Anomalous Coronary Arteries
A State-of-the-Art Approach

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KEYWORDS

• Sudden cardiac death • Anomalous aortic origin of a coronary artery • Coronary artery anomalies • Advanced imaging • Cardiac catheterization

KEY POINTS

- Congenital anomalies of the coronary arteries may affect up to 1% of the population and lead to myocardial ischemia and sudden death.
- Echocardiography can diagnose anomalous coronaries in up to 95% of patients, though advanced imaging has greatly enhanced the ability to define morphologic features that impact outcome.
- Risk stratification remains a challenge in the setting of anomalous aortic origin of a coronary artery (AAOCA), and myocardial functional studies under provocative stress greatly contribute to management decision-making.
- Standardized approach to the evaluation and management of patients with coronary anomalies, with data gathering and collaboration among institutions, are paramount to optimize outcomes in this population.
- Optimal strategies in management will foster a safer environment for patients with coronary anomalies to engage in exercise and sports participation, essential components to successful and healthier lives.

INTRODUCTION

Congenital anomalies of the coronary arteries represent a varied group of lesions and are seen in less than 1% to 5% of the population, depending on method of diagnosis.[1,2] Embryologic development of the coronary artery is not completely understood, although altered coronary embryogenesis may result in abnormal coronary origins from the aorta or pulmonary artery or incomplete development leading to coronary fistulae or sinusoids. It can occur as an isolated anomaly or in association with other congenital heart diseases. Although many coronary artery anomalies are detected as incidental findings with little to no significant consequence, approximately 20% of all may have a potential risk of coronary ischemia leading to myocardial infarction, arrhythmia, and sudden cardiac death (SCD).[1–3] This report focuses on the anatomy, physiology, diagnostic strategy, and management of isolated anomalous origin of a coronary artery from the aorta and from the pulmonary artery.

ANOMALOUS AORTIC ORIGIN OF A CORONARY ARTERY

Prevalence and Clinical Significance

The true prevalence of anomalous aortic origin of a coronary artery (AAOCA) in the general population

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remains unknown because studies have focused primarily on symptomatic patients. The estimated frequency of anomalous aortic origin of the left coronary artery (AAOLCA) is 0.03% to 0.15%, whereas that of anomalous aortic origin of the right coronary artery (AAORCA) is 0.28% to 0.92%.[1,4] AAOCA is known to be the second leading cause of SCD in young athletes, estimated to be responsible for 15% to 20% of sudden death in this population.[3,5] The risk of SCD seems highest in young individuals, particularly during or following a period of strenuous exertion, and particularly in those with interarterial and intramural AAOLCA. Studies of adult cohorts with AAORCA undergoing conservative therapy have observed a very low mortality (<1%) in about 1 to 5 years of follow-up.[4,6]

Anatomic subtypes and pathophysiology

This anomaly can involve either the right coronary originating from the left sinus of Valsalva (reportedly more common) or the left coronary originating from the right sinus of Valsalva (**Fig. 1**), and rarely more posteriorly from the noncoronary sinus or near the posterior commissure with or without an intramural course.[7]

Several pathophysiologic mechanisms have been postulated for the occurrence of sudden cardiac arrest (SCA)/SCD in patients with AAOCA. These include occlusion and/or compression of the anomalous coronary artery (intramural segment, interarterial course) and ostial abnormalities (slit-like and stenotic ostium), particularly during exercise, leading to myocardial ischemia and development of ventricular arrhythmia.[8] In a study by Basso and colleagues, of 27 individuals who experienced SCD due to AAOCA, only 10 presented with symptoms before the event.[5] Given the significant number of patients that are asymptomatic before a critical adverse cardiac event, this highlights difficulties in evaluating patients at risk for adverse sudden cardiac events.

Clinical evaluation

Clinical Presentation and Diagnosis

In recent studies, about 50% of patients have been noted to be asymptomatic at diagnosis.[3,8–12] An increasing number of children and adolescents are being diagnosed with AAOCA following routine preparticipation screening, presence of a murmur, or an abnormal electrocardiogram (ECG).[10,11] Typical presenting symptoms that have been reported are exertional chest pain, palpitations, syncope, as well as SCA.[11,12]

Transthoracic echocardiography (TTE) is the first-line imaging modality for the initial diagnosis.[13,14] Recent report by Lorber and colleagues, found variable agreement between TTE and surgical findings.[14] In another study, TTE reliably and prospectively diagnosed AAOCA in more than 95% of the cohort, and the echo findings were always consistent with the surgical descriptions of the anatomy.[10] Lorber and colleagues also suggested that, apart from the use of TTE in the diagnosis of the abnormal coronary origins, TTE can be helpful in identifying critical anatomic features such as intramural/interarterial course, which may influence surgical management. However, they demonstrated that the assessment of coronary ostium as well as intramyocardial course was not well delineated by TTE. Thus, advanced imaging modalities, including computed tomography angiography (CTA) or cardiac magnetic resonance imaging (CMR) are extremely helpful in comprehensively defining the anatomy of the AAOCA, including ostial morphology, interarterial, intramural, or intramyocardial course.[15–22]

Noninvasive Testing Under Provocative Stress

Exercise stress test Exercise stress test (EST) is recommended in the evaluation of patients with coronary anomalies to assess for ischemic changes during exercise.[23,24] It has been used widely in children with coronary artery anomalies who can tolerate exercise, although it has a low sensitivity to detect inducible ischemia in this population.[5,10,23–29] Moreover, the interpretation of inducible ischemia may vary according to different studies when EST is reported "abnormal," which may reflect blunted blood pressure response, occurrence of premature ventricular contractions, or ST segment depression/elevation, the latter clearly with high specificity indicating inducible myocardial ischemia.[10,22,27,30] SCD during exertion has been reported in patients with coronary artery anomalies who had a normal EST before the event.[5] Brothers and colleagues reported a patient with AAOCA who initially had ischemic changes on EST but a repeat EST 1 week later was reassuring, which raised the question of intermittent nature of ischemia in the setting of AAOCA.[31] Current guidelines state that asymptomatic patients with AAORCA would be considered low-risk if EST is normal.[23,24] However, compelling data by Qasim and colleagues demonstrated the addition of cardiopulmonary exercise testing improved sensitivity of EST in patients with AAOCA, although EST is not well correlated with dobutamine stress CMR (DSCMR; **Fig. 2**).[26] Additionally, ischemic changes were recorded in only 1% of EST in a group of 164 patients with AAORCA.[25] Despite having a poor sensitivity, EST remains a valuable tool and seems to be specific in the presence of ST segment changes

