Anomalous Aortic Origin of a Coronary Artery: Toward a Standardized Approach

Carlos M. Mery, MD, MPH,[*,†] Silvana M. Lawrence, MD, PhD,[*,‡] Rajesh Krishnamurthy, MD,[*,§] S. Kristen Sexson-Tejtel, MD, PhD,[*,‡] Kathleen E. Carberry, RN, MPH,[*,‖] E. Dean McKenzie, MD,[*,†] and Charles D. Fraser Jr, MD[*,†]

Anomalous aortic origin of a coronary artery (AAOCA) is a congenital abnormality of the origin or course of a coronary artery that arises from the aorta. It is the second most common cause of sudden cardiac death in young athletes. Its exact prevalence, the pathophysiological mechanisms that cause sudden cardiac death, the actual risk of death for the different types of AAOCA, the optimal way to evaluate these patients, and whether any treatment strategies decrease the risk of sudden cardiac death in patients diagnosed with AAOCA are unknown. This article analyzes what is currently known and unknown about this disease. It also describes the creation of a dedicated multidisciplinary coronary anomalies program and the development of a framework in an initial attempt to standardize the evaluation and management of these patients.

Semin Thoracic Surg 26:110–122

Keywords: anomalous aortic origin of a coronary artery, coronary anomalies, sudden cardiac death

Anomalous aortic origin of a coronary artery (AAOCA) is a congenital abnormality of the origin or course of a coronary artery that arises from the aorta. This condition, especially when the anomalous coronary originates from the opposite sinus of Valsalva, represents the second leading cause of sudden cardiac death (SCD) among young athletes in the United States.[1] This is particularly important, as the societal burden of premature death is greater for SCD than for any individual cancer or other leading causes of death.[2] Most of the deaths associated with AAOCA occur unexpectedly in healthy children or young athletes during or immediately after exercise.[1,3,4] Furthermore, an increasing number of children and young adults are being incidentally found to have AAOCA on imaging studies performed for other reasons or as part of screening campaigns with magnetic resonance imaging (MRI).[5]

The exact prevalence of AAOCA, the actual risk of SCD associated with different types of coronary anomalies, the mechanisms responsible for the occurrence of SCD, and the benefits conferred by different management strategies are unclear. As such, there is no consensus on how to best evaluate and manage these patients.

The objective of this article is to provide an overview of what is known and unknown about AAOCA and to propose an overall framework to evaluate and treat patients with this condition. We also describe the creation of a dedicated coronary anomalies program at our institution in an attempt to standardize the evaluation and management of these patients.

PREVALENCE

Several published series based on autopsies,[6,7] echocardiography,[8-10] cardiac catheterization studies,[11-13] and cross-sectional imaging[14,15] have tried to estimate the exact prevalence of AAOCA in the

[*]Coronary Anomalies Program, Texas Children's Hospital, Houston, Texas
[†]Michael E. DeBakey Department of Surgery, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas
[‡]Division of Pediatric Cardiology, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas
[§]E. B. Singleton Department of Pediatric Radiology, Texas Children's Hospital/Baylor College of Medicine, Houston, Texas
[‖]Outcomes & Impact Service, Texas Children's Hospital, Houston, Texas

Address reprint requests to Carlos M. Mery, MD, MPH, Division of Congenital Heart Surgery, Texas Children's Hospital, 6621 Fannin St MC 19345H, Houston, TX 77030.. E-mail: cmmery@gmail.com

1043-0679/$-see front matter
http://dx.doi.org/10.1053/j.semtcvs.2014.08.001

general population. Based on these series, the prevalence of AAOCA is reported to be between 0.06% and 0.9% for anomalous right coronary artery (ARCA), 0.025% and 0.15% for anomalous left coronary artery (ALCA), and 0.02% and 0.67% for anomalous circumflex coronary artery. Obviously, these studies can suffer from a selection bias as the prevalence of AAOCA may be higher in patients with SCD or undergoing these studies than in the general population.

The best data on prevalence of AAOCA can probably be obtained from a recent study where 1836 middle-school students underwent a limited screening cardiac MRI to detect hypertrophic cardiomyopathy and coronary anomalies. Of all patients screened, 11 (0.6%) had ARCA and 2 (0.1%) had ALCA.[5]

RISK OF SCD

The annual incidence of SCD among young athletes is between 1:43,800[16] and 1:200,000,[17] with AAOCA from the opposite sinus of Valsalva accounting for 14%-17% of all cardiac-related deaths.[1,18,19] These deaths occur most commonly during or just after physical exertion and tend to be mainly associated with sports such as basketball, soccer, track and field, swimming, and cross-country running. To the best of our knowledge, there have been no reports of SCD in children younger than 10 years, with most events occurring in patients between 10 and 30 years of age.[20,21]

Despite the available evidence that suggests that ARCA is approximately 6 times more prevalent than ALCA, ALCA seems to be responsible for up to 85% of SCDs related to AAOCA.[3,4,20] This has led to the conclusion that ALCA is a more lethal anomaly than ARCA.

Estimating the actual risk of SCD from AAOCA is difficult. Eckart et al[22] analyzed all deaths that occurred among 6.3 million military recruits undergoing basic military training from 1997-2001. Of the 277 deaths encountered, 21 were due to AAOCA (0.33 deaths due to AAOCA per 100,000 recruits), all from ALCA. Based on an estimated prevalence of ALCA of 0.1%, 6300 recruits could be estimated to have been ALCA carriers at the time of military training. This would translate into a 0.33% mortality risk in recruits with ALCA during the 6 weeks of military training. However, how this translates into an ongoing annual mortality risk of SCD in the general population who are not subjected to military training is unclear.

Maron et al[1] estimated an incidence of SCD in athletes of 0.61 per 100,000 person-years with 17% of those deaths caused by AAOCA and among those deaths, ALCA was responsible for 4 times more deaths than ARCA. Assuming a prevalence of AAOCA in the general population of 0.6%, a prevalence ratio of ALCA to ARCA of 1:6,[3,11] and using a similar analysis as the one performed by Brothers et al,[23] the annual mortality risk would be calculated at 0.1% for ALCA and 0.004% for ARCA. However, a different study among National Collegiate Athletic Association athletes showed a much higher incidence of SCD (1 per 43,770 persons per year).[16] This would translate into a higher risk of SCD: 0.36% for ALCA and 0.015% for ARCA. If the prevalence of AAOCA is assumed to be lower, the risk would be even higher. It is obviously difficult to determine what the annual risk of SCD would be among nonathlete children and young adults, but one would assume it to be relatively lower.

