

Outcomes of Kidney Transplantation in Patients With Systemic Lupus Erythematosus

A Single-center Study

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Introduction. This study aimed to compare outcomes of kidney transplantation in patients with systemic lupus erythematosus (SLE) and a matched control group of non-SLE kidney recipients. **Materials and Methods.** In a case-control study, 33 patients with kidney transplantation due to end-stage renal disease caused by SLE were matched to a control group consisted of 33 non-SLE patients who had been transplanted during the same period of time in our center. The clinical characteristics, complications, and patient and graft survival were compared between the two groups. **Results.** In each group, 12 patients (36.4%) received a kidney from a deceased donor, 15 (45.4%) from a living unrelated donor, and 6 (18.2%) from a living related donor. There was no significant difference between the outcome in SLE patients and duration of dialysis before transplantation. The mean duration of hospital stay was 23.4 ± 18.1 days in the SLE group, while it was 13.0 ± 7.3 days in the controls ($P = .006$). One-year graft survival was 79.0% in patients with SLE and 90.9% in non-SLE patients ($P = .17$). One-year patient survival was 93.9% in patients with SLE versus 81.8% in the controls ($P = .26$). Nine patients in the SLE group versus 11 patients in the control group developed posttransplant complications ($P = .59$). **Conclusions.** Although hospital stay after transplantation was longer in the SLE kidney recipients than controls, safety of kidney transplantation was comparable. Graft failure in the SLE patients was not significantly different between patients with different sources of kidneys.

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INTRODUCTION

Kidney transplantation is an established practice among patients with end-stage renal disease (ESRD) caused by lupus nephritis. This is achieved from reports demonstrating that early graft survival in these patients was comparable to that of patients with other causes of ESRD.¹ About 50% of patients with systemic lupus erythematosus (SLE), have lupus nephritis and about 10% of these patients

progress to ESRD.² Systemic lupus erythematosus is an immune-complex-mediated disease with gradual rising in its incidence in our area. The autoimmune nature of this disease caused excessive doubts about its recurrence in kidney allograft after transplantation. Current data, although are inconsistent, alleviate this theory. However, Clinical outcome of kidney transplantation among SLE patients still remains a topic of controversy.

With more than 1800 kidney transplant patients in our center, we lack comparative data between SLE and non-SLE patients. This study aimed to compare outcome of kidney transplantation in patients with SLE and a matched control group of non-SLE patients.

MATERIALS AND METHODS

Patients

In a case-control study, we reviewed charts of 33 patients who underwent kidney transplantation due to ESRD caused by SLE in Shiraz Organ Transplant Center between 1990 and 2004. We collected data on gender, age, source of kidney donation, duration of hospital stay, complications, and serum creatinine level during hospitalization. All patients included in the study met at least 4 of the American College of Rheumatology criteria for the diagnosis of SLE, and had a pretransplant kidney biopsy result consistent with the diagnosis of lupus nephritis.

The control group was consisted of 33 non-SLE patients who had been transplanted during the same period of time in our center. One control was selected for each SLE patients by an investigator who was blinded to outcomes of controls. Cases and controls were matched for age, sex, race, source of kidney donation (cadaveric versus living related and living unrelated), and number of previous transplants. Patients with diabetes mellitus or those who developed posttransplant diabetes mellitus were excluded from both cases and control groups. Both cases and controls had been receiving steroid as induction therapy. All study subjects either in case or control groups were receiving cyclosporine and mycophenolate mofetil as immunosuppression regimen. The study protocol was carried out in accordance with the Helsinki Declaration revised in 1989.

Statistical Analyses

Survival analysis was used to compare the probabilities of graft failure and patient mortality between patients with ESRD caused by lupus nephritis and patients with ESRD due to other causes. The starting date for these analyses was the date of transplantation. All data were expressed as mean \pm standard deviation. Parameter comparisons were performed with the Student *t* test and the chi-square test, and correlation analyses were performed using the Pearson correlation test. *P*

values less than .05 were considered significant. Statistical analyses were performed using the SPSS software (Statistical Package for the Social Sciences, version 12.0, SPSS Inc, Chicago, Ill, USA).

RESULTS

There were 29 women (87.9%) and 4 men (12.1%) in each of the SLE and control groups. Twelve patients (36.4%) received a kidney from a deceased donor, 15 (45.4%) from a living unrelated donor, and 6 (18.2%) from a living related donor. All of the patients were first-time kidney transplant recipients. Causes of ESRD in the control group are outlined in Table 1. Source of the kidney in the SLE patients did not have any significant correlation with mortality rate, graft failure, complications, and days of hospital stay. There was no significant difference between the outcome in SLE patients and duration of dialysis before transplantation (Table 1).