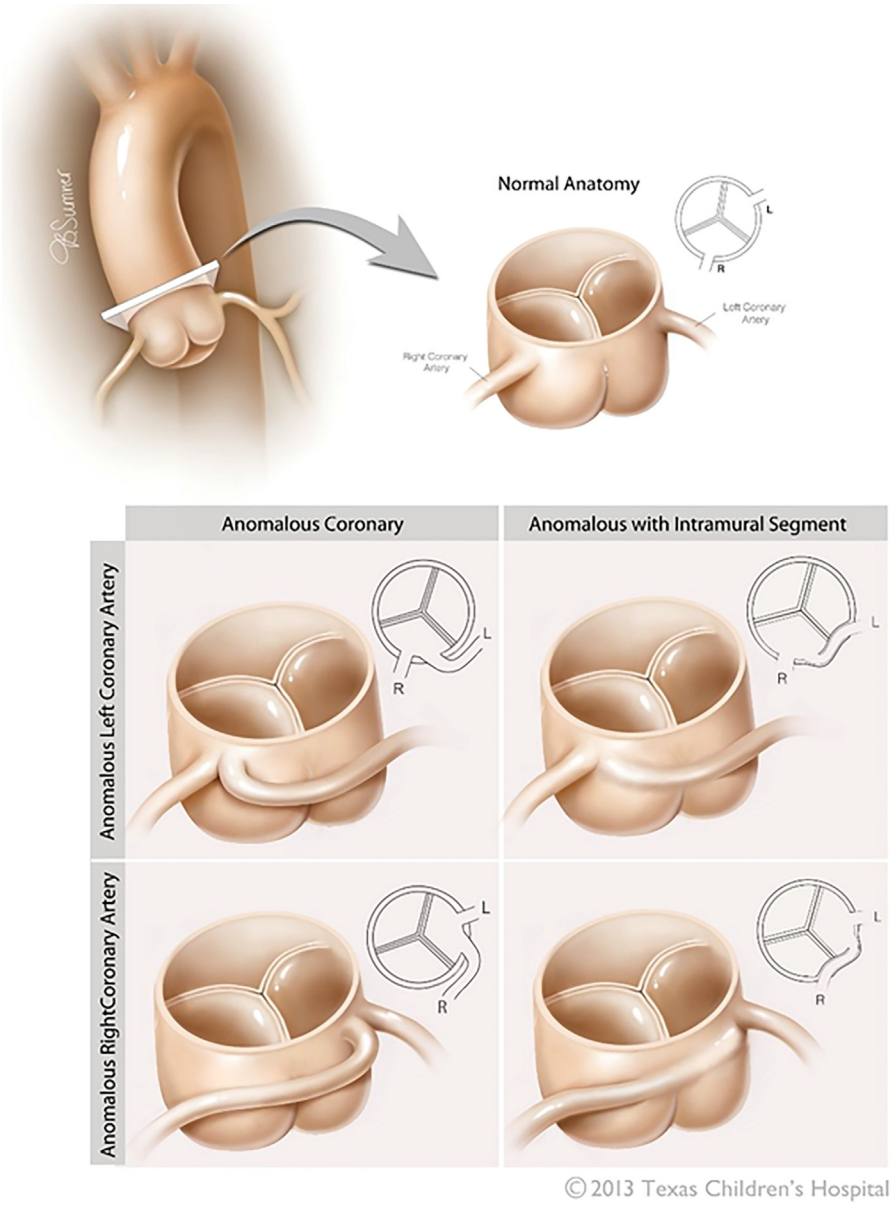

Fig. 1. Normal coronary anatomy and AAOCA subtypes. Printed with permission from Texas Children's Hospital.

suggestive of myocardial ischemia. Continued data gathering and correlation with other provocative tests investigating inducible myocardial ischemia is needed to further define its role in this young population with AAOCA.

Stress echocardiography Stress echocardiography has been established to identify new regional wall motion abnormalities or valvular dysfunction indicative of inducible myocardial ischemia following exercise (treadmill/cycloergometer) or during pharmacologic stress using dobutamine/atropine or adenosine/dipyridimole.[32–38] Heart rate decreases quickly, particularly in young children, a limitation that may prevent accurate acquisition and reading of images. Pharmacologic stimuli, however, allow for sustained peak heart rate with optimal image acquisition during peak stress, including in smaller children or infants.[39] It is available in most centers, portable, and less expensive than other advanced imaging modalities. Notwithstanding, training and expertise is important in the assessment of regional wall motion abnormalities, which may limit its use in centers with low patient volume and/or with variable readers. Yet, stress echocardiography has been

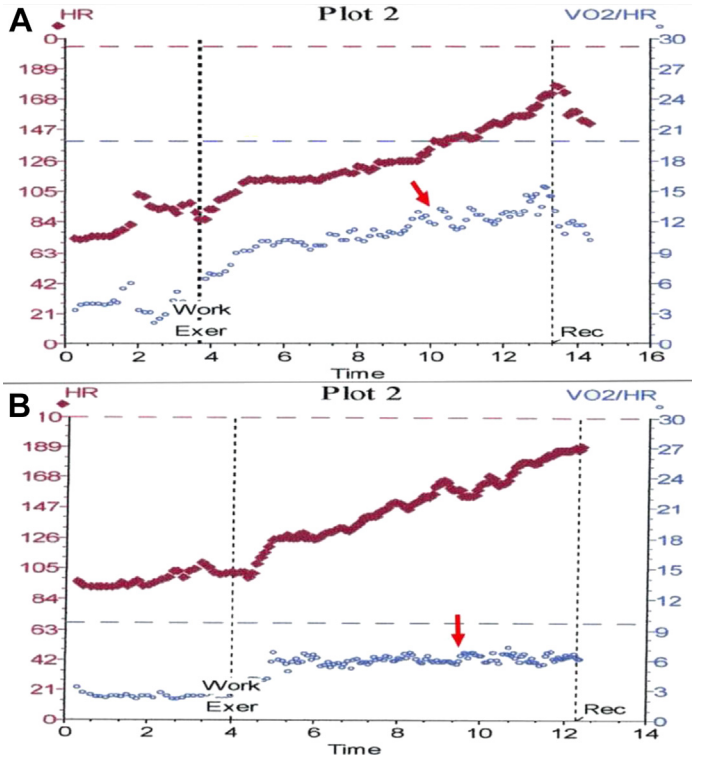

Fig. 2. Cardiopulmonary exercise testing (CPET) graphs showing normal upsloping O_2 pulse curve (*blue arrow*) (*A*) in a patient with AAORCA and abnormal flattening of O_2 pulse curve (*blue arrow*) (*B*) in a patient with AAORCA (patient also had subendocardial hypoperfusion in anterior and inferior septum on DSCMR). The horizontal dotted line on CPET graphs represents the maximal percentage predicted O_2 pulse for body mass. (*From* Qasim A, Doan TT, Pham TDN, Molossi S. Poster: Exercise stress testing in risk stratification of Anomalous Aortic Origin of a Coronary Artery. In: Pediatric Reseacrh Symposium at Texas Children's Hospital. ; 2021. https://www.texaschildrens.org/sites/default/files/uploads/documents/symposia/2021/posters/90.pdf. Printed with permission from Texas Children's Hospital.)

used in the pediatric population with a wide variety of indications where coronary lesions are suspected, such as acquired coronary disease and repaired/unrepaired congenital heart disease,[34,35,40,41] and as the preferred method to evaluate inducible myocardial ischemia in children/adolescents with AAOCA in some centers.[10,22,39,42–44] Currently, studies comparing different noninvasive testing modalities in the assessment of myocardial perfusion in AAOCA is lacking.

Advanced imaging on provocative stress

Nuclear perfusion imaging Nuclear perfusion imaging (NPI) with provocative stress is well established in adults for the evaluation of coronary artery/ischemic heart disease. Its use in the evaluation of inducible ischemia in the young with AAOCA has been reported by several groups (**Fig. 3**B).[22,27,30,44–47] However, concerns with patient exposure to ionizing radiation, high incidence of false-positive and false-negative findings, low spatial resolution, and attenuation artifacts are all factors that have resulted in decreasing interest for the use of NPI in this population. These are reasons that led our institution to transition to DSCMR as its safety, feasibility, and utility in a large cohort of children and adolescents with AAOCA have been recently published.[27,28,48–50]

