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My Approach to Sudden Death Risk Evaluation in Athletes, Who Should Play and Who Can Return to Play?

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Abstract

Purpose of Review Although the absolute risk of sudden death in the athlete is low, pre-articipation evaluation is an important opportunity to assess risk as well as establish a working relationship with the patient. In this chapter, we review the basis for our approach to pre-participation evaluation of an athlete.

Recent Findings To date, no randomized study has compared the additive benefit of the screening ECG; however, the false positive rate is now in an acceptably low range. Different imaging modalities and/or exercise stress testing may provide important adjunctive information.

Summary Thoughtful assessment of the athlete should account for exercise-induced adaptation and shared decision-making in challenging cases. Future research continues on distinguishing between the physiologic and pathologic changes in the athlete's heart. No matter what screening program is in place, a well-thought-out and well-rehearsed emergency action plan is paramount.

Keywords Athlete · Sudden death · Pre-participation · Exercise · Imaging · Electrocardiography

Introduction

Sudden death (SD) in any athlete greatly impacts families and communities and attracts immense media attention and public response. Although they are rare occurrences, exercise can serve as a trigger for SD events, especially in those with cardiovascular conditions, inherited or acquired. Thus, comprehensive risk stratification algorithms could mitigate risk. Genetics, race, gender/sex, level of training, type of sport, and concurrent medical conditions all factor into calculating risk. In general, the substrate for SD in young athletes < 35 years old is inherited channelopathies and/or cardiomyopathies; in older adults, the main culprit is coronary heart disease and/or associated comorbidities [1, 2].

In this chapter, we briefly review common causes of SD in athletes. We will also summarize our approach to pre-participation evaluation (PPE) and return to play decisions.

Sudden Death in Young Athletes

Calculation of the estimated incidence varies depending on methodology and population studied. The annual incidence of SD in athletes has been estimated at 0.5 in 100,000 athletes in Minnesota to 2.3 in 100,000 in Europe to 1:50,000 in US collegiate athletes [1, 3]. A recent study of soccer players in the UK reported an incidence of 6.8 deaths per 100,000 person years despite undergoing routine PPE that included ECG and echo [5]. SD among athletic young adults has been shown in some studies to be higher than nonathletes [5–7]. In an observational analysis by Corrado et al. [5], young adults involved in competitive sports had nearly a 2.5-fold higher risk of death compared to their age-matched cohorts of young adults who were not involved with competitive sports. However, in the study by Risgaard et al. [7], the higher risk in athletes was not observed. In a study of US collegiate athletes, male African-American basketball players represented the highest risk group [8]. This study by Harmon et al. also found, in line with

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data from the UK, that "autopsy-negative" was the most common finding at autopsy.

In athletes >35 years of age, coronary artery disease remains the most likely etiology, especially in males. Historically, the most common etiologies attributed to SD in younger athletes have been hypertrophic cardiomyopathy (US), arrhythmogenic right ventricular cardiomyopathy (Italy), coronary artery anomalies, aortic dissection secondary to Marfan's syndrome, channelopathies, conduction system abnormalities (e.g., Wolff Parkinson White syndrome), and valvular heart disease including aortic stenosis and mitral valve prolapse [9, 10]. Undiagnosed congenital heart disease is rare. Channelopathies involving cardiac ion channels include long QT syndrome, catecholaminergic polymorphic VT (CPVT), and Brugada syndrome. Commotio Cordis is an "acquired" potential cause of SD death whereby direct blow to the chest wall triggers VF and SD. Myocarditis has been increasingly recognized as a potential risk for SD events and, indeed, was the third most common cause in the study on US collegiate athletes [8]. In a seminal autopsy based paper on military recruit deaths, 51% had an identifiable cardiac anomaly and 35% remained unexplained; of the former group, 61% had coronary anomalies, 20% had myocarditis, and 13% had HCM [11].

Additional Conditions to Consider

In addition to the study by Eckart et al., more recent registry studies have also shown that nearly 40% of cases of SD do not have a clearly defined etiology [11–13]. Undiagnosed channelopathies and/or cardiac substrates (e.g., ventricular scar) that do not conform to commonly known etiologies are the probable causes.

Non-ischemic LV Myocardial Scar

In the study by Zorzi et al. from Italy [14], 35 athletes with non-ischemic LV scar identified by MRI were compared to 35 age-matched athletes without LV scar. After 3–5-year follow-up, the investigators noted that the athletes with LV scar had a significantly higher risk of malignant ventricular arrhythmias and SD compared to their counterparts without LV scar. They also noted that these scars are difficult to identify using echocardiography. From a recent pathology study [15], these scars are thin, with a gray rim of mid-myocardial or sub-epicardial gadolinium enhancements usually noted around the LV posterior wall. Pathologically, they represent fibrous and fibro-adipose tissue.

Subtle ECG changes may help identify these athletes. Low-voltage QRS (< 0.5 mv) may be seen [15]. If serial ECGs are available, then progressive decrease in QRS voltage may be observed over time [15]. Although this pathology is suspected be prevalent in 25% of athletes with SD, the ECG may not detect subtle signs of scar.

