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Remodeling of the Aorta After Successful Balloon Coarctation Angioplasty

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The purpose of this study was to examine whether remodeling of the aorta takes place after successful balloon angioplasty of aortic coarctation. During the 35 month period ending in December 1987, 30 children, aged 14 days to 13 years, underwent balloon angioplasty of unoperated aortic coarctation, with a resultant reduction in mean coarctation gradient from 44 ± 20 to 10 ± 8 mm Hg ($p < 0.001$). On the basis of results of 6 to 30 months' follow-up catheterization data in 20 children, the patients were classified into group A (13 patients with good results; gradient ≤20 mm Hg and no recoarctation on angiography) and group B (7 patients with fair or poor results; gradient >20 mm Hg with or without recoarctation on angiography).

Measurements of the aorta at five sites (the ascending aorta, isthmus, coarcted segment and descending aorta distal to the coarctation and at the level of the diaphragm) were made in two angiographic views, corrected for magnification and averaged. A standardized diameter of the aorta at the five locations was calculated for each case before angioplasty and at follow-up study, and variance of the diameter was then determined. The variance of standardized aortic measures (0.233 versus 0.287) was similar ($p > 0.05$) in both groups before angioplasty, whereas at follow-up study (0.057 versus 0.129) they were different ($p = 0.01$). There was a greater percent improvement at follow-up study (0.233 versus 0.057) in the group with good results than in the group with fair or poor results (0.287 versus 0.129). Cluster analysis was also indicative of remodeling of the aorta in the group with good results.

These data indicate a greater remodeling and normalization of the aorta after successful balloon angioplasty of aortic coarctation, suggesting that normalized flow across the dilated coarctation allows optimal growth of the aortic segments.

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Several immediate and a few intermediate-term follow-up results of balloon angioplasty of previously unoperated cases of aortic coarctation have been reported (1–18). The major objective in relieving aortic obstruction is to alleviate heart failure and hypertension and improve blood flow to the lower part of the body. There should also be a certain degree of "remodeling" of the aorta after successful relief of aortic obstruction. In this context, remodeling may be defined as a change in size of various segments of the aorta, such that the aorta is uniform and closely approximates that in normal children. Whether such a remodeling occurs has not been investigated. The purpose of this study was to examine whether remodeling of the aorta takes place after balloon angioplasty of native aortic coarctation; data on the size of various aortic segments at intermediate-term follow-up study after balloon angioplasty were utilized for this purpose.

Methods

Study patients. During the 35 month period ending in December 1987, 30 infants and children, aged 14 days to 13 years, underwent balloon dilation of unoperated aortic coarctation. Informed consent was obtained from the parents of each patient. The technique of balloon angioplasty of aortic coarctation has been described in detail in previous publications (11,12,18) and will not be described here. Follow-up cardiac catheterization and angiography were performed 6 to 30 months (mean 12 ± 6) after balloon angioplasty. Twenty of the 30 infants and children have follow-up data. These patients were not selected for any specific

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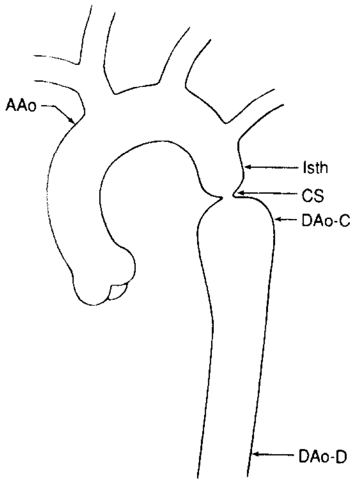

Figure 1. Line drawing of the aorta to show the five locations where the aortic measurements were obtained. AAo = ascending aorta; CS = coarcted segment; DAo-C = descending aorta immediately distal to coarctation; DAo-D = descending aorta at diaphragm; Isth = aortic isthmus.

reason and included all patients in whom we have been able to perform follow-up study. Patients were classified into two groups (19): group A (Patients 1 to 13) with good results, and group B (Patients 14 to 20) with fair or poor results.

