Long-term outcomes of end-stage kidney disease for patients with lupus nephritis

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Patient outcomes in end-stage kidney disease (ESKD) secondary to lupus nephritis have not been well described. To help define this we compared dialysis and transplant outcomes of patients with ESKD due to lupus nephritis to all other causes. All patients diagnosed with ESKD who commenced renal replacement therapy in Australia and New Zealand (1963–2012) were included. Clinical outcomes were evaluated in both a contemporary cohort (1998–2012) and the entire 50-year cohort. Of 64,160 included patients, 744 had lupus nephritis as the primary renal disease. For the contemporary cohort of 425 patients with lupus nephritis, the 5-year dialysis patient survival rate was 69%. Of 176 contemporary patients with lupus nephritis who received their first renal allograft, the 5-year patient, overall renal allograft, and death-censored renal allograft survival rates were 95%, 88%, and 93%, respectively. Patients with lupus nephritis had worse dialysis patient survival (adjusted hazard ratio 1.33, 95% confidence interval 1.12–1.58) and renal transplant patient survival (adjusted hazard ratio 1.87, 95% confidence interval 1.18–2.98), but comparable overall renal allograft survival (adjusted hazard ratio 1.19, 95% confidence interval 0.84–1.68) and death-censored renal allograft survival (adjusted hazard ratio 1.05, 95% confidence interval 0.68–1.62) compared with ESKD controls. Similar results were found in the entire cohort and when using competing-risks analysis. Thus, the ESKD of lupus nephritis was associated with worse dialysis and transplant patient survival but comparable renal allograft survival compared with other causes of ESKD.

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Systemic lupus erythematosus (SLE) is a clinically heterogeneous autoimmune disease that can involve multiple systems, including the kidneys. The prevalence of SLE is 20 to 150 cases per 100,000 population and is greater in individuals of African, Hispanic, or Asian ethnicities.[1,2] It primarily affects women of childbearing age, with a female-to-male ratio of about 9:1.[3] It has been reported that 30% to 60% of patients with SLE have renal involvement and 10% to 30% of those with lupus nephritis World Health Organization class III and above will progress to ESKD within 15 years from the time of diagnosis.[4,5]

Previous retrospective, single-center observational studies of Chinese cohorts[4,6,7] and registry studies from the United States[8,9] and Taiwan[10] have reported that ESKD due to lupus nephritis is associated with increased mortality on dialysis compared with other forms of ESKD. However, these studies were variously limited by small sample size, single-center design, failure to consider the competing risk of kidney transplantation, and limited or no adjustment for baseline differences in comorbid illness or smoking status. There have also been 3 analyses of the United Network for Organ Sharing/Organ Procurement and Transplantation Network database and the United States Renal Data System database in the United States in the 1990s. Two of these analyses found similar renal allograft and patient survival outcomes between lupus nephritis transplant recipients and non–lupus nephritis recipients.[9,11] A third analysis reported worse renal allograft and patient survival in lupus nephritis transplant recipients, but the reference group comprised patients with diabetes mellitus ESKD rather than all non–lupus nephritis ESKD.[12] Overall, previous studies have suggested that patients with lupus nephritis ESKD have worse survival on dialysis but comparable outcomes following renal

transplantation compared to patients with non–lupus nephritis ESKD.

The aim of this study was to evaluate patient survival, renal function recovery, renal allograft survival, and renal transplant patient survival in patients with ESKD secondary to lupus nephritis in the Australian and New Zealand dialysis populations, using data from the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry.

RESULTS

Patient characteristics

Between 15 May 1963 and 31 December 2012, 64,160 individuals started renal replacement therapy (RRT) for ESKD. Of these, 744 individuals (1.2%) had ESKD secondary to lupus nephritis (80% biopsy proven). In the contemporary cohort (1998–2012), 447 (1.13%) ESKD patients had lupus nephritis (87% biopsy proven). For all the participants, median follow-up time was 3.8 years (interquartile range: 1.6–8.3 years), during which 483 (0.75%) patients were lost to follow-up with a median time of 4.3 years (interquartile range 0.75–11.4 years) during the study period. The baseline characteristics of contemporary and entire cohorts are displayed in Table 1 and in Supplementary Table S1 online, respectively. ESKD patients with lupus nephritis were younger, disproportionately female, and less likely to have comorbidities (diabetes, coronary artery disease, peripheral vascular disease, cerebrovascular disease) and had lower body mass index compared with other forms of ESKD.

