Outcomes after anomalous aortic origin of a coronary artery repair: A Congenital Heart Surgeons' Society Study

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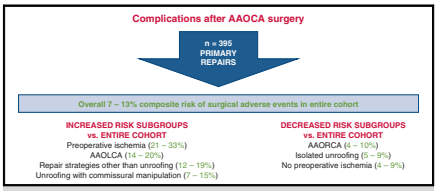
ABSTRACT

Objectives: It remains unclear when sudden cardiac event risk outweighs surgical risk for patients with anomalous aortic origin of a coronary artery. The Congenital Heart Surgeons' Society sought to characterize the surgical risks by determining the techniques, complications, and outcomes of repair.

Methods: Between January 2000 and September 2018, 682 patients with anomalous aortic origin of a coronary artery aged 30 years or less were enrolled. Demographic, morphologic, operative, imaging, and ischemia-related data were analyzed.

Results: There were 395 of 682 (57%) surgical patients (45 centers, median follow-up 2.8 years). In addition to primary repair (87% unroofing, 26% commissural manipulation), 13 patients had 15 coronary-related reoperations. Of 358 patients with pre/postoperative aortic insufficiency assessment, 27 (8%) developed new mild or greater aortic insufficiency postoperatively, and 7 (2%) developed new moderate or greater aortic insufficiency. Freedom from mild aortic insufficiency differed in those with versus without commissural manipulation (85%/91% at 6 months, 83%/90% at 1 year, and 77%/88% at 3 years, respectively) ($P = .05$). Of 347 patients with preoperative/postoperative ejection fraction, 6 (2%) developed new abnormal ejection fraction (<50%) within 30 days of surgery which persisted. Although 64 of 395 patients (16%) had preoperative ischemia, after surgery 51 of 64 patients (80%) no longer had ischemia (13 = new postoperative ischemia, $P < .0001$). Four patients died postoperatively (preoperatively 2 asymptomatic, 1 symptomatic, 1 in extremis). Composite surgical adverse event rates were 7% to 13% in the entire cohort (increasing/decreasing by presentation/anatomy/repair strategy).

Conclusions: Anomalous aortic origin of a coronary artery surgery may relieve ischemia with low mortality; however, it can result in a variety of important morbidities, varying by the group evaluated. Strategies avoiding commissural manipulation may



Primary findings related to the surgical risks of AAOCA repair.

CENTRAL MESSAGE

AAOCA repair may relieve ischemia with low mortality, but can result in important morbidity varying by presentation/anatomy/repair. Avoiding commissural manipulation may reduce the risk of developing AI.

PERSPECTIVE

Past AAOCA studies have been mainly small single-center series with short follow-up. We studied 395 surgical patients (45 centers, median 2.8 years follow-up). Mortality was low, but there was a range of important morbidities (varying by presentation/anatomy/repair), which may have long-term sequelae. Avoiding commissural manipulation may reduce AI. These should inform risk stratification and management.

See Commentaries on pages 772, 774, and 775.

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Abbreviations and Acronyms

AAOCA = anomalous aortic origin of a coronary artery
AAOLCA = anomalous aortic origin of a left coronary artery
AAORCA = anomalous aortic origin of a right coronary artery
AI = aortic insufficiency
CHSS = Congenital Heart Surgeons' Society
CPET = cardiopulmonary exercise test
ECMO = extracorporeal membrane oxygenation
EF = ejection fraction

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decrease the risk of developing aortic insufficiency. Understanding these risks should inform surgical decision-making and support the need for standardized assessment and management. (J Thorac Cardiovasc Surg 2020;160:757-71)

Anomalous aortic origin of a coronary artery (AAOCA) is a rare congenital cardiac anomaly that may be associated with myocardial ischemia and has an estimated prevalence of 0.01% to 2% of the population.[1] There are numerous anatomic variants wherein 1 or both coronary arteries arise from the contralateral sinus of Valsalva or with a high (supra-sinus) origin, with or without ostial abnormalities, and most often with an abnormal course. Most commonly, the courses are interarterial and/or intramural or intraconal. Patients may present with symptoms of ischemia or sudden cardiac events, including death, but most are asymptomatic and diagnosed incidentally.[2,3] Numerous knowledge gaps remain, including the prevalence in the general population, the mechanism of sudden cardiac events, the morphologies predictive of ischemia, and which patients may benefit from surgical repair. Despite this, numerous patients including many who are asymptomatic, undergo repair every year without a clear understanding of whether the risks of sudden cardiac events outweigh the risks of surgery.

Currently, surgical repair in AAOCA is primarily intended to mitigate the risk of sudden cardiac events in those who have experienced them or prevent lingering uncertainty related to the potential risk of sudden cardiac death in asymptomatic patients, especially those wanting to continue high-level athletics. However, the short-, mid-, and long-term outcomes of repair are incompletely understood. Most studies in the literature are primarily from single centers and have limited long-term follow-up. Attempts to draw lessons from these are further confounded by the fact that they include numerous morphologic variants that require nuanced surgical strategies; as well, surgeons and institutional teams have variable preferences for surgical referral and techniques. This has resulted in unclear risk stratification with limited surgical guidelines.[4,5]

Because of the many unknowns surrounding this lesion and its repair, the Congenital Heart Surgeons' Society (CHSS) established the AAOCA Registry in 2009 to examine the natural and unnatural (surgical) history of AAOCA, including the long-term outcomes, with the goals of guiding both risk stratification and management. The primary aims of this study were to evaluate the outcomes of AAOCA repair by (1) characterizing both the operations and reoperations that patients underwent; (2) evaluating complications, including those pertaining to changes in ejection fraction (EF) and aortic valve competence; (3) evaluating changes in ischemia status following surgery; and (4) examining survival after surgery.

MATERIALS AND METHODS

Patients

This cohort includes patients aged 30 years or less who met the inclusion criteria retrospectively between January 1, 2000, and January 20, 2009, and prospectively between January 21, 2009, and September 31, 2018, from 47 CHSS institutions. A list of all enrolling institutions is shown in Appendix E1. The inclusion and exclusion criteria for this cohort are shown in Appendix E2. Previous studies from the CHSS cohort have focused on the Registry design and implementation, descriptions of the cohort, surgical procedures performed, correlation between echocardiographic and intraoperative evaluation, how exercise restriction affects body mass index, and the morphologic features associated with ischemia and sudden cardiac events.[2,6-11]

For this study, we evaluated all patients who underwent AAOCA repair. Baseline (demographic, morphologic, imaging, ischemia testing), surgical, and follow-up data (complications, imaging, ischemia testing, reoperations, and mortality) were evaluated. Echocardiogram reports were reviewed to determine if patients had developed changes in aortic valve competence as demonstrated by aortic insufficiency (AI) on the latest study (because of the potential for worsening over time) or left ventricular function based on abnormal EF (<50%) within 30 days and at latest follow-up. Results of ischemia testing, including data from cardiopulmonary exercise tests (CPET), stress echocardiograms, and nuclear perfusion scans, were also analyzed. All operative reports were abstracted by Data Center staff, followed by review and adjudication by 2 surgeons. Discharge summaries and clinic notes were reviewed for complications.

In this study, a patient was determined to have ischemia if he/she had at least 1 positive provocative ischemia test (CPET, stress echocardiograms, and nuclear perfusion scans) or met the criteria for ischemic symptoms or presentations described in Table 1, *A*. Chest pain in the absence of positive biomarkers or electrocardiographic changes was not sufficient to be classified as ischemia. Commissural manipulation is defined as takedown

TABLE 1. Criteria for preoperative or postoperative ischemia and criteria for surgical adverse events

A. **Criteria for preoperative or postoperative ischemia**
- I. Any of the following events:
  - a. Sudden cardiac death (only postoperative)
    and/or
  - b. Sudden cardiac arrest
    and/or
  - c. Requirement for cardiopulmonary resuscitation
    and/or
  - d. Requirement for ECMO

OR
- II. Presenting symptom of:
  - a. Syncope during or after exercise not explained by dehydration or a vasovagal event

OR
- III. Abnormal test:
  - a. Biomarkers (creatine kinase-muscle/brain or troponin I) above normal in the setting of congruent symptoms
    and/or
  - b. Ventricular tachycardia, infarction or ischemia on electrocardiogram in the same coronary artery territory as the anomalous coronary artery[12]
    and/or
  - c. Abnormal CPET with ST-segment changes in the same coronary artery territory as the anomalous coronary artery, exercise-induced hypotension, and/or significant arrhythmia (eg, ventricular tachycardia)[13]

OR
- IV. Abnormal imaging:
  - a. Abnormal perfusion scan with perfusion defect in the same coronary artery territory as the anomalous coronary artery
    and/or
  - b. Abnormal stress echocardiogram with wall motion abnormality in the same coronary artery territory as the anomalous coronary artery
    and/or
  - c. Abnormal MRI with evidence of fibrosis or scar in the same coronary artery territory as the anomalous coronary artery
    and/or
  - d. Wall motion abnormalities in any modality with or without stress in the same coronary artery territory as the anomalous coronary artery

B. **Criteria for surgical adverse events**
- I. Calculated as new moderate or greater AI postoperatively on last echocardiogram
- II. New abnormal EF (<50%) postoperatively on last echocardiogram
- III. Any positive ischemia test or symptoms after surgery (as described in Table 1, A) or need for a coronary-related reoperation
- IV. Requirement for ECMO at the end of surgery or after surgery
- V. Death after an elective case

ECMO, Extracorporeal mechanical oxygenation; *CPET*, cardiopulmonary exercise test; *MRI*, magnetic resonance imaging; *AI*, aortic insufficiency; *EF*, ejection fraction; *ECMO*, extracorporeal membrane oxygenation.

and/or resuspension of the commissure. Surgical adverse events were defined on the basis of the criteria listed in Table 1, *B*. An elective repair was defined as a surgery performed in a patient, either symptomatic or asymptomatic, in a nonurgent setting.

All imaging, provocative testing, and management decisions (including the decision to perform surgery and the type of operation performed) were based on institutional team and surgeon preference. The CHSS AAOCA Registry does not have mandated study protocols for patient management.

