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Outcome of shared care for pediatric cardiac transplantation between two nations with different health care systems

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BACKGROUND: No data are available for the outcome of children undergoing cardiac transplantation with shared care programs in different countries. We sought to investigate the outcome of a shared care transplant program between 2 countries given the complex immunologic, cardiac, and psychologic needs of these young people.

METHODS: We investigated the results of a shared care program for children who underwent cardiac transplantation between our center in the Republic of Ireland and 2 centers in the United Kingdom over 2 decades.

RESULTS: Between 1990 and 2013, 22 patients underwent 23 cardiac transplants. The median age at transplant was 3.2 years (range, 0.3–13.3 years), median age at listing was 30 months (range, 0.1–13.3 years), and the median waiting list time was 2.8 months (range, 0.3–14 months). The median time to return to the referral center from the time of transplant was 3 weeks (range, 2–8 weeks). The referral center treated 4 of 5 late rejection episodes. Angiography was undertaken in the transplant center at annual or biannual review. Outcomes for rejection, coronary vasculopathy, and survival were comparable between the referral and transplant centers.

CONCLUSIONS: This report of shared care for pediatric transplant patients between 2 sovereign nations demonstrates good results, with comparable outcomes to the specialist transplant center. These data may encourage liberalization of follow-up in other centers.

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Children with end-stage congestive heart failure, irrespective of the underlying mechanism, are surviving longer with improved medical therapies, ventricular assist devices (VADs), and increasing referral for cardiac transplantation.[1–7] The post-transplant patients often have the added complexities of human leukocyte antigen (HLA) and ABO incompatibilities. Follow-up also requires careful psychosocial input because of concern over adolescent nonadherence.[8]

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Smaller pediatric cardiology centers traditionally have worked in collaboration with larger tertiary pediatric cardiac centers in listing and bringing patients to cardiac transplantation. Yet, basing follow-up in the specialist transplant center for patients living a long distance away can mean huge family disruption in the early months post-operatively and financial difficulties with travel in the later years. It also de-skills the local team if complex rejection occurs.

There are limited data on shared care programs but no data on outcomes of shared care programs between different countries.[9] However in a Western European setting, high-quality health care can exist across borders and we have opted to devolve care wherever possible. The Republic of Ireland, owing to its relatively small population, does not support a pediatric cardiac transplant program and thus refers its patients to 1 of 2 centers in the United Kingdom (UK): Freeman Hospital in Newcastle upon Tyne and Great Ormond Street Hospital in London.

Methods

The medical records of all children who were referred to Great Ormond Street Hospital or to Freeman Hospital and underwent cardiac transplantation between January 1990 and September 2013 were retrospectively studied. We report the outcome of our shared care program for pediatric transplantation between the referral center in Ireland and the 2 specialist transplantation centers in the UK.

Patient demographics, diagnosis, and medical and surgical treatment before transplant were collected. The duration of listing, ABO compatibility, post-operative recovery, number of rejection episodes, and extent of coronary arteriopathy were also documented for each patient. Survival curves and freedom from graft rejection were generated using Kaplan-Meier curves. In addition, a more detailed comparative analysis was undertaken between patients from the referral center and the transplant center at Great Ormond Street Hospital to explore differences before and after transplant. Because many factors of transplantation, including donation rates, surgical technique, and immunosuppression regimens, have significantly changed during the 20-year study period, only patients who received transplants in the most recent 10 years were included.

Health care setting

The National Health Service in UK is free at the point of care. Care can be provided for patients from other European Union countries using the E112, where the referring government agrees to pay the UK for the services at an agreed price. In the Republic of Ireland there, is a mixture of public and private health care services, with some patients having private insurance. English is spoken in both countries, although Irish is taught in Ireland.

Transplant listing and transfer

After multidisciplinary assessment and agreement between the referral and transplant center, patients were listed for transplantation. Where possible, parents and the patient travelled to the transplant center for a formal assessment and were placed on the transplant list, if suitable. Patients who required inotropic or ventilatory support in the referral center did not travel for assessment although their parents often did. Patients who required mechanical support were transferred by air transport to the transplant center because this was not available in the referral center. Patients resided within short distance of the referral center to allow rapid transfer to the transplant center.

Transplant regimen and shared care pathway

The induction immunosuppression regimens varied in the transplant centers. Great Ormond Street Hospital used basiliximab as standard practice from 2002, and the Freeman Hospital used anti-thymocyte globulin (ATG). In the longer-term, however, all patients received tacrolimus-based immunosuppression. Some local autonomy regarding tacrolimus levels was agreed; however, all levels were reported to the transplant center, with standard target trough levels after the first year of 5 to 8 μg/liter.

Patients initially received anti-microbial prophylaxis after transplant, including nystatin/corsodyl, cotrimoxazole, and acyclovir for 3 months. Both transplant centers used preemptive treatment for cytomegalovirus (CMV) rather than prophylaxis. Biopsy regimens varied slightly in the transplant centers, but return for biopsy at 3 and 6 months was arranged for most patients. The shared care pathway used in most patients is presented in Table 1.

Patients were transferred back to the center in the Republic of Ireland as early as 2 weeks after transplant in some cases. Patients were seen in the outpatient transplant clinic weekly for the first 3 months and then every 2 months for 1 year, 3 months for the second year, and then every 6 months after that. Drug levels were checked weekly for the first 3 months, monthly for the first year, every 2 months for the second year, and every 3 months after the second year. Angiography to assess the coronary arteries was performed at 1 year and then biannually after transplant on the follow-up visit at the specialist transplant center.

Most of the rejection episodes during the last decade were treated at the referral center. Exceptional cases required return to the transplant center. One such patient with a complex case of combined cellular and antibody-mediated rejection was transferred to the specialist center after treatment in the Irish center with rituximab, intravenous immunoglobulin (IVIG), steroids, ATG, and plasmapheresis in addition to hemodialysis.

Telemedicine was used to discuss complex medical decisions between the referral and the specialist transplant centers and the families of patients. This was particularly important in discussing severe complications such as coronary vasculopathy and rejection.

Statistics

The entire data set was used for all analyses, unless stated. All data were tested for normality with the Kolmogorov-Smirnov test. Continuous non-normally distributed parameters (age and weight at transplant, waiting list time, mean and maximum intimal thickness, and stenosis) were analyzed with the Mann-Whitney U test. Categoric data (recipient weight <20 kg, Stanford grade) were analyzed with Pearson's χ^2 or Fisher's exact test when the cell count was <5 (death on waiting list, need for extracorporal life support [ECLS] pre-transplant, infant transplants). Freedom from rejection and graft survival were investigated with Kaplan-Meier curves and Mantel-Cox log-rank.

Results

During the 23-year period between January 1990 and September 2013, 22 patients (16 girls, 6 boys) underwent 23