeling during accelerated body growth during adolescence [40]. The phenotypic expression during this time is part of the rationale supporting

pre-participation screening of high school and college athletes with interval repeat exams and history every several years [40].

HCM may be first suspected on routine history and physical or screening examination. However, frequently, SCD is the first clinical presentation of an athlete with HCM [37]. If an athlete presented in-season with symptoms concerning for HCM, it would usually be from a syncopal episode associated with exertion. Physical exam is frequently normal, but if an outflow tract obstruction exists, a systolic murmur may be heard best at the left lateral sternal border in positions that decrease preload, (Valsalva maneuver or squat-to-stand) emphasizing the importance of dynamic cardiac auscultation at physical exam.

Abnormalities on 12-lead ECG may precede development of overt structural cardiac disease [43–45]. If ECG abnormalities exist but the heart is found to be structurally normal, athletes should be allowed to participate but should be followed annually for the development of structural disease [43], as 6–7% of athletes with abnormal ECGs and initially structural normal hearts went on to develop structural pathology or cardiomyopathy at follow-up [44, 45].

Consultation of a cardiologist with expertise in sports cardiology should be sought for any athlete with suspected or known HCM. Routine diagnostic testing for those being evaluated for HCM includes an ECG, echocardiogram, exercise ECG test, and a minimum 24-hour Holter monitor test. If echocardiography is non-diagnostic or apical or antero-lateral HCM is suspected, contrast-enhanced cardiac MRI should be a standard component of the assessment as echocardiogram may not provide a reliable assessment of those areas. MRI provides a superior assessment of myocardial hypertrophy, and if gadolinium enhancement is present, can also suggest myocardial fibrosis [43]. Two-dimensional (2D) myocardial strain imaging is a new tool that has shown promise in discriminating subclinical functional differences in variant forms of left ventricular hypertrophy (LVH), like athlete's heart, from HCM [46, 47]. Detraining for 6 weeks to 6 months has been utilized as a method for distinguishing physiological LVH or "athlete's heart" from pathologic LVH or HCM, as most cardiac parameters regress and then completely normalize by 6 months of detraining [48, 49]. However, detraining is undesirable by athletes and not practical to implement, limiting its usefulness. Genetic screening and family evaluation may also be considered.

Treatment options depend on an individualized risk assessment for sudden death but include medication management (i.e., beta blockers), implantable defibrillators, surgical septal myectomy, and percutaneous alcohol septal ablation for outflow tract obstruction [37].

Currently, the risk for sudden death in the genotype-positive–phenotype-negative population appears very low, likely no higher than in the general population, and participation in competitive athletics is reasonable for this population [42]. For phenotype-positive HCM athletes, the current expert opinion is that they should not participate in competitive sports with the exception of low-intensity class IA sports (Table 15.2), which include bowling, golf, and yoga, even if treated medically or surgically [42] including an implantable defibrillator (See ICD under Screening and Prevention), given that intense exertion is a known arrhythmogenic substrate in a

Table 15.2 Classification of sports based on static/dynamic component [50]

	A. (Low dynamic < 50%)	B. (Moderate dynamic 50–75%)	C. High dynamic (>75%)
III. High static (>30%)	Gymnastics; Field (throwing); Martial arts; Weightlifting	Wrestling; Downhill skiing; Snowboarding; Bodybuilding	Boxing; Cycling; Rowing; Triathlon
II. Moderate static (10–20%)	Diving; Equestrian sports	*Football;* Field (jumping); Track (sprint)	Swimming; Track (mid-distance); Basketball; Lacrosse
I. Low static (<10%)	Golf; Yoga; Bowling	Softball; Volleyball	Soccer; Track (distance)/ Cross Country

patient with the impaired myocardial tissue of HCM. American-style football (ASF) is a class IIB sport (moderate static and dynamic components) [50]. There are genetic mutations associated with a higher risk of sudden SCD, including several *ß-MYH7* mutations and those involving the cardiac troponin T (*cTnT*) gene [41], and in general, sport participation recommendations for individuals with these mutations are dependent upon their phenotype status, as previously mentioned.

Aortic Diseases

Aortic dissection or rupture accounted for 5% of SCD in one decade-long study of collegiate athletes, but none were football athletes [1] and 6% of SCD in another study, over a 2-year duration, of middle school-aged through professional competitive athletes [10]. Aortopathies, including Marfan syndrome and a bicuspid aortic valve (BAV), are possible predisposing factors for aortic dissection.

