Predictors and Outcome of Extracorporeal Life Support After Pediatric Heart Transplantation

Jacob Simmonds, MD, Troy Dominguez, MD, Joanna Longman, MBBS, Nitin Shastri, MS, Maura O'Callaghan, MS, Aparna Hoskote, MD, Matthew Fenton, MBBS, Michael Burch, MD, Victor Tsang, MD, and Kate Brown, MPH

Cardiac Unit, Great Ormond Street Hospital, London, United Kingdom

CONGENITAL HEART

Background. Extracorporeal life support (ECLS) has proven success after conventional cardiac surgery. Its use after pediatric heart transplantation is less well documented. We reviewed ECLS after pediatric heart transplantation, to understand better predisposing factors, morbidity, and mortality.

Methods. The notes of all patients at Great Ormond Street Hospital undergoing orthotopic heart transplantation from 1999 to 2009 were reviewed (202 transplants; patients aged 0.06 to 17.91 years). Patients were grouped by diagnosis: restrictive cardiomyopathy (n = 17), nonrestrictive cardiomyopathy (n = 134), and anatomic heart disease (n = 51).

Results. Twenty-eight patients (13.9%) required ECLS after transplantation. Those requiring ECLS had longer ischemic times (4.2 versus 3.7 hours, $p = 0.02$). More restrictive cardiomyopathy patients (35.3%) required ECLS—higher than dilated cardiomyopathy (10.4%) or anatomic heart disease (15.7%; χ^2 7.99; $p = 0.018$). Factors associated with posttransplant ECLS were restrictive cardiomyopathy, longer ischemic time, and extracorporeal membrane oxygenation before transplant. Graft survival was higher in the non-ECLS group, with 1-year survival of 98.2% versus 57.7%; however, medium-term survival was comparable, with 5-year survival for those surviving to hospital discharge being 84.7% versus 100%.

Conclusions. The requirement for ECLS was higher than expected for conventional cardiac surgery. Although just over one half of patients requiring ECLS survived to discharge, they had excellent medium-term survival, with all still alive. Although ECLS is an expensive, invasive therapy, with significant morbidity and mortality, without it, those patients would have perished. Its judicious use, therefore, can be recommended.

(Ann Thorac Surg 2015;99:2166–72)

Modern improvements in cardiac surgery, intensive care, and transplant medicine have enhanced outcomes for pediatric heart transplantation over the last 2 decades [1]. In addition, conventional surgical techniques now palliate children that previously would not have survived infancy, a proportion of whom will require transplantation [2]. Unfortunately, in contrast to this growing pool of potential recipients, donation rates are relatively static [3]. This imbalance has led to transplant programs being burdened with a more heterogeneous—and technically demanding—group of recipients, waiting longer on the transplant list (and deteriorating further, with potential for increasing pulmonary vascular resistance [PVR]), and being forced to accept organs from marginal donors.

One consequence of these changes is further strain on the critical immediate postoperative period, accentuating the possibility of early graft failure. In response, programs increasingly rely on additional rescue measures, such as nitric oxide and extracorporeal life support (ECLS) [4], while waiting for graft recovery. The indications, risk factors, and outcomes of ECLS in this setting are not well documented, particularly in children. We reviewed ECLS as rescue therapy after pediatric heart transplantation at our institution, to uncover risk factors predisposing patients to ECLS.

Patients and Methods

This retrospective review of all pediatric orthotopic heart transplants at Great Ormond Street Hospital covers an 11-year period (January 1999 to December 2009 inclusive), using institutional transplant and ECLS databases. The start reflects the date when ECLS became standard treatment for early graft failure. In all, 202 orthotopic transplants were performed (103 female recipients), including 8 retransplants (patients aged 0.06 to 17.9 years, median 9.6); in addition, 2 heterotopic heart transplants were conducted—these were excluded from analysis. Patients were grouped by pretransplant diagnosis (Fig 1): of 151 transplants for cardiomyopathy, 17 were for restrictive cardiomyopathy (RCM); dilated cardiomyopathy (n = 129) and hypertrophic cardiomyopathy (n = 5) were considered together, as the nonrestrictive cardiomyopathy group (n = 134). The third group consisted of transplants for anatomic disease (n = 51), 48 congenital heart disease and 3 acquired surgical heart disease

Accepted for publication Feb 12, 2015.

