Anomalous aortic origin of a coronary artery: 2020 year in review

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While at first, managing patients with anomalous aortic origin of a coronary artery (AAOCA) may seem straightforward, in reality it involves a nuanced understanding of the ever-evolving literature in the field. The primary conundrum that clinicians face is determining which patients require repair, because their risk of sudden cardiac death is greater than the risks of surgery. It is difficult to determine the answer to this question because we do not know the true prevalence of this lesion in the general population, and as a result we do not know the risk of ischemia and sudden cardiac death. Currently, the management of patients often occurs at the discretion of cardiologists and surgeons who have a varying perception of how to interpret the literature and the complexity of a procedure that was once thought to be benign.

The guidelines also have evolved. Although it was initially recommended that all patients with left AAOCA and those with right AAOCA who have ischemia undergo surgery, the latest 2018 American College of Cardiology/American Heart Association guidelines for the management of adults with congenital heart disease recommend that all patients with symptoms or ischemia during diagnostic testing undergo repair (Class I); however, for patients with left AAOCA who do not meet this criteria, surgical intervention is now only a Class IIa recommendation, which decreases to IIb in right AAOCA, unless patients have ventricular arrhythmias.¹ As such, the purpose of this review is to highlight some of the key publications in the last year and provide our readers with a current understanding of how to evaluate and manage these patients.

SURGICAL TECHNIQUES

Jegatheeswaran and colleagues² reviewed the surgical outcomes of 395 surgical patients in a cohort of 682 patients from 45 North American centers in the Congenital Heart Surgeons' Society cohort. They found that the most

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CENTRAL MESSAGE

Many unknowns remain regarding AAOCA. However, our knowledge of new surgical procedures, outcomes, and the utility of advanced techniques for imaging and risk stratification continues to evolve.

commonly used repair strategies were isolated unroofing (87%), unroofing with commissural manipulation (25%), patch ostioplasty (6%), reimplantation (6%), and pulmonary artery translocation (6%), followed by other strategies. Of note, intimal tacking was used in 74% of patients and commissural manipulation was performed in 26% of patients. It should be noted that these strategies each only address 1 or 2 anatomic issues and can only be used interchangeably in select situations.

The latest thinking is that all abnormal components of an anomalous vessel must be addressed to bring the coronary as close as possible to having a normal anatomy. This means that any issues related to the ostium (ie, stenosis or slit-like origin) and course (ie, an acute take-off and intramural or interarterial course) must be addressed during repair, in addition to ensuring the anomalous vessel is relocated to the appropriate sinus. This is in contrast to thinking that simply unroofing an intramural course is adequate if the vessel remains interarterial or is still not in the appropriate sinus. Gaillard and colleagues³ report the results of 35 patients (15 left and 20 right AAOCAs) who underwent anatomic repair in their cohort of 61 patients. Although

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there were no early or late postoperative mortalities and all patients within this group were free from ischemia at last follow-up, 3 symptomatic patients had acute postoperative events (1 translocation, 1 septal release/reimplantation, and 1 anatomic repair). Mean follow-up was 38 months (range, 1-15 years). With respect to late results, 2 patients with right AAOCA required angioplasties, 1 with stenting who ultimately underwent coronary artery bypass grafting for in-stent thrombosis. Three asymptomatic patch aneurysms were also found in patients who received anatomic repair using long saphenous vein patches, one of which was operated on but found to have no sign of rupture or infection, preventing operation in the other 2 patients. At latest follow-up, only 1 patient was symptomatic. It should be noted that although surgeons use multiple different patch materials during coronary repair, we still do not know which has the best durability and outcomes.^{4,5}

