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Outcome of renal transplantation in patients with systemic lupus erythematosus

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Abstract Renal transplantation is considered to be a good treatment option for patients with systemic lupus erythematosus (SLE) and end-stage renal disease. However, in patients with glomerular diseases, the outcome of renal transplantation can be adversely affected by recurrence of the original disease. Furthermore, the post-transplant course might be complicated by pre-transplant morbidity and treatment history. We studied the outcome of renal transplantation in patients with SLE who underwent transplantations in our center between 1968 and 2001. Patient and graft survival were compared with a matched control group. We specifically looked for any evidence of recurrent disease. There were 23 patients (two male, 21 female) with a mean ±SD age of 34±12 years at transplantation. One patient developed renal failure with serological evidence of SLE activity at 61 months after transplantation. In the absence of urine abnormalities we favored the diagnosis of rejection, although recurrence of lupus nephritis could not formally be excluded. This was the only case of a possible recurrence of lupus nephritis. Two other patients developed extra-renal manifestations of SLE at 6 and 17 months after transplantation. Patient and graft survival rates at 5 years after transplantation were 86% and 68%, respectively. Survival rates were not significantly different from those of a matched control group, 95% and 78%, respectively. Recurrence of SLE after transplantation is rare. The results of renal transplantation in patients with SLE do not differ significantly from a matched control group. Renal transplantation is a good alternative for renal replacement therapy in patients with lupus nephritis.

Keywords SLE · Relapse · Renal transplantation · Lupus nephritis

Introduction

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disorder that is characterized by the production of antibodies against auto-antigens, in particular nuclear, cytoplasmic, and cell membrane antigens. SLE can affect multiple organ systems, including the kidney. Lupus nephritis is one of the most serious manifestations of the disease, and overt nephritis is found in up to 60% of adults with SLE [2, 14]. End-stage renal disease (ESRD) requiring hemodialysis or renal transplantation develops in 5–22% of patients with lupus nephritis [17]. Transplantation is considered to be a good therapeutic option for patients with ESRD due to lupus nephritis, although recurrent disease may occur more frequently than initially thought [4]. The reported recurrence rate of lupus nephritis ranges from less than 1% to 8% [12, 23].

Most studies have reported equal graft survival rates in patients with lupus nephritis and those with other underlying diseases [1, 7, 18, 20, 24]. However, recent data have suggested that graft survival in renal transplant patients with SLE may be less [21, 22], especially in cadaveric allograft recipients treated with cyclosporine [15]. The aim of this retrospective study was to evaluate the outcome of renal transplantation in patients with SLE and to assess the rate of relapse of SLE.

Patients and methods

We examined the records of patients diagnosed with lupus nephritis who received a kidney transplant at our hospital between 1968 and 2001. Patients younger than 15 years at the time of transplantation were excluded. Only patients who fulfilled at least four of the criteria for SLE revised by the American Rheumatism Association were included in the study [10, 25].

From 1968 to 1983 basic immunosuppressive therapy consisted of prednisone (25 mg/day for 1 month tapered to 10 mg/day after 4 months) and azathioprine (3 mg/kg per day). From 1983 to 1985 patients were treated in a randomized study with either cyclosporin A (CyA; starting with 17.5 mg/kg per day and tapering to 5 mg/kg per day at 3 months) and prednisone for the first 3 months followed by conversion to azathioprine and prednisone thereafter, or azathioprine and prednisone for the whole period [11]. From 1985 to 1989 all patients received CyA and prednisone during the first 3 months and azathioprine and prednisone thereafter. In the period from 1989 to 1992, patients were treated with CyA (starting with 12 mg/kg per day and tapering to 4 mg/kg per day at 3 months) and prednisone for the first 3 months and thereafter randomized for continued treatment with either azathioprine and prednisone or CyA monotherapy [9]. From 1992 to 1997 patients were treated with a combination of CyA and prednisone, and from 1997 patients have been treated in a randomized study with mycophenolate mofetil (MMF; 1 g b.i.d.), prednisone, and high-dose (10 mg/kg per day) or low-dose (6 mg/kg per day) CyA [6]. Since 2000, patients have been treated with tacrolimus and mycophenolate mofetil in combination with either prednisone or daclizumab. Patients who received an HLA-identical living related-donor kidney have been treated with different immunosuppressive regimens. Until 1985 these patients received azathioprine and prednisone. Thereafter, they were treated with CyA (starting with 12 mg/kg per day and tapering to 4 mg/kg per day at 3 months) and prednisone for the first 3 months, followed by conversion to azathioprine and prednisone.

