Contemporary Reviews in Cardiovascular Medicine

The Heart of Trained Athletes

Cardiac Remodeling and the Risks of Sports, Including Sudden Death

Barry J. Maron, MD; Antonio Pelliccia, MD

Young competitive athletes are widely regarded as a special subgroup of healthy individuals with a unique lifestyle who are seemingly invulnerable and often capable of extraordinary physical achievement.[1–3] For more than 100 years, there has been considerable interest in the effects of intense athletic conditioning on the cardiovascular system.[4–27] The advent of echocardiography more than 30 years ago provided a noninvasive quantitative assessment of cardiac remodeling associated with systematic training, and consequently, a vast body of literature has been assembled that is focused on the constellation of alterations known as "athlete's heart."[4–27]

Athlete's heart is generally regarded as a benign increase in cardiac mass, with specific circulatory and cardiac morphological alterations, that represents a physiological adaptation to systematic training.[1,6–27] However, the clinical profile of athlete's heart has expanded considerably over the last several years as a result of greater accessibility to large populations of trained athletes studied systematically with echocardiography, ECG, cardiac magnetic resonance, and ambulatory Holter ECG monitoring. As a consequence, there is increasing recognition of the impact that prolonged conditioning has on cardiac remodeling, which may eventually mimic certain pathological conditions with the potential for sudden death or disease progression.

Over the last several years, sudden deaths of trained athletes, usually associated with exercise, have become highly visible events fueled by news media reports and with substantial impact on both the physician and lay communities.[1,28–36] Interest in these tragic events has accelerated owing to their increased recognition; awareness that underlying, clinically identifiable cardiovascular diseases are often responsible; and the availability of treatments to prevent sudden death for high-risk athlete-patients. In the present review, we offer a comprehensive assessment of many issues that target the interrelation of intense physical exertion with cardiac structure and function, as well as the rare, potentially adverse consequences of sports.

Athlete's Heart

Historical Perspectives

The concept that the cardiovascular system of trained athletes differs structurally and functionally from others in the normal general population remarkably extends over a century.[4] During that time, there has also been periodic controversy about the true nature of athlete's heart, ie, whether the findings are physiologically adapted, benign, and related only to training, or alternatively are potentially pathological and the harbinger of disease and disability.

The clinical entity of athlete's heart has been defined with increasing precision using a variety of techniques. Henschen is credited with the first description in 1899, using only a basic physical examination with careful percussion to recognize enlargement of the heart caused by athletic activity in cross-country skiers.[5] Henschen concluded that both dilatation and hypertrophy were present, involving both the left and right sides of the heart, and that these changes were normal and favorable: "Skiing causes an enlargement of the heart which can perform more work than a normal heart."[5]

Subsequent investigators used quantitative chest radiography to show that heart size was increased in athletes, particularly those engaged in endurance sports with large aerobic requirements. Some early observers even regarded the heart of the trained athlete to be weakened owing to the "strain" created by continuous and excessively strenuous training and believed that athletes were subject to deteriorating cardiac function and heart failure.[4]

Physiology

Cardiovascular adaptations to exercise have been systematically defined and differ with respect to the type of conditioning: endurance training (sometimes also described as dynamic, isotonic, or aerobic) such as long-distance running and swimming; and strength training (also referred to as static, isometric, power, or anaerobic) such as wrestling, weightlifting, or throwing heavy objects.[37] Sports such as cycling and rowing are examples of combined endurance and strength exercise. Most athletic disciplines to some extent combine endurance and strength modes of physical conditioning, and training-related physiological alterations represent a complex set of central and peripheral mechanisms operating at structural, metabolic, and regulatory levels.

Acute responses to endurance exercise training include substantial increases in maximum oxygen consumption, cardiac output, stroke volume, and systolic blood pressure,

From the Hypertrophic Cardiomyopathy Center, Minneapolis Heart Institute Foundation, Minneapolis, Minn, and the Institute of Sports Medicine and Science, Rome, Italy.

Correspondence to Barry J. Maron, MD, The Hypertrophic Cardiomyopathy Center, Minneapolis Heart Institute Foundation, 920 East 28th St, Suite 60, Minneapolis, MN 55407. E-mail hcm.maron@mhif.org

(*Circulation.* **2006;114:1633-1644.**)

Circulation **is available at http://www.circulationaha.org** **DOI: 10.1161/CIRCULATIONAHA.106.613562**

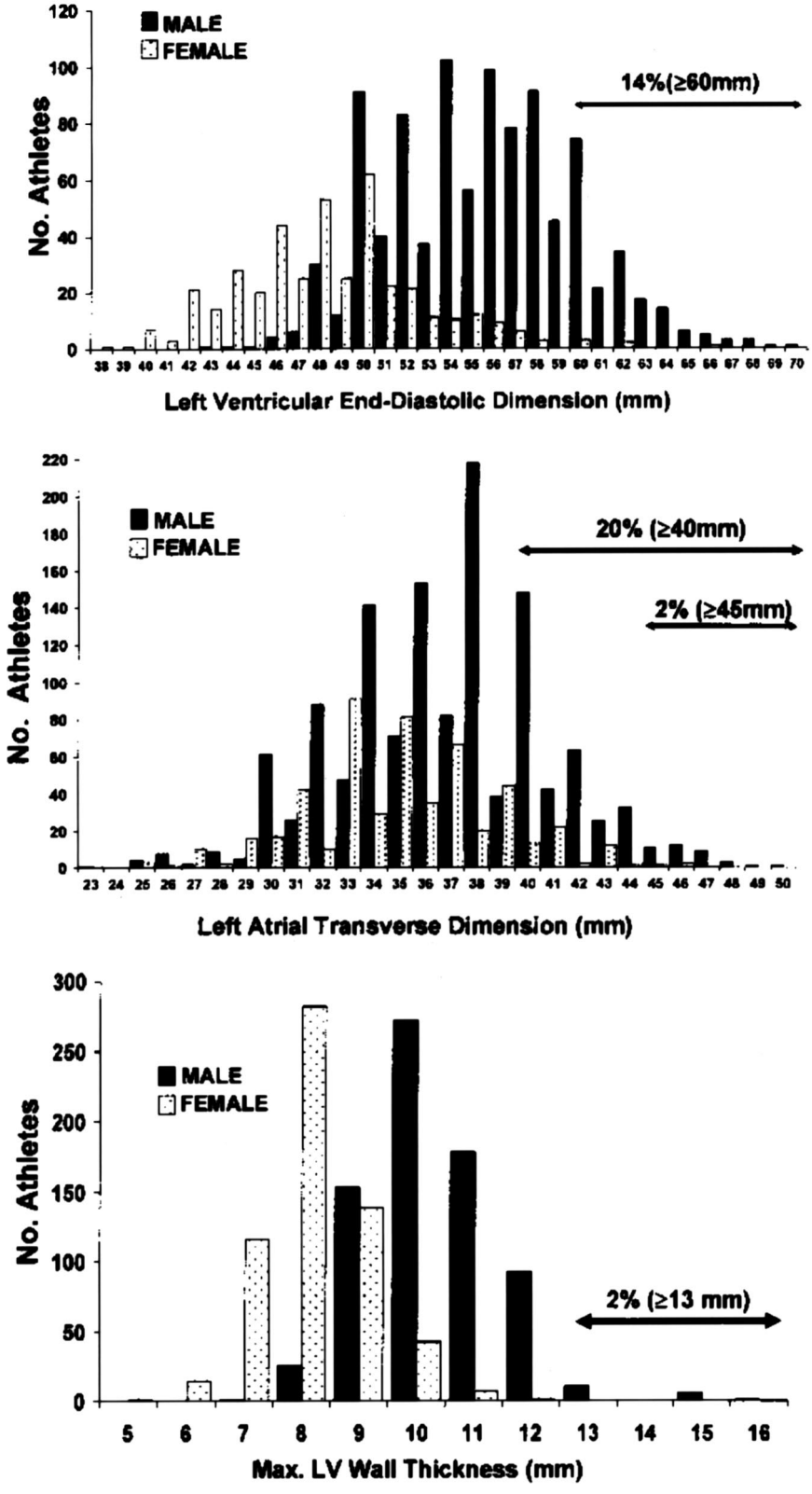

Figure 1. Distribution of cardiac dimensions in large populations of highly trained male and female athletes. Top, LV end-diastolic cavity dimension; 14% of athletes have enlargement of 60 to 70 mm. Reproduced from Pelliccia et al[10] with permission of the American College of Physicians. Copyright 1999. Middle, Transverse left atrial dimension; 20% of athletes have transverse left atrial dimension ≥40 mm. Reproduced from Pelliccia et al[22] with permission of the American College of Cardiology. Copyright 2005. Bottom, Maximum (Max.) LV wall thickness; 2% of men and 0% of women have wall thickness ≥13 mm. Reproduced from Pelliccia et al[9] with permission of the Massachusetts Medical Society. Copyright 1991.

associated with decreased peripheral vascular resistance. The immediate results of strength conditioning include only mildly increased oxygen consumption and cardiac output but substantial increases in blood pressure, peripheral vascular resistance, and heart rate.

