Systemic Lupus Erythematosus Risk Probability Index: ready for routine use? Results from a Chinese cohort

Lin Zhang, Wentian Lu, Dong Yan, Zhichun Liu, Leixi Xue

ABSTRACT

Objectives To evaluate the performance of Systemic Lupus Erythematosus Risk Probability Index (SLERPI) in patients with SLE using a Chinese cohort.

Methods The Chinese cohort included 352 patients with and 385 without SLE (control group). The clinical data of patients, including demographic data, clinical findings and serological profiles, were collected. Patients with an SLERPI score >7 were classified as SLE. The performance of the American College of Rheumatology (ACR)-1997, Systemic Lupus International Collaborating Clinics (SLICC)-2012 and European League Against Rheumatism (EULAR)/ACR-2019 criteria were used as references.

Results Of these four classification criteria, SLERPI has the highest sensitivity (98.3% (95% CI 96.3% to 99.4%)), but lowest specificity (89.4% (95% CI 85.8% to 92.2%)). In the control group, patients eligible for the classification criteria for SLE were mainly those with primary Sjögren’s syndrome (pSS) and undifferentiated connective tissue disease (UCTD), which adversely affected the specificity of the classification criteria. Moreover, significantly more patients with pSS and UCTD met SLERPI than those who met other classification criteria. After excluding patients with pSS and UCTD from the control group, the specificity and accuracy of SLERPI improved to 94.3% (95% CI 91.0% to 96.6%) and 96.5% (95% CI 95.0% to 97.9%), respectively, and both outperformed the EULAR/ACR-2019 criteria. The time to SLERPI classification was the same as their clinical time to diagnosis in 261 patients, earlier than the clinical diagnosis in 23 patients and later than the clinical diagnosis in 9 patients. A total of 280 patients had the same time to SLERPI classification as EULAR/ACR-2019, 8 patients had earlier than EULAR/ACR-2019 and 1 patient had later than EULAR/ACR-2019.

Conclusion SLERPI performed well in patients with SLE, particularly for the earlier diagnosis of SLE.

WHAT IS ALREADY KNOWN ON THIS TOPIC
⇒ In managing patients with SLE, the diagnosis has always been a great challenge, and there is still no diagnostic standard.
⇒ Although there are classification criteria for SLE that aimed at identifying relatively homogeneous groups of patients for inclusion in clinical trials, their use for diagnostic purposes is common in clinical practice.

WHAT THIS STUDY ADDS
⇒ The present study evaluated the performance of Systemic Lupus Erythematosus Risk Probability Index (SLERPI) in a Chinese cohort and revealed that SLERPI has good diagnostic efficacy, particularly for the earlier identification of SLE.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY
⇒ The use of SLERPI in clinical practice may lead to more timely interventions for patients with SLE and contribute to improved patient prognosis.
⇒ Therefore, SLERPI deserves to be promoted in clinical practice.

INTRODUCTION

SLE is a common connective tissue disease (CTD) characterised by high clinical heterogeneity and unpredictable flares. In managing patients with SLE, the diagnosis has always been a great challenge, and there is still no diagnostic standard. Therefore, SLE is mainly diagnosed based on the experience of rheumatologists. Although there are classification criteria that aimed at identifying relatively homogeneous groups of patients for inclusion in clinical trials, their use for diagnostic purposes is common in clinical practice. In the past few decades, several versions of the classification criteria for SLE have been proposed by different international organisations, including the American College of Rheumatology (ACR)-1997 classification criteria, Systemic Lupus International Collaborating Clinics (SLICC)-2012 classification criteria and European League Against Rheumatism (EULAR)/ACR-2019 classification criteria. Meta-analysis results showed that the sensitivity of SLICC-2012 (0.96 (95% CI 0.93 to 0.97)) and EULAR/ACR-2019 (0.95 (95% CI 0.92 to 0.97)) were higher than that of ACR-1997 (0.86 (95% CI 0.82 to 0.89)), and SLICC-2012 and EULAR/ACR-2019 are more conducive to identifying patients with early disease course.
Based on common clinical and serological features, Adamichou et al recently developed a new, simple and interpretable model, the Systemic Lupus Erythematosus Risk Probability Index (SLERPI), to help diagnose SLE early. This model includes 14 variably weighted items, with >7 patients being classified as SLE. In the European population, the sensitivity, specificity and accuracy of this model were estimated at 94.2%, 94.4% and 94.2%, respectively. Another study from Australia suggested that this model has high sensitivity (98.5%) but low specificity (84.6%). Due to differences in diagnostic performance with the existing classification criteria to diagnose patients with SLE in different races, the performance of SLERPI should be further validated in other races.

