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Early outcomes in kidney transplant recipients with systemic lupus erythematosus

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Abstract

Kidney transplant (KT) is the best treatment for patients who progress to end-stage renal disease. Short-term outcomes in patients with systemic lupus erythematosus (SLE) following KT are not well known. To describe the postoperative outcomes and complications in SLE patients undergoing KT, we conducted a case–control study from 2010 to 2015 including SLE recipients compared to non-SLE controls matched by age and sex. Demographics, comorbidities, donor characteristics, and preoperative tests were retrieved. Main outcomes were 30-day postoperative allograft function, development of infectious or non-infectious complications, and mortality. 68 patients (34 SLE, 34 non-SLE) were included. SLE recipients had median disease duration of 9 years; SLEDAI-2K of 2, and SLICC/ACR damage index of 3; 16 (47%) were taking prednisone (median dose 5 mg daily) before KT. SLE recipients had a lower frequency of diabetes (0 vs. 27%, $p=0.002$). No differences were found in the development of any complication (50% SLE vs. 47% non-SLE, $p=1.00$); infectious (44% vs. 41%, $p=1.00$), or non-infectious (15% vs. 21%, $p=1.00$). There were no deaths in either group, and none of the SLE recipients presented lupus disease activity 30 days after the KT. Allograft function determined by serum creatinine, estimated glomerular filtration rate, delayed graft function, and allograft loss was similar in both groups ($p>0.05$). There were no differences between SLE recipients with and without complications. Early postoperative outcomes in SLE patients who undergo KT, including allograft function, development of infectious, non-infectious complications, and mortality, are similar to patients without SLE.

Keywords Allografts · Delayed graft function · Kidney transplantation · Lupus nephritis · Postoperative complications

Introduction

Systemic lupus erythematosus (SLE) is the prototype autoimmune disease that affects several organs and systems, including skin, joints, nervous system, heart, lungs, and kidneys. Lupus nephritis (LN) represents the major cause of morbidity and mortality affecting almost 40% of SLE patients; from these, 11–16% will develop end-stage renal disease (ESRD) at 5 years requiring renal replacement therapy (RRT), a figure that has remained stable around 10% in recent times [1, 2]. Kidney transplant (KT) is the treatment of choice for ESRD.

The first KT in SLE patients was performed in 1959, and until 1975, it was considered a contraindication. The American College of Surgeons/National Institutes of Health (ACS/NIH) Transplant Registry reported that SLE patients undergoing KT had outcomes comparable to those of non-SLE patients [3]. One of the major concerns in that era was the potentially higher risk of allograft loss due to recurrence of

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LN, but several studies have demonstrated that allograft and overall survival are similar than those being transplanted for other causes [4].

There are recognized risk factors for recurrence of LN in kidney transplant recipients (KTR), such as black ethnicity, female gender, younger age, antiphospholipid antibodies and patient compliance with immunosuppression [5, 6]. It is estimated that LN recurrence may be as high as 30%; however, most of the cases are subclinical and detected only by histological findings. The clinical relevance of LN recurrence in SLE recipients is reported around 10% [7–10].

It is recommended by some experts to delay KT procedure until 6 months of clinical remission and at least 6 months with minimal immunosuppression to avoid a potential LN recurrence, yet the recommendation about the adequate immunological status remains controversial [9, 11, 12]. Besides clinical status, some other factors may influence the long-term outcomes of the kidney allograft, such as drugs used for immunosuppression, donor source, modality and duration of dialysis before KT, and presence of antiphospholipid antibodies [5, 13].

Several studies have reported long-term outcomes in LN recipients after transplantation, and found that graft and overall survival are comparable with patients transplanted due to other causes [14, 15]. To our knowledge, there is only one study describing early outcomes after KT in patients with SLE. It identified acute rejection and perirenal hematomas as the most frequent early complications [14]. Therefore, we aimed to describe the short-term (30 day) postoperative outcomes, including allograft function, development of infectious and non-infectious complications as well as mortality in SLE patients undergoing KT.

Materials and methods

Patients and design

We conducted a case–control study, including patients > 18 years old with established SLE diagnosis according to the American College of Rheumatology revised criteria [16] who underwent KT between January 2010 and December 2015 in the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, a tertiary care center in Mexico City with more than 1300 KT performed since 1971.

SLE patients with LN leading to ESRD who underwent KT were randomly matched 1:1 for age (±5 years) and sex with patients who underwent KT due to non-autoimmune causes of ESRD. Controls without SLE were selected randomly from the kidney transplant registry at our Institution. Patients with SLE and secondary or associated antiphospholipid syndrome (APS) were included, whereas patients with primary APS or other overlapping connective tissue diseases were excluded.