Stress cardiac magnetic resonance imaging Stress cardiac magnetic resonance imaging has been reported to improve patient outcome when used to guide revascularization decision in adults with ischemic heart disease.[51–60] Several studies have demonstrated its safety and feasibility in children with coronary artery involvement following a diagnosis of Kawasaki disease and repaired complex congenital heart disease that include coronary artery transfer (ie, following arterial switch operation).[61–65] In these studies, hyperemia was achieved using adenosine or its selective alpha-2A receptor agonist (Regadenoson) to potentially unmask fixed obstructive coronary lesions. The proposed mechanism by which inducible ischemia may occur in patients with AAOCA has been postulated to relate to dynamic obstruction during exertion, although ostial abnormalities may be contributory as a fixed mechanism. Dobutamine has been viewed to closely mimic exercise because it increases contractility and decreases systemic vascular resistance,[56,57,65,66] thus inducing wall motion abnormalities at a time of maximal myocardial oxygen demand. DSCMR has demonstrated excellent performance with good prediction of ischemic events in adults.[54,66,67] First-pass perfusion, in addition to assessment of wall motion abnormalities, has increased the sensitivity of DSCMR, in keeping

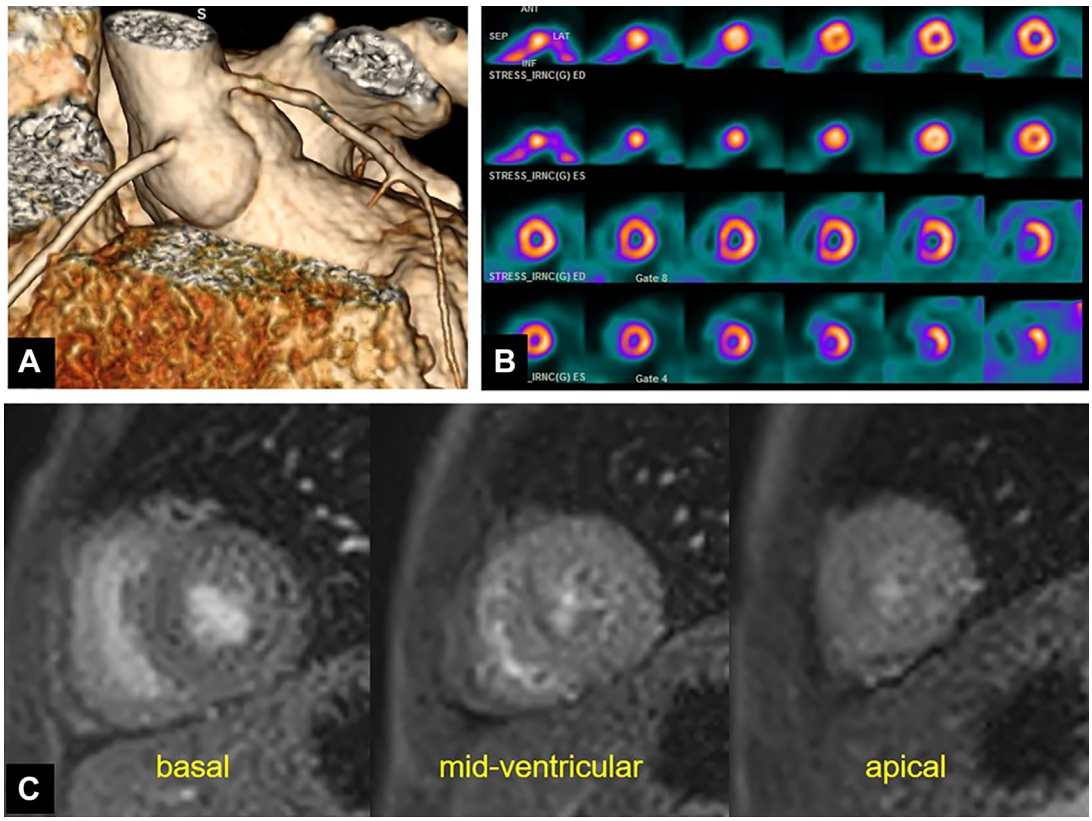

Fig. 3. A 9-year-old boy with AAOLCA at the sinotubular junction near the intercoronary commissure on CTA (*A*). Patient had a reassuring nuclear stress perfusion study (*B*), and no subendocardial hypoperfusion on DSCMR (*C*).

with the mechanism in demand ischemia cascade (where impaired perfusion precedes wall motion abnormalities).[56–58,60] Stress CMR additionally provides high-quality cardiac imaging with excellent spatial resolution and avoids ionizing radiation, an important factor especially in children/adolescents.[68–71] Doan and colleagues reported the largest cohort of children with AAOCA undergoing DSCMR,[48] including 224 studies in 182 patients younger than 20 years and median age of 14 years. Most studies were successfully completed with no sedation and 99% were free of major events, with only 12.5% reported minor events (Fig. 3; Fig. 4). Inducible perfusion defects were seen in 14%, and 42% among these had associated wall motion abnormalities. This study demonstrated safety and feasibility of DSCMR in the young patient with AAOCA and greatly contributed to management decisions.[48] Moreover, agreement between DSCMR and invasive fractional flow reserve (FFR) during dobutamine challenge was demonstrated in 13 young patients with AAOCA.[72] Comparable data was demonstrated in isolated case reports and intraseptal AAOLCA in a cohort of 19 patients reported by Doan and colleagues.[73–75] These authors reported stress perfusion imaging studies in 14 patients and 50% had inducible perfusion defects.[75] Given these more recent data, DSCMR clearly seems to have a defining role for the detection of perfusion abnormalities in AAOCA, allowing for comparison of results after surgical repair (in those patients for whom this intervention is indicated) with resolution of the inducible ischemia determined postoperatively (see Fig. 4).[27,28,48,49] However, image quality and expertise are paramount for the visual assessment of first-pass perfusion of gadolinium, specifically to differentiate dark rim artifacts from a true inducible perfusion defect. Risk stratification in AAOCA continues to be a challenge to determine those patients at risk for myocardial ischemia and DSCMR is clearly contributing to decision-making in this population.

Invasive Testing Under Provocative Stress

Angiography Angiography is generally not the first choice of imaging to diagnose anomalous coronary arteries in children. However, it is part of invasive assessment of coronary artery flow and has been performed in recent years when there is