MECHANISMS OF SCD IN AAOCA

Despite the evident association between AAOCA and SCD, no study has consistently found a clear mechanism to explain this association. It is believed that the anomalous coronary is subject to occlusion or compression during exercise, leading to severe myocardial ischemia and ventricular tachycardia or fibrillation.[23,24] The mechanism by which this occlusion or compression occur is unclear. However, the following mechanisms have been proposed.[25]

Interarterial Course

Based on the observation that most anomalous coronaries travel between the aorta and the pulmonary artery, it has been suggested that the vessel may be compressed between the great vessels during vigorous exercise. However, studies of AAOCA using intravascular ultrasound (IVUS) have found that narrowing of the proximal segment of the anomalous coronary happens even as the pulmonary artery is displaced away during the cardiac cycle.[26] Furthermore, it is unlikely that the pulmonary artery will compress the coronary artery given the much lower pressure of the pulmonary artery when compared with the pressure within the coronary artery.

Intramural Course

Many patients with AAOCA have a variable length of the proximal anomalous coronary artery that travels within the aortic wall before entering the mediastinum (Fig. 1). It is therefore plausible that aortic expansion during exercise may compress the intramural portion of the coronary artery. Using IVUS on patients with AAOCA, studies have shown the following: (1) the proximal intramural segment is 20%-70% smaller in circumference than the distal

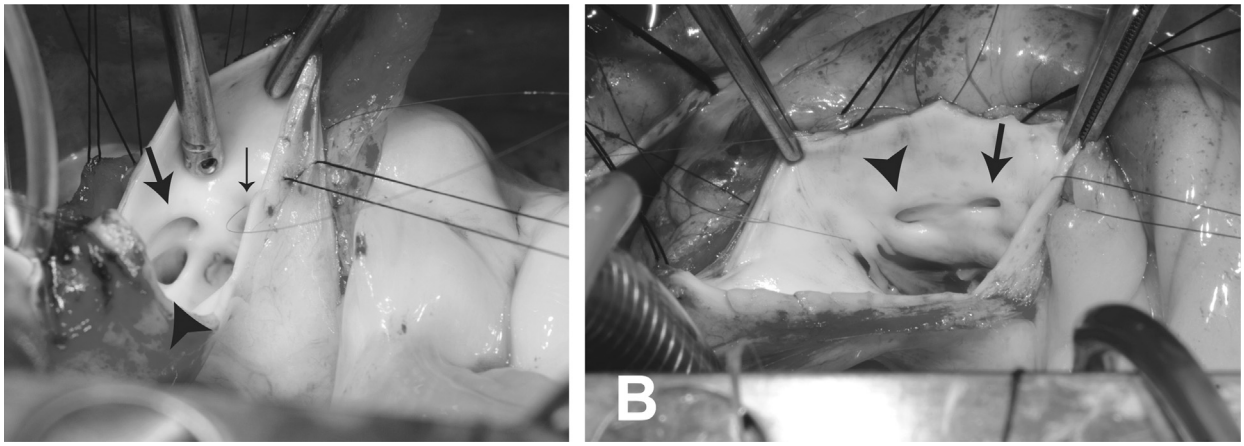


Figure 1. Surgical findings in patients with AAOCA. (A) A normal round left coronary ostium arising from the left sinus of Valsalva (arrowhead). The right coronary ostium is slitlike (large arrow) and arising from above and to the left of the intercoronary commissure of the aortic valve. The transmural fine stitch (small arrow) marks the location where the anomalous coronary arises from the aorta; the segment between the ostium and the stitch is intramural. (B) A patient that presented with aborted sudden cardiac death. The left coronary ostium (arrowhead) is stenotic with an ostial ridge and arises from the right sinus of Valsalva, above and to the right of the intercoronary commissure. The right coronary artery ostium (arrow) is also abnormal with a smaller ostial ridge. © 2014 Texas Children's Hospital (reprinted with permission).

segment of the same coronary artery because of lateral compression, (2) this segment is further compressed during systole, and (3) stimulation with fluids and dobutamine to simulate exercise conditions can worsen the systolic compression of the vessel.[26-29]

Ostial Abnormalities

Owing to the oblique proximal course that the anomalous coronary usually takes, the coronary ostium may be slitlike instead of having a round appearance (Fig. 1). This slitlike ostium may collapse in a valvelike manner with aortic expansion during systole and during exercise, compromising blood supply. In addition, in our experience, it is not uncommon to see ostial stenosis as part of this entity. These ostial anomalies could limit the necessary exercise-related increase in coronary blood flow.

CLINICAL PRESENTATION

The clinical presentation of patients with AAOCA is variable. In some instances, an episode of SCD may be the first presentation. In most series, approximately half of the patients with AAOCA present with other associated symptoms that include nonspecific chest pain, palpitations, chest pain on exertion, and dizziness or syncope on exertion.[3,4,22]

The value of exercise stress testing (EST) in patients with AAOCA is unclear. In a study analyzing 27 cases of SCD in athletes, a maximal EST had been performed and deemed to be normal in 6 patients 6-18 months before their death.[3] Upon reviewing the literature, the authors compiled data on 18 patients with AAOCA that had EST findings reported. The findings of EST were positive in only 4 (22%) patients, including 2 patients that were symptomatic. All 5 patients that died of AAOCA in this literature-based series had a negative EST finding within 6 months before their death. In a separate study, Brothers et al[30] found that only 1 (6%) of 16 patients that underwent surgical intervention for AAOCA had a positive EST finding before surgery.

IMAGING

Imaging plays an important role in the detection, categorization, and risk stratification of patients with AAOCA. Cross-sectional imaging using either MRI or computerized tomographic angiography (CTA) is often obtained to make or confirm the diagnosis. MRI has the advantages that it offers correlative information on myocardial function, perfusion, viability, and flow, without imparting any ionizing radiation. However, MRI often requires sedation in younger children and more importantly, it lacks the required spatial resolution and contrast to evaluate the ostium and proximal course of the coronary arteries to distinguish an intramural from an interarterial course. In addition, MRI does not provide information regarding dynamic changes of the coronary lumen across the cardiac cycle.

CTA has evolved as a reliable method to image the coronary arteries. Over the last year, we have implemented at our institution a dynamic CTA protocol specifically designed for the evaluation of

