Rapid Two-Stage Arterial Switch Operation
Evaluation of Left Ventricular Systolic Mechanics Late After an Acute Pressure Overload Stimulus in Infancy

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Background  Banding of the pulmonary artery to induce left ventricular (LV) hypertrophy followed by arterial switch operation (ASO) within 2 weeks has been performed when a primary ASO was considered high risk because of inadequate LV hypertrophy.

Methods and Results  Potential adverse myocardial effects of the two-stage procedure were examined by comparing outcome in 18 patients after a rapid two-stage ASO with 33 patients after a primary ASO. Regional wall motion was assessed. Echocardiographic and noninvasive pressure data were combined to obtain LV dimension, wall thickness, mass, fractional shortening, rate-corrected mean velocity of shortening, and end-systolic wall stress. Afterload-adjusted velocity of shortening was obtained as a load-independent index of contractility. In the two-stage ASO group, the magnitude and rate of hypertrophy after pulmonary artery banding were measured serially. No wall motion abnormalities were seen in either group. Systolic dysfunction due to higher afterload and lower contractility was observed in the two-stage ASO group. Contractility below the limits of normal was seen in 25% of two-stage ASO compared with 3% of primary ASO; however, symptomatic or progressive LV dysfunction was not observed. There was a significant inverse relation between the peak rate of hypertrophy immediately after banding and contractility at late exam. Lower ejection fraction before and early after pulmonary artery banding correlated with depressed contractility on late examination.

Conclusions  Myocardial contractility is lower after the two-stage ASO than after a primary repair. Severe or progressive dysfunction was not seen. A very high peak rate of hypertrophy and severe LV dysfunction after banding predict a greater reduction in late contractility. (Circulation. 1994;90:1294-1303.)

Key Words  • ventricles • systole • hypertrophy • transposition of great vessels • heart defects, congenital • echocardiography

Numerous reports indicate that a primary arterial switch operation (ASO) is preferable to intraatrial baffle repair for correction of transposition of the great arteries (TGA), in part because the incidence of arrhythmias and ventricular dysfunction is lower.1-4 A two-stage ASO consisting of banding of the pulmonary artery to induce left ventricular (LV) hypertrophy followed by ASO after a variable period has been performed when the primary ASO was considered high risk because of systemic LV pressure and presumed inadequate LV hypertrophy. LV function has been shown to be better preserved when a primary ASO was performed compared with a two-stage approach when the ASO was delayed beyond infancy.1,5 Specific reasons for this difference are unclear, but the duration of the LV preparatory period has been proposed as a possible mechanism.1,3,5-14 Preliminary data from our group15 indicated that LV performance early after a two-stage procedure was preserved when the interval between banding of the pulmonary artery and the ASO was shortened to 1 to 2 weeks compared with prior reports in which preparatory banding was continued for 5 months up to several years.5 However, the late myocardi...
Echocardiographic and Hemodynamic Data Early After ASO

In the two-stage ASO group, echocardiographic examinations were performed before pulmonary artery banding and as frequently as every 12 hours after surgery until the time of ASO. LV mass and volumes were obtained from each examination by hand-digitizing the end-diastolic and end-systolic endocardial and epicardial surface of the LV with a Dextra D-200 cardiac analysis system. The rate and magnitude of LV mass accrual after banding and the ejection fraction before and after pulmonary artery banding were measured. Cardiac catheterization data before banding and again before the ASO were reviewed, and the ratio of LV to right ventricular (RV) pressure was obtained. The clinical data during the interval between banding and arterial switch were also reviewed.

Late Echocardiographic Assessment

All patients from both groups had one or more complete imaging and Doppler echocardiographic evaluations performed after the ASO at Boston Children’s Hospital. Patients were sedated when judged necessary with chloral hydrate 50 to 100 mg/kg. The echocardiographic examination was performed with a Hewlett-Packard Sonos 500, 1000, or 1500 or an Acuson 128 echocardiographic machine, using transducers appropriate for body size. All examinations included two-dimensional echocardiographic imaging of the LV from sub-costal, apical, and parasternal views. The presence and degree of aortic insufficiency were assessed by color Doppler in both groups and categorized as absent, trace, mild, moderate, or severe according to proximal jet width. Patients with evidence of elevated RV systolic pressure by pulmonary or tricuspid regurgitant Doppler or RV volume overload due to pulmonary or tricuspid regurgitation were excluded from quantitative analysis of cardiac mechanics. After a circular short-axis LV configuration throughout the cardiac cycle was confirmed by visual inspection, a high-speed (100-mm/s) hard-copy two-dimensional echocardiography–directed M-mode of the LV in the parasternal short-axis view was performed simultaneously with an ECG, a phonocardiogram, a carotid or axillary pulse tracing, and peripheral monitoring of the blood pressure. A Dinamap 845 vital signs monitor (Critikon) was used to obtain brachial blood pressure.

