Influence of HLA AB and DR antigen matching in transfused cadaver renal transplant patients[1]

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This is a retrospective analysis of the results of HLA AB and DR antigen matching in 56 transfused cadaver transplant patients. Maintenance immunosuppression in these patients comprised Imuran, prednisone, and an initial two-week course of ALG. Matching for HLA AB or DR antigens alone failed to yield subgroups with significant differences in graft outcome. However, with combined HLA AB and DR matching criteria, a subgroup of 0 DR, < 2 AB matched recipients was identified with significantly diminished graft survival. These preliminary data support a role for tissue matching in cadaver transplantation and suggest that combined matching for HLA AB and DR antigens may be more useful than matching for either alone.

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Conflicting data from both European and North American centers have been published on the role of matching for histocompatibility locus (HLA) A and B antigens in cadaver renal transplantation.[1–5] By comparison, a more widespread consensus appears to be emerging regarding the importance of matching for HLA DR antigens. Since the early report by Ting and Morris,[6] several studies have demonstrated improved cadaver allograft success with better DR matched donor kidneys, particularly when the donor and recipient share both identified DR antigens.[7–10] Some authors have suggested that the beneficial effect of DR matching may equal or outweigh the acknowledged importance of preliminary blood transfusions in cadaver renal transplantation.[9,10] The present retrospective study

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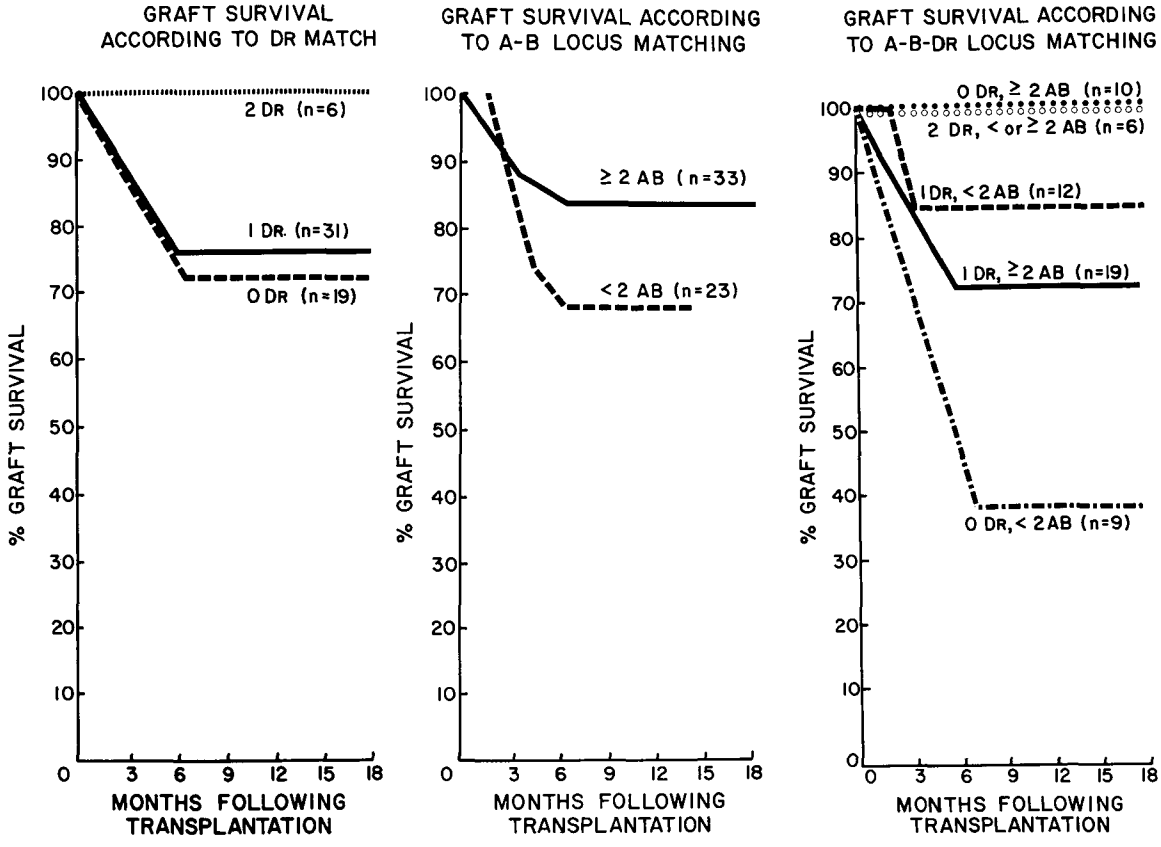

Figure 1. Graft survival according to matching for HLA DR antigens.
Figure 2. Graft survival according to matching for HLA A and B antigens.
Figure 3. Graft survival according to matching for HLA AB and DR antigens.

was undertaken to more clearly define the combined role of HLA AB and DR antigen matching in transfused cadaver allograft recipients.

