

## PEDIATRIC AND CONGENITAL HEART DISEASE

### Original Studies

# Stenting of Aortic Coarctation: Acute, Intermediate, and Long-Term Results of a Prospective Multi-Institutional Registry—Congenital Cardiovascular Interventional Study Consortium (CCISC)

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**Introduction:** Since the 1980s, stent implantation has evolved as an important therapeutic strategy for coarctation of the aorta. However, available data is frequently flawed by short follow-up, lack of adequate follow-up imaging, and retrospective nature of data collection. **Methods:** Data was prospectively collected using a multicenter registry congenital cardiovascular interventional study consortium (CCISC). Between 2000 and 2009, 302 patients from 34 centers with a median weight of 58 kg underwent stent implantation for coarctation. Eligible patients (44%) completed intermediate follow-up (3–18 months) with integrated imaging (cath, CT, MRI), whereas 21% completed long-term follow-up (>18–60 months). Procedural success was defined as UL/LL systolic gradient of less than 20 mm Hg, lack of significant recurrent obstruction, and freedom from unplanned repeat intervention. **Results:** Acute procedural success was 96%. Cumulative intermediate success was 86%, and cumulative long-term success was 77%. Unplanned repeat interventions were required in 4%, and aortic wall complications were seen in 1% of patients (dissection  $n = 1$  and aneurysm  $n = 3$ ). Other adverse events ( $n = 15$ ) occurred mainly acutely and included technical complications such as stent malposition ( $n = 9$ ). At long-term follow-up, 23% of patients continued to have systolic blood pressure above the 95th centile, 9% had an upper-to-lower limb blood pressure gradient in excess of 20 mm Hg, and 32% were taking antihypertensive medication. **Conclusions:** This study documented acute, intermediate, and long-term outcome data comparable or superior with other surgical or interventional series. However, even with successful initial stent therapy, patients continue to require long-term follow-up and have associated long-term morbidity, relating to aortic wall complications, systemic hypertension, recurrent obstruction as well as need for repeat intervention. © 2010 Wiley-Liss, Inc.

**Key words:** pediatric interventions; congenital heart disease in adults; coarctation

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## INTRODUCTION

Coarctation of the aorta represents one of the more common congenital cardiac lesions and accounts for ~5–10% of all cases of congenital heart disease. The reported natural history of untreated coarctation is poor; the mean age of death for patients with coarctation surviving the 1st year of life is 34 years (control: 72 years) [1]. The anatomic simplicity of coarctation is in sharp contrast to the clinical challenges faced when trying to improve upon the poor natural history. Treatment options for aortic coarctation include surgical approaches, transcatheter balloon angioplasty, or stent placement. Although surgical approaches have been performed for more than 50 years [2], transcatheter treatment alternatives have only evolved since the late 80s [3–5]. Even though a variety of articles have reported institutional results of surgical or transcatheter strategies, most are retrospective single center experiences with the chosen treatment strategies usually depending on operator or institutional preference and with lack of intermediate and long-term follow-up data. Very little prospective data is available on the incidence of recurrent obstruction, aortic wall complications, or blood pressure recording. Intermediate and long-term follow-up after aortic stent implantation have been poorly documented, and only very few of the series focusing on aortic stent included 50 or more patients [6–10]. Congenital cardiovascular interventional study consortium (CCISC) has evolved as a prospective interventional registry, which captures all types of treatment for coarctation (surgical, balloon angioplasty, and stent implantation). This article reports on the results of stent implantation for aortic coarctation. The primary purpose of this report is to provide a detailed review of composite procedural success including recurrent obstruction/repeat interventions, aortic wall complications, with a particular focus on intermediate and long-term outcomes. Comparison among treatment approach to coarctation from CCISC registry is reported elsewhere (Forbes et al.).

## METHODS

### Study Population and Design

The study was designed as a prospective, multi-institutional, observational registry from the CCISC [7], and included 302 patients from 34 centers who underwent aortic stent placement over a 9-year period between December 2000 and November 2009. Although the registry also captured data on patients who underwent balloon angioplasty or surgical repair of coarctation, this will be reported elsewhere, as the main objective of this article was the more detailed presentation of the data collected prospectively on endovascular stenting. IRB approval

**TABLE I. Inclusion and Exclusion Criteria**

Inclusion criteria
Presence of significant coarctation based on one or more of the following:
UL/LL gradient $\geq 20$ mm Hg
UL/LL gradient $\geq 10$ mm Hg plus either decreased LV function or aortic insufficiency
UL/LL gradient $\geq 10$ mm Hg plus significant collateral flow
Exclusion criteria
Weight $< 10$ kg
Refusal to sign consent
Known or suspected arteriitis

was obtained from all participating institutions. Inclusion and exclusion criteria pertinent to aortic stent implantation procedures are listed in Table I. Data was collected at the time of the procedure, as well as at intermediate (3–18 months), and long-term follow-up ( $> 18$ –60 months), and submitted electronically using a secure web-based interface, with data storage occurring at a secure server at Wayne State University Medical School. Additional data collection was performed for any reintervention during the follow-up period. The data integrity was reviewed by the site-administrator and institutions were asked to provide core documents, such as data entry sheets and original catheterization reports, for a random 10% of the procedures. Missing data and data that fell out of normal ranges were also queried from the primary site. In addition, all imaging studies (Cath, CT, MRI) were reviewed by corelab physicians from different sites.

