Coronary Artery Anomalies – State of the Art Review

Weiren Lau, MBBS, BSc, MRCP(UK), MMed(IM)[a], Phong Teck Lee, MBChB, MRCP(UK)[a,b], and Choong Hou Koh, MBBS, MRCP(UK), DAvMed[a,b,c*]

From the [a] Department of Cardiology, National Heart Centre Singapore, Singapore, [b] Duke-NUS School of Medicine, National University of Singapore, Singapore and [c] Changi Aviation Medical Centre, Changi General Hospital, Singapore.

Abstract: Coronary artery anomalies (CAAs) comprise a wide spectrum of anatomic entities, with diverse clinical phenotypes. We present a case of an anomalous right coronary artery arising from the left aortic sinus with an interarterial course, a potentially fatal condition that can precipitate ischemia and sudden cardiac death. CAAs are increasingly detected in adults, mostly as incidental findings in the course of cardiac evaluation. This is due to the expanding use of invasive and noninvasive cardiac imaging, usually in the work-up for possible CAD. The prognostic implications of CAAs in this group of patients remain unclear. In AAOCA patients, appropriate work-up with anatomical and functional imaging should be performed for risk stratification. An individualized approach to management should be adopted, considering symptoms, age, sporting activities and the presence of high-risk anatomical features and physiologic consequences (such as ischemia, myocardial fibrosis, or cardiac arrhythmias) detected on multimodality imaging or other functional cardiac investigations. This comprehensive and up to date review seeks to crystallize current data in the recent literature, and proposes a clinical management algorithm for the clinician faced

*Corresponding author: Koh Choong Hou MBBS, MRCP(UK), DAvMed, National Heart Centre Singapore, 5 Hospital Dr, 169609, Singapore. E-mail: koh.choong.hou@singhealth.com.sg
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with the conundrum of managing such conditions. (Curr Probl Cardiol 2023;48:101935.)

Introduction

Coronary artery anomalies (CAAs) are a heterogenous group of congenital conditions, defined as abnormalities in the origin, course or termination of the epicardial coronary arteries, encountered in <1% of the general population.[1,2] Although uncommon, they constitute the second most common cause of sudden cardiac death (SCD) amongst competitive athletes,[3] rendering it a subject of clinical interest. Among the CAAs, the anomalous aortic origin of the coronary artery (AAOCA), in particular when it traverses between the aorta and pulmonary artery (ie, interarterial course), has been most frequently associated with SCD.[4] The majority of patients are asymptomatic, and CAAs are usually diagnosed incidentally on coronary angiography or imaging, or on autopsy following SCD.[4] Patients may also report symptoms of myocardial ischemia, heart failure, and/or arrhythmias.[4]

The rapid development in invasive and noninvasive coronary imaging techniques has increased the reported prevalence of CAAs in the adult population, mostly as incidental findings. The prognostic implications of CAAs diagnosed in this manner remain unclear,[1] and current management guidelines are supported by a lower level of scientific evidence, mostly consisting of observational and small study series.[5-7] This poses a significant challenge in the management of such patients. For certain high-risk groups, surgery is generally recommended. Other treatment options include conservative medical management and percutaneous coronary intervention (PCI). As the majority of deaths associated with CAAs occur during exercise,[8] exercise restrictions and eligibility for competitive sports should also be carefully evaluated, taking into consideration both the coronary anatomy and presence of inducible ischaemia.[2]

In this paper, we describe a patient with an anomalous origin of the right coronary artery (RCA) from the left sinus of Valsalva (LSV) with an interarterial course. We aim to examine the current literature on the types, epidemiology, prognosis, investigation, and management of CAAs.

Case Report

A 67-year-old gentleman with hypertension, type 2 diabetes mellitus and hyperlipidemia, was referred to the cardiology clinic by his general

practitioner. He had an 8 months history of exertional dyspnea and chest tightness. Transthoracic echocardiogram showed a normal left ventricular ejection fraction with no regional wall motion abnormalities. Apart from aortic valve sclerosis, the valves were morphologically normal. Dobutamine stress echocardiogram showed inducible myocardial ischemia in the RCA territory at 88% maximum predicted heart rate. He was then started on aspirin, statins, beta-blockers, and nitrates.

A coronary angiogram was performed (See Fig 1), revealing an anomalous origin of the RCA from the LSV, and nonobstructive coronary atherosclerosis in the left anterior descending (LAD) and left circumflex (LCX) arteries. The RCA was of large caliber and with a right dominant coronary circulation. Coronary computed tomography angiography (CCTA) confirmed the anomalous origin of the RCA from LSV (See Fig 2), arising adjacent to the LMCA origin. The proximal course of RCA traversed between the main pulmonary artery and aorta (ie, interarterial course).

The patient was subsequently referred to cardiothoracic surgery, where surgical options including coronary unroofing, reimplantation, and coronary artery bypass grafting (CABG) were discussed. Following a multidisciplinary discussion, he opted for conservative management and was placed on regular follow-up.

Normal Coronary Anatomy and Normal Variants

Angelini and colleagues[1] have proposed to define normal coronary anatomy as every morphological feature with >1% prevalence in the general population. This includes normal variants, which are relatively

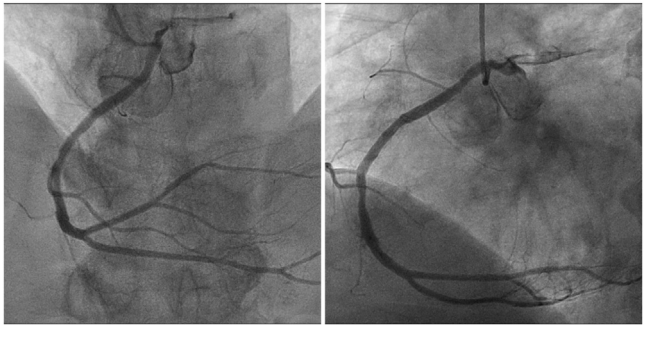

FIG 1. Coronary angiogram images showing an anomalous right coronary artery (RCA) from the left sinus of Valsalva (LSV). Left: Posterior-anterior (PA) cranial view; Right: left anterior oblique (LAO) view. (Color version of figure is available online.)

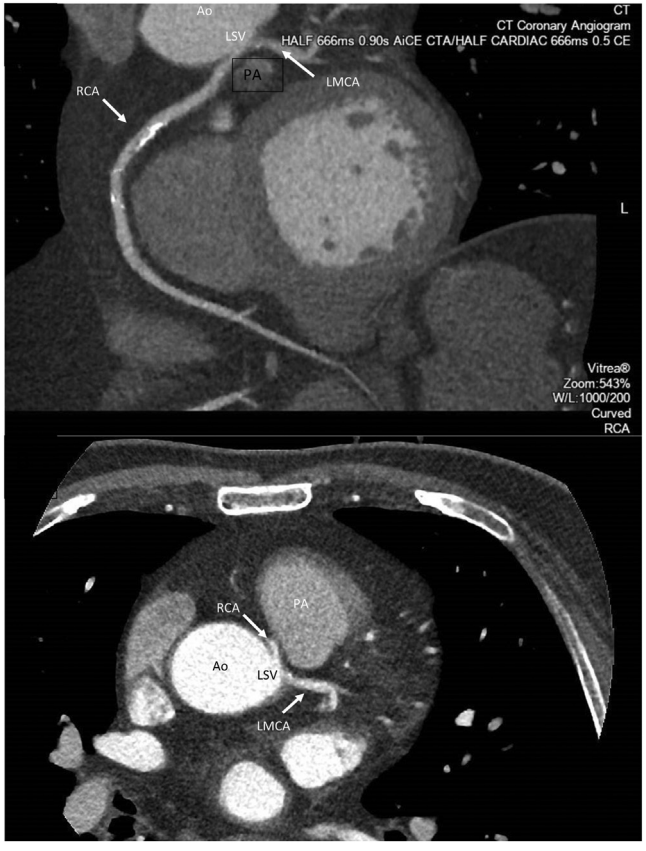

FIG 2. Coronary computed tomography angiography (CCTA) images showing an anomalous right coronary artery (RCA) from the left sinus of Valsalva (LSV). Top: Oblique coronal view showing the origin and course of the RCA with nonobstructive coronary plaques; bottom: axial view showing the interarterial course between the main pulmonary artery and the aorta. Ao, aorta; LSV, left sinus of Valsalva; PA, pulmonary artery; RCA, right coronary artery. (Color version of figure is available online.)

