Registry of the International Society for Heart and Lung Transplantation: Twelfth Official Pediatric Heart Transplantation Report—2009

Richard Kirk, MA, FRCP, FRCPCH, Leah B. Edwards, PhD, Paul Aurora, MRCP, PhD, David O. Taylor, MD, Jason D. Christie, MD, MS, Fabienne Dobbels, PhD, Anna Y. Kucheryavaya, MS, Axel O. Rahmel, MD, Josef Stehlik, MD, and Marshall I. Hertz, MD

The first pediatric heart transplantation reported to the International Society of Heart and Lung Transplantation (ISHLT) Registry was in 1982; since then, more than 8,000 children have been registered. Many have survived into adult life, and some have had their own children. This 12th Report continues to document the evolving management of pediatric transplant recipients and their outcomes.

REGISTRY DATA SOURCE AND STATISTICAL METHODS

The ISHLT Registry data are provided by individual centers or a data-sharing arrangement with a national or regional organ procurement or exchange organization. Approximately 450 pediatric heart transplants are reported to the Registry each year. Most the data are provided from North American centers, but significant contributions come from centers in Europe and the rest of the world (Figure 1). The Registry Committee is actively seeking participation from all centers performing pediatric heart transplants.

The tables and figures in this report and additional slides are all available from the ISHLT Web site.[1] Contributing centers are recognized in the Introduction to the 2009 Annual Reports.

Survival rates were calculated using the Kaplan-Meier method and compared using the log-rank test. Multivariable analyses were performed using Cox proportional hazard regression analysis. Results of the multivariable analyses are reported as relative risks (RR) with a corresponding p-value or 95% confidence interval, or both. A RR significantly > 1 indicate that the factor is associated with an increased likelihood of the event occurring, such as death, development of coronary allograft vasculopathy, or others. Conversely, a RR < 1 indicates that the event is less likely to occur when that factor is present.

CENTERS AND ACTIVITY

The total of 8,058 pediatric (age < 18 years) heart transplants were reported to the Registry between 1982 and 2007, with an annual transplant rate of 450 during the last 3 years. This represents about 12.5% of the 3,300 adult heart transplants per annum.[2] The number of centers reporting transplant activity increased rapidly in the 1980s and early 1990s to a peak of 106 in 1994. It has decreased slightly since then and has now plateaued at 80 centers.

A gradual trend has developed during the last 10 years toward centers undertaking larger volumes of transplants. For the 1997 to 2000 cohort, 82% of centers undertook 4 or fewer transplants per year, accounting for 34% of all transplants reported to the Registry. Only 6% of centers undertook more than 10 transplants per year, accounting for 31% of total transplants. Since the year 2001, there has been a trend toward slightly fewer centers (79%) undertaking a small number of transplants (1 to 4 per annum), accounting for 28% of all transplants. There has been a corresponding increase in centers (9%) undertaking more than 10 transplants per year, accounting for 44% of all pediatric heart transplants reported to the Registry (Figure 2). In general, European centers had smaller annual volumes, with 44% of centers undertaking 4 or fewer transplants per year compared with 23% in North America (Figure 3).

The annual center volume is one of the factors influencing survival; the RR of 1-year mortality is less than 0.9 for those centers undertaking 15 or more transplants per year compared with 1.06 for those undertaking 4 or less (Figure 4).

DONOR CHARACTERISTICS

There was a significant difference in donor demographics between transplant centers in North America and other centers. In North America, only 20% are adult donors (Figure 5), whereas in the rest of the world,

International Society for Heart and Lung Transplantation, Addison, Texas.

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

Reprint requests: Dr Marshall I. Hertz, University of Minnesota, Pulmonary/Critical Care Medicine, 301 E River Rd, 350G VCRC, Minneapolis, MN 55455. Telephone: 612-624-5481. Fax: 612-625-2174. E-mail: hertz001@umn.edu

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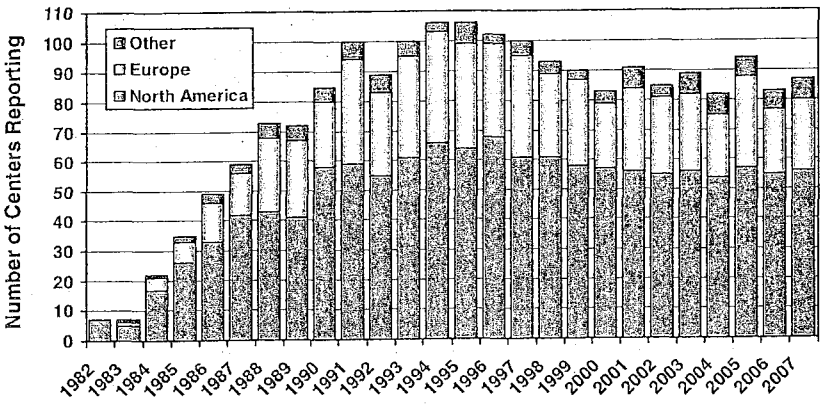

Figure 1. Number of centers reporting pediatric heart transplants by location.

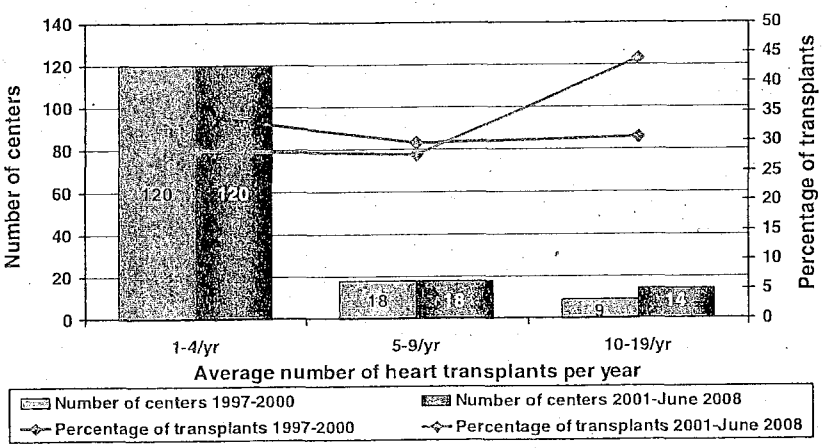

Figure 2. Average center volume for transplants from January 1997 through June 2008.

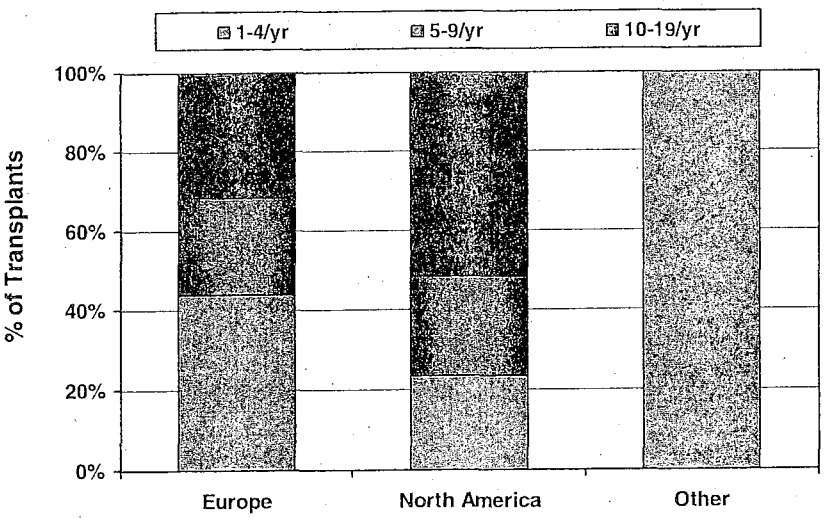

Figure 3. Average center volume distribution by location for transplants from January 2000 through June 2008.

