EXTENDED REPORT

Prolonged remission in Caucasian patients with SLE: prevalence and outcomes

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ABSTRACT

Aim To assess the prevalence of prolonged remission in Caucasian patients affected with systemic lupus erythematosus (SLE) and its relationship with damage accrual.

Methods Caucasian patients diagnosed with SLE between 1990 and 2009 and quarterly seen from 2009 to 2013 were included in the study. We defined remission as prolonged when lasting ≥5 consecutive years. Three levels of remission were defined using the SLE Disease Activity Index-2000 (SLEDAI-2K): complete remission: no disease activity in corticosteroid-free and immunosuppressant-free patients; clinical remission off corticosteroids: serologically active clinical quiescent (SACQ) disease in corticosteroid-free patients and clinical remission on corticosteroids: SACQ disease in patients taking prednisone 1–5 mg/day. Damage was measured by the SLICC/American College of Rheumatology Damage Index (SDI).

Results 224 patients fulfilled inclusion criteria: 196 (87.5%) were women, mean±SD disease duration 11.2 ±6.8 years. During the 5-year follow-up, 16 patients (7.1%) achieved prolonged complete remission, 33 (14.7%) prolonged clinical remission off corticosteroids and 35 (15.6%) prolonged clinical remission on corticosteroids. At the multivariate analysis, vasculitis (OR 4.95), glomerulonephritis (OR 2.38) and haematological manifestations (OR 2.19) over the patients' disease course were associated with an unremitted disease. SDI increased more frequently in unremitted (72/140, 51.4%) than in remitted patients (22/84, 26.2%; p=0.001); SDI median increase was higher in unremitted than in remitted patients: 1 (0–3) vs 0 (0–2), respectively (p<0.001). At multivariate analysis, unremitted disease (OR 2.52) and high-dose corticosteroid intake (OR 2.35) were risk factors for damage accrual.

Conclusions Thirty-seven percent of our Caucasian patients achieved a prolonged remission, which was associated with a better outcome in terms of damage accrual.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune rheumatic disease characterised by a variety of clinical manifestations.[1 2] Despite the improvement of SLE prognosis in the last decades, patients with SLE are still at high risk of disease-related complications and premature death.[3 4]

Disease activity is one of the major causes of morbidity and mortality in patients with SLE, since it is responsible for the higher use of corticosteroids and immunosuppressants and for the development of new organ damage.[5 6] Three major patterns of disease activity have previously been reported using the SLE Disease Activity Index (SLEDAI) or SLEDAI-2000 (SLEDAI-2K): chronic active disease (CAD), relapsing-remitting disease (RRD) and clinical quiescent disease (CQD).[5–10] While there is a substantial agreement in the definitions of CAD and RRD, different definitions of CQD have been proposed.[5–10] Major differences are whether to include active serology, durability of the quiescence period and treatment in the definition of CQD. It has to be pinpointed that inconsistent definitions of CQD could have contributed to the large variability of results among studies assessing disease activity patterns and their effects on disease outcome.[5–10]

Recently, the concept of remission gained a great interest when evaluating disease activity and treat-to-target therapies in several autoimmune rheumatic diseases. Unfortunately, the definition of remission in SLE still remains elusive owing to the heterogeneity of the disease and the multiple activity scores used[4 11]; indeed, which disease or treatment variables should be considered in order to define a patient as in remission have not been established and no definition of remission has been validated yet.

Cohort studies carried out in patients with SLE underlined that remission, when defined as complete or clinical, is a rare occurrence reported in less than 10% of patients.[7 9 12–17]

However, it has to be highlighted that the majority of studies assessing remission in SLE included patients diagnosed with SLE from the 50s to the 80s,[9 12–18] when diagnostic tools and treatments were less effective, leading to a worse long-term prognosis. In addition, many of these studies were performed in adult patients followed in North America (particularly Canada), thus the results may not be completely extended to other clinical settings.

