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The impact of cytomegalovirus serology for 7-year graft survival in cadaveric kidney transplantation – the Newcastle experience

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Abstract To analyse the contribution of cytomegalovirus (CMV) serology to long-term graft survival in cadaveric kidney transplantation, 404 transplants from a single centre were divided into four subgroups with respect to the combination of donor and recipient CMV antibody status. Graft survival was estimated according to Kaplan-Meier for 1, 3, 5 and 7 years post-transplantation. The single-centre results confirm a negative impact of CMV-positive donor organs for initial graft survival in CMV-negative recipients within the first 3 years after transplantation. However, when 5- and 7-year long-term graft survival was studied, Donor +/Recipient – pairs showed a favourable long-term result, whilst D +/R – pairs had surprisingly a poorer outcome. Therefore, the concept of avoiding transplantation in the D +/R + CMV serology group should be ignored whereas attempts could be made to improve the poor long-term outcome of D +/R + pairs or to reduce its size by organ allocation.

Key words Cytomegalovirus infection · Kidney transplantation · Long-term outcome · Organ allocation · Single centre experience

Introduction

Cytomegalovirus (CMV) serology in donors (D) and recipients (R) is widely thought to have an impact on graft survival in kidney transplantation [5–7]. CMV-positive donor organs are identified as being high-risk transplants in the first 3 post-transplant years, and prophylactic treatment is commonly used in D +/R – pairs to avoid graft and patient loss due to active CMV disease [4, 8, 9]. It is controversial, however, as to whether the CMV serology should be taken into account whilst allocating donated cadaveric kidneys to improve the long-term outcome [11]. This study was conducted to analyse the CMV contribution to graft survival for up to 7 years after transplantation.

Patients and methods

Four hundred and four cadaveric kidney transplants which were performed between 1.1. 1987 and 31.12. 1993 in a single regional centre and whose CMV serology status was known were included in this retrospective study. Overall graft survival was estimated by using the bivariate Kaplan-Meier method. The 95% confidence interval was calculated. Transplants were divided into 4 subgroups with respect to the combination of donor (D) and recipient (R) CMV antibody status (D –/R –, D –/R +, D +/R –, D +/R +. The sample of transplants was representative for the total group in regard to recipient age and HLA mismatch (Tables 2, 3). The graft survival was followed up at 1, 3, 5 and 7 years. Yearly graft loss rates in the different follow-up intervals were estimated.

Results

At the time of retrieval 247 (61.1%) donors had a positive CMV antibody status. Graft survival was 83.3% at 1 year post-transplantation. 75.4% at 3 years, 66.3% at

Table 1 Kaplan-Meier graft survival estimates for cadaveric kidney transplants in Newcastle upon Tyne from 1987 to 1993

Survival period	Donor/recipient CMV serology pair	Number at risk at day 0	Survival estimate (%)	95% Confidence interval
1 year	D −/R −	60	81.5	71.6–91.4
	D −/R +	97	83.3	75.8–90.8
	D +/R −	68	77.8	67.9–87.7
	D +/R +	179	85.9	80.7–91.0
3 years	D −/R −	60	74.4	63.3–85.6
	D −/R +	97	75	66.1–83.9
	D +/R −	68	71.8	61.0–82.5
	D +/R +	179	77.3	71.1–83.6
5 years	D −/R −	60	65.6	52.7–78.4
	D −/R +	97	67.8	57.7–77.9
	D +/R −	68	65.7	53.7–77.7
	D +/R +	179	66	58.4–73.6
7 years	D −/R −	60	56.2	39.9–72.5
	D −/R +	97	53.7	35.9–71.5
	D +/R −	68	56.3	40.5–72.1
	D +/R +	179	48.9	36.7–61.0

5 years and 52.4% at 7 years. There were 179 pairs (44.3%) within the CMV serology subgroup D +/R +. They showed the poorest 7-year survival rate of 48.9% and the highest annual graft loss rate of 6%. The D +/R − subgroup had the poorest 1-year graft survival of 77.8% and improved its ranking to the best graft survival rate of the 4 subgroups at 7 years post-transplantation with 56.3% (Table 1). Recipient age distribution as well as HLA mismatching are listed in Tables 2 and 3.

