Coronary Artery Anomalies
An Entity in Search of an Identity

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Coronary artery anomalies (CAAs) are a diverse group of congenital disorders whose manifestations and pathophysiological mechanisms are highly variable. The subject of CAAs is undergoing profound evolutionary changes related to the definition, morphogenesis, clinical presentation, diagnostic workup, prognosis, and treatment of these anomalies. To understand the clinical impact of CAAs, the fundamental challenge is the firm establishment, for a particular type of CAA, of a mechanism capable of interference with the coronary artery's function, which is to provide adequate blood flow to the dependent myocardium. The present review focuses on anomalous origination of a coronary artery from the opposite sinus—the subgroup of CAAs that has the most potential for clinical repercussions, specifically sudden death in the young. For this subgroup, solid diagnostic screening protocols should be established, especially for athletes and other young individuals subjected to extreme exertion. Intravascular ultrasonography is the preferred means to evaluate the mechanisms responsible for ischemia in anomalous origination of a coronary artery from the opposite sinus and other potentially significant CAAs. Patients symptomatic of anomalous origination of a coronary artery from the opposite sinus may undergo medical treatment/observation, coronary angioplasty with stent deployment, or surgical repair. To be competent to advise CAA carriers, especially in the context of sporting or military activities, cardiologists should undergo specific training in these disorders. Only multicenter collaboration on protocols dedicated to CAAs can give rise to the large-scale studies needed to define the prognosis and optimal treatment of these disorders. **(*Circulation.* 2007;115:1296-1305.)**

Key Words: coronary disease ■ death, sudden ■ diagnosis ■ heart defects, congenital ■ ischemia

The subject of coronary artery anomalies (CAAs) is undergoing profound evolutionary changes related to the definition, morphogenesis, clinical presentation, diagnostic workup, prognosis, and treatment of these anomalies.[1–11] Initially, CAAs were the subject of anatomic discussions that centered around the description and classification of unusual morphologies.[1] Eventually, the ischemic mechanisms of CAAs[9,12–14] and the incidence of these anomalies in the normal human population were addressed in autopsied patients and coronary angiography populations.[10] More recent studies have dealt with vexing questions related to pathophysiological mechanisms and clinical prognoses for different forms of CAAs.[10,15] The present review focuses on anomalous origination of a coronary artery from the opposite sinus (ACAOS) with intussusception of the ectopic proximal vessel, which is the subgroup of CAAs that has the most potential for clinical repercussions, specifically sudden death in the young.

Definition of Coronary Anomalies

Classification criteria for CAAs have been extensively discussed in the literature. Some authors prefer to categorize CAAs only as "major," "severe," "important," or "hemodynamically significant" anomalies versus "minor" ones.[10] Our group has concluded that a comprehensive and widely agreed-upon scheme to define and classify CAAs should initially consider all possible coronary anatomic variations independently from the clinical and hemodynamic repercussions of individual CAAs.[10] Such a scheme should include 2 basic steps: (1) The normal coronary anatomy (Table 1) should be described in terms of quantitative and qualitative criteria, and (2) once the normal features have been excluded, the remaining features should be considered to define abnormality and should be used to generate a classification order.[10]

The basic issue in the definition of a normal coronary artery (and, hence, an anomaly) is the normal spectrum of variation. For example, whereas most experts agree that it is normal to have 2 coronary arteries (the right and the left), how should one consider the frequent presence of independent conal or infundibular branch ostia? This question leads to the next: How is a coronary artery differentiated from a smaller artery such as a conal branch?[10] A further related question deals with the case of an absent left main stem: Is it normal to have a separate ostium for the circumflex and left anterior descending arteries? Such questions cannot be answered without an accepted solid criterion that defines the normal spectrum of variants. We have proposed that, when possible, one should use quantifiable criteria such as, "Any

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TABLE 1. Normal Features of the Coronary Anatomy in Humans

Feature	Range
No. of ostia	2 to 4
Location	right and left anterior sinuses (upper midsection)
Proximal orientation	45° to 90° off the aortic wall
Proximal common stem or trunk	only left (LAD and Cx)
Proximal course	direct, from ostium to destination
Mid-course	extramural (subepicardial)
Branches	adequate for the dependent myocardium
Essential territories	RCA (RV free wall), LAD (anteroseptal), OM (LV free wall)
Termination	capillary bed

LAD indicates left anterior descending artery; Cx, circumflex artery; RCA, right coronary artery; RV, right ventricular; OM, obtuse marginal artery; and LV, left ventricular.

form observed in >1% of an unselected general population is normal."[11] The literature continues to entertain these and similar considerations while the field awaits a widely accepted endorsement by representative professional groups.[10,16]

Table 2 shows our group's proposed comprehensive classification scheme. A basic principle of coronary classification should be that the nature and name of a specific coronary artery are assigned, not according to the site of origin or proximal course, but according to the dependent territory. Figures 1 and 2 show 2 complex CAAs that exemplify the methods used to describe any given complex case.[10] Furthermore, 3 main coronary vessels (the left anterior descending, circumflex, and right coronary) (Figure 3) should probably be termed arteries, but the most distal vessels should be called coronary branches. We have proposed that a common proximal trunk, which joins 2 or 3 coronary arteries, should be named a mixed trunk. The only normally observed mixed trunk is the left main (common trunk or stem).[10] The following criteria are proposed to define each coronary artery:

