



Technical success and long-term outcomes after anomalous right coronary artery stenting with cardiac computed tomography angiography correlation

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Abstract

Introduction: Anomalous origin of coronary arteries has been observed in about 0.35–2.10% of the population. Patients with anomalous right coronary artery (ARCA) may present with significant symptoms, arrhythmias or ACS, and at times sudden death. Traditionally, surgical correction has been the recommended treatment. However, these may be technically challenging, and bypass grafting for such anomalies has the potential for graft failure because of competitive flow. We sought to determine the intermediate and long-term outcomes of drug-eluting stent placement for patients with symptomatic ARCA. We also looked at angiographic findings suggestive of interarterial course as confirmed by subsequent computed tomography (CT) findings.

Methods: Between January 2005 and December 2012, we enrolled 11 patients for elective percutaneous coronary intervention (PCI) of ARCA in a single center, prospective, nonrandomized fashion. Patients were followed up in clinic at 1 week, 3 months, 6 months, and 1 year, and then annually or more frequently if needed. All patients underwent a cardiac CT, as well as functional stress testing when needed to assess for recurrence of disease.

Results: All 11 of our patients, who presented with significant symptomatic stenosis with an ARCA, were successfully treated with PCI. Mean follow-up duration was 8.5 years. The only two deaths during follow-up were related to noncardiac causes (sepsis), with a mortality rate of 18.2%. Two patients had a positive functional study and on subsequent coronary angiography, one of them had significant in-stent restenosis (target lesion revascularization of 9.1%) and one distal to the stent (target vessel revascularization 9.1%). We found the observation of a “slit-like lesion” on angiography to have a sensitivity of 100% and specificity of 86% for the diagnosis of interarterial course of the anomalous vessel seen on subsequent CT.

Conclusions: Our study results suggest that PCI of ARCA is an effective and low-risk alternative to surgical correction, with good procedural success and long-term outcomes. It can provide symptomatic relief in such patients and may reduce the risk of sudden death in younger patients, without the inherent risks associated with surgical repair.

KEYWORDS

coronary artery disease, congenital heart disease in adults, coronary anomaly, electron beam CT/multidetector CT imaging, percutaneous coronary intervention

1 | INTRODUCTION

Anomalous origin of coronary arteries occurs in about 0.35–2.10% of the population, with anomalies of origin of the right coronary artery (RCA) being more common than left coronary artery.^{1,2} The presence of coronary artery anomalies may lead to restriction of flow through the anomalous artery related to their anatomic course, causing myocardial ischemia and ventricular arrhythmias. The presence of such anomalies may also be associated with an increased predisposition to developing significant epicardial atherosclerotic disease.³ Patients with anomalous right coronary artery (ARCA) may remain asymptomatic and may come to attention only as an incidental diagnosis. Others may present with exertional chest pain, syncope, ventricular tachycardia, or myocardial infarction although, the first clinical presentation may also be sudden cardiac death (SCD). SCD appears to be most common in cases where the anomalous artery takes an intramural or interarterial course.

The preferred choice of treatment for ARCA is still controversial, although because of the propensity for sudden death, especially in association with exercise in younger individuals, most of the literature advocates definitive surgical correction. This is recommended for anomalous coronary anomalies associated with symptoms or with evidence of ischemia on stress testing (class I recommendation).⁴ Options for surgical correction include CABG (coronary artery bypass grafting), reimplantation of the coronary ostia, unroofing of the coronary artery (excision of the common wall between the aorta and the RCA), or pulmonary artery translocation.^{5,6} However, bypass grafting for such anomalies, especially without proximal ligation of the native coronary artery, has the potential for graft failure because of competitive flow.⁵ Percutaneous stenting of the anomalous coronary artery is another approach that has been proposed, though outcome data for this approach are limited mainly to case reports/series.

We sought to determine the intermediate and long-term outcomes of drug-eluting stent placement for patients with symptomatic ARCA. We also looked at angiographic findings suggestive of interarterial course as confirmed by subsequent computed tomography (CT) findings.

2 | METHODS

2.1 | Study design and population

Between the dates of January 2005 and December 2012, we enrolled 11 consecutive patients at Loyola University Medical Center for elective percutaneous coronary intervention (PCI) of ARCA in a single center, prospective, nonrandomized fashion. Institutional review board approval was obtained.

