

Myocardial Performance After Arterial Switch Operation for Transposition of the Great Arteries With Intact Ventricular Septum

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Left ventricular dimensions, wall thickness, wall stress, and indexes of afterload, preload, contractility, and early diastolic function, as well as regional wall motion, were determined by echocardiographic methods in patients with transposition of the great vessels after arterial switch operation and in age-matched normal controls. In patients evaluated early after surgery, body surface area-adjusted left ventricular dimensions were smaller, and wall thickness was increased compared with controls. Ventricular performance (fractional shortening) was normal in most patients but was abnormally low in 10%. Nevertheless, contractility was normal or augmented in all subjects, with a mean value higher than the control group. The reduction in systolic function was related to altered loading conditions with a combination of reduced afterload and preload combined with augmented contractility. These altered myocardial mechanics appeared to be secondary to routine therapy with digitalis and diuretics. Diastolic function was also normal with differences in the rate of peak filling and rate of wall thinning entirely attributable to differences in ventricular size and function, and normalized indexes of diastolic function were not different between patients and controls. Patients evaluated late after repair were found to have normal regional wall motion with no evidence to suggest regional dysfunction as might be seen with regional ischemia. Ventricular size, wall thickness, systolic function, afterload, preload, contractility, and early diastolic function were indistinguishable from control values. Indexes of diastolic function demonstrated the same relation to age, body surface area, and ventricular size and function in both patients and controls. Thus, patients evaluated up to 4 years after arterial switch operation for transposition of the great vessels with intact ventricular septum have left ventricular mechanics that are identical to age-matched controls, at least in the absence of right ventricular hypertension. This outcome appears to represent a measurable improvement over the results of the two-stage repair, perhaps related to the early age of definitive surgery. (*Circulation* 1988;78:132-141)

Long-term complications of atrial baffle repair of transposition of the great arteries (TGA) with intact ventricular septum (IVS), including right ventricular dysfunction, have stimulated

interest in the arterial switch operation (ASO) as an alternative surgical approach. Although the feasibility of performing an arterial-level repair, even as a one-stage operation in neonates, has been clearly demonstrated,¹ the long-term outlook for left ventricular performance is uncertain.²⁻¹¹ Studies performed in survivors of the two-stage approach (initial pulmonary artery banding followed by definitive repair at >0.5 years) have indicated decreased shortening fraction,¹⁰ elevated ventricular volumes,² and abnormal contractility⁴ in some patients. Although the cause of this is uncertain, it has been suggested that earlier definitive repair may improve the ultimate outlook for the left ventricle.² The status of the left ventricular myocardium after single-stage repair with arterial switch and coronary reim-

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plantation in the neonatal period is, therefore, of considerable interest.

In 1983, we undertook a program of prospective evaluation of all patients with TGA before and serially after ASO. Using recently developed sensitive indexes of left ventricular mechanics,¹²⁻¹⁷ we have documented the global and regional performance of the left ventricle, including afterload, preload, and contractility. In addition, echocardiographic parameters of early diastolic function were evaluated in this patient group.

Subjects and Methods

Subjects

The study group comprised 49 sequential survivors of primary ASO for TGA with either IVS or hemodynamically insignificant (i.e., resulting in no significant shunt on oximetry and requiring no surgical intervention) ventricular septal defect. The median age at the time of repair was 4 days, and three patients were older than 28 days. Data were divided into early and late categories for analysis. The early postoperative infant data (TGA1) were derived from studies performed in patients examined at the time of discharge from the hospital after the primary repair (5-10 days after surgery), except in one patient evaluated at the first clinic visit 6 weeks after surgery. In 28 of 49 patients, either inadequate echocardiographic windows or residual distortion of left ventricular configuration on two-dimensional echocardiography (2D-Echo) was present at the time of hospital discharge, precluding quantitative assessment of left ventricular systolic and diastolic function. The TGA1 group therefore comprised 21 patients with normal left ventricular configuration in whom the 2D-Echo windows were adequate for evaluation of global left ventricular mechanics. At the time of evaluation, two of 21 patients were being treated with only diuretics while 19 of 21 patients were taking digitalis (5-10 $\mu\text{g/kg/day}$) and diuretics. The exact diuretic regimen varied, with six of 21 receiving furosemide (1-3 mg/kg/day), 12 of 21 receiving furosemide (1-3 mg/kg/day) with spironolactone (1-2 mg/kg/day), and three of 21 receiving Diuril (5-10 mg/kg/day) with spironolactone (1-2 mg/kg/day).

The late postoperative group (TGA2) comprised 32 older patients (age, 5-50 months) in whom subsequent exams ($n=47$) were obtained at the time of hospital visits for postoperative catheterization or at the time of routine clinical evaluation. In addition to the 21 patients included in the early study group (TGA1), 11 additional subjects had normalization of left ventricular configuration by the time of the later evaluation. Regional wall motion analysis was performed in 26 of these 31 patients in whom adequate 2D-Echo windows were available for complete visualization of the left ventricle in long and short axis. There were eight patients with significant right ventricular hyperten-

sion detected on 2D-Echo, Doppler, or cardiac catheterization who were excluded from analysis because left ventricular geometry is distorted in the presence of right ventricular pressure or volume overload.¹⁸ There were two patients in whom adequate echocardiographic windows could not be obtained, and seven of the patients were not available for follow-up. Ten of 47 late studies were performed with patients receiving digoxin (2-7 $\mu\text{g/kg/day}$, mean = 3.5 $\mu\text{g/kg/day}$), one of whom was receiving furosemide (1 mg/kg/day), and two of whom were receiving furosemide (1 mg/kg/day) plus spironolactone (1 mg/kg/day). With a single exception, the patients receiving medications at the time of their late evaluation had not had an increase in their dosages between the two evaluations despite a doubling of body mass.