We have previously established a Chinese cohort that included patients with and without SLE and examined the overall performance of SLERPI in the diagnosis of SLE, we included the results of our previous studies on the ACR-1997, SLICC-2012 and EULAR/ACR-2019. Therefore, this study aimed to further evaluate the performance of SLERPI in patients with SLE using the cohort.

**METHODS**

**Study design and participants**

The Chinese cohort comprised 352 patients with and 385 without SLE (control group) who were recruited from the Department of Rheumatology and Immunology at the Second Affiliated Hospital of Soochow University between January 2016 and December 2020. The SLE diagnosis was established by rheumatologists with ≥8 years of clinical practice. Patients with other CTD, infections, cirrhosis, malignant solid tumours or haematological tumours or who were pregnant were excluded from the SLE group. The control group included patients with primary Sjogren’s syndrome (pSS) (n=56), undifferentiated CTD (UCTD) (n=32), rheumatoid arthritis (n=85), idiopathic inflammatory myopathies (n=24), systemic sclerosis (n=24), mixed CTD (n=14), primary systemic vasculitis (n=25), Behcet’s disease (n=12), rheumatoid polyarthritis (n=25), spondyloarthritis (n=18), lymphoma (n=10), immune thrombocytopenic purpura (n=3), Crohn’s disease (n=8), ulcerative colitis (n=7), liver cancer (n=5), lung cancer (n=16), pneumonia (n=11) and urinary tract infection (n=10).

**Data collection**

Demographic, clinical and laboratory data associated with the classification criteria were extracted from electronic medical records. The ANA titre was measured using an immunofluorescence antibody assay in the immune laboratory of the Second Affiliated Hospital of Soochow University, and positive ANA was set at a serum dilution of 1:100.

During the project establishment and training of data collectors, this study emphasised that care should be taken to identify similar disorders when collecting clinical data such as signs and symptoms. If more alternative explanations were available, they would not be considered as positive items for the classification criteria. Arrangements were made for another staff member to review the clinical data after collection and before starting the study analysis. If there was any doubt, it would be reconfirmed by the two clinical experts to avoid attribution errors where possible.

**RESULTS**

**Sample description**

Compared with the control group, the SLE group consisted of younger patients and a higher proportion of women (online supplemental table 1). In the SLE group, the proportion of patients with a disease course of ≤1, 1–3, 3–5 and >5 years was 23.9%, 6.3%, 10.8% and 59.1%, respectively. Of the 14 SLERPI items, differences in the clinical variables were significant between the SLE and control groups, except for the second item (subacute cutaneous lupus erythematosus or discoid lupus erythematosus) (table 1). As a score reduction item, the SLE group had fewer interstitial lung disease than the control group. The remaining 12 items are indeed more common in the SLE group.

The overall performance of SLERPI in the diagnosis of SLE

The accuracy of SLERPI was 93.6% (95% CI 91.9% to 95.4%), with a specificity of 89.4% (95% CI 85.8% to 92.2%) and sensitivity of 98.3% (95% CI 96.3% to 99.4%) (table 2). To clarify the performance of SLERPI in the diagnosis of SLE, we included the results of our previous studies on the ACR-1997, the SLICC-2012 and the EULAR/ACR-2019 criteria in the same cohort. The results showed that SLERPI had the highest sensitivity, but lowest specificity.

The clinical characteristics and disease composition of patients in the control group meeting SLERPI

In order to elucidate the reasons for the low specificity of SLERPI, we further investigated the clinical characteristics and disease composition of patients in the control group meeting SLERPI (total score >7). Among the 385 patients in the control group, 41 were eligible for the SLERPI. We first compared the SLERPI items for patients with SLERPI >7 and ≤7 (online supplemental table 2).
We next investigated the disease composition of these 41 patients in the control group, including 15 patients with pSS, 9 with UCTD, 5 with rheumatoid arthritis, 4 with idiopathic inflammatory myopathies, 3 with systemic sclerosis, 2 with mixed CTD and 2 with pneumonia, and 1 with primary systemic vasculitis (table 3). pSS and UCTD accounted for >50% of patients eligible for SLERPI in the present study; however, their total proportion was only 23% of the control group. Similar findings were confirmed by the analysis of other classification criteria, namely, that control patients meeting the classification criteria for SLE were predominantly those with pSS and UCTD.

