ARTHRITIS & RHEUMATISM
Vol. 41, No. 8, August 1998, pp 1438–1445

OUTCOME OF RENAL TRANSPLANTATION IN NINETY-SEVEN CYCLOSPORINE-ERA PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND MATCHED CONTROLS

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Objective. **To evaluate the effectiveness of renal transplantation in systemic lupus erythematosus (SLE).**

Methods. **A total of 97 SLE patients who underwent renal transplantation between January 1984 and September 1996 were selected for study and were matched with a group of non-SLE controls (1 control for each SLE patient) who also received transplants during that period. SLE patients and controls were matched on 6 covariates: age, sex, race, type of allograft (cadaveric versus living-related), number of previous transplants, and year of transplantation. All study subjects received either cyclosporine or FK-506/tacrolimus as part of their immunosuppressive regimen. In a rigorous medical records review, the status of each allograft and the cause of each graft loss was determined. Using a stratified Cox proportional hazards model, the transplantation outcomes of the SLE patients were compared with those of the controls. The effects of 9 individual variables on transplantation outcomes were also examined, and the statistically significant variables were compared in a stratified, multivariate Cox proportional hazards model.**

Results. **The control group included patients with 20 different causes of end-stage renal disease (ESRD). The mean followup times for the SLE patients and controls were 323 weeks and 320 weeks, respectively. During the followup period, 52 SLE patients and 37 controls lost their allografts. The 1-, 2-, 5-, and 10-year allograft survival probabilities for the 2 groups (SLE versus controls) were as follows: 81.7% versus 88.2% (1-year); 74.7% versus 84.4% (2-year); 45.9% versus 75.0% (5-year); and 18.5% versus 34.8% (10-year). In the multivariate model, the relative hazard of allograft loss associated with SLE as the cause of ESRD was 2.1 (95% confidence interval 1.06–4.06, $P = 0.0328$). The total number of HLA mismatches, smoking status, and delayed allograft function were also associated with allograft loss in the multivariate model.**

Conclusion. **Compared with matched controls, renal transplant patients with SLE had inferior transplantation outcomes, with more than twice the risk of allograft loss.**

Despite advances in the treatment of renal disease secondary to systemic lupus erythematosus (SLE) over the past 2 decades (1,2), lupus nephritis (LN) remains a marker of severe disease (3,4), a strong predictor of adverse SLE outcomes (5), and a leading cause of damage associated with SLE (6). LN becomes clinically evident in 50% of patients with SLE, and perhaps as many as 10% show progression to end-stage renal disease (ESRD) (7). SLE patients now account for 4% of all renal transplantation procedures performed in the United States (8).

Because SLE has been viewed as the prototypic human immune complex disease, transplant physicians in the 1960s and early 1970s believed that recurrent LN would rapidly destroy the renal allograft. Thus, in the early days of renal transplantation, there was reluctance to offer renal transplantation to SLE patients (9–11). The initial published experience with renal transplantation in SLE, however, allayed these fears. In 1975, an international, multicenter study reported that the allograft survival of 56 renal transplant patients with SLE was 55% (at an average followup of 2 years), a rate claimed to be comparable with that of non-SLE patients from the same centers at that time (12). After the publication of that study, renal transplantation became an accepted treatment for SLE patients with ESRD.

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Submitted for publication November 24, 1997; accepted in revised form March 19, 1998.

In the past 20 years, there has been relatively little critical examination of renal transplantation outcomes in SLE patients. Published studies related to the topic have varied widely in size, design, and quality (13). The median number of patients in all of the studies, including 5 multicenter studies, was 18.5. Fewer than half of the studies included comparison groups for the SLE patients, and many comparison groups were not ideally suited for determining the effect of SLE on transplantation outcome. For example, most of the studies (14–17) failed to control for the demographic distributions within the compared groups (age, race, and sex), or for other group characteristics (e.g., the percentage of patients who received living-related renal transplants and the number with previous renal allografts). Thus, the actual effectiveness of renal transplantation in SLE, compared with other patients with ESRD, remains an underexamined question.