2.1.1 | Inclusion criteria

Patients were included in the study if they were age 18 or above and able to give consent, agreeable to clinical follow-up per protocol, willing to take dual antiplatelet for at least 12 months, and had symptoms attributable to an ARCA with either: a “high risk” course defined as anomalous origin of RCA that runs between the pulmonary artery and aorta, or significant atherosclerotic disease in the ARCA. Patients with non-ST-elevation myocardial infarction (NSTEMI) or unstable angina at presentation and found to have significant disease in an ARCA were also included.

2.1.2 | Exclusion criteria

Patients were excluded from the study if they had left main or three vessel disease, any significant valvular disease, syncope or sudden cardiac death, hypertrophic or arrhythmogenic right ventricular cardiomyopathy, intolerance or contraindication to antiplatelet therapy, or congenital heart disease.

2.2 | Interventional procedure

Arterial access was established via right or left femoral arteries. The size of the guiding catheter used for the procedure was 7 or 8Fr in the majority of cases. All patients were pretreated with aspirin 325 mg and clopidogrel 600 mg or prasugrel 60 mg. After the procedure, patients continued dual antiplatelet therapy for at least 1 year at which time the decision to continue DAPT was left to the discretion of the treating cardiologist. Only drug-eluting stents were implanted. Angiographic success was defined as post-PCI residual stenosis <10% with TIMI 3 flow in the culprit artery.

2.3 | Cardiac CT

Cardiac CT studies were independently reviewed by an imaging cardiologist who was blinded to angiography results. On follow-up CTs, in addition to describing the takeoff and course of the ARCA, we also sought to assess stent patency, and any evidence of stent fracture or anatomic distortion. Ten of eleven patients had a cardiac CT in addition to cardiac catheterization.

2.4 | Follow-up

Patients were scheduled for follow-up in cardiology clinic at 1 week, 3 months, 6 months, and 1 year. Patients were then followed annually in clinic or by phone contact if followed by an outside referring

TABLE 1 Baseline demographics

Baseline biographical data	
Mean age (years)	64.4 ± 9.9
Female gender (%)	36.4
Mean ejection fraction (%)	57.2 ± 10.3
CAD risk factors	
Diabetes mellitus (%)	36.4
Hypertension (%)	90.9
Hyperlipidemia (%)	90.9
Known prior CAD (%)	27.3
Smokers (%)	63.6
Chronic kidney disease (%)	18.2
Medications prior to PCI	
ACEI/ARB (%)	63.6
Beta blocker (%)	45.5
Calcium channel blocker (%)	0
Aspirin (%)	63.6
Statin (%)	90.9
Clinical presentation	
Functional study prior to cardiac catheterization (%)	54.5
Type of functional study	
Treadmill nuclear stress (%)	9.1
Pharmacological nuclear stress (%)	27.3
Treadmill stress echo (%)	18.2
Unstable angina/NSTEMI at presentation (%)	36.4

Abbreviations: NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention.

cardiologist. They were followed more frequently than annually if needed, based on the discretion of the primary cardiologist.

3 | RESULTS

A total of 11 patients were enrolled in the study. These patients underwent PCI of an ARCA at our institution between 2005 and 2012. Baseline characteristics of the patients are shown in Table 1.

All (11 out of 11) patients were symptomatic at presentation. Thirty-six percent (4 out of 11) of patients had NSTEMI/unstable angina at the time of presentation. Six of the eleven patients (54.5%) had a functional study prior to getting LHC (left heart catheterization). The types of functional study are shown in Table 1. Among the patients who had functional studies, two had significant wall motion abnormalities induced with exercise in the territory of the RCA, three had fixed perfusion defects on their nuclear stress tests but developed abnormal electrocardiographic findings during stress. One patient had normal perfusion on their stress test but was taken to the catheterization lab due to significant resting wall motion abnormalities on echo and nuclear stress test and found to have significant RCA disease with nonobstructive disease of the left system.

TABLE 2 Site of stenosis and length of narrowing in the anomalous RCA on angiography, and type of catheter and guidewire used for each intervention

Patient	Site of stenosis in anomalous RCA	Lesion length (mm)	Catheter	Guidewire
1	Proximal RCA	11	AL1	Choice PT
2	Ostial RCA	2.61	AL2	BMW
3	Proximal RCA	5.51	AL1	Choice PT
4	Proximal RCA	3	AL2	Sport
5	Proximal RCA	11	AL3	Choice PT
6	Proximal RCA	8	AL2	BMW
7	Proximal RCA	9.44	MP	BMW
8	Proximal RCA	4	AL1	Fielder
9	Ostial RCA	3.1	XB 3.5	BMW
10	Ostial RCA	3.48	AL2 SH	BMW
11	Ostial RCA	10.4	AL2	BMW

Abbreviation: RCA, right coronary artery.

