Registry of the International Society for Heart and Lung Transplantation: Tenth Official Pediatric Heart Transplantation Report—2007

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Pediatric heart transplantation celebrates its twenty-fifth birthday in 2007, and the first recipients are now entering adulthood. This, the Tenth Official Pediatric Report of the Registry of the International Society for Heart and Lung Transplantation (ISHLT), is dedicated to the courageous recipients and their families, and to the generous donor families who have made this possible. This report documents decades-long survival enjoyed by many pediatric heart transplant recipients. We can now look back over the past 25 years and evaluate indications, survival and morbidity by age of the recipient and era of transplantation. Because much has changed over one-quarter century, we can only be reasonably certain that the late outcomes of the earliest pediatric transplants will be reflected accurately in current recipients. However, these data form a standard and a point of reference to predict future outcomes and perhaps compare actual outcomes in the years to come, as new therapies and management protocols are developed and tested.

The data stream for the Registry of the ISHLT is global, and geographic differences have emerged. Geographic comparisons for age at transplant and indication for transplantation are presented for the first time in this tenth report. Previous publications have reported on a steadily improving early survival.[1] We now have a more complete knowledge base for late survival and we report, for the first time, morbidity as late as 10 years after transplantation. Re-transplantation as an indication for transplant has been slowly increasing in North America, but is almost non-existent elsewhere in the world. This report documents the recent rise in the number of re-transplant procedures and further evaluates the late outcomes after re-transplantation. Questions remain about the role of re-transplantation for pediatric recipients who become adults. Will adult transplant programs worldwide accept the burden of re-transplantation for pediatric recipients who are now in need of a second heart transplant, or perhaps a kidney transplant, due to calcineurin inhibitor–induced renal failure? Certainly this challenge will grow and the pediatric transplant community must evaluate potential changes at the point of care in childhood that could reduce the demand for re-transplantation and perhaps increase the likelihood of multi-decade survival with less morbidity.

The two main post-transplant morbidities that have steadily increased are coronary artery vasculopathy and renal failure. Malignancy has remained an important but low-frequency event. In this report, we continue to evaluate late outcomes as a function of early events such as rejection, induction therapy and choice of calcineurin inhibitor. The risk of coronary vasculopathy is still $<$20% as late as 10 years after transplantation, which is quite different from the experience of adult transplant recipients. The data continue to strengthen earlier observations regarding a relative sparing of infant recipients from the risks of rejection, coronary vasculopathy and even late mortality. Perhaps the apparent better late survival seen in infant recipients is due to decreased rejection early after the transplant procedure.

In this investigation, we add to the experience and update many of the comparisons to the most recent era. Still we generally look back in our efforts to define contemporary outcomes. The transplant experience is a complicated process and many of the observations may reflect management styles and protocols perhaps more than correlations related to specific drug therapies or even the diagnosis of rejection. For pediatric recipients who survive the first year of transplant, the estimated overall median survival was beyond 15 years, and for the infant age group the median survival was not yet calculable because median survival exceeded the 20-year

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All of the figures and tables from this report and a more comprehensive set of Registry slides are available at http://www.ishlt.org/registries/.

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period of observation. Late survivors have continued to show excellent rehabilitation in terms of functional status, but renal dysfunction now threatens nearly 20% of surviving recipients at 10 years post-transplant.

STATISTICAL METHODS

Survival rates were calculated using the Kaplan–Meier method and were compared using the log-rank test described previously.[2] Multivariate analyses were performed using proportional hazards regression models. The impact of continuous risk factors was examined with restricted cubic splines. Predicted survival curves were again generated for specific hypothetical patient/donor/transplant profiles, as reported previously.[1]

PEDIATRIC HEART TRANSPLANTATION

Volumes and Indications

The total number of pediatric heart transplant procedures reported to the Registry of the ISHLT has remained reasonably stable for the past 15 years at approximately 400 procedures per year (Figure 1). As reported previously, the first year of life is the single most common year for a heart transplant procedure during the first 18 years of life. The total number of donors is also greatest in the early childhood years.