Materials and methods

Serological typing for HLA A, B, and DR locus antigens was done in 56 cadaver donor-recipient pairs as defined in the 1980 Histocompatibility Workshop.[11] Donor-recipient HLA matching was on a scale of 0–2 and 0–4 for DR and AB locus antigens, respectively, according to the number of shared antigens. Blank alleles were considered as undefined antigens and not assumed to be compatible, although it is possible that detection of only one antigen may, in some cases, have represented homozygosity for that antigen. There were 48 first graft and 8 second graft recipients who underwent transplantation between January 1980 and September 1981. All patients had received one or more blood transfusions prior to transplantation. All cadaver kidneys were harvested with a warm ischemia time less than 10 minutes and preserved under hypothermic pulsatile perfusion with Plasmanate. Postoperatively, these patients were managed with a maintenance immunosuppressive regimen including Imuran, prednisone, and an initial 14-day course of Minnesota antilymphoblast globulin (ALG). The preparation and testing of the latter drug are described elsewhere.[12] Episodes of acute rejection were treated with either a second 10-day course of ALG or high-dose steroids in the form of intravenous methylprednisolone.

Results

The interval following transplantation in these patients ranges from 10 to 30 months, and complete follow-up information has been obtained in all patients. Graft and patient survival rates were determined by actuarial calculation.[13] Graft loss was calculated on the basis of the date of transplant nephrectomy or the date the patient was returned to maintenance dialysis. Patient mortal-

ity from any cause was also considered a graft loss.

In the present series, overall patient and graft survival at one year was 88% and 78%, respectively. *Figure 1* illustrates the influence of DR matching alone on graft success in these patients. One-year graft survival in recipients of 0 DR (n = 19), 1 DR (n = 31), and 2 DR-matched (n = 6) grafts was 73%, 75%, and 100%, respectively. In considering the role of HLA AB matching alone, one-year graft survival in recipients of < 2 AB (n = 23) and ≥ 2 AB (n = 33) matched grafts was 68% and 84%, respectively (*Fig. 2*).

Figure 3 demonstrates the effect of combined HLA AB and DR matching on graft survival. In the category of 1 DR matched recipients, those with < 2 AB (n = 12) and ≥ 2 AB (n = 19) matched grafts had equivalent one-year graft survival rates of 83% and 72%, respectively. However, among 0 DR matched recipients, those with < 2 AB (n = 9) and ≥ 2 AB (n = 10) matched grafts had significantly different one-year graft success rates of 37% and 100%, respectively ($p < .02$). Graft survival in the 0 DR, < 2 AB matched group was also significantly different ($p < .05$) from that observed in the 2 DR matched group. Although the graft success rate was much lower in 0 DR, < 2 AB matched recipients compared to 1 DR matched recipients (37% versus 75%), the sample size at this time precludes a statistically significant difference.

Discussion

The role of HLA DR antigen matching in cadaver transplantation is currently being evaluated in many centers. Initial reports from Europe[6–9] and North America[10] have indicated improved graft survival with better DR matched donor kidneys. One international multicenter study[5] showed no correlation between graft success and the number of mismatched or shared DR locus antigens; however, in considering only North American transplant centers, graft survival was significantly better in 0 versus 1 or 2 DR mismatched grafts. In a recent editorial, Svejgaard[14] suggested that criteria which combine HLA AB and DR antigen matching may ultimately prove most beneficial in determining suitable cadaver donor-recipient combinations.

In considering other determinants of cadaver transplant success, the evidence supporting a beneficial effect of preliminary blood transfusion is overwhelming.[15] In our program, a recent controlled prospective randomized study also demonstrated significantly better graft survival in recipients treated with an adjunctive initial 14-day course of ALG compared to those managed with Imuran and prednisone alone.[16] The purpose of the present study was to evaluate a possible superimposed influence of HLA A, B and DR antigen matching in transfused cadaver patients with received prophylactic ALG.

In this analysis, matching for HLA AB or DR antigens alone failed to yield subgroups with significant differences in graft outcome, although graft success was improved in 2 DR versus < 2 DR and ≥ 2 AB versus < 2 AB matched recipients. However, by combining HLA AB and DR matching criteria, a subgroup of 0 DR, < 2 AB matched recipients was identified with particularly diminished graft survival. These preliminary data support the role of tissue matching in cadaver transplantation, even among transfused patients receiving prophylactic ALG, and suggest that combined matching for HLA AB and DR antigens may be more useful than matching for either alone.

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