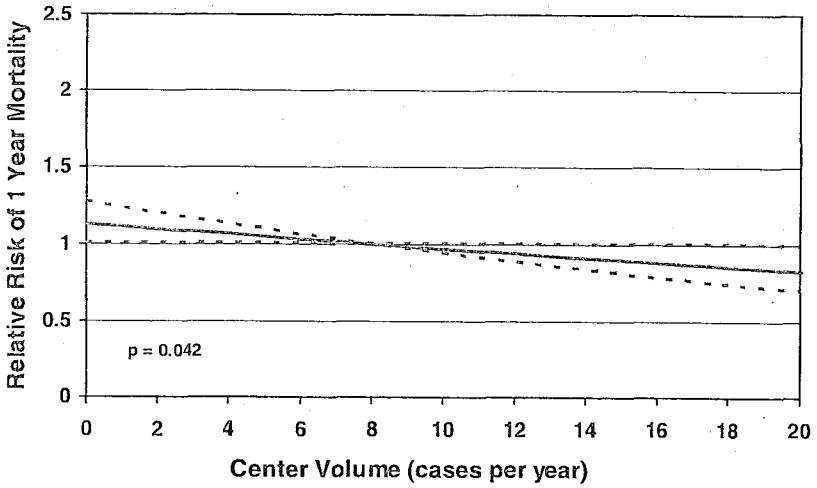

Figure 4. Center volume risk factor for 1-year mortality for transplants from January 1995 to 2007. The dotted lines show the 95% confidence interval for the relative risk.

more than 40% of heart transplant donors for pediatric recipients were from the adult pool. This is of significance, because increasing donor age is associated with reduced 1-year survival (Figure 6).

TRANSPLANT DEMOGRAPHICS

Very few infants (age < 1 year) received an allograft in the early years of transplantation; however, since the early 1990s, approximately 25% of all pediatric heart transplants are undertaken in infancy, with the remainder split amongst other ages (Figure 7). In North America, the proportion transplants performed in infants is 27%, compared with 11% in the rest of the world (Figure 8). The commonest indication for transplant during infancy is congenital heart disease (63%), followed by cardiomyopathy (31%). In older patients the reverse is true, and cardiomyopathy predominates (64%) over congenital heart disease (24%). This contrasts with the adult population,[2] where cardiomyopathy accounts for 50% of transplants, congenital heart disease for 3%, and coronary disease for 34%.

There are also geographic differences in the diagnoses leading to transplant (Figure 9). For all age groups, cardiomyopathy is the reason for transplant in 69% in Europe compared with 49% in North America, where a much higher number of transplants have been for congenital heart disease.

Retransplants (considered as a diagnostic category) occur in 1% infant recipients but now account for 5% of pediatric recipients. This compares with 3% in the adult population.[2] The sudden increase from about 20 retransplants yearly to 35 retransplants in 2005 fell back to 21 reported in 2006, but increased again in 2007 to 36. Retransplants are now being reported in Europe (1.6%), in contrast to previous years. Fifty percent of all retransplants occur more than 5 years after the initial transplant.

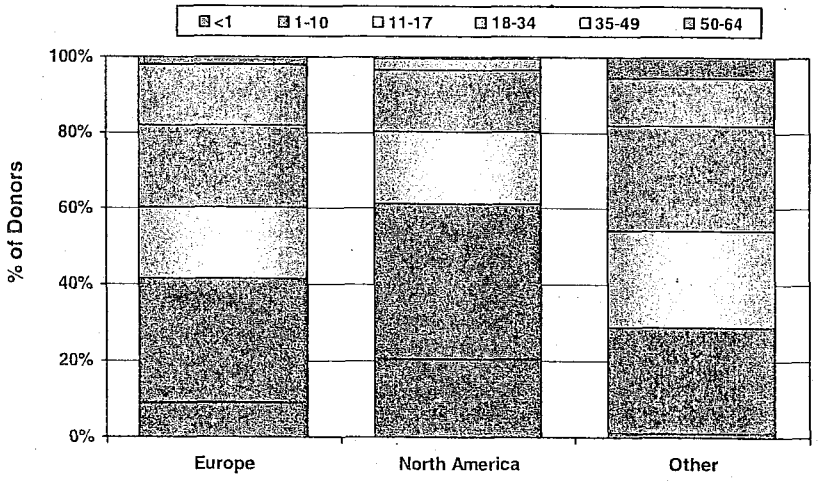

Figure 5. Donor age distribution by location for transplants from January 2000 through June 2008.

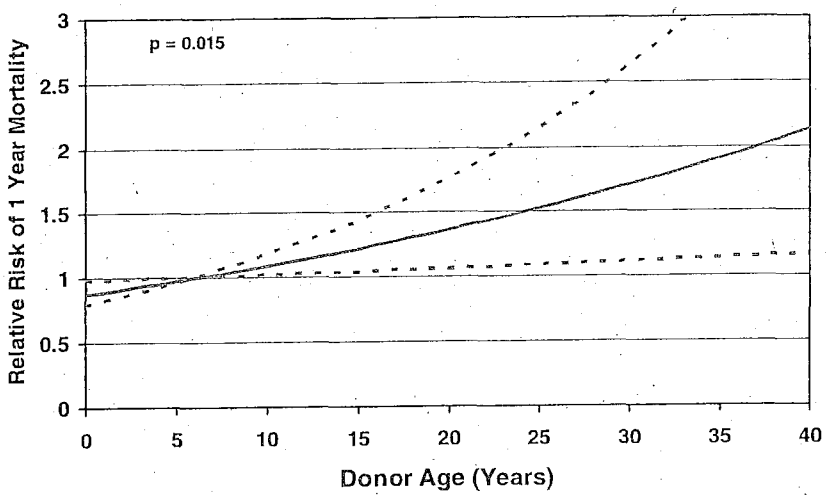

Figure 6. Donor age risk factor for 1-year mortality for transplants from January 1995 through June 2007. The dotted lines show the 95% confidence interval for the relative risk.

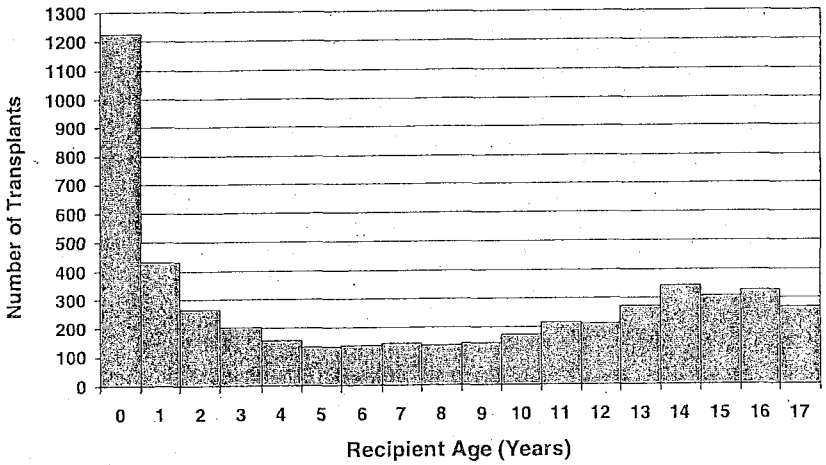

Figure 7. Age distribution of pediatric heart recipients for transplants from January 1996 through June 2008.