Compliance with ethical standards

The hospital Institutional Review Board (Comité de Ética en Investigación) approved the study (approval reference IRE-2002-16/17-1), and compliance with the Helsinki Declaration was followed. Informed consent was not obtained due to the retrospective nature of the study.

Evaluation and measurements

Kidney transplant recipients and living donors underwent a standardized protocol at our Institution, based on local and international recommendations, consisting on a multidisciplinary approach, as well as standardized post-operatory care protocol.

Renal variables included duration and modality of dialysis prior to KT; donor characteristics, number of shared HLA haplotypes and HLA-sensitized KTR (panel reactive antibodies, PRA), as well as causes of ESRD in non-SLE patients.

All data were abstracted from the medical records and included: demographic variables; SLE clinical characteristics at diagnosis and at the time of the KT; disease duration and presence of secondary APS; comorbidities (obesity, smoking, arterial hypertension, diabetes mellitus, dyslipidemia, heart failure, cancer and cerebrovascular disease); use of oral anticoagulants or aspirin; SLE treatment at the time of surgery, including dose of prednisone, and disease activity and damage accrued at the time of surgery using SLEDAI-2K (Systemic Lupus Erythematosus Disease Activity Index) and SLICC/ACR-DI (Systemic Lupus International Collaborating Clinics, American College of Rheumatology Damage Index), respectively [17, 18].

Preoperative variables (< 3 months prior to KT) included laboratory parameters and SLE serologic disease activity markers such as anti-double stranded DNA (anti-dsDNA), complement C3 and C4 levels. Antiphospholipid antibodies, including IgG and IgM anti-cardiolipin (aCL), IgG, and IgM anti-beta 2 glycoprotein 1 (anti-B2GPI), and lupus anticoagulant (LA) were considered as ever positive since SLE diagnosis until the surgery. Preoperatory risk assessment was evaluated using the Charlson comorbidity index [19]. Intervention times, bleeding, cold ischemia time, duration of mechanical ventilation, days in intensive care unit (ICU), length of hospital stay, second intervention or re-hospitalization, induction and maintenance immunosuppression were also retrieved. Renal biopsies prior to the transplant and 30-days renal graft biopsies were retrieved when available.

Outcomes

The main outcomes were allograft function, the development of infectious or non-infectious complications, and mortality 30 days after surgery. Allograft outcomes were evaluated at 30 days with serum creatinine, estimated glomerular filtration rate (eGFR) using the Chronic Kidney Disease Epidemiology Collaboration (CKD EPI) equation [20], allograft loss, and delayed graft function (DGF). Allograft loss was defined as persistent renal replacement therapy (RRT) requirement or eGFR < 15 mL/min/1.73 m^2 over 30 days or more, and DGF as the need of dialysis within the first week of transplantation. Infectious and non-infectious complications were documented through radiological and microbiological tests.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) or median with minimum and maximum range; categorical variables are expressed as counts and percentages. Differences between groups were evaluated with the Student *t* test or Mann–Whitney *U* test for continuous variables and Chi-square or Fisher's exact test for categorical variables; one-way ANOVA was used to assess differences when more than two groups were compared. Univariate logistic regression analyses were performed, using logistic regression to analyze associations between significant variables ($p \leq 0.10$) identified from the bivariate analyses and postoperative complications. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated. A value of $p < 0.05$ was set and two-sided values are reported. All analyses were done using Stata 12 (Stata Corp LLC, College Station, TX, USA).

Results

A total of 68 patients (34 SLE and 34 non-SLE) were included, 79% female in both groups, with a median age at surgery of 32 and 33 years in SLE and non-SLE recipients, respectively.

Characteristics of SLE recipients

Age at SLE diagnosis was 21 years (range 12–43), only 3 patients (9%) fulfilled criteria for secondary APS (1 of them thrombotic and 2 obstetric APS), and 76% presented renal involvement at SLE diagnosis. The most frequent antiphospholipid antibody was IgM aCL, positive in 48% of the patients.

At the time of KT, median duration of SLE was 9 years, disease activity assessed by SLEDAI-2K was 2 points (range 0–16), and damage according to SLICC/ACR damage index was 3 points (range 3–5). Although 16 (47%) patients with SLE were taking prednisone at the time of KT, median dose was 5 mg (1.25–10 mg/day). All the subjects had been in SLE clinical remission at least for 6 months prior to KT.

