Transplant Int (1992) 5 [Suppl 1]: S32–S34

TRANSPLANT
International


# Renal retransplantation in patients with HLA-antibodies

**L. Mjörnstedt[1], J. Konar[2], G. Nyberg[1], M. Olausson[1], L. Sandberg[2], and I. Karlberg[1]**

[1] Transplant Unit and [2] Blood Centre, Sahlgrenska Hospital, University of Göteborg, Sweden

**Abstract.** The results of 92 consecutive renal retransplantations, performed during a 5-year period in recipients with HLA-antibodies, were retrospectively analysed. The actuarial 1-year graft survival (1-y GS) was 65% for all retransplantations, as compared with 63% for first grafts in sensitized recipients. For the second ($n = 56$), third ($n = 24$) and fourth-fifth ($n = 12$) grafts 1-y GS was 64%, 71% and 58%, respectively. Acute rejection was the major cause of graft loss (45%). Recipients with > 3 years GS of the preceding transplant had significantly better GS at retransplantation. Also, grafts with no HLA mismatches had significantly prolonged GS. One-y GS was 78% when PRA (panel reacting antibody) was less than 50%, and 60% when PRA was more than 50%. A benefit of repeated mismatches was demonstrated in the subgroup with PRA < 50%, in contrast to recipients with PRA > 50%, suggesting that, in some patients, an absence of antibody response against certain antigens might be used as a basis for future deliberate mismatching.

**Key words:** Renal retransplantation – HLA antibodies – Graft survival

Regrafting and the presence of HLA-antibodies are factors, which alone or taken together have been reported to impair kidney graft survival [1, 5]. The purpose of the present study was to analyse consecutive renal retransplantations, performed in recipients with preformed HLA-antibodies in our centre during a 5-year period.

## Materials and methods

During 1985–89, 92 renal retransplantations were performed in Göteborg in patients with preformed HLA-antibodies. Of these patients, 56 (61%), were second grafts, 24 (26%) third, 10 (11%) fourth and 2 (2%) fifth grafts. All grafts but one were cadaveric (CD). Cross matches (CM) with the lymphocytotoxicity test against T and B cells were negative in historical and current symples. Mean cold ischaemia time was 22.1 ± 0.6 h in a range of 9–39 h (CD only). Triple-drug basal immunosuppression with cyclosporine A (CyA) + azathioprine (Aza) + Prednisolone (Pred) was used in 87 (95%) transplantations, Cya + Pred in four cases, and Aza + Pred in one case. ATG induction therapy was given in 47 (51%) transplantations. A group of 38 primary transplantations, also performed in presensitized recipients during this period, was in certain instances used for comparison. The follow-up time was 1–6 years.

### *Patients*

A majority of the recipients were male (67%) and on haemodialysis (69%). The causes of uraemia were: glomerulonephritis (38%), diabetes (14%), chronic pyelonephritis (13%) and polycystic kidney disease (13%). More than 50% panel reacting antibodies (PRA) in current sera were found in 71% of the patients and less than 50% in 25%. Reactivity only against B cells was found in 4% of patients, while 36% of the recipients had a remaining previous graft at the time of transplantation.