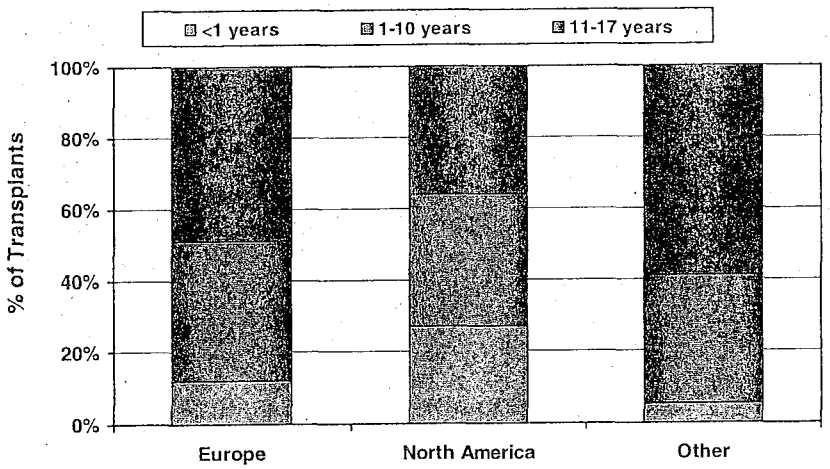

Figure 8. Age distribution by location for transplants from January 2000 through June 2008.

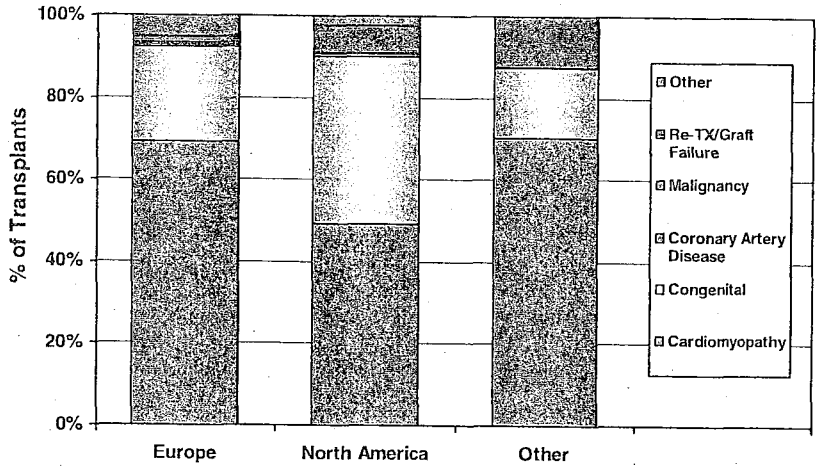

Figure 9. Diagnosis distribution by location for transplants from January 2000 through June 2008.

IMMUNOSUPPRESSION

Induction

Induction therapy is designed to reduce the incidence of early rejection and allow a delay, if necessary, of the introduction of maintenance immunosuppression. The tendency for induction has increased during the past 6 years, with 37% receiving induction in 2001 and 60% in 2008 (Figure 10). This can mainly be accounted for by an increase in polyclonal anti-lymphocyte antibody use from 23% to 39%, although the use of interleukin-2 receptor (IL-2R) antagonists has also increased from 12% to 22%. The overall use of induction agents in the adult population is similar, although the use of IL-2R antagonists is greater. Rejection episodes between transplant discharge and 1 year were not reduced by induction therapy (Figure 11). Neither did the induction strategy (none, polyclonal anti-lymphocyte antibodies, or IL-2R antagonists) influence survival regardless of age at transplant (Figure 12).

There has been some concern that induction therapy might increase the risk of cytomegalovirus (CMV) disease or the development of post-transplant lymphoproliferative disease, driven by Epstein-Barr virus (EBV). However, no relationship has been found between the reported rate of CMV disease according to donor/recipient status combinations and the use or otherwise of induction therapy. Likewise, the use of induction therapy did not increase the likelihood of developing post-transplant lymphoproliferative disease (Figure 13).

Maintenance

Most immune suppressive regimens include a combination of a calcineurin inhibitor (CNI) and cell cycle inhibitor, with a significant number of patients also

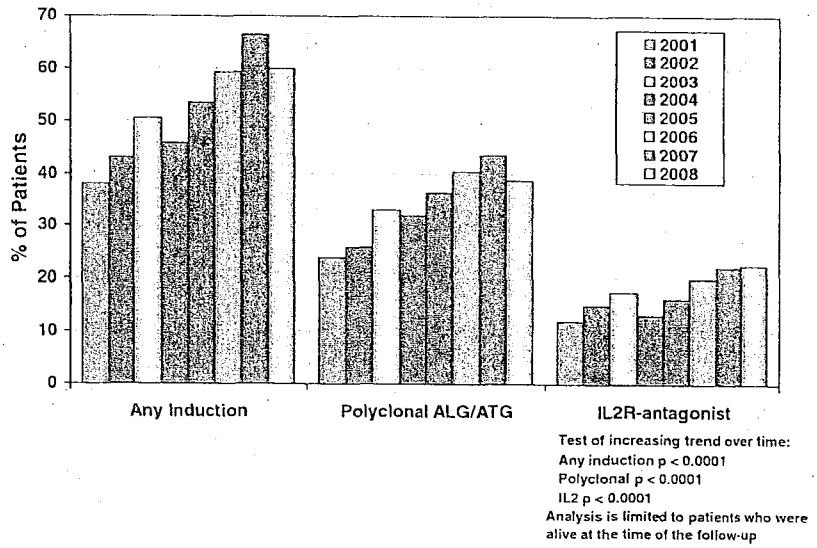

Figure 10. Induction immunosuppression for transplants from January 2001 through June 2008. ALG, anti-lymphocyte globulin; ATG, anti-thymocyte globulin; IL2R, interleukin 2 receptor.

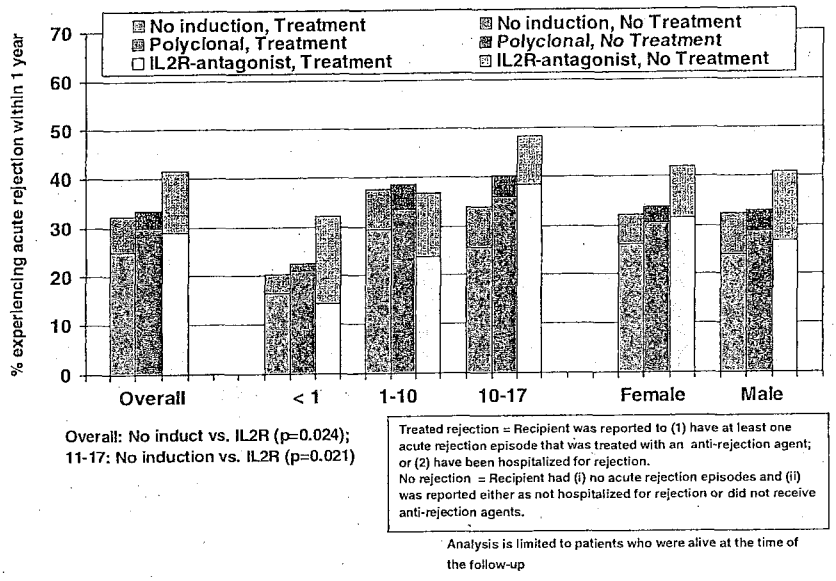

Figure 11. Percentage of pediatric heart transplant recipients experiencing acute rejection between transplant discharge and 1-year follow-up stratified by type of induction for follow-up occurring from July 2004 through June 2008. IL2R, interleukin 2 receptor.