Discussion

The single-centre results can confirm a trend of a negative impact of CMV-positive donor organs for 1- and 3-year graft survival in CMV-negative recipients, though statistical significance was not achieved. Prophylactic acyclovir treatment was given in the D +/R − subgroup to avoid active CMV-disease-related complications. This was successful in terms of 5- and 7-year graft survival, which were similar to the D − graft survival rates. Although CMV-positive donor organs are widely identified as high-risk transplants, long-term follow-up studies to confirm this observation for the period longer than 3 years post-transplantation are lacking [8]. In this analysis there is a lack of correlation between poor outcome and the D +/R − subgroup after the 5-year period following transplantation, and surprisingly, this combination actually shows the best 7-year graft survival rate with 56.3%. This indicates that the concept of avoiding transplantation in this combination should be ignored as long as early graft loss due to active CMV disease can be avoided by prophylactic and therapeutic CMV treatment. The poor 7-year long-term outcome of the D +/R + subgroup in a single centre with a graft survival rate of only 48.9% is certainly unsatisfactory. Factors contributing to the graft loss in this particular group

Table 2 Recipient ages (years) for cadaveric kidney grafts of each cytomegalovirus (CMV) serology group in Newcastle upon Tyne

CMV	0–9	10–19	20–29	30–39	40–49	50–59	60–69	> 69	Total
D −/R −	8	5	16	13	9	8	1	0	60
D −/R +	2	3	8	13	28	25	15	3	97
D +/R −	2	4	16	13	16	11	6	0	68
D +/R +	1	5	19	26	38	51	33	6	179
Total	13	17	59	65	91	95	55	9	404

Table 3 HLA mismatch for cadaveric kidney grafts of each cytomegalovirus (CMV) serology group in Newcastle upon Tyne

	CMV serology D −/R −	CMV serology D −/R +	CMV serology D +/R −	CMV serology D +/R +	Total group
Number of HLA mismatches					
0–2	35 (58.3%)	50 (51.5%)	35 (51.5%)	83 (45.8%)	203 (50.3%)
3–4	24 (40.0%)	47 (48.5%)	29 (42.6%)	91 (50.8%)	191 (47.3%)
5–6	1 (1.7%)	0 (0%)	4 (5.9%)	5 (2.8%)	10 (2.5%)
Total	60	97	68	179	404
Number of DR mismatches					
0	38 (63.3%)	63 (65.0)	41 (60.3%)	115 (64.3%)	257 (63.6%)
1	18 (30.0%)	26 (26.8%)	25 (36.8%)	53 (29.6%)	122 (30.2%)
2	4 (6.7%)	8 (8.2%)	2 (2.9%)	11 (6.1%)	25 (6.2%)
Total	60	97	68	179	404

need to be analysed further. These patients are certainly susceptible for active CMV disease and long-term graft damage caused by CMV since a positive CMV antibody status does not protect from reinfection with a different virus strain [2, 3]. They also carry the highest viral load of all four subgroups, which in combination with the immunosuppression and the inefficiency of the recipient immune system to clear the virus from the allograft cells due to HLA mismatch could account for subsequent graft loss [1, 10]. We found similar trends and even statistical significance in a larger study including the long-term outcome of all cadaveric kidney transplants performed in the UK and the Republic of Ireland (manuscript in preparation). It seems necessary to improve graft survival in this D +/R + subgroup of renal transplants which was not specifically addressed before. These patients may also benefit from prophylactic antiviral treatment. In addition, efforts could possibly be made to reduce the size of this subgroup with the poorest long-term outcome by organ allocation.

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