Role of Socioeconomic Status in Kidney Transplant Outcome

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There is controversy regarding the influence of genetic *versus* environmental factors on kidney transplant outcome in minority groups. The goal of this project was to evaluate the role of certain socioeconomic factors in allograft and recipient survival. Graft and recipient survival data from the United States Renal Data System were analyzed using Cox modeling with primary variables of interest, including recipient education level, citizenship, and primary source of pay for medical service. College (hazard ratio [HR] 0.93, $P < 0.005$) and postcollege education (HR 0.85, $P < 0.005$) improved graft outcome in the whole group and in patients of white race. Similar trends were observed for recipient survival (HR 0.9, $P < 0.005$ for college; HR 0.88, $P = 0.09$ for postcollege education) in the whole population and in white patients. Resident aliens had a significantly better graft outcome in the entire patient population (HR 0.81, $P < 0.001$) and in white patients in subgroup analysis (HR 0.823, $P < 0.001$) compared with US citizens. A similar effect was observed for recipient survival. Using Medicare as a reference group, there is a statistically significant benefit to graft survival from having private insurance in the whole group (HR 0.87, $P < 0.001$) and in the black (HR 0.8, $P < 0.001$) and the white (HR 0.89, $P < 0.001$) subgroups; a similar effect of private insurance is observed on recipient survival in the entire group of patients and across racial groups. Recipients with higher education level, resident aliens, and patients with private insurance have an advantage in the graft and recipient outcomes independent of racial differences.

Clin J Am Soc Nephrol 1: 313–322, 2006. doi: 10.2215/CJN.00630805

Kidney transplantation is the treatment of choice for the majority of patients with ESRD and is associated with improved survival and quality of life compared with patients who remain on the waiting list (1). Kidney transplantation is one of the major success stories of the 20th century by virtually doubling the chance of survival for all patients independent of age, gender, underlying diagnoses, race, or ethnicity. One-year graft survival now exceeds 90% for the majority of transplant programs in the United States, and rejection rates have dropped to <20% as a result of improved immunosuppressive strategies, surgical techniques, and improved posttransplantation care (2–5). Despite these dramatic successes in the past 50 years, important long-term problems persist, namely racial and ethnic disparities, the complications of long-term immunosuppression, and chronic allograft nephropathy. The predictive factors of graft survival have been studied extensively in adults (5,6) and children (7). These factors include donor and recipient age, preexisting donor hypertension and diabetes, non–heart-beating donor, prolonged cold storage time, retransplantation, multiple blood transfusions, and body mass index (BMI) of donor and recipient (5,7–9), yet the role of socioeconomic status (SES) of the donor and the recipient remains controversial and poorly understood. We and other authors previously demonstrated that donor and recipient race plays an important role in allograft survival (6,10) and that long-term transplantation outcomes in black patients remain significantly lower than those in all other ethnic groups, independent of genetic matching (11). However, it is not clear what impact genetic and environmental factors have on these racial disparities in allograft survival. Furthermore, it has been demonstrated that racial differences affect the access to specific transplant procedures, in particular kidney-pancreas transplant (12), and are associated with different levels of compliance (13). In addition, there are apparent disparities in chronic kidney disease care that is provided to ethnic minorities. Disparities exist in wait-list time and kidney transplantation rates for Native American and black patients, independent of insurance status (11). Black patients were less likely than white patients to want a transplant and less likely to be referred for evaluation at a transplantation center and placed on a waiting list. These differences, however, explain only a small fraction of the substantial racial differences in access to transplantation (14). Al-

Received August 3, 2005. Accepted December 8, 2005.

Published online ahead of print. Publication date available at www.cjasn.org.

The data reported here have been supplied by the US Renal Data System. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as official policy or interpretation of the US government.

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ISSN: 1555-9041/102-0313

though certain genetic factors that are associated with race might potentially play a role, literature reports suggest the presence of poorly understood social aspects contributing to the survival differences. We hypothesized that certain socioeconomic factors, such as education level, citizenship/immigration status, and source of payment for medical service, play an important role in graft and recipient outcome. The goal of this project was to evaluate the role of the above factors in kidney allograft and recipient outcome.

Materials and Methods

Data Set

We analyzed the records of all kidney and kidney-pancreas allograft recipients (both pediatric and adult) who underwent transplantation during the period January 1, 1990, through December 31, 1999, using ESRD-course data collected by the United States Renal Data System (USRDS) and transplant-related data collected by the United Network for Organ Sharing (UNOS). The follow-up period was extended through December 31, 2000. For recipients of multiple transplants, the most recent procedure was considered the transplant of interest. Patient records with missing information regarding graft or patient survival were excluded from the study.

Outcome Measures and Definitions

There were two outcomes in this study. The first outcome, graft survival, was the time between the study transplantation and the failure of its graft. The graft failure date was defined as the date of return to dialysis or retransplantation. The second outcome, recipient survival, was the time between study transplantation and recipient death. Both outcomes were modeled using continuous survival time variables.

