Surgical management of anomalous coronary arteries

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Anomalies in the coronary arterial circulation have been described since classical antiquity by Galen and through the Medical Renaissance by Vesalius, but their clinical significance and association with sudden cardiac death (SCD) has only been appreciated over the last 4 decades. Advances in cardiac surgery and cardiovascular intensive care have led to decreasing overall postoperative mortality and morbidity associated with cardiac surgery. The decision whether to surgically treat an anomaly of coronary artery origin and course, and the risk-to-benefit ratio of surgical treatment in preventing a potentially lethal complication of SCD, requires careful, deliberate consideration based on the best available evidence. In this keynote lecture, we aim to deliver a concise discussion of the current surgical management of anomalous coronary arteries.

Keywords: Cardiac surgery; congenital heart disease; surgical management; anomalous coronary arteries



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Introduction

Coronary artery anomalies have been described since classical antiquity by Claudius Galenus (Galen) (1) and have been documented in various anatomical treatises of the inquisitive Renaissance scholars Vesalius, Bartholin, Fallopius, Morgagni and Thebesius (2,3). Yet it was only in the mid-1970s that the clinical significance of anomalies of coronary artery origin and course with respect to sudden death became more widely known and the first successful surgical unroofing procedure was performed (4). Congenital anomalies of the coronary arteries occur in 0.2% to 1.2% of the population (5,6). Given the heterogeneity of coronary artery anomalies, multiple classification systems have been proposed, based on anatomy, function or clinical significance (5,7). With the intent of creating a unified database, members of the STS-Congenital Heart Surgery Database Committee (8) and representatives from the European Association for Cardiothoracic Surgery met from 1998 to 1999 to standardize the nomenclature and categories of coronary artery anomalies (9). The latest data specification of this database (10) classifies coronary artery anomalies into 5 categories:

- Coronary artery anomaly, anomalous aortic origin of a coronary artery (AAOCA);
- Coronary artery anomaly, anomalous pulmonary origin (includes ALCAPA; Bland-Garland-White);
- Coronary artery anomaly, fistula;
- ✤ Coronary artery anomaly, aneurysm;
- Coronary artery anomaly, other, including coronary artery bridging, coronary artery stenosis, and secondary coronary artery variations.

AAOCA

AAOCA can be further subdivided into anomalous left main coronary artery (ALMCA) from the right aortic sinus of Valsalva (RASV), anomalous right coronary artery (ARCA) from the left aortic sinus of Valsalva (LASV), circumflex artery (Cx) from RASV or RCA, and inverted coronary arteries (rare) (11). "Wrong sinus origin" of the right coronary artery is more common than "wrong sinus origin" of the left coronary artery, by ratios ranging from 3:1, to as high as 9:1 in various reports (3,12). The risk of sudden death is widely acknowledged to be higher when the LMCA arises from the RASV than when the RCA arises from the LASV, though precise estimation of these risks remains elusive. For the remainder of this report, we shall use AAORCA to indicate anomalous aortic origin of the right coronary artery, most often from the left sinus of Valsalva), and we shall use AAOLCA to indicate anomalous aortic origin of the left main coronary artery, most often from the right, or anterior sinus of Valsalva. Instances where only the left anterior descending (LAD) branch or only the circumflex (Cfx) coronary artery has an anomalous origin will be described separately and specifically.

One of the landmark papers that drew attention to the potential association of AAOCA with SCD was published by in 1974 by Cheitlin and associates from the Armed Forces Institute of Pathology (Washington DC) (4). They reviewed all cases of single coronary artery origin or both coronary arteries arising from the same sinus of Valsalva among autopsy cases. They found a total of 51 cases of AAOCA out of 475,000 records. Among patients in whom both coronary arteries arose from the anterior ("right coronary") sinus (AAOLCA), 27% (9/33) had experienced SCD. There were no cases of SCDs among the 18 patients in whom the RCA arose from the left coronary sinus (AAORCA). The authors noted that slit-like orifices and intramural courses were commonly noted in the cases with SCD. They proposed that these features contributed to the mechanism for sudden death.