Data Collection and Aggregation of Anatomic Features

A detailed description of data collection, and the technique used for aggregation of morphologic features for each patient from their various sources (echocardiogram, computed tomography, magnetic resonance imaging, and surgery reports) is available in Appendix E2. The atomization form used to collect detailed morphologic features is shown in Online Data Supplement.

Consent

Ethics approval was obtained from the institutional review board at all participating CHSS sites. Informed consent and assent were obtained from participating parents or patients as required. Institutional and patient participation were voluntary.

Statistical Methods

Standard descriptive statistics were performed for the group of patients who underwent surgery. Surgical procedures were evaluated and classified on the basis of their individual components (eg, unroofing, reimplantation, pulmonary artery translocation). Categorical variables are presented as frequencies with corresponding percentages, with between group differences evaluated using chi-square and Fisher exact testing. The change in preoperative and postoperative (paired) ischemia status was assessed using McNemar's test. Continuous variables were assessed for normality using the Shapiro–Wilk test and then presented as means with standard deviations (if normal) or medians with interquartile ranges (if non-normal). Differences between groups for normal continuous

variables were evaluated with the Student *t* test, and non-normal continuous variables were evaluated using the Wilcoxon signed-rank test. Multiphase parametric modeling was performed to determine freedom from mild or greater AI with stratification by commissural manipulation (using log-rank testing), coronary-related reoperation, noncoronary-related reoperation, and any reoperation. Statistics were performed using SAS 9.4 (SAS Institute, Inc, Cary, NC) (Appendix E2).

RESULTS

Of 682 patients enrolled in the CHSS AAOCA cohort, 395 (58%) underwent surgery. These 395 patients were enrolled (70 retrospectively and 325 prospectively) from 45 centers and underwent surgery between May 9, 2000, and September 10, 2018. Of these patients, 108 were left AAOCA (AAOLCA), 282 were right AAOCA (AAORCA), and 5 had both AAOLCA and AAORCA.

Baseline Characteristics

The baseline characteristics of the surgical cohort are presented in Table 2. This cohort consisted of 66% male patients, with a median age at surgery of 13.3 years (IQR, 9.9-15.5) and a median follow-up after surgery of 2.8 years (IQR, 1.1-5.0). Table 3 details the coronary morphology of the surgical cohort.

The nonsurgical patients (n = 287) consisted of 57 (20%) with AAOLCA, 224 (78%) with AAORCA, 2 (1%) with anomalous left anterior descending artery, 2 (1%) with anomalous circumflex, and 2 (1%) with both AAOLCA and AAORCA. The nonsurgical group had 9 (3%) deaths (3 AAOLCA, 6 AAORCA), 3 of whom died after sudden cardiac arrest secondary to exertion. The other 6 patients died from non–AAOCA-related causes as follows: 2 secondary to cancer, 1 secondary to injuries related to abuse, 1 had multiple congenital anomalies including cerebral dysgenesis and multiorgan failure, 1 had complications of prematurity and bronchopulmonary dysplasia after patent ductus arteriosus ligation, and 1 had renal failure in the setting of viral myocarditis.

Surgical Procedures

Table 2 provides a description of the surgical procedures. In Table 2, patients can be listed on more than 1 line. For a detailed description of the mutually exclusive surgical procedure groups (each patient described once), see Table 4. Use of extracorporeal membrane oxygenation (ECMO) occurred in 2 patients only before surgery, 3 patients both preoperatively and postoperatively, and an additional 3 patients were placed on ECMO after leaving the operating room (1 for aortic dehiscence). One additional patient had ECMO support before surgery at the time of cardiac arrest, was discharged, and had repair after recovery.

Preoperative and Postoperative Ischemia Testing

There were 250 patients who underwent a preoperative and/or postoperative ischemia test; of these, 163 patients had a preoperative ischemia test and 190 patients had a postoperative ischemia test (Table 2). Patients had a median of 2 preoperative tests (IQR, 1-2; range, 1-7) and a median of 2 postoperative tests (IQR, 1-3; range, 1-25). Of these patients, 103 had both preoperative and postoperative ischemia testing (22 AAOLCA, 80 AAORCA, 1 with both). Of the 348 patients who did not present with ischemia-related symptoms or presentations, 201 (58%) did not undergo any preoperative ischemia testing.

TABLE 2. Baseline, follow-up, and surgical characteristics of cohort

Patient characteristics (n = 395)	Median (range, Q1-Q3) OR Number, %
Baseline and follow-up characteristics	
Median age at surgery	12.9 y (range, 0.01-30.6, Q1-Q3: 8.8-15.2)
Gender (M:F)	261:134 = 66%: 34%
Preoperative ischemia testing	163/395 (41%)
AAOLCA	36/163 (22%)
AAORCA	125/163 (77%)
Both	2/163 (1%)
Median age at surgery	13.3 y (range, 0.9-30.7, Q1-Q3: 9.9-15.5)
Median follow-up	2.8 y (range, 0-16.2, Q1-Q3: 1.1-5.0)
Surgical characteristics (note that patients can be included in more than 1 group below)	
Type of procedure	
Unroofing	344/395 (87%)
Unroofing with tacking	280/395 (71%)
Unroofing with commissural manipulation	98/395 (25%)
Unroofing with patch ostioplasty	13/395 (3%)
Unroofing with PA translocation	9/395 (2%)
Patch ostioplasty	25/395 (6%)
PA translocation	22/395 (6%)
Reimplantation	24/395 (6%)
Neo-ostial creation	11/395 (3%)
Aortocoronary window*	3/395 (1%)
Bypass graft	3/395 (1%)
Commissural manipulation as an adjunct	104/395 (26%)
Tacking as an adjunct	294/395 (74%)
Cardiopulmonary bypass time (min)	68 (range, 17-276, Q1-Q3: 50-92), missing = 20
Crossclamp time (min)	46 (range, 0-217, Q1-Q3: 30-62), missing = 15
Postoperative characteristics	
Postoperative ischemia testing	190/395 (48%)
AAOLCA	49/190 (26%)
AAORCA	140/190 (74%)
Both	1/190 (1%)

AAOLCA, Anomalous aortic origin of a left coronary artery; *AAORCA*, anomalous aortic origin or a right coronary artery; *PA*, pulmonary artery. *Figure E2 shows a figure demonstrating aortocoronary window repair.

TABLE 3. Morphologic characteristics

Patients who underwent surgery (n = 395)									
	Total	Dead	Interarterial	Intramural	Intraconal	Intramural length (mm)		High orifice	Slit-like orifice
Anomalous coronary artery	n (%)	n (%)	n (%)	n (%)	n (%)	Median (IQR) (min, max)	Missing	n (%), missing	n (%)
AAOLCA	108 (27)	4/108 (4)	96/108 (89)	92/108 (85)	6/108 (6)	7 (5-9) (1, 20)	18	19/79 (24), 29	68/95 (72), 13
AAORCA	282 (71)	0	281/282 (100)	273/282 (97)	1/282 (0.4)	7 (5-10) (1, 28)	50	76/212 (36), 70	203/241 (84), 41
Both	5 (1)	0	5/5 (100)	4/5 (80)	0	1, 4, 12*	1	5/5 (100), 0	3/4 (75), 1
Total	395 (100)	4/395 (1)	382/395 (97)	369/395 (93)	7/395 (2)	7 (5-10) (1, 28)	69	100/296 (34), 99	274/340 (81), 55

For interarterial, intramural, and intraconal, there were no missing values. *IQR*, Interquartile range; *AAOLCA*, anomalous aortic origin or a left coronary artery; *AAORCA*, anomalous aortic origin of a right coronary artery. *Note that where the anomalous coronary is both, there are only 5 intramural values; thus, these have been listed.

If a definition of postoperative ischemia is used that includes ischemia by testing or symptoms, coronary reoperations, postoperative ECMO, and death after an elective case, then there were 26 patients with postoperative ischemia. Unclassified patients did not have testing and did not present with symptoms of ischemia. See Figure 1, *A-C*. Of these 26 patients, 11 had ischemia by testing or symptoms, 8 had coronary reoperations alone, 2 had coronary reoperations and ischemia by symptoms or testing, 1 had coronary reoperation/ischemia by testing or symptoms/ECMO, 2 died, 1 died after reoperation, 1 died after reoperation and postoperative ECMO. Table E1 details the anatomy with morphology, operations that these patients underwent, and their reason for inclusion in the ischemia group.

Overall, we found that 64 of 395 patients (16%) had preoperative ischemia, whereas after surgery 51 of 64 (80%) no longer had ischemia (and 13 became ischemic, $P < .0001$). In this scenario, we considered unclassified patients as patients without ischemia, because this would be how the data would be clinically interpreted (Figure 1, *D*).

Upon review of the postoperative management of the 10 patients with ischemia by testing we found the following. In 1 case, clinicians thought it did not warrant further intervention, in 6 cases clinicians decided to repeat the tests that then had negative results, 2 were pending repeat testing with interim exercise restriction, and 1 patient was exercise restricted indefinitely. Four patients were included because of ischemia by symptoms, of whom 3 had symptoms despite a negative test result, and 1 did not have any testing but had symptoms. For an expanded description of this section, Appendix E3 and Figure E1 include an assessment and discussion of postoperative ischemia testing with respect to patient follow-up.

Aortic Insufficiency

There were 358 patients with preoperative and postoperative assessment of AI, who had none or trivial AI preoperatively. Of these, 27 (8%) developed new mild or greater AI postoperatively, and 7 (2%) developed new moderate or greater AI postoperatively. The median follow-up for AI was 8.9 months (IQR, 0.2-30.9).

Freedom from mild or greater AI was significantly different ($P = .05$) for those with commissural manipulation (85% [81%-89%] at 6 months, 83% [78%-87%] at 1 year, and 77% [71%-82%] at 3 years) versus those without commissural manipulation (91% [89%-92%] at 6 months, 90% [88%-92%] at 1 year, and 88% [85%-90%] at 3 years) (Figure 2, *A*). The less common development of moderate or greater AI was not statistically significantly associated with commissural manipulation (4/95 [4%] in those with manipulation vs 3/263 [1%] in those without manipulation, $P = .08$, odds ratio 3.81, 95% confidence interval 0.84-17.35). Although we evaluated the last echocardiogram, there were 10 patients who had a decrease in their echo grade with mild AI at some time, who at last follow-up had less than mild.

