Long-term activity index after renal failure in a cohort of 32 patients with lupus nephritis

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Abstract

Objective

To characterise long-term activity levels after renal failure (RF) in lupus patients.

Methods

A retrospective activity analysis was performed of 32 lupus nephritis (LN) patients in RF over a maximum of 34 years. Activity was recorded every 6 months using the BILAG index and serological involvement (SI) (C3 and anti-dsDNA antibodies). 'Inactive' disease was defined as no BILAG A/B and no SI, 'moderate disease' as at least BILAG 1A/ 2B or 'major' SI (C3<0.73g/L and/or anti-dsDNA>149IU/ml, and 'severe' as both BILAG 1 A/2B and major SI. Patients on dialysis (n=32) were compared to patients who had a renal transplantation (n=14).

Results

In the dialysis group, 12.5% were inactive and 87.5% had at least mild-moderate activity (92.8% due to SI; 85.7% due to clinical activity) of which 37.5% demonstrated severe activity. BILAG involvement was mainly haematological (59.4%) and mucocutaneous (25%). In the renal transplantation group, 92.8% were active (100% due to SI, 84.6% due to clinical activity) of which 28.6% displayed severe activity. BILAG involvement was mainly haematological (57.1%) and renal (50%).

Conclusion

Although lupus activity is highly prevalent after RF, when a more restrictive cut off is established, activity decreases from 87.5% to 37.5% in the dialysis group and 92.8% to 28.6% in the renal transplantation group. Serological markers and haematological BILAG activity were the predominant indicators for post-RF lupus activity. We were unable to rule out whether activity derived from an intercurrent process or was intrinsic to the renal failure itself.

Key words

Lupus nephritis, disease activity, renal failure, outcome, BILAG index.

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Introduction

Renal involvement is one of the most serious complications of systemic lupus erythematosus (SLE), usually presenting early in the course of the disease (1). It can appear in over 50% of the patients (2, 3) and 20–30% may progress to end-stage renal disease (ESRD) necessitating renal replacement therapy and/or renal transplantation (2, 4, 5). In the early 1970s, Coplon *et al*. (6) and Fries *et al*. (7) were the first to report a marked clinical and serological improvement of disease activity following the onset of ESRD; a phenomenon they coined "burn-out". Since then, many authors have attempted to confirm this observation (8).

The BILAG (The British Isles Lupus Assessment Group) index is a valid and sensitive activity index based upon the principle of the physician's intention to treat (3, 9-11). The present study is the first to use the BILAG activity index to analyse a cohort of SLE patients with lupus nephritis (LN) who have gone into RF, including patients on dialysis (Dp) and patients with kidney transplants (RTp). In particular, we aimed to elucidate whether there is a difference in the grade of activity between Dps and RTps, and in which organs and/or systems activity remains.

Materials and methods

Patients

Between January 1975 and February 2012, 182 patients were diagnosed with LN at the Middlesex Hospital and University College Hospital, London. Of this cohort, 154 patients followed up until 2005 were reported previously by Croca *et al*. (12). LN was confirmed by a renal biopsy consistent with the World Health Organisation (WHO) classification criteria (n=133), or when a biopsy was not available, unequivocal clinical, serological and urinary evidence of renal involvement (n=21). 30 developed ESRD as defined by the need for dialysis [haemodialysis (HD) and/or peritoneal dialysis (CAPD)] and/or RTp.

Between 2005 and February 2012, 28 new patients have been added to the cohort, 4 of whom developed ESRD. Two of these patients were not included due to insufficient data. Patients on dialysis for less than 6 months were included. Thus, our final cohort consisted of 32 patients in ESRD. Every patient was characterised by sex, ethnicity, time from the diagnosis of SLE to LN, time from LN to ESRD, type and time of dialysis, outcome (notably mortality and its cause), and whether they had a renal transplantation. The cohort was divided into two distinct groups; the first consisted of 32 patients on Dp and the second consisted of 14 patients who had RTp.