Current evidence underlines that both persistent high disease activity and medication-related toxicity are associated with increased damage accrual,[5] while the beneficial effect of achieving a disease remission on damage accrual has not been fully elucidated.

The aim of our study was to assess the prevalence of prolonged remission in a cohort of Caucasian patients diagnosed with SLE after 1990. In addition, we evaluated the effect of remission on organ damage.

PATIENTS AND METHODS

We used our Lupus Database which includes patients recruited in Padova lupus cohort between

1970 and 2014. We analysed a 5-year period from January 2009 to December 2013. Patients with SLE were enrolled in the study if they fulfilled the following inclusion criteria: (1) ≥4 revised American College of Rheumatology (ACR) Classification Criteria for SLE[19]; (2) Caucasian ethnicity; (3) diagnosis of SLE between 1990 and 2009; (4) active disease at study entry or remission lasting no more than 12 months and (5) at least three visits per year between January 2009 and December 2013.

Local ethics committee approved the study. Each patient signed the informed consent for the use of clinical and laboratory data for study purposes.

Clinical and laboratory findings were recorded at each visit according to a standardised protocol[6] and were stored in a dedicated database. Clinical manifestations were defined using ACR definitions.[20]

Data regarding therapy, including corticosteroids, antimalarials, immunosuppressants and B cell targeted therapy (rituximab), were recorded; corticosteroid doses were converted to milligrams (mg) of prednisone equivalent. The cumulative oral prednisone dose received by patients before enrolment (g) was calculated for each subject.

Disease activity and definitions of different levels of prolonged remission

Disease activity was monitored using the SLEDAI-2K Index, which was calculated at each visit.

We defined prolonged remission as a 5-year consecutive period of no disease activity based on SLEDAI-2K. We defined three levels of remission according to disease activity and treatment (table 1):

A. *Complete remission:* no clinical and serological disease activity (SLEDAI-2K=0) in corticosteroid-free and immunosuppressant-free patients; antimalarials were allowed.
B. *Clinical remission off corticosteroids:* serologically active clinical quiescent (SACQ) disease according to SLEDAI-2K in corticosteroid-free patients; immunosuppressants and antimalarials were allowed.
C. *Clinical remission on corticosteroids*: SACQ disease according to SLEDAI-2K in patients taking a daily dose of prednisone or equivalent 1–5 mg; immunosuppressants and antimalarials were allowed (table 1).

Moreover, SLE manifestations not included in the SLEDAI-2K (haemolytic anaemia, myelitis and gastrointestinal lupus involvement) were recorded in the database.

Definition of flare

Flares were defined according to Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI criteria.[21] We registered constitutional (fever, anorexia, lymphadenopathy or unintentional weight loss due to SLE), renal, musculoskeletal, skin, haematological, serosal, neuropsychiatric and vasculitic flares.

Definition of damage accrual

Organ damage was evaluated at baseline and at the end of the follow-up using the Systemic Lupus International Collaborating Clinics/ACR Damage Index for SLE (SDI). Following definitions by Gladman *et al*,[22] damage was categorised as related to or independent of corticosteroids.

Moreover, risk factors other than corticosteroids, for example, personal and family history of some SDI features such as cardiovascular disease and diabetes, were taken into account in the attribution of damage to corticosteroids. When risk factors other than corticosteroids were considered more relevant in triggering the event, damage was recorded as non-corticosteroid related.

Laboratory testing

Standard laboratory tests were used to determine antinuclear antibodies, anti-double-stranded (ds)DNA antibodies,[23] haemoglobin, white cell and platelet counts, blood urea nitrogen, creatinine and creatinine clearance, C3, C4 and urinalysis.

