

Long-Term Outcome and Impact of Surgery on Adults With Coronary Arteries Originating From the Opposite Coronary Cusp

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Background—An anomalous coronary artery from the opposite sinus of Valsalva may increase sudden death risk in children and young adults, and surgical intervention is often recommended. The impact of this lesion when recognized in the adult and its management are ill defined.

Methods and Results—We reviewed 210 700 cardiac catheterizations performed over a 35-year period at a single institution and identified 301 adults with an anomalous coronary artery from the opposite sinus of Valsalva, either anomalous right coronary artery from the left cusp or anomalous left main coronary artery from the right cusp. Patients were stratified by the pathway of the anomalous artery and the chosen treatment. Among the 301 patients with anomalous coronary artery from the opposite sinus of Valsalva (0.14% of the cohort), 79% had anomalous right coronary artery from the left cusp, and 18% had an interarterial course (IAC). Patients with IAC were younger (52 ± 13 versus 59 ± 13 years; $P=0.001$) and more likely to undergo surgical intervention (52% versus 27%; $P<0.001$), but mortality was not increased with IAC. Among the 54 patients with IAC, 28 underwent surgical repair with no perioperative deaths. Patients evaluated since 2000 were significantly more likely to be referred for surgery ($P=0.004$). Surgical patients were more likely to have abnormal stress tests (90% versus 43%; $P=0.01$) and had more extensive atherosclerosis but less diabetes mellitus (0% versus 23%; $P=0.01$). Long-term survival at 10 years appeared similar in both groups.

Conclusions—In this single-center cohort study of patients with an anomalous coronary artery from the opposite sinus of Valsalva, surgical management appears to have been favored recently. Despite no perioperative mortality, a positive impact on long-term survival was not observed. The impact of surgery in older adults with anomalous coronary arteries arising from the opposite coronary sinus with IAC deserves further study. (*Circulation*. 2011;123:154-162.)

Key Words: coronary arteries ■ catheterization ■ heart defects, congenital ■ outcomes ■ revascularization ■ surgery

Congenital anomalies of the coronary arteries are common, occurring in 0.3% to 1.3% of the population, and they have become increasingly recognized with wider use of new imaging technologies including cardiac computed tomography and magnetic resonance imaging. Although most cases are clinically insignificant, some anomalies have been associated with an increased risk of myocardial ischemia and infarction, congestive heart failure, and sudden cardiac death (SCD). In the United States, congenital coronary malformations are the second leading cause of SCD in the young, exceeded only by hypertrophic cardiomyopathy.¹⁻⁵ The highest-risk lesions are believed to be anomalous origin of the coronary arteries that arise from the opposite sinus of Valsalva (ACAOS) (Figure 1), including anomalous left main coronary artery arising from the right sinus (ALCA-R) and anomalous right coronary artery arising from the left sinus

(ARCA-L), particularly in the presence of an interarterial course (IAC) between the aorta and pulmonary artery.^{2,4,6-10} The presumptive mechanism of SCD in these patients is ischemia and generally occurs in close proximity to physical exertion.^{5,9,11-14} The risk of SCD in athletes with these lesions may as much as 79-fold higher than in nonathletes,¹⁵ and, as a result, patients with ACAOS have been excluded from competitive athletics. Unfortunately, attempts to identify the patients at greatest risk for fatal and nonfatal cardiac events have been largely unsuccessful.^{5,16} Coronary artery morphology,¹⁷ the presence of premonitory symptoms,^{4,5,16,18} and exercise stress testing^{11,16,19,20} are all inadequate in stratifying SCD risk. The only generally accepted risk factor for SCD is age <30 years at presentation.^{2,5,9,18} Older patients (≥ 30 years) appear to have a lower risk of SCD, although some risk may still exist. Thus, physicians are left with a quandary

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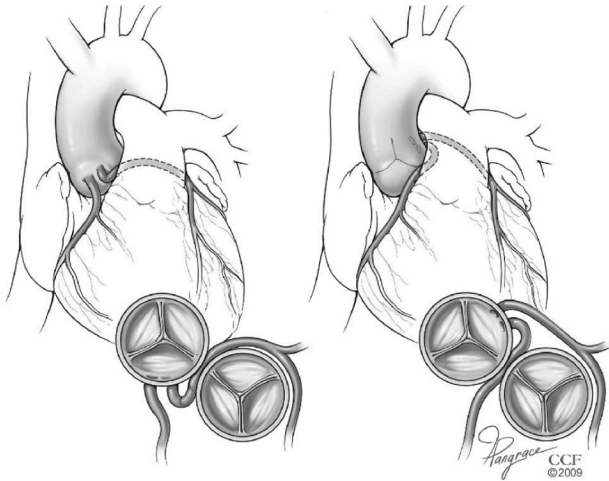


Figure 1. Illustration of an ALCA-R passing between the aorta and the pulmonary artery (left) and ARCA-L passing between the aorta and the pulmonary artery (right).

when faced with an older adult with so-called malignant coronary anatomy, particularly in the absence of worrisome symptoms or documented ischemia.

