

Coronary Artery Anomalies and Sports Activities

Paolo Angelini, MD

From the Department of Cardiology, Texas Heart Institute at St. Luke's Episcopal Hospital, Houston, Texas

Address for correspondence: Paolo Angelini, MD, P.O. Box 20206, Houston, TX

77030. Telephone 713-790-9401; fax 713-790-0353; e-mail

PAngelini@leachmancardiology.com

*Your vision will become clear only when you can look into your heart.
Who looks outside, dreams; who looks inside, awakes. (Carl Jung)*

INTRODUCTION: THREE STORIES

Case 1: Sudden Cardiac Death in a Top High-School Athlete

A 19-year-old African-American male basketball player had trained and competed intensively for at least 5 years without having cardiovascular signs or symptoms. He excelled at this sport and was the star of his high-school basketball team. He had passed multiple annual preparticipation examinations without showing any evidence of disease. At the end of the first half of a citywide championship game, he was the top-scoring player. After completing a successful offensive play, he switched to a defensive position and became suddenly confused. A few seconds later, he fell onto his back, hit his head, and became unconscious. He remained motionless on the floor while the coaching staff attended to him. When emergency medical personnel arrived, 10 minutes later, the electrocardiographic monitor showed a straight line. Resuscitation efforts were initiated and continued until hospital admission. Despite intravenous infusion of epinephrine, repeated external defibrillation, and hour-long cardiopulmonary resuscitation, the patient never regained a spontaneous, stable pulse. At autopsy, he was found to have a structurally normal, moderately hypertrophied heart, with anomalous origin of the right coronary artery (RCA), which arose from the left sinus of Valsalva, just a few millimeters to the left of the anterior aortic commissure (Fig. 17-1A,B). The dominant RCA penetrated into the aortic wall and pursued a tangential proximal course, remaining within the aortic wall for 5 mm. Figure 17-1C shows a cross-section of the intramural segment. Detailed examination revealed no histologic

changes characteristic of focal necrosis. Figure 17-2 provides a further description of this anomaly by means of radiologic methods.

Case 2: Sudden Crib Death in an Infant

Thirty minutes after being seen by his grandparents in his normal healthy state, a 2-month-old boy was found motionless in his crib. He could not be resuscitated by the emergency medical team, which arrived 15 minutes later. An autopsy showed only an abnormal coronary pattern, characterized by anomalous origination of the RCA from the left sinus of Valsalva with an intramural proximal course (Fig. 17-3). Histologic examination revealed no signs of a myocardial infarction.

Case 3: A Surprising Accidental Finding in an 83-Year-Old Woman

An 83-year-old asymptomatic, physically active woman underwent heart catheterization because a routine nuclear pharmacologic stress test had shown probable reversible ischemia of the inferior wall. On coronary angiography, the left coronary artery (LCA) was found to originate from the RCA at the right sinus of Valsalva. The LCA had an intramural course, which crossed from right to left between the aorta and pulmonary artery, as confirmed by magnetic resonance imaging (MRI). No atherosclerotic stenosis was observed. The patient refused to undergo further testing. Figure 17-4 shows a typical angiographic image of this anomaly.

Comment

These 3 case histories illustrate the spectrum of clinical manifestations that may be seen in patients with coronary artery anomalies (CAAs). In the first case, an ectopic RCA was associated with sudden cardiac death (SCD) in a star athlete who had previously been asymptomatic. In the second case, an apparently healthy infant died

suddenly and unexpectedly in his crib. In the third case, an asymptomatic elderly woman was incidentally found to have the anomaly generally considered to be the most lethal CAA (LCA originating from the right sinus of Valsalva with an intramural course). The patient had had a long, cardiologically uneventful life until the diagnosis was accidentally made, as a consequence of what was probably a false-positive nuclear stress test.

This chapter focuses on current anatomic, physiologic, and clinical concepts regarding CAAs in the context of sports activities. The author discusses some newly defined principles and urges a structured approach to this confusing area of cardiology and sports medicine.

CORONARY ARTERY ANOMALIES: A BRIEF APPRAISAL OF A COMPLEX ENTITY

For some 40 years, the medical literature has reported a worrisome association between competitive sports activities and CAA-related SCD.¹⁻⁷ Cheitlin and colleagues⁷ initially raised this issue in 1974 when they reported a limited series. Since then, the belief has become widely pervasive in the medical community, as well as the public at large, that any kind of CAA entails an increased risk of SCD, especially during sports activities. This belief was underscored by the guidelines published in 1994 by the 26th Bethesda Conference for determining eligibility for competition in athletes with cardiovascular abnormalities.⁸ The authors alluded to “coronary anomalies” as a generic label and stated that 19% of deaths in athletes were due to CAAs (not including 5% due to muscular bridging, which is also a CAA but was listed separately in that document). Recent, more advanced studies have clarified that only a few types of CAAs, by means of specific, plausible and possibly quantifiable mechanisms, have a

high risk of severity in individual cases; these few CAAs can indeed cause transient ischemic symptoms and—only rarely—SCD,⁹⁻¹¹ typically in the context of extreme exertion^{12,13} (Capsule 17-1).

Today, CAAs are increasingly being recognized by clinical screening techniques such as standard coronary angiography or computed tomographic angiography (CTA). Although our understanding of these anomalies continues to evolve, our current knowledge is far from satisfactory or comprehensive, mainly because the medical community has not yet fully understood the involved pathophysiologic mechanisms or established definite severity criteria for identifying individual risk.

