The clinically quiescent phase in early-diagnosed SLE patients: inception cohort study

Nuntana Kasitanon¹, Tulaporn Intaniwet¹, Suparaporn Wangkaew¹, Saowanee Pantana¹, Waraporn Sukitawut¹ and Worawit Louthrenoo¹

Abstract

Objectives. The aims of this study were to evaluate the incidence of clinical quiescence in early-diagnosed SLE patients and to determine factors associated with a prolonged clinically quiescent phase.

Methods. We used an inception cohort of SLE patients seen between May 2007 and June 2012. All patients were assessed for clinical quiescence [modified SLEDAI 2000 (mSLEDAI-2K) score = 0, no new features of lupus activity or increase in treatment] then evaluated for the occurrence of flare (mSLEDAI-2K increase ≥ 4 and increased disease activity in one or more organ systems or an increase in treatment).

Results. Ninety-five patients (88 females) with a mean age of 33.22 years (± 13.24) and mean disease duration 2.79 months (± 3.19) at cohort entry were enrolled during a mean observation period of 3.04 years (± 1.38). Sixty-six patients (69.5%) reached clinical quiescence within 11.31 months (± 1.10) of enrolment. Thirty-six patients (54.5%) had a disease flare during the observation period. The clinically quiescent phase was 28.2 months (± 3.4). Cox regression analysis revealed that age ≤ 25 years at diagnosis [hazard ratio (HR) 2.57 (95% CI 1.23, 5.40)] and continued antimalarial drug treatment [HR 2.80 (95% CI 1.40, 5.58)] were associated with a longer clinically quiescent phase.

Conclusion. Most early-diagnosed SLE patients could have a good prognosis. Age at diagnosis ≥ 25 years or continued treatment with antimalarial drugs after reaching clinical quiescence may result in a longer clinically quiescent phase. More studies are needed to elucidate the mechanism of action for these protective effects.

Key words: SLE, early-diagnosed, clinically quiescence, remission, flare, antimalarial drugs.

Introduction

SLE is a chronic remitting and relapsing disease. Relapse in SLE is associated with increased morbidity [1] and mortality [2, 3] and decreased quality of life and affects the economic status of the individual patient and society [4–6]. Therefore, one goal of SLE treatment is to control disease activity to the lowest level possible or to induce remission. However, the remission rate in SLE is low: in one Canadian study only 1.7% of SLE patients experienced prolonged remission of ≥ 5 years without treatment [7]. Generally some SLE patients can achieve a state of no disease activity (remitting or clinical quiescence), but they still need some treatment to maintain or prolong the clinically quiescent phase, e.g. the regimen of treatment in LN with induction and maintenance therapy [8, 9].

With the exception of one study focused on factors associated with a prolonged clinically quiescent phase [10], most studies focus on specific organ damage prevention in diseases such as LN [11, 12] or cutaneous lupus erythematosus [13]. The aims of this study were to determine the incidence of clinical quiescence within the first year in early-diagnosed SLE patients from an inception lupus cohort and to identify factors associated with a prolonged clinically quiescent phase.
**Clinical quiescence in SLE**

**Patients and methods**

**Patients**

This cohort was recruited from Chiang Mai University and Maharaj Nakorn Chiang Mai Hospital and included all consenting, newly diagnosed SLE patients from May 2007 to June 2012. All patients satisfied at least four of the 1997 ACR revised criteria for the classification of SLE [14] and had been observed for at least 1 year at the Division of Rheumatology. Patients with \( \leq 50\% \) of the data required for analysis were excluded. This study was approved by Research Ethics Committee 3, Faculty of Medicine, Chiang Mai University, and informed consent was obtained at the time of cohort entry according to the Declaration of Helsinki.

At cohort entry, basic demographic characteristics, including presenting and cumulative clinical manifestations, laboratory tests, modified SLEDAI 2000 (mSLEDAI-2K) scores, which was the mSLEDAI-2K without serology [15], the SLICC/ACR Damage Index (SDI) for SLE [16] and immunological markers (anti-dsDNA and aCL) were all recorded. Patients were seen at regular intervals of 1–3 months, or more frequently if medically indicated. At each patient visit a complete history (including severe infection events and treatments), physical examination and routine laboratory testing were performed in a systematic fashion. All treatments (antimalarial drugs, immunosuppressants and corticosteroids) were given by physician judgment according to the standard of care.