The following data were documented from the patients' records: gender, age, onset of disease, onset of clinical renal disease defined as proteinuria of more than 0.5 g/24 h or urinary sediment abnormalities (according to the ARA criteria for SLE), clinical symptoms, presence of ANF, anti-double-stranded DNA (anti-dsDNA), anti-phospholipid antibodies, duration of dialysis prior to transplantation, biopsy result, follow-up time after transplantation, age at transplantation, donor source, age of donor, number of mismatches at the HLA-A, B, and DR loci, immunosuppressive therapy, relapse rate, malignancy, graft failure and patient failure, coronary heart disease (myocardial infarction, angina pectoris), stroke, and peripheral vascular disease (aortic aneurysm, intermittent claudication). For each patient with SLE, one control patient was selected from our database. The controls were matched for age, gender, time of transplantation, and donor source. Information obtained from the control patients included: gender, age, donor source, age of donor, original disease, day of transplantation, follow-up time after transplantation, age at transplantation, malignancy, and date and cause of graft failure and patient failure.

The values are given as mean ± SD or median (range) when appropriate. For comparison between groups, the unpaired *t*-test or Mann–Whitney U test were used for continuous data, and Fisher's exact test was used for categorical data. Patient and graft survival rates were calculated with Kaplan–Meier survival curves. The log-rank test was used for comparison of survival curves and incidence of cardiovascular events. A P value of 0.05 was considered as the level of statistical significance.

Results

We identified 23 patients (two male and 21 female) with lupus nephritis who received a first allograft at our hospital. Twenty patients were Caucasian, one patient was Moroccan, and two patients were black. Characteristics of the individual patients with SLE at the time of SLE diagnosis and transplantation are given in Tables 1 and 2. SLE disease activity index, ANF, and anti-dsDNA activity is given in Table 3.

Before transplantation, all 23 patients had been treated with prednisone for a mean of 9.3 ± 5.4 years. Seventeen patients continued using prednisone during dialysis until transplantation. Furthermore, before dialysis, 15 patients received concomitant treatment with azathioprine for a mean of 4.5 ± 4.7 years, and three patients were treated with cyclosporine. In the early course, before the onset of ESRD, ten patients had 20 flares of disease activity of SLE, seven at extra-renal sites and 13 involving the kidney. The flares were treated with more intensified immunosuppressive therapy; however, only three patients were treated with cyclophosphamide. During chronic dialysis no patient had any new flares of SLE activity. Around the time of transplantation, 17 patients were tested for ANF. A positive ANF was found in ten patients. Anti-dsDNA was tested in 13 patients, and only two patients (who were also positive for ANF) were positive, with relatively low titers of 63 and 29 U/l, respectively.

After transplantation, two patients showed evidence of extra-renal SLE disease activity, whereas another patient had a probable recurrence of lupus nephritis. The first patient (no. 5) developed arthritis of the right ankle at 17 months after transplantation while receiving maintenance immunosuppressive therapy that consisted of cyclosporine and prednisone. Physical examination revealed a red, swollen right ankle. Synovial fluid could not be aspirated. The anti-dsDNA titer increased from 42 U/ml to 79 U/ml. Before transplantation anti-dsDNA was also positive with a titer of 30 U/ml. The patient was treated with a transient increase in prednisone dose, and azathioprine was added to the maintenance immunosuppressive regimen. With this treatment her symptoms subsided and the anti-dsDNA became negative.

