Expert consensus guidelines: Anomalous aortic origin of a coronary artery

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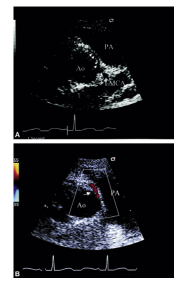

Anomalous aortic origin of the right coronary artery.

Central Message

We sought to establish evidence-based guidelines for the management anomalous aortic origin of a coronary artery.

Perspective

Anomalous aortic origin of a coronary artery is associated with sudden cardiac death. Although the risk for any single affected individual is small, the loss of an otherwise healthy person is particularly devastating. Surgical and interventional therapies have been developed that appear to be protective but these therapies carry risks. The challenge is identifying those individuals at such risk.

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RATIONALE AND OBJECTIVES

The objective of this project was to establish consensus 2016 American Association for Thoracic Surgery (AATS) evidence-based guidelines for the management of anomalous aortic origin of a coronary artery. In many types of coronary anomalies, the risk of sudden cardiac death (SCD) is largely unknown, as the anomalies are quite rare. However, observational studies have identified the coronary anomalies that appear to be most prevalent and in which the SCD risk appears to be the greatest: when both coronary arteries arise from the same aortic sinus with either a single ostium or 2 separate ostia (Table 1). The aberrant vessel may arise above the inappropriate sinus or above the commissure and not truly from the sinus itself. For this article, we refer to this as anomalous aortic origin of a coronary artery (AAOCA) from the inappropriate coronary sinus. The course the anomalous coronary artery takes appears to have an impact on its risk of SCD. The anomalous aortic origin of the left main coronary artery (AAOLCA) or right coronary artery (AAORCA) can course in front of the pulmonary artery (pre-pulmonic) or posterior to the aorta (posterior/retroaortic). The AAOLCA or left anterior descending coronary artery alone can course through the conal septum (intraseptal or intraconal or intramyocardial). These previous subtypes are generally not believed to be clinically significant. However, the course becomes important if either the aberrant left main coronary artery or right coronary artery travels between the 2 great vessels. This review and recommendations are directed at AAOCA from the opposite sinus of Valsalva with an interarterial course (Figure 1).

METHODS OF REVIEW

The AATS Guidelines Committee identified the management of AAOCA as a key topic in cardiothoracic surgery suitable for the establishment of clinical guidelines. The Guidelines Committee selected James S. Tweddell, MD, as chair of the AAOCA Working Group and asked him to appoint an AAOCA Guidelines writing committee to create evidence-based guidelines for the AATS Guidelines Committee. The chair assembled a multidisciplinary group of experts, the coauthors of this article, who include congenital cardiac surgeons and adult and pediatric cardiologists. Members were tasked with performing comprehensive literature searches, and making recommendations based on a review of the literature. Members also graded the quality of the evidence supporting the recommendations and with assessing the risk-benefit profile for each recommendation. The level of evidence was graded by the work force panel according to standards published by the Institute of Medicine (Figure 2). For the development of the guidelines, we followed the recommendations of the Institute of Medicine's 2011 *Clinical Practice Guidelines We Can Trust: Standards for Developing Trustworthy Clinical Practice Guidelines* (http://www.nationalacademies.org/hmd/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx). Scheduled teleconferences were used to organize the topics to be covered by the guidelines, review the literature review summaries, and propose recommendations. For all meetings, agendas were circulated beforehand. Summaries of the conference calls were circulated to the writing committee members. The final recommendations were voted on by the writing committee to present to the Councilors of the AATS and review the final manuscript. The writing committee unanimously agreed on all recommendations. Therefore, the process followed the recommendations of the Institute of Medicine, but an extensive consultation with all other stakeholders, including patients, was not performed. Instead, the AATS guidelines attempt to provide a rapid response to the rapidly changing medical literature and provide clinicians with the recommendations of senior content experts based on the best available information. The expert consensus provides important guidance to clinicians, particularly when the quality of the evidence is limited or contradictory. These consensus guidelines provide the best opinion of a group of content experts.

The following recommendations are based on expert consensus opinion as well as on the best available evidence. Despite important knowledge gaps, we feel it is important and timely to review the available evidence and present expert opinion based on best practices. The guidelines were prepared for publication in *The Journal of Thoracic and Cardiovascular Surgery.*

SECTION I: BACKGROUND

Prevalence

The true prevalence of congenital coronary anomalies that are potentially pathologic in the general population is difficult to ascertain. Several studies have attempted to quantify this value, with estimates ranging between 0.1% and 1.0% in both the adult and pediatric populations.[1-7] The wide difference in prevalence rates is likely due to

TABLE 1. Variations of anomalous aortic origin of a coronary artery

1. Left main coronary artery (LMCA) arises from right sinus of Valsalva, either directly from right coronary artery or as a separate ostia
   a. LMCA course anterior to pulmonary artery (anterior)
   b. LMCA course posterior to aorta (posterior)
   c. LMCA course through interventricular septum (intraseptal/intraconal)
   d. LMCA course between aorta and pulmonary artery (interarterial)
2. Left anterior descending coronary or left circumflex coronary artery may originate from the right sinus alone
3. Right coronary artery (RCA) arises from left sinus of Valsalva, either from LMCA or as a separate ostia
   a. RCA courses anterior to pulmonary artery (anterior)
   b. RCA courses posterior to aorta (posterior)
   c. RCA courses between aorta and pulmonary artery (interarterial)
4. Single LMCA arises from left sinus of Valsalva and bifurcates into the left anterior descending coronary and left circumflex coronary arteries. The left circumflex coronary artery crosses the crux and continues as the RCA.
5. Single RCA arises from right sinus, crosses crux, continues as left anterior descending coronary and left circumflex coronary arteries

Adapted from Brothers JA, Gaynor JW. Coronary artery anomalies in children. In: Kaiser LR, Kron IL, Spray TL, eds. *Mastery of Cardiothoracic Surgery.* 3rd ed. Philadelphia, PA: Lippincott, William and Wilkins; 2014:1055-73.

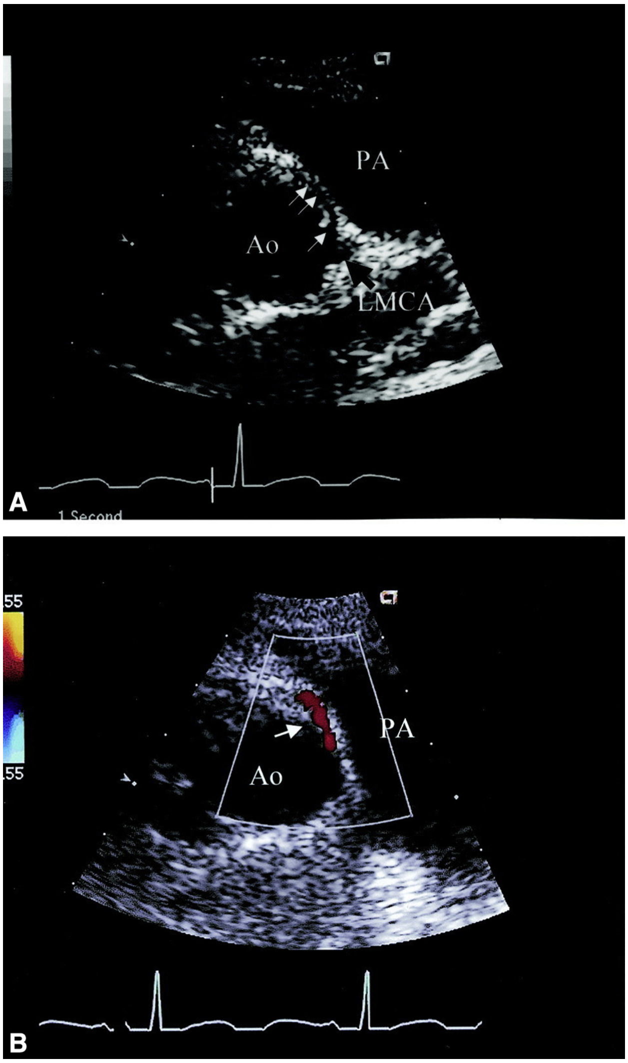

FIGURE 1. Transthoracic echocardiography from a short-axis plane in a patient with anomalous origin of the right coronary artery from the left sinus of Valsalva and an intramural course of the anomalous coronary. A, The anomalous right coronary artery can be seen arising from the left sinus of Valsalva near the origin of the left main coronary artery (*LMCA*) and coursing intramurally within the anterior aortic wall (*arrowheads*) between the aorta (*Ao*) and the pulmonary artery (*PA*) toward the right sinus of Valsalva. B, Color Doppler imaging shows the linear diastolic flow of the anomalous coronary within the anterior aortic wall (*arrow*); the *red color signal* confirms anomalous coronary flow towards the transducer anteriorly, consistent with the coronary originating from the left sinus and coursing toward the more anteriorly positioned right sinus. Reprinted with permission.[53]

choice of imaging modality, patient population chosen to study, and/or the how coronary anomalies were defined.[8]

When looking specifically at the estimated prevalence of interarterial AAOCA, this has ranged between 0.1% and 0.7%.[1-7] Yamanaka and Hobbs[1] found the incidence to be approximately 0.3% of more than 100,000 adults evaluated with coronary angiography. In a large population-based prospective study in asymptomatic children using transthoracic echocardiography, the incidence of AAOCA was found to be 0.17%.[5] Because this study evaluated only asymptomatic patients, the true prevalence was likely underestimated, as they did not include those children with symptomatic AAOCA. Recently, Angelini[7] reported on a magnetic resonance imaging screening program designed to identify high-risk cardiac lesions, and found 0.7% of the population screened had interarterial AAOCA, with 0.5% interarterial AAORCA. If we extrapolate this to the population of young people (ages 12-35) in the United States, this could mean more than 600,000 children and young adults have interarterial AAOCA. In most studies, interarterial AAORCA is from 3 to 6 times more common than AAOLCA.[1,7]

Genetics

Little is known about the genetics of coronary anomalies, especially those that have the potential for sudden death, including interarterial AAOCA. The development of the coronary arteries is complex, with many different sites at which a mutation leads to a potentially lethal coronary anomaly. There are minimal data regarding the genetic patterns of AAOCA. Bloor et al[9] reported on the coronary artery anatomy in albino rats and found that the genetic variation in newborn rats and their parents was likely determined from multiple genes and not of classical Mendelian inheritance. There are no published data about the genetic inheritance in humans. However, there have been reports of families with at least 2 first-degree relatives affected by AAOCA.[10-12] Genetic testing in association with focused imaging of the relatives of the AAOCA patient may help elucidate any potential genetic factors. In a more general, nonspecific sense, there are multiple population studies demonstrating familial clustering of sudden cardiac arrest (SCA) as a first clinical manifestation of ischemia.[13-16] This suggests a yet-undefined genetic basis for an arrhythmic response to ischemia, distinct from, but in addition to, any genetic basis for the primary structural defect itself.

SCD and the Mechanism of Ischemia

Since the exact mechanism of SCD associated with coronary anomalies is not known, several hypotheses have been put forth based on anatomic and physiologic properties of the anomalous coronary. Certain factors appear to predispose to myocardial ischemia and/or lethal ventricular arrhythmias, likely due to limitation of coronary reserve. These include 1 or more of the following: ostial stenosis in association with an oblique take-off from the aorta, ostial ridge, vessel spasm, intussusception, noncompliant pericommissural area, and compression of the anomalous coronary artery intramurally and/or between the great arteries.[17-19] It remains unknown whether these mechanisms act alone or in combination to provide the substrate for SCD.

