Coronary artery anomalies

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INTRODUCTION

While coronary artery anomalies (CAAs) are relatively rare overall, they are one of the most common types of congenital heart disease.[1 2] Multiple classification schemes have been proposed, typically taking into account abnormalities of vessel origin, course, number and ventricular myocardium supply.[3 4] These anomalies can occur in otherwise structurally normal hearts or associated with other types of congenital heart disease. While many CAAs are not associated with untoward outcomes, some may have a more concerning clinical course resulting in presentation with sudden cardiac death (SCD).[5 6] Unfortunately, this dramatic presentation may be the first presenting symptom, though patients may have had prior symptoms that were not linked to the underlying potentially fatal diagnosis.[5] This review will focus on the evaluation and management of CAA among adolescents and young adults with otherwise structurally normal hearts, primarily focusing on anomalous aortic origin of a coronary artery (AAOCA) at or above the opposite sinus of Valsalva, the second leading cause of SCD in the young.[6]

AAOCA may involve the right coronary artery (AAORCA) originating from the left (opposite anterior) sinus of Valsalva, the left coronary originating from the right (opposite anterior) sinus of Valsalva (AAOLCA), or, more rarely, the origin of a coronary artery from or near the 'non-coronary' (posterior) sinus.[7] They are typically also categorised into the following groups based on their course: interarterial, subpulmonic (also called intraseptal or intraconal), pre-pulmonic, retroaortic and retrocardiac (figure 1). Based on this anatomical definition, lesions have historically been classified as normal variants without increased risk of mortality (typically including those variants without an interarterial course) and variants that could be associated with increased risk of mortality. Defining which variants and factors are associated with SCD is important to help both physicians and patients better understand the risk of any specific lesion and appropriately individualise management.

To date, extensive and long-term data clearly identifying the most appropriate management strategy and outcomes for this diverse and often asymptomatic group of patients are lacking, though substantial efforts have occurred in the past several years toward gathering data prospectively. Thus, while guidelines exist from varying groups such as the American Heart Association/American College of Cardiology (AHA/ACC),[2] the European Society of Cardiology (ESC)[8] and the American Association of Thoracic Surgeons (AATS),[9] all of these recommendations are based on limited data, typically cohort studies and often expert opinion. Given the need to more systematically evaluate this population, several large, multicentre registry studies have been undertaken and are ongoing including the Congenital Heart Surgeon's Society (CHSS),[10] ANOCOR[11] and J-CONOMALY.[12] Initial data have been published from these cohorts, which each has a somewhat different design. Forthcoming, multi-institutional, longitudinal data will help improve our understanding of this complex disease process and guide our management into the future.

Learning objectives

⇒ Understand the appropriate diagnostic work up for patients with anomalous coronary arteries.
⇒ Understand the approach to risk stratification for patients with anomalous coronary arteries.
⇒ Understand the appropriate management strategy for patients with anomalous coronary arteries.

EPIDEMIOLOGY

Assessing the true epidemiology is difficult given the general rarity of CAA lesions and frequent lack of associated symptoms. Among patients with otherwise structurally normal hearts, the incidence of these abnormalities in the general population varies widely depending on the sampling strategy, the specific abnormalities included and differences in the modality used for inclusion, with most studies noting a prevalence ranging from 0.1% to 1.7%. A recent review by Cheezum *et al* including a total of 250 620 patients from 28 studies noted a weighted prevalence of AAOCA of 0.70% by non-invasive cardiac testing (mostly computed tomography angiography (CTA)).[1] However, the observed prevalence of AAOCA with interarterial course in this study was much lower, with AAORCA noted in 0.23% and AAOLCA noted in 0.03% of patients. All patients in these studies were referred for cardiac testing due to some degree of clinical concern; thus, it is possible this may not represent the true prevalence of AAOCA in the general population. A recent prospective study by Angelini *et al* sought to evaluate this further using cardiac MRI (CMRI) to identify high-risk cardiac lesions among unselected school-age children and noted an AAOCA incidence of 0.44%, identifying 23 cases among 5169 screened children; of these, 6 (0.12%) were AAOLCA with an intramural course, and 17 were AAORCA (0.33%).[13]

While SCD among young people is devastating and often widely publicised, it is quite rare overall. In a landmark description of 1866 sudden deaths among athletes in the USA, coronary anomalies were the second most common identified cardiac aetiology, representing 17% of these cases.[6] In a