The second patient (no. 23) had suffered three flares of disease activity of SLE (two involving the kidney and

Table 1 Characteristics of patients at the time of their diagnosis of SLE (*P* prednisone, *Aza* azathioprine, *Chloro* chloroquine, *Cyclo* cyclophosphamide)

Patient number	Gender	Age at diagnosis (years)	Age at start of nephritis (years)	Clinical signs and symptoms at diagnosis	Kidney biopsy	Immuno suppressive treatment before transplantation	Interval between onset of nephritis and dialysis (months)	Time on dialysis (months)
1	F	47	51	Malar rash, arthritis, leukopenia	Focal segmental glomerulonephritis (type IIIb)	P–Aza	146	25
2	F	29	31	Malar rash, arthritis, pleuritis, fever	Diffuse glomerulonephritis (type IVb)	P–Cyclo–Chloro	182	80
3	F	18	21	Malar rash, arthritis	No biopsy	P–Aza	42	22
4	F	11	14	Malar rash, arthritis, oral ulcers, pleuritis, seizures	Diffuse glomerulonephritis (type IVc)	P–Aza	231	11
5	F	23	23	Malar rash, arthritis, leukopenia, hematuria	Diffuse glomerulonephritis (type IVb)	P–Cyclo–Chloro	54	3
6	F	14	14	Malar rash, arthritis, leukopenia, thrombopenia, hematuria	No biopsy	P–Aza	52	59
7	F	30	30	Arthritis, pericarditis proteinuria, hematuria	Diffuse glomerulonephritis (type IVb)	P–Aza	41	20
8	F	17	19	Fever, seizure, anemia	No biopsy	P	21	41
9	F	16	23	Malar rash, arthritis, thrombopenia	Sclerosing glomerulonephritis (type VI)	P–Chloro	86	13
10	F	17	30	Malar rash, arthritis, oral ulcer, photosensitivity	Diffuse glomerulonephritis (type IVb)	P–Aza	15	32
11	F	17	26	Malar rash, arthritis, pleuritis, leukopenia	Diffuse glomerulonephritis (type IVc)	P–Aza–Chloro	29	9
12	M	10	10	Malar rash, oral ulcer, proteinuria, hematuria	Diffuse glomerulonephritis (type IVb)	P–Aza–Chloro	88	31
13	F	19	23	Malar rash, arthritis, pericarditis	Diffuse glomerulonephritis (type IVb)	P–Chloro	10	83
14	F	17	20	Arthritis, pleuritis, malar rash, pericarditis, seizure	Focal segmental glomerulonephritis (type IIIb)	P–Aza–Chloro	101	11
15	F	35	35	Malar rash, arthritis	No biopsy	P	49	6
16	F	23	26	Malar rash, arthritis, oral ulcer, hemolytic anemia	Diffuse glomerulonephritis (type IVb)	P–Aza	30	64
17	F	19	19	Malar rash, hematuria, proteinuria	Diffuse glomerulonephritis (type IVc)	P–Cyclo	2	11
18	F	40	50	Thrombocytopenia, arthritis, pleuritis	Diffuse glomerulonephritis (type IVd)	P–Aza–Chloro	43	27
19	F	18	19	Malar rash, arthritis, seizures	Focal segmental glomerulonephritis (type IIIc)	P–Aza	158	11
20	M	14	14	Fever, hematuria, proteinuria	Diffuse glomerulonephritis (type IVb)	P–Aza	3	52
21	F	42	47	Malar rash, arthritis	Diffuse glomerulonephritis (type IVc)	P–Aza	22	17
22	F	18	29	Arthritis, seizure	No biopsy	P	86	54
23	F	6	13	Malar rash, arthritis, oral ulcers, seizure	Diffuse glomerulonephritis (type IVc)	P–Aza	121	9