Preoperative serologic characteristics in SLE recipients showed positive anti-dsDNA in 63% and low complement C3 and C4 in 53% and 41%, respectively. Twenty (59%) SLE recipients had renal biopsy prior to KT; the most frequent type of LN was Class IV in half of the cases. Table 1 summarizes these data.

Comparative analysis of SLE and non-SLE recipients

Causes of ESRD in non-SLE recipients were unknown in 16 (47%); diabetes mellitus in 9 (26%); vesicoureteral reflux in 4 (12%); focal and segmental glomerulosclerosis and polycystic kidney disease in 2 (6%), and fibrillary glomerulopathy in 1 (3%).

Non-SLE recipients had more frequency of diabetes mellitus (26% vs. 0, $p = 0.002$), compared to SLE recipients. There were no differences in the Charlson comorbidity index between groups. As expected, more SLE recipients were taking prednisone at the time of the surgery (47% vs. 6%, $p < 0.0001$). There were no differences between groups with regard to dialysis vintage (length of time on dialysis), modalities of dialysis or preemptive transplant. Living related donor (LRD) was the most frequent source of allograft in SLE recipients (18/34, 53%), similar to non-SLE recipients (14/34, 41%) ($p = 0.46$). Deceased donor source was similar between SLE recipients (13/34, 38%) and non-SLE recipients (17/34, 50%) ($p = 0.46$). With regard to the number of shared HLA haplotypes, more SLE recipients had two-shared HLA haplotypes compared to non-SLE recipients (24% vs. 3%, $p = 0.02$).

Preoperatory lymphopenia (< 1000 cells/mm^3) was more frequent in SLE recipients compared with non-SLE recipients (41% vs. 15%, $p = 0.02$). Other laboratory parameters, such as anemia or hypoalbuminemia, were not different between groups (Table 2). Induction and maintenance immunosuppression after KT were similar between groups, including methylprednisolone in combination with Thymoglobulin or Basiliximab for induction; and the combination of either Azathioprine or Mycophenolate Mofetil with Tacrolimus and Prednisone for the maintenance regimens.

Outcomes

There were no differences between SLE recipients and non-SLE recipients with regard to surgical intervention time, cold ischemia time, amount of bleeding, or length of hospital stay. At least one postoperative complication was present in 17 (50%) of SLE recipients, compared to 16 (47%) of non-SLE

Table 1 Characteristics of SLE recipients

Variable[a]	
Sex, female/male, *n/n*	27/7
Age at SLE diagnosis, years	21 (12–43)
Length from SLE diagnosis to KT, months	110 (15–312)
SLE criteria at diagnosis	
Malar rash	16
Discoid lupus	3
Photosensitivity	10
Oral ulcers	14
Arthritis	27
Serositis	7
Renal involvement	26
Neurologic involvement	3
Hematologic	17
Immunologic, *n* + /*n*	29/32
Positive ANA, *n* + /*n*	26/31
Positive anti-dsDNA, *n* + /*n*	26/30
Secondary APS	3
Positive IgG aCL (ever), *n* + /*n*	8/31
Positive IgM aCL (ever), *n* + /*n*	15/31
Positive IgG B2GP1 (ever), *n* + /*n*	11/32
Positive IgM B2GP1 (ever), *n* + /*n*	8/32
Positive LA (ever), *n* + /*n*	6/25
SLEDAI-2K before surgery, points	2 (0–16)
SLICC/ACR damage index before surgery, points	3 (3–5)
Preoperative SLE treatment	
Prednisone	16
Prednisone dose (mg)	5 (1.25–10)
Azathioprine	8
Tacrolimus	1
Antimalarials	12
Preoperative serologic characteristics	
Positive anti-dsDNA, *n* + /*n*	17/27
Anti-dsDNA titers, UI/mL	17.4 (0.7–1130)
Low complement C3, *n* + /*n*	16/30
Low complement C4, *n* + /*n*	12/29
Lupus nephritis histopathology	*n* = 20
Class IV	10
Class IV + V	8
Class V	1
Class VI	1
Activity index, points	4 (1–13)
Chronicity index, points	8 (5–11)

SLE systemic lupus erythematosus, *KT* kidney transplant, *ANA* antinuclear antibodies, *APS* antiphospholipid syndrome, *SLEDAI-2K* Systemic Lupus Erythematosus Disease Activity Index, *SLICC/ACR damage index* Systemic Lupus International Collaborative Clinics/American College of Rheumatology, *anti-dsDNA* anti-double stranded DNA, *aCL* anti-cardiolipin, *anti-B2GPI* anti-beta 2 glycoprotein 1, *LA* lupus anticoagulant

[a]Values are expressed as n or median (minimal–maximal range)

recipients ($p = 1.00$), occurring in a median of 4 and 5 days after the surgery, respectively. There were no differences in the frequency of infectious (44% vs. 41%, $p = 1.00$), and non-infectious (15% vs. 21%, $p = 0.75$) complications between SLE and non-SLE recipients. Urinary tract infections and graft dysfunction were the most frequent infectious and non-infectious complications respectively in both groups (Table 3).