Long-term cardiovascular adaptation to dynamic training produces increased maximal oxygen uptake due to increased cardiac output and arteriovenous oxygen difference. Strength exercise results in little or no increase in oxygen uptake. Thus, endurance exercise predominantly produces volume

load on the left ventricle (LV), and strength exercise causes largely a pressure load.

Chamber Morphology

Cardiac dimensional alterations associated with athletic training have been defined over the past 35 years in a number of cross-sectional echocardiographic (or cardiac magnetic resonance) studies, usually performed in highly trained individuals.[1,6,9–26,38–42] The responses of individual athletes to systematic conditioning are not uniform. Training induces in ≈50% of trained athletes some evidence of cardiac remodeling, which consists of alterations in ventricular chamber dimensions, including increased left and right ventricular and left atrial cavity size (and volume), associated with normal systolic and diastolic function (Figure 1). For example, marked enlargement of the LV chamber (≥60 mm) occurs in ≈15% of highly trained athletes.[10] This chamber enlargement may very occasionally be accompanied by a relatively mild increase in absolute LV wall thickness that exceeds upper normal limits (range 13 to 15 mm).[9] LV remodeling with changes in mass is dynamic in nature and may appear to develop relatively rapidly, or more gradually, after the initiation of vigorous conditioning. Such changes, which are reversible with cessation of training, are most impressive in endurance athletes.[18–20,27] However, there is considerable overlap in cardiac dimensions between a trained athlete population and age- and sex-matched sedentary controls.[42] Athletes show relatively small (but statistically significant) increases of ≈10% to 20% for wall thickness or cavity size, and these values in most individual athletes remain within accepted normal limits.[42]

The pattern and magnitude of physiologically increased LV mass may vary with respect to the nature of sports training[13,27,41] (Figure 2). One metaanalysis[15] and also the large database assembled at the Institute of Sports Medicine and Science (Rome, Italy)[9–11,20–22,39,41] support in part an earlier hypothesis[6] that specific morphological adaptations and changes in LV mass result from systematic training in different sports disciplines. The most extreme increases in cavity dimension or wall thickness have been observed in those elite athletes training in rowing, cross-country skiing, cycling, and swimming,[9–11,20–22,26,39,41] whereas limited data in athletes participating in ultraendurance sports (such as triathlons) paradoxically show more modest alterations in cardiac dimensions.[1,12] Of note, some misunderstanding persists as to whether strength training alone results in LV hypertrophy. Such sports are associated with only mildly increased wall thicknesses (often disproportionate relative to cavity size), whereas absolute values uncorrected for body surface area usually remain within the accepted normal range (≤12 mm; Figure 2).[1,15,38,39,41,42]

Increases in LV cavity size and calculated mass associated with athletic training are determined in part by body surface area (or lean body mass).[9–11,13] Larger athletes (particularly men) will generally demonstrate greater absolute LV cavity and wall thickness dimensions. However, the relative contributions of demographic and environmental or genetic determinants to LV remodeling in trained athletes has long been a subject of controversy.[43] Data assembled in large athlete populations assessed with multivariate analysis show that 75% of variability in LV cavity size is attributable to nongenetic factors, such as body size, type of sport, gender, and age, with body surface area the largest of these components[10] (Figure 3). The remaining 25% of cavity size variability is otherwise unexplained[10,43] and possibly caused in small part by genetic factors. Indeed, recent investigations in trained athletes have demonstrated an association between LV remodeling (and increased LV mass in response to training) and the angiotensin-converting enzyme gene I/D (ACE I/D) and/or angiotensinogen (AGT M/T) polymorphisms.[43,44] There is no compelling evidence linking the magnitude of training-related cardiac dimensional changes in athletes with the level of performance during competition.

Left atrial remodeling is an additional physiological adaptation frequently present in highly trained athletes, most commonly those in combined static and dynamic sports (ie, cycling and rowing), and is largely explained by associated LV cavity enlargement and volume overload.[22] Increased transverse left atrial dimensions (≥40 mm) are present in 20% of athletes and more substantially enlarged dimensions (≥45 mm) are evident in 2%. These latter dimensions overlap

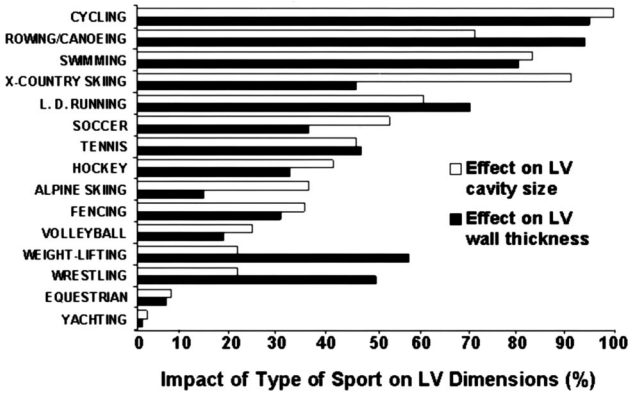

Figure 2. Effect of specific sports training on LV cavity dimension or wall thickness in elite athletes, representing 27 different sporting disciplines. X-Country indicates cross-country; L.D. Running, long-distance running.

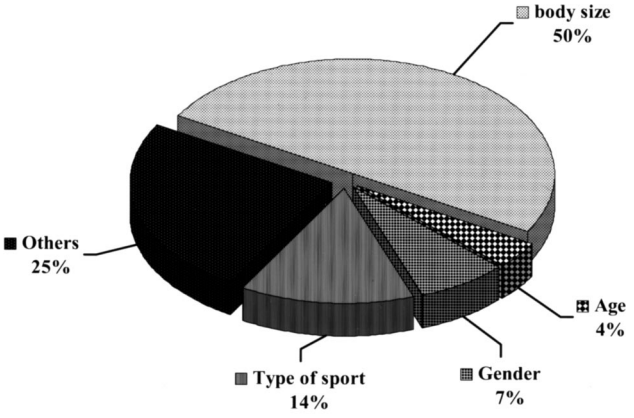

Figure 3. Impact of different clinical variables on LV end-diastolic cavity dimensions in a large population of male and female elite athletes. The relative impact of the examined variables (body size, gender, age, and type of sport) are shown here as a proportion of overall variability in LV cavity size.

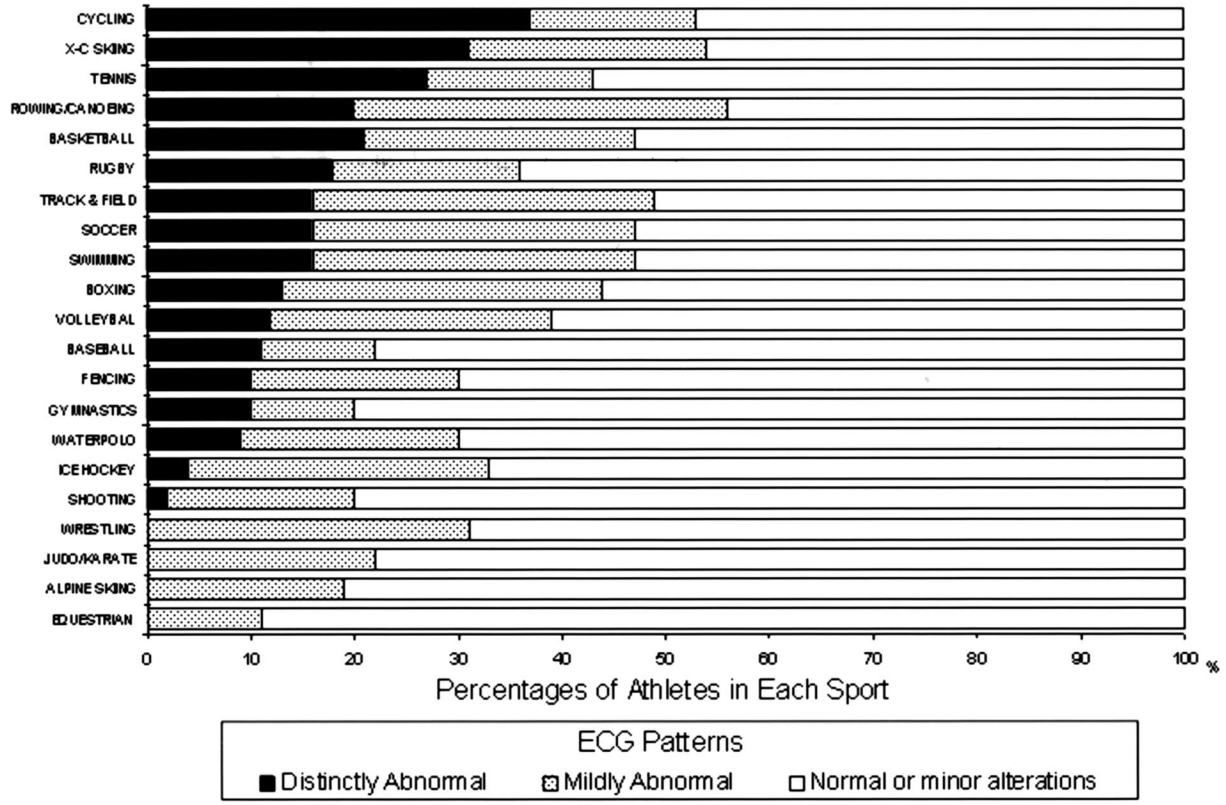

Figure 4. Relation of ECG patterns to sporting disciplines in 1005 highly trained athletes. ECGs that were distinctly abnormal (black bars), mildly abnormal (gray bars), and normal or with minor alterations (white bars) are depicted as proportions of all the athletes participating in each sporting discipline. X-C indicates cross-country. Reproduced from Pelliccia et al[25] with permission of the American Heart Association. Copyright 2000.