Marfan syndrome (MFS) is an autosomal dominant (AD) condition with an estimated prevalence of 2–3 per10,000 individuals caused by abnormal fibrillin-1 due to mutations in the fibrillin-1 (*FBN1*) gene, of which approximately 75% are inherited and 25% are de novo mutations [51]. Marfan syndrome is a multisystem disorder of connective tissue, with cardiovascular manifestations a major cause of morbidity and mortality. The main features of MFS consist of aortic root aneurysm, ectopia lentis, and disproportionate long bone overgrowth [52]. The most common cardiovascular manifestation of MFS is ascending aorta dilatation at the level of the aortic sinuses [51]. Diagnosis is made using the revised Ghent criteria, which evaluates based on the presence of a dilated aorta, ectopia lentis, FBN1 mutation, systemic features of MFS, and family history [52, 53].

MFS would usually be suspected during pre-participation screening, as opposed to in-season, due to typical stigmata seen on physical exam.

The largest correctly measured aortic root diameter obtained from at least three transthoracic images should be corrected for body size and age and interpreted as a *Z*-score [52].

Individuals diagnosed with MFS typically have a transthoracic echocardiogram along with an ECG-gated CT scan of the entire aorta at the time of diagnosis followed by yearly echocardiograms to monitor; more frequently if the aortic diameter is approaching a surgical threshold [54]. Adults with repeatedly normal aortic root measurements may escalate to echocardiograms every 2–3 years [52]. Medication management with beta blockers, unless contraindicated, is the standard of care of prevention of complications, although there are research trials looking at other medications [52].

Prophylactic surgery should be considered when the aortic root diameter at the sinuses of Valsalva approaches 5.0 cm to prevent acute dissection of the ascending aorta which is a medical emergency [52].

Bicuspid aortic valve (BAV) is another often encountered aortic disease. It is one of the most common congenital heart defects with a prevalence of 0.5–2% in the general population [55–57] and may be associated with other aortic abnormalities such as aortic root and ascending aorta dilation, aneurysm, and coarctation [56, 57]. Aortic dilation can be found with BAV even in the absence of aortic valve stenosis or regurgitation and is believed to be due to abnormalities in the aortic media rather than primarily from hemodynamic alterations [56]. BAV may be suspected if a murmur is heard on physical exam, typically auscultated as an ejection murmur heart best at the apex. If symptoms present in-season, they are typically secondary to complications or associated conditions (i.e., aortic stenosis, aortic regurgitation, dissection).

Management of BAV consists of surveillance with serial echocardiography biannually or annually for those with aortic root diameters greater than 40 mm or valve lesions; medical therapy typically with beta-blockers to control blood pressure and reduce the pressure gradient across the valve, slowing progression of the disease; and surgical management for those meeting specific criteria [57].

One study showed ascending aortic dimensions were significantly larger in former National Football League (NFL) athletes compared to controls after adjusting for other factors; however, it is currently unknown if this translates to any increased risk [58].

Athletic participation decisions for those with abnormalities affecting the aorta should be made on an individual basis. A cardiologist experienced with athletes and an experienced cardiovascular surgeon should be consulted. Guidelines to consider when making a decision include the American Heart Association/American College of Cardiology (AHA/ACC) guidelines [59]. These guidelines recommend it is reasonable for athletes with MFS to participate in class IA and IIA competitive sports (see Table 15.2) provided they do not have any specified criteria placing them at higher risk [59]. In general, athletes with MFS should avoid contact sports and isometric activities involving a Valsalva maneuver [52], which precludes ASF.

The AHA/ACC guidelines [59] recommend athletes with BAV without a dilated aortic root or ascending aorta can participate in all competitive athletics. The function (stenosis, regurgitation) of the BAV also needs to be assessed. Athletes with BAV and dilated aortic dimensions should undergo serial aortic imaging to look for

progression. Athletes with BAV and a mild to moderately dilated aorta may consider participation in low and moderate static and dynamic competitive sports with a low likelihood of bodily impact [59]. Athletes with BAV and a more severely dilated aorta should avoid any competitive sports that involve the potential for bodily collision and may consider participation in class IA (see Table 15.2) sports [59].