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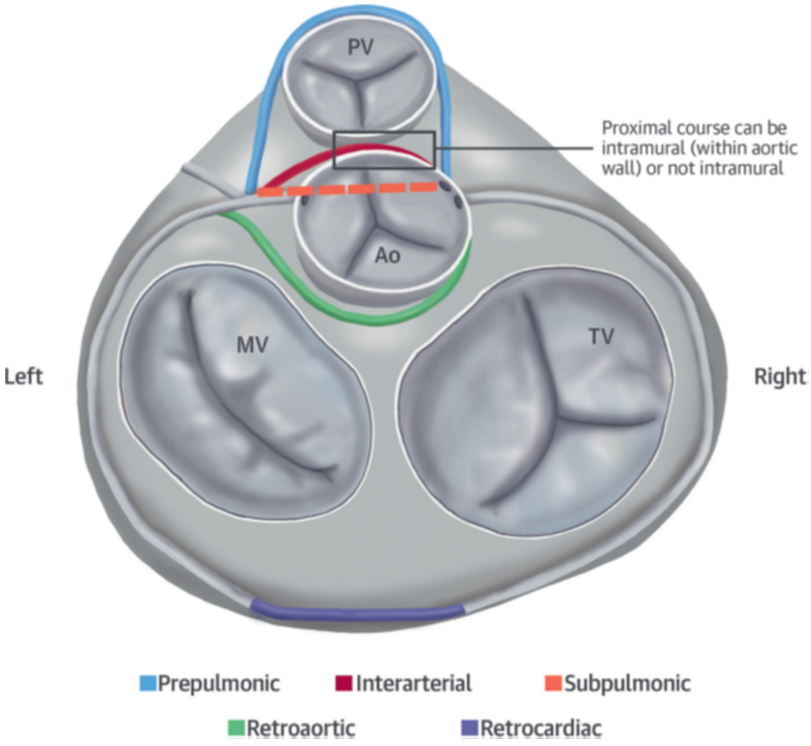

Figure 1 Demonstration of the five main course subtypes of anomalous aortic origin of a coronary artery. Subpulmonic course may also be referred to as intraseptal or intraconal. Used with permission from Cheezum *et al*.[1] Ao, aorta; MV, mitral valve; PV, pulmonary valve; TV, tricuspid valve.

foundational study of 27 patients who experienced SCD related to AAOCA, 23 of 27 had AAOLCA and 4 of 27 had AAORCA.[5] Similarly, among a cohort of 126 non-traumatic deaths in 6.3 million US military recruits, 21 were associated with an anomalous coronary, all of which were AAOLCA.[14] Thus, while AAORCA is significantly more common, more cases of SCD are associated with AAOLCA, suggesting that AAOLCA is likely associated with a much higher risk. Using conservative figures, previous estimates[9] suggest that there may be more than 600 000 cases of interarterial AAOCA in young adults in the USA. Given the relatively large number of overall cases and that potential sudden deaths would be preventable if identified and treated, there is interest in potentially screening at-risk populations, though this would require imaging as ECG is typically normal in these patients. It is of critical importance, thus, to determine who is at high risk of SCD related to AAOCA.

RISK STRATIFICATION

Risk stratification is the 'holy grail' sought after in AAOCA. Many morphological factors are thought to play a significant role, though other factors are also important as similar morphological features may have different clinical evidence of ischaemia and, possibly, outcomes. Mechanisms postulated to cause SCD in AAOCA include a combination of morphological features such as ostial abnormalities and compression or occlusion of the vessel in its intramural and/or interarterial course[7] as well as physiological changes associated with exercise (loading conditions, hydration status, electrolyte imbalance, etc) that lead to myocardial ischaemia, ultimately fatal ventricular arrhythmias, and SCD.

Many studies have sought to identify specific structural, physiological, and demographic characteristics that identify patients at risk of developing myocardial ischaemia and, ultimately, SCD; selected high-risk anatomical features are shown in figure 2. However, given the relatively small numbers of patients, these factors often vary in importance between studies. Recent data from the CHSS registry support that patients with AAOLCA are at increased risk of ischaemia in comparison with patients with AAORCA.[10] Additionally, for those with AAOLCA, the presence of an intramural course, a high orifice and a slit-like orifice were associated with ischaemia, while intramural length was associated with ischaemia for AAORCA. Other studies have noted that intramural course, interarterial course, slit-like orifice, acute angle takeoff and proximal coronary hypoplasia are high-risk features.[15 16] Recent data from Molossi *et al* evaluating 163 paediatric patients with AAOCA followed prospectively identified older age at diagnosis (among paediatric patients), black race, intramural course and exertional syncope as predictors of high risk.[17] Given the importance of coronary artery origin and course and to facilitate accurate communication between providers, a topographical map was created to precisely describe the origin and course of the anomalous coronary in relation to the sinus of Valsalva and ascending aorta (figure 3).

Historically, patients underwent ECG exercise stress testing (EST). While this can be helpful, particularly if positive for ischaemia, the foundational paper from Basso *et al* showed the inadequacy of stress ECG testing alone to adequately identify patients at risk of sudden death, with six patients who suffered SCD having normal maximal stress ECG testing within 24 months of their event.[5] Preliminary data from Qasim *et al* reported maximal EST (ECG and cardiopulmonary EST) results in 147 paediatric patients with AAOCA followed prospectively and correlating with myocardial perfusion on dobutamine stress CMRI (DS-CMRI); there was poor EST sensitivity and no correlation between EST and DS-CMRI findings.[18] Additionally, the presence of ischaemia may sometimes be variable on EST, as demonstrated by Brothers *et al* in an AAOLCA case report with two studies performed 1 week apart noting different results.[19] This idea of intermittent ischaemia may relate to the fact that some patients tolerate high levels of exertion for many years before dying suddenly, without any clear differences to the circumstances leading to the fatal event. Given that most SCD associated with AAOCA occurs with exercise, there is likely a dynamic component of the ischaemia that may only be provoked at high workloads with elevated blood pressure and heart rate. Thus, among patients without prior SCD, we recommend exercise/stress testing with an imaging component that simulates increased workload such as a dobutamine stress