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Surgical interventions in patients with ACAOS (Figure 2) are generally performed to prevent ischemia and/or SCD and generally include bypass (with or without native vessel ligation), reimplantation into the correct sinus, and unroofing (in the event of an intramural coronary course). Not only are the indications for surgery in adults with ACAOS and IAC poorly supported by the medical literature, but the procedure of choice is uncertain, and its impact on long-term survival is unknown. With this background, we sought to examine our experience with these lesions and determine the long-term impact of surgical repair.

Methods

Study Design and Patients

We reviewed >210 700 cardiac catheterizations in the Cleveland Clinic Cardiovascular Information Registry from 1966 to 2007 and identified 530 patients with suspected ACAOS who were at least 18 years of age at the time of presentation and underwent coronary angiography as part of their diagnostic evaluation. The electronic and paper records of each of these patients were carefully reviewed, and any available catheterization films were reviewed by a single reviewer (R.A.K.) blinded to patient outcome. The final cohort consisted of 301 patients with confirmed ACAOS, 54 of whom had IAC between the aorta and pulmonary artery. The patients were further stratified on the basis of clinical management (surgical or medical). The study was approved by the institutional review board at the Cleveland Clinic.

Clinical Data

In addition to the information prospectively collected and validated within the Cardiovascular Information Registry, we reviewed the individual electronic and paper medical records of each patient, collecting additional demographic information, presenting signs and symptoms, results of diagnostic workup including stress testing, specific details of the surgical procedure that was performed, and date of last follow-up at the Cleveland Clinic. We defined "cardiovascular symptoms" as the presence of any of the following: exertional chest pain, shortness of breath, syncope, myocardial

infarction in the distribution of the anomalous coronary, or aborted SCD. Survival was confirmed for all patients with the use of the Social Security Death Index.

Statistical Analysis

The study population was divided into those with an IAC and those without and those who underwent surgery and those who did not. Continuous data were compared with 2-tailed *t* tests, and nominal data were compared with χ^2 likelihood ratios or Fisher exact test when appropriate. Follow-up time was compared with the Wilcoxon rank sum test. Survival free of death was estimated with Kaplan-Meier curves beginning with the date of catheterization. Survival comparison was made with the log-rank test at 10-year follow-up. Significance was set at 0.05 for all analyses. Data management and statistical analysis were performed in JMP 8.0 (SAS Institute, Inc; 2008).

Results

Demographics and Clinical Data

ACAOS Stratified by Presence of IAC

The demographic information and clinical data of the 301 patients with ACAOS (0.14% of the total cohort) stratified by the presence or absence of an IAC are listed in Table 1. Patients with an IAC were younger (52 ± 13 versus 59 ± 13 years; $P=0.001$) and more likely to have ALCA-R (33% versus 19%; $P=0.02$) than patients without an IAC. Patients with IAC presented with chest pain more commonly (82% versus 62%; $P=0.01$), although other signs and symptoms were similar. Patients with IAC had less extensive atherosclerosis ($P=0.01$), although coronary disease risk factors were similar. Patients with IAC had similar rates of abnormal stress tests (74% versus 88%; $P=0.12$) and incidence of significant ($\geq 60\%$ stenosis) coronary artery disease in the distribution of the anomalous artery (26% versus 20%; $P=0.20$). Patients with IAC were significantly more likely to undergo surgical intervention (52% versus 27%; $P<0.001$) and, among those receiving bypass, were more likely to receive an arterial graft to the anomalous vessel (53% versus 25% of surgical interventions; $P=0.03$).

ACAOS Stratified by Clinical Management

Table 2 compares patients with ACAOS on the basis of their clinical management (surgical or medical). Surgical intervention was more common in men (72% versus 57%; $P=0.01$) and in those with more extensive coronary disease ($P<0.001$). Patients managed with surgery more frequently had peripheral atherosclerosis (carotid disease in 22% versus 7% [$P<0.001$] and peripheral vascular disease in 21% versus 10% [$P=0.01$]). Surgical intervention was more common when the anomaly involved the left coronary artery than the right coronary artery (30% versus 17%; $P=0.02$) and in those who presented with chest pain (77% versus 61%; $P=0.01$) or had suffered a myocardial infarction (32% versus 21%; $P=0.04$). Surgically managed patients were also more likely to have had an abnormal stress test (97% versus 74%; $P=0.002$) and were more likely to have significant coronary artery disease in the distribution of the anomalous vessel (50% versus 25%; $P=0.02$).