One patient had mild AI preoperatively, but this patient did not have AI postoperatively. In addition, 1 patient had severe preoperative AI secondary to rheumatic disease and underwent aortic and mitral mechanical valve replacements, with residual mild AI.

Ejection Fraction

There were 347 patients with preoperative and postoperative EF assessment via echocardiogram, who had normal preoperative EF. Of these, 6 (2%) developed new abnormal EF within 30 days that persisted to the patient's last study (2 mild, 1 moderate, 2 severe, 1 missing [patient died]). The median follow-up of EF was 9.5 months (IQR, 0.2-30.5). There were 3 patients who had abnormal left ventricular function preoperatively, 1 of whom had abnormal left ventricular function postoperatively.

Complications

Complications included the following: 3 (1%) stroke, 3 (1%) wound infection requiring antibiotics, 14 (4%) postpericardiotomy syndrome requiring medical therapy, 2 (1%) chest tube for pleural effusion, and 6 (2%) chest tube for a pneumothorax.

Reoperation

Reoperations after primary AAOCA repair were divided into coronary and noncoronary-related reoperations.

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TABLE 4. Primary procedures in surgical patients

Primary surgical repairs (N = 395)	No. of patients (with tacking, without tacking)							
					Surgical adverse events			
					All patients		Patients without ischemia	
	Total	Right	Left	Both	Mild	Moderate	Mild	Moderate
					50	34	29	19
Unroofing alone	27+197T	25+159T	2+37T	1T	5+16T	4+11T	4+8T	4+5T
Unroofing with commissural manipulation	14+71T	6+42T	7+29T	1	1+12T	1+7T	7T	4T
Unroofing with ostioplasty	1+2T	1+2T						
Unroofing with ostioplasty and commissural manipulation	2T	2T						
Unroofing with patch ostioplasty	7+3T	6+3T	1		1			
Unroofing with patch ostioplasty and commissural manipulation	2	1	1					
Unroofing with PA translocation	3+4T	2+2T	2T	1	1+2T	2T	1+2T	2T
Unroofing with PA translocation and commissural manipulation	2	2						
Ostioplasty alone	1+1T		1+1T					
Ostioplasty with commissural manipulation	1	1			1	1		
Ostioplasty with patch augmentation	2	1	1					
Ostioplasty with patch augmentation and commissural manipulation	1+1T	1T	1		1	1		
Ostioplasty with patch augmentation and PA translocation	3	3						
Ostioplasty with PA translocation	1T		1T		1T	1T	1T	1T
PA translocation alone	8	1	6	1				
Planned bypass graft alone	1		1					
Planned bypass graft with unroofing	1	1						
Planned bypass graft with unroofing, and commissural manipulation	1		1		1	1		
Reimplantation alone	11	5	5	1	2	2	1	1
Reimplantation with ostioplasty	1	1						
Reimplantation with commissural manipulation	2	2						
Reimplantation with PA translocation	1		1					
Reimplantation with patch ostioplasty	4	1	3		1	1	1	1
Reimplantation with patch ostioplasty and commissural manipulation	1	1						
Reimplantation with unroofing	1	1						
Reimplantation with unroofing and commissural manipulation	2	2			1		1	
Reimplantation with unroofing and patch ostioplasty and commissural manipulation	1T		1T					
Neo-ostial creation	10T	6T	4T		1T	1T		
Neo-ostial creation with commissural manipulation	1T	1T						
Aortocoronary window with unroofing*	1		1		1		1	
Aortocoronary window with unroofing,* commissural manipulation	2	1	1		2	1	2	1

N = 395. The primary procedure of each patient is represented once in this table, and cases that included tacking of the intima are denoted with a T. *T*, Tacking; *PA*, pulmonary artery. *Figure E2 shows a figure demonstrating aortocoronary window repair.

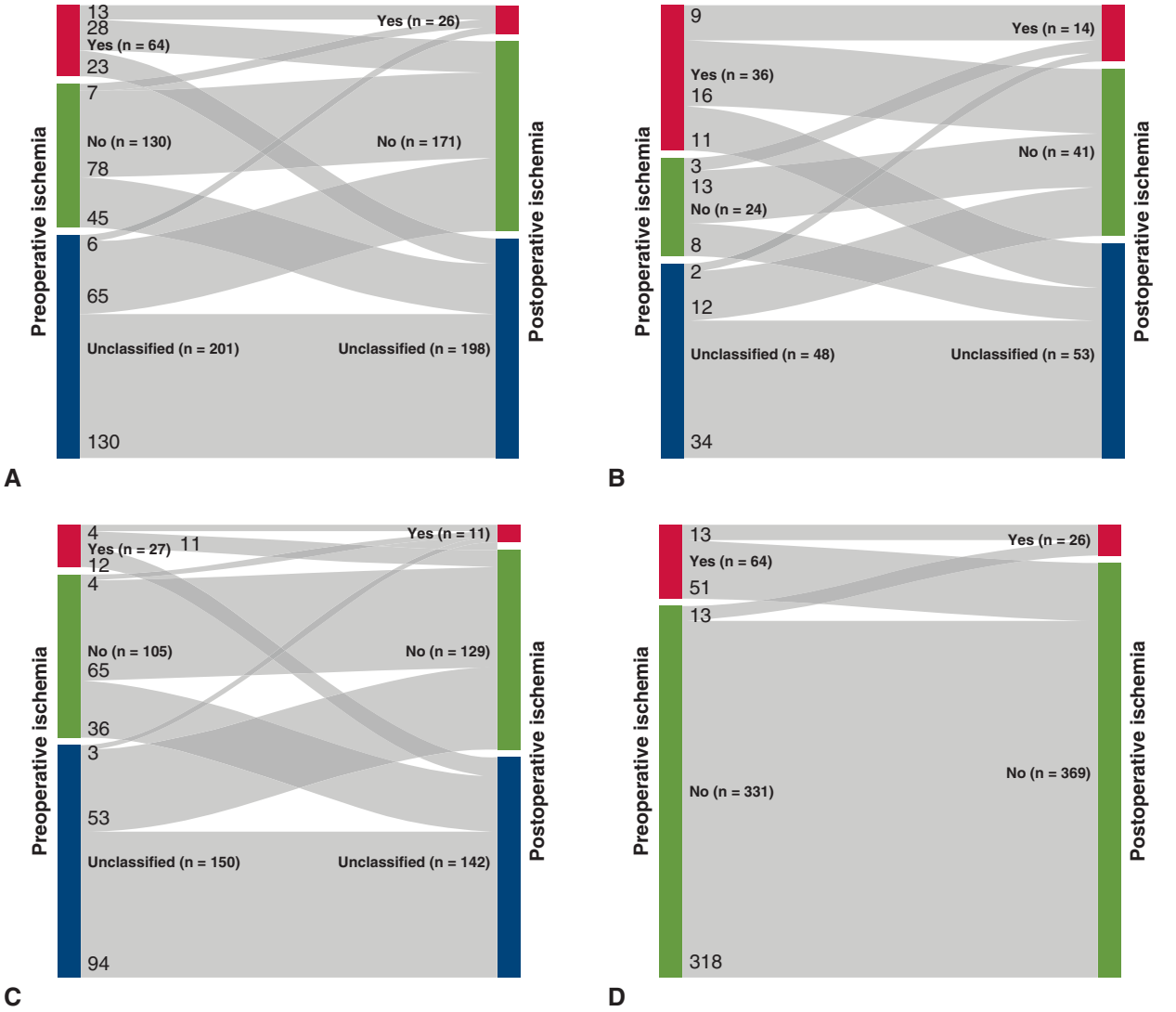


FIGURE 1. Sankey diagrams of preoperative and postoperative ischemia status. Patients could have ischemia based on ischemia testing, symptom-based criteria, coronary reoperations, or death after elective surgery. To be classified as not having ischemia, patients had to have undergone ischemia testing. If patients were unclassified, they did not undergo ischemia testing. A, All patients with unclassified patients as a group. B, Only patients with AAOLCA. C, Only patients with AAORCA. D, Without unclassified patients as a group.

There were 15 coronary-related reoperations (5 predischarge and 10 postdischarge) in 13 patients, and 27 noncoronary-related reoperations (9 predischarge and 18 postdischarge) in 21 patients. In total, there were 42 reoperations in 30 patients (14 in the perioperative period and the remainder after discharge).

From Table 5, the 15 coronary-related reoperations are broken down into 5 that occur predischarge and 10 that occur postdischarge. Eight (4 predischarge and 4 postdischarge) were reoperations for coronary issues (1 had a concomitant biventricular assist device, 1 had concomitant ECMO, and 1 had concomitant aortic valve repair). One additional patient had a short-term left ventricular assist device preoperatively. Six additional postdischarge procedures included 2 internal cardiac defibrillator placements for residual postoperative arrhythmias, 2 procedures for myocardial bridge unroofing (1 of which also included coronary translocation), 1 pseudoaneurysm repair, and 1 heart transplant. Further descriptions of the noncoronary-related reoperations are shown in Table 5.

Freedom from coronary-related reoperations was 99% at 1 month, 98% at 1 year, and 95% at 7 years (Figure 2, *B*). Freedom from noncoronary-related reoperations was 96% at 1 month, 95% at 1 year, and 94% at 7 years (Figure 2, *C*). Freedom from any reoperation was 96% at 1 month, 93% at 1 year and 90% at 7 years (Figure 2, *D*).