All patients were assessed for clinical quiescence criteria and subsequently for the occurrence of flares and prolonged complete remission. We compared factors putatively associated with prolonged clinically quiescent phases between patients. These factors were demographic data, clinical variables, treatments and severe infections. Patients with late-onset SLE (age of onset \( \geq 50 \) years) had lower disease activity and less renal involvement [17–19]. To investigate whether age may have some effect on disease activity in SLE, the clinically quiescent phase was compared between patients with age at diagnosis of SLE \( \geq 50 \) vs \( <50 \) years (the definition of late-onset SLE) and compared between patients with age at diagnosis of SLE \( \geq 25 \) vs \( <25 \) years, which was proposed by Ines et al. [20]. Moreover, several studies have reported an association between infection and flares in SLE patients [21–24], while another study evaluated the impact of marital status and health outcomes in SLE and found that patients who were married had better scores on physical functioning and general health than patients who were unmarried [25]. Thus we also considered the presence of severe infection and marital status in this study.

**Definition**

Clinical quiescence was considered when the following criteria were met: mSLEDAI-2K score zero with no increase in treatment and no new features of lupus activity compared with the previous assessment. The patients could be taking antimalarial drugs, low-dose steroid (equivalent to prednisolone \( \leq 7.5 \) mg/day or other corticosteroid in an equivalent dose) or immunosuppressive drugs for the maintenance phase. Prolonged complete remission was defined as a period of at least 5 years with clinical and laboratory quiescence (mSLEDAI = 0) and the absence of pharmacotherapy for lupus, specifically no corticosteroid, antimalarial or immunosuppressant, according to Urowitz et al. [7]. Disease flare was determined by at least one of the following criteria: (i) mSLEDAI-2K score increased \( \geq 4 \) as compared with the score assessed in the previous visit, modified from the flare definition in SLE proposed by Gladman et al. [26–28]; (ii) increased disease activity in one or more organ systems involving new or worse clinical signs and symptoms and/or laboratory measurements or (iii) consideration of a change or an increase in treatment, defined by international consensus for a definition of disease flare in lupus [29]. Severe infections were defined as an infection requiring i.v. antimicrobial therapy, hospitalization or caused by opportunistic pathogens such as Mycobacterium species, herpes zoster, cytomegalovirus, Pneumocystis jiroveci, etc.

**Statistical analysis**

Statistical analyses were performed using the Statistical Package for Social Sciences software version 17.0 (SPSS, Chicago, IL, USA). The times from cohort entry to clinical quiescence and from clinical quiescence to flare (within the clinically quiescent phase) were analysed using a Kaplan–Meier plot; the censor was obtained patients either when met outcome criteria, were lost to follow-up or reached the end of the study. Univariable analysis for the difference between the clinically quiescent phase with respect to categorical and continuous variables used the log rank test. Cox regression analysis was used to assess the associated factors of a prolonged clinically quiescent phase. For all statistical evaluations, \( P \)-values < 0.05 were considered statistically significant.

**Results**

The study included 117 patients at the beginning of the study and then excluded 2 patients with incomplete data and 20 patients with a follow-up period of <1 year, 3 of whom were referred to other hospitals, 9 lost to follow-up before 1 year, 8 who died within 1 year (3 from sepsis, 1 from severe autoimmune hepatitis, 1 from pulmonary haemorrhage, 1 from pulmonary artery hypertension, 1 from iatrogenic pneumothorax and 1 from severe mitral valve stenosis). Therefore 95 patients were included in this analysis. Eighty-eight patients (92.6%) were female with a mean age of 33.2 years (s.d. 13.2). Fifty patients (52.6%) were married, with an income of 18.7 \( \times 10^4 \) Thai baht/year (s.d. 29.4 \( \times 10^4 \)) (the national income of Thailand in 2010 was 7.9 \( \times 10^4 \) Thai baht/year). Mean time from SLE diagnosis to cohort entry was 2.8 months (s.d. 3.2) and the mean follow-up was 3.04 years (s.d. 1.38).
During the first year of treatment, all patients were treated with corticosteroids and only 7.4% were treated with pulse methylprednisolone. Concomitant treatment included CYC (54.7%) and antimalarial drugs (74.7%). Of 95 patients, 66 (69.5%) met the clinical quiescence criteria, which occurred in the first year of follow-up. The comparison of baseline clinical and treatment data between these two clinically quiescent groups is presented in Table 1. The estimated time from cohort entry to reach clinical quiescence criteria was 11.31 months (s.d. 1.10). Median time was 7.40 months (s.d. 1.02).