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test. We feel that this likely provides a more accurate assessment of potentially important dynamic conformational changes of the aorta and coronary arteries than vasodilator testing alone. Vasodilators such as adenosine result in myocardial hyperemia and evaluate lesions with fixed obstruction to coronary flow. While this may play a role in AAOCA, there is also a significant dynamic component related to the presence of intramural course and the flattening of the coronary lumen related to the distensibility of the aortic wall in many patients, especially during exercise.

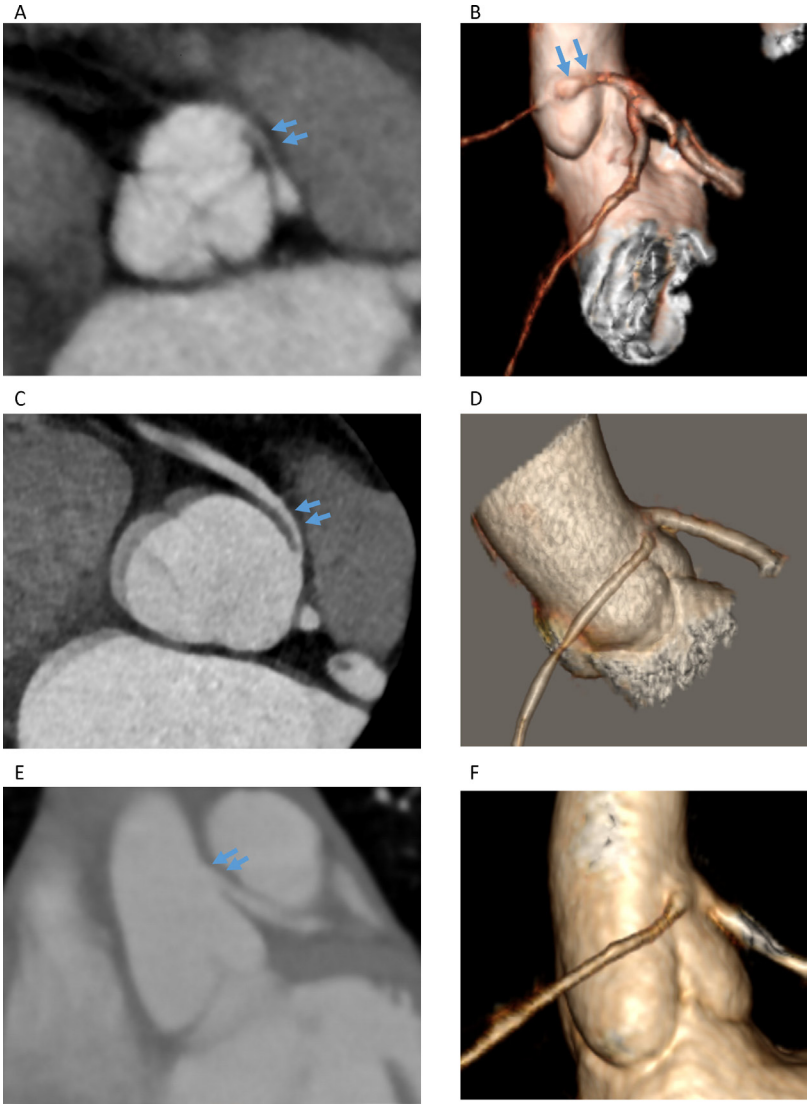

Figure 2 Selected high-risk anatomical features of patients with anomalous aortic origin of a coronary artery. (A, B) Anomalous left coronary artery from the right sinus of Valsalva with intramural and intra-arterial course (blue arrows). There is an acute angle takeoff and proximal narrowing of the left main coronary artery. On the 3D reconstruction, the left main coronary appears to take an intramural course posteriorly from the superior portion of the right sinus of Valsalva (blue arrows). (C,D) Anomalous right coronary artery from the left sinus of Valsalva with intramural and intra-arterial course (blue arrows). There is an acute angle takeoff and proximal narrowing of the right coronary artery. On the 3D reconstruction, the right coronary can be seen coursing just superior to the intercoronary pillar. (E,F) High origin of both the left and right coronary arteries from the ascending aorta above the level of the sinus of Valsalva. (E) The high origin of the left main without significant proximal narrowing (blue arrows). On the 3D reconstruction (F), the right coronary artery appears to originate on the ascending aorta just above the left sinus of Valsalva.

