

TWELVE YEARS' EXPERIENCE WITH NATIONAL SHARING OF HLA-MATCHED CADAVERIC KIDNEYS FOR TRANSPLANTATION

STEVEN K. TAKEMOTO, PH.D., PAUL I. TERASAKI, PH.D., DAVID W. GJERTSON, PH.D., AND J. MICHAEL CECKA, PH.D.

ABSTRACT

Background In October 1987, the United Network for Organ Sharing (UNOS) established a national kidney-sharing program to increase the number of HLA-matched transplantations. Since then, over 7500 cadaveric kidneys have been shipped to centers in 48 states for transplantation to HLA-matched patients. We evaluated the efficacy of the program during its first 12 years of operation.

Methods We compared the rates of rejection and actuarial graft survival for 7614 HLA-matched and 81,364 HLA-mismatched cadaveric kidney transplantations reported to the UNOS Scientific Registry between October 1987 and September 1999. To assess the effects of the extended period of ischemia associated with shipping HLA-matched kidneys, we identified 3562 pairs of cadaveric kidneys in which one kidney went to an HLA-matched recipient and the other went to an HLA-mismatched recipient.

Results The estimated 10-year rate of graft survival was 52 percent for HLA-matched transplants, as compared with 37 percent for HLA-mismatched transplants. The estimated half-lives of the transplants were 12.5 years and 8.6 years, respectively, and the mean duration of cold ischemia was 23 hours and 22 hours, respectively. After adjustment for the effects of demographic characteristics, at 10 years the overall rates of graft survival and the rates of functional-graft survival (with data censored on patients who died with a functioning graft) were 10 percent and 11 percent higher, respectively, for HLA-matched transplants than for HLA-mismatched transplants. Among 3562 pairs of kidneys, HLA-matched transplants had higher rates of survival, a lower incidence of episodes of rejection, and a lower risk of loss as a result of rejection.

Conclusions A superior graft outcome with little increase in the duration of cold ischemia justifies national sharing of HLA-matched kidney transplants. (N Engl J Med 2000;343:1078-84.)

©2000, Massachusetts Medical Society.

THROUGH an agreement among U.S. transplantation centers, the United Network for Organ Sharing (UNOS) established a program in 1987 to ship kidneys anywhere in the United States to a recipient who had the same HLA-A, B, and DR antigens as the donor. By September 1999, 7614 HLA-matched kidney transplantations had been performed. Despite concern about the cost effectiveness and value of this program, the results of the first 1386 HLA-matched transplantations were very promising.¹ Since that time, there have

been substantial improvements in immunosuppression protocols, the criteria for the acceptance of organs have been broadened to include older donors,² and the definition of an HLA-matched kidney has been expanded.³ We therefore reexamined the results of the national kidney-sharing program after more than 10 years of operation and compared the survival rates of HLA-matched and HLA-mismatched kidney transplantations.

METHODS

According to the UNOS Scientific Renal Transplant Registry, 7614 patients received kidney transplants from HLA-matched donors and 81,364 patients received kidneys from HLA-mismatched donors through September 1999. The 10 factors with the most influence on graft survival were the recipient's race, age, level of reactive HLA antibodies before transplantation (defined as the percentage of a panel of normal-donor cells that reacted with the recipient's serum — that is, the panel-reactive antibody value),⁴ number of previous transplantations, and the cause of end-stage renal disease; the transplantation center; the donor's age and cause of death (excluding trauma); the duration of cold ischemia; and the year of transplantation.⁵ The distributions of these covariates among the HLA-matched and HLA-mismatched patients and donors are summarized in Table 1. The mean (\pm SD) duration of cold ischemia was 23 ± 8 hours for the patients who received HLA-matched kidneys, as compared with 22 ± 10 hours for the patients who received HLA-mismatched kidneys ($P < 0.001$). More than 83 percent (6387 of 7614) of the HLA-matched kidneys were shipped by the organ-procurement organization for transplantation at a distant transplantation center, whereas 77 percent (62,895 of 81,364, $P < 0.001$) of the HLA-mismatched kidneys were shipped within the organization's local service area.