In SLE recipients, the causes of graft dysfunction were thrombotic microangiopathy ($n = 3$), pre-renal acute kidney injury ($n = 1$), and calcineurin inhibitors toxicity ($n = 1$), whereas in non-SLE recipients were pre-renal acute kidney injury ($n = 3$), acute tubular necrosis ($n = 1$), calcineurin inhibitors toxicity ($n = 1$), and humoral rejection ($n = 1$).

None of the SLE recipients presented extrarenal severe activity (i.e., thrombocytopenia, autoimmune hemolytic anemia, diffuse alveolar hemorrhage, myocarditis, serositis, seizures, and cutaneous manifestations), and there were no deaths in either group at 30-day follow-up.

When SLE patients with ($n = 17$) and without ($n = 17$) post-surgical complications (any) were compared, no differences were found with regard to clinical characteristics, treatment, comorbidities or laboratory parameters, as shown in Table 4. Moreover, no differences in the 30 days renal outcome (serum creatinine and eGFR) were found between SLE recipients that developed infectious complications (15/34, 44%) compared to those without them (19/34, 56%) ($p = 0.47$).

There were no differences in the renal outcomes between SLE recipients and non-SLE recipients, assessed with serum creatinine, eGFR, percentage of recipients who presented DGF or allograft loss, as shown in Table 5.

One patient in the SLE group with a living non-related donor kidney source and none in the non-SLE group had allograft loss. In this patient, graft nephrectomy and Tenckhoff catheter placement were performed 1 month after the KT. Two months later, the patient continued with peritoneal dialysis and developed an infected hematoma in the area of graft nephrectomy.

The outcomes and complications between SLE recipients and non-SLE recipients were not different according to graft source (living or deceased donor), or number of shared haplotypes (Supplementary Material 1–4).

SLE recipients from LRD had longer surgical intervention time (4.5 vs. 3.7 h, $p = 0.03$), and shorter cold ischemia time (65 vs. 1020 min, $p < 0.001$) compared to deceased donors, without differences in the incidence of complications (infectious or non-infectious) or renal outcome between groups (Supplementary Material 5).

The analysis of SLE ($n = 17$) and non-SLE ($n = 16$) recipients with postoperative complications showed that SLE patients had more frequency of hypertension (94% vs. 63%, $p = 0.03$); more frequency of prednisone use (35% vs. 0, $p = 0.01$), and a tendency for lower frequency of dyslipidemia (35% vs. 69%, $p = 0.08$), and lower leukocyte count

Table 2 Characteristics of SLE recipients and non-SLE recipients

Variable[a]	SLE ($n=34$)	Non-SLE ($n=34$)	p
Sex, female/male, *n/n*	27/7	27/7	1.00
Age at surgery, years	32 (18–53)	33 (18–50)	0.96
Comorbidities			
Obesity	12	13	1.00
Smoking	10	8	0.78
Diabetes mellitus	0	9	0.002*
Hypertension	31	23	0.03*
Dyslipidemia	13	19	0.22
Heart failure	2	1	1.00
Cerebrovascular disease	1	1	1.00
Cancer	3	0	0.23
Charlson comorbidity index[b]	81 ± 15	88 ± 9	0.11
Use of prednisone before surgery	16	2	< 0.0001*
Use of aspirin	4	5	1.00
Use of oral anticoagulants	2	0	0.49
ESRD characteristics			
Time in RRT, months	24 (2–108)	24 (3–132)	0.37
Peritoneal dialysis	8	10	0.78
Hemodialysis	14	11	0.60
Both modalities of RRT	9	10	1.00
Preemptive transplant	3	3	1.00
Donor kidney source			
Deceased	13	17	0.46
Living related	18	14	0.46
Living non-related	3	3	1.00
Shared HLA haplotypes			
0	18	20	0.80
1	8	13	0.29
2	8	1	0.02*
HLA-sensitized KTR (PRA > 20%)	11	8	0.59
Preoperative tests			
Hemoglobin, g/dL	10.6 (6.9–14)	11.1 (6.6–14.6)	0.50
Leukocytes, cells/mm^3	5.7 (2.1–10.3)	7.3 (3–10.7)	0.006*
Neutrophils, cells/mm^3	3.5 (1.2–6.6)	4.9 (1.6–8.5)	0.01*
Lymphocytes, cells/mm^3	1.1 (0.1–3)	1.6 (0.6–2.9)	0.01*
Platelets, × 1000/mL	205 (120–463)	233 (109–412)	0.36
Serum creatinine, mg/dL	7.3 (2.6–21.4)	9.1 (3–20.4)	0.84
Albumin, g/dL	4.1 (3–5.2)	3.9 (1.6–5)	0.14
Hemoglobin < 10 g/dL	12	9	0.60
Albumin < 3.5 g/dL	4	11	0.07
Lymphopenia < 1000/mm^3	14	5	0.02*