Risk of SCD. The most common anomaly that appears to carry some increased risk of SCD is AAORCA. However,

Applying Classification of Recommendations and Level of Evidence			
Class I Benefit >>> Risk Procedure/Treatment **SHOULD** be performed / administered	**Class IIa** Benefit >> Risk Additional studies with focused objectives needed **IT IS REASONABLE** to perform procedure/administer treatment	**Class IIb** Benefit ≥ Risk Additional studies with broad objectives needed; Additional registry data would be helpful. Procedure/Treatment **MAY BE CONSIDERED**	**Class III** Risk ≥ Benefit No additonal studies needed. Procedure/Treatment should **NOT** be performed/adminsitered **SINCE IT NOT HELPFUL AND MAY BE HARMFUL**

Level A:	Recommendation based on evidence from multiple randomized trials or meta-analyses. Multiple (3-5) population risk strata evaluated. General consistency of direction and magnitude of effect.
Level B:	Recommendation based on evidence from a single randomized trial or non-randomized studies. Limited (2-3) population risk strata evaluated.
Level C:	Recommendation based on expert opinion, case studies, or standard-of-care. Very limited (1-2) population risk strata evaluated.

FIGURE 2. Schema used to guide the grading of available published evidence and the expected effect of the intervention for their impact on patient outcomes.

interarterial AAOLCA is proportionally far more prevalent among individuals who have died suddenly with no other explanation.[17-21] Despite not knowing the exact mechanism of ischemia in those with AAOCA, identifying and treating those anomalies that place the patient at risk of SCD is of utmost importance, and management should ideally be based on the risk assessment. Although the true risk is unknown, an estimation based on some assumptions can be calculated. The mortality rates frequently cited and used for risk assessment are from autopsy series data and include 0% to 57% for AAORCA and 27% to 100% for AAOLCA.[17-21] What is necessary to understand is that these rates reflect the prevalence of AAOCA in those who have already died and not the risk of SCD in those living with AAOCA. Recently, 2 studies reported on the incidence of SCD or SCA in people 35 years and younger.[22,23] In the combined cohorts, there were 4 cases of AAOCA associated with SCD or SCA in a combined 34 million patient-years; in 1 study, the 2 cases of SCD (ages <19 years) were both interarterial AAOLCA and known to be associated with vigorous physical activity.[23] These studies demonstrate that the risk of SCD or SCA in the young, in the absence of participation in competitive sports, is exceedingly low.[24]

Exercise and SCD risk. Vigorous physical activity increases the risk of SCD in those with interarterial AAOCA.[6,23,25] Maron et al[25] published a comprehensive analysis of sudden deaths among competitive athletes in the United States over a 27-year period. Of the 690 SCD episodes ascribed to a cardiovascular cause, 119 of these were due to AAOCA. Based on their data, the incidence of SCD would be approximately 0.1 per 100,000 person-years from AAOCA. A similar incidence of SCD was found among Minnesota high school athletes over a 26-year period, with 2 SCD events occurring due to AAOCA, both of which were AAOLCA.[26] Using the data of Maron et al,[25] Brothers et al[27] calculated the cumulative risk of death over a 20-year period in children and young adults with AAOCA (ages 15-35 years) participating in competitive sports was 6.3% for AAOLCA and 0.2% for AAORCA. Even though these analyses are prone to ascertainment bias as well as underreporting, it does seem that the risk of SCD ascribed to AAOCA is far less than reported in autopsy series.

It is important to understand that most risk estimates are based on the presumed incidence of SCD in those who are participating in competitive athletics, which is only approximately 10% to 15% of children and adolescents. They do not assess risk among those who have SCA during high-intensity recreational sports, or in the general population not participating in higher-level sports. Competitive athletes are defined as individuals of middle school age and older (generally ≥11 years of age) who are engaged in exercise training on a regular basis and participate in official sports competition organized by a recognized athletic association. Competitive athletes place a high premium on athletic excellence and these individuals typically exercise more than 10 hours per week. In contrast, recreational athletes are defined as individuals engaged in recreational or leisure-time sports activities, on either a regular basis or intermittently. Usually, they exercise less than 10 hours per week. Recreational sports do not necessarily require systematic training or the pursuit of excellence.[28] Although there are rare case reports of SCD from AAOCA at rest or while participating in recreational activity, these reports are just that: individual cases that occur rarely, and not derived from any formal databases. Notably, a recent study from France demonstrated that many more SCDs occur during recreational sports than during competitive activities, albeit at an older age.[29] This increasing number of older individuals (eg, ages late 20s to 40s) with reports of SCD or SCA from AAOCA may be due to the growth of sanctioned sporting events for adults, such as triathlons and running and bicycle races. In fact, these older athletes may now be exerting themselves at a higher level than they did when they were young. Taking a conservative prevalence rate of AAOCA in the population of approximately 0.2%, which may be underestimating the prevalence based on recent studies, then there are at least 600,000 young people in the United States with AAOCA. Besides the competitive athlete, in whom there are only a small number of SCD events reported every year, the risk of SCD for the asymptomatic young person with interarterial AAOCA, even AAOLCA, who is not participating in competitive sports does not appear to be significantly greater than the SCD risk for those without AAOCA who are participating only in recreational athletics.

SECTION II: PRESENTATION AND DIAGNOSIS

Presentation

There is not a typical way that patients present with AAOCA. For some, the initial presentation is aborted SCD or true SCD. However, most patients with AAOCA are diagnosed when the anomaly is found incidentally on a transthoracic or transesophageal echocardiogram or computed tomography (CT) angiogram that is performed for another reason, such as a heart murmur or abnormal electrocardiogram (ECG). The patient may also have an echocardiogram performed for symptoms related to exertion, such as chest pain, palpitations, dizziness, presyncope, or syncope. Although many of these symptoms are often seen in those without coronary anomalies, these complaints prompt the referral to a cardiologist and an echocardiogram is performed. Chest pain should be considered ischemic if it is accompanied by evidence of myocardial injury, noted by ST segment depression at rest or with exercise, ventricular arrhythmias that increase with exercise, lack of increase or a decrease in blood pressure with exercise, evidence of wall motion abnormality on echocardiography, perfusion defect on nuclear scan in the correct distribution of the anomalous coronary artery, and/or evidence of past fibrosis/scar or perfusion abnormality seen by cardiac magnetic resonance imaging (MRI). Recent large-scale screening programs have increased the frequency of incidentally diagnosed AAOCA.

Diagnostic Studies

A screening ECG is not reliable for suspecting or recognizing AAOCA.[30] The presence of a q-wave consistent with a previous myocardial infarction scar is rarely, if ever, seen in AAOCA. Exertional chest pain or dyspnea in a relatively young individual not otherwise suspected to be at risk for coronary atherosclerosis may be helpful; however, 2 reports suggest that 50% of SCD associated with coronary artery anomalies were first events without previous symptoms.[24,31] As well, stress tests are not uniformly positive among individuals with these anomalies.[24,32]

In the past, cardiac catheterization with coronary angiography was routinely used for diagnosis of AAOCA; however, due to the invasive nature of the test and its inherent exposure to ionizing radiation, it is rarely used in the pediatric population. Cardiac catheterization is indicated if the anatomy cannot be defined with noninvasive imaging and in adults with suspected or echocardiographically defined anomalous vessels, for both complete definition of the anatomy and concomitant evaluation for coronary atherosclerotic disease.[1,33-52] Obviously, it is not used for routine screening in the absence of ischemic symptoms or clues from other imaging studies. The best method for initially identifying AAOCA is a carefully performed transthoracic echocardiogram with Doppler color flow mapping.[11,27,32,53-65] This is generally the initial diagnostic modality due to availability, cost-effectiveness, ease of performance, and absence of radiation exposure. Imaging should clarify origin of left or right, as well as the presence or absence of an intramural course. Additional imaging is indicated when the anatomy cannot be accurately defined.[64] Coronary CT angiography or cardiac MRI is commonly used to obtain better visualization of the coronary artery anatomy to confirm the diagnosis.[40,46,52,59,63,66-95] Once the anatomy has been established, a maximal exercise stress test should be used to help assess the potential ischemic burden of the anatomic variant, especially in competitive athletes or high-intensity recreational athletes. We also recommend that the exercise test be combined with a nuclear perfusion scan or stress echocardiogram to optimize the sensitivity of identifying ischemia[27,32,40,96-99]; however, it must be emphasized that a normal stress test, nuclear perfusion scan, or stress echocardiogram is, at best, incompletely reassuring. These studies have a low negative predictive value, and are most helpful only if they are positive.

Recommendations on Diagnostic Imaging

1. Individuals with suspected AAOCA should undergo transthoracic echocardiography to identify the origin and course of the proximal coronary arteries. *(Class I, Level of Evidence B—supporting references[11,27,32,53-65])*
2. Additional imaging studies, such as coronary CT angiography or cardiac MRI are reasonable to better visualize

the coronary artery anatomy and to confirm the diagnosis. *(Class IIa, Level of Evidence B—supporting references*[40,46,52,59,63,67,69-87,89-95,100]*)*

3. In those individuals without a history of ischemic chest pain or aborted SCD, exercise stress testing combined with nuclear perfusion scan or echocardiographic imaging should be used to help assess the potential ischemic burden of the anatomic variant. *(Class I, Level of Evidence B—supporting references*[27,32,40,98,99]*)*
4. Cardiac catheterization should be performed in those individuals with anomalous origin of a coronary artery if the anatomy cannot be defined with noninvasive imaging, and in adults with risk factors for coexistent atherosclerotic coronary artery disease. *(Class I, Level of Evidence B—supporting references*[1,33-52]*)*

SECTION III: TREATMENT

Overview

Most would agree that activity restriction and surgical intervention is indicated in any patient with AAOCA who presents with signs and/or symptoms of myocardial ischemia, or has inducible ischemic changes with exercise testing. The treatment dilemma occurs when this diagnosis is made in the asymptomatic patient, especially the patient with AAORCA, as provocative testing is often negative. Treatment options for AAOCA include surgical and nonsurgical interventions and/or medical management.

Surgical Intervention

The clinical indication for intervention, even in those who are asymptomatic, is based on the calculated risk of SCD. Although an intervention is not warranted in most cases of coronary anomalies, there are some instances in which intervention may be warranted, including syncope associated with documented or reasonably suspected ventricular arrhythmia (nonvagally mediated), high-risk ambient ventricular arrhythmias, chest pain consistent with angina, aborted sudden death/cardiac arrest, and evidence of ischemia on provocative testing.[101,102] In those with interarterial AAOLCA, most children ages 10 and older are referred for surgical intervention, even if asymptomatic, due to the significantly increased risk of SCD with this anomaly, especially with exercise.[103] In contrast, there is far less agreement about whether patients with AAORCA without symptoms should undergo operation. Until recently, American College of Cardiology (ACC) and American Heart Association (AHA) guidelines have suggested avoidance of athletic activity for all patients with AAOCA and so for asymptomatic young patients with AAORCA, surgery has sometimes been performed to permit them to participate in competitive athletics.[104,105] The recent AHA/ACC Scientific Statement now differentiates between the much higher-risk interarterial AAOLCA and the lower-risk interarterial AAORCA, with the potential for those with AAORCA who are asymptomatic to return to competitive sports after a complete evaluation.[105] AAOLCA with intraseptal, prepulmonic, or retroaortic courses are generally considered benign with only rare case reports of ischemia.[106-108] These patients are generally not referred for surgery and are not exercise-restricted, but should have a stress test as part of preparticipation clearance for competitive athletics.

Once the decision to perform surgery has been made, several surgical procedures are available. These various approaches have not been compared in any rigorous fashion, and so the superiority of any one remains speculative. Each type of operation is performed to address 1 or more of the proposed mechanisms of myocardial ischemia in patients with AAOCA, as discussed previously.

Specific surgical procedures.

Unroofing. Among the various surgical options, perhaps the most technically and conceptually simple is the so-called ''unroofing'' procedure. It is the procedure of choice for interarterial, intramural AAOCA in the young patient.[109,110] The operation is accomplished via an anterior aortotomy and consists of incising the common wall between the aorta and intramural segment of the anomalous coronary artery (Figure 3). This incision has several salutary consequences in that it relocates the functional orifice to the appropriate sinus, enlarges the orifice significantly, eliminates the intramural component of the artery, and eliminates the portion of the vessel that lies between the great arteries.

