Endovascular stenting for aortic (re)coarctation in adults

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Objectives. Stenting for native and recurrent coarctation (COA) in adults has become an important therapeutic strategy. In this prospective observational study we evaluated the intermediate-term outcome of stent implantation for either native or recurrent (re)COA in adults.

Methods. All adults who underwent stent implantation in our institution between January 2003 and December 2008 were included. Diagnosis of (re)COA was based upon a combination of clinical signs, noninvasive imaging or invasive gradient measurements. NuMED stents were implanted under general anaesthesia.

Results. Twenty-four patients (50% male) underwent stent implantation for native (n=6) or reCOA (n=18) at a median age of 36 (18 to 60) years. There was significant improvement in pre- versus post-stent invasive systolic gradient (19 vs. 0 mmHg, $p<0.001$) and COA diameter (10 vs. 16 mm, $p<0.001$). Acute complications (12.5%) included death due to aortic rupture despite immediate successful coverage with a covered stent (n=1) and groin haemato-

ma (n=2). During a median follow-up period of 33 (8 to 77) months (n=22), late complications occurred in three patients (13.6%): stent migration to the ascending aorta (n=1), pseudoaneurysm at the site of the initial stent (n=1), and occluded external iliac artery (n=1). Stent implantation did not reduce the need for anti-hypertensive medication or blood pressure at last follow-up.

Conclusion. COA stenting results in a significant gradient decrease and increase in vessel diameter. However, serious complications do occur and hypertension remains in the majority of patients. (Neth Heart J 2010;18:430-6.)

Keywords: Congenital Heart Disease; Aortic Coarctation; Catheter Intervention

Over the past 15 years endovascular treatment of native aortic coarctation (COA) and recurrent COA (reCOA) has gained widespread acceptance in older children and adolescents.^{1,2} In analogy of coronary angioplasty, there has been a shift in the interventional treatment of COA from balloon angioplasty to balloon expandable intravascular stent placement.³⁻¹¹ Although the acute haemodynamic improvements are well known, there are concerns about aortic rupture, especially in patients with native COA. In the longer term, pseudoaneurysm formation and reCOA may occur.^{12,13} In our institution stent implantation for COA was started in 2003. This prospective, single-centre, observational study reports the acute and intermediate results in adult patients who underwent endovascular stent placement for both native COA and reCOA.

Patients and Methods

Study population

Between January 2003 and December 2008, a total of 24 adult patients received endovascular stent implantation for (re)COA. Diagnosis of (re)COA was based upon a combination of clinical signs (arm-leg blood pressure (BP) difference ≥ 20 mmHg), non-

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invasive imaging (echocardiography, CT scan or MRI) and/or invasive gradient measurements. The choice for stent implantation was made by a team of cardiac surgeons, interventional cardiologists and cardiologists specialised in adult congenital heart disease. In our institution there is a tendency to opt for surgical treatment in patients with native COA, unless specific conditions in the patient, such as pregnancy, exist. In reCOA, stenting is the preferred choice.

Intervention

All procedures were performed under general anaesthesia and full heparinisation. Retrograde aortic catheterisation was performed. The peak systolic gradient was measured invasively before and after stent implantation. Biplane aortography was performed for optimal delineation of the stenosis, including measurements of the distal arch before the narrowing, the stenosis and the descending aorta. The procedure was considered successful if the systolic gradient was reduced to ≤ 10 mmHg and/or the angiographic diameter had increased $\geq 50\%$. A covered or bare CP stent (NuMED CP stent, Heart Medical Europe BV, Best, the Netherlands) was hand crimped on a balloon (Balloon-in-Balloon, NuMED Inc, Heart Medical Europe BV, Best, the Netherlands). The balloon-stent assembly was advanced through a long 11 to 14 F sheath (William Cook Europe, Bjaeverskov, Denmark). The inner balloon was inflated, and with angiographic control through the long sheath, the stent position could be adjusted before the outer balloon was inflated. Control angiography and pressure measurements were performed. When a waist persisted and the residual gradient was significant, further dilatation with a high pressure balloon (Zymed or Mullins NuMED, Heart Medical Europe BV, Best, the Netherlands) was performed. At final angiography special attention was given to possible signs of dissection. After the intervention, patients received acetylsalicylic acid for six months.

