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Original Article

Mid-term effects of implanting stents for relief of aortic recoarctation on systemic hypertension, carotid mechanical properties, intimal medial thickness and reflection of the pulse wave

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Abstract *Objective:* Primary implantation of stents is an accepted technique for treating aortic recoarctation, albeit that the effects of stenting on pressure profiles, carotid mechanical properties, intimal medial thickness, and reflection of the pulse wave have not been systematically investigated. *Methods:* Over the period from 1 January, 1999, to 31 December, 2002, we implanted stents to relieve aortic recoarctation in 15 patients, with a median age of 17 years, and a range from 7 to 29 years, with a median weight of 56 kilograms, ranging from 20 to 96 kilograms. Indications were a gradient of 20 millimetres of mercury or more measured in all, systemic hypertension at rest in 8, and systemic hypertension at exercise in all. Of the patients, 5 were receiving anti-hypertensive treatment. Before implantation of the stents, and after a mean follow-up of 22 months, all patients underwent an exercise test, vascular echography, and examination of the common carotid artery so as to determine its cross sectional compliance and distensibility, and the augmentation index. *Results:* The stents were implanted successfully in all patients. The mean gradient was reduced from 27 to 4 millimetres of mercury ($p < 0.001$). Systolic blood pressure at rest diminished from 140 to 131 millimetres of mercury ($p = 0.04$), while hypertension at rest regressed in 4 patients. Systolic blood pressure at exercise diminished from 245 to 222 millimetres of mercury ($p = 0.018$), and hypertension at exercise regressed in 1 patient. Anti-hypertensive treatment is still required for 4 patients. A correlation was found between systolic blood pressure at rest and initial peak-to-peak gradient ($r = 0.8$), and between initial gradient and percentage reduction of systolic blood pressure at rest at follow-up ($r = -0.73$). Compliance and distensibility of the common carotid artery were not significantly modified, albeit that the intimal medial thickness diminished from 0.64 to 0.57 millimetres ($p = 0.04$), and the augmentation index decreased from 5 to -1 ($p = 0.012$). *Conclusions:* Primary implantation of stents is effective in mid-term repair of aortic recoarctation. Although there is an improvement in systemic hypertension, the tensional profile and vascular sonography are not normalized. At long term follow-up, the suppression of an early reflection site of the pulse wave could decrease the wall stress of the great elastic vessels, reducing the thickness of the arterial walls.

Keywords: Aortic coarctation; balloon dilatation; stent; exercise test

After first being trialled in an experimental model,[1] stenting is now considered the elective treatment for recoarctation of the aorta in adolescents and adults.[2] More recently, some have advocated primary stenting of the aortic isthmus.[2,3] This has potential advantages over balloon dilation, carrying a lower incidence of recoarctation, providing a theoretical lower incidence of dissection or tearing of the aortic wall, and thus diminishing the risk of formation of aneurysm.[4]

Immediate results of implantation of stents are generally good,[2–7] although concern exists regarding

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Table 1. Previous surgery and interventions.

N	Diagnosis	First surgery (age)	Second surgery (age)	Previous catheter interventions (age)
1	Aortic coarctation	Direct suture (4 years)		None
2	Aortic coarctation and VSD	Extended reconstruction and VSD closure (10 days)		None
3	Aortic coarctation and VSD	Direct suture and PB (12 days)	Direct suture and de-banding (1 year)	None
4	Aortic coarctation	Direct suture (5 days)		BA (4 months)
5	Aortic coarctation	Extended reconstruction (2 months)		None
6	Aortic coarctation	Direct suture (2 years)		None
7	Aortic coarctation	Extended reconstruction (2 years)		None
8	Aortic coarctation	Extended reconstruction (1.5 years)		None
9	TGA, aortic coarctation, VSD	Extended reconstruction, ASO, VSD closure (15 days)		BA (8 years)
10	Aortic coarctation	Extended reconstruction (3 years)		None
11	Aortic coarctation and VSD	Direct suture and PB (3 months)	VSD closure, de-banding (2 years)	None
12	Aortic coarctation and VSD	Extended reconstruction and PB (3 months)	Direct suture and de-banding (2.5 years)	None
13	Aortic coarctation	Synthetic patch (11 years)	Direct suture (19 years)	None
14	Aortic coarctation	Extended reconstruction (14 years)		None
15	Aortic coarctation	Extended reconstruction (10 days)		Pulmonary BA (1 day)

