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Posttransplant Recoarctation of the Aorta: A Twelve Year Experience

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Objectives. This study was undertaken to investigate the incidence of posttransplant recoarctation of the aorta, delineate the mode of presentation, identify risk factors that predict recoarctation and examine the results of intervention for posttransplant recoarctation.

Background. Patients with aortic arch hypoplasia require extended arch reconstruction at transplant, with an inherent possibility of subsequent recoarctation of the aorta.

Methods. This was a retrospective review of all children (age <18 years) who underwent cardiac transplantation over a 10-year period. Collected data included pretransplant diagnosis, details of the transplant procedure and posttransplant data including development of recoarctation of the aorta, interventions for recoarctation and the most recent follow-up assessment of the aortic arch.

Results. Two hundred eighty-eight transplants were performed on 279 children (follow-up = 1,075 patient-years; range 0 to 133 months, median 43.7). Thirty-two of 152 patients (21%) who underwent extended aortic arch reconstruction subsequently developed recoarctation. All but one patient developed recoarctation within 2 years after transplant; 87% were hypertensive at presentation. Of 30 patients who underwent intervention for recoarctation (balloon angioplasty [n = 26] and surgical repair of recoarctation [n = 4]), 26 (87%) have remained recurrence-free (follow-up = 133 patient-years; range 8 to 106 months, median 47).

Conclusions. The high frequency of recoarctation after cardiac transplantation with extended aortic arch reconstruction mandates serial echocardiographic evaluation of the aortic arch. Patients typically present with systemic hypertension within the first two years after transplantation. Balloon angioplasty is a safe, effective and durable method of treatment.

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Severe congenital structural defects of the left side of the heart are major indications for referral to cardiac transplantation in infancy. This group of defects often includes a hypoplastic aortic arch and is typified by hypoplastic left heart syndrome (HLHS). Studies have shown that in HLHS, ductal tissue frequently extends circumferentially from the ductal orifice into the aortic wall (1,2). Whereas transplant surgery in infants with arch hypoplasia necessarily includes ductal tissue resection and extended aortic arch reconstruction beyond the ductus arteriosus (Fig. 1), this may not be adequate to prevent subsequent posttransplant recoarctation (3). This condition has been addressed anecdotally, but has not been studied systematically in a large population of transplant recipients (4,5).

Our objectives were to study the incidence and mode of presentation of posttransplant recoarctation of the aorta, identify risk factors that predict recoarctation and examine the results of intervention for posttransplant recoarctation.

Methods

The records of all cardiac allotransplants performed on children younger than age 18 years over a 10-year period (from November 1985 to November 1995) at Loma Linda University Children's Hospital and Medical Center were retrospectively reviewed in August 1997. Recorded pre-transplant variables included year of transplant, gender, age at transplant, cardiac diagnosis and indication for transplantation, previous surgery for coarctation and stent implantation in the ductus arteriosus. Transplant operation reports were reviewed for the identity of the surgeon, the need for extended aortic arch reconstruction, donor and recipient weight and donor ischemic time. Patient
charts were reviewed for the date, type and results of the most recent diagnostic test that visualized the aortic arch. Autopsy reports were reviewed for references to recoarctation. For patients who had undergone repeat transplantation, the surgeon’s description of the aortic arch at repeat transplantation was used as the most recent diagnostic test for the first transplant.

For all patients who developed posttransplant recoarctation, the mode of presentation, date of diagnosis, indications for intervention, date of intervention, type (surgery or balloon angioplasty) and number of interventions, intraprocedure and postprocedure complications and duration of follow-up were noted. All aortic arch angiograms were reviewed to assess recoarctation anatomy prior to intervention.

Surgical technique. The techniques used for cardiac transplantation and extended aortic arch reconstruction were similar to those described previously (3); a continuous 7-0 polypropylene suture was used for aortic arch reconstruction. In the past year, the surgical technique has been modified to decrease the circulatory arrest time; thus, only the aortic and left atrial anastomoses are being performed under circulatory arrest.

Screening for posttransplant recoarctation. Recoarctation was defined as anatomic narrowing in the juxtaductal region of the thoracic aorta, with or without a significant pressure gradient across the area of narrowing. All patients who underwent transplantation were screened for recoarctation using clinical criteria including arm-leg blood pressure differentials. Echocardiographic surveillance including Doppler evaluation of the aortic arch was scheduled 1, 3, 6 and 12 months and then annually after transplant. In addition, echocardiography or cardiac catheterization, or both, were performed when indicated by clinical criteria.

