Journal of the American College of Cardiology
© 2000 by the American College of Cardiology
Published by Elsevier Science Inc.
Vol. 35, No. 4, 2000
ISSN 0735-1097/00/$20.00
PII S0735-1097(99)00646-4

**Pediatric Cardiology**

# Balloon Angioplasty of Native Coarctation: Clinical Outcomes and Predictors of Success

Caroline Ovaert, MD,* Brian W. McCrindle, MD, MPH, FRCPC, FACC,*
David Nykanen, MD, FRCPC,* Cathy MacDonald, MD,† Robert M. Freedom, MD, FRCPC, FACC,*
Lee N. Benson, MD, FRCPC, FACC, FSCAI‡
*Toronto, Canada*

**OBJECTIVES** We sought to investigate the clinical impact of balloon angioplasty for native coarctation of the aorta (CoA) and determine predictors of outcome.

**BACKGROUND** Balloon dilation of native CoA remains controversial and more information on its long-term impact is required.

**METHODS** Hemodynamic, angiographic and follow-up data on 69 children who underwent balloon angioplasty of native CoA between 1988 and 1996 were reviewed. Stretch, recoil and gain of CoA circumference and area were calculated and related to outcomes.

**RESULTS** Initial systolic gradients (mean ± SD, 31 ± 12 mm Hg) fell by −74 ± 27% ($p < 0.001$), with an increase in mean CoA diameters of 128 ± 128% in the left anterior oblique and 124 ± 87% in the lateral views ($p < 0.001$). Two deaths occurred, one at the time of the procedure and one 23 months later, both as a result of an associated cardiomyopathy. Seven patients had residual gradients of >20 mm Hg. One patient developed an aneurysm, stable in follow-up, and four patients had mild dilation at the site of the angioplasty. Freedom from reintervention was 90% at one year and 87% at five years with follow-up ranging to 8.5 years. Factors significantly associated with decreased time to reintervention included: a higher gradient before dilation, a smaller percentage change in gradient after dilation, a small transverse arch and a greater stretch and gain, but not recoil.

**CONCLUSION** Balloon dilation is a safe and efficient treatment of native CoA in children. Greater stretch and gain are factors significantly associated with reintervention, possibly related to altered elastic properties and vessel scarring. (J Am Coll Cardiol 2000;35:988–96) © 2000 by the American College of Cardiology

Percutaneous balloon angioplasty of unoperated or native coarctation of the aorta (CoA), first described by Singer et al. (1) appears a viable, although controversial, management option. Clinical concerns regarding potential weakening of the aortic wall, aneurysm formation and recurrence exist (2).

The largest clinical studies currently available, with follow-up up to nine years, describe aneurysm formation in <5% of patients (3–5), with their development potentially, although not convincingly, related to intrinsic vessel wall abnormalities more than to the extent of the vessel wall tears (6,7). Young patient age (neonates) and the presence of associated transverse aortic arch hypoplasia have been associated with a higher incidence of recurrence (3–5,8). To this end, the elastic properties of the aortic vessel wall, as studied by the stretch-recoil-gain relationships, may also influence immediate and long-term response to balloon angioplasty (9,10).

In this study, we reviewed our clinical experience with balloon angioplasty of native CoA, detailing immediate and late outcomes and complications. Age, hemodynamic data, aortic arch measurements and biophysical characteristics of the vessel wall were further analyzed as possible factors associated with long-term success.

## METHODS

**Indications for intervention.** From June 1988, patients presenting with a discrete CoA and a resting systolic gradient by sphygmanometry between the upper and lower limbs of >20 mm Hg were offered balloon angioplasty as an alternative to surgery (2). Neonates and young infants (<1 year of age) were not, on a routine basis, considered for transcatheter treatment.

From the *Department of Pediatrics and †Diagnostic Imaging, Division of Cardiology and the Variety Club Cardiac Catheterization Laboratories, ‡Hospital for Sick Children, University of Toronto School of Medicine, Toronto, Canada.

Manuscript received February 28, 1999; revised manuscript received October 20, 1999, accepted December 2, 1999.

Present address for Dr. C. Ovaert is: Pediatric Cardiology, Cliniques Universitaires St-Luc, Université Catholique de Louvain, Avenue Hippocrate 10, 1200 Brussels, Belgium. E-mail: ovaert@pedi.ucl.ac.be.

**Abbreviations and Acronyms**

| | |
|---|---|
| CoA | = coarctation of the aorta |
| LAO | = left anterior oblique |
| LAT | = lateral |
| MRI | = magnetic resonance imaging |

**Technique.** General anesthesia was used in all procedures. The initial approach to the procedure was a right heart catheterization followed by transseptal entry to the left atrium. A balloon tipped catheter (Berman, Arrow International, Reading, Pennsylvania) was directed into the left ventricle and ascending aorta, from where an aortogram was obtained (1–2 cc/kg, Hexabrix, Mallinkodt Inc. or Isovue, Bracco Diagnostics, Ontario) in the 15°–20° left anterior oblique (LAO) and lateral (LAT) angiographic projections. Occasionally, to improve the lesion profile due to overlap of the isthmus upon the descending aorta, a caudal tilt (10° to 20°) was used on the LAO projection. Subsequently, an arterial catheter was placed from a retrograde approach, simultaneous ascending and descending aortic pressures obtained and the angioplasty performed. An 0.035 in, 260 cm exchange guide wire (Cook Inc., Bloomington, Illinois) was placed through an end hole catheter positioned above the aortic valve and maintained in the ascending aorta throughout the procedure. The balloon catheters were inserted over this wire without a vascular sheath. The transatrial catheter in the ascending aorta allowed continual arterial pressure monitoring and repeat aortography to judge the anatomic impact of the procedure, avoiding arterial catheter exchange and thereby lessening trauma to the femoral vessel. Patients were administered 150 IU/kg of heparin sulfate intravenously after vascular access was achieved, (maximum dose 5,000 IU), with an additional dose of 75 IU/kg given if the duration of the study exceeded 2 h. Activated clotting times were not measured.