with those observed in patients with cardiac disease (Figure 1). Nevertheless, left atrial enlargement in athletes appears to be benign and largely confined to training in endurance sports, and is only rarely associated with atrial fibrillation (<1% of cases).[22,45]

12-Lead ECGs

In cross-sectional analysis, a spectrum of abnormal ECG patterns is present in ≈40% of trained athletes, occurring 2-fold more commonly in men than women, and particularly in those participating in endurance sports[25] (Figure 4). Therefore, most athletes have ECGs that are within normal limits or that show only minimal alterations. However, the frequency with which these ECG patterns occur is highly dependent on the type, intensity, level of training, and precise criteria used to define normality (Figure 4). The most commonly reported alterations are early repolarization patterns, increased QRS voltages, diffuse T-wave inversion, and deep Q waves.[8,25,46,47] Distinctly abnormal and bizarre ECGs, intuitively suggestive of cardiac disease, are encountered in an important minority of elite athletes (≈15%).[25] The vast majority of such ECGs represent only extreme manifestations of physiological athlete's heart.

Arrhythmias

Because of the heightened vagal tone that accompanies physical conditioning, trained athletes are known to commonly incur innocent arrhythmias and conduction alterations, such as sinus bradyarrhythmia, junctional rhythm, and first-degree or Wenckebach AV block (Mobitz type I).[1,26,46,47] However, the application of ambulatory (Holter) ECG monitoring to trained athletes unexpectedly documented substantial ectopy with frequent premature beats and complex ventricular tachyarrhythmias (including couplets and bursts of nonsustained ventricular tachycardia) in many such individuals.[48,49] These findings suggest that a variety of arrhythmias are part of the athlete's heart spectrum (Figure 5). Indeed, such rhythm disturbances have not been associated with adverse clinical events and are usually abolished or substantially reduced after relatively brief periods of deconditioning (as well as during physical training sessions and exercise testing). Even in athletes with heart disease, resolution of ventricular tachyarrhythmias with deconditioning is common and may represent a potential mechanism by which sudden death risk is reduced by withdrawal of these individuals from training and competition,[49,50] in accord with consensus panel recommendations.[2]

A few observational studies have reported mild-to-moderate postrace elevations in biochemical cardiac-specific markers (plasma cardiac troponin T and I) suggestive of transient myocardial injury in some participants after prolonged and strenuous endurance athletic events, such as triathlons and marathons.[51,52] At present, there is no evidence that these subclinical findings are associated with permanent

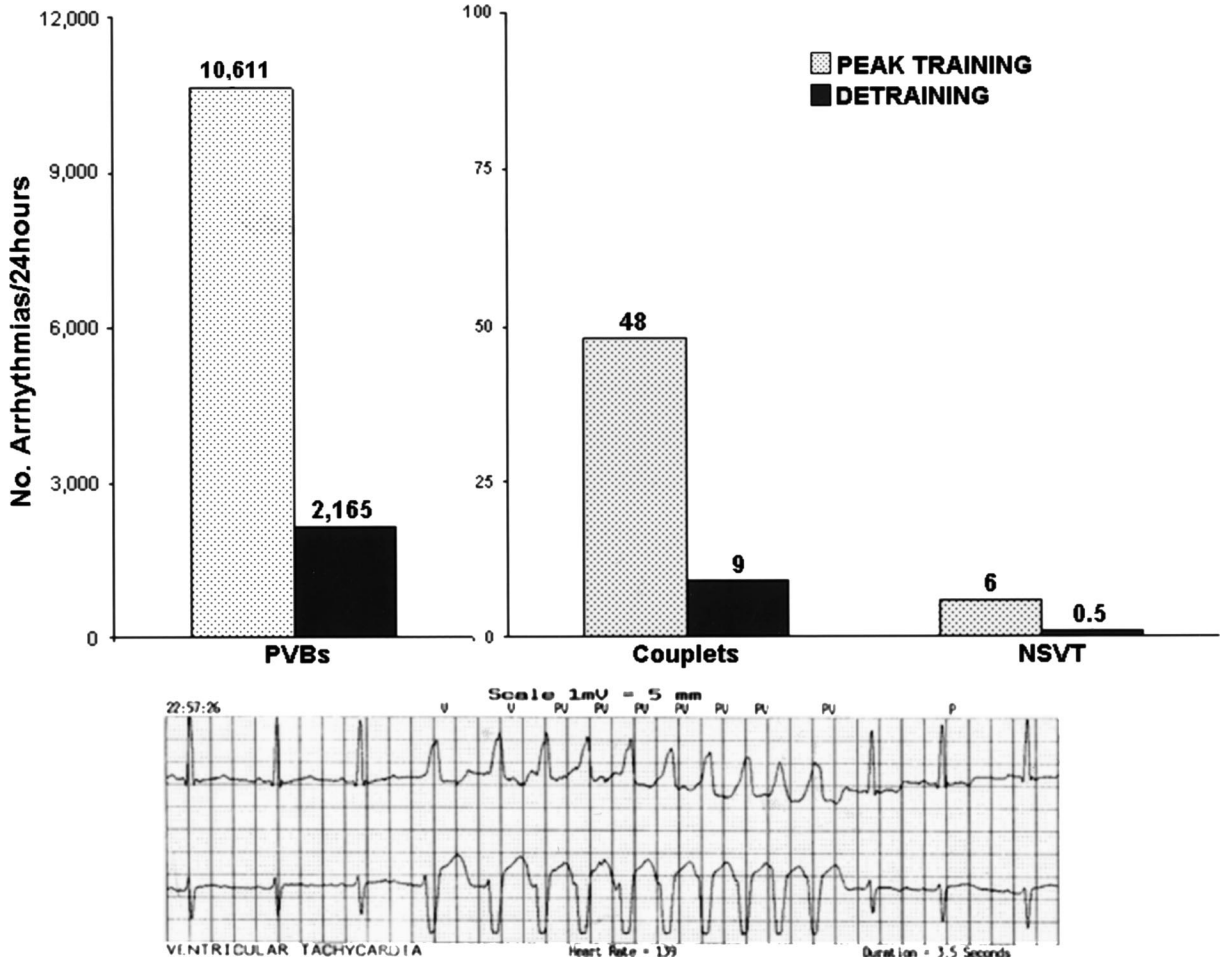

Figure 5. Ventricular arrhythmias in trained athletes. Top, Frequency of premature ventricular beats (PVBs), ventricular couplets, and bursts of nonsustained ventricular tachycardia (NSVT) recorded during a 24-hour (Holter) ECG at peak training and after a deconditioning period. Bottom, Ambulatory Holter ECG recording from 24-year-old male basketball player with frequent palpitations showing asymptomatic 10-beat burst of nonsustained ventricular tachycardia. Reproduced from Biffi et al[49] with permission of the American College of Cardiology Foundation. Copyright 2004.

clinical consequences. Some studies have also identified transient and reversible systolic and diastolic dysfunction after extreme athletic events.[51,52]

Although data defining the physiological and morphological adaptations of systematic training are considerable, it nevertheless remains unresolved whether the current profile of athlete's heart can be extrapolated to all subgroups within this physically active and diverse population: those of different ages, sports disciplines, and racial or ethnic origin.[9–18] Much of the available cardiac dimensional data have been assembled from white European athletes, particularly the large cohort at the Institute of Sports Medicine and Science comprising elite Italian national and international level competitors.[9-11,20-22,25,39,48,49,51] Indeed, there are limited data defining the adaptations of athlete's heart in females, in modestly trained individuals in youth sports programs, and in blacks and other minorities.

Sudden Death in Young Athletes

Background and Frequency

Sudden death occurring in young athletic individuals was once regarded as a mysterious and undefined syndrome; however, a voluminous body of literature defining the cardiovascular and other causes of these catastrophes has been assembled over the last several years.[1,28–36,50,53–57] Nevertheless, the perception persists in the community that it is counterintuitive for young and highly trained high school, college, or professional athletes to unknowingly harbor potentially lethal cardiovascular disease susceptible to sudden and unexpected death.