SLE systemic lupus erythematosus, *ESRD* end-stage renal disease, *RRT* renal replacement therapy, *KTR* kidney transplant recipient, *PRA* panel reactive antibodies

*Statistically significant p values

[a]Values are expressed as n or median (minimal–maximal range)

[b]Mean ± SD

(5.1 vs. 6.7 cells/mm^3, $p=0.09$). However, none of these differences reached statistical significance in the univariate regression analysis (Supplementary Material 6 and 7).

Table 6 summarizes the results of the renal transplant graft biopsies performed during the first 30 days after surgery in some of the patients. Of notice, three patients with

Table 3 Outcomes in kidney transplant recipients with and without SLE

Variable[a]	SLE ($n=34$)	Non-SLE ($n=34$)	p
Surgical time, h	4.2 (1–8.4)	3.9 (2–6.9)	0.66
Cold ischemia time, min	88 (20–1640)	540 (53–1920)	0.17
Bleeding, mL	200 (100–2350)	300 (20–900)	0.59
Mechanical ventilation > 1 day	0	1	1.00
Stay in intensive care unit > 1 day	4	11	0.07
Length of hospital stay, days	8 (5–30)	8 (6–21)	0.42
Postoperative complications			
Any complication	17	16	1.00
Time to complication diagnosis, days	4 (1–12)	5 (3–21)	0.07
Infectious postoperative complications (any)	15	14	1.00
Urinary tract infection	14	12	0.80
Surgical wound	1	0	1.00
Bacteremia	0	1	1.00
Abdominal sepsis	0	1	1.00
Non-infectious postoperative complications (any)	5	7	0.75
Thrombosis	0	1	1.00
Graft dysfunction	5	6	1.00
Second intervention	1	1	1.00
Second hospitalization	2	6	0.25

[a]Values are expressed as n or median (minimal–maximal range)

SLE presented renal thrombotic microangiopathy; one of them had double positivity for antiphospholipid antibodies and thrombotic APS, and also developed renal transplant infraction despite anticoagulation; one had positive LA with obstetric APS, and the third patient did not have APS diagnosis.

Discussion

In this study, we described the short-term outcomes in SLE and non-SLE recipients during the first 30 days after KT, and found no differences in the development of complications (infectious or non-infectious), renal outcomes, and mortality between groups.

There is controversy regarding the allograft and overall long-term survival in SLE patients undergoing KT and the possible effects of recurrence of LN. Most of the authors have reported that these patients have the same prognosis as patients undergoing KT due to other causes of ESRD [15, 21, 22], in line with our results. In counterpart, few studies have concluded that SLE recipients have a worse allograft and overall survival. For example, Lionaki et al. described that non-SLE recipients have better overall survival with living-related donors than SLE-patients [23]. In this regard, the analysis of our patients according to kidney donor source did not show any differences, a finding similar to other series [5, 8].

Renal transplant recipients, including SLE and non-SLE, often have multiple comorbid conditions which may be more predictive of early overall success than immunologic and transplant-related factors [24]. Rates of early non-immunological complications after KT of up to 16% have been described, particularly due to vascular and urological problems, and are frequently a source of bias in cohorts [25].

Previously, Golebiewska et al. [14] described that the most common early complications in SLE patients were acute rejection and perirenal hematomas. Nevertheless, the exact period of time after KT when these complications occurred was not specified. Our cohort showed that overall complications and outcomes are not affected particularly by SLE condition compared to other ESRD patients without immunological causes.

In our study, the most frequent complication after the surgery was urinary tract infection in both groups, without a significant difference between them (41% vs. 35%, $p=0.8$), as it was also reported in the study of Nieto-Ríos et al. [22]. The only study that emphasized short-term mortality described a patient that died of sepsis [26]. In this regard, there were no deaths in our cohort in the first 30 days after the surgery.

