CLINICAL RESEARCH

Benefit of endovascular stenting for aortic coarctation on systemic hypertension in adults

Bénéfices d’un stenting cardiovasculaire dans la coarctation aortique chez des adultes hypertendus

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KEYWORDS
Aortic coarctation; Systemic hypertension; Coarctation stenting

Summary
Background. — Endovascular stenting is a recognised treatment strategy for aortic coarctation (CoA) in adults. We assessed systemic hypertension control and the need for antihypertensive therapy after CoA stenting in adults.

Methods. — Data were collected prospectively on 54 patients (36 men; mean age: 34 ± 16 years) who underwent endovascular stenting for CoA over a 7-year period. Five patients were excluded as they did not attend follow-up appointments. Patients underwent clinical examination, including right arm systolic blood pressure (SBP) and 24-hour ambulatory blood pressure monitoring at baseline, 6–12 weeks and 9–12 months.

Results. — There was a significant fall in mean peak-to-peak systolic gradient (PG) across the CoA after stenting (26 ± 11 mmHg vs. 5 ± 4 mmHg; P < 0.01). There were successive reductions in right arm SBP and ambulatory SBP at baseline, 6–12 weeks and 9–12 months post-procedure (right arm: 155 ± 18 mmHg vs. 137 ± 17 mmHg vs. 142 ± 16 mmHg, respectively; all P-values <0.01; ambulatory: 142 ± 14 mmHg vs. 132 ± 16 mmHg vs. 131 ± 15 mmHg, respectively; all P-values <0.01). Twenty-four patients had severe CoA (PG >25 mmHg before stenting); baseline

Abbreviations: AUC, area under the curve; CI, confidence interval; CoA, aortic coarctation; PG, peak-to-peak systolic gradient; ROC, receiver-operating characteristic; SBP, systolic blood pressure.

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SBP was significantly higher in severe versus non-severe patients (160 mmHg vs. 148 mmHg; \( P = 0.02 \)). The absolute reduction in PG after stenting was significantly higher in the severe group (31 \( \pm \) 7 mmHg vs. 14 \( \pm \) 5 mmHg; \( P < 0.0001 \)), but there was no significant difference in SBP between groups at 6–12 weeks (141 mmHg vs. 135 mmHg; \( P = 0.21 \)) or 9–12 months (139 mmHg vs. 139 mmHg; \( P = 0.96 \)).

**Conclusion.** — Endovascular stenting of CoA results in a significant reduction in SBP at 6–12 weeks, which is sustained at 9–12 months, with similar outcomes in severe and non-severe CoA groups.

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**Background**

Aortic coarctation (CoA) is a congenital narrowing of the upper descending thoracic aorta adjacent to the site of attachment of the ductus arteriosus (ligamentum arteriosum) [1]. CoA represents 5–10% of all congenital cardiac lesions [2]. CoA has a male predominance and has been associated with conditions that include gonadal dysgenesis (Turner’s syndrome), Shone’s complex, bicuspid aortic valve, intracranial aneurysms, patent ductus arteriosus, ventricular septal defect and mitral stenosis or regurgitation [1,3]. If left untreated, CoA is associated with high morbidity and mortality [4,5]. The first surgical repair for CoA was performed in 1945 [6]. Various surgical techniques were developed across age groups, including resection with end-to-end anastomosis, extended end-to-end anastomosis, end-to-side anastomosis, extra-anatomical bypass, tube graft replacement, patch augmentation and subclavian flap aortoplasty [1]. Surgical repair is performed depending on age of presentation, ranging from newborns to adults [7].
Patients can develop restenosis of the previously repaired CoA with the passage of time, because of fibrous scar tissue or residual ductal tissue contracting.

In 1982 [8], the first percutaneous balloon dilatation was successfully performed in an infant and, since then, has also been successfully performed in recurrent CoA [9–11]. While balloon dilatation showed promising results in the short-term, because of the elastic recoil properties of the aorta, restenosis was common, being reported in up to 20–30% of patients [10,11]. In 1991, O’Laughlin et al. [12] successfully used balloon-expandable endovascular stents, and this technique is currently an established management strategy in adults with CoA [13–16].

The main objectives of this study were to assess systemic hypertension outcomes and the need for antihypertensive therapy in adolescent and adult patients undergoing primary stenting for CoA.