Significantly more patients with pSS and UCTD met SLERPI (n=24) than those meeting other classification criteria (n=8 for ACR-1997, 16 for SLICC-2012, 15 for EULAR/ACR-2019), while the number of patients with other diseases meeting SLERPI in the control group (n=17) was similar to the number of those meeting SLICC-2012 (n=14) and EULAR/ACR-2019 (n=18) criteria (table 3). Numerous studies have shown that patients with pSS and UCTD may progress to SLE in the future. Therefore, the inclusion of patients with pSS and UCTD in the control group in this study reduced the specificity of each classification criterion, especially for SLERPI.

### Table 1 Evaluation of patients in the SLE group and control group according to SLERPI

<table>
<thead>
<tr>
<th>Condition</th>
<th>SLE group (n=352)</th>
<th>Control group (n=385)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malar rash or maculopapular rash</td>
<td>167 (47.4)</td>
<td>12 (3.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Subacute cutaneous lupus erythematosus</td>
<td>2 (0.6)</td>
<td>1 (0.3)</td>
<td>0.938</td>
</tr>
<tr>
<td>Alopecia</td>
<td>132 (37.5)</td>
<td>14 (3.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mucosal ulcers</td>
<td>62 (17.6)</td>
<td>22 (5.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Arthritis</td>
<td>182 (51.7)</td>
<td>124 (32.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Serositis</td>
<td>78 (22.2)</td>
<td>9 (2.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Leucopenia &lt;4000/μL (at least once)</td>
<td>265 (75.3)</td>
<td>103 (26.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Thrombocytopenia or autoimmune haemolytic anaemia</td>
<td>158 (44.9)</td>
<td>37 (9.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Neurological disorder</td>
<td>15 (4.3)</td>
<td>0 (0.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Proteinuria &gt;500 mg/24 hours</td>
<td>171 (48.6)</td>
<td>9 (2.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ANA</td>
<td>349 (99.1)</td>
<td>186 (48.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Low C3 and C4</td>
<td>235 (66.8)</td>
<td>32 (8.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Immunological disorder (any of: anti-DNA, anti-Sm, anti-phospholipid antibodies)</td>
<td>281 (79.8)</td>
<td>20 (5.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>20 (5.7)</td>
<td>53 (13.8)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Values are n (%).

Malar rash or maculopapular rash, alopecia, serositis, leucopenia, thrombocytopenia or autoimmune haemolytic anaemia, proteinuria, ANA positivity, low C3 and C4, and neurological disorder were all significantly more common in the SLERPI group with >7. No significant differences were found in patients with subacute cutaneous lupus erythematosus or discoid lupus erythematosus, mucosal ulcers, arthritis, neurological disorder and interstitial lung disease.

### Table 2 Overall performance of ACR-997 criteria, SLICC-2012 criteria, EULAR/ACR-2019 criteria and SLERPI

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensitivity (95% CI), %</th>
<th>Specificity (95% CI), %</th>
<th>Accuracy (95% CI), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR-997</td>
<td>82.1 (77.7, 86.0)</td>
<td>96.4 (94.0, 98.0)</td>
<td>89.6 (87.1, 91.7)</td>
</tr>
<tr>
<td>SLICC-2012</td>
<td>98.0 (95.9, 99.2)</td>
<td>92.2 (89.1, 95.7)</td>
<td>95.0 (93.1, 96.4)</td>
</tr>
<tr>
<td>EULAR/ACR-2019</td>
<td>97.4 (95.2, 98.8)</td>
<td>91.4 (88.2, 94.0)</td>
<td>94.3 (92.4, 95.9)</td>
</tr>
<tr>
<td>SLERPI</td>
<td>98.3 (96.3, 99.4)</td>
<td>89.4 (85.8, 92.2)</td>
<td>93.6 (91.9, 95.4)</td>
</tr>
</tbody>
</table>

ACR, American College of Rheumatology; EULAR, European League Against Rheumatism; SLERPI, Systemic Lupus Erythematosus Risk Probability Index; SLICC, Systemic Lupus International Collaborating Clinics.
Lupus Science & Medicine

was the same as their clinical time to diagnosis in 261 patients, earlier than the clinical diagnosis in 23 patients, and later than the clinical diagnosis in 9 patients. Subsequently, a subgroup analysis was performed based on the involvement system, indicating that the SLERPI classification was earlier than the clinical diagnosis in 15 patients with cutaneous mucosal lesions, 15 with arthritis, 5 with serositis, 20 with haematological involvement and 12 with lupus nephritis, whereas only 5, 2, 3, 6 and 4 patients had a later SLERPI classification, respectively.