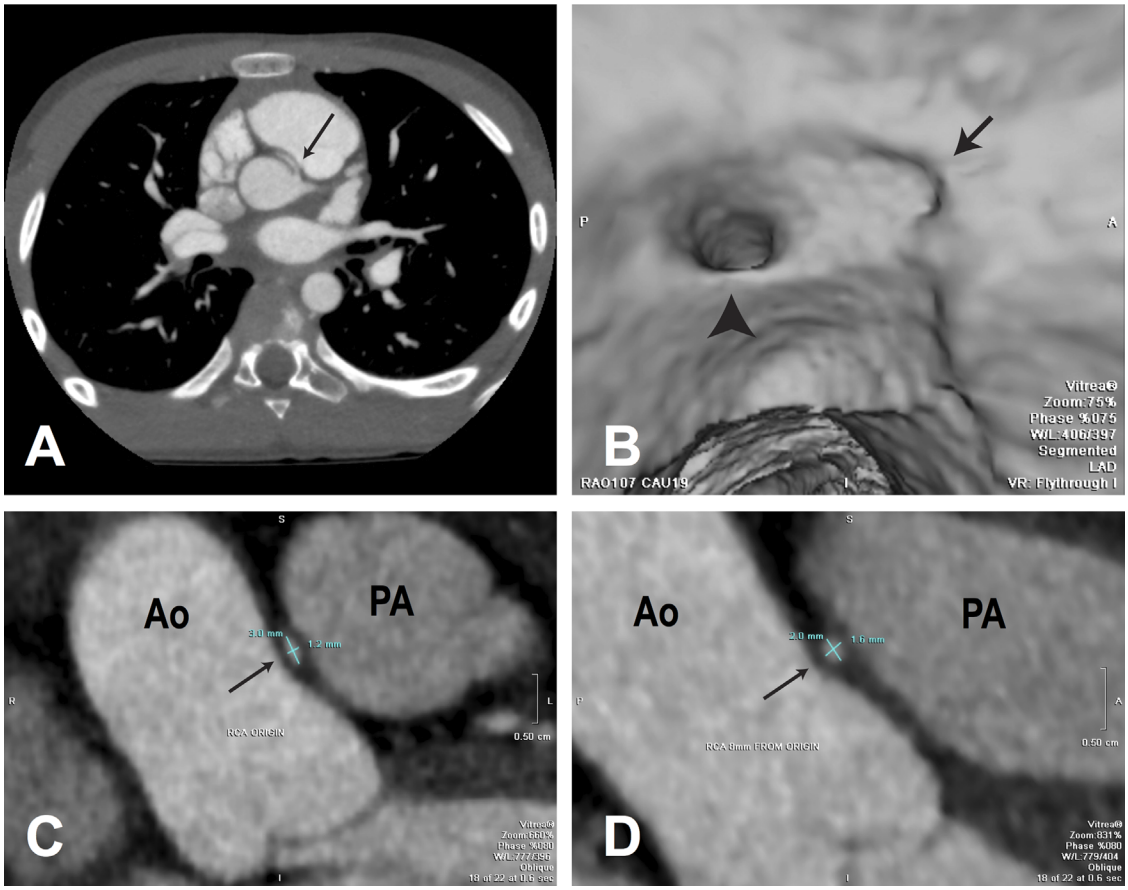


Figure 2. CTA imaging in AAOCA. (A) An ARCA (arrow) arising from the left sinus of Valsalva and traveling intramurally and interarterially. (B) A virtual angioscopy that demonstrates a normal left coronary ostium (arrowhead) and an abnormal, small, and slitlike ostium of the right coronary (arrow) arising just above and to the left of the intercoronary commissure of the aortic valve. (C and D) A transverse cut of an anomalous right coronary artery (arrow) demonstrates an oval morphology close to its origin (likely due to intramurality) and a normal round morphology 8 mm from its origin. Intramurality is determined by quantification of the density of the tissue around the coronary (presence or absence of pericoronary fat between the coronary and the aorta) and the shape of the coronary artery. Ao, aorta; PA, pulmonary artery; RCA, right coronary artery. © 2014 Texas Children's Hospital (reprinted with permission). (Color version of figure is available online.)

coronary anomalies. We obtain a retrospective electrocardiographically gated CTA of the heart, and the images are postprocessed using a 3-dimensional workstation. The use of new-generation volume scanners has allowed a 60%-90% reduction in ionizing radiation dose when compared with the older 64-slice and 16-slice scanners owing to the lack of overlapping helical imaging and iterative reconstruction techniques.[31] Using this protocol, patients receive a cumulative radiation dose of 2-5 mSv depending on age and size of the patient, which is lower than that received during the course of a coronary catheterization or a nuclear stress perfusion test.

By analyzing the dimensions of the proximal coronary artery, the status of the pericoronary mediastinal fat, and the morphology of the ostium on virtual angioscopy, our group has been able to reliably determine the location and morphology of the coronary ostia, their relationship to each other, their variation during the cardiac cycle, and the presence and length of an intramural segment (Fig. 2). We have found good correlation between radiologic and surgical findings on the 25 patients with AAOCA that have undergone surgical intervention at our institution since implementation of this protocol (unpublished results).

MANAGEMENT CONTROVERSIES

Given all the uncertainties surrounding AAOCA, it is not surprising that the treatment of these anomalies is highly variable and controversial, as demonstrated in a recent survey of more than 100 health care providers from member institutions of the Congenital Heart Surgeons Society.[32]