These events convey a devastating emotional impact to families and the community at large.[1,28,29] Once regarded as rare personal and family tragedies, sudden deaths in young athletes have been increasingly integrated into the public discourse. Although initially reported in the United States in the early 1980s,[55] the causes of sudden death in young athletes and related issues (eg, preparticipation screening and disqualification criteria)[1–3,57,58] have more recently become the focus of increasing concern in other parts of the world, including Europe, where a cluster of 7 recent deaths in elite athletes competing in soccer, hockey, and skating has occurred.[58]

Data establishing the prevalence of sudden death in athletes with precision are quite limited, although it is evident

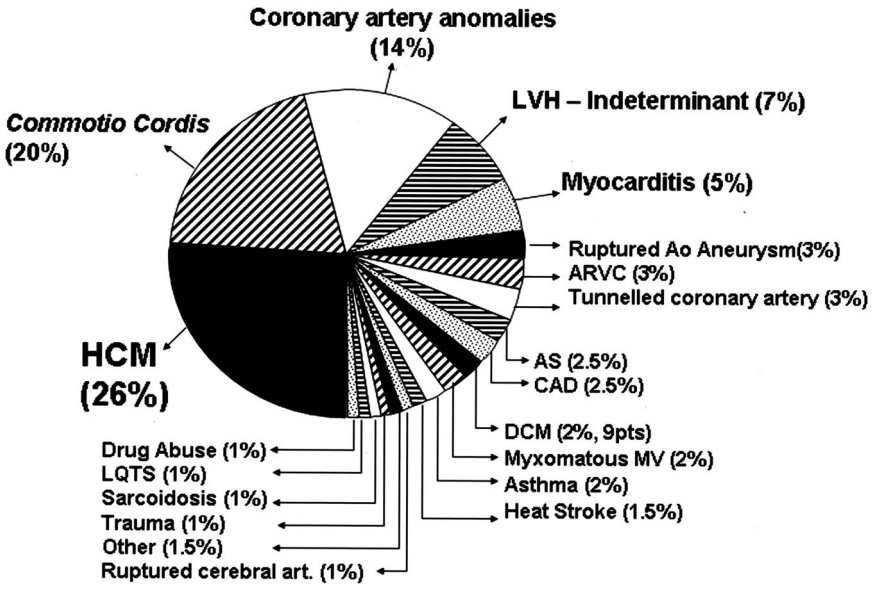

Figure 6. Causes of sudden death in young competitive athletes, as reported to the Minneapolis Heart Institute Foundation national registry. Ao indicates aorta; art., artery; AS, aortic stenosis; CAD, coronary artery disease; DCM, dilated cardiomyopathy; LQTS, long-QT syndrome; LVH, LV hypertrophy; MV, mitral valve; and pts, patients.

that the overall risk in this population is low. A 12-year survey from Minnesota reported a frequency of sudden death caused by undiagnosed cardiovascular disease in high school athletes of 1:200 000/year (based on only 3 deaths among 1.4 million student-athlete sports participations in 27 sports).[34]

Mechanisms and Causes

Sudden death in young athletes usually occurs on the athletic field and is related to physical activity, in the absence of prior symptoms.[1,28–36,50,53–56,59] Indeed, the incremental risk for sudden death in adolescents and young adults is significantly higher (ie, 2.8-fold greater) when associated with vigorous physical exertion during competitive sports.[36] Exercise acts as a trigger for lethal ventricular tachyarrhythmias, given the susceptibility imposed by underlying (and usually unsuspected) cardiac disease.[33,36]

A number of largely congenital and often clinically silent cardiovascular diseases have been causally linked to sudden deaths in young trained athletes in autopsy surveys (Figures 6 and 7). In the United States, hypertrophic cardiomyopathy (HCM)[1,32,33,35] has been consistently reported to be the single most common cardiovascular cause, accounting for approximately one third of the deaths. Indeed, 3 recent and highly visible sudden deaths or cardiac arrests that occurred in US professional athletes were each caused by HCM (Jason Collier [sudden death], Thomas Herrion [sudden death], and Jiri Fischer [cardiac arrest]), as was 1 notable sudden death in a Cameroon soccer player with previously diagnosed HCM that occurred during a televised international match.[58] The second most frequent cause of these deaths in athletes is a congenital coronary artery anomaly of wrong sinus origin (most commonly, left main coronary artery origin from right sinus of Valsalva).[1,33,53] Diagnosis requires a high index of suspicion in young athletes presenting with exertional chest pain and/or syncope, because 12-lead or exercise ECG abnormalities suggestive of ischemia are usually absent.[53]

A diverse array of ≈15 other diseases each accounts for a much smaller proportion (5% to 8%) of the cardiovascular deaths in young athletes (Figures 6 and 7).[1,32,33] These include myocarditis, valvular heart disease (aortic stenosis and myxomatous mitral valve disease), premature atherosclerotic coronary artery disease, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy (ARVC), or aortic dissection and rupture (usually associated with Marfan syndrome). Of note, 3 professional basketball players in the United States were recently diagnosed with aortic root dilatation that required prophylactic surgery.[60]

Approximately 2% of young athletes who die suddenly are reported to show normal cardiac structure on standard autopsy examination.[1,33] Many of these deaths are likely caused by ion-channel disorders (long-QT and Brugada syndromes and catecholaminergic polymorphic tachycardia), Wolff-Parkinson-White syndrome, coronary artery vasospasm, or abnormalities of the conducting system and microvasculature.[33] Occasionally, a tunneled segment of the left anterior descending coronary artery is the only structural abnormality evident at autopsy to explain sudden death[33]; however, it is unresolved whether this malformation can be regarded as the sole cause of sudden death.[1] In contrast, sudden deaths in older athletes (>35 or 40 years) are caused predominantly by atherosclerotic coronary artery disease.[1] Primary ventricular tachyarrhythmias are the mechanism of the vast majority of sudden deaths in athletes, with Marfan syndrome and aortic dissection the exceptions.

An alternative demographic profile has emerged from the Veneto region of northeastern Italy in which ARVC[61] is reported to be the most common cause of athletic field deaths.[36] Such a predisposition to ARVC, which contrasts sharply with the US experience, could be based on a unique genetic substrate or the consequence of the long-standing Italian national preparticipation screening program,[62] or both. Such systematic screening is less likely to identify and disqualify from competition athletes with ARVC than those with diseases more readily identified by screening, such as HCM.[63]

Demographics

Sudden cardiovascular death may occur in a wide variety of more than 30 competitive athletic disciplines, most com-

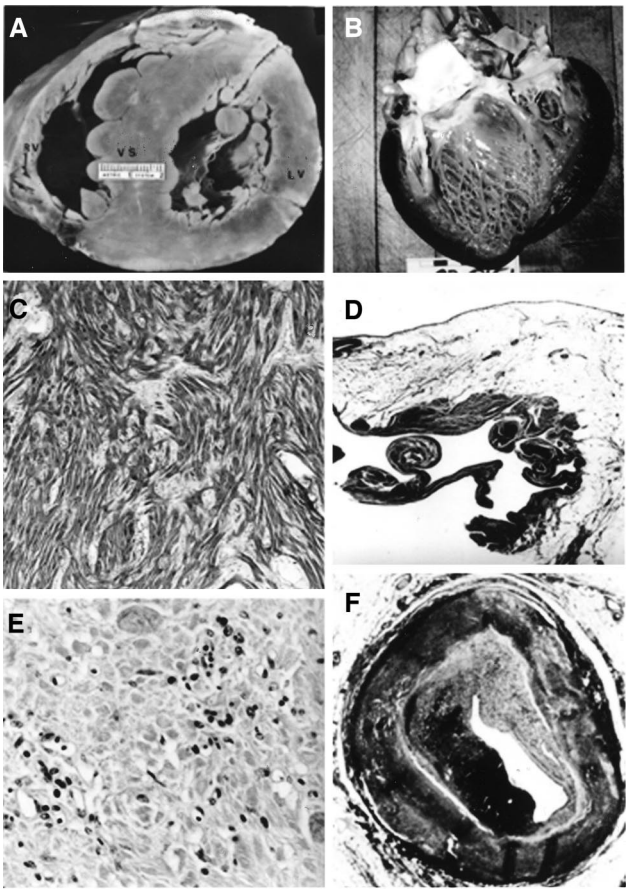

Figure 7. Causes of sudden cardiac death in young competitive athletes. A, HCM. Gross heart specimen showing asymmetrical ventricular septal (VS) thickening. B, Idiopathic dilated cardiomyopathy showing greatly enlarged LV cavity. C, HCM. Histopathology showing substrate of disorganized cardiac muscle cells and chaotic architectural pattern. D, ARVC. Histological section of right ventricle showing extensive fatty replacement adjacent to small area of residual myocytes. E, Myocarditis. LV myocardium with clusters of inflammatory mononuclear cells. F, Premature coronary artery disease. Portion of right coronary artery with atherosclerotic narrowing and ruptured plaque. Adapted from Maron[1] with permission of the Massachusetts Medical Society. Copyright 2003.

monly basketball and American football in the United States (and soccer in Europe), intense sports that also have high participation levels.[1,32,33,35] These sudden death events also occur much more frequently in males (by 9:1); young women are probably less frequently affected because of their lower overall participation rates and absence from sports such as football.[1,33,35]

Blacks account for a disproportionate number of sports-related sudden deaths owing to previously undiagnosed HCM.[1,33,35] This observation contrasts sharply with the striking underrepresentation of blacks in clinically identified HCM populations, suggesting that socioeconomic status and ethnicity may play an important role in determining access to echocardiography and consequently the clinical diagnosis of HCM.