Our previous study found that the EULAR/ACR-2019 criteria showed the best early diagnostic performance compared with the ACR-1997 and SLICC-2012 criteria; therefore, we further compared the classification time of SLERPI with that of EULAR/ACR-2019 criteria (table 5). The time to SLERPI classification was the same as the EULAR/ACR-2019 criteria in 280 patients, earlier in 8 patients and later in only 1 patient. SLERPI also had better early diagnostic performance in skin mucosal lesions, arthritis, haematological involvement and lupus nephritis, with 6, 4, 7 and 5 patients diagnosed earlier than the EULAR/ACR-2019 criteria, respectively.

**DISCUSSION**

The new classification criteria are developed to improve the sensitivity and specificity, and the early discrimination of the classification criteria is also particularly important for SLE. The present study evaluated the performance of SLERPI in a Chinese cohort and revealed that SLERPI has good diagnostic efficacy, particularly for the earlier identification of SLE.

Previously, this cohort was used to investigate the performance of ACR-1997, SLICC-2012 and EULAR/ACR-2019 criteria.

### Table 3 The disease composition of the control group meeting different classification criteria

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>ACR-997 (n=14)</th>
<th>SLICC-2012 (n=30)</th>
<th>EULAR/ACR-2019 (n=33)</th>
<th>SLERPI (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Sjogren's syndrome</td>
<td>4 (28.6)</td>
<td>9 (30.0)</td>
<td>8 (24.2)</td>
<td>15 (36.6)</td>
</tr>
<tr>
<td>Undifferentiated connective tissue disease</td>
<td>4 (28.6)</td>
<td>7 (23.3)</td>
<td>7 (21.2)</td>
<td>9 (22.0)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1 (7.1)</td>
<td>3 (10.0)</td>
<td>10 (30.3)</td>
<td>5 (12.2)</td>
</tr>
<tr>
<td>Idiopathic inflammatory myopathies</td>
<td>4 (28.6)</td>
<td>3 (10.0)</td>
<td>3 (9.1)</td>
<td>4 (9.8)</td>
</tr>
<tr>
<td>Systemic sclerosis</td>
<td>0</td>
<td>3 (10.0)</td>
<td>2 (6.1)</td>
<td>3 (7.3)</td>
</tr>
<tr>
<td>Mixed connective tissue disease</td>
<td>1 (7.1)</td>
<td>2 (6.7)</td>
<td>2 (6.1)</td>
<td>2 (4.9)</td>
</tr>
<tr>
<td>Primary systemic vasculitis</td>
<td>0</td>
<td>1 (3.3)</td>
<td>0</td>
<td>1 (2.4)</td>
</tr>
<tr>
<td>Behcet’s disease</td>
<td>0</td>
<td>2 (6.7)</td>
<td>1 (3.0)</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (4.9)</td>
</tr>
</tbody>
</table>

Values are n (%).
ACR, American College of Rheumatology; EULAR, European League Against Rheumatism; SLERPI, Systemic Lupus Erythematosus Risk Probability Index; SLICC, Systemic Lupus International Collaborating Clinics.

### Table 4 The performance of ACR-997 criteria, SLICC-2012 criteria, EULAR/ACR-2019 criteria and SLERPI after excluding patients with pSS and UCTD from the control group

<table>
<thead>
<tr>
<th>Classification Criteria</th>
<th>Sensitivity (95% CI), %</th>
<th>Specificity (95% CI), %</th>
<th>Accuracy (95% CI), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR-997</td>
<td>82.1 (77.7, 86.0)</td>
<td>98.0 (95.7, 99.3)</td>
<td>89.4 (87.0, 91.7)</td>
</tr>
<tr>
<td>SLICC-2012</td>
<td>98.0 (95.9, 99.2)</td>
<td>95.3 (92.2, 97.4)</td>
<td>96.8 (95.4, 98.1)</td>
</tr>
<tr>
<td>EULAR/ACR-2019</td>
<td>97.4 (95.2, 98.8)</td>
<td>93.9 (90.6, 96.4)</td>
<td>95.8 (94.3, 97.4)</td>
</tr>
<tr>
<td>SLERPI</td>
<td>98.3 (96.3, 99.4)</td>
<td>94.3 (91.0, 96.6)</td>
<td>96.5 (95.0, 97.9)</td>
</tr>
</tbody>
</table>

ACR, American College of Rheumatology; EULAR, European League Against Rheumatism; pSS, primary Sjogren’s syndrome; SLERPI, Systemic Lupus Erythematosus Risk Probability Index; SLICC, Systemic Lupus International Collaborating Clinics; UCTD, undifferentiated connective tissue disease.
presented with more malar rash or maculopapular rash, alopecia, serositis, leukopenia, thrombocytopenia or auto-immune haemolytic anaemia, proteinuria, ANA positivity, low C3 and C4, and immunological disorder. Therefore, the above items facilitate the identification of SLE, which may conversely lead to a decreased specificity of SLERPI.

