

# Coarctation of the Aorta

## Strategies for Improving Outcomes

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### KEYWORDS

- Congenital heart disease • Aortic coarctation • Bicuspid aortic valve • Cardiac surgery • Stent
- Aneurysm • Aorta • Treatment outcome

### KEY POINTS

- Coarctation of the aorta is defined by a discrete narrowing of the aorta.
- Transcatheter systolic coarctation gradient  $\geq 20$  mm Hg is an indication for intervention with treatment choice guided by patient age and anatomy of obstruction.
- Follow-up imaging should be tailored to early identification of recoarctation/aneurysm with directed intervention.
- Hypertension is common in the aging patient with coarctation despite successful repair.
- Lifelong routine evaluation by cardiology specialists with expertise in adult congenital heart disease is required to identify late-onset complications.

### INTRODUCTION

Coarctation of the aorta (CoA) is a common congenital heart defect (CHD) found in approximately 1 per 2900 live births<sup>1–3</sup> and is the seventh most common type of CHD.<sup>4</sup> Still, this is likely an underestimate, because the diagnosis may be delayed, even in the pediatric population.<sup>4,5</sup> In simple terms, coarctation is characterized by discrete narrowing of the thoracic aorta adjacent to the ligamentum arteriosum. Importantly, discrete coarctation is an aortopathy that lies within a spectrum of arch abnormalities ranging from discrete narrowing to a long segment of arch hypoplasia. The prognosis of untreated coarctation was extremely poor during the presurgical era with median survival age of 31 years and a quarter of patients dying before the age of 20 years.<sup>6</sup> Since the first surgical repair of aortic coarctation performed in the 1940s, treatment of coarctation has dramatically changed. Overall, survival into adulthood is now expected. However, these

patients continue to require lifelong follow-up for management of associated problems including arterial hypertension, atherosclerotic disease, recoarctation, and aneurysm formation.

### CAUSE AND PATHOGENESIS OF COARCTATION

Histologic examination of localized aortic coarctation lesions has demonstrated the presence of a tissue ridge extending from the posterior aortic wall and protruding into aortic lumen. This ridge consists of ductal tissue with in-folding of the aortic media.<sup>6</sup> In older patients, aortic intimal proliferation also contributes to the narrowing at the site of coarctation.<sup>7</sup> The cause of discrete aortic coarctation remains unclear, but is likely multifactorial. Prenatal environmental exposures have been associated with CoA and other left-sided lesions.<sup>8</sup> However, there is a growing body of literature that suggests a genetic basis for development of these lesions. Case series have described

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clustering of coarctation cases in families. Evaluation of families with an index case of left ventricular outflow tract abnormalities of aortic valve stenosis, CoA, or hypoplastic left heart syndrome suggest a strong genetic influence, with an estimated sibling recurrence risk of greater than 30-fold.<sup>9</sup> Recently, mutations in the NOTCH1 gene have been identified in individuals with left ventricular outflow tract malformation, including coarctation.<sup>10</sup> In particular, the NOTCH1 variant R1279H seems to be more common in individuals with aortic coarctation.<sup>11</sup> NOTCH1 mutations have also been shown to contribute to abnormal epithelial-to-mesenchymal transition in endothelial cells, which is an important step in the development of the left ventricular outflow tract. Mechanical models have suggested that abnormalities of blood flow, defective endothelial cell migration, and excessive deposition of aortic duct tissue at the aortic isthmus can result in coarctation. Furthermore, embryonic studies in zebrafish have highlighted the importance of intracardiac hemodynamics in epigenetic control of distal chamber development.<sup>12</sup>