Coronary Artery Anomalies/Coronary Artery Disease

Anomalous coronary arteries are an important cause of SCD in sport with more recent estimates at prevalence as the etiology of 11% of SCD in the National Collegiate Athletic Association (NCAA) while Coronary Artery Disease (CAD) was the etiology in 9% [1]. In a cohort including a wider age range of athletes from middle school to professional, coronary artery anomalies accounted for 15.7% of cases of SCD over a 2-year period while CAD accounted for 2.4% of SCD [10].

Anomalous coronary arteries are a heterogeneous group of congenital anomalies involving an aberrant anatomy as they arise from the aortic root and sinuses of Valsalva. In one study of 27 cases of SCD in young athletes with anomalous coronary arteries, 85% had the left main coronary artery aberrantly from the right aortic sinus [60]. All of the athletes died either during (93%) or immediately following intense exertion [60]. Only 37% of those athletes had experienced premonitory symptoms which included syncope and/or chest pain, and if experienced, symptoms occurred within 2 years of their death [60]. Only two of the symptomatic athletes underwent echocardiography and all of the cardiovascular testing done on the symptomatic athletes was normal [60].

If anomalous coronaries are suspected, an experienced cardiologist and cardiothoracic surgeon should be consulted.

Imaging is needed to diagnose anomalous coronary arteries. The best methods include computed tomography angiography (CTA), magnetic resonance angiography (MRA) or coronary angiography [61]. However, in one study of intercollegiate athletes, the origin and proximal course of the coronary arteries were reliably and readily observed on echocardiogram, suggesting that if echocardiogram is performed, the protocol should include assessment of the coronary arteries [62].

In general, athletes with an anomalous coronary artery should be restricted from sports, with the possible exception of class IA (see Table 15.2), pending surgical repair [61]. After surgical repair of an anomalous coronary artery from the wrong sinus, sports participation may be considered 3 months post-surgery if symptom free with a normal exercise stress test [61].

There is increased concern about football players having an increased incidence of cardiovascular disease (CVD) due to a high prevalence of obesity and early HTN [63]. These concerns are increased in lineman who engage in short repetitive bouts of intense static activity, with little aerobic conditioning. Studies have actually shown a lower rate of CVD risk factors and mortality in several overall cohorts of retired NFL players [64, 65] compared to controls; however, ASF athletes are a heterogenous group with different cardiovascular demands depending on their position. When a position subgroup of defensive linemen were examined, they had a 42% higher CVD mortality compared to controls [64]. Retired NFL linemen also

have shown a significant increased rate of moderate-to-severe subclinical atherosclerosis [66].

Athletes with CVD leading to CAD may present with chest pain, dyspnea, or decreased exercise tolerance, or they may experience "silent ischemia" seen only on provocative testing, or coronary artery calcification seen on imaging. The assumption for recommendations on participation in the risk of an exertion-related event is greater in those who have had a previous acute coronary syndrome [67].

As with all conditions, individual management and consultation with a cardiologist are recommended. General recommendations for athletes with atherosclerotic CAD include maximal exercise stress testing, an assessment of left ventricular (LV) function, and aggressive risk factor reduction including statin therapy to reduce the chance of plaque disruption [67]. Asymptomatic athletes with appropriate LV function, no inducible ischemia or electrical instability should generally be allowed to continue to participate in full ASF activity [67]. Symptomatic athletes, or those with impaired LV function, inducible ischemia or electrical instability should usually be restricted from ASF football, in addition to those <3 months out from an acute myocardial infarction or coronary revascularization procedure [67].

Electrical

Wolff-Parkinson-White Syndrome

Wolff-Parkinson-White syndrome (WPW) refers to ventricular pre-excitation which occurs due to one or more accessory pathways occurring between the atria and ventricles bypassing the atrioventricular (AV) node [68]. Sudden death can be provoked when atrial flutter and atrial fibrillation (AF) are rapidly conducted to the ventricle by the accessory pathway, triggering ventricular fibrillation (VF) [68, 69]. In one study looking at cause of SCD in NCAA athletes over a decade, WPW was responsible for 3% of deaths [1]. In another study on cause of sudden cardiac arrest/deaths (SCA/D) of competitive athletes 11–29 years of age, WPW was the etiology of 6.8% of cases. WPW syndrome can present with presyncope, lightheadedness, and palpitations caused by an atrioventricular reciprocating tachycardia (AVRT) or atrial tachycardia. It can also be diagnosed incidentally on an asymptomatic person on ECG done for screening or other purposes. The pathognomonic ECG findings include: (1) delta wave/slurred upstroke in the QRS complex, (2) short PR interval (<120 ms in adults) during sinus rhythm, (3) QRS duration >120 ms in adults, and (4) secondary ST and T-wave changes [70].

