Impact of Fontan Operation on Left Ventricular Size and Contractility in Tricuspid Atresia

Marc H. Gewillig, MD, Ulla R. Lundström, MD,
John E. Deanfield, MD, Catherine Bull, MD, Rodney C. Franklin, MD,
Thomas P. Graham Jr., MD, and Richard K. Wyse, MD

Left ventricular dimensions and contractility were determined by echocardiography in 33 patients with tricuspid atresia in 1985 and again in 1988. Eight patients remained palliated throughout the 3-year period; neither the left ventricular end-diastolic diameter (153±15% of normal vs. 157±19%, \(p=NS\)) nor a load-independent index of contractility (rate-corrected velocity of shortening [VCFc]/end-systolic meridional stress [ESSM]) changed. Eleven patients underwent a Fontan operation during the study and were reevaluated at least 6 months after surgery; left ventricular dimension decreased (130±15% vs. 114±19%, \(p<0.001\)), and the contractility index VCFc/ESSM improved (\(p<0.05\)). Fourteen patients had undergone a Fontan operation 0.9–9.5 years (mean, 4.2 years) before initial examination in 1985. Over the 3-year period, left ventricular dimensions did not change (121±17% vs. 118±11%, \(p=NS\)), but the contractility index showed significant improvement (\(p<0.01\)). Eight additional patients were studied just before and after a Fontan operation to examine the early effects of surgery. Left ventricular dimensions decreased from 130±14% to 100±13% by 10 days \(p<0.001\) with no further change at 2 months. An inappropriate degree of ventricular hypertrophy was observed in only the early postoperative period. Successful Fontan repair results in rapid reduction of left ventricular size, followed by regression of hypertrophy to a normal mass-to-volume ratio. Operating at more favorable dimensions and loading conditions results in an early increase in left ventricular contractility, which further improves in the medium term follow-up. (*Circulation* 1990;81:118–127)

There have been numerous reports of abnormal left ventricular dimensions and function in patients with tricuspid atresia, both before and after a Fontan operation.1-12 Various factors might contribute to these morphologic and functional abnormalities, including preoperative chronic volume overload and cyanosis, perioperative myocardial damage, and adverse postoperative hemodynamics. All previous studies, however, have measured left ventricular pump function in terms of variables that are affected not only by abnormal contractility but also by afterload, preload, and myocardial hypertrophy.

Colan et al13 reported an echocardiographically derived index of left ventricular function that is a sensitive measure of contractile state and is relatively independent of abnormal loading conditions. In 1985, we reported a cross-sectional study using this index to compare left ventricular function in patients palliated for tricuspid atresia with those who had undergone a Fontan operation.14 Reexamining these patients after a 3-year period, we now report a prospective longitudinal study that reports the effect of the altered loading conditions on left ventricular size and function after a Fontan operation. Our aim was to understand whether the Fontan operation represents a beneficial long-term investment for ventricular function in patients with tricuspid atresia.

**Methods**

In 1985, we studied all patients with tricuspid atresia who underwent surgery (palliation or Fontan procedure) at The Hospital for Sick Children, London, from January 1970 to January 1985 and were
living in the UK. Patients were excluded if they were less than 18 months old or had transposed great arteries with subvalvar aortic stenosis. Four additional patients with pulmonary atresia and intact ventricular septum, severe tricuspid stenosis, and diminutive right ventricles were also included as their hemodynamics were believed to be functionally similar to tricuspid atresia. Of the total of 42 patients studied in 1985, 33 were reevaluated in 1988 (study interval, 2.7–3.1 years; mean, 2.8 years). Four patients died during the study period (two early and two late after a Fontan procedure). The remaining five patients declined reevaluation for nonmedical reasons, but all are known to be alive and well.

All patients were studied electively and were considered to be in stable clinical condition. No patient had edema, effusions, or protein losing enteropathy; all had a mild degree of hepatomegaly. The 33 patients were divided into three groups. Group 1 consisted of eight patients who remained palliated throughout the study period. Since the initial evaluation, four shunt procedures were performed in three patients. Five patients are considered potential candidates for a Fontan repair; the other three have pulmonary vascular problems (pulmonary artery hypoplasia in one and severe distortion in two) (Table 1).

Group 2 consisted of 11 patients who had a Fontan operation by direct right atrial-pulmonary artery connection between 1985 and 1988. During this period, only patients who were increasingly symptomatic, typically from cyanosis, were selected for a Fontan operation. All patients were studied before and at least 6 months after Fontan repair (Table 2).

The 14 patients in group 3 had undergone a Fontan operation 0.9–9.5 years (mean, 4.2 years) before initial examination in 1985. Longitudinal comparison was, therefore, available between two postoperative studies (Table 3).

To examine the early effects of the Fontan operation on left ventricular function and size, a fourth group (group 4) of eight consecutive patients with tricuspid atresia undergoing the Fontan operation between September 1987 and April 1988 was investigated. Echocardiographic examination was performed just before surgery and 10 days and 2 months after the Fontan procedure. All patients in this group were taking digitalis, diuretics, and vasodilators at the first postoperative evaluation; at 2 months, medication in all patients had significantly been reduced (Table 4).

Echocardiographic Studies

All patients underwent echocardiographic examination with an Advanced Technology Laboratory Mark 600 Ultrasound System in 1985 and with an Ultramark 8 in 1988. Studies were performed with patients supine or in a slight left lateral decubitus position in a darkened, quiet room, with sedation required in a few young patients in 1985. Mitral regurgitation, residual ventricular septal defect, sub-aortic stenosis, and aortic regurgitation were excluded in all patients by Doppler echocardiographic analysis.

Precordial long- and short-axis views of the left ventricle were used to detect regional wall motion abnormalities; two patients in 1985 and one patient in 1988 were excluded because of marked septal dyskinesia. Simultaneous recordings of left ventricular echocardiogram, phonocardiogram, indirect carotid pulse tracing, and electrocardiogram were obtained. Systolic and diastolic blood pressures were recorded with a cuff sphygmomanometer.