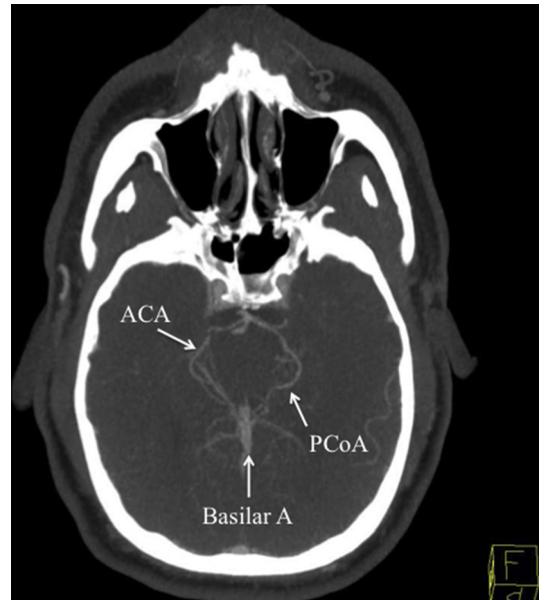
### ASSOCIATED CONGENITAL HEART LESIONS

Although CoA can be an isolated CHD, it is also commonly found in other congenital syndromes and cardiovascular anomalies. Thus, deliberate investigation for the presence of coarctation should be made in these patients. The most common cardiovascular malformation associated with CoA is bicuspid aortic valve (BAV). Prior autopsy examination showed 46% of patients with CoA have congenital BAV.<sup>13</sup> More modern studies in patients with repaired coarctation found similar results with up to 45% to 62% prevalence of BAV.<sup>14–16</sup> The coincidence of BAV and CoA is difficult to determine, because BAV is very common and not everyone is screened for the presence of coarctation. In a study of 102 patients with BAV diagnosed by computed tomography (CT) imaging, 22% of patients either had prior coarctation repair, or were found to have CoA.<sup>17</sup> The coexistence of BAV and coarctation is important to consider, because it places the patient at a higher risk of aortic complications.<sup>18</sup> In a study following 341 patients with BAV over a median of 7 years, patients with bicuspid valve in the presence of coarctation had 7.5 times increased risk of ascending aortic complications, most commonly dilation of the ascending aorta.<sup>19</sup> The same group also found that among patients with aortic coarctation, the presence of a BAV was an independent risk factor for the development of aortic wall complications.<sup>16</sup>

Turner syndrome has a strong association with CoA. In a study of 132 girls diagnosed with aortic coarctation who subsequently underwent karyotyping, Turner syndrome was diagnosed in 5.3%.<sup>20</sup> CoA is found in 18% of patients with Turner syndrome.<sup>21</sup> Williams syndrome, a congenital and multisystem genetic disorder, has been associated with supravalvular aortic stenosis. Aortic arch abnormalities, including coarctation, are present in 10% of patients with Williams syndrome.<sup>22</sup> Coarctation can also be present in congenital cardiovascular anomalies involving multiple left-sided lesions, including Shone syndrome and hypoplastic left heart syndrome.

### NONCARDIAC ASSOCIATIONS

The link between intracranial aneurysms and CoA was described well before the surgical era, accounting for 5% deaths in patients with aortic coarctation on autopsy review.<sup>23</sup> In the modern era, with the availability of brain MRI the reported prevalence of intracranial aneurysms in patients with CoA is approximately 10%,<sup>24</sup> which is five times more common than the average population (Fig. 1). In one study, hypertension was more common in the population of coarctation patients with



**Fig. 1.** Computed tomography angiography of the head showing normal anatomy of the circle of Willis without cerebral artery aneurysm in a 36 year old with coarctation of the aorta. Given that hypertension may play a role in the growth of intracranial aneurysm, these patients should be monitored and treated if indicated. ACA, anterior cerebral artery; basilar A, basilar artery; PCoA, posterior communicating artery.

intracranial aneurysms.<sup>24</sup> Most of the aneurysms described are small, and therefore have a low risk of spontaneous rupture. Currently the benefits of routine screening for intracranial aneurysms in coarctation remain unclear.

## CLINICAL PRESENTATION

The clinical presentation of coarctation differs significantly in pediatric patients in comparison with adults. Although infants with severe coarctation may present with signs and symptoms of heart failure and cardiogenic shock as the ductus closes, most adults with unrepaired coarctation are generally asymptomatic. A common presentation of coarctation is systemic arterial hypertension. In young adults presenting with severe upper extremity hypertension, coarctation should be excluded. Patients presenting with severe hypertension may experience symptoms including angina, headache, epistaxis, and heart failure.

