Anomalous origination of a coronary artery from the opposite sinus

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Abstract | Anomalous origination of a coronary artery from the opposite sinus (ACAOS) is estimated to be present in 0.2–2.0% of the population. In the majority of individuals, ACAOS has no hemodynamic or prognostic implications, but in a minority of cases, typically where the anomalous coronary artery takes an interarterial course to reach its correct myocardial territory, it can precipitate ischemia and sudden cardiac death (SCD). With the growing use of CT coronary angiography (CTCA) in the investigation of ischemic heart disease, we can expect increasing rates of incidental detection of this anomaly. Although CTCA and magnetic resonance coronary angiography can effectively characterize these lesions anatomically, they fail to describe and quantitatively assess the basic defect that leads to coronary insufficiency, such as mural intussusception. The key challenge lies in the identification of which patients are at risk of SCD and, therefore, who should be offered corrective surgical or (potentially) percutaneous intervention. Conventional, noninvasive stress testing has limited sensitivity, but emerging, invasive stress tests, which utilize intravascular ultrasonography and measurements of fractional flow reserve, show the potential to provide more-accurate hemodynamic and prognostic assessment.

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Introduction

The term 'coronary artery anomalies' encompasses a spectrum of morphological variants of coronary anatomy arising *in utero*, the majority of which do not cause symptoms and bear no prognostic implications.[1] However, certain coronary anomalies have an established association with sudden cardiac death (SCD), particularly in young and fit individuals.[1–5] CT coronary angiography (CTCA) has been endorsed by the UK National Institute for Health and Clinical Excellence for the investigation of chest pain and suspected ischemic heart disease.[6] This technique also enables the 3D architecture of the coronary tree to be imaged, and is likely to increase the detection rate of coronary anomalies. Clinicians must, therefore, understand the different types of anomaly, their respective prognostic implications, and the indications for treatment. In this Review, we focus on the anomalous origination of a coronary artery from the opposite (or 'improper') coronary sinus (ACAOS), a scenario often discovered during invasive investigation of angina. We discuss the various classification systems of coronary artery anomalies, the methods used to quantify the risk to individuals with ACAOS, and available treatment modalities for these patients.

Competing interests
The authors, the journal Chief Editor B. Mearns and the CME questions author C. P. Vega declare no competing interests.

Classification

Early classification schemes, which were developed largely on the basis of surgical and autopsy specimens, divided coronary anomalies into those of 'major' and 'minor' importance.[7,8] Major anomalies were those associated with substantial hemodynamic consequences and were further subdivided into 'primary' and 'secondary' anomalies. Primary major anomalies were defined as those with physiological implications, but in the absence of coexisting structural heart disease, typically involving an arteriovenous-like shunt, as in the case of anomalous origination of a coronary artery from the pulmonary artery.[7,8] Secondary major anomalies were defined as those that

occurred in conjunction with structural congenital heart disease, usually as a compensatory mechanism, and potentially with retrograde coronary flow.[7] All other anomalous arteries originating from the aorta were prematurely assumed not to bear any physiological importance, apart from the potential technical challenges during surgery or angiography, and were consequently referred to as 'minor' anomalies, including abnormalities of number, size, origination, and course.[7,8]

The subsequent demonstration that some of these so-called minor anomalies might, in fact, be associated with SCD and carry prognostic implications led to a shift in terminology.[9] Abnormalities with hemodynamic implications that were potentially associated with the development of symptoms and SCD were termed 'potentially serious' or 'malignant' coronary anomalies, while the remainder were designated 'benign'.[10] Malignant anomalies include anomalous origination of a coronary artery from the pulmonary artery, ACAOS with an interarterial course, coronary artery fistulas, single coronary artery, and certain variants of myocardial bridge.[2,10] In addition to this prognostic form of classification, accumulation of data from both invasive angiography and CTCA has demonstrated the vast array of potential permutations in origin, course, and termination of anomalous arteries and detailed anatomical classifications have been developed to assimilate these variations. The most comprehensive of these schemes is by Angelini and colleagues,[3,11] and proposed categorization according to anomalies of coronary origination and course (Box 1), intrinsic coronary arterial anatomy (Box 2), coronary termination (Box 3), and anastomotic vessels.

ACAOS constitutes just one category in the broad spectrum of coronary anomalies, and can be further subdivided into four categories: anomalous origination of the right coronary artery from the left coronary sinus; anomalous origination of the left coronary artery from the right coronary sinus; anomalous origination of the left anterior descending coronary artery or left circumflex artery from the right coronary sinus; and anomalous origination of the right or left coronary artery from the noncoronary sinus.[12] These arteries then follow one of four courses to reach their dependent myocardial territory: interarterial, retroaortic, prepulmonic, or subpulmonic (Figure 1).[2,10] This information is vital in the analysis of coronary anomalies because anomalous arteries with an interarterial course, and more specifically the intramural course, can behave in a malignant fashion and cause SCD.[9]

On the basis of the terms already introduced, a broad terminology is applied to coronary anomalies. For example, some researchers refer to anomalous arteries with an intramural course by a different name (AAOCA, anomalous aortic origination of a coronary artery from the opposite sinus with an intramural course between the great arteries),[13] whereas others refer to anomalous arteries with an interarterial course, again using different names (ALCA, anomalous origination of the left coronary artery from the right coronary sinus with an interarterial course, and ARCA, anomalous origination of the right coronary artery from the left coronary sinus with an interarterial course).[14] This lack of fixed nomenclature can be confusing, particularly because these acronyms do not include letters to indicate whether they refer to intramural or interarterial subsets. In this Review, we have applied the acronym ACAOS literally, to encompass the whole group of anomalies included in the fourth section of Box 1. Where applicable, we have then made specific reference to an intramural or interarterial course.

Key points

- Anomalous origination of a coronary artery from the opposite sinus (ACAOS) is a recognized cause of sudden cardiac death (SCD), typically associated with exercise
- Insights from intravascular ultrasonography (IVUS) studies suggest that the pathophysiological mechanism by which ACAOS causes SCD involves systolic compression of the anomalous artery within the aortic wall
- Cardiac catheterization was regarded as the gold standard for diagnosis and anatomical characterization of ACAOS, but has been superseded by CT and magnetic resonance coronary angiography
- Standard, noninvasive stress tests have limited sensitivity in predicting the risk of SCD in patients with ACAOS
- Invasive stress tests using IVUS and measurements of fractional flow reserve might provide a means of establishing the hemodynamic and prognostic significance of ACAOS
- Case reports of successful percutaneous coronary intervention for treatment of ACAOS exist, but surgery remains the first-line treatment of choice

Prevalence

Estimates of the prevalence of coronary anomalies are made on the basis of data from coronary artery catheterization, echocardiography, CTCA, and autopsy databases, but each modality has inherent limitations. Cardiac catheterization is likely to be performed only on individuals with suspected cardiac disease, so is not representative of the general population and is unlikely to account for young, previously asymptomatic patients who suffer SCD.[14] To a lesser extent, the same applies to echocardiographic and CTCA data. Autopsies potentially provide a more-accurate estimation of the prevalence of coronary anomalies in the whole population, but not everyone who dies has an autopsy. In addition, autopsy data on coronary anomalies tend to be from studies investigating SCD and, although they can provide useful information on the likelihood of SCD being caused by coronary anomalies, they do not provide an accurate estimate of the prevalence of coronary anomalies in the general population.