Methods

Study population

The data were collected prospectively for 54 adolescent and adult patients who underwent transcatheter stenting of CoA over a 7-year period. These patients were followed up as part of a non-randomized observational protocol. Informed written consent was obtained from all patients before the stenting procedure, according to local guidelines. Patients were defined as being hypertensive if they had blood pressure readings (right upper limb) >140/90 mmHg on more than one occasion at rest [17]. Blood pressure was measured at 6–12 weeks and 9–12 months at clinical follow-up, and included outpatient ambulatory blood pressure monitoring. Clinical blood pressure was measured 10 minutes after arrival of the patient at the outpatient department, in an upright position in the right upper limb with an automated cuff.

Stent deployment technique

A single lead operator performed all procedures with either covered or uncovered stents, according to operator preference and angiographic findings. All procedures were performed under general anaesthesia. The covered stents used were the Cheatham Platinum (CP) stent (NuMED, Hopkinton, NY, USA) and the Adventa V12 stent (Atrium, Mijdrecht, Netherlands); the uncovered stents used were the Max LD stent (EV3, Plymouth, MN, USA), the PALMAZ stent (Cordis [Johnson & Johnson], Roden, the Netherlands), the CP Stent (NuMED, Hopkinton, NY, USA) and the JOSTENT (Abbott Vascular Devices, Santa Clara, CA, USA). The balloons used for deployment of non-premounted stents included the balloon-in-balloon (BIB; NuMED, Hopkinton, NY, USA) and Cristal balloons (Balt, Montmorency, France).

Vascular access was achieved from the femoral artery in all patients. Further arterial access was achieved using the right radial artery in all patients except one, in whom brachial artery access was obtained. In two patients, the CoA site could not be crossed from the femoral approach, and the wire was snared from the femoral artery after antegrade crossing of the coarctation from an upper limb vessel. Femoral arterial access sites were preclosed using a Perclose A-T™ or Proglide™ device (Abbott Vascular Devices, Santa Clara, CA, USA) in 49 (91%) patients. Patients received 5000 IU heparin. Aortic pressures were simultaneously recorded in the ascending aorta and descending thoracic aorta to measure the peak-to-peak systolic gradient (PG) across the CoA segment. An aortic arch angiogram was taken in the left lateral and right anterior oblique views. Measurements were then obtained from the images, including the diameter of the aorta proximal and distal to the site of obstruction. The diameter of the balloon was chosen to equal that of the normal portion of the transverse arch or proximal isthmus at the level of the take off of the left subclavian artery.

The location of the CoA relative to landmarks within the chest was noted for reference during positioning and implantation. Implantation was performed using standard techniques. After successful deployment of the CoA stent, the femoral artery access site was closed with the Perclose A-T™ or Proglide™ preclosure device.

Major complications were defined as mortality or complications requiring surgical intervention — either cardiac or vascular — including the need for blood transfusions.

Statistical analysis

Analysis was performed using SPSS 17.0 (SPSS, Chicago, IL, USA). Group means were compared using paired or unpaired Student’s t tests as appropriate. Absolute PG reduction (baseline PG — post-stenting PG) and percentage PG reduction (absolute PG reduction/baseline PG) × 100 were calculated for each procedure. The correlations between baseline PG and baseline systolic blood pressure (SBP), and between PG reduction (absolute and percentage change) and SBP reduction (baseline — post-stenting SBP) at 6–12 weeks and 9–12 months were assessed using Pearson’s correlation coefficients. Additionally, the predictive accuracy of absolute and percentage PG reduction to predict adequate SBP control (<140/90 mmHg) was determined using receiver-operating characteristic (ROC) analysis, and expressed as area under the curve (AUC). To determine statistical significance, various AUCs were compared with 0.5 and their 95% confidence intervals (CIs) calculated. Based on invasive haemodynamic data we divided patients into severe CoA (PG >25 mmHg) and non-severe CoA (PG ≤25 mmHg) groups for comparison. All statistical tests were two-tailed and a P-value <0.05 was considered significant. Stepwise univariate and multivariable logistic regression analyses were performed for the outcome of SBP <140 mmHg at 12 months using the following variables: age, sex, preprocedural SBP, preprocedural PG, post-procedural PG, absolute and percentage PG reduction. An alpha level of 0.05 was used for entry into multivariable analysis.

Stepwise logistic regression

On univariate logistic regression, only preprocedural SBP significantly predicted a 12-month outcome of SBP <140 mmHg (P < 0.05). All the other variables tested failed to reach significance (all P-values >0.05). Multivariable analysis was therefore not performed.
Results

Study population

Over a 7-year period, a total of 54 consecutive patients underwent CoA stenting. Five patients were excluded, as they did not attend follow-up appointments within the specified time periods for blood pressure monitoring. Forty-nine patients had complete measurements; their mean age was 34 ± 16 years (range: 15–72 years). Patient demographics, lesion characteristics and associated conditions are given in Table 1.