### Data Collection

Collected data included demographic variables (age, weight, and gender) as well as associated anomalies. The coarctation morphology was further specified by its baseline classification (native and recurrent) and the location (transverse arch proximal: after origin of RIA/RCCA or proximal to LCCA, transverse arch distal: after origin of LCCA or proximal to LSCA, complex: transverse and isthmus obstruction, isthmus proximal:  $\leq 5$  mm from LSCA, isthmus distal:  $> 5$  mm from LSCA, and abdominal/mid-thoracic). The presence of transverse arch hypoplasia was noted, defined as a ratio between the narrowest segment of the transverse arch and the aorta at the diaphragm of less than 0.65.

Clinical data was collected at baseline, before discharge, and at follow-up and included upper and lower extremity systolic/diastolic blood pressure, as well as the need for antihypertensive medication. A blood pressure exceeding the 99th centile obtained for children of similar age (using the 50th centile for height) was defined as hypertensive [11]. Similarly, for adults, a systolic blood pressure in excess of 145 mm Hg or a diastolic blood pressure in excess of 95 mm Hg was defined as hypertensive.

Procedural data included stent type/length, balloon type/length/diameter, wire position for stent delivery, cardiac output control measures (adenosine, pacing), flaring of stent, type of sedation/anesthesia, and the use of inotropes to unmask a potentially significant coarctation with a low-baseline gradient under anesthesia. Hemodynamic data collected before and after stent placement included ascending and descending aortic pressures (systolic, diastolic, and mean), as well as left ventricular end-diastolic pressures. In the presence of a residual gradient >10 mm Hg after stent placement, pressure recordings were obtained in the distal transverse aortic arch to evaluate for the presence of a potential obstruction at the level of the transverse aortic arch. Angiographic data was obtained before stent implantation using two separate projections (AP or LAO, as well as lateral), and included the diameter of the coarctation (minimum), transverse aortic arch, as well as aorta at level of diaphragm. Angiography was repeated using two projections after stent implantation to evaluate for the presence of residual or new arch pathology.

Valid follow-up data required provision of integrated imaging data, provided either by CT and/or MRI and/or cardiac catheterization. All baseline and follow-up imaging data was evaluated for the presence of aortic wall injury (dissection and aneurysm), stent-related pathology (intimal proliferation and stent fracture), and recurrent/residual obstruction. The degree of recurrent or residual obstruction was classified as percent of stent lumen (<10%: mild, 11–30%: moderate, and >30%: severe). If a patient required a reintervention, all procedural data was recorded similar to the original intervention. Dissection was defined as the presence of contrast extravasating within the aortic wall into the region of the wall media that was not present before the intervention. An aneurysm was defined as a diameter more than 20% greater than the diameter of the aorta at level of the diaphragm, or an abnormal localized enlargement with abrupt, localized change in the aortic lumen diameter of greater than 10% compared with the aorta immediately proximal to the enlargement.

### Outcome Parameters

Outcome parameters included the incidence of adverse events as well as the rate of acute, intermediate, and long-term procedural success. A procedure was classified as procedural failure, if any of the following criteria were met:

1. Unplanned surgical or transcatheter repeat intervention,
2. Moderate or severe reobstruction on imaging at follow-up, and

3. Upper-to-lower limb systolic blood pressure gradient of 20 mm Hg or more for nonstaged procedures, or for staged procedures after first repeat intervention.

Because of the lack of reported data defining a successful procedural outcome, the procedural success was analyzed separately for different thresholds using the immediate postprocedural systolic pressure gradient obtained invasively in the catheterization laboratory (<10 mm Hg, <15 mm Hg, <20 mm Hg, 20 mm Hg, or above). In contrast to unplanned repeat interventions, a planned repeat intervention was defined as a repeat intervention performed to accommodate interval growth or staged stent re-expansion.

Secondary outcome parameters included the immediate postprocedural systolic gradient obtained in the catheterization laboratory, the systolic and diastolic blood pressure, the need for anti-hypertensive medication, as well as the incidence of aortic wall complications and other adverse events.