Consequently, estimates of the overall prevalence of coronary anomalies according to the largest invasive angiographic studies range from 0.78% to 1.30%, with the prevalence of ACAOS estimated at 0.15–0.39%.[10,15–26] The overall prevalence of anomalies according to the largest CTCA studies range from 0.99% to 5.80%, with the prevalence of ACAOS estimated at 0.35–2.10%.[27–32] Anomalous origination of the right coronary artery from the left coronary sinus, and anomalous origination of the left circumflex artery from the right coronary sinus are the most-commonly reported anomalies (Table 1). Studies using CTCA data indicate a greater prevalence of coronary anomalies compared with those using cardiac catheterization data, but investigators apply different definitions to the

Box 1 | Anomalies of coronary artery origination and course[3,11]

Absent left main trunk (split origination of the left coronary artery)

Anomalous location of coronary ostium within aortic root or near proper aortic sinus of Valsalva (for each artery): (i) high, (ii) low, (iii) commissural

Anomalous location of coronary ostium outside normal 'coronary' aortic sinuses

- Right posterior aortic sinus
- Ascending aorta
- Left ventricle
- Right ventricle
- Pulmonary artery

  Left coronary artery that arises from posterior facing sinus; circumflex artery that arises from the posterior facing sinus; left anterior descending coronary artery that arises from the posterior facing sinus; right coronary artery that arises from the anterior right facing sinus; or ectopic location (outside facing sinuses) of any coronary artery from the pulmonary artery: (i) from the anterior left sinus, (ii) from the pulmonary trunk, (iii) from the pulmonary branch
- Aortic arch
- Innominate artery
- Right carotid artery
- Internal mammary artery
- Bronchial artery
- Subclavian artery
- Descending thoracic aorta

Anomalous location of a coronary ostium at the improper sinus (which can involve joint origination or 'single' coronary pattern)

- Right coronary artery that arises from the left anterior sinus, with anomalous course

  Posterior atrioventricular groove or retrocardiac; retroaortic; between the aorta and the pulmonary artery (intramural); intraseptal; anterior to the pulmonary outflow; or posteroanterior interventricular groove (wraparound)
- Left anterior descending coronary artery that arises from the right anterior sinus, with anomalous course

  Between the aorta and the pulmonary artery (intramural); intraseptal; anterior to the pulmonary outflow; or posteroanterior interventricular groove (wraparound)
- Circumflex artery that arises from the right anterior sinus, with anomalous course

  Posterior atrioventricular groove; or retroaortic
- Left coronary artery that arises from the right anterior sinus, with anomalous course

  Posterior atrioventricular groove; retroaortic; between the aorta and the pulmonary artery; intraseptal; anterior to the pulmonary outflow; or posteroanterior interventricular groove

Single coronary artery

term 'coronary anomalies'. For example, myocardial bridging and separate origination of the left anterior descending and left circumflex arteries are considered anomalies by some researchers, but not by others. Inclusion of coronary fistula depends on whether only anomalies of origin and course are being classified. Interpretation is further limited by the lack of a universally accepted classification scheme. Despite these limitations, the higher reported prevalence of coronary anomalies from the CTCA-based studies compared with cardiac catheterization data is also likely to reflect the greater sensitivity of CTCA in detecting coronary anomalies.[33] Clinicians must, therefore, understand the prognosis and management of coronary anomalies, as the use of CTCA becomes more widespread and increasing numbers of patients with the condition are diagnosed.

Relationship between ACAOS and SCD

Prognosis

Patients with ACAOS can be asymptomatic, despite potentially having an increased risk of SCD. The association between ACAOS and SCD has been demonstrated in retrospective cohort analyses of autopsy reports for SCDs. In a study of 134 athletes with SCD, hypertrophic cardiomyopathy was the most-common cause of death (36%), followed by ACAOS (13%).[34] In a study of 126 nontraumatic deaths of military recruits, 64 were attributed to cardiac causes, 33% of which were attributed to ACAOS.[35] All these cases featured anomalous origination of the left coronary artery from the right coronary sinus with an interarterial course. Notably, ACAOS was a more-common cause of cardiac death than cardiomyopathy, myocarditis, and atherosclerosis in this study. A history of prodromal symptoms that included chest pain, syncope, or breathlessness was reported in only 52% of the cases of SCD.[35]

Although anomalous origination of the left coronary artery from the right coronary sinus with an interarterial course is the abnormality most-commonly associated with SCD, anomalous origination of the right coronary artery from the left coronary sinus with an interarterial course has also been associated with this phenomenon.[36–39] In a review by Basso and co-workers of two large registries of young athletes with SCD, 23 deaths were attributed to anomalous origination of the left coronary artery from the right coronary sinus, and four deaths were attributed to anomalous origination of the right coronary artery from the left coronary sinus.[36] SCD in such cases usually occurs during or after exercise.[36–38] In a review of 51 cases of congenital coronary anomalies accessioned at the American Institute of Forensic Pathology, 81.3% of the individuals who suffered unexpected SCD were engaged in, or had just stopped, physical exercise.[9] Likewise, in the study by Basso and colleagues, all SCDs occurred either during or immediately after intense physical exercise.[36]

Pathophysiology

A number of putative mechanisms have been proposed to account for the association between SCD and ACAOS with an interarterial course. The downstream event is presumed to be ischemic, usually following an episode of strenuous exercise, leading to a reduction in cardiac output, followed by bradycardia or asystole, syncope, and death.[3,14] Ventricular fibrillation might also have a role, precipitated by ischemia or reperfusion.[3,14,40] Because the left coronary system usually supplies a larger proportion of the myocardium than the right, ischemia or infarction of its dependent territory is more likely to produce fatal consequences, possibly explaining the stronger association between SCD and anomalous origination of the left (compared with the right) coronary artery.[14]

Box 2 | Anomalies of coronary artery anatomy[3,11]

Congenital ostial stenosis or atresia (left coronary artery, left anterior descending coronary artery, right coronary artery, or circumflex artery)

Coronary ostial dimple

Coronary ectasia or aneurysm

Absent coronary artery

Coronary hypoplasia

Intramural coronary artery (muscular bridge)

Subendocardial coronary course

Coronary crossing

Anomalous origination of the posterior descending artery from the anterior descending branch or a septal penetrating branch

Split right coronary artery

- Proximal and distal posterior descending branches that both arise from the right coronary artery
- Proximal posterior descending branch that arises from the right coronary artery; distal posterior descending branch that arises from the left anterior descending coronary artery
- Parallel posterior descending branches ×2 (arising from the right coronary artery or the circumflex artery) or 'codominant'

Split left anterior descending coronary artery

- Left anterior descending coronary artery and first large septal branch
- Left anterior descending coronary artery, double

Ectopic origination of first septal branch

- Right coronary artery
- Right sinus
- Diagonal
- Ramus
- Circumflex artery

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Box 3 | Anomalies of coronary artery termination[3,11]

Inadequate arteriolar or capillary ramifications

Fistulas from right coronary artery, left coronary artery, or infundibular artery to the:

- Right ventricle
- Right atrium
- Coronary sinus
- Superior vena cava
- Pulmonary artery
- Pulmonary vein
- Left atrium
- Left ventricle
- Multiple, right and left ventricles

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The mechanism by which ACAOS triggers this intermittent ischemia is not clearly understood, but several theories have been proposed. First, that exercise precipitates expansion of the great vessels, which compresses the anomalous artery along its interarterial course between the aorta and the pulmonary artery.[9,14,41] However, the pulmonary artery is unlikely to exert sufficient pressure to occlude a coronary artery in the absence of pulmonary hypertension.[9,41] Second, that exercise and vigorous expansion of the pulmonary artery and aorta causes spasm, torsion, or kinking of the aberrant coronary artery.[1,14,41] Third, that the acute leftward passage of the aberrant left coronary artery along the aortic wall causes intraluminal narrowing of the vessel and gives rise to a slit-like ostium. During increased cardiac activity and expansion of the great vessels, the left coronary artery is further stretched, which precipitates flap-like closure of the orifice of the left coronary artery and sudden myocardial infarction.[9,14,41] Fourth, that formation of a congenitally small left coronary artery system causes ischemia;[41] and fifth, that ACAOS is associated with obstructive coronary atherosclerotic disease, although considerable evidence against this last hypothesis exists.[41]

Transthoracic echocardiography has shown that anomalous arteries often assume a trajectory within the aortic wall to reach their dependent territories (an 'intramural course'),[42] and this observation has been supported by the results of studies using intravascular ultrasonography (IVUS).[3,43] In a small case series, Angelini and colleagues described three symptomatic patients, one with anomalous origination of the left coronary artery from the noncoronary sinus, another with anomalous origination of the left coronary artery from the right coronary sinus, and the third with anomalous origination of both coronary arteries superior to the left coronary sinus.[43] Three common features were documented in each of these patients: intussusception of the anomalous coronary artery into the aortic wall; substantial narrowing of the anomalous vessel during its proximal intramural course compared with the distal vessel, consistent with segmental hypoplasia; and asymmetrical lateral compression of the vessel lumen, most marked during systole and during exercise conditions simulated pharmacologically with atropine and dobutamine.

If corroborated by further studies on a larger scale, these results would indicate that development of the aberrant coronary artery is hampered by its intramural setting and is further aggravated by asymmetrical lateral compression that occurs with exercise and with advancing age as the aortic wall becomes thicker and stiffer.[3] Furthermore, these findings might affect what constitutes a 'malignant' anomaly. Rather than assuming that the interarterial course of the ACAOS confers the risk of SCD (presumably because of compression between the great vessels), the intramural course of the vessel might constitute the key pathophysiological mechanism. The theory

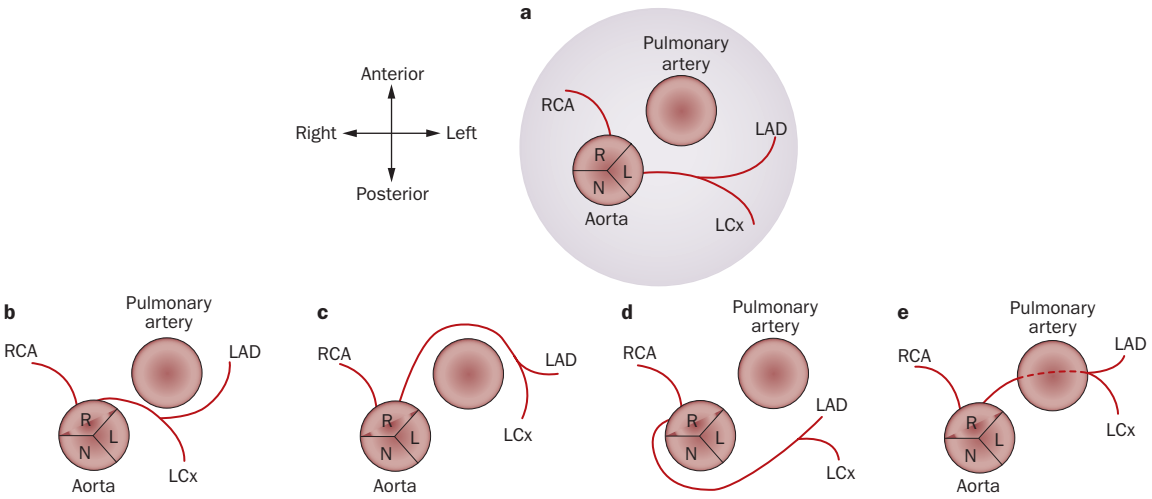

Figure 1 | Anomalous origination of the left coronary artery from the right coronary sinus: variations in the course of the anomalous artery. **a** | Normal coronary-artery anatomy. **b** | ACAOS with an interarterial course. **c** | ACAOS with a prepulmonary course. **d** | ACAOS with a retroaortic course. **e** | ACAOS with a subpulmonic course. Abbreviations: ACAOS, anomalous origination of a coronary artery from the opposite sinus; L, left coronary sinus; LAD, left anterior descending coronary artery; LCx, left circumflex artery; N, noncoronary sinus; R, right coronary sinus; RCA, right coronary artery.

is supported by the case of a patient who presented with critical ischemia attributed to an anomalous left coronary artery arising from the correct sinus, but with an acute proximal angulation of the ostium and an intramural course with the same features of lateral compression and hypoplasia seen on IVUS.[44]

Diagnosis

The various imaging modalities available for investigating coronary artery disease or anomalies in general can equally be employed in the diagnosis of ACAOS, and are compared in Table 2.

Echocardiography

Echocardiography has a role in identifying coronary anomalies and is particularly useful in children, where the coronary ostia can be appreciated in the majority of cases.[13,45] In adults, however, echocardiography has limited sensitivity for small-caliber vessels, and those with diameters <2 mm can easily be missed.[27] Sensitivity and specificity are operator-dependent and can be limited further by patient anatomy and poor echogenic windows.[46]

Invasive coronary angiography

Before the advent of CTCA, invasive coronary angiography was the only technique available to fully assess the coronary architecture, but although it was considered to be the gold standard for diagnosis of coronary anomalies, it has a number of limitations. Cannulation of anomalous vessels can require a considerable degree of skill and, therefore, outcomes are operator-dependent. Overlap of the proximal coronary segments can make distinguishing the anatomy difficult, and complex 3D relationships with the great vessels might not be fully defined.[33,46,47] Furthermore, the invasive nature of this test carries associated risks of morbidity and mortality, with early risk of major complications (myocardial infarction, stroke, or death) estimated at 0.2–0.3% and risk of minor complications (usually related to peripheral vascular access) at 1.0–2.0%.[47] The equipment and personnel required for invasive coronary angiography are expensive and although the procedure itself can be of short duration if performed by an experienced operator, the whole process of angiography is lengthy when preparation and aftercare of the patient and laboratory are taken into account.[47]