Once WPW is diagnosed, risk stratification must be performed to determine if an athlete has a high-risk pathway for lethal arrhythmias and sudden death or a low-risk pathway. Risk assessment is best completed through a referral to cardiology. Noninvasive tests used to help determine risk include echocardiogram (to look for structural heart disease associated with WPW), Holter monitor test (low risk if intermittent loss of pre-excitation at physiologic heart rates or high risk for multiple accessory pathway morphologies), and exercise stress test (EST) (low risk only with abrupt and complete loss of pre-excitation on EST) [68]. If a low-risk pathway

cannot be confirmed with noninvasive testing, electrophysiological evaluation should be undertaken with ablation of the bypass tract if it is deemed high risk for SCD [71].

Transcatheter ablation offers a potential cure for WPW and is recommended for high-risk pathways and symptomatic athletes. An athlete who has undergone an ablation and is asymptomatic with normal follow-up ECG can usually return to sport within 1 week [68]. Asymptomatic athletes with low-risk pathways should be monitored for development of new symptoms [68].

Atrial Fibrillation

Atrial fibrillation (AF) is the most commonly encountered clinically significant arrhythmia [72]. Risk factors for AF include increasing age, hypertension (HTN), hyperthyroidism, structural heart disease, male sex, tall stature, left atrial remodeling, increased vagal tone, alcohol intake, endurance sport, and total lifetime exercise dose of over 1500–2000 hours [72–75]. When AF is not associated with known medical disease, it is termed lone atrial fibrillation (LAF).

Endurance sporting activity is a known, well-established risk factor for the development of AF, but Mont and colleagues [76] showed that the cumulated hours of moderate- and heavy-intensity sport activity and moderate occupational physical activity were also significantly higher in lone AF patients than in controls. Symptoms of AF may include palpitations, lightheadedness, and weakness. Most athletes (70%) present with "vagal AF" that occurs during rest or sleep, post-exercise, and post-prandial [73, 76]. Exercise-provoked symptoms, seen with "adrenergic AF," are less common and can also include fatigue and reduced exercise capacity [73]. AF usually presents initially as paroxysmal, occurring infrequently, and is self-limited, progressing to more frequent and prolonged over the years and then to persistent AF [72].

Evaluation of all athletes with AF should include blood pressure, thyroid function tests, ECG, echocardiograms, drug use (including illicit and performance-enhancing), supplement use, and alcohol use. Some athletes may warrant further testing such as cardiac magnetic resonance imaging and stress testing.

Athletes with AF that is well tolerated and self-terminating may participate in all competitive sports without therapy [71]. The need for anticoagulation for stroke prophylaxis should be determined for athletes the same as the general population, using a risk score such as CHA_2DS_2-VASc score. Most athletes are at low risk. When antithrombotic therapy, other than aspirin, is indicated, it is reasonable to consider the bleeding risk of sport prior to making clearance decisions [71]. This would preclude a football athlete from being able to participate while on antithrombotic therapy due to high risk of bleeding.

Management of AF in athletes includes rate or rhythm control. Rate control is not ideal for athletes due to the need to elevate heart rate for athletic performance. Rhythm control can be achieved with medication or ablation procedures, and ablation should be considered due to some evidence of sustained benefit, particularly in paroxysmal AF, and the risk of side effects with antiarrhythmic drug therapy [71].

In some cases, a reduction of physical activity can stabilize sinus rhythm and allow athletes to resume training after several months [72].

Long QT Syndrome

Long QT syndrome (LQTS) is an inherited cardiac ion channelopathy with electrocardiographic manifestations of QT prolongation and increased susceptibility to life-threatening arrhythmias such as torsades de pointes and ventricular fibrillation [77, 78]. The estimated prevalence is 1 in 2000 individuals [79]. It was responsible for 1% of SCD in NCAA athletes over a 10-year period [1] and 6% of SCA/D in competitive athletes between 11 and 29 years old over a 2-year period [10].