TABLE 3 Procedure details for anomalous RCA interventions

Lesion and intraprocedural characteristics	
Mean number of stents per patient	1.6 ± 0.7
Mean stent length (mm)	23.3 ± 7
Mean stent diameter (mm)	3.1 ± 0.3
Drug-eluting stents (% of stents placed)	
Cypher (%)	72.7
Xience (%)	27.3
Mean total fluoroscopy time (min)	17.4 ± 4.7
Mean total amount of contrast used (ml)	217.7 ± 50
Significant non-RCA lesion present (% of patients)	81.8

Abbreviation: RCA, right coronary artery.

The site of lesion as well as the length of narrowing within the ARCA on angiography is shown in Table 2. Table 2 also shows the type of catheter and guidewire used for the RCA intervention. As shown in the table, 4 of our patients (36.4%) had stenosis at the ostium of the ARCA. Four of the eleven patients (36.4%) undergoing coronary angiography were identified to have a “slit-like lesion” in the ARCA.

The mean number of stents placed per patient was 1.6 ± 0.7 with an average diameter and length of 3.1 ± 0.3 mm and 23.3 ± 7 mm respectively. All were DES (drug-eluting stents), with 72.7% being Cypher and the remaining being Xience. Table 3 describes the procedural details for the ARCA interventions.

Angiographic success, defined as post-PCI residual stenosis <10% with TIMI 3 flow in the culprit artery, was achieved in 100% of cases. There were no major bleeding or vascular complications reported in any of our patients, and no instances of aortic or coronary dissection. Post-PCI, all the patients were placed on DAPT, with aspirin being the primary agent and the secondary agent being clopidogrel (81.8%), Prasugrel (9.1%), or Ticlopidine (9.1%).

Patient	Takeoff level	Ostia	Takeoff angle	Vessel course	Intramural course
2 ^a	Above commissure	Separate	≥45	Subpulmonic	Not intramural
3	Above commissure	Separate	<45	Interarterial	Intramural
4	Above commissure	Separate	<45	Subpulmonic	Not intramural
5	Above commissure	Separate	<45	Interarterial	Intramural
6	Above commissure	Separate	<45	Subpulmonic	Not intramural
7	Above commissure	Separate	<45	Subpulmonic	Not intramural
8	Below commissure	Separate	≥45	Subpulmonic	Not intramural
9	Above commissure	Separate	≥45	Subpulmonic	Not intramural
10	Below commissure	Separate	≥45	Subpulmonic	Not intramural
11	Above commissure	Separate	<45	Interarterial	Intramural

TABLE 4 Cardiac CT findings of anomalous RCA

Abbreviations: CT, computed tomography; RCA, right coronary artery.

^aPatient 1 did not undergo cardiac CT.

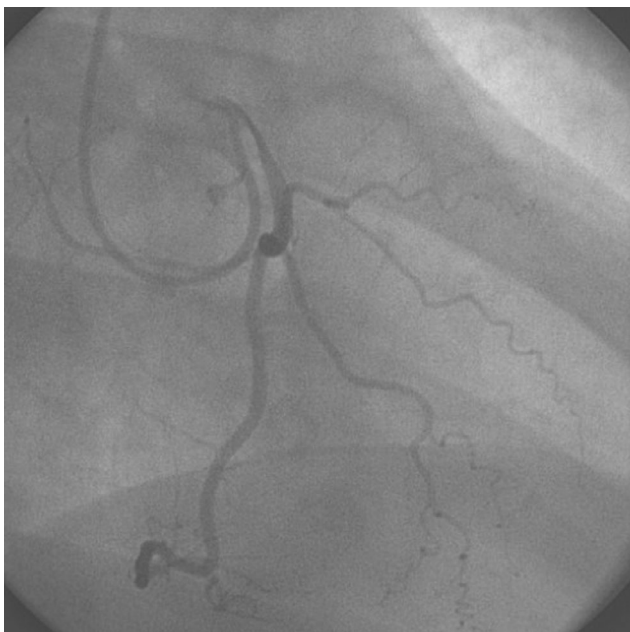


FIGURE 1 Coronary angiography of our patient demonstrating an anomalous RCA with a “slit-like lesion” at its ostium. This patient went on to have a PCI to this segment of the vessel. PCI, percutaneous coronary intervention; RCA, right coronary artery

Cardiac CT was performed on all but one of our study patients. On cardiac CT, six of the patients were seen to have an acute angle (less than 45°) at takeoff. Table 4 describes cardiac CT findings of the ARCA for each of our patients, including angle at takeoff, take off level, whether the ARCA had a separate ostium, as well as the course, including whether an intramural course was present.

