Long-term effects of balloon angioplasty on systemic hypertension in adolescent and adult patients with coarctation of the aorta

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Aims To define the long-term effect of balloon angioplasty of aortic coarctation on hypertension, in adolescent and adult patients.

Methods Balloon angioplasty of discrete, native aortic coarctation was performed on 50 patients (34 male) aged 23 ± 8 (mean ± standard deviation) years. In 42 of these patients cardiac catheterization and angiography were repeated 1 year later, and on the basis of sphygmomanometric blood pressure determination at that time, they were divided into 31 patients (group A) with normalized blood pressure and 11 patients (group B) who still needed antihypertensive medication. Both groups were followed annually thereafter for 12–123 (66 ± 37) months.

Results Coarctation gradient values before, immediately after and 1 year after angioplasty were 69 ± 24 mmHg, 12 ± 8 mmHg (P<0.001) and 7 ± 6 mmHg. The corresponding systolic blood pressure values were 165 ± 17 mmHg, 128 ± 12 mmHg (P<0.001) and 115 ± 10 mmHg (P<0.001) in group A; 182 ± 21 mmHg, 141 ± 24 mmHg (P<0.001) and 134 ± 18 mmHg (P<0.001) in group B. Echocardiographic left ventricular mass index before angioplasty and at follow-up was 130 ± 31 g . m⁻² and 105 ± 23 g . m⁻² in group A; 157 ± 38 g . m⁻² and 132 ± 35 g . m⁻² in group B (P<0.001 for both comparisons).

Conclusion Normalization of blood pressure without medication occurred in 74% of patients after angioplasty for aortic coarctation, with subsequent long-term regression of left ventricular hypertrophy. In comparison to reported surgical results, balloon angioplasty should be considered as first line treatment for native, discrete aortic coarctation in adolescent and adult patients.

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Key Words: Balloon angioplasty, coarctation of the aorta, hypertension.

Introduction

In patients with coarctation of the aorta, morbidity and mortality are mainly determined by complications of systemic hypertension associated with the coarctation. Patients may suffer from ischaemic cerebrovascular disease, intracranial haemorrhage, myocardial infarction, congestive heart failure or aortic rupture. More than 80% of untreated patients do not survive beyond the age of 50[1].

Although surgical repair of coarctation has significantly improved survival, morbidity and mortality remain elevated in comparison to controls, even in the absence of associated cardiovascular malformations. Postoperative persistent hypertension is thought to represent the main risk factor[2–6]. Balloon coarctation angioplasty is now accepted as an alternative method of treatment in infants and children with aortic coarctation[7–11]. The results in adolescent and adult patients have also been encouraging[12–15]. In this retrospective study we report on the long-term results of 42 adolescent and adult patients submitted to balloon angioplasty for native, discrete aortic coarctation, with special emphasis on the effect of this modality on systemic hypertension.
Methods

Study population

Since July 1966, we have performed balloon angioplasty in 51 consecutive patients with native, discrete, ‘shelf-like’ aortic coarctation. One patient was excluded after he developed aortic dissection for which he was submitted to immediate surgical repair without sequelae. The remaining 50 patients (34 male) whose age ranged 14–54 (23 ± 8; mean ± 1 standard deviation) years were included in the study. Systemic hypertension, defined as blood pressure ≥140/90 mmHg, was present in 49 of these patients with systolic blood pressure of 182 ± 17 (range 140–260) mmHg, despite medical treatment. All 49 patients had native, discrete, ‘shelf-like’ aortic coarctation not associated with isthmic stenosis. Concomitant cardiovascular disease was present in 24 patients. Thus, bicuspid aortic valve was present in 19 patients (two of whom had moderate aortic regurgitation), small atrial septal defect in two, subaortic membrane in one, small ventricular septal defect in one, and moderate mitral regurgitation in one.

Initial evaluation

Clinical evaluation before angioplasty included blood pressure measurement, chest radiograph, 12-lead electrocardiogram, and M-mode, two-dimensional and Doppler echocardiogram. The blood pressure was measured by cuff sphygmomanometer from the right arm in the supine position and under conditions of physical and emotional rest, in accordance with the criteria set by the American Heart Association[16]. In 37 patients with technically adequate echocardiographic examinations, the left ventricular mass index was calculated by echocardiography before angioplasty and after 32 ± 22 months of follow-up, as detailed below.

