Transplant Int (1992) 5 [Suppl 1]: S 138–S 139

TRANSPLANT
International

Factors affecting the long-term outcome following non-living kidney transplantation

J. Thorogood[1,3], J. C. van Houwelingen[3], J. J. van Rood[2], F. A. Zantvoort[1], G. M. Th. Schreuder[2], and G. G. Persijn[1]

[1] Eurotransplant Foundation, Leiden, The Netherlands
[2] Department of Immunohaematology and Blood Bank, Leiden University Hospital, Leiden, The Netherlands
[3] University Department of Medical Statistics, Leiden, The Netherlands

The aims of the study were threefold: (1) to analyse the long-term overall kidney graft survival within Eurotransplant for the period 1971–1987; (2) to examine the effect of matching for HLA over the years, with the aid of half-lives after the first post-transplant year; and (3) to take prognostic factors into account for the period 1981–1987, comparing their influence on the long-term outcome of the graft and to predict half-lives for various combinations of factors.

Key words: Kidney transplantation – Long-term-results

Patients and methods

Data on 12883 first unrelated kidney grafts from non-living donors, transplanted between 1971 and 1987, in 52 renal transplant centres within Austria, Belgium, Germany, Luxembourg and the Netherlands were analysed. Four separate time periods were examined: 1971–1975, 1976–1980, 1981–1984 for patients not treated with cyclosporine (CsA) and 1981–1987 for patients treated with CsA. Estimates of half-lives were obtained from a Weibull model and, for the analysis with prognostic factors, from an exponential model (see Appendix). The half-life estimates the time by which half the grafts would be lost, of those surviving for at least 1 year post-transplant.

Results

Table 1 shows the improvement in graft survival over the years 1971–1987. It can be seen that the half-lives increased by approximately 2 years. The main contribution to better long-term survival came from improvements in the first post-transplant year. Table 2 shows the changes over the years with respect to number of HLA-B mismatches. The effect of matching for HLA was clearly shown to be important even after the first post-transplant year and in patients receiving CsA. Examining previously identified prognostic factors [1], we observed that donor and recipient age and sex, recipient diagnosis of diabetes and number of HLA-B mismatches all remained of prognostic importance in the longer term. Table 3 shows that the half-lives varied from 14.5 years to 4.9 years, depending on the combination of factors for a given patient.

Discussion

Half-lives increased from 9.7 years for 1971–1975 for patients treated without CsA, to 11.6 years for 1981–1987 for patients treated with CsA. The 30% gain in overall 5-year graft survival may be largely attributed to improvements in the first post-transplant year, due to such factors as preoperative blood transfusions, prospective HLA-DR matching and use of CsA. The benefits in prolonged renal allograft survival gained by matching for HLA are maintained in the CsA era. Other factors also affect the long-term outcome, namely donor and recipient age and sex and recipient diagnosis of diabetes. Together with number of HLA-B mismatches, these factors in combination lead to large differences in half-lives, estimates ranging from 14.5 to 4.9 years.

Appendix

The Weibull distribution is a generalization of the exponential distribution, allowing for a power dependence of the hazard on time. The survivor function, $S(t)$, for this distribution is $S(t) = \exp(-(\lambda t)^p)$. The hazard function, $\lambda(t)$, is $\lambda(t) = \lambda p(\lambda t)^{p-1}$ and is monotone decreasing for $p < 1$ and monotone increasing for $p > 1$. For $p = 1$ the Weibull model reduces to the exponential model with constant hazard function $\lambda(t) = \lambda$. In the earlier periods, p was significantly smaller than 1, indicating a decreasing hazard rate. In the final

Supported in part by the Dutch Foundation for Medical and Health Research (MEDIGON), the J. A. Cohen Institute for Radiopathology and Radiation Protection (IRS) and the Kuratorium für Dialyse und Transplantation.