**TABLE 1** Baseline clinical and treatment data comparing patients by clinical quiescence status within 1 year

<table>
<thead>
<tr>
<th>1 year clinical and treatment data</th>
<th>Clinical quiescence positive (n = 66)</th>
<th>Clinical quiescence negative (n = 29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time between SLE diagnosis and cohort entry, mean (s.d.), months</td>
<td>2.6 (3.2)</td>
<td>2.9 (4.5)</td>
<td>0.731</td>
</tr>
<tr>
<td>mSLEDAI-2K score at cohort entry, mean (s.d.)</td>
<td>12.4 (4.9)</td>
<td>15.3 (6.4)</td>
<td>0.021</td>
</tr>
<tr>
<td>SDI score, mean (s.d.)</td>
<td>0.5 (0.8)</td>
<td>0.2 (0.6)</td>
<td>0.144</td>
</tr>
<tr>
<td>Patients with SDI score = 0, n (%)</td>
<td>45 (68.2)</td>
<td>25 (86.2)</td>
<td>0.080</td>
</tr>
<tr>
<td>Cumulative prednisolone within 1 year after cohort entry, mean (s.d.), g</td>
<td>4.5 (1.9)</td>
<td>6.2 (2.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Patients treated with pulse methylprednisolone, n (%)</td>
<td>4 (6.1)</td>
<td>3 (10.3)</td>
<td>0.433</td>
</tr>
<tr>
<td>Patients treated with antimalarial drugs, n (%)</td>
<td>50 (75.8)</td>
<td>21 (72.4)</td>
<td>0.799</td>
</tr>
<tr>
<td>Patients treated with CYC, n (%)</td>
<td>34 (69.5)</td>
<td>18 (62.1)</td>
<td>0.378</td>
</tr>
</tbody>
</table>

mSLEDAI-2K: modified SLEDAI 2000; SDI: SLICC/ACR Damage Index.

**Fig. 1** The Kaplan–Meier plot of time from cohort entry to first clinical quiescence

Mean estimated time from cohort entry to reaching clinical quiescence criteria was 11.31 months (s.d. 1.10). Median time was 7.40 months (s.d. 1.02).

**Fig. 2** The Kaplan–Meier plot of time from clinical quiescence to the first flare

Mean estimated time from reaching clinical quiescence criteria to the first disease flare (clinically quiescent phase) was 28.2 months (s.d. 3.4). The median was 19.2 months (s.d. 7.0).

**Clinically quiescent phase**

During the first year of treatment, all patients were treated with corticosteroids and only 7.4% were treated with pulse methylprednisolone. Concomitant treatment included CYC (54.7%) and antimalarial drugs (74.7%).

Of 95 patients, 66 (69.5%) met the clinical quiescence criteria, which occurred in the first year of follow-up. The comparison of baseline clinical and treatment data between these two clinically quiescent groups is presented in Table 1. The estimated time from cohort entry to reach clinical quiescence criteria from the Kaplan–Meier plot was 11.31 months [s.d. 1.10 (95% CI 9.16, 13.47)] and the median was 7.40 months [s.d. 1.02 (95% CI 9.16, 13.47)], as shown in Fig. 1. Of the 66 patients who reached clinical quiescence criteria within 1 year, only 6 patients (9.1%) were able to discontinue prednisolone, antimalarial drugs and immunosuppressants. Two of the six patients were disease flare free for 5 years after discontinuing medication. In other words, only 2 of 95 patients (2.1%) in this cohort achieved prolonged complete remission. The 64 patients who reached clinical quiescence criteria remained on low-dose prednisolone, antimalarial drugs and/or immunosuppressive drugs for the maintenance phase [60 patients (90.9%) received low-dose prednisolone at a median dose of 5 mg/day, 44 patients (66.7%) received an antimalarial drug and 31 patients (47.0%) received at least one immunosuppressant].

During the observation period, 36 of 66 patients (54.5%) had a disease flare. The estimated time from reaching clinical quiescence criteria to the first disease flare (clinically quiescent phase) was 28.2 months [s.d. 3.4 (95% CI 22.3, 34.1)] and the median was 19.2 months [s.d. 7.0 (95% CI 5.3, 33.0)] (Fig. 2).
At cohort entry, the three initial most common manifestations were leucopenia, arthritis and LN. Twenty-eight of 36 patients (77.7%) with a flare had a repeated flare of the same organ (Fig. 3). LN was the flare in 14 of 36 patients (38.9%). Of these 14 patients, 12 (85.7%) had LN at presentation while the other 2 patients (14.3%) had not had LN before.