Activity was assessed at 6-monthly intervals. In the Dp group, assessments were made from the beginning of dialysis at our Unit until February 2012, death, loss of follow-up or renal transplantation. In the RTp group, assessments were made from the time of transplantation until February 2012, death, graft rejection or loss of follow-up. Assessments were performed by three parallel methods: (1) Both the 'classic' BILAG and BILAG-2004 index. For patients diagnosed prior to the instigation of the BILAG assessment (1988) we undertook a careful review of the hospital notes in order to complete a 'classic' BILAG. (2) Levels of complement C3 (0.9–1.8 g/L), measured using laser nephelometer. (3) Levels of anti-dsDNA antibodies detected by ELISA (Shield Diagnostics, Dundee, UK) (0-50 IU/ml), or by Crithidia and ELISA. The definition of grades of activity is summarised in Table I. For patients on dialysis, renal assessment by BILAG was excluded but assessed again after RTp.

Statistics

Clinical, serological and epidemiological features were collected and descriptively analised in contingency tables. Results were expressed as mean ± standard deviation (if normally distributed) or, alternatively, as median and range. All values were expressed to 1 or 2 decimal place. For comparisons between the two groups a univariant analysis was performed using Chi-square test (with Yates' correction for expected frequencies less than 5), Fisher test, Mann-Whitney non-parametric *t*-test and Wilcoxon signed-rank

test, where necessary. A 2-tailed value of $p<0.05$ indicates statistical significance. The statistical analysis was performed using the 19.0 SPSS programme (SPSS, Chicago, IL).

Results

1. General characterisation

(Tables II and III)

Of the 32 Dps, 31 were female. Ethnically, 12 (37.5%) were Afro-Caribbean (AC), 9 (28.1%) Caucasian (C), 8 (25.0%) Asian (A) (including Indian, Pakistani and Bangladeshi) and 3 (9.4%) were others. The mean age at diagnosis of RF was 33.9 (SD 12.8). The majority (40.6%; n=13) developed ESRD 6-10 years after initial renal involvement [6 A (46.1%), 4 AC (30.8%), 3 C (23.1%)]. For 12.5%, ESRD was the first manifestation of renal disease (n=4; 100% AC), 28.1% developed ESRD 2–3 years after LN began [(n=9; 4 AC (44.4%), 2 C (22.2%), 1 A (11.1%), 2 others)], and a further 18.7% developed ESRD after >10 years [n=6; 4 C (66.7%), 1 A and 1 other (16.6%)]. All of the patients had dialysis for a time ranging from 1 to 144 months. Five patients received treatment mostly in other hospitals for a mean time of 69.9±27.4 months. In our hospital, 15 patients received dialysis for a period of between 1-5 years (46.9%). Eleven patients (34.4%) died after a mean time of 3.5±2.4 years on dialysis. The causes of death are summarised in Table II. Patients during dialysis remained on inmunosupression using prednisolone plus azathioprine in most of cases or plus micofenolate (MMF) in the past few years. We do not have information in 2 cases.

Of the 14 RTps, 7 grafts were from cadaveric donors, 6 from a living relative donor, and unknown in 1. All transplant patients were female, with a mean age of 33.8±12.1 years. Ethnically, 6 were A, 5 C and 3 AC. The mean time from ESRD to transplantation was 38.5 months. All patients were on dialysis prior to transplantation, the majority for 1-5 years (n=6). Treatment after renal transplantation included triple therapy (Table III). Four patients (28.6%) had transplant failure (50% in less than 2 years after RTp) due to renal flare

Table I. Activity criteria.

		Not Active	Active			
			Mild	Moderate		Severe
BILAG	No A or B	✓	✓			
	1B			✓		
	1A/2B				✓	✓
Serology	C3=0.9-1.8 g/L and anti-dsDNA= 0-50 IU/ml	✓	✓		✓	
	C3 <0.9≥ 0,73 and/or anti-dsDNA>50≤ 150		✓	✓		
	C3<0,73 and or anti-dsDNA>150			✓		✓

Table II. Characteristics of patients in dialysis.

	n (%)		n (%)
Sex: female	31 (9.9)	Years in dialysis	
Ethnic:		<1	9 (28.1)
AC	12 (37.5)	>1<5	15 (46.9)
C	9 (28.1)	>5<10	6 (18.7)
A	8 (25)	>10	2 (14.3)
Others	3 (9.4)	B- cell deplection	9 (28.1)
Age at RF [mean (SD)]	33.9 (12.8)	Deceased	11 (34.4)
Years from RD to RF:		Cause of death:	
<1	4 (12.5)	Infections	4 (12.5)
>1<3	9 (28.1)	Cardioavscular	2 (6.2)
<6<10	13 (40.6)	Cancer	1 (3.1)
>10	6 (18.7)	Lupus flare	1 (3.1)
Dialysis	32 (100)	Traffic accident	1 (3.1)
HD	12 (37.5)	Maior bleeding	1 (3.1)
CAPD	11 (34.4)	Unknown	1 (3.1)
Both	9 (28.1)	Months of Follow-up [median (IQR)]	24 (12-35.1)
		Patients treated in others hospitals	5
		Months of follow-up	69.9 (SD+27.4)

AC: Afrocaribean; C: Caucassian; A: Asian; RD: renal disease; RF: renal failure; HD: haemodialysis; CAPD: peritoneal dialysis.