Table 17-I and Figure 17-5 present most of the known CAAs. Several recent comprehensive reviews^{14,15} give a more complete description of these anomalies, which may be considered to involve a congenital defect in coronary origination, course, and/or termination (Capsule 17-2). All CAAs are due to a defect in embryologic development that occurs during the first trimester of human gestation. The ultimate cause of such defects can occasionally be traced to a genetic disorder; most CAAs are due to biologic variations in a complex process that is influenced by multiple redundant, morphogenetic factors.¹⁶

Table 17-II lists various postulated or proven pathophysiologic mechanisms capable of impairing the function (ie, supplying blood flow to the dependent myocardium) of an abnormally shaped coronary artery.¹⁵ The only anomaly that has an intrinsic consistent pathophysiologic mechanism capable of causing ischemia is number 3, in Figure 17-5 (see also Figs. 17-4, 17-6, and 17-7), which features anomalous origin and crossing of the ectopic vessel in a preaortic course (“between the aorta and

pulmonary artery”). This anomaly is a case of “anomalous origin of a coronary artery from the opposite sinus of Valsalva” with an intramural course in the aortic wall (ACAOS). Recent experience, as reflected in the medical literature, has shown that ACAOS is the culprit in most cases of SCD in athletes and other persons undergoing extreme exertion (Capsule 17-3).^{9,10,12-15,17-19} As shown in Figures 17-1 through 17-4, the peculiar, insidious, and only recently recognized mechanism of ischemia in ACAOS is related to the abnormal vessel’s ectopic proximal course inside the aortic wall.

The basic mechanisms of stenosis in ACAOS (Figs. 17-6 and 17-7) are 1) hypoplasia of the proximal lumen with respect to the distal vessel; 2) lateral compression of the intramural segment, which runs inside the aortic media; and 3) further compression of the same segment during systole (Fig. 17-7) and tachycardia.¹⁷

At baseline, only occasional cases of ACAOS involve critical stenosis (Fig. 17-4), but severe stenosis can develop during extreme exertion or a hypertensive crisis, resulting in an increased stroke volume, systolic pressure, and/or “systolic time/minute” (as in severe tachycardia).¹⁷ Unfortunately, the methods typically used to establish the severity of coronary stenosis—even stress nuclear scintigraphy or measurement of the pressure decrease at the coronary ectopic origin¹⁹—usually fail to provide objective evidence of significant ischemia.

A major limitation of the literature (especially the early literature) concerning the clinical implications of CAAs is related to the fact that necropsy case series were initially the basis for generalized statements about these disorders and that the “denominator” of the reported cases (involving the same anomalies) was not available or taken into account.^{10,15} Additionally, in cases of otherwise unexplained death, the “mere presence”

of a CAA was automatically assumed to be the “cause” of death. More recently, clinicians have realized that most CAAs are quite benign and compatible with a normal, and even an active, lifestyle.^{10,15,18}

The recent pursuit of large population-based studies has enabled researchers to evaluate the real risk of SCD in the context of a definite exercise program. Thus far, the most significant study has been one by Eckart and colleagues,¹⁹ who studied 6.35 million US Army recruits over 25 years. The recruits underwent an initial 2-month period of boot-camp training, which included running long distances and lifting or carrying heavy weights. These activities entailed some degree of dehydration in addition to maximal physical exertion. Two hundred sixty-three recruits died of nontraumatic causes. At necropsy, a third of these deaths were found to be related to the presence of a CAA—specifically ACAOS of the LCA (L-ACAOS) in all cases. No other types of CAAs were responsible for the lethal events. Nevertheless, one cannot conclude that all other CAAs may be considered benign because they cannot cause exercise-related death. Coronary anomalies have been claimed to be the cause of some 20% of death in athletes¹⁻⁷ (Capsule 17-4). Other studies (unfortunately without a denominator) have shown that ACAOS of the RCA (R-ACAOS) and anomalous origination of the LCA from the pulmonary artery are additional culprits.^{2,5,12,13,20} Most studies, though, do not describe the population at risk: in terms of either the total population from which the target patients were derived²⁰ or the expected incidence of CAAs, especially ACAOS.

In addition to SCD, other symptoms may be seen during exertion or even at rest in patients with some CAAs (see Screening, Diagnosis, and Counseling, below). The clinically important concept that has resulted from recent CAA series is not only that

each type of CAA has fundamentally different clinical implications but also that each individual patient with a given type of CAA may have a different severity of the disorder, depending on the mechanism responsible for ischemic events.¹⁷ As a consequence, the popular concept that CAAs generically pose a high risk of ischemic consequences during exertion should, in fact, be qualified by asking “what type of anomalies?” and “what level of severity?” Unfortunately, the subclassification of each anomaly, and especially of the markers of severity in individual cases, is still subject to guesswork and speculation.^{9,17-19,21,22}

With regard to athletics, it is largely unknown whether the most serious forms of CAAs cause physical limitations and, if so, whether they automatically imply preclusion from involvement in competitive sports. Both of these possibilities are likely, and both warrant investigation.