Even though more than 50% of SLE recipients presented positive anti-dsDNA antibodies and low C3 levels before the surgery, these markers did not distinguish between patients with and without complications, including rejection or extra-renal manifestations of lupus. Previous studies have included

Table 4 SLE recipients with and without postoperative complications

Variable[a]	With complications ($n=17$)	Without complications ($n=17$)	p
Sex, female/male, *n*/*n*	15/2	12/5	0.39
Age at SLE diagnosis, years	21 (12–35)	21 (13–43)	0.79
Age at surgery, years	30 (18–46)	35 (19–53)	0.97
Length from SLE diagnosis to KT, months	108 (23–312)	113 (15–269)	0.79
Comorbidities			
Obesity	7	5	0.72
Smoking	4	6	0.70
Hypertension	16	15	1.00
Dyslipidemia	6	7	1.00
Heart failure	0	2	0.48
Cerebrovascular disease	0	1	1.00
Cancer	2	1	1.00
Donor source			
Deceased	6	7	1.00
Living related	9	9	1.00
Living non-related	2	1	1.00
Surgical time, h	4 (2.8–8.4)	4.3 (1–7.3)	0.55
Cold ischemia time, min	108 (40–1640)	78 (20–1440)	0.48
Secondary APS	2	1	1.00
SLEDAI-2K before surgery, points	2 (0–4)	2 (0–16)	0.29
SLICC/ACR damage index before surgery, points	3 (3–4)	3 (3–5)	0.05
Preoperative SLE treatment			
Prednisone	6	10	0.30
Prednisone dose, mg	6.25 (1.25–10)	5 (2.5–5)	0.11
Azathioprine	3	5	0.68
Antimalarials	7	5	0.72
Aspirin	3	1	0.60
Oral anticoagulants	1	1	1.00
Preoperative serologic characteristics			
Positive anti-dsDNA, *n* +/*n*	8/13	9/14	1.00
Anti-dsDNA titers, UI/mL	14.4 (2.8–75)	19.2 (0.7–1130)	0.43
Low complement C3, *n* +/*n*	5/14	11/16	0.14
Low complement C4, *n* +/*n*	3/13	9/16	0.13
Preoperative tests			
Hemoglobin, g/dL	10.2 (7.9–13)	11 (6.9–14)	0.34
Leukocytes, cells/mm^3	5.1 (2.1–10.3)	5.7 (3.7–8.3)	0.54
Neutrophils, cells/mm^3	3 (1.2–6.6)	3.7 (2.5–5.9)	0.29
Lymphocytes, cells/mm^3	1.2 (0.1–3)	0.9 (0.2–1.9)	0.12
Platelets, × 1000/mL	211 (124–380)	199 (120–463)	0.90
Albumin, g/dL	4.1 (3.1–4.9)	4.3 (3–5.2)	0.22
Hemoglobin < 10 g/dL	6	6	1.00
Albumin < 3.5 g/dL	3	1	0.60
Lymphopenia < 1000/mm^3	5	9	0.29

SLE systemic lupus erythematosus, *KT* kidney transplant, *APL* antiphospholipid antibodies, *APS* antiphospholipid syndrome, *SLEDAI-2K* Systemic Lupus Erythematosus Disease Activity Index, *SLICC/ACR damage index* Systemic Lupus International Collaborative Clinics/American College of Rheumatology

[a]Values are expressed as *n* or median (minimal–maximal range)

Table 5 Renal outcomes

Variable	SLE ($n=34$)	Non-SLE ($n=34$)	p
Serum creatinine at 30 days, mg/dL[a,b]	0.9 (0.6–2.2)	0.9 (0.5–1.9)	0.51
eGFR at 30 days, mL/min/1.73 m^2 [a,b]	77.6 (28.8–126.2)	79.8 (47.7–120.4)	0.55
Delayed graft function	1	1	1.00
Allograft loss	1	0	1.00

[a]Serum creatinine and eGFR data from three recipients in dialysis were excluded

[b]Values are expressed as median (minimal–maximal range)

Table 6 30-Days renal transplant graft biopsies

Histopathological findings (n)[a]	SLE ($n=5$)	Non-SLE ($n=4$)[b]
Thrombotic microangiopathy	3	0
Humoral rejection	1	3
Calcineurin inhibitors toxicity	1	0
Tubular atrophy	0	1
Cellular rejection	0	1
Nonspecific changes	1	0

[a]Some biopsies have more than one histopathological finding

[b]One patient had two biopsies

disease status according to SLEDAI and/or SLICC [15, 26]; however, the inclusion of anti-dsDNA and complement levels before surgery as potential risk factors for complications had not been described before. In our cohort, SLEDAI and SLICC/ACR damage index scores before the procedure were low, as requested by the KT protocol at our Institution, where a minimal period of 6 months in remission is required.