Three of our patients were found to have a typical interarterial course of the ARCA on cardiac CT. All three of these patients had a “slit-like ostium” identified on initial cardiac cath. Figure 1 shows the finding of slit-like origin on one of our patients. Figure 2a,b shows the subsequent cardiac CT for the same patient confirming an ARCA with an interarterial course. We found the observation of a “slit-like lesion” on angiography to be very sensitive (sensitivity of 100% and

specificity of 86%) for the diagnosis of interarterial course of the anomalous vessel seen on subsequent CT.

The cardiac CT was performed at a mean duration of 536 days after the ARCA PCI. All patients with post-PCI cardiac CT were found to have patent ARCA stents (Figure 3). On follow-up cardiac CT, we did not find any evidence of stent fracture or any anatomic distortion in any of our patients.

All patients were symptom free postintervention. All the patients were followed clinically until 2017 (mean follow-up of 8.5 years). Patients who did not continue to follow at LUMC were contacted by phone periodically for follow-up. Table 5 shows the clinical endpoints at mean 8.5 years of follow-up. There were 2 deaths (18.2%) in our patient group, both occurring due to sepsis well beyond the date of the index PCI. Among the remaining nine patients, eight had a future functional study per discretion of their primary cardiologist. One of these patients had stenosis within the stent at follow-up. Another patient had progression of his CAD in a segment distal to the prior stent (posterior descending artery) of the ARCA. The stent itself was widely patent with no evidence of stent fracture on angiogram. One patient had a positive functional study but no obstructive CAD on the subsequent LHC. One patient had a fixed defect on the functional study and was followed clinically. Another one had a fixed defect but went on to have a LHC for persistent angina. He was found to have multivessel disease needing subsequent CABG, although the ARCA was found to be patent.

4 | DISCUSSION

In selected patients with symptomatic ARCA, PCI with DES is a viable treatment option for symptomatic relief as well as alleviating the risk of sudden cardiac death in younger patients. We found PCI of ARCA to be associated with excellent procedural outcomes and good long-term outcomes with no evidence of stent fracture or distortion on follow-up imaging. We also looked at the angiogram finding of “slit-like ostium” of an ARCA and found it to be highly sensitive for detection of interarterial course of the artery on a subsequent cardiac CT.