Patients were followed up for 24 ± 17 months (range: 3–65 months, median: 17 months). A total of 17/54 (31%) patients had a follow-up angiogram, while the rest had non-invasive assessment using a computed tomographic scan. One patient had successful redilatation of his stent 28 months later for stent recoil with increasing gradients. No other patient required reintervention for the CoA, and there was no evidence of aneurysm formation. One patient needed deployment of a covered stent because of fracture of stent struts in the previously deployed stent. Two patients underwent additional cardiac procedures unrelated to the CoA stenting procedure, including percutaneous aortic balloon valvuloplasty for aortic stenosis (bicuspid aortic valve) and device closure of a left-sided ascending vein for partial anomalous pulmonary venous drainage [17]. One patient had a stroke 5 months after the procedure, was thrombolysed and made a satisfactory recovery. One patient underwent successful surgical aortic valve replacement and one patient underwent mastectomy for carcinoma of breast in the follow-up period. There was one death in the follow-up period resulting from non-cardiac causes.

Procedural data

Previous balloon dilatations had been performed in 10 patients. Two patients had undergone three previous balloon dilatation procedures each. None of these was performed as part of the stenting procedure. Covered stents were used in 40 (74%) patients: the CP Stent™ was used in 24/54 (44%) patients and the Advanta V12™ stent was used in 16/54 (30%) patients. Uncovered stents were used in 14 (26%) patients: the CP Stent™, the Max LD™ and the JOSTENT™ (Abbott Vascular Devices, Santa Clara, CA, USA) were used in 11 patients, 2 patients and 1 patient, respectively. The stent length varied from 28 to 40 mm. In 40/54 (74%) patients the femoral access site was closed using a preclosure technique with a Perclose™ closure device. Femoral artery sheath sizes ranged from 10–14 Fr (French).

Complications

There was no procedure-related mortality or need for emergency cardiac or vascular surgery. All patients were mobilized within 6 hours after the procedure, except one patient who had a femoral artery dissection, which was successfully managed conservatively. None of the patients had an endovascular leak after intervention. Major vascular access site complication was seen in one additional patient, who developed an arteriovenous fistula that was diagnosed 2 weeks after the stenting procedure and required vascular surgical repair. There was one non-cardiac related death, but no cardiac mortality in the follow-up period. One patient with a very tortuous aorta had stent mobilization; this stent was safely redeployed in the descending abdominal aorta.

Peak-to-peak systolic gradients

There was a weak but significant linear correlation between baseline PG and baseline SBP (r = 0.45; P = 0.001; Fig. 1). There was a significant fall in PG across the CoA after

Table 1 Patients’ demographics and associated conditions (n = 54).

<table>
<thead>
<tr>
<th>Variable</th>
<th></th>
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<tbody>
<tr>
<td>Men</td>
<td>36</td>
</tr>
<tr>
<td>Age (years)</td>
<td>34 ± 16</td>
</tr>
<tr>
<td>Native CoA</td>
<td>35</td>
</tr>
<tr>
<td>Previous surgical repair</td>
<td>14</td>
</tr>
<tr>
<td>Previous balloon dilatation</td>
<td>10</td>
</tr>
<tr>
<td>Stent strut fracture in previous CoA stent</td>
<td>1</td>
</tr>
<tr>
<td>Associated conditions</td>
<td></td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>18</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>5</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>3</td>
</tr>
<tr>
<td>Turner’s syndrome</td>
<td>3</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>3</td>
</tr>
<tr>
<td>Wolff-Parkinson-White syndrome</td>
<td>2</td>
</tr>
<tr>
<td>Cerebral aneurysm</td>
<td>1</td>
</tr>
<tr>
<td>Dextrocardia</td>
<td>1</td>
</tr>
<tr>
<td>Parachute malformation of mitral valve</td>
<td>1</td>
</tr>
<tr>
<td>Dysplastic aorta</td>
<td>1</td>
</tr>
<tr>
<td>Waardenberg’s syndrome</td>
<td>1</td>
</tr>
</tbody>
</table>

Data are expressed as number or mean ± standard deviation; CoA: aortic coarctation.

Figure 1. There was a weak but significant linear correlation between baseline peak gradient (PG) across aortic coarctation and baseline systolic blood pressure (SBP) in the right arm (r = 0.45; P = 0.001). The line of best fit is shown in black.
stenting, from $26 \pm 11$ mmHg (range: 10–50 mmHg) to $5 \pm 4$ mmHg (range: 0–20 mmHg; $P < 0.01$). The changes in PG for individual lesions are shown in Fig. 2.