Other Risks of Sports

A substantial number of other sudden deaths in athletes occur in the absence of cardiac disease and under diverse circumstances.[1,54,56] These deaths are caused by severe blunt head, spine, and other bodily trauma (eg, during football or pole vaulting), heat stroke, uncontrolled bronchial asthma, ruptured cerebral artery aneurysm, and possibly sickle cell trait. Stroke, myocardial infarction, and sudden death have been linked to substance abuse with cocaine, anabolic steroids, or nutritional supplements (including ephedrine).[64]

Two other circumstances in which trauma-related sudden death occurs during sports involve blunt, nonpenetrating, and often innocent-appearing blows to the precordium or neck[54,56] (Figures 8 and 9). Virtually instantaneous death has been reported during ice hockey in which high-velocity blows to the neck by the puck trigger arterial rupture and subarachnoid hemorrhage[54] (Figure 9). The likely mechanism is reflex

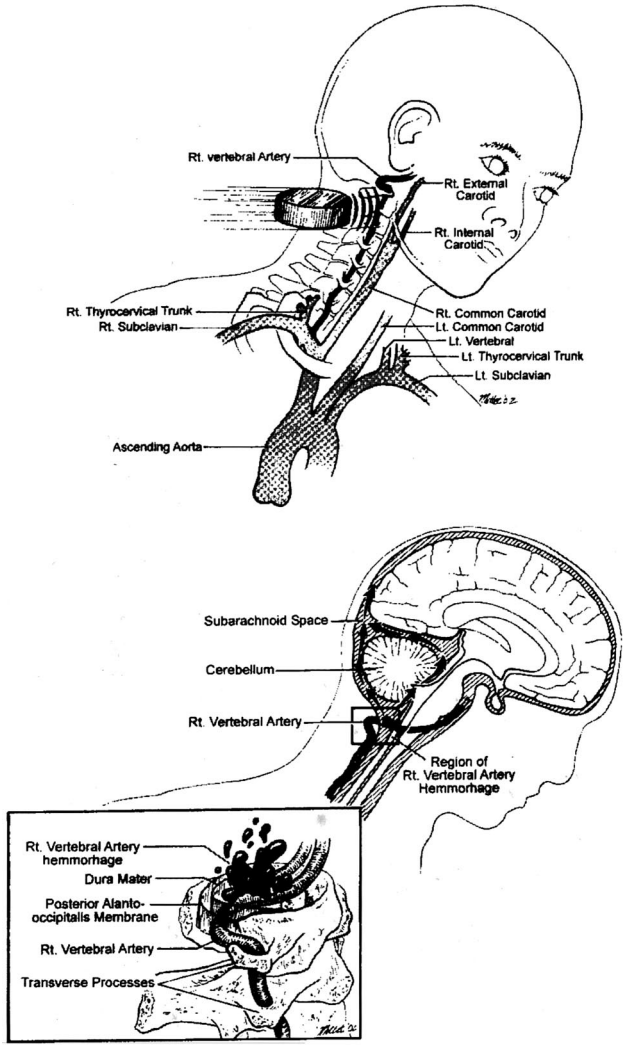

Figure 8. Blow to an unprotected area of the upper neck by a hockey puck (accompanied by abrupt reflex hyperextension) can result in sudden death (upper panel). Mechanism involves arterial dissection and rupture at the anatomic point where the vertebral artery courses through the boney canal of the foramina transversarium and penetrates the posterior atlanto-occipital membrane or dura mater (lower panel). Vertebral artery is rigidly anchored at this point (as it enters the transverse process of the first cervical vertebra) and becomes the point of rupture leading to massive hemorrhage into the subarachnoid space and instantaneous death. Lt. indicates left; Rt., right.

Figure 9. Stop-frame images of an aborted commotio cordis event during a televised professional hockey game. A, Flight of the puck from a slap shot (arrowheads and arrow) toward the victim (*). B through F, After precordial blow, victim (*) is seen progressively falling toward the surface of the ice. E and F, Enlarged stop frames showing final collapse.

hyperextension of the head that causes vertebral artery dissection at its fixed anchor point within the foramina transversarium.

More commonly, precordial blows may trigger ventricular fibrillation without structural injury to ribs, sternum, or the heart itself (commotio cordis[56,65]; Figure 10). These events are more common causes of athletic field deaths than most of the aforementioned cardiovascular diseases (Figure 6). Commotio cordis is most frequently caused by projectiles that are implements of the game and strike the chest at a broad range of velocities (eg, hockey pucks or lacrosse balls [up to 90 mph]), but more frequently result from blows with only modest force (eg, a pitched Little League baseball striking a batter at 30 to 40 mph) or by virtue of bodily contact (eg, a karate blow or when 2 outfielders tracking a baseball collide).[56]

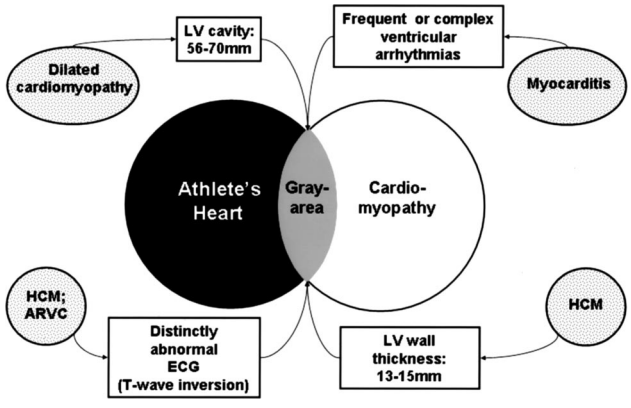

Figure 10. Differential diagnosis between athlete's heart and cardiac disease. Gray zone of overlap between physiological hypertrophy and pathological cardiomyopathies (including myocarditis, HCM, and ARVC). Adapted from Maron[1] with permission of the Massachusetts Medical Society. Copyright 2003.

On the basis of clinical observations and an experimental animal model (which replicates commotio cordis), the mechanism by which ventricular fibrillation and sudden death occur requires a blow directly over the heart, exquisitely timed to within a narrow 10- to 30-ms window just before the T-wave peak during the vulnerable phase of repolarization.[65] Basic electrophysiological mechanisms of commotio cordis are largely unresolved, although selective K^+_{ATP} channel activation appears to play a role.[1]

Only ≈15% of commotio cordis victims survive, usually in association with timely cardiopulmonary resuscitation and defibrillation.[56] However, there are reports of both successful[66] and unsuccessful resuscitation with automated external defibrillators.[67] Strategies for primary prevention of commotio cordis include innovations in sports equipment design. However, although softer-than-normal ("safety") baseballs reduce the frequency of ventricular fibrillation under exper-

imental conditions,[65] they do not provide absolute protection in the field.[56] At present, chest barriers with proven efficacy in preventing commotio cordis are not yet available. In fact, under laboratory conditions, commercial chest protectors are uniformly ineffective in preventing chest blow–induced ventricular fibrillation.[68]

Several sudden cardiac deaths have been reported in Belgian cyclists, with the suggestion that athletic participation produced ventricular tachyarrhythmias.[69] Mechanisms responsible for this disproportionate rate of cardiac events are largely undefined. An infectious cause, with vector-borne pathogens (and myocarditis), has been implicated in a cluster of sudden deaths among Swedish orienteers.[70]

Athlete's Heart and Cardiovascular Disease

Because of the potentially adverse consequences of underlying cardiovascular disease in young athletes, considerable attention has been focused on clinically distinguishing physiologically based athlete's heart from a variety of structural heart diseases (Figure 10).[1,7,19,20,22,24,71,72] This differential diagnosis has critical implications for dedicated athletes (and their physicians) because cardiovascular disease may represent the basis for disqualification from competitive sports to reduce the risk of sudden death.[2,57] Furthermore, some athletes with cardiac disease judged to be at high risk may subsequently become candidates for an implantable defibrillator and prophylactic prevention of sudden death.[1,73]

Diagnostic dilemmas arise when the remodeling adaptations of athlete's heart mimic certain pathological conditions, such as hypertrophic and dilated cardiomyopathies and ARVC (Figure 10). This circumstance may arise in athletes because of distinctly abnormal ECGs, or when absolute cardiac dimensions fall outside clinically accepted partition values (eg, >12 mm for LV wall thickness and ≥55 to 60 mm for LV cavity size at end diastole; somewhat lower cut points apply to female and adolescent athletes).[11,24] For example, ≈2% of elite adult male athletes have been reported to show modestly increased LV wall thickness of 13 to 15 mm, which defines a "gray zone" of overlap between the extreme expressions of athlete's heart and a mild HCM phenotype (without marked hypertrophy or outflow obstruction; Figure 11).[7,9] This ambiguity can be resolved by the application of a number of noninvasive parameters, such as reduced cardiac mass with short deconditioning periods (best assessed with serial magnetic resonance imaging) or absolute LV diastolic dimension >55 mm, both of which suggest athlete's heart.[7] In contrast, an HCM diagnosis would be favored by abnormal Doppler-derived LV diastolic filling or relaxation indices or by the existence of a family member with HCM. Magnetic resonance imaging has value in resolving the HCM-versus–athlete's heart differential diagnosis in selected athletes by virtue of its superiority over echocardiography in identifying segmental LV hypertrophy in the anterolateral free wall or apex.[74]

Rapid commercial laboratory testing is now available for both HCM[75] and cardiac ion channel mutations,[76] with the potential for achieving a DNA-based diagnosis. If a proband is positive for one of the known disease-causing mutant genes in the panel, the result is definitive. On the other hand, genetic testing has certain potential limitations. For example, negative tests are common but nondiagnostic because they may represent false-negative results. In addition, such commercial testing is costly (in the range of $5000), and it is uncertain whether that expense will be covered by insurance carriers. However, if the family gene defect is known, then all other relatives can be tested definitively and inexpensively.