**Associated factors of a prolonged clinically quiescent phase**

From the demographic data shown in Table 2, 7 of 66 patients (10.6%) had late-onset SLE. There was no difference in the clinically quiescent phase between patients with and without late-onset SLE. However, patients who had an age at diagnosis of SLE ≥25 years had a longer clinically quiescent phase than patients who had an age at diagnosis <25 years. We also found that patients who were married had a longer clinically quiescent phase than patients who were single. There was no difference in the clinically quiescent phase of patients with a household income greater than or equal to the national income of Thailand in 2010 and patients with a low household income. Among SLE-related variables, there was no difference between the clinically quiescent phase of patients with and without high disease activity (mSLEDAI-2K ≥6), positive serology test or specific organ involvement at cohort entry. After reaching the clinical quiescence criteria, 9 of 66 patients (13.6%) had a severe infection, 13 events in total. When comparing

**Table 2** Comparison of the clinically quiescent phase of 66 patients with and without study variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number (with vs without)</th>
<th>Clinically quiescent phase, mean (s.d.), months</th>
<th>P-valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Late-onset SLE</td>
<td>7 vs 59</td>
<td>28.0 (3.3) vs 26.7 (3.5)</td>
<td>0.142</td>
</tr>
<tr>
<td>Age at diagnosis ≥25 years</td>
<td>19 vs 27</td>
<td>36.2 (4.6) vs 14.9 (2.8)</td>
<td>0.003</td>
</tr>
<tr>
<td>Married</td>
<td>35 vs 31</td>
<td>36.0 (4.9) vs 17.5 (3.1)</td>
<td>0.009</td>
</tr>
<tr>
<td>Household income ≥ national incomeb</td>
<td>33 vs 33</td>
<td>26.4 (4.5) vs 25.8 (3.89)</td>
<td>0.517</td>
</tr>
<tr>
<td><strong>SLE-related variable</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mSLEDAI-2K ≥6</td>
<td>60 vs 6</td>
<td>6.4 (3.4) vs 26.4 (3.4)</td>
<td>0.165</td>
</tr>
<tr>
<td>Malar rash</td>
<td>26 vs 39</td>
<td>27.6 (5.5) vs 29.2 (4.4)</td>
<td>0.942</td>
</tr>
<tr>
<td>Oral ulcer</td>
<td>14 vs 52</td>
<td>13.6 (3.7) vs 31.0 (3.8)</td>
<td>0.052</td>
</tr>
<tr>
<td>Photosensitive</td>
<td>11 vs 55</td>
<td>27.5 (3.4) vs 27.9 (3.7)</td>
<td>0.820</td>
</tr>
<tr>
<td>Discoid rash</td>
<td>20 vs 46</td>
<td>23.8 (4.6) vs 27.9 (4.0)</td>
<td>0.960</td>
</tr>
<tr>
<td>Arthritis</td>
<td>39 vs 27</td>
<td>22.4 (3.4) vs 30.8 (5.3)</td>
<td>0.332</td>
</tr>
<tr>
<td>Serositis</td>
<td>14 vs 52</td>
<td>33.5 (7.6) vs 26.6 (3.9)</td>
<td>0.472</td>
</tr>
<tr>
<td>Seizure or psychosis</td>
<td>4 vs 62</td>
<td>25.2 (5.6) vs 27.5 (3.4)</td>
<td>0.396</td>
</tr>
<tr>
<td>Coomb’s test positive</td>
<td>19 vs 47</td>
<td>27.7 (4.4) vs 26.8 (4.1)</td>
<td>0.442</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>41 vs 25</td>
<td>26.6 (3.9) vs 22.2 (5.2)</td>
<td>0.096</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>7 vs 59</td>
<td>33.7 (6.4) vs 26.6 (3.5)</td>
<td>0.235</td>
</tr>
<tr>
<td>Nephritis</td>
<td>31 vs 35</td>
<td>24.1 (3.5) vs 29.3 (5.4)</td>
<td>0.709</td>
</tr>
<tr>
<td>Anti-dsDNA antibody</td>
<td>51 vs 15</td>
<td>25.5 (3.8) vs 34.5 (7.4)</td>
<td>0.198</td>
</tr>
<tr>
<td>aCL</td>
<td>13 vs 53</td>
<td>13.4 (3.0) vs 30.7 (3.8)</td>
<td>0.103</td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe infection</td>
<td>9 vs 56</td>
<td>29.4 (3.6) vs 15.5 (4.4)</td>
<td>0.272</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimalarial drugs</td>
<td>44 vs 22</td>
<td>33.0 (4.2) vs 18.1 (5.3)</td>
<td>0.005</td>
</tr>
<tr>
<td>Immunosuppressant</td>
<td>31 vs 35</td>
<td>27.6 (5.0) vs 28.4 (4.7)</td>
<td>0.944</td>
</tr>
</tbody>
</table>