Of the 13 patients who had coronary-related reoperations (8 AAOLCA, 4 AAORCA, 1 both), 12 of 13 (92%) were

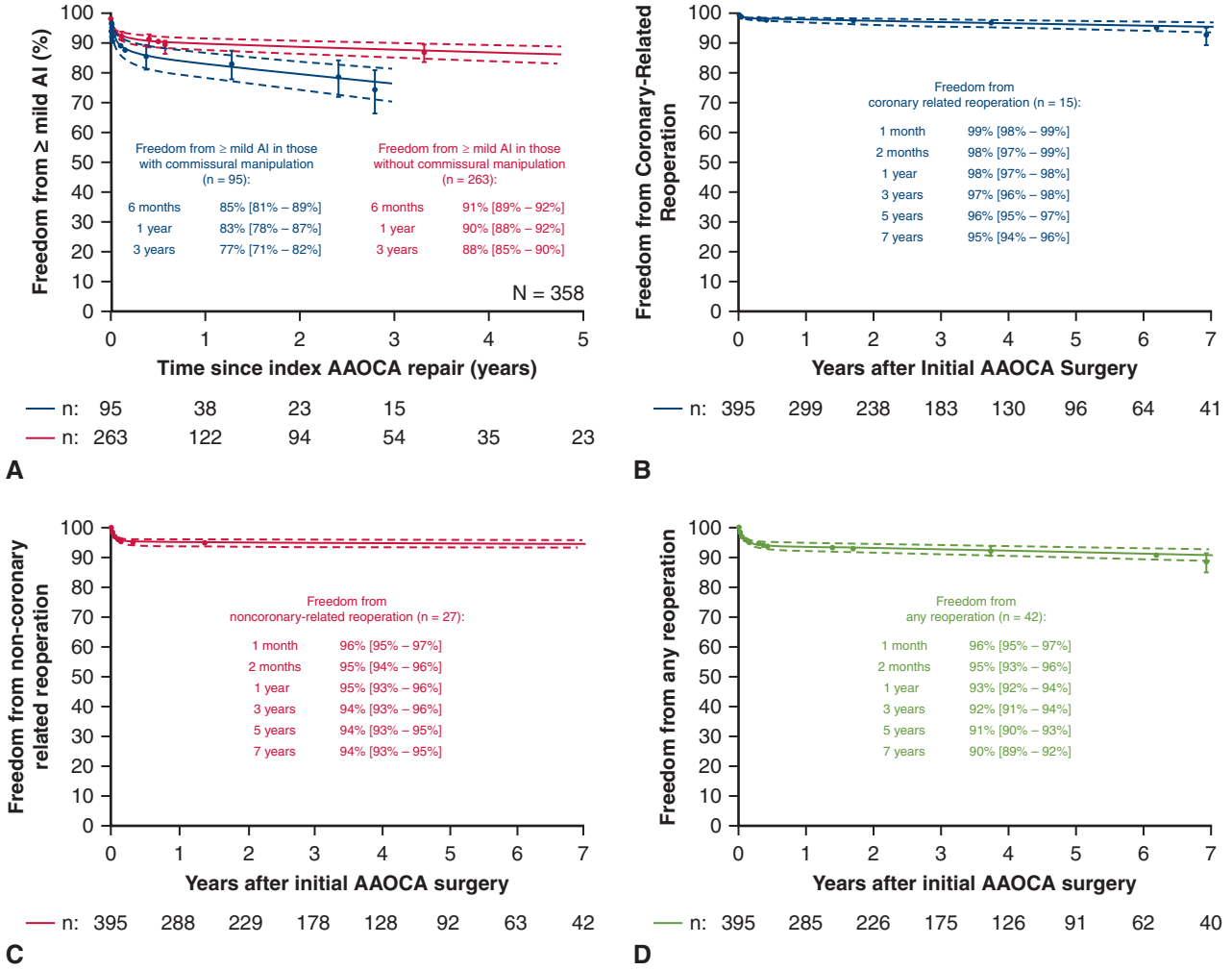


FIGURE 2. Freedom from mild or greater AI, coronary-related reoperations, noncoronary-related reoperations, and from any reoperation. A, Freedom from mild or greater AI after initial AAOCA surgery stratified by the occurrence of commissural manipulation during repair. B, Freedom from coronary-related reoperations after initial AAOCA surgery. C, Freedom from noncoronary-related reoperations after initial AAOCA surgery. D, Freedom from any reoperation after initial AAOCA surgery. Solid lines represent parametric point estimates. Dashed lines represent 70% confidence intervals. *AI*, Aortic insufficiency; *AAOCA*, anomalous aortic origin of a coronary artery.

interarterial and intramural (with a median length of 6 mm [IQR, 3-8, missing = 5]), 1 of 13 (8%) was intraconal, 4 of 13 (31%) were high (at or above the sinotubular junction), and 10 of 12 (83%, missing = 1) had a slit-like orifice. Appendix E3 shows a detailed description of the anatomy with morphology and operation that each of these 13 patients underwent.

Mortality

Of the 395 patients within the cohort who underwent surgery, 4 patients (1%) with AAOLCA died within 30 days of surgery, 3 (<1%) of whom died after elective surgery (the other presented in extremis after sudden cardiac arrest).

Of these 4 patients who died, 1 presented in extremis preoperatively (6 years old, AAOLCA with single coronary, interarterial, intramural 9 mm), underwent a repair with an aortocoronary window (surgery shown in Figure E2) and patch ostioplasty, and died secondary to stroke. Another patient was discharged and returned to the hospital just before arrest (7 years old, asymptomatic AAOLCA, intraconal, underwent reimplantation with trapdoor patch ostioplasty and muscular unroofing, returned with neurologic complaints). After arrest and re-repair with coronary artery bypass grafting, the patient died after having a stroke. Two patients with AAOLCA died postoperatively in the hospital. One of these patients was 15 years old, asymptomatic and intraconal; underwent ostioplasty, muscular unroofing, and pulmonary artery translocation; and died of hypotension. The other patient was 11 years old, had symptomatic AAOLCA (interarterial, intramural 6.25 mm), underwent elective repair with an aortocoronary window and patch ostioplasty, required re-repair using a coronary bypass graft, and died

TABLE 5. Causes of reoperation

Causes of reoperation	Predischarge	Postdischarge
Coronary-related reoperations	5	10
Coronary issue (1 with BIVAD, 1 with ECMO, 1 with aortic valve repair)	4	4
ICD for arrhythmia/SCD	0	2
Myocardial bridge (1 with coronary translocation)	0	2
Short-term LVAD	1	0
Pseudoaneurysm repair	0	1
Heart transplant	0	1
Noncoronary-related reoperations	9	18
Postoperative bleeding	7	2
Pericardial drainage	1	11
Aortic valve repair	0	2
ICD for secondary prevention	0	1
Supraventricular tachycardia	0	1
Mediastinitis	0	1
Bilateral embolectomy and fasciotomy	1	0

BIVAD, Biventricular assist device; *ECMO*, extracorporeal membrane oxygenation; *ICD*, internal cardiac defibrillator; *SCD*, sudden cardiac death; *LVAD*, left ventricular assist device.

after brain death was declared. When those patients who had a sudden cardiac arrest before surgery were reviewed, 1 patient died postoperatively (described earlier); however, the remaining 22 were alive (6 of whom were discharged before returning for surgery).

Surgical Adverse Events Summary

By using the definition in Table 1, *B*, we found the following adverse events after surgery.

In the entire cohort, 7 patients had new moderate or greater AI, 6 patients developed new abnormal EF, 14 patients had postoperative ischemia (10 by testing, 4 by symptoms), 13 patients required coronary-related reoperations, 3 patients required ECMO after surgery, and 3 patients died after elective repair. This totals 34 (9%) mutually exclusive patients (16 AAOLCA, 17 AAORCA, 1 both) patients who had surgical adverse events if calculated using moderate or greater AI and a positive ischemia test at any time postoperatively (Table 4, "All patients").

Of the 331 asymptomatic patients (patients without preoperative ischemia), there were 19 (6%) (6 AAOLCA, 12 AAORCA, 1 both) patients with surgical adverse events (Tables 4 and E2). There were 15 of 64 patients (23%) (10 AAOLCA, 4 AAORCA, 1 both) with surgical adverse events, who had ischemia before surgery by testing or symptoms. Surgical adverse event rates were 15 of 224 patients (7%) (4 AAOLCA, 11 AAORCA) in those who only had unroofing (with or without tacking), 8 of 85 patients (9%) (5 AAOLCA, 3AAORCA) in who had unroofing with commissural manipulation (with or without tacking), and 11 of 86 patients (13%) (7 AAOLCA, 3 AAORCA, 1 both) who had surgeries other than these. Surgical adverse event rates were 17 of 282 (6%) for patients with AAORCA and 16 of 108 (15%) for patients with AAOLCA. These calculations were done counting any positive postoperative ischemia test as an adverse event. Table E2 shows an expanded description of surgical adverse events in the patient groups described in this section, in addition to calculations if mild or greater AI is considered adverse as it has been in other manuscripts, and calculations using last positive postoperative ischemia test.[14]

DISCUSSION

This study presents the results of a uniquely large multi-institutional cohort of patients who have undergone AAOCA repair and captures the numerous techniques which multiple surgeons have used to repair the variants of this lesion. The primary findings from this large cohort of AAOCA patients are as follows: (1) The majority of patients had unroofing, followed by patch ostioplasty, pulmonary artery translocation, and reimplantation (6% each) (these are not exclusive); (2) the development of mild or greater AI was associated with commissural manipulation, although the long-term consequences of this are unclear, and strategies avoiding the commissure such as neo-ostial creation and reimplantation may avoid this; (3) surgery for AAOCA has low mortality rates and is generally associated with elimination of ischemia postoperatively; (4) there is a low but important risk of reoperation; and (5) the composite risk of surgical adverse events was 7% to 13% in the entire cohort and varied depending on the group of patients evaluated (lowest for those without ischemia preoperatively and highest in those with preoperative ischemia). Figure 3 shows a graphical representation of these take-home messages.

Many studies evaluating patients with AAOCA have focused on anatomy and ischemia status and are often case reports, autopsy series, and single-institution studies.[15-24] There are limited reports of surgical outcomes, including several contemporary reports, but these often reflect continually evolving management paradigms.[14,25-34] In comparison with our study, these primarily single-center studies often describe the surgical outcomes of a small number of patients with a short duration of follow-up. Past work has suggested complication rates ranging from 0% to 67%.[3,25,30,31] The large range of complication rates suggests there is significant variation among the many CHSS institutions. However, in the hands of expert surgeons who do a large volume of these cases and have a standardized approach to carefully evaluate and follow patients, we speculate that there is potential for this surgery to be performed with low risk.