unusual coronary anatomy variations that are encountered in >1% in the general population.[9,10]

Angelini used several quantitative and qualitative criteria to define normal coronary anatomy (Table 1).[1] There are 3 main epicardial coronary arteries: the RCA, left anterior descending artery (LAD), and the left circumflex artery (LCX) with the LCX and LAD arising from the left main coronary artery (LMCA). There are 2-4 coronary ostia located at the upper midsection of the anterior aspect of the left and right sinuses of Valsalva, part of the ascending aorta.

The LMCA originates from the LSV and passes between the main pulmonary artery and left atrial appendage, before bifurcating into the LAD

TABLE 1. Features of normal coronary anatomy

Feature	Description
No. of ostia	2 to 4
Location	Right and left coronary sinuses (upper midsection)
Proximal orientation	45˚ to 90˚ off the aortic wall
Proximal common stem or trunk	Only left main coronary artery (LAD and LCX)
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, left anterior descending artery; LCX, left circumflex artery; LV, left ventricular; OM, obtuse marginal artery; RCA, right coronary artery; RV, right ventricular.

and LCX. The LAD descends towards the cardiac apex along the anterior interventricular sulcus, then gives rise to the diagonal and septal branches, supplying the anterior wall, apex, and the anterior 2/3 of the interventricular septum. The LCX courses towards the left, in the coronary sulcus on the diaphragmatic cardiac surface, giving rise to the obtuse marginal branches. It supplies the lateral wall of the left ventricle.

The RCA stems from the right sinus of Valsalva (RSV) and courses in between the pulmonary artery and right atrial appendage. It descends across the right atrioventricular sulcus and continues over the posterior surface of the heart, supplying the right side of the heart. It may give rise to the following branches: the conus branch, sinoatrial branch, right ventricular branch, atrioventricular nodal branch, posterior descending artery (PDA), and the posterolateral branch.[4,10,11]

The PDA runs in the posterior interventricular groove and supplies the inferior wall and inferior 1/3 of the interventricular septum. In 70% of the population, the RCA supplies the PDA, termed a right-dominant coronary circulation. Left-dominance, where the LCX gives rise to the PDA, is seen in 20%. The remaining 10% of the population have a co-dominant circulation, where both the left and right systems supply the PDA and posterolateral branches. Left and co-dominance are considered normal anatomical variants.[12] In the case of a small PDA, supply to the inferior wall may be provided by the RCA, LCX, OM branches, or a "wraparound LAD," where the LAD extends beyond the cardiac apex into the inferior interventricular groove.[10,11,13]

Another variant is the presence of a ramus intermedius (RI), arising as a third branch from the LMCA (~20% of cases). It typically takes the route of a diagonal or OM branch, supplying the lateral and inferior walls.[10,12,14] The sinoatrial branch (supplying the sinoatrial node) may

arise from the LCX instead of the RCA,[15] and the atrioventricular nodal branch (perfusing the atrioventricular node) may be supplied by the distal portion of the dominant artery.[12] The conus branch may arise directly from the aorta instead of the proximal RCA. Prevalence ranges from 10% to 50%.[10,12] Other variants include an acute take-off of the LCX (where there is an angle of ≤45° between the LMCA and LCX, caused by an unusually distal point of origin from the LMCA, ∼2% prevalence),[16] a "shepherd's crook" RCA (in which there the RCA takes a high and tortuous course, ∼5% prevalence)[12] and a high take-off (a coronary ostium ≥5 mm above the aortic sinotubular junction).[1,17]

The aforementioned normal variants are clinically benign, but may pose technical challenges during coronary angiography or intervention.[4,10]

Modified From Angelini

Classification of CAAs

Several classification systems for CAAs have been proposed, although no single classification scheme is widely used.[1,10,12,18] Some authors prefer to categorize CAAs as "major," "severe," vs "important," or "hemodynamically significant" vs "minor."[1] The 2007 classification scheme by Angelini is based on anatomical features, and 4 categories are recognized: (1) anomalies of origin and course; (2) anomalies of intrinsic coronary anatomy; (3) anomalies of coronary termination; and (4) anomalous collateral vessels (Table 2).[1]

Anomalies of Origin and Course

Anomalous Pulmonary Origin of a Coronary Artery (APOCA). This is a group of rare CAAs where one or more of the coronary arteries arise from the pulmonary artery (PA). It is associated with myocardial ischemia to varying degrees, depending on the vessel involved and the presence of collateral circulation.[2]

Of this group, anomalous origin of the LCA from PA (ALCAPA), also known as Blande-White-Garland syndrome, is the most common, occurring in 0.008% of the general population. Prognosis is abysmal, with only a minority surviving into adulthood.[4,10] Approximately 2/3 are symptomatic, reporting symptoms of angina, dyspnea, palpitations, or fatigue. Patients may also present with syncope, ventricular arrhythmias, and SCD.[19] Anomalous origin of the RCA from PA (ARCAPA) is the next

TABLE 2. Classification of types of coronary artery anomalies

Modified from Angelini (2007) [1]
A. Anomalies of origin and course
Absence of LMS
Anomalous location of coronary ostium within aortic root or near proper aortic sinus of Valsalva
Anomalous location of coronary ostium outside normal coronary aortic sinuses
Right posterior aortic sinus
Ascending aorta
Left ventricle
Right ventricle
Pulmonary artery
Aortic arch
Innominate artery
Right carotid artery
Internal mammary artery
Bronchial artery
Subclavian artery
Descending thoracic aorta
4. Anomalous location of coronary ostium at improper sinus
a. RCA that arises from left anterior sinus, with anomalous course
b. LAD that arises from right anterior sinus, with anomalous course
c. LCX that arises from right anterior sinus, with anomalous course
d. LCA that arises from right anterior sinus, with anomalous course
5. Single coronary artery
B. **Anomalies of intrinsic coronary arterial anatomy**
1. Congenital ostial stenosis or atresia (LMCA, LAD, RCA, LCX)
2. Coronary ostial dimple
3. Coronary ectasia or aneurysm
4. Absent coronary artery
5. Coronary hypoplasia
6. Myocardial bridging
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. Dual/split coronary artery
11. Ectopic origination of first septal branch
C. Anomalies of coronary termination
1. Inadequate arteriolar/capillary ramifications
2. Coronary artery fistulas
3. Termination of a coronary artery into a systemic artery
D. Anomalous anastomotic vessels

