

PERIPHERAL

Immediate Outcomes of Covered Stent Placement for Treatment or Prevention of Aortic Wall Injury Associated With Coarctation of the Aorta (COAST II)



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ABSTRACT

OBJECTIVES This study aimed to describe the safety and short-term efficacy of the Covered Cheatham-Platinum stent (CCPS) in treating or preventing aortic wall injury (AWI) in patients with coarctation of the aorta (CoA).

BACKGROUND The COAST II trial (Covered Cheatham-Platinum Stents for Prevention or Treatment of Aortic Wall Injury Associated with Coarctation of the Aorta Trial) is a multicenter, single-arm trial using the CCPS for the treatment and/or prevention of AWI in patients with CoA and pre-existing AWI or increased risk of AWI.

METHODS Patients were enrolled if they had a history of CoA with pre-existing AWI (Treatment group) or with increased risk of AWI (Prevention group). Pre/post-implant hemodynamics and angiography were reported. A core laboratory performed standardized review of all angiograms. One-month follow-up was reported.

RESULTS A total of 158 patients (male = 65%; median age 19 years) underwent placement of CCPS. Eighty-three patients had pre-existing AWI. The average ascending-to-descending aorta systolic gradient improved from 27 ± 20 mm Hg to 4 ± 6 mm Hg. Complete coverage of pre-existing AWI was achieved in 66 of 71 patients (93%) with AWI who received a single CCPS. Ultimately, complete coverage of AWI was achieved in 76 of 83 patients (92%); 7 patients had minor endoleaks that did not require repeat intervention. Four patients experienced important access site vascular injury. There were no acute AWI, repeat interventions, or deaths.

CONCLUSIONS The CCPS can effectively treat and potentially prevent AWI associated with CoA. Access site arterial injury is the most common important complication. Longer-term follow-up is necessary to define mid- and late-term outcomes. (J Am Coll Cardiol Intv 2016;9:484-93) © 2016 by the American College of Cardiology Foundation.

Coarctation of the aorta (CoA) occurs in approximately 4 of 10,000 live births and comprises 5% to 8% of congenital heart disease (1). When present without additional defects, CoA may not be detected until late childhood or adulthood (2). Infants and young children with native CoA are typically treated surgically, but remain at risk for recurrent obstruction (3). Older children and

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adults may be managed either surgically or percutaneously. Although surgical repair in this age group may be definitive, up to 10% of older children or adults require further intervention (4,5).

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Balloon angioplasty of native CoA, carries a relatively higher risk of aortic wall injury (AWI) and recurrent obstruction (6-8). This has led to the “off-label” use of bare-metal stents in older patients (9-14). Although such interventions are generally safe, aortic dissection, aneurysm, and rupture have been reported, particularly in the context of severe or complex lesions (15-17). To prevent AWI during the primary stent implantation procedure, covered stents, currently unavailable for use within the United States, have been used in Europe and elsewhere with reports of safety and efficacy (11,18-23).

The balloon-expandable Covered Cheatham-Platinum (CP) stent (CCPS) (NuMED, Hopkinton, New York) was developed for the transcatheter treatment of native and recurrent CoA. It received the European Union C.E. mark in 2003 and is widely available outside of the United States. The Covered CP stent is composed of a bare-metal CP stent, covered its entire length with an expandable sleeve of ePTFE. Dilation of the CP stent to 22-mm diameter results in stent shortening of approximately 20%. The ePTFE sleeve has a wall thickness of 0.005-inch with an internodal distance of 35 to 55 μm. The tubing is attached to each end of the CP stent with a cyanoacrylate adhesive on a physically etched section of the sleeve.

The COAST (Coarctation of the Aorta Stent Trial) multicenter study began in 2007, demonstrating the safety and efficacy of bare-metal CP stents for treatment of CoA (24,25). As part of the investigational device exemption protocol and the COAST trial, CCPS was available at participating sites for compassionate use and emergency implantation in case of AWI during the procedure. Informed consent included trial information. Although such implants preceded the start of the COAST II (Covered Cheatham-Platinum Stents for Prevention or Treatment of Aortic Wall Injury Associated With Coarctation of the Aorta) study, patients were prospectively followed using COAST protocol. Once the COAST II study opened, these patients were included and identified as “legacy patients.” The prospective arm of the COAST II study began in 2010 and continued through December 14, 2011. Subsequent to closure of enrollment, ongoing use of the CCPS was made available under a Continued Access protocol. We report technical results, short-term efficacy, and safety of the CCPS for

prevention and treatment of AWI associated with CoA through September 2014.

METHODS

SCREENING/INTAKE EVALUATION. The COAST II trial is a multicenter, single-arm clinical study of the safety and efficacy of CCPS for treating AWI in patients with a history of CoA (Treatment group) or preventing AWI in patients with CoA and presumed risk factors for developing AWI with bare-metal stent placement (Prevention group). **Table 1** summarizes inclusion and exclusion criteria. **Figures 1 and 2** demonstrate representative baseline and post-implant angiography of patients in the Treatment and Prevention groups. Nineteen pediatric cardiac centers in the United States participated in the COAST II trial. The study received approval by the Johns Hopkins Institutional Review Board and by institutional review boards of all participating centers.