The HLA-matching criteria were modified twice during the program. Initially, all six HLA-A, B, and DR antigens (two antigens at each locus) had to be identical in the donor and the recipient. In August 1990, donors and recipients who were both homozygous for the same loci were considered to be phenotypically matched for HLA antigens. Finally, in March 1995, the criteria were expanded further to include any donor who had no HLA-A, B, or DR antigens that were not also detected in the recipient (referred to as no mismatches); in other words, the recipient was matched with respect to these HLA antigens, but the recipient could still have had antigens that were not present in the donor. Microcytotoxicity tests were used for HLA typing in the majority of donors,⁴ and kidneys were allocated on the basis of the results of tests at 14 HLA-A loci, 45 HLA-B loci, and 10 HLA-DR loci.

To analyze the effect of the extended duration of cold ischemia associated with nationwide shipping of organs, we identified pairs of kidneys from 3562 cadaveric donors in which one kidney was transplanted into an HLA-matched recipient and the other kidney into an HLA-mismatched recipient. We also used these pairs to determine whether shipping was associated with delayed graft

From the United Network for Organ Sharing Scientific Renal Transplant Registry and the Department of Pathology, University of California at Los Angeles, Los Angeles. Address reprint requests to Dr. Takemoto at the Department of Pathology, UCLA, 950 Veteran Ave., Los Angeles, CA 90095, or at stakemot@ucla.edu.

TABLE 1. CHARACTERISTICS OF THE PATIENTS ACCORDING TO WHETHER THEY RECEIVED AN HLA-MATCHED OR AN HLA-MISMATCHED KIDNEY TRANSPLANT.*

CHARACTERISTIC	HLA-MATCHED TRANSPLANT (N=7614)	HLA-MISMATCHED TRANSPLANT (N=81,364)	P VALUE
Recipient			
Female sex (%)	43	39	<0.001
Race (%)			<0.001
White	83	61	
Black	8	25	
Other	9	14	
Age (yr)	44±14	43±14	<0.001
Diabetes mellitus (%)	24	25	0.02
Panel-reactive antibody level (%)†			<0.001
0–10%	59	66	
11–40%	14	17	
41–80%	10	7	
>80%	14	6	
Previous transplantation (%)	21	12	<0.001
Donor			
Death not due to trauma (%)	59	64	<0.001
Age (yr)	34±16	33±16	<0.001
Transplant			
Duration of cold ischemia (hr)	23±8	22±10	<0.001
Transplantation center (%)‡			<0.001
Top 20 centers	9	10	
Middle 140 centers	78	76	
Bottom 20 centers	9	10	
Year of transplantation (%)			<0.001
1987–1990	13	28	
1991–1995	44	45	
1996–1999	43	27	

*Plus-minus values are means ±SD. To allow for multiple comparisons, only P values of less than 0.002 were considered statistically significant.

†The values are the percentage of a panel of normal-donor cells that reacted with a transplant recipient's serum. Because of missing data, the percentages do not total 100.

‡The centers in this analysis had each performed at least 100 transplantations. Centers are ranked according to the five-year rates of graft survival. Data from centers that performed fewer than 100 transplantations were excluded from the analysis.

function (defined as anuria on the day after transplantation or the need for dialysis during the first week after surgery), episodes of rejection, or graft failure.

We used the Kaplan-Meier product-limit method for univariate analyses of survival. We determined statistical significance by making log-rank comparisons of survival curves using two-sided P values. We calculated half-lives of grafts at one year, assuming that the rate of failure was constant thereafter, as previously described.⁶ A multifactor analysis of the variables listed in Table 1 was performed with the use of Cox proportional-hazards analysis. We examined the proportional-hazards assumption by plotting the graft-survival curves for each subgroup of a covariate on a log-log scale. (For continuous variables, we created four to five equal-sized groups for diagnostic comparisons.) Since the curves appeared reasonably parallel, we regarded the proportional-hazards model as appropriate. Data on patients who died with a functioning graft were censored at the time of death in the calculation of the survival of functional grafts. The effects of the ages of the recipients and the donors were approximated with both linear and quadratic terms.⁵ We used Stata statistical software (College Station, Tex.) for all statistical analyses.