Regional wall motion data in the TGA2 group were compared with data from 27 normal infants and children age 24 days to 6 years that have been previously reported.¹⁷ For analysis of global left ventricular mechanics, patient data (21 studies in TGA1 and 47 studies in TGA2) were compared with data obtained from 68 normal control subjects aged 1 week to 4 years who were matched for the patient age at the time of evaluation and divided into infant (NORM1) and older (NORM2) categories. Control subjects were free of known cardiovascular disease, were taking no cardioactive medications, and had normal physical examination and intracardiac anatomy by 2D-Echo.

Echocardiogram

All echocardiograms were performed at Children's Hospital in Boston with previously described methods.^{12,15-17,19-21} Patients were sedated with 50-100 mg/kg chloral hydrate when necessary. Complete Doppler and 2D-Echo evaluation of residual anatomic defects, valve function, and surgical anastomotic sites were performed in all subjects. Standard subxiphoid short-axis (parasagittal plane) and long-axis (about 60° superior angulation from a horizontal plane) views of the left ventricle were recorded in patients under 1 year of age for regional wall motion analysis with a Hewlett-Packard 77020 Cardiac Imager equipped with a 5.0-MHz transducer. In addition, high-speed (100 mm/sec) hard copy 2D-Echo-directed M-mode recordings of the left ventricular minor axis were obtained with simultaneous recording of the electrocardiogram, phonocardiogram, indirect axillary or carotid pulse tracing, and peripheral blood pressure. Blood pressures were obtained with a Dinamap 845 Vital Signs Monitor (Critikon, Tampa, Florida).

Analysis of Left Ventricular Shape and Wall Motion

Analysis of regional wall motion was performed with a Franklin Quantic 1200 echocardiographic review system (Bruce Franklin). All studies were digitized by one of the authors. The endocardial

border of the end-diastolic and end-systolic frames (defined as the largest and smallest enclosed areas, respectively) of the selected cardiac cycle were manually digitized. The endocardial border of each intervening frame was automatically digitized with use of an edge-detection algorithm. The validity and reproducibility of analyses performed with this software have been previously documented.²² The contours were then reviewed frame by frame and manually corrected as needed.

The method of regional wall motion analysis performed with this computer has been previously reported.^{17,23} The center of mass of the left ventricle is calculated for each frame, and 64 equally spaced radii are calculated from the center of mass to their respective intersections with the endocardial border for all frames in both long and short axes. The radial shortening fraction for each radius is then obtained as the systolic change in radial length divided by the diastolic length. Superimposition of the individual centers of mass is used to correct for translational motion of the heart, and alignment of anatomic reference points is used to correct for rotational motion. The landmarks used for this adjustment are the anterior and posterior junctions of the right ventricular free wall with the interventricular septum and the position of the papillary muscles in the short axis. In the long axis, the ventricle is aligned with respect to the aortic root and apex of the left ventricle.

The endocardial border was divided into six short-axis and seven long-axis segments according to well-defined anatomic landmarks (Figure 2). This scheme permits comparison of patients according to anatomically defined segments as previously discussed in detail.¹⁵ The segmental shortening fraction was calculated as the average of the fractional shortening of the radii contained within each segment.

Calculation of Left Ventricular Dimensions, Thickness, and Stress

The indirect carotid or axillary pulse tracing, as well as the left ventricular echocardiogram including the endocardial border of the septum and the endocardial and epicardial borders of the left ventricular posterior wall, were hand-digitized on a microcomputer-based digitizing station by one of the authors with custom software. This system is programmed to adjust the sampling rate to 200 Hz, which is adequate to obtain at least 50 nonaliased harmonics at the heart rates encountered in the present study population. After data input, the pulse transmission delay is corrected by electronically aligning the dirotic notch on the pulse tracing with the first high-frequency component of the aortic valve closure sound. From the digitized data, the following instantaneous measurements are then obtained by averaging from three to six cardiac cycles: 1) pressure during left ventricular ejection calculated by assignment of diastolic pressure to the minimum and systolic pressure to the maximum of

the pulse trace and calculation of intervening values by linear interpolation according to the method of Stefadouros et al²⁴ (see also Marsh et al²⁵). This method has been previously verified against an intra-arterial standard in our laboratory^{19,20}; 2) left ventricular internal diameter; 3) first derivative of dimension with respect to time. The derivative is calculated by a Savitzky-Golay modified least-squares algorithm with a 25-msec convolution kernel; 4) left ventricular posterior wall thickness; 5) first derivative of wall thickness with respect to time, calculated as in 3) above; and 6) left ventricular meridional wall stress, calculated according to Grossman et al²⁶:

$$WS = \frac{(P)(D)1.35}{(h)[1 + 1(h/D)](4)}$$

where WS is wall stress (g/cm²), P is pressure (mm Hg), D is dimension (cm), h is the wall thickness (cm), and 1.35 is the conversion factor from millimeters mercury to grams per centimeter squared.

From the continuous data, end-diastolic values for dimension (EDD) and wall thickness (EDh) were taken at the time of maximum left ventricular dimension, and end-systolic values for dimension (ESD), wall thickness (ESh), blood pressure (ESP), and wall stress (ESS) were determined at the time of aortic valve closure (first high-frequency component of the second heart sound). In subjects with no significant left ventricular outflow obstruction by Doppler echocardiography, peak systolic stress (PSS) was calculated as the peak value for ejection wall stress. Left ventricular ejection time was measured from the pulse tracing and adjusted to a heart rate of 60 beats/min by dividing by the square root of the R-R interval on the electrocardiogram. The fractional wall thickening (FWT) was calculated as (EDh - ESh)/EDh. The left ventricular percent fractional shortening (%FS) was calculated as (EDD - ESD)/EDD. The rate-adjusted mean velocity of shortening (VCFc) was calculated as %FS divided by rate-adjusted ejection time.