In the mid-1980s, the field of organ transplantation entered a new era. With the introduction of a more effective immunosuppressive agent, cyclosporine, the success of organ transplantation procedures increased significantly (16). We therefore examined our center's experience with renal transplantation in SLE patients during the "cyclosporine era," comparing the transplantation outcomes of patients with SLE with those of a group of non-SLE controls matched on 6 important characteristics.

PATIENTS AND METHODS

Selection of SLE patients. All SLE patients who underwent renal transplantation at the University of California, San Francisco (UCSF) between January 1, 1984 and September 1, 1996 were included in the study. Transplant patients with SLE were identified by diagnosis through the Organ Transplantation & Immunogenetics System (OTIS), a computer database of all patients who have received organ transplants at UCSF. We cross-checked the list of SLE patients in OTIS with a list of all UCSF hospital and clinic patients with diagnoses of SLE and LN in order to identify any transplant patients with SLE whose causes of ESRD were miscoded in OTIS. Patients' diagnoses of SLE were confirmed in a rigorous review of all pre- (and post-) transplantation medical records. All patients included in the study met at least 4 of the American College of Rheumatology revised criteria for the diagnosis of SLE (18), or met 3 criteria *and* had a pretransplant renal biopsy result consistent with the diagnosis of LN (19).

Selection of controls. We chose 1 control for each SLE patient. The controls were chosen from the pool of 2,583 patients who received kidney transplants at UCSF during the same period, but who had non-SLE diseases as their causes of ESRD (Table 1). Because age at transplantation, sex, race, type of allograft (cadaveric, living-related, or living-unrelated), number of previous transplants, and year of transplantation have all been demonstrated to affect the outcome of renal transplantation (20–22), we matched the controls with the cases on all 6 of these variables.

Table 1. Etiologies of end-stage renal disease among the control subjects*

Etiology	Number
Chronic GN	16
Unknown	15
Diabetes mellitus	14
Hypertensive nephrosclerosis	12
IgA nephropathy	6
Focal sclerosing GN	6
Rapidly progressive GN	5
Congenital urologic disease	5
Polycystic kidney disease	4
Poststreptococcal GN	4
Obstructive uropathy	3
Chronic pyelonephritis	3
Membranoproliferative GN	3
Interstitial nephritis	3
Hereditary nephritis	2
Anti-GBM disease	1
Cyclosporine toxicity	1
Renal carcinoma	1
Drug-induced nephropathy	1
Lipoid nephrosis	1
Total	106

* GN = glomerulonephritis; unknown = none had clinical histories consistent with systemic lupus erythematosus; GBM = glomerular basement membrane.

The controls were selected by an investigator (JHS) who was blinded to the controls' transplantation outcomes. First, the list of potential controls was sorted by sex, race, and year of renal transplantation. Thus, for each SLE patient, the group of potential controls was narrowed to include only patients of the same sex and race who had undergone transplantation within 1 year of the SLE patient's year of transplantation. This list was narrowed further by eliminating those potential controls who received a different type of allograft (e.g., living-related as opposed to cadaveric) or who had a different number of previous renal allografts. Finally, the remaining patients were grouped according to their ages at transplantation, and the patient closest in age to that of the SLE patient was selected as the control. Patients who received dual-organ transplantations, such as diabetic patients who simultaneously received renal and pancreatic allografts, were excluded as controls. In general, however, diabetic patients were *not* excluded from serving as controls, because we wanted the control group to be representative of our population of non-SLE renal transplant patients. Each control was used only once.

Data collection. We ascertained the transplantation outcomes of all SLE patients and their controls, including the current status of each allograft, the cause of each allograft loss, and the cause of every death in patients who had functioning allografts or who returned to dialysis. Complete followup, defined as the time period from transplantation until September 1, 1996, was achieved for all SLE patients and controls through review of the subjects' 1) hospital charts, containing

Table 2. Data collected on all transplant patients with systemic lupus erythematosus and controls

Pretransplant
Demographic information (age, race, sex)
Cause of end-stage renal disease
Length of pretransplantation dialysis
Immunosuppression received prior to transplantation
Diabetic status (type I versus type II)
Smoking history (ever smoked prior to transplantation?)
Donor age
Number of mismatches at the HLA–A, B, and DR loci
Panel-reactive antibodies*
Blood-product transfusions prior to transplantation
Posttransplant
Type of allograft received (cadaveric, living-related, or living-unrelated)
Occurrence of delayed allograft function
Posttransplant blood pressure measurements
Posttransplant renal biopsy results
Current allograft status
Cause of allograft loss
Cause of death