one at extra-renal sites) before transplantation. The extra-renal flare consisted of a malar rash, oral ulcers, arthritis, and a positive anti-dsDNA titer of 500 U/ml. The last flare, a reactivation of her lupus nephritis, occurred 1 year before transplantation. Six months after undergoing a living related-donor transplantation, she presented with ataxia, paralysis of the facial nerve, arthritis, and skin lesions. Immunosuppressive therapy consisted of prednisone and cyclosporine. Anti-dsDNA was initially negative, but became positive with 33 U/l, and complement levels remained normal. MRI of the brain showed a lesion in the basal ganglia consistent with ischemia due to extensive arteritis. The symptoms diminished spontaneously and anti-dsDNA titers became negative again. Seven months later she suffered a grand mal insult probably related to SLE. Although anti-dsDNA titers remained negative, a CT scan of the brain showed an increase in the lesions in the basal ganglia, consistent with extensive vasculitis. Blood pressure was very high at 240/130 mmHg, and labora-

Table 2 Characteristics of patients at their time of transplantation (*CAD* cadaveric donor, *LRD* living related donor, *NA* not available, *AIR* acute interstitial rejection, *AVR* acute vascular rejection, *CTA* cyclosporine toxicity, *P* prednisone, *CyA* cyclosporin A, *Aza* azathioprine, *Tacro* tacrolimus, *MMF* mycophenolate mofetil)

Patient number	Age at transplantation (years)	Donor source	Donor age (years)	Donor gender	Cold ischemia time (h)	Number of rejection episodes	Histological type of rejection	Baseline[a] immunosuppression after transplantation	Maintenance immunosuppression after transplantation	Follow-up time (months)
1	65	CAD	22	M	29	0		P–CyA–MMF	MMF–CyA	36
2	53	LRD	50	F	0.5	2	AIR + AVR	P–Aza	P–Aza–CyA	92
3	26	CAD	30	F	33	0		P–Aza	Graft failure	0
4	34	CAD	73	M	20.9	1	AIR	P–Aza	P–Aza	4
5	27	LRD	55	F	0.6	1	AIR	P–CyA	P–Aza–CyA	96
6	23	CAD	57	F	19.5	0		P–MMF–Tacro	P–Tacro	5
7	35	CAD	20	M	34.8	1	No biopsy	P–CyA	P–Aza	64
8	24	CAD	34	M	33.1	0		P–CyA	P–CyA	98
9	31	LRD	65	F	0.3	0		P–MMF–Tacro	P–Tacro	7
10	34	CAD	29	F	25.4	0		P–CyA	P–Aza	182
11	29	CAD	30	F	14.6	2	AIR	P–Aza	P–CyA	73
12	20	CAD	10	M	20.3	4	AIR	P–CyA	P–Aza	14
13	31	CAD	14	M	38.1	0		P–CyA	P–CyA	92
14	30	CAD	12	M	36.4	1	AVR	P–Aza	P–Aza	200
15	40	LRD	41	F	0.2	0		P–Aza	P–Aza	234
16	34	CAD	15	F	24	1	No biopsy	P–CyA	P–Aza	190
17	20	CAD	27	F	21.7	2	AIR	P–CyA	P–Aza	117
18	56	CAD	31	F	37.4	0		P–CyA	P–Aza	103
19	33	CAD	18	M	26.8	0		P–CyA	Graft failure	3
20	19	CAD	NA	NA	26.7	1	AVR	P–Aza	P–Aza	3
21	50	CAD	53	F	25	1	AIR	P–CyA	P–CyA	78
22	41	CAD	37	F	23	2	AVR + AIR	P–Aza	Graft failure	2
23	24	LRD	52	F	1	2	CTA	P–CyA	P–CyA	13

[a]Initial immunosuppressive therapy, used in the first 3 months after transplantation