CT coronary angiography

Multidetector-row CT provides 3D information on the blood vessels and adjacent structures (Figure 2).[48] Several techniques have been used to minimize respiratory and cardiac-motion artifacts, including breath holding, electrocardiogram (ECG) gating, and post-processing algorithms.[46,48,49] Image quality has been shown to correlate inversely with patient heart rate, so pharmacological preparation of patients with β-blockers or calcium-channel antagonists can be required.[47,49] Dysrhythmias and extensive coronary calcification can interfere with the quality of the image obtained.[47]

CTCA has been shown to be an accurate means of diagnosing coronary anomalies.[50–53] Early studies focused on demonstrating noninferiority of CTCA compared with invasive coronary angiography.[50–52] Furthermore, a number of studies have, in fact, demonstrated superiority of CTCA in diagnosing coronary anomalies when compared with invasive coronary angiography.[28,33,54] In a blinded analysis of matched CTCA and invasive angiography images of 16 patients with coronary anomalies, all the anomalies were detected using CTCA, but only 53% were correctly identified using coronary angiography.[54] Two similar studies found that invasive angiography identified only 53% and 55% of the coronary anomalies diagnosed using CTCA, respectively.[28,33] The results of these small, observational studies consistently demonstrate improved sensitivity

Table 1 | Prevalence of coronary artery anomalies, and specifically of ACAOS, according to imaging modality

Study location, year	Cohort size	Prevalence of coronary artery anomalies	Prevalence of ACAOS	Prevalence of specific ACAOS subgroups
Angiography				
US, 1990[10]	126,595	1.3%	0.155%	RCA from LCS 0.107% LCA from RCS 0.017% LAD from RCS 0.030%
Turkey, 2010[15]	12,457	0.9%	0.168%	RCA from LCS 0.080% LCA from RCS 0.008% LAD from RCS 0.000% LCx from RCA 0.080%
Portugal, 2010[16]	3,906	0.54% (anomalies of origination only)	0.154%	RCA from LCS 0.026% LCA from RCS 0.051% LAD from RCS 0.026% LCx from RCS 0.051%
Lebanon, 2010[17]	4,650	0.73% (excluding anomalous origination of a coronary artery from the pulmonary artery, fistulae, and aneurysms)	0.387%	RCA from LCS 0.194% LCA from RCS 0.108% LAD from RCS 0.022% LCx from RCS 0.065%
Tunisia, 2009[18]	7,330	0.27% (anomalies of origination only)	NA	NA
Turkey, 2005[19]	12,059	0.829%	0.232%	RCA from LCS 0.058% LCA from RCS 0.075% LAD from RCS 0.008% LCx from RCS 0.091%
Turkey, 2004[20]	10,042	NA	NA	LCA from RCS 0.020% LCA from NCS 0.010%
Italy, 2003[21]	5,100	1.216%	0.294%	RCA from LCS 0.235% LCA from RCS 0.039%
India, 2002[22]	7,400	0.460% (excluding fistulae)	0.216%	RCA from LCS 0.095% LCA from RCS 0.028% LAD from RCS 0.014% LCx from RCS 0.081%
Turkey, 2002[23]	5,253	NA	NA	RCA from LCS 0.095%
India, 2000[24]	4,100	0.951%	NA	NA
Hungary, 1997[25]	7,694	1.34%	NA	NA
US, 1988[26]	10,661	0.78%	0.309%	RCA from LCS 0.281% LCA from RCS 0.028%
CTCA				
China, 2010[27]	1,879	1.3%	0.905%	RCA from LCS 0.639% LCA from RCS 0.053% LCA from NCS 0.160% LAD from RCS 0.000% LCx from RCS 0.053%
China, 2010[28]	3,625	0.99%	NA	NA
Germany, 2009[29]	748	2.3%	2.139%	RCA from LCS 1.070% LCA from RCS (SCA) 0.134% LCx from RCS 0.936%
Turkey, 2009[30]	700	2.139%	1%	RCA from LCS 0.571% LCA from RCS 0.286% LCx from RCS 0.143%
Turkey, 2006[31]	725	5.793%	0.551%	LCA from RCS 0.138% LCx from RCS 0.413%
Japan, 2005[32]	1,153	0.43% (anomalies of origination only)	0.347%	RCA from LCS 0.260% LCx from RCS 0.087%
Echocardiography				
US, 2001[45]	2,388 (pediatric)	NA	0.167%	RCA from LCS 0.084% LCA from RCS 0.084%
Autopsy				
Australia, 1994[92]	7,857 (pediatric)	0.5%	0.216%	NA

Abbreviations: ACAOS, anomalous origination of a coronary artery from the opposite sinus; CTCA, CT coronary angiography; LAD, left anterior descending coronary artery; LCA, left coronary artery; LCS, left coronary sinus; LCx, left circumflex artery; NA, not available; NCS, noncoronary sinus; RCA, right coronary artery; RCS, right coronary sinus; SCA, single coronary artery.

Table 2 | Comparison of imaging modalities for diagnosis and anatomical characterization of ACAOS

Technique	Duration	Radiation*	Spatial resolution	Temporal resolution	Advantages	Disadvantages
Echocardiography	20–30 mins	0 mSv	<1.0 mm[96]	<33 ms[97]	Noninvasive No radiation No contrast	Operator-dependent[46] Limited by patient anatomy and echo windows[46]
Invasive coronary angiography	10–30 mins	3–10 mSv[47,55,56]	0.2 mm[48]	8 ms[98]	High spatial resolution High temporal resolution	2-dimensional Procedural morbidity (1.5%) and mortality (0.15%)[48] Operator-dependent[48] Radiation Iodinated contrast
CTCA	5–20 s on a 64 row MDCT scanner with single-breath hold[48,49]	5–32 mSv[47–49,55–57] 1.1–3.3 mSv[58,59] (though possible underestimation)[60]	0.40–0.75 mm[47–49]	Previously as high as 250 ms,[93] now as low as 83 ms with 64 slice dual source CT[94,95]	Noninvasive High spatial resolution	Radiation Iodinated contrast Potential for artifact from cardiac motion (but minimized by ECG gating) Potential for artifact from respiratory motion (but only single-breath hold required) Low heart rates required for optimal imaging[46]
MRCA	25–50 min[47,48]	0 mSv	0.7–3.0 mm[47,48]	120–150 ms[99]	Noninvasive No radiation No contrast	Low spatial resolution Low temporal resolution High potential for artifact from cardiac motion (but minimized by ECG gating) High potential for artifact from respiratory motion, particularly if patient is claustrophobic or anxious with altered breathing pattern

*Average background radiation per year = 3 mSv.[54] Abbreviations: ACAOS, anomalous origination of a coronary artery from the opposite sinus; CTCA, CT coronary angiography; ECG, electrocardiogram; MDCT, multidetector-row CT; MRCA, magnetic resonance coronary angiography.

of CTCA compared with invasive angiography in the detection of coronary anomalies.