Treatment of posttransplant recoarctation. Balloon angioplasty of recoarctation was performed using techniques similar to those previously described (6–9). Angioplasty catheter selection criteria were operator-dependent; five different operators performed balloon angioplasty over the 10-year study period. The procedure for surgical repair of posttransplant recoarctation consisted of resection followed by end-to-end repair of recoarctation.

Statistical methods. Because continuous variables were not normally distributed, nonparametric testing with the Mann-Whitney U test was performed. Discrete variables were analyzed using chi-square analysis. Analysis of variance was used wherever appropriate. Kaplan-Meier survival curves were used to determine freedom from recoarctation, and separately, to determine freedom from reintervention after the initial intervention for recoarctation. The equality of event-free survival (freedom from recoarctation) between HLHS and non-HLHS patients was compared using the log-rank test. Patients were censored at the date of first intervention for recoarctation (for those who have developed recoarctation), or at the date of the most recent study confirming absence of recoarctation (for those who have not developed recoarctation).

Results

Two hundred eighty-eight cardiac transplants were performed on 279 children during the study period, including 9 retransplants. The median duration of follow-up was 43.7 months (range 0 to 133), representing a total of 1,075 patient-years of follow-up. The pretransplant cardiac diagnosis was HLHS in 128 patients (44%), other structural heart defects in 108 patients (38%), cardiac tumors in 3 patients (1%) and cardiomyopathy in 49 patients (17%) including 9 retransplants.

Figure 1. Schematic diagram of extended aortic arch reconstruction as part of cardiac transplantation for aortic arch hypoplasia. **Left panel**, severe aortic arch hypoplasia extends up to the level of the insertion of the ductus arteriosus into the descending thoracic aorta. Cardiopulmonary bypass cannulas are in place and snares have been placed around the proximal ends of the aortic arch branches. **Right panel**, the donor atria are anastomosed to the posterior collar of recipient atria. An extended length of donor aorta is used to reconstruct the aortic arch; anastomotic suture lines are seen on the undersurface of the arch, extending beyond the level of the ductus arteriosus.
for coronary arteriopathy (n = 8) and early posttransplant graft failure (n = 1).

The most recent test available for the 197 children who are alive to date was catheterization in 165 and echocardiography in 32. Autopsy data were available for 74 of the 82 children who died; either the most recent cardiac catheterization (n = 6) or echocardiographic data (n = 2) were used for the remaining 8 patients.

Incidence and presentation. Posttransplant recoarctation occurred in 32 of 152 patients (21.1%) who underwent aortic arch reconstruction; there were no cases of posttransplant recoarctation among patients who did not require prior arch augmentation (0 of 136 patients, p < 0.0001). Of 32 patients with recoarctation, antemortem diagnosis was possible in 30 cases. Twenty-nine patients were diagnosed at less than 2 years after transplant; one patient first developed recoarctation 5 years after transplant (median time from transplant to diagnosis 8.7 months, range 0 to 60.8). Twenty-six of 30 patients (87%) exhibited systolic hypertension (systolic blood pressure greater than or equal to the 95th percentile for age and gender) within the 2 months before intervention (10). The remaining 4 children were asymptomatic and in these, recoarctation was first detected by surveillance echocardiograms (n = 3) or catheterization (n = 1).

Two patients were not diagnosed antemortem; recoarctation was found at autopsy. A 2-year-old child who underwent transplantation for HLHS was followed for respiratory symptoms (tachypnea and dyspnea attributed to reactive airways disease) until her death; severe recoarctation was found at autopsy. The second patient was an infant with interrupted aortic arch who underwent transplant surgery and did not wean off cardiopulmonary bypass; at autopsy, residual coarctation was found distal to the arch reconstruction. Undiagnosed recoarctation was probably a significant contributor to the demise of both children.

Risk factors. Of the 152 patients requiring arch reconstruction, the pretransplant diagnosis was HLHS in 128, 28 of whom (21.9%) developed recoarctation. The remaining 24 patients requiring arch reconstruction had structural heart defects other than HLHS (including double-outlet right ventricle with mitral atresia, unbalanced atrioventricular canal defects or other malformations); 4 of these patients (16.7%) developed recoarctation. The difference between recoarctation rates for the two diagnostic groups (HLHS vs. non-HLHS) was not statistically significant. Thus, the need for extended arch reconstruction predicted subsequent recoarctation regardless of specific pretransplant cardiac diagnosis. The Kaplan-Meier survival function showing freedom from recoarctation for all patients undergoing extended arch reconstruction is shown in Figure 2. Log-rank analysis revealed no differences between rates of freedom from recoarctation for patients with versus without HLHS (p = 0.57).