Echocardiographic examinations

All echocardiographic examinations were conducted in the standard left parasternal long- and short-axis views using a commercially available phased-array system, equipped with a 2-25 or 3-5 MHz transducer, and recorded on a 0-5-inch video tape. Measurements of the left ventricular end-diastolic dimension, and the thickness of the interventricular septum and posterior left ventricular wall, were averaged over five cardiac cycles and used to calculate left ventricular mass according to the Penn convention[17]. The left ventricular mass was then divided by the body surface area to provide the left ventricular mass index.

Balloon angioplasty technique

The technique used for balloon angioplasty has been reported previously[15]. An angioplasty balloon was selected with a diameter equal to that of the aortic isthmus or 1–2 mm smaller than the diameter of the descending thoracic aorta at the level of the diaphragm. Heparin 2000 units were given intravenously prior to angioplasty. The angioplasty balloon was inflated by hand for 5 to 10 s until the stenotic waist disappeared. Haemodynamic measurements and biplane aortic angiography were performed immediately before and after balloon angioplasty. Special precaution was taken to avoid manipulating the tip of the catheter or guidewire over the area of freshly dilated coarctation. Upon completion of the procedure, haemostasis was achieved by manual compression of the femoral artery and application of pressure dressing. Patients were advised to remain supine in bed until the next morning and were discharged 24 h following the procedure.

Follow-up evaluation

Follow-up evaluation of 42 patients for 66 ± 37 (range 12–123) months was conducted at regular clinic visits and included blood pressure measurements, magnetic resonance imaging and echocardiography. Repeat cardiac catheterization was performed 12 months after dilation of the coarctation. Following angioplasty, patients were placed on appropriate antihypertensive treatment and the need for continuation of such treatment was assessed 1 year later. By July 1998, 42 patients who had completed ≥12 months of follow-up were assigned to one of two groups, based on the absence (group A: 31 patients) or presence (group B: 11 patients) of hypertension after a 1-month trial period of treatment withdrawal. To assess the blood pressure response to exercise, 30 patients of group A underwent treadmill exercise testing according to the Bruce protocol.

Statistical analysis

Data are presented as mean value ± standard deviation and 95% confidence intervals (CI). The paired Student t-test was used to compare data before and after angioplasty. Association of various risk factors with normalization of blood pressure was studied using two group comparisons, chi-square test for contingency tables, or the Fisher exact test for small sample size/cell frequencies. Age, baseline gradient, residual gradient, baseline blood pressure and blood pressure at 1 year post dilation follow-up visit were entered in multiple logistic regression analysis to identify possible covariates (risk factors) for normalization of blood pressure after coarctation angioplasty. Statistical analyses were performed using commercially available software (JMP v 3.2.SAS).

Results

Immediate results

The peak-to-peak systolic pressure gradient across the coarctation decreased from 69 ± 24 mmHg (95% CI 61
to 12 ± 8 mmHg (95% CI 10 to 15, *P* <0.001; Table 1). A reduction in gradient to ≤20 mmHg was achieved in all patients. Neither paradoxic hypertension nor post-coarctation syndrome was observed after dilation of coarctation. The systolic blood pressure in group A decreased from 165 ± 17 mmHg (95% CI 159 to 171) to 128 ± 12 mmHg (95% CI 124 to 133, *P* <0.001) immediately after dilation and in group B from 182 ± 21 mmHg (95% CI 169 to 196) to 141 ± 24 mmHg (95% CI 125 to 157, *P* <0.001; Table 2).

### Complications

There were no immediate or late deaths. Thrombosis of the right femoral artery developed in one patient and required thrombectomy.

### Follow-up results

Follow-up catheterization and angiography were performed 1 year after dilation in all 42 patients of groups A and B. In comparison to values obtained immediately after dilation, there was a small, further reduction in gradient across the coarctation to 7 ± 6 mmHg (95% CI 4 to 8; *P* <0.001; Table 1). All 42 patients were followed-up by magnetic resonance imaging performed annually over a period of 12–123 months. A total of three aneurysms were observed at the site of dilation by both angiography and magnetic resonance imaging (incidence 7%). These aneurysms were small, measuring 2–2.3 cm in diameter, and could not be detected on chest radiograph. No appreciable change in the size of the aneurysm was noted on follow-up magnetic resonance imaging, up to 10 years later.