There are 3 particular pitfalls to be avoided in the performance of the operation. The intramural course typically runs behind the intracoronary commissure, which might be damaged or distorted by the unroofing incision, potentially causing aortic insufficiency. Strategies for approaching this anatomic variant include resuspension of the commissure if it has been injured or creating a neo-ostium of the anomalous vessel by unroofing only that portion which is not behind the commissure (Figure 4).[53,111] Another potential difficulty with the unroofing procedure is the exposure of the layers of the aortic wall to systemic pressure at the site of the neo-ostium, creating the possibility for a localized dissection, which might occlude the coronary artery. This can be prevented by the placement of fine ''tacking'' sutures to approximate the layers of the aortic wall at the neo-ostium. An additional hazard of unroofing is seen with overly aggressive unroofing, whereby the incision is inadvertently carried through the aortic or coronary wall in an area in which the coronary is not actually intramural. This is particularly easy if the intramural component of the vessel is very short. If not recognized, this can result in troublesome bleeding, which requires very precisely placed sutures for repair, possibly necessitating an

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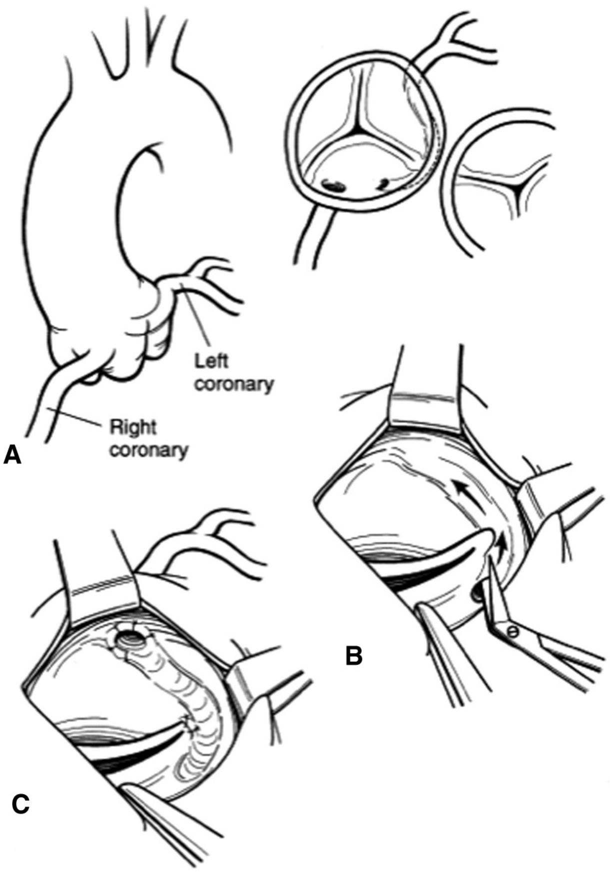

FIGURE 3. The unroofing technique in a patient with anomalous origin of the left coronary artery from the right sinus of Valsalva with an intramural course. The normally positioned right coronary artery orifice and the anomalous left coronary artery orifice can both be seen arising from the right sinus (A). The intramural segment of the anomalous coronary is unroofed and the common wall debulked (B) to create a neo-orifice in the left sinus (C). Reprinted with permission.[53]

additional period of cardioplegic arrest. Clearly the best approach to this complication is prevention.

Pulmonary artery translocation. This operation is based on the concept that the anomalous vessel is compressed or pinched between the great arteries in AAOCA, and therefore the goal of the operation is to reposition the main pulmonary artery (Figure 5).[112,113] This technique is mainly used when the anomalous coronary is not intramural but the ostia are in close approximation or if there is a single coronary artery in the presence of ischemia. This procedure consists of an initial meticulous dissection to permit full mobilization of the proximal pulmonary root. In one version of the operation, the main pulmonary artery is transected, the pulmonary confluence is patched, and the main pulmonary artery is anastomosed to a "neo-confluence" location created by making an incision well out onto the left pulmonary artery. In effect, this moves the course of the main pulmonary artery leftward, preventing it from compressing the anomalous coronary. An alternative version of the operation is accomplished by dividing the proximal right pulmonary artery at its origin and then transposing it anterior to the aorta, where it is re-anastomosed to its original site. This is usually accomplished by a tissue-to-tissue posterior wall suture line, with a generous augmentation patch placed anteriorly to prevent stenosis in the stretched right pulmonary artery. This version of the operation has the effect of moving the main pulmonary artery anteriorly and away from the anomalous coronary artery.

Reimplantation (ostial translocation). Reimplantation is perhaps most useful when there is little or no intramural component of the anomalous coronary and there are 2 separate ostia.[65,114-117] In this operation, the anomalous vessel is mobilized over its proximal course. Ideally, a few millimeters of aortic wall containing the ostium of the anomalous coronary is excised from its abnormal location, and then reimplanted in the correct sinus of Valsalva (Figure 6). Sometimes a patch of autologous pericardium is used to enlarge the connection. It is somewhat technically challenging in that it requires full mobilization of the anomalous vessel to avoid kinking as well as very precise patching and reimplantation.

Ostioplasty. In the ostial approach, a neo-ostium is created for the anomalous vessel in the sinus from which it would normally have exited. An incision is created in the aortic sinus with a matching incision in the coronary artery away from the aortic wall. By joining these incisions and augmenting the opened areas with a patch, typically of autologous pericardium, a neo-ostium is fashioned (Figure 7), and the course of the artery is no longer either intramural or between the great vessels.[118-120] The operation is facilitated by transection of the main pulmonary artery to optimize exposure, and requires meticulous reconstruction of the coronary artery itself. Of all of the surgical options, this is therefore probably the most technically challenging.

Bypass grafting. An indirect approach for AAOCA is to use standard coronary artery bypass techniques, with either a mammary artery or saphenous vein conduit.[121] This approach has generally been unsatisfactory because flow in the anomalous vessel is typically only compromised during periods of stress or exercise, so that there is substantial competitive flow the vast majority of the time.[122] The patency of a bypass graft in such a setting is likely to be disappointing. Ligation of the native vessel at its origin has been advocated by some as a solution to the issue of competitive flow, but concern has also been raised that a native mammary artery may have inadequate flow early on to replace all of the flow produced by a nonstenotic native coronary artery. Therefore, bypass grafting has a very limited role for AAOCA, and should probably be limited to settings in which the anomaly is accompanied by significant atherosclerotic narrowing or in which an alternative approach has been technically unsatisfactory.

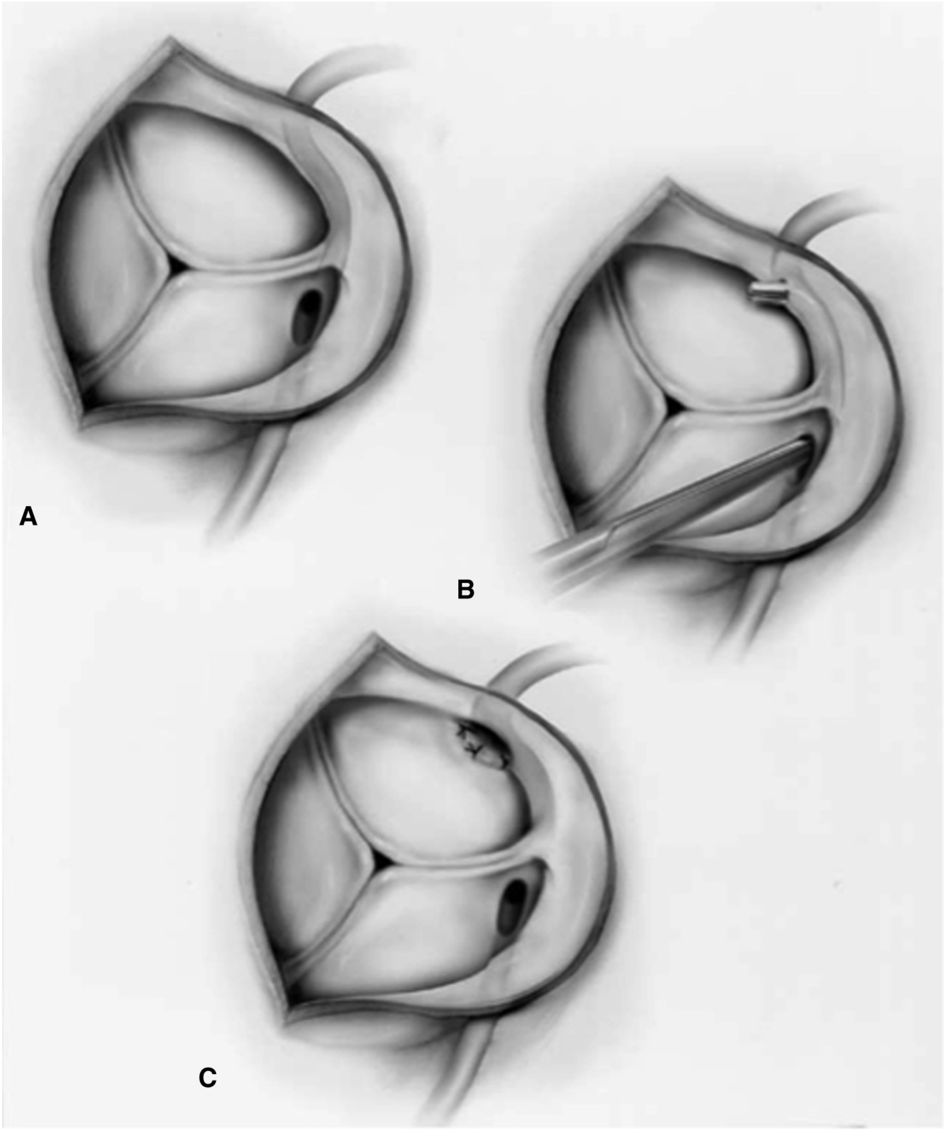

FIGURE 4. Unroofing procedure in which a neo-ostium was created without taking down the intercoronary commissure. A, The left coronary artery arises from the right sinus of Valsalva with an intramural course. The site for creation of a neo-ostium is identified by passing an instrument into the coronary (B). The anomalous coronary is unroofed into the appropriate sinus (C). Because the commissure between the left and right sinuses is not disrupted, this may decrease the risk of aortic valve regurgitation. A neo-ostium is created in that sinus at the point at which the artery leaves the aortic wall. Reprinted with permission.[111]

Summary of surgical approaches to AAOCA. In summary, surgical address of AAOCA may take 1 of several forms. For patients with significant intramural length of the anomalous vessel, unroofing is generally the preferred procedure. For patients with a very short or minimal intramural course, reimplantation or ostial reconstruction would be more appropriate. If the AAOCA is accompanied by atherosclerotic narrowing or if an alternative reconstruction technique has failed, coronary bypass grafting is reasonable. Pulmonary artery translocation techniques may be used to supplement any primary reconstruction, and are relatively low risk and technically simple adjuncts to other procedures.

The risk of surgery for AAOCA in published series is extremely low, with excellent intermediate-term survival.[32,40,56,58,59,65,72,82,96,105,111-113,119,123,124] Nevertheless, despite a patent coronary ostium, 1 study found that subclinical changes suggestive of ischemia occur on stress testing in more than one-third of postoperative patients.[96] Furthermore, although the surgical procedures may remove the hypothesized mechanism of ischemia leading to SCD, the long-term impact of surgery on the coronary arteries is unknown. Specifically, we do not know if these procedures place the patient at long-term risk of coronary stenosis due to scarring or accelerated atherosclerosis.

