Defining the Limits of Athlete's Heart
Implications for Screening in Diverse Populations

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Whereas consensus exists on the need for preparticipation examinations in young athletes, the best approach to such screening is debated. Preparticipation examinations help athletes avoid musculoskeletal injury and repeated concussion, but most attention is focused, understandably, on the avoidance of sudden cardiac death. To this end, in the United States, a brief clinical examination and questionnaire focusing on symptoms and family history (Table 1) are recommended by the 36th Bethesda Conference guidelines.[1–3] Meanwhile, the International Olympic Committee and the European Society of Cardiology, drawing from the 25-year Italian experience,[4] have recommended the inclusion of a 12-lead ECG in the preparticipation examination of young athletes.[5–7] Debate surrounding these different approaches focuses on cost, effectiveness, differences in cause distribution in different countries, and the consequences of false-positive ECG findings.[3,8] In relation to the last, whereas cost-effectiveness analysis can account for financial implications of secondary testing, the psychological burden is harder to quantify. Indeed, even between studies, the percentage of athletes screened with ECG who are deemed to require follow-up varies widely. In the Italian experience, 8% of athletes qualified for secondary screening,[4] whereas an earlier US study with 501 athletes suggested a secondary screening rate as high as 15%.[9] In the largest study to date, Pelliccia et al reported that 4.8% of 32 642 athletes exhibited findings classified as "distinctly abnormal" on ECG.[10] In fact, others have reported a follow-up rate as low as 1.5% with adapted ECG criteria.[11] In this context, the consistent and accurate definition of "normal" becomes paramount.

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It is against this background that we view the most recent data from Rawlins and coauthors in this issue of *Circulation*.[12] These authors compared 240 nationally ranked black female athletes with 200 white female athletes from two countries, France and the United Kingdom. Participants were well matched for age, body size, and sport. The findings are important for several reasons. First, the data serve as a starting point to correct the overrepresentation of data from white male athletes in the existing literature. Second, these authors noted that matched black female athletes showed a higher prevalence of early repolarization on the ECG and greater echocardiographic left ventricular hypertrophy. In particular, mean maximal wall thickness and left ventricular mass were 0.6 mm and 15 g greater in the matched black athletes, respectively. Finally, in a multivariate model, only ethnicity and age were significant independent predictors of left ventricular wall thickness. Of importance, both height and weight were also greater in the black athletes, although *P* values only approached significance for this comparison.

These findings are of particular importance because of the increasing discussion relative to the use of the ECG to screen athletes for silent cardiovascular disease. The key challenge in such screening examinations is the distinction of normal from abnormal. Currently, little account is taken of body size, sex, ethnicity, or sport in the determination of "normal." Yet, life-altering decisions are made on the basis of our current definitions. For example, although scaling for body size is routine in pediatric clinical practice, it is uncommon in adult medicine despite a similar body size range over which values are assessed.[13] Furthermore, the inadequacy of body surface area equations derived from a small number of cadavers to factor out the effect of size often goes unnoticed. More robust correction for body size, with the use of allometric scaling indices and fat-free mass,[14] is challenging in everyday clinical practice but relatively easy to apply to large populations of consecutively screened athletes. In addition, sport-specific changes in the ECG have recently been reported: percentages of abnormal ECG were highest for participants in football, track and field, and rowing and lowest in sailing and floor sports.[15] Finally, an understanding of differences such as those between men and women[8,9] and different ethnicities will serve to limit false-positive results in the future.

Others have examined the effect of ethnicity on ECG changes in athletes and have observed results consistent with those in the current study. Magalski and coauthors examined 1959 American football players and observed that electrocardiographic abnormalities were twice as common in black as in white male athletes.[16] In multivariate analysis, ethnicity was an independent determinant of ECG pattern. In a recent analysis of young athletes in Africa undergoing preparticipation surveys with screening ECGs, nearly a quarter of the athletes were found to have abnormal ECGs.[17] Even among different ethnicities of Africans, there was considerable variation in the ECGs. Such changes mirror but do not necessarily explain the differences in prevalence of sudden cardiac death in these different groups.[18] In a large registry study of sudden death in young athletes,[18] the absolute

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Table 1. Medical History*

Personal history
Exertional chest pain/discomfort
Unexplained syncope/near-syncope†
Excessive exertional and unexplained dyspnea/fatigue, associated with exercise
Previous recognition of heart murmur
Elevated systemic blood pressure
Family history
Premature death (sudden and unexpected, or otherwise) before age 50 years due to heart disease, in ≥1 relative
Disability from heart disease in a close relative <50 years of age
Specific knowledge of certain cardiac conditions in family members: hypertrophic or dilated cardiomyopathy, long-QT syndrome or other ion channelopathies, Marfan syndrome, or clinically important arrhythmias
Physical examination
Heart murmur‡
Femoral pulses to exclude aortic coarctation
Physical stigmata of Marfan syndrome
Brachial artery blood pressure (sitting positions)§

The 12-Element AHA Recommendations for Preparticipation Cardiovascular Screening of Competitive Athletes.[2]

*Parental verification is recommended for high school and middle school athletes.