Unlike other studies where the majority of SLE recipients received an allograft from deceased donors [22, 27, 28], in our study, 53% of KTR received an allograft from a LRD. In short-term, the type of donor did not impact the outcome, although it would be important to follow the long-term outcomes as mentioned by Lionaki et al. in patients without SLE [23].

In addition to the optimal circumstances around living related donation in this cohort, almost one quarter of SLE recipients shared two HLA haplotypes, which may be associated to improved outcomes given a lower risk of immunological rejection. Nevertheless, we did not find differences in graft outcomes according to number of mismatches. In addition, HLA matching is not associated to better short-term results in general population according to findings from contemporary cohorts [29].

In the first 30 days after the surgery, 11 patients (5 SLE and 6 non-SLE) of our cohort suffered graft dysfunction resulting in 9 renal transplant graft biopsies (5 SLE and 4 non-SLE). None of the biopsies in the SLE patients showed LN recurrence. In this regard, Norby et al. reported in 41 SLE recipients that more than 50% had LN recurrence during an 8-year period of follow-up. The biopsies where performed as per protocol and the majority showed type I or II LN without clinical impact. Only three KTR from LRD presented proliferative nephropathy in association with positive LA and proteinuria [10]. Moreover, a Chinese group made an analysis of transplanted kidney biopsies in 32 SLE patients [30]. In line with the results of Norby et al., most of the biopsies showed type I or II LN, without clinical significance; nevertheless, the patients received aggressive treatment without differences in the outcome compared to SLE patients with another histopathology different from LN. These findings suggest that early renal transplant graft biopsies should only be performed when there is a clinical change in recipient condition.

In our cohort, three allograft biopsies in SLE recipients presented thrombotic microangiopathy; two of them had secondary APS. In this regard, Oliveira et al. [26] reported one graft loss associated to vein thrombosis in a patient with secondary APS. Other studies have addressed the role of APS as a risk factor for allograft failure [14]. Considering this information, we propose that each SLE patient that will be accepted as a candidate for KT must have a recent determination of antiphospholipid antibodies to evaluate risk for allograft failure and need for therapy.

Limitations of our study include the small sample of patients, the retrospective design, and the very small number of patients having secondary APS, which prevented the analysis of the impact of this condition in the renal outcome. Among the strengths are the analysis of variables related to SLE both before and after the procedure, such as clinical manifestations, serologic markers, treatment, disease activity and damage; the inclusion of a well-matched control group for the comparison of the outcomes, and the homogenous evaluation of all patients following an established protocol prior to KT.

In conclusion, early postoperative outcomes in SLE recipients that undergo KT, including allograft function, development of infectious, non-infectious complications and mortality, are similar to recipients without SLE.

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analyzed and interpreted data; JMLM, LQG, AHA and JCRS drafted the manuscript; JMLM, LQG, AHA and JCRS revised the manuscript.