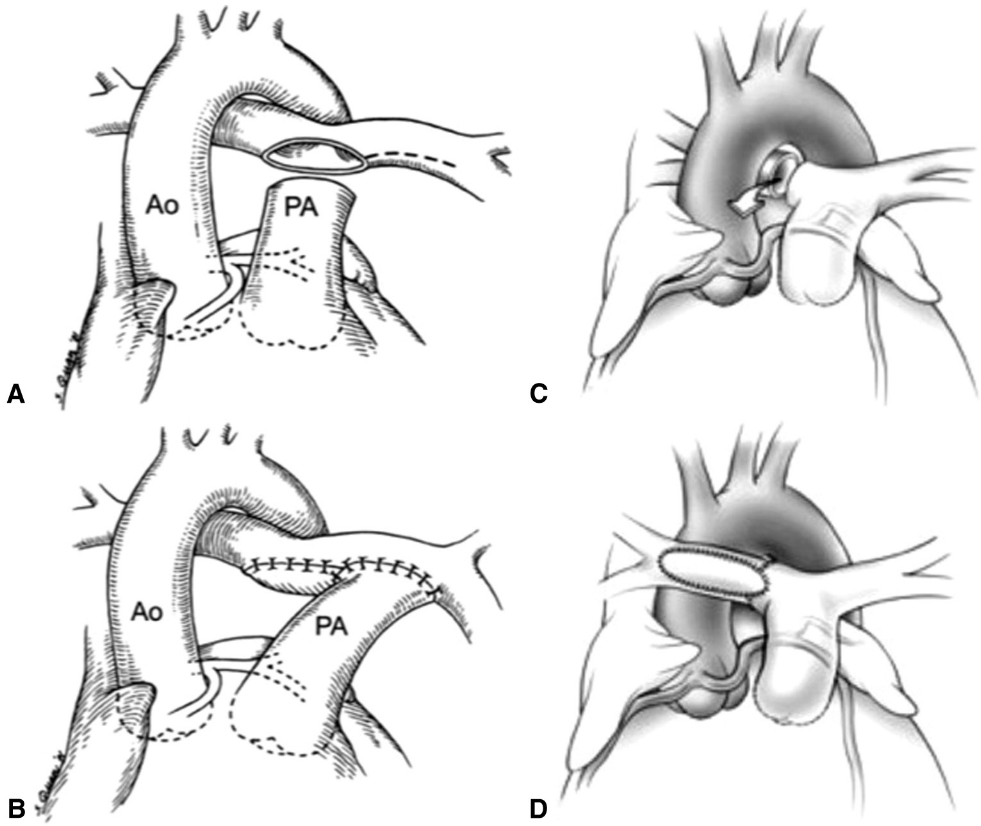

FIGURE 5. Illustration of the pulmonary artery translocation procedure. The distal main pulmonary artery is transected (A) and then relocated into the left pulmonary artery (B) to prevent compression of the anomalous coronary artery between the 2 great vessels. An alternative method involves transection of the right pulmonary artery at its origin (C). The right pulmonary artery is then brought anterior to the aorta and re-anastomosed to the main pulmonary with anterior patch augmentation (D). *Ao*, Aorta; *PA*, pulmonary artery. Reprinted with permission.[112]

Ongoing assessment of patients who have undergone surgery for AAOCA is essential to define the risks both short- and long-term.

Percutaneous Coronary Intervention

Before the development of the field of percutaneous coronary interventions (PCI), management of symptomatic or high-risk coronary arteries with anomalous origins, with or without superimposed atherosclerotic lesions, was limited to surgery and medical therapy directed at superimposed coronary vasospasm. The development of PCI technology has added the strategy of stenting the anomalous vessels, based on their anatomic take-off anatomy and coexisting lesions, with or without vasospasm. It has been suggested that intravascular ultrasound technology aids in the PCI approach to identifying and intervening for an ischemic burden associated with AAORCA, especially in those with a partial intramural course and proximal intramural stenosis.[125] There are no large-scale studies or registries comparing outcomes of surgery versus PCI, leaving evaluation limited to objective ischemic burden testing before and after interventions. Furthermore, long-term follow-up data are limited regarding this procedure in adults. Due to safety issues with stenting anomalous coronary arteries in growing children, this procedure is not advisable in the pediatric population, but may be considered in select cases in the adult population.

Medical Therapy

Beta-blockers. There are a small number of case reports using beta-blockers in adults to treat AAOCA.[126,127] The single largest series in the literature described 56 adult patients (average age 55.9 years) with beta-blockade and reported no episodes of SCD over a 5-year period.[99] In this study, however, there were no patients with AAOLCA and no patients younger than 30, both variables known to increase the risk of sudden death in patients with AAOCA. There are no reports of the use of beta-blockers in patients with AAOCA younger than 30 years. Presently, there does not appear to be adequate data to justify medical therapy for AAOCA.

Exercise restriction from competitive athletics. In the young patient, exercise restriction from competitive athletics is the most common nonsurgical strategy. The

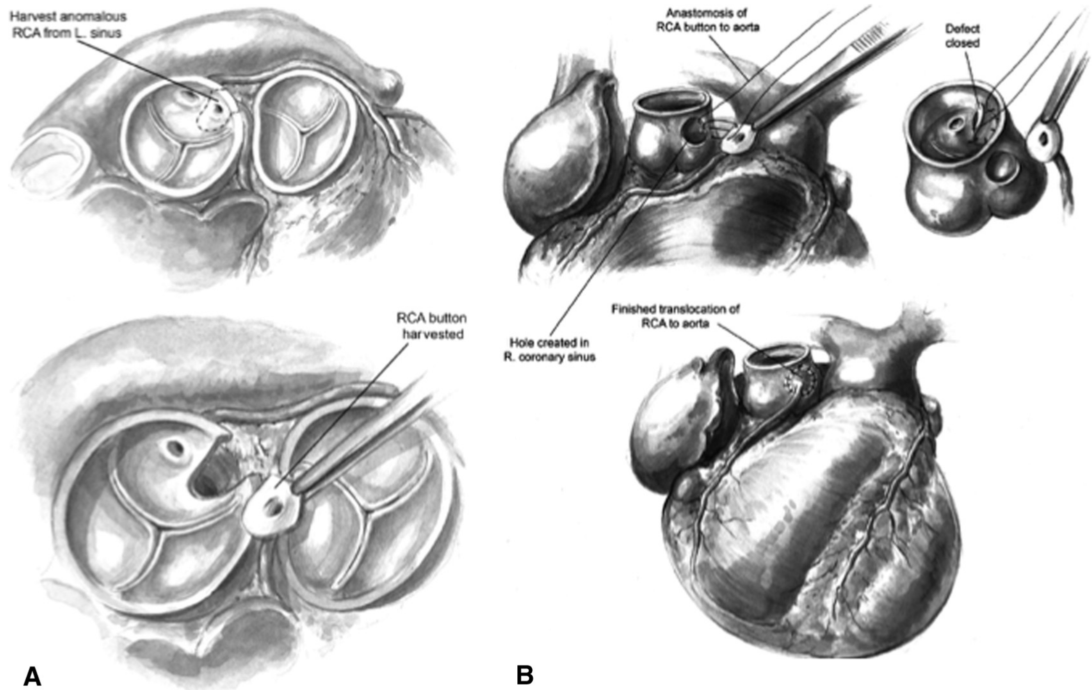

FIGURE 6. Direct reimplantation of an anomalous right coronary artery arising from the left sinus of Valsalva. A button of aortic sinus containing the anomalous coronary is excised and mobilized (A). The anomalous coronary is then reimplanted into the right sinus of Valsalva (B). *RCA*, Right coronary artery; *L*, left; *R*, right. Reprinted with permission.[116]

recommendation to avoid competitive athletics in patients with AAOCA is based on 2 observations: (1) the mortality risk associated with AAOCA is high, and (2) sudden death in patients with AAOCA occurs most frequently during or after peak exercise.[6,18,21-23,29] However, because children should remain active and discouraging exercise may lead to other issues with long-term cardiovascular health, asymptomatic children are encouraged to participate in physical education class and other recreational activities.

In contrast to previous recommendations, the current recommendations by the AHA/ACC permit individuals with unrepaired AAORCA who are without symptoms or a positive exercise stress test to participate in competitive sports.[105,128] It is important to note, however, that as of this report, there are no short- or long-term follow-up studies on unoperated patients with AAOCA who have been observed and restricted from competitive sports. The guidelines are generally based on Level of Evidence C, expert consensus opinions, in the absence of reliable objective clinical or epidemiological data. The one exception is surgery for interarterial AAOLCA, for which intervention is based on Level of Evidence B. To better address this issue, the Congenital Heart Surgeons' Society has established a Registry of Anomalous Aortic Origin of the Coronary Artery.[129] The overall purpose of the registry is to determine the outcome of surgical intervention versus observation in children and young adults with AAOCA, and to describe the natural and "unnatural" history of these patients over the course of their lifetime.

Observation without exercise restriction. If the cumulative risk for interarterial AAORCA is estimated at 0.2%, is it safer to observe than to recommend surgery? We must also take into account the risks of surgical intervention, the lack of long-term follow-up for these patients, and the few scattered reports of postoperative sudden death, ischemia, and other complications from surgery.[58,96,111,130]

We agree with the current AHA/ACC guidelines[51] in that participation in competitive sports may be a reasonable option for the asymptomatic patient with AAORCA without evidence of inducible ischemia, as this appears to be a more benign lesion than previously recognized. It is essential that we have a clear definition of "symptoms." Palpitations, chest pain, and even presyncope are common in the pediatric population and rarely have a cardiac etiology, whereas frank syncope and true anginalike chest pain with exercise are much less common and could be considered related to the coronary anomaly. Thus, even in the symptomatic patient, if all provocative testing for ischemia is negative, especially in the case in which the symptoms are replicated during the test and the test is normal, there is little reason to limit these individuals. In the absence of inducible ischemia on testing, there should be convincing historical evidence that the symptoms are likely due to ischemia or

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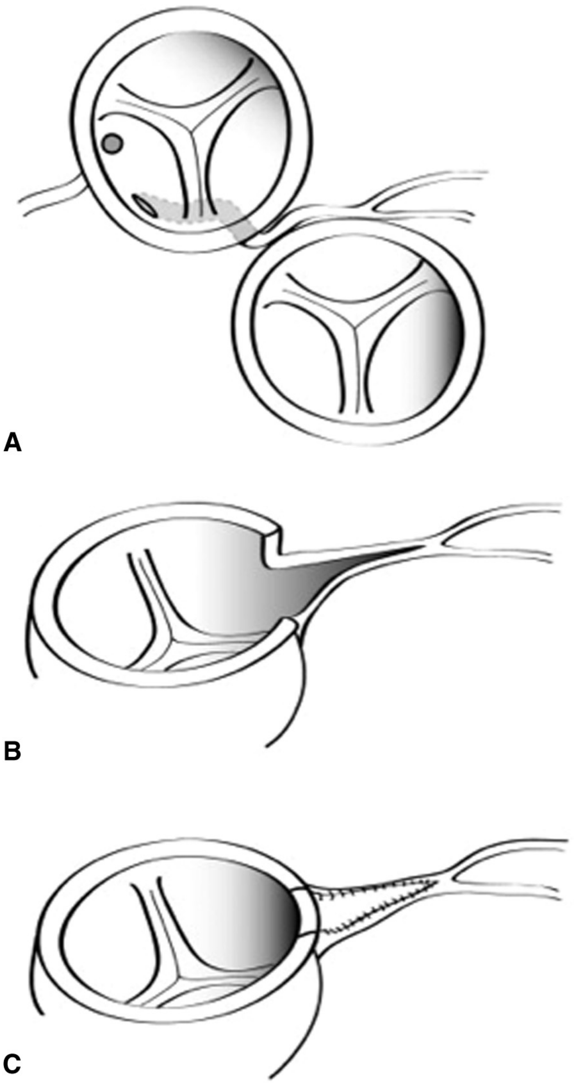

FIGURE 7. An ostioplasty for anomalous origin of the left coronary artery from the right sinus of Valsalva. A, The aorta and pulmonary artery have been transected above the commissures. The eccentric slit orifice in the opposite sinus of Valsalva, proximal intramural segment, nonorthogonal angle of exit, and interarterial course of the left coronary artery are demonstrated. B, The left coronary artery has been opened from its origin in the aorta to the bifurcation. C, An autologous pericardial patch is sutured into the coronary artery and aortic wall. Reprinted with permission.[119]

arrhythmias before restricting the individual from competitive athletics.