Cx, circumflex artery; LCA, left coronary artery; LSV, left sinus of Valsalva; RCA, right coronary artery; RSV, right sinus of Valsalva.

most common, and has a prevalence of 0.002%. While most patients are asymptomatic or mildly symptomatic, serious complications such as syncope, heart failure, and SCD have also been reported. Anomalous origin of the LAD from PA (ALADPA) is extremely rare (0.0008% prevalence)

and is associated with myocardial ischemia and SCD.[4,10,20-24] All coronary arteries from the PA has also been reported.[4,23,25]

The American College of Cardiology (ACC)/American Heart Association (AHA) and the European Society of Cardiology (ESC) guidelines recommend surgery in patients with ALCAPA (class I recommendation), and in those with ARCAPA and symptoms attributed to the anomalous coronary artery (class I recommendation). Surgery should be considered in an asymptomatic patient with ARCAPA with ventricular dysfunction or myocardial ischemia (class IIa recommendation).[5,7]

Athletes with APOCA should only be allowed to compete in low-intensity sports, pending repair of the anomaly. After repair, the decision regarding exercise restriction should be based on the presence of complications such as myocardial infarction or ventricular dysfunction.[26]

Anomalous Aortic Origin of a Coronary Artery From an Improper Sinus (AAOCA)

Anomalous AAOCA is a heterogenous group of CAAs that affects at least 1-7 in 1000 individuals.[146] The anomalous origin from the opposite sinus, that is, anomalous aortic origin of the RCA from the LSV (AAORCA) and anomalous aortic origin of the LCA from the RSV (AAOLCA), is the most clinically relevant and usually not associated with other congenital abnormalities.[147] They are associated with an interarterial course and an increased risk of SCD, especially in young athletes.[4] AAORCA is more common, with a prevalence of 0.03%-0.92%, while that of AAOLCA is 0.03%.[10]

Anomalous LCX from the RSV is a relatively common coronary artery anomaly, with a prevalence of 0.37%-0.64%.[10,24,30] Rarer CAAs include LMCA, LCA, and RCA from the posterior sinus of Valsalva (PSV). These CAAs are rarely associated with symptoms or complications, and can be considered benign.[10]

In patients with AAOCA, the course of CCAs is of clinical importance, especially in anomalous origin from the opposite sinus. It should be further classified, in order of frequency, as retroaortic, interarterial, subpulmonic (intraconal or intraseptal), prepulmonic, or retrocardiac (Table 3).[148,149]

The exact mechanism of SCD associated with AAOCA is unknown and hypotheses include the predisposition to myocardial ischemia and/or ventricular arrhythmias, likely due to limited coronary reserve.[150] Myocardial ischemia may be precipitated by several possible mechanisms. Firstly, an acute angled-take off from the ascending aorta, results in a

TABLE 3. Classification of anomalous courses of coronary arteries

Anomalies of course	Description of anomalies
Retroaortic	Posterior to aortic route
Interarterial	Between aorta and pulmonary artery
Subpulmonic	Between the aorta, right ventricular outflow trat, pulmonary infundibulum, and interventricular septum (ie, below the pulmonary valve)
Prepulmonic	Anterior to right ventricular outflow tract
Retrocardiac	Between mitral and tricuspid valves, in the posterior atrioventricular groove

slit-like lumen at its point of origin.[8] Secondly, the anomalous artery may take an intramural course, as demonstrated in autopsy and IVUS studies. The intussuscepted segment is more prone to compression due to its smaller circumference, ovoid cross section, and thinner inner and outer aortic wall layers, compared its distal segment.[1,27] A third cause, the interarterial coronary compression between the aorta and PA via a scissors-like mechanism, has been frequently suggested. However, this has not been observed in IVUS studies, and several authors have proposed that low-pressure PA is less likely to generate enough force to occlude the anomalous coronary artery.[8,28,29] It remains unclear whether these mechanisms work in isolation or in combination to provide a substrate for SCD.

The absolute risk of SCD attributable to these anomalies is unclear. Published SCD risks from autopsy studies and small series are likely to be grossly overestimated due to referral bias.[151-153] Larger registries have demonstrated very low SCD rates (4 cases of AAOCA associated SCD in a combined 34 million patient-years) in these anomalies.[154,155] In a cohort of competitive athletes, ages 15-35 years, the cumulative risk of death over a 20-year period was estimated to be 6.3% for AAOLCA and 0.2% for AAORCA.[156] Vigorous physical activity is known to increase the risk of SCD in those with interarterial AAOCA and most prior studies included younger athletes.[157,155] As such, the risks of these anomalies in older individuals, as well as the general population who do not participate in higher-level sports, is less certain.

European and American guidelines recommend surgery for those with AAOCA who have typical angina symptoms and evidence of myocardial ischemia in a matching territory (class I recommendation). Surgery may be considered for asymptomatic patients with evidence of myocardial ischemia (class IIa recommendation), symptomatic patients with no

evidence of myocardial ischemia (IIa) recommendation, and in the setting of ventricular arrhythmias (IIa) recommendation.[5,7]

When considering sports, evaluation with an exercise stress test should be performed to look for inducible myocardial ischemia (class IIa recommendation). In asymptomatic patients without evidence of myocardial ischemia, cardiac arrhythmias, or high-risk features (ie, interarterial course, slit-like orifice, or an intramural course), competitive sports may be considered after adequate counseling to the patient and his/her parents (if the patient is a minor) (class IIb recommendation). If an athlete with AAOCA does exhibit any of such features, however, participation in most competitive sports with a moderate/high cardiovascular demand is not recommended (class III recommendation). After successful repair of AAOCA, participation in all sports may be considered 3 months after surgery, if there are no symptoms or evidence of ischemia or arrhythmias during an exercise stress test.[6,26]

Other Anomalous Location of Coronary Ostia

Within the coronary sinus, a coronary artery may originate at a higher or lower level compared to normal. Coronary ostia may also be located outside the proper coronary sinus in various locations, such as ectopic sites in the aorta, other arteries (anonymous artery, carotid arteries, internal thoracic artery) or the ventricles.[4]

Single Coronary Artery (SCA)

Single coronary artery (SCA) describes anatomy in which an isolated coronary artery arises from 1 coronary ostium, providing blood supply to the entire myocardium. It is rare, with an incidence of 0.024% to 0.06%,[31] and often occurs with other congenital cardiac anomalies.[4,10] Lipton et al. proposed an anatomical classification system that was later modified by Yamanaka et al., based on the aberrant artery's origin, anatomical distribution and course.[24,32] (Table 4).