1. The right coronary artery (RCA) is the vessel that provides blood flow to the right ventricular free wall. It is not essential for the posterior descending branch to originate from the RCA (the most common pattern) or that the ostium of the RCA be located at the right anterior sinus of Valsalva (which is normal).
2. The left anterior descending artery is the vessel that provides blood flow to the anterior interventricular septum. It is not essential for the diagonal branch to originate from this vessel (as is normal).
3. The circumflex artery is the vessel that provides blood flow to the free wall of the left ventricle, on the obtuse margin of the heart.[10]

Incidence of Coronary Artery Anomalies

Curiously, the literature shows that the overall incidence of CAAs is consistently mentioned by most authors, even the hundreds of them who report individual cases. This practice has led the nonspecialized audience to assume that CAAs, as a whole, are a serious threat (not simply that some rare individual forms may be so).[10] The greatest confusion in this regard is about myocardial bridges: Are they an anomaly, a pathological anomaly, or simply a normal feature of some coronary arteries in humans? The fact that such bridges are surely present in >1% of the general population suggests that they may be a normal variant.[10,17] Should only "severe" myocardial bridges be counted as pathological anomalies, and, if so, by what criteria?[10]

In one of the few prospective analyses to involve strict diagnostic criteria, which was performed in a continuous series of 1950 patients studied by coronary angiography, our group found that CAAs had a global incidence of 5.64% (Table 3), which is much higher than usually reported. Particularly noteworthy were the 0.92% incidence of anomalous origination of the RCA from the left sinus and the 0.15% incidence of anomalous origination of the left coronary artery from the right sinus (for a total incidence of 1.07% for ACAOS).[10]

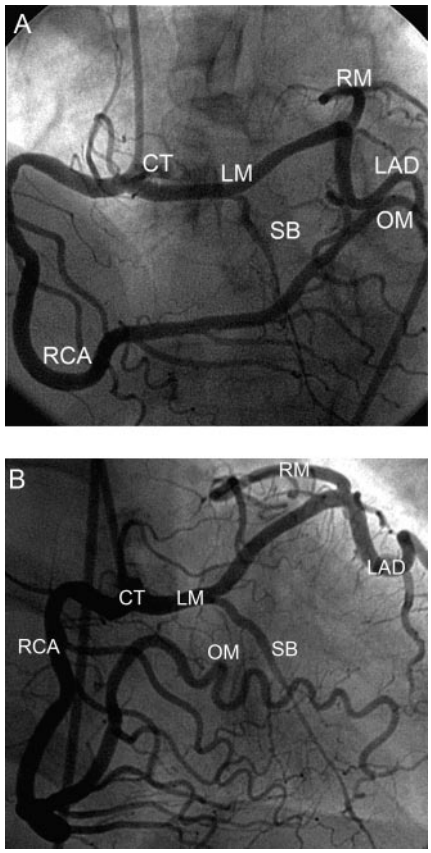

Figure 1. Angiograms from a 52-year-old man, in the left anterior oblique cranial (A) and right anterior oblique (B) projections. The patient had atypical chest pain and borderline nuclear stress test results. In these views, the whole coronary system is visualized from a single ostium, located at the right sinus. The right coronary artery (RCA) splits off from a short common trunk (CT), and continues into a terminal obtuse marginal branch (OM). The left main trunk (LM) crosses to the left off the CT, and courses intraseptally to give off a large septal branch (SB). The left coronary artery ends in the left anterior descending (LAD) and ramus (RM) branches. This is a case of clinically benign single coronary artery, which should more properly be called single coronary ostium because all the coronary arteries are present, though they are anomalous in their origin and course.

TABLE 2. Classification of Coronary Anomalies in Human Hearts

A. Anomalies of origination and course
- 1. Absent left main trunk (split origination of LCA)
- 2. Anomalous location of coronary ostium within aortic root or near proper aortic sinus of Valsalva (for each artery)
  - a. High
  - b. Low
  - c. Commissural
- 3. Anomalous location of coronary ostium outside normal "coronary" aortic sinuses
  - a. Right posterior aortic sinus
  - b. Ascending aorta
  - c. Left ventricle
  - d. Right ventricle
  - e. Pulmonary artery
    - (1) LCA that arises from posterior facing sinus
    - (2) Cx that arises from posterior facing sinus
    - (3) LAD that arises from posterior facing sinus
    - (4) RCA that arises from anterior right facing sinus
    - (5) Ectopic location (outside facing sinuses) of any coronary artery from pulmonary artery
      - (a) From anterior left sinus
      - (b) From pulmonary trunk
      - (c) From pulmonary branch
  - f. Aortic arch
  - g. Innominate artery
  - h. Right carotid artery
  - i. Internal mammary artery
  - j. Bronchial artery
  - k. Subclavian artery
  - l. Descending thoracic aorta
- 4. Anomalous location of coronary ostium at improper sinus (which may involve joint origination or "single" coronary pattern)
  - a. RCA that arises from left anterior sinus, with anomalous course
    - (1) Posterior atrioventricular groove or retrocardiac
    - (2) Retroaortic
    - (3) Between aorta and pulmonary artery (intramural)
    - (4) Intraseptal
    - (5) Anterior to pulmonary outflow
    - (6) Posteroanterior interventricular groove (wraparound)
  - b. LAD that arises from right anterior sinus, with anomalous course
    - (1) Between aorta and pulmonary artery (intramural)
    - (2) Intraseptal
    - (3) Anterior to pulmonary outflow
    - (4) Posteroanterior interventricular groove (wraparound)
  - c. Cx that arises from right anterior sinus, with anomalous course
    - (1) Posterior atrioventricular groove
    - (2) Retroaortic
  - d. LCA that arises from right anterior sinus, with anomalous course
    - (1) Posterior atrioventricular groove
    - (2) Retroaortic
    - (3) Between aorta and pulmonary artery
    - (4) Intraseptal
    - (5) Anterior to pulmonary outflow
    - (6) Posteroanterior interventricular groove
- 5. Single coronary artery (see A4)

