Prognosis of Surgically Corrected Coarctation of the Aorta

A 20-Year Postoperative Appraisal

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SUMMARY
A long-term retrospective analysis of 248 patients, 11–25 years after surgical correction of coarctation of the aorta, revealed a high incidence of premature cardiovascular disease. Twelve percent of patients with follow-up have died. It is suggested that premature death in patients with adequate surgical repair may be related to the duration of preoperative hypertension. Fifty-nine patients were evaluated on a standard hospital protocol. Seventy-eight percent had evidence of cardiovascular disease and over 40% had no change or had increased blood pressure over the preoperative value. These data emphasize the importance of early diagnosis and treatment for patients with coarctation of the aorta as well as the need for close postoperative follow-up.

Additional Indexing Words: Congenital heart disease, Hypertension, Sudden death

CORRECTIVE surgery for coarctation of the aorta has been practiced with success since 1945. The immediate and short-term effects of surgery have been the subject of previous studies, which demonstrated clinical improvement and reversal of blood pressure abnormalities in most patients.

However, the long-term cardiovascular status of patients with surgically corrected coarctation of the aorta is not known. Theoretically, prolonged preoperative hypertension may have adverse effects on the cardiovascular system despite adequate surgical intervention. This study investigates the long-term condition of 248 patients, 11–25 years after surgical correction of coarctation of the aorta.

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Laboratory evaluation included electrocardiogram (ECG), exercise ECG, vectorcardiogram (VCG), chest radiograph, phonocardiogram, intravenous pyelogram, serum electrolytes, cholesterol, triglycerides, complete blood count, urinalysis, and creatinine clearance.

Individual variables of the study were examined by quantitative and qualitative statistics, including chi-square tests of independence and Student's t test. The possible relationships between variables were also examined by regression and covariance analysis where applicable.

Results

Current information was obtained (fig. 1) regarding the health of 194 of the 248 patients (78%). One hundred seventy-one of the 194 are known survivors, including the 59 subjects having a 3-day hospital evaluation. Twenty-four of the 194 patients have died; 54 other patients are lost to follow-up (22%).

The youngest patient in the study group at the time of surgery was 2½ years and the oldest 40 years (fig. 1); mean age at operation was 20.0 years. The period of follow-up ranged from 11 to 25 years.

Nonsurvivors

Twenty-three (12%) of 194 patients with follow-up died of cardiovascular disease and are summarized in table 1. One other patient died in an automobile collision. Mean age at death was 35.1 years. Survival after surgery ranged from 6 months to 16.2 years (mean 8.8 years). Sixty-four percent of the premature cardiovascular deaths occurred in patients having surgery after 25 years of age, although only 33% of the study population had surgery at these ages.

Mean age at operation was 32.9 years in nonsurvivors without intracardiac defects, compared with 19.5 years in survivors. Therefore, nonsurvivors experienced significantly longer periods of preoperative hypertension ($P < 0.001$).

Complete postmortem information was available in eight of the 22 nonsurvivors (table 1). Death was sudden (in less than 1 hour) and unexpected in 11 of the 14 patients without autopsy. Ruptured major arterial vessel was probable in four of these patients and myocardial infarction in two others.

There was no significant difference in the magnitude of preoperative hypertension between survivors (mean 164/92) and nonsurvivors (mean 167/94), nor in the severity of preoperative symptoms.

Survivors with Examination in the Hospital

Fifty-nine patients were studied in the hospital on a standard protocol (fig. 2). Age at the time of examination ranged from 19 to 58 years (mean 40.6 years). Mean age at operation was 22.0 years and average follow-up period was 18.4 years. Fifty-three of the 59 patients were asymptomatic; five had angina pectoris and one, a previous myocardial infarction.

Twenty-two of the 59 patients (37%) had systemic hypertension, including six subjects with systolic hypertension, five with diastolic hypertension, and 11 others with both systolic and diastolic blood pressure elevations (figs. 3 and 4). Sixteen of the 22 hypertensive patients had systolic blood
Table 1