receiving corticosteroids. With regard to the choice of CNI, 38% of patients at the 1-year follow-up received cyclosporine, and 58% received tacrolimus. Cell cycle inhibitors were used by 80% of patients (20% azathioprine, 59% mycophenolate mofetil [MMF]). Prednisone was given to 55%, and 8% received a target of rapamycin inhibitor (Figure 14). These figures broadly reflect the adult practice.[2] A total of 631 patients were tracked for Years 1 to 5 to see how their immunosuppression regimens changed (Figure 15). There were many combinations of therapies, and some uncommon combinations were therefore categorized as "other," accounting for 8% of combinations at 1 year and 19% at 5 years. The percentage change of the more common regimens has been calculated after this "other" category was removed. At Year 1, 15% were receiving cyclosporine and azathioprine, and this decreased to 9% by Year 5. The percentage of patients in this cohort who were receiving a combination of cyclosporine and MMF halved, from 23% to 13%. Overall, the proportion of these 631 patients receiving cyclosporine regimens reduced from 45% to 28%, whereas the proportion with tacrolimus-based regimens rose from 46% to 52%. The proportion taking azathioprine fell from 24% to 16%, and those taking MMF fell from 51% to 43%.

SURVIVAL

The average survival—the time at which 50% of recipients remain alive—varies with the age of the recipient at transplant. The average survival is 11 years for those who receive an allograft as teenagers and 18 years for infants. The highest risk of dying is in the first 6 months after transplant (Figure 16). By estimating survival for those who have exceeded this high-risk period and

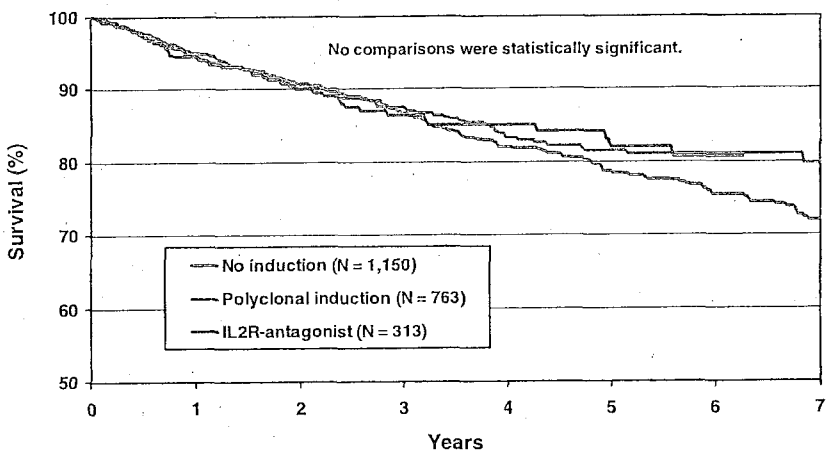

Figure 12. Kaplan-Meier survival by induction group conditional on survival to 14 days for transplants from January 2000 through June 2007.

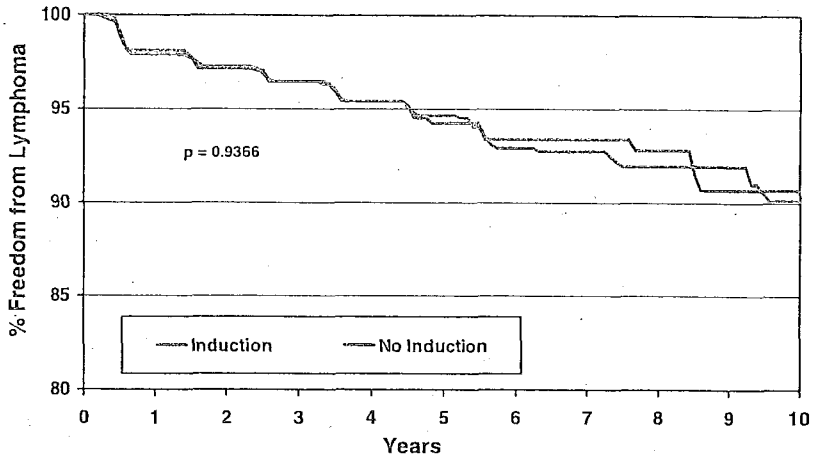

Figure 13. Freedom from lymphoma stratified by induction for follow-up from April 1994 through June 2008.

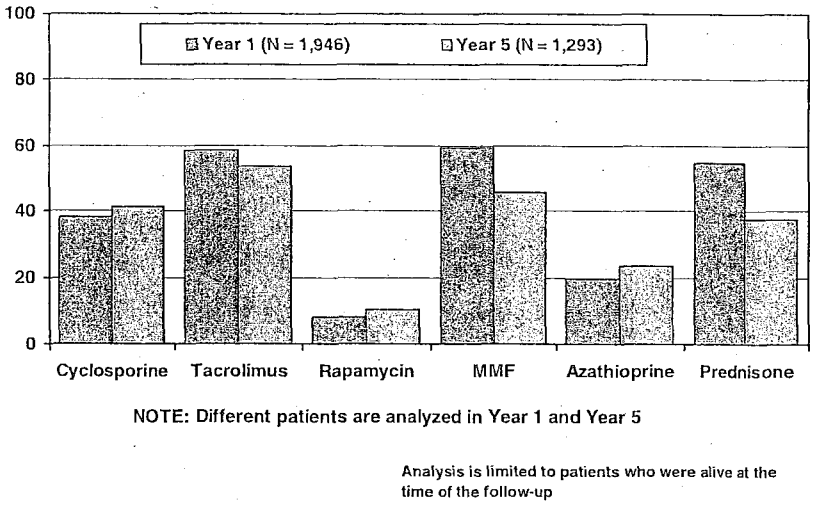

Figure 14. Maintenance immunosuppression at time of follow-up from January 2001 through June 2008. MMF, mycophenolate mofetil.

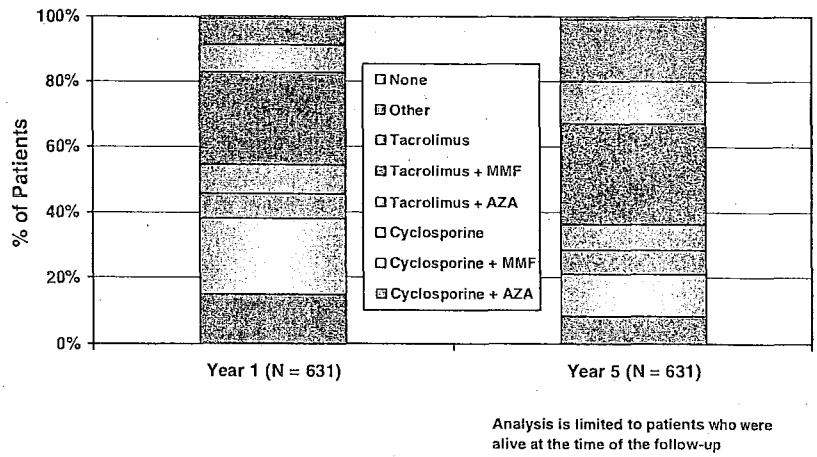

Figure 15. Maintenance immunosuppression at time of follow-up for same patients at each time point from January 2001 through June 2008. AZA, azathioprine; MMF, mycophenolate mofetil.