Follow-up

All patients were scheduled for echocardiography, 24-hour ambulatory blood pressure monitoring (ABPM) and CT scan or MRI during clinical follow-up. Echocardiographic Doppler study was performed to evaluate left ventricular function and flow velocity over the distal arch. A possible reCOA was diagnosed by a diastolic run-off on echocardiography. Ventricular function was evaluated as good, moderate or poor. Twenty-four hour ABPM was measured on the right arm (Spacelabs Healthcare, Buck, UK). Recordings were performed every 30 minutes during the daytime (07.00 to 22.00 hours) and every 60 minutes during the night (22.00 to 07.00 hours). The monitor display was switched off during ABPM to avoid possible

impact on the BP readings. Hypertension was defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg. Either a CT scan or MRI was performed to document arch morphology and to demonstrate possible pseudoaneurysm formation during follow-up.

Statistics

Normally distributed continuous data are presented as mean $\pm$ standard deviation (SD) and nominal variables as counts and/or percentages. Non-normal distributed continuous data are presented as median and ranges. The (paired) Student's *t* test was used for continuous variables, when normally distributed. In case of skewed distributed data, the Wilcoxon signed-rank was considered for paired observations and the Mann-Whitney *U* test for unpaired observations. Unpaired nominal variables were analysed using the Fisher's exact test. All statistical tests were two-sided and a *p* value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS 15.0 for Windows (SPSS, Chicago, Ill, USA).

Results

Study population

Between January 2003 and December 2008, 24 patients were diagnosed with native COA (25%) or reCOA (75%) and accepted for endovascular stent implantation at our institution (table 1). Three patients with repaired COA had previously been treated with endovascular balloon angioplasty for reCOA. One patient was diagnosed with a native COA at nine weeks' gestation and very high blood pressure in the upper extremities. She underwent a two-step approach; a stent implantation at 12 weeks gestation and additional stent dilatation six months after delivery. Other patients who underwent stent implantation for native COA had a history of multiple cardiac operations ($n=3$), mental retardation ($n=1$) and Turner's syndrome ($n=1$).

Procedural characteristics

A total of 25 stents were implanted. Procedural characteristics are shown in table 2. In one patient a second covered stent was placed immediately after the bare stent to treat aortic rupture. The median invasively measured systolic gradient decreased significantly ($p < 0.001$, figure 1A) and reduced to ≤ 10 mmHg in 21 patients (88%, 5 native COA, 16 reCOA). The diameter of the distal aortic arch was 17 ± 3 mm, the distal aorta 20 ± 4 mm. The median minimum diameter at the side of the COA increased significantly from 10 (2 to 17) to 16 (10 to 28) mm ($p < 0.001$, figure 1B). An increase in diameter of $\geq 50\%$ after the procedure was seen in 15 patients (65%, all reCOA). The procedure was considered successful in 22 patients (92%, 6 native COA, 16 reCOA).

Table 1. Baseline patient characteristics.

	All patients (n=24)	Native COA (n=6)	ReCOA (n=18)
Age (years)	35±13	28±9	38±13
Gender (male)	12 (50)	4 (67)	8 (44)
BMI (kg/m ²)	24±4	24±6	24±4
Antihypertensive treatment	18 (75)	3 (50)	15 (83)
Previous repair type			
- End-to-end anastomosis	13	-	13
- Subclavian flap	3	-	3
- Graft interposition	1	-	1
- Patch angioplasty	1	-	1
Associated cardiac anomalies			
- Bicuspid aortic valve	7	3	4
- Aortic valve stenosis	5	1	4
- Ventricular septal defect	4	1	3
- Patent arterial duct	2	0	2
- Aortic regurgitation	2	2	0
- Mitral valve insufficiency	2	1	1
- Atrioventricular septal defect	1	1	0
- Discrete subaortic stenosis	1	1	0
- Tricuspid valve insufficiency	1	0	1
- None	6 (25)	0 (0)	6 (33)
Associated comorbidities			
- Turner's syndrome	2	1	1
- Mohr's syndrome	1	1	0

BMI=body mass index, COA=aortic coarctation, reCOA=recurrent aortic coarctation. Values are expressed as mean ± SD for continuous variables and numbers (percentages) for dichotomous variables. There are no significant differences between the native COA and reCOA group concerning age, gender, BMI and antihypertensive treatment.

Table 2. Procedural characteristics.

	All patients (n=24)	Native COA (n=6)	ReCOA (n=18)
Stent length (mm)	45 (34-45)	42 (34-45)	45 (34-45)
Balloon size (mm)	18 (12-24)	18 (12-24)	18 (14-22)
Covered	6 (25)	1 (17)	5 (28)
Invasive gradient (mmHg)			
- Pre-stent	19 (6-50)	25 (18-30)	17 (10-50)
- Post-stent	0 (0-35)*	1 (0-11)*	0 (0-35)*
Diameter lesion (mm)			
- Pre-stent	10 (2-17)	9 (2-17)	10 (7-15)
- Post-stent	16 (10-28)*	17 (10-28)*	16 (12-19)*
Diameter increase (%)	58 (20-400)	86 (58-400)	50 (20-99)†

COA=aortic coarctation, reCOA=recurrent aortic coarctation. Values are expressed as median (ranges) for continuous variables and number (percentages) for dichotomous variables. * p<0.05 vs. pre-stent, † p<0.05 vs. native COA.