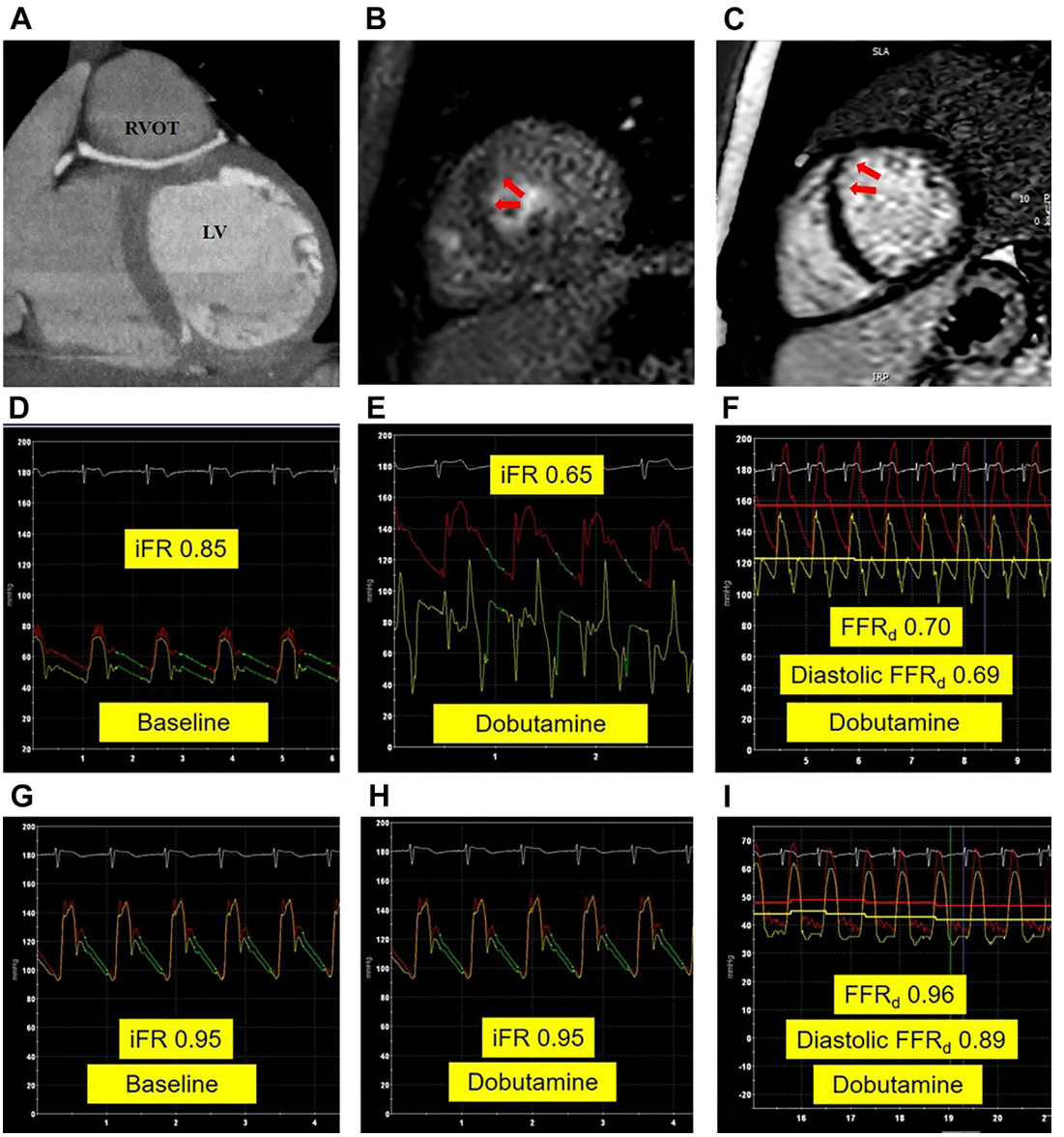

Fig. 4. A 16-year-old male patient with recurrent chest pain during wrestling practice. CTA showed AAOLCA with intraseptal course of the LCA (*A*). DSCMR showed subendocardial hypoperfusion in the anteroseptal wall (*red arrows*) (*B*), and late-gadolinium enhancement (*red arrows*) (*C*) indicates inducible ischemia and likely history of subendocardial infarction. Baseline iFR <0.89 (*D*), which further decreased to 0.65 (*E*), and diastolic FFR 0.69 <0.80 (*F*) consistent with impaired coronary flow. Following supraarterial myotomy of the intraseptal segment through a right ventriculotomy and direct reimplantation of the LCA, there were normalization of baseline iFR to 0.95 (*G*); at peak dobutamine stress, normal values of iFR at 0.95 (*H*), FFR at 0.96, and diastolic FFR at 0.89 (*I*). (*From* Doan TT, Molossi S, Qureshi AM, McKenzie ED. Intraseptal Anomalous Coronary Artery With Myocardial Infarction: Novel Surgical Approach. Ann Thorac Surg. 2020 Oct;110(4):e271-e274.)

conflict between clinical data and results from noninvasive studies.[76,77] Using pharmacologic stressors to mimic physiologic changes that occur during exercise may disclose hemodynamically significant lesions that would benefit from intervention, including measurement of coronary flow and angiographic assessment of the vessel diameter (**Fig. 5**B, C).

Fractional flow reserve FFR is a pressure-derived index of severity in the setting of coronary artery stenosis, calculated as a ratio between mean

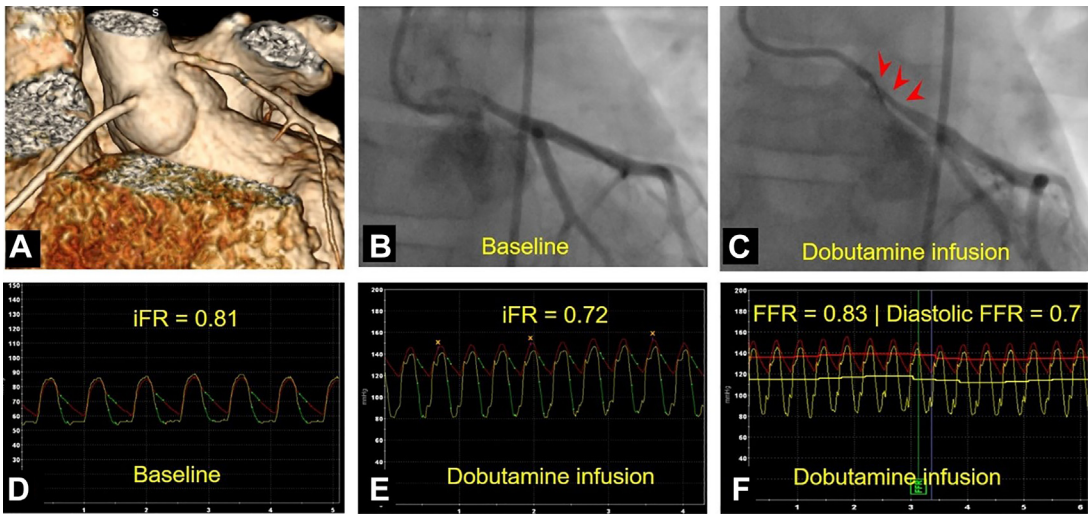

Fig. 5. Angiogram and intracoronary hemodynamic assessment in a 9-year-old boy with AAOLCA at the sinotubular junction near the intercoronary commissure on CTA (*A*). Despite reassuring DSCMR and nuclear stress perfusion study (see Fig. 3), the proximal LCA caliber changed from subtle narrowing (*B*) to severely compressed (*red arrowheads*) during dobutamine infusion (*C*). Baseline iFR <0.89 indicates significant coronary artery compression (*D*) and iFR further reduced during dobutamine infusion (*E*). Diastolic FFR <0.8 consistent with significant coronary flow impairment during provocative testing with dobutamine (*F*).

intracoronary pressure distal to the lesion (Pd) and mean aortic pressure (Pa) obtained during the entire cardiac cycle (see Fig. 4; Fig. 5). It requires the use of a coronary vasodilator to unmask a fixed obstructive coronary lesion. In adults with ischemic heart disease, coronary revascularization is typically indicated with FFR less than 0.8. In the setting of dynamic mechanisms leading to coronary compression, such as in AAOCA with intramural course or intraseptal course, dobutamine is considered the preferred pharmacologic agent to induce provocative stress mimicking some physiologic changes that occur with exercise.[48,65,78] Dobutamine induces positive inotropy and increased cardiac output, as it also induces decrease in systemic and coronary vascular resistance.[79–81] Diastolic FFR (dFFR), however, might constitute a better indicator of intracoronary hemodynamic assessment during dobutamine infusion given a potential overshooting of distal systolic pressure, which in turn may nullify a significant diastolic pressure gradient.[82] The initial data on the use of FFR in children with AAOCA was presented by Agrawal and colleagues in 2017, although in a small cohort that included 4 patients with AAOCA, stating its contribution in risk stratification in select patients.[76] As dFFR is calculated manually (average of 3 Pd/Pa ratio using digital calipers at end systole), it comprises a major limitation. In addition, the use of dobutamine is contraindicated in patients presenting with SCA, further limiting the assessment of FFR in AAOCA.