There are 17 currently known gene mutations associated with LQTS, of these LQT1, LQT2, and LQT3 account for 75% of cases [78]. LQT1 patients have an increased susceptibility to events with physical exertion, especially swimming, and emotional stress [80]. LQT2 are most often triggered by emotional stressors, followed by sleep and auditory events (alarm clocks), while LQT3 are most susceptible to events during sleep [80].

Athletes with LQTS can present with palpitations, presyncope, syncope, and cardiac arrest, or may be detected asymptomatically with prolonged QTc (men >470 ms, women >480 ms) on ECG.

Per the HRS/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of Patients with Inherited Primary Arrhythmia Syndromes [81], LQTS can be diagnosed:

1. A. In the presence of an LQTS risk score ≥3.5 and in the absence of a secondary cause for QT prolongation

   B. In the presence of an unequivocally pathogenic mutation in one of the LQTS genes

   C. In the presence of a QT interval corrected for heart rate using Bazett's formula (QTc), ≥500 ms in repeated 12-lead electrocardiogram (ECG), and in the absence of a secondary cause for QT prolongation
2. In the presence of a QTc between 480 ms and 499 ms in repeated 12-lead ECGs in a patient with unexplained syncope in the absence of a secondary cause for QT prolongation and in the absence of a pathogenic mutation

All football athletes should be referred to a clinical (heart rhythm or genetic cardiologist) expert for an evaluation of risk [81].

Treatment of LQTS includes avoidance of QT-prolonging drugs; beta-blocker therapy with propranolol or nadolol is typically first-line treatment [77, 81]. Left cardiac sympathetic denervation (LCSD) is recommended for high-risk patients who cannot have either an implantable cardioverter-defibrillator (ICD) inserted or undergo beta-blocker therapy [81]. ICD is recommended for patients with LQTS who survive cardiac arrest [81].

It is recommended that suspected or symptomatic athletes from a cardiac channelopathy be restricted from sports until evaluation is complete, the patient and their family are well-educated about the treatment, the treatment is implemented, and the

athlete is asymptomatic on therapy for 3 months [82]. It is reasonable for an asymptomatic athlete with genotype-positive/phenotype-negative LQTS to participate in football and competitive sports with appropriate precautionary measures [82]. For an athlete with symptomatic LQTS or ECG-manifest LQTS, competitive football and sport may be considered after institution of treatment and appropriate precautionary measures if the athlete has been asymptomatic on treatment for at least 3 months [82].

Situational/Other

Hypertension

Hypertension (HTN) is a major risk factor for CVD [83]. ASF athletes have consistently demonstrated a higher level of HTN than the general population. Compared with healthy controls, active NFL players had significantly higher incidence of prehypertension and HTN [63]. In collegiate ASF athletes, one season of participation was associated with significant increases in systolic blood pressure (SBP) and diastolic blood pressure (DBP), with the lineman position being one of the strongest independent predictors of postseason BP [84]. In a separate study of collegiate ASF athletes, the linemen also demonstrated a significantly larger increase in SBP than non-linemen in addition to a decreased (impaired) global longitudinal strain (GLS), suggesting a maladaptive remodeling at the lineman position [85].

In 2017, the ACC/AHA updated their guidelines on HTN and lowered the values for diagnosis (Table 15.3). The diagnosis should be based on an average of ≥2 readings on ≥2 separate occasions, and those with SBP and DBP in separate categories should be placed in the higher category [83].

The renaming of BP categories was based on the interpretation of data of the benefit of lowering BP in CVD risk and the earlier identification and intervention, even if with non-pharmacological treatment [83].

To diagnose HTN, blood pressure should be measured after the patient has been made to sit in a chair for more than 5 minutes with feet on the floor, relaxed, with an appropriate-sized cuff that encircles 80% of the arm (too small cuff leads to falsely elevated reading), and an average of ≥2 readings obtained on ≥2 occasions should be used [83].

Secondary causes of HTN should be evaluated for the onset of HTN in an athlete <30 years old or in the setting of history and physical exam findings suggestive of a secondary cause. The most common secondary causes of HTN include renal disease

Table 15.3 Categories of blood pressure in adults [83]

Blood pressure category	SBP		DBP
Normal	<120 mmHg	AND	<80 mmHg
Elevated	120–129 mmHg	AND	<80 mmHg
Stage 1 HTN	130–139 mmHg	OR	80–89 mmHg
Stage 2 HTN	≥140 mmHg	OR	≥90 mmHg

(especially fibromuscular hyperplasia in women), primary aldosteronism, obstructive sleep apnea, and drug or alcohol induced [83].