Indexes of Contractility and Preload

The relation between VCFc and ESS has been previously shown to be an afterload-adjusted, preload-independent index of contractility.¹² To facilitate comparison of patient groups, the position of the relation of ESS to VCFc for each patient was determined relative to the distribution of this index in controls and calculated as the stress-velocity index (SVI) = number of standard deviations from the population mean VCFc for the ESS (see Figure 1 for detailed explanation). In contrast, the relation of %FS to ESS is an afterload-adjusted index of contractility, which is sensitive to alterations in preload.^{12,14,16} The ESS-%FS relation was correspondingly quantified as the stress-shortening index (SSI) = number of standard deviations from the population mean %FS for the given ESS (Figure 1). The

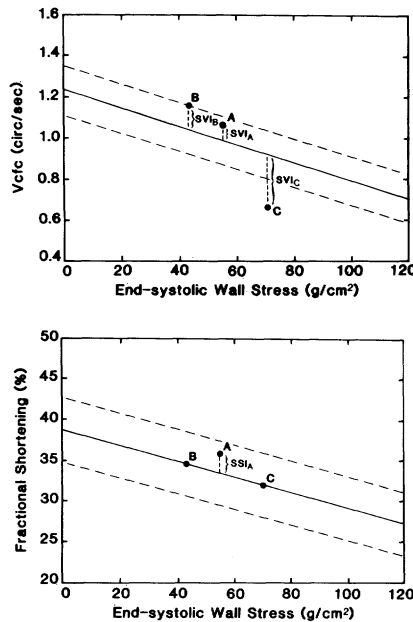


FIGURE 1. Plots of method of calculation of indexes of contractility and preload. Normal relations of rate-adjusted velocity of shortening (VCFc, top panel) and fractional shortening (%FS, bottom panel) to afterload (end-systolic stress, ESS) are shown (solid lines) with 95% confidence intervals (dashed lines). Point A illustrates a patient with ESS-VCFc and ESS-%FS relations that are both in the normal range and that have positions approximately the same with respect to the normal range. Quantitatively, the position of patient A with respect to the normal population regression line for the ESS-VCFc relation (stress-velocity index, SVI) can be expressed as the number of standard deviations of VCFc from the mean VCFc at that ESS. For patient A, $SVI_A = 1.75$. Similarly, the position of patient A with respect to the normal population regression line for the ESS-%FS relation (stress-shortening index, SSI) can be expressed as the number of standard deviations of %FS from the mean %FS at that ESS. For patient A, $SSI_A = 1.80$. The difference in position between these two indexes is determined by preload status and can be quantitatively expressed as the functional preload index (FPI) where $FPI = SSI - SVI$. For patient A, $FPI = SSI_A - SVI_A = 0.05$. Patient A has a FPI typical of normal preload, that is, concordance of SVI and SSI. In contrast, for patient B, the ESS-VCFc relation is just above the 95% confidence level ($SVI_B = 2.00$), and the ESS-%FS relation is equal to the population mean ($SSI_B = 0.00$), giving an FPI of -2.00 , the pattern typical of reduced preload. For patient C, the ESS-VCFc relation is substantially below the 95% confidence level ($SVI_C = -3.00$), implying reduced contractility, and the ESS-%FS relation is equal to the population mean ($SSI_C = 0.0$), giving an FPI of -3.00 , the pattern typical of augmented preload.

relative magnitude of VCFc compared with %FS for any level of ESS is a measure of the preload status, reflecting the fact that fractional shortening is directly related to end-diastolic fiber stretch,

whereas VCFc is independent of preload.^{12,14,16,27-29} Differences between the ESS-VCFc relation and the ESS-%FS relation therefore reflect the functional consequences of altered preload, which was quantified as the functional preload index ($FPI = SSI - SVI$).

Indexes of Diastolic Function

The peak rate of filling (PFR) and the time from the Q wave to maximal filling rate (tPFR) were determined as the maximum early-diastolic value for the first derivative of dimension with respect to time.^{30,31} Normalized PFR (NPFR) was calculated as PFR/EDD .³⁰ Similarly, the peak rate of wall thinning (PTR) and the time from the Q wave to maximal thinning rate (tPTR) were determined as the maximum early-diastolic value for the first derivative of wall thickness with respect to time.^{30,31} Normalized PTR (NPTR) was calculated as $PTR/(EDh - ESh)$.³⁰

Statistical Analysis

Values are reported as mean \pm SD unless otherwise noted. Left ventricular dimension and wall thickness at end diastole and end systole were indexed to body surface area (BSA) by division by the cube root of BSA. All corresponding measurements in patient and control groups (TGA1 vs. NORM1, TGA2 vs. NORM2) were compared by *t* tests. The indexes of systolic and diastolic function were compared in all four subject groups by one-way analysis of variance. The variation in regional wall motion was evaluated within and among groups by unbalanced two-way analysis of variance. In the older patient and control groups (TGA2 and NORM2), the relation of the indexes of diastolic function to subject age, BSA, and ventricular size and function were examined with linear regression techniques, testing for differences in slope or intercept.