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References

1. Tektonidou MG, Dasgupta A, Ward MM (2016) Risk of end-stage renal disease in patients with lupus nephritis, 1971–2015: a systematic review and bayesian meta-analysis. Arthritis Rheumatol 68:1432–1441
2. Marinaki S, Lionaki S, Boletis JN (2013) Glomerular disease recurrence in the renal allograft: a hurdle but not a barrier for successful kidney transplantation. Transpl Proc 45:3–9
3. Barnes B, Bergan J, Braun W et al (1975) Renal transplantation in congenital and metabolic disease. A report from the ASC/NIH renal transplant registry. J Am Med Assoc 232:148–153
4. Burgos P, Perkins E, Pons-Estel G et al (2009) Risk factors and impact of recurrent lupus nephritis in transplanted patients with systemic lupus erythematosus: data from a single US institution. Arthritis Rheumatol 60:2757–2766
5. Contreras G, Mattiazzi A, Guerra G et al (2010) Recurrence of lupus nephritis after kidney transplantation. J Am Soc Nephrol 21:1200–1207
6. Kasiske BL, Ramos EL, Gaston RS et al (1995) The evaluation of renal transplant candidates: clinical practice guidelines. Patient Care and Education Committee of the American Society of Transplant Physicians. J Am Soc Nephrol 6:1–34
7. Signori Baracat AL, Ribeiro-Alves MA, Alves-Filho G, Mazzali M (2008) Systemic lupus erythematosus after renal transplantation: is complement a good marker for graft survival? Transpl Proc 40:746–748
8. Ponticelli C, Moroni G (2005) Renal Transplantation in lupus nephritis. Lupus 14:95–98
9. McIntyre JA, Wagenknecht DR. Antiphospholipid antibodies (2001) Risk assessment for solid organ, bone marrow, and tissue transplantation. Rheum Dis Clin North Am 27:611–631
10. Norby GE, Strom EH, Midtvedt K et al (2010) Recurrent lupus nephritis after kidney transplantation: a surveillance biopsy study. Ann Rheum Dis 69:1484–1487
11. Aygül ÇeltİK A, Sen S, Furkan Tamer A et al (2016) Recurrent lupus nephritis after transplantation: clinicopathological evaluation with protocol biopsies. Nephrology (Carlton) 21:601–607
12. Kasiske BL, Cangro CB, Hariharan S et al (2001) The evaluation of renal transplant candidates: clinical practice guidelines. Am J Transpl Suppl 2:3–95
13. Goral S, Ynares C, Shappell SB et al (2003) Recurrent lupus nephritis in renal transplant recipients revisited: it is not rare. Transplantation 75:651–656
14. Golebiewska J, Debska-Ślizień A, Bułło-Piontecka B, Rutkowski B (2016) Outcomes in renal transplantation recipients with lupus nephritis—a single-center experience and review of the literature. Transpl Proc 48:1489–1493
15. Ramírez-Sandoval JC, Chavez-Chavez H, Wagner M, Vega-Vega O, Morales-Buenrostro LE, Correa-Rotter R (2018) Long-term survival of kidney grafts in lupus nephritis: a Mexican cohort. Lupus 27:1303–1311
16. Tan EM, Cohen AS, Fries JF et al (1982) The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheumatol 25:1271–1277
17. Gladman DD, Ibañez D, Urowitz MB (2002) Systemic lupus erythematosus disease activity index 2000. J Rheumatol 29:288–291
18. Gladmann DD, Ginzler E, Goldsmith C et al (1996) The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index for systemic lupus erythematosus. Arthritis Rheumatol 39:363–369
19. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 40:373–383
20. Levey AS, Stevens LA, Schmid CH et al (2011) A new equation to estimate glomerular filtration rate. Ann Intern Med 155:408
21. Chelamcharla M, Javaid B, Baird BC, Goldfarb-Rumyantzev AS (2007) The outcome of renal transplantation among systemic lupus erythematosus patients. Nephrol Dial Transpl 22:3623–3630
22. Nieto-Ríos JF, Serna-Higuita LM, Builes-Rodriguez SA et al (2016) Clinical outcomes of kidney transplants on patients with end-stage renal disease secondary to lupus nephritis, polycystic kidney disease and diabetic nephropathy. Colomb Med 47:51–58
23. Lionaki S, Kapitsinou PP, Kostakis A, Moutsopoulos HM, Boletis JN (2008) Kidney transplantation in lupus patients: a case–control study from a single centre. Lupus 17:670–675
24. Wu C, Evans I, Joseph R et al (2005) Comorbid conditions in kidney transplantation: association with graft and patient survival. J Am Soc Nephrol 16:3437–3444
25. Khandoga A, Thomas M, Kleespies A et al (2018) Surgical complications and cardiovascular comorbidity—substantial non-immunological confounders of survival after living donor kidney transplantation. Surgeon. https://doi.org/10.1016/j.surge.2018.04.005
26. Oliveira CS, d'Oliveira I, Bacchiega ABS et al (2012) Renal transplantation in lupus nephritis: a Brazilian cohort. Lupus 21:570–574
27. Naranjo-Escobar J, Manzi E, Posada JG et al (2017) Kidney transplantation for end-stage renal disease in lupus nephritis, a very safe procedure: a single Latin American transplant center experience. Lupus 26:1157–1165
28. Contreras G, González-Suárez M, Isakova T et al (2014) Kidney allograft survival of African American and Caucasian American recipients with lupus. Lupus 23:151–158
29. Meier-Kriesche HU, Scornik JC, Susskind B, Rehman S, Schold JD (2009) A lifetime versus a graft life approach redefines the importance of HLA matching in kidney transplant patients. Transplantation 88:23–29
30. Yu TM, Wen MC, Li CY et al (2012) Impact of recurrent lupus nephritis on lupus kidney transplantation. Clin Rheumatol 31:705–710