* Panel-reactive antibodies are determined using a standard test performed at the time of transplantation, which quantifies the number of preformed recipient antibodies that are reactive against a group of lymphocytes whose antigens are representative of the population pool of HLA antigens.

details of the transplant hospitalization as well as subsequent hospitalizations, 2) transplant clinic charts, containing records of longitudinal followup visits after transplantation, and 3) pertinent outside medical records. After the medical records review, any missing patient information was obtained by telephone interviews with the patients themselves, their physicians, or surviving family members, or by inquiries to the United Organ Sharing network.

In addition to information about allograft status, cause of allograft loss, and cause of death, we also collected data on pre- and posttransplantation variables potentially associated with transplantation outcome. These variables are displayed in Table 2. As a rule, the posttransplantation immunosuppressive regimens administered at our institution do not differ between SLE and non-SLE patients.

Statistical analysis. Because of the matched study design, we used a *stratified* Cox proportional hazards model (23) to analyze the survival of renal allografts in the 2 patient groups. In the analysis, we defined "allograft loss" as any event resulting in the permanent cessation of allograft function, including death in a patient who died with a functioning allograft. Patients who did not lose their allografts during the period of the study were treated as censored observations. We calculated the relative hazard (RH) of allograft loss associated with a diagnosis of SLE (the RH of allograft loss is the ratio of the instantaneous probability of allograft loss among SLE patients to that among controls [23]). Then, in crude analyses, we examined the effects of 9 additional variables on transplantation outcomes, including weeks of dialysis, donor age, smoking history, posttransplantation hypertension, total number of HLA mismatches, number of blood-product transfusions prior to transplantation, number of preformed antibodies, pretransplant history of immunosuppression, and the occurrence of delayed allograft function. We corrected for multiple comparisons using the method of Bonferroni (24), and results with associated P values of 0.006 or less were considered statistically significant. We then examined the statistically significant variables in a stratified, multivariate Cox proportional hazards model.

RESULTS

SLE patients. One hundred transplant patients with ESRD secondary to SLE were identified through the computer search described above. Three patients were excluded because review of their records failed to confirm the diagnosis of SLE and suggested other diagnoses (specifically, IgA nephropathy, hemolytic-uremic syndrome, and non-SLE "familial nephropathy"). Thus, 97 SLE patients, recipients of a total of 106 renal transplants at our center, comprised the study group. The 106 transplantation procedures in the SLE patients included 92 first transplants and 14 second transplants (3 patients received their first transplants at other medical centers, and the outcomes of those procedures were not included in our study). Seventy-six (71.2%) of the transplantation procedures in the SLE patients involved cadaveric allografts, 28 (26.4%) were living-related transplants, and 2 (1.9%) were living-unrelated transplants.

Matching. The SLE group included 81 women (83.5%) and 16 men (16.5%). All of the SLE patients were matched successfully with controls of the same sex, and all SLE/control pairs had equal numbers of previous renal allografts. Among the SLE group, there were 35 patients of Caucasian ancestry (36.1%), 27 Hispanics (27.8%), 17 African Americans (17.5%), 6 Filipinos (6.2%), 3 Japanese, 3 Chinese, and 3 Vietnamese (3.1% each), and 1 Korean, 1 Indian, and 1 Pacific Islander (1.0% each). Precise matching on ethnicity was possible in 102 (96.2%) of the 106 SLE/control pairs. Considering all 6 matching variables, the most precise matches for 1 Vietnamese patient and 1 Indian patient (who received 2 renal allografts) were 3 different controls of Chinese ancestry. Similarly, the best match for the only Pacific Islander among the SLE patients was a control of Japanese ancestry. Among the SLE/control pairs, the SLE and control patients underwent transplantation within 1 calendar year of each other in 102 (96.2%) of the 106 cases. Patients in all SLE/control pairs except 1 received the same types of allografts, the lone exception being an African-American patient with SLE who received a living-unrelated transplant from her husband. That patient was matched to a female African-American recipient of a cadaveric allograft. Finally, 98 (92.4%) of