Results

Study Population

There were no significant differences between TGA1 and NORM1 or between TGA2 and NORM2 for age (Table 1). The BSA in TGA1 was smaller than in age-matched controls, and the heart rate was lower, but no differences were found between TGA2 and NORM2 for BSA or heart rate. Peak-systolic and end-systolic blood pressures were lower in TGA1 than in NORM1, with no difference in diastolic pressure. Peak-systolic, end-systolic, and diastolic blood pressures were not different between TGA2 and NORM2.

Regional Wall Motion

The short- and long-axis regional wall motion patterns for TGA2 are shown in Figures 2A and 2B compared with the normal values for our laboratory in this age group.¹⁷ All left ventricular segments in

TABLE 1. Clinical and Echocardiographic Data on Patients and Controls

	TGA1 (mean \pm SD)	NORM1 (mean \pm SD)	<i>p</i> value	TGA2 (mean \pm SD)	NORM2 (mean \pm SD)	<i>p</i> value
Age (yr)	0.08 \pm 0.13	0.09 \pm 0.03	NS	1.38 \pm 1.14	1.38 \pm 1.15	NS
BSA (m ²)	0.23 \pm 0.03	0.27 \pm 0.02	<0.05	0.45 \pm 0.11	0.45 \pm 0.11	NS
HR (beats/min)	117 \pm 14	136 \pm 8	<0.05	119 \pm 17	112 \pm 17	NS
PSP (mm Hg)	80 \pm 8	95 \pm 11	<0.001	91 \pm 11	91 \pm 11	NS
ESP (mm Hg)	67 \pm 8	80 \pm 7	<0.001	73 \pm 12	75 \pm 13	NS
DBP (mm Hg)	45 \pm 8	47 \pm 7	NS	46 \pm 12	46 \pm 12	NS
EDD (cm)	1.65 \pm 0.22	2.14 \pm 0.18	<0.001	2.67 \pm 0.56	2.80 \pm 0.46	NS
EDDi [cm/m ^(2/3)]	2.70 \pm 0.34	3.29 \pm 0.22	<0.05	3.48 \pm 0.52	3.66 \pm 0.45	NS
ESD (cm)	1.06 \pm 0.18	1.38 \pm 0.15	<0.001	1.71 \pm 0.39	1.79 \pm 0.35	NS
ESDi [cm/m ^(2/3)]	1.74 \pm 0.29	2.13 \pm 0.19	<0.05	2.22 \pm 0.37	2.33 \pm 0.37	NS
%FS (%)	35.8 \pm 4.1	35.4 \pm 2.0	NS	36.3 \pm 2.7	36.4 \pm 3.2	NS
PFR (cm/sec)	5.49 \pm 1.26	6.10 \pm 1.13	NS	7.29 \pm 1.86	7.76 \pm 1.58	NS
NPFR (sec ⁻¹)	3.44 \pm 1.14	2.89 \pm 0.65	NS	2.74 \pm 0.50	2.81 \pm 0.57	NS
TPFR (msec)	318 \pm 32	341 \pm 14	<0.05	419 \pm 49	381 \pm 94	NS
EDh (cm)	0.49 \pm 0.09	0.42 \pm 0.06	NS	0.54 \pm 0.09	0.52 \pm 0.09	NS
EDhi [cm/m ^(2/3)]	0.81 \pm 0.13	0.65 \pm 0.05	<0.05	0.71 \pm 0.12	0.68 \pm 0.10	NS
ESh (cm)	0.71 \pm 0.09	0.67 \pm 0.05	NS	0.85 \pm 0.14	0.86 \pm 0.13	NS
EShi [cm/m ^(2/3)]	1.16 \pm 0.14	1.03 \pm 0.06	<0.05	1.12 \pm 0.16	1.13 \pm 0.15	NS
FWT (%)	-45.0 \pm 15.5	-60.3 \pm 15.3	NS	-59.6 \pm 20.2	-66.8 \pm 19.3	NS
PTR (cm/sec)	-2.78 \pm 1.00	-2.44 \pm 0.44	NS	-3.79 \pm 1.09	-3.98 \pm 1.03	NS
NPTR (sec ⁻¹)	13.0 \pm 3.3	10.0 \pm 1.4	NS	12.6 \pm 3.3	11.9 \pm 2.0	NS
TPTR (msec)	317 \pm 30	348 \pm 17	<0.05	403 \pm 60	380 \pm 92	NS
PSS (g/cm ²)	53 \pm 11	108 \pm 30	<0.001	100 \pm 32	106 \pm 25	NS
ESS (g/cm ²)	21 \pm 5	38 \pm 6	<0.001	34 \pm 12	36 \pm 9	NS
VCF (circ/sec)	2.02 \pm 0.25	1.70 \pm 0.16	<0.001	1.49 \pm 0.21	1.51 \pm 0.19	NS
VCFc (circ/sec)	1.33 \pm 0.17	1.13 \pm 0.08	<0.001	1.10 \pm 0.09	1.10 \pm 0.09	NS
SVI (SD)	3.25 \pm 2.67	1.15 \pm 1.09	<0.05	0.37 \pm 1.24	0.53 \pm 1.18	NS
SSI (SD)	-0.45 \pm 1.96	0.19 \pm 0.86	NS	0.47 \pm 1.08	0.58 \pm 1.46	NS
FPI (SD)	-3.71 \pm 1.51	-0.96 \pm 0.31	<0.001	0.09 \pm 0.97	0.05 \pm 1.07	NS