Many paediatric patients are initially diagnosed with AAOCA by echocardiography due to improved coronary visualisation in this patient population, while most adult patients will be diagnosed either by angiography or cross-sectional imaging. The current AHA/ACC guidelines have a class I recommendation to use catheterisation, CTA or CMRI for evaluation of AAOCA.[2] While the AHA/ACC guidelines do not recommend one form over the another, the ESC guidelines[8] favour CTA and the AATS guidelines[9] recommend either CTA or magnetic resonance angiography. In our institution, retrospectively gated coronary CTA is used as this provides the highest spatial resolution (~0.5 mm) of the non-invasive studies and allows for clear characterisation of proximal course. CMRI angiography can also provide high resolution images (~1 mm) and is reasonable to consider based on centre experience and additional data provided by the CMRI including functional assessment and stress perfusion imaging.

The specific imaging modality used for stress testing will vary based on institutional preferences. In our institution, we initially used single photon emission computed tomography (SPECT) imaging; however, based on concerns for possible high false-positive and false-negative testing,[20] we have transitioned to DS-CMRI. Our recent data evaluating adolescents with stress CMRI suggest that it is feasible with good reproducibility and safety; this study noted evidence of inducible hypoperfusion in 14% of patients using a first-pass perfusion technique, which improves the sensitivity of stress CMRI.[21] There are not currently any data available directly comparing stress imaging modalities in this population.

A recent study from the ANOCOR group evaluated the use of estimating fractional flow reserve using CT (FFR-CT) to risk stratify patients with AAOCA in a middle-aged cohort.[11] While FFR-CT has been validated as a useful tool to assess for ischaemia in typical atherosclerotic coronary disease, it has not been found to have significant prognostic utility in patients with AAOCA. This study noted a moderate reduction in FFR-CT among patients with AAOCA, but this was not different between patients considered at risk of ischaemia and those not at risk. No differences were noted between groups with a low event rate over a median follow-up of 7.5 years. Based on the lack of incorporation of dynamic changes during stress and these data, we do not feel that rest FFR-CT has yet been shown to provide added diagnostic utility in this population.

In young patients with unexplained symptoms and/or equivocal results regarding inducible myocardial ischaemia on provocative stress testing, cardiac catheterisation with FFR measurement and intravascular ultrasound (IVUS) should be considered. Our team has published the safety and feasibility of performing invasive FFR and IVUS during cardiac catheterisation in children with AAOCA.[22] While normative values for evaluation of ischaemia in this

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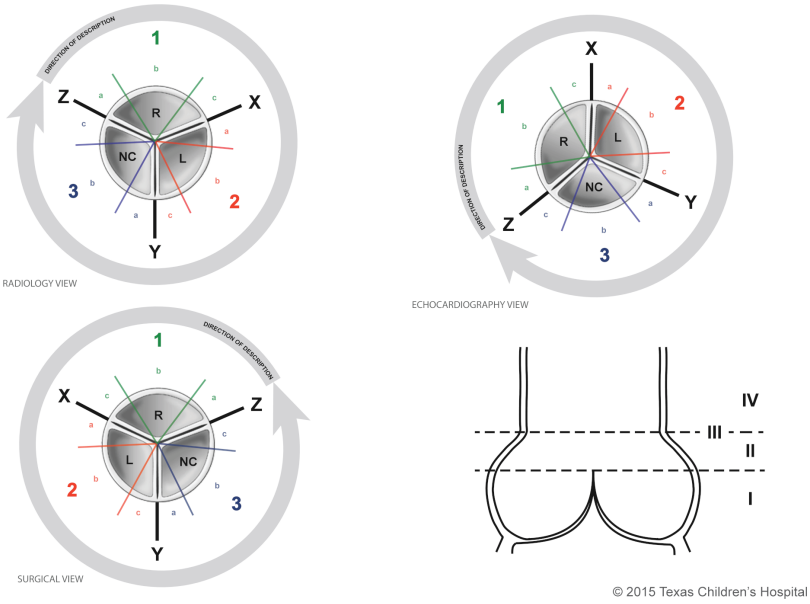

Figure 3 Topography map for optimal determination of ostium location. Used with permission from Texas Children's Hospital. L, left coronary cusp; NC, noncoronary cusp; R, right coronary cusp.

population do not currently exist, we currently use a cut-off of 0.80, similar to Driesen *et al*.[23]

Important demographic factors also play a role, with the vast majority of sudden deaths attributed to AAOCA occurring between the ages of 15 and 35 years.[24] A recent study from the Cleveland clinic[25] evaluating their experience in older adult patients (mean age 53 years) described surgery for AAOCA repair in approximately 22% of these patients, with their general approach being to determine need for operation based on high-risk anatomical features and comorbidities. Most of these patients were referred for cardiac symptoms, but only 18 of 31 had an ischaemic imaging evaluation before surgery with 7 patients having diagnostic findings of ischaemia. Only two of their patients had the same ischaemic diagnostic modality repeated before and after surgery; one of these had improvement in their ischaemia while the other did not. Given the lack of clearly demonstrated SCD risk, the benefit of surgical intervention in patients without definite ischaemia, particularly in those patients older than 35 years, has not clearly been demonstrated at this time.