Participants described in this report were enrolled in the COAST II study and are referred to as: 1) prospectively enrolled patients, if enrolled directly into the COAST II study; 2) legacy patients, if a CCPS was implanted during the original COAST trial via Food and Drug Administration (FDA) Emergency Use or FDA Compassionate Use guidelines; or 3) continued access patients, if treated after pivotal trial enrollment closed, under FDA-approved continued access,

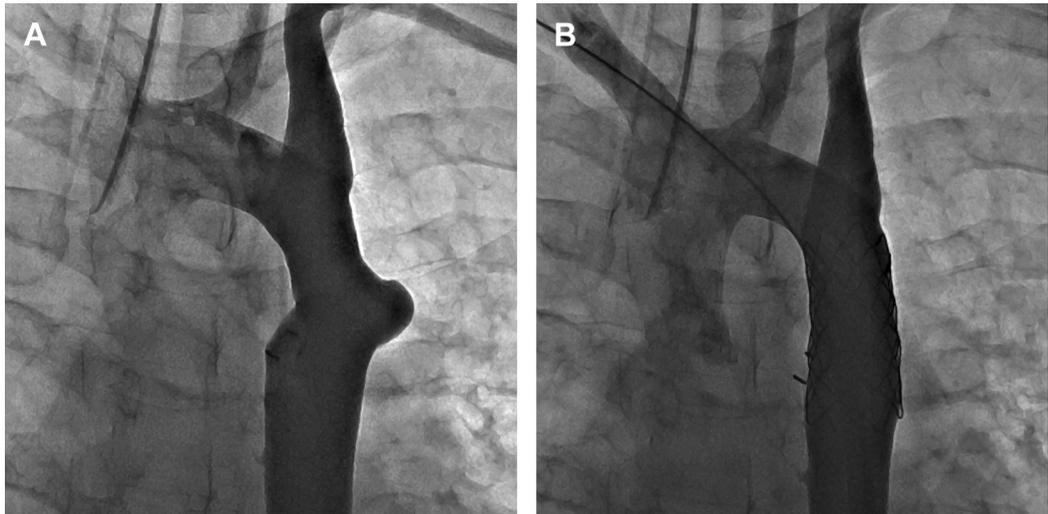
ABBREVIATIONS AND ACRONYMS

- AE** = adverse event(s)
- AWI** = aortic wall injury
- CP** = Cheatham-Platinum (stent)
- CCPS** = Covered Cheatham-Platinum stent
- CoA** = coarctation of the aorta
- CT** = computed tomography
- FDA** = Food and Drug Administration
- SBP** = systolic blood pressure

TABLE 1 Patient Selection

Inclusion criteria	
<ul style="list-style-type: none"> • Native or recurrent aortic coarctation* associated with 1 or more of the following: • Acute or chronic aortic wall injury† • Nearly atretic descending aorta to 3 mm or less in diameter • Genetic syndromes associated with aortic wall weakening (e.g., Marfan syndrome, Turner syndrome, familial bicuspid aortic valve with ascending aortic aneurysm) • Advanced age (60 yrs or older) 	
Exclusion criteria	
<ul style="list-style-type: none"> • Patient size too small for safe delivery of the device (absolute exclusion of patients <20 kg), possible exclusion of patients 20 to 30 kg after discussion of risk with parents/guardians • Planned deployment diameter of stent <10 mm or >22 mm • Location of coarctation would require placement across a carotid artery‡ • Adults lacking capacity to consent • Pregnancy 	

*The significance of aortic obstruction was left to the judgment of the participating investigator. Indications might include mild resting aortic obstruction associated with: exercise related upper extremity hypertension; severe coarctation with multiple and/or large arterial collaterals; single-ventricle physiology; left ventricular dysfunction; ascending aortic aneurysm. †Aortic wall injury might include descending aortic aneurysm; descending aortic pseudoaneurysm; contained aortic wall rupture; noncontained rupture of the aortic wall. ‡Crossing or covering of a subclavian artery was permissible in certain situations, but only after alternative treatments had been considered.

