Rapid Two-Stage Arterial Switch Operation

Acquisition of Left Ventricular Mass After Pulmonary Artery Banding in Infants With Transposition of the Great Arteries

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Background. Banding of the pulmonary artery (PAB) in preparation for arterial switch operation (ASO) in patients with transposition of the great arteries (TGA) represents a unique model of acute left ventricular pressure overload in humans.

Methods and Results. To establish the rate, magnitude, and determinants of left ventricular hypertrophy and the acute effect on ventricular function, serial bidimensional echocardiographic evaluations were performed on 26 patients with TGA after PAB. Mass, volume, and ejection fraction of the left ventricle were measured. Cardiac catheterization data before PAB and again before ASO were reviewed. The mean interval between the PAB and ASO was 9 ± 4 days. The left ventricular to right ventricular pressure ratio before PAB was 0.5 and increased to 1.0 before ASO. The mean percentage increase in left ventricular mass from PAB to ASO was 96%, 95% of which was achieved in the first 7 days. The average rate of left ventricular hypertrophy for the entire period was 0.06 g/h and was 0.19 g/h during the interval from PAB to attainment of maximum left ventricular mass. The most rapid rate of hypertrophy was seen by day 2, with an exponential fall in the growth rate thereafter approaching zero by day 7. Ejection fraction was significantly reduced at 12 hours after PAB, but mean values returned to pre-PAB levels by 3.5 days after banding. The absolute rate of left ventricular hypertrophy correlated directly with body surface area but not to other hemodynamic variables.

Conclusions. Doubling of left ventricular mass can be achieved in 1 week after PAB. Function falls acutely due to afterload excess and/or depressed contractility but recovers rapidly as compensatory hypertrophy occurs. (Circulation. 1994;90:1304-1309.)

Key Words • ventricles • transposition of great vessels • heart diseases • echocardiography • arterial switch operation

Follow-up of patients who have had a primary anatomic repair for transposition of the great arteries (TGA) consisting of an arterial switch operation (ASO) performed in the first weeks of life has demonstrated preserved right and left ventricular function, a low incidence of significant arrhythmias, and few short-term or midterm surgical complications when compared with intra-atrial baffle correction.1-4 A two-stage approach for anatomic correction of TGA was reported by Yacoub et al5 in 1977. With this procedure, pulmonary artery banding was performed and the ASO was delayed until age 1 year or more, when the left ventricle was judged to be adequately prepared to sustain the systemic circulation.5-8 However, the prolonged period of cyanosis, evidence of time-related left ventricular injury,9 branch pulmonary artery injury, and insufficiency of the neoaoartic valve prompted a move to a primary, single-stage ASO during the first weeks of life,10 when the left ventricle is still capable of supporting the systemic circulation. Since not all patients with TGA can undergo early one-stage ASO because of prematurity, extracardiac disease, or late referral, a two-stage repair is still necessary in some patients.

In 1989, we11 reported that the left ventricle could be adequately prepared for an ASO after a preparatory period of approximately 1 week with excellent results at early follow-up. To evaluate the response of the left ventricle after banding of the pulmonary artery, the present study was performed to establish the specific rate of left ventricular mass acquisition, the magnitude of hypertrophy, and the possible determinants influencing left ventricular hypertrophy after banding of the pulmonary artery. We also examined the effect of banding on left ventricular function during the preparatory period.

Methods

In December 1986, we undertook a prospective evaluation of patients with TGA who had pulmonary artery banding in preparation for ASO.12 All patients were judged to be at risk for left ventricular failure if a primary ASO was performed based on interventricular pressure ratio at cardiac catheterization or an interventricular septal position on echocardiogram consistent with significantly systemic left ventricular pressure. Therefore, pulmonary artery banding with or without an aortopulmonary shunt was done in these patients. For those in whom a shunt was not performed at the time of pulmonary artery banding, all had the shunt placed as a second procedure within the following 2 days. Study entrance criteria therefore included (1) TGA with intact or virtually intact ventricular septum and low left ventricular pressure and (2) pulmonary artery banding for induction of left ventricular hypertrophy. Clinical details and preliminary results of the echocardiographic evaluation of these patients have been reported previously.12

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Echocardiographic Assessment

Patients underwent serial two-dimensional echocardiographic and Doppler examinations before surgery and starting in the first 12 hours after banding of the pulmonary artery until the second-stage ASO was performed. Evaluations were done every 12 to 24 hours during the first 5 to 7 days and every 24 hours thereafter when possible.