Measurements and Calculations

Left ventricular internal dimensions (D) and posterior wall thickness (h) were measured at end diastole (ed) and end systole (es) for five beats, and mean values were computed. Ed was defined as the onset of the QRS, and es was estimated by the first high-frequency component of the second heart sound. Left ventricular ejection time (ET) was measured from the carotid pulse tracing and rate-corrected to a heart rate of 60 beats/min by dividing by the square root of the R-R interval (ETc). Es pressure (Pes) was estimated by the method of Borow et al by assigning maximum systolic blood pressure to the peak and diastolic pressure to the nadir of the carotid pulse, with subsequent linear interpolation to the level of the incisura. Fractional shortening (FS) was calculated as (Ded–Des)/Ded, and endocardial velocity of circumferential fiber shortening corrected for heart rate (VcFe) was determined as FS/ETc. Endocardial es meridional stress (ESSM) was determined by the method of Grossman et al in which ESSM (g/cm²)=Pes×Des×1.35/4×hcs(1+hcs/Des) where Des and hcs are in centimeters, Pes in millimeters of mercury, 1.35 is a conversion factor (from mm Hg to g/cm²), and 4 is a geometric factor that results from conversion of radius to internal diameter.

Normal values for Des were estimated as 37.75+12.88 log (body surface area [BSA]) from the study of Gutgesell et al.17 Dimensions and contractility indexes were compared with literature data and our own results from 42 normal controls studied in our laboratory.18

Statistical Analysis

Data were stored in a sir (version 2) database on an Amdahl mainframe computer and analyzed using SAS statistical packages (version 10, Northwestern University). A Shapiro-Wilk normality test was performed on the differences of paired data; the significance level was set at 0.10. Depending on the normality of the distribution, the t test for paired data or the Wilcoxon ranked sum test was used; p values obtained by the latter test are identified in the tables. Associations between variables were analyzed with the Pearson product-moment correlation coefficient. A p value of less than 0.05 was considered statistically significant. All data are expressed as mean±SD.
TABLE 2. Patients With Palliation Only (Group 1)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>%BSA</td>
<td>%BSA</td>
<td>%BSA</td>
<td>%BSA</td>
</tr>
<tr>
<td>1</td>
<td>8.1</td>
<td>BT 0.1, BT 0.1, CS 2.4</td>
<td></td>
<td>0.687</td>
<td>0.893</td>
<td>67.2</td>
<td>188</td>
<td>59.2</td>
<td>161</td>
</tr>
<tr>
<td>2</td>
<td>13.3</td>
<td>WAT 0.2, BT 8.0</td>
<td></td>
<td>0.842</td>
<td>0.931</td>
<td>59.4</td>
<td>161</td>
<td>65.1</td>
<td>174</td>
</tr>
<tr>
<td>3</td>
<td>5.3</td>
<td>Band 0.4</td>
<td></td>
<td>0.511</td>
<td>0.775</td>
<td>48.5</td>
<td>142</td>
<td>47.6</td>
<td>131</td>
</tr>
<tr>
<td>4</td>
<td>6.4</td>
<td>BT 0.01, BT 1.7</td>
<td>BT 4.5</td>
<td>0.661</td>
<td>0.837</td>
<td>48.2</td>
<td>136</td>
<td>54.2</td>
<td>147</td>
</tr>
<tr>
<td>5</td>
<td>6.8</td>
<td>BT 0.02</td>
<td></td>
<td>0.528</td>
<td>0.676</td>
<td>61.5</td>
<td>180</td>
<td>64.5</td>
<td>181</td>
</tr>
<tr>
<td>6</td>
<td>17.9</td>
<td>WAT 0.03, BT 8.3, BT 10.3</td>
<td>CS 16.0</td>
<td>1.34</td>
<td>1.46</td>
<td>64.8</td>
<td>164</td>
<td>73.6</td>
<td>185</td>
</tr>
<tr>
<td>7</td>
<td>7.4</td>
<td>CS 0.01, BT 1.7</td>
<td>CS 6.0, CS 6.7</td>
<td>0.627</td>
<td>0.817</td>
<td>42.8</td>
<td>122</td>
<td>50.9</td>
<td>139</td>
</tr>
<tr>
<td>8</td>
<td>9.0</td>
<td>BT 0.3, BT 3.0</td>
<td></td>
<td>0.645</td>
<td>0.798</td>
<td>47.2</td>
<td>134</td>
<td>52.3</td>
<td>143</td>
</tr>
</tbody>
</table>

Mean 9.3 ±SD 4.2

*p <0.001 NS NS

Interobserver and intraobserver variability were assessed for all variables for 30 cardiac cycles in five patients. Values for the coefficients of variation ranged between 0.2% and 4.9% for interobserver variability and between 0.3% and 4.2% for intraobserver variability.

Results

Although left ventricular end-diastolic dimensions increased in six of the eight patients who remained palliated throughout the study period (group 1), the overall change for the group did not reach statistical significance (153±15% of normal vs. 157±19% of normal, p=NS) (Figure 1). In contrast, the end-diastolic dimension of patients who had received a Fontan repair during the study period (group 2) decreased significantly both in absolute values (−9±8%, p<0.02) and when expressed as percentage of normal (130±15% vs. 114±19%, p<0.001). Only two patients in group 2 showed no decrease in ventricular size. One of these patients had developed