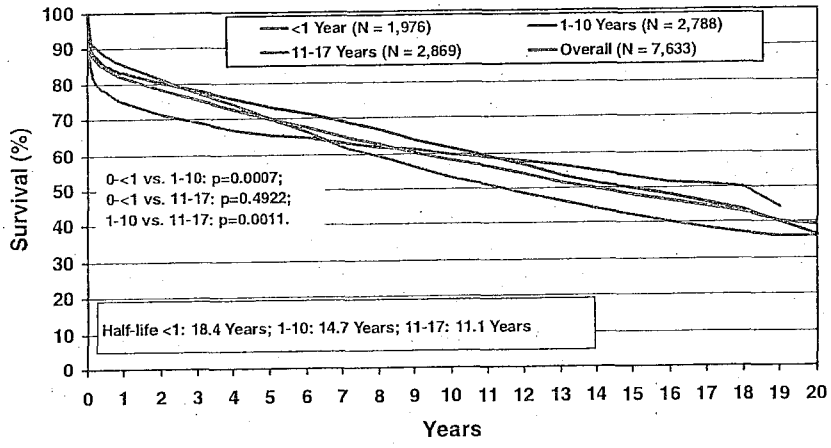

Figure 16. Kaplan-Meier survival for transplants from January 1982 through June 2007.

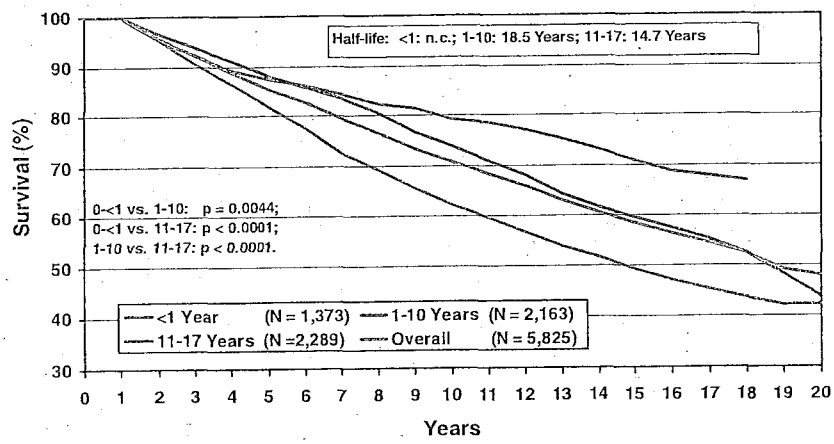

Figure 17. Kaplan-Meier survival conditional on survival to 1 year for transplants from January 1982 through June 2007.

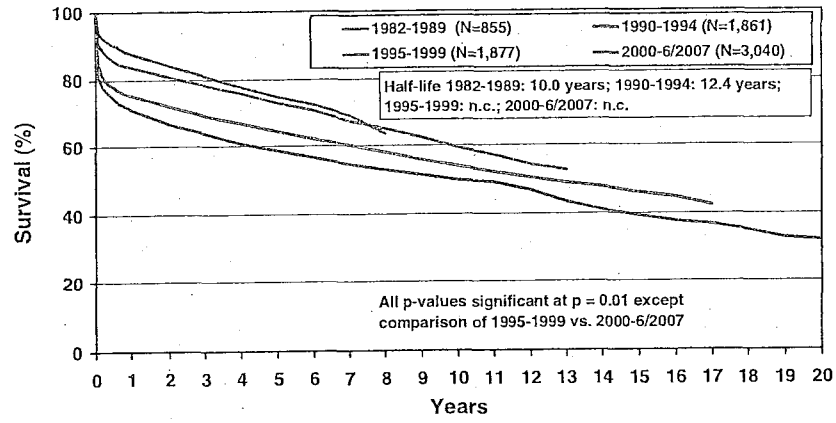

Figure 18. Kaplan-Meier survival by era for transplants from January 1982 through June 2007.

Table 1. Risk Factors for Mortality Within 1 Year for 3,756 Transplants Performed January 1995 Through June 2007

Variable	No.	RR	95% CI	*p*-value
Congenital diagnosis, age = 0, on ECMO	74	2.70	1.57–4.63	0.0003
Congenital diagnosis, age > 0	893	2.17	1.67–2.83	<0.0001
Retransplant	225	2.09	1.42–3.07	0.0002
On ventilator	706	1.80	1.45–2.23	<0.0001
On dialysis	91	1.62	1.08–2.43	0.0210
Year of transplant: 1995–1996 vs 2001–2002	506	1.55	1.14–2.09	0.0049
Panel reactive antibody ≥ 10%	344	1.37	1.04–1.79	0.0228
IV drug therapy for infection ≤2 wk HTx	565	1.29	1.03–1.62	0.0267
Donor cause of death = anoxia vs head trauma	863	0.80	0.64–1.00	0.0468
Not ABO identical	843	0.79	0.63–0.99	0.0384
Diagnosis other than congenital, no ECMO, age = 0	295	0.46	0.27–0.78	0.0042
Recipient age	...	...	...	0.0230
Donor age	...	...	...	0.0150
Creatinine	...	...	...	0.0230
Pediatric transplant volume	...	...	...	0.0420
Recipient height	...	...	...	0.00013
Donor height	...	...	...	0.0470

CI, confidence interval; ECMO, extracorporeal membrane oxygenation; HTx, heart transplantation; IV, intravenous; RR, relative risk.

NOTE: Reference diagnosis = cardiomyopathy.

including only those who survived at least 1 year after transplant (conditional survival), the average conditional survival is 15 years for teenagers and nearly 19 years for those who undergo transplantation between age 1 and 10 years. The infant average survival is not calculable, because 50% have not yet died (Figure 17). The average survival in the adult population is approximately 1 year less, and conditional average survival is 2 years less than the teenager group.

Survival can also be shown to be improving in relation to the date of transplantation (Figure 18), with the transplant average survival improving from 9.9 years for the period 1982 to 1989 to 12.4 years for the period 1990 to 1994. The transplant average survival is not calculable for more recent eras because the 50% failure rate has not yet been reached. This improvement has occurred primarily due to a decrease in early death (within the first 3 months).

Post-transplant care after the first few months of life appears not to have significantly improved medium to late outcomes. This is also borne out by a recent detailed analysis of pediatrics recipients using the ISHLT Registry. Although data showed the risk-adjusted 5-year survival after transplant has improved by 30% in the recent era, all of this effect appears to be due to improved survival during the first 6 months after transplantation.[3]

Risk factors predictive of 1-year mortality are listed in Table 1. In general, these risk factors follow common sense, with patients requiring the most pre-transplant support (eg, mechanical support and ventilation) having the greatest risk of dying in the first year. Similarly, factors reflecting recipient illness, such as pre-transplant creatinine levels, influenced the 1-year survival (Figure 19). However, other recipient markers of severity of illness (eg, hospitalization and intravenous inotrope use) had no influence on 1-year mortality. Transplant center volume had an influence: busier centers had better survival (Figure 4).