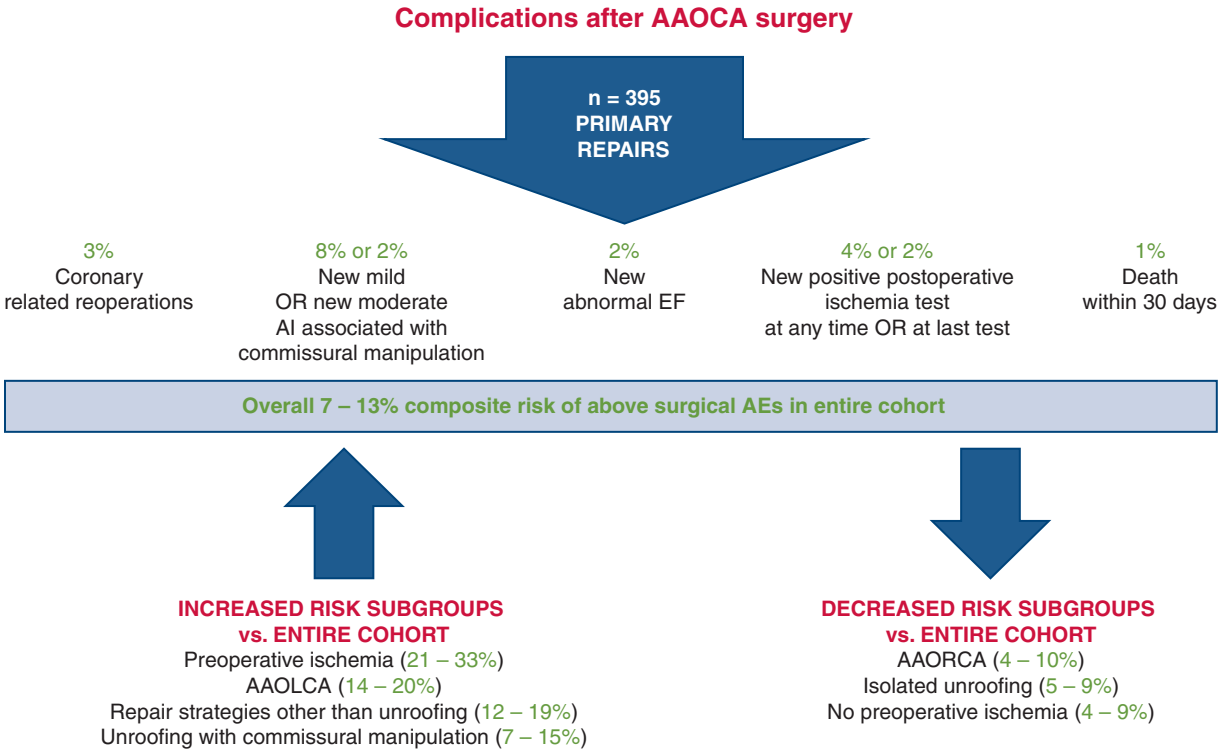


FIGURE 3. Primary findings related to the surgical risks of AAOCA repair. Ranges for surgical adverse events based on calculations using occurrence of new mild or new moderate AI associated with commissural manipulation and new postoperative ischemia based on any or last postoperative ischemia test (Table E2). *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 or a right coronary artery.

Surgery and Repair Strategies

This study is unique because it demonstrates for the first time that surgical repair can effectively eliminate ischemia in most patients. Similar to the 2 prior studies from the CHSS, the primary technique used to repair AAOCA is unroofing (344/395, 87%), because the majority of patients have an intramural course (93%).[9,11] Of note, the use of commissural manipulation during repair was found to be associated with the development of AI, as in another study.[14] This can be difficult to avoid when the majority of patients have an intramural course. Our findings suggest that commissural manipulation should be avoided if possible, potentially in favor of strategies which avoid the commissure, such as neo-ostial creation and reimplantation (despite the lack of knowledge regarding the long-term outcomes of either). This alternative is already being advocated for by certain centers.[32,35] Of note, in those patients who developed AI but did not have commissural manipulation, we speculate that (1) unroofing with tacking may not have been the procedure done, that is, surgeons did take down the commissure, but failed to describe it in their operative note; (2) somehow the process of unroofing weakens the aortic wall in this region and perhaps causes a distortion of the valve resulting in AI; or (3) the type of aortotomy used (eg, hockey stick) may be prone to distorting the valve at the time of closure, especially in small patients.

Although often the surgical repair strategy is dictated by a patient's individual anatomy, the surgical adverse event rates by strategy provide important information that can be provided to patients. Those who solely underwent unroofing had a 7% rate of surgical adverse events, whereas if unroofing with commissural manipulation was performed, the rate increased to 9%, followed by all other repair strategies, which had a rate of 13% (Table E2). Patients without ischemia preoperatively had a 6% rate of surgical adverse events, whereas in comparison those with preoperative ischemia had the highest rate of 23% (composite rates use new moderate or greater AI).

Reoperations and Complications

A total of 26 of 395 (7%) mutually exclusive patients had postoperative ischemia after surgery, including 13 patients with coronary-related reoperations. This suggests that patients may benefit from intraoperative coronary flow assessment, perioperative completion angiography, and further follow-up incorporating advanced imaging and provocative ischemia testing as suggested by the consensus guidelines.[7]

Although the majority of complications were easily resolved with minimal consequences, of importance are the 3 patients who experienced a stroke, as well as those patients whose complications were directly related to the AAOCA repair (13 patients underwent 15 coronary-

related reoperations [including 1 heart transplant, 2 requiring ventricular assist devices], 2 patients requiring aortic valve repair, 1 with mediastinitis and postoperative bleeding from aortic dehiscence, and 1 requiring embolectomy and fasciotomy). Similar to our series, in which we conservatively only included those patients undergoing drainage, pericardial effusions have been noted to be the most common complication (9%-46%) in patients undergoing AAOCA repair.[28,32] One strategy reported to manage this potential complication is leaving the right pleural space and pericardium open in all patients.[32]

Surgical Success

Balancing the risk of surgery with the potential for a sudden cardiac event in an asymptomatic patient is perhaps the biggest emotional burden caregivers and patients face when given a diagnosis of AAOCA. Although we have attempted to create a definition of surgical success, it is admittedly difficult to compare the potential elimination of sudden cardiac events with the creation of other issues that may have long-term consequences. For example, it is difficult to compare the potential deterioration of AI created at the time of surgery with its consequent risks, to the risk of sudden death. Perhaps a better comparison would have been freedom from reoperation or complication; although without the dates that complications occur (something very difficult to capture), this is hard to ascertain.

Ischemia Status

As expected, there was a lack of consistency with respect to the preoperative and postoperative ischemia testing that patients underwent. Because this is a contemporary cohort, it was surprising to find that only 41% had testing preoperatively, with 26% of patients undergoing both preoperative and postoperative testing. Although it may be the case that some patients were too young to be tested, the lower quartile of age at surgery was 9.9 years, suggesting that approximately 75% of patients would have been eligible. Likewise, if we consider the age at diagnosis, the lower quartile of age at diagnosis was 8.8 years. The current consensus guidelines (although more recent than our initial enrollment dates) also recommend that all patients without a history of ischemic chest pain or an aborted sudden cardiac death undergo ischemia testing as part of their workup, but 58% in our cohort without symptoms did not undergo testing.[4] These guidelines similarly suggest that patients with AAORCA undergo ischemia testing; however, only 125 patients with AAORCA of the 282 (44%) who underwent surgery were tested preoperatively. In addition, of those who had preoperative and postoperative ischemia testing, although we found 5 of 90 patients (6%) newly positive after surgery, this is likely an underestimation because not all patients had postoperative testing, and we know there were an additional 4 patients without preoperative testing.

Study Limitations

Due to the nature of CHSS cohorts, we do not know if we are able to capture all patients at a given site, which may potentially bias our results. Another potential source of bias related to our study design is that it is unknown whether patients cared for at CHSS institutions are different from those treated at nonparticipating sites. In addition, patient testing and surgical strategies were not protocol driven. As such, patients may or may not have undergone ischemia testing or had ischemia assessed using different tests before and after surgery, and the repair strategies used on similar lesions varied. Finally, the quality of our data is based on the completeness of information sent from participating member institutions. This is important as related to coronary artery dominance, something that is rarely assessed, and the relationship of blood flow with dominance and which artery is anomalous. It is also important to our abstraction of patient complications, because these are taken from discharge summaries and follow-up clinic notes. Thus, although our complications represent those patients undergoing AAOCA surgery, the numbers may underestimate the true value. Likewise, coronary artery anatomy and procedures were determined using institutional imaging reports and surgical operative notes (a small proportion of which had surgeon abstracted anatomic atomization) as opposed to the expert review of images. Finally, some patients had arrhythmia postoperatively (which could be considered as postoperative ischemia); however, this may be a result of scar created preoperatively secondary to ischemia, despite undergoing anatomically successful AAOCA repair.

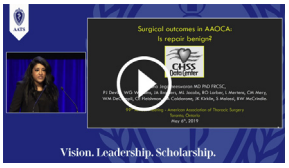
CONCLUSIONS

The primary question faced by patients and families is, "Do the risks of sudden cardiac events outweigh the risks of surgery?" The goal of this study was to help patients, families, and their healthcare team decipher part of the answer to this question, because it remains impossible to determine the risk of sudden cardiac events without knowing the number of patients in the general population with AAOCA. However, the answers related to the risk of surgery, just one side of the equation, can now be answered with some of our findings. Figure 3 shows a summary of our primary findings. We found that although mortality related to AAOCA repair is relatively low and surgery had only up to 80% probability of eliminating ischemia (when unclassified patients were considered to not have ischemia) (Figure 1, *D*), there is an important number of patients who experience morbidity and mortality that varies according to the group evaluated (by anatomy, presence of ischemia, repair strategy) (Table E2) and includes those without preoperative ischemia. There also remains a strong need for guideline-directed

standardized workup, risk stratification, and management of these patients to prevent morbidity in those who actually do not require surgery. In addition, because the long-term surgical outcomes of AAOCA repair remain unknown, it is essential that these patients are followed for life, and deliberate transition to an adult congenital heart disease cardiologist is imperative.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/19%20AM/Monday_May6/1.%20PLENARY/1.%20PLENARY/1.%20Presidential%20Plenary/8.%20Is%20surgical%20repair%20of%20anomalous%20aortic%20origin%20of%20a%20coronary%20artery.mp4.



Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: anomalous aortic origin of a coronary artery, complications, congenital heart disease, database, epidemiology, surgery

Discussion

Presenter: Dr Anusha Jegatheeswaran

Dr Charles D. Fraser, Jr *(Austin, Tex)*. It's a great privilege to discuss yet another outstanding presentation by Dr Anusha Jegatheeswaran on the subject of anomalous aortic origin of a coronary or AAOCA. Anusha, just 1 year ago at that AATS plenary session, you brought us important information from the CHSS AAOCA Registry. Important points from last year include ischemia or sudden death is more frequent in anomalous left coronaries, but it also occurs in anomalous right coronary arteries; patients with clinically significant anomalous right coronary arteries are more likely to have a long intramural segment; and patients undergoing surgery for AAOCA were thought to have at least a 10% risk of needing reoperation. Last year, we talked about you bringing us more information about the operations, what people are doing, and what are our patient outcomes.

So it is great to hear from you again on this very vexing subject. Unfortunately, this year you've brought us some really sobering information, in my estimation. Of the subgroup of 395 primary surgical patients of the original 682 patient cohort, I'll revisit some of what I heard of your important findings. Clinical observation of the patients and expectant management is not always successful. Of the 287 patients who did not undergo surgery, 9 died, including 6 with anomalous right coronary arteries. As you just related, surgery has risks. Despite the fact that study centers were exclusively congenital programs with operations being performed by experienced, largely board certified, congenital heart surgeons, there is significant morbidity and mortality associated with surgery for AAOCA.

In your study, 26 patients had postoperative ischemia and 3% of patients had new postoperative, ischemia. A total of 34 patients developed new, iatrogenic AI, and this appears to be related to commissural manipulation. Two percent of patients who had normal function going in to the operating room had a decreased EF coming out. Of the patients who are operated on without symptoms (eg, primarily for morphology), 51% did not undergo provocative testing before surgery. There were 42 reoperations in thirty patients. Fifteen patients required reoperation for a coronary artery misadventure. Freedom from any reoperation at 7 years was only 90%, and 4 patients died, 3 of whom had elective operations. So, we still have a long way to go with this challenging subject. In deciding on whether to operate on a given patient, it's easy if the patient had symptoms or sudden cardiac death. The tough ones are the asymptomatic patients. Among many important findings, you've documented that congenital heart surgeons are operating on the majority of patients solely based on morphologic determinants. Should we be more tempered in our decision-making after your data?

Dr Anusha Jegatheeswaran *(Toronto, Ontario, Canada)*. You are correct. From these data, we can see that the many surgeons operate on patients solely for morphology. Part of the reason for this occurring is that the guidelines suggest that patients with interarterial left AAOCA should undergo surgery, without the need to demonstrate ischemia via testing, even in asymptomatic patients. From the data we presented last year, we know that a high proportion of patients have an interarterial course, perhaps rendering this a less useful discriminating feature.

What I would advocate for is the need for a collaborative team including surgeons, cardiologists, radiologists, nursing, and social work, all with a specific interest in AAOCA, to manage patients at each institution. We should be making decisions together regarding whether or not a patient needs surgery and should be maintaining a critical eye on whether the patient has been adequately evaluated. Especially because we increasingly coming to understand the risks involved with surgery. One approach would be to serially evaluate asymptomatic patients without proceeding to surgery immediately. However, we still don't know is the natural history of various lesions without surgery. This would allow us to determine how to balance the risk of surgery with the risk of ischemia.

Dr Fraser. I might also suggest that we need to involve, in an objective way, the patients or the parents in this decision-making. As per the above, it seems that our congenital heart surgeon colleagues have been slow to adopt the guidelines that we've developed. Specifically, we are not

adhering to the recommendation of preoperative provocative testing. Why is this, and should the guidelines be revisited?

Dr Jegatheeswaran. As I mentioned, for a patient with an interarterial left AAOCA, the guidelines seem to suggest that you don't need testing and can proceed to surgery based solely on morphology. However, more concerning was the fact that there a large proportion of patients within our cohort with right AAOCA who did not have preoperative testing. One thing to note is that our cohort starts in 1999 because of the retrospective aspect component, and the various guidelines were not available at that time. As such, physicians seem to have been doing what they felt like at that time.

However, we are doing this repair to get rid of ischemia. So, first, it would be nice to know if there is ischemia in patients who are asymptomatic, and second, it would be nice to follow up and see whether we really corrected ischemia through surgical repair.

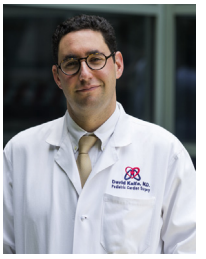
With respect to the guidelines, I think the information from this study can add some useful information. I think we still have a lot of ways to go in terms of having high-level evidence that will allow for Class A recommendations. What we really need is a protocol for assessment and management of patients before we can provide definitive answers.

Dr Fraser. As I did last year, I would like you to offer another management opinion based on a theoretical, but a realistic scenario: A 12-year-old girl is incidentally found to have anomalous right coronary artery from the left sinus and an 8-mm intramural course behind the left-right commissure. All provocative testing is normal. Would you recommend surgery, and, if so, what operation?

Dr Jegatheeswaran. We don't have the answer to a very important question yet, because we still don't know the risk of ischemia and sudden cardiac death, in comparison with the risk of surgery. As such, I don't know if I would be able to provide a definitive answer because this study was not intended to answer that question. However, using our current understanding, this patient does have a high-risk feature for ischemia and sudden cardiac death that we elucidated last year, that of a long intramural course. We know that in that our cohort there were patients who had a long course, in the setting of right AAOCA, who had sudden events. So, although patients with right AAOCAs were previously thought to have a benign lesion, this is no longer the case. However, other than an appreciation that a long intramural course is a risk factor, we do not yet have a cutoff, and most centers would not operate on patients with right AAOCA without some kind of positive testing. In the setting of negative testing, centers doing a large number of these cases often perform serial evaluation.

What we really need before we can answer this question is more research, more protocolized studies, and international collaboration, which will allow the capture of thousands of patients. This is required because the sudden cardiac event rate is so low.

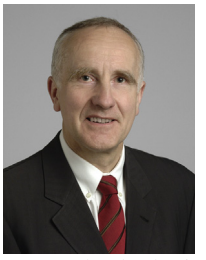
In the interim, the pros and cons of surgery need to be balanced and discussed with the family. This patient would require an unroofing with careful resuspension of the commissural post or creation of a neo-ostial window, which may decrease the risk of new aortic regurgitation.



Dr David M. Kalfa *(New York, NY).* Congratulations on your work. Your work shows that a surgery doesn't always treat or prevent coronary ischemia and can even sometimes lead to ischemia. You also stated that coronary unroofing was by far the most frequent technique applied to these patients.

I strongly believe that, from a technical standpoint, a coronary unroofing procedure needs to be done in an adequate and proper way to be effective. You need to be aggressive in terms of unroofing the coronary artery to really "open" the coronary ostium, open the commissure-related or fibrosis-related obstruction of the coronary ostium. So my question for you is do you have any granular data about how these coronary unroofing procedures that you included in your study were performed? Do you have granular data coming from the operative notes? And, if yes, did you analyze this data in your study?

Dr Jegatheeswaran. For this study, I personally reviewed all the operative notes, which totaled just under 400 in number. The problem that we have with all studies of this nature, where we are using retrospective data is that we do not always have the granular data we need. Sometimes surgeons will just write "We did an unroofing." They do not always clearly write whether they simply resected a small flap at the ostium or whether they have tacked the intima after takedown. As such, although we reviewed the data we collected carefully, what we really require is, as you mentioned, granular data collection with all those details, which likely needs to be prospectively collected.



Dr Gosta Pettersson *(Cleveland, Ohio).* Thank you for presenting this sobering data. I do a fair number of reoperations, and even in this category of patients, there is a number of patients who had previous operations for their anomaly—in the last one we did the entire root had been destroyed by a surgeon who had tried a minimally invasive approach to unroofing of an anomalous right coronary only to recognize that the artery did not after all did not have an intramural course, and ending up having to reconstruct the root and bypass both coronary arteries.

We need to separate the different anomalous carefully, take them one by one and analyze the approach risk, indication for intervention and choice of intervention for each one. We are very critical when it comes to preoperative evaluation of these patients and require not only symptoms but functional testing and use all available technology, including intravascular ultrasound and fractional flow reserve to prove significance. We also try to convince patients preoperatively to submit themselves to postoperative examinations as well. I'd like to congratulate you on this very important study, again demonstrating that we still have a long way to go.

Dr Jegatheeswaran. We have a long way to go.

Dr Sabine Hellevi Daebritz *(Zürich, Switzerland)*. I've done a lot of those cases, and I used to do a thoracic artery bypass in addition for security for the postoperative period being aware that this will occlude after 6 months if it's not needed. There is obviously another peak in the fourth decade in those patients; they never present with myocardial infarction and they often have symptoms but you cannot reproduce ischemia. These patients are often reluctant to undergo surgery. Can you comment on implanting a defibrillator because, obviously, they are not prone to infarction but to sudden cardiac death because of rhythm problems due to ischemia.

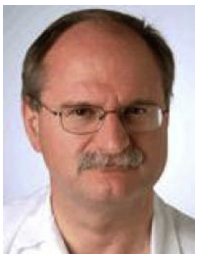
Dr Jegatheeswaran. With respect to our cohort, all patients were aged less than 30 years of at enrollment, with mostly medium-term follow-up, a median of 2.8 years, and we only had 3 patients in our cohort who had an implantable cardioverter defibrillator. Two implantable cardioverter defibrillators were for prevention based on scar, and one was for secondary prevention after an event that occurred after the repair. As such, unfortunately this Registry does not contain adequate data to provide you with an answer regarding whether or not patients should receive an implantable cardioverter defibrillator.

Dr Pravana Sinha *(Washington, DC)*. I have a question specifically about the intramural anomalous coronaries. In your data you show that commissural manipulation leads to more AI. Do you think that in itself is a surrogate for the anatomic variation where the intramural course runs below the commissure? Rather than the message that you should avoid commissural manipulation, should the message be that that's a different anatomy that requires commissural manipulation?