### Statistical Analysis

For all procedural and patient characteristics, median and range were calculated for continuous variables, and frequency with percentage for categorical variables. StatsDirect software (StatsDirect, Cheshire, UK) was used for all statistical calculations. The impact of various procedural and patient characteristics on acute, intermediate, and long-term success was evaluated using Chi-square and Fisher's exact test. The same tests were used to evaluate the relationship between incidence of stent migration, and the balloon type, stent type, wire position, as well as the use of cardiac output control measures. The relationship between incidence of aortic wall complications and balloon-to-coarctation ratio, stent type, balloon type, and use of compliance testing was evaluated Chi-square and Fisher's exact test. Pre- and post-procedural angiographic measurements and hemodynamic data for continuous variables were compared using the paired *t*-test. The percentage of patients with a systolic blood pressure above the 95th/99th centile was compared between preprocedure, postprocedure, intermediate follow-up, and long-term follow-up using the Chi-Square test. The same test was used to compare the percentage of patients requiring anti-hypertensive medication between preprocedure, postprocedure, intermediate follow-up, and long-term follow-up. Similarly, the percentage of patients who had upper-limb to lower-limb blood pressure gradients above/below certain thresholds (10 mm Hg, 15 mm Hg, and 20 mm Hg) was compared between preprocedure, postprocedure, intermediate follow-up, and long-term follow-up using the Chi-Square test. All tests were performed at  $\alpha = 5\%$ .

**TABLE II. Basic Demographic Data and Coarctation Morphology**

Demographics and coarctation morphology	Median (range) or <i>n</i> (%)
Weight (kg)	58 (11–156)
Age (years)	15 (2–63)
Gender	
Male	211 (70%)
Female	91 (30%)
Coarctation classification	
Native	167 (55%)
Recurrent	135 (45%)
Coarctation location	
Transverse arch, proximal	9 (3%)
Transverse arch, distal	33 (11%)
Complex	20 (7%)
Isthmus, proximal	66 (22%)
Isthmus, distal	168 (56%)
Abdominal/mid-thoracic	2 (1%)
Arch hypoplasia	31 (10%)
Associated anomalies	
Bicuspid aortic valve	123 (41%)
Single ventricle	6 (2%)
Shone's	8 (3%)
Other complex CHDz	44 (15%)

Median and range are provided for continuous variables as well as frequency with percentage for categorical variables.

## RESULTS

### Demographics and Coarctation Morphology

Basic demographic and clinical data are listed in Table II. The median weight was 58 kg (11–156 kg). Approximately half of the cases were native coarctation (55%), located at the distal isthmus (56%). Out of 135 patients with recurrent coarctation, 87 (64%) had isolated previous surgical repair of coarctation, whereas the remainder had previous transcatheter balloon angioplasty ( $n = 15$ ), stent placement ( $n = 22$ ), or a combination of different treatment/unspecified modalities ( $n = 11$ ). Associated transverse arch hypoplasia was present in 31/302 (10%) of procedures.

### Procedural Data

Three hundred fifty-one stents were implanted in 302 procedures, and general anesthesia was used in 247 of 302 (82%) procedures. In 17% (50/302) of cases, the procedures were intentionally staged with subsequent electively planned repeat intervention.

Inotropes were used to assess for the presence of an exercise-induced gradient as under anesthesia in 8/302 (3%) procedures, most commonly using either dopamine ( $n = 4$ ) or dobutamine ( $n = 3$ ). In most patients, inotropes were used when the baseline gradient across the coarctation is low due to anesthesia-induced hypotension.

Compliance testing before stent implantation (using a low-pressure balloon to evaluate for distensibility of

**TABLE III. Procedural Data**

Procedural data	Median (range) or <i>n</i> (%)
Procedures with >1 stent	64 (21%)
Compliance testing	41 (14%)
Inotropes	8 (3%)
Cardiac output control	65 (22%)
Sheath size (Fr)	10 (5–14)
Stents used	Total stents $n = 351$
Genesis XD <sup>®</sup>	153 (44%)
Cheatham-Platinum <sup>®</sup> (CP)	39 (11%)
Covered Cheatham-Platinum <sup>®</sup>	18 (5%)
Max LD <sup>®</sup>	23 (7%)
Mega LD <sup>®</sup>	59 (17%)
Palmaz 10 Series <sup>®</sup>	28 (8%)
Other/unspecified	31 (9%)
Balloons used	Total balloons $n = 313$
BiB <sup>®</sup>	186 (59%)
Cordis	44 (14%)
ZMed <sup>®</sup>	54 (17%)
Other	29 (9%)
Balloon diameter (mm)	15 (4–25)
Balloon/CoA ratio	2 (1–9.2)
Balloon/CoA ratio >3	57 (19%)
Balloon/CoA ratio <1.5	38 (13%)

Median and range are provided for continuous variables as well as frequency with percentage for categorical variables. The Max LD<sup>®</sup> and Mega LD<sup>®</sup> stents are manufactured by EV3 (EV3, Plymouth, MN). The Palmaz 10 Series<sup>®</sup> stents, the Genesis XD<sup>®</sup> stents as well as the Cordis balloons are manufactured by Cordis (Cordis, Warren, NJ). The (covered) Cheatham-Platinum stents<sup>®</sup> as well as the BiB<sup>®</sup> and ZMed<sup>®</sup> balloons are manufactured by NuMED (NuMED, Hopkinton, NY).

the coarctation segment) was performed only occasionally (14%; 41/302 procedures). In 65/302 (22%) procedures, cardiac output control was used to facilitate stent placement, with the majority being rapid RV pacing ( $n = 61$ ), followed by rapid RA pacing ( $n = 4$ ). Information on wire position for stent placement was available for 254 procedures. The most common wire position was the ascending aorta (135/254, 44%), followed by the right subclavian artery (79/254, 31%), the left subclavian artery (34/254, 13%), and the carotid arteries (6/254, 2%). The median balloon-to-coarctation ratio was 2 (1–9.2).