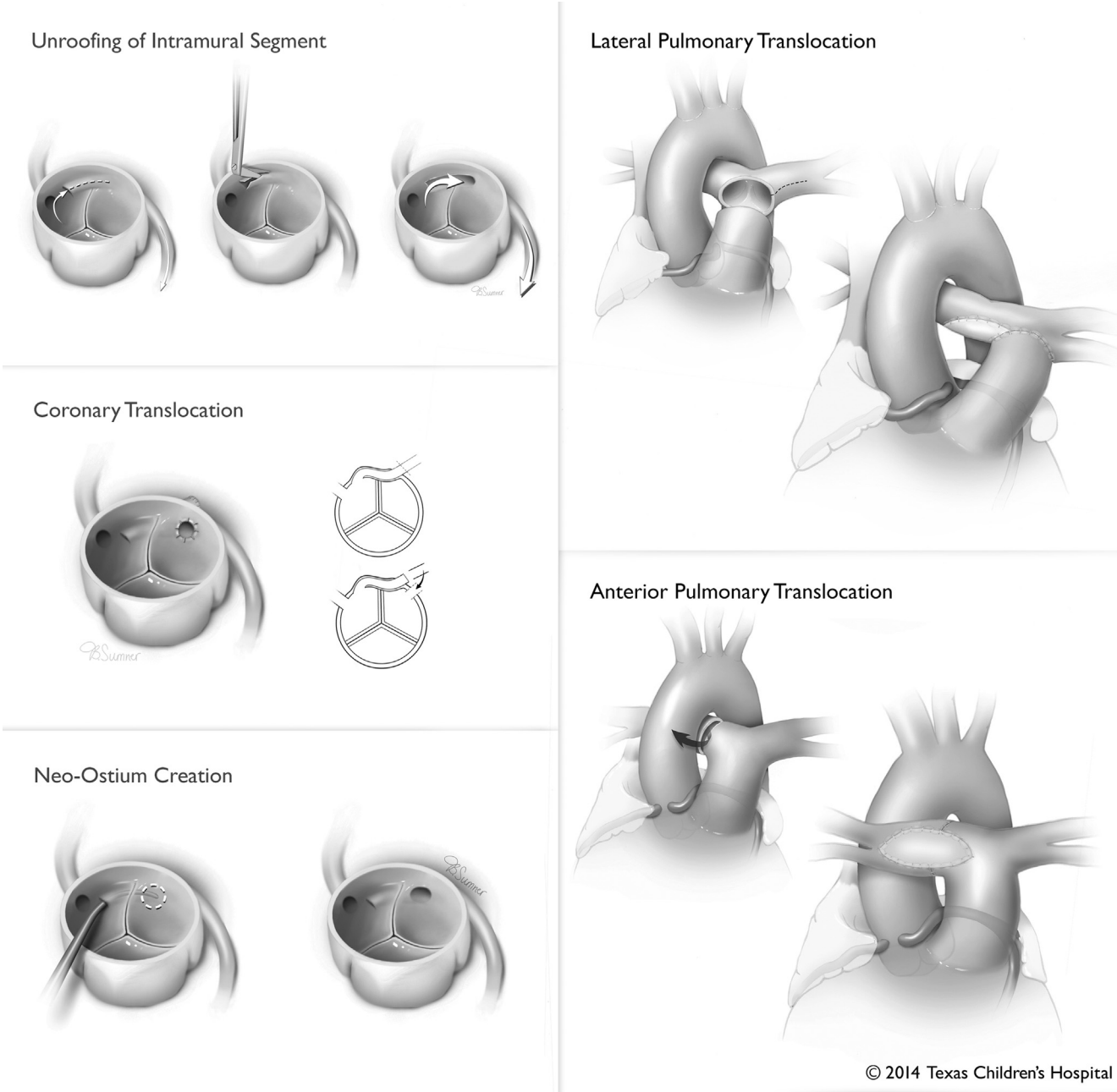


Figure 3. Surgical techniques currently used for treatment of patients with AAOCA. © 2014 Texas Children's Hospital (reprinted with permission).

Several strategies, such as exercise restriction and different surgical procedures, have been used in an attempt to decrease the risk of SCD in patients with AAOCA. Problems with recommending exercise restriction, either comprehensive or selective for competitive sports, include the difficulty of children following the recommendation, the possibility of SCD with minimal activity that would not necessarily be prevented with exercise restriction, the psychological and emotional consequences of restricting exercise in a child or adolescent, and the known health consequences of not exercising. Surgical procedures that have been proposed in an attempt to decrease the risk of SCD in these patients include (Fig. 3) the following.

Unroofing of an Intramural Segment

The most commonly used technique is unroofing of the intramural segment of the anomalous coronary.

It has been postulated that excising the intervening roof of the intramural segment may prevent coronary compression and therefore SCD. When the intramural segment travels below the level of one of the aortic commissures, some have advocated detaching the involved commissure, unroofing the intramural segment, and resuspending the aortic valve.[30] However, there have been reports of patients developing severe aortic insufficiency months after this procedure.[33]

Creation of a Neo-ostium

When the intramural segment of the anomalous coronary artery crosses an aortic valve commissure before exiting the wall, a new coronary ostium can be created in the exit sinus by unroofing the anomalous coronary at this level.[34] This procedure avoids taking down the aortic valve but requires the presence of a long intramural segment within the exit sinus of Valsalva.

Coronary Reimplantation

In certain situations, the anomalous coronary can be divided at its exit point from the aorta and reimplanted into the correct sinus. This is the technique we favor when the intramural segment crosses the aortic valve below the level of the commissures.

Ostioplasty

When the coronary ostium is found to have an ostial ridge in the absence of a significant intramural segment, the additional fibrous tissue may be removed, essentially improving the size of the coronary ostium. Patch angioplasty has also been used by some surgeons to enlarge the ostium.

Pulmonary Artery Translocation

Owing to the concern for compression of the interarterial segment of the anomalous coronary as it travels between the aorta and the pulmonary artery, some groups have advocated moving the pulmonary artery either anteriorly or laterally to prevent compression of the coronary.[35] This has been specifically used in cases where there is a single coronary ostium and no intramural segment.

Coronary Artery Bypass Graft Surgery

Coronary bypass surgery has been used to treat patients with AAOCA, especially adults.[12] The use of this strategy is discouraged owing to the risk of thrombosis of the graft as a result of competitive flow or the risk of leaving the distal circulation fully dependent on a graft if the proximal coronary is ligated to prevent competitive flow.

Results

Table 1 summarizes the results from the largest surgical series for treatment of AAOCA available in the literature.[30,33-40] The complication rate is reported to be 7%-20% with no operative mortality. Long-term results have overall been good although up to 15% of patients may have symptoms postoperatively. Most series that report results on postoperative EST show negative findings on most patients. The exception is a study from Children's Hospital of Philadelphia where 24 patients of 5-18 years of age underwent unroofing ($n = 23$, 12 with commissure takedown) or coronary reimplantation ($n = 1$). In total, 9 patients (56%) presented with symptoms preoperatively and, of the 16 patients undergoing preoperative EST, all patients but 1 had negative results. However, postoperatively, 9 patients (56%) were found to have some evidence of ischemia, including 5 abnormal EST findings a median of 15 months after surgery.[30]

The incidence of symptoms after surgery and the reports of positive EST findings after intervention raise the question of the real benefit of surgical intervention and its efficacy in preventing SCD. So far, to our knowledge, there has been only 1 report of SCD after surgical intervention for AAOCA.[41] This report from the Netherlands describes a 15-year-old high-school athlete who collapsed in the field and was found to have a myocardial infarction secondary to ALCA. At the time of surgical intervention, a slitlike orifice and intramural and interarterial courses were found. The patient underwent ostioplasty and a lateral pulmonary translocation. No unroofing of the intramural segment was performed because of the proximity of the coronary ostium to the aortic valve commissure. He was cleared for exercise 2 months later and that same day, while playing basketball, he collapsed and was unable to be resuscitated.

TOWARD A STANDARDIZED APPROACH

Owing to the uncertainty surrounding AAOCA, standardized clinical guidelines are lacking. We believe that establishing a protocol with a standardized approach for workup and management of patients with AAOCA may improve outcomes and will nourish an area that desperately needs data.

Therefore, in an effort to manage patients with AAOCA in a more consistent way, our group decided to create a dedicated multidisciplinary coronary anomalies program in December 2012. A small group of cardiologists, congenital heart surgeons, radiologists, and researchers was assembled to create

Table 1. Surgical Series of Patients With AAOCA

References	Population	Basic Anatomy	Clinical Presentation	Treatment	Outcome/Comments
Turner et al,[36] (1995-2009)	$n = 53$ 14 y (4-65 y) Pts with AAOCA and IAC undergoing repair	75% ARCA 25% ALCA 87% Of ARCA IM 85% Of ALCA IM	Symptomatic in 46% ALCA and 57% ARCA 1 ARCA with aborted SCD	Unroofing: 43 (81%) Reimplantation: 6 (11%) Creation neo-ostium: 3 (6%) CABG: 1 (2%)	F/u: 29 mo No operative mortality Surgical complications (7%): Pneumothorax Pleural effusion Bleeding requiring reoperation AI requiring reintervention Retained foreign body 8 Pts with postoperative symptoms 92% with no exercise restriction 23/24 (−) EST findings
Mainwaring et al,[35] (1999-2010)	$n = 50$ 14 y (5 d-47 y) Pts undergoing repair	62% ARCA (82% IM) 34% ALCA (59% IM) All interarterial	52% Symptomatic Symptoms in: 87% With IM 40% With no IM 16% Of cases diagnosed intraoperatively (28% had other CHD)	Unroofing: 35 (70%) for pts with IM segment. One CABG to circumflex for atherosclerotic disease Coronary reimplantation: 6 (12%) for separate coronary with no IM segment PA translocation: 9 (18%) for pts with single coronary and no IM segment. 7 Anterior and 2 lateral	No early mortality Surgical complications: 7 (14%) 3 Pleural effusions 3 Postcardiotomy syndrome 1 Heart block Long-term f/u (5.7 y): 1 Transplant (multiple infarctions before dx) 85% Unrestricted activities 15% Activity restriction No symptoms after surgery