TGA1, TGA2, early and late postoperative study groups, respectively; NORM1, NORM2, infant and older control groups, respectively. BSA, body surface area; DBP, diastolic blood pressure; EDD, end-diastolic dimension; EDDi, EDD indexed to BSA; EDh, end-diastolic wall thickness; EDhi, EDh indexed to BSA; ESD, end-systolic dimension; ESDi, ESD indexed to BSA; ESh, end-systolic wall thickness; EShi, ESh indexed to BSA; ESP, end-systolic pressure; ESS, end-systolic stress; FPI, functional preload index; %FS, percent fractional shortening; FWT, fractional wall thickening; HR, heart rate; NPFR, normalized PFR; NPTR, normalized PTR; PFR, peak filling rate; PSP, peak systolic pressure; PTR, peak thinning rate; PSS, peak systolic stress; SSI, stress-shortening index; SVI, stress-velocity index; tPFR, time to PFR; tPTR, time to PTR; VCF, velocity of shortening; VCFc, rate-corrected VCF.

both the long and short axes exhibited similar segmental shortening fractions in the patients and controls. There was neither significant segment-to-segment variation in the short axis for patients or controls nor did any individual patient demonstrate short-axis intersegmental variation in excess of the norm. The patients demonstrated the normal pattern of intersegmental variation in the long axis with reduced shortening in the lateral-apical (LAP), apical (AP), and basilar-septal (BS) regions.

Left Ventricle Size, Wall Thickness, and Function (Table 1)

In TGA1, the EDD and ESD were significantly lower than in age-matched controls with no differences in EDh or ESh. Because of the smaller BSA in TGA1 patients, smaller dimensions and wall thickness would be anticipated, and therefore, BSA-

adjusted values were also examined. When indexed to the cube root of BSA, EDDi and ESDi were significantly smaller, and EDhi and EShi were significantly larger in TGA1 compared with NORM1. In older subjects, no differences were found in the absolute or BSA-indexed values for ventricular dimensions and wall thickness at end systole or end diastole (EDD, EDDi, ESD, ESDi, EDh, EDhi, ESh, or EShi) between TGA2 and NORM2. No differences were noted in %FS or FWT among TGA1, NORM1, TGA2, and NORM2. In contrast, VCF and VCFc were significantly higher in TGA1 compared with all other groups. In NORM1, VCF was higher compared with NORM2 and TGA2, while there was no difference in VCF between TGA2 and NORM2. When VCF was adjusted to heart rate, no difference in VCFc was noted among the NORM1, NORM2, or TGA2 groups.

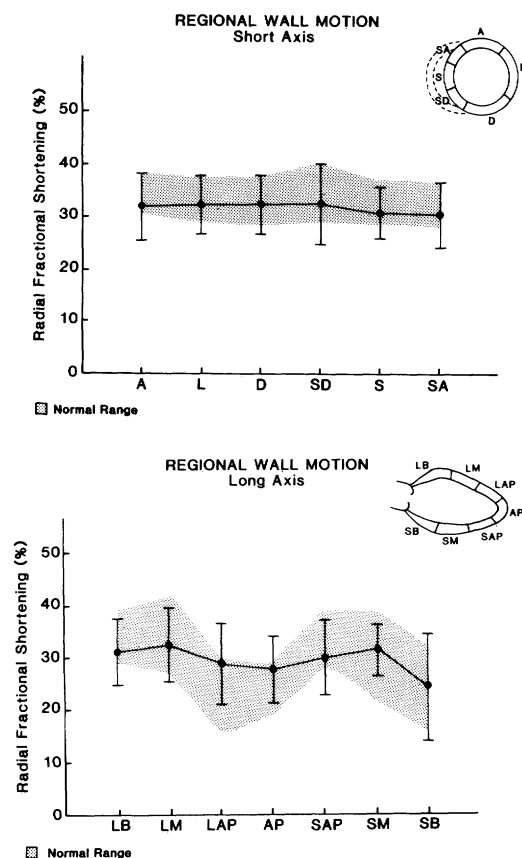


FIGURE 2. Plots of short-axis and long-axis regional wall motion. Normal range (shaded area) and segmentation scheme are shown. Range and pattern of motion were not different from controls for all segments, and no individual subject demonstrated intersegmental variation out of the range of normal.

Left Ventricle Wall Stress, Preload, Afterload, and Contractility (Table 1)

Peak-systolic stress was lower in TGA1 than in all other groups, while PSS was not different among the NORM1, TGA2, or NORM2 groups. Afterload (ESS) was significantly reduced in the TGA1 group compared with NORM1, TGA2, and NORM2, with no significant differences in afterload among the other three groups. As we have previously demonstrated, when VCFc is adjusted for afterload, the resulting relation is a load-independent index of contractility.¹² The ESS-VCFc and ESS-%FS relations for the TGA1 and TGA2 groups are shown in Figures 3A and 4A respectively, and the 95% confidence limits for this relation in our laboratory are given for comparison. None of the patients in TGA1 or TGA2 had SVI values below the lower limits of normal; that is, contractility was normal in all patients in TGA1 and TGA2. Similarly, the ESS-%FS relation represents an afterload-adjusted index of ventricular performance, which is affected by contractility and preload.¹⁹ The ESS-VCFc relation for the TGA1 and TGA2 groups with the normal 95% confidence limits are shown in Figures 3B and