The initial balloon diameter was chosen to be equal to or within 1 to 2 mm of the diameter of the aorta at the level of the subclavian artery and not greater than the diameter of the aorta at the diaphragm. Short inflation times were employed (<10 s) but repeated (two to four times) before repeat aortography was obtained. If no significant change in lesion diameter was noted (a diameter increase within 80% to 90% of the diameter of the aortic isthmus), the next larger balloon diameter was used within the above guidelines.

One hour after the conclusion of the procedure, an intravenous heparin sulfate infusion was begun if the pedal arterial pulse was absent. Administered was a bolus of 75 IU/kg followed by an intravenous infusion at 20 IU/kg/h, adjusting the activated partial thrombin time to between 60 to 100 s. The infusion was maintained for 24 h, and thrombolytic therapy was administered if the pulse did not return (11).

Informed consent was obtained from all patients in accordance with the Human Subjects Protection Committee of the Hospital for Sick Children, University of Toronto.

**Data collection, measurements and calculations.** *Cardiac catheterization data.* Invasive blood pressures were measured above and below the areas of CoA before and after balloon dilation, as well as the maximal balloon size employed. The clinical impact of all complications was also noted.

*Aortic arch measurements.* All cineangiograms were reviewed, and the diameters of the following regions were recorded prior to angioplasty: ascending aorta, transverse aortic arch (between the brachiocephalic and left common carotid arteries), isthmus (area beyond the left subclavian artery), the CoA site and the descending aorta at the level of the diaphragm and after the procedure: transverse aortic arch, isthmus and CoA site. All measurements were from systolic frames and corrected for magnification using the known diameter of the angiographic catheter.

*Assessment of transverse arch hypoplasia.* Transverse aortic arch dimensions were normalized to aortic arch dimensions previously obtained from age-matched controls without aortic pathology at our institution (unpublished data). Transverse aortic arch hypoplasia was defined as a transverse aortic arch z-score $<-2$.

*Biophysical measurements.* Balloon inflation stretches the CoA segment. As a result of elasticity of the vessel wall, it recoils, determining the vessel dimension after dilation. The gain is the difference between pre- and post-angioplasty dimensions (induced enlargement). The stretch-recoil-gain relationship for the cross-sectional area and circumference of the CoA segment were calculated. The fully inflated balloon was considered as a perfect circle (area = pi $r^2$, circumference = 2 pi r). As the balloons were inflated to within rated pressures by hand until the CoA waist disappeared, the nominal balloon diameters were used in the calculations. The CoA segment was considered an ellipse, using the measured diameters in the LAO and the LAT angiographic projections for calculations of area (= pi ab) and circumference (= 4aE; E being derived from a table of elliptic integrals, based on a k value = square root $a^2 - b^2/a$, a being the largest diameter of the ellipse) (12). Area and circumference stretch was calculated as the difference between the inflated balloon dimensions and those of the CoA segment before angioplasty, normalized to the balloon dimensions. Area and circumference recoil was calculated as the difference between the inflated balloon dimensions and those of the CoA segment after balloon angioplasty, normalized to the balloon dimensions. Gain was calculated as the difference between area or circumference of the CoA segment before and after angioplasty, normalized to the area or circumference before balloon angioplasty. All values were multiplied by 100 to calculate percent stretch, recoil and gain (Fig. 1, Table 1).

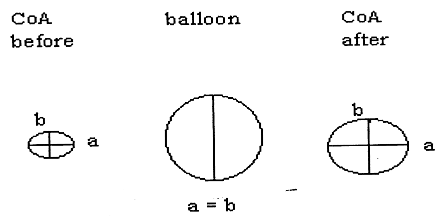


**Figure 1.** Representation of the measurements of the CoA before and after angioplasty **(ellipse)** and of the fully inflated balloon **(circle).**

**Follow-up.** Patients were followed as clinically indicated. Sphygmanometric blood pressure measurements in the right arm and the noncatheterized leg were performed at each follow-up visit. The morphology and dimensions of the thoracic aorta were assessed by magnetic resonance imaging (MRI) or by repeat angiography in 61 patients (90%). An aneurysm of the aorta at the site of the dilation was defined as the presence of wall contour deformation, whose diameter was 1.5 times the aorta at the level of the diaphragm (13,14). Magnetic resonance imaging was performed in a 1.5 Tesla superconducting magnetic scanner, using a spin echo technique with cardiac gating and respiratory compensation. Imaging which eluded axial, oblique coronal and oblique sagittal planes with 5 mm thick images were obtained with 1 mm interspersing. In addition, gradient recalled acquisition scanning of the pelvic vessels was carried out in an axial plane in 23 of 68 patients (34%) (15).