Basso et al. (13) reviewed two registries of young competitive athletes in the US and Italy who died suddenly during exercise and found 27 athletes with coronary anomalies (i.e., 24 AAOLCA and 3 AAORCA, 22 men and 5 women, ages 9 to 32). Ten of these athletes had experienced symptoms (e.g., chest pain, syncope, palpitations). Twelve athletes had normal testing in life, including all 10 symptomatic patients. Every heart, on pathological examination, had a slit-like orifice and a partially or completely intramural course. Maron and associates reviewed the distribution of cardiovascular causes of sudden death in 1,435 US athletes less than 35 years of age from 1980 to 2005 and reported that 17% were due to coronary artery anomalies (14). The only cardiovascular anomaly associated with a larger number of cases of sudden death was hypertrophic obstructive cardiomyopathy.

There have been a number of possible mechanisms suggested for sudden death in AAOCA (15), such as aortic pressure on an intramural segment, slit-like orifice "closed" by increased aortic pressure, kinking or sharp angulation at take-off, an inter-arterial segment "squeezed" by aorta and pulmonary artery (PA) and spasm of the AAOCA.

With respect to AAOCA with an inter-arterial course (i.e., between the aorta and the PA), there are certain additional details of morphology that may be associated with increased risk of ischemic events. These include the presence of an intramural segment (and possibly the length of the intramural segment), abnormally high take-off from the aorta, slit-like orifice, acute angulation of the proximal segment and an exaggerated degree of "ellipticity" (i.e., non-roundness) of the proximal segment of the coronary artery (16,17). Conversely, within the entire spectrum of AAOCA with "wrong sinus origin", there are a number of variants that are thought to be relatively benign (e.g., AAOCA with posterior looping course or anterior "prepulmonic course") as well as AAOLCA with "intra-septal" or "intraconal" courses, which have traditionally been thought of as "low risk", but this potentially requires reevaluation.

In possibly the largest series of patients with anomalies of coronary artery origin and course from the Congenital Heart Surgeons' Society (CHSS) AAOCA registry, 560 patients ≤ 30 years of age at diagnosis were enrolled from 40 institutions between January 1998 and December 2016. There were 415 AAORCA patients, 128 AAOLCA patients and 17 with anomalous origin of both the left and right coronaries-most often a single coronary origin outside the sinus of Valsalva and above the "inter-coronary" commissure. Of these, 55% of AAORCA patients, 64% of AAOLCA patients and 41% of ARCA/ALCA patients underwent surgery (i.e., 57% of all patients) (18). Operated and unoperated patients in this registry are all being followed longitudinally, in hopes of shedding light on both the natural and unnatural history of these anomalies and possibly to address unanswered questions regarding risk stratification and indications for surgery in certain groups. A recent analysis of this registry sought to characterize patients with ischemia or a sudden event [sudden cardiac arrest (SCA) or death (SCD)] at presentation. Findings of this study were presented by Jegatheeswaran and associates at the 2018 meeting of the American Association for Thoracic Surgery (19). Characteristics were evaluated among those who have had documented ischemia (i.e., 49 patients with sudden death, aborted sudden death, lethal arrhythmia, syncope with exercise, or positive exercise stress test documenting ischemia) and were compared to those who had undergone exercise stress tests that did not reveal ischemia (n=236 patients). The remainder, who had not been subjected to provocative physiologic stress testing, were not included in the analysis. Of the 49 patients in the

ischemia group, 28/49 (57%) had AAOLCA, 20/49 (41%) had AAORCA and 1/49 (2%) had anomalous aortic origin of both LMCA and RCA. Anomalous left outnumbered anomalous right by approximately 1.4:1. In the smaller sub-group who had experienced sudden events (SCA or SCD, 18 patients), 12/18 (67%) had AAOLCA and 6/18 (33%) had AAORCA. So, in the sudden event sub-group, anomalous left outnumbered ARCA by 2:1. Ischemic AAOLCA patients were more likely to have an intramural course, high orifice, or slit-like orifice, than non-ischemic patients. And ischemic right AAOCA (AAORCA) patients had a longer intramural course compared to non-ischemic patients.

The subsequent discussion pertains to AAOCA ("wrong sinus origin") with inter-arterial course.