Table 3. Characteristics of the patients with systemic lupus erythematosus (SLE) and controls

Characteristic	SLE	Controls
Mean age at transplantation, years	35.0	38.0
Mean pretransplantation dialysis, weeks	134.0	123.1
Mean donor age, years	41.8	49.0
Positive smoking history, no.*	38	34
Mean PRA at transplantation, no.†	11.9	11.8
Mean HLA mismatches (maximum 6), no.	4.11	3.72
Posttransplantation hypertension, no.‡	14	9
Immunosuppression, no.§	94¶	25
Insulin-dependent diabetes mellitus, no.#	2	13
Delayed allograft function, no.**	11	15
Biopsy-proven, acute rejection reactions, no.	66	54
Mean posttransplantation followup, weeks	323.0	320.0

* Defined as ever having smoked cigarettes before receiving a renal transplant.
† See Table 2 for definition of panel-reactive antibodies (PRA).
‡ Defined as either a mean systolic blood pressure of >140 mm Hg or a mean diastolic blood pressure of >90 mm Hg in either the first posttransplantation year or subsequent years.
§ Defined as treatment with corticosteroids, cyclophosphamide, azathioprine, or other immunosuppressive medications in the pretransplant period as part of therapy for the cause of end-stage renal disease.
¶ $P < 0.006$ versus controls.
# None of the SLE patients had type I diabetes mellitus. Twelve of the 13 controls with diabetes mellitus as the cause of their end-stage renal disease had type I diabetes.
** Defined as the requirement for dialysis in the first week following transplantation.

the 106 SLE/control pairs were matched on age within 7 years of each other. In the other 8 pairs, differences in age ranged from 9 years to 21 years.

Characteristics of the 2 groups are displayed in Table 3. The SLE patients were more likely than controls to have received pretransplantation immunosuppression as part of the treatment for their disease leading to ESRD (98.1% versus 25.5%; $P = 0.001$).

Allograft survival. The mean followup periods for the 2 groups were nearly identical (323 weeks for the SLE group, 320 weeks for the controls). During followup, 52 SLE patients (49.1%) lost their allografts, compared with 37 controls (34.9%). The RH of allograft loss associated with having SLE as the cause of ESRD was 1.7 (95% confidence interval [95% CI] 1.03–2.83, $P = 0.0372$). Renal allograft survival curves for the 2 groups are displayed in Figure 1. The 1-, 2-, 5-, and 10-year allograft survival probabilities for the 2 groups were as follows: 1-year SLE 81.7% versus controls 88.2%; 2-year SLE 74.7% versus controls 84.4%; 5-year SLE 45.9% versus controls 75.0%; and 10-year SLE 18.5% versus controls 34.8%.

We examined the impact of individual variables on transplantation outcome, including disease status (i.e., SLE versus control), in every model. The RHs of

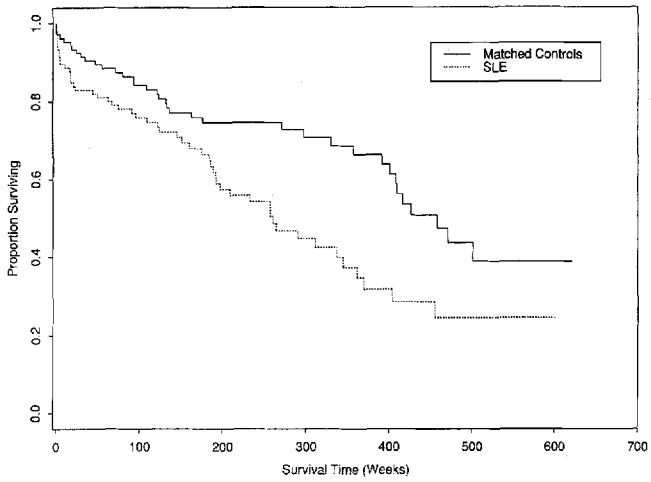

Figure 1. Renal allograft survival in patients with systemic lupus erythematosus (SLE) and matched controls using a Kaplan-Meier survival curve for renal allografts in the 2 groups. The 2 curves separate in the immediate posttransplant period, and remain separated throughout the followup period, thus indicating significant differences in survival probabilities.