STANDARDISED DIAGNOSTIC APPROACH

The approach to defining risk in AAOCA varies between institutions, though most use advanced imaging to define anatomy and course of the anomalous coronary and myocardial functional studies to evaluate for ischaemia. The recent evaluation of the CHSS registry suggests that there is wide variation in preoperative evaluation and management; among 560 patients, 298 did not undergo provocative testing.[10] Only 23 of these patients met criteria for ischaemia at diagnosis, leaving 275 without diagnostic criteria for ischaemia. Of these, 168 of 275 (61%) underwent an operation despite the lack of provocative testing. While some of these patients may have been early in the experience, this suggests that a significant portion of patients are not being evaluated in a manner consistent with recent guidelines.[2 8 9]

Our recommended approach (see figure 4) begins with cardiology consultation and diagnostic testing. Initial diagnostic testing includes advanced imaging with retrospective ECG-gated coronary CTA, maximal EST (ECG/cardiopulmonary EST) and an imaging stress test (we typically use DS-CMRI, though other methods such as stress echocardiograms are used in other institutions). In select patients in whom appropriate management is not clear, we recommend cardiac catheterisation with measurement of FFR and IVUS.[17] Those patients who experienced sudden cardiac arrest (SCA) do not undergo EST or DS-CMRI prior to surgical intervention. Once evaluation is completed, patients are discussed at a multidisciplinary meeting including cardiologists, cardiac surgeons, cardiovascular radiologists, nurses and research staff to develop a consensus recommendation. While centres may vary in diagnostic algorithms due to differences in local expertise, we feel that a standardised approach is useful for consistency in management. Given the relative rarity of these lesions and the lack of consensus guidelines available for their management (tables 1 and 2), it is reasonable to consider referral to centres experienced in AAOCA management for evaluation. We believe a multidisciplinary approach is invaluable to determine management in this population, where optimal risk stratification is yet to be defined based on long-term outcomes data.

MANAGEMENT STRATEGIES

In general, patients with AAOCA deemed at risk are recommended to undergo surgical intervention. There are no data as to the effect of exercise restriction in this population, and an adequately powered study comparing these two different approaches would be difficult given the infrequency of sudden death/arrest. Data are also not available on outcomes of patients who do not undergo an operation and are either released to unrestrictive exercise activities or remain restricted. The current AHA/ACC Scientific Statement on Eligibility and Disqualification Recommendations for Competitive Athletes with Cardiovascular Abnormalities recommends no exercise restriction in asymptomatic AAORCA in the presence of a normal maximal EST and exercise restriction until surgical repair in the setting of AAORCA with symptoms/ischaemia/arrhythmia and AAOLCA with an interarterial course.[26] While the current guidelines suggest that it is reasonable to allow patients to have no activity restriction with a normal maximal EST, our data on EST[18] showing poor sensitivity for demonstration of ischaemia in comparison with

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Table 1 Guideline recommendations for patients with anomalous aortic origin of a left coronary artery (AAOLCA) stratified by symptoms, ischaemic evaluation and high-risk features

AAOLCA					
Presence of symptoms	**Evidence of ischaemia**	**High-risk anatomy**	**AHA/ACC 2018[2]**	**ESC 2020[8]**	**AATS 2017[9]**
Symptoms	Ischaemia	High risk	I—surgery is recommended	I—surgery is recommended	I—surgery is recommended
		Not high risk			
	No ischaemia	High risk			
		Not high risk		IIb—surgery may be considered	
No symptoms	Ischaemia	High risk		IIa—surgery should be considered	
		Not high risk			
	No ischaemia	High risk	IIa—surgery is reasonable		
		Not high risk	IIa—surgery is reasonable OR IIb—surgery or observation may be reasonable	IIb—surgery may be considered (age less than 35)	Not clearly defined

AATS, American Association of Thoracic Surgeons; AHA/ACC, American Heart Association/American College of Cardiology; ESC, European Society of Cardiology.

perfusion imaging (such as DS-CMRI) suggest caution in broad applicability of this. Furthermore, exercise restriction may vary not only among centres but also among patients and families, depending on their desire to continue to exercise.

For patients with ischaemic symptoms and/or evidence of ischaemia corresponding to the at-risk territory, surgery is recommended, if feasible, which is supported by guidelines from multiple societies.[2 8 9] Among young patients without clear evidence of ischaemia, surgery is typically suggested for AAOLCA with an interarterial or intramural course, in keeping with previously mentioned guidelines. Among patients with other coronary anomalies (including AAORCA with an interarterial course) with a negative diagnostic evaluation for ischaemia, surgical intervention is not recommended nor is exercise restriction.