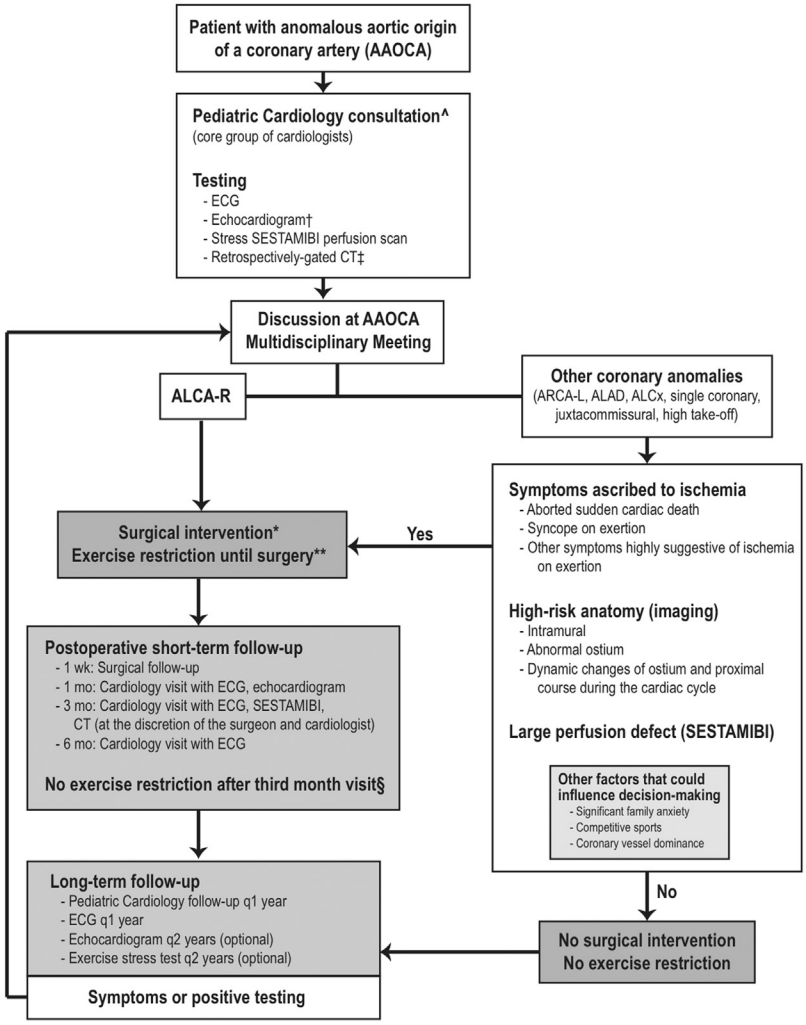
Table 1. Continued

References	Population	Basic Anatomy	Clinical Presentation	Treatment	Outcome/Comments
Davies et al,[37] (1992-2008)	$n = 36$ 47 y (13–82 y) Pts undergoing repair	58% ARCA 36% ALCA 2% ALAD 95% IM and 5% unknown 58% slitlike orifice All IAC All ACOS	81% Symptomatic 9 Of 21 (42%) had (+) EST findings 5 Pts with hx of MI due to AAOCA (2 ALCA, 2 ARCA, and 1 ALAD) 1 Pt had prior ARCA repair with CABG at another institution, now with ischemia	Unroofing: 22 (61%) CABG: 14 (39%)	No early mortality Surgical complications: 6 Atrial fibrillation 1 Subdural hematoma Long-term f/u: 1 Pt with chest pain 1 Pt catheter ablation for atrial fibrillation 1 Pt aortic homograft replacement for endocarditis
Frommelt et al,[38] (1999-2009)	$n = 27$ 13 y (4-20 y) Pts undergoing repair of IM AAOCA	74% ARCA 26% ALCA All 7 ALCA with IM—only 1 slitlike ostium All 20 ARCA with IM—4 with slitlike ostium	55% Symptomatic (3 Pts aborted SCD—all ALCA during exercise)	Unroofing: 27 (100%). 4 Pts with takedown of commissure	All pts symptom free at 1.8 y 19/19 With (−) EST findings
Brothers et al,[30] (2001-2006)	$n = 24$ 12 y (5-18 y) Pts undergoing repair (2 excluded for lack of f/u)	67% ARCA 33% ALCA	56% Symptomatic 1 Of 16 pts had (+) EST findings	Unroofing: 23 (95%). 12 Pts had detachment of commissure Coronary reimplantation: 1 (5%) for pt with ARCA	Surgical complications: 2 (8%) 1 Emergent re-exploration for aortic disruption 1 Pericardial effusion EST 15 mo postoperation: 1 ALCA and 8 ARCA (+) for ischemia
Mumtaz et al,[34] (1998-2008)	$n = 22$ 15 y (5-54 y) Pts undergoing repair AAOCA	68% ARCA 32% ALCA All IM and IAC	All symptomatic except for 1 ALCA	Unroofing: 22 (100%). All procedures without taking down commissure.	F/u: 1-63 mo No early or late deaths. All asymptomatic except for 1 with chest pain but negative studies

Table 1. Continued

References	Population	Basic Anatomy	Clinical Presentation	Treatment	Outcome/Comments
Erez et al,[39] (2003-2005)	*n* = 9 12 y (4 mo-23 y) Pts with AAOCA	55% ARCA 45% ALCA 33% IM with slitlike ostium	All patients symptomatic except for 1 (4 mo) All with normal EST findings 1 With (+) perfusion scan	Reimplantation: 6 (66%). 1 Pt pericardial patch enlargement of ARCA before reimplantation Unroofing: 2 (22%) None: 1 (11%)—awaiting surgery (4 mo)	5/5 (−) EST findings F/u: 12 mo All asymptomatic All (−) EST findings
Romp et al,[33] (1995-2001)	*n* = 9 11 y (7-65 y) Pts undergoing repair ACOS	33% ARCA 66% ALCA	All patients symptomatic except for 1	Unroofing only: 2 (22%) on pts with IM above commissure Unroofing and resuspension: 5 (55%) on pts with IM at level of valve Neo-ostium creation: 2 (22%) on pts with IM at level of valve	F/u: 4-85 mo 1 Pt (11 y) with unroofing and resuspension developed severe AI at 42 mo—Ross procedure All other pts with normal function All (−) EST findings. 2/2 (−) Thallium scan 2/2 Normal cardiac catheterization
Alphonso et al,[40]	*n* = 5 11 y (10-14 y) Pts undergoing repair AAOCA	40% ARCA 60% ALCA 2 single coronary 4 slitlike 3 IM 4 IAC	All symptomatic (1 with ventricular tachycardia and 1 with aborted SCD)	Patch angioplasty proximal coronary: 5 (100%). 4 With IAC with additional PA translocation.	No operative deaths All pts asymptomatic 3/3 (−) EST findings 2/2 Normal cardiac catheter