Although the USRDS reports whether a graft is still functioning at the time of patient death, our definition of graft failure excludes these functioning grafts. In cases in which this variable was missing, we used *International Classification of Diseases, Ninth Revision* codes to impute graft failure (the cause of death was coded as one of the following: 3200, graft failure: primary failure; 3201, graft failure: rejection; 3202, graft failure: technical; 3299, graft failure: other; or 3903, miscellaneous: renal failure). Allograft outcome was censored at the earliest of the following events: Loss to follow-up, patient death, or the study completion date (December 31, 2000) and was analyzed as days to graft failure or censor. Patient follow-up was censored at the earliest of loss to follow-up or study completion date and was analyzed as days to recipient death or censor.

Statistical Analyses

Primary Variables of Interest. The following three primary variables of interest were evaluated: Recipient education level, primary source of payment for medical services, and the citizenship/immigration status. Recipient education level was divided into the following categories: None, from grade school to high school (0 to 12), from some college to bachelor's degree, postcollege graduate degree, N/A (<5 yr old), and missing or unknown. The following categories of citizenship or immigrations status were studied: US citizen, resident alien, nonresident alien, and missing or unknown. Resident aliens are citizens who are of another country and live in the United States and/or have resident status by law or visa. Nonresident alien is a person who is not a US citizen and who does not meet either the "green card" test or the "substantial presence" test.

Primary source of pay was divided into the following categories: Medicare, Medicaid, US/state government agency, private insurance, health maintenance organization/preferred provider organization (HMO/PPO), missing or unknown, and others (self, donation, free care, Veterans Administration, pending, and foreign government). An HMO is a prepaid health plan that delivers comprehensive care to members through designated providers, has a fixed monthly payment for health care services, and requires members to be in a plan for a specified period of time. A PPO is an arrangement whereby a third-party payer contracts with a group of medical care providers who furnish medical services at lower-than-usual fees in return for prompt payment and a certain volume of patients. Although the patient does have some flexibility in health care decisions and selecting providers, patients have financial incentives to select PPO network providers.

All of the primary variables of interest were evaluated in a single Cox model, which therefore was adjusted for all three of the primary variables of interest in addition to covariates mentioned below (*i.e.*, the results of the role of the education level should be interpreted as adjusted for primary source of pay and immigration status).

Covariates. The Cox models were adjusted for covariates that were believed to be potential confounders for graft survival and SES. On the basis of our previous work (6) and that of others (5,15–17), all models were adjusted for the following variables:

1. Recipient variables: Recipient age, gender, race, BMI, history of hypertension and diabetes, total duration of ESRD, cause of ESRD, total number of transplants, mean and peak panel reactive antibody levels, number of previous blood transfusions, and number of different renal replacement therapy modalities used during the pretransplant ESRD course
2. Donor variables: Type of donor (cadaveric or living), heart-beating donor or not, donor age, gender, race, BMI, and history of diabetes
3. Transplant procedure variables: Number of matched HLA antigens and cold storage time

To adjust for recipient comorbidities, we calculated a comorbidity score similar to the one proposed by Davies *et al.* (18). The comorbidity score used in this study was calculated on the basis of the following coexisting conditions, each of them contributing 1 point to the score: Cardiovascular disease (defined in USRDS as symptomatic cardiovascular disease or angina/coronary artery disease), symptomatic peripheral vascular disease, diabetes, and hypertension. Information about coexisting conditions was obtained from the TXUNOS file (available on the Transplant Candidate Registration Form); therefore, the comorbidities that were used for this study are those that the patient had at the time of listing for the study transplantation. We did not use data from the CMS-2728 form so as not to exclude patients who were not Medicare eligible before 1995 (before 1995, dialysis units and transplant centers were required to fill out the Medicare Evidence form only for Medicare-eligible patients). To reduce lead time bias, we also adjusted the models for total duration of ESRD before the follow-up time included in the Cox models. Unrealistic values of the independent variables that were used in the study were eliminated. In particular, for donors and recipients who were younger than 13 yr, the Centers for Disease Control and Prevention growth charts were used as a guide for determining valid ranges. The heights and weights of recipients and donors who were 13 yr and older were based on the acceptable ranges: Height, 122 to 274 cm; and weight, 23 to 180 kg.

Statistical Models. Kaplan-Meier graphs were used to display hypothesized relationships, and Cox regression models were used to analyze time to event. Data were analyzed using SAS (SAS Institute, Cary, NC).

Results

This study was approved by the University of Utah's Institutional Review Board. A total of 92,844 patients with kidney transplants were identified and studied.

Baseline Characteristics

The characteristics of the study population are presented in Tables 1 (covariates) and 2 (primary variables of interest). The recipients (n = 92,844) were 60% male, 70% white, 23% black, and 3% Asian; 27% had diabetes; and the average age was 43 yr at the time of the study transplantation. Roughly one (12.6%) in eight had at least one previous transplant. These recipients were 59% male and 78% white; 16% had diabetes; and the average age was 38.5 yr at the time of the study transplantation. Other characteristics, including socioeconomic factors of the recipients (primary source of payment, education level, and citizenship), are presented in Table 2.