Congenital diagnosis predicts a worse outcome. Donor gender had no effect, but increased donor age did adversely affect survival (Figure 6). Transplant factors

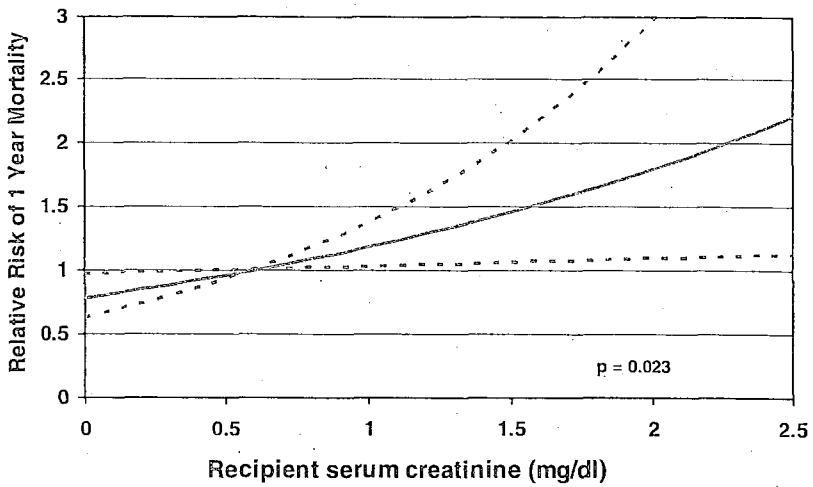

Figure 19. Pre-transplant creatinine risk factor for 1-year mortality is shown with the 95% confidence interval (dotted lines) for transplants January 1995 through June 2007.

Table 2. Risk Factors for Mortality Within 5 Years for 2,364 Transplants Performed January 1995 Through June 2003

Variable	No.	RR	95% CI	*p*-value
Congenital diagnosis, age = 0, on ECMO	36	2.12	1.23–3.67	0.0072
Retransplant, age > 0	131	1.86	1.34–2.59	0.0002
On dialysis	49	1.59	1.04–2.43	0.0337
Panel reactive antibody ≥ 10%	240	1.45	1.15–1.83	0.0019
Congenital diagnosis, age > 0	586	1.38	1.11–1.71	0.0039
On ventilator	445	1.30	1.05–1.61	0.0169
Female recipient	1,006	1.25	1.06–1.47	0.0081
Diagnosis other than congenital, no ECMO, age = 0	185	0.53	0.34–0.83	0.0050
Recipient age	...	...	...	<0.0001
Donor age	...	...	...	0.0230
Pediatric transplant volume	...	...	...	0.0078

CI, confidence interval; ECMO, extracorporeal membrane oxygenation; RR, relative risk.

NOTE: Reference diagnosis = cardiomyopathy.

that had no influence included CMV mismatch, ischemia time, and human leukocyte antigen mismatch.

Risk factors for 5-year mortality include congenital diagnosis with extracorporeal membrane oxygenation (RR, 2.1), dialysis (RR, 1.59), ventilation (RR, 1.3), or female recipient (RR, 1.25; Table 2). Donor age influenced survival, with adult donors leading to poorer survival. The RR of death using a 40-year-old donor was 1.8 compared with that of a 6-year-old donor. Risk factors for 10-year mortality were detailed in last year's report.[4]

Rejection during the first year after transplant appears not to affect short- to medium-term survival (Figure 20). Survival for those discharged with cyclosporine therapy was 69% compared with 63% for tacrolimus at 9 years. This effect persisted for those who continued taking cyclosporine at 1 year, demonstrating 5-year survival of 87% compared with 81% for those maintained on tacrolimus at discharge through to 1 year. This effect also persisted at 9 years, with 73% survival in the cyclosporine group compared with 68% in the tacrolimus group (Figure 21). Patients who changed from one CNI to the other had worse survival times. At the 1-year follow-up, patients who were still receiving corticosteroids as part of their immunosuppression regimen had a worse survival of 69% at 9 years with compared with 81% for those who were not receiving corticosteroids. This may well reflect the occurrence of rejection managed with the inclusion of corticosteroids in the first year, which is known to be associated with a worse outcome rather than a direct effect of corticosteroids.

TRANSPLANT MORBIDITY

Functional status in the Registry is available for 557 transplant recipients who survived at least 10 years. Although the Registry measures of functional status are limited, they do show that 92% of recipients have no limitations on physical activity, and only 1% require total assistance. There is little change in functional status of patients with time, with those having little or no limitations initially continuing to have few limitations later. Rehospitalization during the first year after transplantation is significant, with 50% of the patients requiring readmission for infection (35%), rejection (25%), and for both infection and rejection (15%; Figure 22). By 10 years, hospitalization is much less frequent, with 36% hospitalized for infection, 15% for rejection, and 4% for both infection and rejection. These figures are very similar to the adult data.

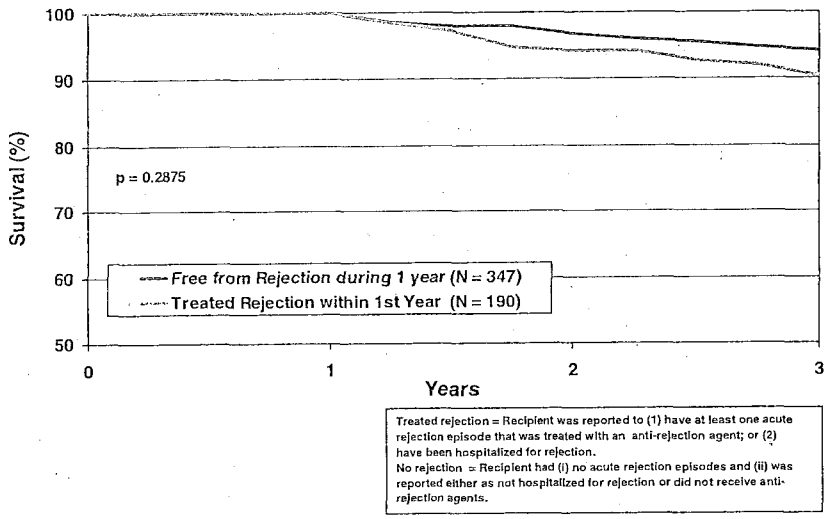

Figure 20. Kaplan-Meier survival based on treated rejection within 1st year conditional on survival to 1 year for 1-year follow-up from July 2004 through June 2007.

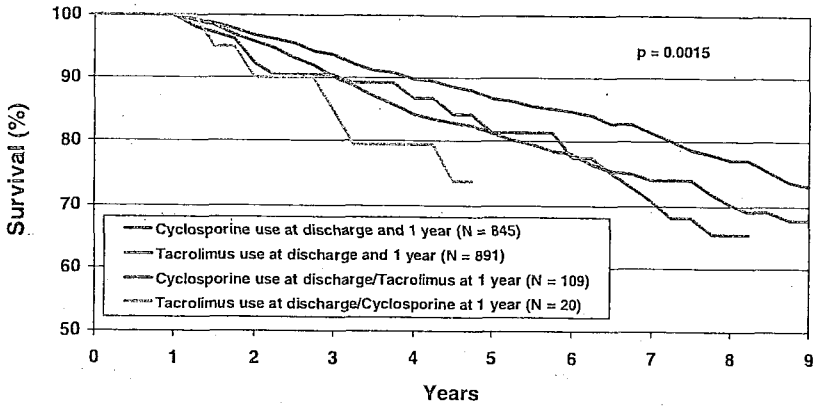

Figure 21. Kaplan-Meier survival stratified by tacrolimus vs cyclosporine use conditional on survival to 1 year for transplants from January 1998 through June 2007.