Aortic measurements. Measurements of the aorta (Fig. 1) are the average of measurements made in anteroposterior and lateral views in all but two cases (in which the left anterior oblique and right anterior oblique views were used) after correction for magnification. The ascending aorta was measured immediately proximal to the origin of the right innominate artery and was high enough not to have the significant "post-stenotic dilation" effect of associated aortic stenosis in some of these children. The aortic isthmus was measured midway between the origin of the left subclavian artery and the coarcted aortic segment. The coarcted segment was measured at the narrowest part of aortic coarctation. The descending aorta distal to the coarcted segment was measured at an area at which the post stenotically dilated descending aorta attained a stable size (Fig. 1). The descending aorta was also measured at the level of the diaphragm. These measurements were taken from aortic cineangiographic frames obtained before and immediately after initial balloon angioplasty and at the time of follow-up catheterization, without the knowledge of whether there was a successful outcome at follow-up study. When data on aortic segment sizes before and immediately after angioplasty were compared, there was no change, with the exception of the coarcted aortic segment. Therefore, preangioplasty data were compared with data obtained at follow-up catheterization and angiography.

Statistics. Student's *t* test was used for comparison of the data obtained before and after angioplasty as well as for the comparison of the groups. The level of statistical significance was set at $p < 0.05$. Values are presented as mean values ± SD. Data analysis and statistical methods used with regard to aortic remodeling will be described in conjunction with the results.

Results

Immediate results. Thirty children, 23 boys and 7 girls with a weight range of 2.1 to 50.0 kg (mean 14.7), underwent cardiac catheterization and balloon angioplasty of aortic coarctation. Twelve of the 16 infants were in moderate to severe heart failure, and all but 3 patients were hypertensive. After balloon angioplasty, the mean systolic pressure gradient across the aortic coarctation decreased from 44 ± 20 to 10 ± 8 mm Hg ($p < 0.001$) and the coarcted aortic segment increased in mean diameter from 3.5 ± 2.0 to 8.3 ± 3.6 mm ($p < 0.001$). None of the patients required immediate surgical intervention.

Follow-up results. Twenty children had repeat cardiac catheterization and angiography 6 to 30 months (mean 12) after balloon angioplasty. Of the remaining 10 children, 2 were lost to follow-up and in 8 patients it was too soon to perform repeat catheterizations. For the 20 children in whom follow-up catheterization data were available, the systolic pressure gradient across the coarctation (51 ± 22 versus 10 ± 8 mm Hg) and the size of the coarcted aortic segment (3.5 ± 1.7 versus 8.7 ± 3.4 mm) improved ($p < 0.001$) immediately after balloon angioplasty. At follow-up study approximately 1 year later, the systolic pressure gradient across the coarctation (15 ± 13 mm Hg, $p < 0.001$) and the size of the coarcted segment (9.4 ± 3.4 mm, $p < 0.001$) remain improved when compared with the preangioplasty values. Despite improvement as a group, several children developed recoarctation. On the basis of individual results at repeat catheterization and angiography, these 20 children were divided into two groups: group A (Patients 1 to 13) with good results, with a pressure gradient across the dilated coarctation of ≤20 mm Hg and no recoarctation on angiography, and group B (Patients 14 to 20) with fair results (gradient 21 to 30 mm Hg, with or without angiographic recoarctation) or poor results (gradient >30 mm Hg and recoarctation on angiography), with a coarctation pressure gradient ≥21 mm Hg with or without recoarctation on angiography.