**Success.** Early success was defined as a reduction in the sphygmanometric blood pressure gradient between the upper and lower limbs <20 mm Hg, precluding the need for early reintervention (<1 year). Long-term success was defined as a compound outcome of an arm to leg gradient by sphygmanometry of <20 mm Hg and freedom from reintervention.

**Data analysis.** Patient and procedural characteristics were described as frequencies, medians with ranges and means with standard deviations as appropriate. Where there were missing data, the number of nonmissing values was reported for that variable. All statistical analyses were performed using SAS Version 6.12 statistical software (SAS Institute, Inc., Carey, North Carolina) using default settings. Changes in hemodynamic parameters and vascular dimensions were tested with paired *t* tests. The proportion of patients with an immediate (during cardiac catheterization) residual peak-to-peak systolic pressure gradient across the obstruction of 20 mm Hg or more, and the proportion of patients that needed early versus late reintervention were noted. Factors associated with acute procedural outcomes were sought with *t* tests and Kruskal-Wallis analysis of variance. Outcomes during follow-up were described, and estimates of freedom from reintervention for residual or recurrent obstruction were plotted as Kaplan-Meier curves. The association of patient and procedural characteristics, acute results and biophysical parameters with freedom from reintervention were each tested in univariable Cox's proportional hazard regression modeling. A $p < 0.05$ was set as the level of statistical significance.

## RESULTS

**Patient characteristics.** From June 1988 through December 1996, 74 patients underwent transcatheter treatment of native CoA. Of the 74 patients, 69 underwent balloon dilation and five patients underwent endovascular stent placement. Those five patients are not described in this study and were excluded from further analyses.

Of the 69 patients, 46 were male (67%) and 23 were female (33%). A bicuspid aortic valve was present in 42 patients (61%). Other associated cardiac anomalies are described in Table 2. The median patient age at procedure was 5.8 years (range, six months to 16.8 years). Only three

**Table 1.** Formulas for Calculation of Stretch, Recoil and Gain

$$\%\ \text{Circumference Stretch} = \frac{\text{Balloon circumference} - \text{CoA circumference pre}}{\text{Balloon circumference}} \times 100$$

$$\%\ \text{Area Stretch} = \frac{\text{Balloon area} - \text{CoA area pre}}{\text{Balloon area}} \times 100$$

$$\%\ \text{Circumference Recoil} = \frac{\text{Balloon circumference} - \text{CoA circumference post}}{\text{Balloon circumference}} \times 100$$

$$\%\ \text{Area Recoil} = \frac{\text{Balloon area} - \text{CoA area post}}{\text{Balloon area}} \times 100$$

$$\%\ \text{Circumference Gain} = \frac{\text{CoA circumference post} - \text{CoA circumference pre}}{\text{CoA circumference pre}} \times 100$$

$$\%\ \text{Area Gain} = \frac{\text{CoA area post} - \text{CoA area pre}}{\text{CoA area pre}} \times 100$$

**Table 2.** Associated Cardiac Lesions

| | N | % |
|---|---|---|
| Bicuspid Aortic Valve | 42 | 61 |
| Associated intracardiac anomalies | 21 | 30 |
| Aortic valve stenosis | 6 | |
| Ventricular septal defect | 7 | |
| Subaortic stenosis | 8 | |
| Transposition of the great arteries | 1 | |
| Mitral valve anomaly | 3 | |
| Other cardiovascular anomalies | 12 | 17 |
| Patent arterial duct | 7 | |
| Persistent left superior vena cava draining to the coronary sinus | 3 | |
| Aberrant origin of the left subclavian artery | 2 | |
| Severely reduced left ventricular function at presentation | 4 | 6 |

patients were <1 year, the youngest being 6 months of age, presenting with severe left ventricular failure. The median weight at intervention (n = 68) was 19 kg (range, 8 to 64 kg), with a median height (n = 68) of 112 cm (range, 69 to 177 cm).

The mean z-value for the transverse aortic arch (n = 63) was −1.66 ± 1.48 ($p < 0.001$ vs. normal) with hypoplasia, as defined above, noted in 46% of the patients.

**Early results.** Median balloon diameter was 12 mm (range, 7 to 20 mm), with a mean ratio of balloon to isthmus diameter (n = 58) of 1.2 ± 0.4, a mean ratio of balloon to aortic diameter at the level of the diaphragm of 1.0 ± 0.2 and a mean ratio balloon to CoA segment diameter (n = 65) of 3.1 ± 1.3.

Hemodynamic and angiographic data before and after angioplasty, expressed as mean values ± 1 standard deviations, are shown in Table 3. The systolic pressure gradients across the CoA sites and the ratio between the peak systolic pressures in the ascending and the descending aorta decreased significantly after angioplasty, with mean percentage changes, respectively, of −74 ± 28% (n = 67, $p < 0.001$) and −21 ± 9% (n = 67, $p < 0.001$).

The dimensions of the CoA segments, as well as the ratio of diameters of the CoA segments to diaphragmatic aorta from both angiographic projections (LAO, LAT), increased significantly, with mean percentage increases, respectively, of 129 ± 29% (n = 62, $p < 0.001$) and 124 ± 87% (n = 66, $p < 0.001$).