FIGURE 1 Treatment of Existing AWI

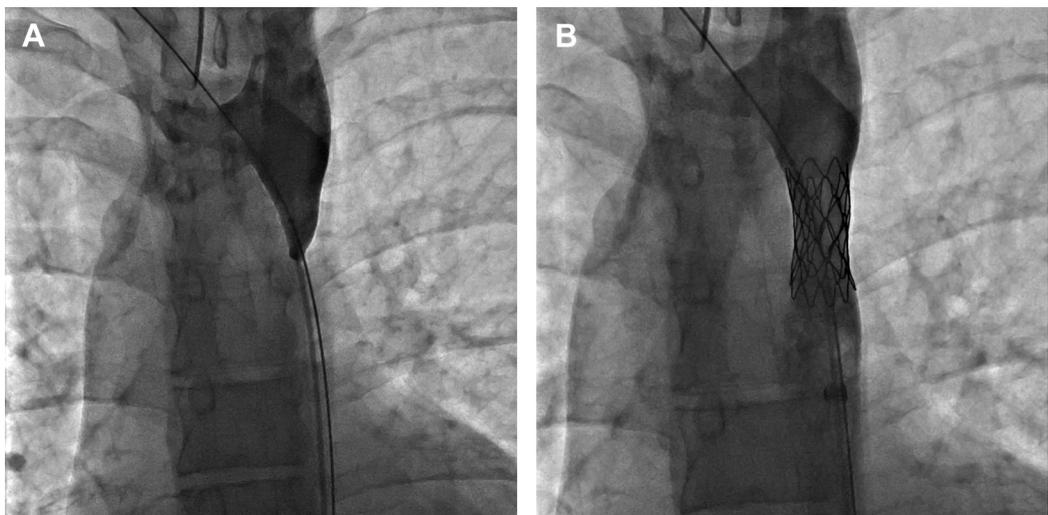
(A) Posterolateral aneurysmal outpouching in the region of previous aortic coarctation. **(B)** Covered Cheatham-Platinum stent placement effectively excludes the aneurysm. AWI = aortic wall injury.

following protocols identical to the COAST II study. Before enrollment, all patients and/or guardians signed informed consent for CCPS implantation and to participate in study follow-up. All patients were followed prospectively.

Pre-procedure assessment required a complete history and physical, including measurement of 4-extremity

automated oscillometric blood pressure, performed in triplicate. The upper-lower extremity gradient was defined as the difference between the highest of the upper extremity and the highest of the lower extremity systolic blood pressure (SBP) measurements.

CATHETERIZATION PROCEDURE. Participants received aspirin 325 mg (clopidogrel 75 mg if aspirin-allergic)

FIGURE 2 Prevention of AWI

(A) Nearly atretic coarctation of the aorta. **(B)** Covered Cheatham-Platinum stent placement treats the coarctation and prevents injury to the surrounding aortic wall. AWI = aortic wall injury.

before the procedure. Catheterization was performed according to accepted standards. There was no trial-specified implantation protocol. Analgesia and/or anesthesia were administered at the discretion of the catheterizing physician. Pressure measurements were obtained proximal and distal to the CoA. Contrast angiography was performed for measurements of the aortic arch, CoA, and descending aorta at the level of the diaphragm. The diameter of any aortic aneurysm or pseudoaneurysm was measured. Pre-existing AWI was defined as in **Table 2**.

Covered CP stents of various lengths (28, 34, 39, 45 mm) were provided pre-mounted on NuMED BIB (Balloon-in-Balloon) catheters, with outer balloon lengths of 3.0, 3.5, 4.0, and 5.0 cm. Outer balloon diameters of 12, 14, 15, 16, 18, and 20 mm were available. The implanting physician selected stent length and balloon size based upon pre-procedure imaging and angiography at the time of catheterization. Typically, the diameter of the dilated stent did not exceed 110% the distal transverse arch or the descending aorta at the level of the diaphragm.

The selected stent/balloon combination was advanced over a wire through a long sheath into the region of the CoA. The stent was deployed upon inflation of the outer balloon. Rapid right ventricular pacing or other stabilization techniques were optional. Repeat balloon inflations were performed as needed to ensure optimal stent expansion.

After stent placement, pressure measurements were obtained in the ascending aorta, immediately above the stent, and in the descending thoracic aorta. Post-implantation angiography was performed. Further dilation of the stent could be performed based upon hemodynamic and angiographic findings. If endoleak or significant AWI proximal or distal to the initial stent was identified, additional overlapping CCPSs could be placed at the discretion of the physician. A core laboratory reviewer assessed all angiograms. The development of any vessel irregularity, dissection, contained rupture, or aneurysm was noted. Stent position, AWI coverage, and appearance of the aorta were graded as shown in **Table 2**. Endoleak was defined as residual flow of blood into the AWI after stent placement.

Daily antiplatelet therapy was continued for at least 6 months after the procedure. For patients who had received outpatient anticoagulation before the procedure, anticoagulation was resumed in lieu of antiplatelet therapy.

POST-CATHETERIZATION EVALUATION. Patients were monitored in accordance with the practice of each institution. Before hospital discharge and

1 month after stent placement, patients were interviewed and examined, and upper and lower extremity blood pressures documented. Further follow-up was scheduled at 6 months, 12 months, and annually thereafter for 5 years. This report only includes 30-day outcome.