In the 13 group A children with good results, the gradient across the coarctation decreased (46 ± 17 versus 9 ± 7 mm Hg, $p < 0.001$) and the size of the coarcted aortic segment increased (4.0 ± 1.9 versus 10.0 ± 3.1 mm, $p < 0.001$) immediately after balloon angioplasty; these remained essentially unchanged and, respectively, were 8 ± 6 mm Hg and 10.9 ± 3.1 mm at follow-up catheterization. In the seven group B children with fair and poor results, the coarctation gradient decreased from 61 ± 27 to 12 ± 8 mm Hg ($p < 0.01$). However, on follow-up study, the gradient (31 ± 8 mm Hg)

Table 1. Aortic Measurements at Various Sites Before Angioplasty and at Follow-Up Study in 20 Patients

Patient No.	AAo Pre/FU	Isth Pre/FU	CS Pre/FU	DAo-C Pre/FU	DAo-D Pre/FU
Group A					
1	9.9/11.7	7.0/8.8	2.5/7.0	10.2/12.9	8.0/10.3
2	15.3/15.3	9.4/9.4	8.0/8.8	15.2/15.2	13.7/14.1
3	15.8/17.6	7.3/8.8	3.0/8.5	11.3/14.9	8.6/15.5
4	20.6/18.0	12.3/12.3	3.0/12.0	18.8/18.8	12.8/12.8
5	20.5/17.5	17.7/17.7	4.0/12.0	13.1/14.5	10.9/14.0
6	18.2/18.2	14.3/15.0	6.9/13.5	21.2/22.0	15.7/19.5
7	25.0/25.4	13.8/13.9	6.9/10.6	15.8/15.8	11.5/13.3
8	11.6/15.7	9.0/9.0	5.6/9.5	12.7/13.4	9.4/11.0
9	21.0/21.9	16.0/20.3	6.8/16.0	19.4/23.1	15.2/21.9
10	24.6/26.5	12.8/14.4	3.75/11.5	19.8/19.8	16.0/17.9
11	24.3/26.8	13.9/16.1	2.9/13.0	21.5/21.5	23.4/23.8
12	21.7/23.0	18.0/21.5	2.0/14.5	20.1/25.0	16.0/18.4
13	10.3/13.7	5.6/7.7	1.67/5.0	10.0/10.2	6.7/8.7
Mean	18.4/19.3	12.1/13.5	4.4/10.9	16.1/17.5	12.9/15.5
SD	5.4/4.9	4.1/4.6	2.2/3.1	4.3/4.5	4.5/4.6
Group B*					
14	24.6/24.2	12.4/12.9	3.0/12.2	21.8/23.2	17.4/18.6
15	7.7/11.0	4.8/6.4	1.67/3.1	8.7/11.5	6.4/9.4
16	16.8/14.8	5.7/8.2	2.7/6.9	6.3/9.4	8.8/10.5
17	19.7/18.8	8.7/8.7	3.5/6.0	13.1/15.2	10.6/12.1
18	9.2/10.2	4.2/6.4	2.0/4.8	7.3/11.4	6.2/9.5
19	20.5/–	8.1/–	3.0/–	14.6/–	10.1/–
20	8.6/12.0	4.9/8.0	1.7/3.4	6.8/11.5	6.4/9.6
Mean	13.1/15.2	7.0/8.4	2.5/6.1	11.2/13.7	9.4/11.6
SD	5.7/5.4	2.9/2.4	0.7/3.3	5.7/5.0	4.0/3.6

*Criteria for classification into group B (fair and poor results at follow-up): Patient 14 gradient = 30 mm Hg, diffuse narrowing of isthmus. Patient 15 gradient = 24 mm Hg, no discrete recoarctation on angiography. Patient 16 gradient = 30 mm Hg, no discrete recoarctation on angiography. Patient 17 gradient = 25 mm Hg, recoarctation on angiography. Patient 18 gradient = 46 mm Hg, recoarctation on angiography. Patient 19 recoarctation on angiography performed elsewhere; no follow-up angiographic data are available for review. Patient 20 gradient = 31 mm Hg, recoarctation on angiography. AAo = ascending aorta; CS = coarcted aortic segment; DAo-C = descending aorta immediately distal to the coarctation; DAo-D = descending aorta at the level of the diaphragm; FU = at follow-up catheterization and angiography; Isth = aortic isthmus; Pre = preangioplasty.