**Biophysical data: the stretch-recoil-gain relationships.** Mean circumferential stretch was 63 ± 14% (n = 64), mean circumferential recoil 26 ± 12% (n = 63) and mean circumferential gain 123 ± 96% (n = 61). Mean area stretch was 84 ± 12% (n = 64), mean area recoil 44 ± 20% (n = 63) and mean area gain 493 ± 706% (n = 65).

The relation between stretch, gain and recoil for areas and circumferences are represented in Fig. 2. There was an exponential increase in area and circumference gain with stretch. There was no relation between area or circumference recoil and stretch.

**Early complications.** One patient (1%) aged six months died during the procedure as a result of severe left ventricular failure, its severity having precluded a surgical repair. Five patients (7%) had reduced pulses in the catheterized leg treated with heparin sulfate with reappearance of the pulse in all cases. Three additional patients (4%) had mildly reduced pulses in the catheterized leg but were not treated. One patient had to be admitted to the intensive care unit for control of elevated blood pressure (paradoxical hypertension). Nine others required intravenous, sublingual or oral therapy to control elevated blood pressures after the procedure (15%). Seven of those, plus two additional patients were prescribed oral antihypertensive treatment at the time of hospital discharge. Two patients (3%) had a transient

**Table 3.** Hemodynamic and Angiographic Results Immediately Before and After Angioplasty

| | Before Angioplasty | After Angioplasty | p Value* |
|---|---|---|---|
| Pressure gradient (mm Hg) | 31 ± 12 (n = 67) | 8 ± 8 (n = 68) | < 0.001 (n = 67) |
| Ascending/descending aortic systolic pressure ratio | 1.39 ± 0.21 (n = 67) | 1.09 ± 0.10 (n = 68) | < 0.001 (n = 67) |
| CoA dimension (LAO projection) (mm) | 4.6 ± 2.7 (n = 65) | 8.9 ± 3.1 (n = 64) | < 0.001 (n = 62) |
| CoA dimension (LAT projection) (mm) | 4.8 ± 29 (n = 68) | 9.2 ± 2.9 (n = 66) | < 0.001 (n = 66) |
| CoA/diaphragmatic aorta diameter ratio (LAO projection) | 0.36 ± 0.14 (n = 65) | 0.70 ± 0.15 (n = 64) | < 0.001 (n = 62) |
| CoA/diaphragmatic aorta diameter ratio (LAT projection) | 0.36 ± 0.14 (n = 68) | 0.72 ± 0.14 (n = 66) | < 0.001 (n = 66) |

CoA = coarctation; LAO = left anterior oblique view; LAT = lateral view.

JACC Vol. 35, No. 4, 2000
March 15, 2000:988–96

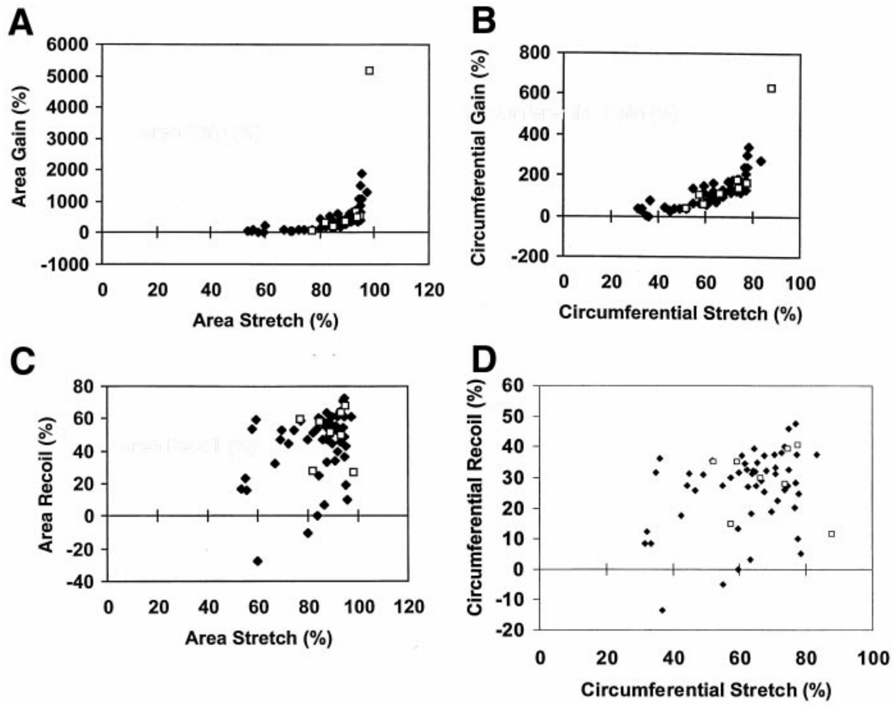


**Figure 2.** Relation between gain and stretch for area **(A)** and circumference **(B)** and relation between recoil and stretch for area **(C)** and circumference **(D).** Reint = reintervention. **Closed diamond** = No Reint; **open square** = Reint.

episode of junctional escape rhythm not requiring treatment.