ACOS, anomalous coronary from the opposite sinus of Valsalva; AI, aortic insufficiency; ALAD, anomalous left anterior descending artery; CABG, coronary artery bypass grafting; CHD, congenital heart disease; dx, diagnosis; f/u, follow-up; hx, history of; IAC, interarterial course; IM, intramural course; MI, myocardial infarction; PA, pulmonary artery; Pt: patient.



AAOCA: Anomalous aortic origin of a coronary artery, ALAD: Anomalous left anterior descending artery, ALCA-R: Anomalous left coronary from the right sinus, ALCx: Anomalous left circumflex artery, ARCA-L: Anomalous right coronary from the left sinus.
^ Consent obtained for participation in prospective CHSS and TCH databases on AAOCA.
† External echocardiograms do not need to be repeated if the study is deemed appropriate.
‡ An external MR or CT may be used if able to upload the images and the study provides all necessary information to make a decision.
* Unroofing if significant intramural segment, neo-ostium creation or coronary translocation if intramural segment behind a commissure, coronary translocation or ostioplasty if no intramural segment. Surgical intervention will be offered for patients between 10 and 35 years of age. Other patients will be considered on a case-by-case basis.
** Restriction from participation in all competitive sports and in exercise with moderate or high dynamic component (>40% maximal oxygen uptake - e.g., soccer, tennis, swimming, basketball, American football). (Mitchell et al, JACC 2005; 1364-7).
§ Postoperative patients will be cleared for exercise and competitive sports based on findings at the third month postoperative visit including results of SESTAMIBI and CT (if performed).

Figure 4. Clinical algorithm used by the Texas Children's Hospital coronary anomalies program to evaluate and manage patients with AAOCA. © 2013 Texas Children's Hospital (reprinted with permission).

a clinical algorithm based on the best available evidence. The first iteration of this algorithm is shown in Figure 4.

This algorithm was not meant to be an inflexible pathway but rather an initial attempt to guide clinical management and make the workup and management of these patients more uniform across our program. It is obviously limited by the large gaps in knowledge surrounding this disease. The goal is to revisit the algorithm periodically as we gather data, gain more experience, and the knowledge about this disease improves.

As part of the effort, a decision analysis model was created using estimates from the literature and sensitivity analyses over a wide range of probabilities to determine the best strategy to follow up patients with ALCA and ARCA. Based on the model (unpublished results), young patients with ALCA were found to benefit from surgical intervention, whereas in patients with ARCA, either surgery or observation alone (with no exercise restriction) were reasonable strategies depending on the perceived annual risk of SCD.

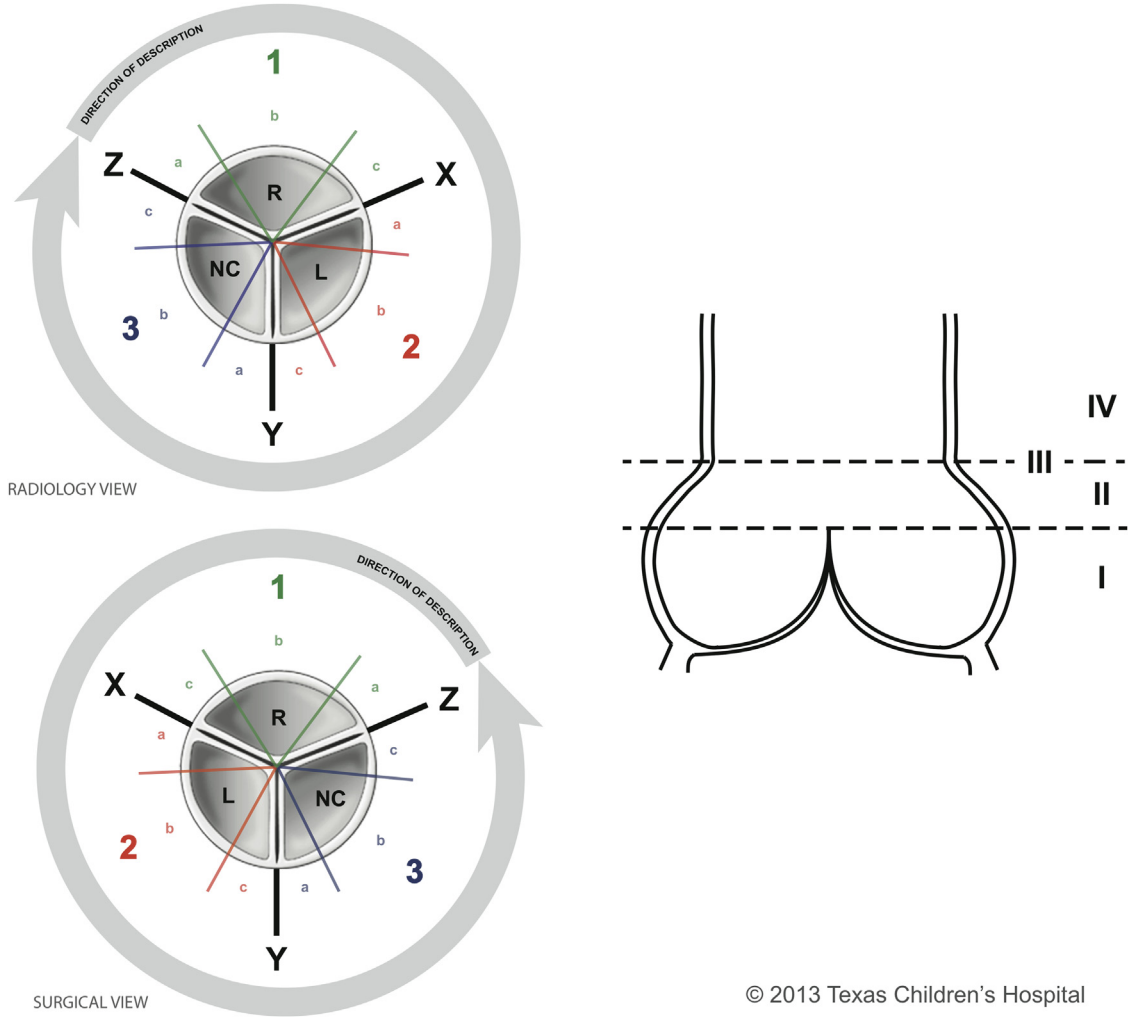


Figure 5. Coronary nomenclature and topography map used to define the origin of the coronary arteries at imaging and surgery. L: Left sinus, NC: Non-coronary sinus, R: Right sinus. © 2013 Texas Children's Hospital (reprinted with permission). (Color version of figure is available online.)