IAC Stratified by Clinical Management

Of the 54 patients with ACAOS and IAC, 28 underwent a surgical intervention. The surgical intervention included by-

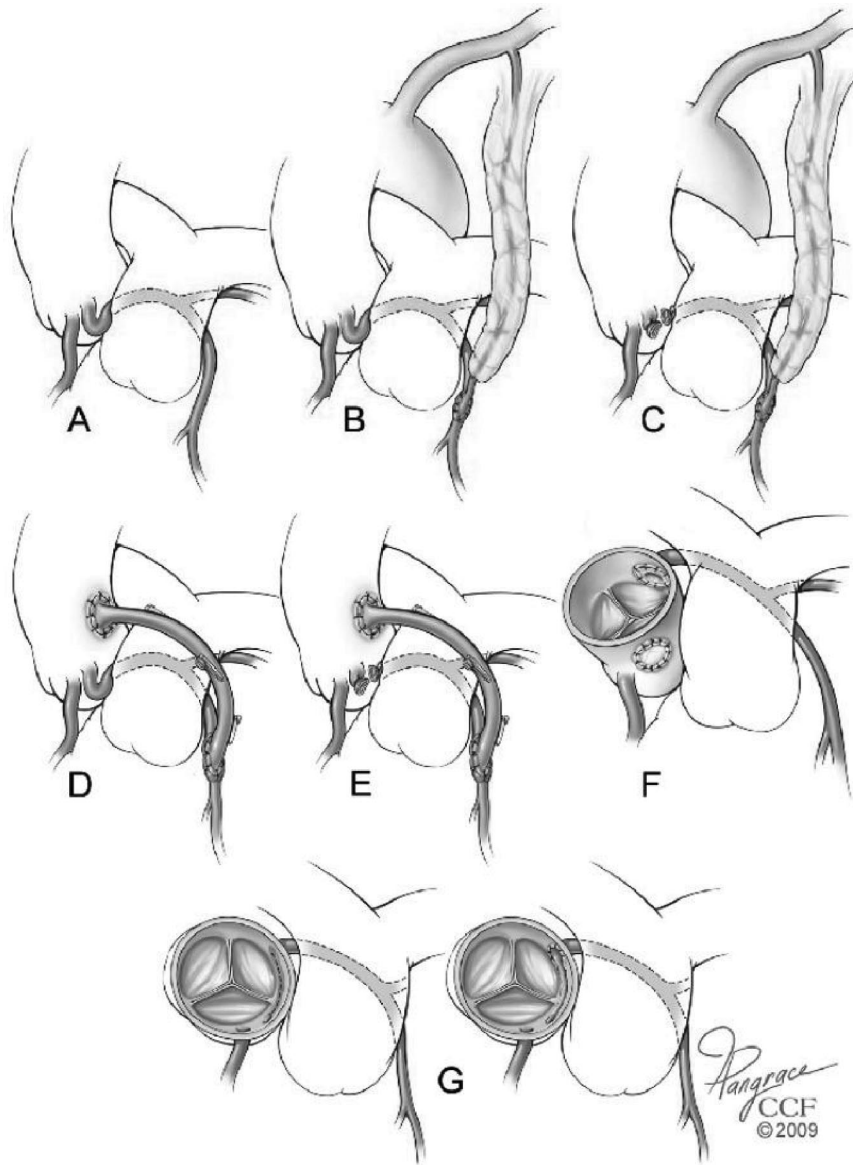


Figure 2. Illustration of a few of the surgical techniques that have been used to correct anomalous coronary arteries; ALCA-R (A) is used for illustrative purposes. These techniques include bypass with an internal thoracic artery (B), bypass with an internal thoracic artery with native vessel ligation (C), bypass with a saphenous vein (D), bypass with a saphenous vein with native vessel ligation (E), reimplantation (F), and coronary unroofing (G).

pass of the anomalous vessel with the use of an arterial graft in 10 patients (with concurrent ligation of the native vessel in 1 case), bypass with the use of a saphenous venous graft in 10 patients (with concurrent ligation of the native vessel in 1 case), reimplantation in 5 patients, and surgical unroofing in 3 patients.

Figure 3 illustrates the frequency of referrals by decade for ACAOS with IAC. Of note, the number of referrals over the past 6 years almost equaled that of the prior 34 years. Equally interesting, the management strategy has shifted over this time from predominantly medical (30% undergoing surgical intervention) to almost exclusively surgical (79% undergoing surgical interventions) ($P=0.004$).