RESULTS

Before the kidney-sharing program was initiated, only 2 percent of transplants were HLA-matched. After the program was initiated, 5 percent of kidneys were transplanted in HLA-matched recipients with use of the six-antigen matching criteria. Use of the phenotypic criteria increased the percentage to 7 percent, and use of the no-mismatch criteria increased it to 13 percent. The survival rate of HLA-matched kidney transplants was similar regardless of the criteria by which they were selected. A total of 3375 transplants were matched for six HLA antigens, 1336 were phenotypically matched, and 2903 had no mismatches. For each type, the survival rates were significantly higher than those for HLA-mismatched transplants ($P<0.001$) (Fig. 1). The similar rates of graft survival among the HLA-matched subgroups indicate that HLA typing techniques were sufficiently accurate that a missing antigen could be interpreted as implying homozygosity rather than the failure to detect the antigen.

The estimated half-life of the entire group of HLA-matched transplants was 12.5 years, significantly longer than the estimate of 8.6 years for the group of HLA-mismatched transplants ($P<0.001$). The estimated 10-year rate of graft survival for the HLA-matched transplants was 52 percent, as compared with a rate of 37 percent for the HLA-mismatched transplants ($P<0.001$).

Although there were no significant differences in the long-term rates of graft survival among the subgroups of HLA-matched transplants, the adoption of the expanded criteria in 1995 broadened the number of HLA-matched recipients that could be identified. Therefore, the rate of transplantation of HLA-matched cadaveric kidneys increased from 7 percent in 1994 to 13 percent in 1995, coincident with the change in criteria.

During the study period, the proportion of kidneys from older cadaveric donors increased steadily in response to the increasing demand for transplants. In 1988, 6 percent of transplanted cadaveric kidneys were from donors over the age of 55 years, and that fraction increased to 13 percent in 1997. The donor's age had a significant effect on long-term graft survival. The 10-year rate of graft survival among recipients of HLA-matched kidneys declined with increasing donor age: the rate was 68 percent among patients whose donor was 15 years of age or younger and 32 percent among those whose donor was older than 55 years. The difference in 10-year rates of graft survival between HLA-matched and HLA-mismatched recipients was greatest (28 percent) among those whose donor was 15 years of age or younger and least (10 percent) among those whose donor was older than 55 years.

Table 2 lists the estimated half-lives of grafts according to several factors that influence long-term survival.

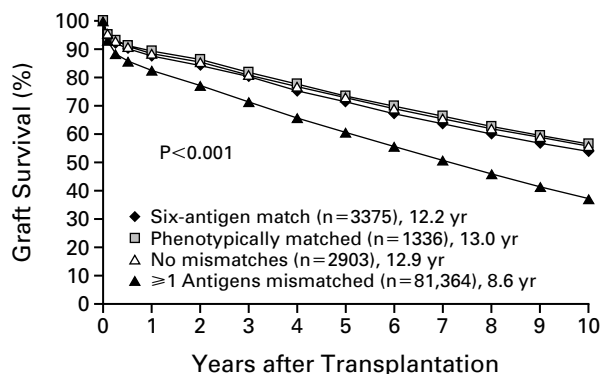


Figure 1. Estimated Rates of Graft Survival among Recipients of HLA-Matched Cadaveric Kidneys Chosen with the Use of Three Different Matching Algorithms and Recipients of HLA-Mismatched Transplants.

There were no significant differences in survival among the three subgroups of HLA-matched grafts. The difference in survival between each subgroup of HLA-matched transplants and the HLA-mismatched transplants was significant ($P<0.001$). The estimated half-life of the grafts in each group is shown.

al of transplants. Transplantations performed between 1994 and 1999 were also analyzed separately because both short- and long-term rates of graft survival improved during this period. Although the variations attributable to each of these factors are made evident by the differences in the graft half-lives, the long-term results for HLA-matched transplants were better for each period.