**Early failure.** In seven patients (10%), the procedure was not successful. Six of these patients underwent early reintervention (<1 year), and one patient was managed with oral antihypertensive treatment and underwent reintervention at a later stage (see below). Table 4 compares the hemodynamic and angiographic data between patients with early success and those with early failure. Patients with early success had significantly lower gradients and ascending to descending aortic systolic pressure ratios measured invasively at catheterization before dilation, with greater ratios of balloon to coarctation and to diaphragmatic aortic diameters. Patients with successful procedures had somewhat lower circumferential and cross-sectional area stretch and significantly lower gain, but did not differ regarding recoil. In multiple logistic regression analysis, only a lower systolic pressure ratio (odds ratio [OR] 0.65 per 0.1 decrease; 95% confidence interval [CI] 0.45 to 0.95; $p = 0.03$) and a greater ratio of balloon to diaphragmatic aortic diameter (OR 0.44 per 0.1 increase; 95% CI 0.22 to 0.89; $p = 0.03$) could be entered significantly into the final model. After controlling for these two variables, no other variable was significantly independently associated with early success.

**Reintervention.** Nine of the 68 early survivors (13%) required reintervention at a median interval of 7.7 months (range, 1.2 months to 7.6 years) after the initial procedure. Reasons for reintervention included an unsuccessful initial procedure in seven (10%) and a recurrent stenosis despite an initially successful procedure in two patients (3%). One patient with an initially unsuccessful procedure had a repeat balloon angioplasty (using a larger balloon) with clinical success. In two other patients, presence of vessel dilation around the site of restenosis precluded repeat balloon dilation and these, together with four additional patients, were referred for surgery. The two patients with late restenosis had successful repeat transcatheter treatment, including one patient in whom an endovascular stent was placed across the recoarcted segment.

**Follow-up.** Of the 61 early survivors with an initially successful procedure, two were lost to follow-up. For the remaining 59 patients, median clinical follow-up interval was 2.8 years (range, 2.4 months to 8.5 years). Two patients underwent reintervention (repeat transcatheter angioplasty, as described above) for late restenosis, both seven years after the initial procedure. One late death occurred 23 months after the initial procedure in a child with persistent severe left ventricular dysfunction, despite the absence of residual or recurrent coarctation after the balloon angioplasty.

For the remaining 56 patients, mean systolic pressure in the right arm at latest clinical follow-up assessment was $110 \pm 12$ mm Hg. Nine patients had required antihypertensive therapy after the angioplasty, but none were being treated at latest follow-up. The median systolic gradient between the right arm and the noncatheterized leg at latest clinical visit ($n = 49$) at a median interval after the initial

**Table 4.** Comparison of Patients With Early Failure Versus Success

| | Early Failure (n = 7) | Early Success (n = 61) | p Value |
|---|---|---|---|
| Median age at intervention (yr) | 7.8 (1.1 to 14) | 5.8 (0.8 to 16.8) | 0.54 |
| Median weight at intervention (kgs) | 26.3 (8.2 to 54) | 19 (8 to 64.5) | 0.70 |
| Mean transverse aortic arch z-value | −2.59 ± 0.74 (n = 6; p < 0.001*) | −1.57 ± 1.50 (n = 57; p < 0.001) | 0.11 |
| Mean peak-to-peak systolic ascending to descending aorta pressure gradient before dilation (mm Hg) | 41 ± 13 | 29 ± 11 (n = 60) | 0.01 |
| Mean ratio of peak systolic ascending to descending aortic pressure before dilation | 1.59 ± 0.17 | 1.37 ± 0.20 (n = 60) | 0.006 |
| Median diameter of CoA segment in LAO projection (mm) | 3.6 (1 to 4) | 3.8 (2 to 12) (n = 57) | 0.08 |
| Median diameter of CoA segment in LAT projection (mm) | 2.5 (1.4 to 6) | 4 (1.8 to 15) | 0.07 |
| Mean ratio of balloon diameter to: | | | |
| Aortic isthmus diameter | 1.18 ± 0.31 (n = 5) | 1.24 ± 0.39 (n = 52) | 0.73 |
| CoA diameter | 4.56 ± 2.58 | 2.98 ± 1 (n = 57) | 0.003 |
| Aorta at diaphragm diameter | 0.83 ± 0.15 | 0.98 ± 0.13 | 0.008 |
| Mean circumferential: | | | |
| Stretch | 71 ± 10% | 62 ± 14% (n = 57) | 0.07 |
| Recoil | 27 ± 12% (n = 6) | 26 ± 13% (n = 57) | 0.81 |
| Gain | 218 ± 204% (n = 6) | 112 ± 73% (n = 55) | 0.01 |
| Mean cross-sectional area: | | | |
| Stretch | 91 ± 6% | 84 ± 12% (n = 57) | 0.11 |
| Recoil | 48 ± 17% (n = 6) | 44 ± 21% (n = 57) | 0.69 |
| Gain | 1,250 ± 1,915% (n = 6) | 410 ± 379% (n = 55) | 0.005 |

*p value represents single sample *t* test versus a hypothesized population mean of 0.
CoA = coarctation; LAO = left anterior oblique view; LAT = lateral view.

procedure of 2.6 years (range, 2.4 months to 8.5 years) was 5 mm Hg (range, −20 to 40 mm Hg). A gradient of ≥20 mm Hg was noted in three patients. In two of these patients, MRI revealed no significant recoarctation, and, in the absence of associated hypertension, conservative management was advocated. The remaining patient had a cardiac catheterization, and was noted to have a diffusely tortuous aorta (invasive gradient, 14 mm Hg), and no further treatment was recommended.