Abbreviations: VSD: ventricular septal defect; TGA: transposition (concordant atrioventricular and discordant ventriculo-arterial connections); PB: banding of the pulmonary trunk; ASO: arterial switch operation; BA: balloon angioplasty

the results over the long term.[2,8] In particular, there has been no systematic examination of the effects of stenting on the profiles of the systemic blood pressure, the mechanical properties or intimal medial thickness of the elastic arteries, and the reflection of the pulse wave. With these deficiencies in mind, we aimed to investigate the mid-term results of implantation of stents for relief of aortic recoarctation in a series of 15 consecutive patients, measuring systemic blood pressure at rest and at exercise. We also performed sonography of the common carotid artery in order to determine its cross sectional compliance and distensibility, and the augmentation index.

Patients and methods

From 1 January, 1999 through 31 December, 2002, we inserted stents for relief of aortic recoarctation in 15 consecutive patients, aged from 7 to 29 years, with a mean age of 17 years, and weighing from 20 to 96 kilograms, with a median weight of 56 kilograms. The diagnoses, along with previous surgical and interventional treatments, are illustrated in Table 1. Their characteristics before and after implantation of the stents are illustrated in Table 2.

The indications for intervention were a gradient of at least 20 millimetres of mercury in all, systemic hypertension at rest in 8, and severe systemic hypertension at exercise in all. Of the patients, 5 required anti-hypertensive treatment.

We performed an exercise test in all on a stationary cycle, following the protocol of Bruce.[9] All patients were assessed by the same investigator, who, had not been blinded to the results of stenting. We interrupted the exercise test if systolic blood pressure exceeded 270 millimetres of mercury, or if the patients claimed of claudication of the legs.

We evaluated the maximal work load, the maximal heart rate, and systolic and diastolic blood pressures at rest and at exercise. Systolic hypertension was defined as systolic blood pressure above the 95th percentile for patients of the same age and sex.

Vascular studies were performed by the same investigator. Having measured the diameter and cross-sectional area of the common carotid artery, we calculated[10] compliance and distensibility from the changes in diameter during systole, and from simultaneously measured pulse pressure, according to the formulas:

- cross-sectional compliance equals $\pi(sD^2 - dD^2)/4\Delta P$
- cross-sectional distensibility equals $(sD^2 - dD^2)/(dD^2 \cdot \Delta P)$.

Having also captured the waveform of the carotid pulse, we were also able to determine the reflection of the pulse wave reflection. We then defined an augmentation index as the ratio of the pulse pressure divided by the difference between reflected wave and systolic peak pressure (PP), according to the following formula

- Augmentation index equals $\Delta P/PP$.

The technique used for stenting remained unchanged during the period of study, following the method

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Table 2. Characteristics of the patients before and after implantation of stents.

N	Age (years)	Weight (kilograms)	Hypoplasia of the transverse arch	Upper/inferior limb gradient (millimetres of mercury)	Drug treatment before stenting	Initial peak to peak gradient (millimetres of mercury)	Final peak to peak gradient (millimetres of mercury)	Drug treatment after stenting
1	14	75	No	20	ACE inhibitors	25	0	ACE inhibitors
2	14	56	No	20	None	20	0	None
3	21	68	No	50	Beta blockers	65	0	None
4	7	20	Yes	95	None	90	25	None
5	21	68	No	40	None	30	0	None
6	23	65	No	20	None	15	0	None
7	25	66	Yes	50	ARA	20	0	ARA
8	13	50	No	20	None	20	0	None
9	8	31	Yes	25	ARA	20	10	ARA
10	20	72	Yes	40	None	30	0	None
11	29	70	Yes	30	None	20	0	None
12	27	62	Yes	40	None	35	10	None
13	19	56	No	20	None	15	5	None
14	15	96	Yes	40	None	35	10	None
15	15	49	Yes	20	Beta blockers	20	5	Beta blockers

Abbreviation: ARA: angiotensin receptor antagonist

described by Bulbul et al.[11] General anaesthesia was used in all patients. After administration of heparin at 100 international units per kilogram, the site of recoarctation was crossed in retrograde fashion. The peak-to-peak gradient was recorded on pullback, and an aortogram was performed and imaged in lateral or left oblique views. The diameter of the aorta was measured proximal to and at the level of the site of recoarctation. A long sheath was advanced over a guide wire across the site of coarctation, positioning the tip of the wire in the right subclavian artery. We implanted 16 Palmaz stents (4014, 308 or 188, Johnson & Johnson Interventional System, Sommerville, New Jersey) in 15 patients, crimping the stents onto a BiB balloon catheter (Numed, Hopkinton, USA). We chose the diameter of the balloons to be at least twice the diameter of the site of coarctation, and not larger than the aortic diameter proximal to the site of coarctation. The inner balloon was inflated first, the position of the stent being checked by making a hand injection of contrast through the delivery sheath. The outer balloon was then inflated to expand the stent to the desired diameter, and both balloons were eventually deflated. Haemodynamic measurements, and angiography, were repeated at the end of the procedure. The patients continued to receive heparin for 24 hours, and antiplatelet therapy with aspirin for 6 months.