B. Anomalies of intrinsic coronary arterial anatomy
- 1. Congenital ostial stenosis or atresia (LCA, LAD, RCA, Cx)
- 2. Coronary ostial dimple
- 3. Coronary ectasia or aneurysm
- 4. Absent coronary artery
- 5. Coronary hypoplasia
- 6. Intramural coronary artery (muscular bridge)
- 7. Subendocardial coronary course
- 8. Coronary crossing
- 9. Anomalous origination of posterior descending artery from the anterior descending branch or a septal penetrating branch
- 10. Split RCA
  - a. Proximal+distal PDs that both arise from RCA
  - b. Proximal PD that arises from RCA, distal PD that arises from LAD
  - c. Parallel PDs ×2 (arising from RCA, Cx) or "codominant"
- 11. Split LAD
  - a. LAD+first large septal branch
  - b. LAD, double (parallel LADs)
- 12. Ectopic origination of first septal branch
  - a. RCA
  - b. Right sinus
  - c. Diagonal
  - d. Ramus
  - e. Cx

C. Anomalies of coronary termination
- 1. Inadequate arteriolar/capillary ramifications
- 2. Fistulas from RCA, LCA, or infundibular artery to:
  - a. Right ventricle
  - b. Right atrium
  - c. Coronary sinus
  - d. Superior vena cava
  - e. Pulmonary artery
  - f. Pulmonary vein
  - g. Left atrium
  - h. Left ventricle
  - i. Multiple, right+left ventricles

D. Anomalous anastomotic vessels

LCA indicates laft coronary artery; LAD, left descending coronary artery; RCA, right coronary artery; Cx indicates circumflex; and PD, posterior descending branch. Adapted from Angelini P et al[10] with permission from Lippincott, Williams & Wilkins. Copyright 1999.

A group at the American Armed Forces Institute of Pathology[18] recently reported some notable and groundbreaking statistics. In a continuous series of 6.3 million 18-year-old recruits who underwent intense military training for 8 weeks, the researchers identified 277 deaths unrelated to trauma. A review of the clinical and necropsy charts showed that, of 64 cardiac deaths, 21 (33%) were related to ACAOS