**Aneurysm formation.** The morphology and dimensions of the thoracic aorta were assessed during follow-up in 61 of the 68 (90%) early survivors, by MRI (n = 60) or by repeat angiography (n = 9), with the latest assessment being performed at a median of 6 months (range one week to 3.5 years) after the initial balloon angioplasty. One patient (1%) had an aneurysm diagnosed by MRI and confirmed by angiography. This aneurysm remained stable in size over the time of observation, and no intervention was required. Four patients (7%) had mild dilation of the aorta at the angioplasty site (not fulfilling the criteria for an aneurysm) without progression over the period of observation. Two additional patients (3%) who required reintervention for residual stenosis had mild dilation at the angioplasty site. In three further patients (5%), early MRI studies showed an intimal flap within the vessel lumen but no aneurysm or dilation. Repeat MRI in those three patients showed disappearance of the intimal flap in two patients, with the remaining patient having an unusual form of vasculopathy (16).

**MRI assessment of femoral artery patency.** Twenty-one patients had early MRI assessment of femoral artery patency. Iliofemoral arteries were described as normal in 7 patients, patent but significantly smaller than the contralateral vessel in 10 and blocked or severely stenosed in 4

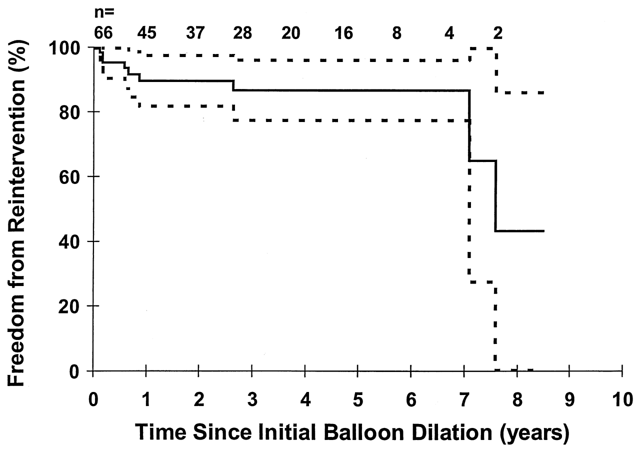


**Figure 3.** Kaplan-Meier plot of freedom from reintervention after initial transcatheter balloon angioplasty. **Dashed lines** represent 95% confidence intervals.

patients. Fourteen patients had a follow-up study of the femoral arteries, showing normal vessels in five patients, patent but smaller illiofemoral arteries in five and severely stenosed or blocked arteries in four patients. Out of 12 patients who had two MRI assessments of the femoral arteries, there was no change or progression between the two assessments in 10 patients. In one patient there was progression from a normal appearing artery to a severely stenosed artery, and in one patient there was progression from a narrow but patent artery to a severely stenosed or blocked artery.

**Freedom from reintervention.** Kaplan-Meier estimates of freedom from reintervention in early survivors were 90% at one year and 87% at five years (Fig. 3). Factors associated with a decreased time to reintervention were sought in univariable Cox's proportionate hazard modeling (Table 5). Significant factors included a lower z-value of the transverse aortic arch diameter, higher predilation ascending to descending aortic peak-to-peak systolic pressure gradient, a lower percentage change in invasive gradient with dilation, a higher ratio of balloon to coarctation segment diameter but a lower ratio of balloon to aorta at level of diaphragm diameter and both increased circumferential and cross-sectional area stretch and gain, but not recoil. In stepwise multiple Cox's proportionate hazard regression modeling, only three variables were independently associated with a reduced time to reintervention ($n = 57$) and included a higher predilation invasive gradient, a reduced percentage change in invasive gradient with dilation and an increased ratio of balloon to coarctation segment diameter. After controlling for these three variables, no other variable met level of significance criteria for entry into the final model.

## DISCUSSION

Transcatheter treatment of native CoA in children remains a highly charged and controversial topic due to the perceived risks to vessel integrity, its influence on long-term vessel stability and the initial success of the procedure (2). In this regard, a more coherent understanding of the mechanism of restenosis and aneurysm formation, as well as longer term follow-up of results after angioplasty, can help toward resolving this management dilemma.

Factors associated with restenosis after balloon angioplasty have been described in many large studies and include: young patient age (neonate), associated arch hypoplasia and a small CoA diameter (3–5,8,17). Aneurysm formation, although in some cases related to technical factors such as use of larger balloons, may be promoted by inherent wall abnormalities such as cystic medial necrosis (7,18). The presence of ductal tissue within the aortic wall as seen in neonates may be an important component of

