



## Original Article

# Anomalous origin of coronary artery from the opposite aortic sinus of Valsalva—a single center experience with a therapeutic conundrum



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## ABSTRACT

**Background:** Coronary artery anomalies are rare congenital abnormalities, most often found incidentally on conventional coronary angiography and CT angiography (CTA). CTA better delineates the origin and course of anomalous coronaries. Anomalous origin of coronary artery from the opposite aortic sinus of Valsalva (ACAOS) has a prevalence of 1% with a very few having an interarterial (malignant) course. There is limited literature, especially in the Indian population, dealing with this topic.

**Methods:** In this retrospective observational study, angiographic data of 8500 consecutive patients from June 2011 to December 2019 at a large tertiary care hospital in western India was analyzed. Patients diagnosed with ACAOS underwent CTA for delineation of the exact anatomy. Those with a non-malignant course with evidence of ischemia clinically or on stress myocardial perfusion imaging (MPI), underwent PCI. Others with a non-malignant course were medically managed. Patients with malignant (interarterial) course were revascularized by coronary artery bypass graft (CABG) surgery in case of LCA involvement or positive MPI test. Asymptomatic patients with negative MPI were managed medically. Clinical follow-up over 12 months of patients undergoing PCI and those with a malignant course showed no major adverse cardiovascular events (MACE).

**Results:** Of the 8500 patients studied, 74 (0.87%) had ACAOS. Of these, 51 (68.9%) patients had anomalous origin of right coronary artery (RCA) from the left aortic sinus, 21 (28.4%) had anomalous origin of the circumflex artery (Cx) from the right aortic sinus and two patients (2.7%) had an anomalous origin of the left main coronary artery (LCA) from the right aortic sinus. Interarterial course was found in five (6.7%) patients. Of these, four patients underwent CABG-one asymptomatic patient with LCA from right aortic sinus and three with positive MPI in anomalous RCA. All five patients with malignant course and ten patients who underwent PCI were free of MACE over 12 months' clinical follow up.

**Conclusions:** ACAOS is a rare anomaly and if interarterial course is excluded, then PCI is feasible in selected cases with significant stenosis. Patients with malignant course with inducible ischemia or LCA involvement should undergo surgical revascularisation.

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## 1. Introduction

Coronary artery anomalies, including anomalous origin of coronary artery from the opposite sinus of Valsalva (ACAOS), are rare. The overall prevalence is reported to be 0.3%–2% of the general population.<sup>1–7</sup> Most patients are asymptomatic throughout life although, some of these anomalies are associated with syncope, angina and sudden cardiac death (SCD).<sup>7–12</sup> Most anomalies are

detected as incidental findings during coronary angiography. Because it is rare, there is paucity of contemporary data on the clinical profile and management of ACAOS in existing literature and delineation and diagnosis is better after the availability of CTA.<sup>13</sup> The aim of this study was to assess the prevalence and clinical presentation of ACAOS, and to assess the outcome of PCI in cases with non-malignant course of the anomalous artery in consecutive patients subjected to CA in a tertiary care centre in western India over a period of nine years.

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## 2. Methods

This was a retrospective study of consecutive patients who underwent coronary angiography from January 2011 to December 2019. Patients with coronary anomalies associated with congenital heart disease were excluded. Of all patients who underwent CA for an appropriate clinical indication, those who were found to have ACAOS underwent CTA to delineate further anatomic details using a 64-slice CT scanner (Philips Diamond Select Brilliance, U.S.A.).<sup>14</sup> Only the patients with ACAOS were studied and other anomalies of the coronaries such as single coronary artery, duplication or hypoplasia of the left anterior descending (LAD) or RCA, coronary artery fistula were excluded because of insignificant numbers and less potential for SCD. A defined case record form was used to collect all data. ACAOS was classified into four different groups mainly based upon the course after the origin as per the classification system proposed by Angelini et al.<sup>2</sup> as follows:

- (1) Anterior or prepulmonic course: anterior to the pulmonary trunk or the right ventricular outflow tract
- (2) Interarterial course: between the pulmonary artery and the aorta
- (3) Septal course: through the interventricular septum
- (4) Retro aortic course: posteriorly between the aortic root and the left atrium.