When the SCA arises from the LSV (L-type), the RCA may originate from the proximal/mid LAD or rarely, from the LCX.[10] This CAA is extremely rare and is found in 0.024%-0.066% of the general population.[33,34] An SCA may also arise from the RSV (R-type). Here, the LCA may arise from the proximal RCA, before it bifurcates into the LAD and LCX. Alternatively, the LAD and LCX may originate separately from the proximal RCA, in the absence of an LCA (RIII type). It has a prevalence of 0.02%-0.05% in an angiographic study.[24,35]

TABLE 4. Modified Lipton classification of a single coronary artery

Origin	R: RSV L: LSV
Anatomical distribution	I: Follows the anatomical course of a normal RCA/LCA II: One coronary artery arises from the proximal part of the normally located opposite coronary artery III: Absent LCA, with the LAD and Cx arising separately from the proximal part of a normal RCA (R-type only)
Course of the transverse trunk	A: Anterior to the great vessels B: Between the aorta and pulmonary artery (interarterial course) P: Posterior course S: Septal course C: Combined type

Most patients are asymptomatic at the time of diagnosis, with the CAA being detected incidentally on coronary angiography. However, patients may also present with chest pain, sudden death (usually after vigorous exercise), syncope, palpitations ventricular tachycardia, and myocardial infarction.[36] Certain subtypes, such as the LI and RI variants, typically have a benign clinical course. On the other hand, variants whereby the aberrant coronary artery takes an interarterial course (R/LIIB or RIII types) are associated with myocardial ischemia and SCD.[4,10,24,32,34,35,37,38]

There is no consensus on the management of SCA, and long-term data on both medical and surgical management is lacking. Several case reports have documented the successful PCI of patients with SCA.[39-42] Options for surgical management include osteoplasty, coronary artery bypass grafting (CABG) of the anomalous artery, re-implantation of the anomalous artery to the aorta, and PA translocation.[43,44]

Modified From Yamanaka and Hobbs

Anomalies of Coronary Arterial Developments

Absent Coronary Artery. An absent LMCA, wherein the LAD and LCX arise from separate ostia in the LSV, is a fairly common anomaly with a prevalence of 0.41%-0.67%. The vessels otherwise follow a normal course. This anomaly has no hemodynamic consequences.[10,23,24]

The congenital absence of the LCX is extremely rare, and only a few cases have been reported in the literature. In this CAA, a large "super dominant" RCA ascends the atrioventricular groove beyond the crux to

perfuse the left ventricular free wall. It is sometimes described as anomalous origin of the LCX from the distal RCA. The LAD arises from the LSV and has a normal distribution.[10,24] It has not been associated with any adverse cardiovascular events in the absence of atherosclerotic coronary artery disease. However, symptoms such as angina and palpitations can occur, particularly on exertion.[10,45] An accepted theory is that this is due to a "steal" phenomenon, whereby the increased arterial supply to the LCX territory results in transient ischemia in the LAD or RCA territories.[46]

Coronary Ostial Atresia

LMCA atresia is a rare congenital malformation that occurs when there is no left coronary ostium or left main stem. Instead, fibrous tissue connects the LSV and a blind-ended LAD-LCX arterial junction.[10] The left ventricle receives its blood supply retrogradely from right-to-left collateral vessels, which are often inadequate to meet myocardial oxygen demands. Pediatric patients present with failure to thrive, syncope, myocardial infarction, tachyarrhythmias, and sudden death.[47-50] Adult patients tend to become symptomatic at an advanced age.[51] Prognosis is unfavorable.

It is generally proposed that surgical revascularization is the treatment of choice, although there is a paucity of long-term survival data. A 2018 review by Tian et al. on 70 cases of LMCA atresia reported the following: 13 of 27 (48.1%) adult cases underwent a CABG, with no in-hospital deaths. In the pediatric group, 12 of 37 (32.4%) went for a CABG, and 10 (27%) underwent surgical left coronary ostial reconstruction with autologous pericardium. Three children died postoperatively, of low cardiac output syndrome and failure of surgical left coronary reconstruction.[52]

Congenital ostial atresia of the RCA is characterized by the absence of the RCA ostial stump. The RCA is supplied retrogradely by 1 or 2 full-caliber connecting collateral vessels, distinguishing from acquired RCA occlusions (causes include atherosclerosis, syphilis, Kawasaki, and Takayasu arteritis), where there is a dense network of collaterals that are smaller than the receiving vessel.[53] It is exceedingly rare, having only been described in sporadic case reports.[15,54-58] This CAA has been associated with typical and atypical angina and dyspnea, but patients may be asymptomatic owing to the well-developed collateral circulation.[15,54,57]

There is little long-term outcome data on management. One case report described a 45 year-old woman with Marfan syndrome who

underwent preimplantation of the RCA.[56] Another patient with solitary RCA atresia was treated with saphenous vein patch angioplasty,[55] while a third responded to medical management with anti-anginal therapy.[15]

Hypoplastic Coronary Artery Disease (HCAD)

In this CAA, 1 or 2 of the main epicardial coronary arteries are greatly narrowed (a luminal diameter <1.5 mm has been proposed as a criterion for diagnosis) or shortened, without nearby compensatory branches.[59] One case series describing autopsy findings of 224 subjects with CAAs found a frequency of 2.2% for HCAD.[60] In another postmortem study, HCAD accounted for 5% of athletes with SCD.[3] The most frequently reported variant is hypoplasia of both the LCX and RCA.[61] Hypoplasia of the LAD alone, both the LAD and RCA, and both the LAD and LCX have also been reported.[59,62,63] Notably, in several cases of myocardial infarction, the anomaly was found distal to atherosclerotic or thrombotic occlusions.[59]

HCAD is associated with myocardial ischemia, heart failure, and arrhythmias, with patients reporting symptoms of syncope, palpitations, dyspnea and chest pain. More frequently, patients have no antecedent symptoms and present with SCD, with the diagnosis typically being made on autopsy.[4,59,61-63] Treatment options are limited. Implantable cardioverter-defibrillator insertion and transmyocardial revascularization have been suggested in the literature.[4,63]

Dual/Split Coronary Artery

This is a diverse group of coronary anomalies and normal variants, describing a pattern whereby the coronary artery bifurcates into 2 or is duplicated. Definitions on what constitutes dual vs split coronary arteries are unclear, and indeed, both terms are often used interchangeably in the literature. Saremi and Shavelle[64] proposed that the terms "dual" and "duplicated" coronary artery (the name "double coronary artery" has also been used) be reserved for when 2 arteries with separate ostia supply the same perfusion territory. Dual/split coronary arteries are seen in 0.2%-2% of patients,[65] and are not infrequently associated with other congenital heart diseases.[66] They can generally be regarded as benign anomalies, with the exception of a type VII dual LAD system, where the LMCA originates from the RSV and courses interarterially.[67] It is important to

recognize this anatomy prior to intervention or surgery. For example, there is a risk of incorrect placement of a bypass graft.[64,68,69]

A split RCA is the most common variant, with a prevalence of 1.23% in patients undergoing coronary catheterization. A frequently reported subtype is where the RCA divides into anterior and posterior branches, each giving off a posterior descending branch that supplies part of the interventricular septum. One branch follows the normal anatomical route of the RCA, running in the right atrioventricular groove and terminating in a PDA that supplies the proximal interventricular groove. The other subdivision travels down the free wall of the right ventricle, continuing to become as second PDA that runs in the distal part of posterior interventricular groove.[4,64] Another subtype that has been described is where the marginal branch originates more proximally from the RCA than usual (high take-off) and continues as a single PDA (high-riding PDA) in the inferior interventricular groove.[70] A "split PDA," when the RCA gives off a single PDA that immediately splits into 2 equal-caliber branches, has also been reported.[64] Duplication of the RCA (with 2 separate ostia) is extremely rare, with only a handful of case reports in the literature.[12]