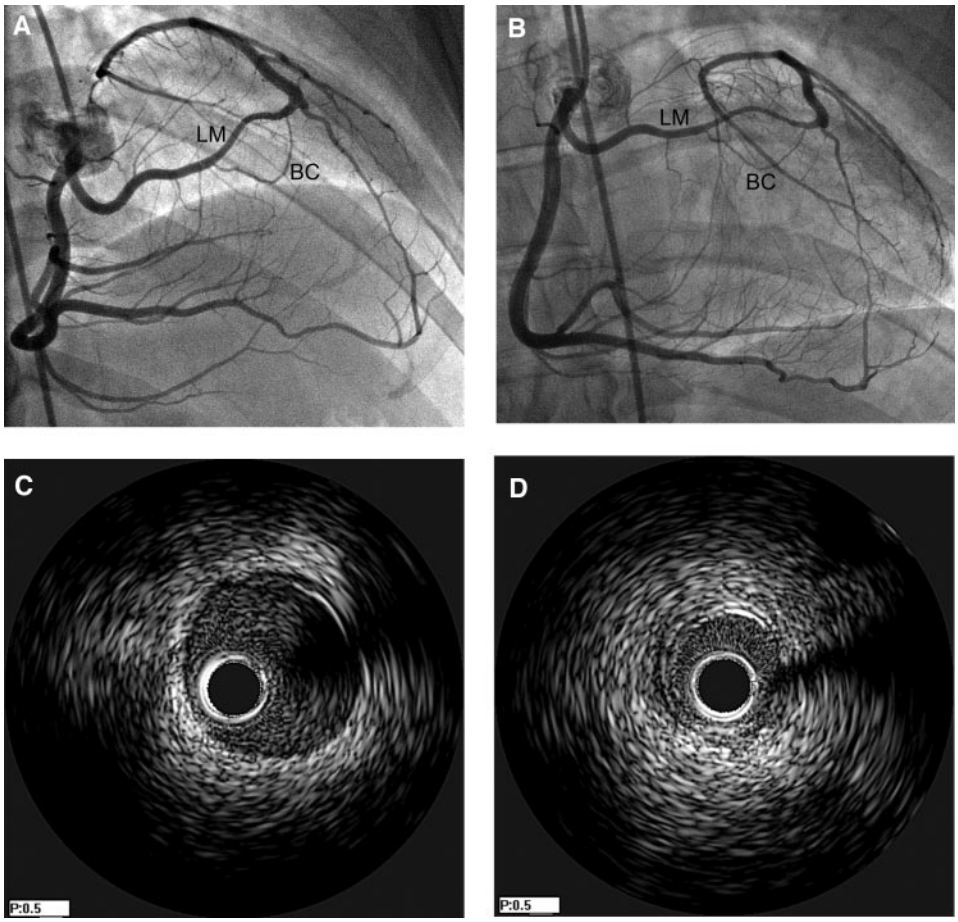

Figure 2. Angiograms from a 30-year-old man with a long-term history of crescendo angina, mainly at rest, accompanied by reversible ECG T-wave changes and lateral ischemia on the nuclear stress test. Angiograms in the right anterior oblique cranial (A) and straight (B) projections reveal a single coronary ostium and a prepulmonic course for the LM. View A was obtained after intracoronary administration of nitroglycerin; note the mildly narrowed mid LM with bridging collaterals (BCs). View B shows the effects of intracoronary infusion of acetylcholine (100 μg over 30 seconds) that reproduced typical angina and ECG changes. The LM stenosis has clearly increased in severity. C, IVUS image of the proximal LM (area, 8.9 mm^2). D, IVUS image of the stenotic area after nitroglycerin administration (area, 6.1 mm^2). This case shows the spastic potential of some anomalous vessels, in this instance at the level of a prepulmonic course. Calcium antagonists successfully abated the presenting angina syndrome.

of the left coronary artery (left-ACAOS) and that no other CAAs resulted in cardiac death. Although the authors did not specify, it is likely that none of these cases of left-ACAOS had been diagnosed before death (in an environment in which medical evaluations are routine). This is the first large-scale study of CAAs in which the denominator (all candidates at risk) was known, the setting of the clinical events was consistent (extreme physical training), and all the fatal events led to necropsy studies.[18]

In comparison, Drory and colleagues[19] studied the incidence of CAAs in a continuous series of 162 patients with sudden unexpected death. The patients were <40 years of age and underwent routine autopsy studies in Israel, where an autopsy is obligatory in such cases. The incidence of CAA-related sudden death was 0.6% (1 of 162 cases); taken together with the recent military recruit series,[18] this result suggests that extreme exercise plays a powerful role in such deaths.

In conclusion, the main interest of current clinical investigators seems to be to establish the incidence of those individual types of CAAs that have become recognized for their clinical consequences.

Pathophysiological Mechanisms and Clinical End Points

To understand the clinical impact of CAAs, the fundamental challenge is to firmly establish, for a particular type of CAA, a mechanism capable of interference with the coronary artery's function to provide adequate blood flow to the dependent myocardium. Table 4 summarizes such mechanisms and the conditions under which they apply.[10] Whereas some CAAs may cause occasional ischemia, others (eg, anomalous origination of the left coronary artery from the pulmonary artery) obligatorily cause ischemia, and yet others only predispose the patient to have a misdiagnosis or complications (clotting, spasm, or atherosclerotic buildup).

The present review is limited to only 1 kind of coronary anomaly, ACAOS, which has recently been recognized as having serious prognostic implications in young individuals.[5–7,9,12,20] In cases of ectopic origination of a CAA, only 1

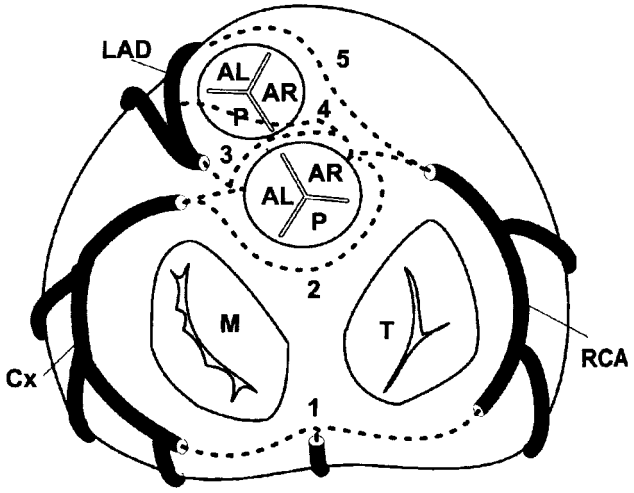

Figure 3. Conceptual diagram that shows most of the possible paths (1 through 5) by which the RCA, left anterior descending artery (LAD), and circumflex artery (Cx) can potentially connect with the opposite coronary cusps. Paths: 1, Retrocardiac; 2, retroaortic; 3, preaortic, or between the aorta and pulmonary artery; 4, intraseptal (supracristal); 5, prepulmonary (precardiac). The aortic and pulmonary cusps are labeled according to their position in space: AL indicates antero-left; AR, antero-right; P, posterior; M, mitral valve; and T, tricuspid valve. Reproduced from Angelini et al[10] with permission from Lippincott Williams & Wilkins. Copyright 1999.