Analysis of Left Ventricular Volume and Mass

Subcostal short- and long-axis views of the left ventricle were used for the determination of left ventricular mass and volume. In some cases, these views were not technically adequate for measurements and the anatomically equivalent parasternal short-axis and apical four-chamber views of the left ventricle were used instead. We have found no significant difference in volumes obtained from these two views in normal subjects. End-diastolic and end-systolic endocardial and epicardial borders of the left ventricle were hand-digitized using a Dextra D-200 Cardiac Analysis System. All analyses were performed by a single investigator (C.B.) to reduce interobserver variability. The modified biplane Simpson's rule was ap

grams, or a mean of 5.5 exams per patient. The mean age and weight at pulmonary artery banding were 0.4±0.3 years and 5.6±2.2 kg, respectively. The mean interval between pulmonary artery banding and ASO was 9±4 days. All patients had a prior balloon atrial septostomy.

Cardiac catheterization data were available in 23 patients immediately before pulmonary artery banding and in 21 cases immediately before ASO. The mean left ventricular to right ventricular pressure ratio before banding of the pulmonary artery was 0.5±0.09 and increased to a mean value of 1.0±0.2 at the end of the preparatory period immediately before ASO.

Left Ventricular Mass

The indexed left ventricular mass before banding of the pulmonary artery was 78.4±28.9 g/m² (range, 41.84 to 141.99 g/m²) and was not significantly related to the patient's age or size at presentation over the narrow range included in the study. This value is not different from the normal value for left ventricular mass using the modified biplane Simpson's method for our laboratory for subjects under 6 months of age, which is 77.1±20.5 g/m². The left ventricular mass was significantly increased compared with preoperative values by 36 hours after banding of the pulmonary artery (Fig 1). The mean increase in left ventricular mass during the preparatory period was 100.1±67%. The rate of acquisition of left ventricular mass for the overall preparatory period was 0.058±0.042 g/h and was 0.2±0.3 g/h during the period from banding of the pulmonary artery to the time of maximum hypertrophy. After banding of the pulmonary artery, the accretion rate of left ventricular mass peaked rapidly and then fell exponentially (Fig 2).

The rate of hypertrophy correlated inversely with time since banding (r=−.88, P<.0001). By 7 days after banding, ventricular mass had increased by 95% and the rate of hypertrophy was no longer significantly different from zero (Fig 2).

To determine factors predicting or influencing left ventricular mass acquisition after banding of the pulmonary artery, clinical parameters (patient age, days of assisted ventilation, duration and quantity of the catecholamine vasopressors dopamine, dobutamine, and

Figure 1. Graph shows evolution of indexed left ventricular mass (g/m²) after acute pulmonary artery banding (PAB). A significant direct relation exists between the mean indexed left ventricular mass (y axis) and time since PAB (x axis). Mean data for each day are expressed as mean±1 SD. Thirty-six hours after PAB, indexed left ventricular mass was significantly different from pre-PAB level. Pre represents the indexed left ventricular mass before PAB.
epinephrine, and length of hospital stay), echocardiographic data (left ventricular mass before banding, ejection fraction before and after banding), and hemodynamic parameters (interventricular pressure ratio before banding and before ASO) were analyzed. None of these factors correlated significantly with the rate or magnitude of left ventricular hypertrophy, with the exception of a significant correlation between the average growth rate after banding and the patient’s weight at initial presentation ($P=.02$, $r=.49$). This association appears to be related to the fact that these are nonindexed growth rates because indexed growth rate was not related to body weight. As expected, the absolute magnitude of left ventricular hypertrophy correlated with the average ($P=.002$, $r=.71$) and peak ($P=.03$, $r=.45$) left ventricular growth rate.

**Left Ventricular Volume**

The mean indexed left ventricular volume determined within 12 hours after banding of the pulmonary artery was $106.5\pm43.4$ mL (range, 59.0 to 173.4 mL) and progressively increased with time until the time of ASO ($r=.65$ versus time, $P=.003$) (Fig 3). However, the increment in volume was not proportional to the increase in mass, so that the mass to volume ratio rose progressively over the first week, reaching a plateau at 7 to 10 days (Fig 4).

**Left Ventricular Function**

To evaluate the impact that pulmonary artery banding had on left ventricular function, ejection fraction before and after banding was echocardiographically determined. The mean ejection fraction before banding was $57\pm16\%$ and significantly decreased to $37\pm19\%$ by 12 hours after banding ($P=.03$). The minimal ejection fraction (mean, 33±8%; range, 2% to 56%) was obtained in the first 3 days after banding of the pulmonary artery. Nine of the 22 patients who were studied in the first 3 days after banding had an ejection fraction of 28% or less, with 5 patients having an ejection fraction below 10%. By 3.5 days after pulmonary artery banding, mean ejection fraction was similar to preoperative values, and by day 7 after banding, mean ejection fraction had reached 95% of the initial value (Fig 5). Age or weight at time of banding, duration of the preparatory period, left ventricular mass before banding, and left to right ventricular pressure ratio before pulmonary artery banding or before ASO did not correlate significantly with ejection fraction. In addition, the ejection fraction before or after banding was not predictive of the postoperative course.