One group of HLA-matched recipients in which there was no significant improvement in the half-life of grafts for the period from 1994 to 1999 was black recipients. We compared various factors among the HLA-matched black recipients and white recipients and found that blacks were more often matched for blood type (A, B, or O) than were whites (62 percent vs. 58 percent, $P=0.03$), more often received a kidney from a donor whose death was not related to trauma (46 percent vs. 40 percent, $P=0.003$), and more often received a kidney for which the duration of cold ischemia was less than 24 hours (63 percent vs. 58 percent, $P=0.007$). Blacks also more often received matched kidneys from donors with no HLA-A, B, or DR antigen mismatches (59 percent vs. 35 percent, $P<0.001$). The factor with the greatest effect on the outcome of transplantation among HLA-matched black recipients was hypertension as the cause of end-stage renal disease. Among hypertensive black recipients of an HLA-matched kidney, the half-life of the transplant was 5.2 years, as compared with 10.8 years for black recipients with other renal diseases ($P=0.005$). Among HLA-matched white recipients, there was no significant difference in the half-life of the transplant between those with hypertension and

those with other causes of renal failure (13.4 vs. 12.8 years, $P=0.39$).

The benefit of HLA matching was most evident at the 20 transplantation centers that had each performed more than 100 cadaveric kidney transplantations overall and had the highest overall rates of five-year graft survival (Table 2). The graft half-life of 11.8 years among HLA-mismatched transplants at these centers was similar to the graft half-life of 12.5 years among HLA-matched transplants as a whole. The graft half-life of 22.6 years among HLA-matched transplants at the 20 centers translates into a difference in 10-year rates of graft survival of 18 percentage points (66 percent for HLA-matched transplants, as compared with 48 percent for HLA-mismatched transplants).

The effect of 11 covariates on the relative likelihood of graft loss between 1 and 10 years after transplantation and of the loss of a functional graft, with data on patients who died with a functioning graft censored, is shown in Table 3. The risk of graft loss was 38 percent higher among recipients of HLA-mismatched transplants than among recipients of HLA-matched transplants. After data on patients who died with a functioning graft were censored, HLA mismatching increased the risk of graft loss by 55 percent. The risk attributed to continuous variables is given as the increased hazard for each increase of one standard deviation above the mean. For example, the mean duration of cold ischemia was 23 ± 8 hours for HLA-matched kidneys. The risk of functional-graft loss was 4 percent higher among transplants with 31 hours of cold ischemia than among those transplanted within 23 hours. The risk of graft loss was particularly high for black patients and patients with a panel-reactive antibody level of more than 80 percent.

The risk of functional-graft loss between 1996 and 1999 was half that for the period from 1987 to 1990. Figure 2 shows survival curves for the grafts as a whole and for functional grafts after adjustment for the effects of the covariates listed in Table 3. At 10 years, the overall rates of graft survival and the rates of functional-graft survival were 10 percent and 11 percent higher, respectively, for HLA-matched transplants than for HLA-mismatched transplants.

For a closer evaluation of the effect of the duration of cold ischemia on the national organ-sharing program, we analyzed the results for pairs of kidneys from 3562 donors in which one kidney was transplanted into an HLA-matched recipient and the other kidney was transplanted into an HLA-mismatched recipient. The incidence of delayed graft function did not differ significantly between the HLA-matched and HLA-mismatched kidneys (21 percent vs. 19 percent, $P=0.15$). The recipients of HLA-matched transplants had slightly higher serum creatinine concentrations at discharge (median, 1.8 mg per deciliter [$159\ \mu\text{mol}$ per liter] vs. 1.7 mg per deciliter [$150\ \mu\text{mol}$ per liter]; $P<0.001$), but they had a lower incidence of treated

TABLE 2. ESTIMATED HALF-LIFE OF HLA-MATCHED GRAFTS AND HLA-MISMATCHED GRAFTS FOR THE PERIODS FROM 1987 TO 1999 AND 1994 TO 1999, ACCORDING TO FACTORS THAT INFLUENCE THE LONG-TERM SURVIVAL OF GRAFTS.*