The decision to participate in competitive or high-intensity recreational sports should include a thorough family discussion and counseling regarding the risks and benefits of observation versus surgical management of this lesion. We recommend that automated external defibrillators (AEDs) should be available and accessible for sporting practices and competition.[131-143] The immediate availability of AEDs during competitive athletics is also recommended in the scientific statement concerning eligibility and disqualification of competitive athletes with cardiovascular abnormalities by the AHA and ACC.[144] For those with interarterial AAOLCA, even if asymptomatic, surgical repair is usually recommended, However, if after consultation with the family, they opt for no surgical intervention, the patient with AAOLCA should be restricted from competitive athletics.

RECOMMENDATIONS ON TREATMENT

5. Individuals with AAOCA and symptoms of ischemic chest pain or syncope suspected to be due to ventricular arrhythmias, or a history of aborted SCD, should be activity restricted and offered surgery. *(Class 1; Level of Evidence B—supporting references*[6,18,21-23,29,32,40,58,72,82,105,113,123,124]*)*
6. Individuals with AAOCA and symptoms of ischemic chest pain or syncope suspected to be due to ventricular arrhythmias, or a history of aborted SCD, should be activity restricted and if deemed prohibitively high risk for surgery, catheter-based intervention may be considered. *(Class IIb; Level of Evidence C)*
7. Individuals with or without symptoms with an unrepaired anomalous origin of a left coronary artery from the right sinus of Valsalva, with an interarterial course, should be restricted from participation in all competitive sports. *(Class 1; Level of Evidence B—supporting references*[6,18,21-23,29,105]*)*
8. Individuals without symptoms with anomalous origin of a left coronary artery from the right sinus of Valsalva with an interarterial course should be offered surgery. *(Class 1; Level of Evidence B—supporting references*[17-24]*)*
9. Individuals with an anomalous origin of a right coronary artery from the left sinus of Valsalva should be evaluated for inducible ischemia, using an exercise stress test with additional imaging, including stress echocardiography or nuclear perfusion imaging. For those without symptoms concerning for ischemia or a positive exercise stress test, and after counseling concerning the risk of SCD, participation in competitive athletics is permissible. *(Class IIa; Level of Evidence C)*
10. Surgery for repair of AAOCA from the opposite sinus of Valsalva should include elimination of the intramural course and any associated ostial narrowing by unroofing, ostioplasty, or reimplantation. *(Class I; Level of Evidence B—supporting references*[56,59,65,82,117,123]*)*
11. Repositioning of the pulmonary artery confluence away from the anomalous artery (laterally or anteriorly) may be considered as an adjunctive procedure. *(Class IIb; Level of Evidence C)*

TABLE 2. Recommended follow-up for AAOCA, surgical repair

Postoperative short-term follow-up (timeline respective to surgical date)
- 7-10 d: Cardiology appointment with ECG and echocardiogram
- 4-6 wk: Cardiology appointment with ECG and echocardiogram
- 3 mo: Cardiology appointment with exercise stress test with imaging
- 6 mo: Cardiology appointment with ECG and cardiac MRI, if available
- Remain on 1 baby aspirin daily indefinitely

Postoperative long-term medical follow-up
- Cardiology follow-up annually
- ECG annually
- Echocardiogram annually
- Exercise stress test every 1-3 y, depending on activity level
  - If participating in high-level recreational or competitive sports, exercise stress test annually
  - With nuclear perfusion or stress echocardiogram only if new symptoms
- Holter monitor as needed, if symptoms

Physical activity
- No competitive athletics until at least 3 mo after surgery and after a complete evaluation has been performed by the pediatric cardiologist
- No competitive athletics for at least 12 mo after surgery and after a complete evaluation has been performed by the pediatric cardiologist in those whose presentation was sudden cardiac arrest/aborted sudden death
- Patients should be counseled that they are to cease exercise until further evaluation by the cardiologist if any symptoms develop, such as chest pain, palpitations, or fainting, during or just after exercise
- Patient should be allowed to rest if he or she gets tired
- Patient should stay well-hydrated with water, aiming for at least 60 ounces of water daily, or more, based on his or her activity level

AAOCA, Anomalous aortic origin of a coronary artery; *ECG*, electrocardiogram; *MRI*, magnetic resonance imaging.

TABLE 3. Long-term follow-up and physical activity recommendations, unrestricted

Medical follow-up
- Cardiology follow-up annually
- Electrocardiogram annually
- Echocardiogram every 1-2 y
- Exercise stress test every 1-3 y, depending on activity level
  - If participating in high-level recreational or competitive sports, exercise stress test annually
  - With nuclear perfusion only if new symptoms
- Holter monitor as needed, if symptoms

Physical activity
- Full participation in competitive athletics
- Recommend automated external defibrillator at all team practices and sporting events
- Patients should be counseled that they are to cease exercise until further evaluation by a cardiologist if any symptoms develop, such as chest pain, palpitations, or fainting, during or just after exercise
- Patient should be allowed to rest if he or she gets tired
- Patient should stay well-hydrated with water, aiming for at least 60 ounces of water daily, or more, based on his or her activity level

SECTION IV: FOLLOW-UP

Ongoing Risk

The follow-up for patients with AAOCA will depend somewhat on the management chosen; however, all patients should be followed by a cardiologist for their lifetime. This should include a transition from a pediatric to an adult cardiologist, if necessary. Lifelong follow-up is especially important for those who undergo surgical repair, as long-term outcomes from surgical repair are largely unknown. Short- and mid-term complications have been noted, including mild aortic valve insufficiency, severe aortic valve insufficiency requiring aortic valve replacement, pericardial effusions, and ischemic changes on postoperative provocative testing.[96,109,111,145] Postoperative death has been reported rarely in the literature in both the pediatric and adult age groups.[82,146,147] The authors are aware of a handful of other pediatric deaths postoperatively that have not been published. It is interesting to note that, at least in the young, if a patient presents with SCD or SCA and survives the surgery, he or she may still be at increased risk for an SCD event once the patient returns to sport.[146]

Those who have undergone surgery will need close follow-up in the initial postoperative period, but will be able to lengthen the interval between visits after the first postoperative year. According to the recent AHA/ACC guidelines, these patients may return to competitive sports at least 3 months postoperatively and if an exercise stress test reveals no evidence of myocardial ischemia or ventricular arrhythmias.[104,105] However, those who present with true aborted SCD appear to remain at increased risk, even after surgical repair.[146] We would recommend those

TABLE 4. Follow-up and activity recommendations for AAOCA, restricted from competitive athletics

Medical follow-up
- Cardiology follow-up annually
- Electrocardiogram annually
- Echocardiogram every 1-2 y
- Exercise stress test every 1-3 y, depending on activity level
  - With nuclear perfusion only if new symptoms
- Holter monitor as needed, if symptoms

Physical activity
- No competitive sport at the middle school level or higher that requires moderate to vigorous activity levels (<40% maximum oxygen uptake and <20% maximal voluntary contraction)
  - Examples include running, soccer, tennis, swimming, basketball, baseball, football
- Participation at the middle school level or higher is allowed in those sports that require low activity levels
  - Examples include golf, bowling, cricket, archery, equestrian, karate
- Participation is allowed in recreational athletics, including gym class
- Patient should be allowed to rest if he or she gets tired
- Patient should stay well-hydrated with water, aiming for at least 60 ounces of water daily, or more, based on his or her activity level

patients with true SCA or aborted SCD should not return to competitive athletics for at least 1 year postoperatively and then only return to competitive athletics if they are free of symptoms and have a negative exercise stress test. Those managed conservatively with exercise restriction will need follow-up annually. Those patients who are not exercise-restricted should be seen annually, especially if they are participating in competitive athletics. Finally, when there is a family history of clustering of SCD as a first manifestation of any ischemic event, more specific counseling of risk-versus-benefit should be undertaken with both the athlete and family so they can make an informed decision about participation.[148] For further details, please refer to Tables 2-4, which are suggested protocols that we have created for follow-up of patients with AAOCA, based on their management.

Recommendations on Follow-up

12. Following surgical repair of an anomalous coronary artery, individuals without a history of aborted SCD should be offered the opportunity to return to competitive or recreational athletics after waiting at least 3 months after surgery, provided they have remained without symptoms concerning for ischemia or arrhythmia and an exercise stress test does not show evidence of myocardial ischemia or concerning arrhythmia. *(Class I; Level of Evidence C)*
13. Following surgical repair of an anomalous coronary artery, in an individual who presented with aborted SCD, it is reasonable to permit return to competitive athletics after a longer waiting period of 12 months after surgery provided the patient has remained without symptoms concerning for ischemia or arrhythmia and an exercise stress test does not show evidence of myocardial ischemia or concerning arrhythmia. *(Class IIa; Level of Evidence C)*
14. After surgical repair of an anomalous coronary artery, in an individual who presented with aborted SCD, it is reasonable to permit return to recreational sports, including physical education class, 3 months after surgery, provided the patient has remained without symptoms concerning for ischemia or arrhythmia and an exercise stress test does not show evidence of myocardial ischemia or concerning arrhythmia. *(Class IIa; Level of Evidence C)*
15. An automated external defibrillator with trained personnel should be immediately available during competition and training. *(Class 1; Level of Evidence B—supporting references[131-143])*

SECTION V: GAPS IN KNOWLEDGE

One major gap in knowledge regarding AAOCA is our ability to adequately risk stratify patients for surgery versus observation, notably in the asymptomatic young person with AAORCA. Although there are suspected anatomic and physiologic reasons for myocardial ischemia and/or potentially lethal arrhythmias, we are still unable to distinguish which person is at high risk for ischemia and should undergo surgery from the individual who will remain asymptomatic and may be allowed to participate in competitive sports. Another gap arises from our lack of long-term follow-up of patients after surgical repair. Short- and medium-term results are encouraging; however, there are reports of issues, such as new aortic valve regurgitation, that will need to be followed over time.

SECTION VI: SUMMARY AND RECOMMENDATIONS

Summary

AAOCA with an intramural course is associated with SCD, due to ischemia and arrhythmias. Although the risk for any single affected individual is small, the loss of an otherwise healthy person is particularly devastating. Surgical and interventional therapies have been developed that appear to be protective, but these therapies carry risks. The challenge is identifying those individuals at such risk that there is net benefit to the therapy. Although we acknowledge there is still much to be learned with this entity, the guidelines put forth in this article are based on best practice and knowledge regarding the risk of SCD that we have to date.

Recommendations

1. Individuals with suspected AAOCA should undergo transthoracic echocardiography to identify the origin and course of the proximal coronary arteries. *(Class I, Level of Evidence B—supporting references[11,27,32,53-65])*
2. Additional imaging studies, such as coronary CT angiography or cardiac MRI are reasonable to better visualize the coronary artery anatomy and to confirm the diagnosis. *(Class IIa, Level of Evidence B—supporting references[40,46,52,59,63,67,69-87,89-95,100])*
3. In those individuals without a history of ischemic chest pain or aborted SCD, exercise stress testing combined with nuclear perfusion scan or echocardiographic imaging should be used to help assess the potential ischemic burden of the anatomic variant. *(Class I, Level of Evidence B—supporting references[27,32,40,98,99])*
4. Cardiac catheterization should be performed in those individuals with anomalous origin of a coronary artery if the anatomy cannot be defined with noninvasive imaging, and in adults with risk factors for coexistent atherosclerotic coronary artery disease. *(Class I, Level of Evidence B—supporting references[1,33-52])*