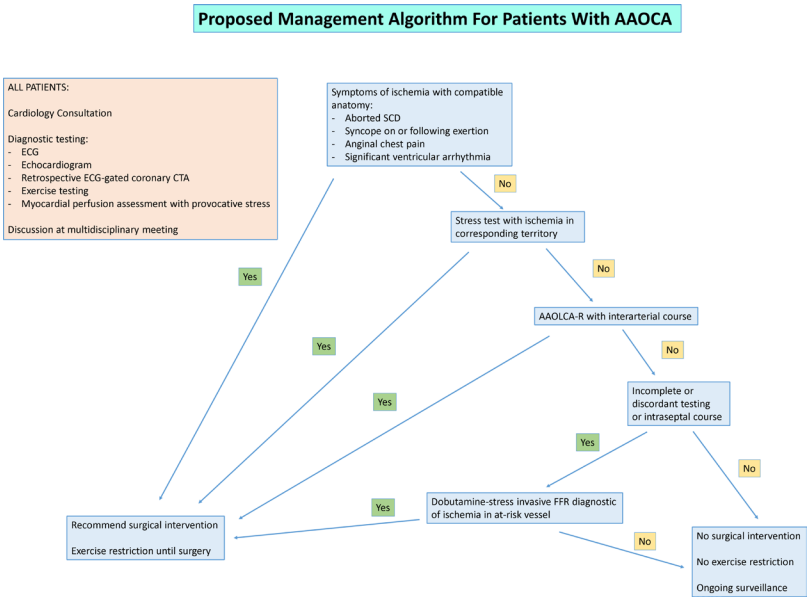

Figure 4 Proposed management algorithm. AAOCA, anomalous aortic origin of a coronary artery; AAOLCA, anomalous aortic origin of a left coronary artery; CTA, CT angiography; FFR, fractional flow reserve; SCD, sudden cardiac death.

As shown in tables 1 and 2, the recommended management for patients with historically high-risk features but without documented evidence of ischaemia is not clearly described in any of the pertinent guidelines. While we include anatomical high-risk characteristics such as intramural course and ostial abnormalities in our decision-making process, the presence of these abnormalities alone in the absence of ischaemia does not result in a recommendation for surgery. Of note, even for the asymptomatic patients without high-risk anatomical or physiological features, the AHA/ACC guidelines[2] provide a IIb recommendation for either surgery or continued observation, highlighting the lack of consensus available for management of this patient population. For patients on whom there are outstanding questions as to the indication for surgery, we recommend cardiac catheterisation with FFR. In the presence of abnormal FFR, consideration to surgical intervention is given, with an emphasis on shared decision-making with the patient and family.

The definitive treatment for patients with AAOCA is surgical repair. A detailed review of surgical management is beyond the scope of this review, but has been well summarised previously.[9] Multiple techniques have been used to repair AAOCA. If technically feasible, unroofing of the intramural segment of the anomalous coronary artery is frequently preferred as it is technically facile and addresses two of the morphological features considered to be high risk: the intramural segment and the narrowed, slit-like, angulated ostium.[9] Ostioplasty may also be undertaken to ensure adequate ostial size. Unroofing also results in relocation of the functional origin to the appropriate sinus, thereby reducing the risk of interarterial compression. However, the extent to which unroofing moves the functional orifice is limited by the length of the intramural portion. Because unroofing may not completely eliminate the interarterial component, coronary artery translocation and

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Table 2 Guideline recommendations for patients with anomalous aortic origin of a right coronary artery (AAORCA) stratified by symptoms, ischaemic evaluation and high-risk features

AAORCA					
Presence of symptoms	**Evidence of ischaemia**	**High-risk anatomy**	**AHA/ACC 2018[2]**	**ESC 2020[8]**	**AATS 2017[9]**
Symptoms	Ischaemia	High risk	I—surgery is recommended	I—surgery is recommended	I—surgery is recommended
		Not high risk			
	No ischaemia	High risk			
		Not high risk		IIb—surgery may be considered	
No symptoms	Ischaemia	High risk		IIa—surgery should be considered	Not clearly defined. It is recommended that these patients be evaluated for ischaemia.
		Not high risk			
	No ischaemia	High risk	Not clearly defined	Not clearly defined	
		Not high risk	IIb—surgery or observation may be considered	III—surgery is not recommended	

AATS, American Association of Thoracic Surgeons; AHA/ACC, American Heart Association/American College of Cardiology; ESC, European Society of Cardiology.

reimplantation has increasingly been employed as a solution. This technique completely restores the anomalous coronary to its usual sinus away from the interarterial groove, thereby eliminating risk of interarterial compression or compromise by the intercoronary pillar.[27] Reimplantation can also be used in conjunction with a patch ostioplasty to further ensure a widely patent proximal course. Among patients who do not have a significant intramural course, pulmonary artery translocation is a possible option to decrease compression of the coronary artery between the aorta and pulmonary artery.[9] In general, unless there are no other options, coronary artery bypass grafting is not preferred due to significant competitive flow from the native ostium when the patient is not exercising resulting in issues with graft patency.

Key messages

⇒ Risk stratification for patients with anomalous coronary arteries should include cross-sectional imaging and exercise stress testing with an imaging component.
⇒ Anomalous aortic origin of the left coronary from the right sinus of Valsalva with an interarterial course is the highest risk anatomical substrate for sudden death among coronary artery anomalies.
⇒ For patients with evidence of ischaemia and amenable anatomy, surgery should be the preferred management strategy.
⇒ After recovery from surgery, if there is no evidence of ongoing ischaemia, it is reasonable for patients to resume exercise activities.