FACTOR	1987-1998			1994-1999		
	HALF-LIFE OF HLA-MATCHED GRAFTS	HALF-LIFE OF HLA-MISMATCHED GRAFTS	P VALUE	HALF-LIFE OF HLA-MATCHED GRAFTS	HALF-LIFE OF HLA-MISMATCHED GRAFTS	P VALUE
	years			years		
Recipient						
Previous transplantation						
No	12.9	8.7	<0.001	15.3	10.3	<0.001
Yes	11.0	7.9	<0.001	20.3	9.0	0.001
Panel-reactive antibody level†						
0-10%	12.9	9.0	<0.001	17.7	10.8	<0.001
80-100%	10.8	7.5	<0.001	12.6	7.9	0.03
Race						
White	12.8	9.8	<0.001	17.1	11.7	<0.001
Black	7.7	5.7	0.02	8.0	6.9	0.25
History of diabetes mellitus						
Yes	10.2	7.9	<0.001	16.5	10.0	0.007
No	13.2	8.8	<0.001	16.1	10.1	<0.001
Transplant						
Transplantation center‡						
Top 20 centers	22.6	11.8	<0.001	24.2	15.7	0.14
Middle 140 centers	12.3	8.7	<0.001	17.0	10.2	<0.001
Bottom 20 centers	8.9	6.5	0.02	12.0	7.4	0.04
Pairs of kidneys§	12.2	9.7	<0.001	17.8	11.3	0.003
Location of center			<0.001			<0.001
Distant¶	12.8	8.6		16.5	9.9	
Local¶¶	11.3	8.7		14.2	10.2	
Duration of cold ischemia						
<24 hours	13.6	8.8	<0.001	18.3	10.3	<0.001
>36 hours	11.2	8.1	0.009	9.7	8.6	0.37

*To allow for multiple comparisons only P values of less than 0.002 were considered statistically significant.

†The values are the percentage of a panel of normal-donor cells that reacted with a transplant recipient's serum.

‡The centers in this analysis had each performed at least 100 transplantations. Centers are ranked according to the five-year rates of graft survival.

§We analyzed pairs of kidneys from 3562 donors in which one kidney was given to an HLA-matched recipient and the other was given to an HLA-mismatched recipient.

¶The P value is for the comparison of shipped HLA-matched kidneys with local HLA-mismatched kidneys.

||The analysis included fewer than 100 grafts.

episodes of rejection (13 percent vs. 19 percent, $P < 0.001$) and fewer days of hospitalization after the initial transplantation procedure (median, 10 vs. 11; $P < 0.001$). The HLA-matched recipients had significantly higher rates of graft survival, and the estimated survival rates were similar to the overall rates of graft survival: 50 percent for the HLA-matched kidneys and 42 percent ($P < 0.001$) for the HLA-mismatched contralateral kidneys (Fig. 3).

During the first year after transplantation, 397 HLA-matched transplants failed, 70 of which (18 percent) were lost because of rejection, and 485 HLA-mismatched contralateral transplants were lost, 117 of which (24 percent, $P = 0.02$) were lost because of rejection. Between one and three years after transplantation, grafts failed in 141 HLA-matched recip-

ients, because of chronic rejection in 36 (26 percent), and 62 of these recipients died (44 percent), whereas the grafts failed in 239 HLA-mismatched recipients, because of chronic rejection in 85 (36 percent), and 75 of these recipients died (31 percent, $P = 0.03$).

DISCUSSION

Since UNOS established the national kidney-sharing program in 1987, many have argued that the resultant increased duration of cold ischemia would offset the benefit of shipping kidneys to HLA-matched patients.^{7,8} In this study, in three separate analyses, we found that graft survival was superior in patients who received HLA-matched kidneys and that the mean increase in the duration of cold ischemia was small. Shipping kidneys to an HLA-matched recipient did not

TABLE 3. HAZARD RATIOS FOR THE LIKELIHOOD OF GRAFT LOSS AND FUNCTIONAL-GRAFT LOSS, ACCORDING TO A PROPORTIONAL-HAZARDS ANALYSIS.*