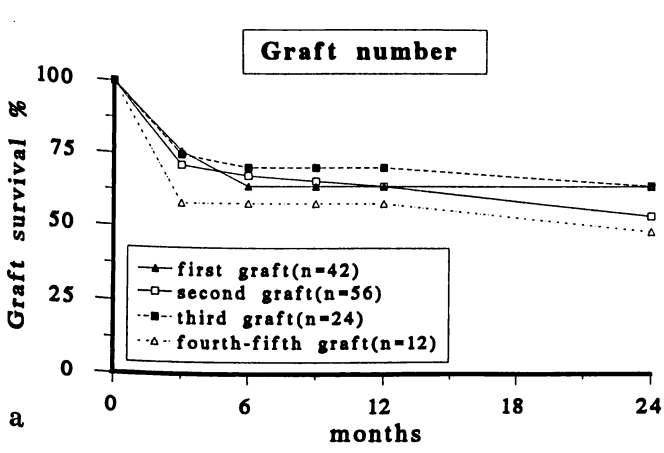
### *Statistical methods*

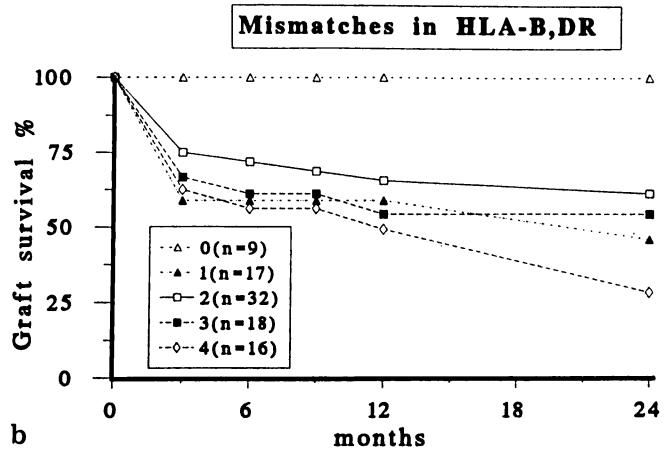
Actuarial graft and patient survival probabilities were estimated by the Kaplan-Meier method. A log-rank test (Mantel-Haenszel) was used to test the equality of survival curves.

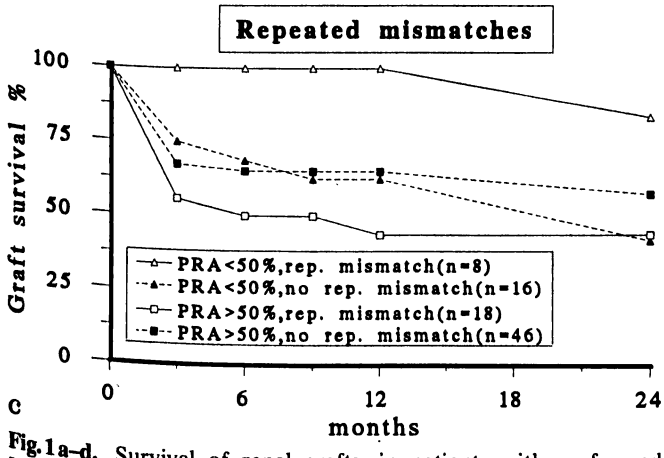
## Results

For all retransplantations in PRA plus patients taken together, 1-, 2- and 3-year graft survival (1-, 2- and 3-y GS) was 65%, 56% and 45%. No statistically significant difference in GS was seen between second, third or fourth-fifth grafts and the survival curves of regrafts were similar to those of primary grafts in presensitized recipients (Fig. 1a). The causes of regraft loss within the follow-up time were: acute rejection ($n = 22$, 45%); 'chronic rejection' ($n = 13$, 27%); patient death ($n = 8$, 16%); or technical, infectious or other reasons ($n = 6$, 12%). The patient

*Offprint requests to:* Lars Mjörnstedt, M. D, Ph. D., Transplant Unit, Department of Surgery, Sahlgrenska Hospital, S-413 45 Göteborg, Sweden



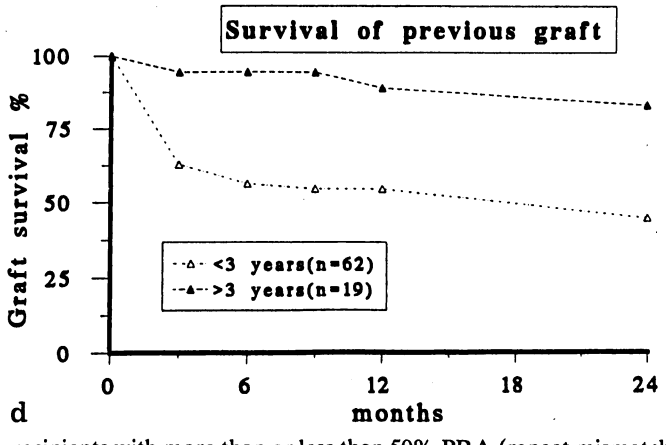




**Fig. 1a–d.** Survival of renal grafts, in patients with preformed HLA antibodies, transplanted in Göteborg 1985–89. Graft survival is shown in relation to: **a** the graft number; **b** the number of mismatches in HLA-B, DR loci (0 vs 1–4 mismatches; $P < 0.05$); **c** the presence or absence of repeated HLA-A, B or DR mismatches in recipients with more than or less than 50% PRA (repeat mismatch vs no repeat mismatch; $P < 0.05$ for PRA < 50%; n.s. for PRA > 50%); **d** the survival time (less than or more than 3 years) of the previous graft ($P < 0.01$)

survival after retransplantation was 92%, 86% and 81% after 1, 2 and 3 years.