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FOLLOW-UP

Follow-up strategies vary among institutions, including time intervals and testing to be performed for both surgical and non-surgical patients. In our programme, all patients are followed at specific time intervals, whether undergoing surgery or not. Following surgical intervention, patients are re-evaluated at 1 month with ECG and echocardiogram, and at 3 months with all initial testing performed prior to surgery. If the evaluation at 3 months is reassuring, patients are allowed to return progressively to full exercise activities and competitive sports participation. Exercise restriction is recommended for patients awaiting surgery, during the 3 months postoperatively, high-risk lesions where surgery has been declined or those deemed unsuitable to undergo surgery given long intraseptal/intramyocardial course.

OUTCOMES

As mentioned above, long-term outcomes of repaired and unrepaired AAOCA populations are lacking at this time. Surgical repairs are usually associated with a very low risk of mortality and minimal morbidity with good outcomes in experienced centres.[27 28] Sachdeva *et al* reported surgical outcomes with the unroofing procedure in 63 patients with no operative mortality. On median follow-up of 3 years, three patients suffered SCA with one death.[28] More recently, Bonilla-Ramirez *et al* published outcomes in 61 patients, median follow-up of 4 years, with no surgical mortality and most patients (94%) with no exercise restrictions; one patient had a second cardiac arrest following initial repair due to residual narrowing as the vessel traversed the intercoronary commissure pillar requiring reoperation.[27] However, recent multicentre data from the CHSS registry[29] show that 8% of patients developed new-onset mild or greater aortic regurgitation after surgery, with commissural manipulation being more frequent in these patients; additionally, 2% of patients developed a persistent decrease in left ventricle ejection fraction after surgery. Overall, a mortality rate of 0.6% (4 of 482 including 2 asymptomatic patients) was

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also noted in this study. Thus, while there is a low overall mortality rate, significant morbidities may be associated with surgery.

Some preliminary data show that percutaneous management with stenting of patients with AAORCA with an intramural course may be feasible, with 42 adult patients undergoing stenting for this; in this study, stenting was associated with improved symptoms at 1-year follow-up in 71% of patients.[30] However, this technique remains under investigation and all of the current guidelines recommend surgical management of these lesions.[2 8 9]

There is no clear diagnostic utility for medical therapy such as beta blockers in most patients with AAOCA. Specifically, our approach rests on the reasoning that if there is an anatomical obstruction associated with ischaemia, it should be addressed definitively in a surgical manner. However, in a small number of cases (usually involving an intraseptal course or a significant myocardial bridge that is not amenable to surgery), it is reasonable to consider beta blocker therapy.[31]

FUTURE DIRECTIONS

Despite numerous efforts across the globe to better understand AAOCA and the mechanisms leading to myocardial ischaemia in certain patients, many questions remain unanswered. Only collaboration among institutions, referral centres, ongoing registries and continued systematic investigation will lead to better answers in the future. More importantly, strategies for longitudinal follow-up ought to be devised for us to understand outcomes many decades into the future. The privacy rules of patient information limit the establishment of large social media networks. Research in this area should be developed to establish seamless ways to maintain contact throughout patients' lifespan.

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Author note References which include a * are considered to be key references.