Table III. Patients with RTp.

	n (%)		n (%)
Sex: female	14 (100)	Years from ESRD to RTp	
Age at RTp	33.8 (12.1)	<1	2 (14.3)
Ethic:		>1<5	10 (71.4)
AC	3 (21.4)	>5<10	1 (7.1)
C	5 (35.7)	>10	1 (7.1)
A	6 (42.9)	B-cell deplection before Tp	3 (21.4)
Years from RD to ESRD		Type of RTp	
<1	2 (14.3)	Cadaver donor	7 (50)
>1<5	2 (14.3)	Relative donor	6 (42.8)
>5<10	6 (42.6)	NA	1 (7.1)
>10	4 28.6)	Treatment after RTp	
Renal biopsy (WHO Clasiffication)		Prednisone	14 (100%)
NA	3 (21.4)	CSA	5 (35.7)
II	1 (7.1)	Tacrolimus	9 (64.3)
IV	10 (71.4)	Mycophenolate	7 (50)
Years in dialysis		Azatioprine	7 (50)
<1	4 (28.6)	RTp outcome	
>!<5	6 (42.9)	Favourable	10 (71.4)
>5<10	2 (14.3)	Failure	4 (28.6))
>10	1 (7.1)	Months of follow-up [mean IQR)]	36 (19.5-58.5)
Type of dialysis		Deceased	3 (21.4)
HD	5 (35.7)	Infection	1 (33.3)
CAPD	6 (42.9)	Renal lupus flare	1 (33.3)
Both	3 (21.4)	Colon carcinoma	1 (33.3)

RTp: renal transplant; NA: not avalaible; CSA: Cyclosporine A.

Table IV. Activity index.

	Dialysis (n=32) n (%)	RTp (n=14) n (%)	*p*-value
1. Inactive disease	4 (12.5)	1 (7.1)	
2. Active disease	28 (87.5)	13 (92.8)	1
SI	26 (92.8)	13 (100)	
BILAG+SI	24 (85.7)	11 (84.6)	
HD/CAPD	10 (83.3)/	10 (90.9)	0.9
Ld/Cd	7 (100)/	5 (83.3)	
A. Moderate disease	22 (68.7)	7 (50)	0.32
SI	21 (95.4)	7 (100)	
BILAG+SI	19 (86.4)	6 (85.7)	
B. Severe disease	12 (37.5)	4 (28.6)	0.74
HD/CAPD	3 (25)/	4 (36.4)	0.9
Ld/Cd		0/4 (66.6)	0.19
Organs/system afected			
Haematological	19 (59.4)	8 (57.1)	
Mucocutaneuous	8 (25)	5 (35.7)	
Musculoeskeletal	7 (21.9)	5 (35.7)	
General	6 (18.7)	3 (21.4)	
Cardiovascular	5 (15.6)	3 (21.4)	
Neurological	1 (3.1)	1 (7.1)	
Vasculitis	0	1 (7.1)	
Renal involvement	X	7 (50)	

Ld: Living relative donor; Cd: Cadaveric donor.

(AC patient, IV WHO Class glomerulopathy in graft biopsy), septic complication, chronic allograft glomerulopathy (after 7 years) and unknown. Three patients died during follow-up; time to death was 1, 2 and 9 years after RTp, and causes of death are in Table III.

2. Activity index

– Global activity (Table IV)

The median follow-up at our hospital was 24 months (IQR 12-35.1) for the 32 Dps, and 36 months (IQR 19.5-58.5) for the 14 RTps. Complete inactivity during follow-up was demonstrated by 4 Dps (12.5%) and only 1 (7.1%) RTp. Some level of activity was shown at some point in follow-up in the remaining 28 Dps (87.5%) and 13 RTps (92.8%) (p=1). This was due to SI in 26 Dps (92.8%) and 13 RTps (100%). In both groups, SI often correlated with BILAG activity [24 Dps (85.7%) and 11 RTps (84.6%)].