Diagnosis

The initial diagnosis of AAOCA is practically always by echocardiography, with exceptions being coronary angiography, mostly in adults, or incidental finding at surgery for another lesion. However, there are limitations of echocardiography (20), such as the relatively lower spatial resolution compared to CT or MRI. While there is no universal consensus regarding the evaluation of AAOCA (21) and the use of various imaging modalities for evaluation is based on physician preferences (12); the general recommendation is that an echocardiographic diagnosis should be supported by additional tomographic scans to assess morphologic details. The detailed morphologic data obtained from these advanced imaging studies may be helpful in risk stratification and are certainly helpful in surgical planning. Stress testing is also important, providing functional assessment to assess for provocation of ischemia (22,23) and as a baseline for further evaluation during follow-up.

Indications for surgery

In the most recent expert consensus guidelines [2017] for AAOCA (22) commissioned by the American Association of Thoracic Surgery (AATS) and written after an extensive literature review, it is recommended that symptomatic AAOCA individuals (e.g., chest pain or syncope suspected to be due to myocardial ischemia or proven/suspected cardiac arrhythmias), or a history of aborted SCD, should be activity restricted and should be offered surgery (class 1; level of evidence B) or catheter-based intervention if surgical risk is deemed too high (class IIb, level of evidence C). Asymptomatic individuals with the left main coronary artery arising from the right sinus of Valsalva should be offered surgery (class 1, level of evidence B). Individuals with an anomalous origin of the RCA from the left sinus of Valsalva should be evaluated for inducible ischemia (class IIa, level of evidence C). Based on these expert consensus guidelines, if the stress testing is negative and the patient is counselled regarding the risk of sudden death, the patient may participate in competitive sports (class IIa; level of evidence C). However, there are many questions that remain unanswered in these guidelines, such as whether there is a lower limit or upper limit in terms of age for surgery and whether to perform corrective procedures if the anomaly is found incidentally at the time of surgery. Management of asymptomatic patients with AAORCA also remains a matter of discussion (15). Practices vary from center to center, and may be individualized based on patient factors. For example, in the management of asymptomatic patients with AAORCA, the Coronary Anomalies Program at the Texas Children's Hospital takes into consideration "high risk anatomy" (24) (i.e., long intramural course, abnormal ostium, dynamic changes of ostium and proximal course during the cardiac cycle), as well as significant family anxiety, competitive sports and coronary vessel dominance.

Types of surgical repair

The pathophysiology of AAOCA is that of ischemia occurring when myocardial oxygen demand exceeds supply. This may be related to multiple surgically correctable anatomical factors (15,25), such as inter-arterial course, ostial morphology (i.e., a round, oval, slit-like, pinhole), ostial location, peri-commissural origin, acute angulation of origin, right-left ostial relationship and the presence and length of intramural course. As such, the aim of surgical repair should be to reduce the likelihood of myocardial ischemia. This can be achieved by establishing or restoring a coronary origin within the "appropriate sinus", optimizing the ostial size and morphology, eliminating the inter-arterial course, eliminating intramurality, while minimizing the likelihood of sclerosis or scarring. Alternatively, the critical features of morphology may occasionally be left in place while providing an extra-anatomic source of myocardial blood supply.

There are several surgical options for treating AAOCA, namely unroofing the intramural segment, including creation of "neo-ostium" in the appropriate sinus, translocation of ostium (i.e., reimplantation), translocation of PA, pericardial patch of the aorta and proximal anomalous coronary artery, either alone or in combination with translocation of ostium or PA. Coronary bypass (i.e., IMA to affected coronary) is occasionally used to provide an extra-anatomic source of blood flow to the myocardium, but it is not generally recommended, as the anomalous vessel is only compromised during stress or exercise. Thus, most of the time, there will be significant competitive flow, leading to the possibility of low graft patency or subclavian steal (26).