Table 3 compares the demographics and clinical data of patients with an IAC on the basis of their management. Surgically managed patients were significantly more likely to have had an abnormal stress test than medically managed patients (94% versus 46%; $P=0.002$) but were no more likely to have coronary artery disease in the distribution of the

anomalous vessel (22% versus 31%; $P=0.059$). Surgical patients also had more extensive coronary atherosclerosis ($P=0.03$) but were less likely to have diabetes mellitus (0% versus 23%; $P=0.01$).

Outcomes

Length of survival follow-up for those with and without IAC was similar (median [interquartile range], 9.2 [3.3 to 16.4] and 9.3 [4.8 to 16.2] years; $P=0.45$; Table 1). Death occurred in 32% of patients with and 46% of patients without IAC. Among the entire cohort of patients with ACAOS, follow-up for patients managed medically was significantly longer than for patients managed surgically (9.9 [4.8 to 18.0] and 8.2 [3.4 to 14.0] years; $P=0.03$; Table 2).

In patients with IAC, long-term survival follow-up time for the surgical patients was significantly shorter (5.1 [2.0 to 11.3] and 11.4 [8.1 to 21.1] years; $P=0.01$) owing to the recent trend toward surgical intervention in these patients (Table 3). There was no perioperative mortality in this cohort.

Table 1. Demographics and Clinical Characteristics for IAC vs No IAC

| | All Patients (n=301) | IAC (n=54) | No IAC (n=247) | <i>P</i> |
|---|-------------------------|----------------|-------------------|----------|
| Demographics | | | | |
| Women, % | 37.9 | 33.3 | 38.9 | 0.44 |
| Age, y | 57.7±14.3 | 52.2±12.7 | 58.7±13.1 | 0.001 |
| Anomalous coronary artery, L%/R% | 20.9/79.1 | 33.3/66.7 | 18.4/81.6 | 0.02 |
| Body mass index, kg/m ² | 27.6±5.1 | 27.6±4.4 | 27.5±5.2 | 0.95 |
| Presenting symptoms | | | | |
| Chest pain, % | 65.8 | 81.5 | 62.4 | 0.01 |
| Shortness of breath, % | 57.8 | 57.4 | 57.9 | 0.95 |
| Syncope, % | 4.7 | 9.3 | 3.6 | 0.10 |
| Myocardial infarction, % | 24.2 | 16.7 | 25.9 | 0.14 |
| Comorbidities | | | | |
| Hypertension, % | 36.4 | 29.6 | 37.3 | 0.28 |
| Diabetes mellitus, % | 13.7 | 11.1 | 14.2 | 0.54 |
| Smoking, % | 36.9 | 31.5 | 38.1 | 0.36 |
| Atrial fibrillation, % | 4.3 | 0.0 | 5.3 | 0.02 |
| No. of diseased vessels, 0/1/2/3 | 97/77/64/63 | 17/21/12/4 | 80/56/52/59 | 0.01 |
| Peripheral vascular disease, % | 13.3 | 7.4 | 14.6 | 0.14 |
| Carotid disease, % | 12.0 | 14.8 | 11.3 | 0.49 |
| Chronic obstructive pulmonary disease, % | 5.6 | 3.7 | 6.1 | 0.47 |
| Chronic renal disease, % | 2.7 | 1.9 | 2.8 | 0.67 |
| Stress testing | | | | |
| Abnormal stress test, n (%) | 72 (82.8) | 23 (74.2) | 49 (87.5) | 0.12 |
| Coronary artery disease in anomalous distribution,* n (%) | 30 (21.1) | 8 (25.8) | 22 (19.8) | 0.20 |
| Clinical course | | | | |
| Surgical management, % | 31.4 | 51.9 | 26.7 | <0.001 |
| Anomalous bypass, % | 28.7 | 37.0 | 26.8 | 0.14 |
| Clinical follow-up | | | | |
| Follow-up time, y | 9.2 (4.5–16.1) | 9.2 (3.3–16.4) | 9.3 (4.8–16.2) | 0.45 |
| Death during follow-up, % | 43.5 | 31.5 | 46.2 | ...† |

Data are presented as mean±SD or percentage except follow-up time, which is presented as median (interquartile range). L indicates left; R, right.

*≥60% stenosis.

†Underpowered for comparison.

Survival during the entire follow-up period in patients with IAC appeared better in the surgical cohort (82% versus 53%) but did not appear to differ after 10 years (92.9% versus 92.3%). Figure 4 compares the survival for patients with IAC managed either surgically or medically up to 10 years after catheterization. At 10 years, no difference in survival was observed between those managed surgically or medically ($P=0.65$).