Statistical analysis

Statistics were performed by the SPSS software for Windows (V.20.0, SPSS, Chicago, Illinois, USA). Comparison of continuous data with a parametric distribution was performed using t test or one-way analysis of variance with Bonferroni's post hoc analysis; continuous data with a non-parametric distribution were analysed using the Wilcoxon's rank-sum test and the Kruskal–Wallis test. Comparison of categorical data was performed using χ^2 test (Fischer's exact test) or the McNemar test for dependent samples. The association between the different types of remission and demographic and clinical variables was tested by logistic regression analysis.

The following variables were considered in the univariate analysis: age, gender, age at SLE onset, disease duration, lag time between SLE onset (first symptom) and diagnosis (by a qualified rheumatologist), SLEDAI-2K score, anti-dsDNA antibodies, low C3 or C4, type of organ involvement, number and type of flares before the study and therapy including immunosuppressants, corticosteroids, hydroxychloroquine, chloroquine and cumulative dose of corticosteroids.

Factors associated with different levels of prolonged remission at univariate analysis ($p<0.2$) were entered into the multivariate model. Backward stepwise multivariate logistic regression was performed with significance set at 5%.

Logistic regression was also used to assess the relationship between organ damage accrual during the follow-up (present or absent) and prolonged remission.

RESULTS

Among 386 consecutive patients who were evaluated, 224 (58%) fulfilled inclusion criteria. Reasons for exclusion were non-Caucasian ethnicity (9, 2.3%); SLE diagnosis before 1990 (72, 18.7%); remission lasting more than 12 months at study entry (39, 10.1%); less than three visits per year during the follow-up (16, 4.0%); incomplete data records (11, 2.8%) and lost-to-follow-up (15, 3.9%).

Demographic and clinical features of patients are summarised in table 2; 196 patients (87.5%) were women, mean±SD age at disease onset was 26.5±11.6 years, mean±SD age at study entry was 37.5±11.6 years and mean±SD disease duration was 11.2±6.8 years.

During the 5-year follow-up, 16 patients (7.1%) achieved a prolonged complete remission, 33 (14.7%) a prolonged clinical remission off corticosteroids and 35 (15.6%) a prolonged clinical remission on corticosteroids, whereas 140 patients (62.5%) did not achieve any level of prolonged remission.

We did not find any difference in terms of age, gender, age at SLE onset, lag time between SLE onset and diagnosis and disease duration among patients achieving one of the three levels of prolonged remission, nor between remitted and unremitted patients (table 2).

We did not observe any patient with haemolytic anaemia, myelitis and gastrointestinal lupus involvement.

Table 1 Definitions of remission according to clinical, serological and therapeutic status

	Disease activity		Treatment		
Prolonged remission	**Clinical**	**Serological**	**Prednisone**	**Antimalarials (allowed)**	**Immunosuppressants (allowed)**
Complete remission	No	No	No	Yes	No
Clinical remission off corticosteroids	No	Yes	No	Yes	Yes
Clinical remission on corticosteroids	No	Yes/No	1–5 mg/day	Yes	Yes

Disease activity was assessed by Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K).

Univariate analysis

At the univariate analysis, positive anti-dsDNA antibodies, glomerulonephritis, vasculitis, haematological abnormalities and serositis over the patients' disease course were more frequently observed in unremitted compared with remitted patients (p=0.005, p=0.002, p=0.003, p=0.008, p=0.008, respectively) (table 2).

Among patients in prolonged remission, glomerulonephritis (ever) was less frequent in patients in complete remission compared with those in clinical remission off corticosteroids or in clinical remission on corticosteroids (6.3% vs 42.4 vs 48.6%, p=0.029).

Remitted patients were less frequently treated with immunosuppressants and biological agents than unremitted patients during the disease course (table 3).

Multivariate analysis

At the multivariate analysis, glomerulonephritis (OR 2.38, 95% CI 1.32 to 4.29, p=0.004), vasculitis (OR 4.95, 95% CI 1.33 to 18.37, p=0.017) and haematological abnormalities (OR 2.19, 95% CI 1.17 to 4.12, p=0.014) over the patients' disease course were independently associated with the absence of prolonged remission.