In comparison to values obtained immediately after dilation, significant (*P* <0.001) further reductions in blood pressure at follow-up were noted in group A (115 ± 10 mmHg; 95% CI 111 to 119) and group B (134 ± 18 mmHg; 95% CI 122 to 141). Multiple regression analysis conducted on the whole group of 42 patients failed to identify valid risk factors for persistent hypertension.

### Regression of left ventricular hypertrophy

Significant regression in left ventricular hypertrophy was observed in both groups. Thus, the left ventricular mass index measured in 28 patients of group A decreased from a pre-dilation value of 130 ± 31 g·m⁻² (95% CI 118 to 142) to 105 ± 23 g·m⁻² (95% CI 96 to 114; *P* <0.001) at follow-up. Similarly, in nine patients in group B the index fell from a pre-dilation value of 157 ± 38 g·m⁻² (95% CI 127 to 185) to 132 ± 35 g·m⁻² (95% CI 105 to 159; *P* <0.001) at follow-up (Table 3).

### Response of blood pressure to exercise

All 30 patients of group A who were submitted to exercise testing, demonstrated normal blood pressure response (systolic ≤200 mmHg at peak effort).

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**Table 1** Response of invasively measured pressure gradient to balloon dilation of native aortic coarctation

<table>
<thead>
<tr>
<th></th>
<th>Gradient (mean ± SD) (mmHg)</th>
<th>95% confidence intervals (mmHg)</th>
</tr>
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<tbody>
<tr>
<td>All patients</td>
<td>n=42</td>
<td></td>
</tr>
<tr>
<td>Before balloon dilation</td>
<td>69 ± 24</td>
<td>61–76</td>
</tr>
<tr>
<td>Immediately after balloon dilation</td>
<td>12 ± 8*</td>
<td>10–15</td>
</tr>
<tr>
<td>At 1 year follow-up</td>
<td>7 ± 6†</td>
<td>5–9</td>
</tr>
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*P*<0.001 in comparison to values before dilation; †*P*<0.001 in comparison to values immediately after dilation.

**Table 2** Response of invasively measured systolic blood pressure to balloon dilation of native aortic coarctation

<table>
<thead>
<tr>
<th></th>
<th>Group A Mean ± SD (n=31)</th>
<th>Group A 95% CI (n=31)</th>
<th>Group B Mean ± SD (n=11)</th>
<th>Group B 95% CI (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before balloon dilation</td>
<td>165 ± 17</td>
<td>159–171</td>
<td>182 ± 21</td>
<td>169–196</td>
</tr>
<tr>
<td>Immediately after balloon dilation</td>
<td>128 ± 12*</td>
<td>124–133</td>
<td>141 ± 24*</td>
<td>125–157</td>
</tr>
<tr>
<td>At 1-year follow-up</td>
<td>115 ± 10*†</td>
<td>111–119</td>
<td>134 ± 18*</td>
<td>122–141</td>
</tr>
</tbody>
</table>

CI=confidence intervals; *P*<0.001 in comparison to values before dilation; †*P*<0.001 in comparison to values immediately after dilation; All values are in mmHg.
Table 3  Long-term response of left ventricular mass index to balloon dilation of native aortic coarctation

<table>
<thead>
<tr>
<th></th>
<th>Group A Mean ± SD (n=28)</th>
<th>Group A 95% CI (n=28)</th>
<th>Group B Mean ± SD (n=9)</th>
<th>Group B 95% CI (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before balloon dilation</td>
<td>130 ± 31</td>
<td>118–142</td>
<td>157 ± 38</td>
<td>127–185</td>
</tr>
<tr>
<td>At follow-up (12–123 months)</td>
<td>105 ± 23*</td>
<td>96–114</td>
<td>132 ± 35</td>
<td>105–159</td>
</tr>
</tbody>
</table>

*P<0.001 in comparison to values before dilation; All values are in g·m⁻².