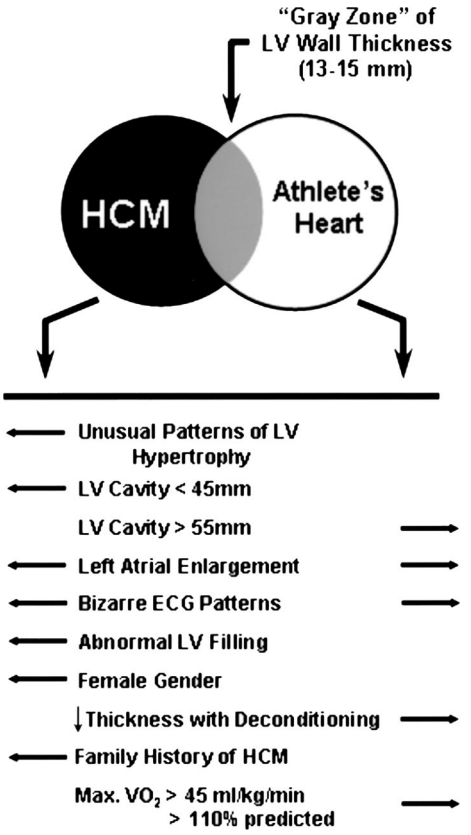

Figure 11. Clinical criteria used to distinguish nonobstructive HCM from athlete's heart when maximal LV wall thickness is within shaded gray area of overlap, consistent with both diagnoses. Adapted from Maron et al[7] with permission of the American Heart Association. Copyright 1995.

Marked LV cavity enlargement in an athlete, even in the absence of cardiac symptoms, may intuitively raise the differential diagnosis between physiological hypertrophy and pathological cardiomyopathies,[1,10,21] particularly when ejection fraction is judged to be at the lower range of normal or mildly depressed. This difficult clinical situation can often be resolved by surveillance with serial testing of ejection fraction at rest and with exercise, after disqualification from sports.

Complex and frequent ventricular tachyarrhythmias evident on ambulatory Holter ECG in trained athletes without cardiovascular abnormalities[48,49] can raise the possibility of disease states such as myocarditis, for which a high index of clinical suspicion is required.[1,48] Periods of forced deconditioning may not be useful in resolving such differential diagnoses, because detraining is associated with reduction (and even abolition) of ventricular tachyarrhythmias in athletes both without and with underlying pathological substrates (Figure 5).[49]

Long-Term Consequences of Athlete's Heart

Extreme LV remodeling evident in some highly trained athletes has intuitively raised a concern of whether such exercise-related morphological adaptations are always innocent. For example, ≈15% of highly trained athletes show striking LV cavity enlargement, with end-diastolic dimensions ≥60 mm, similar in magnitude to that evident in pathological forms of dilated cardiomyopathy.[1,10,21] One longitudinal echocardiographic study reported incomplete reversal of extreme LV cavity dilatation with deconditioning; substantial chamber enlargement persisted in 20% of retired and deconditioned former elite athletes after 5 years (Figure 12).[21] There is no evidence at present showing that athlete's heart remodeling leads to long-term disease progression, cardiovascular disability, or sudden cardiac death. The possibility that persistence of extreme remodeling after prolonged and intensive conditioning will ultimately convey deleterious cardiovascular consequences to some athletes is perhaps unlikely but at this time cannot be excluded with certainty.

Cardiovascular Criteria for Disqualification From Sports

The devastating impact of even relatively infrequent sudden deaths in young athletes offers justification for restriction from competition to reduce the risk related to silent and unsuspected cardiac disease. For athletes in whom cardiovascular disease has been identified (either by preparticipation screening[3,63] or under other circumstances), important considerations arise with respect to the appropriate formulation of eligibility and disqualification decisions for competitive sports. The 2005 American College of Cardiology 36th Bethesda Conference[2] and European Society of Cardiology (ESC)[57] consensus documents offer expert panel recommendations and clear benchmarks for clinical practice, largely focused on amateur competitive athletes. Panel recommendations for athletic eligibility are based on the premise that intense sports training and competition increase risk for sudden death or disease progression in susceptible athletes with heart disease[1,28–33,36,50] and that this risk can be reduced or minimized by either temporary or permanent withdrawal from sports.[2,49,57] Indeed, the US appellate court decision in *Knapp v Northwestern*[30] supports the use of national association medical guidelines (such as those of the Bethesda Conference) in justifying disqualification decisions in athletes. Therefore, team physicians would be prudent to rely on Bethesda Conference No. 36 in making difficult disqualification decisions, because it will likely play an important role as precedent in resolving future medical-legal disputes.

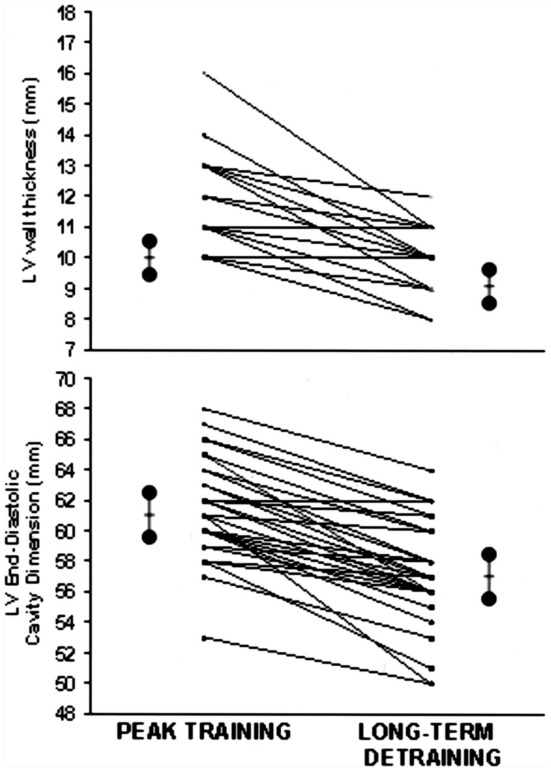

Figure 12. Cardiac remodeling caused by long-term deconditioning. Serial LV end-diastolic cavity dimensions and maximum LV wall thicknesses at peak training compared with measurements after an average detraining period of 5.6 years. Reproduced from Pelliccia et al[21] with permission of the American Heart Association. Copyright 2002.

The recent ESC consensus report[57] assessing eligibility criteria for competitive athletes with cardiovascular disease is modeled after the Bethesda Conference.[2] Although the 2 guidelines are very similar, the European recommendations are selectively more restrictive in advising disqualification for certain cardiac conditions, including long-QT syndrome, HCM, and Marfan syndrome, particularly when diagnostic cardiac findings are borderline.

The assumptions with regard to sports, cardiovascular disease, and sudden death in these consensus guidelines are intuitive and justified, although the precise risks for sports participants with cardiac disease are not easily quantifiable, nor can this problem be subjected to formally controlled and evidence-based study designs. Nevertheless, there is preliminary evidence that the disqualification strategies of the Bethesda Conference[2] and the ESC[57] may minimize risk and thereby reduce the number of sudden deaths in young athletes.

Italian investigators attribute a decline in the rate of sudden cardiac death during sports to their long-standing systematic national preparticipation screening program, which routinely includes a 12-lead ECG.[19] They report an almost 90% decline in the annual incidence of sudden cardiovascular death in competitive athletes (largely owing to reduced mortality from cardiomyopathy) from the Veneto region of northeastern Italy.[19] This positive change occurred in parallel with progressive implementation of nationwide mass screening and the increasing identification of affected athletes who were then disqualified from competitive sports.

However, decisions to withdraw elite athletes from sports because of heart disease may be confounded by complex societal considerations and can prove difficult to implement, particularly when elite sports careers are involved.[28–30] Many such athletes are highly motivated to remain in the competitive arena, may not fully appreciate the implications of the relevant medical information, or are willing to accept risks while resisting prudent recommendations to withdraw. In

contrast to countries such as Italy,[62] national standards linked to mandatory disqualification are not part of the US healthcare system. Improper overdiagnosis of cardiac disease may lead to unnecessary disqualification from athletics, thereby depriving some individuals of the psychological and economic benefits of competitive sports. As a cautionary note, physician judgment in making these medical eligibility/disqualification decisions can be impaired insidiously by extrinsic pressures imposed by relatives, fans, alumni, coaching staff, administrators, and other interested parties, particularly when athletes "shop" for multiple medical opinions.