SPORTS ACTIVITIES AND CORONARY ANOMALIES

Sports activities are intrinsically competitive, involving a need for maximal physical performance. During training and especially during the competition itself, athletes exceed their usual level of physical activity, going well beyond that reached during submaximal clinical stress testing. The following three facts are well established: 1) Of persons who have a “potentially lethal” CAA variant, nonathletes have a much lower probability of SCD than do athletes with the same condition;^{3,13,18,23} 2) most CAA-related deaths occur during or immediately after exertion;^{2,3,4,7,12,13,16,23-25} and 3) older patients with ACAOS do not have a clearly increased incidence of either SCD or myocardial infarction.^{2,10,12,18}

What sports-related factors increase the likelihood that a CAA will have catastrophic consequences? In general, with any CAA that has an intrinsic ischemic potential, the chance of clinical manifestations may be expected to increase when the myocardial oxygen demand is maximal and the oxygen supply limited. Additionally, peak exercise conditions (characterized by a cardiac output and workload up to 5 times baseline levels), emotion-related catecholamine surges, and dehydration can extend the intrinsic ischemic burden and risk of complications beyond tolerable limits. In this setting, ACAOS-related functional changes that occur during or early after peak exertion, or both, may be related to the unique mechanism of (unexpected) ischemia.

The basic pathophysiologic mechanism in ACAOS seems to be related to lateral compression of the intramural aortic segment: the ectopic artery originates tangentially, and the initial segment is embedded in the aortic media (see Figs. 17-1 through 17-5). At baseline, intravascular ultrasonography (IVUS) shows a variable amount of cross-sectional narrowing that may be compatible with a lack of symptoms during physical training. However, maximal physical exertion may cause critical worsening of the stenosis because of 1) an increased cardiac output and, more especially, an increased stroke volume (leading to increased pulsatility and systolic expansion of the aortic root); 2) increased systolic compression of the intramural ectopic artery (Figs. 17-6 and 17-7); and 3) extreme tachycardia (frequently >200 beats/min), which increases the systolic time with respect to the diastolic time to an exceptional degree. Interestingly, in the above-mentioned military recruits, 86% of the SCDs occurred during or soon after exercise²⁴ (Capsule 17-5).

Other, more frequent coronary anatomic variants such as myocardial bridges or small coronary fistulas are occasionally reported to cause symptoms or even SCD during exertion.^{2,3,23,25} Speculation about the cause/effect of these events is ongoing. Even in the military recruits,¹⁹ for example, about 25% of the SCDs were unexplained by necropsy findings; any such cases involving a minor CAA could give rise to an unjustified association between that anomaly and SCD.

It is not clear whether any particular sports activity is specifically associated with an increased risk of SCD in individuals who have a given type of CAA. It has long been suspected that the aorta may be unusually elastic or distensible in persons with Marfanoid phenotypes, especially tall basketball players.¹⁷ In the presence of an intramural ectopic coronary artery, such an association might have specific repercussions (possibly resulting in increased systolic compression). Heavy weight lifting, which is transiently associated with an extremely high intrathoracic pressure, may be associated with similar levels of aortic root dilatation during exertion. In itself, regular training can lead, over time, to dilatation of both the left ventricle and the aortic root.²⁶

In addition to SCD, the clinical manifestations of myocardial ischemia normally seen in ischemic heart disease have also been observed in ACAOS and should be detectable during preparticipation screening: unusual dyspnea on exertion, with or without chest pain or pressure, and/or dizziness or syncope.²⁷ These symptoms should be properly evaluated, because they are frequently the only ones an athlete reports before succumbing to SCD in the context of ACAOS. Recently, the popularization of CTA screening for coronary artery disease in adults has resulted in the fortuitous

detection of a growing number of CAAs, causing anxiety and uncertainty for both patients and physicians.²⁸

The few reports of ACAOS-related SCD that have included clinical details^{29,30} suggest that in athletes with CAAs, SCD has the following specific functional and electrocardiographic features: 1) initially, hypotension and bradycardia; 2) later, asystole (primary ventricular fibrillation is probably unusual under such conditions) (Capsule 17-6); and 3) finally, reperfusion-related rapid ventricular arrhythmias (ventricular fibrillation), usually after resuscitative treatment.^{10,31} These features are relevant to the planning of effective resuscitative efforts (see Prevention and Treatment of Sudden Coronary Death in Athletes, below).

SCREENING, DIAGNOSIS, AND COUNSELING

Whereas ACAOS is relatively rare in the general population, it must be similarly rare⁵ or even more so in trained athletes, because of a spontaneous selection bias due to symptoms or physical limitations. Maron and colleagues^{6,32} estimated that the incidence of SCD risk factors is about 1/10,000 in marathon runners older than age 45 years (mostly because of atherosclerotic coronary artery disease) but is only 1/200,000 in runners below that age. Crawford and coauthors³³ indicated that the incidence of SCD is 1-2/100,000 per year in high school athletes, 1/50,000 in marathon runners, and 1/15,000 in recreational joggers of any age. If the healthcare system could (or would) support generalized screening by means of echocardiography, coronary magnetic resonance angiography (MRA), or CTA^{28,34-37} (Figs. 17-4 and 17-8), at least in athletes, it should be technically easy to reliably diagnose serious CAAs (essentially, ACAOS). The cost-effectiveness of such a policy can be grossly based on the fact that probably

close to 1% of the general population has ACAOS.¹⁴ If young athletes in the United States number 5 million per year,^{6,38} about 50,000 of these athletes would be expected to have a CAA. Moreover, because experience in the catheterization laboratory¹⁵ has shown that 0.1% of the general population has L-ACAOS, 5000 young athletes would be at the highest risk in any given year. About 0.9% of the general US population is estimated to have the other significant variant, R-ACAOS, accounting for 45,000 cases.