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REFERENCES

*1 Cheezum MK, Liberthson RR, Shah NR, *et al*. Anomalous Aortic Origin of a Coronary Artery From the Inappropriate Sinus of Valsalva. *J Am Coll Cardiol* 2017;69:1592–608.
*2 Stout KK, Daniels CJ, Aboulhosn JA, *et al*. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American heart association Task force on clinical practice guidelines. *J Am Coll Cardiol* 2019;73:e81–192.
3 Angelini P. Coronary artery anomalies: an entity in search of an identity. *Circulation* 2007;115:1296–305.
4 Cheezum MK, Ghoshhajra B, Bittencourt MS, *et al*. Anomalous origin of the coronary artery arising from the opposite sinus: prevalence and outcomes in patients undergoing coronary CTA. *Eur Heart J Cardiovasc Imaging* 2017;18:224–35.
5 Basso C, Maron BJ, Corrado D, *et al*. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. *J Am Coll Cardiol* 2000;35:1493–501.
6 Maron BJ, Doerer JJ, Haas TS, *et al*. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980-2006. *Circulation* 2009;119:1085–92.
7 Molossi S, Sachdeva S. Anomalous coronary arteries: what is known and what still remains to be learned? *Curr Opin Cardiol* 2020;35:42–51.
*8 Baumgartner H, De Backer J, Babu-Narayan SV, *et al*. 2020 ESC guidelines for the management of adult congenital heart disease. *Eur Heart J* 2021;42:563–645.
9 Brothers JA, Frommelt MA, Jaquiss RDB, *et al*. Expert consensus guidelines: anomalous aortic origin of a coronary artery. *J Thorac Cardiovasc Surg* 2017;153:1440–57.
10 Jegatheeswaran A, Devlin PJ, McCrindle BW, *et al*. Features associated with myocardial ischemia in anomalous aortic origin of a coronary artery: a congenital heart surgeons' Society study. *J Thorac Cardiovasc Surg* 2019;158:822–34.
11 Adjedj J, Hyafil F, Halna du Fretay X, *et al*. Physiological evaluation of anomalous aortic origin of a coronary artery using computed Tomography-Derived fractional flow reserve. *J Am Heart Assoc* 2021;10:e018593.
12 Nagashima K, Hiro T, Fukamachi D, *et al*. Anomalous origin of the coronary artery coursing between the great vessels presenting with a cardiovascular event (J-CONOMALY registry). *Eur Heart J Cardiovasc Imaging* 2020;21:222–30.
13 Angelini P, Cheong BY, Lenge De Rosen VV, *et al*. High-Risk cardiovascular conditions in sports-related sudden death: prevalence in 5,169 schoolchildren screened via cardiac magnetic resonance. *Tex Heart Inst J* 2018;45:205–13.
14 Eckart RE, Scoville SL, Campbell CL, *et al*. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med* 2004;141:829–34.
15 Lee H-J, Hong YJ, Kim HY, *et al*. Anomalous origin of the right coronary artery from the left coronary sinus with an interarterial course: subtypes and clinical importance. *Radiology* 2012;262:101–8.
16 Opolski MP, Pregowski J, Kruk M, *et al*. Prevalence and characteristics of coronary anomalies originating from the opposite sinus of Valsalva in 8,522 patients referred for coronary computed tomography angiography. *Am J Cardiol* 2013;111:1361–7.
17 Molossi S, Agrawal H, Mery CM, *et al*. Outcomes in anomalous aortic origin of a coronary artery following a prospective standardized approach. *Circ Cardiovasc Interv* 2020;13:e008445.
18 Qasim A, Doan T, Pham TD, *et al*. Abstract 15075: exercise stress testing and stress cardiac magnetic resonance imaging for detection of inducible ischemia in a large cohort of children with anomalous aortic origin of a coronary artery. *Circulation* 2020;142.
19 Brothers J, Carter C, McBride M, *et al*. Anomalous left coronary artery origin from the opposite sinus of Valsalva: evidence of intermittent ischemia. *J Thorac Cardiovasc Surg* 2010;140:e27–9.
20 Brothers JA, McBride MG, Seliem MA, *et al*. Evaluation of myocardial ischemia after surgical repair of anomalous aortic origin of a coronary artery in a series of pediatric patients. *J Am Coll Cardiol* 2007;50:2078–82.
21 Doan TT, Molossi S, Sachdeva S, *et al*. Dobutamine stress cardiac MRI is safe and feasible in pediatric patients with anomalous aortic origin of a coronary artery (AAOCA). *Int J Cardiol* 2021;334:42–8.
22 Agrawal H, Wilkinson JC, Noel CV, *et al*. Impaired myocardial perfusion on stress CMR correlates with invasive FFR in children with coronary anomalies. *J Invasive Cardiol* 2021;33:E45–51.
23 Driesen BW, Warmerdam EG, Sieswerda G-JT, *et al*. Anomalous coronary artery originating from the opposite sinus of Valsalva

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(ACAOS), fractional flow reserve- and intravascular ultrasound-guided management in adult patients. *Catheter Cardiovasc Interv* 2018;92:68–75.
24 Eckart RE, Shry EA, Burke AP, *et al*. Sudden death in young adults: an autopsy-based series of a population undergoing active surveillance. *J Am Coll Cardiol* 2011;58:1254–61.
25 Jiang MX, Blackstone EH, Karamlou T. Anomalous aortic origin of a coronary artery in adults. *Ann Thorac Surg* 2020;21.
26 Van Hare GF, Ackerman MJ, Evangelista J-AK, *et al*. Eligibility and Disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task force 4: congenital heart disease: a scientific statement from the American heart association and American College of cardiology. *Circulation* 2015;132:e281–91.
27 Bonilla-Ramirez C, Molossi S, Sachdeva S, *et al*. Outcomes in anomalous aortic origin of a coronary artery after surgical reimplantation. *J Thorac Cardiovasc Surg* 2021. doi:10.1016/j.jtcvs.2020.12.100. [Epub ahead of print: 05 Jan 2021].
28 Sachdeva S, Frommelt MA, Mitchell ME, *et al*. Surgical unroofing of intramural anomalous aortic origin of a coronary artery in pediatric patients: single-center perspective. *J Thorac Cardiovasc Surg* 2018;155:1760–8.
*29 Jegatheeswaran A, Devlin PJ, Williams WG, *et al*. Outcomes after anomalous aortic origin of a coronary artery repair: a congenital heart surgeons' Society study. *J Thorac Cardiovasc Surg* 2020;160:757–71.
30 Angelini P, Uribe C, Monge J, *et al*. Origin of the right coronary artery from the opposite sinus of Valsalva in adults: characterization by intravascular ultrasonography at baseline and after stent angioplasty. *Catheter Cardiovasc Interv* 2015;86:199–208.
31 Doan TT, Zea-Vera R, Agrawal H, *et al*. Myocardial ischemia in children with anomalous aortic origin of a coronary artery with intraseptal course. *Circ Cardiovasc Interv* 2020;13:e008375.

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