Extra large diameter stents expandable beyond 20 mm were implanted in 108/352 (31%) instances. Stents were flared at the distal end in 59/302 (20%) procedures. In 49/302 (16%) procedures, more than one stent was implanted. Indications for implantation of a second stent, reported in only 19/49 (41%) patients, were to fully cover the coarctation segment ( $n = 11$ ), migration of the initial stent ( $n = 7$ ), and aortic dissection ( $n = 1$ ). Other procedural data including specific stent and balloon type are presented in Table III.

### Immediate Angiographic and Hemodynamic Result

Using the average between AP and lateral dimensions, the median ratio of smallest coarctation diameter

**TABLE IV. Hemodynamic and Angiographic Data at Time of Stent Implantation**

	Pre-stent	Post-stent	<i>P</i> -value
<b>Dimensions</b>			
Transverse arch (mm)	14.3 (6–26)	–	
Aorta at diaphragm (mm)	15.8 (4.5–41.2)	–	
Coarctation (avg. AP/Lat) (mm)	6.9 (1.3–15.5)	13.8 (5.5–23)	<0.0001
Ratio: CoA/Ao at diaphragm	0.44 (0.09–1.7)	0.85 (0.28–3.11)	<0.0001
% pts with ratio >0.65	11%	82%	<0.0001
<b>Hemodynamics</b>			
Syst. Gradient AAO-DAO (mm Hg)	26 (4–101)	2 (–18 to 61)	<0.0001
% pts with gradient <10 mm Hg	5%	84%	<0.0001
% pts with gradient <15 mm Hg	17%	91%	<0.0001
% pts with gradient <20 mm Hg	28%	95%	<0.0001
% pts with gradient ≥20 mm Hg	72%	5%	<0.0001
LVEDP (mm Hg)	12 (3–33)	14 (3–27)	0.1122

A negative upper limb to lower limb blood pressure gradient signifies that the lower limb blood pressure was higher than the upper limb blood pressure. % pts, percent of patients.

to diameter of the aorta at the diaphragm increased significantly from 0.44 (0.09–1.78) to 0.85 (0.28–3.11) after stent implantation ( $P < 0.0001$ ), and the coarctation diameter improved significantly from 6.9 mm (13.5–15.5 mm) before stent implantation to 13.8 mm (5.5–23 mm) post stent implantation ( $P < 0.0001$ ) (Table IV). After stent implantation, the median preprocedural systolic blood pressure gradient was reduced significantly from 26 mm Hg to 2 mm Hg ( $P < 0.0001$ ). In 287/302 (95%) procedures, the gradient was reduced to less than 20 mm Hg. There was no significant difference between median LVEDP before and after intervention (12 mm Hg vs. 14 mm Hg,  $P = 0.1122$ ).

Stents overlapped arch-vessels in 39/302 (13%) of procedures, most commonly the subclavian artery ( $n = 30$ ), followed by the carotid artery ( $n = 9$ ). Vessels were overlapped to less than half of the vessel diameter in 15 procedures, and to more than half the vessel diameter in 24 procedures. Closed-cell design stents were used in 12 procedures where the stent overlapped an arch vessel by 50% or more. Only in three procedures was obstruction of flow seen to an arch vessel caused or worsened by the implanted stent. The majority of patients (250/302, 83%) were discharged within 24 hr of the procedure, with the remainder staying in hospital for a median of 2 days (2–46 days).

### Follow-Up and Procedural Outcome

Ninety-four percent of patients were eligible for intermediate follow-up (at least 3 months as stent implantation), whereas 73% were eligible for long-term follow-up (at least 18 months as stent implantation). However, only 124/283 (44%) eligible patients had intermediate follow-up data with integrated imaging provided by the participating institutions, whereas so far only 46/221 (21%) had long-term follow-up data with

**TABLE V. Type of Follow-Up Imaging Provided**

	Intermediate follow-up ( $n = 147$ )	Long-term follow-up ( $n = 50$ )
CT	92 (63%)	31 (62%)
Cardiac catheterization	15 (10%)	11 (22%)
MRI	17 (12%)	4 (8%)
No imaging provided	23 (16%)	4 (8%)

Frequency and percentage of all patients at follow-up is provided for each imaging modality.

integrated imaging provided. The median follow-up of patients who had at least one follow-up evaluation was 1.1 years (3.6 months to 4.8 years). Table V lists the type of follow-up imaging provided. At intermediate follow-up 23/147 (16%) and at long-term follow-up 4/50 (8%), patients had only clinical information, but no imaging data provided. Data from these patients were not included in the procedural success analysis.