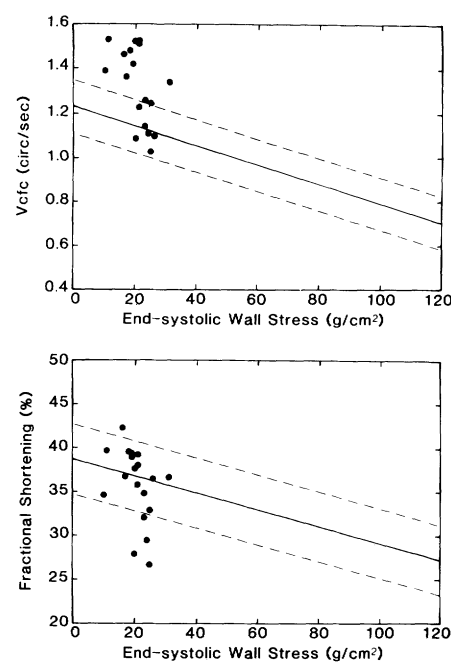


FIGURE 3. Plots of relation of rate-adjusted velocity of shortening (VCFc, top panel) and percent fractional shortening (%FS, bottom panel) to afterload (end-systolic wall stress, ESS) in subjects evaluated early after arterial switch operation. Mean population regression line and 95% confidence intervals for normals in our laboratory are displayed as described in Figure 1. Increased contractility (high ESS-VCFc relation) was typical of these patients. Additionally, the ESS-%FS relation tended to be normal or low, consistent with reduced preload. In two subjects, preload reduction was of sufficient magnitude to result in abnormal %FS (%FS < 28%).

4B, respectively. Differences in these two indexes represent changes in preload.^{16,19} The ESS-VCFc and ESS-%FS relations were quantified in each individual as the stress-normalized value relative to the normal distribution and expressed as the number of standard deviations from the mean (Figure 1). Contractility (SVI) was significantly elevated in the TGA1 group compared with NORM1, TGA2, and NORM2. Although there was a trend toward higher SVI in NORM1 compared with TGA2 and NORM2, this did not attain statistical significance. There was no difference in SVI in the TGA2 and NORM2 groups. The relation between afterload and %FS and SSI did not differ significantly among the four groups. Left ventricular preload (the degree of concordance between the ESS-VCFc and ESS-%FS relations as quantified in the FPI) was significantly reduced in the TGA1 group compared with the other three groups and was reduced in NORM1 compared with TGA2 and NORM2. No difference in FPI was noted between TGA2 and NORM2.

Left Ventricle Diastolic Function (Table 1)

All indexes of diastolic function (PFR, NPFR, PTR, and NPTR) were similar between TGA1 and

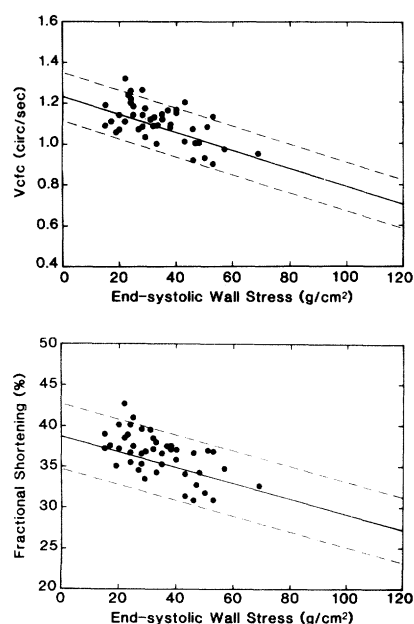


FIGURE 4. Plots of relation of rate-adjusted velocity of shortening (Vcfc) and percent fractional shortening to afterload (end-systolic wall stress) in subjects 5–50 months after arterial switch operation. Mean population regression line and 95% confidence intervals for normals in our laboratory are also shown as in Figure 1. No significant differences compared with control subjects were noted.

NORM1 as well as between TGA2 and NORM2 (Figure 5). When the younger groups (TGA1 and NORM1) were compared with the older groups (TGA2 and NORM2), the nonadjusted indexes (PFR and PTR) were significantly lower. However, when these indexes were adjusted for their known³⁰ dependencies on ventricular size (NPFR) and systolic thickening (NPTR), these differences were no longer detected. Similarly, although the times at which these derivative maxima occurred (tPFR and tPTR) did not differ between either TGA1 and NORM1 or TGA2 and NORM2, they were significantly earlier in the cardiac cycle in TGA1 and NORM1 compared with TGA2 and NORM2. This finding is expected because of the more rapid heart rates in the younger groups. Because of the complex dependency of these indexes on age and left ventricle size, wall thickness, systolic function, and afterload,³⁰ we examined the relation between PFR and PTR and their previously identified dependencies with regression analysis in TGA1 and NORM1 (Tables 2 and 3, Figures 6 and 7). For all regressions, no significant differences were noted in either the slope or intercept.

Discussion

Patients treated with the ASO for TGA are at risk for myocardial injury due to the surgical procedure itself; to transfer of the systemic arterial load to the ventricle, which had previously supported the pulmonary circulation; and to the potential for coronary

insufficiency after coronary reimplantation. In this prospectively evaluated group of patients with TGA and intact or almost intact ventricular septum in whom the ASO had been performed as a one-stage procedure in infancy, we found no evidence of regional or global left ventricular dysfunction, abnormalities of contractility, or detectable diastolic dysfunction.

Evidence of left ventricular functional abnormalities has been reported by several investigators after two-stage anatomic correction of TGA with IVS.^{2–4} Of 12 patients evaluated up to 7 years postoperatively, nine were noted to have angiographic left ventricular volumes significantly above normal despite normal ejection fractions.² When Sievers et al³ examined the afterload-adjusted ejection fraction, four of 12 patients who were 10–29 months after two-stage repair had abnormally low values, indicating either low contractility or reduced preload. Borow et al⁴ used afterload augmentation to determine the end-systolic pressure-dimension rela-