The name "dual LAD" has been commonly used to refer to both duplicate and split LAD systems. This group of CAAs has an incidence of approximately 1%. It has been traditionally divided into 4 subtypes, in a classification system introduced by Spindola-Franco et al.[71] Since then, another nine subtypes have been added to the nomenclature (Table 5).[67,72-75] Types I-III, VII and IX are when the LMCA bifurcates into a short and long LAD (ie, a split LAD), each giving rise to septal perforators. The long LAD may descend on the left ventricular (type I, VII, and IX) or right ventricular (type II) side of the short LAD, or within the anterior interventricular groove (type III). In a type VII system, the LMCA originates from the RSV and may have an interarterial course. For types IV-VI, VIII, X, and XII, the long LAD originates from the RCA or RSV, and takes either a pre-pulmonic (type IV and X), intramyocardial (type V) or interarterial (type VI) course, or travels down the RV and round the apex (type IX), before entering the distal anterior interventricular groove. The short LAD has a separate ostium in the LSV and runs in the proximal anterior interventricular groove. Al-Umairi et al.[72] identified an eleventh subtype in 2018, whereby both short and long LAD arteries originate from the RSV. The short LAD takes an intramyocardial course within the proximal septum before emerging in the proximal anterior interventricular groove, while the long LAD travels anterior to the RVOT and terminates in the distal anterior interventricular groove. In a

TABLE 5. Types of dual left anterior descending artery variants

Type	Short LAD artery		Long LAD artery	
	Origin	**Course**	**Origin**	**Course**
I	*LMCA*	*Proximal AIVG*	*LAD proper*	*LV side of the proximal AIVG and then re-enters the distal AIVG*
II	LMCA	Proximal AIVG	LAD proper	RV side of the proximal AIVG and then re-enters the distal AIVG
III	LMCA	Proximal AIVG	LAD proper	Intramyocardial course in the proximal septum, then emerges epicardially in the distal AIVG
IV	LMCA	Proximal AIVG	RCA	Prepulmonic course anterior to the RVOT and then enters the distal AIVG
V	LSV	Proximal AIVG	RSV	Intramyocardial course within the septal crest and then emerges in the distal AIVG
VI	LMCA	Proximal AIVG	RCA	Between the RVOT and aortic root and then enters the mid or distal AIVG
VII	LAD proper	Proximal AIVG	LAD proper	LV side of the proximal AIVG and then re-enters the distal AIVG (LMCA originates from RSV, and has a malignant interarterial course)
New variant of type VII	LMCA	Proximal AIVG	RSV	Intramyocardial course within the septial crest, emerging epicardially in the distal AIVG
VIII	LMCA from RSV (with a retroaortic course)	Proximal AIVG	Mid-RCA	Inferior wall of the RV and then turns around the apex and reaches the distal AIVG
IX	LAD proper	Mid AIVG	LAD proper	LV side of the proximal AIVG and then re-enters the distal AIVG and terminates before reaching the apex
X	LMCA	Proximal AIVG	RSV	Prepulmonic course anterior to the RVOT and then enters the distal AIVG

(*continued*)

TABLE 5. (*continued*)

Type	Short LAD artery		Long LAD artery	
	Origin	**Course**	**Origin**	**Course**
XI	RSV	Intramyocardial course within the proximal septum, then emerges in the proximal AIVG	RSV	Prepulmonic course anterior to the RVOT and then enters the distal AIVG
XII	LMCA from RSV	Proximal AIVG	RSV	Anterior to the main pulmonary artery and terminates in the distal AIVG
XIII	None	Not applicable	LAD proper	Two long LADs which both leave the AIVG and travel towards the apex, 1 lateral and 1 medial to the AIVG

AMI, acute myocardial infarction; CABG, coronary artery bypass graft; LCA, left coronary artery; LCX, left circumflex artery; PCI, percutaneous coronary intervention.

type XIII dual LAD system, the LAD bifurcates into 2 long LADs that course on either side of the AIVG.

Duplicate left circumflex arteries have been described in a few case reports. In this anomaly, one LCX artery arises from the LMCA, and the other from the RSV or the ostial RCA. It has been associated with symptoms of myocardial ischemia, possibly due to a predisposition to selective atherosclerosis in the aberrant artery originating from the right circulation.[76] Nevertheless, this CAA has generally been considered benign, with the majority of patients being asymptomatic.[21,30]

LAD = left anterior descending; LMCA = left main coronary artery; AIVG = anterior interventricular groove; LV = left ventricular; RV = right ventricular; RCA = right coronary artery; RVOT = right ventricle outflow tract; LSV = left sinus of Valsalva; RCS = right sinus of Valsalva.

Myocardial Bridging

A myocardial or muscular bridge occurs when an epicardial coronary artery takes an intramuscular course, usually spanning 10 to 50 mm,[4] most commonly affecting the proximal LAD.[10] It has been debated whether myocardial bridging should be considered an anomaly or normal variant. There is a broad range of the reported prevalence of this anomaly, ranging from 0.15% to 0.25% in angiographic studies, 5% to 86% in postmortem studies, and up to 25% in CT imaging studies.[1,4,10,77]

The bulk of patients do not display any symptoms nor evidence of myocardial ischemia on functional testing.[10] Rarely, patients may present with typical or atypical angina.[78] This may be a result of the systolic compression and delayed diastolic reopening of the intramural segment, as well as endothelial dysfunction.[4,10,79] Myocardial bridging has traditionally been considered benign, although more recent evidence has suggested otherwise. A 2014 meta-analysis by Hong et al demonstrated that subjects with myocardial bridging had a higher risk of myocardial infarction, but not with major adverse cardiac events (MACE).[80] Conversely, another meta-analysis showed that myocardial bridging was associated with higher rates of MACE, but not with acute myocardial infarction, cardiovascular death, or evidence of myocardial ischemia on functional testing.[81] More research is needed to provide clarity on the subject.

In symptomatic patients, medical therapy with beta-blockers is first-line, in view of their negatively chronotropic and inotropic effects. Calcium channel blockers (negatively inotropic) or ivabradine (negatively chronotropic) may be used as adjunct therapy. Vasodilators are not indicated as they may increase heart rate and cause proximal vessel dilatation, reducing downstream flow.[2] For those who do not respond to medical therapy, PCI (although high rates of stent failure have been reported[82]) or surgical treatment with a CABG or supra-arterial myotomy can be considered.[2]

Current sports cardiology guidelines advise that, for patients with myocardial bridging and no symptoms or evidence of myocardial ischemia during stress testing, it is reasonable to permit participation in competitive and leisure-time sports (class IIa indication)[6,26] For those with symptoms, evidence of myocardial ischemia or prior myocardial infarction, prohibition of competitive sports is recommended (class III indication as per ESC, class IIa recommendation as per ACC)[6,26] Athletes may participate in low-intensity sports for the first 6 months following stenting or surgical treatment. Thereafter, should they demonstrate no evidence of myocardial ischemia, competitive sporting activities may be resumed.[26]

Anomalies of Coronary Termination

Coronary Artery Fistulae (CAF). A coronary fistula is a congenital or acquired abnormal communication between the termination of a coronary artery or its branches, with a cardiac chamber, great vessel or other vascular structure, in the absence of an intervening capillary network.[83] This anomaly is relatively common, with an incidence of 0.02%-0.87% in

angiographic studies,[4,24,84] and up to 0.9% in patients undergoing cardiac computed tomography angiography (CCTA).[85]

Any coronary artery can be involved. The RCA is the most common site of origin (50%-55%), followed by the LAD (35%-40%) and LCX (5%-20%). When divided by drainage site, fistulas draining into the cardiac chambers (termed coronary cameral fistulas) are the most common type, with the right heart chambers (accounting for ~60%) being more commonly affected than the left. Other types include fistulas draining into the PA (15%-30%), coronary sinus (7%), bronchial artery (0.5%-0.61%).[83] In addition to origin and drainage site, CAFs may classified according to etiology, number of fistulous tracts, complexity and the presence of accompanying anomalies (Table 6).[86]