Discussion

When an anomalous coronary artery originates from the opposite sinus of Valsalva and passes between the great vessels, there is believed to be an increased risk of SCD. Most of the literature to support this hypothesis consists of small case series and autopsy reports rather than comparative studies and is derived mainly from experience collected in children. The long-term impact of this lesion when recog-

nized in the adult was previously unknown. In the largest reported cohort of such patients coming from a single institution's database collected over a 40-year period, we have found survival to be similar regardless of whether medical or surgical therapy was employed. This is a critically important finding because the frequency of such referrals appears to have increased 4-fold over the past decade. This increase has coincided with the proliferation of less invasive imaging techniques, including computed tomography and magnetic resonance imaging, now available to most physicians working in the ambulatory setting in the United States.

It is even more important to note the dramatic shift in clinical care over this same time period from favoring medical observation (2:1 over surgical management between 1970 and 2000) to most recently favoring surgery (4:1 over medical management between 2000 and 2006), despite any published evidence that such a strategy alters

Table 2. Demographics and Clinical Characteristics for Surgery vs Medical Management

| | All Patients (n=301) | Surgical Management (n=94) | Medical Management (n=207) | P |
|---|-------------------------|-------------------------------|-------------------------------|--------|
| Demographics | | | | |
| Women, % | 37.9 | 27.7 | 42.5 | 0.01 |
| Age, y | 57.7±14.3 | 58.4±13.4 | 57.2±13.2 | 0.48 |
| Anomalous coronary artery, L%/R% | 20.9/79.1 | 29.8/70.2 | 17.4/82.6 | 0.02 |
| Interarterial course, % | 17.9 | 29.8 | 12.6 | 0.001 |
| Body mass index, kg/m ² | 27.6±5.1 | 27.8±4.0 | 27.4±5.4 | 0.65 |
| Presenting symptoms | | | | |
| Chest pain, % | 65.8 | 76.6 | 60.9 | 0.01 |
| Shortness of breath, % | 57.8 | 52.1 | 60.4 | 0.18 |
| Syncope, % | 4.7 | 5.3 | 4.4 | 0.71 |
| Myocardial infarction, % | 24.2 | 31.9 | 20.8 | 0.04 |
| Comorbidities | | | | |
| Hypertension, % | 36.4 | 38.3 | 34.8 | 0.56 |
| Diabetes mellitus, % | 13.7 | 11.7 | 14.5 | 0.51 |
| Smoking, % | 36.9 | 35.1 | 37.7 | 0.67 |
| Atrial fibrillation, % | 4.3 | 2.1 | 5.3 | 0.36 |
| No. of diseased vessels, 0/1/2/3 | 97/77/64/63 | 6/20/27/41 | 91/57/37/22 | <0.001 |
| Peripheral vascular disease, % | 13.3 | 21.3 | 9.7 | 0.01 |
| Carotid disease, % | 12.0 | 22.3 | 7.3 | <0.001 |
| Chronic obstructive pulmonary disease, % | 5.6 | 3.2 | 6.8 | 0.29 |
| Chronic renal disease, % | 2.7 | 5.3 | 1.5 | 0.11 |
| Stress testing | | | | |
| Abnormal stress test, n (%) | 72 (23.9) | 33 (35.1) | 39 (18.9) | 0.002 |
| Coronary artery disease in anomalous distribution,* n (%) | 30 (21.1) | 17 (50.0) | 13 (24.5) | 0.02 |
| Extended clinical follow-up | | | | |
| Follow-up time, y | 9.2 (4.5–16.1) | 8.2 (3.4–14.0) | 9.9 (4.8–18.0) | 0.03 |
| Death during follow-up, % | 43.5 | 38.3 | 45.9 | ... |

Data are presented as mean±SD or percentage except follow-up time, which is presented as median (interquartile range). L indicates left; R, right.