Damage

Median (range) SDI values in 2009 and in 2013 were 0 (0–5) and 1 (0–6), respectively (p=0.003). An increase in SDI from baseline was observed in 94 patients (41.9%), occurring more frequently in unremitted patients (72/140) than in those with clinical remission on corticosteroids (13/35), clinical remission off corticosteroids (6/33) or complete prolonged remission (3/16) (p=0.001).

The median (range) increase in SDI during follow-up was higher in unremitted patients compared with patients with any level of prolonged remission: 1 (0–3) vs 0 (0–2), p<0.001. Median (range) increase in corticosteroid-related SDI ((0 (0–2) vs 0 (0–1), p<0.001)) and in corticosteroid-independent SDI (0 (0–3) vs 0 (0–2), p=0.014) was significantly higher in unremitted patients compared with patients with any level of prolonged remission.

Among remitted patients, increase in damage accrual was more frequently observed in patients with clinical remission on corticosteroids than in those with clinical remission off corticosteroids or complete remission: 13/35 (37.1%) vs 9/49 (18.4%), p=0.05. The proportion of patients with clinical remission off corticosteroids or complete remission who accumulated damage were similar (18.1% vs 18.7%), with a similar median increase in SDI (0 (0–2) vs 0 (0–2)).

Among remitted patients, those with clinical remission off corticosteroids and complete prolonged remission tended to accumulate less damage than did patients with clinical remission on corticosteroids (0 (0–2) vs 0 (0–1), p=0.066). Moreover, the former accumulated less corticosteroid-related organ damage compared with the latter (p=0.039); conversely, the median increase in SDI not related to corticosteroid was similar.

Table 2 Demographic and cumulative disease manifestations since the diagnosis in 224 patients included in the cohort: overall and according to the type of remission achieved during the follow-up

	Overall	**Prolonged complete remission**	**Prolonged clinical remission off CS**	**Prolonged clinical remission on CS**	**Unremitted disease**	**p Value**
Patients (N)	224	16	33	35	140	
Age, years, mean±SD	37.5±11.6	39±13	36±8.6	37.9±11.4	36.5±11.4	n.s.
Female, N (%)	196 (87.5)	13 (81.3)	31 (93.9)	32 (91.4)	120 (85.7)	n.s.
SLE duration at 2009, years, mean±SD	11.2±6.8	13.9±7.6	12.1±7.4	10.9±9.7	10.5±7.9	n.s.
Lag time onset–diagnosis, months, mean±SD	17.2±19.2	18.5±24	17.5±15.2	17.4±16.6	16.5±21.2	n.s.
ANA positivity, N (%)	224 (100)	16 (100)	33(100)	35(100	140 (100)	n.s.
Anti-dsDNA Ab, N (%)	188 (83.9)	10 (62.5)	30 (90.3)	27 (77.1)	125 (89.3)	0.005
Low C3 or C4 serum levels, N (%)	191 (85.3)	12 (75)	29 (87.9)	30 (85.7)	120 (85.7)	n.s.
Disease manifestations						
Systemic involvement, N (%)	189 (84.3)	11 (68.8)	30 (90.9)	28 (80)	120 (85.7)	n.s.
Skin rashes, N (%)	138 (61.6)	6 (37.5)	17 (51.5)	23 (65.7)	92 (65.7)	n.s.
Arthritis, N (%)	163 (72.7)	14 (87.5)	22 (66.7)	24 (68.6)	103 (73.6)	n.s.
Serositis, N (%)	59 (25.4)	1 (6.3)	7 (21.2)	5 (14.3)	44 (31.4)	0.039
Glomerulonephritis, N (%)	115 (51.3)	1 (6.3)	14 (42.4)	17 (48.6)	83 (59.3)	0.001
Neuropsychiatric manifestations, N (%)	26 (11.6)	1 (6.3)	2 (6.1)	3 (8.6)	20 (14.3)	n.s.
Vasculitis, N (%)	27 (12)	1 (6.3)	1 (3.0)	1 (2.9)	24 (17.1)	0.026
Haematological involvement, N (%)	108 (47.8)	3 (18.8)	12 (36.4)	10 (28.6)	83 (59.3)	0.049