Instantaneous wave-free ratio Instantaneous wave-free ratio (iFR) is a drug-free pressure-derived index of coronary artery flow during a period of naturally constant and low resistance due to minimal competing pressure waves in diastole (see Figs. 4 and 5).[83] In theory, advantages of this index include no need of a vasodilator to reduce coronary vascular resistance and better procedure tolerance due to shorter procedure time.[84] iFR showed better agreement with coronary flow velocity reserve when compared with (JUSTIFY-CFR study)[85] and noninferior to FFR because it relates to health outcomes in guiding coronary revascularization in adults with ischemic heart disease.[84,86] Doan and colleagues very recently first reported the use of iFR in children with AAOCA.[78] Data showed that iFR correlated with adenosine FFR and dobutamine dFFR, thus being an alternative to those patients in which pharmacologic stressors (eg, dobutamine) are contraindicated. Moreover, the authors stated the data contributed to decision-making regarding coronary intervention. Additional recent data from the same authors published resting iFR and dFFR with dobutamine challenge guiding decision-making in a subset of patients with concerning clinical symptoms but negative noninvasive perfusion studies under provocative stress.[87] These abnormal values of intracoronary flow were shown to completely resolve on repeat invasive studies following surgical intervention (see Fig. 4G–I).

Of interest, the principles of iFR during dobutamine challenge neutralizes the systolic overshooting phenomenon in the assessment of potential dynamic compression in AAOCA, indicating that dynamic compression during provocative stress could be of value in unfolding hemodynamic significant coronary obstruction in the setting of AAOCA. Specifically, Ghobrial and colleagues published their center experience in symptomatic adult AAOCA patients using iFR and dobutamine challenge.[88] Similarly, these authors reported improvement in dobutamine iFR in 18 patients following surgical repair of the anomalous vessel. We have observed similar pattern of provocative pharmacologic stress with dobutamine affect iFR values in children with AAOCA compared with those seen at rest in our center (unpublished data). As promising as these data on significant improvement in iFR and FFR following surgical repair of AAOCA are,[89] it is important to keep in perspective that such cutoff values derive from ischemic coronary artery disease in adults and may not be the optimal values in the setting of AAOCA, which likely includes mostly a dynamic component leading to myocardial ischemia and sudden events, especially in the young population.

Intravascular ultrasound Intravascular ultrasound (IVUS) in AAOCA has been widely used in adults and considered the gold standard for the assessment of the intramural segment given its excellent spatial determination and evaluation of dynamic lateral compression at rest and compared with pharmacologic stress.[4,90–92] Angelini and colleagues published data in adult patients with AAORCA where IVUS showed the worst area of stenosis in the intramural segment of the RCA proximally, immediately distal to its ostium.[90] IVUS performed under pharmacologic stress includes administration of saline bolus, atropine, and dobutamine. The diameter (minimal and maximal) of the anomalous coronary in the compromised area is measured in both systole and diastole. Significant coronary compression includes an area ratio greater than 50% at baseline and/or greater than 60% during provocative stress.[90] Its use has also guided stent placement in the proximal intramural segment in select adults patients with AAORCA.[90] Although IVUS is used in pediatric patients for the evaluation of certain congenital heart lesions,[93] its use in the setting of AAOCA is hardly existent. Agrawal and colleagues reported a small cohort of pediatric patients with AAOCA and myocardial bridges describing the feasibility and safety of IVUS, and its significant contribution in management decision-making.[76] This seems promising in a very selected group of patients with AAOCA but substantial data are needed to determine its role in risk stratification in young patients. More importantly, perhaps, this should not be considered a common technique in the evaluation of young patients with AAOCA because expertise is essential to mitigate potential serious coronary complications with the procedure.

Management decision-making

Medical Management

At our institution, we use a previously published standardized approach in the assessment and management of AAOCA (**Fig. 6**).[27] Clinical follow-up without medication or intervention is indicated when the provocative testing is negative for ischemic changes in the asymptomatic patient with AAORCA.[94] Exercise restriction with or without beta-blocker therapy (in the setting of intraseptal AAOLCA) is indicated when surgery is recommended in a patient with AAOCA but surgery is either denied or not feasible given the anatomy.[73] In our experience, medical management in a young athlete with beta-blocker therapy is challenging given its effect in athletic performance. Therefore, surgical intervention is favored when it outweighs the risks. Following surgical repair of the anomalous coronary artery, we empirically recommend antiplatelet therapy with aspirin for 3 months, with discontinuation following reassuring postoperative studies at this time.

Surgical Approach

To date, the exact mechanisms of ischemia leading to SCA in AAOCA remain undefined, as do clinical and morphologic features that increase the risk of ischemia and SCA.[95–98] Surgical repair of AAOCA has been performed to potentially address this risk and mitigate the occurrence of SCA, although surgical indications and benefits remain unclear with significant variation in practice.[10,12,28,49,99,100] Current consensus guidelines provide a standardized approach that surgical intervention is recommended for those with signs and/or symptoms of ischemia (class I).[23,24,94] In asymptomatic patients with reassuring diagnostic testing, surgery is recommended (class IIa) for patients with AAORCA who had ventricular arrhythmia and in AAOLCA.[94] Patients who are diagnosed with AAORCA can be considered for surgery despite reassuring testing and no other clinical concern (class IIb).[94] The goals of AAOCA repair are to yield an unobstructed coronary artery from the appropriate aortic sinus while minimizing the risk of procedural complications.[28,101] Surgical repair of AAOCA should aim at eliminating the intramural course and its associated ostial narrowing by unroofing,