**Procedural success.** Complete data entry including presence of recurrent obstruction, need for repeat intervention, upper and lower limb blood pressure recordings, and documentation of aortic wall complications to evaluate the procedural success was provided for 260/302 (86%) of procedures at the time of discharge, 115/147 (78%) procedures at intermediate follow-up, and 43/50 (86%) procedures at long-term follow-up. Only these procedures with a complete dataset were included into the procedural success analysis.

Using the criteria defined in the method section, acute procedural success was 249/260 (96%) at the time of discharge. Cumulative procedural success was 99/115 (86%) at intermediate follow-up and 33/43 (77%) at long-term follow-up. Acute, intermediate, and long-term procedural success was unrelated to patient weight, presence of transverse arch hypoplasia, use of compliance testing, as well as stent type, and balloon type. Even though not statistically significant, there

TABLE VI. Blood Pressure and Anti-Hypertensive Medication Use

Blood pressure and anti-hypertensive medication	Median (range) or <i>n</i> (%)				<i>P</i> -value
	Pre-procedure	Pre-discharge	Intermed. follow-up	Long-term follow-up	
Systolic BP (UL) (mm Hg)	138 (85–216)	124 (79–187)	122 (78–161)	126 (90–150)	
>95th Centile	229/299 (77%)	125/297 (42%)	37/147 (25%)	11/48 (23%)	<0.0001
>99th Centile	177/299 (59%)	68/297 (23%)	20/147 (14%)	3/48 (6%)	<0.0001
Diastolic BP (UL) (mm Hg)	73 (35–110)	66 (31–104)	66 (32–90)	65 (45–85)	
>95th Centile	78/295 (26%)	34/296 (11%)	4/147 (3%)	0/48 (0%)	<0.0001
>99th Centile	32/295 (11%)	14/296 (5%)	0/147 (0%)	0/48 (0%)	<0.0001
Systolic UL-LL gradient					
% pts <10 mm Hg	30/284 (11%)	204/274 (74%)	94/135 (70%)	35/46 (76%)	<0.0001
% pts <15 mm Hg	52/284 (18%)	233/274 (85%)	110/135 (81%)	38/46 (83%)	<0.0001
% pts <20 mm Hg	66/284 (23%)	248/274 (91%)	117/135 (87%)	42/46 (91%)	<0.0001
% pts ≥20 mm Hg	218/284 (77%)	26/274 (9%)	18/135 (13%)	4/46 (9%)	<0.0001
% of pts on anti-HTN Meds	129/302 (43%)	181/302 (59%)	66/147 (45%)	16/50 (32%)	<0.0001

Only those patients were included where the relevant blood pressure information was available. Median and range are provided for continuous variables as well as frequency with percentage for categorical variables. Fraction and percentage of patients with systolic and diastolic blood pressures above the 99th and the 95th centile. UL, upper limb; LL, lower limb; anti-HTN, anti-hypertension.

was a trend toward higher intermediate (89 vs. 73%) and long-term procedural success (79 vs. 70%) when the coarctation was located at the isthmus, as opposed to any other location.

As it has been unclear whether operators should aim to achieve a gradient reduction (measured invasively after stent implantation) to less than 10 mm Hg, less than 15 mm Hg, or less than 20 mm Hg, we compared these three invasive gradient thresholds with regards to procedural success at discharge, at intermediate, and at long-term follow-up. There was no significant difference between procedural success when comparing patients with an immediate postprocedural invasive systolic gradient of <10 mm Hg, <15 mm Hg, and <20 mm Hg. This applied to acute procedural success (96% vs. 96% vs. 96%,  $P = 0.9822$ ), intermediate procedural success (87% vs. 86% vs. 86%,  $P = 0.9915$ ), and long-term procedural success (80% vs. 82% vs. 79%,  $P = 0.9717$ ). 9/13 (76%) procedures with an immediate postprocedural gradient of 20 mm Hg or more were planned staged procedures.

**Blood pressure and anti-hypertensive medication.** Blood pressure obtained during the follow-up period is listed in Table VI. Although the percentage of patients with a residual upper limb to lower limb gradient of >20 mm Hg remained fairly constant from discharge to long-term follow-up, there appeared to be a continued improvement in the percentage of patients with a systolic blood pressure above the 99th percentile (Table VI). The incidence of systolic hypertension was higher at all time points (preprocedure, discharge, intermediate follow-up, and long-term follow-up) when compared with diastolic hypertension.

Patients were arbitrarily defined as being at “hypertensive risk,” if they had either a hypertensive systolic blood above the 99th centile, or an upper limb to lower

limb systolic gradient above 20 mm Hg, or the need for antihypertensive medication. The percentage of patients at “hypertensive risk” decreased significantly from 261/284 (92%) before the procedure, 181/260 (70%) at discharge, 59/115 (51%) at intermediate follow-up, and 16/43 (37%) at long-term follow-up ( $P < 0.0001$ ).