Mitral Valve Prolapse

Once considered a common benign variant with an estimated prevalence of 2% in the general population, mitral valve prolapse (MVP) is likely an underestimated etiology of SD. Several studies have reported an association between SD and MVP [16–18]. Nearly 0.5%/year of those with MVP are reported to have malignant arrhythmias, with 0.2%/year of them experiencing SD. Pathology studies have shown that myxomatous degeneration causing MVP was noted in 7% of SD victims. Inferobasal LV and papillary muscle fibrosis close to the posterior leaflet were noted in these SD victims [19, 20]. This fibrosis and subsequent scar can often be noted in gadolinium-enhanced MRI studies [18–20]. An athlete with MVP is often a young adult (most commonly female) and may present with mid-systolic click on auscultation, bileaflet involvement of the mitral valve on echocardiography, T wave abnormalities on inferior ECG leads, and/or ventricular arrhythmias with a right bundle branch block morphology on ECG monitoring [20]. LGE is not easily seen on the papillary muscles on cardiac MRI. A recent study demonstrated the promise of FDG-PET imaging in identifying inflammation or ischemia in the MV apparatus that accompanies fibrosis and scar [21].

Myocarditis

Inflammation of the heart, typically after a viral illness, can result in a substrate with increased predilection for ventricular arrhythmias. As mentioned earlier, in a seminal study of sudden death in presumably asymptomatic military recruits, myocarditis was implicated in about 20% of those with a cardiac structural abnormality, representing about 10% of all cases [11]. Patients may present with flu-like or heart failure symptoms. ECG changes might include sinus tachycardia, PVCs, T wave inversions, diffuse ST elevation (concave pattern), and diffuse PR segment depression. Follow-up cardiac biomarkers, ECG, and echocardiogram findings should all be within normal prior to resumption of activity, usually after at least 3 months after initial diagnosis [22]. Cardiac MRI can be useful for detecting sub-acute inflammation as well as long-term fibrotic changes [23•]. Any findings of residual scar or fibrosis will have to be taken into account in return to play decisions.

Pre-participation Evaluation

The pre-participation evaluation (PPE) is an important opportunity to engage the athlete with the medical team, discuss

lifestyle choices, and assess mental health needs. At the heart of the PPE is assessment of risk of sudden cardiac death due to known, suspected, and/or newly discovered cardiovascular disease. Several societal guidelines, including those from the American Heart Association (AHA) and European Society of Cardiology (ESC), recommend pre-participation screening for young adults [19, 20, 24]. However, the ESC recommends the addition of the 12-ECG as part of the PPE. A detailed history and thorough physical exam should be the key component of any PPE and offers a pragmatic approach. However, most young athletes are healthy and often have limited prior history of illness, symptoms, and/or signs. A systematic review highlighted the significantly higher sensitivity of the ECG for detecting potential cardiovascular conditions [19]. Family history can raise red flags and identify those who might need further workup. However, on the condition and penetrance of disease, family history may also not be so helpful. Physical exam can identify conditions such as HCM, MVP, aortic stenosis, Marfans syndrome, and coarctation of the aorta, but the overall sensitivity is low in athletes [19].

For the better part of the last 3 decades, the role and implementation of the 12 lead ECG in the PPE has greatly evolved. A 12-lead ECG significantly enhances screening for channelopathies including long QT, short QT, Brugada, and pre-excitation [19]. Other conditions with limited sensitivity include HCM, ARVC, DCM, and LVH. The most compelling evidence for using the ECG as a pre-participation tool comes from Italy. A 26-year follow-up study (1979–2004) from the Veneto region in Italy showed a significant decline in mortality rates after implementation of a nationwide screening program [24]. There was a remarkable reduction of 89% in SD among athletes (3.6 per 100,000 athlete-years in the pre-screening period (1979–1981) to 0.4 per 100,000 athlete-years in the late-screening period (1993–2004)). The incidence of SD in unscreened non-athletic adult population remained unchanged in this time period. That said, most of the reduced death rate in screened athletes was due to fewer cases of SD from cardiomyopathies (HCM and ARVC) and there was a parallel increase of the number of asymptomatic athletes diagnosed with cardiomyopathies at pre-participation screening during the same time period. Also, awareness of SD in the athlete and emergency action planning improved during this time frame. Furthermore, no randomization was performed comparing H&P alone versus H&P with ECG. So the reduction in SD reported in the Italian study might have been an overestimation of the effect [25]. Since 1997, the ECG has been a mandated component of the PPE in Israel, yet the annual incidence of SD in athletes has remained similar [26]. Data collection concerns may have impacted the reliability of this study.