Survival Analysis

Although the models described here were not adjusted for the year of the transplantation because of a relatively short study period, we realize that the time of the transplantation might still confound the results. Therefore, additional analysis was performed after adjustment for the model for the year of the transplantation. Also, because using the year of the transplantation as an indicator of transplant era may introduce bias in the statistical analysis, we selected the use of mycophenolate mofetil, that came on the market in mid-1990s, as a surrogate for the transplant era. Using both approaches revealed results very similar to our original analysis and are not presented here.

Role of Education Level. Kaplan-Meier plots suggested incremental improvement in the outcome with increased education level (Figure 1). The proportional hazard model demonstrated improved outcome associated with more advanced education. Compared with patients who receive grade to high school (0 to 12) education, those with some college to bachelor's degree had significantly better graft (hazard ratio [HR] 0.93, $P < 0.005$) and recipient (HR 0.90, $P < 0.005$) survival. Furthermore, recipients with postcollege graduate degrees had even better outcome, with HR of 0.85 ($P < 0.005$) for the graft and HR of 0.88 ($P = 0.09$) for recipient failure (Table 3). When different racial groups were analyzed separately, black and white patients (but not Asian patients) had a similar trend for the graft survival. A similar trend for the recipient survival was observed only in white patients (Tables 4 and 5).

Primary Source of Pay. On the basis of Kaplan-Meier plots, recipients with private insurance had better outcome than those with Medicare, Medicaid, or other sources of payment. As far as recipient survival, patients who have Medicare seem to have worse outcome than other groups, which could be confounded by older age (data not shown). In the entire patient population, using Medicare as a reference group, the proportional hazard model demonstrated statistically significant benefit to graft survival from having private insurance (HR 0.87, $P < 0.001$; Table 3). This effect was not observed in Asian recipients but remained in the black patients (HR 0.8, $P < 0.001$) and white patients (HR 0.89, $P < 0.001$). Private insurance in comparison with Medicare also had an advantage for recipient survival in the entire group of patients (HR 0.8, $P < 0.001$) as well as in Asian (HR 0.66, $P < 0.05$), black (HR 0.71, $P < 0.001$), and white patients (HR 0.83, $P < 0.001$), when analyzed separately. HMO/PPO was associated with significantly higher risk for graft failure (HR 1.2, $P < 0.05$) but improved patient survival (HR 0.52, $P < 0.001$; Tables 4 and 5). Having Medicaid, US/

Table 1. Baseline characteristics of the study population[a]

Variable	Mean (SD)
Recipient	
age (yr)	43.31 (14.19)
height (cm)	169.01 (13.68)
weight (kg)	72.61 (17.22)
history of diabetes	27%
history of hypertension	47%
race	
white	71%
black	23%
Asian	3%
other	3%
gender	
female	40%
male	60%
Donor	
living donor	25%
age (yr)	34.4 (15.5)
gender	
female	43%
male	57%
height (cm)	164.3 (21.9)
weight (kg)	72.8 (19.0)
no. of HLA matched antigens	1.82 (1.49)
Cause of ESRD	
diabetes	25%
hypertension	17%
glomerulonephritis	26%
other	32%
Mean PRA level (%)	5.27 (14.67)
Peak PRA level (%)	12.09 (21.45)
Comorbidity score	0.83 (0.80)
Total no. of transplants	1.16 (0.43)
Previous transplant	13%
Predominant RRT modality	
hemodialysis	67%
peritoneal dialysis	23%
transplant	6%
none	4%

[a]Continuous variables are presented as mean (SD), categorical variables are presented as class percentages. Variables included in multivariate analysis, except for the primary variables of interest (Table 2), are described in this table. PRA, panel reactive antibody; RRT, renal replacement therapy.

Table 2. The distribution of the primary variables of interest in the subgroup of patients divided by the race[a]

	Asian (n = 3,127)	Black (n = 21,393)	White (n = 65,214)	Total (n = 92,844)
Recipient education level				
none	25 (0.8)	62 (0.3)	205 (0.3)	318 (0.3)
grade to high school: grades 0 to 12	536 (17.1)	4,999 (23.4)	14,528 (22.3)	20,410 (22.0)
some college to bachelor's degree	565 (18.1)	2,684 (12.6)	9,942 (15.3)	13,384 (14.4)
postcollege graduate degree	116 (3.7)	263 (1.2)	1,301 (2.0)	1,728 (1.9)
N/A: <5 yr old	12 (0.4)	51 (0.2)	347 (0.5)	419 (0.5)
missing or unknown	1,873 (59.9)	13,334 (62.3)	38,891 (59.6)	56,585 (61.0)
Primary source of payment				
Medicare	1,135 (36.3)	9,424 (44.1)	22,733 (34.9)	34,484 (37.1)
Medicaid	115 (3.7)	721 (3.4)	1,319 (2.0)	2,259 (2.4)
US/state government agency	40 (1.3)	205 (1.0)	482 (0.7)	764 (0.8)
private insurance	621 (19.9)	2,715 (12.7)	13,593 (20.8)	17,775 (19.2)
HMO/PPO	52 (1.7)	124 (0.6)	477 (0.7)	703 (0.8)
other	8 (0.3)	67 (0.3)	152 (0.2)	239 (0.3)
missing	1,156 (37.0)	8,137 (38.0)	26,458 (40.6)	36,620 (39.4)
Registered patients' citizenship				
US citizen	2,606 (83.3)	20,720 (96.85)	62,064 (95.2)	86,628 (93.3)
resident alien	374 (12.0)	164 (0.77)	1,292 (2.0)	1,955 (2.1)
nonresident alien	29 (0.9)	16 (0.07)	83 (0.1)	147 (0.2)
missing or unknown	118 (3.8)	493 (2.3)	1,775 (2.7)	4,114 (4.4)