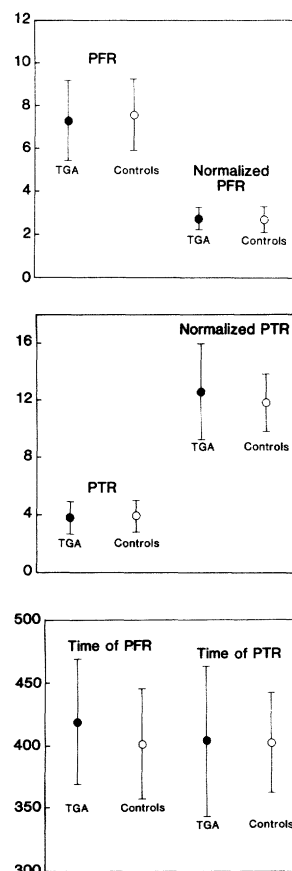


FIGURE 5. Plots of comparison of peak filling rate (PFR) and PFR normalized to end-diastolic dimension (top panel, cm/sec), peak thinning rate (PTR) and PTR normalized to systolic change in wall thickness (middle panel, cm/sec), and the time at which these peak rates occurred (in msec) relative to the Q wave (bottom panel) in controls and patients 5–50 months after arterial switch operation for transposition of the great arteries (TGA). No differences were noted.

TABLE 2. Comparison of Correlation of PFR to Age, BSA, EDD, ESS, and %FS in Older Patient and Control Groups (TGA2 and NORM2)

	Patients	Controls	<i>p</i> value
PFR versus age			
<i>r</i> value	0.61 ($p<0.0001$)	0.56 ($p<0.0001$)	
Slope	0.90 ± 0.21	0.66 ± 0.32	NS
Intercept	6.04 ± 0.37	6.47 ± 0.67	NS
PFR versus BSA			
<i>r</i> value	0.48 ($p<0.0001$)	0.56 ($p<0.0001$)	
Slope	6.81 ± 1.64	6.46 ± 1.21	NS
Intercept	4.13 ± 0.66	4.57 ± 0.59	NS
PFR versus EDD			
<i>r</i> value	0.70 ($p<0.0001$)	0.54 ($p<0.0001$)	
Slope	1.94 ± 0.25	1.72 ± 0.35	NS
Intercept	2.15 ± 0.62	2.70 ± 0.99	NS
PFR versus ESS			
<i>r</i> value	0.34 ($p<0.05$)	0.19 (NS)	
Slope	0.051 ± 0.02	0.036 ± 0.02	NS
Intercept	5.52 ± 0.78	6.27 ± 0.88	NS
PFR versus FS			
<i>r</i> value	-0.005 (NS)	0.13 (NS)	
Slope	-0.03 ± 0.07	0.07 ± 0.07	NS
Intercept	6.84 ± 2.72	4.84 ± 2.71	NS

r value, correlation coefficient for regression in each group with associated significance level; Slope, Intercept, slope and intercept of regression equation in each group; *p* value, significance between slope and intercept values in normals versus controls; PFR, peak filling rate; BSA, body surface area; EDD, end-diastolic dimension; ESS, end-systolic wall stress; %FS, percent fractional shortening.

tion in 12 patients ages 1–5 years after two-stage repair and found depressed contractility in two patients. In the latter study, a strong relation between age at repair and contractile state was noted. Similar findings have led several authors to suggest that primary repair in infancy may result in improved left ventricular performance.^{2–4} Although our findings would support this contention, at least one difference in the patient populations should be emphasized. Because of the strikingly different clinical courses of patients with TGA depending on the presence or absence of a hemodynamically significant ventricular septal defect (VSD),⁸ we have included only patients without significant VSD in the present study. Although some authors have similarly reported patients with intact ventricular septa separately,^{2,3} many reports contain data from both types of patients,^{4,10,11} making comparison more difficult.

Coronary reimplantation carries an associated risk of primary ischemic injury and late problems with coronary artery kinking or ostial stenosis.^{7,11} No evidence of regional dysfunction suggestive of coronary insufficiency was noted in subjects 6 months or more after ASO. Because of the age of these patients, it has not yet been possible to evaluate the adequacy of coronary blood flow dur-

TABLE 3. Comparison of Correlation of PTR to Age, BSA, EDh, ESS, and FWT in Older Patient and Control Groups (TGA2 and NORM2)

	Patients	Controls	<i>p</i> value
PTR versus age			
<i>r</i> value	-0.47 ($p<0.0001$)	-0.48 ($p<0.0001$)	
Slope	-0.49 ± 0.11	-0.38 ± 0.09	NS
Intercept	-3.00 ± 0.17	-3.29 ± 0.19	NS
PTR versus BSA			
<i>r</i> value	-0.44 ($p<0.0001$)	-0.43 ($p<0.0001$)	
Slope	-3.89 ± 1.04	-3.23 ± 0.89	NS
Intercept	-1.99 ± 0.42	-2.42 ± 0.43	NS
PTR versus FWT			
<i>r</i> value	0.62 ($p<0.0001$)	0.53 ($p<0.0001$)	
Slope	0.036 ± 0.006	0.033 ± 0.007	NS
Intercept	-1.47 ± 0.33	-1.81 ± 0.45	NS
PTR versus EDh			
<i>r</i> value	-0.08 (NS)	-0.26 ($p<0.05$)	
Slope	-0.96 ± 1.56	-2.87 ± 1.38	NS
Intercept	-2.98 ± 0.84	-2.38 ± 0.75	NS
PTR versus ESS			
<i>r</i> value	-0.22 (NS)	-0.05 (NS)	
Slope	-0.019 ± 0.02	-0.006 ± 0.02	NS
Intercept	-3.12 ± 0.48	-3.69 ± 0.59	NS

r value, correlation coefficient for regression in each group with associated significance level; Slope, Intercept, slope and intercept of regression equation in each group; *p* value, significance between slope and intercept values in normals versus controls; PTR, peak thinning rate; BSA, body surface area; FWT, fractional wall thickening; EDh, end-diastolic wall thickness; ESS, end-systolic wall stress.

ing the stress of exercise. After two-stage ASO, some patients have been noted to have thallium perfusion defects elicitable by isoproterenol infusion.¹¹ Thus, ongoing evaluation of the status of the coronary anastomoses in this patient group remains a critical issue.