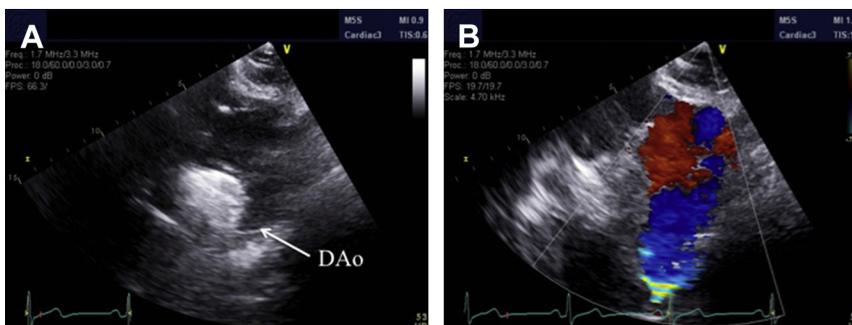
On physical examination, femoral arterial pulses are diminished and usually delayed. Rarely, claudication may be reported because of lower extremity ischemia. Auscultation of the left sternal border may demonstrate a harsh systolic murmur with radiation to the back. An associated thrill may be palpable in the suprasternal notch. If left ventricular pressure or volume overload have developed, a left ventricular lift can be present. The finding of a continuous murmur may suggest the presence of arterial collaterals in those with long-standing unrepaired significant coarctation.<sup>25</sup> Arterial pulsations from collaterals to the intercostal and interscapular arteries can also be palpated. In patients with suspected coarctation, it is important to assess for systolic blood pressure discrepancy between upper and lower extremities. The upper extremity systolic blood pressure is usually 20 mm Hg higher than the lower extremities in patients with significant coarctation. In rare instances of coarctation patients with concomitant anomalous subclavian artery origin distal to the coarctation, systolic blood

pressure differences may not be detected between ipsilateral arm and legs.<sup>25</sup> Therefore, complete evaluation should involve measurement of blood pressure in all four extremities.

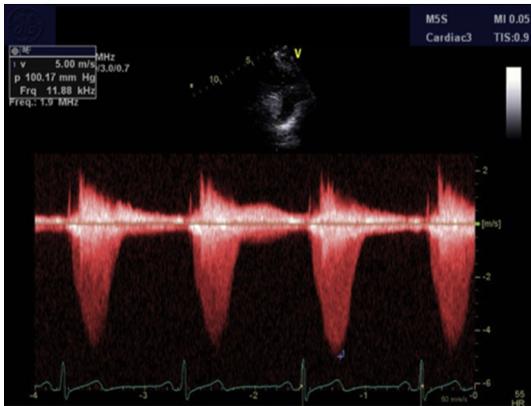
## DIAGNOSTIC EVALUATION

The electrocardiogram of a patient with coarctation may be normal or demonstrate evidence of left ventricular hypertrophy from chronic left ventricular pressure overload. On chest radiograph, a “figure of three” sign formed by the aortic knob, the stenotic segment, and the dilated poststenotic segment of the aorta suggests CoA. The heart border can be normal or mildly enlarged. Inferior rib notching can also be seen in the third to eighth ribs bilaterally caused by the presence of dilated intercostal collateral arteries.

Among the noninvasive modalities to evaluate CoA, transthoracic echocardiography is the most accessible for the practicing physician. A comprehensive echocardiogram is recommended in the initial evaluation of a patient with repaired or suspected CoA. In addition to characterization of the coarctation itself, it is important to evaluate for evidence of left ventricular pressure or volume overload, left ventricular hypertrophy, size, and left ventricular systolic and diastolic dysfunction. Particular attention should be placed in identifying associated cardiac defects especially left-sided lesions. The morphology of the aortic valve, and evidence of subvalvular, valvular, and supra- valvular aortic stenosis should be interrogated. The dimensions of the aortic root and ascending aorta can be followed serially to assess for associated aortopathy. Suprasternal windows are important to view the aortic arch from the long-axis view, in two-dimensional imaging and by color flow Doppler. Visualization of the aortic arch in the long axis may demonstrate a focal area of narrowing of the thoracic aorta distal to the takeoff of the left subclavian artery with associated flow turbulence on color flow Doppler (Figs. 2 and 3).