[a]Values are presented as an absolute number of patients (percentage of the subgroup). All of the differences between the subgroups using ANOVA for the continuous variables and χ^2 for the categorical variables are statistically significant ($P < 0.001$). HMO/PPO, health maintenance organization/preferred provider organization.

state government agency, or other sources of payment for medical services did not show any significant association with outcome as compared with Medicare either in the whole patient population or in the subgroups divided by race.

Role of Citizenship. Kaplan-Meier plots suggested that resident and nonresident alien recipients had the best graft outcome and patient survival as compared with US citizens (Figure 2). Using the Cox model in the entire patient group with US citizens as the reference group, resident aliens had significantly better graft outcome (HR 0.81, $P < 0.001$; Table 3). When analysis was stratified by race, only in white patients did this association reach statistical significance (HR 0.823, $P < 0.001$; Table 4). Similar results were observed for recipient survival: when compared with US citizens, legal aliens had a survival advantage (HR 0.7, $P < 0.001$; Table 2). This effect was observed in Asian patients (HR 0.66, $P < 0.05$) and white patients (HR 0.7, $P < 0.001$) but not in black patients (Table 5). In addition, similar to resident aliens, nonresident aliens have better outcome than the US citizens, but this finding did not reach statistical significance, likely because of the very small sample size of this group.

Subgroup Analysis: Adult Patients with the First Transplant. We reanalyzed the subset of patients who were older than 18 yr and had the first transplant (n = 78,181). In this subset of the data, we found associations similar to those in the whole data set. Compared with patients with high school attendance, those with college education had a trend toward better graft (HR 0.96, 95% confidence interval [CI] 0.91 to 1.01, $P = 0.0965$) and recipient (HR 0.90, 95% CI 0.84 to 0.97, $P < 0.01$) outcome. Those with more advanced education had even better outcome for the graft (HR 0.88, 95% CI 0.78 to 1.00, $P < 0.05$) and recipient (HR 0.90, 95% CI 0.77 to 1.05, $P = 0.173$) survival. Compared with patients with Medicare (n = 28,882), recipients who had private insurance (n = 15,339) had lower risk for the long-term graft failure (HR 0.86, 95% CI 0.82 to 0.90, $P < 0.001$) and recipient death (HR 0.80, 95% CI 0.76 to 0.85, $P < 0.001$). Having HMO/PPO (n = 618) was associated with worse graft survival (HR 1.27, 95% CI 1.07 to 1.51, $P < 0.01$) but better recipient survival (HR 0.54, 95% CI 0.37 to 0.78, $P < 0.005$). Also, resident aliens (n = 1739) had an advantage over US citizens for graft (HR 0.81, 95% CI 0.74 to 0.90, $P < 0.005$) and recipient (HR 0.70, 95% CI 0.62 to 0.81, $P < 0.001$) survival.

Discussion

Socioeconomic factors have been shown to affect health care outcomes. Poverty, unemployment, and low education level have been listed among the factors that adversely affect health (19). SES has been suggested to play a significant role in kidney transplant outcome. Among others, the following socioeconomic factors have been listed as risk factors for posttransplantation noncompliance: occupational status, educational level, language or cultural barriers, and ethnic background (20). Race and income have substantial effects on mortality and use of services among Medicare beneficiaries (21). Poor individuals are less likely than wealthy individuals to be medically suit-

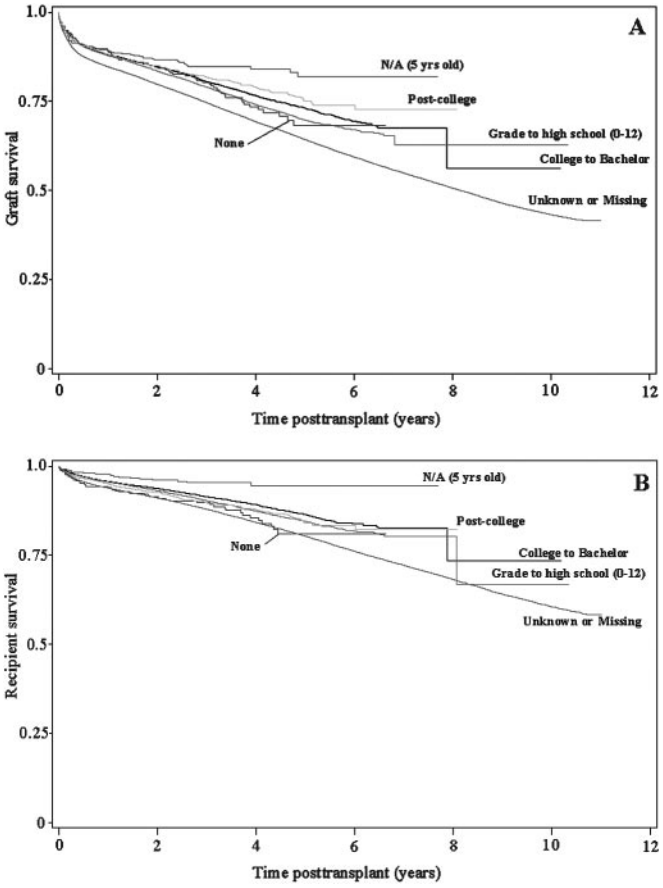

Figure 1. Kaplan-Meier analysis illustrates the association of recipients' education level with graft (A) and recipient (B) survival (for both analyses, $P < 0.001$ by log-rank test).

able, to be interested in transplantation, and to complete the pretransplantation workup (22).