ADVERSE EVENTS. Five patients entered the COAST II study after sustaining minor AWI during CoA balloon pre-dilation as part of the COAST bare-metal stent protocol and were treated with a CCPS. All were successfully treated, and these pre-stenting events are reported in the COAST study. All adverse events (AE) related to CCPS implantation were classified by

TABLE 2 Core Lab Angiographic Interpretation

<p>Pre-existing aortic wall injury</p> <ul style="list-style-type: none"> No AWI or trivial aortic wall irregularity defined as outpouching or bulging of the aortic wall with a diameter that is <1/4 the aortic diameter at the level of the diaphragm. Small aneurysmal, pseudoaneurysmal, or contained wall rupture with bulging or outpouching of the aortic wall to a diameter that is 1/4 to 1/3 the aortic diameter at the level of the diaphragm. Moderate aneurysmal, pseudoaneurysmal, or contained wall rupture with bulging or outpouching of the aortic wall to a diameter that is >1/3 to 1/2 the aortic diameter at the level of the diaphragm. Large aneurysmal, pseudoaneurysmal, or contained wall rupture with bulging or outpouching of the aortic wall to a diameter that is >1/2 the aortic diameter at the level of the diaphragm or any noncontained rupture. This classification includes acute or rapidly expanding moderate or large aneurysmal, pseudoaneurysmal, or contained outpouching >1/3 the aortic diameter or any acute, uncontained rupture.
<p>Stent placement</p> <ul style="list-style-type: none"> Well-positioned: The stent(s) is/are located within the region of coarctation or target aortic wall injury such that the stent does not unnecessarily cross a brachiocephalic artery and does not distort the contour of the aorta. Minor malposition: The stent(s) is/are well-centered in the region of the coarctation or target aortic wall injury, but would not be considered well positioned by unnecessarily crossing and partially obstructing flow into a brachiocephalic artery and/or by causing mild distortion of the aortic contour. Major malposition: The stent(s) is/are outside of the region of coarctation or target aortic wall injury, unnecessarily crosses and totally occludes a brachiocephalic artery, or causes major distortion of the aortic contour
<p>Coverage of aortic wall injury</p> <ul style="list-style-type: none"> Not Applicable. No aortic wall injury defined at baseline or after Covered Stent implantation Complete coverage of target aortic wall injury, (aneurysm, pseudoaneurysm, wall rupture) Minor endoleak* (contained residual leakage into the target wall defect with the expectation of spontaneous closure) Moderate residual contained endoleak, likely to require additional therapy Large residual endoleak or persistent uncontained, extraluminal leak requiring additional surgical therapy
<p>Appearance of aorta</p> <ul style="list-style-type: none"> Smooth angiographic appearance to the vessel Therapeutic tear: Tear in the intima/media that is confined to the aortic wall in radial dimension and to the target region or irregular appearance of the vessel without dissection or aneurysm Dissection: Tear in the intima/media that extends proximally or distally from the narrowed aortic segment. <ul style="list-style-type: none"> Subcategory A: Dissection without obstruction to distal flow Subcategory B: Dissection with obstruction to distal flow New aneurysm or contained rupture: New bulging or outpouching of the aortic wall to a diameter that is >1/4 the aortic diameter at the level of the diaphragm

Endoleak refers to residual leak of blood into the pre-existing wall injury.
 AWI = aortic wall injury.

TABLE 3 Baseline Patient Demographics

	Entire Cohort (N = 158)	Treatment (n = 83)*	Prevention (n = 75)	Treatment vs. Prevention p Value
Sex				
Male	102 (65)	49 (59)	53 (71)	NS
Female	56 (35)	34 (41)	22 (29)	
Age, yrs	19 (5-70)	17 (5-61)	26 (5-70)	0.007
Weight, kg	67 (17-142)	67 (17-110)	69 (20-142)	NS
Prior aortic interventions†	79 (50)	66 (80)	13 (17)	<0.0001
Surgical intervention	40 (25)	31 (37)	9 (12)	0.0003
End-to-end anastomosis	19 (12)	17 (20)	2 (3)	0.0006
Patch repair	12 (8)	7 (8)	5 (7)	NS
Subclavian flap	4 (3)	4 (5)	0 (0)	NS
Interposition graft	3 (2)	3 (4)	0 (0)	NS
Bypass or jump graft	3 (2)	1 (1)	2 (3)	NS
Not specified	1 (1)	1 (1)	0 (0)	NS
Transcatheter intervention	52 (33)	45 (54)	7 (9)	0.0001
Balloon angioplasty	29 (18)	25 (30)	4 (5)	0.0001
Stent placement	34 (22)	30 (36)	4 (5)	0.0001
Antihypertensive medications				
Any	102 (65)	50 (60)	52 (69)	NS
>1 Medication	47 (30)	17 (20)	30 (40)	0.01

Values are n (%) or median (interquartile range). *Two patients (weights = 16.8 kg and 18.8 kg) were each implanted with a Covered Cheatham-Platinum stent and were enrolled into COAST II and COAST II Continued Access, respectively. †Patients may have undergone more than 1 intervention.
NS = not significant.

the implanting physician, then adjudicated by the Data and Safety Monitoring Board, as being related to 1 of the following: stent (e.g., stent positioning, stent fracture, new or progressive AWI); catheterization or implantation procedure (e.g., femoral or iliac arterial injury); or not attributable to stent, implantation, or catheterization (e.g., due to a pre-existing or independent condition). The seriousness of the AE was described as being “not serious,” “somewhat serious,” or “serious,” based upon previously described standards (26).