returned toward preangioplasty values. Similarly, the size of the coarcted aortic segment increased (2.5 ± 0.7 versus 6.2 ± 2.5 mm, $p < 0.01$) immediately after angioplasty and remained unchanged (6.1 ± 3.3 mm, $p > 0.1$) on follow-up. At follow-up study, group A children (with good results) had a lower pressure gradient across the coarctation (8 ± 6 versus 31 ± 8 mm Hg, $p < 0.001$) and a larger segment of dilated aortic coarctation (10.9 ± 3.1 versus 6.1 ± 3.3 mm, $p < 0.01$) than did group B children. None of the group A children required surgical repair or repeat balloon angioplasty. Four infants from group B at restudy approximately 12 months after initial balloon angioplasty required repeat balloon angioplasty (Patients 15 and 20) or surgical resection (Patients 18 and 19). The remaining three children, all from the fair results subgroup, did not require further intervention because of a low pressure gradient and near normal systolic blood pressure.

Results of aortic remodeling. Inter-and intragroup comparisons of the shape of the aorta, as defined by measurements of the ascending aorta (AAo), isthmus (Isth), coarcted segment (CS) and descending aorta immediately distal to the site of coarctation (DAo-C) and at the level of the diaphragm (DAo-D) were performed before angioplasty and at follow-up study to assess aortic remodeling (raw data are listed in Table 1). For this purpose, it seemed appropriate to standardize the measurements to create a pure measure of shape. This was done by dividing each of the five aortic measurements by their average for each subject before and after treatment. The resulting standardized measures would be on the same scale for each subject at each time point. An example is shown in Table 2. The method of obtaining standardized aortic measures is also illustrated in Figure 2. Once the standardized aortic measures were determined, the variance* from norm or unity was determined for each patient before angioplasty and at follow-up study.

Inter- and intragroup comparisons were made by using

*Variance is the sum of the squared differences of each measure divided by the degrees of freedom.

Table 2. Example of Standardized Measurements Based on the Five Aortic Measurements

	Aortic Measurements					
	AAo	Isth	CS	DAo-C	DAo-D	Average
Patient 1	5	3	1	6	4	3.8
Patient 2	11	7	3	13	6	8.0
	Corresponding Standardized Measurements					
	AAo	Isth	CS	DAo-C	DAo-D	
Patient 1	1.32	0.79	0.26	1.58	1.05	
Patient 2	1.38	0.88	0.38	1.63	0.75	

AAo = ascending aorta; CS = coarcted segment; DAo-C = descending aorta immediately distal to the site of coarctation; DAo-D = descending aorta at the level of the diaphragm; Isth = aortic Isthmus.

the variance of five standardized diameter values (Table 3). This procedure was designed to assess how much the aorta deviated from the norm (an aorta with a uniform diameter throughout). The test statistic for the intergroup comparison was the nonparametric Mann-Whitney U statistic. To test for the effect of balloon angioplasty within each group, Wilcoxon's signed rank test was used. The data suggest that group A and group B were not statistically different ($p > 0.05$) before angioplasty, though the variability of the aortic diameters in group B tended to be greater. At follow-up study, aortic measurements from group A patients were significantly more uniform ($p = 0.01$) suggesting a better remodeling in these patients with good results. There was improvement within both groups after angioplasty ($p < 0.05$); there was a greater percent improvement (0.233 versus 0.057) in group A patients than in group B patients (0.287 versus 0.129).

Cluster analysis was used to determine whether patients with good results could be differentiated from those with poor results on the basis of the shape of the aorta (Table 4). Using Anderberg's "nearest centroid sorting" method (20) with the variance of the standardized diameter values as the defining characteristic, the subjects were sorted into two clusters before and after treatment. In examining the 2 × 2 tables of clusters and groups, it is apparent that cluster analysis does not distinguish between groups A and B before angioplasty (meaning that both groups are similar) as well as it does at follow-up study. Inspection of schematic diagrams of the aorta (Fig. 3) graphically indicates that there was a definite remodeling of the aorta in group A (with good intermediate-term follow-up results), whereas there was less remodeling in group B (with poor and fair results).