In a study similar in design to our project and based on UNOS data, in patients with liver transplant, it has been shown that neighborhood income had no effect on graft or patient survival, education had only marginal influence on the outcome (survival was lower in those with a high school education than in those with graduate education), and patients with Medicaid and Medicare had lower survival when compared with those with private insurance (23). The results of our study that was done in kidney transplant recipients are similar. In the entire patient group, there is a statistically significant benefit to graft and patient survival from having private insurance compared with Medicare. This effect was observed across almost all racial groups (except for Asian patients, for whom there was no significant association between private insurance and graft survival). HMO/PPO was associated with significantly higher risk for graft failure but improved patient survival. These results are similar to those reported in liver transplant recipients (23).

Compliance with regard to immunosuppressive medication use is one of the key factors in prolonging graft survival. Until 1993, Medicare regulations allowed for coverage of immunosuppressive medications only for 1 yr posttransplantation unless the recipients maintain their Medicare beneficiary status through disability or age. Between 1993 and 1995, that duration was gradually extended to 3 yr posttransplantation, which was extended further by 8 mo in 2000. Woodward *et al.* (24) have shown that extending the coverage from 1 yr to 3 yr posttransplantation has eliminated the 4.5% difference in graft survival between low-income and high-income recipients. In a follow-up analysis (25), the same authors estimated that if Medicare provided life-long immunosuppressive medications to all of the recipients, then graft failure would be reduced by 1.2% annually beginning in the fourth year posttransplantation. Furthermore, Medicare beneficiaries who are eligible to receive the immunosuppressive medication coverage must still pay 20% of the cost of these medications as Medicare covers only 80% of the total cost. With many HMO/PPO or private insurance carriers, subscribers may be required to pay substantially lower copayments. This could also contribute to better compliance with immunosuppressive medications and, subsequently, better graft outcome among HMO/PPO or private insurance subscribers compared with Medicare beneficiaries. Medicare beneficiaries who undergo kidney transplantation do not have coverage for nonimmunosuppressive prescription drugs. This could explain the poor recipient survival seen in our analysis. Medicare beneficiaries were shown to be more likely to take required prescription medications if they had prescription drug coverage (26). Finally, even though we included age as an independent variable in our analysis, there may be a residual confounding effect of age on the outcome. As Medicare patients tend to be older compared with HMO/PPO or private insurance patients, Medicare beneficiaries may have poor outcome compared with non-Medicare recipients.

A possible reason for inferior outcome in Medicaid beneficiaries is as follows: Previous studies have shown that Medicaid beneficiaries are less likely to receive optimal treatment, and their outcome is worse compared with privately insured patients for common conditions such as myocardial infarction and bronchial asthma (27,28). Restricted access to medical care because of lower reimbursement by Medicaid and highly variable coverage benefits between different states are some of the possible explanations for such poor outcomes. Low income and poverty indicated by Medicaid may contribute directly or indirectly to worse health outcomes in general. Indeed, cost-related skipping of medications has been shown to be associated with the level of drug coverage and the income level (29). A potential explanation for better outcomes among those with private insurance could be better quality of care. Furthermore, these patients might be either healthy enough to be employed or have high personal income to be able to afford private insurance, both of which may potentially influence the outcomes.

Our study demonstrated that better recipient but worse graft survival is associated with HMO/PPO coverage. Better graft survival does not always translate into improved recipient survival. In this particular case, we hypothesized that the HMO population is likely to consist of relatively young employed patients. The residual confounding effect of age might explain longer recipient survival as compared with Medicare beneficiaries. Poor graft survival among HMO/PPO recipients is in-

Table 3. Proportional hazard model of the graft and recipient survival for the whole group of patients[a]