Interarterial course between the aorta and pulmonary artery was defined as malignant and other courses as non-malignant. Patients with malignant course but with no symptoms or insignificant stenosis were subjected to stress myocardial perfusion imaging (MPI) to rule out inducible ischemia. Of the 74 patients with ACAOS, 10 underwent PCI for significant stenosis. The patients with malignant course and those with non-malignant course who underwent PCI were clinically followed up for MACE for a period of one year. MACE was defined as a composite of death due to myocardial infarction, non-fatal myocardial infarction, stroke and repeat revascularization. Follow-up involved clinical and echocardiographic evaluation every three months for a period of one year after diagnosis or revascularization, whichever was later.

Statistical analysis: Case record forms for data collection and analysis was performed using Microsoft Excel software and SPSS Version 2.0 was used to compute means and standard deviations.

## 3. Results

### 3.1. Patient population

Of the 8500 patients- 6100 men (72%) and 2400 (28%) women- 74 (0.87%) had anomalous origin of coronary artery from the opposite aortic sinus. The mean age was  $57 \pm 12$  years (age range: 32–73 years). The baseline clinical characteristics of these patients are shown in [Table 1](#).

Types of ACAOS observed:

- 1) Anomalous right coronary artery from left sinus of Valsalva was the commonest anomaly (51 patients, 68.9%) with four having an interarterial course and the rest had retroaortic and inter-ventricular course. The origin of the left coronary artery was normal in all the cases.
- 2) The next commonest anomaly is origin of circumflex artery from right aortic sinus (21 patients, 28.4%) with all of them following a retroaortic course. They had a normal distribution. The left anterior descending arose from the left coronary cusp in all these patients.

- 3) Two patients (2.7%) had LCA arising from the right aortic sinus. One of them had an interarterial and the other one had a retroaortic course with normal distal distribution.
- 4) Malignant course: Five (6.7%) patients were found to have a malignant course, four of whom had an anomalous RCA arising from left aortic sinus. All four were subjected to stress perfusion imaging and three had reversible ischemia so they were subjected to CABG. One patient had no reversible ischemia on stress MPI and was managed medically. One patient had LCA arising from right coronary aortic sinus and was subjected to CABG without stress imaging ([Table 2](#)).
- 5) Overall course: The course of arteries were as follows: Retroaortic in 40 (54%) patients, septal in 15 (20.2%) and prepulmonic in fourteen (18.9%) patients.

### 3.2. Clinical presentation

Typical angina was present in 40 patients, 18 patients had previous myocardial infarction, three had previous PCI and two presented with heart failure. 11 patients had atypical symptoms with positive exercise stress test. There was no personal or family history of sudden cardiac arrest in any patient. None of the patients suffered a sudden cardiac death in the followup upto a year after diagnosis.

### 3.3. PCI in ACAOS

In our center, 10 patients with non-malignant course on CTA underwent PCI for significant stenosis (>70% luminal narrowing). Of these, five involved RCA originating from the left sinus and four involved the (Cx) arising from right sinus. One patient with LCA arising from the right sinus with a non-malignant course underwent PCI as well. Femoral route was used in nine and one patient underwent radial PCI. Guide catheters used for cannulation of ACAOS included various sizes of Judkins left, Amplatz and Judkins. Through the transfemoral route, 6 Fr JL 3.5 and 3.0 cm guide catheters were used for more antero-inferior origin of RCA and AL1 guide catheter was used for more posterior superior origin of RCA in relation to the left main coronary artery origin. Transradially, the 6 Fr Tiger guide catheter was used to provide stable cannulation. For anomalous Cx from the right sinus, the 6 Fr JR 3.5 cm guide catheter was used. Second generation drug eluting stents were used in all patients. The patient with anomalous origin of the LCA from right sinus with retroaortic course and mid-stem significant stenosis was cannulated using 6 F JR 4 guide catheter. There were no procedure related complications.

### 3.4. Follow up

All patients with malignant course and those subjected to revascularization in the form of PCI or CABG were clinically followed for the next one year for major adverse cardiovascular events. Outcomes were favourable with no MACE in any of these 15 patients at the end of one year.