Information on 22 Deaths Related to Cardiovascular Disease

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age at operation (yrs)</th>
<th>Age at death (yrs)</th>
<th>Clinical information</th>
<th>Autopsy findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.3</td>
<td>17.4</td>
<td>CHF after surgery for recurrent coarctation</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>3.9</td>
<td>5.3</td>
<td>CHF</td>
<td>EFE of LV and mitral regurgitation</td>
</tr>
<tr>
<td>3</td>
<td>5.9</td>
<td>10.8</td>
<td>CHF</td>
<td>Insufficient and stenotic mitral valve</td>
</tr>
<tr>
<td>4</td>
<td>12.2</td>
<td>23.0</td>
<td>Chest pain; died 10 min later; postmortem X-ray suggested hemothorax</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>15.0</td>
<td>28.0</td>
<td>Severe AI and CHF; secondary to SBE</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>17.8</td>
<td>23.1</td>
<td>Severe chest pain; died 45 min later</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>18.0</td>
<td>18.5</td>
<td>Sudden death 2½ wks after ligation aortic aneurysm</td>
<td>Ruptured “false” aortic aneurysm at site of anastomosis</td>
</tr>
<tr>
<td>8</td>
<td>20.7</td>
<td>29.7</td>
<td>Chest pain and hypotension postop resection aortic aneurysm; coarctation resection 9 yrs previously</td>
<td>Ruptured dissecting aneurysm ascending aorta</td>
</tr>
<tr>
<td>9</td>
<td>26.4</td>
<td>29.5</td>
<td>Died suddenly with severe chest pain</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>26.8</td>
<td>34.1</td>
<td>Sudden death</td>
<td>None</td>
</tr>
<tr>
<td>11</td>
<td>27.7</td>
<td>40.8</td>
<td>Acute CHF and pulmonary edema</td>
<td>None</td>
</tr>
<tr>
<td>12</td>
<td>28.3</td>
<td>36.5</td>
<td>Suggested cerebral hemorrhage</td>
<td>None</td>
</tr>
<tr>
<td>13</td>
<td>30.8</td>
<td>39.2</td>
<td>Died suddenly with chest pain</td>
<td>None</td>
</tr>
<tr>
<td>14</td>
<td>31.1</td>
<td>44.0</td>
<td>Suggested subarachnoid hemorrhage</td>
<td>None</td>
</tr>
<tr>
<td>15</td>
<td>31.9</td>
<td>48.1</td>
<td>5-mo history CHF; valvular aortic stenosis</td>
<td>None</td>
</tr>
<tr>
<td>16</td>
<td>35.3</td>
<td>38.6</td>
<td>Died suddenly on train</td>
<td>None</td>
</tr>
<tr>
<td>17</td>
<td>37.7</td>
<td>47.1</td>
<td>Suggested subarachnoid hemorrhage</td>
<td>Ruptured aneurysm internal carotid artery</td>
</tr>
<tr>
<td>18</td>
<td>41.5</td>
<td>52.7</td>
<td>Pulmonary edema; angina pectoris</td>
<td>Severe atherosclerosis of LAD; calcific aortic stenosis</td>
</tr>
<tr>
<td>19</td>
<td>42.6</td>
<td>47.3</td>
<td>Died suddenly; previous myocardial infarction</td>
<td>None</td>
</tr>
<tr>
<td>20</td>
<td>45.2</td>
<td>51.4</td>
<td>Lobar pneumonia; CHF</td>
<td>EFE of LV; aortic insufficiency and mitral stenosis, probably rheumatic; lobar pneumonia</td>
</tr>
<tr>
<td>21</td>
<td>46.3</td>
<td>50.8</td>
<td>Died in sleep; history angina pectoris</td>
<td>None</td>
</tr>
<tr>
<td>22</td>
<td>48.9</td>
<td>57.1</td>
<td>CHF and atrial fibrillation</td>
<td>Moderate atherosclerosis of LAD</td>
</tr>
</tbody>
</table>

Abbreviations: SBE = subacute bacterial endocarditis; EFE = endocardial fibroelastosis.

pressures over 160 mmHg and/or diastolic exceeding 95 mmHg. These figures exclude six patients with aortic insufficiency and systolic hypertension. Eight patients with hypertension had left ventricular hypertrophy (LVH) on ECG or cardiac enlargement on chest radiograph.

Only four of the 17 patients with systolic hypertension had suspected residual coarctation, with brachial blood pressure exceeding popliteal blood pressure by more than 10 mmHg. Therefore, 18 of 59 patients (31%) had unexplained systemic hypertension even after subjects with aortic insufficiency and possible residual coarctation are excluded.

Simultaneous popliteal blood pressure exceeded brachial blood pressure in 20 subjects (34%). In 29 patients (66%) brachial pressure was equal to or greater than the popliteal.
No patient had abnormalities in serum electrolytes, creatinine clearance, or intravenous pyelogram. Eye examination showed minimal arteriolar changes in 19 of 59 patients (32%). Five patients had elevations in serum cholesterol and/or triglycerides compatible with hyperlipoproteinemia, including three with hypertension and two with angina pectoris.

Twenty-five of the 59 patients (42%) had no change or an increase in systolic blood pressure at long-term examination compared with the preoperative value (fig. 5). Residual coarctation could not be excluded in 10 patients. Twenty-seven of the 59 patients (46%) had no change or an increase in diastolic blood pressure postoperatively.