Table 3 Serological manifestations of SLE and SLE disease activity index score (+ positive result, – negative result, *NA* not available, *Tx* transplantation)

Patient number	SLE disease activity index score				ANF				Anti dsDNA			
	At the time of diagnosis	At the start of dialysis	At Tx	After Tx	At the time of diagnosis	At the start of dialysis	At Tx	After Tx	At the time of diagnosis	At the start of dialysis	At Tx	After Tx
1	9	0	0	0	+	+	–	–	+	+	–	–
2	12	0	0	0	+	+	+	+	+	+	–	–
3	7	0	0	0	+	–	–	–	NA	–	–	–
4	19	0	0	0	+	+	+	+	NA	–	NA	NA
5	16	6	2	4	+	+	NA	+	+	+	+	+
6	20	0	0	0	+	+	–	NA	+	–	–	NA
7	23	0	0	0	+	+	NA	NA	+	+	–	NA
8	9	0	0	0	+	+	NA	NA	NA	–	NA	–
9	7	0	0	0	NA	+	–	NA	NA	+	NA	NA
10	8	0	0	0	+	+	+	+	+	+	NA	–
11	9	0	0	0	+	+	+	NA	+	+	+	–
12	12	0	0	0	+	+	+	NA	+	+	–	–
13	15	8	0	8	+	+	–	–	NA	+	–	–
14	18	0	0	0	+	+	+	+	NA	–	NA	–
15	7	0	0	0	+	+	+	+	+	+	–	–
16	8	0	0	0	+	+	NA	+	+	–	NA	–
17	10	0	0	0	+	+	+	+	+	+	–	–
18	9	0	0	0	+	+	+	+	+	–	NA	–
19	21	0	0	0	+	+	+	+	+	+	–	NA
20	9	0	0	0	+	NA	NA	NA	+	NA	NA	NA
21	7	0	0	0	+	+	–	–	NA	NA	NA	–
22	12	0	0	0	+	+	NA	+	NA	–	NA	–
23	19	8	0	9	+	+	–	+	+	+	–	+

tory studies revealed an increase in creatinine and thrombocytopenia, without micro-angiopathic hemolytic anemia. Fundoscopic examination was normal. A renal biopsy showed thrombi in the arterioles and glomeruli without signs of lupus nephritis. Immunofluorescence examination of the renal biopsy was consistent with intravascular coagulation. No lupus anticoagulant activity or anti-cardiolipin antibodies were detected. The grand mal insults responded well to treatment with high doses of methylprednisolone, but renal function deteriorated further, necessitating hemodialysis.

The patient who developed a probable recurrence of lupus nephritis (no. 7) received a cadaveric graft after 21 months on hemodialysis. Pre-transplant serology showed an anti-dsDNA titer of less than 1:20 (negative) and normal complement. Post-transplant immunosuppressive therapy consisted of prednisone and azathioprine. Sixty-one months after transplantation, she developed edema, proteinuria of 0.5 g/day, and a new butterfly rash. Urinalysis did not show any erythrocytes. Laboratory studies revealed elevated creatinine levels of 4.1 mg/dl, a C3 level of 514 mg/l (normal: 750–1,250 mg/l), a C4 level of 63 mg/l (normal: 180–400 mg/l), and a positive ANF. Because of a prolonged bleeding time, no renal biopsy was performed. The activated partial thromboplastin time and prothrombin time were normal. The patient was treated with prednisone (0.5 mg/kg per day). Initially, the serum creatinine level declined to 2.7 mg/dl and the C3 and C4 levels increased to 827 mg/l and 142 mg/l, respectively. However, after 2 months the creatinine level increased again, with no response to high doses of prednisone (1.5 mg/kg per day). Because of graft failure, she was subsequently placed on CAPD. Four months after the graft failed she was admitted to the hospital for acute operative repair of an aneurysm of the thoracic aorta. Postoperatively, she died from sepsis. Post-mortem examination was refused.