The proportion of highly sensitized (> 50% PRA) recipients increased after regrafting (Table 1). Patients given their fourth-fifth grafts had the largest proportion of grafts with more than 24 h ischaemia time, grafts lost due to acute rejection and well matched grafts, and were more often male than female (Table 1).

In the regrafted group the influence of various parameters on GS was analysed. In recipients with < 50% PRA ($n = 26$), 1-, 2- and 3-y GS was 78%, 78% and 60%, as compared with 60%, 54% and 41% in those with > 50% PRA ($n = 62$). There was a better GS when no mismatches were present in the HLA-B, DR loci (Fig. 1b). A similar, but not statistically significant, benefit of 0 vs > 0 mismatches was seen with matching for the HLA-A + B + DR or HLA-DR. In highly sensitized patients repeat mismatch gave a 1-y GS of 43%, whereas a beneficial effect of repeat mismatch was seen in eight patients with PRA < 50% (Fig. 1c). A significant difference in GS was observed between recipients who had lost their previous graft in rejection after less than 3 years, compared with those with more than 3 years function (Fig. 1d). Other factors, such as ATG induction therapy, cold ischaemia time more than 24 h, and remaining previous graft at the time of transplantation, did not influence GS significantly.

## Discussion

In the present report the survival rate of second and subsequent grafts was similar to first grafts in presensitized recipients, consistent with other reports [1]. This was true despite the fact that the group of regrafted recipients had a higher proportion of highly sensitized recipients and a tendency for longer graft ischaemia as compared with primary grafts. However, in the fourth-fifth grafted group better HLA-matching was obtained, possibly compensating for the other risk factors. A benefit of zero mismatches was demonstrated, particularly when matching for the HLA-B, DR loci. This finding is supported by previous studies [3], whereas others have reported conflicting results [1]. It has been suggested that transplantation across previous mismatches should be avoided, since it increases the risk of early graft loss [2]. In the present report the small subgroup of patients with PRA < 50% showed significantly better survival of kidneys bearing prevous mismatches, as compared with organs without such antigens. Other centres have reported successful retransplantations with the policy

**Table 1.** Proportions (%) of various parameters in groups of first or repeated renal transplantations in recipients with performed HLA-antibodies

| | First graft ($n = 38$) | Second graft ($n = 56$) | Third graft ($n = 24$) | Fourth-fifth graft ($n = 12$) |
|---|---|---|---|---|
| PRA > 50% | 45 | 69 | 67 | 83 |
| Cold ischemia time > 24 h | 35 | 37 | 35 | 56 |
| Graft loss due to acute rejection | 47 | 42 | 40 | 63 |
| 0–1 mismatches in HLA-B, DR | 24 | 25 | 21 | 58 |
| Male recipients | 47 | 55 | 75 | 92 |

of allowing repeated mismatches, provided no antibody response against these antigens had previously been detected [6]. As also shown, but not concluded, in the latter report, a majority of the recipients with successful transplantations had no or < 50% PRA. The lack of antibody responses against previously-presented foreign HLA antigens could perhaps therefore be used as a basis for 'intelligent mismatching' in the subsequent transplantations. The duration of the previous graft survival was another factor, which in this and earlier [4] reports was found prognostic for the survival of retransplants.

We conclude that in many cases retransplantation of CM-negative kidneys to presensitized patients could be justified. For this group of patients the international programs for kidney exchange are probably even more important, making it possible to obtain HLA-compatible, or in the future perhaps 'intelligently mismatched', organs.

*Acknowledgement.* This study was supported by grants from The Professor L-E. Gelin Memorial Foundation, Föreningen för njursjuka i Väst-Sverige och Riksförbundet för njursjuka.

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