TABLE 6. Classification of coronary artery fistulae

Basis of classification	Description
Aetiology	Congenital: embryonic Acquired: • Iatrogenic: caused by PCI, CABG placement, cardiac transplantation, permanent pacemaker insertion, myocardial biopsy • Disease related: caused by AMI, cardiomyopathy (hypertrophic, dilated), Kawasaki disease, tumor • Trauma related: caused by penetrating or non-penetrating trauma • Radiation injury
Origin	RCA LCA: LAD and its branches, LCX and its branches, ramus intermedius RCA and LCA Other anomalous coronary arteries
Segment of origin	Sakakibara type A: originating from proximal native vessel; distal artery is normal Sakakibara type B: originating from distal native vessel; entire coronary artery is dilated
Drainage site	Coronary cameral fistula: involving any cardiac chamber (right atrium, right ventricle, left atrium, left ventricle) Coronary arteriovenous fistula: involving pulmonary artery, coronary sinus, superior and inferior vena cavas, bronchial vessels, other extracardiac veins (eg, azygos, costal, brachiocephalic veins)
No. of fistulous tracts	Single or multiple
Morphology and complexity	Simple CAF: has a single origin and drains through a single vascular course Complex CAF: involves entangled blood vessels with multiple fistulous structures
Presence of accompanying anomalies	Isolated CAF: no accompanying anomaly CAF accompanied by ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot, or other valvular disease

Most patients are asymptomatic, and coronary fistulae generally have a benign clinical course. Those with large intracardiac shunts often become symptomatic in childhood. The remaining minority may present in the 5th or 6th decade of life with SCD, myocardial ischemia, pulmonary hypertension, heart failure, arrhythmia, rupture, or endocarditis.[10,85]

There are several pathophysiological mechanisms by which CAFs cause symptoms. Firstly, blood preferentially drains from the high-pressure coronary arterial circuit into a low-resistance venous system, instead of the small arterioles and capillaries. This results in a persistent or intermittent steal phenomenon whereby blood bypasses the myocardium, thus leading to ischemia. Myocardial ischemia may also be caused by the stenosis of side branches, which are prone to thrombosis, ulceration, and atherosclerosis. Pretricuspid valve CAFs with left-to-right shunts may cause right ventricular volume overload, eventually leading to pulmonary hypertension and heart failure. On the other hand, post-tricuspid valve CAFs may result in left-sided cardiac chamber dilatation and heart failure. Another mechanism is related to the feeding coronary artery becoming dilated and tortuous due to increased flow. This results in not only vascular wall degeneration and predisposition to rupture, but also distortion of the aortic root and ensuing valvular incompetence.[4,83,87]

Current management options of surgical ligation and percutaneous transcatheter closure are controversial.[7] Indications for intervention are not well-established. Indications for surgery may include large symptomatic fistulas with high blood flow, complex fistulas with multiple communications, and drainage sites and tortuous and aneurysmal fistulous arteries, and the need for simultaneous bypass surgery. Percutaneous transcatheter closure may be preferred in those with a proximal fistula origin and single drainage site, nontortuous coronary artery whose distal end is accessible and in older patients with a high risk of perioperative complications.[83] In a case series of 46 CAF patients with angina and heart failure symptoms, 11% of those treated with surgery had post-operative myocardial infarction, due to low flow in the dilated coronary artery proximal to fistula closure. There was also significantly reduced late survival compared to an age-matched population.[88] The current ACC/AHA guidelines on adults with congenital heart disease suggest that CAFs should be managed by a knowledgeable multidisciplinary team, that may involve congenital or non-congenital cardiologists and surgeons, to determine the role of medical treatment or intervention.[7]

Modified From Reddy et al.[86]

Systemic Termination

This refers to when a coronary artery terminates into a systemic artery. This is distinct from a coronary artery fistula, in that the anomalous artery not dilated nor tortuous, due to the lack of a significant pressure difference between the coronary and systemic arteries. It is an uncommon finding,[12] although it has been suggested that its prevalence has been underestimated in CT studies, due to the narrow caliber of the involved vessels.[89] This anomaly is not hemodynamically significant in the absence of stenosis of the involved vessels (eg, from atherosclerosis), which may then create a pressure gradient.[12]

Imaging of CAAs

Although patients with CAA may present with ischemia-like symptoms, the majority of patients are diagnosed incidentally during work-up for ischemic heart disease.[2,4] Further investigation with anatomic studies is warranted to establish the type of CAA, identify high-risk features, and to plan for invasive corrective procedures[28] Various modalities of noninvasive anatomic imaging (such as CCTA and cardiac magnetic resonance imaging [CMR]) have demonstrated increasing utility for this purpose, decreasing the need for coronary angiography.[90-92]

Myocardial ischemia has been proposed to be the most likely mechanism of SCD in patients with CAAs.[1,65] In certain high risk CAAs, or if the clinical significance of an anomaly is uncertain, functional testing (eg, with nuclear cardiac imaging, stress CMR, or stress echocardiography) may be indicated to look for inducible myocardial ischemia.[2,6,7]

Coronary Computed Tomography Angiography (CCTA)

With substantial technical advances in the last few decades, CCTA has become the gold standard technique for the imaging of CAAs.[90,92-95] It offers a high spatial resolution ($0.5 \times 0.5 \times 0.6$ mm), and advanced post-processing rendering methods have enabled 3D visualization of the coronary arteries and its relation to surrounding cardiac and noncardiac structures. This allows detailed characterization of the coronary anatomy and high risk anatomical features, even of the distal vessels and small side branches.[96,97] Among its other advantages, CCTA may be acquired throughout the cardiac cycle with a high temporal resolution of up to 66 ms, even at fast heart rates.[96] Ventricular function, valves and the

presence of concomitant atherosclerotic coronary artery disease (CAD) can also be simultaneously assessed[93,96] Compared to magnetic resonance imaging (MRI), CCTA is more precise in confirming the anomalous origin, proximal course and severity of stenosis of the coronary arteries.[28]

The main drawbacks of this imaging modality include the use of ionizing radiation, which is relevant considering that most patients are young, as well as the need for intravenous contrast and rate-limiting agents in some cases.[10,28] With recent technological developments and the introduction of ECG gating, however, there have been dramatic reductions in radiation exposure, to an average of 0.5-3mSv in routine clinical practice.[98-101]

CT fractional flow reserve (CT-FFR) is a novel technique that uses fluid dynamic analysis to assess for vessel-specific ischemia, primarily in the evaluation of CAD.[102,103] A value of <0.8 is deemed to be significant. The use of CT-FFR in the evaluation of AAOCS are currently limited to a few case reports, but results have been promising so far.[104-107] The role of stress myocardial CT perfusion imaging in the study of AAOCA and other coronary anomalies is yet to be determined.[108]

Cardiac Magnetic Resonance Imaging (CMR)

CMR has emerged as an alternative to CCTA for the imaging of CAAs.[2] It has a high spatial resolution (slightly lower than CCTA) and 3D capabilities, to allow detailed examination of the of the coronary arteries and their relationship to the great vessels.[93,96,109-111] CMR has some advantages over other imaging modalities, in that it can be done without radiation exposure or contrast agents, making it particularly appealing for use in the pediatric population.[96,110] It can capture a wealth of additional information, including valvular function, ventricular function, regional contractility, and characterization of myocardial tissue.[112] The finding of late gadolinium enhancement (LGE) can unveil the presence of myocardial fibrosis, a substrate for potentially fatal ventricular arrhythmias,[8] thus offering more information for risk stratification.[110] A surface-rendered angiographic view may be used to evaluate the shape and caliber of the coronary ostia, in particular looking for the high-risk feature of a slit-like ostium.[112-114]