5. Individuals with AAOCA and symptoms of ischemic chest pain or syncope suspected to be due to ventricular arrhythmias, or a history of aborted SCD, should be activity restricted and offered surgery. *(Class 1; Level of Evidence B—supporting references*[6,18,21-23,29,32,40,58,72,82,105,113,123,124]*)*
6. Individuals with AAOCA and symptoms of ischemic chest pain or syncope suspected to be due to ventricular arrhythmias, or a history of aborted SCD, should be activity restricted and if deemed prohibitively high risk for surgery, catheter-based intervention may be considered. *(Class IIb; Level of Evidence C)*
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8. Individuals without symptoms with anomalous origin of a left coronary artery from the right sinus of Valsalva with an interarterial course should be offered surgery. *(Class 1; Level of Evidence B—supporting references*[17-24]*)*
9. Individuals with an anomalous origin of a right coronary artery from the left sinus of Valsalva should be evaluated for inducible ischemia, using an exercise stress test with additional imaging, including stress echocardiography or nuclear perfusion imaging. For those without symptoms concerning for ischemia or a positive exercise stress test, and after counseling concerning the risk of SCD, participation in competitive athletics is permissible. *(Class IIa; Level of Evidence C)*
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11. Repositioning of the pulmonary artery confluence away from the anomalous artery (laterally or anteriorly) may be considered as an adjunctive procedure. *(Class IIb; Level of Evidence C)*
12. After surgical repair of an anomalous coronary artery, individuals without a history of aborted SCD should be offered the opportunity to return to competitive or recreational athletics after waiting at least 3 months after surgery, provided they have remained without symptoms concerning for ischemia or arrhythmia and an exercise stress test does not show evidence of myocardial ischemia or concerning arrhythmia. *(Class I; Level of Evidence C)*
13. After surgical repair of an anomalous coronary artery, in an individual who presented with aborted SCD, it is reasonable to permit return to competitive athletics after a longer waiting period of 12 months after surgery, provided the patient has remained without symptoms concerning for ischemia or arrhythmia and an exercise stress test does not show evidence of myocardial ischemia or concerning arrhythmia. *(Class IIa; Level of Evidence C)*
14. After surgical repair of an anomalous coronary artery, in an individual who presented with aborted SCD, it is reasonable to permit return to recreational sports, including physical education class, 3 months after surgery, provided the patient has remained without symptoms concerning for ischemia or arrhythmia and an exercise stress test does not show evidence of myocardial ischemia or concerning arrhythmia. *(Class IIa; Level of Evidence C)*
15. An automated external defibrillator with trained personnel should be immediately available during competition and training. *(Class 1; Level of Evidence B—supporting references*[131-143]*)*

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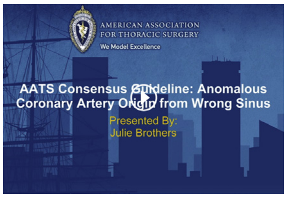

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

References

1. Yamanaka O, Hobbs RE. Coronary artery anomalies in 126,595 patients undergoing coronary arteriography. *Cathet Cardiovasc Diagn*. 1990;21:28-40.
2. Tuo G, Marasini M, Brunelli C, Zannini L, Balbi M. Incidence and clinical relevance of primary congenital anomalies of the coronary arteries in children and adults. *Cardiol Young*. 2013;23:381-6.
3. Labombarda F, Coutance G, Pellissier A, Mery-Alexandre C, Roule V, Maragnes P, et al. Major congenital coronary artery anomalies in a paediatric and adult population: a prospective echocardiographic study. *Eur Heart J Cardiovasc Imaging*. 2014;15:761-8.
4. Pelliccia A, Spataro A, Maron BJ. Prospective echocardiographic screening for coronary artery anomalies in 1,360 elite competitive athletes. *Am J Cardiol*. 1993;72:978-9.
5. Davis JA, Cecchin F, Jones TK, Portman MA. Major coronary artery anomalies in a pediatric population: incidence and clinical importance. *J Am Coll Cardiol*. 2001;37:593-7.
6. Maron BJ, Shirani J, Poliac LC, Mathenge R, Roberts WC, Mueller FO. Sudden death in young competitive athletes. Clinical, demographic, and pathological profiles. *JAMA*. 1996;276:199-204.

7. Angelini P. Novel imaging of coronary artery anomalies to assess their prevalence, the causes of clinical symptoms, and the risk of sudden cardiac death. *Circ Cardiovasc Imaging*. 2014;7:747-54.
8. Angelini P. Coronary artery anomalies: an entity in search of an identity. *Circulation*. 2007;115:1296-305.
9. Bloor CM, Leon AS, Pitt B. The inheritance of coronary artery anatomic patterns in rats. *Circulation*. 1967;36:771-6.
10. Laureti JM, Singh K, Blankenship J. Anomalous coronary arteries: a familial clustering. *Clin Cardiol*. 2005;28:488-90.
11. Brothers JA, Stephens P, Gaynor JW, Lorber R, Vricella LA, Paridon SM. Anomalous aortic origin of a coronary artery with an interarterial course: should family screening be routine? *J Am Coll Cardiol*. 2008;51:2062-4.
12. Devanagondi R, Brenner J, Vricella L, Ravekes W. A tale of two brothers: anomalous coronary arteries in two siblings. *Pediatr Cardiol*. 2008;29:816-9.
13. Friedlander Y, Siscovick DS, Weinmann S, Austin MA, Psaty BM, Lemaitre RN, et al. Family history as a risk factor for primary cardiac arrest. *Circulation*. 1998;97:155-60.
14. Jouven X, Desnos M, Guerot C, Ducimetiere P. Predicting sudden death in the population: the Paris Prospective Study I. *Circulation*. 1999;99:1978-83.
15. Dekker LR, Bezzina CR, Henriques JP, Tanck MW, Koch KT, Alings MW, et al. Familial sudden death is an important risk factor for primary ventricular fibrillation: a case-control study in acute myocardial infarction patients. *Circulation*. 2006;114:1140-5.
16. Kaikkonen KS, Kortelainen ML, Linna E, Huikuri HV. Family history and the risk of sudden cardiac death as a manifestation of an acute coronary event. *Circulation*. 2006;114:1462-7.
17. 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*. 1974;50:780-7.
18. Taylor AJ, Byers JP, Cheitlin MD, Virmani R. 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*. 1997;133:428-35.
19. Roberts WC, Siegel RJ, Zipes DP. Origin of the right coronary artery from the left sinus of valsalva and its functional consequences: analysis of 10 necropsy patients. *Am J Cardiol*. 1982;49:863-8.
20. Taylor AJ, Rogan KM, Virmani R. Sudden cardiac death associated with isolated congenital coronary artery anomalies. *J Am Coll Cardiol*. 1992;20:640-7.
21. 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*. 1988;62:771-7.
22. Meyer L, Stubbs B, Fahrenbruch C, Maeda C, Harmon K, Eisenberg M, et al. Incidence, causes, and survival trends from cardiovascular-related sudden cardiac arrest in children and young adults 0 to 35 years of age: a 30-year review. *Circulation*. 2012;126:1363-72.
23. Pilmer CM, Kirsh JA, Hildebrandt D, Krahn AD, Gow RM. Sudden cardiac death in children and adolescents between 1 and 19 years of age. *Heart Rhythm*. 2014;11:239-45.
24. Basso C, Maron BJ, Corrado D, Thiene G. 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.
25. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980-2006. *Circulation*. 2009;119:1085-92.
26. Maron BJ, Haas TS, Ahluwalia A, Rutten-Ramos SC. Incidence of cardiovascular sudden deaths in Minnesota high school athletes. *Heart Rhythm*. 2013; 10:374-7.
27. Brothers J, Carter C, McBride M, Spray T, Paridon S. Anomalous left coronary artery origin from the opposite sinus of Valsalva: evidence of intermittent ischemia. *J Thorac Cardiovasc Surg*. 2010;140:e27-9.
28. Solberg EE, Borjesson M, Sharma S, Papadakis M, Wilhelm M, Drezner JA, et al. Sudden cardiac arrest in sports—need for uniform registration: a position paper from the Sport Cardiology Section of the European Association for Cardiovascular Prevention and Rehabilitation. *Eur J Prev Cardiol*. 2016;23: 657-67.
29. Marijon E, Tafflet M, Celermajer DS, Dumas F, Perier MC, Mustafic H, et al. Sports-related sudden death in the general population. *Circulation*. 2011;124: 672-81.
30. Roberts WO, Asplund CA, O'Connor FG, Stovitz SD. Cardiac preparticipation screening for the young athlete: why the routine use of ECG is not necessary. *J Electrocardiol*. 2015;48:311-5.
31. Eckart RE, Scoville SL, Campbell CL, Shry EA, Stajduhar KC, Potter RN, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med*. 2004;141:829-34.
32. Osaki M, McCrindle BW, Van Arsdell G, Dipchand AI. Anomalous origin of a coronary artery from the opposite sinus of Valsalva with an interarterial course: clinical profile and approach to management in the pediatric population. *Pediatr Cardiol*. 2008;29:24-30.
33. Sivri N, Aktoz M, Yalta K, Ozcelik F, Altun A. A retrospective study of angiographic ally determined anomalous coronary arteries in 12,844 subjects in Thrace region of Turkey. *Hippokratia*. 2012;16:246-9.
34. Turkmen S, Cagliyan CE, Poyraz F, Sercelik A, Boduroglu Y, Akilli RE, et al. Coronary arterial anomalies in a large group of patients undergoing coronary angiography in southeast Turkey. *Folia Morphol (Warsz)*. 2013; 72:123-7.
35. Sarkar K, Sharma SK, Kini AS. Catheter selection for coronary angiography and intervention in anomalous right coronary arteries. *J Interv Cardiol*. 2009; 22:234-9.
36. Jim MH, Siu CW, Ho HH, Miu R, Lee SW. Anomalous origin of the right coronary artery from the left coronary sinus is associated with early development of coronary artery disease. *J Invasive Cardiol*. 2004;16:466-8.
37. Topaz O, DeMarchena EJ, Perin E, Sommer LS, Mallon SM, Chahine RA. Anomalous coronary arteries: angiographic findings in 80 patients. *Int J Cardiol*. 1992;34:129-38.
38. Donaldson RM, Raphael M, Radley-Smith R, Yacoub MH, Ross DN. Angiographic identification of primary coronary anomalies causing impaired myocardial perfusion. *Cathet Cardiovasc Diagn*. 1983;9:237-49.
39. Uthayakumaran K, Subban V, Lakshmanan A, Pakshirajan B, Solirajaram R, Krishnamoorthy J, et al. Coronary intervention in anomalous origin of the right coronary artery (ARCA) from the left sinus of valsalva (LSOV): a single center experience. *Indian Heart J*. 2014;66:430-4.
40. Cho SH, Joo HC, Yoo KJ, Youn YN. Anomalous origin of right coronary artery from left coronary sinus: surgical management and clinical result. *Thorac Cardiovasc Surg*. 2015;63:360-6.
41. Heo W, Min HK, Kang DK, Jun HJ, Hwang YH, Lee HC. Three different situations and approaches in the management for anomalous origin of the right coronary artery from the left coronary sinus: case report. *J Cardiothorac Surg*. 2014;9:21.
42. Yuksel S, Meric M, Soylu K, Gulel O, Zengin H, Demircan S, et al. The primary anomalies of coronary artery origin and course: a coronary angiographic analysis of 16,573 patients. *Exp Clin Cardiol*. 2013;18:121-3.
43. Yildiz A, Okcun B, Peker T, Arslan C, Olcay A, Bulent Vatan M. Prevalence of coronary artery anomalies in 12,457 adult patients who underwent coronary angiography. *Clin Cardiol*. 2010;33:E60-4.
44. Ouali S, Neffeti E, Sendid K, Elghoul K, Remedi F, Boughzela E. Congenital anomalous aortic origins of the coronary arteries in adults: a Tunisian coronary arteriography study. *Arch Cardiovasc Dis*. 2009;102:201-8.
45. Hamzeh G, Crespo A, Estaran R, Rodriguez MA, Voces R, Aramendi JI. Anomalous origin of right coronary artery from left coronary sinus. *Asian Cardiovasc Thorac Ann*. 2008;16:305-8.
46. Zemanek D, Veselka J, Kautznerova D, Tesar D. The anomalous origin of the left coronary artery from the right aortic sinus: is the coronary angiography still a 'gold standard'? *Int J Cardiovasc Imaging*. 2006;22:127-33.
47. Mavi A, Ayalp R, Sercelik A, Pestemalci T, Batyraliev T, Gumusburun E. Frequency in the anomalous origin of the left main coronary artery with angiography in a Turkish population. *Acta Med Okayama*. 2004;58:17-22.
48. Rigatelli G, Docali G, Rossi P, Bovolon D, Rossi D, Bandello A, et al. Congenital coronary artery anomalies angiographic classification revisited. *Int J Cardiovasc Imaging*. 2003;19:361-6.
49. Ayalp R, Mavi A, Sercelik A, Batyraliev T, Gumusburun E. Frequency in the anomalous origin of the right coronary artery with angiography in a Turkish population. *Int J Cardiol*. 2002;82:253-7.
50. Yip H, Chen MC, Wu CJ, Yeh KH, Fu M, Hang CL, et al. Primary angioplasty in acute inferior myocardial infarction with anomalous-origin right coronary arteries as infarct-related arteries: focus on anatomic and clinical features, outcomes, selection of guiding catheters and management. *J Invasive Cardiol*. 2001;13:290-7.
51. Garg N, Tewari S, Kapoor A, Gupta DK, Sinha N. Primary congenital anomalies of the coronary arteries: a coronary: arteriographic study. *Int J Cardiol*. 2000;74:39-46.
52. Post JC, van Rossum AC, Bronzwaer JG, de Cock CC, Hofman MB, Valk J, et al. Magnetic resonance angiography of anomalous coronary arteries. A

new gold standard for delineating the proximal course? *Circulation*. 1995;92: 3163-71.