STATISTICAL ANALYSIS. Categorical data are summarized as frequency (percent); continuous data are summarized as mean \pm SD for normally distributed variables and median (range) otherwise. Comparisons between treatment groups were performed using Fisher exact test or the Wilcoxon rank sum test. Post-intervention measurements were compared to baseline using the paired Student *t* test for continuous data and McNemar test for categorical variables.

RESULTS

PRE-IMPLANTATION CHARACTERISTICS. Demographics.

A total of 158 patients (65% male, median age 19

[range 5 to 70] years) were enrolled in the COAST II study (29 prospectively enrolled, 53 legacy, and 76 continued access). No significant differences were noted in baseline demographic information, noninvasive blood pressure measurements, or invasive hemodynamic and angiographic measures by enrollment strategy (legacy, prospective, continued access). Therefore, these groups were combined for analysis.

Table 3 summarizes demographic data including operative and interventional history. No patients had single ventricle heart disease. The Treatment group consisted of 83 patients (53% of the cohort); the Prevention group consisted of 75 patients (47%). Seven patients in the Treatment group who received CCPS for small, localized intimal tears with diameters $<1/4$ the aortic diameter identified by the implanting physicians after CoA balloon dilation did not meet trial criteria for significant AWI (**Table 2**). However, because these patients received a CCPS to treat an existing injury, they were included in the Treatment cohort.

Noninvasive blood pressure. The Prevention group demonstrated a higher mean SBP (149 ± 24 mm Hg vs. 133 ± 16 mm Hg; $p < 0.0001$) and a greater upper-lower extremity SBP gradient (35 ± 23 mm Hg vs. 14 ± 24 mm Hg; $p < 0.0001$) than the Treatment group (**Table 4**). Among the entire cohort, 62 patients (39%) had a resting upper extremity SBP of 120 to 139 mm Hg; 72 patients (46%) had a SBP of 140 mm Hg or greater.

Pre-implantation angiography and hemodynamics. Baseline invasive pressure measurements are shown in **Table 5**. On average, the Prevention group had a greater ascending-descending aorta gradient (36 ± 20 mm Hg vs. 19 ± 15 mm Hg; $p < 0.0001$) and tighter CoA (5 ± 4 vs. 10 ± 4 ; $p < 0.0001$) than the Treatment group. Of the 83 patients in the Treatment group, 44 (53%) were graded by the core as having large or rapidly expanding AWI, 17 (20%) moderate, and 15 (18%) patients were graded as having small wall injuries (**Table 6**). The remaining 7 (8%) patients had only trivial localized AWI, but the implanting physician, concerned that additional enlargement of the coarcted segment might lead to a serious tear, elected to proceed with CCPS implantation and enrollment into the COAST II study.

STENT IMPLANTATION. Stent implantation was performed with technical success in all patients. Fifteen patients (9%) received >1 CCPS at the discretion of the implanting physician. Three of these implants occurred among the Prevention group due to malposition of the first CCPS.

TABLE 4 Noninvasive Blood Pressure at Baseline and 1-Month Follow-Up*

	Entire Cohort			Treatment			Prevention		
	Baseline	1-Month	p Value	Baseline	1-Month	p Value	Baseline	1-Month	p Value
Upper extremity SBP	(N = 158)	(n = 154)		(n = 83)	(n = 81)		(n = 75)	(n = 73)	
Mean ± SD (mm Hg)	140 ± 22	124 ± 15	<0.0001	133 ± 16	121 ± 15	<0.0001	149 ± 24	126 ± 15	<0.0001
Lower extremity SBP	(n = 153)	(n = 143)		(n = 81)	(n = 76)		(n = 72)	(n = 67)	
Mean ± SD (mm Hg)	117 ± 22	125 ± 20	<0.0001	119 ± 20	124 ± 18	0.03	114 ± 24	126 ± 22	<0.0001
SBP gradient	(n = 153)	(n = 143)		(n = 81)	(n = 76)		(n = 72)	(n = 67)	
Mean ± SD (mm Hg)	24 ± 26	-1 ± 15	<0.0001	14 ± 24	-2 ± 14	<0.0001	35 ± 23	1 ± 15	<0.0001
Gradient ≥20 mm Hg, n (%)	79 (52)	11 (8)	<0.0001	25 (31)	5 (7)	<0.0001	54 (75)	6 (9)	<0.0001

*Changes in blood pressures and gradients remained statistically significant when analyses were repeated using generalized estimating equations models to account for the correlation of patients within sites.
 SBP = systolic blood pressure.

Of the 83 patients in the Treatment group, 71 were treated with a single CCPS. Among these patients, complete coverage of AWI by the CCPS was documented in 66 patients (93%). The remaining 5 patients had minor residual endoleaks that did not require additional intervention.