As discussed above, the mortality rate during maximum physical exertion has been only approximately established. The best available evidence for L-ACAOS has been provided by the US Army Recruits study²⁴ and by a database established in Veneto, Italy.^{23,39} Specifically, of the 6,350,000 recruits, about 6300 would have been expected to have L-ACAOS, of whom 36 (4/1000) died during the 2-month exposure to an unusually high level of physical exertion; therefore, we may conclude that SCD affects about 1.4/100,000 recruits during the 2-month exposure period, or 8.4/100,000 recruits per year. In the same population, there were 263 “nontraumatic deaths,” for a mortality of 25/100,000 over the 2-month period.²⁴ In comparison, in the state of Minnesota, the general risk of SCD in high-school athletes was reported to be about 0.5/100,000 per year, while the CAA-related risk was 20% of the total, or 0.1/100,000 athletes.³⁸ In a similar study performed in Washington state, the estimated annual incidence of cardiac arrest was 1.8/100,000.⁴⁰ Evidently, the risk of CAA-related SCD in army recruits would be about 16.8 times higher (or more frequently diagnosed) than in athletes of an equivalent age. In professional athletes, the reported incidence of SCD is 1/3500 (or 30/100,000) per year.⁴¹

If policy guidelines were instituted regarding CAAs, screening would initially apply only to athletes. Sedentary persons with ACAOS have a lower probability of SCD (although their risk—and that associated with less aggressive sports activities—has not been evaluated in reasonable detail). This selection policy would greatly improve the cost-efficiency of screening. In athletes and possibly military recruits, one could further restrict the use of expensive and possibly risky (in the context of a large population study) screening, by subselecting candidates who have clinical symptoms such as unusual shortness of breath, dizziness, syncope, or chest pain. Unfortunately, however, when retrospectively studied, only about 20% of SCD victims who had ACAOS with an intramural course were found to have reported suspicious symptoms that could have warranted such screening (Capsule 17-7).

In general, athletes are highly motivated, aggressive individuals who tend to under-appreciate or under-report symptoms. To be useful, a history-taking session would need to be highly structured and informative.^{6,8,22,33,39} Therefore, athletes and their coaches should be made generally aware of the current thinking about CAAs and other causes of SCD during sports activities and should necessarily be included in relevant discussions.

Electrocardiography, both at rest and during treadmill exercise, is a relatively inexpensive screening method that is frequently used to identify cardiomyopathies and coronary artery disease. Unfortunately, however, electrocardiography is not a sensitive method for identifying ACAOS.^{12,16,27,38,42-44} Similarly, in this setting, nuclear stress testing is of dubious utility, yielding an unacceptably high level of false-positive and false-negative data.¹⁰ A dedicated, prospective echocardiographic study of ACAOS

patients has not yet been carried out; however, preliminary testing³⁴ suggests that echocardiography can reliably diagnose L-ACAOS (without determining the specific course of the ectopic artery) in nonobese young individuals. Likely, the positive predictive value would be near 90% in L-ACAOS^{34,37} but 50% to 70% in R-ACAOS.^{27,45}

Currently, we prefer to use cardiac MRA, CTA, or traditional coronary angiography to identify the presence of CAAs.²⁷ Although coronary angiography is almost 100% successful in expert hands, it has three main limitations:

1) The diagnosis of ACAOS implies that the ectopic proximal coronary artery courses inside the anterior wall of the aorta. Selective catheter cannulation for angiography may be difficult, because of the tangential proximal course of the ectopic artery. Additionally, a similar anatomic variant, ectopic LCA with an intraseptal course, is frequently mistaken for L-ACAOS (with an intramural aortic course) by nonexpert interpreters of CTA or MRA studies.²⁷ Unlike true L-ACAOS, this variant does not involve a clear mechanism of ischemia; its prognosis is generally benign, so no intervention is required, and no physical restrictions are indicated.

2) Mere recognition of ACAOS is inadequate to identify the specific risk incurred by a given patient, especially during sports activities. As discussed above, a fundamental issue involves determining the severity of the anomaly in each individual case, which basic screening methods do not allow.

3) The diagnosis of ACAOS (or some other CAA) may negatively affect an athlete's emotional outlook if he or she has to abandon sports activities. Therefore, referral to an expert center for disease subclassification and counseling is advised.

Criteria for increased risk in L-ACAOS patients are still being defined. Our group has suggested that high-risk criteria should include both specific symptoms (reproducible exercise-related chest pain, dyspnea, objective signs of ischemia, and especially syncope or a history of SCD) and also features that are quantifiable on IVUS examination (>50% baseline cross-sectional area stenosis, with further phasic systolic worsening of >10% during simulated exercise testing¹⁷). Until validated recommendations are issued, as approved by a representative professional organization, many authors^{6,21,22,42} suggest that all L-ACAOS patients should be strongly discouraged from participating in maximal sports activities and should be referred to a specialized center. In contrast, R-ACAOS apparently has a more benign prognosis with respect to SCD,^{10,12,13,18,21,22,24} but this prognosis varies in individual patients, probably depending on the clinical history,²⁷ coronary dominance pattern, and IVUS findings.¹⁷ Multicenter investigations are underway to establish reliable guidelines based on general principles. At specialized centers dedicated to CAAs, current efforts are concentrated on establishing solid criteria by which to judge the severity of individual cases.¹⁷