This year also brought additional data regarding novel surgical solutions for intraconal/intraseptal anomalous coronaries. Although these lesions originally were largely thought to be benign, with the use of aggressive strategies for testing, including both fractional flow reserve and intravascular ultrasound, ischemia has been more clearly documented in these patients, leading to the requirement for repair.⁶ Najm and colleagues⁷ described the results of their novel technique for repair of these left AAOCAs in 7 patients. In their technique, they describe opening the right ventricular outflow tract below the pulmonary valve, dividing the posterior wall, and dissecting the right ventricular outflow tract muscles over the left main coronary artery until the bifurcation. This is followed by placement of an anteriorly tapered rectangular patch of fresh autologous pericardium in a rectangular shape to bridge the gap (Figure 1). With a median follow-up of 9 months (range, 0.48-12 months), there were no mortalities or major complications. Doan and colleagues⁸ reported the use of a myotomy over the intraseptal vessel after a transverse infundibular ventriculotomy, and Gaillard and colleagues³ reported 5 patients who underwent septal release (Figure 2).

SURGICAL OUTCOMES

Surgical repair of AAOCA was once thought to be a straightforward procedure with minimal morbidity and mortality, but this notion has been challenged. Jegatheeswaran and colleagues² evaluated the surgical outcomes of 395 patients in the Congenital Heart Surgeons' Society cohort with a focus on the adverse outcomes after repair. They reviewed the surgical management in patients aged 30 years or less. The median age at surgery was 13.3 years (interquartile range, 9.9-15.5), and median follow-up in this cohort was 2.8 years (interquartile range, 1.1-5.0). Mortality was low with only 4 deaths (1%) (3 elective, 1 urgent) within 30 days of surgery, but there was a surprisingly high composite risk of adverse events after repair. Of those

who died, 2 patients were asymptomatic preoperatively. Adverse outcomes included 3% coronary-related reoperations (15 reoperations in 13 patients), 8% new mild or more aortic insufficiency ($n = 27$) or 2% new moderate or more aortic insufficiency ($n = 7$) in those evaluated before and after repair, 2% new abnormal ejection fraction ($n = 6$), and 4% new positive postoperative ischemia at any time after repair ($n = 14$) or 2% if considered only on the basis of their last test ($n = 8$). Overall, when these events were reviewed together, the adverse event rate ranged from 7% to 13% based on whether the degree of aortic insufficiency considered was mild or more, or moderate or more, and whether the presence of postoperative ischemia was considered at any time or at the last test. They also calculated the adverse event rate for specific subgroups of interest. Subgroups that had higher risk than the entire cohort included those with preoperative ischemia (21%-33%), those with left AAOCA (14%-20%), those who underwent repair strategies other than unroofing (12%-19%), and those who received unroofing with commissural manipulation (7%-15%). Subgroups who had lower risk than the entire cohort included those with right AAOCA (4%-10%), those who underwent isolated unroofing (5%-9%), and those without preoperative ischemia (4%-9%) (Figure 3). Of note, freedom from mild aortic insufficiency differed in those who underwent commissural manipulation during repair versus those who did not (85% vs 91% at 6 months, 83% vs 90% at 1 year, and 77% vs 88% at 3 years).

A large review of 167 adult patients with isolated AAOCA over a 2-year period from the Cleveland Clinic Foundation gave us our first major look at diagnosis, concomitant lesions, and surgical management in adult patients.⁹ Jiang and colleagues¹⁰ reviewed 167 cases of AAOCA over a 2-year period that had the diagnosis code of congenital coronary anomaly. Among these patients, 96 had right AAOCA, 39 had AAOCA, 4 had left anterior descending AAOCA, 26 had circumflex AAOCA, and 2 had multiple anomalous vessels. They found that patients with right AAOCA were diagnosed significantly later than those with left AAOCA (55 vs 51 years, $P = .03$). Of these patients, 74% (124/167) were diagnosed secondary to evaluation of cardiac symptoms, followed by advanced imaging for cardiac or noncardiac surgery. Symptoms were most commonly chest pain (63%) and dyspnea (51%), with a small proportion who were asymptomatic (8%). Surgical repair occurred as follows: A total of 61 patients (31%) underwent open surgery, with the AAOCA addressed in 59% (36/61). Concomitant procedures were performed in 39% (14/36) of those in whom surgery addressed the anomalous vessel. During the follow-up period (median, 2.5 years), there were no mortalities and reoperations or cardiac events. The most common concomitant procedures included aortic valve surgery