Twelve patients in the Treatment group were treated with multiple CCPSSs, including seven for coverage of persistent moderate (n = 6) or large (n = 1) endoleak. The other 5 patients received multiple CCPSSs for other reasons, such as residual coarctation or nonstudy stent fracture. Of the 7 patients who received multiple CCPSSs for persistent endoleak, 5 ultimately achieved complete coverage. The remaining 2 patients had minor persistent endoleaks, one after placement of 2 CCPSSs and the other after 3 CCPSSs. Angiography for both patients suggested that complete aneurysm thrombosis was likely to occur after the procedure. Neither patient has required additional surgical or catheter intervention. Thus, CCPS implantation accomplished complete AWI coverage in 76 of 83 (92%) patients and eliminated the need for surgical repair in all 158 patients.

POST-IMPLANT HEMODYNAMICS AND COARCTATION DIAMETER. Table 5 demonstrates post-implant hemodynamics and aortic diameter by angiography. The ascending-descending gradient decreased

significantly in both groups (p < 0.0001). Similarly, the minimum stent diameter increased significantly from the pre-implant CoA diameter (p < 0.0001).

HOSPITAL STAY AND AEs. Median length of hospital stay after stent implantation for the entire cohort was 1 day (range 0 to 8). Seventeen serious or somewhat serious AEs occurred in 13 patients (8%) within 30 days attributable to stent, catheterization, or implantation procedure (Table 7). Four patients experienced important access site vascular injuries: dissection of the iliac artery (n = 2), extending to the aorta in 1 patient; femoral artery pseudoaneurysm (n = 1); and femoral artery occlusion related to suture-mediated vascular closure (n = 1). All of these AEs occurred before hospital discharge, although for 1 patient with iliac artery dissection, the extent of injury was not appreciated until after discharge.

There were no new, acute AWIs produced by stent implantation. There were no strokes, deaths, or episodes of bacteremia/endocarditis. There were no repeat interventions, CoA-related surgeries, or deaths within 30 days of the initial implant.

ONE-MONTH FOLLOW-UP. Of the original 158 patients, 154 (97%) had documentation of upper extremity SBP, and 143 had documentation of upper and lower extremity blood pressure measurements at

TABLE 5 Invasive Hemodynamic and Angiographic Measures Pre-/Post-Stent Implantation*

	Entire Cohort			Treatment			Prevention		
	Pre	Post	p Value	Pre	Post	p Value	Pre	Post	p Value
AAo-DAo systolic gradient, mm Hg	(n = 156)	(n = 152)		(n = 81)	(n = 82)		(n = 75)	(n = 70)	
Mean ± SD	27 ± 20	4 ± 6	<0.0001	19 ± 15	4 ± 7	<0.0001	36 ± 20	3 ± 6	<0.0001
Aorta/stent minimal diameter, mm	(n = 153)	(n = 154)		(n = 78)	(n = 80)		(n = 75)	(n = 74)	
Mean ± SD	8 ± 5	14 ± 3	<0.0001	10 ± 4	15 ± 3	<0.0001	5 ± 4	14 ± 4	<0.0001

*Changes in gradients and minimum diameters remained statistically significant when analyses were repeated using generalized estimating equations models to account for the correlation of patients within sites.
 AAo = ascending aorta; DAo = descending aorta.

TABLE 6 Core Lab Angiographic Assessment	
Pre-existing aortic wall injury	
None/trivial*	82 (52%)
Small	15 (9%)
Moderate	17 (11%)
Large or rapidly expanding	44 (28%)
Position of first implanted stent	
Well-positioned	142 (90%)
Minor malposition	13 (8%)
Major malposition	3 (2%)
Final appearance of aorta	
Smooth	157 (99%)
Therapeutic tear	1 (1%)
Dissection	0 (0%)
New aneurysm	0 (0%)
Final coverage of aortic wall injury (Treatment group only)	
Complete	76 (92%)
Minor endoleak	7 (8%)
Moderate or large endoleak	0 (0%)
<small>Values are n (%). *Includes 7 patients in the Treatment group who were treated for small, localized intimal tears with diameters <1/4 the aortic diameter identified by the implanting physicians after balloon dilation of the coarctation, but who were not classified by the core laboratory as having pre-existing aortic wall injury by trial definition.</small>	

1-month follow-up. **Table 4** summarizes these data. Both groups saw a significant improvement in resting SBP and SBP gradient.

At follow-up, most patients still had an upper extremity SBP of 120 mm Hg or greater, but there was a significant decrease from baseline (60% vs. 85%; $p < 0.0001$). Fewer patients had a SBP ≥ 140 mm Hg (13% vs. 46%; $p < 0.0001$). Ninety-two patients (60%) demonstrated a decrease in SBP of more than 10 mm Hg from baseline, and 106 patients (74%) had an upper-lower extremity SBP gradient ≤ 10 mm Hg.

SUBCLINICAL ARTERIAL ACCESS SITE INJURY.