**Fig. 2.** Suprasternal notch view in a 50-year-old woman with known bicuspid aortic valve demonstrating narrowing of the proximal descending aorta (A, arrow) aided by color Doppler interrogation (B). DAo, descending aorta.



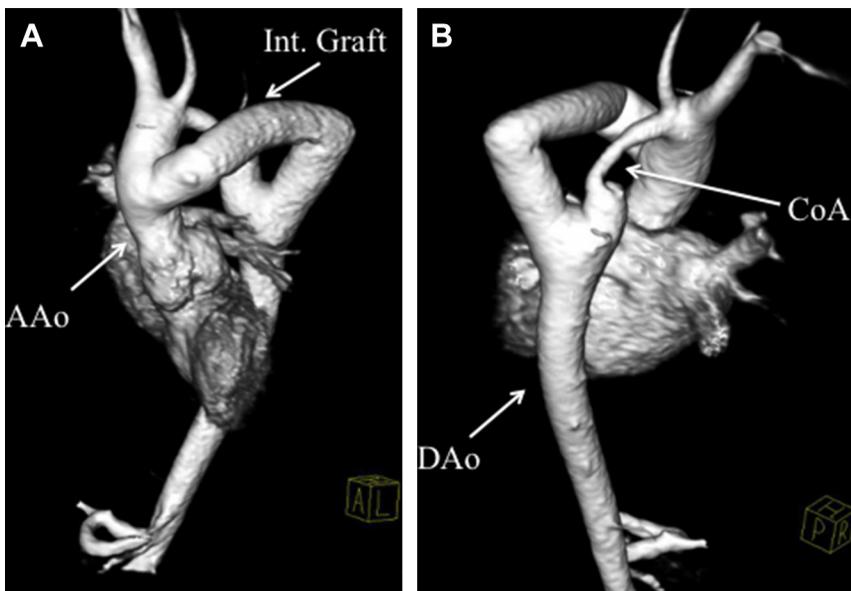
**Fig. 3.** Spectral Doppler interrogation demonstrates severe arch obstruction.

Doppler interrogation shows increased velocity across the site of coarctation. Typically, the modified Bernoulli equation can be used to calculate the peak instantaneous gradient across the coarctation. However, because patients with CoA may have multiple left-sided lesions (eg, stenotic, BAV, subaortic membrane) leading to an increased velocity before the CoA site, the expanded Bernoulli equation should be used to avoid overestimation of the peak gradient. Yet with long-standing coarctation, significant collaterals may have developed thereby reducing the peak systolic gradient across the site of stenosis. A saw-tooth pattern seen on continuous-wave Doppler reflects the persistent forward flow in

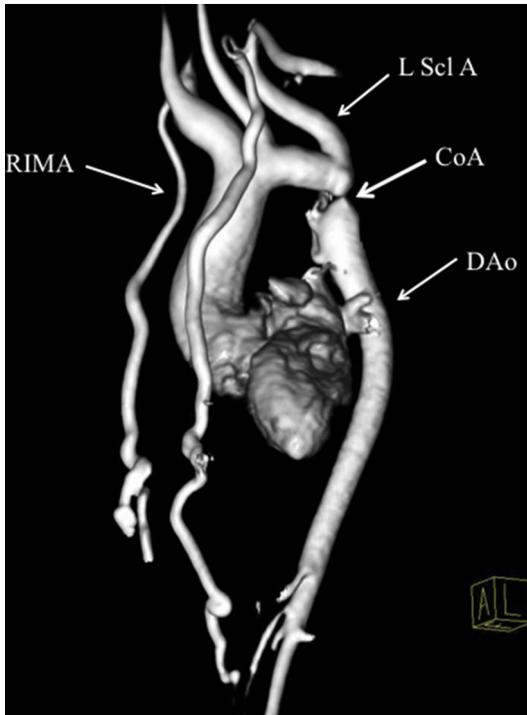
diastole because of diastolic run-off. Higher gradient across the coarctation and longer duration of diastolic forward flow in the thoracic aorta suggest more significant coarctation. Similarly, Doppler examination of the abdominal descending aorta provides useful information in the presence of significant coarctation. Here, Doppler demonstrates a continuous antegrade flow signal without evidence of flow reversal.