PREVENTION AND TREATMENT OF SUDDEN CARDIAC DEATH IN ATHLETES

On the sports field, SCD is a tragic experience, not only for the victim but also for witnesses, while survival in that setting is much less likely than in a hospital environment. Society has come to recognize that it has a moral duty both to prevent such incidents and to facilitate rescue efforts when SCD occurs. Several specific considerations apply to the rescue of athletes affected by a CAA: 1) These individuals generally have a healthy heart, so expeditious resuscitation should result in a good

chance of recovery (Capsule 17-8).⁴⁶ 2) Unlike older patients who have a coronary event caused by atherothrombotic disease, these patients are unlikely to have had an anatomic event that would necessitate recanalization. 3) In patients with L-ACAOS (and in the few with R-ACAOS) the mechanism of SCD probably depends on a specific, unique behavior that, though still unclear, seems initially to involve hypotension and bradycardia more than ventricular fibrillation. Likely, a critical hemodynamic overload and increased compression of the intramural, ectopic artery leads to a dramatic (“suicidal”) negative spiral of events, whereby bradycardia leads to hypotension, and hypotension to bradycardia, as observed in patients with acquired >50% stenosis of the left main coronary artery.^{47,48} Whereas some of these episodes result in SCD, others abort, usually owing to the cessation of exertion, resulting only in syncope and spontaneous recovery, as in L-ACAOS patients who have a sudden cardiac arrest followed by successful recovery. Early recovery from a sudden cardiac arrest in L-ACAOS patients is likely if early resuscitation is aggressively instituted, especially with rapid external cardiac massage (Capsule 17-9).⁴⁹⁻⁵¹

If resuscitation efforts are delayed or inadequate, SCD frequently results in secondary complications: 1) Ventricular tachycardia and fibrillation (as a likely manifestation of myocardial reperfusion arrhythmias, which may be potentiated by high levels of circulating catecholamines); 2) refractory, persistent hypotension or a low cardiac output that is poorly responsive to vasopressors; and 3) ischemic brain damage caused by head trauma, the initial syncopal fall, or the cardiac arrest itself. In such cases, resuscitation may necessitate more aggressive support than medical treatment alone. An easily implantable ventricular assist device such as the TandemHeart

(Cardiac Assist Inc., Pittsburgh, Pa.), or the Impella pump (Abiomed, Danvers, Mass.)^{52,53} may stabilize the patient's condition, allowing myocardial unloading and eventual recovery. In this context, the diagnosis of L-ACAOS is generally established by echocardiography in the emergency room and confirmed by traditional angiography, CTA, or MRA in the catheterization laboratory.^{16,17}

After recovery from SCD, the causes of the event should be quickly ascertained insofar as possible, because secondary prevention is mandatory and may be not only lifesaving but also quite cost-effective. Clearly, in the absence of effective correction, syncope or SCD resulting from L-ACAOS is likely to recur. Both echocardiography and CTA are urgently indicated for survivors of a sudden cardiac arrest. Counseling about interventions and/or discontinuation of sports activities should be pursued at specialized centers (Capsule 17-10). Most experts believe that such activities should be routinely curtailed unless the causative problem is effectively treated, for example with surgical correction of L-ACAOS followed by a negative appropriate follow-up study.^{18,21}

In the absence of established, evidence-based guidelines concerning CAAs,^{6,22,27,41,54,55} we can only make reasonable temporary and tentative recommendations while awaiting further experience and documentation, as well as official statements by representative professional societies. Aborted SCD in the presence of L-ACAOS constitutes an adequate basis for intervention (generally surgical); in the presence of R-ACAOS, however, aborted SCD or other symptoms (such as dyspnea, syncope, or chest pain on exertion) necessitate further diagnostic workup. At our center, IVUS imaging of the pertinent coronary anatomy is routinely

used to evaluate the severity of R-ACAOS. Unfortunately, the recommendations for treating ACAOS that have been issued by official organizations include few details and little supporting evidence. In general, it is currently agreed that ACAOS patients who have severe symptoms (dyspnea, chest pain, or syncope during exertion) or objective proof of ischemia on stress testing should have a revascularization procedure: surgery for L-ACAOS^{11,21} as well as for R-ACAOS.^{21,56-58} For symptomatic R-ACAOS, our institution and other centers have recently implemented an experimental, institutional-review-board–approved protocol that calls for stent-angioplasty of the intramural segment, if a significantly stenosed segment is identified,⁵⁷ as an attractive alternative to surgical treatment.⁴ Treatment of patients who have minor symptoms or who lack evidence of ischemia on stress testing is subject to an ongoing discussion.¹⁸ In addition, the question of genetic studies in familial cases of CAAs remains unsettled.^{18,48,56}

CONCLUSIONS

Recently, ACAOS has been recognized as one of the most frequent causes of SCD in athletes. Because L-ACAOS is the dominant pathology in these cases, the current emphasis is on excluding the presence of this condition in competitive athletes. In specific individuals, the severity of a given form of L-ACAOS or of some cases of R-ACAOS needs to be ascertained, by means of IVUS. Because SCD on the sports field should be avoided “at all costs,” we recommend that relevant new information regarding the causes of SCD in athletes be disseminated to coaches and other staff members, as well as athletes themselves. Victims of SCD should undergo aggressive resuscitation on the playing field, followed by referral to a specialized center for further

diagnosis and treatment. As widespread screening for CAAs is introduced in clinical and population-based studies and as mechanisms of ischemia in ACAOS are clarified, more effective means of preventing the catastrophic consequences of CAAs can be expected to become available.