aFrom log rank test. bThe national income of Thailand in 2010 was 7.9 × 10^4 Thai baht/year mSLEDAI-2K: modified SLEDAI 2000.
patients with and without severe infection, there was no difference in the clinically quiescent phase between groups. With regard to concurrent treatment, patients who continued treatment with antimalarial drugs had a longer clinically quiescent phase when compared with patients who discontinued treatment or were treated without antimalarial drugs, whereas there was no difference in the clinically quiescent phase between patients treated with and without an immunosuppressant.

The Cox regression analysis was computed to identify independent associated factors of a prolonged clinically quiescent phase. Significant independent factors included age at SLE diagnosis $\geq 25$ years and continued treatment with antimalarial drugs after reaching clinical quiescence criteria. However, different from univariable analysis, married status was no longer an independent factor, as shown in Table 3.

### Discussion

SLE is a complicated autoimmune disease with diverse clinical presentation and degrees of severity. Current knowledge of SLE manifestations and serology testing allows physicians to make diagnoses early in the course of the disease. We demonstrated that disease activity, particularly during early diagnosis, can be regulated in most of our patients (69.5%). During the first year of our inception cohort, which observed patients with mean disease duration 3 months, only a minority of patients (30.5%) did not meet the clinical quiescence criteria. These data are consistent with the Sapienza Lupus Cohort study from Italy, which observed patients with mean disease duration 137 months. The Sapienza Lupus Cohort study reported that 9% of patients had persistent disease activity during the 2-year follow-up [30]. However, in contrast, a contemporary multinational European inception cohort that included new-onset SLE patients (mean disease duration was not stated) reported that only 27.5% of patients achieved disease quiescence according to the physician global assessment (PGA) during the first years of disease [31]. These significant differences may stem from diverse study population characteristics and/or the definition of clinical quiescence. In the first year of disease, i.v. pulse methylprednisolone was given to 33% of cases in the European cohort vs only 7% of the cases in our cohort. Moreover, the European cohort defined disease quiescence according to the PGA, while we defined clinical quiescence according to the mSLEDAI score and treatment.

In our patients, the incidence rate of flare was 54.5%, which is comparable to the 46-66% range found in the first year of previous studies [31–33]. Disease activity in SLE can be intermittently active, often with patients in the clinically quiescent phase experiencing a flare within 1 year. Thus regular follow-up of patients in clinical quiescence remains crucial.

This study sought to determine the factors associated with a prolonged clinically quiescent phase. It should be noted that no clear-cut consensus definition of remission in SLE exists. Some studies define prolonged clinical remission as no disease activity and no immunosuppressive treatment for 5 years [7, 34]. However, these studies found that only 2% of patients meet those criteria. In clinical practice, even when SLE disease status is clinically inactive, patients still receive preventative treatment (typically for either flares or LN), including low-dose steroids, antimalarial drugs or low-dose immunosuppressive drugs. Therefore, instead of the term remission, we use the term clinical quiescence for an mSLEDAI-2K score of zero without an increase in treatment and with no new features of lupus activity since the previous assessment.

In our study, age $\geq 25$ years at SLE diagnosis was an independent factor associated with a prolonged clinically quiescent phase. Patients with age at onset of SLE $\geq 25$ years had a longer duration of the clinically quiescent phase, which was confirmed by multivariable analysis. However, due to the small number of older patients, this study cannot distinguish between the clinically quiescent phase of patients with and without late-onset SLE ($\geq 50$ years). A shorter duration of the clinically quiescent phase in young adults may be due to several possible factors, including the level of oestrogen, compliance, lifestyle and exposure to sunlight.