TABLE 2. Patients With Fontan Repair During Study Period 1985–1988 (Group 2)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>%BSA</td>
<td>%BSA</td>
<td>%BSA</td>
<td>%BSA</td>
</tr>
<tr>
<td>1</td>
<td>4.6</td>
<td>BT 0.3, BT 0.3</td>
<td>3.7</td>
<td>0.495</td>
<td>0.713</td>
<td>34.3</td>
<td>188</td>
<td>33.3</td>
<td>161</td>
</tr>
<tr>
<td>2</td>
<td>5.0</td>
<td>BT 0.2, WAT 1.8</td>
<td>2.6</td>
<td>0.491</td>
<td>0.690</td>
<td>40.3</td>
<td>119</td>
<td>37.8</td>
<td>106</td>
</tr>
<tr>
<td>3</td>
<td>5.6</td>
<td>BT 0.9, BT 2.0</td>
<td>3.8</td>
<td>0.519</td>
<td>0.728</td>
<td>46.7</td>
<td>137</td>
<td>41.6</td>
<td>116</td>
</tr>
<tr>
<td>4</td>
<td>5.7</td>
<td>BT 1.5</td>
<td>4.8</td>
<td>0.507</td>
<td>0.713</td>
<td>43.2</td>
<td>127</td>
<td>35.8</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>6.9</td>
<td>BT 0.1, BT 4.6</td>
<td>6.3</td>
<td>0.661</td>
<td>0.906</td>
<td>48.2</td>
<td>136</td>
<td>42.4</td>
<td>114</td>
</tr>
<tr>
<td>6</td>
<td>7.1</td>
<td>BT 3.5</td>
<td>4.9</td>
<td>0.594</td>
<td>0.846</td>
<td>41.3</td>
<td>119</td>
<td>38.4</td>
<td>104</td>
</tr>
<tr>
<td>7</td>
<td>9.4</td>
<td>BT 0.01, BT 3.6</td>
<td>8.0</td>
<td>0.841</td>
<td>1.140</td>
<td>57.1</td>
<td>155</td>
<td>52.0</td>
<td>135</td>
</tr>
<tr>
<td>8</td>
<td>9.5</td>
<td>BT 0.02, BT 3.6</td>
<td>8.3</td>
<td>0.784</td>
<td>1.010</td>
<td>47.5</td>
<td>131</td>
<td>39.8</td>
<td>105</td>
</tr>
<tr>
<td>9</td>
<td>9.8</td>
<td>BT 0.1, BT 1.0</td>
<td>8.0</td>
<td>0.759</td>
<td>0.900</td>
<td>46.1</td>
<td>127</td>
<td>38.5</td>
<td>103</td>
</tr>
<tr>
<td>10</td>
<td>11.7</td>
<td>BT 0.01, BT 6.2</td>
<td>11.1</td>
<td>0.809</td>
<td>1.050</td>
<td>47.5</td>
<td>130</td>
<td>48.0</td>
<td>126</td>
</tr>
<tr>
<td>11</td>
<td>13.6</td>
<td>BT 2.2, CS 7.6</td>
<td>11.3</td>
<td>0.905</td>
<td>1.180</td>
<td>57.5</td>
<td>154</td>
<td>62.3</td>
<td>161</td>
</tr>
</tbody>
</table>

Mean 8.1 ±SD 3.0

*p <0.001 <0.05 <0.001 NS

BSA, body surface area; %BSA, % of normal for BSA; BT, Blalock-Taussig shunt (classic or modified); CS, central shunt; Ded, ventricular end-diastolic dimension; %Ded, % of normal for Ded; G, glycosides; hed, ventricular end-diastolic posterior wall thickness; NYHA, New York Heart Association; WAT, Waterston shunt; D, diuretics; V, vasodilator (angiotensin converting enzyme inhibitor).

All p values refer to a paired t test unless stated otherwise.
asymptomatic atrial flutter between 14 and 22 months after the Fontan operation with a ventricular rate of 110–140 beats/min on a 24-hour Holter monitor. A postoperative echocardiogram in atrial flutter 22 months after the Fontan operation showed a substantial increase in end-diastolic dimension. With diuretics and control of the ventricular rate with digitalis, this improved but still remained above preoperative values. In group 2, there was a highly significant correlation between end-systolic and end-diastolic dimensions (r=0.92, p<0.001; r=0.88, p<0.001, respectively).

There was no significant change in end-diastolic dimension in group 3 patients in whom both measurements were made during follow-up after the Fontan procedure (121±17% vs. 118±11%, p=NS).

In the eight group 4 patients whose dimensions were measured immediately before and early after the Fontan procedure, there was a significant decrease in end-diastolic dimension (130±14% vs. 100±13%, p<0.001). There was no further change at the 2-month evaluation (101±12%, p=NS). The variable pattern of end-diastolic dimension during both evaluations may reflect differences in medical therapy. As in group 2, the postoperative end-diastolic dimension at 10 days correlated best with preoperative end-systolic dimensions (r=0.91, p<0.002) but also with end-diastolic dimensions (r=0.89, p<0.003).

**Wall Thickness**

Left ventricular wall thickness did not change significantly in patients who remained palliated (group 1) (Figure 2). It was increased when compared with normal values for BSA but was decreased when related to end-diastolic dimension (Dved), suggesting ventricular dilatation (BSA: 129±27% vs. 126±19%, p=NS; Dved: 76±11% vs. 77±8%, p=NS). After a Fontan operation in both group 2 and 3, the wall thickness was appropriate for the ventricular size. In group 2, there was a significant decrease in wall thickness during the study (−20±22%, p<0.02), whereas in group 3, there was no significant change.

The patients studied during the perioperative period after a Fontan operation (group 4) showed a major increase in wall thickness 10 days after their operation, especially when related to diastolic dimension (90±9% vs. 175±30%, p<0.001). This inappropriate degree of wall thickness for heart size had decreased significantly by 2 months but was still elevated above normal (126±13%, p<0.001). In the early postoperative measurements, increases in wall thickness correlated closely with decreases in dimension (r=0.88, p<0.005).

**Contractility-Stress Data**

In the patients who remained palliated (group 1), FS, which is load dependent, increased from 29.7±4.6% to 31.2±4.8% (p<0.05), but VCFc did not change (Figures 3–5). ESSM remained above normal throughout but decreased (67.5±23.3 to 57.7±20.4 g/cm², p<0.05), mainly due to an increase in end-systolic wall thickness (mean increase, 1.6 mm; p<0.02). The load-independent relation of VCFc to ESSM showed no significant change perpendicular to its regression line,13 suggesting no alteration of left ventricular contractility during the 3-year period.