allograft loss associated with the individual variables are displayed in Table 4. The RH findings describe the impact of each of the variables on allograft survival, after adjusting for disease status (i.e., cause of ESRD). In the crude analyses, the total number of HLA mismatches (RH 1.46, 95% CI 1.06–2.01, $P = 0.0205$), pretransplantation smoking history (RH 4.68, 95% CI 1.73–12.67, $P = 0.0024$), and delayed allograft function (defined as the requirement for dialysis within 1 week of transplantation) (RH 3.81, 95% CI 1.12–12.99, $P = 0.0327$) were

Table 4. Relative hazard of allograft loss for variables with potential effects on transplantation outcome*

Variable	Relative hazard	P
Weeks of pretransplantation dialysis	1.00	0.939
Total no. of HLA mismatches	1.46	0.021
Donor age	0.98	0.127
History of smoking prior to transplantation	4.68	0.0024
Panel-reactive antibodies†	1.00	0.788
No. of blood-product transfusions before transplantation	1.00	0.529
Delayed allograft function‡	3.81	0.033
No pretransplantation immunosuppression	0.41	0.139
Posttransplantation hypertension	5.90	0.101

* All Cox proportional hazards models included systemic lupus erythematosus as the cause of end-stage renal disease in addition to each listed variable.
† See Table 2 for definition.
‡ Defined as the requirement for dialysis within 1 week of transplantation.

Table 5. Multivariate Cox proportional hazards model of variables associated with renal allograft loss*

Variable	Relative hazard	*P*
SLE	2.08	0.0328
History of smoking prior to transplantation	6.69	0.0030
Total no. of HLA mismatches	1.86	0.0043
Delayed allograft function	7.88	0.0166

* These 4 variables were the only ones included in this model. SLE = systemic lupus erythematosus.

all associated with an increased risk of allograft loss during the followup period. Posttransplantation hypertension (RH 5.9, 95% CI 0.71–49.38, $P = 0.101$) was also associated with an increased risk of allograft loss, but this variable did not achieve statistical significance. Conversely, patients who received no immunosuppression prior to transplantation had a lower risk of allograft loss (RH 0.41, 95% CI 0.13–1.33, $P = 0.139$), but this variable was also not statistically significant.

We included the statistically significant variables in a stratified, multivariate Cox proportional hazards model. The results are displayed in Table 5. In the multivariate analysis, the RHs for all 4 variables included in the model *increased* compared with those in the crude analyses. All 4 variables (total number of HLA mismatches, pretransplantation smoking history, delayed allograft function, and SLE as the cause of ESRD) remained statistically significant. The RH for smoking history increased from 4.68 in the crude analysis to 6.69 in the multivariate model. The RHs for the total number of HLA mismatches and delayed allograft function also increased, from 1.46 to 1.86 for the former, and from 3.81 to 7.88 for the latter. Finally, the RH of allograft loss associated with SLE as the cause of ESRD increased from 1.7 to 2.1 (95% CI 1.06–4.06; $P = 0.0328$).

Causes of allograft loss. The causes of allograft loss in both patient groups are displayed in Table 6. The distribution of causes of allograft loss were similar for the 2 groups ($P = 0.524$, by chi-square test with 8 degrees of freedom). Recurrent LN complicated the posttransplantation course of 9 SLE patients (8.5% of all transplantation procedures in that group), and contributed to allograft loss in 4 cases (3.8%) (24). The most common cause of allograft loss in both groups, however, was chronic rejection, which accounted for 50% of the allograft failures (n = 26) in the SLE group, and 62.1% of the failures (n = 23) among the controls. Biopsy-proven, acute rejection reactions and allograft losses due to acute rejection were more common among the SLE patients than the controls (66 versus 54 and 9 versus 5, respectively), but neither comparison reached statistical significance. Eight allograft losses in the SLE group (5 thromboses and 3 deaths with functioning grafts) were attributed to complications of antiphospholipid antibodies (aPL; $P = 0.012$ compared with controls). Two allograft thromboses occurred in the control group, and were of uncertain etiology.

