The heart of the athlete has intrigued cardiologists since the original description of increased cardiac dimensions in elite Nordic skiers more than a century ago.1 Athletes exhibit structural and electric cardiac abnormalities that mimic findings associated with cardiovascular disease.2 Some early observers regarded the heart of a conditioned athlete as weakened by strenuous training and thereby subject to progressive deterioration in function.3 Structural findings include chamber enlargement and ventricular hypertrophy.2,3 Electric abnormalities include increased QRS voltage, abnormal Q waves, and T-wave inversions.2,3 Currently, the athlete’s heart is regarded as a benign increase in cardiac mass with circulatory and morphological alterations in response to athletic training.2,3 Contemporary evidence supports the notion that this represents adaptive physiology, not preclinical disease.2,3 Despite considerable advances in diagnostic tests, significant challenges remain in differentiating the athlete’s heart from some types of cardiac disease.2–4 ECG and morphological changes found in athletes can mimic findings of hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular (RV) cardiomyopathy (ARVC), and other cardiovascular diseases.2–4 The absence of a definitive diagnostic test or gold standard for many cardiovascular common results in diagnostic uncertainty.2–4

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This overlap of normal and abnormal findings has represented a clinical challenge because diagnostic criteria lacked sufficient sensitivity and specificity to reliably distinguish physiological enlargement of the athlete’s RV from ARVC.5 The importance of this distinction is underscored by the fact that in the United States, ARVC is responsible for 4% of cases of athletic sudden deaths.2 Sudden deaths are attributed to ARVC in 22% of athletes in the Veneto region of Italy.2 Because of the recognized shortcomings of the 1994 International Task Force Criteria for the diagnosis of ARVC, a revised set of diagnostic criteria were developed recently.5,6 The revised criteria increase the sensitivity for early disease and refined ECG criteria.5,6 The additional diagnostic criteria are related to genetic testing, imaging (3-dimensional echocardiography and magnetic resonance imaging [MRI]), and electroanatomic mapping.6

The criteria were developed by analyzing quantitative MRI, echocardiographic, signal-averaged ECG, and Holter monitor data from 108 patients with newly diagnosed ARVC who were enrolled in the National Institutes of Health–funded Multidisciplinary Study of Right Ventricular Dysplasia.6 Comparing the data with data from normal subjects resulted in extensive modification of the diagnostic criteria.6 Strict MRI and echocardiographic quantitative measures were introduced in both major and minor criteria.5 Specific criteria for myocardial biopsy positivity were delineated.6 To fulfill a major RV morphological criteria, quantitative MRI or echocardiographic abnormalities must be accompanied by RV akinesia, dyskinesia, or aneurysm.6 Inverted T waves in the ECG precordial leads were elevated from minor to major criterion, and ARVC confirmed in a first-degree relative was also made a major diagnostic criterion for diagnosis.6 However, there remains no gold standard for the diagnosis of ARVC. Because of the segmental nature of the disease, biopsy carries a very high false-negative rate resulting from sampling with the risk of perforation.6 On the basis of these considerations, transmural biopsy is not performed in most patients being evaluated for ARVC.

Previous reports have noted that abnormalities of the RV are present in trained athletes.7–9 In a study comparing 40 athletes with 40 control subjects and 40 subjects with ARVC, the athletes exhibited significant enlargement of the RV.7 These athletes had RV outflow tract enlargement and a reduced RV ejection fraction, and no athlete had T-wave inversion beyond V1 on the ECG.7 Thus, none of the athletes met ECG criteria for the diagnosis of ARVC.7 Data from preparticipation screening of competitive athletes from northeast Italy revealed an incidence of T-wave inversion in subjects >14 years of age of 1.4%.8 In a separate study, 154 African players exhibited a greater incidence of ECG T-wave inversion compared with 62 white competitive soccer players.9 The incidence of this finding in leads V5 through V6 was 6% in the African players.9

In the current issue of Circulation, Zaidi et al10 compared the ECGs and RV echocardiographic data of 300 consecutive black athletes with data from 375 white athletes and 153 control subjects.10 The control group consisted of a similar proportion of blacks who were not athletes.10 Anterior T-wave inversion (leads V5–V6) was more common in black athletes (14.3%; P = 0.001) compared with either white athletes or control subjects of either race.10 Both black and white athletes had greater RV dimensions compared with control subjects of the same ethnicity, including RV outflow tract dimensions.10 Compared with white athletes, black athletes had significantly lower values for all 3 measures of RV

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outflow tract dimensions and RV longitudinal dimensions.10 On echocardiogram, 4 white and 4 black athletes had RV apical wall motion abnormalities on the apical 4-chamber view.10 The combination of T-wave inversion in V1 through V3 and RV dilation meeting the modified ARVC diagnostic criteria occurred in 3% of black athletes and only 0.3% of white athletes.10 To meet the revised criteria for a diagnosis of ARVC, RV wall motion abnormalities needs to accompany dilatation.6 Only 2 of the 4 black athletes with RV wall motion abnormalities on echocardiogram had the combination of all 3 findings (wall motion abnormalities, RV dilatation, and T-wave inversion).10 Cardiac MRI of those athletes revealed normal RV wall motion, thereby excluding the diagnosis of ARVC. The authors conclude that highly trained athletes, regardless of ethnicity, exhibit RV enlargement, but because of the higher incidence of T-wave inversion in V1 through V3 in black athletes, the potential for erroneous diagnosis of ARVC exists.10