In patients who had received a Fontan repair during the study period (group 2), FS did not change significantly (30.7±4.8% vs. 32.5±8.5%, p=NS), but

<table>
<thead>
<tr>
<th>TABLE 1. (Continued)</th>
<th>VCFc (cycles/sec)</th>
<th>ESM (g/cm²)</th>
<th>Medication</th>
<th>NYHA class</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.1 101 61 0.656 0.760 115 103 G III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.0 130 73 0.881 0.910 79.6 50.5 G II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.8 120 85 1.117 1.020 51.9 38.9 G II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.0 119 76 1.030 1.030 52.4 52.0 — II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.9 166 82 0.942 1.000 63.1 46.6 — II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.2 110 66 0.790 0.833 81.2 68.9 — II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.5 129 87 1.040 1.110 49.2 44.8 — III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.5 130 85 0.849 0.863 47.7 56.9 — II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.5 126 77 0.916 0.928 67.5 57.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.9 19 8 0.153 0.104 23.3 20.4 NS NS NS NS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NS NS NS &lt;0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

left ventricular absolute dimensions before the Fontan procedure and the postoperative end-diastolic measurements (r=0.92, p<0.001; r=0.88, p<0.001, respectively).

In the eight group 4 patients whose dimensions were measured immediately before and early after the Fontan procedure, there was a significant decrease in end-diastolic dimension (130±14% vs. 100±13%, p<0.001). There was no further change at the 2-month evaluation (101±12%, p=NS). The variable pattern of end-diastolic dimension during both evaluations may reflect differences in medical therapy. As in group 2, the postoperative end-diastolic dimension at 10 days correlated best with preoperative end-systolic dimensions (r=0.91, p<0.002) but also with end-diastolic dimensions (r=0.89, p<0.003).

**Wall Thickness**

Left ventricular wall thickness did not change significantly in patients who remained palliated (group 1) (Figure 2). It was increased when compared with normal values for BSA but was decreased when related to end-diastolic dimension (Dved), suggesting ventricular dilatation (BSA: 129±27% vs. 126±19%, p=NS; Dved: 76±11% vs. 77±8%, p=NS). After a Fontan operation in both group 2 and 3, the wall thickness was appropriate for the ventricular size. In group 2, there was a significant decrease in wall thickness during the study (−20±22%, p<0.02), whereas in group 3, there was no significant change.

The patients studied during the perioperative period after a Fontan operation (group 4) showed a major increase in wall thickness 10 days after their operation, especially when related to diastolic dimension (90±9% vs. 175±30%, p<0.001). This inappropriate degree of wall thickness for heart size had decreased significantly by 2 months but was still elevated above normal (126±13%, p<0.001). In the early postoperative measurements, increases in wall thickness correlated closely with decreases in dimension (r=0.88, p<0.005).

**Contractility-Stress Data**

In the patients who remained palliated (group 1), FS, which is load dependent, increased from 29.7±4.6% to 31.2±4.8% (p<0.05), but VCFc did not change (Figures 3–5). ESSM remained above normal throughout but decreased (67.5±23.3 to 57.7±20.4 g/cm², p<0.05), mainly due to an increase in end-systolic wall thickness (mean increase, 1.6 mm; p<0.02). The load-independent relation of VCFc to ESSM showed no significant change perpendicular to its regression line,13 suggesting no alteration of left ventricular contractility during the 3-year period.

In patients who had received a Fontan repair during the study period (group 2), FS did not change significantly (30.7±4.8% vs. 32.5±8.5%, p=NS), but
TABLE 3.  Patients With Fontan Operation Before 1985 (Group 3)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age in 1988 (yr)</th>
<th>Previous surgery age (yr)</th>
<th>Age at Fontan (yr)</th>
<th>Type of connection</th>
<th>BSA 1985 (m²)</th>
<th>BSA 1988 (m²)</th>
<th>Ded 1985 mm %BSA</th>
<th>Ded 1988 mm %BSA</th>
<th>hed 1985 mm %BSA</th>
<th>%Ded 1988 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.6</td>
<td>BT 0.01</td>
<td>2.7</td>
<td>RA-PA(H)</td>
<td>0.670</td>
<td>0.871</td>
<td>43.5</td>
<td>122</td>
<td>42.9</td>
<td>116</td>
</tr>
<tr>
<td>2</td>
<td>8.6</td>
<td>—</td>
<td>4.3</td>
<td>RA-RV(H)</td>
<td>0.767</td>
<td>0.954</td>
<td>39.3</td>
<td>108</td>
<td>43.4</td>
<td>115</td>
</tr>
<tr>
<td>3</td>
<td>9.2</td>
<td>BT 0.6</td>
<td>5.4</td>
<td>RA-PA(D)</td>
<td>0.745</td>
<td>1.021</td>
<td>39.5</td>
<td>109</td>
<td>41.0</td>
<td>108</td>
</tr>
<tr>
<td>4</td>
<td>10.2</td>
<td>BT 0.1</td>
<td>6.3</td>
<td>RA-PA(H)</td>
<td>0.803</td>
<td>0.980</td>
<td>50.2</td>
<td>136</td>
<td>50.2</td>
<td>133</td>
</tr>
<tr>
<td>5</td>
<td>11.3</td>
<td>BT 3.5</td>
<td>7.5</td>
<td>RA-PA(D)</td>
<td>0.920</td>
<td>1.232</td>
<td>49.1</td>
<td>131</td>
<td>48.6</td>
<td>125</td>
</tr>
<tr>
<td>6</td>
<td>11.4</td>
<td>Band 0.3</td>
<td>3.9</td>
<td>RA-RV(H)</td>
<td>0.943</td>
<td>1.158</td>
<td>41.5</td>
<td>111</td>
<td>49.2</td>
<td>127</td>
</tr>
<tr>
<td>7</td>
<td>11.6</td>
<td>—</td>
<td>4.2</td>
<td>RA-RV(H)</td>
<td>0.943</td>
<td>1.153</td>
<td>40.5</td>
<td>108</td>
<td>40.2</td>
<td>104</td>
</tr>
<tr>
<td>8</td>
<td>12.0</td>
<td>BT 0.01</td>
<td>4.2</td>
<td>RA-PA(H)</td>
<td>1.060</td>
<td>1.302</td>
<td>64.0</td>
<td>168</td>
<td>52.6</td>
<td>134</td>
</tr>
<tr>
<td>9</td>
<td>14.2</td>
<td>BT 0.1</td>
<td>5.8</td>
<td>RA-PA(H)</td>
<td>1.039</td>
<td>1.340</td>
<td>38.2</td>
<td>102</td>
<td>39.2</td>
<td>100</td>
</tr>
<tr>
<td>10</td>
<td>14.7</td>
<td>BT 0.3</td>
<td>8.2</td>
<td>RA-RV(H)</td>
<td>1.300</td>
<td>1.632</td>
<td>48.0</td>
<td>122</td>
<td>48.9</td>
<td>121</td>
</tr>
<tr>
<td>11</td>
<td>16.2</td>
<td>WAT 1.9</td>
<td>7.0</td>
<td>RA-PA(H)</td>
<td>1.278</td>
<td>1.638</td>
<td>47.9</td>
<td>122</td>
<td>51.1</td>
<td>126</td>
</tr>
<tr>
<td>12</td>
<td>16.6</td>
<td>Band 0.2, BT 3.8</td>
<td>11.5</td>
<td>RA-RV(H)</td>
<td>1.342</td>
<td>1.357</td>
<td>47.3</td>
<td>120</td>
<td>43.2</td>
<td>109</td>
</tr>
<tr>
<td>13</td>
<td>17.1</td>
<td>BT 0.4, BT 6.0</td>
<td>9.9</td>
<td>RA-RV(X)</td>
<td>1.401</td>
<td>1.612</td>
<td>43.6</td>
<td>110</td>
<td>43.6</td>
<td>108</td>
</tr>
<tr>
<td>14</td>
<td>24.9</td>
<td>Brock 2.0, BT 6.8</td>
<td>12.7</td>
<td>RA-PA(C)</td>
<td>1.460</td>
<td>1.420</td>
<td>53.0</td>
<td>133</td>
<td>51.6</td>
<td>130</td>
</tr>
</tbody>
</table>