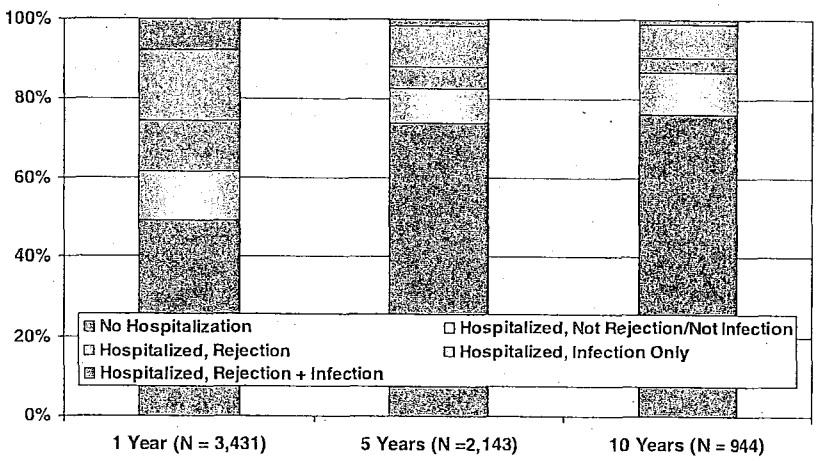

Figure 22. Rehospitalization after transplantation of surviving recipients from April 1994 through June 2008.

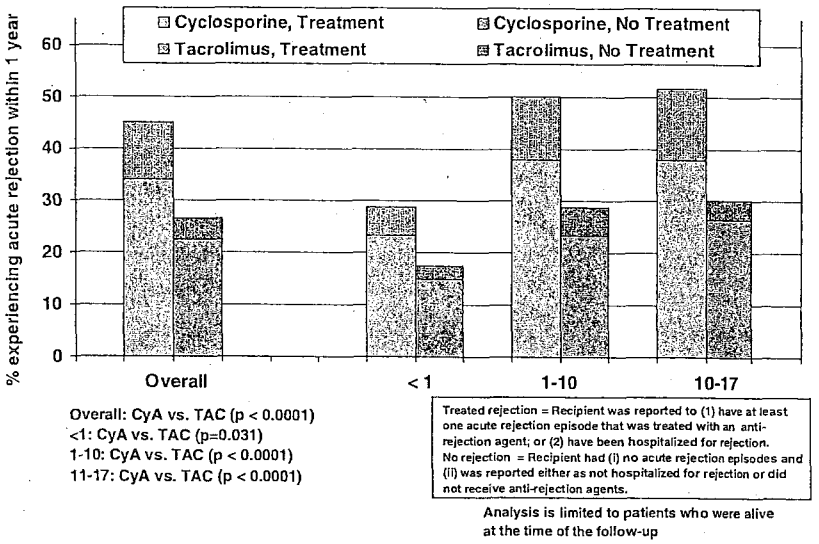

Figure 23. Percentage of pediatric heart transplant recipients experiencing acute rejection between transplant discharge and 1-year follow-up stratified by calcineurin inhibitor use at discharge for follow-up from July 2004 through June 2008.

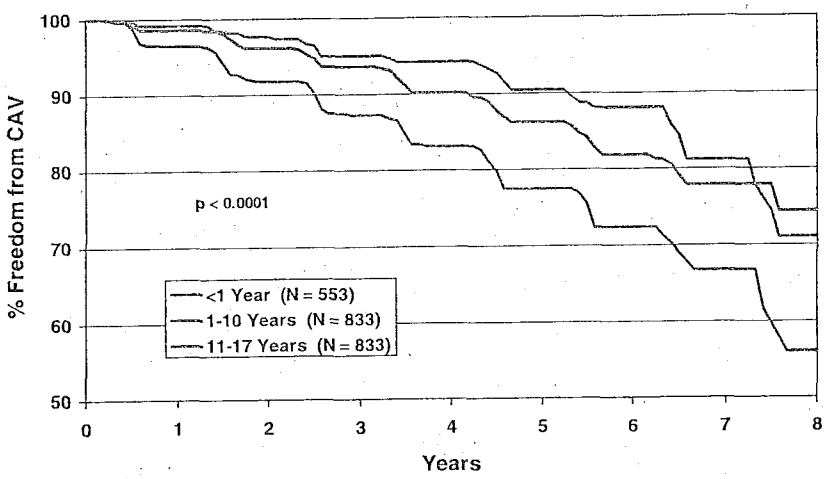

Figure 24. Freedom from cardiac allograft vasculopathy (CAV) stratified by age group for follow-up from January 1999 through June 2008.

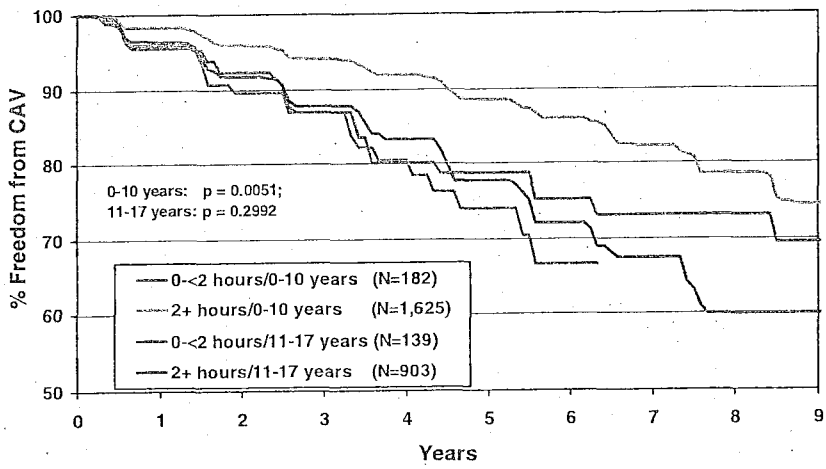

Figure 25. Freedom from cardiac allograft vasculopathy (CAV) stratified by ischemia time and recipient age for follow-up from April 1994 through June 2008.

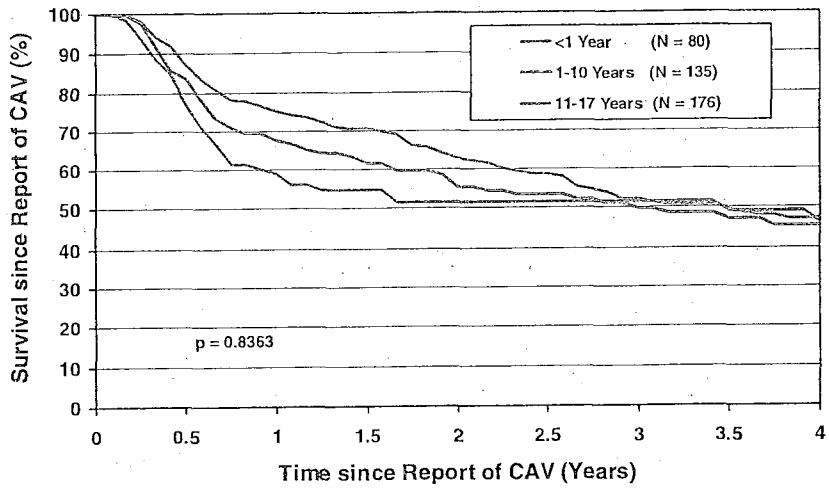

Figure 26. Graft survival after a report of cardiac allograft vasculopathy (CAV) stratified by age group for follow-up from April 1994 through June 2008.

Table 3. Malignancy After Heart Transplantation for Pediatric Recipients, Cumulative Prevalence in Survivors for Follow-up From April 1994 through June 2008

Malignancy and type[a]	1-year survivors No. (%)	5-year survivors No. (%)	10-year survivors No. (%)
No malignancy	3,361 (98.1)	1,343 (95.2)	332 (92.2)
Malignancy (all types)	64 (1.9)	68 (4.8)	28 (7.8)
Lymph	59	64	26
Other	4	5	2
Skin	...	1	...
Type not reported	1	...	...

[a]Patients may have more than one type, thus, sum of types may be greater than total number with malignancy.