specific abnormal course, traditionally called interarterial, or "between the aorta and pulmonary artery," is associated with a severe prognosis.[20–25] Indeed, that anomaly has recently been observed, on intravascular ultrasound (IVUS) imaging, to consist of intramural proximal intussusception of the ectopic artery at the aortic-root wall.[26] Never has an extramural course been observed with IVUS in such a scenario.[21,26,27] The traditional terminology (between the aorta and pulmonary artery) implied that the aberrant artery was liable to a scissors-like mechanism, created by the close proximity of the aorta and pulmonary artery, especially during exertion.[22] Such a mechanism is unlikely, however, because at the site of closest aortopulmonary proximity the anomalous artery lies inside the aortic wall.[26] In our more recent extensive experience with IVUS examination of CAAs, we have occasionally found an intramural aortic course in some type of ACAOS without an interarterial course. Specifically, only 2 patients had an unusual intramural anomalous "retroaortic" course: In 1 case, the left coronary arose from the posterior sinus[27]; in the other case, the circumflex artery arose from the right sinus.

TABLE 3. Incidence of Coronary Anomalies and Patterns, as Observed in a Continuous Series of 1950 Angiograms

Variable	N (%)
Coronary anomalies (total)	110 (5.64)
Split RCA	24 (1.23)
Ectopic RCA (right sinus)	22 (1.13)
Ectopic RCA (left sinus)	18 (0.92)
Fistulas	17 (0.87)
Absent left main coronary artery	13 (0.67)
Circumflex arising from right sinus	13 (0.67)
LCA arising from right sinus	3 (0.15)
Low origination of RCA	2 (0.1)
Other anomalies	3 (0.27)
Coronary dominance patterns	
Dominant RCA	1641 (89.1)
Dominant LCA (circumflex)	164 (8.4)
Codominant arteries (RCA, circumflex)	48 (2.5)

LCA indicates left coronary artery. Adapted from Angelini P et al[10] with permission from Lippincott, Williams & Wilkins. Copyright 1999.

The reasons for our insistence on the intussusception of anomalous arteries are related to the following newly discovered mechanisms of stenosis (Figure 4):

1. Coronary hypoplasia. Our group has discovered that the intramural intussuscepted segment of the proximal ectopic artery is smaller in circumference than the more distal extramural vessel. With IVUS, we found it valuable to quantify this parameter with the hypoplasia index (ie, the ratio of the circumference of the intramural segment with respect to the circumference of the more distal segment).[26,27] Arteries that arise congenitally inside the aortic media likely cannot grow normally either before or after birth.
2. Lateral compression. The cross section of the intramural segment is characteristically not circular but ovoid (Figure 4). The lateral compression results in a smaller area than that possessed by a circle of the same circumference.[17] This parameter can be quantified with the asymmetry ratio (the ratio of the smallest to the largest diameter in an IVUS cross section).[27] Additionally, our group has observed that the smaller diameter is further compressed during each systole, as manifested by pulsatile behavior observed with IVUS during the cardiac cycle. This liability to undergo intermittent worsening is most likely related to changes in stroke volume (and pulsatility of the ascending aorta) and to tachycardia, which is a behavior that becomes manifest during IVUS imaging when an experimental pharmacological challenge simulates exercise conditions.[26] For instance, in 3 symptomatic patients with left-ACAOS, we found 49% to 70% area stenosis at baseline, which increased by 8% to 10% with stimulation.[27] Such lesions are in the range of what the Coronary Artery Surgery Study (CASS) defined as critical stenosis of the left main coronary, which can cause sudden death.[28] In this context, it is important to recognize the hemodynamic changes that occur during sports activities that involve maximal exertion; for example, from the resting state, the heart rate increases from 65 to 180 bpm, the cardiac output from 5 to 22 L/min, and the stroke volume from 77 to 122 cc.[29]
3. Stenotic segment length. With any coronary stenosis, the segmental length is another measure of severity. In ACAOS that involves the RCA, as well as in left-ACAOS, the length of the stenosis varies between 5 and 15 mm.[26,27]

In our series, all 3 of the aforementioned parameters showed great individual variability. It is likely that aortic wall distensibility (degree of cross-sectional area enlargement associated with a certain increase in pressure) is a further related variable that depends on intrinsic anatomic changes in the aortic wall (as in medial cystic necrosis or aortic dissec-

TABLE 4. Pathophysiological Mechanisms and Coronary Anomalies (Functional Classification)