Dr Jegatheeswaran. I don't believe that should be the message. When you have a coronary that is running behind the commissure, you have to decide what surgical strategy you are going to use. The most common option is unroofing, with commissural take-down and hopefully with resuspension. Some surgeons don't always resuspend, especially if the coronary is just at the top of the pillar. After reading almost 400 operative notes, it is clear that different surgeons use different strategies with respect to resuspension.

Our study simply found that there is an association between commissural takedown and new AI. At the present time, we do not know what the right repair is. We do not know the long-term outcomes for the various repair strategies that could be used in this setting, such as neo-ostial windows and reimplantation after transection from outside the aorta without the use of a button. As a result, we still do not know which one has the best outcomes in this setting.

Dr Sinha. I mean, the surgeon should not have to balance between doing a complete unroofing and commissural resuspension because one will lead to more AI, the other will lead to more ischemia. So we have adopted a technique that we presented last year. It's a small series of 26 patients because I believe that no matter what the anatomy is, when you unroof the coronary, there is a decrease in the commissure that is equal to the diameter of the intramural segment. So we prophylactically suspend the commissure in 100% of our cases and at the same time achieve complete unroofing of the coronary.



Dr Antonio F. Corno *(Leicester, United Kingdom)*. Don't you think that instead of only sharing the outcomes of surgery, you should also collect all possible data from all the patients with myocardial ischemia in the presence of anomalous coronary artery? These are the data we're missing, the common denominator, and there are alarming data reported from the pathology registries.

Dr Jegatheeswaran. I would definitely agree with that. Our Registry does collect data from all patients with AAOCA, whether or not they're medically treated or surgically treated. The focus of this study was surgical risks, but we do also have that data. However, I will make this plea: We need everyone's data, especially medically treated patients who may not be seen by surgeons, for us to figure out what is happening.

APPENDIX E1. MEMBER INSTITUTIONS

USA

Phoenix Children's Hospital, Phoenix, Arizona
Cedars-Sinai Medical Center, Los Angeles, California
Loma Linda University Children's Hospital, Loma Linda, California
Lucile Packard Children's Hospital, Palo Alto, California
Rady Children's Hospital, San Diego, California
Yale New Haven Children's Hospital, New Haven, Connecticut
Nemours/Alfred I. Dupont Hospital for Children, Wilmington, Delaware
Children's National, Washington, District of Columbia
AdventHealth for Children, Orlando, Florida
Arnold Palmer Hospital for Children, Orlando, Florida
Johns Hopkins All Children's Hospital, Tampa, Florida
Nicklaus Children's Hospital, Miami, Florida
Children's Healthcare of Atlanta, Atlanta, Georgia
Ann & Robert H. Lurie Children's Hospital, Chicago, Illinois
Norton Children's Hospital, Louisville, Kentucky
Tulane Hospital for Children, New Orleans, Louisiana
Johns Hopkins Children's Center, Baltimore, Maryland
Boston Children's Hospital, Boston, Massachusetts
Children's Hospital of Michigan, Detroit, Michigan
C.S. Mott Children's Hospital, Ann Arbor, Michigan
Children's Minnesota, Minneapolis, Minnesota
Masonic Children's Hospital, Minneapolis, Minnesota
Mayo Clinic Children's Center, Rochester, Minnesota
Cardinal Glennon Children's Hospital, St. Louis, Missouri
Children's Mercy, Kansas City, Missouri
St. Louis Children's Hospital, St. Louis, Missouri
Children's Hospital of Omaha, Omaha, Nebraska
Children's Hospital at Montefiore, Bronx, New York
Golisano Children's Hospital at Strong Memorial Hospital, Rochester, New York
Hassenfeld Children's Hospital, New York, New York
Kravis Children's Hospital at Mount Sinai, New York, New York
Levine Children's Hospital, Charlotte, North Carolina
Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio
Cleveland Clinic Foundation, Cleveland, Ohio
Doernbecher Children's Hospital, Portland, Oregon
Children's Hospital of Philadelphia, Philadelphia, Pennsylvania
Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania
MUSC Children's Hospital, Charleston, South Carolina
Texas Children's Hospital, Houston, Texas
University of Texas Health Science Center at San Antonio, San Antonio, Texas
University of Texas Southwestern Medical Center, Dallas, Texas
Primary Children's Hospital, Salt Lake City, Utah
Inova Children's Hospital. Fall's Church, Virginia
Seattle Children's Hospital, Seattle, Washington
Children's Hospital of Wisconsin, Milwaukee, Wisconsin

CANADA

Stollery Children's Hospital, Edmonton, Alberta, Canada
The Hospital for Sick Children, Toronto, Ontario, Canada

APPENDIX E2. INCLUSION AND EXCLUSION CRITERIA, DATA COLLECTION, AND DATA AGGREGATION OF ANATOMIC FEATURES

Inclusion and Exclusion Criteria

Inclusion criteria for the Registry are a diagnosis of AAOCA at age 30 years or less, with a structurally normal heart or a hemodynamically insignificant concomitant cardiac lesion (eg, patent ductus arteriosus, atrial septal defect, restrictive ventricular septal defect, mild pulmonary valve stenosis, or bicuspid aortic valve without stenosis) not requiring surgical or catheter-based intervention.

Exclusion criteria are coronary artery ostial atresia, coronary artery aneurysm, myocardial bridging, coronary-cameral fistula, AAOCA from the pulmonary artery, and any concomitant hemodynamically significant structural heart lesion.

Data Collection

Patient data were abstracted from copies of institutional medical records submitted to the CHSS Data Center, for initial and subsequent assessments, hospitalizations, and procedures, and entered into a database by CHSS Data Center staff. These variables have been defined and described in our previous work and include patient demographics, presentation and symptoms from clinic notes, operative details from reports, and anatomical details from imaging reports, operative records, and autopsy reports.[2] Coronary artery anatomy was depicted as individual morphologic components for classification and analysis as demonstrated in the standardized atomization form given to participating centers, as previously described (Online Data Supplement). Anatomic components collected included which coronary artery is anomalous, the morphology of the origin (2 orifices, common orifice, single orifice with common trunk, slit-like orifice, high take off, acute angulation), and the course of the coronary artery.

The anatomic features collected for each patient were based on data obtained from preoperative echocardiogram, computed tomography, and/or magnetic resonance imaging reports. In addition, surgical atomization reports completed by the surgeon were used, if the patient underwent an operation. If these were not provided, a report was completed by Data Center staff using the operative report. In several cases, the only anatomic description available was from an autopsy report (n = 4). We have also previously

described our method for using multiple patient reports to obtain missing data or clarify contradictory data for the same patient.

Data Aggregation of Anatomic Features

Aggregated composite morphology for each patient was based on available diagnostic studies, and surgical data. Similar to the technique used in our previous manuscript, only preoperative diagnostic studies were used, before any surgical procedures. These were concatenated to reflect the global morphology of each patient using an algorithm which first retained all values which were similar among all sources (echocardiograms, computed tomography, magnetic resonance imaging, operative notes, and surgeon-completed data forms), it then added those variables that were only available from one source. Finally, if a variable had differing values, these were adjudicated by Data Center staff. The gold standard was considered to be a data form that was completed by the surgeon based on his/her intraoperative findings, followed by operative notes, magnetic resonance imaging or computed tomography, and echocardiography.

APPENDIX E3. EXPANDED DESCRIPTION OF PREOPERATIVE AND POSTOPERATIVE ISCHEMIA TESTING

Of those 103 patients who had preoperative and postoperative testing, 5 of 90 (6%) who tested negative preoperatively (1 patient CPET, 3 patient CPET and nuclear perfusion scan, 1 patient nuclear perfusion scan) subsequently tested positive postoperatively (2 by nuclear perfusion scan, 3 by CPET). Of the 13 patients who tested positive preoperatively (and had a postoperative test), only 1 of 13 (9%) remained positive after surgery. There were 4 additional patients without preoperative testing, who tested positive for ischemia after repair, for a total of 10 of 190 patients (5%) with postoperative ischemia. There were 7 patients who were positive preoperatively but did not have postoperative testing. Figure E1 highlights that there were a total of 29 patients (7 + 12 + 1 + 5 + 4) who had a positive ischemia test at any time, 9 of whom were newly positive after surgery (although 4 did not have any preoperative testing). The 10 patients with positive postoperative ischemia testing are all alive (5 had a negative test preoperatively, 4 did not have a preoperative test, 1 was positive preoperatively and postoperatively).

Patient Follow-up

Within our cohort, 352 of 395 patients (98%) have at least 3 months of follow-up; however, only 188 of 352 (53%) have an ischemia test postoperatively at any time, of whom 183 had an exercise stress test with or without a stress echocardiogram or nuclear perfusion scan. Only 102 of 188 of those patients had an ischemia test within 4 months, 99 of which were at least exercise stress tests (this increases to 129 of 188 and 125 tests, if the time frame is increased to $\leq$6 months).

Currently, it is recommended that patients undergo a CPET 3 months after surgery and a cardiac magnetic resonance image at 6 months.[4] In our cohort, if we give the allowance of considering any ischemia test within the first 6 postoperative months (in those patients with at least 3 months of follow-up), we found that only 129 of 352 underwent testing. Long-term follow-up suggests CPET every 1 to 3 years (based on activity level, annually if high-level sports participation), with a nuclear perfusion scan if new symptoms occur.[4] However, within our cohort, we found that only 190 of 395 patients (48%) had ischemia testing after surgery.