Analysis of Regional Wall Motion

Regional wall motion was quantitatively assessed on the two-dimensional echocardiograph with a Dextra D-200 cardiac analysis system (software version 1.20, Dextra Medical Inc). Planimetry of the endocardial border was performed on end-diastolic and end-systolic images from subxiphoid short-axis and apical four-chamber views. A floating-center-of-mass algorithm was used to correct for translational and rotational motion during the cardiac cycle. The radial method was used to calculate wall motion. In this method, each image is divided into 100 segments, and for each segment the percentage area reduction during systole is obtained. The 100 segments were grouped into seven anatomically defined regions for the apical four-chamber view and six for the short-axis view as previously described.16 Regional wall motion was assessed by three distinct methods. Mean percent area reduction was computed for each anatomic region as the average of all segments contained within that region (nonnormalized approach). Normalized percent area reduction was obtained by dividing the mean area reduction for each region by the average area reduction for all segments combined. The normalized analysis demonstrates regional wall motion abnormalities after correction for globally reduced wall motion. Finally, analysis of the intrasegmental variance in area reduction was performed to identify variability in the anatomic region. A group of 60 age-matched healthy children was used as a control population to establish normal values for this analysis.

Analysis of Ventricular Size, Wall Thickness, and Mechanics

The indirect carotid or axillary pulse tracing, the endocardial border of the ventricular septum, and the endocardial and epicardial borders of the posterior wall of the LV on the M-mode recording were hand-digitized on a custom-programmed microcomputer-based digitizing station by one of the authors. Measurements obtained by averaging data from three cardiac cycles were ventricular short-axis dimensions, LV posterior wall thickness, fractional shortening (FS), mean velocity of circumferential fiber shortening corrected for heart rate (VCF), LV mass using the equation of Devereux et al,17 and LV meridional wall stress calculated according to Grossman et al18:

\[ WS = \frac{[(P)(D)]}{(h)[1-(h/D)](4)} \]

where WS is the wall stress (g/cm²), P is the pressure (mm Hg), D is the internal LV dimension (cm), h is the LV posterior wall thickness (cm), and 1.35 is the conversion factor from mm Hg to g/cm². End-diastolic dimension was taken as the maximum dimension. End-systolic measurements were determined at the first high-frequency component of the aortic valve closure sound recorded on the phonocardiogram. The end-systolic pressure was obtained by assigning the systolic pressure to the peak and the diastolic pressure to the nadir of the pulse tracing and calculation of intervening values by linear interpolation according to the method of Stefanouros et al19 and Marsh et al.20

The relation between VCF, and LV wall stress at end systole (ESS) has been shown to be a preload-independent and afterload-adjusted index of contractility.21 In contrast, the relation between FS and ESS is a contractility index that is adjusted for afterload but sensitive to preload. These relations were determined relative to a large population of normal control subjects and expressed as z scores of the distribution in normal subjects as follows. The relation of VCF, to ESS was calculated relative to the distribution of this relation in normal subjects as the stress-velocity index (SVI) defined as the number of SDs from the normal population mean VCF, for the given level of ESS. Thus, an SVI of 0 is the normal mean value, and the normal 95% confidence interval is −2 to 2. The ESS-FS relation was quantified as the stress-shortening index (SSI), which is the number of SDs from the population mean FS for the given ESS. The effect of preload on LV performance is represented by the difference between these two indices and is quantified as the functional preload index (FPI) defined as SSI−SVI.

