

ORIGINAL CLINICAL SCIENCE

Outcomes after percutaneous coronary artery revascularization procedures for cardiac allograft vasculopathy in pediatric heart transplant recipients: A multi-institutional study



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KEYWORDS:

heart transplant;
pediatric;
cardiac;
allograft;
vasculopathy

BACKGROUND: Cardiac allograft vasculopathy is an important cause of long-term graft loss. In adults, percutaneous revascularization procedures (PRPs) have variable success with high restenosis rates and little impact on graft survival. Limited data exist in pediatric recipients of transplants.

METHODS: Data from the Pediatric Heart Transplant Study (PHTS) were used to explore associations between PRPs and outcomes after heart transplant in patients listed ≤ 18 years old who received a first heart transplant between 1993 and 2009.

RESULTS: Revascularization procedures were done in 28 of 3,156 (0.9%) patients; 13 patients had multiple PRPs giving a total of 51 PRPs performed across 15 centers. Mean recipient age at time of transplant was 7.7 ± 6.7 years; mean donor age was 15.9 ± 15.4 years. The mean time to first PRP was 5.7 ± 3.2 years. Vessels involved were left anterior descending artery (41%), right coronary artery (25%), circumflex artery (18%), other coronary branches/unknown (16%). PRPs consisted of 38 (75%) stent implantations and 13 (25%) balloon angioplasties with an overall procedural success rate of 73%. Freedom from graft loss after PRPs was 89%, 75%, and 61% at 1, 3, and 12 months. In addition, patients with transplants from donors >30 years old were found to have less freedom from the need for a revascularization procedure than patients with transplants from younger donors ($p < 0.0001$).

CONCLUSIONS: In this large pediatric heart transplant cohort, use of PRPs for cardiac allograft vasculopathy was rare, likely related to procedural feasibility of the interventions. Despite technically successful interventions, graft loss occurred in 39% within 1 year post-procedure; relisting for heart transplant should be considered.

J Heart Lung Transplant 2015;34:1163–1168

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7.0%, 32.3%, and 45.7% among adult recipients at 1, 5, and 8 years post-transplantation.⁵ Therapies targeted to prevent the development of CAV include using statins and modifying immunosuppression regimens.^{6,7} However, after CAV has developed, the therapeutic interventions are limited and have variable success rates. These interventions include percutaneous revascularization procedures (PRPs) such as balloon angioplasty, coronary artery stent implantation, and coronary artery bypass grafting. Percutaneous interventions in adult patients with CAV have reported high angiographic success and low complication rates. However, restenosis rates were high, and overall incidence of graft loss was increased, highlighting the progressive nature of CAV post-heart transplant.^{8–10} Limited data exist on the true incidence of CAV in pediatric patients. A study by Pahl et al³ from the Pediatric Heart Transplant Study (PHTS) database between 1993 and 2001 revealed that 751 of 1,221 (62%) patients with transplants underwent 2,049 coronary angiography procedures. In this cohort, 30 patients (4%) had moderate to severe CAV showing that the incidence of moderate to severe CAV was less than in the adult population; however, the prognosis with moderate to severe disease was poor. There are fewer data with respect to coronary artery revascularization procedures in pediatric patients. Shaddy et al¹¹ reported their experience with 3 pediatric patients requiring a revascularization procedure. All 3 patients had severe stenosis on angiography with a normal ejection fraction, lipid profile, and blood pressure. These patients also had successful procedures by angiography; however, all patients subsequently underwent retransplantation. Tham et al¹² reported on a single-center pediatric experience with percutaneous coronary interventions in which 7 patients underwent a revascularization procedure. Major procedural complications in this study included death ($n = 1$) and a resuscitated cardiac arrest ($n = 1$). Of the 7 patients, 3 underwent retransplantation, and 3 died. The aforementioned single-center studies reveal an alarming amount of graft loss among patients who develop CAV and undergo revascularization procedures.

The purpose of our study was to conduct a multi-institutional review, from the PHTS participating centers, of the procedural and clinical outcomes of all children who underwent a PRP for CAV from 1993 to 2009. This study composes the largest review to date of coronary revascularization in pediatric patients with transplants.

Methods

All participating centers had approval from their institutional review boards to participate in this study.

Data collection

The PHTS database includes patient demographic, medical, and procedural data that were collected and submitted by operating centers at the time of the procedure. Data collection forms described the location and degree of stenosis in the diseased vessel, the type of coronary artery intervention—either balloon angioplasty or stent placement—and procedural success identified by

angiographic improvement of the percent stenosis. Clinical outcomes were also measured with regard to the development of a complication during the procedure and long-term graft and/or patient survival. Patients who had not undergone angiography prior were excluded from the study.

Design

This was a retrospective review of the PHTS database of all patients listed ≤ 18 years old with an orthotopic heart transplant who have moderate or severe CAV as defined by angiography. Moderate stenosis was defined as major epicardial coronary vessel narrowing between 51% and 70% and severe stenosis $\geq 71\%$ as defined by the published Cardiac Transplant Registry Database criteria.¹³ The type of coronary revascularization procedures, location, and lesion characteristics were described. Recipient and donor risk factors were analyzed for predictors of the need for coronary revascularization. Outcomes of the revascularization procedure were divided into 2 categories: short-term and long-term outcomes. Short-term outcomes include procedural success and complication rates. Procedural success was defined as $\leq 20\%$ residual stenosis after the intervention. Long-term outcomes include survival after intervention and/or graft loss secondary to death or retransplantation. Additional comparisons were made within recipient and donor age groups as potential risk factors for survival or the need for a PRP.

Data analysis

Data were described using frequencies, means with SDs, and medians with ranges. The time-related freedom from revascularization for all patients and for patients with CAV were analyzed using Kaplan-Meier estimates, and associated factors were sought using Cox's proportionate hazard models. Confidence limits of ± 1 SE were used for comparison of means and survival proportions. A similar analysis was performed for the time-related events of restenosis and graft loss.

Results

Baseline characteristics

From January 1, 1993, to December 31, 2009, 3,156 pediatric heart transplants were performed in 35 PHTS participating institutions on patients ranging in age from birth to 21 years. During that time period, 11,430 angiograms were performed and 51 revascularization procedures in 28 patients with a first heart transplant were conducted at 15 of the 35 participating institutions. Baseline patient demographic data and characteristics for the study group are presented in [Table 1](#). The mean age of patients at the time of PRP was 13.4 ± 5.95 years, and the mean donor age was 15.9 years (range, 0.7–48.7 years).

Angiographic and procedural data

The mean time to first coronary intervention was 5.7 ± 3.2 years with 38 (75%) patients undergoing stent implantation and 13 (25%) undergoing balloon angioplasty. The left anterior descending coronary artery was the most common vessel requiring intervention ($n = 21$; 41%)

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