### CARDIAC MRI

Cardiac MRI (cMRI) has become a valuable noninvasive modality to assess patients with unrepaired and repaired coarctation. In adults with suboptimal echocardiographic imaging window, cMRI can be used to characterize the aortic valve, aortic root, left ventricular size, and function. cMRI, along with gadolinium-enhanced magnetic resonance angiography, provides excellent resolution of cardiac anatomy and vascular structures (Fig. 4). Additionally, phase contrast flow analysis can be used to estimate flow and peak gradient through the coarctation.<sup>26</sup> Compared with echocardiography, cMRI demonstrates superior visualization of the aortic arch with precise characterization of the location and extent of coarctation, and assessment of the presence and extent of collateral vessels (Fig. 5). In the unrepaired patient, the measured minimum aortic cross-sectional area and heart rate–corrected deceleration time in the descending aorta can be used to predict a significant gradient by cardiac catheterization<sup>27</sup> and



**Fig. 4.** Volume-rendered magnetic resonance angiographic reconstruction (A, anterior; B, posterior view) in a 35-year-old patient with coarctation of the aorta who underwent surgical repair with an interposition graft. AAo, ascending aorta; Int. Graft, interposition graft.



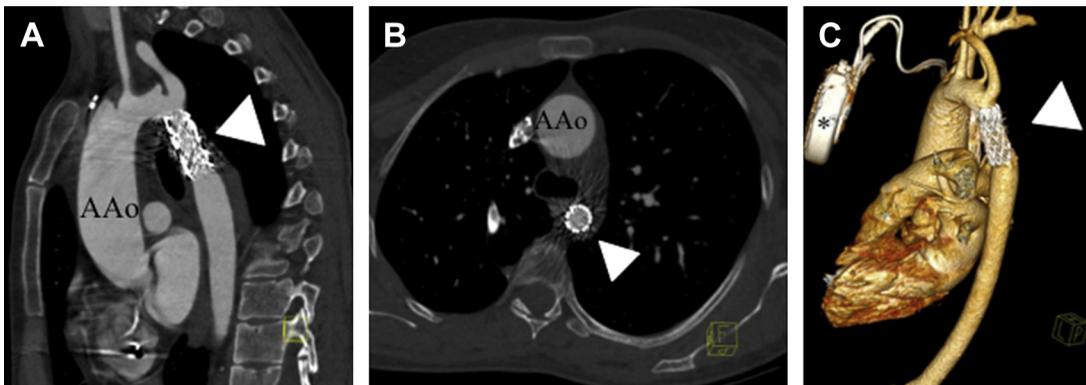
**Fig. 5.** Severe, native coarctation of the aorta in a 51-year-old patient presenting with severe hypertension refractory to antihypertensive therapy identified by contrast-enhanced magnetic resonance angiography. Dilated left and right internal mammary arteries suggest collateral circulation. L Scl A, left subclavian artery; RIMA, right internal mammary artery.

future need for intervention.<sup>28</sup> Compared with conventional echocardiography, cMRI provides exceptional visualization of the aortic arch and detection of postrepair complications including arch “kinking” and pseudoaneurysm.<sup>29</sup> Thoracic aortic magnetic resonance angiography also

provides assessment of poststenotic dilation or aneurysmal formation at the site of a previous repair. Importantly, the lack of ionizing radiation provides an advantage of cMRI over CT, in the serial evaluation of late complications after repair. Recognizing the benefits of advanced cMRI and CT the 2008 American College of Cardiology/American Heart Association Guidelines for the Management of Adults with Congenital Heart Disease recommend that patients with coarctation have serial evaluation with CT or MRI at least every 5 years.