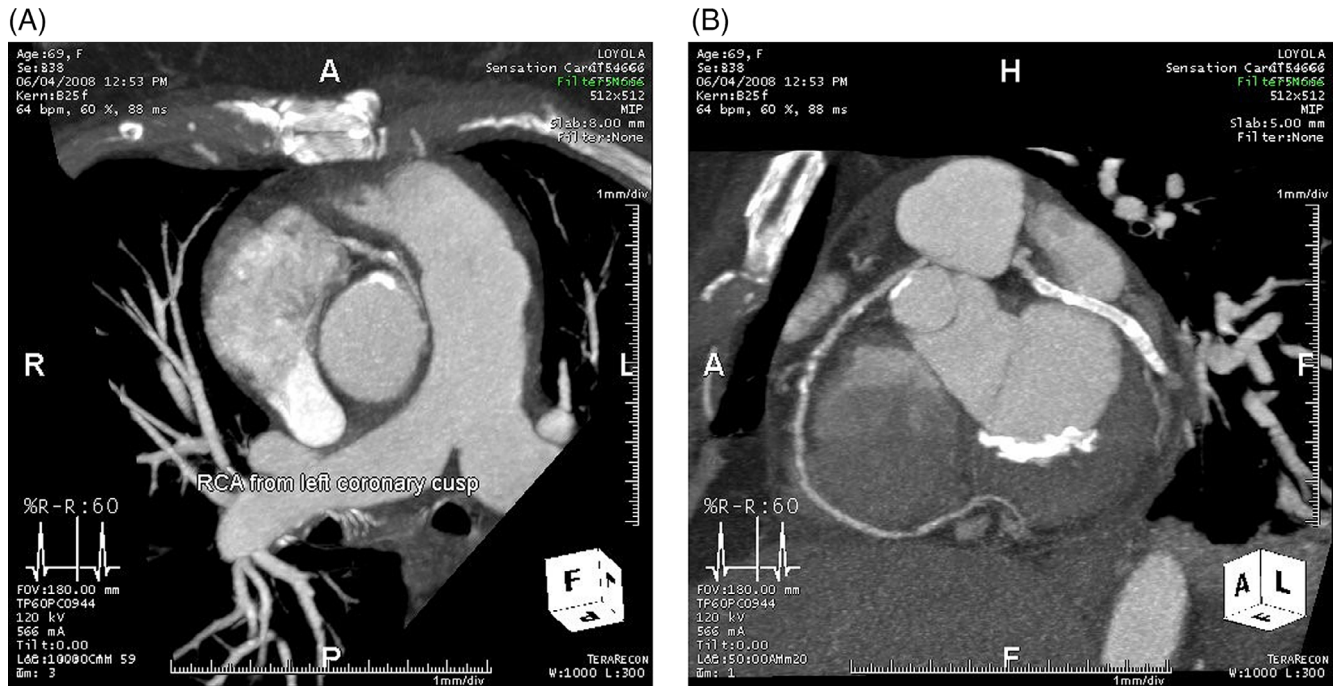


FIGURE 2 (a) Cardiac CTA image of the patient in Figure 1 showing an anomalous RCA arising from left coronary cusp. The proximal RCA courses between the ascending aorta and the main pulmonary artery. (b) The same cardiac CT showing mid and distal RCA. CT, computed tomography; RCA, right coronary artery [Color figure can be viewed at wileyonlinelibrary.com]

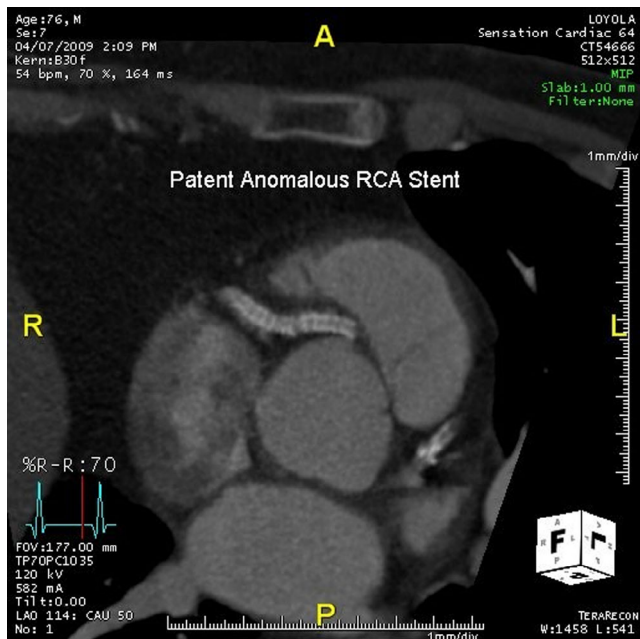


FIGURE 3 Cardiac CTA, done 11 months post-PCI, showing a patent stent in the proximal segment of an anomalous RCA. PCI, percutaneous coronary intervention; RCA, right coronary artery [Color figure can be viewed at wileyonlinelibrary.com]

Anomalous origin of the RCA constitutes a large fraction of congenital coronary artery anomalies.⁷ The ARCA may originate from high above the coronary sinus, from the left or noncoronary sinus, left main coronary artery, pulmonary artery or other anomalous locations on the aorta and aorto-left ventricular canal. The morphological spectrum

TABLE 5 Clinical endpoints at mean 8.5 years of follow-up

Clinical end points	Clinical end points	
	Number of patients	Percentage of total patients (%)
Overall mortality (%)	2	18.2
Cardiac mortality (%)	0	0
Major adverse cardiovascular events (%)	2	18.2
Target vessel revascularization (%)	1	9.1
Target lesion revascularization (%)	1	9.1

also encompasses an intramural course in the wall of the aorta versus nonintramural course, single (common) ostium shared with the normal coronary artery versus separate ostium, and varying degrees of ostial and angulation abnormalities.^{8,9} These anomalous coronary arteries may lead to myocardial ischemia by a variety of mechanisms, including a slit or flap like opening or an acute angulation as the vessel exits the aorta, both of which may be flow limiting. Direct compression when coursing between the great vessels (interarterial course) has also been thought to be a mechanism, especially during exertion when the great vessels dilate, although many believe that the increased aortic wall tension relative to the wall tension in the coronary artery results in coronary deformation and decrease in coronary flow.^{5,10} A partial intramural course of the anomalous vessel, that is, embedded within the tunica media of the aorta in some patients, may also be prone to obstruction during exercise.³