The mean duration of hospital stay was 23.4 ± 18.1 days in the SLE group, while it was 13.0 ± 7.3 days in the controls ($P = .006$). One-year graft survival was 79.0% in patients with SLE and 90.9% in non-SLE patients ($P = .17$). One-year patient survival was 93.9% in patients with SLE versus 81.8% in the controls ($P = .26$). Nine patients in the

Table 1. Characteristic of Kidney Transplant Recipients With Systemic Lupus Erythematosus and Controls*

Characteristic	SLE	Control	<i>P</i>
Mean age, y	26.8 \pm 8.0	26.7 \pm 8.0	.80
Organ source			
Living unrelated	15	15	
Living related	6	6	
Cadaver	12	12	> .99
Mean hospital stay, d	23.4 \pm 18.1	13.0 \pm 7.3	.006
Cause of ESRD			
SLE	33	0	
Chronic GN	0	8	
Reflux nephropathy	0	5	
FSGS	0	3	
Nypertension	0	2	
Alport syndrome	0	2	
RPGN	0	1	
MGN	0	1	
Unknown	0	11	> .99
Mean pretransplant dialysis, mo	24.25 \pm 23.96	14.33 \pm 8.97	.06
PRA positivity	2	4	.60

*SLE indicates systemic lupus erythematosus; ESRD, end-stage renal disease; GN, glomerulonephritis; FSGS, focal segmental glomerulosclerosis; RPGN, rapidly progressive glomerulonephritis; MGN, membranous glomerulonephritis; and PRA, panel reactive antibodies.

Table 2. Outcome and Complications of Kidney Transplant Recipients With Systemic Lupus Erythematosus (SLE) and Controls

Characteristic	SLE	Control	P
1-year graft survival	79.0	90.9	.17
1-year patient survival	93.9	81.8	.26
5-year patient survival	90.9	60.6	.06
Complications	9	11	.59
Type of complication			
Cardiac disorder	1	3	
Pulmonary edema	1	2	
Pneumonia	2	1	
Uremia	1	1	
Leakage	1	1	
Thrombocytopenia	1	0	
Gastroenteritis	1	0	
Hypocalcemia	1	0	
Urinary tract infection	0	1	
Hyperkalemia	0	1	
Kidney calculus	0	1	...
Death	3	10	.03
Causes of death			
Cardiopulmonary arrest	1	2	
Myocardial infarction	0	2	
Sepsis	1	2	
Pulmonary edema	0	1	
Accident	0	1	
Uremia	1	1	
Hypovolemic shock	0	1	...

SLE group versus 11 patients in the control group developed posttransplant complications ($P = .59$). The mean serum creatinine level 2 weeks after transplantation was 2.28 ± 1.80 mg/dL and 1.60 ± 1.20 mg/dL in the SLE and non-SLE patients, respectively ($P = .11$). The complications and causes of death in the SLE and control groups are outlined in Table 2.

DISCUSSION

In this case-control study, we showed that the general outcomes of kidney transplantation in patients with ESRD caused by SLE were not significantly different from those who underwent transplantation due to other causes of ESRD. However, the mean duration of hospitalization after kidney transplantation was significantly higher in the SLE patients. This difference may originate from the higher incidence of early posttransplant graft failure and subsequent creatinine rising in SLE patients compared to controls. Assessment of the outcomes of kidney transplantation in patients with ESRD caused by lupus nephritis is limited, because

the few of the studies that compared the risk of graft failure between transplant patients with and without lupus nephritis adjusted these comparisons for differences in potential confounding factors.^{3,4} As we know, transplant patients with ESRD caused by lupus nephritis tend to be younger than transplant patients with ESRD from other causes. On the other hand, graft survival is higher among younger recipients; hence, differences in graft survival attributed to the primary kidney disease may merely reflect differences in the ages of the groups. Recipient gender, race, and other factors may have similar or countervailing influences on estimates of relative graft survival. To defeat these confounding factors, especially age of patients, our cases and controls were matched for their age, gender distribution, source of organ donation, and number of previous transplants along with immunosuppression medications.

Most of the conducted studies since 1987 have reported a low mortality rate following kidney transplantation of patients with lupus nephritis.⁵⁻¹¹ Complications and graft survival rates were also similar in SLE patients compared to matched controlled non-lupus patients in most of case-control studies.¹²⁻¹⁵ However, some recent studies have demonstrated significant differences in major complications and graft survival among transplanted SLE patients in comparison with control groups. In a study performed by Moroni and coworkers, as well as another Spanish case-control study by Villaverde Verdejo and colleagues, the risk for thrombosis was higher among SLE patients.^{16,17} Systemic lupus erythematosus was associated with worse allograft and recipient survival rates compared with diabetic nephropathy in another case-control study.¹⁸ In a recent study, Lionaki and coworkers explained that SLE patients compared with controls had significantly higher rates of hypertension, cardiovascular disease, infections, and malignancies. They also had worse graft survival, but patient survivals were similar in both groups.¹⁹ Another Iranian study showed that Long-term patient and graft survivals were similar in SLE and non-SLE kidney transplant recipients, although the risk for thrombotic complications was greater among SLE patients.²⁰

In our study, although duration of hospital stay after transplantation was longer in SLE kidney recipients than non-lupus recipients, safety of

kidney transplantation was comparable to the control group. As some abovementioned studies reported, there was a nonsignificant tendency to a higher 1-year graft failure rates^{18,19}; however, patient survivals were not significantly difference between the SLE and non-SLE patients. Source of allograft may affect outcomes after transplantation. The source of kidney in our study was matched between the two groups, and graft failure rate in the SLE patients was not different among patients with different sources of kidneys.