Unroofing is the simplest surgery, both technically and conceptually (22). Through a median sternotomy, the pericardium is opened and conventional cardiopulmonary bypass is established. After cardioplegic arrest, the ascending aorta is opened either by an oblique aortotomy or by transecting well above the coronary origins, to allow for the identification of the orifice(s) from which the coronary arteries arise. The courses of the coronary arteries are ascertained. In cases of AAOLCA, the intramural course of the ALMCA, if present, may be above or below the commissure, requiring slightly different unroofing techniques (27). When the intramural course of the ALMCA is above the commissure, a sharp scalpel incision is made within the aorta, along the course of the ALMCA (12) guided by a coronary probe or other fine instrument, while taking precautions to prevent a transaortic or transcoronary incision to the outside of the heart. Tacking sutures are then placed, either along the entire course of the "unroofing" or only at the site of the neo-orifice. If the intramural course of the ALMCA is below the commissure, the unroofing is performed separately in the LASV and RASV, with tacking sutures then placed at the neo-orifice. This technique, which is often referred to as "neo-ostial creation" avoids the need to take-down and later resuspend the inter-coronary commissure, which in some series has been associated with development and eventual progression of aortic insufficiency. The aorta is repaired, the heart reperfused, and the patient is rewarmed. During this time, ECG findings are closely examined for changes reflective of myocardial ischemia and transesophageal echocardiography is performed to assess the function of the aortic valve. A similar technique applies for AAORCA with proximal intramural segment.

Methods other than unroofing can also be applied. Cubero *et al.* (28) opined that the major limitation of unroofing is that it does not universally eliminate the interarterial segment of the coronary artery with anomalous origin. In instances with only a short intramural segment, unroofing may still leave the coronary artery origin in the "wrong sinus," with persistence of an interarterial segment. In such cases, additional PA relocation may be performed. Additionally, unroofing may require manipulation of the inter-coronary commissure, which may predispose to aortic regurgitation, even if the commissure is resuspended at the time of repair. Reimplantation (29) can be performed, such as in the case of AAORCA from the left coronary sinus with inter-arterial course and intramural segment. The RCA is divided immediately distal to the intramural segment and is directly reimplanted in an end-to-side fashion, without button, into the RASV (30,31). Reimplantation of the AAOLCA is felt by some to be more technically difficult (28) and unroofing is felt by many to be more suitable for AAOLCA from the RASV.

An anatomical surgical repair as suggested by Gaudin et al. (32) (i.e., Vouhe repair, Paris, France) may also be performed, where the aorta and pulmonary trunk are transected to expose the course of the ALMCA. The proximal epicardial course of the ALMCA is incised and a patch of either pericardium or saphenous vein is used to fashion a neo-ostium in the appropriate sinus, with incorporation of the patch into the aortic suture line. Proponents of this technique point out that the abnormal interarterial and/or intramural segment is left intact but is bypassed. A new, enlarged coronary ostium is created in the appropriate sinus, restoring a normal angle of take-off.

In AAOCA patients with a single coronary ostium and no intramural component, a PA translocation (33) can be performed, either as an anterior PA translocation (i.e., LeCompte maneuver) or a lateral PA translocation. In a variation of the LeCompte maneuver, the right PA is transected, mobilized, translocated anterior to the aorta and re-anastomosed to the main PA, with patch augmentation. PA translocation has been proposed by the Stanford group (18,34,35) for instances in which unroofing of a relatively short intramural segment results in the ostium remaining in the wrong sinus, resulting in persistence of an inter-arterial course. Repairs that rely upon extranatomic sources of coronary blood flow, such as coronary artery bypass grafting using either saphenous vein grafts or internal mammary artery grafts, are generally not preferred in children and young adults, due to possible long-term graft patency issues, but may be considered in older adults (36). Other less common methods not covered in the video lecture include simple osteoplasty without unroofing, creation of ostial window-partial unroofing to fashion a neo-ostium in the distal intramural segment-and aortocoronary anastomosis

from outside the aorta without unroofing (12).

Surgical outcomes

Turner *et al.* (37) (Duke University series) reviewed 53 AAOCA patients from 1995 to 2009, with a mean age of 13.9 years old (range, 4–65 years). There were 40 patients with AAORCA and 13 with AAOLCA. There were symptoms of angina or syncope in 58% of the AAORCA patients and 46% of the AAOLCA patients. The lack of an intramural course was noted intra-operatively in 5 AAORCA patients and 2 AAOLCA patients, with TTE accurately predicting an intra/extramural course in 92.5% of cases. There were no mortalities with a mean follow up of 29 months, with complications in 9.4% of all patients (e.g., aortic insufficiency, pneumothorax, pleural effusion, bleeding and retained foreign body).