When at least moderate activity markers were considered to define the presence of SLE disease, activity was present in 22 Dps (68.7%) and 7 (50%) RTps (p=0.32); In the Dps, activity was due to SI in the majority (21 patients; 95.4%) of whom 19 (86.4%) had associated BILAG activity. In the RTps, activity was demonstrated by both SI and BILAG markers (85.7%). Severe activity was present in 12 Dps (37.5%) and 4 RTps (28,6%) (p=0.74). One patient with severe activity died in each group (8.3% and 25% each). Ethnically, there was no statistical significance difference in Dps or RTps with severe activity (AC: 5 vears 2, p=0.61; C: 3 vears 1, p=0.54, A: 3 vears 1, p=0.49). Patients with severe activity during dialysis had a mean time of 7.9 years from SLE diagnosis to RF (IC 95%; 4.40-11.50) and stayed on dialysis for a mean of 1.25 years (CI 95% 0.64-1.86). There was no significant difference in these parameters compared with those who did not have severe activity (p=0.46 and 0.369, respectively). Lupus activity was also analysed between patients on different types of Dp (12 patients on HD versus 11 patients on CAPD) but statistical significance was not found not in neither global nor severe activity (p=0.9).

In RTps, the mean time from SLE to RF in patients with severe activity was 11.8 years (CI 95% 5.39-18.21) and the mean time on dialysis until renal transplantation was 0.8 years (IC 95% 0.24-1.36%), again without significant difference to the rest of the cohort (p=0.13 and 0.10, respectively). Activity was compared between those patients who received a graft from living donors (RLD) (n=7) or cadaveric donors (CD) (n=6). 100% presented with activity during follow-up in the first group and 83.3% (n=5) in the second group. Severe activity was not present in any case in the first group. In contrast, in the second group 4 patients presented severe lupus disease (66.6%), but this was not statistically significant (p=0.19)

In both groups, the most frequent organ/system in which BILAG activity was recorded was haematological [(Dp: 19 patients (59.4%); RTp: 8 patients (57.1%)]. This was predominantly due to anaemia [Dp: 19 (100%); RTp: 7 (87.5%)], lymphopenia [Dp: 16 (84.2%); RTp: 6 (75%)], thrombocytopenia [Dp: 3 (15.8%); RTp: 3 (37.5%)], neutropenia [Dp: 3 (15.8%); 1 (12.5%)] and one case (5.3%) of haemolytic anaemia in Dps. The most common organs/systems were mucocutaneous (8 patients; 25.0%), musculoskeletal (7 patients; 21.9%) and general manifestations (6 patients; 18.7%). In the RTp group, renal abnormalities were the second most frequent BILAG finding in 7 cases (50.0%), followed by musculoskeletal and mucocutaneous manifestation in 5 each (35.7%).

– Activity though the follow up

The presence and grade of SLE activity was described and compared between the two groups for 36 months, starting from 6 months either after starting dialysis or 6 months after renal transplantation. As some patients were treated in other hospitals during the period of follow-up, some periodical measurements were not available. There was no significant decrease in either the grade or severity of activity in either group (p=1). Assessments ranging from 42 to 144 months after the beginning of the dialysis or after renal transplantation were described, but could not be compared due to loss of sample size (Table V).

Discussion

Since the 1970s, several reports have documented resolution of clinical and/or serological activity in SLE after RF (2, 4, 6, 7, 13, 14). The pathophysiological mechanisms involved in this process are not well understood. Some

Table V. Activity though the follow-up.