**Clinical Outcome**

Among these 26 patients, there were no deaths between the time of presentation and ASO. One patient died early after the ASO of pneumonia complicated by adult respiratory distress syndrome. One patient did well after the operation but died suddenly after return to his country of origin. The echocardiographic data on function, mass, and volume for these two patients was not out of the range observed in the other patients.
Discussion

The purpose of this study was to evaluate the response of the left ventricle to acute imposition of outflow obstruction in a relatively homogeneous group of patients. All patients had TGA with intact or virtually intact ventricular septum and underwent banding of the pulmonary artery in infancy as a first stage in preparation for an ASO. The left ventricular mass before banding of the pulmonary artery was normal for body surface area and was similar to the values observed in patients before one-stage ASO, in accord with data published by Maroto et al in 1983.16 We have no data about whether changes in the composition of the myocardium may have occurred despite maintaining a normal mass. After banding of the pulmonary artery (tightened to achieve a left ventricular pressure of at least 75% of systemic pressure), a rapid increase in left ventricular mass was observed, being significantly different from the baseline as early as 36 hours after pulmonary artery banding. During a mean preparatory period of 9 days, the left ventricular mass doubled (mean increase of 100%), with a plateau after 7 days. These findings indicate that the left ventricle has the capacity to hypertrophy very rapidly in response to a sufficient pressure stimulus and that a longer period does not result in further increase in the left ventricular mass over the short term.

Acute Left Ventricular Hypertrophy

The conceptual basis for the two-stage ASO in TGA with intact ventricular septum is the ability to induce acute hypertrophy of the left ventricle by banding the pulmonary artery. The intent is to prepare the left ventricle to support the pressure load of the systemic circulation after the arterial switch. To our knowledge, other data on left ventricular hypertrophy in humans in response to an acute pressure overload do not exist. There are many studies on the acquisition of left ventricular mass after acute pressure loading in animal models.17-31 However, in animal models of aortic or pulmonary banding, cardiac output remains dependent on maintaining adequate stroke volume from the banded ventricle, thereby limiting the severity of stenosis that can be imposed acutely. The typical intraoperative and acute mortality rates of 30% to 50% reported for aortic banding experiments30 are a direct consequence of a limited tolerance for acute outflow obstruction. Due to the presence of transposed great arteries and the placement of an aortopulmonary shunt at the time of pulmonary artery banding, the patient is not dependent on left ventricular output for either systemic or pulmonary blood flow. Consequently, this model of acute outflow obstruction is unique because survival is possible even with an afterload mismatch severe enough to cause isovolumic left ventricular contraction. Most studies of pressure-overload hypertrophy in neonatal animals have avoided this problem by using a very gradual imposition of load by means of a minimal imposed gradient at the time of aortic banding, which is then augmented over the next several weeks or months by the normal process of growth. Thus, the data gathered in neonatal animals concerning rate of hypertrophy may have limited applicability to human neonates with a sudden, severe imposition of outflow obstruction.

Despite the large number of animal studies on acute pressure overload, few have examined the rate of change in ventricular function and structure. Studies in aortic-banded rats have documented a significant rise in cardiac mass as early as day 1 after banding.32 A study in aortic-banded guinea pigs reported a substantial rise in wet weight of the left ventricle by 5 days due to intracellular edema but no change in dry weight.33 However, a similar study in rats documented an increase in dry weight of the left ventricle by day 6 to day 9 after banding with a normal left ventricular dry weight to left ventricular wet weight ratio.34 Lambs with 4 days of an intermittently obstructing pulmonary artery balloon catheter experienced a significant rise in dry heart weight.35 In an ultrastructural examination of abdominal aortic-banded rats, a 20% increase in myocyte size was noted by 20 hours after banding, which resulted from a 36% rise in mitochondrial volume and a 78% increase in volume occupied by sarcoplasmic reticulum but only a 4% increase in myofibrillar volume.36 Our reliance on echocardiographic estimation of left ventricular mass precludes any estimate of the time course or relative contribution to the change in mass of the synthesis of new cellular elements. However, there are also data concerning the rate of biochemical response after aortic banding in animals indicating that the time course of change in mass that we observed represents accrual of new protein. After initial activation of a program of immediate early gene expression, which appears to be an essential feature of both in vivo and in vitro models of hypertrophy,24,37-40 there is a rise within hours to days after banding in cardiac RNA.41-46