Figure 1. A) Invasively measured peak systolic gradient before and after stent implantation. B) Minimum diameter at the side of the lesion before and after stent implantation. Box plots indicate the median, interquartile ranges, highest and lowest values; * $p < 0.001$ vs. pre-stent.

Table 3. Echocardiographic follow-up.

	All patients (n=24)	Native COA (n=6)	ReCOA (n=18)
Peak systolic velocity (proximal of lesion, m/s)			
- Pre-stent	1.3±0.5	1.2±0.2	1.3±0.4
- Post-stent	1.2±0.3	1.5±0.1	1.3±0.3†
Peak systolic velocity (maximum, m/s)			
- Pre-stent	3.6±0.6	3.6±0.7	3.6±0.6
- Post-stent	2.4±0.7*	2.0±0.4*	2.3±0.7*
Diastolic run-off (%)			
- Pre-stent	67	75	65
- Post-stent	15*	17	14*
Left ventricular function (%)			
- Pre-stent			
- Good	79	50	89
- Moderate	14	17	-
- Poor	17	33	11
- Post-stent			
- Good	90	67	100†
- Moderate	10	33	-
- Poor	-	-	-

COA=aortic coarctation, reCOA=recurrent aortic coarctation. Values are expressed as mean ± SD for continuous variables and percentages for dichotomous variables. * $p < 0.05$ vs. pre-stent, † $p < 0.05$ vs. native COA.

Acute complications

One major complication occurred in a patient with reCOA in whom the aorta ruptured. Despite immediate successful placement with a covered stent, the clinical condition remained critical due to an unexplained massive pulmonary haemorrhage into the left main bronchus, which, despite selective ventilation of the right lung, could not be controlled and the patient died the same day. Postmortem examination excluded an aortic bronchial fistula as possible cause for the bleeding. Two other patients developed a groin haematoma after the procedure.

Follow-up

During a median follow-up period of 33 (range 8 to 77) months, data were collected for 22 patients. Echocardiographic follow-up was collected in 20 (91%) patients, 28 (2 to 77) months after implantation (table 3). Maximum peak systolic velocity, measured at the side of the lesion, decreased from 3.6 ± 0.6 to 2.4 ± 0.7 m/s and no differences were found between the native vs. reCOA group. The percentage of patients with a diastolic run-off decreased from 67 to 15%. Left ventricular function improved slightly after the procedure (not significant).

Additional imaging by CT scan or MRI was obtained in 20 patients (91%) at a median follow-up of eight (0.3 to 33) months. No pseudoaneurysm or dissection was found. Late complications occurred in three patients (13.6%, all reCOA). One patient had a stent migration to the ascending aorta 18 months after the procedure which was identified by echocardiography and confirmed by a CT scan. This was treated by surgical correction of the aortic arch by means of graft interposition. The second patient had drug-resistant hypertension and a pseudoaneurysm was discovered during a diagnostic angiography for assessment of the invasive gradient over the stent. This was treated by a covered stent. One patient with groin haematoma after the index procedure was diagnosed with an occluded external iliac artery and neurological symptoms of the right leg. The occlusion was opened by urokinase treatment followed by iliac stent placement.

Blood pressure results are shown in table 4. Before stenting, 19 patients (79%) were hypertensive and 18 (75%) were treated with antihypertensive agents. After a median follow-up of 27 (1 to 65) months, BP data were available for 22 patients. A small decrease in BP was observed (not significant) and 14 patients (67%) were treated

Table 4. Blood pressure.