Variables	Graft Survival		Recipient Survival	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Recipient education level				
missing or unknown	1.07 (1.03 to 1.12)	<0.001	1.101 (1.04 to 1.17)	<0.001
N/A: <5 yr old	1.26 (0.98 to 1.62)	0.076	2.36 (1.5 to 3.72)	<0.001
none	1.05 (0.83 to 1.31)	0.7	1.17 (0.87 to 1.59)	0.298
grade to high school: grades 0 to 12	Reference			
some college to bachelor's degree	0.93 (0.89 to 0.97)	<0.005	0.9 (0.84 to 0.96)	<0.005
postcollege graduate degree	0.85 (0.76 to 0.95)	<0.005	0.88 (0.76 to 1.02)	0.09
Primary source of payment				
Medicare	Reference			
Missing or unknown	1.00 (0.96 to 1.05)	0.865	1.12 (1.05 to 1.19)	<0.001
Medicaid	1.00 (0.91 to 1.09)	0.916	0.92 (0.80 to 1.05)	0.214
US/state government agency	1.00 (0.87 to 1.15)	0.957	0.84 (0.69 to 1.04)	0.108
private insurance	0.87 (0.83 to 0.90)	<0.001	0.80 (0.76 to 0.85)	<0.001
HMO/PPO	1.20 (1.02 to 1.42)	<0.05	0.52 (0.36 to 0.74)	<0.001
other: self, donation, free care, VA, pending, foreign government	1.08 (0.85 to 1.38)	0.515	0.91 (0.63 to 1.32)	0.608
Recipient citizenship				
US citizen	Reference			
missing or unknown	1.03 (0.97 to 1.10)	0.357	0.99 (0.91 to 1.08)	0.849
resident alien	0.81 (0.74 to 0.88)	<0.001	0.70 (0.62 to 0.80)	<0.001
nonresident alien	0.78 (0.54 to 1.13)	0.190	0.64 (0.35 to 1.15)	0.134

[a]Only primary variables of interest are presented. The model was adjusted for the following covariates: Recipient age, gender, race, body mass index (BMI), history of diabetes, history of hypertension, total duration of ESRD, cause of ESRD, mean and peak PRA levels, number of pretransplantation transfusions, total number of transplants, number of different RRT modalities used, donor type, donor age, gender, race, BMI, heart-beating or not, donor history of diabetes, cold ischemia time, and number of matched antigens.

triguing and difficult to explain. It is interesting that in another study, no difference in clinical outcome was demonstrated between HMO and fee-for-service patients (30). We speculate that higher copays and deductibles in these plans for specialist physician visits and expensive immunosuppressive medications compared either with private insurance plans or with Medicare/Medicaid may be a hindrance for the patients to comply with required posttransplantation treatment. Indeed, the HMO membership was associated with higher degree of cost-related skipping of medications as compared with Medicare beneficiaries (29).

Also, in our analysis, recipients with higher education level had better graft and patient survival. There is a clear trend in incremental lowering of the HR for both graft failure and recipient survival with advanced education level. Theoretically, people with a higher level of education are more likely to be well informed and have better awareness of posttransplantation care, which could potentially improve outcomes. The correlation between the better education status and compliance is arguable. We also contemplated the possibility of the association between education level and insurance status so that the effect of these variables on the outcome is not independent. It seems logical that the insurance status would be associated with education level of the recipients. To address this question, we evaluated the potential association between these variables in a bivariate (χ^2) analysis. We found a significant association between education level and insurance status ($P < 0.001$). In general, people with a higher level of education tend to earn higher income. For example, according to US Census Bureau data (31), annual average earnings of workers with a bachelor's degree was $45,678 in 1999 compared with $24,572 for those with only a high school diploma. Higher income may translate into better medical care and greater ability to pay for medication, which in turn may translate in to better graft and recipient survival. This effect of the higher education on the outcome might or might not be independent of the insurance status. To address this potential confounding effect of the education level on the insurance status, we constructed two separate models with each one having either the level of education or the type of insurance coverage and found that the results were very similar to the main analysis that included both the variables. This similarity suggests an independent association between the outcomes and the level of education and the type of insurance coverage.

Finally, in our analysis, resident aliens seem to have a significantly better outcome than US citizens in terms of both graft and recipient survival. This effect was observed in white but not in black patients and may be explained by a number of

Table 4. Proportional hazard model of the graft survival stratified by recipient race[a]

	Asian		Black		White	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Recipient education level						
missing or unknown	1.05 (0.79 to 1.39)	0.735	1.20 (1.12 to 1.29)	<0.001	1.02 (0.97 to 1.07)	0.496
N/A: <5 yr old	0.90 (0.12 to 6.63)	0.920	1.04 (0.58 to 1.84)	0.907	1.38 (1.04 to 1.84)	<0.05
none	1.37 (0.55 to 3.41)	0.5	1.24 (0.80 to 1.93)	0.344	0.87 (0.64 to 1.19)	0.379
grade to high school: 0 to 12	Reference					
some college to bachelor's degree	1.06 (0.77 to 1.44)	0.736	0.92 (0.84 to 1.01)	0.072	0.92 (0.87 to 0.97)	<0.005
postcollege graduate degree	1.06 (0.64 to 1.75)	0.828	0.72 (0.54 to 0.96)	<0.05	0.84 (0.74 to 0.95)	<0.01
Primary source of payment						
Medicare	Reference					
missing or unknown	0.96 (0.73 to 1.26)	0.744	0.94 (0.86 to 1.03)	0.180	1.04 (0.98 to 1.10)	0.215
Medicaid	0.64 (0.37 to 1.11)	0.115	0.92 (0.80 to 1.06)	0.248	1.07 (0.96 to 1.21)	0.236
US/state government agency	0.47 (0.17 to 1.27)	0.136	0.93 (0.73 to 1.19)	0.576	1.06 (0.88 to 1.27)	0.531
private insurance	0.88 (0.69 to 1.13)	0.306	0.80 (0.74 to 0.87)	<0.001	0.89 (0.85 to 0.93)	<0.001
HMO/PPO	0.97 (0.47 to 1.98)	0.924	0.95 (0.64 to 1.39)	0.776	1.36 (1.12 to 1.65)	<0.005
other: self, donation, free care, VA, pending, foreign government	0.67 (0.09 to 4.79)	0.688	0.88 (0.58 to 1.33)	0.534	1.24 (0.92 to 1.67)	0.167
Recipient citizenship						
US citizen	Reference					
missing or unknown	1.10 (0.77 to 1.57)	0.592	0.88 (0.76 to 1.01)	0.072	1.10 (1.01 to 1.20)	<0.05
resident alien	0.84 (0.66 to 1.07)	0.156	0.78 (0.60 to 1.00)	0.052	0.82 (0.74 to 0.92)	<0.001
nonresident alien	0.54 (0.22 to 1.30)	0.166	1.18 (0.53 to 2.63)	0.686	0.98 (0.60 to 1.61)	0.947