In the SLE group, overall patient survival was 86%, 86%, and 51% at 1, 5, and 10 years, respectively (Fig. 1). Seven patients (30%) died with functioning allografts. No patient died from recurrence of SLE. The causes of death were: infections ($n=4$), myocardial infarction ($n=1$), cerebral hemorrhage ($n=1$), and malignancies ($n=1$). Graft survival was 78% at 1 year, 68% at 5 years, and 38% at 10 years (Fig. 2). Five grafts were lost after transplantation. Graft failure was caused by recurrent lupus nephritis ($n=1$; patient no. 7), chronic rejection ($n=1$), arterial and venous thrombosis as a complication of compression by large hematomas due to direct postoperative bleeding at the anastomosis ($n=1$), acute rejection ($n=1$), and intraglomerular thrombosis ($n=1$; patient no. 23). Graft survival for cyclosporine-treated patients with a cadaveric graft ($n=7$) was 75% at 1 and 5 years.

The control group consisted of 23 patients, three male and 20 female. The mean age at transplantation was 35 ± 13 years. The original disease was chronic pyelonephritis ($n=6$), polycystic kidney disease ($n=3$), hemolytic uremic syndrome ($n=1$), membranoproliferative glomerulonephritis ($n=3$), membranous glomerulopathy ($n=2$), interstitial nephritis ($n=1$), Alport's syndrome ($n=1$), IgA nephropathy ($n=1$), reflux nephropathy ($n=1$), and unknown ($n=4$). The control group was comparable to the SLE group with respect to several donor and transplant characteristics (Table 4). Patient survival in the control group was 95%, 90%, and 77% at 1, 5, and 10 years, respectively (Fig. 1). Graft survival in the control group was 83% at 1 year, 78% at 5 years, and 46% at 10 years (Fig. 2). Graft survival in the cyclosporine-treated control group with cadaveric grafts ($n=8$) was 75% after 1 and 5 years, respectively. Although survival rates were numerically lower in SLE patients, the difference did not reach statistical significance. There was also no statistically significant difference in graft survival of pre-cyclosporine-era and post-cyclosporine-era lupus cadaver grafts compared with controls.

In the study group, three patients (13%) developed a malignancy after transplantation, one had skin cancer,

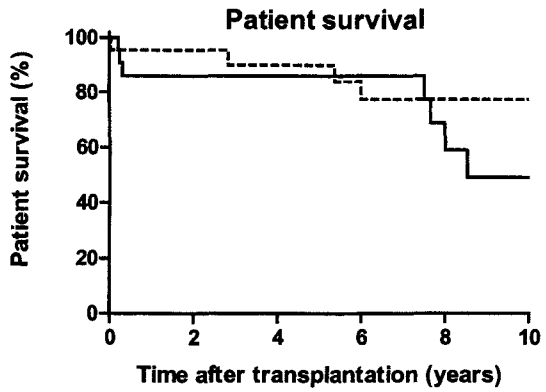

Fig. 1 Patient survival rates after renal transplantation in patients with systemic lupus erythematosus (*solid line*) and in the control group (*dotted line*)

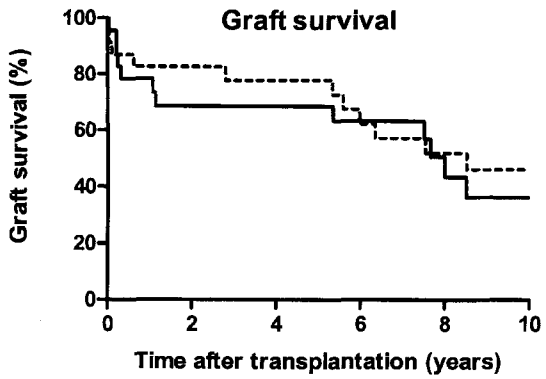

Fig. 2 Graft survival after renal transplantation in patients with systemic lupus erythematosus (*solid line*) and in the control group (*dotted line*)