Early postoperative blood pressure at hospital discharge was compared with preoperative and late postoperative values in 57 patients. A significant relationship existed between systolic and diastolic preoperative blood pressure and short-term postoperative blood pressure ($P < 0.01$). Systolic and/or diastolic blood pressure had returned to normal by the time of hospital discharge in only 30% of patients.

The relationship between early and late postoperative blood pressure is shown in figure 6. The higher the systolic blood pressure at hospital discharge, the greater the blood pressure at late follow-up ($P < 0.001$). Although this result demonstrates a positive relationship between early and late postoperative blood pressure, accurate predictions of ultimate blood pressure response cannot be made since the correlation coefficient is relatively low ($r = 0.51$).

Patients with systolic hypertension at late follow-up examination had significantly higher blood pressures on discharge from the hospital compared with nonhypertensives ($P < 0.001$). Therefore, subjects with hypertension in the immediate postoperative period are likely to have persistent hypertension. Mean age at operation for patients with late postoperative systolic hypertension was earlier (mean 17.0 years) than for nonhypertensives (mean 24.9 years).

Auscultatory and phonocardiographic findings are summarized in table 2. Forty-one of the 59 patients (70%) had either decrescendo diastolic blowing murmurs of aortic insufficiency or aortic

Figure 3

Late postoperative systolic brachial blood pressures in 59 patients.
systolic ejection murmurs associated with systolic ejection clicks. Nine of the 12 patients with aortic insufficiency had either widened pulse pressure, LVH on ECG, or radiographic evidence of cardiac enlargement.

Fifty-six ECG and/or VCG abnormalities were present in 38 patients (table 3). Conduction system defects occurred in 18 patients, ranging in age from 25.0 to 55.4 years (mean 43.3 years). Three of the 10 patients with left-axis deviation had LVH on ECG. The ECG was entirely normal in only 14 patients. In one half of the 18 patients with ECG conduction defects, conduction abnormalities were present preoperatively.

Exercise ECGs were positive in eight of the 54 patients (15%) with adequate testing. Three of the eight patients with abnormal exercise ECGs had normal standard ECGs.

Overall morbidity in the hospital follow-up group was determined by tabulating patients by their most significant cardiovascular abnormality (table 4). Considered in this context, 46 of 59 patients (78%) had evidence of cardiovascular disease. Mean age of these patients was 40.0 years.

Comparison of patients having operation before 15 years of age (19 patients) and those with surgery after 15 years of age (40 patients) indicated no difference in the incidence of late postoperative cardiovascular abnormalities.

Survivors with Follow-up from Physicians Outside the Hospital

Thirteen of the 112 survivors without hospital follow-up had significant cardiovascular disease (12%). The age distribution of these patients was 18 to 57 years (mean 38.4 years). This group includes four patients with severe hypertension secondary to residual coarctation, two patients with significant aortic insufficiency, two with previous myocardial infarctions, and one each with severe mitral regurgitation secondary to bacterial endocarditis, angina pectoris, aortic aneurysm, and ventricular septal defect with Eisenmenger’s reaction.

Discussion

There was a significant (12%) incidence of premature death in the study population. Cardiovascular disease was the primary cause of death in 21 patients and a contributing cause in another. All
22 deaths occurred prior to 58 years of age, with an average age of only 34 years.

Since a significant number of the 248 study patients were lost to follow-up (54 patients), the precise incidence of premature cardiovascular deaths in this population could not be determined. However, many of those patients lost to follow-up are probably dead and the reported mortality figure is likely a conservative estimate.

Death in this study was most commonly due to a ruptured major arterial vessel; aortic or cerebral rupture was implicated in one third of our cases.

Table 2
Postoperative Auscultatory and Phonocardiographic Findings in 59 Patients

<table>
<thead>
<tr>
<th>Auscultatory/phonocardiographic abnormality</th>
<th>Pt (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreasing diastolic murmur (aortic insufficiency)</td>
<td>12</td>
</tr>
<tr>
<td>Aortic systolic ejection murmur and ejection click</td>
<td>29</td>
</tr>
<tr>
<td>Aortic ejection murmur only</td>
<td>14</td>
</tr>
<tr>
<td>Ejection click only</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
</tr>
</tbody>
</table>

Aneurysms of the Circle of Willis occur in 10% of patients with coarctation of the aorta and may have been the underlying cause of ruptured cerebral vessels in many of these patients.