Statistical Analysis

Values are reported as mean±SD unless otherwise indicated. To adjust for age- and growth-related changes in ventricular mechanics, all echocardiographic variables were expressed as z scores relative to the normal distribution. Normal data for these parameters were determined in 180 normal children 1 week to 10 years old studied in our echocardiographic laboratory following a protocol similar to that for the study population. This normal population has been described in detail.22 For FS, VCF, wall stress, and contractility, the z score relative to age was used, and for LV dimension, wall thickness, and mass, the z score relative to body surface area (BSA) was used. Z scores indicate the position of each measurement relative to the normal population expressed as SD from the mean, where both the mean and SDs are specific for the age or BSA. In addition, to facilitate comparison with data reported by others, we also report dimension, thickness, and mass adjusted for BSA. Linear measurements (dimension and wall thickness) were divided by BSA13,14 and wall motion by BSA15. All corresponding measurements in patients within the same group were analyzed by one-sample ANOVA. Linear regression analysis was used to evaluate the relation between potential predictors of outcome and the
systolic function indices. Comparisons between two-stage ASO and one-stage ASO group values were done by two-sample ANOVA. The variation in regional wall motion was evaluated by $\chi^2$ test. A Fisher's exact test was used to compare the one-stage ASO group to the two-stage ASO group in regard to the incidence of decreased contractility and aortic insufficiency. The relation between time and the echocardiographic indices measured on the serial examinations in the two-stage group was assessed by repeated-measures ANOVA.

**Results**

**Patients**

The two-stage ASO group consisted of 19 patients, 14 boys and 5 girls. Sixteen patients had TGA with intact ventricular septum, and 3 had TGA with a hemodynamically insignificant ventricular septal defect. The ventricular septal defect was considered hemodynamically insignificant on the basis of a negligible shunt and a large transseptal pressure difference in these patients. Mean age at the time of pulmonary artery banding was 0.3±0.2 year (0.1 to 1.0 year), and mean age at ASO was 0.3±0.2 year (0.1 to 1.0 year). The interval between the two procedures was 12.8±14.4 days (5 to 69 days; median, 8 days). In the two-stage ASO group, 9 of 19 patients had only one complete echocardiographic assessment of ventricular function, 4 in the first postoperative month and 5 at least 6 months after the ASO. The other 10 patients had two or more serial echocardiographic evaluations of LV performance. The mean echocardiographic follow-up was 2.0±2.0 years (0.02 to 5.3 years). The one-stage ASO group included 33 patients with TGA and intact ventricular septum or with a hemodynamically insignificant ventricular septal defect who underwent a primary ASO at a mean age of 0.07±0.09 year (0.02 to 0.37 year). This group is significantly younger compared with the two-stage group ($P<.0001$). All patients in the one-stage ASO group had at least two ventricular function assessments late after surgery. The mean age at follow-up was 3±2 years (0.2 to 8 years), with an echocardiographic follow-up of 3±2 years (0.5 to 8 years) after surgery, which is not significantly different from the two-stage group.

**Aortic Insufficiency**

In the one-stage ASO group, 20 of 33 patients had no aortic regurgitation, and 13 had trivial or mild aortic insufficiency at the last Doppler examination. In the two-stage ASO group, aortic insufficiency was absent in 6 of 15 patients and trivial or mild in 9 patients. No case of moderate or severe neoaoartic (native pulmonary valve) regurgitation was found in either group. There was no significant difference between the one-stage ASO and the two-stage ASO groups for the presence and the severity of aortic insufficiency. The degree of aortic insufficiency was not related to differences in ventricular mechanics between the one- and two-stage ASO groups.

**LV Regional Wall Motion**

The number of individual short- and long-axis segments with a regional percent shortening outside the 95% confidence interval was not different from normal in the one-stage ASO group for either the nonnormalized, normalized, or intrasegmental regional wall motion analysis. In the two-stage ASO group, there was a significantly increased number of abnormally functioning segments (30 of 126, 24%, $P<.001$) on the nonnormalized analysis of regional function. However, this appeared to be related to global dysfunction, since normalized shortening (regional shortening adjusted for global shortening) failed to detect an increased number of abnormally functioning segments (9 of 126, 7%; $P=.22$). Intrasegmental variance was also not different from normal.

**LV Mass, End-Diastolic Dimension, and Wall Thickness**

The means for values indexed for BSA and for z scores of LV mass, end-diastolic dimension, and wall thickness for the one-stage ASO and two-stage ASO groups are shown in the Table. When considered as overall groups or when subdivided into early and late postoperative examinations, LV mass z score and end-diastolic dimension and wall thickness z scores were not different from normal, and no significant difference existed between one-stage ASO and two-stage ASO groups for mean values of LV mass, end-diastolic dimension, or wall thickness z scores. However, there was a trend toward lower early postoperative LV mass z scores in the one-stage ASO group, and there was a significant direct relation between LV mass z score and duration of postoperative follow-up in this group that was not noted in the two-stage ASO group. For both groups, there was a nonsignificant reduction in end-diastolic dimension on the early studies compared with late examinations but a significant rise in dimension over time by regression analysis. In the one-stage ASO group, wall thickness z score was stable over time, whereas in the two-stage group, the posterior wall thickness z score correlated inversely with follow-up.