VARIABLE	GRAFT LOSS		FUNCTIONAL-GRAFT LOSS†	
	HAZARD RATIO (95% CI)	P VALUE	HAZARD RATIO (95% CI)	P VALUE
HLA mismatch	1.38 (1.31–1.46)	<0.001	1.55 (1.45–1.65)	<0.001
Race of recipient‡				
Black	1.44 (1.40–1.48)	<0.001	1.55 (1.50–1.59)	<0.001
Other	0.79 (0.76–0.84)	<0.001	0.82 (0.78–0.87)	<0.001
Age of recipient (for each SD above the mean)	1.08 (1.07–1.13)	<0.001	1.02 (1.01–1.03)	<0.001
Diabetes mellitus	1.22 (1.18–1.25)	<0.001	0.99 (0.96–1.03)	0.6
Serum panel-reactive antibodies§				
11–40%	1.09 (1.06–1.12)	<0.001	1.11 (1.07–1.15)	<0.001
41–80%	1.22 (1.17–1.27)	<0.001	1.28 (1.22–1.34)	<0.001
>80%	1.41 (1.35–1.48)	<0.001	1.47 (1.40–1.55)	<0.001
Previous transplantation	1.18 (1.14–1.22)	<0.001	1.18 (1.13–1.22)	<0.001
Donor's death not due to trauma	1.11 (1.08–1.14)	<0.001	1.13 (1.09–1.16)	<0.001
Age of donor (for each SD above the mean)	1.12 (1.11–1.13)	<0.001	1.14 (1.13–1.16)	<0.001
Duration of cold ischemia (for each SD above the mean)	1.04 (1.03–1.05)	<0.001	1.05 (1.04–1.07)	<0.001
Transplantation center¶				
Top 20	0.80 (0.77–0.84)	<0.001	0.79 (0.76–0.83)	<0.001
Bottom 20	1.23 (1.18–1.27)	<0.001	1.25 (1.20–1.31)	<0.001
Year of transplantation				
1987–1990	1.81 (1.73–1.89)	<0.001	2.02 (1.92–2.13)	<0.001
1991–1995	1.37 (1.31–1.43)	<0.001	1.40 (1.33–1.47)	<0.001

*To allow for multiple comparisons, only P values of less than 0.002 were considered statistically significant. CI denotes confidence interval.

†In the analysis of functional-graft survival, data on patients who died with a functioning graft were censored.

‡The reference category was white race.

§The values are the percentage of a panel of normal-donor cells that reacted with a transplant recipient's serum. The reference category was 0 to 10 percent.

¶The reference category was the middle 140.

||The reference category was 1996 to 1999.

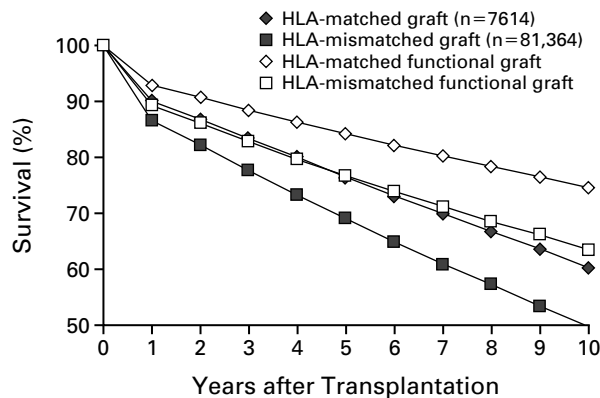


Figure 2. Actuarial Rates of Graft Survival and of Functional-Graft Survival for HLA-Matched and HLA-Mismatched Cadaveric Kidneys after Adjustment for the Effects of the Recipient's Race, Age, and Level of Panel-Reactive HLA Antibodies; the Presence or Absence of Diabetes Mellitus and a History of Transplantation in the Recipient; the Donor's Age and Cause of Death; the Duration of Cold Ischemia; the Transplantation Center; and the Year of Transplantation.

For functional-graft survival, data on patients who died with a functioning graft were censored.

result in a higher rate of delayed graft function, a complication that may reflect ischemic damage. In fact, there were fewer episodes of rejection during the first three years among the recipients of HLA-matched kidneys than among the recipients of HLA-mismatched kidneys, and fewer transplants failed in this group as a result of either acute or chronic rejection. Moreover, the half-lives of HLA-mismatched kidneys that were transplanted locally were shorter than those of kidneys that were shipped to HLA-matched patients.