p Values refer to analysis of variance test for continuous variables and χ^2 test (3 degrees of freedom) for dichotomous variables.
ANA, antinuclear antibodies; Anti-dsDNA Ab, anti-double-stranded DNA antibodies; C3/C4, complement fractions; CS, corticosteroids; SLE, systemic lupus erythematosus.

Table 3 Previous treatments according to the level of remission achieved during the follow-up

	Prolonged complete remission	Prolonged clinical remission off CS	Prolonged clinical remission on CS	Unremitted disease	p Value
Patients (N)	16	33	35	140	
Hydroxychloroquine, N (%)	16 (100)	32 (97)	31 (88.6)	125 (89.3)	n.s.
Methylprednisolone iv, N (%)	5 (31)	15 (45.5)	18 (51.4)	97 (69.3)	0.007
Cumulative average prednisone dose >180 mg/month, N (%)	6 (37.5)	11 (33.3)	23 (65.7)	96 (68.5)	0.02
Immunosuppressants, N (%)	4 (25)	9 (27.3)	25 (71.2)	122 (87.1)	<0.001
Azathioprine, N (%)	3 (18.8)	1 (3.0)	12 (34.3)	64 (45.7)	0.001 0.02*
Mycophenolate, N (%)	1 (6.3)	3 (9.1)	12 (34.3)	82 (58.6)	<0.001
Ciclosporin, N (%)	1 (6.3)	1 (3.0)	6 (14.3)	33 (23.6)	0.05
Cyclophosphamide, N (%)	0	5 (15.2)	10 (28.6)	51 (36.4)	0.001
Methotrexate, N (%)	0	1 (3.0)	5 (14.3)	27 (19.3)	0.01
Rituximab, N (%)	0	1 (3.0)	1 (2.8)	8 (5.8)	0.05

p Values refer to χ^2 test with 3 degrees of freedom.
*Comparing only patients who achieved a remission; p level is 0.02.
CS, corticosteroids.

At the multivariate analysis, unremitted disease (OR 2.527, 95% CI 1.27 to 4.99; p=0.008) and previous intravenous corticosteroid therapy (OR 2.35, 95% CI 1.10 to 5.00; p=0.026) were independent risk factors for damage accrual; notably, none of the clinical manifestations was independently associated with damage increase (table 4).

DISCUSSION

In our cohort of patients with SLE diagnosed after 1990, complete prolonged remission was rare, occurring in only 16 out of 224 patients (7.1%). By contrast, when prolonged remission was defined as clinical remission off corticosteroids or clinical remission on corticosteroids (low-dose corticosteroid allowed), the percentage of patients achieving these levels of remission was considerably higher, being 14.7% (33 patients) and 15.6% (35 patients), respectively.

Previous studies addressing the issue of remission in SLE reported divergent results.[7–9 12 16 18 24] The main reasons for discrepancies among these studies are the use of different definitions of remission. In fact, the more stringent the definition of remission, the lower the number of patients fulfilling the criteria for remission.