**LV End-Systolic Wall Stress**

Values of LV end-systolic wall stress and z scores are shown in the Table and Fig 1. In the one-stage ASO group, the end-systolic stress was within normal limits throughout the study period and was not significantly related to time since surgery. In the two-stage ASO group, LV end-systolic wall stress was also within the normal range and was not significantly different from the one-stage ASO group, but there was a direct correlation with time since surgery.

**LV Systolic Performance**

In the one-stage ASO group, parameters of systolic function (FS, VCF, VCFC) and contractility (SVI, SSI) were within the normal range throughout the period of follow-up and were not influenced by time since ASO or age at follow-up (Figs 2 through 4). The FPI, reflecting the preload status, was significantly below the normal range in the early postoperative period and increased toward the normal mean over the period of observation, as previously reported. In the two-stage ASO group, parameters of systolic function (FS, VCF,), and contractility (SVI, SSI) were not different from normal when all echocardiographic examinations were considered together. However, when only studies that were performed more than 1 month after surgery were included, all indices were significantly decreased compared with normal and with the one-stage ASO group. When studies done beyond the early postoperative period...
Left Ventricular Echocardiographic Parameters, Presented as Overall Values and Subdivided Into Early* and Late† Studies

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
<th>Early</th>
<th>Late</th>
<th>Early</th>
<th>Late</th>
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</thead>
<tbody>
<tr>
<td>LVMi, g/m³</td>
<td>99±22</td>
<td>119±38</td>
<td>114±32</td>
<td>141±40</td>
<td>96±21</td>
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<tr>
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<td>0.2±0.9</td>
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<tr>
<td>EDDi, cm/m</td>
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<td>4.2±0.4</td>
<td>3.9±0.6</td>
<td>3.9±0.4</td>
<td>4.0±0.5</td>
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<tr>
<td>EDDz, SD</td>
<td>0.1±1.2</td>
<td>0.3±1.1</td>
<td>-0.4±1.1</td>
<td>-0.4±0.8</td>
<td>0.3±1.0</td>
</tr>
<tr>
<td>EDhi, cm/m</td>
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<td>0.9±0.2</td>
<td>0.9±0.2</td>
<td>1.1±0.2</td>
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</tr>
<tr>
<td>EDhz, SD</td>
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<td>0.7±1.6</td>
<td>0.4±1.4</td>
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</tr>
<tr>
<td>ESSz, SD</td>
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<td>0.2±1.9</td>
<td>-0.4±1.0</td>
<td>-0.9±1.5</td>
<td>0.0±1.0</td>
</tr>
<tr>
<td>VCFcz, SD</td>
<td>0.4±1.9</td>
<td>-0.8±2.9</td>
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<td>0.0±2.0</td>
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<tr>
<td>FSz, SD</td>
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<td>-0.9±2.3</td>
<td>0.0±1.7</td>
<td>0.6±2.9</td>
<td>-0.2±1.0</td>
</tr>
<tr>
<td>SSI, SD</td>
<td>0.6±1.5</td>
<td>-0.6±2.2</td>
<td>1.9±1.8</td>
<td>1.1±2.2</td>
<td>0.2±1.0</td>
</tr>
<tr>
<td>FPI, SD</td>
<td>0.0±1.5</td>
<td>-0.9±2.1</td>
<td>-0.5±1.7</td>
<td>0.1±1.7</td>
<td>0.2±2.6</td>
</tr>
</tbody>
</table>

1S-ASO indicates single-stage arterial switch operation; 2S-ASO, two-stage arterial switch operation; LVMi and LVMz, left ventricular mass indexed to body surface area (BSA)⁰.⁵ and z score with respect to BSA, respectively; EDDi and EDDz, left ventricular end-diastolic dimension indexed to BSA⁰.⁵ and z score with respect to BSA, respectively; EDhi and EDhz, left ventricular end-diastolic posterior wall thickness indexed to BSA⁰.⁵ and z score with respect to BSA, respectively; ESSz, end-systolic stress z score with respect to age; VCFcz, rate-corrected velocity of fiber shortening z score with respect to age; FSz, fractional shortening z score with respect to age; SSI, stress-shortening index; and FPI, functional preload index.