A potential disadvantage of CTCA is the associated radiation, particularly the increased lifetime risk of cancer that this exposure might confer in young patients.[47] Initial reports of radiation dosages with CTCA were higher than for invasive coronary angiography (5–32 mSv compared with 3–10 mSv, respectively).[47–49,55–57] However, with the use of prospective imaging and techniques to reduce the optimal dose (such as ECG-controlled tube-current modulation, in which the current of the X-ray tube is reduced during systole),[47,49] the radiation delivered during CTCA has been reduced to as low as 1.1–4.5 mSv.[58–60] Although the true radiation burden is not clearly established, overall these results seem encouraging and suggest that, while radiation remains an important consideration when referring patients for CTCA, the doses are at least comparable with those for invasive coronary angiography and not as high as initially reported. Another disadvantage of CTCA, albeit one shared with invasive angiography, is the required administration of intravenous contrast with associated risks of nephrotoxicity and allergic reaction.[61]

Magnetic resonance coronary angiography

Magnetic resonance coronary angiography (MRCA), like echocardiography and CTCA, is a noninvasive option for the diagnosis of coronary anomalies. The key advantage that MRCA holds over both CTCA and invasive coronary angiography is that neither ionizing radiation nor iodinated contrast media are used.[47] MRCA also carries the potential benefits of allowing concomitant assessment of cardiac function, blood flow, and myocardial viability, although these tests are of limited use in the assessment of ACAOS where noninvasive functional tests are often normal, as discussed below. As with CTCA, MRCA produces 3D images of the coronary anatomy.

An evaluation of 36 patients with coronary anomalies suspected on the basis of invasive coronary angiograms, and who were then referred for MRCA blind analysis, demonstrated 100% agreement between the two imaging modalities in differentiating anomalous origination of the coronary arteries from normal anatomy. However, in three cases, MRCA successfully demonstrated the proximal course of the vessel whereas invasive angiography did not.[62] Not all studies have demonstrated superiority of MRCA compared with invasive coronary angiography for the identification of coronary anomalies. In a blinded analysis of 16 patients with anomalies of coronary origination identified by invasive angiography, the coronary anomaly was correctly identified using MRCA in 14 patients, but was incorrectly identified in one individual, and the course of the artery was not clearly delineated in two patients.[63]

As with CTCA, ECG gating can be applied to minimize artifact from cardiac motion, and β-blockade can also be necessary to maximize time spent in diastole.[47] A limitation of ECG-gated MRCA is the need to breath hold to avoid respiratory artifacts,[62,63] but improved outcomes have been achieved with free-breathing 3D MRCA.[47] In an examination of 25 symptomatic patients with coronary anomalies identified using invasive coronary angiography, free-breathing 3D MRCA successfully identified the proximal course of the anomalous vessels in relation to the great vessels in all cases, but invasive angiography

failed to do so in 11 of the 25 cases, eight of which had anomalous origination with an interarterial course.[64]

To our knowledge, the sensitivities of MRCA and CTCA for the detection of coronary anomalies have not been directly compared. However, the spatial resolution of MRCA is inferior to that of CTCA, meaning that MRCA can fail to adequately delineate the distal course of the artery.[44,48,63] Respiratory motion can interfere with both imaging modalities, but CTCA requires just a single-breath hold and takes 5–20 s,[46,48,49] whereas MRCA needs more prolonged compliance with breathing instructions. Even in free-breathing 3D MRCA, patients are required to breathe quietly and regularly, which can prove difficult if they are anxious or claustrophobic.

The AHA Committee on Cardiovascular Imaging has offered a class IIa/b recommendation that evaluation of anomalous coronary arteries can be performed by either CTCA or MRCA; radiation-protection concerns mean that MRCA is preferred when available.[47] The European Society of Cardiology recommends CTCA for first-line investigation in patients with known or suspected coronary anomalies.[49]

Functional assessment

Not all patients with ACAOS who suffer SCD were previously symptomatic,[3] so the absence of symptoms does not necessarily indicate a benign prognosis. Functional assessment offers a means of evaluating the potential risk of SCD in these patients, incorporating a number of noninvasive and invasive strategies.

Noninvasive strategies

Electrocardiography

Evaluation of the resting and exercise ECG has been shown to predict poorly the hemodynamic implications of ACAOS, with regard to both symptoms and risk of SCD. In a cohort of eight patients undergoing surgery for ACAOS, all had symptoms of syncope or chest pain during exertion, but normal resting and exercise ECGs.[65] Similarly, in a cohort of 24 pediatric patients undergoing surgery for ACAOS, nine patients with symptoms suggestive of ischemia underwent exercise-ECG testing, but only one result was abnormal.[66] Furthermore, in an autopsy study of 27 young athletes who suffered SCD as a result of ACAOS, 55% had shown no previous clinical cardiovascular symptoms; 37% had shown preceding symptoms, but cardiovascular tests had yielded normal results, including evaluation of the resting ECG in nine patients and the exercise ECG in six patients.[36] Therefore, a normal ECG during rest or exercise cannot be used to exclude the presence of ACAOS with hemodynamic implications.

Stress echocardiography

Few data exist on the sensitivity and specificity of stress echocardiography for the prediction of SCD in patients with ACAOS. In a study of 31 pediatric patients with ACAOS with an interarterial course, 17 patients underwent dobutamine stress echocardiography. No abnormalities in regional wall motion were demonstrated, although four patients had abnormal flow detected using Doppler ultrasonography and two had ECG changes. Patients with evidence of ischemia were referred for surgery.[67] These findings suggest that stress echocardiography can detect the hemodynamic effects of ACAOS in some cases, and these patients might reasonably be inferred to be at increased risk of SCD. However, the sensitivity of stress echocardiography for prediction of SCD risk, and what the natural history of these patients would have been without surgical intervention, are unknown.

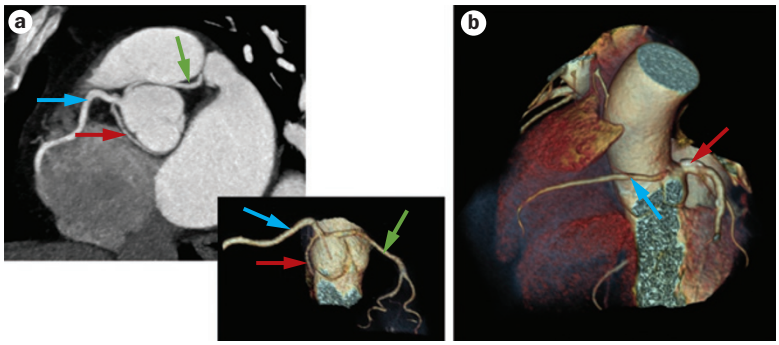

Figure 2 | CT coronary angiograms of anomalous origination of a coronary artery from the opposite sinus. **a** | Maximum intensity projection of an anomalous left anterior descending coronary artery (green arrow) and left circumflex artery (red arrow), both arising from the right coronary artery (blue arrow), with the same patient's anatomy viewed using a volume-rendered technique (inset). **b** | A volume-rendered image of a different patient with a right coronary artery (blue arrow) arising from the left coronary sinus with an anterior malignant course. Left main coronary artery (red arrow).