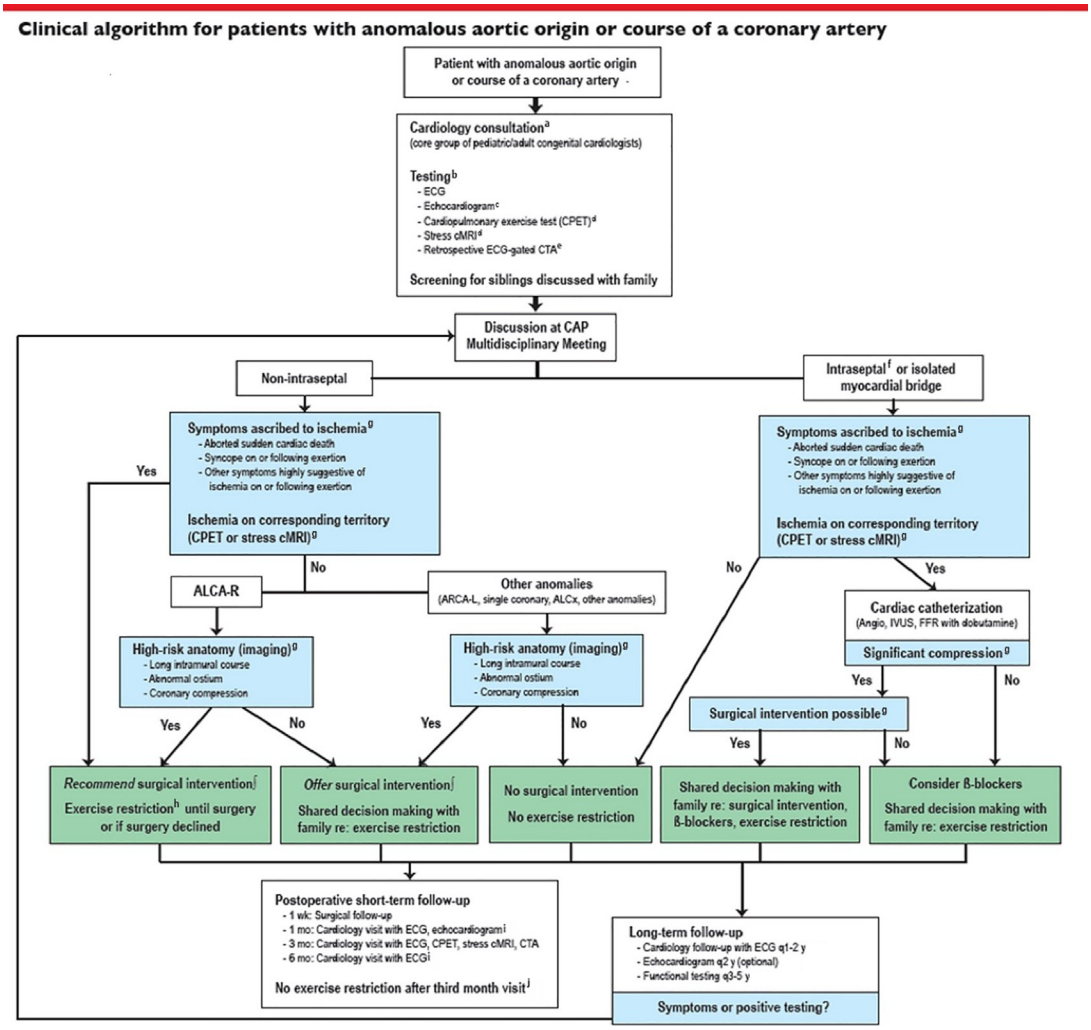

Fig. 6. Clinical algorithm for patients with anomalous aortic origin of a coronary artery.ALCA-R, anomalous left coronary from the right sinus; ALCx, anomalous left circumflex artery; ARCA-L, anomalous right coronary from the left sinus; CAP, coronary anomalies program. [a]Consent abtained for participation in prospective CHSS aand TCH databases. [b]Additional studies (Holter,cardiac catheterization, etc) may be performed depending on the clinical assessment.[c]External echocardiograms do not need to be repeated if the study is deemed appropriate. [d]CPET or stress cMRI not necessary on patients that present with aborted sudden cardiac death. These studies may be deferred in young patients. [e]An external CTA may be used if able to upload the images and the study provides all necessary information to make a decision. CTA should ne deferred in patients <8 years unless clinical concerns. [f]An intraseptal coronaru is as an abnormal vessel(usually a left coronary arising from the right sinus)that travels posteriorly into the septum below the level of the pulmonary valve. [g]Unrollfing if significant intramural segment, neo-ostium creation or voronary translocation if intramural segment behind a commissure,coronary translocation if short or no intramural segment. Surgical intervention will be offered for patients between 10 and 35 years of age. Other patients will be considered on a case-by-case basis. Aspirin will be administered for 3 months after surgery. [h]Restriction form participation in all competitive sports and in exercise with moderate or high dynamic component(> 40% maximal oxygen uptake-e.g.,soccer, tennis, swimming, basketball, American football). (Mitchell et al, JACC 2005:1364-1367). [i]Patient may be seen by outside primary cardiologist. [j]Postoperative patients will be cleared for exercise and competitive sports based on findings at the third month postoperative visit including results of CPET, stress cMRI and CTA. Printed with permission from Texas Children's Hospital.

ostioplasty, or transection and reimplantation (TAR).[24] Unroofing of an intramural course is most commonly reported, although other techniques including TAR or neo-ostium creation have also been performed.[10,28,49,99,102,103] Repositioning of the pulmonary artery confluence away from the anomalous artery may be considered as an adjunctive procedure but less widely

used.[24] Surgical intervention is generally successful, although complication and reoperation due to coronary artery stenosis have been reported up to 5% in the 7 years following the index operation in a multicenter study.[99]

Anomalous aortic origin of a coronary artery with interarterial course or anomalous aortic origin of the left coronary artery from the noncoronary sinus The primary surgical strategies described at our center included unroofing of an intramural course and coronary TAR (**Fig. 7**). We do not favor takedown of the aortic commissure at the time of surgical unroofing due to the potential risk of postoperative aortic insufficiency.[28] Unroofing has been our surgical procedure of choice for patients with an intramural segment above the aortic valve in which the technique is believed to move the ostium to the correct sinus. TAR has been used for patients with short intramural length and the intramural segment traveling below the level of the aortic valve commissure, in whom surgical unroofing would not result in placing the ostium in its correct aortic sinus (**Fig. 8**).[28,49,101]

Coronary unroofing is a widely used technique and is considered relatively safe in the surgical repair of AAOCA.[10,103–106] Coronary TAR has been performed in both adults and children when the unroofing technique is deemed to have potential disruption of the aortic valve integrity.[49,100,107,108] TAR requires extensive coronary manipulation involving transection followed by reimplantation of the anomalous coronary artery without an aortic button. It is important to emphasize that it is still unknown which surgical technique is superior, and that TAR should only be considered in select candidates and performed in centers with expertise given the technical complexity with potential iatrogenic complications.[109]

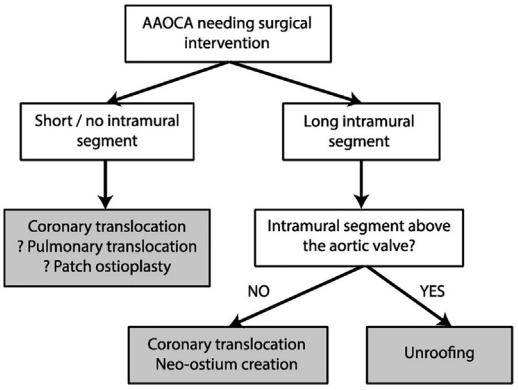

Fig. 7. Proposed algorithm to select surgical intervention techniques for patients with AAOCA based on coronary artery anatomy using computerized tomography angiography and surgical inspection. (*From* Mery CM, De León LE, Molossi S, Sexson-Tejtel SK, Agrawal H, Krishnamurthy R, Masand P, Qureshi AM, McKenzie ED, Fraser CD Jr. Outcomes of surgical intervention for anomalous aortic origin of a coronary artery: A large contemporary prospective cohort study. J Thorac Cardiovasc Surg. 2018 Jan;155(1):305-319.e4.)

Anomalous aortic origin of the left coronary artery with intraseptal course Surgical intervention for this anomaly is challenged by the limitation of current surgical techniques and the uncertainty of long-term outcomes. Najm and colleagues performed unroofing of the intraseptal LCA by circumferentially transecting and extending the right ventricular infundibulum using autologous pericardium.[110,111] The authors reported excellent surgical outcome in 14 patients who have been followed between 1.5 and 45 months.[111] Others have reported anterior translocation of the right pulmonary artery and division of the muscle overlying the LCA externally between the aortic root and pulmonary artery.[12] We have reported a successful supraarterial myotomy of the intraseptal segment through a right ventriculotomy and direct reimplantation of the left coronary artery. This patient recovered well with improved physiologic provocative testing following surgery and has returned to competitive wrestling without issues.[74]

Recommendations to physical activities

Consensus guidelines state that 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.[24] The asymptomatic patient with AAORCA and no evidence of ischemia clinically and with provocative testing can participate in competitive athletics. However, patients and family should be appropriately informed and counseled of the known risk of SCD, although rare, and the uncertain accuracy of a negative stress test.[23] It is important to recommend preparedness for cardiac events such as having an automated external defibrillator (AED) available with individuals who know how to use it, as part of an emergency action plan. However, individuals with untreated AAOLCA from the opposite (right) anterior sinus of Valsalva, regardless of symptomatology, are restricted from all competitive sports.[23,24,94]

Following successful surgical repair of AAOCA, athletes may consider participation in all sports 3 months after surgery if the patient remains free of symptoms, an EST shows no evidence of ischemia or cardiac arrhythmias, and a stress perfusion imaging study shows no inducible perfusion defect or regional wall motion abnormalities.[24,27,28] In patients