Mean 13.3 ± SD 4.6; p < 0.001; NS (W) NS (W) < 0.05

Band, pulmonary artery band; BSA, body surface area; %BSA, % of normal for BSA; BT, Blalock-Taussig shunt (classic or modified); Ded, ventricular end-diastolic dimension; %Ded, % of normal for Ded; G, glycosides; hed, ventricular end-diastolic posterior wall thickness; NYHA, New York Heart Association; PA, pulmonary artery; WAT, Waterston shunt; C, Hancock conduit; D, direct anastomosis; H, valved homograft; W, Wilcoxon rank-sum test; X, valved xenograft.

All p values refer to a paired t test unless stated otherwise.

VCFc increased from 0.929±0.149/sec to 1.050±0.230/sec (p<0.05). The relation of VFCfc to ESSM showed a significant shift toward enhanced contractility after the Fontan procedure (p<0.05).

In the post-Fontan group (group 3 patients), FS and VFCfc increased significantly (29.7±4.9% to 34.0±3.4%, p<0.005; 1.017±0.173/sec to 1.140±0.131/sec, p<0.005). There was a net improvement of

TABLE 4.  Patients with Fontan Operation In 1987–1988 (Group 4)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age in 1988 (yr)</th>
<th>Previous surgery age (yr)</th>
<th>Age at Fontan (yr)</th>
<th>BSA (m²)</th>
<th>Ded preop mm %BSA</th>
<th>Ded 10 days mm %BSA</th>
<th>Ded 60 days mm %BSA</th>
<th>hed preop mm %BSA</th>
<th>%Ded</th>
<th>hed 10 days mm %Ded</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.6</td>
<td>BT 0.01</td>
<td>0.463</td>
<td>37.8</td>
<td>113</td>
<td>29.0</td>
<td>87</td>
<td>30.2</td>
<td>90</td>
<td>5.4</td>
</tr>
<tr>
<td>2</td>
<td>1.9</td>
<td>BT 0.01</td>
<td>0.531</td>
<td>44.4</td>
<td>129</td>
<td>29.5</td>
<td>86</td>
<td>28.7</td>
<td>83</td>
<td>6.5</td>
</tr>
<tr>
<td>3</td>
<td>2.6</td>
<td>BT 0.2</td>
<td>0.550</td>
<td>38.4</td>
<td>111</td>
<td>29.3</td>
<td>85</td>
<td>33.9</td>
<td>99</td>
<td>5.4</td>
</tr>
<tr>
<td>4</td>
<td>3.0</td>
<td>—</td>
<td>0.685</td>
<td>44.4</td>
<td>124</td>
<td>34.9</td>
<td>98</td>
<td>33.6</td>
<td>95</td>
<td>7.3</td>
</tr>
<tr>
<td>5</td>
<td>4.7</td>
<td>BT 1.5</td>
<td>0.624</td>
<td>51.3</td>
<td>146</td>
<td>41.2</td>
<td>117</td>
<td>36.6</td>
<td>104</td>
<td>8.6</td>
</tr>
<tr>
<td>6</td>
<td>6.8</td>
<td>BT 0.01, BT 4.5</td>
<td>0.837</td>
<td>54.2</td>
<td>147</td>
<td>37.6</td>
<td>102</td>
<td>42.4</td>
<td>115</td>
<td>7.0</td>
</tr>
<tr>
<td>7</td>
<td>7.9</td>
<td>—</td>
<td>0.928</td>
<td>51.9</td>
<td>139</td>
<td>43.3</td>
<td>116</td>
<td>–</td>
<td>–</td>
<td>7.8</td>
</tr>
<tr>
<td>8</td>
<td>12.8</td>
<td>Glenn 5.0, BT 10.2</td>
<td>1.433</td>
<td>53.8</td>
<td>135</td>
<td>44.0</td>
<td>110</td>
<td>46.0</td>
<td>115</td>
<td>9.1</td>
</tr>
</tbody>
</table>

Mean 5.1 ± SD 3.8; p < 0.001; < 0.001; < 0.001; < 0.001; < 0.001

BSA, body surface area; %BSA, % of normal for BSA; BT, Blalock-Taussig shunt (classic or modified); Ded, ventricular end-diastolic dimension; %Ded, % of normal for Ded; G, glycosides; hed, ventricular end-diastolic posterior wall thickness; D, diuretics; FS, fractional shortening; V, vasodilator.