Myocardial perfusion imaging

Myocardial perfusion imaging is routinely used to quantify the extent of ischemia during rest and stress, as a result of coronary artery obstruction. A number of case reports exist in which inducible ischemia has been demonstrated by myocardial perfusion imaging in patients with ACAOS.[68,69] In a study of eight patients with ACAOS with an interarterial course who were referred for surgery, only one had demonstrable ischemia using perfusion imaging, despite all patients being symptomatic.[65] Whether the remaining seven patients underwent perfusion imaging was not, however, specifically documented. In a cohort study, 14 patients with coronary anomalies in the absence of atherosclerotic disease were evaluated using stress–rest ^{99m}Tc-sestamibi myocardial-perfusion single-photon emission CT (SPECT).[70] Perfusion defects were successfully demonstrated in four of the five patients with ACAOS with an interarterial course (the fifth patient did not reach the target heart rate). The researchers argue that stress–rest SPECT allows the reliable selection of those patients who should be referred for corrective surgery.[70] The demonstration with this technique that the ACAOS has hemodynamic implications would add weight to the case for surgery, but the sensitivity of this test for prediction of SCD is still unknown.

The ischemia associated with ACAOS with an interarterial course might be induced only by intense physical exertion beyond the level normally experienced in a standard stress test, and these tests might consequently fail to detect ACAOS with hemodynamic effects. To

improve sensitivity, higher levels of stress might need to be induced during existing tests (without compromising patient safety), or alternative tests such as PET might be required to detect potential early indicators of ischemia. PET has the advantage of higher spatial resolution than SPECT, and the potential to detect perfusion or metabolic effects of the ACAOS at a microscopic level by using radiolabeled glucose (^{18}F-fluorodeoxyglucose) or other radiolabeled molecular ligands.[71] However, the use of PET has not, to our knowledge, been evaluated in this field.

Invasive strategies

Intravascular ultrasonography

The behavior of coronary artery anomalies can be visualized directly under controlled stress testing. In a series of symptomatic patients with ACAOS evaluated using IVUS with concurrent dobutamine stress testing, intussusception of the proximal anomalous vessel with associated hypoplasia and lateral luminal compression were described in all three cases.[43] However, in the two cases where additional dobutamine stress testing was performed, one patient developed chest pain, ventricular tachycardia, and syncope. The other patient experienced chest pain and worsening of the proximal stenosis on IVUS, to the extent that urgent surgery was warranted. Other investigators have reported similar findings.[72] IVUS with concurrent dobutamine stress testing would, therefore, seem to allow detailed, dynamic assessment of anomalous coronary arteries both at rest and under stress. The effects of physiological or pharmacological stress on vessel morphology, the ECG, and clinical symptoms have been effectively demonstrated, and produce positive results that make a clear case for instigating treatment.

Fractional and coronary flow reserve

Few case reports exist on the functional evaluation of ACAOS using measurement of either fractional flow reserve (FFR) or coronary flow reserve, which are well-documented, invasive techniques used primarily to assess obstructed coronary flow.[73,74] In one report, a patient aged 14 years with anomalous origination of the left coronary artery from the right coronary sinus (diagnosed using angiography) had been undergoing regular surveillance with serial perfusion scans.[75] These scans had been normal for 6 years, but she then developed mild anterior and lateral wall defects. She subsequently underwent FFR assessment across the left coronary artery ostial segment. The ratio of the pressures in the distal coronary artery and the aorta at rest was 0.96; this ratio fell to 0.87 with adenosine hyperemia and to 0.86 with dobutamine challenge. Although the ratio did not fall below the threshold of 0.75 established for ischemic lesions, this demonstration of a dynamic gradient, induced by conditions that simulated exercise, was felt to offer a good rationale for surgical intervention.[75]

In another small series, IVUS of three patients with anomalous origination of the right coronary artery from the left coronary sinus revealed the characteristic asymmetrical ovoid luminal cross-section, subject to varying degrees of compression during systole.[76] One patient was asymptomatic, but had a positive exercise test and subsequently underwent percutaneous coronary intervention (PCI). The other two patients underwent pressure-wire assessment, which revealed FFRs of 0.94–1.00. On this basis, these patients were managed medically, despite one being symptomatic with chest pain and breathlessness. Notably, IVUS in this series was performed at rest, not stress, and whether the FFR measurements were taken under rest or stress conditions was not recorded.[76] Although no trials have been performed to compare FFR and coronary flow reserve with other modalities for the assessment of ACAOS, potential exists for its use in risk stratification of coronary anomalies, and this technique could be used as an adjunct where ischemic discrepancies are noted with noninvasive stress imaging.

Recommendations for functional assessment

Angelini and colleagues have proposed that, after ACAOS is identified, a nuclear stress test should be performed, followed by coronary angiography to identify any additional obstructive disease, and then IVUS of the anomalous vessel to guide whether or not intervention is indicated.[3] They also suggest that the severity of the ACAOS should be graded according to IVUS criteria, on the basis of the amount of hypoplasia of the proximal vessel compared with the circumference of the distal vessel, and of the amount of lateral compression of the proximal vessel that occurs at baseline and with pharmacological stress and advancing age.[43] The need to create an international database of patients with ACAOS to record investigations, interventions, and outcomes, to formulate and validate appropriate parameters for each level of severity is generally acknowledged.

We would argue that, in addition to characterizing the morphology of the lesion with IVUS, combined FFR assessment would allow a more-complete appreciation of the hemodynamic importance of these lesions. Furthermore, IVUS and FFR assessment should be performed both at rest and under conditions of pharmacologically-induced stress. First, SCD is normally associated with exercise. Second, dobutamine stress can induce worsening of the ostial-segment stenosis on IVUS,[43] thereby providing a good rationale for intervention. Third, FFR measurements can be normal at rest, but fall during pharmacological stress.[75] Although full invasive testing with IVUS and FFR might provide the most-comprehensive form of risk assessment, such tests are not without their own risks, and whether asymptomatic patients with normal results from noninvasive stress tests should be subjected to invasive tests is unclear.

Treatment

Medical management

Patients with ACAOS can be managed medically, surgically, or by PCI. Medical management consists of β-blockers and avoidance of physical exertion.[77,78] In a retrospective review of 56 patients with ACAOS (mean age 55.9 years, range 32–85 years), all of whom were conservatively, medically managed as described above, no

deaths attributable to ACAOS were reported during the follow-up (mean 5.6 years, range 2 months–14.5 years).[78] However, the cohort included no patients with anomalous origination of the left coronary artery from the right coronary sinus with an interarterial course, who potentially carry an increased risk of SCD.

Surgical management

Surgical correction of anomalous vessels could improve the functional impairment that might occur with ACAOS. The various strategies are described below.