**Table 5.** Factors Associated With Decreased Time to Reintervention*

| | n | Beta Coefficient (Standard Error) | p Value | RR (95% CI) |
|---|---|---|---|---|
| Age at intervention (yr) | 66 | −0.0513 (0.0842) | 0.55 | 0.95 (0.81, 1.12) |
| Weight at intervention (yr) | 66 | −0.0209 (0.0237) | 0.38 | 0.98 (0.93, 1.03) |
| z-value of transverse aortic arch diameter | 61 | −0.9667 (0.3962) | 0.02 | 0.38 (0.17, 0.83) |
| Ascending to descending peak-to-peak systolic pressure gradient predilation (mm Hg) | 65 | 0.0818 (0.0293) | 0.006 | 1.09 (1.02, 1.15) |
| Percentage change in invasive gradient | 64 | 0.0305 (0.0083) | < 0.001 | 1.03 (1.01, 1.05) |
| Ratio of balloon to CoA segment diameter | 62 | 0.3979 (0.1379) | 0.004 | 1.45 (1.14, 1.95) |
| Ratio of balloon to aorta at level of diaphragm diameter | 66 | −5.7089 (2.6201) | 0.03 | 0.003 (0.00002, 0.56) |
| Circumferential stretch (%) | 62 | 0.0845 (0.0366) | 0.02 | 1.09 (1.01, 1.17) |
| Circumferential recoil (%) | 61 | 0.0364 (0.0331) | 0.28 | 1.04 (0.97, 1.11) |
| Circumferential gain (%) | 59 | 0.0049 (0.0021) | 0.02 | 1.01 (1.00, 1.02) |
| Cross-sectional area stretch (%) | 62 | 0.1289 (0.0634) | < 0.05 | 1.14 (1.00, 1.29) |
| Cross-sectional area recoil (%) | 61 | 0.0275 (0.0228) | 0.23 | 1.03 (0.98, 1.07) |
| Cross-sectional area gain (%) | 59 | 0.0005 (0.0002) | 0.03 | 1.00 (1.00, 1.00) |

*From univariable Cox's proportionate hazard modeling.
CI = confidence interval; CoA = coarctation; RR = risk ratio.

restenosis when balloon dilation is applied in this age group (17).

Our results are very similar to those of previously reported studies. Early success was achieved in 87% of the patients. Complications were rare and mainly related to femoral artery damage and paradoxical hypertension. Aneurysm formation occurred in only 1% of the patients in whom MRI or angiography was performed during follow-up, but an additional 7% had vessel irregularities, albeit stable in size, at the dilation site. Longer follow-up remains important in such patients. Reintervention was required in 13%, and factors associated with reintervention reported in previous studies were also found to be significant in our study: a high predilation gradient, a reduced percentage change in invasive gradient with dilation and an increased ratio of balloon to coarctation segment diameter were associated with a decreased time to reintervention. Age was not a factor, but most of our patients were >1 year of age. Repeat angioplasty, including stent placement in one patient, was performed successfully in three out of the nine patients requiring reintervention, the remainder (n = 6) having uncomplicated surgical reintervention.

The biophysical properties of the vessel wall may also play an important role in the response to balloon dilation. To better predict the response of atheromatous coronary arteries to balloon angioplasty, Rensing et al. measured the stretch-gain-recoil relationship during angiography as a marker of the biophysical properties of the coronary vessel wall (19,20). They reported that greater gain was associated with more severe luminal narrowing at follow-up and hypothesized that extensive damage caused by dilation (greater gain) promoted intimal hyperplasia and proliferation of muscle cells responsible for restenosis (20). Ino et al. used the same approach to study the aortic vessel wall in patients undergoing balloon dilation of CoA and found that greater stretch and gain was associated with late restenosis (9). However, their patient group was heterogeneous, including those with native CoA and recurrent CoA after surgical repair, infants, young children and adolescents. Such divergent populations may have different vessel wall properties influencing vessel response to dilation. Rao et al. (10) applying a similar method of assessment to CoA, found that recoil was greater in the group without restenosis. Their hypothesis was that in the group with recurrent stenosis after dilation, the elastic properties of the wall had not been preserved, thereby causing restenosis. However, in their analysis, the method of calculation of stretch, gain and recoil was different than that used by Ino et al. (9) making comparisons difficult.

Our cohort included only patients with native CoA and excluded neonates and young infants. Stretch, recoil and gain were measured from CoA cross-sectional areas as well as circumference, suggested by Rao et al. (10). However, as in Ino et al.'s study (9), stretch and recoil were normalized to the balloon diameters and gain normalized to the CoA dimensions before dilation, to minimize the effect of body size. Also considered was the geometry of the CoA, being closer to an ellipse than to a circle, for calculation of the CoA cross-sectional areas and circumferences, using the dimensions measured from two nearly orthogonal projections. Thus, it is difficult to compare our findings with the previously described studies (9,10). However, as did Ino et al. (9), we found an exponential relationship between gain and stretch. Reasonable cross-sectional area gain seems to be obtained with an area stretch between 80% and 90% and a reasonable circumferential gain with a circumferential stretch between 60% and 70%. Similarly, we found that larger gain and stretch were significantly associated with early failure and reintervention, while recoil was not found to be associated with reintervention. However, one critical difference between Ino's study and ours was that seven of the nine patients who underwent reintervention did so for an unsuccessful procedure, therefore representing the effect of residual stenosis rather than late restenosis or recurrence. The small group of patients with late restenosis (n = 2) precludes meaningful analysis. The hypothesis that greater gain and stretch, by promoting more extensive vessel damage, produces more intimal hyperplasia and, thus, late restenosis was difficult to confirm in this group of patients. Greater gain and stretch could, however, alter elastic properties and favor residual stenosis. Our results may also simply reflect the notion that severe coarctations, in which stretch and gain would be expected to be more important, are more difficult to dilate due to their smaller circumference compared with that of the normal aortic wall. Furthermore, the morphology of the obstructing shelf may importantly impact dilation results, not influenced by the elasticity of the vessel, but the histological features of the shelf, where a more inelastic shelf may be more easily torn than a more compliant one. In those patients with the most severe obstructive lesions, there appeared to be more of an invagination of the wall rather than an intraluminal shelf, which could be enlarged through dilation (tearing) within the shelf. More studies on larger populations with residual and late restenosis will be required to fully determine and understand the possible impact of stretch, gain and recoil on outcome. Finally, small measurement errors in the area and circumference normalization can effect results. To limit this effect, an elliptical lesion model was used (rather than assuming a circular lesion) and multiple measurements of the lesion taken in optimal orthogonal projections.