## 4. Discussion

### 4.1. Prevalence and course

The overall prevalence of ACAOS in the present study was found to be 0.87%. This agrees with most other studies as the prevalence ranges from 0.6 to 1.3%. In the largest study (n = 1,26,595) published from the Cleveland Clinic Foundation in North America in 1990, the incidence was 1.3% (n = 1686).<sup>1</sup> A previous Indian study

**Table 1**  
Baseline clinical characteristics of 74 patients with Anomalous origin of coronary artery from opposite coronary sinus.

Age in year (range)	57 ± 12 (32–73)	Percentages
Gender	M: F = 4:1	
Presenting symptoms		
Angina	52	70%
Atypical chest pain	11	14.8%
No chest pain		
Dyspnea	11	14.8%
Syncope	0	0
Palpitation	3	4.0%
Patient who was going for noncardiac surgery	6	8.1%
Risk factor		
Diabetes mellitus	29	39.18%
Hypertension	30	40.5%
Dyslipidemia	10	13.5%
Current smoker	17	22.9%
Cerebrovascular accident	01	1.3
Family history of sudden cardiac death	00	0.00%
Underlying cardiac problem		
Previous myocardial infarction	18	24.3%
Previous coronary intervention	05	6.7%
Idiopathic dilated cardiomyopathy	02	2.7%
Detector number of multidetector computed tomography		
64 slice MDCT	70	94.6%
320 slice MDCT	04	5.4%

**Table 2**  
Details of Anomalous origin of coronary artery from opposite coronary sinus patients with malignant course.

Coronary anomaly	No of patients (n = 74,0.87%)	Anomaly incidence among 8500 patients (%)	Constituent ratio among 74 patients (%)
Left main originating from opposite sinus			
Total	02	0.00028	2.7
Malignant course	01	0.00014	1.35
Percutaneous coronary intervention	01	0.00014	1.35
Left circumflex coronary originating form opposite sinus			
Total	22	0.25	29.7
Malignant course	00	00	00
Percutaneous coronary interventions	4	0.048	5.1
Right coronary originating form opposite sinus			
Total	51	0.6	70.2
Malignant course	04	0.047	5.4
Percutaneous coronary intervention	05	0.058	6.7
Total patient with anomalous origin of coronary from opposite sinus			
Total	74	0.87	
Malignant course	05	0.059	6.7
percutaneous coronary intervention	10	0.117	13.5
Route of anomalous origin of coronary artery from opposite coronary sinus on CT angiography			
Retro-aortic	40(54%)		
Inter-arterial	5(6.7%)		
Pre-pulmonary	14 (18.9%)		
Inter-septal	15(20.2%)		

AWMI- anterior wall myocardial infarction, IWMI- inferior wall myocardial infarction, HTN-hypertension, DM-diabetes mellitus, LAD-left anterior descending artery, LCX-left circumflex artery, RCA-right coronary artery, M-male, F- female, NSTEMI-non ST elevated myocardial infarction. CABG: Coronary Artery by-pass grafting.

by Garg et al<sup>5</sup> also found similar prevalence of 0.95% ACAOS. Male predominance (M: F 4:1) in the study can be explained by the fact that more males underwent angiography in our center. In previous studies, the most frequent coronary anomaly was the origin of the circumflex artery from the right aortic sinus.<sup>4,6,9</sup> However, in the present study though, origin of the RCA from the left aortic sinus was the most common anomaly at 68.9%. This appears consistent with the previous study by Garg et al in the Indian population<sup>5</sup> indicating suggesting a possible higher prevalence of this subtype in our population. All those with the circumflex artery arising from right coronary sinus had a retroaortic course suggesting this anomaly is low risk from a sudden cardiac death perspective. Origin of LCA from the right aortic sinus is rare and our study found only two patients which is less than Topaz et al<sup>18</sup> who found 11 percent with this anomaly. The incidence of interarterial course in ACAOS

was 6.7%, mostly those with anomalous RCA from left aortic sinus and one LCA arising from right aortic sinus similar to the paper by Angelini et al. This can vary as in the paper by Garg et al where they had found a high percentage of interarterial course, a significant 38.46 percent. It must be noted that we didn't include in this study anomalous coronaries associated with congenital heart disease, separate ostium of conal arteries, high take-off of coronaries, coronary artery fistula and anomalous left coronary artery from pulmonary artery.