Patients studied early (5–10 days) after surgical repair had significantly altered myocardial mechanics and hemodynamics compared with controls. Elevated contractility with reduced preload, heart rate, blood pressure, wall stress, and ventricular volumes were typical of this group. These findings are likely related to the routine treatment of all patients with digitalis and potent diuretics. The increased contractility and lower heart rates are typical of acute digitalis therapy.³² Diuretic therapy with reduced filling pressures results in reduced preload and end-diastolic volume, factors responsible for the reduction in peak systolic wall stress.¹² The reduction in arterial resistance associated with diuretic therapy results in lower blood pressure, including end-systolic pressure. Lowered end-systolic pressure, as well as enhanced contractility, results in reduced end-systolic volume.³³ Reduced cavity volumes with normal left ventricular mass results in elevated wall thickness, as was observed. Thus, the differences between patients evaluated

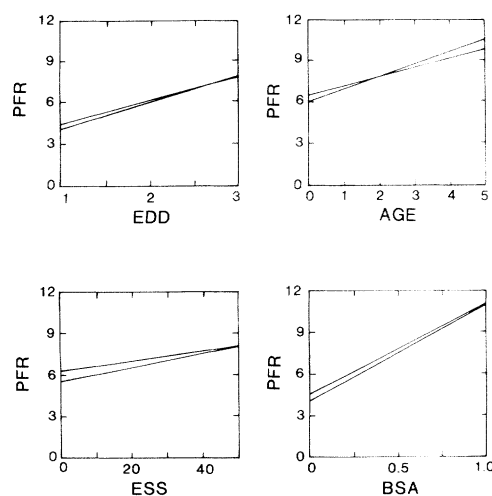


FIGURE 6. Regressions of relation of peak filling rate (PFR; cm/sec) to end-diastolic dimension (EDD; cm), end-systolic stress (ESS; g/cm²), age (years), and body surface area (BSA; m²) in patients 5–50 months after arterial switch operation compared with age-matched normal controls. Slope and intercept of these regressions were not different in the two groups.

shortly after ASO and age-matched controls are most likely related to routine drug therapy in the surgical group. The high incidence of abnormal loading conditions in this patient subgroup emphasizes the need for evaluation with a load-independent index of contractility. As shown in Figure 3B, some patients were noted to have abnormally low fractional shortening secondary to reduced preload, in spite of normal contractility.

Methodological Issues

The index of contractility used in the present study (the relation of VCFc to end-systolic stress) has been previously shown to be independent of preload, to incorporate afterload, and to be responsive to changes in contractility.¹⁹ The inversely linear nature of this relation has been observed in several patient subgroups in addition to normal subjects.^{34,35} In contrast to the preload independence of VCFc,^{27–29} fractional shortening is highly dependent on end-diastolic fiber length, while demonstrating an inversely linear relation to afterload, which is contractility dependent.^{36,37} This difference between the preload independence of VCFc and the preload dependence of fractional shortening can be exploited to yield a clinically useful functional index of preload.¹⁶ The indexes of systolic and diastolic function used here are valid only in the presence of a normal left ventricular configuration without regional dysfunction, conditions confirmed by regional wall motion analysis. Subjects with significant right ventricular hypertension were excluded from evaluation of ventricular performance because of the associated leftward septal displacement and consequent abnormal

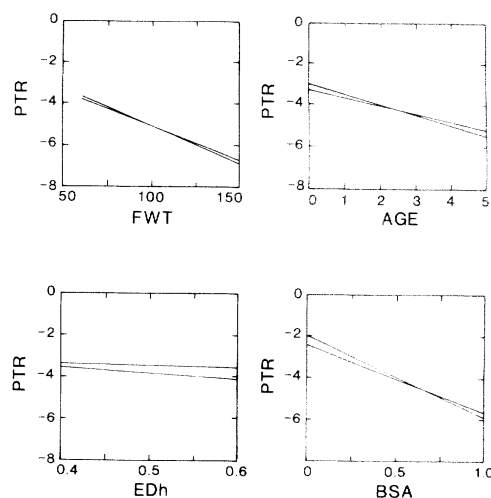


FIGURE 7. Regressions of relation of peak thinning rate (PTR; cm/sec), fractional wall thickening (FWT; %), end-diastolic wall thickness (EDH; cm), age (years), and body surface area (BSA; m²) in patients 5–50 months after arterial switch operation compared with age-matched normal controls. Slope and intercept of these regressions were not different in the two groups.

left ventricular configuration under these circumstances. Therefore, it is not possible to apply these findings to patients with significant right ventricular hypertension after ASO who may in fact experience secondary left ventricular systolic or diastolic dysfunction.

Conclusions

In a large group of patients followed as long as 4 years after neonatal ASO for TGA and IVS, no evidence of abnormal systolic or diastolic function was noted in patients without residual right ventricular hypertension. In the early postoperative period, patients with normal left ventricular configuration demonstrated elevated contractility with reduced afterload and preload, findings attributable to the usual pharmacological management of these patients with digitalis and diuretics. Although this optimal outcome is achievable in the short term, the potential late complications of coronary insufficiency or left ventricular myocardial dysfunction remain concerns that must continue to be evaluated in a prospective fashion.

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KEY WORDS • ventricular function • diastole • systole • transposition of great arteries • congenital heart disease • surgical results