Initial testing for primary HTN should include fasting glucose; complete blood count; lipid profile; renal function; serum sodium, potassium, and calcium; thyroid-stimulating hormone; urinalysis; and ECG, while optional testing can include an echocardiogram, urinary albumin-to-creatinine ratio, and uric acid test [83].

Non-pharmacologic therapies such as exercise and healthy diet are typically not effective in athletes as they are typically already engaging in these behaviors, and weight loss is typically undesirable in football athletes. However, football athletes should be educated about these as they may be able to incorporate healthier behaviors both during and after their football career.

Pharmacological therapy is recommended for primary prevention of CVD in adults with no history of CVD, <10% atherosclerotic CVD (ASCVD) 10-year risk with Stage 2 HTN, or with an ASCVD 10 year risk >=10% and Stage 1 HTN, or for secondary prevention of recurrent CVD events in patients wtih clinical CVD and Stage 1 HTN [83].

Angiotensin-converting enzyme (ACE) inhibitors or aldosterone receptor blockers (ARB) are typically a first-line medication of choice for treating HTN in athletes due to their lack of negative effect on exercise performance or hydration and electrolyte status seen in some of the other classes of medications such as beta blockers and diuretics [86]. ACE inhibitors block the enzyme which coverts angiotensin I to angiotensin II, producing a vasodilatory effect. ARBs block the receptor for type 1 angiotensin II, which leads to vasodilation, decreased aldosterone, and decreased renal reabsorption of sodium and water. The most common side effect of ACE inhibitors is a dry cough which can be occur in up to 10% of people. This does not occur with ARBs. Calcium channel blockers should be considered first line in black athletes as they were found to be more effective in this population [86]. They should also be considered first line in females of child-bearing age because of potential teratogenic effects of ACE inhibitors [87].

It is reasonable to consider restriction from high static activities such as those lineman participate in and weightlifting for those with an SBP >160 mmHg or a diastolic BP >100 mmHg until HTN is controlled [88].

Myocarditis

Myocarditis is an inflammatory heart muscle disease associated with cardiac dysfunction and histologically with inflammatory infiltrates associated with myocyte degeneration and necrosis [89]. It has both infectious and noninfectious etiologies [89]. The most common noninfectious etiology is the hypersensitivity type from acute drug-related injury while infectious causes can include viral (coxsackievirus, adenovirus, HIV, coronavirus), bacterial (streptococcus), rickettsial (typhus, rocky mountain spotted fever), fungal, and parasitic agents [89].

Myocarditis accounted for 9% of NCAA athlete's SCD over a 10 year period but 19% of football players [1] and 4.3% of SCA/D in competitive athletes between 11 and 29 years of age over a 2-year period [10].

Myocarditis may present in many different ways, from mild symptoms of chest pain and palpitations to life-threatening cardiogenic shock and ventricular arrhythmia [90].

Endomyocardial biopsy (EMB) is the gold standard to diagnose myocarditis; however, this is not always practical nor recommended by current guidelines [90].

The AHA/ACC Eligibility and Disqualification Recommendations for Competitive Athletes with Cardiovascular Abnormalities [42] recommends diagnosis of acute myocarditis based on the presence of two clinical criteria: (1) A clinical syndrome that includes acute heart failure, angina-type chest pain, or myopericarditis for a duration of <3 months and (2) an otherwise unexplained elevation in serum troponin; ECG features of cardiac ischemia; otherwise unexplained high-degree AV block or arrhythmias; wall motion abnormalities; pericardial effusion on echocardiography or CMR imaging. Additional CMR findings that suggest myocarditis in the acute clinical setting include characteristic alterations in tissue signal on T2 or T1 weighted images and the presence of late gadolinium enhancement (LGE).

Myocarditis has been linked to sudden death, and strenuous physical exertion appears to increase that risk [42]. Athletes with suspected or diagnosed myocarditis should not participate in competitive sports while active inflammation is present independent of age, gender, and LV function [42].