Table 4 Multivariate analysis: risk factors for damage accrual over the follow-up

	B	p Value	OR	95% CI	
Unremitted disease	**0.927**	**0.008**	**2.527**	**1.279**	**4.992**
High-dose intravenous methylprednisolone	**0.856**	**0.026**	**2.355**	**1.107**	**5.009**
Pre-existing organ damage	0.298	0.355	1.348	0.716	2.537
Glomerulonephritis	−0.349	0.353	0.705	0.337	1.474
NP-SLE	0.795	0.111	2.215	0.834	5.883
Vasculitis	0.366	0.453	1.442	0.555	3.746
Haematological manifestations	−0.034	0.914	0.966	0.517	1.807
Skin involvement	0.159	0.708	1.172	0.511	2.687
Gender (female)	−0.434	0.331	0.648	0.271	1.552
Low C3 or C4	−0.910	0.095	0.403	0.138	1.171
Anti-dsDNA Abs	0.513	0.281	1.671	0.657	4.250
Constant	−1.138	0.048	0.321		

Significant variables are given in bold. Anti-dsDNA Abs, anti-double-stranded DNA antibodies; C3/C4, complement components; NP-SLE, neuropsychiatric SLE; SLE, systemic lupus erythematosus.

A critical aspect in the definition of remission is whether to consider lupus treatment, particularly in the definition of complete remission. In fact, remission in patients on treatment is more frequent than in those who are therapy-free. In a previous study by Steiman *et al*,[15] 2.4% of patients (38/1613) achieved a clinical remission without taking corticosteroids and immunosuppressants, but this percentage doubled (4.5%, 72 patients) when considering remitted patients on medications.

In our study, remitted patients who were taking only antimalarials were considered in complete remission in order to be adherent to our daily clinical practice, since we usually discontinue antimalarials a long time after the achievement of complete remission. Hence, animalarials are used in remitted patients with the aim of preventing disease relapses and not as a therapeutic strategy. Thus, our definition more closely identifies the real percentage of patients who are inactive, but have not discontinued antimalarials yet.

Nikpour *et al*[16] evaluated disease activity in a group of 417 Canadian patients with SLE followed for 2 years (2004–2005) and found an annual incidence of remission, defined as no clinical activity on SLEDAI-2K in patients treated with antimalarials, of 16.8% in 2004 and 21.5% in 2005. These results are in keeping with ours, since we found an annual incidence of clinical remission ranging from 21% to 33% according to different levels of remission.

In our definition of clinical remission on/off corticosteroids, we allowed the use of immunosuppressants since clinically remitted patients often continue the treatment which yielded remission for an indefinite period of time, likely with the aim of preventing relapses and not as a therapeutic strategy. The recommended length of immunosuppressant use after achieving clinical remission has not been defined yet and it largely depends on the physician experience and belief. In lupus glomerulonephritis, data from randomised controlled studies suggest to continue immunosuppressants for at least 3 years, but no data which can drive the treatment strategy after this period are available.[25]

Similarly, we allowed the use of corticosteroids at low dose in the clinical remission on corticosteroids group, strictly defining

the cut-off ≤5 mg/day, based on data regarding the safety of long-term low-dose steroid therapy in SLE.[26 27] Notably, other studies did not specify the dose of corticosteroids allowed in the definition of remission,[7 15 18] thus including cases in which the disease was clinically quiescent, thanks to medium-to-high dose of steroids.

In our study, we excluded patients diagnosed with SLE before 1990, since the therapeutic approach in SLE has greatly changed and improved in the last two decades, thus the inclusion of patients treated with previous regimens may cause our study to depict a scenario not consistent with current disease management.[28 29]

This can explain why in the study by Urowitz *et al*[13] enrolling patients diagnosed between 1970 and 1997, the frequency of prolonged remission was much lower than in our cohort, occurring overall in 20 patients (2.8%). In Urowitz's study, remission was defined as SACQ disease in patients taking antimalarials, thus resembling our definition of clinical remission off corticosteroids, which was achieved by 33 (14.7%) of our patients.