The total number of transplant centers reporting data has stabilized at approximately 80. There has been a steady increase in the average number of heart transplant procedures per center per year, with almost 45% of patients now transplanted at a center performing >10 heart transplants each year (Figure 2).

In this report we document geographic differences in age at the time of transplant. Teenage recipients accounted for >50% of patients in Europe and other areas worldwide, whereas in North America infants, children and adolescents were more balanced in terms of the overall percentage of recipients (Figure 3). The indications for transplantation also show some geographic variation (Figure 4). The most striking differences are that North American patients were more likely to have a congenital diagnosis and more likely to undergo

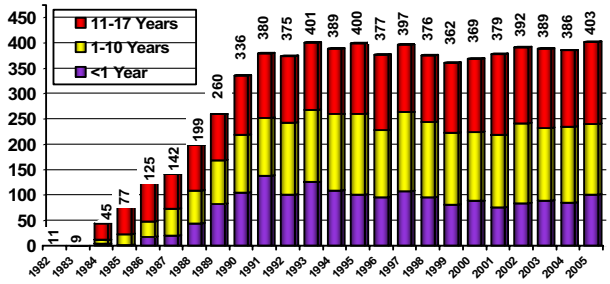

Figure 1. Age distribution for pediatric heart transplants by year of transplant.

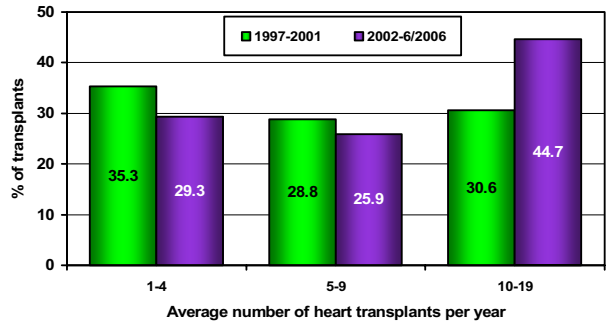

Figure 2. Distribution of transplants by center volume for pediatric heart transplants performed between January 1997 and June 2006.

re-transplantation. Compared with previous Registry reports, the indications for transplantation have remained remarkably stable. The infant age group was most likely to have recipients with a congenital cardiac diagnosis, accounting for about two-thirds of recipients between 1996 and 2006. Recipients between the ages of 1 and 10 years were more evenly split between a congenital and a myopathic diagnosis. A slight majority of children had myopathy leading to transplant and these numbers have changed a little over the years. The shift to a majority of the patients having myopathy occurred in the adolescent age group recipients. Almost two-thirds of adolescents had myopathy, whereas only one-quarter had a congenital diagnosis. The percent of patients requiring re-transplantation has increased to 7% among adolescents.

Most re-transplant procedures were performed >5 years after the initial transplant (Figure 5). This is an important consideration when one evaluates the results of re-transplantation presented later in this report. Although re-transplantations have made up a small proportion of the total number of transplantations, the number of re-transplant procedures has been slowly increasing until the most current reporting period when there was a large jump (Figure 6); this potential trend will be monitored in future Registry reports. The

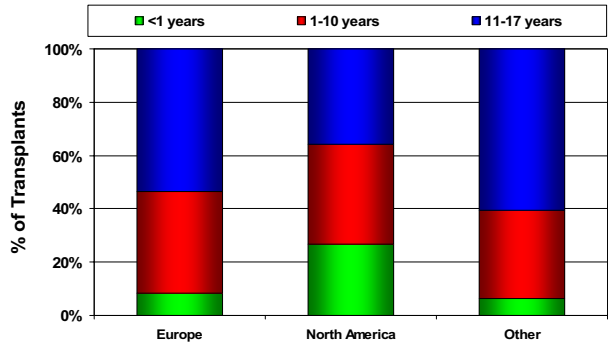

Figure 3. Age distribution of recipients by geographic location for pediatric heart transplants performed between January 2000 and June 2006.

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