Figure 2. Method of obtaining standardized aortic measures. Absolute sizes (**dashed lines**) at all five locations were averaged (represented by **solid lines**). The standardized aortic measure of each site was then calculated by dividing the absolute size by the average (mean) of all the five measurements. The **dotted lines** represent the aortic shape and the latter can be compared with that of other patients or that measured after an intervention. Abbreviations as in Figure 1.

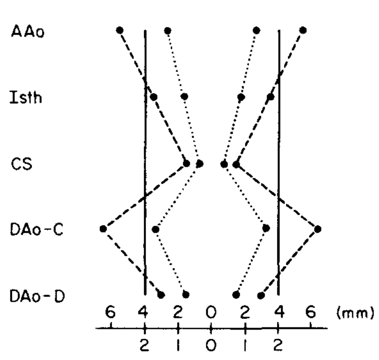

Table 3. Nonparametric Comparison of Standardized Variance of Aortic Measures Between Groups

	Preangioplasty Median	Follow-up Median	p Value (Wilcoxon)
Group A	0.233	0.057	0.002
Group B	0.287	0.129	0.04
p value (Mann-Whitney)	0.08	0.01	

Discussion

Immediate results. Immediate successful results in the 30 infants and children reported in the present study are similar to those observed by other investigators (1,3–12,15–18). Heart failure and hypertension were alleviated and immediate surgical intervention was avoided in all patients.

Follow-up results. Several investigators (2,5,14–18) restudied 7 to 14 patients 1 to 31 months after balloon angioplasty and reported a 10% to 43% recoarctation rate and an 8% to 55% aneurysmal formation rate. The recoarctation rate of 35% at intermediate-term follow-up in our group (7 of 20 patients if both poor and fair results are included) or of 15% (3 of 20 if only poor results are included) is similar to that reported by the previous authors. In young infants, a high incidence of coarctation recurrence after balloon angioplasty is comparable with that seen with surgical resection of coarctation (21–26). Aneurysm at the site of coarctation

Table 4. Two by Two Tables of Cluster Analysis* of Standardized Variance of Aortic Measures in Both Groups

	Preangioplasty		Follow-Up	
	Group A	Group B	Group A	Group B
Cluster 1	7	3	9	2
Cluster 2	6	4	4	4
p value†	0.4		0.025	

*By Anderberg's "nearest centroid sorting" method (20). †By chi-square analysis.