ACKNOWLEDGMENTS

The author thanks Virginia Fairchild, of the Texas Heart Institute's Department of Scientific Publications, for editorial assistance in preparing this chapter. He also thanks Melissa Mayo and Isabel Vasquez, of the Texas Heart Institute's Visual Communications Services, for help in preparing the figures.

REFERENCES

1. Maron BJ, Roberts WC, McAllister HA, Rosing DR, Epstein SE. Sudden death in young athletes. *Circulation*. 1980;62(2):218-229.
2. Frescura C, Basso C, Thiene G, et al. Anomalous origin of coronary arteries and risk of sudden death: a study based on an autopsy population of congenital heart disease. *Hum Pathol*. 1998;29:689-695.
3. Corrado D, Basso C, Rizzoli G, Schiavon M, Thiene G. Does sports activity enhance the risk of sudden death in adolescents and young adults? *J Am Coll Cardiol*. 2003;42:1959-1963.
4. Maron BJ. Sudden death in young athletes. *N Engl J Med*. 2003;349:1064-1075.
5. Mirchandani S, Phoon CK. Management of anomalous coronary arteries from the contralateral sinus. *Int J Cardiol*. 2005;102:383-389.
6. Maron BJ, Thompson PD, Ackerman MJ, et al; American Heart Association Council on Nutrition, Physical Activity, and Metabolism. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation*. 2007;115:1643-1655.
7. Cheitlin MD, De Castro CM, McAllister HA. Sudden death as a complication of anomalous left coronary origin from the anterior sinus of Valsalva, a not-so-minor congenital anomaly. *Circulation*. 1974;50:780-787.

8. Maron BJ, Thompson PD, Puffer JC, et al. Cardiovascular preparticipation screening of competitive athletes. A statement for health professionals from the Sudden Death Committee (clinical cardiology) and Congenital Cardiac Defects Committee (cardiovascular disease in the young), American Heart Association. *Circulation*. 1996;94:850-856.
9. Taylor AJ, Byers JP, Cheitlin MD, Virmani R. Anomalous right or left coronary artery from the contralateral coronary sinus: “high-risk” abnormalities in the initial coronary artery course and heterogeneous clinical outcomes. *Am Heart J*. 1997;133:428-423.
10. Angelini P, Velasco JA, Flamm S. Coronary anomalies: incidence, pathophysiology, and clinical relevance. *Circulation*. 2002;105:2449-2454.
11. Angelini P, Walmsley RP, Liberos A, Ott DA. Symptomatic anomalous origination of the left coronary artery from the opposite sinus of valsalva. Clinical presentations, diagnosis, and surgical repair. *Tex Heart Inst J*. 2006;33:171-179.
12. Taylor AJ, Rogan KM, Virmani R. Sudden cardiac death associated with isolated congenital coronary artery anomalies. *J Am Coll Cardiol*. 1992;20:640-647.
13. 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.
14. Angelini P. Normal and anomalous coronary arteries: definitions and classification. *Am Heart J*. 1989;117:418-434.

15. Angelini P, Villason S, Chan AV, Diez JG. Normal and anomalous coronary arteries in humans. In: Angelini P, ed. *Coronary Artery Anomalies*. Philadelphia, Pa: Lippincott, Williams & Wilkins; 1999:27-150.
16. Roberts WC. Congenital coronary arterial anomalies unassociated with major anomalies of the heart and great vessels. In: WC Roberts, ed. *Adult Congenital Heart Diseases*. Philadelphia, Pa: Davis Co; 1987:583-663.
17. Angelini P, Flamm SD. Newer concepts for imaging anomalous aortic origin of the coronary arteries in adults. *Catheter Cardiovasc Interv*. 2007;69:942-954.
18. Cheitlin MD. Finding asymptomatic people with a coronary artery arising from the wrong sinus of valsalva: consequences arising from knowing the anomaly to be familial. *J Am Coll Cardiol*. 2008;51:2065-2067.
19. Eckart RE, Scoville SL, Campbell CL, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med*. 2004;141:829-834.
20. Tomanek RJ. Formation of coronary vasculature during development. *Angiogenesis*. 2005;8:273-284.
21. Gersony WM. Management of anomalous coronary artery from the contralateral sinus. *J Am Coll Cardiol*. 2007;50:2083-2084.
22. Corrado D, Pelliccia A, Bjørnstad HH, et al; Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. Consensus Statement of the Study Group of Sport Cardiology of the

- Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. *Eur Heart J.* 2005;26:516-524.
23. Basso C, Frescura C, Corrado D, et al. Congenital heart disease and sudden death in the young. *Hum Pathol.* 1995;26:1065-1072.
 24. Dimopoulos K, Di Mario C, Barlis P, et al. Haemodynamic significance of an anomalous right coronary with inter-arterial course assessed with intracoronary pressure measurements during dobutamine challenge. *Int J Cardiol.* 2008;126:e32-e35.
 25. Waller BF, Hawley DA, Clark MA, Pless JE. Incidence of sudden athletic deaths between 1985 and 1990 in Marion County, Indiana. *Clin Cardiol.* 1992;15:851-858.
 26. Maron BJ, Pelliccia A. The heart of trained athletes: cardiac remodeling and the risks of sports, including sudden death. *Circulation.* 2006;114:1633-644.
 27. Glover DW, Glover DW, Maron BJ. Evolution in the process of screening United States high school student-athletes for cardiovascular disease. *Am J Cardiol.* 2007;100:1709-1712.
 28. Budoff MJ, Ahmed V, Gul KM, Mao SS, Gopal A. Coronary anomalies by cardiac computed tomographic angiography. *Clin Cardiol.* 2006;29:489-493.
 29. Taylor AJ, Farb A, Ferguson M, Virmani R. Myocardial infarction associated with physical exertion in a young man. *Circulation.* 1997;96:3201-3204.
 30. Devanagondi R, Brenner J, Vricella L, Ravekes W. A tale of two brothers: anomalous coronary arteries in two siblings. *Pediatr Cardiol.* 2008;29:816-819.

31. Iskandar EG, Thompson PD. Exercise-related sudden death due to an unusual coronary artery anomaly. *Med Sci Sports Exerc.* 2004;36:180-182.
32. Maron BJ, Poliac LC, Roberts WO. Risk for sudden cardiac death associated with marathon running. *J Am Coll Cardiol.* 1996;28:428-431.
33. Crawford MH. Screening athletes for heart disease. *Heart.* 2007;93:875-879.
34. Pelliccia A, Spataro A, Maron BJ. Prospective echocardiographic screening for coronary artery anomalies in 1,360 elite competitive athletes. *Am J Cardiol.* 1993;72:978-979.
35. Pelliccia A. Congenital coronary artery anomalies in young patients: new perspectives for timely identification. *J Am Coll Cardiol.* 2001;37:598-600.
36. Davis JA, Cecchin F, Jones TK, Portman MA. Major coronary artery anomalies in a pediatric population: incidence and clinical importance. *J Am Coll Cardiol.* 2001;37:593-597.
37. Maron BJ, Leon MB, Swain JA, Cannon RO 3rd, Pelliccia A. Prospective identification by two-dimensional echocardiography of anomalous origin of the left main coronary artery from the right sinus of Valsalva. *Am J Cardiol.* 1991;68:140-142.
38. 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.
39. Corrado D, Basso C, Pavei A, Michieli P, Schiavon M, Thiene G. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. *JAMA.* 2006;296:1593-1601.

40. Lotfi K, White L, Rea T, et al. Cardiac arrest in schools. *Circulation*. 2007;116:1374-1379.
41. Harris KM, Sponsel A, Hutter AM, Maron BJ. Brief communication: cardiovascular screening practices of major North American professional sports teams. *Ann Int Med*. 2006;145:507-511.
42. Chaitman BR. An electrocardiogram should not be included in routine preparticipation screening of young athletes. *Circulation*. 2007;116:2610-2614.
43. Lawless CE, Best TM. Electrocardiograms in athletes: interpretation and diagnostic accuracy. *Med Sci Sports Exerc*. 2008;40:787-798.
44. Myerburg RJ, Vetter VL. Electrocardiograms should be included in preparticipation screening of athletes. *Circulation*. 2007;116:2616-2626.
45. Frommelt PC, Frommelt MA, Tweddell JS, Jaquiss RD. Prospective echocardiographic diagnosis and surgical repair of anomalous origin of a coronary artery from the opposite sinus with an interarterial course. *J Am Coll Cardiol*. 2003;42:148-154.
46. Lawless CE, Best TM. Electrocardiograms in athletes: interpretation and diagnostic accuracy. *Med Sci Sports Exerc*. 2008;40:787-798.
47. Liberman L, Pass RH, Kaufman S, Hordof AJ, Printz BF, Prakash A. Left coronary artery arising from the non-coronary sinus: a rare congenital coronary anomaly. *Pediatr Cardiol*. 2005;26:672-674.
48. Caracciolo EA, Davis KB, Sopko G, et al. Comparison of surgical and medical group survival in patients with left main coronary artery disease. Long-term CASS experience. *Circulation*. 1995;91:2325-2334.

49. SOS-KANTO study group. Cardiopulmonary resuscitation by bystanders with chest compression only (SOS-KANTO): an observational study. *Lancet*. 2007;369:920-926.
50. Bobrow BJ, Clark LL, Ewy GA, et al. Minimally interrupted cardiac resuscitation by emergency medical services for out-of-hospital cardiac arrest. *JAMA*. 2008;299:1158-1165.
51. Peberdy MA, Ornato JP. Progress in resuscitation: an evolution, not a revolution. *JAMA*. 2008;299:1188-1190.
52. Angelini P. Surgical standby: state of the art. In: Topol EJ, ed. *Textbook of Interventional Cardiology*. Philadelphia, Pa: Saunders; 2008:541-548.
53. Maron BJ, Isner JM, McKenna WJ. 26th Bethesda conference: recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities. Task Force 3: hypertrophic cardiomyopathy, myocarditis and other myopericardial diseases and mitral valve prolapse. *J Am Coll Cardiol*. 1994;24:880-885.
54. Thompson PD, Franklin BA, Balady GJ, et al; American Heart Association Council on Nutrition, Physical Activity, and Metabolism; American Heart Association Council on Clinical Cardiology; American College of Sports Medicine. Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. *Circulation*. 2007;115:2358-2368.