Rejection

Despite the increasing use of induction agents, rejection episodes do not appear to have been reduced, at least as recorded after discharge. In fact, 36% of patients rejected after receiving induction therapy compared with 32% of those who received no induction therapy (Figure 11). The increase in rejection episodes with induction therapy was, however, only true for IL-2R antagonists (41% vs 32%), because only a small difference in rejection episodes if a polyclonal anti-lymphocytic antibody was used (35% vs 32%). This effect was noted across all age groups. The adult data are comparable to the pediatric data. Patients receiving cyclosporine at discharge have a 45% incidence of rejection in the first year compared with 27% for those discharged with tacrolimus therapy (Figure 23).

Cardiac Allograft Vasculopathy

Overall, 66% of patients are still free of cardiac allograft vasculopathy (CAV) 10 years after transplant. Age at the time of transplant (Figure 24) has an influence. Patients who undergo transplantation in infancy or early childhood have a reduced incidence of CAV at 8 years after transplant (freedom from CAV of 71% and 74%, respectively) compared with those aged older than 11 years (freedom from CAV 56%).

A short ischemic time of less than 2 hours in children undergoing transplantation when aged younger than 10 years (but not older than 10 years) reduced the freedom from CAV (Figure 25); the explanation for this phenomenon is unclear. Once CAV has occurred, the 3-year graft survival is only 45% for all age groups but then appears to plateau (Figure 26).

Renal Dysfunction

Severe renal dysfunction, defined as a patient requiring renal dialysis, transplant, or with a serum creatinine level more than 2.5 mg/dl (221 μmol/liter), analyzed by the Kaplan-Meier method, shows a linear increase after transplantation, occurring in 11% of pediatric recipients 10 years after transplant. This contrasts with the adult group, in which 60% have severe renal dysfunction by 10 years. The type of CNI selected had no influence on late renal function.

Malignancy

A malignancy had occurred in 8% of patients by 10 years after transplant using the cumulative prevalence in survivor's method (Table 3). In the pediatric age range, almost all malignancies are lymphomas. This contrasts with adults, in whom malignancy is more common (32% by 10 years after transplant) and in which most are skin and other non-lymphoma tumors.

Table 4. Cause of Death in Pediatric Heart Recipients From January 1998 through June 2008

Cause of death	0–30 days (n = 213) No. (%)	31 days–1 year (n = 241) No. (%)	1–3 years (n = 192) No. (%)	3–5 years (n = 153) No. (%)	5–10 years (n = 286) No. (%)	>10 years (n = 165) No. (%)
CAV	2 (0.9)	14 (5.8)	33 (17.2)	43 (28.1)	77 (26.9)	47 (28.5)
Acute rejection	22 (10.3)	45 (18.7)	36 (18.8)	23 (15.0)	36 (12.6)	10 (6.1)
Lymphoma	...	6 (2.5)	7 (3.6)	4 (2.6)	28 (9.8)	11 (6.7)
Malignancy, other	...	1 (0.4)	1 (0.5)	...	4 (1.4)	10 (6.1)
CMV	...	7 (2.9)	1 (0.5)	...	...	...
Infection, Non-CMV	26 (12.2)	31 (12.9)	11 (5.7)	3 (2.0)	13 (4.5)	11 (6.7)
Primary failure	44 (20.7)	9 (3.7)	4 (2.1)	6 (3.9)	10 (3.5)	5 (3.0)
Graft failure	31 (14.6)	25 (10.4)	48 (25.0)	44 (28.8)	66 (23.1)	42 (25.5)
Technical	14 (6.6)	...	2 (1.0)	...	4 (1.4)	1 (0.6)
Other	19 (8.9)	20 (8.3)	24 (12.5)	17 (11.1)	26 (9.1)	10 (6.1)
Multiple organ failure	27 (12.7)	40 (16.6)	10 (5.2)	5 (3.3)	8 (2.8)	8 (4.8)
Renal failure		4 (1.7)	1 (0.5)	1 (0.7)	1 (0.3)	3 (1.8)
Pulmonary	11 (5.2)	27 (11.2)	10 (5.2)	6 (3.9)	7 (2.4)	5 (3.0)
Cerebrovascular	17 (8.0)	12 (5.0)	4 (2.1)	1 (0.7)	6 (2.1)	2 (1.2)

CAV, cardiac allograft vasculopathy; CMV, cytomegalovirus.

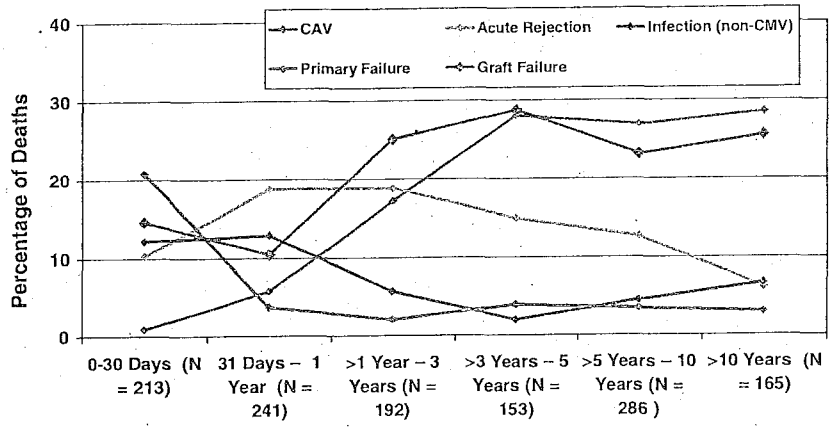

Figure 27. Relative incidence of leading causes of death from January 1998 to June 2008. CAV, cardiac allograft vasculopathy; CMV, cytomegalovirus.

Hypertension

Approximately 69% of patients surviving to 8 years after transplant were documented to have hypertension. By comparison, hypertension had developed in 94% of the adult population 94% by 5 years after transplant.

CAUSE OF DEATH

Nearly 50% of all deaths in the first 30 days after transplant occurred due to graft failure, either primary or secondary to rejection, and technical factors, among others (Table 4); with acute rejection, infection, and multiple organ failure each accounting for about 10% of deaths. Trends in causes of death are shown in Figure 27. Acute rejection remains an ever-present threat, accounting for about 20% of all deaths through 3 years after transplant, with a gradual decline thereafter. CAV and graft failure may well reflect the same pathologic process, that is, individual centers may classify graft failure as CAV and vice versa, but these have traditionally been identified separately in the database. Infection and CAV/graft failure mirror each other, with the risk of infection leading to death declining rapidly after the first year and an increasing number of deaths from CAV/graft failure, which become the leading cause of death (approximately 60% between them) more than 3 years after transplant.

A recent report from Loma Linda University and Children's Hospital[5] similarly identified acute graft dysfunction and technical issues as being implicated in 66% of deaths in the first 30 days after transplant. Their late cause of death was somewhat different, however, with 30% due to acute rejection and 24% to CAV. These differences are likely to relate to ascertainment—the ISHLT Registry data are from many centers, whereas the Loma Linda data were from a detailed retrospective review of all deaths at a single institution with a 75% postmortem rate. This discrepancy highlights the different information from registry and single-center data, with pros and cons of each approach.

In conclusion, this Registry report continues to document the outcome in pediatric heart transplant recipients. It is a registry report, and not a double-blind randomized trial of treatment options and outcomes. The information is therefore imperfect and often poses more questions than answers. The Report will have achieved its objective if it stimulates discussion and suggests areas fruitful for research.

DISCLOSURE STATEMENT

All relevant disclosures for the Registry Director, Executive Committee members and authors are on file with ISHLT and can be made available for review by contacting the Executive Director of ISHLT.

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