Patient survival on dialysis

Survival times of patients with ESKD secondary to lupus nephritis specified according to the different causes of death are displayed in Supplementary Table S2 and Supplementary Figure S1. In the contemporary cohort, death occurred in 138 (32%) lupus nephritis ESKD patients and 18,410 (48%) patients with ESKD due to other causes. The causes of death were cardiac (32% vs. 37%, respectively), dialysis withdrawal (20% vs. 29%), infections (17% vs. 12%), vascular (13% vs. 8%), malignancy (8% vs. 7%), and other (9% vs. 6%) (overall $P = 0.018$). Detailed information on the types of fatal infection and malignancy is displayed in Supplementary Table S3. Adjusted respective survival rates in the 2 groups were 94% versus 96% at 1 year, 69% versus 77% at 5 years, and 40% versus 52% at 10 years.

Lupus nephritis was independently associated with higher mortality during dialysis treatment in the contemporary (1998–2012) cohort (adjusted hazard ratio [HR] 1.33, 95% confidence interval [CI] 1.12–1.58, $P = 0.001$) (Figure 1) and the entire cohort (HR 1.19, 95% CI 1.06–1.33, $P = 0.002$). Lupus nephritis ESKD patients had worse survival than ESKD controls on both hemodialysis (HR 1.28, 95% CI 1.05–1.56, $P = 0.01$) and peritoneal dialysis (HR 1.50, 95% CI 1.08–2.08, $P = 0.02$). In light of the possibility of informative censoring due to differential rates of renal transplantation (31.98% vs. 16.96%) and renal function recovery (4.75% vs. 1.61%) in the lupus nephritis and non–lupus nephritis groups, competing-risks survival analyses were performed that showed that lupus nephritis was significantly associated with higher mortality on dialysis in the contemporary cohort (sub-hazard ratio 1.38, 95% CI 1.15–1.64, $P < 0.001$) but not in the entire cohort (sub-hazard ratio 1.10, 95% CI 0.99–1.23, $P = 0.09$) (Table 2). When only Maori and Pacific Islander (MPI) patients were considered, lupus nephritis ESKD was associated with patient survival comparable to that of individuals with other

Table 1 | Characteristics of contemporary cohort patients (1998–2012) with ESKD secondary to lupus nephritis or other causes in Australia and New Zealand

Characteristics	Lupus nephritis ($n = 447$)	Other ESKD ($n = 38,866$)	*P* value
Age (years)	39 (29, 51)	61 (49, 72)	<0.001[a]
Gender: female	357 (80%)	15,340 (39%)	<0.001
Racial origin			<0.001
European	258 (58%)	28,380 (73%)	
ATSI	25 (5%)	2977 (8%)	
MPI	81 (18%)	4022 (11%)	
Asian	66 (15%)	2859 (7%)	
Other	17 (4%)	628 (1%)	
RRT era			<0.001
1998–2002	142 (32%)	10,852 (28%)	
2003–2007	152 (34%)	13,231 (34%)	
2008–2012	153 (34%)	14,783 (38%)	
Smoking status at RRT entry[b]			<0.001
Current	65 (15%)	5028 (13%)	
Former	129 (29%)	14,885 (40%)	
Never	252 (56%)	17,058 (46%)	
Diabetes mellitus[c]			<0.001
Yes	29 (6%)	16,612 (43%)	
No	418 (94%)	22,244 (57%)	
Chronic lung disease[d]			0.03
Yes	52 (12%)	6306 (17%)	
No	395 (88%)	32,554 (83%)	
Missing	0 (0%)	6 (0%)	
Coronary artery disease[d]			<0.001
Yes	85 (19%)	15,341 (39%)	
No	362 (81%)	23,519 (61%)	
Peripheral vascular disease[e]			<0.001
Yes	43 (10%)	9825 (25%)	
No	404 (90%)	29,034 (75%)	
Cerebrovascular disease[d]			0.003
Yes	40 (9%)	5732 (15%)	
No	407 (91%)	33,128 (85%)	
BMI (kg/m^2)	23.32 (20.75, 27.74)	26.50 (23.03, 30.84)	<0.001[a]
Late referral[f]			0.29
Yes	90 (20%)	9039 (23%)	
No	355 (79%)	29,685 (76%)	
First RRT			0.14
Hemodialysis	314 (70%)	27,547 (71%)	
Peritoneal dialysis	111 (25%)	10,051 (26%)	
Renal transplant	22 (5%)	1268 (3%)	

ATSI, Aboriginal and Torres Strait Islander; BMI, body mass index; ESKD, end-stage kidney disease; MPI, Maori and Pacific Islander; RRT, renal replacement therapy.
[a]Wilcoxon–Mann–Whitney test.
[b]One missing value in lupus nephritis group, 132 missing values in control group.
[c]Ten missing values in control group.
[d]Six missing values in control group.
[e]Seven missing values in control group.
[f]Two missing values in lupus nephritis group, 142 missing values in control group.