The clinical algorithm was developed based on the following principles:

- ALCA is associated with a higher risk of SCD than other coronary anomalies.[3,4,20]
- SCD in AAOCA usually happens during or shortly after vigorous physical activity that includes mainly dynamic exercise.[3,4,22]
- Dynamic exercise markedly increases oxygen consumption, heart rate, stroke volume, end-

Table 2. Recent experience of the Coronary Anomalies Program at Texas Children's Hospital With Patients With AAOCA

Strategy	Overall ($n = 66$)	Major Coronary Anomaly			
		ARCA ($n = 42$)	ALCA ($n = 10$)	Single Coronary ($n = 6$)	Others* ($n = 8$)
Observation	28 (42%)	15 (35%)	1 (10%)	4 (67%)	8 (100%)
Surgery	25 (38%)	18 (42%)	7 (70%)	0	0
Unroofing		15	6		
Ostioplasty		1	1		
Translocation		2			
Surgery recommended (family refused)	5 (8%)	4 (9%)	1 (10%)	0	0
Undergoing workup	8 (12%)	5 (12%)	1 (10%)	2 (33%)	0

*Patients with high takeoff, atretic ostium, and anomalous origin of the circumflex artery.

diastolic volume, and systolic blood pressure while decreasing systemic vascular resistance and diastolic blood pressure[42]; therefore, potentially predisposing to coronary ischemia from a combination of increased demand and decreased coronary perfusion from coronary compression and decreased coronary perfusion pressure.
- Patients that have died suddenly have often exercised numerous times at the same or higher level of intensity and duration without symptoms.[21,43]
- Symptoms occur in approximately half of the patients before the sentinel event.[3,4,22]
- Negative EST findings do not preclude the occurrence of SCD.[3]
- Based on IVUS studies, anomalous coronary arteries with an intramural segment have a significant smaller cross-sectional area within the intramural segment and this area seems to narrow even further with stimulation; the same studies show that the pulmonary artery does not seem to compress the coronary artery even if the course is interarterial.[26–29]
- SCD is rare in patients younger than 10 years and older than 30-35 years.[20,21]
- SCD in patients with AAOCA seems to be related to the development of a malignant arrhythmia or coronary ischemia.[23,24]
- Having a multidisciplinary core group of people involved in the care and decision making of these patients may translate into a more consistent approach that could potentially lead to better outcomes.
- Patients with AAOCA (surgically or non-surgically treated) should be carefully followed up in a long-term fashion.

As part of the algorithm, every patient referred to our institution with AAOCA is seen by a core group of 2 cardiologists and undergoes a standardized evaluation process, including echocardiography (to assess for other cardiac anomalies), CTA, and EST with Tc-99m sestamibi. All patients are discussed in a dedicated coronary anomalies program monthly multidisciplinary meeting to decide the best course of action. Patients with ALCA are offered surgical intervention whereas patients with other coronary anomalies are offered intervention if they have concerning characteristics such as cardiac-related symptoms suggestive of ischemia, a positive EST finding or nuclear medicine test with sestamibi, or what we believe to be high-risk anatomy on CTA (i.e., a long intramural segment, ostial abnormalities, or dynamic changes of the ostium with the cardiac cycle). Surgical intervention includes unroofing procedures, coronary translocation, ostioplasty, or neo-ostium creation, as appropriate. As a group, we avoid taking down the aortic valve as part of the unroofing procedure. All patients, regardless of treatment, are followed up clinically at set intervals. Dynamic exercise restriction is used only in patients that are awaiting surgical intervention or refuse surgical intervention. Patients with lesions believed to be low risk not to warrant surgical intervention are allowed to continue exercising. For patients undergoing surgical intervention, the exercise ban is lifted 3 months after surgery provided that the patient is asymptomatic and findings of all the tests are negative.

All patients are entered into a longitudinal database that includes clinical information from each visit, imaging studies, and surgical intervention, if applicable. We have developed a standardized nomenclature and topography map to define the exact location of the coronary ostia within the aorta for both radiologic studies and surgical description (Fig. 5).

Since the inception of the Coronary Anomalies Program in December 2012, 66 patients have been seen and evaluated using this algorithm (Table 2). Of these, 25 patients (7 with ALCA and 18 with ARCA) have undergone surgical intervention in the form of unroofing, coronary translocation, or ostioplasty with low morbidity. Unroofing has been used in most cases. Ostioplasty is performed when there is no significant intramural segment, and coronary translocation is reserved for patients in whom unroofing cannot be safely performed (i.e., the intramural segment travels behind the aortic valve). Close long-term follow-up of them and future patients will be instrumental to evaluate the adequacy of the algorithm and to periodically adapt it as more data become available.

CONCLUSION

There are multiple gaps in knowledge regarding the evaluation and management of patients with AAOCA. In particular, the mechanisms of SCD, the risk of SCD for each of the different types of coronary anomalies, and the potential improvement with the different management strategies are unclear. It is our expectation that prospective collection of data, close patient follow-up, standardization of the evaluation and management of patients within each institution, inter-institutional collaboration in the development of protocols for this disease, and data collection as part of the multi-institutional AAOCA registry recently developed by the Congenital Heart Surgeons Society[44,45] will eventually provide us with the much needed information to define the best management strategy to follow up patients with AAOCA.