*Studies <1 mo after arterial switch; †studies >4 mo after arterial switch.

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**Fig 1.** Plots showing left ventricular end-systolic wall stress in patients considered as an overall group and subdivided into early and late examinations (top left, two-stage arterial switch operation [ASO]; bottom left, one-stage ASO) and evolution of left ventricular end-systolic wall stress with time after surgery (top right, two-stage ASO; bottom right, one-stage ASO). Left ventricular end-systolic wall stress is expressed in z scores relative to age, the mean being 0 and normal range situated within the interrupted lines. SDs are indicated by vertical bars. ESSz indicates left ventricular end-systolic wall stress z score. End-systolic wall stress was normal during the overall period and was not influenced by time since surgery in the one-stage group. In the two-stage group, end-systolic wall stress did not differ from the normal range but significantly correlated directly with time, with a tendency toward higher values at late study.
were analyzed as a group, there was no significant change in LV function or contractility with duration of follow-up. Finally, the FPI was significantly decreased in the early postoperative period, was greater than the FPI value of the one-stage ASO group, and increased to normal during the study time interval. The number of patients in the two-stage ASO group with abnormal contractility at follow-up was significantly greater than the one-stage ASO group \( (P=.002) \). In the two-stage ASO group, 6 of 15 patients had decreased contractility \( (SVI < 2 \ SD) \), 1 at the early postoperative evaluation with no further follow-up. Only 1 of 33 patients from the one-stage ASO group had decreased contractility at late follow-up.

**Determinants of LV Performance**

To determine factors that might influence or be related to the functional outcome in patients who had undergone a rapid two-stage ASO, clinical parameters (hours of ventilation, hospital stay duration, number and duration of use of vasopressors and/or inotropic agents), hemodynamic data from catheterization performed before pulmonary artery banding and ASO (aortic and superior vena cavaal saturation, ratio of LV to RV pressure), the rate and magnitude of LV hypertrophy, and the ejection fraction before and after pulmonary artery banding were compared with the echocardiographic LV functional indices at late evaluation. None of the clinical parameters were found to be predictive of the late contractile status of the LV. However, parameters of LV performance at late follow-up \( (FS, VCF, SVI, SSI) \) were significantly inversely correlated \( (P=.02, .004, .01, and .02, respectively) \) with the peak rate of LV hypertrophy after banding of the pulmonary artery, indicating that more rapid hypertrophy after banding was associated with poorer ventricular function and contractility at late evaluation (Fig 5). These indices \( (FS, VCF, SVI, SSI) \) were also significantly correlated in a direct manner to the LV:RV pressure ratio before ASO \( (P=.01, .006, .04, and .01, respectively) \), indicating that a more hypertensive LV after banding and before arterial switch operation was associated with reduced function and contractility at late follow-up. A direct relation was found between the minimum ejection fraction after banding of the pulmonary artery and indices of LV function \( (FS, P=.003; VCF, P=.003) \) and contractility \( (SVI, P=.0004; SSI, P=.0001) \) at late evaluation (Fig 6).

**Discussion**

The present study examined medium-term results of LV mechanics in a relatively homogeneous population of patients with TGA who had a rapid two-stage ASO in infancy, comparing the outcome with a similar group of patients after a neonatal one-stage ASO. We found that, compared with patients who had a primary neonatal ASO, significantly more patients in the two-stage ASO group had abnormal ventricular function and myocardial contractility when evaluated late after repair. Over the limited period of observation, no deterioration was observed with age or time since surgery beyond the immediate postoperative period. These findings are in accord with previous results published by other groups and tend to confirm that ventricular function may be adversely affected in some individuals by a two-stage approach compared with a primary ap-
We found that a higher rate of acquisition of ventricular mass after pulmonary artery banding was associated with myocardial dysfunction. A higher LV:RV pressure ratio before ASO and a lower ejection fraction after pulmonary artery banding were also found to be associated with lower ventricular contractility at late follow-up. Each of these variables would be anticipated to correlate with the severity of LV obstruction imposed by the pulmonary artery banding relative to the pressure load before banding, indicating that the severity of the acute pressure load is an important factor.