Table 3
Postoperative ECG and VCG Abnormalities in 59 Patients

<table>
<thead>
<tr>
<th>ECG/VCG abnormality</th>
<th>Pt (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left anterior hemiblock</td>
<td>10</td>
</tr>
<tr>
<td>Left posterior hemiblock</td>
<td>2</td>
</tr>
<tr>
<td>Bifascicular block</td>
<td>1</td>
</tr>
<tr>
<td>Left bundle-branch block</td>
<td>3</td>
</tr>
<tr>
<td>Right bundle-branch block</td>
<td>1</td>
</tr>
<tr>
<td>Second-degree A-V block</td>
<td>1</td>
</tr>
<tr>
<td>First-degree A-V block</td>
<td>3</td>
</tr>
<tr>
<td>Intraventricular conduction defect (unspecified)</td>
<td>1</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular bigeminy</td>
<td>11</td>
</tr>
<tr>
<td>Nonspecific ST-T changes</td>
<td>4</td>
</tr>
<tr>
<td>Old myocardial infarction</td>
<td>2</td>
</tr>
<tr>
<td>LVH</td>
<td>8</td>
</tr>
<tr>
<td>Positive exercise ECG</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
</tr>
</tbody>
</table>
Postmortem studies\textsuperscript{9-11} indicate that mean survival with unoperated coarctation of the aorta is 35 years. Death was usually due to aortic rupture, bacterial endocarditis on the aortic valve, rupture of an intracranial aneurysm or cardiac failure. It appears that the longevity of nonsurvivors in this study does not differ significantly from unoperated cases reported in the literature.\textsuperscript{9-11} However, these are not strictly comparable patient populations and no definite conclusions can be made.

Our data suggest that the duration of preoperative hypertension is an important factor influencing late survival following repair of coarctation of the aorta. Patients who died prematurely of cardiovascular disease experienced longer periods of preoperative hypertension. However, the finding that patients who had systolic hypertension at long-term examination experienced shorter periods of preoperative hypertension (17 years compared with 24.9 years for normotensive patients) was unexpected.

Our data substantiate unexplained late postoperative hypertension in about one third of patients. Possible explanations include: (1) residual limitation of the capacity and distensibility of the proximal aorta;\textsuperscript{12} (2) disturbance of the renin-angiotensin system;\textsuperscript{13} (3) associated hyperlipoproteinemia;\textsuperscript{14} or (4) a process unrelated to the coarctation such as "essential" hypertension.

Previous studies on patients with coarctation of the aorta\textsuperscript{2-4,15} document the short-term effects of surgery on blood pressure. March and associates\textsuperscript{4} found the blood pressure to be normal at hospital discharge in only 33\% of patients, although 74\% had normal blood pressures 1–9 years after surgery. These figures in which blood pressure at hospital discharge was normal in 30\% of patients correspond

\begin{table}[ht]
\centering
\begin{tabular}{ll}
\hline
Cardiovascular abnormality & Pt (no.) \\
\hline
Hypertension & 20 \\
Aortic insufficiency & 11 \\
Calciﬁc aortic stenosis & 1 \\
ECG conduction defects & 10 \\
Angina pectoris & 4 \\
Total & 46 \\
\hline
\end{tabular}
\caption{Postoperative Cardiovascular Disease in 59 Patients}
\end{table}
with ours; 11–25 years after surgery blood pressure had returned to normal in 63% of patients.

Although systemic hypertension theoretically predisposes to coronary artery disease, myocardial infarction is not a major cause of death in patients with unoperated coarctation of the aorta. It is possible that adequate coronary blood flow is maintained by collateral circulation or increased coronary artery lumen area. Twelve of the 195 patients (6%) for which follow-up was available had clinical evidence of coronary artery disease. The age distribution of these patients was 31.9–58.1 years (mean 48.7 years).

Evidence of conduction defects was present in about one third of the hospital study group. These defects appeared sometimes before and in others after surgery, and probably are secondary to chronic left ventricular pressure overload or myocardial ischemia.

The association of bicuspid aortic valves with coarctation of the aorta is well recognized; the incidence varies from 25% to 85% in pathologic surveys and appears to be about 70% in this study. However, only six of the 195 study patients (3%) with follow-up had significant aortic valve disease. This low incidence of valvular disease may be explained by the relative youth of the study group; only 13% were over 50 years of age. Bacterial endocarditis was also rare with only two document
ed instances (one on the aortic valve and one on the mitral).

Recommendations regarding the optimum age for elective surgery of coarctation of the aorta vary from 4 to 12 years. Our data suggests that prolonged preoperative hypertension with surgery after 25 years of age is associated with an increased risk of premature cardiovascular death. However, there is no evidence that the timing of surgery and adolescence influences the incidence of postoperative cardiovascular disease.

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