Per the AHA/ACC Eligibility and Disqualification Recommendations for Competitive Athletes with Cardiovascular Abnormalities [42] before returning to competitive sports, athletes suspected of having an acute myocarditis should wait a minimum of 3–6 months before undergoing a resting echocardiogram, 24-hour Holter monitor, and exercise ECG. It is reasonable to consider resuming training if all of the following criteria are met:

- Ventricular systolic function has returned to normal.
- Serum markers of heart failure, myocardial injury, and inflammation have normalized.
- Clinically relevant arrhythmias are absent of Holter monitor and graded exercise ECG.

Guidelines, Shared Decision Making, and Institutional Risk

Medical decisions related to participation in athletics with cardiac conditions can be complicated, with particularly high stakes, given that the outcome could potentially be death. There are some guidelines that exist to help guide the decision-making process.

There are two recent consensus guidelines advising those caring for athletes with cardiac conditions. The 2015 Eligibility and Disqualification Recommendations for Competitive Athletes with Cardiovascular Abnormalities and A Scientific Statement from the American Heart Association and American College of Cardiology [36, 42, 50, 59, 61, 67, 71, 82, 88, 91–96] which is an update to the 2005 36th Bethesda Conference guidelines [97]. The European Society of Cardiology (ESC) also

published guidelines in 2017 regarding Pre-participation cardiovascular evaluation for athletic participants to prevent sudden death [98].

Guidelines are just one factor a physician should consider while exercising best medical judgment, but should not be used in place of individualized recommendations regarding sports participation based on an athlete's medical short- and long-term best interests.

There are several precedent-setting cases involving student-athletes with cardiac conditions and medical disqualification. These specific cases involve basketball players but the principles apply to football athletes as well.

Knapp v. Northwestern University (cite) is a case in which a basketball student-athlete sued Northwestern University over the decision to medically disqualify him to play basketball at Northwestern due to a cardiac condition which had caused a previous cardiac arrest, claiming a violation of the Rehabilitation Act. The court ultimately ruled that a university has a legal right to establish legitimate physical qualifications for its student-athletes and Northwestern did not violate the Rehabilitation Act by accepting its team physician's reasonable medical determination [96].

It is required that a disqualification must have an individualized medical evaluation and a reasonable medical basis. An educational institution does not violate law in accepting its team physician's reasonable medical judgment or violate federal disability discrimination laws, even if other physicians disagree [96]. It is up to an individual institution to analyze the risk and make a medically reasonable decision.

Mobley v. Madison Square Garden LP (cite) is a separate case in which a federal district court ruled that Mobley, a former National Basketball Association player, may have a valid disability discrimination claim against the New York Knicks for his medical disqualification for hypertrophic cardiomyopathy during the 2008–2009 season, after having been medically cleared to play in 1999–2008 subject to his signing a liability waiver. The ruling in *Mobley* suggests it is possible some courts might consider an "athlete informed consent model" for professional athletes as opposed to the "team physician medical judgment model" seen in *Knapp* applied in a collegiate setting [96].

Ultimately, a physician has a duty to protect an athlete's health and safety, should provide sports participation recommendations based on best medical practice after an individualized assessment, and should not be forced to assume a medically unreasonable risk. There may be situations where a physician determines a cardiac condition does not carry a significant risk and medically clear the athlete to play. In these situations, written informed consent with the athlete, reviewing the possible risks of participation, is recommended.

Conclusions

Seemingly healthy football athletes may have cardiac disease ranging from hypertension to cardiovascular conditions that predispose to SCD. The incidence of SCD in football is higher than in most other sports except men's basketball. Screening for

cardiovascular conditions that predispose to sudden death is a primary objective of the PPE. History and physical examination is the recommended screening strategy, although its sensitivity is low. Given that football is higher risk, some programs, typically at the college or professional level, have elected to include ECG or other advanced cardiac testing, which improves the ability to identify cardiovascular issues. The risks, benefits, and resources available need to be considered when deciding upon a screening strategy. The best screening program will not identify all cardiac conditions; therefore, it is important that EAPs be in place where athletes practice and play. Knowledge regarding specific cardiac conditions affecting football players is important for those who provide care. The process of shared decision-making in those identified with cardiovascular conditions has evolved in an attempt to balance prudence with patient autonomy. Decisions involving returning to play after a cardiac diagnosis have led to legal precedent which is important to be aware of.

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