Because of such variations in anomalies, their severity and their mechanism, these patients may present with a wide variety of symptoms, including palpitations, chest pain or angina, dyspnea, syncope or even SCD.⁵ All patients in our study had symptoms prior to undergoing cardiac catheterization. About a third of them (36%) had ACS (NSTEMI or unstable angina) at the time of presentation. However, none of them were reported to have significant arrhythmias or cardiac arrest. Being the most feared complication, the association of anomalous coronaries with sudden cardiac death is based mostly on autopsy series of military recruits or marathon runners who experienced otherwise unexplained sudden cardiac death.^{11,12} Sudden death is thought to be a result of restricted blood flow causing myocardial ischemia and ventricular arrhythmias.

On the other end of the spectrum are patients with benign anomalies and those that remain asymptomatic. A number of these may survive well into adulthood, with no direct clinical consequence from the altered anatomy. They may present for the first time when these arteries have atherosclerotic disease, both within the anomalous coronary artery as well as involving other arterial beds, or are incidentally noted on noninvasive or invasive coronary imaging performed for other reasons. Interestingly, ARCA has been shown to accelerate the evolution of atherosclerosis in the involved artery. These pose a therapeutic challenge in themselves.¹³ These patients may present earlier in life with atherosclerotic CAD, as reported by Jim et al who looked at patients with atherosclerosis in the RCA and found patients with ARCA to be 10 years younger compared to age, sex and risk factor matched controls.³ They hypothesize the altered fluid dynamics as the underlying pathophysiology, specifically the low fluid velocity which can favor formation of slow recirculation and secondary flow or eddy current. This retards transport and removal of atherogenic material and promotes its uptake by the vascular endothelium.³ Mean age for our patient population was 64.4 years, which is closer to a standard coronary artery disease patient population.

Definitive surgical correction is recommended for the treatment of anomalous aortic origin of coronary arteries with symptoms or diagnostic evidence consistent with coronary ischemia attributable to the anomalous coronary artery (class I recommendation)⁵. Surgery may be considered even for some asymptomatic patients, given their propensity for sudden death particularly in younger patients and the relatively reversible nature of the anatomic abnormality. CABG has historically been used for a number of these patients, notwithstanding its own limitations. Because a number of these patients are young, and may be otherwise healthy, some advocate that bypass with an internal thoracic artery (ITA) increases the potential for long-term patency, as compared to placement of a saphenous vein graft.¹⁴ Unfortunately, without proximal ligation, the arterial graft often fails because of competitive native vessel flow. Ligation of the native RCA is also not free of harm, since it is believed that the initial flow from an ITA graft may not be enough to compensate for the sudden ligation of the native vessel. This may lead to early hypoperfusion, ischemia and increased mortality.⁵

Coronary artery translocation and reimplantation has also been advocated, albeit with concerns about the complexity of the

procedure. It involves dissection of a significant length of the coronary artery and precise placement of neo-ostia. The dissection is exceedingly difficult and not advisable if the anomalous artery runs an intramural course, and if it shares a single ostium with a normal coronary artery.⁸ In cases of intramural course of an anomalous artery, coronary artery unroofing may be an effective surgical modality.¹⁵ Some authors suggest that if the anatomy permits, this may be the best approach to correct such anomalies. However, it may be feasible in only a selected few cases.⁵ Pulmonary artery translocation may also be used to relieve the physical compression of the anomalous coronary artery.⁶

Barring surgery, these patients have historically not had many other options for management. Medical therapy with agents such as beta-adrenergic blockers, calcium channel blockers, nitrates and antiarrhythmic agents has been described with some efficacy in literature, however the benefit has not been consistently demonstrated. Such medical therapy may decrease aortic wall tension and myocardial oxygen demand as well as suppress arrhythmias, but it does not treat the underlying cause.¹⁶