[a]Only primary variables of interest are presented. The model was adjusted for the following covariates: Recipient age, gender, race, BMI, history of diabetes, history of hypertension, total duration of ESRD, cause of ESRD, mean and peak PRA levels, number of pretransplantation transfusions, total number of transplants, number of different RRT modalities used, donor type, donor age, gender, race, BMI, heart to beating or not, donor history of diabetes, cold ischemia time, and number of matched antigens.

factors. These results are somewhat counterintuitive, as previously the negative association between foreign immigration status and the health outcome has been suggested (19). Low income, unemployment, low level of education, lack of health insurance and access to quality health care, and anti-immigrant sentiment and discrimination in health care (19) as well as language barrier (32) have been listed as potential reasons. However, because of the selection process, the transplantation population might not reflect the general trends described in immigrants. Also, it is conceivable that people who recently arrived in the United States might have certain differences in environmental factors compared with the people who were born in the United States. In a recent study, women from Poland and more recent migrants had generally more nutritious intakes, compared with US-born women or earlier migrants (33). In the year 2000, people who were born outside the United States composed an estimated 11.1% of the US population (34). In the report published by the Centers for Disease Control and Prevention, women who were born outside the United States had better birth outcomes than their racial/ethnic US-born counterparts (35). In addition, we speculate that the fraction of the foreign population that immigrates to the United States might not be simply a random slice of the foreign society but rather the motivated and active part of it. Therefore, one can hypothesize that there is a degree of selection bias when the outcome of the American citizens is compared with foreign nationals who live in the United States. The attitude toward medical care (*e.g.*, commodity rather than active involved process), such as the physician's authority and subsequent compliance with recommendations, might be different between Americans and foreigners. Although most of these potential reasons are merely speculative, some cultural differences in regard to specific aspects of medical care between Americans and foreign nationals have indeed been described in the literature (36).

In general, on the basis of our results, it seems that some of the socioeconomic factors are significant predictors of the outcome across racial groups. That supports the independent role of these factors from the racial characteristics. Also, in the studies that analyzed the role of race in the transplantation outcome, potentially uneven distribution of the socioeconomic factors (as demonstrated in Table 2) in the different racial

Table 5. Proportional hazard model of the recipient survival stratified by recipient race[a]

Variables	Asian		Black		White	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Recipient education level						
missing or unknown	1.10 (0.72 to 1.70)	0.658	1.10 (0.98 to 1.22)	0.094	1.10 (1.03 to 1.18)	<0.005
N/A: <5 yr old	0.00 (0 to 0.001)	0.969	2.51 (0.80 to 7.84)	0.115	2.34 (1.41 to 3.90)	<0.005
none	2.84 (0.98 to 8.23)	0.055	1.42 (0.73 to 2.74)	0.301	0.98 (0.66 to 1.46)	0.936
grade to high school: grades 0 to 12			Reference			
some college to bachelor's degree	1.12 (0.70 to 1.81)	0.642	0.88 (0.76 to 1.02)	0.100	0.90 (0.83 to 0.97)	<0.01
postcollege graduate degree	0.84 (0.38 to 1.85)	0.673	0.77 (0.52 to 1.13)	0.177	0.89 (0.75 to 1.06)	0.180
Primary source of payment						
Medicare			Reference			
missing or unknown	1.17 (0.79 to 1.74)	0.422	1.07 (0.93 to 1.22)	0.348	1.14 (1.06 to 1.23)	<0.005
Medicaid	0.79 (0.34 to 1.81)	0.571	0.95 (0.76 to 1.19)	0.677	0.91 (0.75 to 1.09)	0.295
US/state government agency	0.59 (0.15 to 2.41)	0.464	0.59 (0.39 to 0.90)	<0.05	1.00 (0.78 to 1.29)	0.995
private insurance	0.66 (0.44 to 0.99)	<0.05	0.71 (0.62 to 0.81)	<0.001	0.83 (0.78 to 0.89)	<0.001
HMO/PPO	0.30 (0.04 to 2.14)	0.229	0.36 (0.13 to 0.96)	<0.05	0.62 (0.41 to 0.93)	<0.05
other: self, donation, free care, VA, pending, foreign government	1.61 (0.22 to 11.72)	0.638	0.61 (0.29 to 1.27)	0.185	1.07 (0.68 to 1.69)	0.757
Recipient citizenship						
US citizen			Reference			
missing or unknown	0.83 (0.48 to 1.45)	0.515	0.86 (0.70 to 1.06)	0.148	0.96 (0.86 to 1.08)	0.528
resident alien	0.66 (0.46 to 0.96)	<0.05	0.78 (0.55 to 1.12)	0.183	0.70 (0.60 to 0.82)	<0.001
nonresident alien	0.78 (0.29 to 2.13)	0.631	0.36 (0.05 to 2.55)	0.305	0.61 (0.25 to 1.46)	0.266