All p values refer to a paired t test unless stated otherwise.
(Continued)

<table>
<thead>
<tr>
<th>%BSA</th>
<th>%Ded</th>
<th>VCFc</th>
<th>ESSM</th>
<th>Mediation</th>
<th>NYHA class</th>
</tr>
</thead>
<tbody>
<tr>
<td>114</td>
<td>105</td>
<td>1.247</td>
<td>4.43</td>
<td>51.5</td>
<td>I</td>
</tr>
<tr>
<td>105</td>
<td>105</td>
<td>1.352</td>
<td>4.60</td>
<td>42.4</td>
<td>I</td>
</tr>
<tr>
<td>92</td>
<td>97</td>
<td>0.963</td>
<td>1.031</td>
<td>97.0</td>
<td>I</td>
</tr>
<tr>
<td>121</td>
<td>132</td>
<td>0.950</td>
<td>1.093</td>
<td>41.1</td>
<td>II</td>
</tr>
<tr>
<td>97</td>
<td>92</td>
<td>1.192</td>
<td>1.290</td>
<td>41.3</td>
<td>G</td>
</tr>
<tr>
<td>117</td>
<td>107</td>
<td>0.980</td>
<td>1.102</td>
<td>65.1</td>
<td>I</td>
</tr>
<tr>
<td>112</td>
<td>112</td>
<td>0.855</td>
<td>0.914</td>
<td>51.9</td>
<td>II</td>
</tr>
<tr>
<td>123</td>
<td>131</td>
<td>1.064</td>
<td>1.100</td>
<td>47.9</td>
<td>G</td>
</tr>
<tr>
<td>96</td>
<td>82</td>
<td>1.056</td>
<td>1.161</td>
<td>79.3</td>
<td>I</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>%BSA</th>
<th>%Ded</th>
<th>VCFc</th>
<th>ESSM</th>
<th>Mediation</th>
<th>NYHA class</th>
</tr>
</thead>
<tbody>
<tr>
<td>118</td>
<td>108</td>
<td>1.017</td>
<td>1.140</td>
<td>56.7</td>
<td>I</td>
</tr>
<tr>
<td>16</td>
<td>14</td>
<td>0.173</td>
<td>0.131</td>
<td>16.8</td>
<td>I</td>
</tr>
<tr>
<td>NS</td>
<td>NS</td>
<td>&lt;0.005</td>
<td>&lt;0.05</td>
<td></td>
<td>I</td>
</tr>
</tbody>
</table>

contractility as analyzed by the VCFc-ESSM relation (p<0.01).

There was no discrete pattern and, therefore, no statistical significant change in FS in group 4 patients in the early and late postoperative evaluation

<table>
<thead>
<tr>
<th>hed 60 days</th>
<th>FS preop (%)</th>
<th>FS 10 days (%)</th>
<th>FS 60 days (%)</th>
<th>Mediation at 10 days</th>
<th>Mediation at 60 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5</td>
<td>143</td>
<td>28.2</td>
<td>27.5</td>
<td>30.0</td>
<td>G</td>
</tr>
<tr>
<td>5.7</td>
<td>118</td>
<td>34.1</td>
<td>40.2</td>
<td>40.2</td>
<td>GDV</td>
</tr>
<tr>
<td>6.3</td>
<td>128</td>
<td>36.1</td>
<td>43.5</td>
<td>33.1</td>
<td>GDV</td>
</tr>
<tr>
<td>7.0</td>
<td>130</td>
<td>30.8</td>
<td>33.1</td>
<td>39.7</td>
<td>GDV</td>
</tr>
<tr>
<td>8.8</td>
<td>170</td>
<td>35.0</td>
<td>27.3</td>
<td>26.2</td>
<td>GDV</td>
</tr>
<tr>
<td>8.0</td>
<td>136</td>
<td>41.0</td>
<td>32</td>
<td>42.8</td>
<td>GDV</td>
</tr>
<tr>
<td>7.6</td>
<td>139</td>
<td>34.6</td>
<td>34.5</td>
<td>38.1</td>
<td>GDV</td>
</tr>
<tr>
<td>1.8</td>
<td>17</td>
<td>3.9</td>
<td>6.6</td>
<td>6.1</td>
<td>NS</td>
</tr>
<tr>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Discussion

Clinicians caring for patients with tricuspid atresia are frequently faced with therapeutic dilemmas. Should patients who are limited by cyanosis and who fulfill criteria for a low-risk Fontan procedure be offered a shunt or a Fontan? Should an elective Fontan procedure be performed in suitable patients who are minimally symptomatic?

Left ventricular hypertrophy and dysfunction are known to compromise long-term survival and symptomatic status in tricuspid atresia as well as to be risk factors for mortality and morbidity after a Fontan operation. Several previous studies of ventricular mass and contractility in groups of patients after palliation and after a Fontan procedure have been reported. However, the relevance of the results is uncertain because these studies used indexes of pump function that are themselves influenced by the loading conditions of the heart. In our previous study, we used a load-independent index and demonstrated impairment of contractility in tricuspid atresia before and after a Fontan procedure. From this cross-sectional study, we were unable to determine whether the documented changes were reversible with relief of chronic volume overload and cyanosis. We have now investigated prospectively the effect of the Fontan operation on left ventricular performance before and after surgery in the same patients. These results have been related to changes in size and function seen in patients remaining palliated and in patients retaining their Fontan status during the same period. Our results indicate that a successful Fontan repair results in rapid reduction of left ventricular size, which is followed by regression of hypertrophy so that a normal thickness-to-size ratio can be achieved. Operating at these more favorable dimensions and loading conditions results in early increase in contractility, which improves further in medium-term follow-up.