Interestingly, pSS and UCTD accounted for >50% of patients eligible for SLERPI in the present study; however, their total proportion was only 23% of the control group. SS can occur as a distinct entity (pSS) and can also precede other CTDs, including SLE. Zufferey et al observed that 4 of 55 patients with SS developed SLE within 1–10 years after the initial diagnosis of SS, with pleuropériditis, glomerulonephritis and focal central nervous system disease being the main clinical events predicting the development of SLE. A recent study suggested that the presence of albuminuria, haematuria, hypoproteinaemia, anti-dsDNA positivity and anti-Sm positivity in patients with SS may indicate the presence of SLE.

Patients with UCTD may also develop SLE. A study of a cohort with early UCTD found that 18 of 213 patients progressed to SLE after a 5-year follow-up. The presence of anti-DNA, anti-Sm, anti-phosphoprotein or multiple-specific antibodies in patients with UCTD, as well as clinical manifestations such as serositis, alopecia, photosensitivity and discoid rash, suggest the possibility of SLE occurrence. Another study found that 39 of 422 patients with UCTD had an SLERPI score of >7 and could be diagnosed as SLE. When the SLERPI score of >7 and ≤7 groups were compared based on the SLERPI criteria, malar rash or maculopapular rash, alopecia, mucosal ulcer, arthritis, thrombocytopenia/autoimmune haemolytic anaemia, proteinuria, ANA positivity, hypocomplementemia and immunological disorders were all significantly more common in the SLERPI score with >7 group, which was similar to our study. The SLERPI may be useful for the early identification of SLE among patients with signs of CTD without fulfilling any definite set of criteria. Therefore, patients with pSS and UCTD with SLERPI of >7 in the present study may develop SLE in the future, and the number of patients with pSS and UCTD eligible for SLERPI was significantly greater than the number of those eligible for the currently widely used classification criteria for SLE, which was consistent with the original intention of developing SLERPI.

Based on the above statements, the inclusion of patients with pSS and UCTD in the control group of this study adversely affected the specificity of classification criteria, especially for SLERPI. The exclusion of these patients resulted in a significant improvement in performance for all classification criteria, most notably for SLERPI, which improved to 94.3% (95% CI 91.0% to 96.6%) and 96.5% (95% CI 95.0% to 97.9%) in specificity and accuracy, respectively, and both outperformed the EULAR/ACR-2019 criteria. Therefore, SLERPI has good diagnostic efficacy for SLE.

Early intervention in SLE is essential to improve short-term and long-term outcomes, and prompt recognition of SLE, especially in hospitalised patients presenting with severe disease, is a prerequisite for initiating treatment. An observational cohort study found that among the 191 hospitalised patients due to manifestations eventually attributed to SLE, although 79.5% of them were diagnosed within 3 months from hospitalisation, the diagnosis was delayed in 39 patients, particularly those with haematological manifestations. Our data revealed that SLERPI enabled earlier diagnosis in some patients compared with the clinical diagnosis and EULAR/ACR-2019 criteria, especially in patients with important organ involvement, such as the kidney and haematological system. Therefore, the use of SLERPI in clinical practice may lead to more timely interventions for patients with SLE and contribute to improved patient prognosis.

Certain limitations of this study must be acknowledged. First, this is a single-centre retrospective study with inherent flaws, including selection bias. Second, this study focused on a Chinese population; thus, the results may not be appropriate for all patients with SLE.

In conclusion, SLERPI performed well in patients with SLE, particularly for the earlier diagnosis of SLE. In addition, compared with SLICC-2012 and EULAR/ACR-2019 criteria, SLERPI, like the ACR-1997 criteria, has fewer items and is easier to implement. Therefore, SLERPI deserves to be promoted in clinical practice.
However, future studies with larger samples and different ethnicities are still needed to validate the performance of SLERPI in detecting SLE.

Contributors All authors took part in revising the article and approved the final version to be published. LX and ZL contributed to the conception and design, and were guarantors of the study. LZ, WL and DY were responsible for collecting the data. LZ, WL and LX performed the analysis and drafted the article.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study complied with the principles of the World Medical Association Declaration of Helsinki and the study protocol was approved by the Ethics Committee of the Second Affiliated Hospital of Soochow University (Approval No. JD-HG-2021-19). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets used and/or analysed during this study are available from the corresponding author on reasonable request.

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