Statistical analysis

Age and weight were recorded as median and a range. Continuous variables were presented as the mean plus or minus the standard deviation. Comparison for individual parameters before and after stenting was performed using the two-tailed paired t test. A p value of less than 0.05 was considered statistically significant. Linear regression analysis was done using the correlation coefficient r.

Results

The stents were implanted successfully in all subjects, success being judged by a reduction in the peak-to-peak gradient of at least half. A significant decrease of the pressure gradient was obtained, values falling from 27 plus or minus 10 to 4 plus or minus 5 millimetres of mercury ($p < 0.001$). No patient had acute hypertensive crises immediately after implantation of a stent. A limited dissection of the aortic wall occurred in our 13th patient, while the first stent implanted migrated proximally in our 14th patient, in whom a second stent was implanted.

At a mean follow-up of 22 plus or minus 11 months, all patients underwent clinical and sonographic re-evaluation and exercise testing. As revealed by cross-sectional trans-thoracic sonography, all patients showed a regular aortic isthmus, with colour flow mapping showing laminar flow through the stent.

Of the patients, 12 completed a maximal exercise test, but the test was interrupted in 1 because of claudication of the legs, and in 2 because systolic blood pressures exceeded 270 millimetres of mercury. Table 3 illustrates the results of exercise testing. Systolic blood pressure at rest diminished from 140 plus or minus 15 to 131 plus or minus 7 millimetres of mercury ($p = 0.04$), and systolic blood pressure at exercise diminished from 245 plus or minus 2 to 222 plus or minus 25 millimetres of mercury ($p = 0.018$). Systemic hypertension persisted in 4 patients at rest,

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Table 3. Results of exercise test: systolic blood pressure before and after aortic stenting.

N	Systolic blood pressure at rest before stenting (millimetres of mercury)	Systolic blood pressure at exercise before stenting (millimetres of mercury)	Systolic blood pressure at rest after stenting (millimetres of mercury)	Systolic blood pressure at exercise after stenting (millimetres of mercury)
1	120	260	125	260
2	130	265	120	215
3	170	220	130	195
4	139	244	130	170
5	150	270	130	210
6	155	265	125	190
7	138	243	150	230
8	130	245	135	250
9	125	210	120	200
10	160	250	140	240
11	130	220	132	222
12	150	260	130	200
13	130	230	140	235
14	140	245	140	270
15	125	240	125	240

while 9 had mild, and 5 severe, systemic hypertension at exercise. The systolic hypertension at exercise regressed in only 1 patient, and 4 patients continued to require anti-hypertensive treatment.

A positive correlation was found between systolic blood pressure at rest and the initial peak-to-peak gradient ($r = 0.8$), and between the initial peak-to-peak gradient and the proportional reduction of systolic blood pressure at rest at follow-up ($r = -0.73$). No correlation at follow-up was found between systolic blood pressure at exercise and the initial gradient, nor between the initial gradient and the proportional reduction of systolic blood pressure at exercise.

Cross-sectional compliance and distensibility of the carotid arteries were not significantly different compared with the initial values, varying from 0.11 plus or minus 0.036 to 0.14 plus or minus 0.08 ($p = 0.13$), and from 0.5×10^{-2} plus or minus 0.1 to 1.2×10^{-2} plus or minus 0.2 millimetres of mercury $\times 10^{-2}$ ($p = 0.19$). The intimal medial thickness decreased from 0.63 plus or minus 0.07 to 0.58 plus or minus 0.08 millimetres ($p = 0.04$), albeit that the mural thickness remained greater than the normal value in all patients. The augmentation index decreased from 5 plus or minus 8 per cent to −1 plus or minus 11 per cent ($p = 0.012$). No correlation was found between haemodynamic values either before or after implantation of the stents and the intimal medial thickness or the augmentation index.