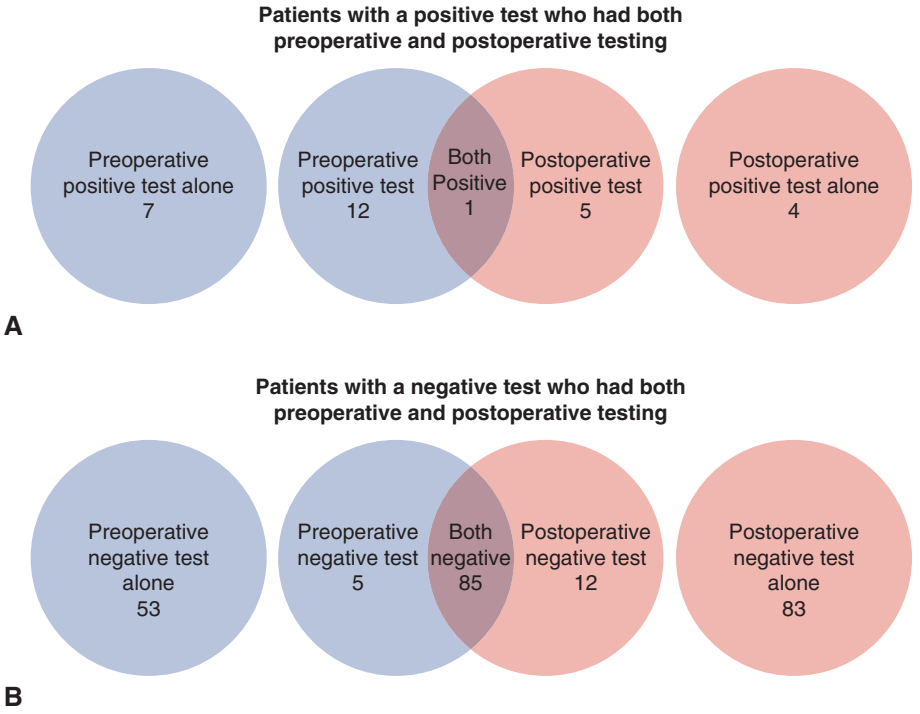


FIGURE E1. Positive and negative ischemia testing in patients undergoing surgery. A, Positive testing. B, Negative testing.

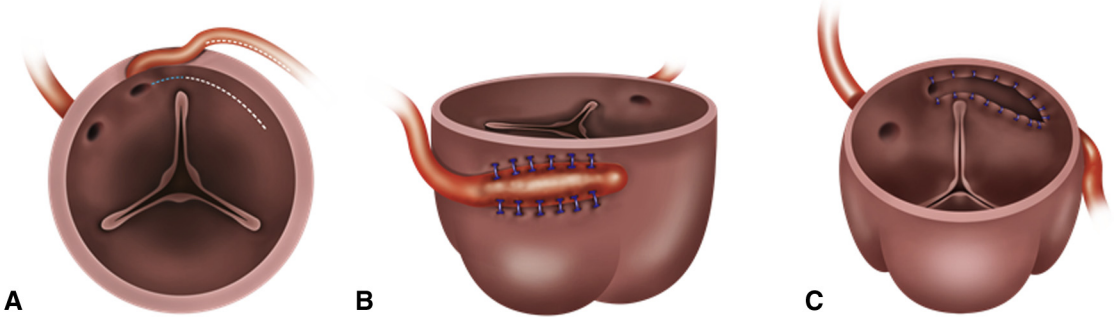


FIGURE E2. Aortocoronary window repair. A, Cross-sectional diagram demonstrating dotted line in blue for segment requiring unroofing and dotted line in white for region of creation of aortocoronary window (often done together). B, External view of aortocoronary window creation. C, Interior view of unroofed segment and aortocoronary window creation.

TABLE E1. Detailed description of 26 patients with postoperative ischemia

Patient	Anomalous coronary	Morphology	Surgery	Reason for ischemia
557	Left	Intraconal	Reimplantation, patch ostioplasty	Reoperation, ECMO, died
368	Left	Intramural (1), intraconal, slit-like orifice	Ostioplasty, tacking, PA translocation	Died
84	Left	Interarterial, intramural (6.25), slit-like orifice	Unroofing, aortocoronary window,* commissural manipulation	Reoperation, died
350	Left	Interarterial, intramural (6), slit-like orifice	Unroofing, tacking, commissural manipulation	Reoperation
581	Left	Interarterial, intramural (5), slit-like orifice	Unroofing, tacking, commissural manipulation	Testing
15	Left	Interarterial, intramural (9), slit-like orifice	Ostioplasty with patch	Died
182	Left	Interarterial, intramural (2), high orifice, slit-like orifice	Reimplantation	Reoperation
12	Left	Interarterial, intramural (missing length)	Ostioplasty with patch, commissural manipulation	Reoperation
652	Left	Interarterial, intramural (4)	Neo-ostial creation, tacking	Testing
578	Left	Interarterial, intramural (missing length), high orifice, slit-like orifice	Unroofing, commissural manipulation	Reoperation, symptoms
604	Left	Interarterial, intramural (5), slit-like orifice	Unroofing, commissural manipulation, bypass graft	Testing
346	Left	Interarterial, intramural (5.5), slit-like orifice	Unroofing, tacking	Reoperation
559	Left	Interarterial, intramural (3), slit-like orifice	Unroofing, tacking	Reoperation
386	Left	Interarterial, intramural (6), slit-like orifice	Unroofing, tacking, commissural manipulation	Testing
241	Right	Interarterial, intramural (1.5), high orifice, slit-like orifice	Unroofing	Testing
446	Right	Interarterial, intramural (missing length), slit-like status missing	Unroofing	Reoperation
463	Right	Interarterial, intramural (3), slit-like orifice	Unroofing	Testing
255	Right	Interarterial, intramural (11.5), high orifice, slit-like orifice	Unroofing, tacking	Symptoms
416	Right	Interarterial, intramural (missing length), slit-like orifice	Unroofing, tacking	Reoperation
462	Right	Interarterial, intramural (6), high orifice missing, slit-like orifice	Unroofing, tacking	Symptoms
68	Right	Interarterial, intramural (missing length), slit-like orifice	Unroofing, tacking, commissural manipulation	Testing
439	Right	Interarterial, intramural (3), slit-like orifice	Ostioplasty, commissural manipulation	Symptoms
552	Right	Interarterial, intramural (8), high orifice, slit-like orifice	Unroofing, tacking	Testing, reoperation, ECMO
645	Right	Interarterial, intramural (missing length), high orifice, slit-like orifice	Unroofing, tacking	Testing
163	Right	Interarterial, intramural (10), slit-like orifice	Unroofing, tacking, commissural manipulation	Reoperation, symptoms
558	Both	Interarterial, intramural (missing length), high orifice, slit-like orifice	Reimplantation	Reoperation

In the column "Morpholgy," the number in parentheses following the term "intramural" represent the intramural length (in mm). Reasons for ischemia presented in this Table are defined in Table 1, *A*. *ECMO*, Extracorporeal membrane oxygenation; *PA*, pulmonary artery. *Figure E2 shows a figure demonstrating aortocoronary window repair.

TABLE E2. Expanded description of adverse surgical events in patients with ischemia preoperatively by testing or symptoms, and by surgical repair type

	All patients	No preoperative ischemia	Preoperative ischemia	Isolated unroofing (with or without tacking)	Unroofing with commissural manipulation (with or without tacking)	Repair strategies other than unroofing	AAORCA	AAOLCA
New mild or greater AI	27	17	21	10	9	8	13	13
New moderate or greater AI	7	3	4	3	2	2	2	5
New abnormal EF	6	4	2	3	0	3	3	3
Postoperative ischemia by symptoms/ any postoperative testing	14 10 by testing 4 by symptoms	6 5 by testing 1 by symptoms	8 5 by testing 3 by symptoms	6 5 by testing 1 by symptoms	5 3 by testing 2 by symptoms	3 2 by testing 1 by symptoms	9 6 by testing 3 by symptoms	5 4 by testing 1 by symptoms
Postoperative ischemia by symptoms/ last postoperative testing	8 4 by testing 4 by symptoms	2 1 by testing 1 by symptoms	6 3 by testing 3 by symptoms	3 2 by testing 1 by symptoms	3 1 by testing 2 by symptoms	2 1 by testing 1 by symptoms	5 2 by testing 3 by symptoms	3 2 by testing 1 by symptoms
Coronary-related reoperations	13	6	7	5	3	5	4	8
Postoperative new ECMO	3	2	1	1	0	2	2	1
Death after an elective case	3	3	0	0	0	3	0	3
Adverse surgical events calculated using mild or greater AI, and any positive postoperative test	50/395 (13%) 22 AAOLCA 27 AAORCA 1 both	29/331 (9%) 10 AAOLCA 18 AAORCA 1 both	21/64 (33%) 12 AAOLCA 9 AAORCA	21/224 (9%) 6 AAOLCA 15 AAORCA	13/85 (15%) 8 AAOLCA 5 AAORCA	16/86 (19%) 8 AAOLCA 7 AAORCA 1 both	27/282 (10%)	22/108 (20%)
Adverse surgical events calculated using moderate or greater AI, and any positive postoperative test	34/395 (9%) 16 AAOLCA 17 AAORCA 1 both	19/331 (6%) 6 AAOLCA 12 AAORCA 1 both	15/64 (23%) 10 AAOLCA 4 AAORCA 1 both	15/224 (7%) 4 AAOLCA 11 AAORCA	8/85 (9%) 5 AAOLCA 3 AAORCA	11/86 (13%) 7 AAOLCA 3 AAORCA 1 both	17/282 (6%)	16/108 (15%)
Adverse surgical events calculated using mild or greater AI, and last positive postoperative test	45/395 (11%) 22 AAOLCA 22 AAORCA 1 both	25/331 (8%) 10 AAOLCA 14 AAORCA 1 both	20/64 (31%) 12 AAOLCA 8 AAORCA	18/224 (8%) 6 AAOLCA 12 AAORCA	12/85 (14%) 8 AAOLCA 4 AAORCA	15/86 (17%) 8 AAOLCA 6 AAORCA 1 both	22/282 (4%)	22/108 (20%)
Adverse surgical events calculated using moderate or greater AI, and last positive postoperative test	28/395 (7%) 15 AAOLCA 12 AAORCA 1 both	14/331 (4%) 5 AAOLCA 8 AAORCA 1 both	15/64 (21%) 10 AAOLCA 4 AAORCA	12/224 (5%) 4 AAOLCA 8 AAORCA	6/85 (7%) 4AAOLCA 2AAORCA	10/86 (12%) 7 AAOLCA 2 AAORCA 1 both	12/282 (4%)	15/108 (14%)

Some patients may have met more than 1 criteria for adverse surgical events as presented in Table 1, *B*. *AAOLCA*, Anomalous aortic origin of a left coronary artery; *AAORCA*, anomalous aortic origin of a right coronary artery; *AI*, aortic insufficiency; *EF*, ejection fraction; *ECMO*, extracorporeal membrane oxygenation.