FIGURE 1. Transconal repair of left AAOCA with pericardial extension of right ventricular outflow tract. A, The right ventricular outflow tract is opened. The *dotted lines* indicate the planned incision line to unroof the coronary segment. The inset (*right*) shows the sagittal view of the anomalous coronary artery, surrounded by muscle. B, The coronary segment is unroofed throughout the entire intraseptal area. C, The coronary artery is bridged from the surrounding structures by a rectangular patch of autologous pericardium. Then inset (*right*) shows the unroofed segment with overlying pericardial patch. D, The completed repair, with the anterior right ventricular outflow tract closed with pericardium. Reproduced from Najm and Ahmad with permission from *The Annals of Thoracic Surgery*.²¹ AAOCA, Anomalous aortic origin of a left coronary artery; RVOT, right ventricular outflow tract.

(64%) and coronary artery bypass grafting (21%), undoubtedly complicating the evaluation of the cause of symptoms. Of the 18 patients who underwent surgery primarily for their AAOCA with follow-up of more than 4 months, 13 (72%) described improvement of their symptoms, and the rest did not report a change. Only 2 patients had the same modality of testing preoperatively and postoperatively. This is something that needs to change, because it is currently suggested that all patients undergo

exercise stress testing at 3 months to clear them after surgery.¹¹

ADVANCED METHODS FOR DELINEATION OF ANATOMY AND RISK STRATIFICATION

Heightened awareness of AAOCA and its potential role in sudden cardiac death have led to an increasing number of children and young adults diagnosed with AAOCA on screening studies without convincing symptoms of

FIGURE 2. Septal release. A, Pulmonary root harvest, as performed for the Ross procedure. B, Division of the myocardial bridge to allow septal relief. C and D, Repositioning of the pulmonary trunk higher on the posterior aspect using a pericardial patch. Reproduced from Gaillard and colleagues with permission from the *European Journal of Cardio-Thoracic Surgery*.³

ischemia. A number of centers have developed diagnostic and treatment protocols to manage these patients, for example, the Texas Children's protocol highlighted in a recent review article by Molossi and Sachdeva.¹² Given the persistent knowledge gaps in understanding the mechanism of ischemia and patients at risk, several articles have assessed the efficacy and accuracy of various advanced imaging methods in anatomic delineation and patient-specific risk stratification.

Krishnamurthy and colleagues¹³ assessed the accuracy of computed tomography angiography (CTA) in the identification of AAOCA and associated anatomic details, and compared CTA readings (3 blinded readers) with surgical findings in 25 patients. CTA was largely accurate in identification of AAOCA and intramural course and moderately accurate in identification of ostial location or lesions. The accuracies were the following: AAOCA presence (100%), intramural course (92%-98%), ostial stenosis (84%-96%), and high ostial origin (76%-82%).

Tang and colleagues¹⁴ assessed the value of noninvasive measurement of functional flow reserve (FFR) using CTA in 94 patients with right AAOCA. They compared those who

had FFR 0.8 or less and greater than 0.8. Patients with FFR 0.80 or less had higher prevalence of typical (29% vs 8%) and atypical (29% vs 7%) angina. Moreover, high-risk anatomic features (high take-off, ostial stenosis, long intramural course) were more prevalent in those with FFR 0.80 or less. They suggested that FFR measurement with CTA might have potential as a noninvasive tool for risk stratification. The same modality was also assessed by Ferrag and colleagues,¹⁵ again suggesting a potential role in patient-specific risk stratification. Although the study was interesting and potentially useful, limitations included the lack of noninvasive FFR validation against catheter-derived FFR and the validation of anatomic features against surgical findings.