Local, direct repair

Surgery to excise the common wall between the ACAOS and aorta, which unroofs the intramural segment and opens up the coronary ostium (Figure 3a),[13,65,79] has been shown using stress testing to be effective in alleviating symptoms and ischemia.[13,79,80] The main disadvantage of this approach is that the intercoronary commissure is temporarily detached and then resuspended, which can lead to aortic insufficiency.[79,80] An alternative approach is to leave the intramural segment *in situ* and create a neo-ostium at the point at which the distal coronary artery segment exits the aortic wall (Figure 3b). This technique avoids disruption of the commissure.[43,79,81]

CABG surgery

CABG surgery is a potentially attractive option for correction of ACAOS, but has a number of limitations. In young patients with a long life expectancy, vein grafts might be considered inappropriate because of their limited longevity.[82] The main disadvantage of arterial conduits is the potential for competitive flow down the ACAOS, which is minimally obstructed at rest, leading to graft closure.[65,83,84] Consequently, some clinicians have recommended ligation of the ACAOS proximal to the anastomosis between the artery and the graft.[81] Others advocate unroofing as the preferred surgical strategy, except where patients have concomitant atherosclerotic coronary disease, in which case CABG surgery is advised.[80,85]

Other surgical strategies

Data from IVUS studies indicate that the slit-like ostium and the intramural course of ACAOS cause ischemia and associated symptoms, and increase mortality.[3] However, some patients with ACAOS and an interarterial course do not demonstrate these features. Gulati and colleagues advocate reimplantation of an anomalous artery with a separate coronary ostium and without an intramural course, on the basis of their work with pediatric populations. Where the patient has an anomalous artery with a single coronary ostium without an intramural course, they advocate pulmonary artery translocation—movement of the main pulmonary artery towards the left pulmonary hilum to create more space and prevent compression.[86] This strategy has also been proposed by other groups.[87,88] Interestingly, the intervention assumes that the key pathophysiological mechanism is compression between the aorta and pulmonary artery, but the most-convincing evidence is from IVUS studies that implicate the slit-like ostium and intramural course. On this basis, patients with ACAOS without either of these features might not be at risk; therefore, surgical repair in these cases might be unnecessary. Further autopsy and *in vivo* studies are required to compare the prognostic and hemodynamic importance of ACAOS with and without an intramural course.

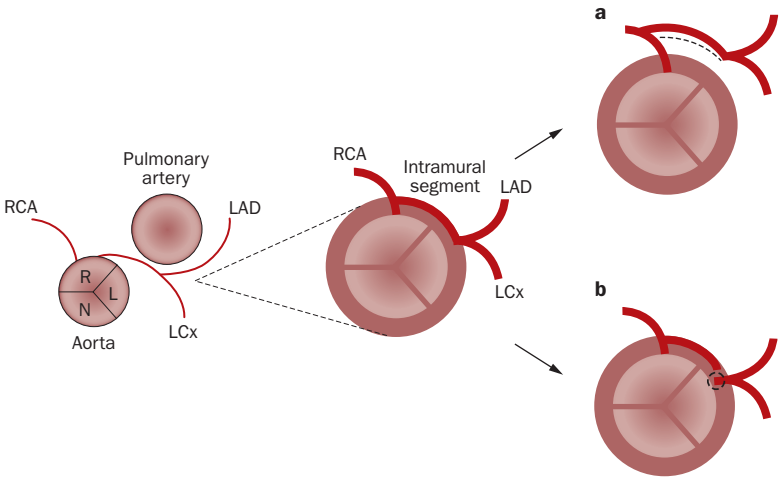

Figure 3 | Two options for surgical repair of ACAOS with an intramural course. **a** | Unroofing of the intramural segment.[13,65,79] **b** | Formation of a neo-ostium in the correct coronary sinus at the point at which the intramural segment exits the wall.[43,79,81] Abbreviations: ACAOS, anomalous origination of a coronary artery from the opposite sinus; L, left coronary sinus; LAD, left anterior descending coronary artery; LCx, left circumflex artery; N, noncoronary sinus; R, right coronary sinus; RCA, right coronary artery.

Outcomes for surgery

In a retrospective review of 36 patients who underwent surgery primarily for ACAOS between 1992 and 2008, 39% were treated with CABG surgery and 61% with unroofing.[85] No perioperative mortality was reported, although one patient who had undergone concomitant redo-aortic valve replacement died 2 months after surgery from a subdural hematoma. One patient treated with CABG surgery had some residual chest pain, but all the other patients were asymptomatic during follow-up (mean 1.1 years). Moustafa and colleagues conducted a systematic review including 264 patients diagnosed with anomalous origination of the left coronary artery from the right coronary sinus between 1966 and 2006.[80] Treatment was reported in 72 patients, of whom 79.2% were managed surgically. Of these patients, 38.5% underwent CABG surgery, 28.1% unroofing, 15.7% ostial splitting with neo-ostial creation and ostium sphincteroplasty, 3.5% ostial reimplantation, 3.5% patch augmentation, and 1.8% surgical angioplasty. Five patients had no surgical details reported. 40% of the patients completed follow-up (mean 18.7 months, range 4 months to 10 years), and only one complication—severe aortic insufficiency in a patient managed with an unroofing procedure—was recorded. All the other patients were asymptomatic with normal functional stress testing on follow-up.[80] Overall, outcomes for ACAOS surgery seem favorable, but these studies highlight the need for long-term follow-up to ascertain the durability of these interventions, particularly in view of potential complications.

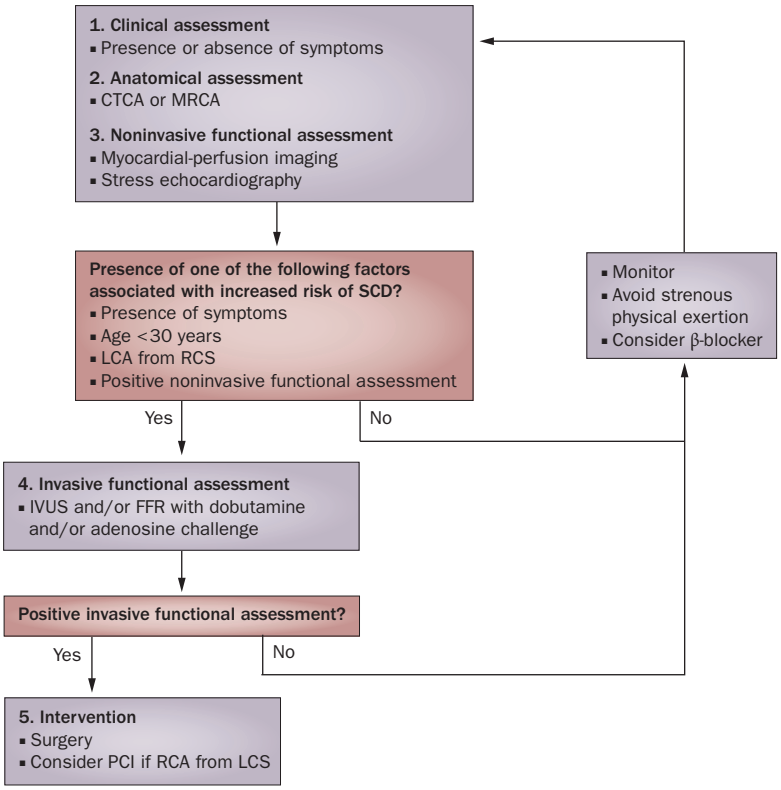

Figure 4 | Proposed algorithm for assessment and management of patients with ACAOS. Patients should be assessed for symptoms, followed by anatomical and noninvasive functional assessment of their coronary arteries. If classified as being at low risk of SCD, a conservative (medical) approach is recommended. High-risk patients should have invasive functional assessment, and those with evidence of ischemia should be discussed in a surgical and PCI multidisciplinary meeting to determine the most-appropriate mode of revascularization. Abbreviations: ACAOS, anomalous origination of a coronary artery from the opposite sinus; CTCA, CT coronary angiography; FFR, fractional flow reserve; IVUS, intravascular ultrasonography; LCA, left coronary artery; LCS, left coronary sinus; MRCA, magnetic resonance coronary angiography; PCI, percutaneous coronary intervention; RCA, right coronary artery; RCS, right coronary sinus; SCD, sudden cardiac death.