*≥60% stenosis.

the clinical outcome. The 2 largest published series of surgical experience in coronary anomalies contain only a few ACAOS cases, and even fewer have an IAC.^{21,22} Although it would be expected that a surgical strategy

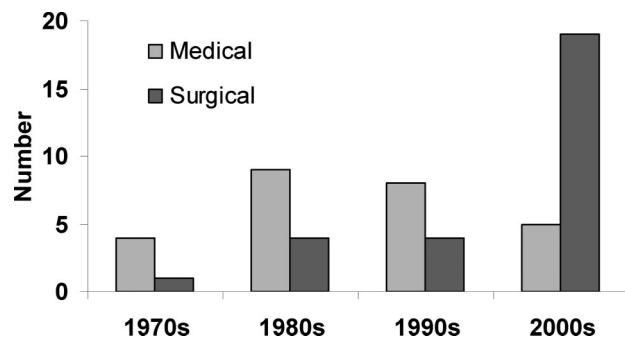


Figure 3. Referrals by decade to the Cleveland Clinic for management of ACAOS passing between the great vessels from the 1970s to 2006. The number of referrals over the last 6 years nearly equals that of the prior 3 decades. In addition, the frequency of surgical intervention has grown exponentially over this same time period ($P=0.004$).

could suffer in the short run because of the expected morbidity and mortality of surgery, no perioperative deaths were seen in the 28 patients undergoing surgery. This is at least in part related to the healthy patient population (young and with few comorbidities) and the expertise of the cardiothoracic surgeons at our institution. Even under these favorable conditions, however, a long-term benefit to surgery could not be demonstrated.

Although assessment of the sudden death risk in the adult with interarterial passage of an anomalous coronary artery would ideally occur in a larger, long-term prospective study, significant barriers to such a strategy exist. This includes the rarity of the lesion (only 0.026% of our total cohort, which itself is a selected, referral-based population that probably overestimates the frequency of these lesions). Therefore, at most, 50 000 such patients exist in the United States, the overwhelming majority of whom remain unrecognized. Further limiting a prospective study design is the expected low risk of clinical events and the often strong opinions of both patients and clinicians about the optimal therapeutic approach.

Table 3. IAC Demographics and Clinical Characteristics for Surgery vs Medical Management

| | IAC Patients (n=54) | Surgical Management (n=28) | Medical Management (n=26) | P |
|---|------------------------|-------------------------------|------------------------------|-------|
| Demographics | | | | |
| Women, % | 33.3 | 39.3 | 26.9 | 0.33 |
| Age, y | 52.2±12.7 | 50.5±14.0 | 54.0±11.2 | 0.32 |
| Anomalous coronary artery, L%/R% | 33.3/66.7 | 28.6/71.4 | 38.5/61.5 | 0.44 |
| Body mass index, kg/m ² | 27.6±4.4 | 27.9±4.0 | 27.3±4.8 | 0.74 |
| Presenting symptoms | | | | |
| Chest pain, % | 81.5 | 89.3 | 73.1 | 0.17 |
| Shortness of breath, % | 57.4 | 46.4 | 69.2 | 0.09 |
| Syncope, % | 9.3 | 10.7 | 7.7 | >0.99 |
| Myocardial infarction, % | 16.7 | 14.3 | 19.2 | 0.72 |
| Comorbidities | | | | |
| Hypertension, % | 29.6 | 28.6 | 30.8 | 0.86 |
| Diabetes mellitus, % | 11.1 | 0.0 | 23.1 | 0.01 |
| Smoking, % | 31.5 | 17.9 | 46.2 | 0.02 |
| No. of diseased vessels, 0/1/2/3 | 17/21/12/4 | 4/14/7/3 | 13/7/5/1 | 0.03 |
| Peripheral vascular disease, % | 7.4 | 3.6 | 11.5 | 0.34 |
| Carotid disease, % | 14.8 | 21.4 | 7.7 | 0.25 |
| Chronic obstructive pulmonary disease, % | 3.7 | 0.0 | 7.7 | 0.23 |
| Renal disease, % | 1.9 | 0.0 | 3.9 | 0.48 |
| Stress testing | | | | |
| Abnormal stress test, n (%) | 23 (74.2) | 17 (94.4) | 6 (46.2) | 0.002 |
| Coronary artery disease in anomalous distribution,* n (%) | 8 (25.8) | 4 (22.2) | 4 (30.8) | 0.59 |
| Extended clinical follow-up | | | | |
| Follow-up time, y | 9.2 (3.3–16.4) | 5.1 (2.0–11.3) | 11.4 (8.1–21.1) | 0.01 |
| Death during follow-up, % | 31.5 | 17.9 | 46.2 | ... |

Data are presented as mean±SD or percentage except follow-up time, which is presented as median (interquartile range). L indicates left; R, right.

*≥60% stenosis.

As a start for assessing the malignant nature of interarterial passage in the adult, we compared the long-term outcome of 54 such patients with 247 patients with what is perceived as a more benign variant (ACAOS in the absence of IAC).