### COMPUTED TOMOGRAPHY

Although cMRI is the preferred mode of serial follow-up for patients after coarctation repair, the use of cardiovascular CT may be considered in selected patients. In particular, cMRI in patients with transcatheter stents may have susceptibility artifact precluding accurate assessment of late complications associated with these interventions. With cMRI, metallic artifact can lead to difficulty in the assessment of vessel lumen patency, identifying restenosis, aneurysm, or stent fracture.<sup>30</sup> Use of CT obviates concerns about metallic artifact impairing accurate assessment (Fig. 6). Other advantages of cardiac CT over cMRI include improved image resolution, shorter scan time, and greater availability across different institutions. CT angiography is also used to assess concomitant coronary anomalies that may not be well visualized with cMRI. Patients with pacemakers or implantable cardioverter defibrillators that are not cMRI compatible may benefit from surveillance with cardiovascular CT. Similar to cMRI, cardiovascular CT can be performed to follow serial aortic dimensions. Small studies of patients postcoarctation repair have shown good correlation of aortic diameter



**Fig. 6.** (A–C) Computed tomography angiography of the aorta in the sagittal and axial planes demonstrates no evidence of in-stent stenosis (arrowheads) in a 38-year-old patient with history of native coarctation presenting after sudden cardiac arrest. Three-dimensional reconstruction displaying previously placed implantable cardioverter defibrillator (asterisk) and luminal surface of the Cheatham-Platinum covered stent.

measurements between helical CT and MRI. Still, considerable variations in measurements between these two modalities have been reported in the same patient, highlighting the importance of using one specific modality in serial assessment.<sup>31</sup> When using cardiovascular CT to assess the patient with repaired coarctation, adhering to radiation safety principles (as low as reasonably achievable) and minimizing radiation dose should be a regulatory requirement for all programs.

### CARDIAC CATHETERIZATION

Cardiac catheterization remains essential in the management of patients with coarctation. However, because of recent advances in noninvasive imaging with cMRI and cardiovascular CT, cardiac catheterization is used more frequently in the setting of intervention than diagnosis. In those patients who are not suitable for transcatheter intervention, cardiac catheterization is performed to accurately assess the coarctation gradient, which is integral to determine need for intervention. In older patients with potential concomitant coronary artery disease (CAD) who require operative intervention for coarctation or aneurysm, coronary angiography should be performed before surgery.

### INDICATIONS FOR INTERVENTION

In patients with a native CoA or recoarctation, a measured peak-to-peak gradient greater than or equal to 20 mm Hg by cardiac catheterization is an indication for intervention, either by transcatheter or surgical approach.<sup>32</sup> Patients with long-standing native coarctation who have developed significant collateral flow over time may have a lower measured gradient despite severe coarctation. Therefore, patients with extensive collaterals should undergo intervention even if the peak-to-peak gradient is less than 20 mm Hg.<sup>32</sup> The decision regarding transcatheter versus surgical intervention depends on a variety of factors including location and complexity of the coarctation, patient preference, and the availability of an interventionalist or cardiac surgeon capable of performing the intervention with a low rate of complication.

### SURGICAL AND TRANSCATHETER THERAPIES

There have been major advances in the treatment of CoA since the first successful surgical repair by Craaford and Nylan in 1944. This was performed with resection of the narrowed segment and reattachment of the transected ends using a circumferential suture line or an end-to-end anastomosis.<sup>33</sup> This technique remains the most common type of surgical repair for children with critical coarctation.

The subclavian flap repair was introduced in the 1960s<sup>34</sup> as an alternative to the end-to-end anastomosis to avoid the circumferential sutures, and reducing the risk of future restenosis. Nonetheless, the rates of restenosis are similar between the two techniques,<sup>35</sup> because the subclavian flap technique leaves behind residual abnormal ductal and coarctation tissue.<sup>34</sup> The synthetic patch aortoplasty approach became popular when first introduced in the 1970s. This approach has since fallen out of favor because of high occurrence of late-term aneurysm formation.<sup>36</sup> Patients with a long segment of coarctation or arch hypoplasia not amenable to resection with an end-to-end anastomosis may require use of an interposition graft or extended end-to-end anastomosis.