Months	Patients (n=32)	Inactive (%)	Dialysis Mild-Moderate (%)	Severe (%)	Patients (n=14)	Inactive (%)	Renal transplant Mild-Moderate (%)	Severe (%)	*p*-value
6	26	5 (19.2)	16 (61.5)	5 (19.2)	14	3 (21.4)	9 (64.3)	2 (14.3)	1
12	21	4 (19.0)	11 (52.4)	6 (28.6)	12	7 (58.3)	3 (25)	2 (16.7)	1
18	16	0	14 (87.5)	2 (12.5)	11	4 (36.4)	6 (54.5)	1 (9.1)	1
24	14	1 (7.1)	11 (78.6)	2 (14.3)	10	4 (40)	5 (50)	1 (10)	1
30	9	1 (11.1)	6 (66.7)	2 (22.2)	8	4 (50)	3 (37.5)	1 (12.5)	1
36	7	0	5 (71.4)	2 (28.6)	6	2 (33.3)	3 (50)	1 (16.7)	1
42	5	0	4 (80)	1 (20)	2	0	1 (50)	1 (50)	*
48	5	0	4 (80)	1 (20)	2	0	1 (50)	1 (50)	*
54	4	0	3 (75)	2 25)	3	0	2 (66.7)	1 (33.3)	*
60	4	0	4 (100)	0	4	1 (25)	1 (25)	2 (50)	*
66	2	0	2 (100)	0	1	0	0	1 (100)	*
72	2	0	2 (100)	0	2	0	1 (50)	1 (50)	*
78	2	0	1 (50)	1 (50)	2	0	1 (50)	1 (50)	*
84	3	1 (25.0)	2 (75)	0	2	0	2 (100)	0	*
90	2	0	2 (100)	0	1	0	1 (100)	0	*
96	1	0	1 (100)	0	2	1 (50)	1 (50)	0	*
102	1	0	1 (100)	0	2	1 (50)	0	1 (50)	*
108	1	0	1 (100)	0	1	1 (100)	0	0	*
114	1	0	1 (100)	0	1	0	1 (100)	0	*
120	2	0	1 (50)	1 (50)	1	1 (100)	0	0	*
126	2	0	0	2 (100)	1	1 (100)	0	0	*
132	2	0	1 (50)	1 (50)	1	1 (100)	0	0	*
138	1	0	1 (100)	0	1	0	1 (100)	0	*
144	2	0	2 (100)	0	1	1 (100)	0	0	*

have suggested roles for the immunodeficient status caused by uraemia during dialysis (15), immunosuppressive treatment used after renal transplant (16, 17) and/or the natural history of the disease. Since then, few studies have been published about this phenomenon, and have argued that SLE does not remain as quiescent after RF as was thought (8, 18-21). These contradictions are not helped by the difficulties of defining a clinical and/or serological "lupus flare" (22) and deciding whether the clinical features are due to the disease, replacement therapy, an intercurrent process, such as infection or treatment itself (23). Indices such as the British Isles Lupus Assessment Group (BILAG) scale, the University of Toronto SLE Disease Activity Index (SLE-DAI), and Systemic Lupus Activity Measure (SLAM) are extremely important in this setting. All of these aforementioned scales have demonstrated good inter-visit and inter-observer reliability (24).

Here, we report a descriptive and retrospective study of a 32 patient cohort with ESRD due to LN, including both those on dialysis and recipients of renal transplantation, measuring activity using the BILAG index over 12 years. Although many studies have compared patients with SLE on dialysis to non-lupus patients or those with SLE after RTp to non-lupus transplant patients, very few studies comment on the long-term outcome of patients with ESRD secondary to SLE for more than 10 years (8, 12, 21, 25-28). Additionally, as far as we know, there have been no attempts to use the BILAG index to measure lupus activity after RF.

Globally, our results demonstrate that almost every patient had activity markers at some point during the follow-up, as summarised in Table IV [Dp: 28 (87.5%); RTp: 13 (92.8%)], this was predominately demonstrated by serological involvement [Dp: 26 (92.8%); RTp: 13 (100%)] though often linked to activity in BILAG assessment. Similar high results have been found in the literature by other authors, including Robdy *et al*. (29) (87.5%), Krane *et al*. (18) (71.4–80.0%), Bruce *et al*. (30) (66.6-80.0%) and Ribeiro *et al*. (31) (84.2%). It is important to consider that the high activity levels after RF could be accounted for by ethnicity, as Afro-Caribbean subjects included in some of these aforementioned studies are well-known to have a poorer prognosis (32, 33) As 37.5% of our cohort was Afro-Caribbean, this could explain the high SLE activity despite a significant difference.