Patients who developed recoarctation were younger at the time of transplantation (median age at transplant 0.8 months, range 0.2 to 3.6) than those who were recoarctation-free (median age at transplant 1.7 months, range 0 to 216, p = 0.001). Reflecting this, recipient weight at transplantation was lower in the recoarctation (median 3.65 kg, range 2.1 to 5.5) than in the recoarctation-free (median 3.9 kg, range 2.1 to 48 kg; p = 0.03) group. Similarly, donor weight was lower in the recoarctation (median 6 kg, range 2.2 to 13) than in the recoarctation-free (median 7.4 kg, range 2.1 to 59 kg; p = 0.005) group. Other tested variables including pretransplant stent implantation in the ductus arteriosus, pretransplant surgery for coarctation, the diagnosis of interrupted aortic arch, ischemic time, year of transplant, identity of the surgeon and donor-recipient weight ratio were not found to be significant predictors of recoarctation.

Nature of posttransplant recoarctation. Aortic arch angiography before intervention revealed a discrete area of recoarctation in 29 of 30 patients. This area was distal to the origin of the left subclavian artery in 27 patients, and was proximal to the origin of the left subclavian artery in 2. One patient had long segment recoarctation. In a separate instance, there was an additional area of stenosis in the ascending aorta.

Intervention for posttransplant recoarctation. Thirty patients underwent 35 procedures; 4 patients required more than one intervention for recoarctation (one patient has required three interventions to date). Transcatheter balloon angioplasty was performed in 31 of 35 patients (89%). Surgery was

Figure 2. Kaplan-Meier curve showing freedom from intervention for recoarctation after cardiac transplantation with extended reconstruction of the aortic arch. Values are shown as mean ± 95% confidence limits (1.96SEM). Numbers above the x-axis represent the number of uncensored patients at each time point.
performed in 4 patients: 2 were diagnosed with recoarctation early (less than 2 months) after transplantation, one patient had obstruction at multiple levels including the ascending aorta and another patient had no arterial access.

Balloon angioplasty resulted in an immediate decrease in the median peak gradient (measured at catheterization) from 35 mm Hg (range 10 to 123) to 2 mm Hg (range 0 to 34; p < 0.0001). Median systolic blood pressure proximal to the recoarctation decreased from 124 mm Hg (range 80 to 156; p < 0.001) immediately after dilation. Median systolic blood pressure distal to the recoarctation increased from 90 mm Hg (range 42 to 148) before dilation to 103 mm Hg (range 90 to 137; p = 0.003) immediately after dilation. At the most recent follow-up study, median systolic blood pressure was 104 mm Hg (range 84 to 140) proximal to the recoarctation, and was 100 mm Hg (range 84 to 140) distal to the recoarctation. The median peak systolic pressure gradient across the site of recoarctation repair was 0 mm Hg (range 0 to 8).

One patient developed transient complete heart block after introduction of a wire into the left ventricle, requiring chest compressions and chemical resuscitation; the patient subsequently recovered uneventfully. Postangioplasty cineangiograms revealed intimal tears in two other patients. One of these patients subsequently underwent surgical repair for multilevel aortic obstruction; the other patient has shown no evidence of aortic luminal irregularity on follow-up angiography. There have been no cases of aortic aneurysms at the angioplasty site.

Patients have been followed for 53 ± 27 months (range 8.4 to 105.8) (total of 132.7 patient-years) since the initial intervention for recoarctation. Twenty-six of 30 children (87%) have remained recurrence-free; 4 children (13%) have required more than one procedure. One of these patients had recoarctation, which responded well to balloon angioplasty, and recurrent ascending aortic stenosis, which required two subsequent operations. The other three patients who required more than one intervention for recoarctation had all undergone balloon angioplasty, and developed recoarctation within 12 to 18 months after the initial intervention. Kaplan-Meier analysis of freedom from recoarctation after the initial intervention for posttransplant recoarctation of the aorta is shown in Figure 3.