#### 4.2. Diagnostic modalities

Coronary artery anomalies are rare and are broadly classified into abnormality of origin, course, destination and number of arteries. Our study focusses on the ACAOS variety as it has maximum

clinical risk of adverse events like sudden cardiac deaths. While these are mostly detected during routine conventional CAG, CTA better delineates the anatomy, origin and course, especially the malignant course wherein the artery lies between the aorta and pulmonary artery. Although Cx origin from right aortic sinus does not have a malignant course, CTA was still performed to rule out intramural course and a slit-like ostium. In contrast to our study, Garg et al<sup>5</sup> only performed an angiographic study of anomalous coronaries. Other investigations that can be used are transthoracic (TTE) and transesophageal (TEE) echocardiography, magnetic resonance angiography (MRA) and intravascular ultrasound (IVUS).<sup>16</sup> TTE and TEE have extremely low yields in screening. In contrast to CTA, MRA provides functional imaging without radiation but has poorer spatial resolution and is costlier. MPI is useful in decision making regarding dynamic ischemia. IVUS offers excellent spatial and temporal resolution making it ideal for dynamic imaging. Stenosis can be graded at the point of maximal narrowing in diastolic phase imaging. However, IVUS catheters are expensive and sometimes difficult to advance into anomalous coronary arteries due to inadequate guide catheter support.

#### 4.3. Clinical significance

Two pointers towards suspecting ACAOS during CAG are failure to demonstrate normal expected origin of the coronary artery from the respective sinus on repeated attempts at cannulation and an unduly long course of the LCA from its origin to the first branch. Non-selective angiograms in the ascending aorta would help to locate the anomalous artery. Attempt to selectively cannulate the anomalous vessel with appropriate catheters can then be made with suitable catheters.

From a clinical standpoint they can be silent, present with angina, myocardial infarction or even sudden cardiac death.<sup>15</sup> Although the incidence of sudden cardiac death in ACAOS is not high, it is those with inter-arterial course i.e. the coronary artery course between the pulmonary artery and aorta, especially for the LCA, that have the highest risk.<sup>16</sup> The exact pathophysiological mechanisms of myocardial ischemia have not been determined. Cheitlin et al<sup>9</sup> reported that an LCA arising as a single or double vessel from the anterior (right) sinus of Valsalva, where it coursed leftward and posteriorly between the aorta and the pulmonary artery, is associated with sudden death. The assumed mechanism of sudden death is ostial closure between the aorta and pulmonary artery and the squeezing of the ostium during exercise by a scissor like mechanism, with sudden interference in coronary arterial flow leading to ischemia mediated ventricular fibrillation.<sup>9–12</sup> Another factor that is important is its angulation with the aorta at its origin with acute angulation associated with a slit like ostium.<sup>17</sup> Recent IVUS studies have shown a high prevalence of coronary hypoplasia and dynamic lateral compression which may induce myocardial ischemia, congestive heart failure or sudden death. This is due to the fact that the intramural segment does not grow adequately. Another point of caution: it is not only those with interarterial course who are at risk. Angelini et al reported two cases, one involving circumflex from right aortic sinus and another with LAD arising from the right aortic sinus, both with a retroaortic course. IVUS revealed intramural course with significant dynamic compression in both cases.<sup>2</sup> In the present study, 6.7% patients had malignant course of which only those involving the RCA were subjected to MPI and revascularized using CABG in those with inducible ischemia. The lone patient with malignant course of LCA was directly referred for CABG due to the risk of sudden cardiac death. Our one-year follow showed that these patients did not suffer any MACE events, suggesting a rational management strategy.

#### 4.4. Challenges in management of ACAOS

There are no guidelines about management of malignant course of coronary artery. It may be appropriate that patients suspected of anomalous coronary artery on CAG should undergo CTA.<sup>13</sup> Those with inter-arterial course of RCA with no significant stenosis and/or symptoms can be subjected to stress MPI test to confirm non-inducibility of ischemia before being managed medically; those who have any reversible ischemia or any family history of SCD should undergo complete revascularization in the form of CABG.

On the other hand, interarterial course of LCA must undergo cardiac surgery and should not be stressed. Rest of the patients may be closely followed up and managed medically.