Patients with broad sensitization to HLA antigens usually wait much longer for a transplant than those with a low degree of reactivity to HLA antigens.⁹ The HLA-matching program has benefited these patients in particular, because the percentage of HLA-matched recipients who had levels of panel-reactive antibody of more than 80 percent was more than twice that of HLA-mismatched recipients with similarly high antibody levels. A panel-reactive antibody value of 80 percent indicates that 80 percent of local donors would have a positive crossmatch with the recipient and that the recipient would therefore be an unsuitable candidate for transplantation because of the high risk of hy-

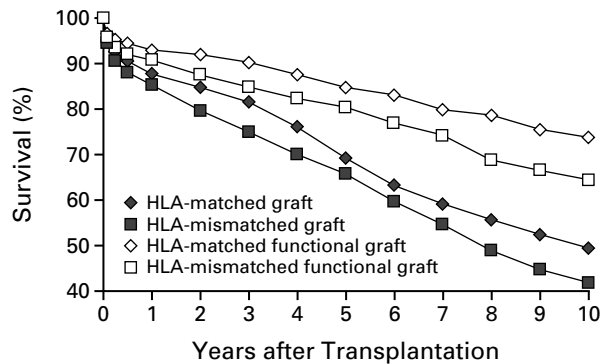


Figure 3. Rates of Graft Survival and Functional-Graft Survival for 3562 Pairs of Kidneys from Donors in Which One Kidney Was Given to an HLA-Matched Recipient and the Other to an HLA-Mismatched Recipient.

For functional-graft survival, data on patients who died with a functioning graft were censored.

peracute rejection.¹⁰ Women usually wait longer than men for a transplant because of the association between pregnancy and sensitization. In our study, the percentage of women in the group of HLA-matched kidney recipients was the same as that on the waiting list (43 percent).⁹

The strongest criticism of the HLA-matching program is that there was no significant improvement in long-term graft survival among black recipients. Only 3 percent of blacks received HLA-matched kidneys during the study period. The more extensive polymorphism of HLA phenotypes among blacks¹¹ makes finding good matches difficult. We had earlier found that changes in the matching criteria increased the rate of HLA matching among black recipients by a factor of 6,³ and, indeed, the percentage of HLA-matched grafts among black recipients was 6 percent in the 1994–1999 cohort, indicating a trend toward increased access for these patients.

Other factors may have a role in the poorer long-term survival of grafts in black recipients. Their allogeneic responses may be stronger,¹² and they may require higher doses of immunosuppressive therapy to maintain the grafts.¹³ Hypertension may also be an important factor. We did not find a long-term benefit of HLA matching for blacks with hypertension, whereas blacks with no hypertension had improved long-term graft survival. Blacks reportedly have an increased rate of graft loss when blood pressure is uncontrolled after transplantation.¹⁴ The outcome for these patients may improve if their blood pressure is lowered before they undergo transplantation.

We had earlier postulated that the decreasing rates of graft survival with increasing donor age might be due to a natural decrease in the number of functional nephrons as the kidney ages.¹⁵ Although HLA match-

ing reduced the risk of loss regardless of the donor's age, the projection that 70 percent of kidneys from donors older than 60 years of age will be lost within 10 years after transplantation suggests that young recipients should not undergo transplantation with organs from older donors, even if they are HLA-matched.

The strong effect of the donor's age illustrates the importance of the physical condition of the kidney transplant. The high rate of success of transplantation of HLA-mismatched kidneys from living unrelated donors has also been cited as evidence that the health of the donor organ is an important factor.¹⁶ In our study, the 12.5-year half-life of HLA-matched cadaveric kidneys is similar to the 12-year half-life of kidney grafts from living unrelated donors.

The estimated half-life of HLA-mismatched kidneys transplanted since 1994 is two years longer than it was in our 1992 report on the HLA-matching program.¹ Many investigators might take this increase to mean that improvements in immunosuppression protocols, crossmatching techniques, and patient care have reduced the need for HLA matching. We found that the expected functional life of HLA-matched transplants has also increased, with notable improvements among patients who had previously undergone transplantation who had a high immunologic risk.

The UNOS national program recognizes that because of the polymorphism of HLA antigens, there must be a large number of patients on the waiting list to find two unrelated people with identical HLA antigens.¹⁷ Approximately 1000 kidneys are transplanted into HLA-matched patients every year. Even with the change in matching criteria implemented in 1995, only 13 percent of the pairs of HLA-matched kidney donors and recipients were from the same geographic region. If the national program of organ sharing were abolished, only 2 percent of patients (about 150 per year) would receive HLA-matched kidneys.