Discussion

Substrate for posttransplant recoarctation. The initial operation for patients with aortic arch hypoplasia associated with a functionally single ventricle, either the Norwood operation or cardiac transplantation, includes aortic arch reconstruction extending beyond the level of the ductus arteriosus (3,11). In HLHS, ductal tissue extends into the thoracic aorta proximally and distally for variable distances, and may encircle the aorta completely; this aortic extension of ductal tissue may be as wide as the ductus itself (1,2). The surgical procedure of cardiac transplantation with arch reconstruction includes resection of the coarctation, removing as much ductal tissue as possible, leaving behind a small posterior rim of the aortic circumference to allow continuity of the aortic wall (3). However, the microscopic extension of ductal tissue into the aortic wall may not be evident to inspection, thus limiting its complete removal. In addition, the posterior remnant of the aortic wall may contain ductal tissue; contraction of ductal tissue and postoperative scarring of the aortic wall are probably the substrate for the development of posttransplant recoarctation. This condition has been addressed in a case report and in a posttransplant follow-up series but has not been systematically analyzed (4,5). In the current study, 20.3% of patients with aortic arch hypoplasia who underwent transplantation with extended aortic arch reconstruction developed recoarctation of the aorta. This is comparable to the 7% to 29% incidence of aortic arch obstruction following the Norwood operation reported from several institutions using the univentricular approach for palliation of HLHS (12–15). Recoarctation occurs more often after extended aortic arch reconstruction than after surgical repair (end-to-end anastomosis or left subclavian artery flap repair) of infantile coarctation; recurrence rates in the latter group have been reported at approximately 14% (16). The high incidence of recoarctation in patients who have undergone extended arch reconstruction emphasizes the need for methodical surveillance.
Diagnosis of posttransplant recoarctation. The diagnosis of posttransplant recoarctation poses several challenges. Patients in the current study were typically less than 2 years old at presentation; accurate blood pressure measurement is a logistic challenge in this age group. Femoral arterial stenosis or occlusion after previous cardiac catheterization or indwelling catheters may obscure the utility of arm-leg differentials in blood pressure. Besides, hypertension may be multifactorial in the setting of immunosuppressive medications and possible renal impairment; thus, the implications of elevated blood pressure may not be readily apparent. Untreated recoarctation of the aorta frequently leads to left ventricular hypertrophy, leading to an echocardiographic profile similar to that seen with allograft rejection. This may lead to more rigorous immunosuppression, with the attendant probability of exacerbating hypertension as an untoward effect. Careful, serial echocardiographic assessment of anastomotic sites is essential after pediatric cardiac transplantation, particularly after extended reconstruction of the aortic arch; at our institution, anastomotic sites are evaluated 1, 3, 6 and 12 months, and then annually after transplant. In addition, the protocol for transcatheter surveillance includes annual aortic arch angiography in all patients who have undergone extended arch reconstruction at transplant.

Treatment of posttransplant recoarctation. Balloon angioplasty has been performed to treat native coarctation of the aorta as well as recoarctation after a variety of initial procedures ranging from coarctation repair to the Norwood operation, with good immediate results (17–21). Fletcher et al. (17) reported a series of 102 patients who underwent angioplasty for native coarctation; 29% of patients either had inadequate relief of coarctation or subsequently developed recoarctation. A multicenter study comparing balloon angioplasty for native versus recurrent coarctation revealed an acute suboptimal outcome in 19% of 422 native coarctations, and in 25% of 548 recurrent coarctations (18). Yetman et al. (22) recently reported a series of 90 consecutive patients who underwent balloon angioplasty for aortic recoarctation after attempted surgical repair; previous surgical techniques included subclavian artery flap repair, end-to-end anastomosis and patch aortoplasty. Twenty-eight percent of patients with an optimal early result required reintervention at long-term follow-up; the presence of transverse arch hypoplasia detected at the time of angioplasty was associated with suboptimal long-term outcome. In the current study, initial treatment of recoarctation of the aorta consisted of extended aortic arch reconstruction at the time of transplantation. Thus, the subsequent development of coarctation in these patients is best classified as recoarctation rather than as new coarctation. We were unable to assess for transverse arch hypoplasia in this cohort because the procedure of transplantation with extended arch reconstruction modifies the contour of the aortic arch; in addition, only four patients required additional procedures on the aortic arch, thus making it difficult to identify risk factors for suboptimal outcome. The current study demonstrates the safety, efficacy and durability of balloon angioplasty in most cases of posttransplant recoarctation of the aorta. Our results compare favorably with published results of balloon angioplasty for native as well as recurrent coarctation of the aorta (17–19, 21, 22).

Limitations. The limitations of this study stem from its retrospective nature, which made it impossible to standardize the procedure of balloon angioplasty for recoarctation. However, extended and complete follow-up has been obtained in every patient in this large cohort. Of patients undergoing arch reconstruction, we were unable to identify those at risk for developing recoarctation. A prospective echocardiographic morphometric analysis may prove useful in assessing such risk factors.

Conclusions. Recoarctation of the aorta occurs often in children requiring cardiac transplantation with extended aortic arch reconstruction. Patients typically present with systemic hypertension within the first 2 years after transplantation. Careful, serial echocardiographic assessment of anastomotic sites is essential after pediatric cardiac transplantation, particularly following extended reconstruction of the aortic arch. Balloon angioplasty is a safe, effective and durable method of treatment.

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