Discussion

Recoarctation is frequent after surgical repair of coarctation of the aorta.[12] It can be treated surgically, by balloon dilation, or by stenting. Stenting is now considered the elective technique in adolescents and adults,[2,3,5–8] having been shown to be superior to simple dilation in providing relief of the gradient.[5,6,8] Primary stenting has also recently been introduced in the clinical practice, with the aim of reducing the incidence of aortic dissection, cerebrovascular accidents and aneurysmal formation, all often caused by dilation of the coarcted segment with balloons.[7] Its immediate results are usually excellent, although rupture or dissection have been occasionally reported.[13] The results over the medium term of either primary stenting or stenting for aortic recoarctation, however, are not available in large series of patients, albeit that the reported data generally show a persistently good anatomical result, without any residual gradient.[3,7,8]

Although major attention is paid to the morphologic and haemodynamic results of implantation of aortic stents,[5–8] changes in the profile of the systemic blood pressure have not, to the best of our knowledge, been systematically investigated. Systolic hypertension at rest has been shown to regress in a variable percentage of patients,[7,8,14] with Harrison et al.[7] reporting that persistent systemic hypertension is less frequent after implantation of stents than after simple balloon dilation. In their series, these authors reported a regression of systemic hypertension at rest in 19 out of 26 patients, although all the patients treated by stenting did not undergo an exercise test. Magee et al.[8] reported that 9 out of 17 patients did not need medical treatment after implantation of stents, although the measurements of systemic blood pressure were taken with the patients supine during visits to the outpatient clinic.

The impact of the repair of coarctation on arterial blood pressure has been systematically studied only in patients undergoing surgery.[15] After surgery, up to one-third of patients continue to have systemic hypertension at rest, while a further third have an abnormal response to exercise.[12,15–17] Systolic blood pressure is significantly higher in patients having had successful treatment of coarctation than in controls.[18] Some authors underlined the need for long term surveillance of patients after surgery for coarctation. Follow-up is recommended to include exercise testing so as to identify those patients with potential hypertension.[15] Various authors[12,16] have also shown that age at operation, systemic blood pressure at the first postoperative visit, and paradoxical hypertension at operative repair all predict the results of surgery for coarctation. In addition, age at operation has been shown to be the only incremental risk factor for recoarctation, late hypertension, and premature death.[17] In our series, we were able to confirm, at mid term follow-up, a good morphologic and haemodynamic result following primary stenting for aortic recoarctation. Systemic blood pressure was significantly diminished after implantation of the stents, either at rest or at exercise, although systemic hypertension persisted at rest in 4 patients, and at exercise in 14 patients. As yet, the determinants of regression of the systemic hypertension regression have not been identified.

Increased stiffness of the transverse aorta has been described in children and adolescents subsequent to repair of coarctation.[18] It has been suggested that the combination of a decrease in distensibility in the proximal arterial bed, and impaired function of the distal arterial bed, could account for the elevation of blood pressure seen at exercise in patients undergoing surgery.[18] Hypertension at exercise has also been shown to be more common after surgery in patients with hypoplasia of the transverse arch.[19,20] Of our patients, 8 had hypoplasia of the transverse arch, and among these, four continued to have hypertension at rest. Our limited number of patients, however, does not permit us to make conclusive inferences.

We showed that patients with higher peak-to-peak gradients at catheterisation had more severe systolic hypertension at rest. At follow-up, however, the higher was the initial gradient, the lower was the proportional decrease of systolic blood pressure at rest. Furthermore, we found no correlation between the peak-to-peak gradient and systolic blood pressure at exercise, neither before nor after aortic stenting. Thus, implantation of the stents generally abolishes the peak-to-peak gradient, but does not produce regression of systemic hypertension, at least at mid-term follow-up.

Our findings were coherent with the results of vascular sonography, which showed that dilation of the stenotic site had an effect on the reflection of the pulse wave, as well as on the intimal medial thickness of the carotid arteries, but that the intimal medial thickness never normalised. Thus, the good anatomic results of stenting induced a significant decrease of systolic blood pressure at rest, but did not change the mechanical parameters of the elastic arteries we analysed. The early return of the incident wave through a less compliant peripheral bed, associated with a poor distension at the isthmic level, could at least in part explain the higher systolic pressure at exercise.

Our findings confirm that aortic recoarctation is a systemic disease, inducing vascular remodelling, and that severe systemic hypertension is not likely to be reversed or improved by successful implantation of stents. Thus, early interventional and medical treatment of these patients could be recommended.

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