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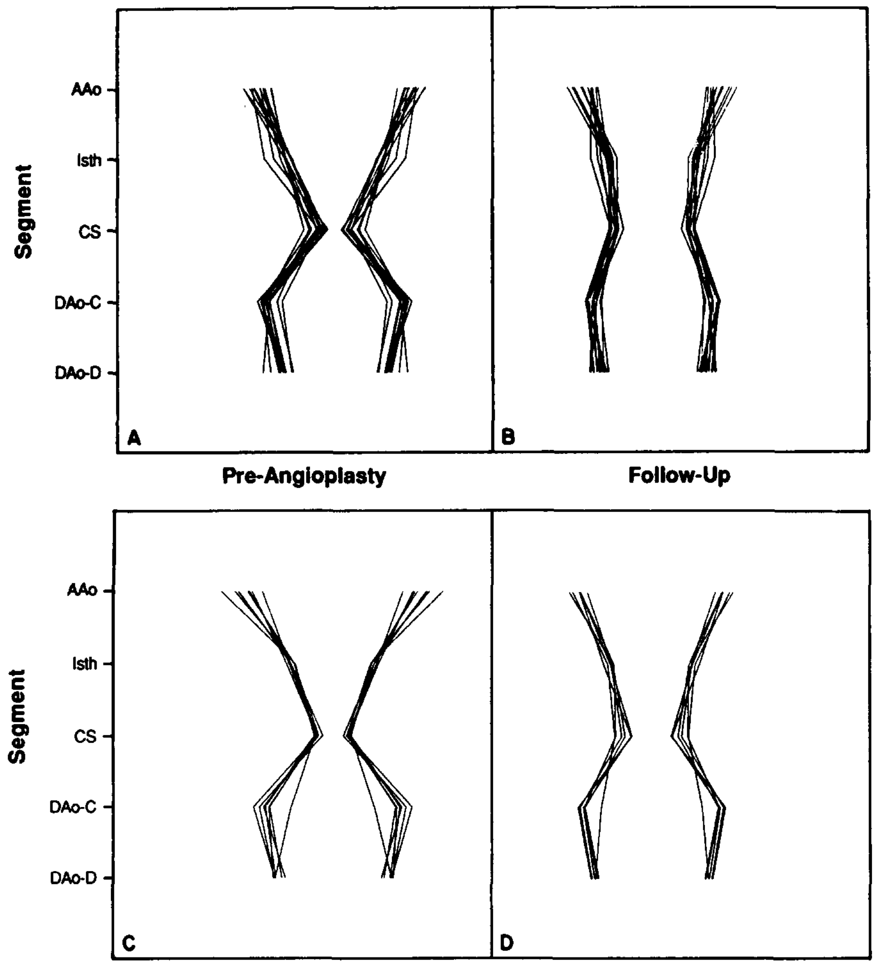

Figure 3. Line drawing of the standardized aortic measurements in Group A (**top**) and Group B (**bottom**). Each pair of lines represents a patient. Note that the aortic shapes appear similar in both groups (**A** and **C**) before angioplasty. The shape of the aorta improved markedly in group A with good results (**B**), whereas in group B the shape looks similar (**D**) to that before angioplasty. Abbreviations as in Figure 1.

dilation at follow-up study has been reported by some workers (13–17), whereas we (12,18,19) and others (5,10) did not find any aneurysm at follow-up study. The reasons for this difference are not known. Lack of attention to the recommendation of not manipulating guidewires and catheters over the area of freshly dilated coarctation (4,18), use of a balloon larger than the descending aorta at the level of the diaphragm (18) or overinterpretation of the results (18) have been suggested as factors responsible for aneurysm formation. The reasons for recoarctation have been discussed elsewhere (19).

Aortic remodeling. Data analysis and statistical treatment of the shape of the aorta as quantitated by measurement of five aortic segments were difficult, and we were unable to locate analysis of similar data elsewhere. Examining the variance of the standardized measures seemed appropriate. Additional cluster analysis by Anderberg's "nearest centroid sorting" method (20) was also used to see if our groups could be formed based on shape consideration alone.

Although surgical treatment of aortic coarctation has been used for >40 years, to our knowledge, no one has examined whether remodeling of the aorta takes place at long-term follow-up study. The reason for this, perhaps, is lack of systematic angiographic follow-up study. Growth of the aortic segment (or segments) as the infant or child gets older plus "normalization" of aortic flow should result in equalization of all aortic segments. The readjustment of size, "remodeling" as we called it, was indeed dramatic as evidenced by a marked decrease in the variance of the standardized aortic measures (Table 3) in the group with good results (Fig. 3) and the small decrease in variance in the group with poor or fair results may be related to the growth. This degree of remodeling was observed at a mean follow-up time of 1 year and, therefore, a longer follow-up period is likely to show greater remodeling and normalization of the aorta. The growth response of the aortic segments to increased blood flow may be similar to that observed in the fetus and neonate (27).

Conclusions. Our data suggest that a greater remodeling of the aorta occurs after successful balloon angioplasty of aortic coarctation, indicating that normalized flow across the dilated coarcted segment allows optimal growth of the aortic segments.

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