Patient survival. Patient survival did not differ significantly between the 2 groups. During the followup period, there were 18 deaths in the SLE group and 15 in the control group ($P = 0.71$). The causes of death for the SLE patients and controls are shown in Table 6. Three deaths in the SLE group were attributed to complications of the antiphospholipid antibody syndrome (APS), including a thrombotic stroke in a young patient, pulmonary artery thrombosis, and complications of peripheral vascular thromboses, all associated with positive tests for aPL.

DISCUSSION

Despite advances in the treatment of LN, a significant number of SLE patients experience progres-

Table 6. Etiologies of allograft loss and death among the patients with systemic lupus erythematosus (SLE) and controls

	SLE	Controls
Allograft loss		
Chronic rejection	26	23
Acute rejection	9	5
Thrombosis	5	2
Death (functioning allograft)	5	3
Recurrent original disease	4	0
Infection	1	1
Uncontrolled hypertension	0	1
Hyperacute rejection	0	1
Other	2	1
Total	52	37
Death		
Cardiopulmonary arrest	7	5
Infection	5	3
Complications of APS*	3	0
Hypertensive stroke	0	1
Uremia	1	2
Liver failure (hepatitis B)	0	1
Lung cancer	0	1
Hemorrhagic pancreatitis	0	1
Hypovolemic shock	1	0
Accidental	1	1
Total	18	15

* Complications of the antiphospholipid antibody syndrome (APS) included a thrombotic stroke in a young patient, pulmonary artery thrombosis, and complications of peripheral vascular thromboses, all occurring in the setting of positive tests for antiphospholipid antibodies.

sion to ESRD and become candidates for renal transplantation. Although most transplantation centers offer the procedure to patients with SLE with little reluctance, the outcome of renal transplantation in SLE patients has not been thoroughly studied. This study represents the largest examination to date of renal transplantation outcomes in SLE patients from a single center. The matched case–control study design permits an accurate estimation of the RH of allograft loss associated with SLE as the cause of ESRD.

The most important finding of our study is that the SLE patients had a 2-fold increase (RH 2.1) in the likelihood of allograft loss during the followup period compared with the controls, despite matching on 6 variables widely acknowledged to have important effects on transplantation outcome (20–22). This decreased allograft survival was noted, *despite* the fact that the renal allografts received by SLE patients were from donors whose mean age was more than 7 years younger than that of the controls', and despite the fact that patients with type I diabetes, who typically have the worst renal transplantation outcomes of any patient group, were included in the control group. Nearly 50% of the SLE patients who received transplants during the cyclosporine era at our institution lost their allografts during followup, compared with 34.9% of the controls. The outcomes in our control group were similar to those reported in patients from a large, multicenter study of renal transplantation outcomes (25). Therefore, unusually good transplantation outcomes in our control group do not appear to explain the discrepancy between the 2 groups.

There are several possible explanations for the decreased allograft survival among our SLE patients. Three other characteristics—number of HLA mismatches, history of smoking prior to transplantation, and the occurrence of delayed allograft function—were also associated with increased risks of allograft loss. However, these variables were evenly distributed among both groups, and thus do not explain the increased likelihood of allograft loss in the SLE group. Indeed, in the multivariate model that included these variables, the RH of allograft loss associated with SLE was increased further relative to the findings of our crude analyses.

Recurrent LN is another potential cause of the SLE patients' inferior transplantation outcomes. As a condition for renal transplantation at our center, SLE patients must demonstrate no overt clinical manifestations of active SLE for a period of 6 months, and must have normal (or near-normal) serologic parameters, i.e., complement levels and anti–double-stranded DNA antibody titers. Thus, none of the SLE patients in this study were known to have active SLE at the time of transplantation. Nevertheless, recurrent LN was detected in 9 SLE patients, and contributed to allograft loss in 4 cases (26). Thus, recurrent LN accounts partially for the discrepancy between the 2 groups. Aside from the cases of recurrent LN, clinically active SLE was unusual in our patients after transplantation, and did not constitute a major source of allograft morbidity.

Morbidity related to the presence of aPL is another possible contributor to poor transplantation outcomes among SLE patients. The occurrence of complications of APS in patients with apparently inactive SLE has been well-described (27), yet the impact of aPL on renal transplantation outcome has been underexamined. In this study, aPL were associated with 8 cases of allograft loss (or 15.4% of all allograft failures in the SLE patients) and 3 deaths. Furthermore, most of the allograft losses caused by complications of APS occurred early in the posttransplant period, partly accounting for the high number of early allograft losses in the SLE group. The contribution of aPL to poor renal transplantation outcomes, particularly in high-risk groups such as SLE patients, requires further study.