		Proof of Action		
Pathophysiological Mechanism	Coronary Anomaly	Certain	Possible	Unlikely
Misdiagnosis	"Missing" coronary artery	x		
	"Hypoplastic" coronary artery		x	
Myocardial ischemia, primary (fixed and/or episodic)	Ostial atresia	x		
	Ostial stenosis	x		
	Coronary fistula		x	
	ALCAPA	x		
	Muscular bridge			x
Myocardial ischemia, secondary (episodic)	Tangential origin (ACAOS) intramural course	x		
	Myocardial bridge, plus spasm and/or clot	x		
	Coronary ectasia (plus mural clot)	x		
	Coronary fistula (plus mural clot)	x		
Increased risk of fixed coronary atherosclerotic disease	Coronary fistula	x		
	ALCAPA	x		
	Coronary ectasia	x		
	Muscular bridge (proximal to)	x		
Secondary aortic valve disease	Coronary aneurysm (ostial)		x	
	Coronary fistula		x	
	ALCAPA		x	
Increased risk of bacterial endocarditis	Coronary fistula		x	
Ischemic cardiomyopathy (hibernation)	ALCAPA	x		
Volume overload	Coronary fistula	x		
	ALCAPA	x		
Unusual technical difficulties during coronary angiography or angioplasty	Ectopic ostia (tangential)	x		
	Split left coronary artery		x	
	Coronary fistula		x	
Complications during cardiac surgery	Ectopic ostia and proximal course	x		
	Muscular bridge	x		

ALCAPA indicates anomalous origination of the left coronary artery from the pulmonary artery. Adapted from Angelini P et al[10] with permission from Lippincott, Williams & Wilkins. Copyright 1999.

tion), changes in the aortic pressure (as at the onset of hypertension or aortic regurgitation), or a rapid weight gain, especially in patients who receive negative chronotropic agents, which increase the stroke volume if the cardiac output remains essentially unchanged. Moreover, a treadmill stress test, which should be transformed into an adenosine test because of an inadequate effort or chronotropic response, may be the most accurate predictive test for ACAOS because it associates an increased cardiac output with nonphysiological bradycardia. Unfortunately, though, such a hybrid protocol is a potential cause of sudden death, specifically in ACAOS carriers, and should generally be avoided or at least closely monitored in a hospital environment.

When a carrier of ACAOS dies suddenly, in the absence of other lethal cardiovascular conditions, a low cardiac output and bradycardia or asystole typically occur early after extreme exercise, after which syncope and/or death ensues. Terminal ventricular fibrillation may also occur as a manifestation of critical ischemia or of reperfusion arrhythmia.[30–32]

Both the anomalous right and left coronary arteries can be responsible for sudden death, although the risk has not been adequately quantified in specific studies. Most likely, predisposing factors include the severity of baseline stenosis, the specific conditions at the time of the crisis, and the myocardial territory at risk.[7,33] Additionally, one must realize that the possible manifestations of ACAOS include not only sudden death but also dyspnea, palpitations, angina pectoris, dizziness, and syncope.[4,10,12,26,32] Whereas sudden death is usually associated with extreme exercise in young adults,[34] the other manifestations of ACAOS are more frequently seen in older adults (in our experience, specifically women) and are related to the onset of hypertension. Interestingly, Cheitlin[33] claimed that sudden death is seen only in young patients, possibly because of progressive hardening of the aortic wall in adults.

During aortic valve replacement, an intramural ectopic coronary artery can also be liable to critical worsening of extrinsic compression by the prosthetic ring, as recently reviewed by Morimoto and colleagues.[35]