Dimensions

Increase in preload leads to enhanced ventricular performance and ventricular dilatation in a variety of clinical and experimental situations. However, it is well known that despite such adaptation, left ventricular failure develops when volume load is sufficiently severe and protracted. This is precisely the situation imposed on the heart by an arterial systemic-to-pulmonary shunt of sufficient size to provide acceptable relief of cyanosis in patients with tricuspid atresia. A resting arterial oxygen saturation of 85% requires a pulmonary to systemic flow ratio of more than 1.5:1 and, therefore, necessitates a minimum volume load to the left ventricle of approximately 250% of normal.
Palliated patients in our own and previous studies have greatly increased left ventricular end-diastolic dimensions when compared with normal. During the 3-year follow-up in this study, there was a further increase in dimension in six of eight patients. Progressive dilatation is a major feature of patients left palliated for a long time. Dick and associates\(^{19}\) reported the clinical course of 101 patients with tricuspid atresia as a gradual attrition due to congestive heart failure that developed in the middle of the second decade, with only very few survivors beyond the third decade.

Our results confirm those of Nakae et al,\(^{12}\) who reported a significant decrease of the left ventricular end-diastolic dimension in six patients after a Fontan procedure. Similar observations have been made after complete relief of left ventricular volume overload in adults with aortic regurgitation or mitral regurgitation, in children after ventricular septal defect closure, and in experimental conditions with aortocaval fistulae.\(^{30–33}\) In our patients, left ventricular dimensions rapidly decreased after Fontan repair to reach a new steady state in most by 10 days. Studies in the post-Fontan group show that this improvement is maintained over a longer period provided that no adverse factors, such as arrhythmia, are present.

Interestingly, the early reduction in size after the Fontan procedure was insufficient to reach levels normal for body surface area. However, with time, values showed a tendency to normalize as the patient’s body surface area increased. When evaluated at least 6 months after repair as in groups 2 and 3, 10 of 25 patients had left ventricular dimensions that were within normal range for their body surface area. Of special interest are the patients of group 4 because they are more representative for current medical and surgical management (less palliative procedures, Fontan operation at younger age): in the early postoper-
end-systolic stress and contractility.

The palliated patients in our study showed myocardial hypertrophy that was not inappropriately high for the cavity size of the ventricle, a situation comparable to that observed in other situations with chronic volume overload. Also, when the preload stress was removed by the Fontan operation, the ventricular thickness gradually decreased to values appropriate for the reduced dimensions.

The rate of decrease in cavity size and wall thickness after the Fontan operation were very different, with reduction of thickness taking much longer than reduction in size. As a result, the ventricles were inappropriately thick for their dimensions in the early postoperative period. This may have implications for the diastolic properties of the left ventricle in the acute postoperative period and requires further study.

**Contractility**

The major changes in dimension and thickness of the left ventricle that follow a Fontan procedure make evaluation of ventricular systolic function with load-dependent indices difficult. When ventricular dimension and wall stress are increased, ejection fraction (EF) and FS underestimate contractility. Furthermore, when dimensions alter during the study period, EF and FS may fail to reflect major changes in contractility.

Sanders et al investigated 11 patients before and after a Fontan procedure with angiocardiography. The EF remained normal in 10 patients and decreased in one, with no overall change for the group. Using radionuclide angiography, Hurwitz et al showed no significant change in mean EF during the early postoperative period; however, at restudy 2 years after surgery, the EF had increased significantly to be within the normal range in all six patients reported. Our own results using a load-dependent index confirm these findings with no significant change of the FS in the early postoperative phase after a Fontan procedure. However, with the gross changes in loading conditions, it would be inappropriate to conclude there was no change in contractility. We, therefore, also made comparisons of the relation of VCFc to ESSM as Colan et al has advocated to produce an index relatively independent of loading conditions but sensitive to altered inotropic state. This relation revealed that there was a significant improvement in contractility by 6 months after a Fontan procedure. It is encouraging to note that the contractility improved further in the medium-term follow-up as has also been shown for patients with aortic regurgitation and a moderate degree of preoperative left ventricular dysfunction. No improvement occurred in the single patient who survived a Fontan repair but had profoundly decreased contractility at initial evaluation. Despite medical therapy, she died in congestive heart failure, suggesting that as in aortic regurgitation, there may be a “point of no return.” We could not, however, evaluate this systematically because the selection criteria for the Fontan operation precluded surgery in patients with left ventricular dysfunction.

**Limitations of the Study**

The limitations of the VCFc-ESSM method have previously been discussed in detail. The assumptions of the model include that the short-axis dimensions are representative for ventricular size and global left ventricular function. As the ventricle in tricuspid atresia is more spherical than normal, this is likely to be the case. All patients were screened for regional wall motion abnormalities to accept the

**FIGURE 5.** Plots of endocardial rate-corrected circumferential fiber shortening (VCFc) as a function of meridional end-systolic stress (ESSM) for groups 1, 2, and 3. Normal values ± 2 SD from Colan et al. Changes parallel to the mean regression line reflect altered loading conditions; changes perpendicular to the mean regression line reflect altered contractility.
M-mode echocardiogram as representative for the global ventricular function. At initial evaluation in
1985, five patients of the post-Fontan group had mild
septal motion abnormalities. We had to exclude one
of these patients because the septal dyskinesia in the
1988 evaluation had increased, although overall left
ventricular function appeared well preserved; the
other four patients showed subsequent improvement
and were, therefore, included. No other regional
dyskinesia was observed in the other groups.

The ESSM model assumes the ventricular cham-
ber to be thin walled. Although all patients had some
degree of hypertrophy when the ventricular thickness
was related to their BSA, the ventricular wall appeared
to be appropriate or even too thin when related to
the ventricular size.