53. Frommelt PC, Frommelt MA, Tweddell JS, Jaquiss RD. Prospective echocardiographic diagnosis and surgical repair of anomalous origin of a coronary artery from the opposite sinus with an interarterial course. *J Am Coll Cardiol*. 2003;42:148-54.
54. Thankavel PP, Lemler MS, Ramaciotti C. Utility and importance of new echocardiographic screening methods in diagnosis of anomalous coronary origins in the pediatric population: assessment of quality improvement. *Pediatr Cardiol*. 2015;36:120-5.
55. Thankavel PP, Balakrishnan PL, Lemler MS, Ramaciotti C. Anomalous left main coronary artery origin from the right sinus of Valsalva: a novel echocardiographic screening method. *Pediatr Cardiol*. 2013;34:842-6.
56. Turner II, Turek JW, Jaggers J, Herlong JR, Lawson DS, Lodge AJ. Anomalous aortic origin of a coronary artery: preoperative diagnosis and surgical planning. *World J Pediatr Congenit Heart Surg*. 2011;2:340-5.
57. Badano LP, Muraru D, Onut R, Lestuzzi C, Toso F. Three-dimensional imaging of anomalous origin of the right coronary artery in a young athlete. *Eur J Echocardiogr*. 2011;12:481.
58. Frommelt PC, Sheridan DC, Berger S, Frommelt MA, Tweddell JS. 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*. 2011;142:1046-51.
59. Mumtaz MA, Lorber RE, Arruda J, Pettersson GB, Mavroudis C. Surgery for anomalous aortic origin of the coronary artery. *Ann Thorac Surg*. 2011;91: 811-4; discussion 814-5.
60. Schreiber C, Libera P, Samprec J, Malcic I, Eicken A, Lange R. Ostial patch plasty of an aberrant right coronary artery in a symptomatic teenager. *Heart Surg Forum*. 2009;12:E57-8.
61. Bria S, Chessa M, Abella R, Frigiola A, Bianco M, Palmieri V, et al. Aborted sudden death in a young football player due to anomalous origin of the left coronary artery: successful surgical correction. *J Cardiovasc Med (Hagerstown)*. 2008;9:834-8.
62. Herrmann JL, Goldberg LA, Khan AM, Partington SL, Brothers JA, Mascio CE, et al. A comparison of perioperative management of anomalous aortic origin of a coronary artery between an adult and pediatric cardiac center. *World J Pediatr Congenit Heart Surg*. 2016;7:721-6.
63. Lee S, Uppu SC, Lytrivi ID, Sanz J, Weigand J, Geiger MK, et al. Utility of multimodality imaging in the morphologic characterization of anomalous aortic origin of a coronary artery. *World J Pediatr Congenit Heart Surg*. 2016;7: 308-17.
64. Lorber R, Srivastava S, Wilder TJ, McIntyre S, DeCampli WM, Williams WG, et al. Anomalous aortic origin of coronary arteries in the young: echocardiographic evaluation with surgical correlation. *JACC Cardiovasc Imaging*. 2015;8:1239-49.
65. Erez E, Tam VK, Doublin NA, Stakes J. Anomalous coronary artery with aortic origin and course between the great arteries: improved diagnosis, anatomic findings, and surgical treatment. *Ann Thorac Surg*. 2006;82:973-7.
66. Ropers D, Moshage W, Daniel WG, Jessl J, Gottwik M, Achenbach S. Visualization of coronary artery anomalies and their anatomic course by contrast-enhanced electron beam tomography and three-dimensional reconstruction. *Am J Cardiol*. 2001;87:193-7.
67. Deibler AR, Kuzo RS, Vohringer M, Page EE, Safford RE, Patron JN, et al. Imaging of congenital coronary anomalies with multislice computed tomography. *Mayo Clin Proc*. 2004;79:1017-23.
68. Schmid M, Achenbach S, Ludwig J, Baum U, Anders K, Pohle K, et al. Visualization of coronary artery anomalies by contrast-enhanced multi-detector row spiral computed tomography. *Int J Cardiol*. 2006;111:430-5.
69. Datta J, White CS, Gilkeson RC, Meyer CA, Kansas S, Jani ML, et al. Anomalous coronary arteries in adults: depiction at multi-detector row CT angiography. *Radiology*. 2005;235:812-8.
70. Hirono K, Hata Y, Miyao N, Nakaoka H, Saito K, Ibuki K, et al. Anomalous origin of the right coronary artery evaluated with multidetector computed tomography and its clinical relevance. *J Cardiol*. 2016;68:196-201.
71. Clark RA, Marler AT, Lin CK, McDonough RJ, Prentice RL, Malik JA, et al. A review of anomalous origination of a coronary artery from an opposite sinus of Valsalva (ACAOS) impact on major adverse cardiovascular events based on coronary computerized tomography angiography: a 6-year single center review. *Ther Adv Cardiovasc Dis*. 2014;8:237-41.
72. Sharma V, Burkhart HM, Dearani JA, Suri RM, Daly RC, Park SJ, et al. Surgical unroofing of anomalous aortic origin of a coronary artery: a single-center experience. *Ann Thorac Surg*. 2014;98:941-5.
73. Rajbanshi BG, Burkhart HM, Schaff HV, Daly RC, Phillips SD, Dearani JA. Surgical strategies for anomalous origin of coronary artery from pulmonary artery in adults. *J Thorac Cardiovasc Surg*. 2014;148: 220-4.
74. Opolski MP, Pregowski J, Kruk M, Witkowski A, Kwiecinska S, Lubienska E, 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.
75. Park JH, Kwon NH, Kim JH, Ko YJ, Ryu SH, Ahn SJ, et al. Prevalence of congenital coronary artery anomalies of Korean men detected by coronary computed tomography. *Korean Circ J*. 2013;43:7-12.
76. Turkvatan A, Guray Y, Altinsoy D. Multidetector computed tomography imaging of coronary artery anomalies. *Cardiol Young*. 2013;23:661-74.
77. Rabelo DR, Barros MV, Nunes Mdo C, Oliveira CC, Siqueira MH. Multislice coronary angiotomography in the assessment of coronary artery anomalous origin. *Arq Bras Cardiol*. 2012;98:266-72.
78. Xu H, Zhu Y, Zhu X, Tang L, Xu Y. Anomalous coronary arteries: depiction at dual-source computed tomographic coronary angiography. *J Thorac Cardiovasc Surg*. 2012;143:1286-91.
79. Miller JA, Anavekar NS, El Yaman MM, Burkhart HM, Miller AJ, Julsrud PR. Computed tomographic angiography identification of intramural segments in anomalous coronary arteries with interarterial course. *Int J Cardiovasc Imaging*. 2012;28:1525-32.
80. Kaushal S, Backer CL, Popescu AR, Walker BL, Russell HM, Koenig PR, et al. Intramural coronary length correlates with symptoms in patients with anomalous aortic origin of the coronary artery. *Ann Thorac Surg*. 2011;92:986-91; discussion 991-2.
81. Tariq R, Kureshi SB, Siddiqui UT, Ahmed R. Congenital anomalies of coronary arteries: diagnosis with 64 slice multidetector CT. *Eur J Radiol*. 2012;81: 1790-7.
82. Davies JE, Burkhart HM, Dearani JA, Suri RM, Phillips SD, Warnes CA, et al. Surgical management of anomalous aortic origin of a coronary artery. *Ann Thorac Surg*. 2009;88:844-7; discussion 847-8.
83. Zhang LJ, Wu SY, Huang W, Zhou CS, Lu GM. Anomalous origin of the right coronary artery originating from the left coronary sinus of Valsalva with an interarterial course: diagnosis and dynamic evaluation using dual-source computed tomography. *J Comput Assist Tomogr*. 2009;33: 348-53.
84. Srinivasan KG, Gaikwad A, Kannan BR, Ritesh K, Ushanandini KP. Congenital coronary artery anomalies: diagnosis with 64 slice multidetector row computed tomography coronary angiography: a single-centre study. *J Med Imaging Radiat Oncol*. 2008;52:148-54.
85. Ichikawa M, Sato Y, Komatsu S, Hirayama A, Kodama K, Saito S. Multislice computed tomographic findings of the anomalous origins of the right coronary artery: evaluation of possible causes of myocardial ischemia. *Int J Cardiovasc Imaging*. 2007;23:353-60.
86. El-Menyar AA, Das KM, Al-Suwaidi J. Anomalous origin of the three coronary arteries from the right aortic sinus Valsalva: role of MDCT coronary angiography. *Int J Cardiovasc Imaging*. 2006;22:723-9.
87. Schmitt R, Froehner S, Brunn J, Wagner M, Brunner H, Cherevatyy O, et al. Congenital anomalies of the coronary arteries: imaging with contrast-enhanced, multidetector computed tomography. *Eur Radiol*. 2005;15:1110-21.
88. Sato Y, Inoue F, Matsumoto N, Tani S, Takayama T, Yoda S, et al. Detection of anomalous origins of the coronary artery by means of multislice computed tomography. *Circ J*. 2005;69:320-4.
89. Brothers JA, Kim TS, Fogel MA, Whitehead KK, Morrison TM, Paridon SM, et al. Cardiac magnetic resonance imaging characterizes stenosis, perfusion, and fibrosis preoperatively and postoperatively in children with anomalous coronary arteries. *J Thorac Cardiovasc Surg*. 2016;152:205-10.
90. Brothers JA, Whitehead KK, Keller MS, Fogel MA, Paridon SM, Weinberg PM, et al. Cardiac MRI and CT: differentiation of normal ostium and intraseptal course from slitlike ostium and interarterial course in anomalous left coronary artery in children. *AJR Am J Roentgenol*. 2015;204:W104-9.
91. Clemente A, Del Borrello M, Greco P, Mannella P, Di Gregorio F, Romano S, et al. Anomalous origin of the coronary arteries in children: diagnostic role of three-dimensional coronary MR angiography. *Clin Imaging*. 2010;34:337-43.
92. Prakken NH, Cramer MJ, Olimulder MA, Agostoni P, Mali WP, Velthuis BK. Screening for proximal coronary artery anomalies with 3-dimensional MR coronary angiography. *Int J Cardiovasc Imaging*. 2010;26:701-10.