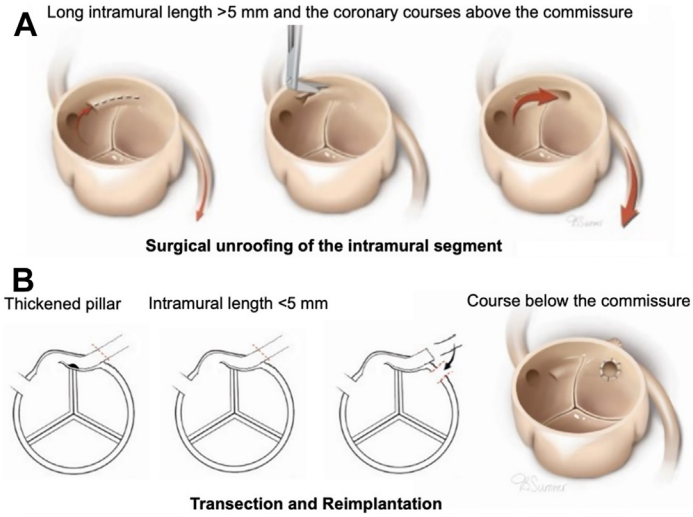

Fig. 8. Diagrams of surgical unroofing of an intramural course (*A*) versus transection and reimplantation (*B*) based on anatomic features on CTA and surgical inspection. Printed with permission from Texas Children's Hospital.

who presented with aborted SCD, a longer postoperative period (12 months) may be necessary to ensure patients are free of symptoms suggesting ischemia or arrhythmia and have no evidence of myocardial ischemia on provocative testing or concerning arrhythmia.[24] An AED should be available for all of these patients with available personnel who are trained in cardiopulmonary resuscitation and how to use an AED.[24]

ANOMALOUS CORONARY ARTERY ORIGIN FROM THE PULMONARY ARTERY

Prevalence, Anatomy, Physiology, and Diagnosis

Prevalence

Anomalous origin of the left coronary artery from pulmonary artery (ALCAPA) is a rare disease, occurring in 1 in 3,00,000 live births or 0.4% of patients with congenital cardiac abnormalities,[112] that if untreated causes heart failure, myocardial ischemia, and death. The incidence of ALCAPA is thought to be higher than that of anomalous origin of the right coronary artery from pulmonary artery (ARCAPA) due to the proximity of the left coronary bud to the pulmonary artery sinus (although ARCAPA may have been underdiagnosed due to its initially relatively innocuous nature compared with ALCAPA).[113,114] ARCAPA is known to occur in 0.002% of patients with congenital cardiac abnormalities.[114–116]

Anatomy

The most common defect of this type is ALCAPA, sometimes known as Bland-White-Garland syndrome.[117,118] In some cases, the left anterior descending and left circumflex coronary arteries have individual origins from the pulmonary artery, with similar pathophysiologic and clinical sequelae.[119,120] The origin of the right coronary artery from the pulmonary artery has been thought to be benign; however, clinical sequelae have been described although later in life.[121]

Physiology

Fetuses with ALCAPA remain asymptomatic because the diastolic pressure in the pulmonary artery and aorta are similar during prenatal circulation. When the pulmonary vascular resistance starts to drop after birth, symptoms start to appear in most infants due to a reversal flow through left coronary artery. This leads to coronary artery steal and further progression of myocardial ischemia. This may be exacerbated during periods of stress, which in infants can occur during feedings. The surrounding arteries start to create collateral blood flow to the affected ventricle. Mitral valve regurgitation occurs in the disease process secondary to ventricular dilatation and papillary muscle ischemia. Patients may initially present with subtle symptoms of extreme fussiness with feeds, due to the ischemia, and ultimately progress toward respiratory distress as heart failure ensues.[122–124] Nevertheless, many patients may do well and be completely asymptomatic, engaging in sports activities until late childhood and adolescence when the diagnosis is established following evaluation for a murmur (commonly mitral regurgitation from chronic ischemia to the mitral valve apparatus).

Due to the reduced ventricular workload and oxygen demands of the right ventricle compared with that of the left ventricle, ventricular ischemia is less prominent in ARCAPA than in ALCAPA and may present in adult life. However, ARCAPA

patients with a right dominant coronary circulation do exhibit chronic ischemia and have increased adverse outcomes than patients with a left dominant circulation.[125,126]

Diagnosis

This condition is usually suspected on echocardiography either by direct visualization of the coronary artery from the pulmonary artery or by secondary signs of ventricular dysfunction, mitral regurgitation, echogenic papillary muscles, dilation of right coronary artery (due to collateral formation in ALCAPA) as well as the presence of flow signals within the myocardium suggesting collateral flow (**Figs. 9** and **10**).[127,128] Noninvasive cross-sectional imaging with either CTA or CMR may assist in more definitive diagnosis and provide additional information.

The electrocardiogram of a patient with ALCAPA may show evidence for anterolateral ischemia or infarction, including transient or chronic ST-segment changes in the anterolateral leads or Q waves in leads I aVL, V5, and V6.[129]

Although patients with ARCAPA may mirror the symptoms of ALCAPA, it is usually diagnosed at autopsy or in asymptomatic children or adults. Electrocardiographic findings are often nonspecific. The diagnosis can be made with careful TTE that includes meticulous attention to the origins of the coronary arteries. CTA of the coronary arteries is also diagnostic. Alternatively, cardiac catheterization provides hemodynamic assessment in addition to coronary angiography to confirm the diagnosis.[114,116,130]

Surgical Approach

All anomalously originating coronary arteries from the pulmonary artery require surgical correction. At this time, there are no percutaneous treatment options to repair this anomaly.

Anomalous origin of the left coronary artery from the pulmonary artery

Regardless of clinical status, patients with ALCAPA would require urgent operation.[130] Creating a two-artery coronary system is indicated in all situations, including critically ill infants. Available pathologic information indicates that either a tunnel (Takeuchi) repair or translocation of the connection to the aortic root, if feasible.[130] Takeuchi described the procedure involving creation of a coronary tunnel inside the pulmonary artery to