In other reports, it is possible that activity could be biased by a lack of validated SLE activity scales (25, 29, 34, 35) or overestimated when clinical parameters are not correlated with alterations in complement and anti-dsDNA antibody levels. In order to avoid overestimating activity, Ribeiro *et al*. (31) established a cut-off of SLEDAI>4 for active SLE. They reported a prevalence of flare-ups of 49% that decreased to 18% when SLEDAI>8 were considered. Many other authors have selected a SLEDAI>10 to define a lupus flare; Nossent *et al*. (2) reported an activity of 14.5% in patients during dialysis (51% when SLEDAI<10 were considered). Lee *et al*. (20) and Goo *et al*. (19) also reported a prevalence of lupus activity of 11.5 and 17.7%, respectively when this cut-off was implemented. In our study, at least moderate activity markers were present in 22 of the Dp group (68.7%) and in 7 (50%) of the RTp group that meant a decrease of activity near 20% and 45%, respectively. When

just severe activity markers in both BILAG and SI was considered to define a real lupus activity, we observed a marked decreased in activity markers in both groups, with just 12 active patients in Dps (37.5%) and 4 (28.6%) in RTps. This is a global decrease of lupus activity of 50% in Dps, and 64.2% in RTps. Although the difference was not statistically significant (p=0,74) we think this might be due to the small size of our sample and discontinuing the follow-up of many patients as some of then move to others cities, countries or were unexplained or lost to follow-up. In both groups, activity was predominately due to SI associated with BILAG activity (mostly haematological) (Table IV). Other well-known risk factors for SLE activity are the duration of the lupus disease, time on dialysis and type (2, 18-22, 36, 37). However, there was no significant difference in these between patients with severe activity and those inactive or with a mild-moderate expression, in either group. Focussing on the assessments obtained, fewer RTps had moderate and severe activity, but again there was no statistical significance. Haematological alterations were the most frequent findings in BILAG assessments in both groups (near 60% in both), followed by musculoskeletal and mucocutaneous (more than 20 in Dps and 30% in RTps). In the RTp group, renal involvement was the second most frequent finding (50%).

We note that although we could not find statistical significance between lupus activity in transplant patients who received the graft from a CD or RLD, severe activity tends to be present much more frequently in this first group of patients (n=4, 66.6% *vs*. n=0) (p=0.19). This could potentially be a more effective rejection mechanism in the group of cadaver donors possibly linked to lupus activity. Although some authors have published better results in those with CD transplant (36), globally, kidney transplants from RLD have been reported to have a better prognosis (37)

A "burn-out" phenomenon shown in lupus while patients are on dialysis has been reported previously (4, 7, 20, 28). However, the present study failed to demonstrate a decline in SLE activity in either Dps or RTps (Table V), in common with several previous reports (2, 18, 19, 38). However, this result could have been biased by some loss of patients during follow-up. Nevertheless, it is difficult to draw complete comparisons between our results and those previously reported in the literature for two main reasons. Firstly, this is the first time the BILAG index has been used at this stage of assessment. Secondly, this is the first study to evaluate and compare activity in the BILAG against serological and global assessments for each patient in renal failure. Furthermore, the validity of our results is hampered by the general limitations of a retrospective non-controlled study, such as an inevitable lost and/or intermittent follow-up and a small sample size.

Objectively, the persistence of SLE activity after RF seems reliable, and has been supported by a recent systematic review which showed that 37.5% of studies demonstrate a similar activity before and after ESRD (8). Activity seems to be less aggressive and life threatening at this stage. In our study, the most prevalent alteration overall in the BILAG index was haematological (anaemia and lymphopenia), followed by mucocutaneous manifestations in Dps, and renal alterations in RTp. In both groups these were accompanied by decreased in C3 and/or rise in anti-dsDNA antibody titres.

In summary, it is reasonable to affirm four conclusions from this study:

(1) Serological activity tends to be the principal, most universal and sensitive finding for patients with SLE in spite of RF (4, 7, 13, 20, 28).

(2) Dialysis decreases lupus activity, but does not abolish it completely. Thus, it is worthwhile to implement strategies and guideline to avoid under recognised and undertreated active disease which could lead to increased morbidity and/or mortality (39, 23).

(3) After RTp, patients tend to show a high prevalence of mild alterations that could be explained by intercurrent processes or, simply, due to the fact of being transplant. Nevertheless, when just moderate-severe markers are considered to demonstrate the presence of real lupus activity the RTp showed a lower activity compared to patients on dialysis. This could be presumably due to the use of immunosuppressive therapy (21). Activity tends to be even lower in those who have received a graft from a relative living donor compared to cadaveric donor (37).

(4) An appropriate scale to measure SLE activity coupled with the determination of serological levels is the most reliable way to identify a real lupus flare (22). We have validated the use of the BILAG index with serological markers for measurement of SLE activity in the long-term.

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