55. Maron BJ, Douglas PS, Graham TP, Nishimura RA, Thompson PD. Task Force 1: preparticipation screening and diagnosis of cardiovascular disease in athletes. *J Am Coll Cardiol.* 2005;45:1322-1326.
56. Brothers JA, Stephens P, Gaynor JW, Lorber R, Vricella LA, Paridon SM. Anomalous aortic origin of a coronary artery with an interarterial course: should family screening be routine? *J Am Coll Cardiol.* 2008;51:2062-2064.
57. Angelini P, Velasco JA, Ott D, Khoshnevis GR. Anomalous coronary artery arising from the opposite sinus: descriptive features and pathophysiological mechanisms, as documented by intravascular ultrasonography. *J Invasive Cardiol.* 2003;15:507-515.
58. Virmani R, Chun PK, Goldstein RE, Robinowitz M, McAllister HA. Acute takeoffs of the coronary arteries along the aortic wall and congenital coronary ostial valve-like ridges: association with sudden death. *J Am Coll Cardiol.* 1984;3:766-771.

LEGENDS

- Figure 17-1.** Autopsy results, Case 1: **A.** Internal view of the aortic root, showing the anomalous location of the orifice of the right coronary artery (RCA), which is positioned to the left of the anterior commissure of the aortic valve at the left sinus of Valsalva (L), next to the normally located left ostium (LCA). Notice the tangential origin of the ectopic RCA, which has a slit-like appearance. N, noncoronary sinus; R, right sinus; **B.** External view of the aortic root, showing the intramural course of a probe, which is introduced into the ostium and is brought out through the transected extramural coronary artery, at its exit from the aortic wall. **C.** Histologic cross-section of the aortic and pulmonary (PA) trunks, showing the intramural course of the RCA. The RCA shows the same lateral compression as seen on intravascular ultrasonography (see Fig. 17-6) and lacks a proper media and adventitia (the RCA intima is free of atherosclerotic buildup and is surrounded by the aortic media). IVS, interventricular septum. (Courtesy of Dwayne A. Wolf, PhD, Office of the Medical Examiner of Harris County, Texas). Figure 17-1C is reprinted from Angelini et al⁵⁷ with permission.
- Figure 17-2.** Angiographic appearance of an anomalous right coronary artery arising from the opposite sinus, in the left anterior oblique (**A**) and right anterior cranial oblique (**B**) projections. In this case (which differs from the ACAOS case seen in Figure 17-1), the right coronary artery (RCA, with an arrow at its ostium) arises ectopically, next to the left coronary

artery (LCA), and both arteries are visualized simultaneously. In **B**, the RCA clearly has an ostial narrowing, unlike in view **A**. See Figure 17-6 for the intravascular ultrasonographic appearance of the same RCA.

Figure 17-3. Autopsy results, Case 2: View from the internal aortic root, showing high origination of the right coronary artery (RCA), above the left sinus of Valsalva, with a slit-like ostium, in a case of sudden crib death involving a newborn boy. Abbreviations as in Figure 17-1. (Courtesy of Dwayne A. Wolf, PhD, Office of the Medical Examiner of Harris County, Texas).

Figure 17-4. **A.** Angiographic appearance of a typical case of anomalous origin of the left coronary artery from the right sinus of Valsalva, with intramural course (between the aorta and pulmonary artery). **B.** Computerized tomographic angiogram of the same case. LCA, left coronary artery; RCA, right coronary artery. **Note that, in this view, the 2 arteries run epicardially, on the same plane, close to the sinu-tubular junction.**

Figure 17-5. Diagrammatic summary of all possible cases of anomalous origin of the coronary arteries from the aortic root (coronal view). The five alternative courses by which an ectopic coronary artery can cross to the normal dependent myocardial area are represented by dotted lines: 1, prepulmonic; 2, intraseptal; 3, intramural, aortic (or “between the aorta and pulmonary artery”); 4, retroaortic; 5, retrocardiac. AL, anterolateral cusp; AR, anterior-right cusp; Cx, circumflex artery; LAD, left anterior descending artery; M, mitral valve; P, posterior cusp; RCA,

right coronary artery; T, tricuspid valve. Reprinted from Angelini et al¹⁵ with permission.

- Figure 17-6.** Intravascular ultrasonographic images of the ostium (**A**) and distal artery (**B**), in cross-section in a case of anomalous right coronary artery arising from the opposite sinus. Only with this method can the investigator evaluate cross-sectional area stenosis: in this case of anomalous right coronary artery arising from the opposite sinus, the stenosis was 63% in diastole. Note the similarity of Figure 17-6A to Figure 17-1C, which shows the corresponding histologic features.
- Figure 17-7.** Diagrammatic reconstruction of the systolic and diastolic dimensions of the cross-sectional area (30 frames/sec), as seen on intravascular ultrasonography in a case of anomalous right coronary artery arising from the opposite sinus. Note the important phasic variations in these parameters: the cross-sectional area decreases by some 40% in systole (from 7.6 to 5.2 mm²). Measurements courtesy of Jonathan Aliota, MD, Texas Heart Institute).
- Figure 17-8.** Computed tomographic images of an anomalous intraseptal left coronary artery arising from the right sinus of Valsalva. The proximal left coronary artery (LCA) is directed inferiorly, below the aortic root (**A**), into the crista supra-ventricularis (view **B**, black arrow) and finally into the ventricular septum. For comparison, see Figure 17-4, which involves an intramural aortic course. The prognosis is quite different in

these two cases, as discussed in the text. MPA, main pulmonary artery; RCA, right coronary artery.