In conclusion, HLA-matched transplants included in the national program of organ sharing were rejected less often and had a higher rate of survival than HLA-mismatched transplants. These results were obtained through the cooperation of all U.S. transplantation centers, and it is likely that the percentage of HLA-matched transplants could be increased by extending the organ-sharing network to include Canada, since many Canadian cities are close to those in the United States.

Supported in part by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases (DK54928-01) and by a subcontract with UNOS, Department of Health and Human Services. The opinions expressed are those of the authors and do not necessarily reflect the opinions or policies of UNOS.

REFERENCES

1. Takemoto S, Terasaki PI, Cecka JM, Cho YW, Gjertson DW. Survival of nationally shared, HLA-matched kidney transplants from cadaveric donors. *N Engl J Med* 1992;327:834-9.

2. Kaufman HM, Bennett LE, McBride MA, Ellison MD. The expanded donor. *Transplant Rev* 1997;11:165-90.
3. Hata Y, Cecka JM, Takemoto S, Ozawa M, Cho YW, Terasaki PI. Effects of changes in the criteria for nationally shared kidney transplants for HLA-matched patients. *Transplantation* 1998;65:208-12.
4. Terasaki PI, Bernoco D, Park MS, Ozturk G, Iwaki Y. Microdroplet testing for HLA-A, -B, -C, and -D antigens: the Phillip Levine Award Lecture. *Am J Clin Pathol* 1978;69:103-20.
5. Gjertson DW. A multi-factor analysis of kidney graft outcomes at one and five years posttransplantation: 1996: UNOS update. In: Cecka JM, Terasaki PI, eds. *Clinical transplants 1996*. Los Angeles: UCLA Tissue Typing Laboratory, 1997:343-60.
6. Takiff H, Cook DJ, Himaya NS, Mickey MR, Terasaki PI. Dominant effect of histocompatibility on ten-year kidney transplant survival. *Transplantation* 1988;45:410-5.
7. Held PJ, Kahan BD, Hunsicker LG, et al. The impact of HLA mismatches on the survival of first cadaveric kidney transplants. *N Engl J Med* 1994;331:765-70.
8. Schnitzler MA, Hollenbeak CS, Cohen DS, et al. The economic implications of HLA matching in cadaveric renal transplantation. *N Engl J Med* 1999;341:1440-6.
9. Harper AM, Rosendale JD, McBride MM, Cherikh WS, Ellison MD. The UNOS OPTN waiting list and donor registry. In: Cecka JM, Terasaki PI, eds. *Clinical transplants 1998*. Los Angeles: UCLA Tissue Typing Laboratory, 1999:73-90.
10. Patel R, Terasaki PI. Significance of the positive crossmatch test in kidney transplantation. *N Engl J Med* 1969;280:735-9.
11. Beatty PG, Mori M, Milford E. Impact of racial genetic polymorphism on the probability of finding an HLA-matched donor. *Transplantation* 1995;60:778-83.
12. Kerman RH, Kimball PM, Van Buren CT, Lewis RM, Kahan BD. Stronger immune responsiveness of blacks vs whites may account for renal allograft survival differences. *Transplant Proc* 1991;23:380-2.
13. Neylan JF. Effect of race and immunosuppression in renal transplantation: three-year survival results from a US multicenter, randomized trial. *Transplant Proc* 1998;30:1355-8.
14. Cosio FG, Falkenhain ME, Pesavento TE, et al. Relationships between arterial hypertension and renal allograft survival in African-American patients. *Am J Kidney Dis* 1997;29:419-27.
15. Terasaki PI, Gjertson DW, Cecka JM, Takemoto S. Fit and match hypothesis for kidney transplantation. *Transplantation* 1996;62:441-5.
16. Terasaki PI, Cecka JM, Gjertson DW, Takemoto S. High survival rates of kidney transplants from spousal and living unrelated donors. *N Engl J Med* 1995;333:333-6.
17. Mickey MR, Cook DJ, Terasaki PI. Recipient pool sizes for prioritized HLA matching. *Transplantation* 1989;47:401-3.