**Restenosis and repeat intervention.** Out of 164 patients who had either early or late follow-up imaging (CT, MRI, or cath), recurrent obstruction was seen in 32 patients (20%), during 35/170 (21%) follow-up evaluation. The severity was mild in 26/35 (74%), moderate in 9/35 (26%), and unspecified in one. The location of recurrent obstruction was identified in 21/35 (60%) follow-up evaluations, being at the stent implantation site in 15 patients, just proximal to the stent in five patients, and in the transverse arch in one patient. In 80% of stent obstructions that were found just proximal to the inserted stent, the cause of recurrent obstruction was hypoplasia of the proximal vessel. Intimal proliferation, defined as intimal growth extending within the lumen of the stent, was seen in at mild degree in 23 cases on follow-up imaging, and at larger degrees in two cases.

Where measurements were provided, a ratio of smallest coarctation diameter to diameter of the aorta at the diaphragm of less than 0.65 was found in 226/259 (87%) of patients before stent implantation, 29/247 (12%) of patients at the end of the procedure, 16/119 (13%) of patients at intermediate follow-up, and 4/41 (10%) at long-term follow-up ( $P < 0.0001$ ).

Twelve percent (36/302) of patients required a total of 42 repeat interventions performed at a median interval of 317 days (1 day to 4.7 years). Six patients had more than one repeat intervention. An early transcatheter repeat intervention was required in one patient a day after the initial procedure due to aortic dissection,

**TABLE VII. Adverse Events Acutely, at Intermediate, and Long-Term Follow-Up**

	Adverse Events		
	Acute (n)	Intermediate (n)	Long-term (n)
All adverse events	15	4	–
Number of patients with AE	15	3	–
Aortic wall complications	2	2	–
Dissection	1	–	–
Aneurysm	1	2	–
Other adverse events	13	2	–
Balloon rupture	1	–	–
Stent migration	9	–	–
Stent fracture	–	2	–
Femoral injury/pulse loss	3	–	–

Number of adverse events is listed (n).

with successful placement of a covered Cheatham-Platinum<sup>®</sup> (covered CP) (NuMED, Hopkinton, NY) stent. Patients [11/302 (4%)] had repeat interventions performed within the intermediate follow-up window, whereas 26/302 (9%) patients had repeat interventions performed within the long-term follow-up window. Repeat interventions [27/42 (64%)] were elective staged procedures performed in 26 patients, whereas 15/42 (36%) were unplanned procedures performed in 13 patients. The reasons for unplanned repeat interventions during the follow-up period were restenosis in 13/15 (87%) procedures, and vascular complications in the remainder. Intimal hyperplasia was the most common cause for recurrent obstruction (7/13, 54%). Stent fracture was the cause for recurrent obstruction in one patient. In total, stent fracture was seen in four patients, two of which occurred in Genesis XD<sup>®</sup> stents, and two in the older Cheatham-Platinum<sup>®</sup> stents.

There was no significant difference in the percentage of patients that on follow-up developed either recurrent obstruction (moderate/severe) or required an unplanned repeat intervention, irrespective on whether the initial invasive postprocedural gradient was less than 10 mm Hg (97/124, 78%), less than 15 mm Hg (99/129, 77%), or less than 20 mm Hg (103/134, 77%) ( $P = 0.719$ ). However, the incidence of recurrent obstruction or the need for repeat intervention was significantly higher (3/8, 38%), when the residual gradient was equal to or in excess of 20 mm Hg ( $P = 0.0287$ ).

**Aortic wall complications and other adverse events.** The incidence of adverse events at the initial procedure, including stent migration, aortic wall injury, and other adverse events was 15/302 (5%) (Table VII).

Stent migration occurred in 9/302 (3%) of procedures, requiring implantation of a second stent in four procedures. No patient required surgical retrieval of a migrated stent. The cause of stent migration was undersized balloon catheter in one procedure, stent migration

during balloon inflation in two procedures, and unspecified in the remaining procedures. There was no significant relationship between incidence of stent migration and balloon type, stent type, use of cardiac output control, or wire position.

Aortic wall complications were seen in 2/302 (1%) at the time of the procedure, 2/126 (2%) at intermediate follow-up, and 0/46 (0%) at long-term follow-up (Table VII). One patient required implantation of a covered CP-stent within 24 hr of the initial procedure, due to a small extravasation of contrast outside the aorta. So far, all aneurysms identified on follow-up were of small size and have not required surgical or transcatheter repeat intervention. Because of the small number of aortic wall complications, we were unable to document any statistical significant relationship between incidence of aortic wall complications and balloon/CoA ratio, stent type, use of cardiac output control, and use of compliance testing. However, one patient who had a tight coarctation treated using a covered CP stent with a balloon-to-coarctation ratio of 7:1 and had evidence of an aortic aneurysm at intermediate follow-up.

Acute adverse events other than stent migration or aortic wall injury were seen in 4/302 (1%) procedures and included femoral artery injury or pulse loss in three procedures, and balloon rupture in one procedure. There was no significant difference in the incidence of aortic wall injury, stent migration, and other adverse events during the initial procedure, when comparing low volume (<25 cases), high volume ( $\geq 25$  cases), and centers (6.2% versus 3.6%,  $P = 0.3671$ ).