The authors should be commended for extending previous observation with emphasis on this issue. It is evident that despite advances in diagnostic criteria, gray zones persist in distinguishing physiological adaptation from cardiac disease in highly trained athletes.4 This dilemma commonly arises for the cardiologist in distinguishing hypertrophic cardiomyopathy from the athlete’s heart.2–4 With the findings of Zaidi et al, it is clear that there also is a considerable potential for erroneous diagnosis of ARVC in black athletes.10 As is the case in cardiovascular trials and registries, there was underrepresentation of minority groups in the ARVD registry.10,11 The Zaidi et al study serves to highlight the higher incidence of suggestive findings for ARVC in highly trained black athletes, primarily because of the observed higher incidence of T-wave inversion in V1 through V3.10 It is important to emphasize that despite ECG findings suggestive of ARVC, none of the subjects in the study met the contemporary diagnostic criteria for ARVC.10

This study brings to the forefront the importance of understanding the methodology and limitations of developing diagnostic criteria for ARVC and many other clinical entities on the basis of registries. Sensitivity and specificity are considerably worse when these criteria are applied to an asymptomatic population with a low prevalence of ARVD. Major and minor criteria for ARVC were selected on the basis of statistical analysis of the data from the 108 probands with diagnosed ARVC and control subjects.10 Major criteria were selected that yielded 95% specificity of diagnosis.4 In general, highly specific criteria or tests are best used in a confirmatory role, in which false negatives are preferable to false positives. In contrast, highly sensitive tests are best used in a screening role, in which false positives are preferable to false negatives.4 Minor criteria were selected that yielded equal sensitivity and specificity.4 The sensitivity and specificity of the criteria are based on the findings in the 108 probands in the ARVC registry who were recently diagnosed with the condition.10 In such a group, the pretest probability of ARVC approaches 100%.4

The sensitivity and specificity of the revised criteria not only depend on the population to which they are applied but also are heavily dependent on the control populations with which the criteria were developed. The control subjects who generated the reference values for the revised criteria come from centers with expertise in the diagnostic test. For example the echocardiographic data were derived from 450 normal subjects in Boston, MA, and Padua, Italy. The authors of the revised guidelines caution that the reference values may not apply to all ethnic populations.10 When the revised criteria are applied to a population with a low (nearly zero) pretest likelihood of ARVC such as in the Zaidi et al study, a larger number of false positives would be expected.10 This represents a vexing clinical issue for a disease that has no diagnostic gold standard. The affected asymptomatic individual with no family history who screens positive or has suggestive findings can be left in diagnostic limbo and excluded from athletics. Even with the knowledge that the Zaidi et al study provides, screening such patients would result in costly further testing and diagnostic uncertainty.

Zaidi and colleagues note that in black athletes without concomitant symptoms or family history, T-wave inversion and RV enlargement may be a benign finding.10 Recognition of this has the potential to reduce the burden of investigations after preparticipation screening and to prevent erroneous disqualification from sport.10 A logical extension of these findings is that screening black athletes with an ECG and echocardiogram meeting the criteria for ARVC could lead to inappropriate diagnosis.10 None of the black athletes in this study fulfilled 2 major criteria required for a diagnosis of ARVC, so the risk of missing true ARVC cases by not screening in this population is very low.10 Of particular importance are the echocardiographic wall motion abnormalities found in the 2 black athletes that would have completed the 2 major criteria for ARVC diagnosis. These were not confirmed on subsequent MRI.10 As the authors point out, visual assessment of RV wall motion on echocardiogram may lead to false positives.10 It is evident that MRI has assumed an important role in establishing a diagnosis of ARVC.

The report by Zaidi et al has important clinical implications that merit emphasis. Use of the ARVC diagnostic criteria as an ECG screening tool in a population with a low prevalence of the disease will reduce the specificity of the criteria and result in a higher number of false positives. This holds particularly true in black athletes.10 The potential for additional expensive testing and inappropriate exclusion of a significant number of young athletes from participation in sports is evident. The ARVC diagnostic criteria were not developed to be applied to subgroups such as black athletes. Black athletes with symptoms possibly attributable to cardiovascular disease or those with a family history of ARVC or sudden cardiac death who have precordial T-wave inversion and RV enlargement may ultimately end up in the gray zone of diagnostic uncertainty. Clinicians should remain mindful that the higher incidence of RV enlargement and ECG T-wave inversion in black athletes represents physiological adaptation rather than cardiac pathology.

Disclosures
None.
References


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The Heart of an Athlete: Black, White, and Shades of Grey With No Gold Standard
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