1. 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 119:1085-1092, 2009
2. Stecker EC, Reinier K, Marijon E, et al: Public health burden of sudden cardiac death in the United States. Circ Arrhythm Electrophysiol 7: 212-217, 2014
3. 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 35:1493-1501, 2000
4. Taylor AJ, Rogan KM, Virmani R: Sudden cardiac death associated with isolated congenital coronary artery anomalies. J Am Coll Cardiol 20:640-647, 1992
5. Angelini P, Shah NR, Uribe CE, et al: Novel MRI-based screening protocol to identify adolescents at high risk of sudden cardiac death. J Am Coll Cardiol 61:E1621, 2013
6. Alexander RW, Griffith GC: Anomalies of the coronary arteries and their clinical significance. Circulation 14:800-805, 1956
7. Drory Y, Turetz Y, Hiss Y, et al: Sudden unexpected death in persons less than 40 years of age. Am J Cardiol 68:1388-1392, 1991
8. Davis JA, Cecchin F, Jones TK, et al: Major coronary artery anomalies in a pediatric population: incidence and clinical importance. J Am Coll Cardiol 37:593-597, 2001
9. Zeppilli P, dello Russo A, Santini C, et al: In vivo detection of coronary artery anomalies in asymptomatic athletes by echocardiographic screening. Chest 114:89-93, 1998
10. Pelliccia A, Spataro A, Maron BJ: Prospective echocardiographic screening for coronary artery anomalies in 1360 elite competitive athletes. Am J Cardiol 72:978-979, 1993
11. Angelini P, Villason S, Chan AV, et al: Normal and anomalous coronary arteries in humans. In: Angelini P, editor. Coronary artery anomalies. Philadelphia: Lippincott Williams & Wilkins; 1999. p. 27-150, 1999
12. Krasuski RA, Magyar D, Hart S, et al: Long-term outcome and impact of surgery on adults with coronary arteries originating from the opposite coronary cusp. Circulation 123:154-162, 2011
13. Kaku B, Shimizu M, Yoshio H, et al: Clinical features of prognosis of Japanese patients with anomalous origin of the coronary artery. Jpn Circ J 60:731-741, 1996
14. Prakken NH, Cramer MJ, Olimulder MA, et al: Screening for proximal coronary artery anomalies with 3-dimensional MR coronary angiography. Int J Cardiovasc Imaging 26:701-710, 2010
15. Schmitt R, Froehner S, Brunn J, et al: Congenital anomalies of the coronary arteries: imaging with contrast-enhanced, multidetector computed tomography. Eur Radiol 15:1110-1121, 2005
16. Harmon KG, Asif IM, Klossner D, et al: Incidence of sudden cardiac death in national collegiate athletic association athletes. Circulation 123:1594-1600, 2011
17. Maron BJ, Gohman TE, Aeppli D: Prevalence of sudden cardiac death during competitive sports activities in Minnesota high school athletes. J Am Coll Cardiol 32:1881-1884, 1998
18. Maron BJ: Sudden death in young athletes. N Engl J Med 349:1064-1075, 2003
19. Harmon KG, Drezner JA, Maleszewski JJ, et al: Pathogeneses of sudden cardiac death in national collegiate athletic association athletes. Circ Arrhythm Electrophysiol 7:198-204, 2014
20. Kragel AH, Roberts WC: Anomalous origin of either the right or left main coronary artery from the aorta with subsequent coursing between aorta and pulmonary trunk: analysis of 32 necropsy cases. Am J Cardiol 62: 771-777, 1988
21. Taylor AJ, Byers JP, Cheitlin MD, et al: Anomalous right or left coronary artery from the contralateral coronary sinus: "high-risk" abnormalities in the initial coronary artery course and heterogeneous clinical outcomes. Am Heart J 133:428-435, 1997
22. 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 141:829-834, 2004
23. 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 140:e27-e29, 2010
24. Cox ID, Bunce N, Fluck DS: Failed sudden cardiac death in a patient with an anomalous origin of the right coronary artery. Circulation 102:1461-1462, 2000
25. Cheitlin MD, MacGregor J: Congenital anomalies of coronary arteries: role in the pathogenesis of sudden cardiac death. Herz 34:268-279, 2009
26. Angelini P, Velasco JA, Ott D, et al: Anomalous coronary artery arising from the opposite sinus: descriptive features and pathophysiologic mechanisms, as documented by intravascular ultrasonography. J Invasive Cardiol 15:507-514, 2003
27. Angelini P: Coronary artery anomalies—current clinical issues: definitions, classification, incidence, clinical relevance, and treatment guidelines. Tex Heart Inst J 29:271-278, 2002
28. Angelini P, Walmsley RP, Libreros A, et al: Symptomatic anomalous origination of the left coronary artery from the opposite sinus of valsalva. Clinical presentations, diagnosis, and surgical repair. Tex Heart Inst J 33:171-179, 2006
29. Angelini P: Coronary artery anomalies: an entity in search of an identity. Circulation 115: 1296-1305, 2007
30. 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 50:2078-2082, 2007
31. Greenberg SB, Bhutta S, Braswell L, et al: Computed tomography angiography in children with cardiovascular disease: low dose techniques and image quality. Int J Cardiovasc Imaging 28:163-170, 2012
32. Brothers J, Gaynor JW, Paridon S, et al: Anomalous aortic origin of a coronary artery with an interarterial course: understanding current management strategies in children and young adults. Pediatr Cardiol 30:911-921, 2009
33. Romp RL, Herlong JR, Landolfo CK, et al: Outcome of unroofing procedure for repair of anomalous aortic origin of left or right coronary artery. Ann Thorac Surg 76:589-595, 2003 [discussion 595-6]
34. Mumtaz MA, Lorber RE, Arruda J, et al: Surgery for anomalous aortic origin of the coronary artery. Ann Thorac Surg 91:811-814, 2011 [discussion 814-5]
35. Mainwaring RD, Reddy VM, Reinhartz O, et al: Anomalous aortic origin of a coronary artery: medium-term results after surgical repair in 50 patients. Ann Thorac Surg 92:691-697, 2011
36. Turner II, Turek JW, Jaggers J, et al: Anomalous aortic origin of a coronary artery: preoperative diagnosis and surgical planning. World J Pediatr Congenit Heart Surg 2:340-345, 2011
37. Davies JE, Burkhart HM, Dearani JA, et al: Surgical management of anomalous aortic origin of a coronary artery. Ann Thorac Surg 88: 844-847, 2009 [discussion 847-8]
38. Frommelt PC, Sheridan DC, Berger S, et al: Ten-year experience with surgical unroofing of anomalous aortic origin of a coronary artery from the opposite sinus with an interarterial course. J Thorac Cardiovasc Surg 142:1046-1051, 2011
39. Erez E, Tam VK, Doublin NA, et al: Anomalous coronary artery with aortic origin and course between the great arteries: improved diagnosis, anatomic findings, and surgical treatment. Ann Thorac Surg 82:973-977, 2006
40. Alphonso N, Anagnostopoulos PV, Nolke L, et al: Anomalous coronary artery from the wrong sinus of Valsalva: a physiologic repair strategy. Ann Thorac Surg 83:1472-1476, 2007
41. Nguyen AL, Haas F, Evens J, et al: Sudden cardiac death after repair of anomalous origin of left coronary artery from right sinus of Valsalva with an interarterial course: case report and review of the literature. Neth Heart J 20:463-471, 2012
42. Mitchell JH, Haskell W, Snell P, et al: Task force 8: classification of sports. J Am Coll Cardiol 45: 1364-1367, 2005
43. Cheitlin MD, De Castro CM, McAllister HA: Sudden death as a complication of anomalous left coronary origin from the anterior sinus of Valsalva: a not-so-minor congenital anomaly. Circulation 50:780-787, 1974
44. Brothers JA, Gaynor JW, Jacobs JP, et al: The registry of anomalous aortic origin of the coronary artery of the Congenital Heart Surgeons' Society. Cardiol Young 20:50-58, 2010(suppl 3)
45. Poynter JA, Williams WG, McIntyre S, et al: Anomalous aortic origin of a coronary artery: a report from the Congenital Heart Surgeons Society Registry. World J Pediatr Congenit Heart Surg 5:22-30, 2014