[a]Only primary variables of interest are presented. The model was adjusted for the following covariates: Recipient age, gender, race, BMI, history of diabetes, history of hypertension, total duration of ESRD, cause of ESRD, mean and peak PRA levels, number of pretransplantation transfusions, total number of transplants, number of different RRT modalities used, donor type, donor age, gender, race, BMI, heart to beating or not, donor history of diabetes, cold ischemia time, and number of matched antigens.

groups may confound the results of the analysis and hypothetically explain some of the differences in the outcome between the races.

This study is a retrospective analysis that used data that were reported to the USRDS. There are limitations as well advantages to large renal transplant database analyses. Database analyses can show long-term differences in outcomes and provide the statistical power to help determine the differences between the primary variables of interest. However, the quality of data is always a concern because of the significant amount of missing and potentially erroneous information (misclassification bias). In particular, SES is difficult to quantify, and subjects might be unwilling to share certain information (*e.g.*, immigration status, education level). For example, in our data set, the education level variable is missing 61% of the data. The analysis of the role of the education status therefore is based on the remaining 39% of the data (>32,000 patients). It would be optimal not to have any missing values, but because of the very large sample size of the remaining observations, the results are still valid. One can assume random pattern of missingness in the data and analyze only records with nonmissing information. Although the random distribution of the missing values is likely, we decided not to discard the records with values missing but rather code and analyze them separately as reported above. Misclassification bias is difficult to address in the retrospective study and remains one of the shortcomings of the data registry analyses. Other potential problems with retrospective data analysis should be considered. As in other retrospective studies, although this analysis establishes the association between independent variables and the outcome, it cannot ascertain causative relationships. In addition, as in most retrospective studies, the results could be distorted by reverse causality

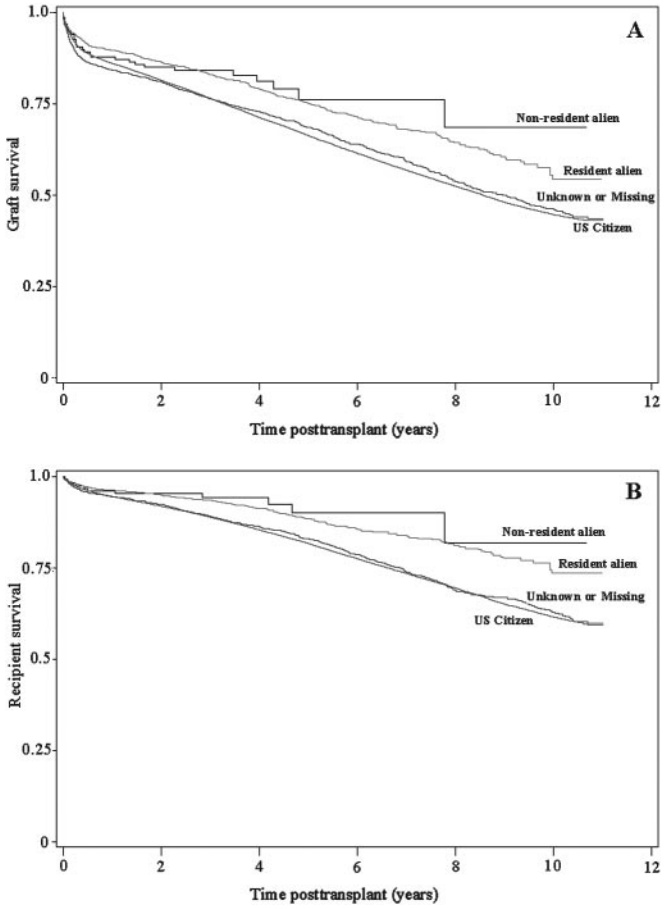

Figure 2. Kaplan-Meier analysis illustrates the association of recipients' citizenship and with graft (A) and recipient (B) survival (for both analyses, $P < 0.001$ by log-rank test).

described elsewhere (37). Finally, as our multivariate models depend on the variables that are available in the data set, certain potential confounders may not be included in the analysis (*e.g.*, annual income, employment status, geographic location, IQ level, marital status). Analysis of the role of these variables may present a new and exciting opportunity for future research.

Conclusion

Recipients with higher education level, resident aliens (as compared with US citizens), and patients with private insurance have an advantage in the graft and recipient outcomes independent of racial differences.

Acknowledgments

This study was supported in part by the Dialysis Research Foundation (Ogden, UT).

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