	All patients (n=24)	Native COA (n=6)	ReCOA (n=18)
BP systolic (mmHg)			
- Pre-stent	162±22	160±18	162±23
- Post-stent	154±12	157±12	153±13
BP diastolic (mmHg)			
- Pre-stent	84±16	87±26	82±12
- Post-stent	80±9	88±6	77±8†
Arm-to-leg gradient (mmHg)			
- Pre-stent	23 (0-54)	12 (3-21)	27 (0-54)
- Post-stent	0 (0-44)	0 (0-21)	0 (0-44)
Hypertension (%)			
- Pre-stent	79	63	78
- Post-stent	82	83	81
Use of antihypertensive medication (%)			
- Pre-stent	75	50	83
- Post-stent	67	67	67
Post-stent 24-hour ABPM (mmHg)			
- Daytime	135 (±23)/79(±10)	133 (±19)/81 (±8)	135 (±25)/78 (±11)
- Night-time	121 (± 21)/68 (±10)	119 (±23)/68 (±9)	121 (±21)/68 (±11)
- 24-hour	130 (±22)/75 (±10)	129 (±19)/77 (±7)	129 (±23)/74 (±11)

ABPM=ambulatory blood pressure monitoring, BP=blood pressure, COA=aortic coarctation, reCOA=recurrent aortic coarctation. Values are expressed as mean ± SD or median (ranges) for continuous variables and percentages for dichotomous variables. † p<0.05 vs. native COA.

with antihypertensive drugs. There was a trend ($p=0.066$) towards a decreased median arm-to-leg BP gradient after stent implantation. Twenty patients also underwent 24-hour ABPM, 15 (6 to 44) months after the procedure. Seven patients (35%) with 24-hour ABPM were hypertensive during daytime measurements. No BP differences were found between the native COA and reCOA group, except a lower diastolic BP in the reCOA group after stent placement ($p=0.038$).

Discussion

In this study we report our six years of experience with stent implantation for native COA and reCOA in adults. Several studies about stent implantations for COA have been published in the past two decades.³⁻¹⁰ Some conclude that, in a selected patient group, stent implantation is feasible, safe and an effective alternative to balloon angioplasty or surgery.^{6,7,10-12} Others describe very promising results regarding BP reduction, but only after short-term follow-up.⁸ Since hypertension is a main determinant of cardiovascular morbidity and mortality in patients with repaired COA,^{14,15} BP reduction is a major goal in this population. Stenting was successful in all but two patients. In addition, the arm-to-leg systolic gradient fell sufficiently. These findings both point to a good relief of the obstruction; however, we found only a small decrease in upper body systolic BP after stenting (not significant). Our data parallel other reports that hypertension may persist after COA stenting in adult life, probably due to structural and functional abnormalities of the arterial wall, which can result in diminished arterial wall compliance and increased rigidity.¹⁶⁻²⁰ Our study confirms that COA is not only a located narrowing of the aorta, but indeed a systemic cardiovascular disease.¹³

COA stenting may result in serious complications, as illustrated in our series. We observed three major complications: fatal vessel rupture, pseudoaneurysm formation during follow-up and stent migration. Vascular complications have been reported in the literature.²¹ The most common complication described is pseudoaneurysm formation occurring in 0 to 11%.^{5,11,22} The use of a covered stent as primary choice remains somewhat controversial.²³ It aims to prevent pseudoaneurysm formation; however, it may result in unwanted occlusion of side branches, also when it has to be deployed in the descending aorta after accidental embolisation. Whether the fatal outcome in the patient with vessel rupture could have been prevented by using a covered stent is unclear. Deployment of a covered stent within the bare stent proved effective on angiographic control, but due to secondary pulmonary haemorrhage with severe respiratory failure the clinical outcome was dramatic. Direct availability of covered stents in the catheterisation laboratory is a prerequisite for inter-

ventional treatment of COA. Distal stent migration or embolisation has also been described before.²¹ It is usually managed by positioning the stent lower in the descending aorta. Proximal migration of the stent has not been described to our knowledge. Surgical removal of the stent with arch reconstruction was even more imminent, because during surgery an ulceration of the ascending aortic wall due to the stent was found. This case illustrates the wide variety in aortic arch morphology in these patients. The balloon expandable stents that are available at present are all closed cell types that adapt poorly to curved vessels. Newer stents should be developed to overcome this problem. The patient with delayed pseudoaneurysm formation underlines the need for CT scan or MRI during follow-up. In the one patient in whom the pseudoaneurysm occurred, this could be successfully treated with a covered self-expanding stent.

Some limitations have to be noted about this study. Only a small number of patients have undergone stent implantation since we started this procedure in 2003. Furthermore, our population included both native and reCOA. Third, this was a single-centre report and patients were not compared with surgery or balloon angioplasty alone. Finally, 24-hour BP monitoring before stenting was not performed in the majority of the patients. Post-stent 24-hour ABPM is therefore difficult to translate in terms of BP reduction.

Conclusion

(Re)COA stenting in adults results in significant gradient decrease and increase in vessel diameter. However, serious complications do occur and hypertension remains in the majority of patients. Large studies comparing surgical techniques, ballooning or ballooning with stent placement are warranted.

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