Address correspondence to Dr Brown, Cardiac Unit, Great Ormond Street Hospital, London WC1N 3JH, United Kingdom; e-mail: katherine.brown@gosh.nhs.uk.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2015.02.047

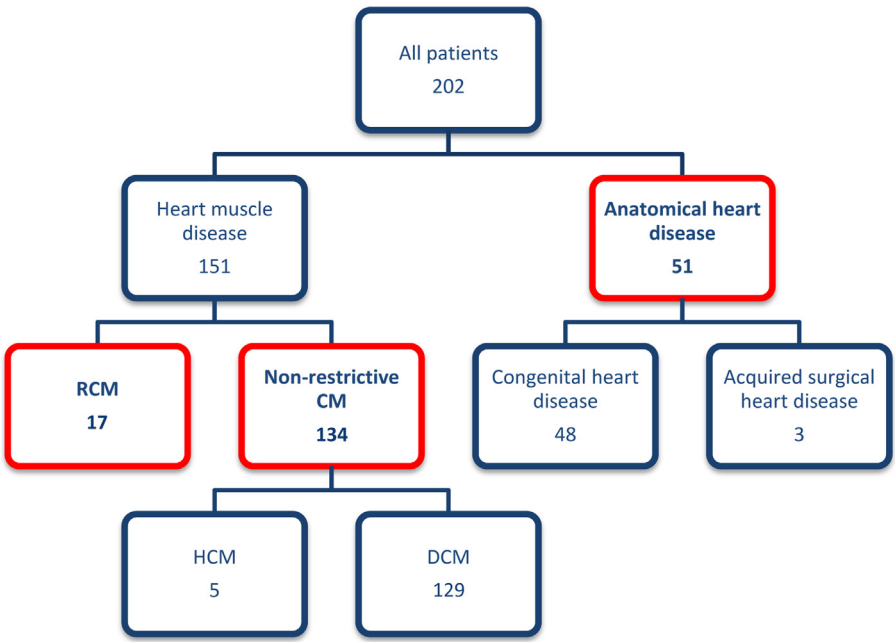

Fig 1. Study population by pretransplant diagnosis. Numbers indicate patients in each group. Red boxes indicate the final groupings used in analysis. (CM = cardiomyopathy; DCM = dilated cardiomyopathy; HCM = hypertrophic cardiomyopathy; RCM = restrictive cardiomyopathy.)

(2 noncongenital valve pathology secondary to Marfan's disease and 1 infective endocarditis).

Pretransplant workup involves formal catheter-based PVR measurements for high-risk patients, including those with suspicion of pulmonary hypertension on echocardiography, and patients with RCM. Twenty-five patients had a ventricular assist device (VAD) before transplantation (all cardiomyopathies), and 38 had a period of pretransplant extracorporeal membranous oxygenation (ECMO); 9 patients overlap both groups, with a period of ECMO followed by VAD. In total, 54 patients had mechanical support before transplantation.

Immediate postoperative care included inotropic support with milrinone, and low-dose epinephrine infusion, if required. Recipients with suspected elevated PVR were begun on inhaled nitric oxide from the operating theater. Renal failure was treated with continuous venoveno hemofiltration. Severe low cardiac output syndrome (with or without cardiac arrest), despite optimum conventional ventilatory and inotropic assistance, resulted in mechanical circulatory support, the majority of cases with ECMO through either transthoracic or peripheral cannulation, depending on patient factors and operator preference; anticoagulation therapy was monitored using activated clotting time, aiming for 215 s to 235 s, or if the patient was actively bleeding, 195 s to 215 s. Complete blood count, clotting times, and antithrombin 3 levels were monitored, and infusions given based on protocolized levels.

During the study, our immunosuppression regime evolved from induction with antithymocyte globulin to basiliximab, and standard maintenance triple immunosuppression from cyclosporin to tacrolimus, and azathioprine to mycophenolate mofetil, in addition to prednisolone, which—in the absence of rejection—is weaned over 3 months. Patients on ECLS support after transplant followed the standard contemporaneous protocol.

Primary outcome measures were ECLS within 30 days of transplantation, and graft loss, comprising death or retransplantation. Secondary outcome measures were length of intubation and in-hospital stay, cerebrovascular accident, seizure (clinical or on electroencephalographic monitoring), laboratory-proven infection, and biopsy-proven rejection (grade 2R or more). Primary graft failure was defined as impaired graft function within 24 hours (in the operating theater or intensive care unit) requiring high-dose inotropes or mechanical support.

Statistical analyses were run using the entire data set, unless stated, using Stata version 12 (StataCorp, College Station, TX). Transplant patients were separated depending on requirement for ECLS immediately after transplant. Demographic and pretransplant variables were compared using two-sample Wilcoxon rank sum (Mann-Whitney *U*) tests for continuous data, and χ^2 tests for categoric data. A small number of variables was missing: ischemic time for 2 patients, donor weight (and donor:recipient weight ratio) for 4, and hours intubated for 3. Rejection and graft survival were analyzed with Kaplan-Meier curves and log rank (Mantel-Cox) tests. Factors associated with posttransplant ECLS were analyzed with a multivariate Cox regression analysis. A p value less than 0.05 was considered significant.

This study was registered as a quality improvement audit, and ethics approval was waived.

Results

Of 202 transplants, 28 (13.9%) resulted in posttransplant ECLS; 24 had venoarterial ECMO only, 2 had right ventricular assist devices only, and 2 had venoarterial ECMO