A common criticism of the ECG as a screening tool has been the potential of false positives. Past iterations of athlete-specific ECG recommendations had unacceptably high false positive rates [27]. However, the International Recommendations on for ECG interpretation in athletes published in 2017 has significantly decreased the rate of false positives to <4% [28, 29]. As mentioned above, echocardiogram is effective to identify structural cardiac pathologies including valvular heart disease like MVP, HCM, and some cases of ARVD. However, it is limited in its ability to identify mid-myocardial and epicardial scarring in which case MRI studies with gadolinium contrast may be of immense value. Use of MRI may be used on a case by case basis to evaluate cardiac structure and function, scar, the aorta, and coronary anatomy. MRI might evolve as an important screening tool in the future but will require normative data in athletes. In one study of 93 endurance athletes, focal late gadolinium enhancement (LGE), the RV insertion/hinge point was 10-fold more likely in highly trained athletes compared to healthy controls [30•].

In older adults, the resting ECG has a limited role as a pre-screening tool because of its limited ability to identify coronary artery disease. Exercise stress testing is considered a valuable tool in this age group because of its ability to screen for CAD, being cost-effective and being readily available. However, the specificity of exercise stress testing depends on pre-test probability. In a general population, the yield may be low but in individuals with several CV risk factors. Accorded to current standards, pre-participation risk assessment in adults follows a European society SCORE risk (based on age, sex, blood pressure, blood cholesterol, and smoking history). Stress testing with or without adjunctive imaging should be reserved for older adults with multiple CV risk factors and those planning intense exercise programs.

An athlete who reports exertional symptoms, however, might warrant early workup via functional exercise stress testing. Ideally, the form of exercise (e.g., running, bicycle) is chosen to best match the primary form of exercise. In addition to risk assessment for coronary artery disease, exercise testing can evaluate:

- exertionally induced symptoms (e.g., palpitations, dyspnea, angina, near syncope)
- functional tolerance and chronotropic competence
- catecholaminergic polymorphic VTs or other exercise-induced arrhythmia
- exercise-induced valvular dysfunction and/or exercise-induced pulmonary hypertension
- cardiorespiratory fitness if VO2 max testing added
- robustness of an accessory pathway noted on ECG if clear disappearance of the delta wave is noted [31]
- blood pressure response to exercise

In general, the exercise stress test can provide a picture of fitness, which has been associated with risk of SCD. Adjunctive imaging, such as echocardiogram (echo) or

nuclear imaging, may be added to increases sensitivity and specificity of diagnosing CAD. Stress echo can also be useful for evaluating for potential causes of dyspnea on exertion, such as exercise-induced LVOT obstruction, valvular regurgitation, pulmonary hypertension, and intracardiac shunting.

The blood pressure (BP) response to exercise should be assessed during the exercise stress test. Any drop of 20 mmHg or more from baseline during the test warrants cessation of the test and could reflect obstructive HCM or valvular heart disease. Athletes can have an exaggerated BP response owing to sympathetic tone, endothelial dysfunction, increased aortic stiffness, and activation of the renin-angiotensin-aldosterone cascade [32]. However, a response in the highest quartile, defined in one study as a systolic blood pressure >183 mmHg, portended a 2.6-fold higher risk of developing systemic hypertension (32).

Conclusions

Pre-participation evaluation represents an important opportunity to assess risk as well as establish a working relationship with the patient. While no randomized study has been performed to compare the additive benefit of the screening ECG, the false positive rate is in an acceptably low range. Different imaging modalities and/or exercise stress testing may provide important adjunctive information. No matter what screening program is in place, a well-thought-out and well-rehearsed emergency action plan is paramount. Future research continues on distinguishing between the physiologic and pathologic changes in the athlete's heart.

Our Practical Approach

Step 1: Detailed history

- Inquire about unexplained syncope and/or exertional symptoms such as chest pain, palpitations, and dyspnea
- Inquire about family history of sudden cardiac death, inherited disease (e.g., LQT, Brugada, HCM, ARVD, MVP, early coronary disease)

Step 2: Thorough physical exam

- Assess for features suggestive of Marfan's syndrome
- Ausculate heart, assess for murmurs, gallops, arrhythmia

Step 3: ECG

- Refer to International Recommendations for ECG Interpretation
- If palpitations reported, consider ambulatory ECG monitoring

Step 4: Cardiac imaging

- Consider if appropriate based on findings from steps 1 to 4
- Obtain echocardiogram, cardiac magnetic resonance imaging as appropriate

Step 5: Exercise stress test

- Assess exercise-induced symptoms and/or arrhythmia; try to duplicate primary mode of exercise if possible (running vs bicycle)
- Assess for catecholaminergic polymorphic VTs, other exercise-induced arrhythmia (PVCs, supraventricular tachycardia)
- Assess functional tolerance and chronotropic competence
- Risk stratify accessory pathways noted on surface ECG [30•]
- Risk stratify patients at risk for significant coronary artery disease
- Consider adjunctive imaging or VO2 assessment if indicated

Step 6: Shared decision discussion

- Review data with patient; discuss known and unknown risks associated with data and sport of choice
- Jointly discuss next steps or reassurance with relevant stakeholders

Compliance with Ethical Standards

Conflict of Interest Eugene H. Chung, MD, and Ghanshyam Shantha, MD, MPH, declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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