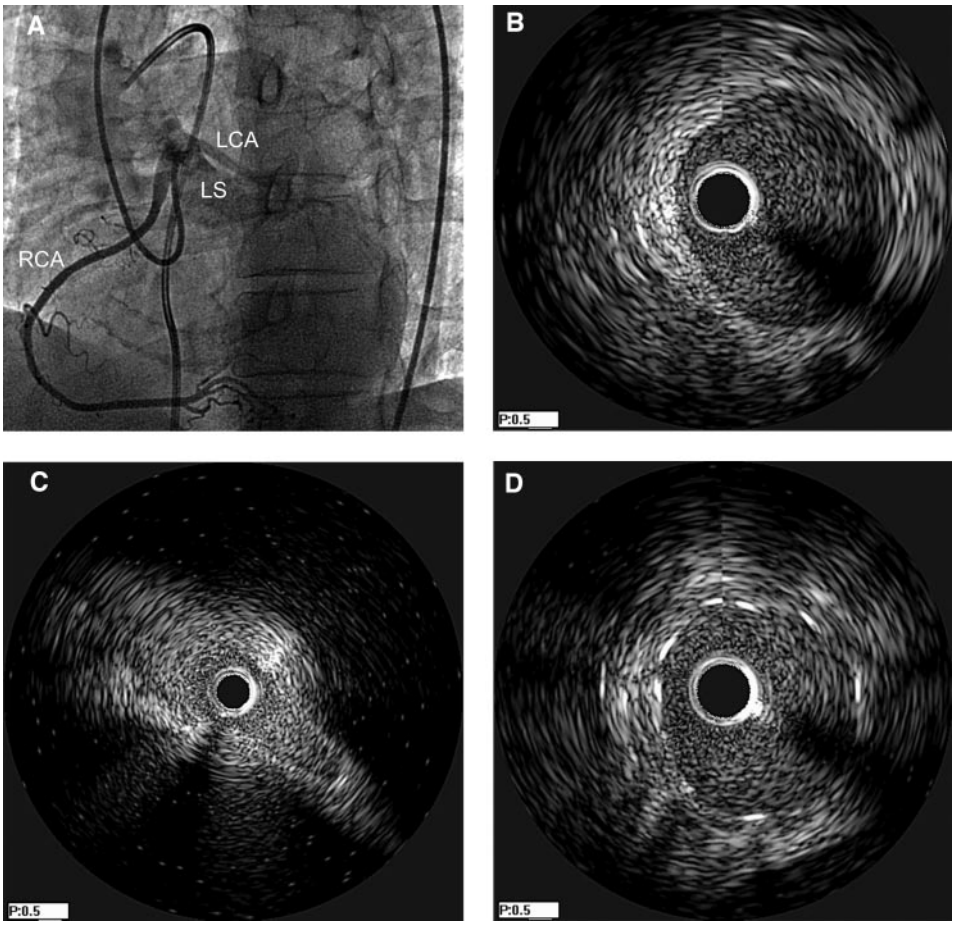

Figure 4. Images obtained from a 42-year-old man with severe angina of recent onset, who had recently developed hypertension. A, Selective angiogram of the RCA in the left anterior oblique projection. In this view, the proximal course appears wider than the more distal vessel, and it originates next to the LCA (which is also ectopic), high above the left aortic sinus (LS). B, IVUS image of the distal RCA. The cross-sectional area is 10.8 mm^2, and the shape is circular. C, IVUS image of the proximal segment of the RCA, whose lumen is severely compressed laterally (minimal diameter, 1.5 mm; maximal diameter, 3.8 mm; cross-sectional area, 4.2 mm^2; area stenosis, 61%). The LCA had also milder ostial stenosis. D, IVUS of the proximal RCA after stent angioplasty (3.5 × 12 mm; postdilated at 18 atm). The shape has become round, and the area has expanded to match that of the distal normal vessel.

Outlines for Diagnostic and Treatment Protocols

In carriers of ACAOS, the clinical histories are consistent in only 1 aspect: Either these patients die suddenly (typically at a young age and after extreme exertion), or they have no characteristic presentation. Most patients are asymptomatic for a large portion of their lives, and an atypical chest-pain syndrome is the most common reason they are referred for coronary angiography, which is when the diagnosis is typically made. The milder cases are more likely to be identified fortuitously (because of a falsely positive stress test and/or coincidental atherosclerotic disease).

The fact that CAAs include many different entities and that no single observer or group has collected a large enough series to clarify the natural prognosis of each entity may contribute to our difficulty in the clinical identification of these lesions, especially the ones that could lead to angina or sudden cardiac death.[21] For most types of coronary anomalies, the fundamental clinical approach could be: "Do not bother to look for these innocent anomalies, but be prepared to recognize them as benign if one is accidentally found, typically at coronary angiography." However, for a few CAAs that are possibly or predictably malignant (fundamentally, ACAOS), we should establish solid diagnostic screening protocols, especially for athletes and other young individuals subjected to extreme exertion.[9,10,29,33] As noted above, ACAOS patients can succumb to sudden cardiac death, usually but not necessarily at a young age, possibly even at the newborn stage.[36]

Retrospectively reviewed, only a few persons reported to have died of ACAOS had significant symptoms, usually atypical chest pain, dyspnea, syncope, or their equivalents, before the final event.[5–7,9,10,13–15] A specific workup protocol is indicated mostly for athletes and military personnel with these symptoms. In view of the fairly rare nature of ACAOS, it would not seem practical or cost-effective to extend the indications for such a workup to all schoolchildren on a routine basis. Nevertheless, larger prospective studies are needed before this decision can become final.[37–39]

In patients with suspected ACAOS, testing should sequentially include electrocardiography, Holter monitoring (basi-

cally to document atrial or ventricular arrhythmias as nonspecific markers of ACAOS), and focused expert echocardiography (transthoracic and, if needed, transesophageal) with Doppler interrogation to identify the coronary origin and proximal course.[40–42] In particular, the reported 0.17% incidence of ACAOS found by examination of a series of 2388 routine echocardiograms[40] must be compared with the 1.07% incidence found at coronary angiography.[10] The implication is that echocardiography is probably not as reliable a means to diagnose this disorder (especially if performed in adults and without specifically looking for ACAOS). The authors of the echocardiographic study[37] reported that 1 of their negative results was followed by sudden death during follow-up observation, the diagnosis of ACAOS becoming apparent only at autopsy.

If at least 2 normally located coronary ostia are identified with echocardiography, which is more often possible in children than adults, no further workup for ACAOS is probably required. If the coronary ostia are not clearly identified echocardiographically, however, or if an alternative method is needed, computed tomography or magnetic resonance imaging is recommended.[21,41,43] These methods not only identify ACAOS more reliably than echocardiography, but also allow description of the dependent territory,[21] which correlates with the prognosis, as discussed above. When ACAOS is identified in this manner, a further workup should include nuclear stress testing. Although the result is usually negative, this method is important both to evaluate effort-induced ischemia and scars and to establish a baseline for follow-up assessment in case of eventual intervention. Furthermore, selective coronary angiography is indicated more to rule out additional obstructive coronary disease of atherosclerotic origin than to evaluate the severity of congenital obstruction at the proximal ectopic vessel. The need for interventional treatment can be substantiated only by IVUS, as discussed above.[26,27]