## DISCUSSION

This prospective registry provides the largest reported experience on stent implantation for aortic coarctation. As in previous reports, stent therapy resulted in significant angiographic improvement and gradient reduction. In this series, the mortality was 0%, whereas 5% of patients had procedure-related adverse events. This study confirms the fairly low rate of acute procedure-related adverse events seen in other recent studies [6,12]. Most of the adverse events were either technical complications or local femoral vascular complications. Although we expected to see a lower incidence of some of the technical complications, such as stent migration or balloon rupture with the use of cardiac output control and the BiB balloon [13], this could not be confirmed in this series, which may be related to the overall fairly small numbers of technical complications.

## Procedural Success

Overall, procedural success was acutely 96% with cumulative long-term success being 77%. However,

this data will have to be interpreted with caution, especially when comparing with surgical series, as most surgical series lack appropriate follow-up imaging, and do rarely report an overall success but instead, report mainly rate of repeat intervention, and very occasionally on incidence of vascular adverse events [14–17]. In our study, decreasing success over time has been related to a large extent to the development of moderate or severe recurrent obstruction. However, in contrast to many surgical series, this study used integrated imaging in a large number of patients to specifically look for recurrent obstruction. Furthermore, the fact that only about 50% of patients had intermediate follow-up data and only 17% long-term follow-up data may have introduced selection bias. Therefore, it is very conceivable that patients with abnormal clinical data and/or evidence of recurrent obstruction on echo were more likely to have been referred for more detailed follow-up imaging, such as MRI, CT, and cath. As such, the percentage of patients with procedural failure as defined per our criteria may be overrepresented in the selected group of patients that underwent integrated follow-up imaging.

Even though acute procedural success is important, the intermediate and long-term follow-up data is what ultimately determines the success of the procedure. In this context, one may have to revise what is considered a successful acute result. Zabal et al. found that an immediate residual gradient of more than 10 mm Hg after transcatheter therapy was associated with a higher composite index of failure (defined as heart-related death, follow-up gradient > 20 mm Hg, need for repeat intervention, vascular complications), compared with patients who achieve a gradient reduction to less than 10 mm Hg [18]. Our study did not find any significant difference in procedural success, as well as incidence of recurrent obstruction or planned repeat intervention, when comparing patients with invasive immediate post-procedural residual gradients of <10 mm Hg, <15 mm Hg, and <20 mm Hg. Therefore, we believe that aiming for an immediate postprocedural gradient of less than 20 mm Hg should be considered adequate.

### Follow-Up Imaging and Aortic Wall Complications

The strengths of this study lie in the number of patients that had either CT, MRI, or angiography as follow-up imaging. This facilitates a much more accurate detection of recurrent obstruction as well as aortic wall complications than just relying on echocardiography and clinical data, as has been the case with many surgical and balloon angioplasty series. In this series, aortic wall complications were seen in 1.3% of

patients, which is very similar to what has been reported in the surgical literature, with less detailed follow-up imaging [16]. Qureshi et al. recently reported an incidence of aortic-wall complications of 7.3% after stent implantation for aortic coarctation [6]. The majority of aneurysms identified in our series were small. Although it is imperative that clinicians be diligent in the performance of evaluations for the presence of aortic wall injury, it remains unclear what long-term effect small aneurysms, will have.

### Repeat Intervention

The overall need for repeat intervention in our series was 12%, and when excluding planned/staged repeat interventions, this rate was only 4%. This compares well to surgical repair, where the incidence of repeat intervention ranges between 6% and 20% [14–17]. In other interventional series that have reported on stent implantation for aortic coarctation, the incidence of repeat interventions was variable, ranging from 6–7% [9,10] to as high as 33–43% [6,12]. However, with only 22% of patients in our series having completed long-term follow-up, it is difficult to draw firm conclusions with regards to the need for repeat intervention. Ultimately more consistent long-term follow-up data of 10–15 years will be required to provide more accurate data on the need for repeat intervention.

The repeat interventions in this study included elective redilatations of adult-size stents that are performed to accommodate interval growth, and accounted in this study for as much as 64% of repeat interventions. Whether elective repeat interventions to accommodate interval growth are desirable is an altogether different question. Some patients may prefer a nonsurgical approach, provided the same long-term result can be achieved, whereas others may opt for a single surgical procedure. The advantage of a single surgical procedure will have to be balanced against the longer initial hospital stay, the surgical scarring, and most importantly the long-term results of either intervention. As long as all treatment alternatives are discussed with the patient and patient's family, an informed decision can be made by the family on the desired and preferred treatment strategy. In addition, practitioners may want to consider economical aspects, with some articles suggesting that stent implantation for aortic coarctation may be the more cost-effective treatment strategy [19].