Some studies on SLE have found increasing anti-dsDNA antibodies, renal disease or neuropsychiatric disease at baseline to be predictors for subsequent flares [35–37], while another [38] did not find any association of anti-dsDNA antibody levels and subsequent flares. In addition, our study found no differences in the clinically quiescent phase between patients with and without specific antibodies (anti-dsDNA and aCL) or specific organ involvement at baseline (e.g. renal or neuropsychiatric diseases). Among our patients, severe infection was not associated with a clinically quiescent phase. Other studies provide evidence of association between infection and clinical flares in SLE, particularly viral infection [21–23]. A previous questionnaire-based cross-sectional study found that patients with a history of infection within 1 month prior to their interview had higher disease activity [24]. In our study, patients with severe infection showed a trend towards shorter duration of the clinically quiescent phase, but the difference did not reach statistical significance.

### Table 3 Adjusted hazard ratios of variables associated with a prolonged clinically quiescent phase

<table>
<thead>
<tr>
<th></th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis $\geq 25$ years</td>
<td>2.57</td>
<td>1.23</td>
<td>5.40</td>
</tr>
<tr>
<td>Married</td>
<td>1.31</td>
<td>0.92</td>
<td>1.88</td>
</tr>
<tr>
<td>Antimalarial drugs</td>
<td>2.80</td>
<td>1.40</td>
<td>5.57</td>
</tr>
</tbody>
</table>

*From Cox regression analysis.*
During our observation, patients who continued antimalarial drug treatment after reaching the clinical quiescence criteria had a longer clinically quiescent phase. Clinical data indicate that antimalarial drugs (HCQ and chloroquine) have therapeutic benefits for patients with SLE due to immunomodulation effects [39–41]. Also, antimalarial drugs may prevent flares in SLE patients [10, 42] and in pregnant SLE patients [43]. The Canadian HCQ Study Group demonstrated that after reaching clinical quiescence, HCQ is effective in reducing the frequency of mild relapses, but not in more severe manifestations like GN [10, 42]. However, phase III belimumab trials, which studied patients with some disease activity and positive serology when entering the study, showed that patients treated with antimalarial drugs since study entry had flare rates similar to those treated without antimalarial drugs [37]. This inconsistent outcome may be due to the timing of the patient’s exposure to antimalarial drugs, continued treatment after reaching clinical quiescence or starting treatment during high disease activity. The clinically quiescent phase characteristics were similar across immunosuppressive drug treatment.

Serology could not be performed every 3 months for all patients in our cohort. Instead, disease activity was measured using the mSLEDAI-2K score (the SLEDAI-2K score without complement level and anti-dsDNA antibody). Thus flare was defined as a combination of the SLEDAI-2K score (score increase ≥4 from the previous visit) and the 2010 international consensus for a definition of disease flare in lupus [29] (increasing disease activity in one or more organ systems involving new or worse clinical signs and symptoms and/or laboratory measurements or consideration of a change or an increase in treatment). The authors agreed that this flare definition represented what is used in daily clinical practice, particularly in countries with economic constraints on frequent serology. It should be noted that the impact of some variables (e.g. late-onset SLE, severe infection etc.) on the clinically quiescent phase could not be studied due to a small sample size. However, these variables should be investigated in the future in a larger cohort.

Each patient in this cohort had been observed for at least 1 year at one centre, long enough for the pattern of disease activity to emerge in early-diagnosed SLE patients. The mean duration from diagnosis to cohort entry was only 3 months, with 74% of patients with an SDI score of zero. Our study is the first to demonstrate the course of disease in early-diagnosed SLE patients, which also showed the effect of certain variables on the clinically quiescent phase by using a specific and appropriate time-to-event analysis [44].

In conclusion, early-diagnosed SLE patients may have a good prognosis despite intermittent disease activity. Age at diagnosis ≥25 years or continuing treatment with an antimalarial drug after reaching clinical quiescence may result in a longer clinically quiescent phase. However, the proper dose of antimalarial drugs for prolonging the clinically quiescent phase requires further investigation.

Rheumatology key messages

- Early-diagnosed SLE patients could have a good prognosis.
- Regular follow-up of SLE patients in their clinical quiescence remains crucial.
- Continued treatment of SLE patients with an antimalarial drug after reaching clinical quiescence may result in a longer clinically quiescent phase.

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