The relationship between sports medicine and the law is complex and involves tenuous relationships between physicians, athlete-patients, teams, and institutions.[77] Indeed, liability issues relevant to the management of competitive athletes with cardiovascular disease have become of increasing concern to the practicing medical community, given that several athlete deaths have triggered attempts in court to hold physicians accountable for alleged grievances.[77] An evolving US medicolegal framework[77] is clarifying the standard of care associated with this clinical practice while upholding the wisdom of withholding selected student-athletes with cardiovascular abnormalities from access to competitive sports programs in an effort to prevent their exposure to medically unacceptable risks.

Disclosures

None.

References

1. Maron BJ. Sudden death in young athletes. *N Engl J Med*. 2003;349:1064–1075.
2. Maron BJ, Zipes DP. 36th Bethesda Conference: eligibility recommendations for competitive athletes with cardiovascular abnormalities. *J Am Coll Cardiol*. 2005;45:1312–1375.
3. Maron BJ, Thompson PD, Puffer JC, McGrew CA, Strong WB, Douglas PS, Clark LT, Mitten MJ, Crawford MH, Atkins DL, Driscoll DJ, Epstein AE. American Heart Association statement for health professionals: cardiovascular preparticipation screening of competitive athletes. *Circulation*. 1996;94:850–856.
4. Rost R. The athlete's heart: historical perspective. In: Maron BJ, ed. *Cardiology Clinics, the Athlete's Heart*. Philadelphia, Pa: WB Saunders Co; 1992:197–207.
5. Henschen S. Skilanglauf und skiwettlauf: eine medizinische sportstudie. *Mitt Med Klin Upsala (Jena)*. 1899;2:15–18.
6. Morganroth J, Maron BJ, Henry WL, Epstein SE. Comparative left ventricular dimensions in trained athletes. *Ann Intern Med*. 1975;82:521–524.
7. Maron BJ, Pelliccia A, Spirito P. Cardiac disease in young trained athletes: insights into methods for distinguishing athlete's heart from structural heart disease, with particular emphasis on hypertrophic cardiomyopathy. *Circulation*. 1995;91:1596–1601.
8. Huston TP, Puffer JC, Rodney WM. The athletic heart syndrome. *N Engl J Med*. 1985;313:24–32.
9. Pelliccia A, Maron BJ, Spataro A, Proschan MA, Spirito P. The upper limit of physiologic cardiac hypertrophy in highly trained elite athletes. *N Engl J Med*. 1991;324:295–301.
10. Pelliccia A, Culasso F, Di Paolo F, Maron BJ. Physiologic left ventricular cavity dilatation in elite athletes. *Ann Intern Med*. 1999;130:23–31.
11. Pelliccia A, Maron BJ, Culasso F, Spataro A, Caselli G. Athlete's heart in women: echocardiographic characterization of highly trained elite female athletes. *JAMA*. 1996;276:211–215.
12. Douglas PS, O'Toole ML, Katz SE, Ginsburg GS, Hiller WD, Laird RH. Left ventricular hypertrophy in athletes. *Am J Cardiol*. 1997;80:1384–1388.
13. Abernethy WB, Choo JK, Hutter AM Jr. Echocardiographic characteristics of professional football players. *J Am Coll Cardiol*. 2003;41:280–284.
14. Longhurst JC, Kelly AR, Gonyea WJ, Mitchell JH. Chronic training with static and dynamic exercise: cardiovascular adaptation, and response to exercise. *Circ Res*. 1981;48(suppl I):I-172–I-178.
15. Pluim BM, Zwinderman AH, van der Laarse A, Van der Wall EE. The athlete's heart: a meta-analysis of cardiac structure and function. *Circulation*. 1999;100:336–344.
16. Scharhag J, Schneider G, Urhausen A, Rochette V, Kramann B, Kindermann W. Athlete's heart: right and left ventricular mass and function in male endurance athletes and untrained individuals determined by magnetic resonance imaging. *J Am Coll Cardiol*. 2002;410:1856–1863.
17. Milliken MC, Stray-Gundersen J, Peshock RM, Katz J, Mitchell JH. Left ventricular mass as determined by magnetic resonance imaging in male endurance athletes. *Am J Cardiol*. 1988;62:301–305.
18. Fagard R, Aubert A, Lysens R, Staessen J, Vanhees L, Amery A. Noninvasive assessment of seasonal variations in cardiac structure and function in cyclists. *Circulation*. 1983;67:896–901.
19. Ehsani AA, Hagberg JM, Hickson RC. Rapid changes in left ventricular dimensions and mass in response to physical conditioning. *Am J Cardiol*. 1978;42:52–56.
20. Maron BJ, Pelliccia A, Spataro A, Granata M. Reduction in left ventricular wall thickness after deconditioning in highly trained Olympic athletes. *Br Heart J*. 1993;69:125–128.
21. Pelliccia A, Maron BJ, de Luca R, Di Paolo FM, Spataro A, Culasso F. Remodeling of left ventricular hypertrophy in elite athletes after long-term deconditioning. *Circulation*. 2002;105:944–949.
22. Pelliccia A, Maron BJ, DiPaolo FM, Biffi A, Quattrini FM, Pisicchio C, Roselli A, Caselli S, Culasso F. Prevalence and clinical significance of left atrial remodeling in competitive athletes. *J Am Coll Cardiol*. 2005;46:690–696.
23. Martin WH III, Coyle EF, Bloomfield SA, Ehsani AA. Effects of physical deconditioning after intense endurance training on left ventricular dimensions and stroke volume. *J Am Coll Cardiol*. 1986;7:982–989.
24. Sharma S, Maron BJ, Whyte G, Firoozi S, Elliott PM, McKenna WJ. Physiologic limits of left ventricular hypertrophy in elite junior athletes: relevance to differential diagnosis of athlete's heart and hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2002;40:1431–1436.
25. Pelliccia A, Maron BJ, Culasso F, Di Paolo FM, Spataro A, Biffi A, Caselli G, Piovano P. Clinical significance of abnormal electrocardiographic patterns in trained athletes. *Circulation*. 2000;102:278–284.
26. Cavallaro V, Petretta M, Betocchi S, Salvatore C, Morgano G, Bianchi V, Breglio R, Bonaduce D. Effects of sustained training on left ventricular structure and function in top level rowers. *Eur Heart J*. 1993;14:898–903.
27. Fagard R. Athlete's heart. *Heart*. 2003;89:1455–1461.
28. Maron BJ. Sudden death in young athletes: lessons from the Hank Gathers affair. *N Engl J Med*. 1993;329:55–57.
29. Maron BJ. Cardiovascular risks to young persons on the athletic field. *Ann Intern Med*. 1998;129:379–386.
30. Maron BJ, Mitten MJ, Quandt EK, Zipes DP. Competitive athletes with cardiovascular disease: the case of Nicholas Knapp. *N Engl J Med*. 1998;339:1632–1635.
31. Burke AP, Farb V, Virmani R, Goodin J, Smialek JE. Sports-related and non-sports-related sudden cardiac death in young adults. *Am Heart J*. 1991;121:568–575.
32. Van Camp SP, Bloor CM, Mueller FO, Cantu RC, Olson HG. Nontraumatic sports death in high school and college athletes. *Med Sci Sports Exerc*. 1995;27:641–647.
33. Maron BJ, Shirani J, Poliac LC, Mathenge R, Roberts WC, Mueller FO. Sudden death in young competitive athletes: clinical, demographic and pathologic profiles. *JAMA*. 1996;276:199–204.
34. Maron BJ, Gohman TE, Aeppli D. Prevalence of sudden cardiac death during competitive sports activities in Minnesota high school athletes. *J Am Coll Cardiol*. 1998;32:1881–1884.
35. Maron BJ, Carney KP, Lever HM, Lewis JF, Barac I, Casey SA, Sherrid MV. Relationship of race to sudden cardiac death in competitive athletes with hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2003;41:974–980.
36. Corrado D, Basso C, Rizzoli G, Thiene G. Does sport activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol*. 2003;42:1964–1966.
37. Mitchell JH, Haskell W, Snell P, Van Camp SP. Task Force 8: classification of sports. In: Maron BJ, Zipes DP, eds. 36th Bethesda Conference:

eligibility recommendations for competitive athletes with cardiovascular abnormalities. *J Am Coll Cardiol*. 2005;45:1364–1367.
38. Longhurst JC, Kelly AR, Gonyea WJ, Mitchell JH. Echocardiographic left ventricular masses in distance runners and weight lifters. *J Appl Physiol*. 1980;48:154–162.
39. Pelliccia A, Spataro A, Caselli G, Maron BJ. Absence of left ventricular wall thickening in athletes participating in intense power training. *Am J Cardiol*. 1993;72:1048–1054.
40. Hauser A, Dressendorfer RH, Vos M, Hashimoto T, Gordon S, Timmis GC. Symmetric cardiac enlargement in highly trained endurance athletes: a two-dimensional echocardiographic study. *Am Heart J*. 1985;109: 1038–1044.
41. Spirito P, Pelliccia A, Proschan MA, Granata M, Spataro A, Caselli G, Biffi A, Vecchio C, Maron BJ. Morphology of the "athlete's heart" assessed by echocardiography in 947 elite athletes representing 27 sports. *Am J Cardiol*. 1994;74:802–806.
42. Maron BJ. Structural features of the athlete heart as defined by echocardiography. *J Am Coll Cardiol*. 1986;7:190–203.
43. Pelliccia A, Thompson PD. The genetics of left ventricular remodeling in competitive athletes. *J Cardiovasc Med*. 2006;7:267–270.
44. Montgomery HE, Clarkson P, Dollery CM, Prasad K, Losi MA, Hemingway H, Statters D, Jubb M, Girvain M, Varnava A, World M, Deanfield J, Talmud P, McEwan JR, McKenna WJ, Humphries S. Association of angiotensin-converting enzyme gene I/D polymorphism with change in left ventricular mass in response to physical training. *Circulation*. 1997;96:741–747.
45. Mont L, Sambola A, Brugada J, Vacca M, Marrugat J, Elosua R, Paré C, Azqueta M, Sanz G. Long-lasting sport practice and lone atrial fibrillation. *Eur Heart J*. 2002;23:477–482.
46. Choo JK, Abernethy WB III, Hutter AM Jr. Electrocardiographic observations in professional football players. *Am J Cardiol*. 2002;90:198–200.
47. Balady GJ, Cadigan JB, Ryan TJ. Electrocardiogram of the athlete: an analysis of 289 professional football players. *Am J Cardiol*. 1984;53: 1339–1343.
48. Biffi A, Pelliccia A, Verdile L, Fernando F, Spataro A, Caselli S, Santorni M, Maron BJ. Long-term clinical significance of frequent and complex ventricular tachyarrhythmias in trained athletes. *J Am Coll Cardiol*. 2002; 40:446–452.
49. Biffi A, Maron BJ, Verdile L, Fernando F, Spataro A, Marcello, Giuseppe, Ammirati F, Colivicchi F, Pelliccia A. Impact of physical deconditioning on ventricular tachyarrhythmias in trained athletes. *J Am Coll Cardiol*. 2004;44:1053–1058.
50. Corrado D, Basso C, Pavei A, Schiavon M, Thiene G. Decline of sudden cardiac death in young competitive athletes after implementation of Italian preparticipation screening. *Circulation*. 2005;112(suppl II):II-831–II-832. Abstract.
51. Rifai N, Douglas PS, O'Toole M, Rimm E, Ginsburg GS. Cardiac troponin T and I, electrocardiographic wall motion analyses, and ejection fractions in athletes participating in the Hawaii Ironman Triathlon. *Am J Cardiol*. 1999;83:1085–1089.
52. Neilan TG, Yoerger DM, Douglas PS, Marshall JE, Halpern EF, Lawlor D, Picard MH, Wood MJ. Persistent and reversible cardiac dysfunction among amateur marathon runners. *Eur Heart J*. 2006;27:1079–1084.
53. Basso C, Maron BJ, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. *J Am Coll Cardiol*. 2000;35:1493–1501.
54. Maron BJ, Poliac LC, Ashare AB, Hall WA. Sudden death due to blunt neck blows in amateur hockey players. *JAMA*. 2003;290:599–601.
55. Maron BJ, Roberts WC, McAllister HA, Rosing DR, Epstein SE. Sudden death in young athletes. *Circulation*. 1980;62:218–229.
56. Maron BJ, Gohman TE, Kyle SB, Estes NAM, Link MS. Clinical profile and spectrum of commotio cordis. *JAMA*. 2002;287:1142–1146.
57. Pelliccia A, Fagard R, Bjørnstad HH, Anestassakis A, Arbustini E, Assanelli D, Biffi A, Borjesson M, Carrè F, Corrado D, Delise P, Dorwarth U, Hirth A, Heidbuchel H, Hoffmann E, Mellwig KP, Panhuyzen-Goedkoop N, Pisani A, Solberg E, van-Buuren F, Vanhees L. A European Society of Cardiology consensus document: recommendations for competitive sports participation in athletes with cardiovascular disease. *Eur Heart J*. 2005;26:1422–1445.
58. Maron BJ. How should we screen competitive athletes for cardiovascular disease? *Eur Heart J*. 2005;26:428–430.
59. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. *JAMA*. 2002;287:1308–1320.
60. Youngblood D. The beat goes on. *Minneapolis Star Tribune*. December 18, 2005;Sports section:10.
61. Corrado D, Basso C, Thiene G, McKenna WJ, Davies MJ, Fontaliran F, Nava A, Silvestri F, Blomstrom-Lundqvist C, Wlodarska EK, Fontaine G, Camerini F. Spectrum of clinicopathologic manifestations of arrhythmogenic right ventricular cardiomyopathy/dysplasia: a multicenter study. *J Am Coll Cardiol*. 1997;30:1512–1520.
62. Pelliccia A, Maron BJ. Preparticipation cardiovascular evaluation of the competitive athlete: perspectives from the 30 year Italian experience. *Am J Cardiol*. 1995;75:827–828.
63. Corrado D, Basso C, Schiavon M, Thiene G. Screening for hypertrophic cardiomyopathy in young athletes. *N Engl J Med*. 1998;339:364–369.
64. Estes NAM III, Kloner R, Olshansky B, Virmani R. Task Force 9: drugs and performance-enhancing substances. In: Maron BJ, Zipes DP, eds. 36th Bethesda Conference: eligibility recommendations for competitive athletes with cardiovascular abnormalities. *J Am Coll Cardiol*. 2005;45: 1368–1369.
65. Link MS, Wang PJ, Pandian NG, Bharati S, Udelson JE, Lee M-Y, Vecchiotti MA, VanderBrink BA, Mirra G, Maron BJ, Estes NAM III. An experimental model of sudden death due to low-energy chest-wall impact (commotio cordis). *N Engl J Med*. 1998;338:1805–1811.
66. Strasburger JF, Maron BJ. Images in clinical medicine: commotio cordis. *N Engl J Med*. 2002;347:1248.
67. Maron BJ, Wentzel DC, Zenovich AG, Estes NAM III, Link MS. Death in a young athlete due to commotio cordis despite prompt external defibrillation. *Heart Rhythm*. 2005;2:991–993.
68. Weinstock J, Maron BJ, Song C, Mane PP, Estes NAM III, Link MS. Failure of commercially available chest wall protectors to prevent sudden cardiac death induced by chest wall blows in an experimental model of commotio cordis. *Pediatrics*. 2006;117:1404–1405, e656–e662.
69. Heidbüchel H, Hoogsteen J, Fagard R, Vanhees L, Ector H, Willems R, Van Lierde J. High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias: role of an electrophysiologic study in risk stratification. *Eur Heart J*. 2003;24:1473–1480.
70. Wesslén L, Pahlson C, Lindquist O, Hjelm E, Gnarpe J, Larsson E, Baandrup U, Eriksson L, Fohlman J, Engstrand L, Linglöf T, Nyström-Rosander C, Gnarpe H, Magnius L, Rolf C, Friman G. An increase in sudden unexpected cardiac deaths among young Swedish orienteers during 1979–1992. *Eur Heart J*. 1996;17:902–910.
71. Sharma S, Elliott PM, Whyte G, Mahon N, Virdee MS, Mist B, McKenna WJ. Utility of metabolic exercise testing in distinguishing hypertrophic cardiomyopathy from physiologic left ventricular hypertrophy in athletes. *J Am Coll Cardiol*. 2000;36:864–870.
72. Vinereanu D, Florescu N, Schulthorpe N, Tweddel AC, Stephens MR, Fraser AG. Differentiation between pathologic and physiologic left ventricular hypertrophy by tissue Doppler assessment of long-axis function in patients with hypertrophic cardiomyopathy or systemic hypertension and in athletes. *Am J Cardiol*. 2001;88:53–58.
73. Maron BJ, Shen W-K, Link MS, Epstein AE, Almquist AK, Daubert JP, Bardy GH, Favale S, Rea RF, Boriani G, Estes NAM III, Casey SA, Stanton MS, Betocchi S, Spirito P. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. *N Engl J Med*. 2000;342:365–373.
74. Rickers C, Wilke NM, Jerosch-Herold M, Casey SA, Panse P, Panse N, Weil J, Zenovich AG, Maron BJ. Utility of cardiac magnetic resonance imaging in the diagnosis of hypertrophic cardiomyopathy. *Circulation*. 2005;112:855–861.
75. Laboratory for Molecular Medicine—Tests. Harvard Medical School–Partners Healthcare Center for Genetics and Genomics Web page. Available at: http://www.hpcgg.org/LMM/tests.html. Accessed May 1, 2006.
76. FAMILION genetic test. PGx Health Web page. Available at: http://www.pgxhealth.com/genetictests/familion/. Accessed May 1, 2006.
77. Paterick TE, Paterick TJ, Fletcher GF, Maron BJ. Medical and legal issues impacting the cardiovascular evaluation of competitive athletes. *JAMA*. 2005;294:3011–3018.

KEY WORDS: cardiomyopathy ■ death, sudden ■ echocardiography ■ electrophysiology ■ exercise ■ hypertrophy ■ remodeling