### Hypertension and Need for Anti-Hypertensive Medication

This study provided detailed follow-up data on blood pressure recording, upper-to-lower limb gradients, and need for antihypertensive medication. Forty-two

percent of patients still had a systolic blood pressure above the 95th centile and 23% above the 99th centile at time of discharge. Although this is slightly higher than expected, the incidence of a residual upper-to-lower limb blood pressure gradient in excess of 20 mm Hg was only 9%, which is similar to the 5% recently reported by Qureshi et al. [6]. The percentage of patients and intermediate or long-term follow-up with a blood pressure gradient of less than 20 mm Hg was 87–90%, which again, compares well with the 77–87% that has been reported after balloon angioplasty or surgical therapy [14,20,21]. It may appear unusual that more patients required anti-hypertensive medication at the time of discharge, when compared with before the procedure, especially when considering a lower percentage of hypertensive patients. However, many operators use  $\beta$ -blockers temporarily after stent implantation to protect the freshly dilated aorta from hypertensive stress with exercise or during activity. Whether this practice may reduce the incidence of early aneurysms or expansion of small dissections is unclear. However, even though there is no evidence to support this, it has been a protocol in several of the centers participating in this study, and the treatment is usually continued for a variable period of time between 1 and 12 months.

Our study documented a significant decline in resting hypertension over the follow-up period. This was more pronounced between discharge and intermediate follow-up when compared with intermediate and long-term follow-up. We suspect that those patients who remain hypertensive at intermediate follow-up are likely to reflect a cohort that will continue to retain a tendency for hypertension, irrespective of the anatomical result. Even though resting hypertension is important, this alone may fall short of identifying patient that may have normal resting blood pressure, but who have a residual gradient across the coarctation leading to significant hypertension with exercise. This is particularly important after stent implantation, as the reduced compliance of the stented aorta may negatively impact upon the blood pressure response to exercise. The exact long-term consequences of reduced elasticity and compliance in a stented aorta and its comparison with surgical scarring are unclear at this stage.

With exercise studies being not included in this study, even a small residual upper-to-lower limb blood pressure gradient may identify those patients who are more likely to develop an even higher gradient (and hypertension) with exercise, albeit this being purely speculative. Interestingly, the percentage of patients with a resting upper limb to lower limb blood pressure gradient of more than 20 mm Hg did not change significantly from discharge (9%) to long-term follow-up

(9%). The need for antihypertensive medication at intermediate and long-term follow-up was 45% and 32%, respectively, which is higher than the 11–33% reported in the literature following stent placement [9,12]. Surgical series have reported need for long-term antihypertensive medication at about 25% [14,22].

### Stents Covering Head and Neck Vessels

Stents overlapped brachiocephalic vessels in 13% of procedures. Although this is common practice among many interventional cardiologists, a concern remains whether this may lead to an increased likelihood of thromboembolism or stenosis. This is specifically important when a stent crosses the carotid artery. Not only can neointimal proliferation potentially narrow the carotid origin but also thromboembolism of even a small clot may have a detrimental result. Holzer et al. reported on stenting of complex aortic arch obstructions and identified no neurological complication of this practice [23]. However, follow-up of these patients is limited and more detailed imaging is often unavailable to detect any potential problems. As such, maintaining patients on aspirin indefinitely may be important when a side branch is crossed. Whenever possible, an open cell-design stent may be the better stent for these patients, as it allows opening the meshwork to the side branches.

Even though this study suggested that procedural success may be lower when the coarctation involved the transverse arch or was of complex type, it is important to emphasize that other studies have shown that treatment of even complex arch obstructions can be performed safely with a good result [23].

### Limitation

This study has several limitations. First and foremost, treatment selection as compared with other treatment alternatives was not randomized, and as such patient selection for stent implantation may be subject to operator and institutional bias. Case capture from participating institutions is incomplete, and therefore, it is unclear how the submitted data relates to the overall number of procedures performed at participating institutions. Follow-up data was incomplete; overall, ~50% of patients had complete follow-up data available. In particular, long-term follow-up was very limited with data available on only 21% of eligible patients. This limited long-term follow-up may have introduced significant and unpredictable bias into our results.

Although data was checked for inconsistencies, and included a randomized audit using source documentation, it is conceivable that there may still be data fields with erroneous data entry. In spite of efforts to obtain

all information from participating centers, we were unable to complete data that was not obtained during the clinical contact (such as blood pressures not recorded during a clinic visit). However, this affected only a small percentage of data fields. Finally, even though this registry represents the largest study to date on stent implantation for aortic coarctation, the incidence of adverse events, aortic wall complications, and stent migration was fairly low, limiting our statistical power to identify predictors of these outcomes.

## CONCLUSIONS

This study is the largest series reported to date on stent implantation for aortic coarctation. It is the only prospective series that collected data on stent implantation for aortic coarctation, as well as other treatment strategies and includes intermediate as well as long-term follow-up with integrated imaging provided by catheterization, CT, or MRI. With a long-term procedural success of 77%, and an incidence of aortic wall complications of 1.3%, and a need for unplanned reintervention of 4%, the results of stent implantation compare well with other surgical and interventional series. On the basis of the data of this study, operators should aim for an immediate postprocedural gradient reduction to less than 20 mm Hg. Longer term follow-up is needed to draw further conclusions from this data.

## Participating Institutions and Investigators

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