Disadvantages of CMR for CAA imaging include long scan times and the need for cooperative patients, therefore sometimes necessitating the use of sedation (especially in children or infants). It has higher costs and a lower spatial resolution compared to CCTA.[96,110] With the use of

respiratory navigation and ECG triggering, CMR can provide detailed images of the origin, proximal, and mid courses of the coronary arteries, but characterization of smaller distal coronary segments remains difficult.[97,110,115] CMR-derived coronary artery measurements also correlate poorly with that obtained by echocardiography in the pediatric population.[96] Lastly, the presence of implanted cardiac devices such as pacemakers or cardioverter defibrillators are relative contraindications, limiting its use in some patients.[96]

Stress CMR can be used to evaluate the hemodynamic significance of a CAA, with a higher accuracy and interobserver agreement than stress echocardiology.[116-118] Inotropic agents (eg, dobutamine) or coronary vasodilators (eg, persantine, adenosine, or regadenoson) are administered as pharmacological stress.[118-120] A matched LGE defect on rest and stress imaging identifies an irreversible perfusion defect, while a perfusion defect seen during stress but not at rest is classified as reversible.[96]

Echocardiography

The use of transthoracic echocardiography (TTE) to image the origin and proximal course of the coronary arteries has been well-described.[110,121-124] The coronary ostia are best seen using a high frequency transducer in the parasternal short-axis view. Turning the transducer clockwise facilitates imaging of the LMCA as it bifurcates into the LAD and LCx, while counterclockwise rotation allows for assessment of the proximal RCA. Other useful views in children include the subcostal view for imaging the LCA origin, and the parasternal long-axis view for imaging the RCA. Additional color flow mapping using Doppler interrogation can be applied to identify an intramural or interarterial course.[96] In a review of 52 pediatric patients undergoing repair of AAOCA, pre-operative TTE accurately identified whether the anomalous artery was intramural or extramural in 92.5%.[125] TTE also provides valuable complementary information, including ventricular and valvular function, and the presence of concomitant congenital heart defects.[93]

TTE is the ideal diagnostic modality in the pediatric population, in whom there are generally good acoustic windows. It does not require radiation exposure or contrast, is portable, widely available, and has a high spatial and temporal resolution.[96,126-129] A notable disadvantage is the limited diagnostic value in adults or children with poor acoustic windows (eg, those with a large body habitus or lung disease), and a transesophageal echocardiography (TEE) may be indicated in such patients. TEE offers superior sensitivity in the identification of CAAs and associated

high-risk features.[110,130] Other limitations include an inability to image the distal coronary arteries, high operator dependence and reliance on institutional experience.[110] The latter was demonstrated in a multicenter study of 159 patients, where there was poor agreement between the "expert" echocardiography core laboratory and other participating centres.[131]

The functional relevance of a CAA can be investigated with stress echocardiography (with either physical or pharmacological [eg, dobutamine] stress). It offers similar advantages to standard TTE, but is limited by high interoperator variability and a lack of standardized protocols.[132]

Invasive Coronary Angiography

For decades, invasive coronary angiography was regarded as the gold standard test for assessment of CAAs.[2,110] Owing to its invasiveness, need for radiation exposure, and inability to visualize noncoronary cardiac structures or provide 3D representation of the coronary anatomy, it has been progressively replaced by CCTA and other non-invasive imaging techniques.[2,90-92] Nevertheless, it plays an important complementary role. Compared to noninvasive imaging modalities, it can better evaluate the distal coronary vessels in infants or children with higher heart rates, in whom ECG gating and spatial resolution remain an issue.[133] The utility of invasive coronary angiography also lies in the application of invasive adjunct techniques such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT), to facilitate precise characterization of the intraluminal geometry. According to Angelini and colleagues, IVUS is the gold standard for evaluation of an intramural segment, with its high spatial and temporal resolution, and ability to assess vessel dimensions (ie, lateral compression) under pharmacological stress conditions.[109,134] OCT is a light-based intravascular imaging modality with a higher spatial resolution but lower penetrance compared to IVUS, and uses a smaller diameter catheter. Hence, it may be useful in evaluating coronary luminal surface anatomy and vessel segments with more severe stenosis.[2,110,134] Finally, fractional flow reserve (FFR) enables quantification of flow changes across a coronary stenosis at rest and during pharmacological stress, providing information on hemodynamic significance.[93,135,136]

Nuclear Cardiac Imaging and Hybrid Imaging

Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are established techniques used in the

assessment of chest pain and risk stratification in patients with CAD.[110] In the setting of ischemic evaluation of CAAs, SPECT-myocardial perfusion imaging (MPI) has been proposed as first line, having shown favorable diagnostic performance in multiple studies.[96,137,138] Exercise PET-MPI could be another option. In 1 study involving 27 patients with AAORCA and an interarterial and intramural course, exercise ^{13}N-ammonia PET identified 13 (48%) patients with myocardial ischemia, which was in turn associated with symptoms of typical angina and exertional dyspnoea.[139]

In patients with a CAA and ischemic symptoms, the CAA may not always be responsible, particularly if there are no high-risk features. Other factors that may cause myocardial ischemia include concomitant atherosclerotic CAD (which must be ruled out in older individuals), or more rarely, coronary vasospasm, and microvascular disease.[110,138,140] In unclear cases, further risk stratification with hybrid imaging (which combines CCTA with SPECT or PET-MPI) is warranted to determine if ischemic areas match the myocardial territories supplied by the CAA in question.[110,138,141] A study using CCTA/SPECT-MPI demonstrated that in a middle-aged population with AAOCA, myocardial ischemia or infarction was more likely to be attributable to co-existent CAD rather than the CAA itself.[142] Stress CMR may also be used for this purpose.[118]

Management Strategy

We propose the following strategy for the evaluation and management of patients with a suspected or an incidental finding of a CAA (Fig 3).

A comprehensive medical history must be taken, including of the patient's symptoms and physical activities.[93] Following this, noninvasive anatomic imaging should be performed to look for high-risk features. These include a slit-like ostium, proximal narrowing, an elliptical vessel shape, an interarterial course between the aorta, and PA, an intramural course and/or an acute take-off angle, AAOCA, APOCA. CCTA or CMR may be considered as an initial diagnostic modality in adults, and TTE in pediatric patients.[93,110] Further investigation can be safely deferred in those with no symptoms or high-risk features.[93,110,143] For patients with suggestive symptoms or high-risk anatomical features, the next step would be an ischemic assessment with SPECT/PET-MPI, stress echocardiography or stress CMR. Hybrid imaging or invasive ischemia testing with FFR/IVUS may also be considered, especially in unclear cases, to further assess the hemodynamic significance of a lesion and obtain more precise measurements of vessel dimensions.[93] In patients above 30 years