We surveyed for subclinical femoral arterial injuries related to vascular access by comparing the instrumented and contralateral leg noninvasive oscillometric SBP measurements. We excluded 2 patients who underwent stent implantation via carotid artery cut-down and the 4 patients with clinically recognized femoral and iliac artery injuries, as noted in the preceding text. Of the remaining 152 patients, 108 had baseline and 1-month bilateral leg blood pressure measurements. We defined suspected femoral artery injury as meeting both of the following criteria: 1) SBP in the accessed leg 10 to 20 mm Hg (mild) or >20 mm Hg (serious) lower than in the non-instrumented leg; and 2) difference between baseline and 1-month lower extremity SBP gradients >10 mm Hg. Patients who met only 1 criterion were classified as “borderline” femoral artery injury.

By these criteria, 9 patients (8.3%) had suspected femoral artery injury; 4 (3.7%) serious, and 5 (4.6%) mild. Ten additional patients (8.9%) were classified as borderline femoral artery injury. Two other patients had a SBP in the accessed leg that was 10 to 20 mm Hg lower than in the contralateral leg but did not have baseline lower extremity SBP for comparison. There was no significant difference in patients weights between those with suspected femoral artery injury (borderline, mild, or serious) and those without (63.6 vs. 69.0 kg; $p = 0.24$). Likewise, there was no difference in the mean arterial sheath size ($p = 0.98$).

DISCUSSION

Once considered a surgical disease, CoA can now frequently be managed via minimally invasive catheter-based methods. Experience using a bare-metal stent for treatment of CoA was first described in the 1990s (9,27,28). Numerous subsequent reports have indicated the safety of stent placement as a primary strategy for treating both recurrent and native CoA, including the short- and intermediate-term results of the COAST study (10,12-14,24,25,29). Current American Heart Association and American College of Cardiology recommendations for the management of CoA in adults support transcatheter stent placement as the preferred therapy for recurrent CoA (30). The 2008 recommendations for management of native, complex, and long-segment CoA are less supportive of transcatheter intervention, citing a paucity of data describing the safety of stent placement in such cases.

Technological and procedural advances in the field of congenital cardiac catheterization have facilitated safer and more effective transcatheter management of CoA. Despite an overall appealing safety profile, bare-metal stent placement for CoA still carries a risk of serious morbidity (16,17). The rate of acute AWI due to bare-metal stent placement has been reported between 1.0% and 4.1%; this is significantly lower than similar complications seen with balloon angioplasty alone (7,13,24). In addition, late AWI is a recognized complication of bare-metal stent placement (14,25,31).

Covered stents represent an appealing option for primary CoA therapy or for treating or preventing AWI. Several studies have reported success using covered stents to manage CoA as a primary therapy for native or recurrent CoA (11,18-23). Others have reported the utility of covered stents for managing acute AWI with or without CoA (15,16,32). Cumulatively, these reports describe a safety profile of covered stents that is similar to bare-metal stents

with the purported added benefit of a covering to prevent or treat AWI. However, these studies primarily consist of self-reported, single-center experiences without standardized data collection, treatment protocols, or follow-up. Before our study, there have not been standardized clinical trials to study the safety and effectiveness of covered stents for treating CoA.

We present procedural and 30-day results for the first multicenter trial of a covered stent for preventing or managing AWI related to CoA. Our cohort of 158 patients all had a history of CoA and either risk factors for AWI or pre-existing AWI. In all patients, CCPS placement was technically successful. Our data suggest that CCPS stent placement is safe with a very low rate of acute complications related to the stent itself. No acute new or expanding AWI resulted from CCPS placement; follow-up magnetic resonance imaging or computed tomography (CT) performed 12 and 24 months after CCPS implantation will provide better information about the incidence of late AWI. We did not identify any distal stent embolization. There were no reinterventions or death within the first 30 days after treatment. The only documented complication related to the stent or stent placement was intentional coverage of the left subclavian artery in a patient with a complex pseudoaneurysm. The patient experienced transient left arm weakness and numbness, which was treated with analgesics and resolved after discharge.

In those with pre-existing AWI, CCPS completely covered the AWI in 92% of patients. Core laboratory review documented minor residual endoleak (i.e., unlikely to require additional therapy) on final angiography in 8% of patients with pre-existing AWI. On clinical follow-up, none of these patients has required further surgical or catheter-based intervention. Collapse of the Advanta V12 covered stent has been reported, presumably due to a residual endoleak, suggesting the need to recognize and treat significant endoleaks (33).

Overall, the most significant acute complications were arterial access injuries, seen in 4 patients (3%). These complications, though uncommon, are serious. The rate of access vascular injury reported in this study is higher than that encountered during the initial COAST trial (24). This difference may reflect our “high-risk” study population. Although the COAST II study specifically targeted older patients and those with genetic arteriopathy syndromes, such patients were excluded from the COAST study. In addition, the larger sheath required for delivery of the CCPS may have contributed an increased risk of arterial injury; the typical sheath size for delivery of a

TABLE 7 Serious and Somewhat Serious Adverse Events Attributable to the Stent or Implantation Procedure