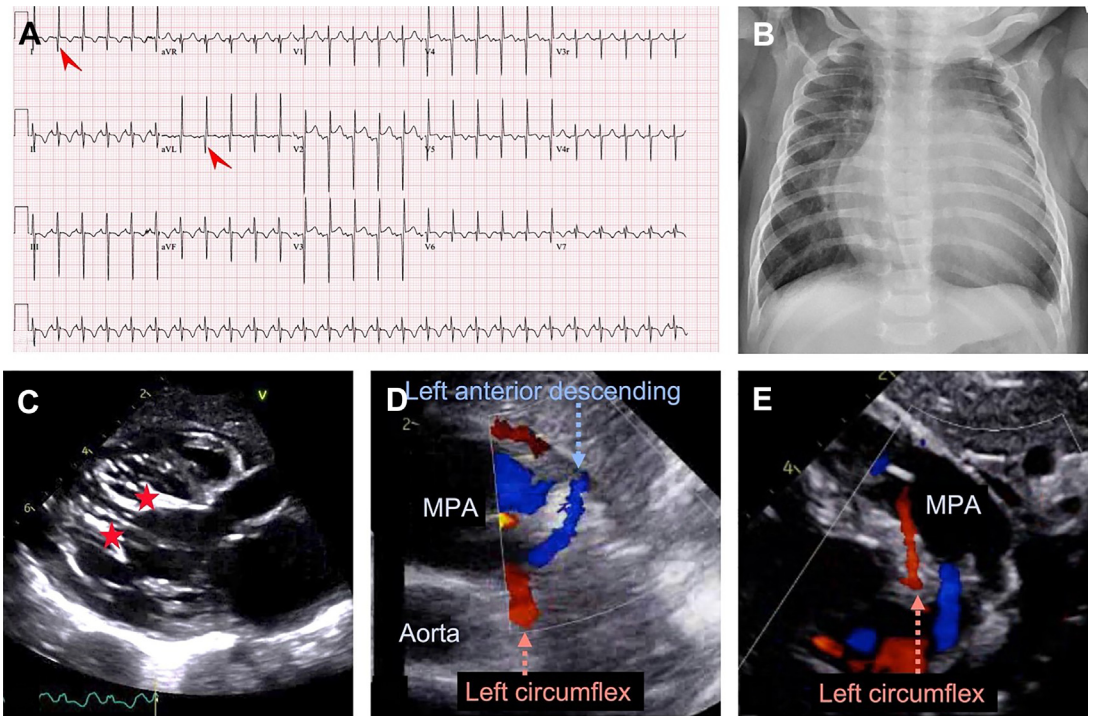

Fig. 9. ALCAPA in a 2-month-old infant who presented with failure to thrive and heart failure. ECG showed normal sinus rhythm, left axis deviation, Q wave in lead I and aVL (*arrowheads*), and T-wave inversion in the inferolateral leads (*A*), severe cardiomegaly and pulmonary edema (*B*), echogenic papillary muscles (*red stars*, C), retrograde flow in the left anterior descending coronary artery (*D*), and circumflex artery (*E*). MPA, main pulmonary artery.

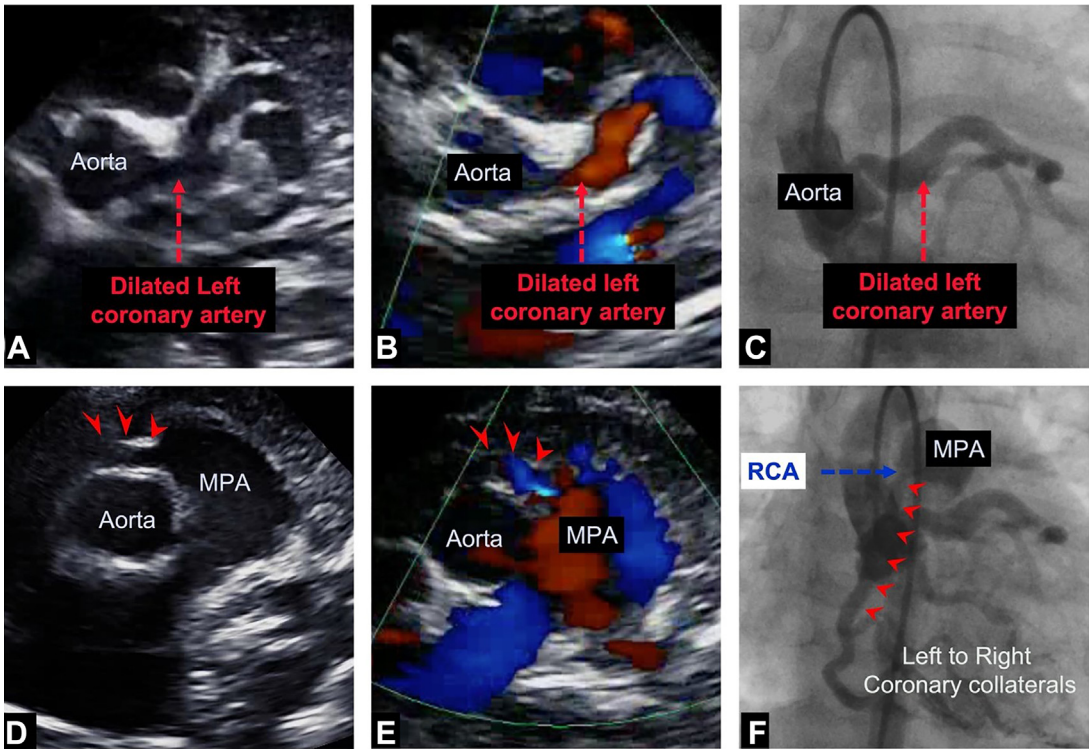

Fig. 10. ARCAPA in a healthy appearing 9-month-old infant who was referred for an evaluation of a heart murmur. Echocardiographic images demonstrated dilated left coronary artery with normal aortic origin and prograde flow (*A–C*), which then provides flow to the right coronary artery (RCA, *arrowheads*), which connects to the main pulmonary artery (MPA) with flow from RCA to MPA (*D–F*).

establish continuity between the aorta and the LCA ostium, in 1979.[131–133] This procedure was useful in cases in which direct implantation was thought to be difficult because of unfavorable coronary anatomy. Use of this method is declining given the high rate of complications including supravalvular pulmonary stenosis, intrapulmonary baffle leaks, and aortic valve insufficiency as well as a 30% chance of reoperation or catheter intervention over time. Thus, direct reimplantation has increasingly become the procedure of choice. Urgent corrective surgery to establish a two-coronary circulation is shown to lead to quick recovery of ventricular function in majority with excellent long-term survival.[131,134–137] A recent cohort study by Patel and colleagues described early surgical outcomes in 37 subjects with ALCAPA with short length of postoperative stay, low morbidity, and no surgical mortality. As in prior studies, they found more late complications with the Takeuchi procedure compared with direct reimplantation.[128] These patients had excellent status at their long-term follow-up, with a significant improvement in the left ventricular ejection fraction and mitral valve regurgitation.[128,138,139] Despite normal ejection fraction, most patients had abnormal measurement of myocardial mechanics.[138]

Anomalous origin of the right coronary artery from the pulmonary artery

According to the latest American Heart Association/American College of Cardiology guidelines, repair is a Class I recommendation for symptomatic patients with ARCAPA and a Class IIa recommendation in asymptomatic patients with ventricular dysfunction or myocardial ischemia attributed to ARCAPA.[94] Surgical intervention consists of reimplantation of the RCA, including excising the anomalous origin of the RCA along with a button of the pulmonary arterial wall and translocating it into the anterior aspect of the ascending aorta.[114,130]

Recommendations to physical activities

Athletes with ALCAPA or ARCAPA can participate only in low-intensity class IA sports, whether or not they have had a prior myocardial infarction, and pending repair of the anomaly.[23] After repair of ALCAPA and ARCAPA, decisions regarding

exercise restriction may be based on the presence of sequelae such as myocardial infarction or ventricular dysfunction.[23]

SUMMARY

Congenital coronary anomalies are not an infrequent occurrence, and their clinical presentation typically occurs during early years, although may be manifested only in adulthood. In the setting of AAOCA, this is particularly concerning because it inflicts sudden loss of healthy young lives. This event, although rare, leads to incalculable grief in families, organizations, and communities. An anomalous origin of one or more coronary arteries from the pulmonary artery is hemodynamically significant and produces myocardial ischemia leading to ischemic cardiomyopathy or SCD, thus surgical intervention in this setting is well defined. However, in AAOCA, current published consensus guidelines for the diagnosis and management of these abnormalities are limited by insufficient evidence due to lack of hard endpoints. There remains significant variability in risk stratification and management decisions, particularly in the asymptomatic patient. Standardized approach to the evaluation of these patients, with careful data collection and collaboration among centers, is likely the way to improve risk stratification and lead to optimal management decision. Such strategies will foster a safer environment for these patients to engage in exercise and sports participation, key components to successful and healthier lives.

CLINICS CARE POINTS

- Coronary artery anomalies may occur in up to 1% of the population and comprise the second most frequent cause of sudden death in the young.
- Echocardiography can diagnose up to 95% of patients, though advanced imaging is essential to define morphologic features.
- Myocardial functional studies under provocative stress are important in risk stratification.
- Surgical intervention may be indicated in a subset of patients.
- Exercise activities should be carefully considered as sedentarism is a great risk factor for lifetime cardiovascular disease.

DISCLOSURE

The authors have nothing to disclose.

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