Left Ventricular Volume

Ventricular dilation was observed and a direct correlation was found between the left ventricular volume and time since banding. However, the left ventricular volume did not increase as rapidly as left ventricular mass, resulting in a gradual rise in the mass to volume ratio from initial values without acute dilation. This is substantially different from other forms of acute hemodynamic stress where acute dilation with a fall in the mass to volume ratio is usually observed before hypertrophy with a trend toward normalization of the mass to volume ratio. In patients with TGA, the left ventricular volume is influenced by many factors including age, pulmonary vascular impedance, and importantly, the size of the atrial septal defect after balloon atrial septostomy. Pulmonary artery banding results in a substantial alteration in left ventricular configuration, which makes it difficult to compare preoperative and postoperative values. In addition to the change in configuration, dilation would be anticipated if left ventricular diastolic pressure rises. The factors expected to lead to a commensurate rise in left and right atrial pressures include the pressure and volume load secondary to pulmonary artery banding in association with an aortopulmonary shunt and the observed ventricular dysfunction. However, because of the atrial septal defect, the rise in left ventricular diastolic pressure is inhibited, accounting for the more gradual evolution of left ventricular volume.

If contractile function is normal, the ability of the left ventricle to sustain the pressure load of the systemic circulation is primarily dependent on the afterload that
results from the ASO. Myocardial afterload is best assessed as wall stress, which is proportional to the product of left ventricular pressure and the left ventricular volume to mass ratio. In transposition, pulmonary blood flow is higher than systemic, and the left ventricular volume load results in left ventricular dilation. For any three-dimensional object, the maximum contained volume for any given surface is a sphere. Because of this, an immediate further increase in left ventricular pressure occurs after the ASO because of the configurational changes that occur when left ventricular pressure rises and right ventricular pressure falls. Although left ventricular mass was normal for body size in these patients at the preoperative evaluation, this proved inadequate for the operative volume needed to sustain a pressure load equivalent to systemic pressure. Whether this relates to a postnatal alteration in the myocardial composition or gene expression is not known. However, it does imply that simply measuring left ventricular mass does not allow one to predict whether or not the ASO will be tolerated. In theory, some method of predicting the postoperative mass to volume ratio should provide the best predictor of operative success. In practice, this is quite difficult because of the complex interplay of factors that determine the postoperative volume.

**Left Ventricular Function**

One of the main concerns about this procedure is the effect of acute, severe left ventricular outflow tract obstruction on left ventricular function. As shown in our study, a significant decrease in the left ventricular ejection fraction occurred immediately after the acute increase in outflow resistance secondary to pulmonary artery banding, even with inotropic support. Although left ventricular function recovered in parallel with hypertrophy, left ventricular function was significantly depressed for as long as 3 days after banding. In some cases, left ventricular function was so reduced that contraction was nearly isovolumic, and both systemic and pulmonary blood flows (through the aortopulmonary shunt) were supplied exclusively by the right ventricle. This supports the notion that a primary ASO in these patients probably would have resulted in severe left ventricular dysfunction. Although the degree of dysfunction is in part related to the acute imposition of afterload excess because of the atrial septal defect, there is also a failure to utilize preload reserve. When the atrial septum is intact, afterload excess results in a rise in diastolic pressure with utilization of the Frank-Starling mechanism to preserve systolic function. However, in these patients the atrial septal defect defeats this compensatory mechanism. The relative contribution of afterload excess and possible depressed contractility is not known.

**Limitations**

It is likely that numerous factors including age and magnitude of stimulus as well as the absolute left ventricular mass before banding can influence the response of the human myocardium to an acute increase in pressure load. We were unable to identify any clinical parameters that correlated with the rate or magnitude of hypertrophy. However, the fact that such associations were not detected does not necessarily imply that they do not have any influence. The small number of patients and the homogeneity of our population limit our ability to confirm the absence of associations. For example, the observed association between body mass and rate of left ventricular mass increase is apparently due to a greater absolute growth rate potential of a larger heart. The fact that no significant association with indexed left ventricular mass was seen probably reflects the larger measurement error inherent in left ventricular mass determination compared with body mass measurements.

**Conclusions**

In this unique model of acute left ventricular pressure overload in humans, we found that the left ventricle of infants with transposition of the great vessels without hemodynamically significant ventricular septal defect has the ability to hypertrophy rapidly, achieving a plateau within 7 days after banding of the pulmonary artery. There is a transient period of severe systolic dysfunction persisting for at least 3 postoperative days. Patient size at time of banding along with the rate of hypertrophy were the only determinants of the magnitude of left ventricular hypertrophy found in this study.

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