Ethnicity can also influence the probability of achieving remission; in fact, Afro-Caribbean and Hispanic patients are at higher risk for a more severe disease.[30] In our cohort, 100% of patients were Caucasian and this could also contribute to the better outcome in terms of remission compared with other studies.[8 9 12–15] The exclusion of patients with different ethnicity can partially explain why our patients had a lower prevalence of glomerulonephritis and vasculitis and took a lower cumulative dose of corticosteroids.[14 15]

How long remission should last to yield significant benefits on patients' outcome has not been proven yet. The durability of remission also varied from study to study, ranging from 6 months to 5 years.[9 12–16 18] In our study, we defined remission as prolonged when lasting at least five consecutive years. Although we are aware that any length of 'prolonged' remission is arbitrary, we thought this cut-off was clinically significant, providing a considerable time interval for damage accrual, thus yielding to detect a difference between remitted and unremitted patients.

Steiman *et al*[15] found that 26/38 patients in remission had renal disease compared with 1/16 remitted patients in our cohort, and 10/38 had vasculitis compared with 1/16 patients in our study. This difference can be due to the different ethnicity and to the different mean disease duration of the two cohorts; in fact, mean disease duration at study entry was longer in Steiman cohort than in ours (21.8±10.3 vs 11.2±6.8 years). Since the achievement of remission requires time, especially in patients with severe disease (eg, in Steiman study the mean time from clinic entry to remission was 9.1±8.8 years), a longer mean disease duration means that more patients have had the time to achieve remission.

In our study, we found that glomerulonephritis, vasculitis and haematological manifestations were independently associated with the absence of prolonged complete or clinical remission. In contrast, Urowitz *et al*[13] and Steiman *et al*[15] showed that the prevalence of major organ involvement was similar in remitted and unremitted patients.

In our cohort, the cumulative dose of corticosteroids differed among patients with different levels of remission, being higher in patients in remission on corticosteroids and in unremitted patients, which could at least in part be due to the different disease severity prior to entry in the study. In fact, we found that glomerulonephritis, vasculitis and haematological involvement were more common in unremitted patients over disease course.

In our study, prolonged remission was associated with a better prognosis in terms of damage accrual. In 2012, Steiman *et al*[17] analysed SDI score in patient with and without a prolonged SACQ and found that after 3 and 10 years of follow-up the mean increase in SDI was significantly lower in the former than in the latter.

Two are the potential reasons why we observed that patients in clinical remission on corticosteroids tended to accrue more damage than patients in clinical remission off corticosteroids or in complete remission. First, patients in clinical remission on corticosteroids might have mild or subclinical manifestations not detected by the SLEDAI-2K, which require the maintenance of corticosteroid therapy. Second, long-lasting corticosteroid therapy, even at very low doses, can itself represent a risk factor for comorbidity and damage.[31 32]

In conclusion, one-third of our Caucasian patients diagnosed with SLE after 1990 experienced a prolonged remission during the follow-up. Glomerulonephritis, vasculitis and haematological manifestations were the major independent predictors of the absence of prolonged remission. Prolonged remission was associated with less damage accrual compared with unremitted disease and an unremitted disease was an independent risk factor for damage accrual. Since patients in remission with corticosteroids, even at low doses, tended to accumulate more damage than did patients in prolonged remission who were corticosteroid free, to avoid long-lasting corticosteroid therapy in cases of CQD could be considered as a treat-to-target goal in these patients.

Contributors MZ contributed to the design of the work and to acquisition, analysis and interpretation of data and she drafted the work; LI gave his contribution in the interpretation of data and he critically revised the work; MG helped in the acquisition of data and in the revision for intellectual content; LN and SB gave their contributions to the acquisition of data and helped in drafting the work; AG helped in the analysis of data and revised the manuscript; LP contributed to the interpretation of data and the critical revision of the final work; AD designed the work, interpreted the data, drafted and revised the manuscript for important intellectual content. All the authors approved the final version of the manuscript and gave their agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests None declared.

Patient consent Obtained.

Ethics approval The study was approved by the ethics committee of the "Azienda Ospedaliera- Università degli Studi di Padova", Padova, Italy. Participants gave informed consent before taking part to the study.

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