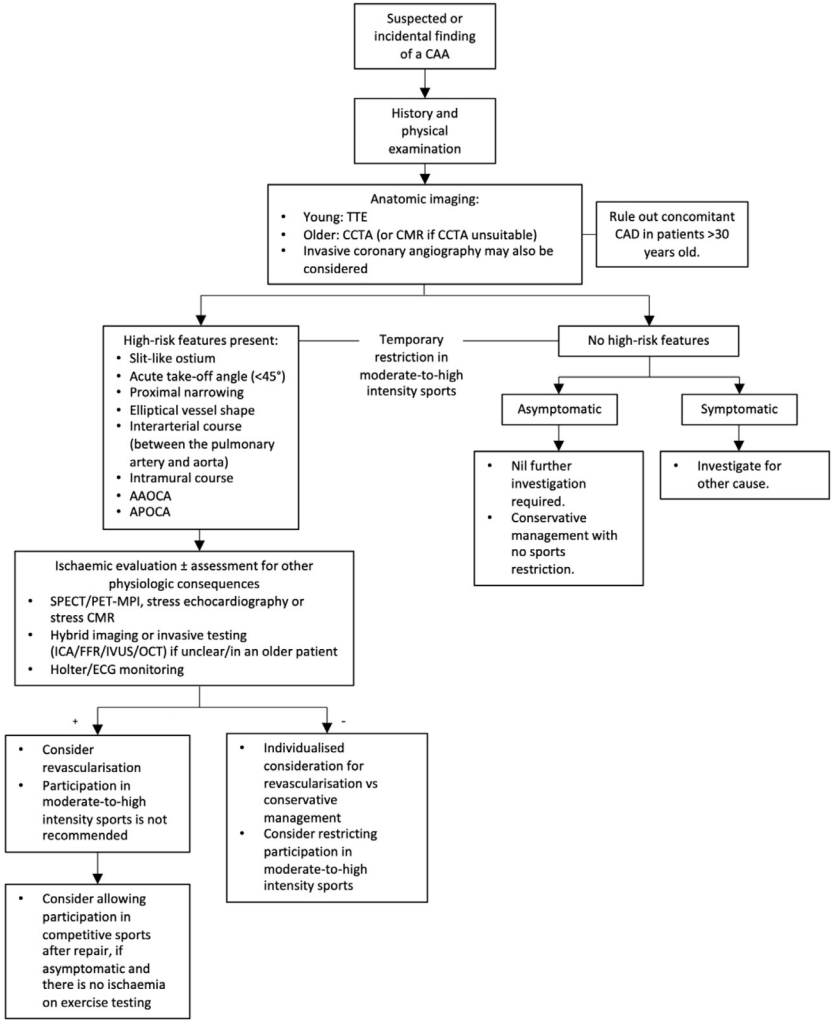

FIG 3. Proposed management algorithm for CAAs. APOCA, anomalous pulmonary origin of a coronary artery; AAOCA, anomalous aortic origin of a coronary artery; CAA, coronary artery anomaly; CAD, coronary artery disease; CCTA, coronary computed tomograpy angiography; CMR, cardiac magnetic resonance; ECG, electrocardiogram; MPI, myocardial perfusion imaging; SPECT, single-photon emission computed tomography; TTE, transthoracic echocardiogram. (Color version of figure is available online.)

of age, concomitant CAD must be ruled out, that is, with invasive coronary angiography or CCTA. This age cut-off was proposed by Gräni and colleagues based on data by Taylor et al., but should be regarded as a guide rather than strict recommendation.[44,110,144] Additionally, electrocardiographic monitoring may be considered in those with suspicious

symptoms (such as palpitations and syncope), to look for arrhythmic events.[5,18]

Regarding revascularization of CAAs (surgically or with PCI), several points should be taken into consideration. Firstly, the benefits of revascularization are unclear and are supported by a low level of evidence. Moreover, cases of SCD following surgical correction of CAAs have been reported.[145] Secondly, the identification of symptoms attributable to the CAA is challenging and may be a coincidental finding.[110] Adding to this dilemma is that 50% of CAA-associated SCD were first events in previously asymptomatic patients.[8,96] Thirdly, while CAAs remain the second most common cause of SCD in competitive athletes, the absolute incidence is very low, at a mere 0.07 per 100,00 person-athlete years.[3]

The decision for revascularization be an individualized one, based on the patient's age, comorbidities, and the presence of ischemia and other physiologic consequences (such as ventricular arrhythmias, ventricular dysfunction and subclinical myocardial infarction on LGE imaging), high-risk features or a high-risk anomaly. The 2018 AHA/ACC guidelines for the management of adult congenital heart disease state that surgery is recommended in patients with ALCAPA, ARCAPA with symptoms, AAOCA with symptoms and evidence of ischemia in a matching territory (class I indication). Surgery is reasonable for AAOLCA in the absence of symptoms or ischemia, AAOCA in the setting of ventricular arrhythmias and ARCAPA in asymptomatic patients with ventricular dysfunction or myocardial ischemia attributable to the coronary anomaly (class IIa recommendation).[5,7]

As the majority of CAA-associated deaths occur during exercise, eligibility for exercise and competitive sports should be carefully considered, taking into account the coronary anatomy, presence of symptoms, inducible myocardial ischemia on imaging and cardiac arrhythmias.[2,8] A temporary restriction on moderate-to-high intensity sports should be placed during the evaluation process.[110] Moderate intensity is defined as 40-69% of an individual's maximal aerobic capacity (VO_{2max}) or 55%-74% of maximum heart rate (HR_{max}) during a cardiopulmonary exercise test (CPET), while the threshold for high intensity are $\geq$70% and $\geq$75% respectively.[6] Current guidelines by ACC/AHA on sports and exercise in patients with cardiovascular disease have put forward the recommendations for AAOCA, APOCA and myocardial bridging (detailed in individual sections above).[6,26] Following successful repair, participation in competitive sports may be considered if the patient is asymptomatic and there is evidence of ischemia on exercise testing (at the earliest 3 months for AAOCA, and 6 months for myocardial bridging).

Low-intensity sports may be considered until 6 months after resection of a myocardial bridge.[6,26]

Conclusion

CAAs comprise a wide spectrum of anatomic entities, with diverse clinical phenotypes. We present a case of an anomalous RCA from the LSV with an interarterial course, a potentially fatal condition that can cause symptoms of ischemia and SCD. CAAs are increasingly detected in adults, mostly as incidental findings in the course of cardiac evaluation. This is due to the expanding use of invasive and non-invasive cardiac imaging, usually in the work-up for possible CAD. The prognostic implications of CAAs in this group of patients remain unclear. In AAOCA patients, appropriate work-up with anatomical and functional imaging should be performed for risk stratification.

An individualized approach to management should be adopted, considering symptoms, age, sporting activities and the presence of high-risk anatomical features and physiologic consequences (such as ischemia, myocardial fibrosis, or cardiac arrhythmias) depicted on multimodality imaging and other investigations. For AAOCA, revascularization should be considered especially in young patients participating in competitive sports, and those with symptoms, evidence of ischemia, and other physiologic consequences. Exercise restriction is a key part of management. Any presumed prognostic benefits from revascularization and exercise restriction should be carefully weighed against the impact on psychoemotional well-being and quality of life in all age groups.

More research is warranted to identify the pathophysiological determinants linking each CAA to myocardial ischemia and other sequelae, and how to determine the individual risk of major cardiovascular events. However, owing to the rarity and variability of CAAs, the design of large prospective studies is likely to be challenging. Research using data from large multicenter registries may be more feasible in this context.

Declaration of Competing Interest

This statement is to certify that all authors have seen and approved the manuscript being submitted, have contributed significantly to the work, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to the journal Current Problems in Cardiology.

I attest that the article is the Author's original work, has not received prior publication and is not under consideration for publication elsewhere.

The corresponding Author shall bear full responsibility for the submission.

The authors report no relationships that could be construed as a conflict of interest.

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