Treatment Options

Symptomatic carriers of ACAOS have 3 treatment options: medical treatment/observation, coronary angioplasty with stent deployment, and surgical repair. Despite the limitations of our current knowledge of such anomalies, intervention may be justified in some cases to prevent sudden death and improve the quality of life. Medical treatment (essentially with β-blockers) is probably as effective as restriction of activity (avoidance of severe exertion) in these patients.[39]

In a significant number of cases, right-ACAOS may not warrant intervention. Precise IVUS/clinical correlations should be prospectively obtained to establish acceptable selection criteria. Stent-angioplasty of the obstructed proximal intramural segment of a patient with right-ACAOS is technically feasible,[26,44] and is probably justifiable in the presence of (1) disabling symptoms and/or a high risk of sudden death, (2) area stenosis more severe than 50% with respect to the distal normal vessel on IVUS, (3) a large dependent myocardial territory (more than a third of the total), and (4) reversible ischemia, as documented by a nuclear stress test.

Besides indicating the need for intervention, IVUS is also essential for proper deployment of a stent. We use IVUS data both to measure the length of the obstructed intramural RCA and to evaluate the cross-sectional area after stent deployment, aiming for a target luminal area similar to that of the distal vessel. Initially, timid dilatation of stents (for fear of aortic-wall dissection if excessively large balloon sizes were used) resulted in incomplete apposition along the longest diameter, some residual stenosis, and sometimes early postoperative restenosis. Presently, we feel confident that the immediate and late results are improved if full luminal restoration, to match the area of the distal vessel, is attained at the intramural segment and for about 4 mm beyond it.

Apparently, only 1 group, in China, has reported the use of stent-angioplasty for left-ACAOS.[45] In this case, the patient was a 14-year-old child with severe symptoms who received a stent at the left main trunk. The early results were favorable, but we prefer to postpone such experimental use of stents until stent-angioplasty is well established for the lower-risk indication of right-ACAOS.

Our initial experience suggests that drug-eluting stents offer the best probability to avoid restenosis, but definitive data need to be collected regarding this off-label use of stents. Moreover, restenosis appears to be rare, and, if it does occur, is related to in-stent fibrocellular growth, not stent compression. Like many others, however, our group considers that left-ACAOS is generically, in itself, a solid indication for surgical intervention.[27] Nevertheless, we continue to acquire IVUS data in these patients to further refine our treatment protocols. Despite the absence of objective studies, surgical treatment of ACAOS has been performed in large series of patients for several years.[43,46] Surgical correction, which is especially recommended for left-ACAOS that involves a large territory at risk, may consist of (1) direct reimplantation of the ectopic artery at the aortic root (a technically difficult and unreliable approach); (2) unroofing of the intramural coronary segment, from the ostium to the exit point, off the aortic wall; or (3) osteoplasty, which creates a new ostium at the end of the ectopic artery's intramural segment (Figure 5).[27,43,46–48]

Athletes and military personnel known to be ACAOS carriers should be advised by a specially trained cardiologist about permitted versus prohibited physical activities before and after intervention. Current guidelines issued by professional associations state that untreated carriers of ACAOS should not be involved in competitive sports or other strenuous activities.[39] Treated patients should be reevaluated before being allowed to resume exercise at maximal capacity.

Conclusions

Coronary artery anomalies should be regarded as an uneven diverse group of congenital disorders whose manifestations and pathophysiological mechanisms are highly variable. To be competent to advise CAA carriers, especially in the context of sporting or military activities, cardiologists should undergo specific training in these disorders. IVUS is the preferred means to evaluate the mechanisms responsible for ischemia in potentially significant CAAs, especially ACAOS.

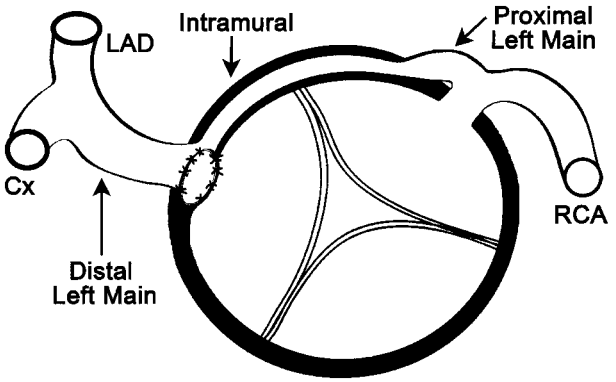

Figure 5. Diagram representation of a case of single coronary ostium at the right sinus. The LM runs intramurally inside the aortic-wall left sinus, just below the anterior aortic commissure, and takes off from the aorta at the center of the left cusp. At this point, a circle with stitches represents the newly created ostium after surgical repair. Cx indicates circumflex. Reproduced from Angelini et al[27] with permission from Texas Heart Institute. Copyright 2006.

Clearly, this aspect of cardiology will not be able to develop fully without extensive collaboration between individual cardiologists and institutions.[16] To further this goal, the Texas Heart Institute has established a Web site designed to promote multicenter collaboration on protocols dedicated to ACAOS patients (http://texasheart.org/Education/Resources/caac.cfm). Only such efforts can give rise to the large-scale studies needed to define the prognosis and optimal treatment of individual forms of CAAs.

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Disclosures

Dr Paolo Angelini is an occasional expert witness in cases of coronary anomalies.

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