PCI is not a reasonable option in interarterial course with stenosis as it may be associated with risk of stent fracture due to compression by the great arteries analogous to a myocardial bridge.

For non-malignant course, when the patient is symptomatic or asymptomatic with significant stenosis and inducible ischemia on stress testing, PCI or CABG may be performed according to standard guidelines.

Patients with non-malignant course and insignificant stenosis may be regularly followed up clinically and by stress test. We have proposed a treatment algorithm for management of ACAOS (Fig. 1).

#### 4.5. PCI in ACAOS:<sup>18–26</sup>

PCI in ACAOS is possible though can be challenging in so far as skills and hardware are concerned.

**Guide catheter selection:** The selective cannulation of aberrant coronary arteries can be technically difficult and time-consuming. Knowledge of the variations in coronary artery origin can help in selecting the appropriate catheters for diagnostic and therapeutic interventions.

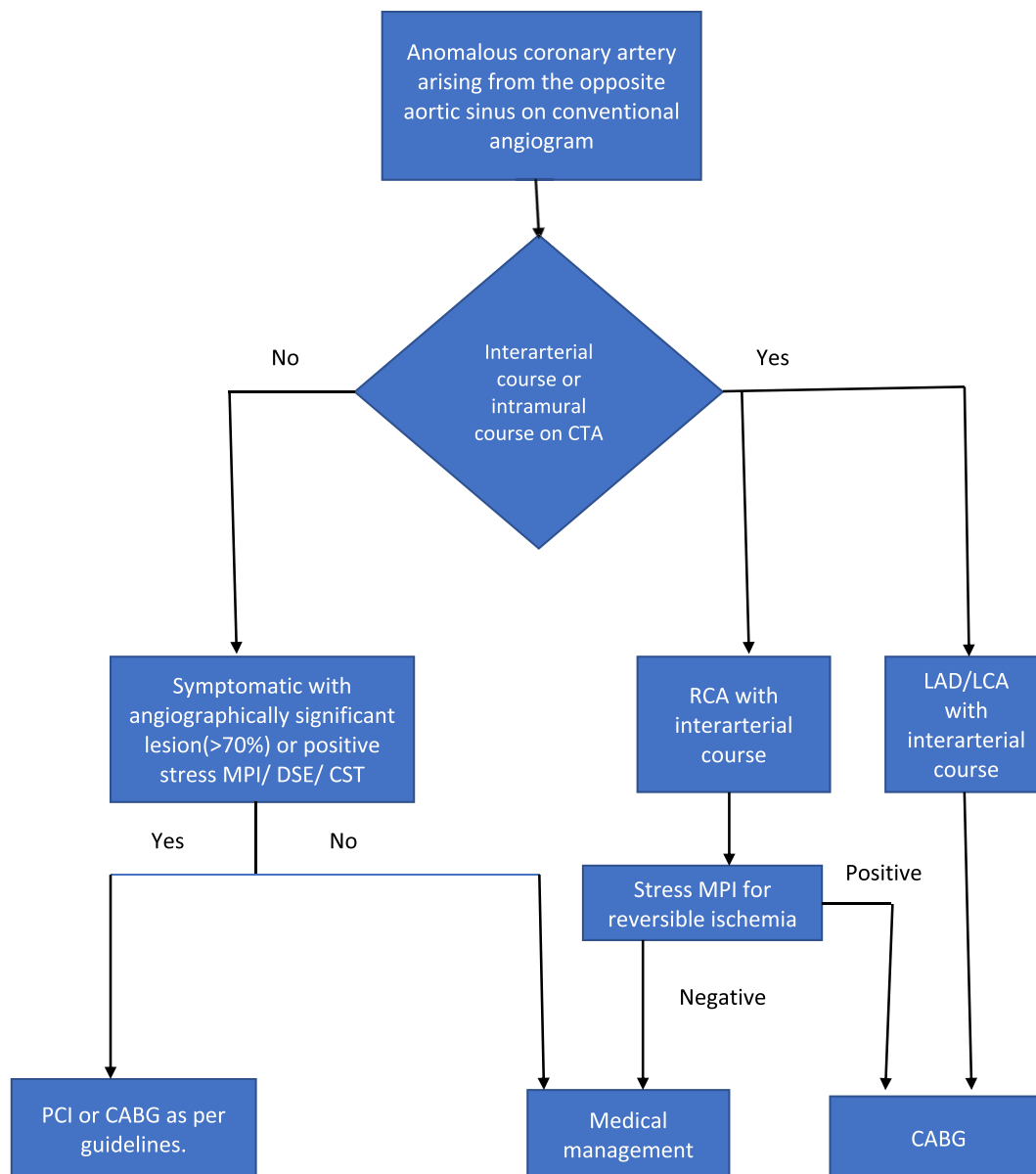
In patients with RCA arising from left sinus of Valsalva, one must understand the take-off of such an artery i.e. Type A in which the origin is just above the LCA, type B in which the origin is just below the LCA and type C in which the origin is in midline. This classification scheme was proposed by Uthayakumaran et al.<sup>19</sup> Femoral route is preferred, and JL 5.0 cm and JL 4.0 cm is useful in Type A, Extra Back Up (EB) 3.5 cm in type B and AL-1 and 2 are useful in type C orientation. Notwithstanding, there may still not be adequate alignment which may need additional manoeuvres.<sup>19</sup> In those patients with the Cx arising from the right sinus, both JR 3.5 cm and AR-1 can be tried. Radial Tiger guide catheter can also provide support in such patients.