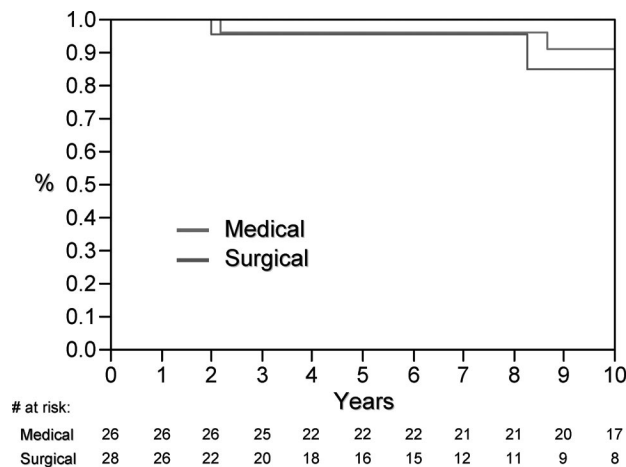


Figure 4. Survival free from death based on initial medical or surgical management in patients with ACAOS passing between the great vessels. At 10-year follow-up, there was no difference in survival ($P=0.65$).

Interestingly, mortality did not appear higher in those with an IAC. Surgical management was, however, nearly twice as common in patients with an IAC, once again emphasizing the perception of this being a higher-risk cohort.

Not only does controversy exist in deciding if and when to proceed to surgical management in patients with ACAOS with IAC, but the choice of operative correction is even less clear. If bypass is the chosen modality, one must decide whether to utilize an internal thoracic artery or a saphenous vein graft and whether the native vessel should be ligated to prevent competitive flow and graft failure (Figure 2). Saphenous vein grafts, by virtue of their larger diameter, allow for higher resting flow rates, which could have hypothetical benefit of increased patency in a lesion with presumed episodic obstruction. Internal thoracic artery grafts are, in general, associated with superior rates of patency in the long term^{23,24} and a higher resistance to atherosclerosis²⁵ and are better able to handle high pressures and flow rates because of intrinsic production of relaxing factors and increased responsiveness to vasoactive substances.²⁶ Furthermore, they appear to be able to grow in length, which may benefit younger patients.^{27,28} Internal thoracic artery grafts have also been shown to

have a positive effect on survival after bypass surgery^{29–31} but, unfortunately, are prone to atrophy and occlusion secondary to competitive flow within the native vessel.^{32–34} Decreased flow through the graft causes it to constrict, placing it at risk of disuse atrophy and occlusion,²⁶ although a growing body of research challenges this assertion.^{26,35,36} It is also important to recognize that younger patients undergoing coronary artery bypass grafting may require repeat bypass at some point, and the use of the internal thoracic artery may limit revascularization options in the future. This issue has helped to fuel the development of newer surgical procedures to repair ACAOS.

When the coronary path is initially within the aortic wall (intramural), surgical unroofing may be possible. First introduced by Mustafa and colleagues³⁷ in 1981, this procedure returns the anomalous vessel to a more normal takeoff point and appears to have promising short-term success.^{38–41} Unfortunately, aortic insufficiency can result, even late after surgery,⁴¹ and myocardial ischemia may persist in this population, particularly in patients with repaired ARCA with IAC.⁴²

The third major surgical option is reimplantation of the coronary artery into the proper sinus. It is a technically demanding procedure that requires extensive dissection and mobilization and can only be performed in patients with very specific coronary anatomy (no slit-like orifice, intramural segment, or common ostium with the other coronary artery). The vessel must also have a considerably sized lumen and be long enough for adequate mobilization. Reimplantation avoids the risks associated with coronary artery bypass grafting and traditional unroofing but carries its own inherent risks, including stretching and kinking of the artery as well as anastomotic stenosis. Direct comparison of outcomes related to these procedures was limited in our cohort because of the small patient populations, although no appreciable differences were seen.

The role of each of these interventions remains the same: to restore perfusion within the anomalous vessel distal to potential points of obstruction. Presumably, ischemia is a trigger for ventricular arrhythmia and sudden death, but the mechanism of this remains far from clear, and several theories have been postulated. The anomalous vessel may be compressed between the great vessels as the aorta dilates during exercise, pushing it against a firmly anchored pulmonary trunk. Studies in which intravascular ultrasound is used have estimated that coronary artery lumen diameter may decrease by 30% to 50% during systole.⁴³ Often, the anomalous artery assumes an intramural course within the aortic wall for a short distance after emerging from the opposite coronary sinus. This close relationship with the aorta places it at risk of being stretched out and flattened as the aorta dilates during exercise as well as being compressed by the intercoronary commissure during diastole when the aortic valve is closed. Atresia of the anomalous artery secondary to altered hemodynamics during its development may also play a role. Some have even postulated that vasospasm of the anomalous vessel can periodically occur and reduce

blood flow. Perhaps the most plausible explanation relates to the acute angle takeoff of the artery (generally $<45^\circ$ between the aortic lumen and coronary ostium), which typically results in a slit-like orifice and an ostial flap-like ridge (a form of ostial stenosis in which a portion of the aortic tissue protrudes into the ostium).