In conclusion, our study supports the previous studies showing that balloon dilation is a safe and effective treatment option for native CoA in children after infancy. Reintervention was more likely when the initial coarctation gradient was very high and when there was associated transverse aortic arch hypoplasia. Modification of vessel wall properties were reflected by the stretch-recoil-gain relationship, which might be an important prognostic factor for outcome, but more data are necessary to sustain this hypothesis and fully understand the mechanism.

**Reprint requests and correspondence:** Dr. Lee N. Benson, Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, Canada M5G 1X8. E-mail: benson@sickkids.on.ca.

## REFERENCES

1. Singer MI, Rowen M, Dorsey TJ. Transluminal aortic balloon angioplasty for coarctation of the aorta in the newborn. Am Heart J 1982;103:131–2.
2. Ovaert C, Benson LN, Nykanen D, Freedom RM. Transcatheter treatment of coarctation of the aorta: a review. Pediatr Cardiol 1998;19:27–44.
3. Fletcher SE, Nihill MR, Grifka RG, O'Laughlin MP, Mullins CE. Balloon angioplasty of native coarctation of the aorta: midterm follow-up and prognostic factors. J Am Coll Cardiol 1995;25:730–4.
4. Rao PS, Galal O, Smith PA, Wilson AD. Five to nine-year follow-up results of balloon angioplasty of native coarctation in infants and children. J Am Coll Cardiol 1996;27:462–70.
5. Mendelsohn AM, Lloyd TR, Crowley DC, Sandhu SK, Kocis KC, Beekman RH. Late follow-up of balloon angioplasty in children with a native coarctation of the aorta. Am J Cardiol 1994;74:696–700.
6. Ho SY, Somerville J, Yip WCL, Anderson RH. Transluminal balloon dilation of resected coarcted segments of thoracic aorta: histological study and clinical implications. Int J Cardiol 1988;19:99–105.
7. Isner JM, Donaldson RF, Fulton D, Bhan I, Payne DD, Cleveland RJ. Cystic medial necrosis in coarctation of the aorta: a potential factor contributing to adverse consequences observed after percutaneous balloon angioplasty of coarctation sites. Circulation 1987;75:689–95.
8. Kaine SF, O'Brian Smith E, Mott AR, Mullins CE, Geva T. Quantitative echocardiographic analysis of the aortic arch predicts outcome of balloon angioplasty of native coarctation of the aorta. Circulation 1996;94:1056–62.
9. Ino T, Ohkubo M, Akimoto K, et al. Angiographic assessment of the stretch-recoil-gain relation after balloon coarctation angioplasty and its relation to late restenosis. Jpn Circ J 1996;60:102–7.
10. Rao PS, Waterman B. Relation of biophysical response of coarcted aortic segment to balloon dilation with development of recoarctation following balloon angioplasty of native coarctation. Heart 1998;79: 407–11.
11. Ino T, Benson LN, Freedom RM, Barker GA, Zipursky A, Rowe RD. Thrombolytic therapy for femoral artery thrombosis after pediatric cardiac catheterization. Am Heart J 1988;115:633–9.
12. Weast RC, Selby SM. Handbook of Tables for Mathematics. 3rd ed. Cleveland, Ohio: CRC Press, 1967:12–769.
13. Bromberg BI, Beekman RH, Rocchini AP, et al. Aortic aneurysm after patch aortoplasty repair of coarctation: a prospective analysis of prevalence, screening tests and risks. J Am Coll Cardiol 1989;14:734–41.
14. Pinzon JL, Burrows PE, Benson LN, et al. Repair of coarctation of the aorta in children: postoperative morphology. Radiology 1991;180: 199–203.
15. Burrows PE, Benson LN, Babyn P, MacDonald C. Magnetic resonance imaging of the iliofemoral arteries after balloon dilation angioplasty of aortic arch obstructions in children. Circulation 1994;90:915–20.
16. Vaillant L, Lorette G, Chantepie A, et al. Multiple cutaneous hemangiomas and coarctation of the aorta with right aortic arch. Pediatrics 1988;81:707–10.
17. Rao PS, Thapar MK, Kutayli F, Carey P. Causes of recoarctation after balloon angioplasty of unoperated aortic coarctation. J Am Coll Cardiol 1989;13:109–15.
18. Rao PS. Aortic rupture after balloon angioplasty of aortic coarctation. Am Heart J 1993;125:1205–6.
19. Rensing BJ, Hermans WRM, Beatt KJ, et al. Quantitative angiographic assessment of elastic recoil after percutaneous transluminal coronary angioplasty. Am J Cardiol 1990;66:1039–44.
20. Rensing BJ, Hermans WRM, Vos J, et al. Angiographic risk factors of luminal narrowing after coronary balloon angioplasty using balloon measurements to reflect stretch and elastic recoil at the dilation site. Am J Cardiol 1992;69:584–91.