Percutaneous coronary intervention

The structural rigidity of intracoronary stents allows the slit-like ostium of the ACAOS to be reconstructed to a more anatomically cylindrical shape and to withstand compression of the vessel lumen during systole. In a report of two symptomatic patients with anomalous origination of the right coronary artery from the left coronary sinus, one patient had previously undergone CABG surgery (right internal mammary artery to right coronary artery), which occluded after 1 year.[89] Both patients had evidence of inferior ischemia on stress testing and systolic lateral compression of the proximal vessel demonstrated on IVUS. Both patients underwent stent implantation to the proximal anomalous right coronary artery. At 4 month follow-up, the former patient reported some persistent atypical chest pain but, overall, the symptoms were much improved and a repeat myocardial-perfusion scan was negative for ischemia. The stent was shown to be patent on repeat angiography, although the IVUS catheter could not be advanced into the stent. At 3 month follow-up, the latter patient also reported some persistent atypical chest pain, but had a normal stress test. Angiography revealed that the stent was well expanded and had corrected the systolic compression, although mild restenosis of the proximal anomalous segment was observed, which was subsequently redilated.

Schrale and co-workers described a patient aged 42 years with anomalous origination of the left coronary artery from the right coronary sinus and reversible anterior ischemia demonstrated on myocardial-perfusion scanning.[72] This patient declined surgery and underwent PCI instead, which successfully overcame the ostial constriction and systolic compression. The patient remained well, with a normal repeat perfusion scan, at 10 month follow-up.[72]

In a systematic review of four patients with anomalous origination of the left coronary artery from the right coronary sinus who underwent PCI, two patients had intracoronary stents to the anomalous left coronary artery, one patient had angioplasty without a stent to the left anterior descending coronary artery, and one patient had angioplasty without a stent to the obtuse marginal branches of the circumflex coronary artery.[80] Three patients completed follow-up at 12 months and were asymptomatic and with normal stress tests. No complications were recorded during the short follow-up periods.

In a report of 14 patients with ACAOS, 13 had objective evidence of ischemia on noninvasive stress testing and successfully underwent PCI with subsequent normalization of stress tests.[90] The other patient developed in-stent restenosis, but resolution of ischemia was eventually achieved with a different type of stent. No complications were reported, although the duration of follow-up was not specified in all cases.

Taken together, these reports suggest that PCI effectively improves symptoms and corrects reversible ischemia from ACAOS, as demonstrated using stress testing. The follow-up of these patients was short, however, and little is known about the long-term efficacy of this treatment. Long-term follow-up studies are required, particularly given the documented risk of in-stent restenosis.[89] Hariharan and colleagues highlighted the technical difficulty in achieving coaxial cannulation of anomalous vessels because of the acute angulation of their origin and the fact that the proximal vessel courses tangentially along the aortic wall, and called for development of catheters specifically designed for this use.[89] Another unresolved issue is the optimal degree of stent dilatation—whether the stent should be postdilated to match the maximum diameter of the ellipsoid intramural segment during systolic compression, or whether it should be matched to the diameter of the distal vessel. A high degree of dilatation might favor increased blood flow and potentially reduce the risk of in-stent restenosis, but this benefit must be offset against the risk of aortic-root dissection.[89] Angelini has argued that PCI for anomalous origination of the right coronary artery from the left coronary sinus is probably justifiable in the presence of disabling symptoms, stenosis >50% compared with the normal distal vessel, a large dependent myocardial territory (more than one-third of the total), and evidence of reversible ischemia on nuclear stress testing.[3] PCI has been reported in patients with anomalous origination of

the left coronary artery from the right coronary sinus,[72,80] but the poor prognosis associated with this condition means that surgery is preferred to PCI.[3]

Selection of the optimal treatment strategy

The key challenge in the management of ACAOS is to determine which patients will benefit from intervention, either surgical or percutaneous, and which can be managed medically. Autopsy studies provide evidence that SCD might be attributable to ACAOS, but they cannot indicate the absolute risk of SCD in the ACAOS patient population as a whole or, indeed, in the individual patient. The ill-defined risk of SCD must be weighed against the risk of surgical or percutaneous intervention when deciding patient treatment strategies.

The consensus of opinion is that symptomatic patients with anomalous origination of the left coronary artery from the right coronary sinus should be offered surgical intervention.[14,65,80,85] For asymptomatic patients with anomalous origination of the left coronary artery from the right coronary sinus, some groups continue to recommend surgery,[80,85] but other groups take into account the results of stress testing and the age of the patient. Patients who are 30 years of age or older are potentially at lower risk of SCD than younger patients.[91] Therefore, conservative medical treatment is recommended for asymptomatic patients over the age of 30 years. In younger asymptomatic patients, surgery is advocated only when ischemia has been demonstrated on stress testing; in the absence of demonstrable ischemia, treatment should be determined on a case-by-case basis.[14]

For symptomatic patients with anomalous origination of the right coronary artery from the left coronary sinus, the consensus of opinion is that intervention—typically surgery—is indicated,[14,85] although a case for PCI has also been made.[3] For asymptomatic patients with anomalous origination of the right coronary artery from the left coronary sinus, more debate exists because of the weaker association between this anomaly and SCD, compared with anomalous origination of the left coronary artery from the right coronary sinus.[14] Thorough assessment with stress testing is advised, with surgical treatment for patients with positive stress tests and very active lifestyles, unless the anomalous right coronary artery is nondominant.[85] Another recommendation supports surgical intervention in asymptomatic patients under 30 years of age with high activity levels.[65] Conversely, the risks of surgery and residual ischemia even after correction might outweigh the small potential risk of SCD in these patients, and conservative medical management is advocated.[14] Given that surgical intervention might not improve patient outcomes, the decision to intervene should be taken cautiously.[77]

Conclusions

With increasing utilization of CTCA, clinicians can expect increased rates of incidental diagnosis of ACAOS. Management of patients with ACAOS is challenging. The aim of treatment is to prevent SCD, yet the precise risk of SCD conferred by ACAOS is unknown. Anomalous origination of the left coronary artery and patients younger than 30 years of age carry a higher risk of SCD compared with anomalous origination of the right coronary artery and patients older than 30 years of age. Although the prognostic importance of positive results from noninvasive and invasive tests have not been proven, they are likely to indicate risk of SCD. The development of comprehensive national and international registries of patients with ACAOS is urgently required in order to improve our understanding of prognosis and risk stratification, to prevent SCD, and to avoid exposing patients to the risks of potentially unnecessary interventions. In the meantime, we cautiously propose a scheme to guide investigation and management of patients with ACAOS (Figure 4).

Review criteria

The PubMed database was searched for Review articles published in English (no time limit), and full-text articles published in English from January 2010 to January 2011 using the following search terms: "anomalous origin coronary artery", "anomalous origin coronary arteries", "coronary anomaly", "coronary anomalies". The reference lists of the articles identified were reviewed for additional papers.

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