**Choice of wires:** Routine workhorse wires and floppy wires may be used to decrease the risk of perforation whereas hydrophilic wires may be used if the artery is extremely tortuous. Sometimes two wires may be used for superior anchoring, especially if guide support is inadequate.

**Choice of stents:** Most of the modern drug eluting stents have excellent trackability. Gentle manipulation is essential to avoid dissecting the other vessel arising from the same aortic sinus. It must be kept in mind that one size does not fit all and a customized approach is necessary for each case of ACAOS.

#### 4.6. Strengths and weakness of the study

This study adds data regarding prevalence of ACAOS in the Indian population and attempts to clear the dilemma regarding management of such patients. Due to the retrospective design of this study, some important clinical characteristics may not have been recorded. This might have also caused some data collection bias. Our study is a descriptive one, and it was not possible to compare the findings with those obtained using other modalities.



**Fig. 1.** Proposed management algorithm of Anomalous coronary origin from opposite sinus. Abbreviations: CTA: CT angiography, MPI myocardial perfusion imaging, DSE dobutamine stress test, CST computerized (treadmill) stress test, PCI percutaneous coronary interventions and CABG coronary artery bypass grafting, RCA right coronary artery, LAD left anterior descending and LCA left coronary artery.

We have not used intravascular ultrasound (IVUS) imaging for additional information of anomalous origin of coronary artery such as a slit or cleft-like origin and proximal intramural course which may impact management. Number of patients undergoing PCI is very small, so the outcomes cannot be generalized.

**5. Conclusions**

Although rare, ACAOS may be life threatening. Adequate evaluation is therefore necessary for deciding about management of patients with it. If ACAOS is suspected on conventional CAG, all patients should undergo CTA. CTA not only confirms the anomaly but also provides accurate information on the origin, course and termination of the coronary arteries. PCI is feasible but challenging in select ACAOS patient who have a non-malignant course and has reasonable outcomes. CABG is advisable for patients with

interarterial course with LCA/LAD involvement or positive MPI. Nevertheless, large prospective studies with long term follow up are required to define the best management strategy for these patients.

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**What is already known about this subject?**

Anomalous origin of coronary artery from the opposite aortic sinus of Valsalva (ACAOS) is rare. It may cause sudden cardiac death especially in cases with a malignant course. There are not many studies regarding prevalence and management of this anomaly from India.



### What does this study add?

This study presents a single centre experience of prevalence and management strategies of ACAOS from India, with patient outcomes at one year after diagnosis.

### How might this impact clinical practice?

ACAOS patients incidentally diagnosed on coronary angiography (CA) should undergo CTA for delineation of anatomical details. ACAOS with borderline stenosis should undergo MPI for demonstration of inducible ischemia. It is feasible for patients with ACAOS and non-malignant course to undergo PCI with good outcomes.

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