Table 4 Donor and transplantation characteristics of SLE patients and controls

Characteristic	SLE ($n=23$)	Controls ($n=23$)
Donor source		
Cadaveric	19	19
Living related	4	4
Donor age (years)	35 ± 18	45 ± 20
Donor gender (M/F)	9/13[a]	15/8
Cold ischemia time (h)	21 ± 13	24 ± 13
Acute tubular necrosis (n)	5	11
Acute rejections (n)	21	22
Follow-up (months)	74 ± 73	85 ± 75
Mean HLA mismatch	0.7 ± 0.6	0.6 ± 0.5

[a]The gender of one donor could not be retrieved

one had cervical cancer (carcinoma in situ), and one developed breast cancer. Seven patients (30%) in the study group suffered from vascular disease. Five patients developed coronary heart disease, one patient had peripheral vascular disease, and one patient died from a stroke. Three patients (13%) in the control group developed a malignancy, one had skin cancer, one developed a renal cell carcinoma, and one had lung cancer. Two patients in the control group suffered from vascular disease, one had coronary artery disease necessitating a coronary artery bypass graft, and one developed a stroke. The difference between cardiovascular events in the SLE group and the control group just failed to reach the level of statistical significance (Fig. 3; $P=0.07$).

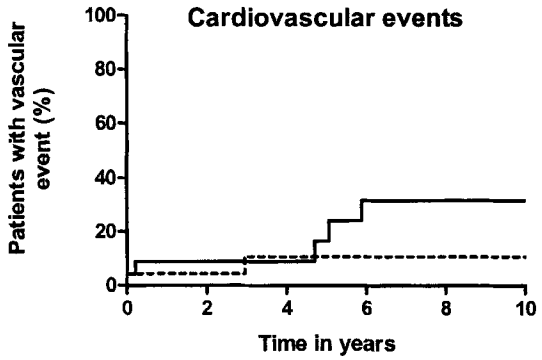

Fig. 3 Cumulative incidence of cardiovascular events in patients with systemic lupus erythematosus (*solid line*) and in the control group (*dotted line*)

Discussion

We studied 23 patients with SLE who received a renal transplant between 1968 and 2001. Three patients (13%) experienced SLE disease activity after transplantation. A possible relapse of lupus nephritis occurred in only one patient (4%). We have no histological proof of the recurrence of lupus nephritis, and the absence of erythrocytes in the urine sediment argues against lupus nephritis. However, the development of renal insufficiency and proteinuria was accompanied by a new butterfly rash, decreased serum complement levels, and a positive ANF. Therefore, to circumvent a bias against under-reporting recurrence rates, we attributed graft failure to possible lupus nephritis, although a rejection process may seem more likely. The recurrence rate in our study group is compatible with the recurrence rates of lupus nephritis reported in the literature, which vary between below 1% and 8%. For a long time it was thought that lupus nephritis had one of the lowest rates of recurrence [2]. Until 1998, there were only seven reported cases of biopsy-proven recurrent lupus nephritis in a total of 331 patients, implying a recurrence frequency of 2.1% [21]. However, this estimate may be too low. In a more recent study by Stone et al. of 97 renal transplant patients with SLE, the recurrence rate of lupus nephritis was higher, at 8.5% [23]. The lower recurrence rate in earlier reports is probably due to difficulties in distinguishing recurrent lupus nephritis from other causes of graft failure. Also, in most studies evaluation of recurrent disease was not the primary question. Admittedly, recurrence of lupus nephritis still remains a relatively rare cause of renal allograft loss.

We have only limited data on the value of routine serological evaluation during follow-up of SLE patients. However, the low recurrence rate suggests that routine laboratory follow-up is not necessary and is only indicated in the case of signs or symptoms comparable with SLE disease activity.