CONCLUSIONS

This study suggests comparable outcomes of first kidney transplantation in patients with SLE and non-SLE patients.

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CONFLICT OF INTEREST

None declared.

REFERENCES

- [No author listed]. Renal transplantation in congenital and metabolic diseases. A report from the ASC/NIH renal transplant registry. *JAMA*. 1975;232:148-53.
- Golbus J, McCune WJ. Lupus nephritis. Classification, prognosis, immunopathogenesis, and treatment. *Rheum Dis Clin North Am*. 1994;20:213-42.
- Bumgardner GL, Mauer SM, Payne W, et al. Single-center 1-15-year results of renal transplantation in patients with systemic lupus erythematosus. *Transplantation*. 1988;46:703-9.
- Krishnan G, Thacker L, Angstadt JD, Capelli JP. Multicenter analysis of renal allograft survival in lupus patients. *Transplant Proc*. 1991;23:1755-6.
- Roth D, Milgrom M, Esquenazi V, Strauss J, Zilleruelo G, Miller J. Renal transplantation in systemic lupus erythematosus: one center's experience. *Am J Nephrol*. 1987;7:367-74.
- Goss JA, Cole BR, Jendrisak MD, et al. Renal transplantation for systemic lupus erythematosus and recurrent lupus nephritis. A single-center experience and a review of the literature. *Transplantation*. 1991;52:805-10.
- Bitker MO, Barrou B, Ourhama S, et al. Renal transplantation in patients with systemic lupus

erythematosus. *Transplant Proc*. 1993;25:2172-3.

- Grimbert P, Frappier J, Bedrossian J, et al. Long-term outcome of kidney transplantation in patients with systemic lupus erythematosus: a multicenter study. *Groupe Cooperatif de Transplantation d'île de France. Transplantation*. 1998;66:1000-3.
- Azevedo LS, Romao JE, Jr., Malheiros D, Saldanha LB, Ianhez LE, Sabbaga E. Renal transplantation in systemic lupus erythematosus. A case control study of 45 patients. *Nephrol Dial Transplant*. 1998;13:2894-8.
- Lochhead KM, Pirsch JD, D'Alessandro AM, et al. Risk factors for renal allograft loss in patients with systemic lupus erythematosus. *Kidney Int*. 1996;49:512-7.
- Stone JH, Amend WJ, Criswell LA. Outcome of renal transplantation in ninety-seven cyclosporine-era patients with systemic lupus erythematosus and matched controls. *Arthritis Rheum*. 1998;41:1438-45.
- Ward MM. Outcomes of renal transplantation among patients with end-stage renal disease caused by lupus nephritis. *Kidney Int*. 2000;57:2136-43.
- Deegens JK, Artz MA, Hoitsma AJ, Wetzels JF. Outcome of renal transplantation in patients with systemic lupus erythematosus. *Transpl Int*. 2003;16:411-8.
- Bunnapradist S, Chung P, Peng A, et al. Outcomes of renal transplantation for recipients with lupus nephritis: analysis of the Organ Procurement and Transplantation Network database. *Transplantation*. 2006;82:612-8.
- Yu TM, Chen YH, Lan JL, et al. Renal outcome and evolution of disease activity in Chinese lupus patients after renal transplantation. *Lupus*. 2008;17:687-94.
- Moroni G, Tantardini F, Gallelli B, et al. The long-term prognosis of renal transplantation in patients with lupus nephritis. *Am J Kidney Dis*. 2005;45:903-11.
- Villaverde Verdejo P, Fernandez Rivera C, Alonso Hernandez A, et al. Evaluation of renal grafts in patients with lupus nephritis as cause of end-stage renal disease. *Transplant Proc*. 2005;37:1426-7.
- Chelamcharla M, Javaid B, Baird BC, Goldfarb-Rumyantzev AS. The outcome of renal transplantation among systemic lupus erythematosus patients. *Nephrol Dial Transplant*. 2007;22:3623-30.
- Lionaki S, Kapitsinou PP, Iniotaki A, Kostakis A, Moutsopoulos HM, Boletis JN. Kidney transplantation in lupus patients: a case-control study from a single centre. *Lupus*. 2008;17:670-5.
- Ghafari A, Etemadi J, Ardalan MR. Renal transplantation in patients with lupus nephritis: a single-center experience. *Transplant Proc*. 2008;40:143-4.

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