Use of PCI for anomalous coronary arteries has been mostly limited to case reports and case series.¹⁷⁻²⁴ However traditionally there has been concern regarding the effectiveness of PCI in such cases, particularly its ability to treat ostial lesions, its durability to be able to withstand compression between great vessels, kinking, angulation, and so on, as well as concerns about the long lengths of stent that may be required. All 11 of our patients, who presented with significant symptomatic stenosis with an ARCA, were successfully treated with PCI. The structural rigidity of a stent may protect the artery from compression between the great vessels or in an intramural segment and help correct angulation and kinking, while correcting the ostial "slit-like" lumen. On follow-up cardiac CT, we did not find any evidence of stent distortion or fracture on any of our patients. Because of the unusual location and the noncircular coronary orifice often associated with these anomalies, as well as the frequently tortuous course and acute angulation involved, selective catheterization and percutaneous intervention can be technically challenging, particularly with regard to adequate guide catheter support.²⁵ A variety of guiding catheters have been used and advocated. These include Judkins left catheter (JL) and its longer and shorter variants, as well as Amplatz left catheter (AL1 and AL2). A modification of the AL1 consisting of a right-angled deviation of the tip (Leya catheter) has also been used successfully in some cases. The Leya catheter with its anteriorly oriented tip at 45° and 90° enables the operator to cannulate the ostium of the ARCA coaxially and at the same time provides good backup support during coronary intervention.²⁶ We found most success with the use of AL1, 2, 3, and Leya catheters in our patients.

To our knowledge, there have been 2 large case series, both involving retrospective review of hospital database, that describe the use of percutaneous interventions for an ARCA in 17 and 24 patients, respectively.^{9,27} Angelini et al reported observational data on 67 patients with ARCA who had intravascular ultrasonography to confirm intramural course of the anomalous arteries. Sixty-three percent of their patients were successfully treated with stent angioplasty of the intramural

RCA.²⁸ However, to our knowledge, there has been no long-term prospective follow-up of such patients which have been reported. Thus, despite a smaller sample size, our study provides a unique and original perspective by reporting long-term outcomes of PCI in patients with ARCA. Our patients were followed clinically for a mean of 8.5 years, with additional testing including cardiac CT and functional stress testing to assess for recurrence of disease. The only two deaths during follow-up were related to noncardiac causes (sepsis), with a mortality rate of 18.2%. This is similar to the mortality rate in the study by Krasuski et al, who reported 17.9% all-cause mortality rate at mean follow-up of 5.1 years after surgical correction in patients with anomalous coronaries with a malignant course. Patients with similar anomalies managed medically had much higher mortality rates (46.2%).²⁹ Our rate of TVR/TLR (target vessel revascularization/target lesion revascularization) of 18.2% appears to be slightly higher than the overall rates of TVR/TLR with Everolimus-eluting stents in major RCTs.^{30,31} However, the comparison is difficult given our small numbers as well as our focus on a small selective and complex cohort of patients. Additionally, we had a long duration of follow-up.

Another unique aspect of our study is the correlation of angiographic with CT findings for anomalous coronaries. Cardiovascular CT has emerged as the standard of reference for identification and characterization of coronary artery anomalies.³² Since angiography provides only a two-dimensional view of a vessel's complex three-dimensional path, the origin and anatomic course of the anomalous vessel, particularly with respect to the aorta and pulmonary artery may be difficult to discern. We found the observation of a "slit-like lesion" on angiography to have an excellent sensitivity and reasonably high accuracy for the diagnosis of interarterial course of the anomalous vessel seen on subsequent CT. The frequent observation of a slit-like lesion also possibly favors the slit-like ostium, with its vulnerability to compression and kinking, as a predominant mechanism by which these anomalies cause hemodynamic significance.

4.1 | Limitations

The most notable limitation of our study is a small sample size. However, given the rarity of anomalous coronary arteries, we hope our case series will shed light on outcomes of patients who underwent PCI for an ARCA.

5 | CONCLUSION

ARCA, although rare, poses a therapeutic challenge for cardiologists and cardiovascular surgeons, especially given symptoms and the risk of sudden death, often at a young age. Surgical modalities including bypass grafting, unroofing, reimplantation are accepted treatment options, although associated with operative risk and the risk of graft failure due to competitive flow. Our study suggests that in select patients, PCI of ARCA is an effective and low-risk alternative with excellent angiographic success and long-term outcomes. It can provide symptomatic relief in such patients, particularly ones who are

deemed too high risk for surgery or have failed prior surgery. It may also mitigate the risk of sudden death in younger patients.

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