In addition to the variety of surgical repairs for coarctation, transcatheter options are now available and are especially useful for adult patients with native coarctation or restenosis of a previous surgical repair. Transcatheter management is now preferred over surgical management in adult patients with discrete coarctation without associated arch hypoplasia.<sup>37</sup> Balloon angioplasty was initially used to treat CoA in children yielding acceptable results in reduction of aortic coarctation gradient.<sup>38</sup> However, midterm follow-up of these patients demonstrated a high rate of restenosis (>20%),<sup>38</sup> likely caused by elastic recoil of the aortic wall. Furthermore, acute complications have been described with balloon angioplasty<sup>39</sup> and subsequent aneurysm development.<sup>40</sup> Currently, balloon angioplasty alone is not recommended for treatment of significant aortic coarctation in adults. Instead, the treatment of choice to treat discrete aortic coarctation involves the use of intravascular stents. This can now be safely performed with a lower rate of complication and restenosis when compared with balloon angioplasty alone.<sup>39,41</sup> A recent report of intermediate outcomes from the Coarctation of the Aorta Stent Trial (COAST) demonstrated that placement of the Cheatham–Platinum bare-metal stent in patients older than the age of 8 years with native or recurrent coarctation can be performed in patients with appropriate anatomy for transcatheter intervention. At 2-year follow-up, 13% of patients required repeat catheterization for stent redilation, but none had need for surgical management. Although stent fractures were observed in 22% of patients, none had significant clinical adverse events. Development of aortic wall injury during catheterization or subsequent aneurysm at the site of stent placement was seen in 9% of patients who subsequently underwent placement of a covered stent.<sup>42</sup> Overall, the results are promising and suggest that transcatheter treatment of

coarctation can be offered to adult patients with unrepaired CoA and recoarctation.

### LONG-TERM COMPLICATIONS

Despite advancements in the treatment of CoA, patients remain at risk for a variety of long-term complications. Patients who have undergone coarctation repair are at a higher risk of death compared with the general population.<sup>43</sup> In one of the largest single-center studies of postsurgical coarctation repair, survivorship was 84% at 20 years and 72% at 30 years follow-up.<sup>44</sup> The most common mode of death was CAD, accounting for 37% of late deaths. Sudden death and heart failure were the next common causes of death in this population. Although early studies suggest an increased prevalence of death caused by CAD,<sup>44</sup> a more recent study demonstrated that coarctation in itself was not an independent risk factor for the development of premature CAD.<sup>45</sup> Cardiac risk factors predisposing to CAD were the same in those with CoA and the general population. These results suggest targeting traditional risk factors rather than untreatable vascular reactivity defects may lead to improved clinical outcomes in this population.

Patients with other cardiac defects in addition to CoA tend to have worse outcomes.<sup>46</sup> Reoperation in patients who have undergone primary repair is often related to associated cardiac defects rather than a direct complication from coarctation repair.<sup>44,47</sup> Aortic valve disease is the most common associated defect requiring surgical management in patients with coarctation who have undergone prior repair.

### RECOARCTATION AND ANEURYSM DEVELOPMENT

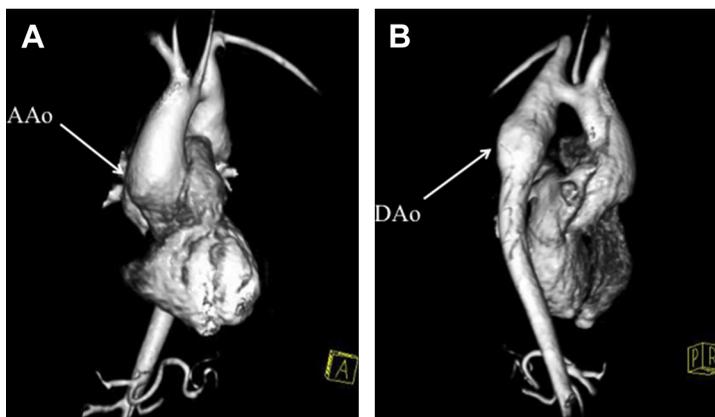
Patients with repaired coarctation are at risk of late recoarctation and aneurysm development. The

rate of recoarctation after surgical repair ranges between 3% and 15% in most studies.<sup>34,44,48</sup> Younger age at the time of surgery is associated with a higher risk of restenosis.<sup>44,48,49</sup> Although earlier studies suggest a high rate of restenosis in patients with end-to-end anastomosis, current reports suggest that an end-to-end anastomosis is comparable with other types of surgical repair.<sup>50</sup> It is difficult to compare long-term outcomes among various types of surgical repair because complication rates are also determined by patient's age at repair and the surgical experience of the operator.