**Blood pressure outcomes**

There was a significant reduction in baseline SBP from $155 \pm 18$ to $137 \pm 17$ mmHg at 6–12 weeks ($P < 0.01; n = 50$) and to $142 \pm 16$ mmHg ($P = 0.001$) at 9–12 months ($n = 47$) after stenting. There was a significant reduction in ambulatory 24-hour SBP from $142 \pm 14$ mmHg at baseline to $132 \pm 16$ mmHg at 6 weeks ($P < 0.01; n = 41$) and to $131 \pm 15$ mmHg at 9–12 months ($P = 0.003; n = 33$) after stenting.

There was no significant difference in the mean number of antihypertensive medications used before and after stenting in the study population overall ($1.9 \pm 0.7$ vs. $1.7 \pm 0.6; P = 0.68$), or specifically in those patients on antihypertensive medication at baseline ($n = 35$; $1.8 \pm 0.7$ vs. $1.8 \pm 0.7; P = 0.38$). Fifteen patients were normotensive at baseline without needing antihypertensive treatment. Similarly, four patients had clinical SBP ≥150 mmHg preprocedure and preferred to wait for the intervention procedure before starting antihypertensive treatment. These four patients went on to have antihypertensive therapy at 12-month follow-up after CoA stenting, despite an excellent gradient reduction (residual gradient <10 mmHg) in all cases, as their blood pressure was not in the target range (140/90 mmHg) at 6-week follow-up. One of these patients also had Turner’s syndrome with a hypoplastic arch.

The antihypertensive treatments used included beta-blockers, angiotensin-converting enzyme inhibitors and calcium channel blockers.

There were no significant correlations between reduction in PG after stenting (absolute or percentage change) and reductions in SBP at 6–12 weeks or at 9–12 months compared with baseline (Table 2). On ROC analysis, neither the absolute nor the percentage PG reduction after stenting significantly predicted adequate control of SBP at 6 weeks (AUC 0.62 and 0.51, respectively) or at 6 months (AUC 0.47 and 0.54, respectively; all 95% CIs traversed zero and all $P$-values were >0.10; Fig. 3).

**Severe versus non-severe aortic coarctation**

Twenty-four patients were classified as having severe CoA (PG >25 mmHg) and 25 as having non-severe CoA (PG ≤25 mmHg) before stenting. The severe CoA group had a significantly higher SBP at baseline compared with the non-severe group (160 vs. 148 mmHg; $P = 0.02$). After stenting, the absolute reduction in PG was significantly higher in the severe versus the non-severe group (31 ± 7 mmHg vs. 14 ± 5 mmHg; $P < 0.0001$), but there was no significant difference in the percentage PG change between the two groups (84 ± 12% vs. 77 ± 19%; $P = 0.12$). At 6 weeks, there was no significant difference in SBP between the severe and non-severe groups (141 mmHg vs. 135 mmHg; $P = 0.21$), and this remained the case at 9–12 months (139 mmHg vs. 139 mmHg; $P = 0.96$).

**Discussion**

The management of CoA is mainly focused on gradient reduction, and the effect on hypertension, especially in adults, is not well described. This study demonstrates that transcatheter treatment for CoA in adolescents and adults with primary stenting results in immediate and sustained haemodynamic benefits. Specifically, the main findings were that there was a significant immediate reduction in absolute and percentage PG across the CoA after stenting in keeping with previous studies [14,16,18–20], which translated into a significant reduction in SBP at 6 weeks and 9–12 months, but that there was a need to maintain medical therapy. Another important finding was that the SBP profiles of severe and non-severe CoAs seem to equilibrate at 6 weeks post-procedure, and this was maintained at 9–12 months, suggesting that both groups may follow a similar risk profile after intervention rather than continuing to diverge. This suggests that patients with non-severe CoA, as defined in this study, may derive benefit in terms of hypertension control with stenting of aortic coarctation, but this will require

![Figure 2](image-url) Individual changes in peak gradient across aortic coarctation immediately after stenting.

<table>
<thead>
<tr>
<th>Correlation with absolute PG reduction</th>
<th>Correlation coefficient r²</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>SBP reduction at 6–12 weeks</td>
<td>0.21</td>
<td>0.14</td>
</tr>
<tr>
<td>SBP reduction at 6–12 months</td>
<td>−0.01</td>
<td>0.94</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Correlation with percentage PG reduction</th>
<th>Correlation coefficient r²</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>SBP reduction at 6–12 weeks</td>
<td>0.03</td>
<td>0.83</td>
</tr>
<tr>
<td>SBP reduction at 6–12 months</td>
<td>−0.11</td>
<td>0.46</td>
</tr>
</tbody>
</table>

PG: peak gradient across aortic coarctation; SBP: systolic blood pressure in right upper limb.