Our study showed no significant difference in overall graft survival between patients with ESRD due to lupus nephritis and the control group. This conclusion was not altered when we analyzed data for the pre-cyclosporine and post-cyclosporine eras. Since only four patients received a living related-donor renal transplant, we are not able to determine whether or not graft survival in these patients is better. Several other studies have been published on graft survival in lupus patients, with varying results. A number of small studies has shown that graft survival in lupus patients is similar to that of a control population [1, 7, 8, 13, 18, 20, 24, 27]. A large study conducted within the US Renal Data System, in which comparisons were adjusted for confounding factors, reported that both cadaveric and living related-donor graft survival in 1,162 patients with lupus nephritis was equivalent to graft survival in controls [27]. However, other studies have reported poorer graft survival in lupus patients [3, 15, 16, 19, 22, 26]. These conflicting results may be due to differences in composition of the control groups, since only few studies on renal transplantation in lupus patients used matched controls [7, 22]. Another explanation could come from differences in type of immunosuppression. Several studies have found lower allograft survival in lupus patients in

the cyclosporine era. Most of these patients received a cadaveric graft [22, 26]. Lochhead et al. [15] reported a significantly lower 5-year graft survival for cyclosporine-treated recipients of cadaveric grafts than for controls and cyclosporine-treated living allograft recipients. Few studies have actually compared graft survival in SLE patients before and after the introduction of cyclosporine. Overall graft survival rates in these studies is higher for patients being treated with cyclosporine than for those on azathioprine, although there is no statistically significant difference [7, 19]. A study by Zara et al. [28] reported a significantly higher 1-year graft survival rate in cyclosporine-treated patients with a cadaveric graft than in patients treated with azathioprine, namely, 62% and 26%, respectively. These studies indicate that immunosuppression with cyclosporine after cadaveric or living related-donor renal transplantation in patients with lupus nephritis is at least as good as with azathioprine. Donor source may also cause differences in graft survival. Living related-donor grafts seem to do better than cadaveric grafts, although only Lochhead et al. reported a statistically significant difference [15, 24, 27, 28]. Due to the heterogeneity of all these studies it is difficult to draw definitive conclusions about the risk of graft failure in patients with lupus nephritis. Based on studies with poorer rates of graft survival after cadaveric renal transplantation, it has been suggested that dialysis might be preferable for patients with ESRD due to lupus nephritis for whom no living related donor is available [15]. However, although one might conclude that living related-donor transplantation is the preferred treatment option for patients with ESRD due to lupus nephritis [4, 21], post-mortal donor transplantation is still a good treatment option. Our own study and a number of others, including the largest study to date by Ward et al. [27], have clearly shown that graft survival after cadaveric renal transplantation is equivalent to graft survival in controls. Furthermore, the majority of SLE patients who undergo renal transplantation experience significant improvement in their quality of life.

Patient survival in the study population with SLE was not significantly different from that in the control group, although the 10-year patient survival rate was much lower in patients with SLE. The reported 10-year patient survival in the literature varies between 60% and 86% [1, 5, 15]. The trend towards poorer 10-year patient survival rates in our study could be explained by a higher morbidity in patients with SLE. Although not statistically significant, the high cumulative incidence of cardiovascular events that we found in our SLE group, compared with controls, supports the idea of an increased morbidity in the SLE group. Another explanation could be a higher rate of infection, due to the use of immunosuppressive medication, in combination with a higher morbidity. Although we did not find a statistically significant difference in the rate of infection, four patients nevertheless died of sepsis in the SLE group, while no patient in the control group died of infectious cause.

The number of malignancies in the study group was the same as that in the control group. Since patients with SLE were treated with immunosuppressive medication before undergoing transplantation, one could expect a higher incidence of malignancies in the study group. Due to the relatively small number of patients, our study was not powerful enough to detect such a difference in the incidence of malignancies.

In summary, recurrence of lupus nephritis is rare. Although living-donor transplantation might be the preferred treatment option, our study shows that both cadaveric and living related-donor transplantations are good treatment options for patients with ESRD secondary to lupus nephritis.

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