As previously reported and further supported by these data, medium-term results indicate that ventricular function is preserved after an early one-stage ASO in patients with TGA with or without a ventricular septal defect. This result, combined with favorable outcome in other respects, led to the acceptance of this procedure as the procedure of choice for patients presenting to our institution within the first weeks of life. However, management of patients with TGA and intact ventricular septum or hemodynamically insignificant ventricular septal defect who do not have a primary ASO in the first weeks of life remains problematic. Since Yacoub et al. introduced the two-stage ASO in 1977, numerous reports have looked at ventricular function after this surgical approach with conflicting results. This can be attributed in part to the heterogeneity within and between groups, methodological differences, and differences in duration of follow-up. Nevertheless, in these studies, later age at pulmonary artery banding and longer duration of the LV preparatory period were identified as factors that might adversely affect late LV function. On the basis of the observation that the myocardial hypertrophic response to acute pressure load in animals occurs rapidly, initiating within hours and reaching completion within days, our group questioned the need for a prolonged banding interval and reported that as little as 1 week of preparatory banding is sufficient to prepare the LV for a subsequent ASO. This approach attempts to minimize both of the factors that have been identified as risk factors for late dysfunction by performance of the pulmonary artery band and subsequent ASO as early in life as feasible and by reducing the duration of banding to the minimal time period possible.

Factors Affecting Outcome

Despite placement of the pulmonary artery band as early in life as possible and minimization of the duration of pulmonary artery banding, the acute imposition of a pressure load on the LV adversely affected myocardial function in some individuals. Because of the intrinsically greater age at surgery in the two-stage group, perinatal maturational changes may have contributed to the observed differences between the groups. In addition, chronic pressure overload myocardial hypertrophy is known to be associated with depressed ventricular function in animals and adult humans, although the mechanism is uncertain. The myocardium responds to a hemodynamic load by myocyte hypertrophy, although hyperplasia has been shown to occur in the first 3 to 6 months of life in rats. The hyperplasia of myofibrillar units results in an increase in oxygen utilization.
and requires a proportional growth of mitochondria responsible for oxygen consumption and energy supply. However, reduction of the ratio of mitochondrial to myofibrillar volume has been found in pressure-overload hypertrophy.32-34 Ventricular hypertrophy secondary to an acute pressure stimulus may also be associated with

Fig 4. Plots showing stress-velocity index (SVI) in patients considered as an overall group and subdivided into early and late examinations (top left, two-stage arterial switch operation [ASO]; bottom left, one-stage ASO) and evolution of the SVI with time after surgery (top right, two-stage ASO; bottom right, one-stage ASO). The SVI is expressed in z scores, the mean being 0 and normal range situated within the interrupted lines. SDs are indicated by vertical bars. The SVI had a tendency to be in the upper normal range in both groups at early studies. At late study, the SVI was significantly decreased in the two-stage group. Neither group showed a significant change over time.

Fig 5. Scatterplots showing relation between peak rate of accrual of left ventricular mass (g/h) after pulmonary artery banding and several parameters of ventricular mechanics at last evaluation. Fractional shortening (FS) z score, rate-corrected velocity of circumferential fiber shortening (VFCf) z score, and the stress-velocity index (SVI) all demonstrated a significant inverse relation to peak growth rate. The direct relation between end-systolic wall stress (ESS) z score and peak growth rate did not attain statistical significance (P=.12).
focal areas of necrosis. Limitations in coronary vascular reserve have also been observed in adult animal and human models of pressure-overload hypertrophy. Cellular and biochemical changes engendered by pressure-overload hypertrophy may also influence ventricular function.

Which of these factors, or others, influence the late outcome of the two-stage ASO is speculative. However, data from a number of sources indicate that the immature myocardium is relatively resistant to the adverse effects of hypertrophy that have been described in the mature animal. Flanagan et al. demonstrated that myocardial angiogenesis and coronary perfusion were preserved in young lambs with pressure-overload hypertrophy. Data from human infants with pressure-overload hypertrophy have similarly indicated preservation of a normal neovascular response. The acute LV pressure overload seen with acute hypertension is associated with altered coronary vascular responsiveness, but this appears to be a direct vascular effect, since it is present in other vascular beds. Because the pulmonary artery band in the infant with TGA does not result in coronary artery hypertension, in contrast to animal models of supracoronary aortic banding and acute hypertension, this model is more comparable to banding of the RV in normally related great vessels. In chronic RV pressure overload animal models induced by pulmonary artery banding, hypertrophy is associated with no or at least less severe abnormalities of coronary perfusion.