Offprint requests to: Ms. J. Thorogood, Eurotransplant Foundation, University Hospital, PO Box 2304, 2301 CH Leiden, The Netherlands

Table 1. Overall graft survival and half-lives

Period	No. of patients	Graft survival (%)		Half-life (years) (95% confidence interval)
		1 year	5 years	
1971–1975	984	57.0	38.8	9.7 (8.4–11.2)
1976–1980	3065	62.2	43.9	10.7 (9.7–11.7)
1981–1984, without CsA	2002	66.0	49.2	10.7 (9.3–12.4)
1981–1987, with CsA	6832	84.5	66.0	11.6 (10.0–13.4)

Table 2. Graft survival and half-lives by number of HLA-B mismatches and period

No. of HLA-B mismatches	No. of patients	Graft survival (%)		Half-life (years) (95% confidence interval)	Standard normal deviate test on half-lives
		1 year	5 years		
1971–1975					
0 HLA-B	320	63.8	45.3	11.1 (8.7–14.3)	$P = 0.042$
1 HLA-B	490	55.1	37.8	9.7 (7.9–12.0)	
2 HLA-B	174	50.0	29.9	7.2 (5.1–10.1)	
1976–1980					
0 HLA-B	992	65.0	50.0	14.5 (12.3–17.2)	$P = 0.001$
1 HLA-B	1741	61.5	41.2	9.3 (8.3–10.4)	
2 HLA-B	332	57.8	39.5	8.7 (6.7–11.3)	
1981–1984, without CsA					
0 HLA-B	550	65.6	51.1	13.0 (10.0–16.7)	$P = 0.005$
1 HLA-B	1193	66.5	49.3	10.8 (9.1–12.8)	
2 HLA-B	259	64.5	44.4	7.5 (5.6–9.9)	
1981–1987, with CsA					
0 HLA-B	1591	87.1	69.7	13.2 (10.6–16.4)	$P = 0.013$
1 HLA-B	3983	84.3	67.0	12.1 (10.2–14.3)	
2 HLA-B	1258	81.7	58.8	9.0 (7.4–11.0)	

Table 3. Half-lives per prognostic group

No. of HLA-B mismatches	Female donor to male recipient	Diabetic recipient	Donor age > 55 years	Recipient < 16 years	Half lives (95% confidence interval)	No. of patients
0	No	No	No	No	14.5 (12.0–17.5)	881
1	No	No	No	No	13.4 (11.8–15.2)	1997
0	Yes	No	No	No	11.1 (8.8–14.1)	210
2	No	No	No	No	10.4 (8.6–12.5)	588
1	Yes	No	No	No	10.3 (8.5–12.4)	496
0	No	Yes	No	No	8.8 (6.2–12.5)	39
1	No	No	No	Yes	8.7 (6.0–12.6)	79
1	No	Yes	No	No	8.1 (5.8–11.2)	101
2	Yes	No	No	No	8.0 (6.3–10.1)	149
0	No	No	Yes	No	6.9 (4.8–9.9)	48
2	No	No	No	Yes	6.7 (4.6–9.8)	51
1	Yes	No	No	Yes	6.6 (4.5–9.8)	22
1	No	No	Yes	No	6.3 (4.5–8.9)	95
2	No	Yes	No	No	6.3 (4.5–8.8)	65
1	Yes	Yes	No	No	6.2 (4.3–8.9)	26
1	Yes	No	Yes	No	4.9 (3.4–7.0)	44
2	No	No	Yes	No	4.9 (3.4–7.2)	24

period (1981–1987, for patients receiving CsA), p was not significantly different from 1 and the exponential model could be used.

Acknowledgement. This work could not have been undertaken without the generous support of all clinicians and their staff from donor hospitals, transplantation centres and tissue typing laboratories, collaborating within Eurotransplant (for a full list, see Thorogood J et al, Transplantation (1989) 48: 231–238).

Reference

1. Thorogood J, van Houwelingen JC, Persijn GG, Zantvoort FA, Schreuder GMTh, and van Rood JJ (1991) Prognostic indices to predict survival of first and second renal allografts. Transplantation (in press)