Other possible explanations for the higher rates of allograft loss among SLE patients include infections and increased rejection reactions. Although 98% of the SLE patients received pretransplantation immunosuppression (versus only 26% of the controls), the rates of posttransplantation infections were similar between the 2 groups. Similarly, the SLE group had more biopsy-proven acute rejection reactions and more allograft losses attributed to acute rejection, but neither comparison was statistically significant. Thus, we conclude that the SLE patients' inferior transplantation outcomes were not attributable to a single factor, but rather to several sources of allograft and patient morbidity, including recurrent LN, presence of aPL, and perhaps a greater overall risk of allograft rejection.

The results of our study refute the common perception (28,29) that renal transplantation outcomes in SLE patients are comparable with those in other transplant patients. Despite this common perception, 2 other studies have reached conclusions that are similar to ours. A report from the University of California, Los Angeles International Transplant Registry (16) focused on the 1-year graft survival rate of first cadaveric renal transplants in patients treated with cyclosporine. The transplantation outcomes of patients with 14 different diseases leading to ESRD were examined, including those of 142 patients with SLE. Allograft survival rates

were consistently high in all disease groups except for the SLE group, in which the 1-year graft survival rate was 67% (compared with 77% overall; $P = 0.009$). However, no adjustments were made for age, sex, or racial differences among the disease groups, which may have been substantial.

More recently, investigators from the University of Wisconsin (30) published what was previously the largest single-center study of renal transplantation outcomes in SLE. The investigators collected data on 69 SLE patients (80 renal transplantation procedures) who underwent transplantation between 1971 and 1994, a period that partly predates the introduction of cyclosporine. The comparison group was the entire nondiabetic cohort of 1,966 patients who received transplants during the same time period. When comparing the subset of 44 SLE patients who received cyclosporine with their non-SLE counterparts, the 5-year allograft survival for cadaveric renal transplants was much poorer among the SLE group (41% versus 71%; $P = 0.02$). In contrast, 5-year graft survival for living-related renal transplants was similar between the groups.

Our series of renal transplant patients with SLE may differ from SLE transplant populations at other centers in terms of ethnic mix and socioeconomic status, particularly in view of the fact that Northern California is populated by a diverse array of ethnic groups. Low socioeconomic status is associated with a number of adverse health outcomes, including renal transplantation. Thus, to the extent that socioeconomic status correlates with ethnic background, the outcomes of our SLE patients may be worse than those of SLE patients at centers with a more affluent patient mix. However, this does not alter the results of our comparison between SLE patients and controls, because the SLE patients and controls were derived from the same population and were matched on ethnic background.

A striking finding of our study was the dramatic association between smoking and transplantation outcome. Although our measurement and quantification of smoking history was relatively crude, since we merely ascertained whether or not the patients had ever smoked prior to renal transplantation, the RH of allograft loss associated with a history of smoking was the highest of any variable measured in the crude analyses (RH 4.68). The reasons for this strong association in our study are complex, and likely confounded in part by associations of cigarette smoking with lower levels of education and socioeconomic status. However, the strength of association that we observed suggests that the impact of smoking on renal transplantation outcomes deserves further study.

In summary, in contrast to the conventional understanding expounded in the literature, the SLE patients in our study had a substantially higher risk of allograft loss compared with controls. Nevertheless, because renal transplantation is a beneficial procedure to many SLE patients, and the majority of SLE patients who undergo renal transplantation have significant improvements in the quality of their lives, the results of our study should not be used to deny this procedure to patients with SLE. Rather, further investigation of the reasons for inferior transplantation outcomes among SLE patients may result in important benefits for patients who develop ESRD secondary to this disease.

ACKNOWLEDGMENTS

The authors thank John Neuhaus, PhD, for his assistance with statistical issues, and Anthony Chamberas for his selfless contribution of computer expertise. Finally, this study would not have been possible without the assistance of Ky Boyd, Calvin Lou, and the rest of the UCSF Transplantation staff.

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