Data derived from animal studies may not be germane to our model for another reason. Because of the presence of TGA and the placement of an aortopulmonary shunt at the time of pulmonary artery banding, the patient is not dependent on LV output for either systemic or pulmonary blood flow. Consequently, severe afterload mismatch can be imposed and LV contraction may be nearly isovolumic, as was true of several of the patients in this report. In animal models of aortic or pulmonary banding, cardiac output remains dependent on maintenance of an adequate stroke volume from the banded ventricle, thereby limiting the severity of stenosis that can be imposed acutely. The typical acute mortality rates of 30% to 50% reported for aortic banding animal experiments are a direct consequence of the limited tolerance for acute outflow obstruction. Because of this, most studies on aortic-banded neonatal animals have applied the band loosely and allowed the pressure load to develop gradually with somatic growth. The rapidity and severity of the imposition of pressure overload are substantially less in animal models of pulmonary artery banding for the same reason, with "rapid" induction of pressure load effected by gradual rise in pulmonary artery pressure over a 2-week period. The importance of the rapidity with which the pressure load is applied is supported by the correlations noted between myocardial dysfunction and both the rate of hypertrophy and the severity of acute postbanding dysfunction, limiting the applicability of results from animal studies to our results.

Study Limitations

Although the "tightness" of the pulmonary band may well represent an important factor with regard to the outcome in two-stage ASO, we were unable to assess this in a meaningful fashion. It should be noted that the surgical approach was similar to pulmonary artery banding in TGA as reported by others, with an attempt
to acutely elevate pressure in the LV to approximately two thirds systemic level. This was no intention to impose a greater acute pressure load to induce more rapid or extreme hypertrophy, but rather the duration of banding was reduced on the basis of the observation that hypertrophy occurs rapidly and longer observation is not needed. Invasive and noninvasive measurements of the pressure drop across the band were recorded after surgery, but because of the variable flow through the orifice and unknown distal pressure, these are unlikely to represent a meaningful measurement of the flow orifice.

It will be important to determine whether the observed myocardial dysfunction in the two-stage ASO group is stable or progressive. We observed no evidence of progression, but only limited serial data are available on the two-stage ASO patients; therefore, our ability to evaluate this possibility is quite limited.

Implications

Some consideration must be given to the alternatives that are available for these patients. Although we prefer a primary neonatal ASO for all patients with TGA, the rationale for considering a two-stage approach to an ASO in some patients is based on the assumption that a primary ASO entails excessive risk. It is possible that more refined selection criteria for the single-stage repair would permit some of these individuals to avoid preparatory banding. However, the results of the present study indicate that the patients at highest risk for myocardial injury are those who experience the most rapid hypertrophic response and who have the most severely depressed function after banding, indicating that they have the least adequate hypertrophy at the time of banding. The overall incidence of myocardial dysfunction is therefore unlikely to be improved, since these individuals are least likely to be candidates for a single-stage repair. Although redirection of venous inflow (Senning or Mustard operation) is possible, it is not clear that mild impairment of contractility of a systemic LV is a worse outcome than the recognized high risk of progressive systemic RV dysfunction, tricuspid regurgitation, and an increased risk of arrhythmia associated with the atrial-level repairs. It is possible that protection of myocardial function can be improved through more gradual imposition of the LV pressure load by means of an adjustable band in patients with the least favorable preoperative interventricular pressure ratio. Finally, a less restrictive band might achieve a lower but still adequate level of “preparedness” of the LV. It should be noted that simply increasing the duration of banding is unlikely to affect outcome, since compensatory hypertrophy is essentially complete within 7 to 10 days of banding. Prolonged band placement associated with somatic growth after banding increases the relative severity of obstruction to LV outflow but prolongs the period of cyanosis, increases the risk of insufficiency of the neoaoartic valve, and may complicate surgical repair because of scar tissue.

Conclusions

The rapid two-stage ASO is associated with a significant incidence of myocardial injury. Although the cause is not known, more rapid hypertrophy and more severe postbanding dysfunction are inversely correlated with late function and contractility. No progression was seen over a limited period of observation of up to 0.5 to 6 years. Continued long-term follow-up of patients after the rapid two-stage ASO is needed. In addition, methods to titrate the rate and magnitude of LV hypertrophy after pulmonary artery banding need to be considered, because extreme acute load appears to adversely affect late outcome.

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Circulation. 1994;90:1294-1303
doi: 10.1161/01.CIR.90.3.1294

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
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