The rate of aneurysm formation has been reported to be between 3% and 20%<sup>44,49,51</sup> in long-term studies of patients who have undergone coarctation repair. Patients repaired with synthetic patch technique are at higher risk of late-term aneurysm development.<sup>52</sup> With the development of cMRI, the prevalence of aneurysm identified by surveillance imaging approaches 46%<sup>36</sup> (Fig. 7). Patients with large aneurysm after coarctation repair often require surgical management with use of an interposition graft.<sup>53</sup> However, there have been several small case series of successful treatment of aneurysm using bare-metal and covered endovascular stents.<sup>54–57</sup> Long-term studies are needed to determine the safety and durability of interventional repairs. Currently, COAST II aims to evaluate the efficacy and safety of covered endovascular stents for treatment of coarctation with associated aortic wall injury, including aortic aneurysm and pseudoaneurysm.

### MEDICAL MANAGEMENT OF SYSTOLIC ARTERIAL HYPERTENSION

Despite excellent early to midterm outcomes of adults with CoA, long-term morbidity remains, especially with respect to premature arterial hypertension. Numerous studies have demonstrated



**Fig. 7.** Volume-rendered magnetic resonance angiographic reconstruction revealing ascending (A, arrow) and proximal descending aortic (B, arrow) aneurysms in a 25-year-old patient who underwent prior patch repair.

that hypertension is prevalent in patients with coarctation. Two studies by Wells and co-workers<sup>58</sup> and Bhat and colleagues<sup>59</sup> sought to evaluate the effect of coarctation repair on systolic blood pressure. In these studies, all patients had hypertension characterized by a systolic blood pressure greater than 140 mm Hg. Following coarctation repair, there was an improvement in systolic blood pressure in all patients and concomitant decrease in the use of antihypertensive medications. Still, systemic arterial hypertension remains in some patients despite coarctation repair. The prevalence of systemic arterial hypertension following coarctation repair ranges from 25% to 68%.<sup>60</sup> The mechanism of late-onset hypertension in repaired coarctation is unclear, although some have implicated the role of abnormal vascular compliance or impaired baroreceptor sensitivity.<sup>60</sup> Factors associated with higher prevalence of late hypertension include older age at time of repair<sup>44</sup> and older age at time of follow-up.<sup>61</sup> Children who underwent subclavian flap repair were found to have higher systolic blood pressure than those who underwent end-to-end anastomosis. Yet, it is unclear whether this trend continues into adulthood.<sup>62</sup>

There are limited data on the efficacy of different classes of antihypertensive medications in hypertensive patients after coarctation repair. A study of 128 young-adult patients with hypertension after coarctation repair reported better control of hypertension with candesartan over metoprolol with fewer side effects.<sup>63</sup> However, in a small crossover study of 18 adult patients, metoprolol was found to be more effective than candesartan at lowering systolic blood pressure.<sup>64</sup> The 2008 American College of Cardiology/American Heart Association Guidelines for the Management of Adults with Congenital Heart Disease recommend use of a  $\beta$ -blocker, angiotensin-converting enzyme inhibitor, or angiotensin II receptor blocker as first-line therapy, with a preference of one agent over another dependent on the presence of aortic root dilation or aortic regurgitation.<sup>32</sup>

## SUMMARY

Patients with CoA who have undergone repair require lifelong surveillance. Because this type of CHD is associated with many long-term complications, collaborative management by cardiologists with expertise in adult CHD is recommended. Current guidelines on the management of adults with CHD recommend at least annual follow-up of patients after coarctation repair<sup>32</sup> to identify long-term complications including restenosis, aortic aneurysm, and systolic arterial hypertension. In

those patients with CoA with associated congenital cardiac defects, additional surveillance is required to identify late-onset complications specific to associated defects that may require additional medical and surgical therapies. Although echocardiography is a fundamental tool in the assessment of patients after coarctation repair, advanced imaging is often necessary for comprehensive evaluation. cMRI is the preferred imaging modality for repaired and unrepaired CoA. Alternatively, cardiovascular CT is best suited to evaluate patients with endovascular stents or those with contraindications to cMRI. Ultimately, multicenter research is needed to determine optimal mode of intervention, medical therapies, safety and efficacy of transcatheter-based therapies, and long-term outcomes in this growing patient population.

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