	Description	Seriousness Classification	Treatment/Outcome
1	Left arm weakness and numbness after intentional occlusion of left subclavian artery to exclude a complex pseudoaneurysm	Somewhat serious	Oral analgesics. Resolved after discharge.
2	Post-procedure chest pain, nonspecific	Somewhat serious	Chest x-ray, IV analgesics. Resolved after discharge.
3	Post-procedure chest pain, nonspecific	Somewhat serious	Analgesics. Resolved by time of discharge.
4	Atrial arrhythmia	Somewhat serious	Cardioversion and single dose of esmolol. Resolved after procedure.
5	Superficial infection of left groin	Somewhat serious	Treated with antibiotics. Resolved after discharge.
6	Femoral artery occlusion after Per-Close device deployed	Somewhat serious	Heparin therapy; vessel recanalized with balloon angioplasty. No further intervention required.
7	Femoral artery pseudoaneurysm	Somewhat serious	Ultrasound of the femoral artery showed a 2 × 4-cm pseudoaneurysm. No additional therapy required.
8	Local stent migration	Somewhat serious	Additional CCPS implanted to secure the stent.
9	Abdominal pain	Somewhat serious	Abdominal CT unremarkable. IV analgesics. Diagnosed with post-coarctation syndrome.
10	Chest pain during procedure	Somewhat serious	General anesthesia initiated. Angiography confirmed no dissection.
11	Blood loss from procedure	Somewhat serious	Transfused 3 units of packed red blood cells post-procedure. Monitored in ICU.
12	Stent malposition	Somewhat serious	Small residual endoleak present after first CCPS slipped. Second CCPS placed to successfully seal leak.
13	Pulmonary embolism	Somewhat serious	Confirmed by CT scan day after procedure. Heparin therapy. Discharged on Coumadin for 6 months.
14	Chest pain	Somewhat serious	IV analgesics. Resolved before discharge.
15	Iliac artery dissection: weakened right pedal pulse	Serious	Treated with low-molecular-weight heparin overnight. At discharge, mildly decreased right leg pressure and pedal pulse. CT scan post-discharge revealed iliac dissection and thrombosis. Persistent exercise-related symptoms prompted bypass grafting 1 year later.
16	Iliac artery dissection, extending just above the renal arteries	Serious	Extensive ilioaortic stent implantation. CICU overnight, treated with esmolol and nitroprusside. Discharged after 2 days on atenolol and enalapril.
17	Left arm muscle fatigue with diminished radial pulse	Somewhat serious	Stenosis of left subclavian artery noted at baseline with additional obstruction from CCPS. Adequate blood flow. No additional therapy.

CCPS = covered Cheatham-Platinum stent; CICU = cardiac intensive care unit; CT = computed tomography; ICU = intensive care unit; IV = intravenous.

bare-metal CP stent is 10- to 12-F compared with 12- to 14-F for the CCPS.

Beyond the safety profile of the CCPS and its utility in treating and preventing AWI, our study shows that it is an effective strategy for primary management of CoA. Notably, the Prevention group, who had more significant CoA at baseline, demonstrated an improvement in peak ascending-descending aorta gradient from 36 mm Hg to 4 mm Hg; the gradient for the entire cohort decreased from 27 mm Hg to 4 mm Hg. At follow-up, 92% of patients had an upper-lower extremity SBP gradient less than 20 mm Hg.

STUDY LIMITATIONS. Although the COAST II study was structured to target patients at high risk of AWI, we do not know the statistical risk among our study population, and our demographics and results do not necessarily reflect what may be observed in other populations. Because the COAST II study was an uncontrolled, single-arm trial, we cannot conclude that CCPS is superior or inferior to other endovascular or surgical options for managing CoA with or without AWI. In addition, we only present acute, procedural, and 30-day outcomes of the COAST II trial and make no suggestions about long-term safety or efficacy. Follow-up is ongoing to better define long-term outcomes including sustained clinical improvement in blood pressure, development of new AWI, risk of stent fracture and endocarditis, and the ability to re-dilate the CCPS. We also acknowledge that our effort to describe arterial access-site injury was a retrospective review of available noninvasive, nonimaging data, and, thus, may not represent the true incidence of arterial injury.

CONCLUSIONS

The CCPS can be used to effectively treat existing AWI and may prevent AWI in patients undergoing stent therapy for CoA. Placement of the CCPS has a high rate of technical success and short-term hemodynamic improvement. We believe that these short-term results support the use of covered stents as a safe and effective treatment option for CoA and AWI. We anticipate that mid- to long-term follow-up of these patients will confirm this conclusion. Although overall, serious complications are uncommon, arterial access injury is a potential complication that should be investigated and treated aggressively.

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PERSPECTIVES

WHAT IS KNOWN? Some patients with coarctation of the aorta may develop AWI, either primary aneurysm formation or secondary injury after transcatheter or surgical intervention. Large-diameter, covered stents are an appealing nonsurgical option for treating AWI, but are currently unavailable for routine clinical use in the United States.

WHAT IS NEW? This large, prospective study shows excellent short-term safety and efficacy of the Covered Cheatham-Platinum stent in managing patients with existing AWI and avoiding AWI in high-risk patients.

WHAT IS NEXT? Longer-term data are necessary and are forthcoming to describe the durability of the CCPS and incidence of aneurysm formation after stent implantation.

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