Current status of HLA matching in renal transplantation

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Summary. The impact of HLA compatibility on the success rate of kidney transplants was studied in over 80,000 recipients of primary transplants. The transplants were done from 1982 to 1991 at over 300 transplant centers in 43 countries. The results show that matching the HLA chromosomes in related donor transplants has a striking influence. It is also important that matching for individual HLA antigens in cadaver transplants provides a highly significant improvement in graft survival ($P < 0.0001$). After 5 years, matched grafts have a survival rate approximately 20% higher than completely mismatched grafts. The matching effect is particularly strong in presensitized and second graft recipients. There is now direct evidence that even if it is necessary to transport well-matched kidneys a long way, they have a significantly higher success rate than locally transplanted poorly matched kidneys. New data based on molecular technology show that the precise identification of HLA-DR antigens by DNA typing further improves the success rate of HLA-matched transplants.

Key words: HLA matching – Renal transplantation – DNA typing

Whether HLA matching should be utilized to improve the success rate of cadaver kidney transplantation continues to be disputed, especially in the United States [1]. Because of the HLA system's great polymorphism, it is difficult to perform perfectly matched cadaver transplants. Most single-center analyses therefore contain small numbers of well-matched grafts which are subject to considerable statistical variation [2]. For a scientifically valid assessment of the impact of HLA matching on graft survival it is necessary to compare large numbers of poorly or well-matched grafts. This recognition led to the initiation 10 years ago of the Collaborative Transplant Study. Currently, more than 300 kidney transplant centers in 43 countries are participating in this unparalleled collaborative scientific effort. This report provides an overview of the results obtained with transplants performed during the 10-year period from 1982 to 1991. Moreover, an update on the results of a recent collaborative substudy employing modern DNA typing technology is given.

Methods

Data were provided on a voluntary basis by more than 300 transplant centers in 43 countries. HLA typings were performed by serological methods at the individual transplant centers' tissue typing laboratories and reported to the study center at the University of Heidelberg for analysis. DNA typings were performed by the restriction fragment length polymorphism (RFLP) method at eight participating laboratories [3]. Clinical follow-up information was obtained at 3, 6, 9, and 12 months, and at yearly intervals thereafter. Graft survival rates were computed by the Kaplan-Meier method. No exclusions were made. Patients dying with functioning grafts were counted as graft failures.

Results

Figure 1 illustrates the impact of matching for the HLA chromosome on kidney graft outcome. Transplants from HLA-identical sibling donors (both HLA chromosomes matched between recipient and donor) have the best survival rate, followed by one-haplotype matched related donor grafts (one HLA chromosome matched, the second HLA chromosome mismatched); cadaver donor transplants (mismatched for both HLA chromosomes) have the lowest graft survival.

Figure 2 illustrates the impact of matching for the HLA-A, -B, and -DR antigens on the survival rate of first cadaver donor transplants. It is evident that the graft survival rate decreases as the number of HLA mismatches increases. At 5 years, grafts with no mismatches have a 20% high-
Fig. 1. Actuarial graft survival rates for HLA-identical sibling (HLA-ID SIB) transplants, HLA one-haplotype matched related (1-HAPL REL) transplants, and cadaver donor transplants. Only first transplants were analyzed.

Fig. 2. Impact of mismatching for HLA-A, -B, and -DR antigens in first cadaver kidney transplants. Transplants in which both recipient and donor were typed for the best-defined HLA-A and -B antigen specificities (splits) were included in the analysis. MM, number of mismatched antigens. The numbers of patients studied are indicated for each mismatch category. Statistical significance: $P$ regression < 0.0001.

Fig. 3. Long-term estimation of graft survival according to the number of HLA-A, -B, and -DR mismatches (MM) in first cadaver transplants. The half-life of zero mismatch grafts is nearly twice as long as that of six mismatch grafts.

...er survival rate than grafts with six mismatched HLA antigens.

To estimate long-term attrition rates, it is appropriate to plot these data on a semilogarithmic scale. Because the long-term failure rate is constant from year to year, it is possible to make reliable 10-year estimations of graft survival. As shown in Fig. 3, grafts with no HLA-A, -B, and -DR mis-