93. Mavrogeni S, Spargias K, Karagiannis S, Kariofilis P, Cokkinos DD, Douskou M, et al. Anomalous origin of right coronary artery: magnetic resonance angiography and viability study. *Int J Cardiol*. 2006;109:195-200.
94. Klessen C, Post F, Meyer J, Thelen M, Kreitner KF. Depiction of anomalous coronary vessels and their relation to the great arteries by magnetic resonance angiography. *Eur Radiol*. 2000;10:1855-7.
95. White CS, Laskey WK, Stafford JL, NessAiver M. Coronary MRA: use in assessing anomalies of coronary artery origin. *J Comput Assist Tomogr*. 1999;23:203-7.
96. Brothers JA, McBride MG, Seliem MA, Marino BS, Tomlinson RS, Pampaloni MH, 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.
97. Cheitlin MD, MacGregor J. Congenital anomalies of coronary arteries: role in the pathogenesis of sudden cardiac death. *Herz*. 2009;34:268-79.
98. De Luca L, Bovenzi F, Rubini D, Niccoli-Asabella A, Rubini G, De Luca I. Stress-rest myocardial perfusion SPECT for functional assessment of coronary arteries with anomalous origin or course. *J Nucl Med*. 2004;45:532-6.
99. Kaku B, Shimizu M, Yoshio H, Ino H, Mizuno S, Kanaya H, et al. Clinical features of prognosis of Japanese patients with anomalous origin of the coronary artery. *Jpn Circ J*. 1996;60:731-41.
100. Sato Y, Inoue F, Kunimasa T, Matsumoto N, Yoda S, Tani S, et al. Diagnosis of anomalous origin of the right coronary artery using multislice computed tomography: evaluation of possible causes of myocardial ischemia. *Heart Vessels*. 2005;20:298-300.
101. Penalver JM, Mosca RS, Weitz D, Phoon CK. Anomalous aortic origin of coronary arteries from the opposite sinus: a critical appraisal of risk. *BMC Cardiovasc Disord*. 2012;12:83.
102. Warnes CA, Williams RG, Bashore TM, Child JS, Connolly HM, Dearani JA, et al. ACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to develop guidelines on the management of adults with congenital heart disease). *Circulation*. 2008;118:e714-833.
103. Poynter JA, Williams WG, McIntyre S, Brothers JA, Jacobs ML. Congenital Heart Surgeons Society AAOCA Working Group. Anomalous aortic origin of a coronary artery: a report from the Congenital Heart Surgeons Society Registry. *World J Pediatr Congenit Heart Surg*. 2014;5:22-30.
104. Warnes CA, Williams RG, Bashore TM, Child JS, Connolly HM, Dearani JA, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Developed in collaboration with the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2008;52:e143-263.
105. Van Hare GF, Ackerman MJ, Evangelista JA, Kovacs RJ, Myerburg RJ, Shafer KM, 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.
106. Chaitman BR, Lesperance J, Saltiel J, Bourassa MG. Clinical, angiographic, and hemodynamic findings in patients with anomalous origin of the coronary arteries. *Circulation*. 1976;53:122-31.
107. Kothari SS, Talwar KK, Venugopal P. Septal course of the left main coronary artery from right aortic sinus and ventricular tachycardia. *Int J Cardiol*. 1998;66:207-9.
108. Murphy DA, Roy DL, Sohal M, Chandler BM. Anomalous origin of left main cononary artery from anterior sinus of Valsalva with myocardial infarction. *J Thorac Cardiovasc Surg*. 1978;75:282-5.
109. Poynter JA, Bondarenko I, Austin EH, DeCampli WM, Jacobs JP, Ziemer G, et al. Repair of anomalous aortic origin of a coronary artery in 113 patients: a Congenital Heart Surgeons' Society report. *World J Pediatr Congenit Heart Surg*. 2014;5:507-14.
110. Mustafa I, Gula G, Radley-Smith R, Durrer S, Yacoub M. Anomalous origin of the left coronary artery from the anterior aortic sinus: a potential cause of sudden death. Anatomic characterization and surgical treatment. *J Thorac Cardiovasc Surg*. 1981;82:297-300.
111. Romp RL, Herlong JR, Landolfo CK, Sanders SP, Miller CE, Ungerleider RM, et al. Outcome of unroofing procedure for repair of anomalous aortic origin of left or right coronary artery. *Ann Thorac Surg*. 2003;76:589-95; discussion 595-6.
112. Mainwaring RD, Reddy VM, Reinhartz O, Petrossian E, MacDonald M, Nasirov T, et al. Anomalous aortic origin of a coronary artery: medium-term results after surgical repair in 50 patients. *Ann Thorac Surg*. 2011;92:691-7.
113. Mainwaring RD, Reddy VM, Reinhartz O, Petrossian E, Punn R, Hanley FL. Surgical repair of anomalous aortic origin of a coronary artery. *Eur J Cardiothorac Surg*. 2014;46:20-6.
114. Rogers SO Jr, Leacche M, Mihaljevic T, Rawn JD, Byrne JG. Surgery for anomalous origin of the right coronary artery from the left aortic sinus. *Ann Thorac Surg*. 2004;78:1829-31.
115. Lee MK, Choi JB, Kim KH, Kim KS. Surgery for anomalous origin of the left main coronary artery from the right sinus of Valsalva, in association with left main stenosis. *Tex Heart Inst J*. 2009;36:309-12.
116. Jaggers J, Lodge AJ. Surgical therapy for anomalous aortic origin of the coronary arteries. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2005;122-7.
117. Law T, Dunne B, Stamp N, Ho KM, Andrews D. Surgical results and outcomes after reimplantation for the management of anomalous aortic origin of the right coronary artery. *Ann Thorac Surg*. 2016;102:192-8.
118. Han WS, Park PW, Cho SH. Neo-ostium formation in anomalous origin of the left coronary artery. *Korean J Thorac Cardiovasc Surg*. 2011;44:355-7.
119. Alphonso N, Anagnostopoulos PV, Nolke L, Moon-Grady A, Azakie A, Raff GW, et al. Anomalous coronary artery from the opposite sinus of Valsalva: a physiologic repair strategy. *Ann Thorac Surg*. 2007;83:1472-6.
120. Gaudin R, Raisky O, Vouhe PR. Anomalous aortic origin of coronary arteries: 'anatomical' surgical repair. *Multimed Man Cardiothorac Surg*. 2014;2014:mmt022.
121. Reul RM, Cooley DA, Hallman GL, Reul GJ. Surgical treatment of coronary artery anomalies: report of a 37 1/2-year experience at the Texas Heart Institute. *Tex Heart Inst J*. 2002;29:299-307.
122. Fedoruk LM, Kern JA, Peeler BB, Kron IL. Anomalous origin of the right coronary artery: right internal thoracic artery to right coronary artery bypass is not the answer. *J Thorac Cardiovasc Surg*. 2007;133:456-60.
123. Mainwaring RD, Murphy DJ, Rogers IS, Chan FP, Petrossian E, Palmon M, et al. Surgical repair of 115 patients with anomalous aortic origin of a coronary artery from a single institution. *World J Pediatr Congenit Heart Surg*. 2016;7:353-9.
124. Law W, DiBardino DJ, Raviendren R, Devaney E, Davis C. Anomalous aortic origin of the left coronary artery: in-hospital cardiac arrest and death despite bed rest. *World J Pediatr Congenit Heart Surg*. 2014;5:580-2.
125. Angelini P, Uribe C, Monge J, Tobis JM, Elayda MA, Willerson JT. 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.
126. Bixby MB. Successful medical management of a patient with an anomalous right coronary artery who declined surgery. *Am J Crit Care*. 1998;7:393-4.
127. Barbou F, Schiano P, Lahutte M. Anomalous right coronary artery from the left coronary sinus, with an interarterial course. *Arch Cardiovasc Dis*. 2010;103:626-8.
128. Graham TP Jr, Driscoll DJ, Gersony WM, Newburger JW, Rocchini A, Towbin JA. Task Force 2: congenital heart disease. *J Am Coll Cardiol*. 2005;45:1326-33.
129. Brothers JA, Gaynor JW, Jacobs JP, Caldarone C, Jegatheeswaran A, Jacobs ML, et al. The registry of anomalous aortic origin of the coronary artery of the Congenital Heart Surgeons' Society. *Cardiol Young*. 2010;20:50-8.
130. Brothers JA, McBride MG, Marino BS, Tomlinson RS, Seliem MA, Pampaloni MH, et al. Exercise performance and quality of life following surgical repair of anomalous aortic origin of a coronary artery in the pediatric population. *J Thorac Cardiovasc Surg*. 2009;137:380-4.
131. Link MS, Myerburg RJ, Estes NA III. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task Force 12: emergency action plans, resuscitation, cardiopulmonary resuscitation, and automated external defibrillators: a scientific statement from the American Heart Association and American College of Cardiology. *Circulation*. 2015;132:e334-8.
132. Fukuda T, Ohashi-Fukuda N, Kobayashi H, Gunshin M, Sera T, Kondo Y, et al. Public access defibrillation and outcomes after pediatric out-of-hospital cardiac arrest. *Resuscitation*. 2017;111:1-7.

133. Kitamura T, Kiyohara K, Sakai T, Matsuyama T, Hatakeyama T, Shimamoto T, et al. Public-access defibrillation and out-of-hospital cardiac arrest in Japan. *N Engl J Med*. 2016;375:1649-59.
134. Thomas VC, Shen JJ, Stanley R, Dahlke J, McPartlin S, Row L. Improving defibrillation efficiency in area schools. *Congenit Heart Dis*. 2016;11:359-64.
135. Cappato R, Curnis A, Marzollo P, Mascioli G, Bordonali T, Beretti S, et al. Prospective assessment of integrating the existing emergency medical system with automated external defibrillators fully operated by volunteers and laypersons for out-of-hospital cardiac arrest: the Brescia Early Defibrillation Study (BEDS). *Eur Heart J*. 2006;27:553-61.
136. Kitamura T, Iwami T, Kawamura T, Nagao K, Tanaka H, Hiraide A, et al. Nationwide public-access defibrillation in Japan. *N Engl J Med*. 2010;362:994-1004.
137. Iwami T, Kitamura T, Kawamura T, Mitamura H, Nagao K, Takayama M, et al. Chest compression-only cardiopulmonary resuscitation for out-of-hospital cardiac arrest with public-access defibrillation: a nationwide cohort study. *Circulation*. 2012;126:2844-51.
138. Mitani Y, Ohta K, Yodoya N, Otsuki S, Ohashi H, Sawada H, et al. Public access defibrillation improved the outcome after out-of-hospital cardiac arrest in school-age children: a nationwide, population-based, Utstein registry study in Japan. *Europace*. 2013;15:1259-66.
139. Hallstrom AP, Ornato JP, Weisfeldt M, Travers A, Christenson J, McBurnie MA, et al. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med*. 2004;351:637-46.
140. Berdowski J, Blom MT, Bardai A, Tan HL, Tijssen JG, Koster RW. Impact of onsite or dispatched automated external defibrillator use on survival after out-of-hospital cardiac arrest. *Circulation*. 2011;124:2225-32.
141. Capucci A, Aschieri D, Piepoli MF. Out-of-hospital early defibrillation successfully challenges sudden cardiac arrest: the Piacenza Progetto Vita project. *Ital Heart J*. 2002;3:721-5.
142. Drezner JA, Toresdahl BG, Rao AL, Huszti E, Harmon KG. Outcomes from sudden cardiac arrest in US high schools: a 2-year prospective study from the National Registry for AED Use in Sports. *Br J Sports Med*. 2013;47:1179-83.
143. Drezner JA, Rao AL, Heistand J, Bloomingdale MK, Harmon KG. Effectiveness of emergency response planning for sudden cardiac arrest in United States high schools with automated external defibrillators. *Circulation*. 2009;120:518-25.
144. Link MS, Myerburg RJ, Estes NA III. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task Force 12: emergency action plans, resuscitation, cardiopulmonary resuscitation, and automated external defibrillators: a scientific statement from the American Heart Association and American College of Cardiology. *J Am Coll Cardiol*. 2015;66:2434-8.
145. Wittlieb-Weber CA, Paridon SM, Gaynor JW, Spray TL, Weber DR, Brothers JA. Medium-term outcome after anomalous aortic origin of a coronary artery repair in a pediatric cohort. *J Thorac Cardiovasc Surg*. 2014;147:1580-6.
146. Nguyen AL, Haas F, Evens J, Breur JM. 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*. 2012;20:463-71.
147. Brothers J, Gaynor JW, Paridon S, Lorber R, Jacobs M. Anomalous aortic origin of a coronary artery with an interarterial course: understanding current management strategies in children and young adults. *Pediatr Cardiol*. 2009;30:911-21.
148. Myerburg RJ, Junttila MJ. Sudden cardiac death caused by coronary heart disease. *Circulation*. 2012;125:1043-52.