†Judged not to be neurocardiogenic (vasovagal); of particular concern when related to exertion.

‡Auscultation should be performed with the individual in both supine and standing positions (or with Valsalva maneuver), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction.

§Preferably taken in both arms.

Table 2. European Society of Cardiology Updated and Simplified Guideline for the Use of the ECG in Screening Athletes

Group 1: common and training-related ECG changes	Group 2: uncommon and training-unrelated ECG changes
Sinus bradycardia	T-wave inversion
First-degree AV block	ST-segment depression
Incomplete RBBB	Pathological Q-waves
Early repolarization	Left atrial enlargement
Isolated QRS voltage criteria for left ventricular hypertrophy	Left-axis deviation/left anterior hemiblock
	Right-axis deviation/left posterior hemiblock
	Right ventricular hypertrophy
	Ventricular preexcitation
	Complete LBBB or RBBB
	Long- or short-QT interval
	Brugada-like early repolarization

RBBB indicates right bundle-branch block; LBBB, left bundle-branch block. Classification of abnormalities of the athlete's electrocardiogram.[7]

number of presumed cardiovascular deaths reported was higher in white than in black athletes (not controlled for participation). However, despite this, deaths due to recognized diseases, including hypertrophic cardiomyopathy and congenital coronary anomalies, were more common in nonwhite than in white athletes, whereas deaths attributed to ion channelopathies were higher among white athletes.

In addition, differences between the sexes in the prevalence of sudden death in sport are well recognized, with some authors finding a 9:1 ratio of male to female deaths.[18,19] This dramatic difference, though previously noted, remains unexplained, although it is clear that morphological changes are reflected differently in the ECG in men and women.[20] Sexual dimorphism has in fact been reported in relation to genetic heart muscle disease in humans and animal models.[21,22]

In an attempt to make more consistent the approach to ECG screening, the European Society of Cardiology recently published an updated and simplified guideline for the use of the ECG in screening athletes (Table 2). Corrado and coauthors [7] divided ECG changes into 2 groups: (1) common and training-related ECG changes and (2) uncommon and training-unrelated ECG changes. This is an evolution from the system adopted widely but informally from Pelliccia et al,[10] which divided ECG changes into 3 groups: (1) normal or with mild alterations, (2) mildly abnormal, and (3) distinctly abnormal. The key features of both schemata relate to the recognition that isolated voltage criteria for left ventricular hypertrophy and early repolarization are likely to be benign and training mediated.

The increasing adoption of ECG screening in sport increases the pool of normal ECGs from which to derive estimates of normal; however, a caveat to the current work that also applies to most of the literature in this area is that the ultimate goal is not to define normal but to distinguish most effectively between 2 populations, one of which is highly underrepresented in these studies (the abnormal group). Indeed, the lower the rate of true positive results in a given study, the less the study has to offer in this regard. An important group of future studies will be those in which results from a large number of individuals with disease are reported and compared with the much larger existing databases of ECGs in athletes. Whereas young patients recruited from clinics may not be the most accurate representation of high-functioning athletes who harbor silent disease, this is likely to be the most appropriate and accessible group to study. Such data would allow much more confidence in our ability to detect abnormalities with high sensitivity and specificity.

Increasing application of ECG screening also offers the potential for digital data collection and analysis. In the present work, ECG interpretation was carried out manually by the use of calipers. Although humans excel at pattern matching, computer algorithms are better able to quantify small changes in voltage, time, their first derivatives, or integrals. It is possible that statistical analysis of digital ECG data will improve our discrimination between normal and abnormal. However, this will once again require ECGs from large cohorts, not just of athletes but of patients with conditions known to be associated with sudden death.

It is interesting to speculate on the underlying biological basis for the ethnic differences observed in this study. Human genetics studies[23] reveal that self-reported ethnicity accurately reflects underlying genetic cluster membership, which suggests that ECG differences such as those described here may have a genetic basis. In the current era, where genome-wide, chip-based tools to quantify common genetic variations are widely and cheaply available and where sequencing costs are declining dramatically, it is disappointing that so few large studies have focused on the genetic basis of myocardial adaptation. In the most important study focused on the genetic basis of cardiac structure and function published to date, Vasan et al identified 16 genetic loci associated with 5 echocardiographic traits[24] in participants of European descent. Although some small studies have suggested biological differences between different ethnic groups—for example, in the sensitivity of activation of the renin-angiotensin system—we await the more definitive high-throughput genetic studies that will inform the biological basis for population differences in myocardial adaptation.

In conclusion, the new data from Rawlins and coauthors move us forward in our understanding of the limits of athlete's heart. With this in hand, we may be able to reduce further the false-positive rate of screening ECGs in diverse populations. In addition to race and sex, accounting for body size and sport, and considering a transition toward digital ECG processing, will likely allow a much clearer differentiation between normal and abnormal for the future benefit of young athletes around the world.

Disclosures

None.

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