Regardless of the mechanisms at work, some patients will develop critical reductions in coronary blood flow to the point of developing symptomatic myocardial ischemia, including chest pain, palpitations, syncope, myocardial infarction, lethal ventricular arrhythmias, and SCD. The most worrisome aspect of this particular coronary malformation, however, is its unpredictable nature, and this has led some to recommend a surgical intervention in nearly all patients.⁴⁴ According to autopsy reviews and small clinical studies, ALCA-R is generally considered to have greater malignant potential than ARCA-L.⁴⁵ When ARCA-L is identified, most authors endorse surgical intervention only in symptomatic patients,^{21,46–48} although some believe that the lesion alone is a strong enough indication for surgery.⁴⁹ These same groups generally take a more aggressive approach to ALCA-R, although a focus remains on demonstrating ischemia. Cohen and colleagues⁵⁰ developed an algorithm for ACAOS in which patients are separated on the basis of age (the only demonstrated risk factor). They suggested that all patients aged <30 years undergo surgery, whereas patients aged ≥ 30 years should first be stratified by presenting symptoms and reversible ischemia on nuclear stress testing. The recently published Guidelines for the Management of Adults With Congenital Heart Disease place a class I recommendation for revascularization in all patients with ALCA-R with IAC.⁵¹ In ARCA-L, revascularization was a class I recommendation in the presence of documented ischemia, sudden death, or unexplained arrhythmia but could also be considered in the absence of symptoms (class IIa recommendation). It is most noteworthy, however, that the authors strongly encourage publication of any data in this field because of its current absence.

Our study provides some reassurance for the adult patient and the treating physician when faced with ACAOS, particularly those in whom the diagnosis was made incidentally. No appreciable improvement in long-term survival was seen in patients with ACAOS and IAC after a surgical intervention. These results do not suggest that higher-risk subsets do not exist with this lesion, nor should they be applied to a child or adolescent in whom this lesion is identified. Because of our tertiary nature as an institution, clinical follow-up (other than immediately postoperative) was scattered, and we were only able to assess nonfatal cardiovascular events in a very limited fashion. It is possible and even likely that hospitalization, frequency of chest pain or syncope, or quality of life was positively altered after surgical revascularization. Although core clinical data were collected prospectively, additional information was acquired through a retrospective chart and electronic medical record review and is therefore subject to various biases. The study population was also small for a cardiovascular study, although it was

quite sizable compared with the previous published studies of these anomalies. Comparisons of management among our cohort of patients with IAC are insightful but very likely underpowered. It is hoped that these results will help physicians to avoid the knee-jerk response of immediate surgical referral in all such patients, particularly those in whom the anomaly is discovered incidentally, and encourage further investigation into this very important field, perhaps even stimulating interest in a randomized multicenter trial of revascularization therapy.

Disclosures

Dr Krasuski has served as a speaker for Actelion, United Therapeutics, AGA Medical, Pfizer, and Roche. He has served as a consultant to Actelion and Gore Medical. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

The presence of an anomalous coronary artery arising from the opposite sinus of Valsalva may increase the risk of sudden death risk in children and young adults, but its impact and management in the adult are poorly defined. The recently published American College of Cardiology/American Heart Association Guidelines for the Management of Adults With Congenital Heart Disease suggest an important role for surgical revascularization when such a lesion is discovered, but the recommendation is based on few clinical data. We examined a large single institution's experience over a 40-year period to further assess the importance of these lesions and the impact of surgery. We identified 301 patients with anomalous coronary artery arising from the opposite sinus of Valsalva, with anomalous right coronary arteries being found more commonly than anomalous left coronaries ($\approx 4:1$). In 54 patients, the lesion passed between the aorta and the pulmonary artery (interarterial course), anatomy that has been believed to place the patient at substantially higher risk. Surgery was more commonly performed in patients with anomalous left coronary arteries, interarterial course, positive stress testing, and in the presence of concurrent coronary disease and appeared to become the highly favored strategy over the past decade. Among the patients with interarterial course, 28 underwent surgical repair with no perioperative deaths but with long-term survival similar to that of the unrepaired cohort. Quality of life was not formally assessed in this study. Our results suggest that anomalous coronary artery arising from the opposite sinus of Valsalva with interarterial course, particularly if incidentally discovered, may not carry the same associated mortality risk in older adults. Prospective studies are desperately needed to formally examine management strategies.