We could not determine the relation between
preoperative ventricular function and long-term
improvement after the Fontan operation over a wide
spectrum of left ventricular function in patients with
tricuspid atresia because poor ventricular function
precluded acceptance for Fontan. The data from this
study relate to a relatively small number of patients
selected by clinical practice and should not be extrap-
olated to all patients with tricuspid atresia.

Four patients died during the study interval, two at
the time of the Fontan operation. This serves to
remind clinicians that the Fontan procedure can still
not be performed with the predictably low risk of a
systemic-to-pulmonary shunt. Interestingly, there was
a relation between age and decreased contractile
function in palliated patients; we could not attempt
to relate age at surgery to change in postoperative
ventricular function.

Conclusion
This prospective study has examined the effect of
palliation and Fontan operation on ventricular size
and function in patients with tricuspid atresia. Abnor-
mal size and contractile function is present in most
patients with palliation alone. A successful Fontan
operation can significantly improve these abnormal-
ities and ventricular contractility may continue to
improve, at least in the medium term. Because left
ventricular dysfunction is the most important deter-
minant of long-term survival, these findings suggest
that a Fontan operation may provide a beneficial
long-term investment and argue in favor of such a
repair, even in mildly symptomatic patients who
fulfill the requirements for a low-risk operation.

References
1. Lacorte MA, Dick M, Scheer G, Lafarge CG, Fyler DC: Left
ventricular function in tricuspid atresia: Angiographic analyses
in 28 patients. Circulation 1975;52:996–1000
2. Sauer U, Mocellin R: Angiocardiographic left ventricular
volume determination in tricuspid atresia: Comparison of patients
with and without palliative surgery. Herz 1979;
4:248–255
ventricular function in cyanotic congenital heart disease. Am J
Cardiol 1980;45:1231–1236
4. Nishioka K, Kamia T, Ueda T, Hayashidera T, Mori C,
Konishi Y, Tatsuka N, Jarmakani JM: Left ventricular volume
characteristics in children with tricuspid atresia before and
5. Gibson DG, Traill TA, Brown DJ: Abnormal ventricular
function in patients with univentricular heart. Herz 1979;
4:226–231
evaluation of the Fontan procedure by radionuclide
angiography. Am Heart J 1982;104:785–793
7. Sanders SP, Wright GB, Keane JF, Norwood WI, Castaneda
WI: Clinical and hemodynamic results of the Fontan operation
for tricuspid atresia. Am J Cardiol 1982;49:1733–1740
8. Peterson RJ, Franch RH, Fajman WA, Jennings JG, Jones
RH: Noninvasive determination of exercise cardiac function
following Fontan operation. J Thorac Cardiovasc Surg 1984;
88:263–272
assessment of the Fontan operation: Combined M-mode,
two-dimensional and Doppler echocardiographic studies. J
Am Coll Cardiol 1984;4:756–764
10. Baker EJ, Jones ODH, Joseph MC, Maisey MN, Tynan MJ:
Radionuclide measurement of left ventricular ejection fraction
in tricuspid atresia. Br Heart J 1984;52:572–574
assessment of ventricular contraction at rest and during exer-
cise following the Fontan procedure for either tricuspid atresia
or single ventricle. Am J Cardiol 1985;55:1127–1132
Y, Ishihara K, Hashimoto H, Koyanagi H, Kanaya M, Nakaza-
wa M, Takao A: Assessment of left ventricular function
before and after Fontan’s operation for ‘the correction of
tricuspid atresia: Changes in left ventricular function deter-
dined by left ventricular volume change. Heart Vessels
1985;1:83–88
13. Colan SD, Borow KM, Neumann A: Left ventricular end-
diastolic wall stress-velocity of fiber shortening relation: A
load-independent index of myocardial contractility. J Am Coll
Cardiol 1984;4:715–724
14. Graham TP Jr, Franklin RCG, Wyse RKH, Gooch V, Dean-
field JE: Left ventricular wall stress and contractile function
in childhood: Normal values and comparison of Fontan versus
palliation only in patients with tricuspid atresia. Circulation
1986;74(suppl):1:61–1:69
aortic pressure using the oscillometric method for analyzing
systemic artery pulsatile flow: Comparative study of indirect
systolic, diastolic, and mean brachial artery pressure with
simultaneous direct ascending aortic pressure measurements.
Am Heart J 1982;103:879–886
of hypertrophy in the human left ventricle. J Clin Invest
1975;56:56–64
17. Gutegess HP, Paquet M, Duff DF, McNamara DG: Evaluation
of left ventricular size and function by echocardiography.
Circulation 1977;56:457–462
18. Lester LA, Sodt PC, Hutcheon N, Arcilla RA: M-mode
echocardiography in normal children and adolescents: Some
new perspectives. Pediatr Cardiol 1987;8:27–33
19. Dick M, Fyler DC, Nadas AS: Tricuspid atresia: Clinical
course in 101 patients. Am J Cardiol 1975;36:327–337
20. Graham TP, Friesinger GC: Complex cyanotic congenital
heart disease, in Roberts WC (ed): Adult Congenital Heart
H: Selection criteria for Fontan’s procedure, in Anderson RH,
Shinebourne EA (eds): Paediatric Cardiology 1977. Edinburgh,
Churchill Livingstone, 1978, pp 559–566
22. Kirklin JK, Blackstone EH, Kirklin JW, Pacifico AD, Bargeron
LM Jr: The Fontan operation: Ventricular hypertrophy, age,
and date of operation as risk factors. J Thorac Cardiovasc Surg
1986;92:1049–1064


**Key Words** • Fontan procedure • contractility • volume loading...
Impact of Fontan operation on left ventricular size and contractility in tricuspid atresia.
M H Gewillig, U R Lundström, J E Deanfield, C Bull, R C Franklin, T P Graham, Jr and R K Wyse

Circulation. 1990;81:118-127
doi: 10.1161/01.CIR.81.1.118

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1990 American Heart Association, Inc. All rights reserved.
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:
http://circ.ahajournals.org/content/81/1/118

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/