Discussion

Our results are in agreement with those of previously reported studies[12–15] demonstrating the efficacy of balloon angioplasty in adolescents and adults with discrete, native coarctation of the aorta. The incidence of aneurysm formation at the site of dilation in our series is comparable to the 1.8% to 5.7% reported from several series[7–10,12–15]. In our series, the size of the aneurysms, as determined by magnetic resonance imaging, remained unchanged for up to 10 years following angioplasty.

Normalization of blood pressure

In 74% of our patients blood pressure remained normal without antihypertensive medication for a follow-up interval of 1–10 years, and of the remaining 26% (group B) who needed long-term treatment none had poorly controlled hypertension (systolic blood pressure >160/90 mmHg). These findings concur with those of Schrader et al.[14] who reported a 79% rate of normalization of blood pressure after balloon angioplasty in adolescents and adults with aortic coarctation. In contrast to the findings of Schrader et al.[14], however, we found no relation between persistence of hypertension and residual gradient of ≥30 mmHg. All of the 11 patients of group B had residual gradient of ≤20 mmHg. Similarly, we found no relation between normalization of blood pressure and either age or coarctation gradient before or after angioplasty, although the study has limitations due to the small sample size.

In a large series from the Mayo Clinic, Cohen et al.[6] reported an incidence of hypertension of 33% in their 320 patients who were ≥15 years of age at the time of surgery. However, the authors defined hypertension as systolic blood pressure ≥150 mmHg. According to this criterion only 7% (three of 42) of our patients would be considered hypertensive. Wells et al.[18] reported a 46% rate of normalization of blood pressure without medication after surgical repair of coarctation in adults of 32 ± 10 years of age. In a series of 68 adults (age: 15–54, mean 27 years) with aortic coarctation submitted to patch aortoplasty and followed for a mean interval of 8.8 years, Ala-Kuul et al.[19] reported an incidence of late postoperative hypertension in excess of 50%.

It has been recommended that patients with an abnormal (≥200 mmHg) systolic blood pressure response to exercise after surgically repaired aortic coarctation should receive antihypertensive treatment and be reassessed, even if the resting blood pressure is normal[20]. This need did not arise in our 30 group A patients, all of whom had a normal blood pressure response to exercise after angioplasty.

Although systemic hypertension persisting after successful correction of aortic coarctation by surgery or balloon angioplasty is not uncommon, its mechanism of production remains unclear. While in many cases the residual gradient ≥20 mmHg across the site of coarctation may provide a plausible pathophysiological mechanism for the hypertension, the lack of such residual gradient in other cases suggests the existence of alternative mechanisms. Thus, altered arterial reactivity involving the pre-coarctation vascular bed has been documented in healthy young adults who had been submitted to successful repair of aortic coarctation in childhood[21]. Persistent hyperdynamic cardiovascular state[22], mismatch in compliance between different vascular segments[23], increased arterial wall stiffness[24], and reduced distensibility and compliance[25,26] of the aortic wall proximal to the coarctation site, have been demonstrated to be among the factors responsible for hypertension persisting after successful repair of coarctation. Altered baroreceptor function has been documented in adolescents with persistent resting hypertension or hypertensive response to exercise, following successful surgical repair of coarctation[27] suggesting, though not proving, a possible cause and effect association.

Both the sympathetic nervous system and the renin-angiotensin system have been implicated in the pathogenesis of paradoxical hypertension[28–31]. Although it is a common complication after surgical correction of aortic coarctation, paradoxical hypertension following balloon dilation is distinctly rare. Thus, in this and nine other studies[7–14,31], collectively involving a total of 1398 patients submitted to this procedure, no case of paradoxical hypertension was observed. On the other hand, a total of 10 cases of paradoxical hypertension after
balloon angioplasty for aortic coarctation were reported in three studies involving a total of 58 patients[32–34], and in two case reports[35,36].

Conclusion
The data presented and those reviewed from published reports suggest that normalization of arterial blood pressure occurs more frequently after balloon angioplasty than after surgery in adolescent and adult patients with native coarctation of the aorta. We found no relation between persistence of hypertension and residual gradient or age in our patients. Balloon angioplasty is a safe and effective procedure in experienced hands and should be considered as first line treatment for native, discrete coarctation of the aorta in adolescent and adult patients.

References