* Pearson’s correlation coefficient.
Systemic hypertension and aortic coarctation

Further large-scale clinical validation and a longer follow-up duration. Finally, the study also showed that the initial PG reduction (absolute or percentage change) is not an accurate predictor of whether normal SBP (<140/90) will be achieved in the long-term, and that other factors therefore need to be considered and studied in the future.

Arterial hypertension has been associated with increased morbidity and mortality from cardiovascular disease [21]. A study by Hager et al. [22] (n = 404) showed persistent hypertension in patients who underwent surgical repair in >50% of patients at a follow-up of 27 years. Our study showed significant improvement in hypertension control after stenting in the immediate period, which persisted at 1 year. Persistent hypertension after CoA repair in the presence or absence of residual stenosis has been reported [18], and was also seen in our patients. While there was a trend towards a decrease in the number of antihypertensive medications after stenting, this did not reach significance. The majority of our patients continued antihypertensive therapy for optimal control, as has been described previously [13,15]. The residual prevalence of hypertension after CoA stenting may be multifactorial, including morphology of the arch, age, poor arterial compliance, the change in target blood pressure guidance [23–25] and the effect of recurrent CoA. Similarly, our results showed that those patients who were not on any medication before intervention remained normotensive, with the need for antihypertensive medication in only four patients. Of those with established hypertension, five had their antihypertensive treatments stopped, indicating that it is may be possible to cease therapy with antihypertensive medication after stenting.

There is evidence in the adult literature that 24-hour blood pressure is a better predictor of end organ damage, and therefore provides a better measure of blood pressure than casual readings [26]. Our study demonstrated improvement in 24-hour blood pressure compared with baseline, which was sustained at 9–12 months, and it is possible that this may be of prognostic benefit in the long-term.
Surgery for CoA and recurrent CoA has been associated with complications, including death, stroke, infection, true and false aneurysm formation, rupture of the anastomosis causing a pseudoaneurysm, spinal cord damage (including paraplegia; 0.3%), unusual gait and aortic dissection and vocal cord palsy [27–30]. Similarly, there is a risk of occlusion of the left subclavian artery or occlusion of other branches of the aorta [31] with covered stents. Strut fracture has been reported with uncovered CoA stents [32–34], as well as aortic dissection or rupture. One of our patients developed a strut fracture in a previously implanted stent, which was successfully treated with implantation of a covered CP Stent™.

The majority of our patients underwent stenting using a covered stent, which may decrease but not eliminate the risk of aortic perforation [35]. Previous studies have demonstrated the safety of CoA stenting in children [25,36]. A review study (comparison between angioplasty [n = 633] and surgery [n = 213]) by Carr [37] showed a lower incidence of restenosis and recurrence in surgically treated patients, while CoA stenting has been associated with the lowest morbidity. Currently, based on the available literature [13,14,16,18–20], primary stent deployment in native or recurrent CoA patients may be considered as first-line therapy in most adolescent and adult patients with CoA.

Our patients underwent additional procedures after CoA stenting, including percutaneous aortic balloon valvuloplasty for aortic stenosis and partial anomalous pulmonary venous drainage device closure [38], aortic valve replacement and mastectomy for carcinoma of breast, without any cardiovascular issues related to the CoA.

Study limitations

This was a cohort study, reflecting the fact that these data are derived from real-world practice in a selected group of patients. There was no controlled or regulated antihypertensive regimen or strategy (i.e. clinician choice was used in the prescription of antihypertensive treatment). We did not have a control arm comprising medical therapy alone. As many patients were referred from outside hospitals to our institution for specialist procedural treatment, additional background data on the study group, including duration of hypertension, left ventricular hypertrophy and renin/aldosterone status, was not complete in all patients to include in the analyses. As it generally takes longer than the presented 12 months of data to safely scale down antihypertensive treatment and to reassess for long-term success and freedom from hypertension treatment, such analyses are the subject of ongoing work to be reported in the future.

Conclusion

This study demonstrates that stenting of both native and recurrent CoA in adults results in a significant reduction in SBP 6 weeks after the procedure, which is sustained after a year. While there is a continuing need for antihypertensive therapy, even patients with non-severe CoA undergoing stenting appear to benefit from better control of systemic hypertension.

Disclosure of interest

The authors declare that they have no competing interest.

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References

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