Agrawal and colleagues¹⁶ examined the role of stress cardiovascular magnetic resonance (sCMR) as a noninvasive tool to evaluate myocardial perfusion in children with coronary anomalies (including but not only limited to AAOCA) and compared that with invasive FFR measurement (performed at baseline using dobutamine or regadenoson as provocative agents). FFR was considered abnormal if less than 0.8 in the affected coronary. The 2 modalities

FIGURE 3. Primary findings related to the surgical risks of AAOCA repair. Ranges for surgical adverse events based on calculations using occurrence of new mild or new moderate aortic insufficiency associated with commissural manipulation and new postoperative ischemia based on any or last postoperative ischemia test. AAOCA, Anomalous aortic origin of a coronary artery; AI, aortic insufficiency; EF, ejection fraction; AE, adverse event; AAOLCA, anomalous aortic origin of a left coronary artery; AAORCA, anomalous aortic origin of a right coronary artery. Reproduced from Jegatheeswaran and colleagues with permission from the *Journal of Thoracic and Cardiovascular Surgery*.²

agreed in approximately 80% of patients especially if done with close time proximity, suggesting that sCMR may help in risk stratification and decision-making in AAOCA and myocardial bridges. Some studies examined the role of nuclear perfusion scans in the assessment of potential ischemia, but the reliability of this seems to vary among centers, with many favoring sCMR.¹²

In an attempt to quantify the pathological behavior of AAOCA and potentially help in patient-specific risk stratification, Lo Rito and colleagues¹⁷ performed computational modeling (finite element analysis) of CTA data (5 patients with right AAOCA and 5 normal controls). They examined simulated dynamic changes in coronary diameter during modeled loading conditions (increasing aortic pressure to 80, 120, and 180 mm Hg to simulate exercise). They showed that right AAOCA was unable to expand its lumen in the intramural segment at loading conditions. The clinical relevance and validity of this model in real life remain to be determined. Another study by Razavi and colleagues¹⁸ assessed coronary wall shear stress using computational flow dynamics models in 6 patients after surgical repair of AAOCA (2 of them also had preoperative models). Coronary wall shear stress usually normalized after unroofing. However, persistence of acute angle of origin continued to alter wall shear stress and affect coronary flow patterns.

Right and left coronary artery flows were also different. Again, the predictability of these models remains to be determined because they involve a small number of patients, and computational flow dynamics techniques have limited the ability to account for various factors such as compression of intramural segment by aortic elastic structures and the intercoronary pillar (both contributors to ischemia).

Several investigators examined the feasibility of transfer of morphologic characteristics of AAOCA from imaging to patient-specific 3-dimensional (3D) printed models. Farooqi and colleagues¹⁹ had 14 cardiac imagers and congenital surgeons review studies of 6 patients (echocardiogram, CTA, and 3D digital models). Participants accurately assessed AAOCA presence, type, and course on CTA and 3D models better than on echocardiogram. The 3D models were superior in the representation of ostial characteristics. Hatoum and colleagues²⁰ had patient-specific 3D printed models for 3 patients with right AAOCA. The models were placed in the aortic position of a pulse duplicator, and FFR and coronary flow rate were measured from the aortic to the mediastinal segment of the anomalous right coronary artery and compared with controls with normal coronaries. In 2 patients with AAOCA and history of ischemia, there was a gradual FFR decrease from the ostium

location (~1.0) to the distal intramural course (0.48). In 1 patient with AAOCA and no history of ischemia and in those with normal coronaries, FFR for all locations did not decrease below 0.9. The decrease in FFR improved after repair. In addition, coronary flow rate decreased with increasing aortic pressure, but the difference was greater in the patients with AAOCA and a history of ischemia. This might explain the origin of ischemia and sudden death risk in these patients and might prove useful in risk stratification. However, these models are associated with several limitations, including a small number of patients, the inability to assess various anatomic features that could affect ischemia (eg, ostial stenosis, long intramural course), and not modeling pulmonary artery pressure.

CONCLUSIONS

Many unknowns remain regarding AAOCA. However, each year there is an evolution of our understanding, with continual advances in our knowledge of new surgical techniques, surgical outcomes, and the utility of advanced techniques for imaging and risk stratification.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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