Mainwaring et al. (35) (Stanford University series) reviewed 50 AAOCA patients from 1999 to 2010. The institutional approach in this center (18,34,35) included recommendation of surgical treatment for all patients identified with AAOCA between the ages of 10 and 30 years, with a more selective approach based upon symptoms and other factors for patients under the age of 10 or over the age of 30. In the initial series reported in 2011, the median age was 14 years (range, 5 days-47 years) and there were 31 AAORCA patients, 17 AAOLCA patients and 2 patients had eccentric single coronary ostium. Overall, 52% of patients had symptoms of ischemia, 28% had associated congenital heart diseases. There was a lack of an intramural course observed intra-operatively in 7 cases (5 AAORCA, 2 AAOLCA). The surgical repair was performed by unroofing in 35 patients (70%), reimplantation in 6 patients (12%) and PA translocation in 9 patients (18%). There was no operative mortality and no sudden deaths during a median follow up of 5.7 years. Complications (14%) included pleural effusion (6%), postcardiotomy syndrome (6%) and heart block (2%). One patient with multiple previous myocardial infarctions prior to AAOCA diagnosis required cardiac transplantation 1 year after AAOCA repair. In their most recent report, updating their experience with surgical management of AAOCA (34), the Stanford group reported data pertaining to a total of 115 patients who underwent surgical repair of AAOCA, with unroofing of an intramural coronary in 86 (75%), reimplantation in 9 (8%) and PA translocation in 20 (17%). There was no mortality and 57 of 59 symptomatic patients (97%) became asymptomatic after surgery. They concluded that these results demonstrate that

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AAOCA surgery can be performed safely and is effective in relieving symptoms of myocardial ischemia. For the first time, an association between AAOCA and myocardial bridges was described in this report.

Herrmann et al. (38) performed a comparative study examining the differences in AAOCA peri-operative management and outcomes in a pediatric vs. an adult center (The Children's Hospital of Philadelphia vs. Hospital of the University of Pennsylvania). Cardiac catheterization was utilized more frequently at the adult center and cardiac magnetic resonance imaging was more commonly employed at the pediatric center. Isolated coronary unroofing was performed in 19 of 20 cases at the pediatric center and in only 2 (22%) cases at the adult institution. They found, as expected, more co-morbidities, more concomitant procedures in the adult group with longer cross clamp times (pediatric 28 minutes vs. adult 120 minutes) and bypass times (pediatric 42 minutes vs. adult 181 minutes). Postoperatively, patients in the adult center were extubated later (pediatric 2 hours vs. adult 15 hours) and had longer ICU stays (pediatric 1.6 days vs. adult 2.7 days) and hospital stays (pediatric 3.6 days vs. adult 8.7 days).

In view of the potential lethality of untreated AAOCA, it is recommended by the American Heart Association and American College of Cardiology (23) that non-operated symptomatic and asymptomatic athletes with AAOLCA from the RASV, especially those with an inter-arterial course, and non-operated symptomatic athletes with AAORCA should be restricted from participation in all competitive sports (class III; level of evidence B for AAOLCA; class III; level of evidence C for symptomatic AAORCA). An exception may possibly be made for class IA sports, such as billiards, bowling and golf (39). Asymptomatic athletes with AAORCA from the LASV should undergo an exercise stress test and those asymptomatic with negative stress tests may compete after adequate counseling (class IIa; level of evidence C). Athletes with AAOCA may consider participation in all sports 3 months after successful surgical repair if asymptomatic and if an exercise stress test is negative for ischemia or arrhythmias (class IIb; level of evidence C).

Conclusions

Anomalous aortic origin of the left or right coronary arteries ("wrong sinus origin") is a rare but important anomaly with potential for exercise-related ischemia which

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may present as SCD in the young. The left main coronary artery arising from the right coronary sinus (AAOLCA) is a higher risk lesion that should be repaired in nearly all patients. The right coronary artery from left sinus (AAORCA) is more common but may be less serious and operation is generally reserved for patients with symptoms attributable to ischemia (such as syncope with exercise), documented ischemia, or history of SCD. Imaging studies to elucidate detailed anatomy of coronary origin and course should be followed by physiologic testing to assess for inducible ischemia. When surgery is indicated, unroofing of the intramural segment is the most commonly performed operation, though several alternative techniques are available. A single surgical strategy is likely not ideal for all patients and operative techniques should be individualized on the basis of anatomy. All potential anatomic culprits should be addressed in patients undergoing operation. Coronary artery bypass grafting has limited application, especially for young patients.

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Footnote

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