**Clinical Science**

**Lupus or not? SLE Risk Probability Index (SLERPI): a simple, clinician-friendly machine learning-based model to assist the diagnosis of systemic lupus erythematosus**

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**ABSTRACT**

**Objectives** Diagnostic reasoning in systemic lupus erythematosus (SLE) is a complex process reflecting the probability of disease at a given timepoint against competing diagnoses. We applied machine learning in well-characterised patient data sets to develop an algorithm that can aid SLE diagnosis.

**Methods** From a discovery cohort of randomly selected 802 adults with SLE or control rheumatologic diseases, clinically selected panels of deconvoluted classification criteria and non-criteria features were analysed. Feature selection and model construction were done with Random Forests and Least Absolute Shrinkage and Selection Operator-Logistic Regression (LASSO-LR). The best model in 10-fold cross-validation was tested in a validation cohort (512 SLE, 143 disease controls).

**Results** A novel LASSO-LR model had the best performance and included 14 variably weighed features with thrombocytopenia/thrombolytic anaemia, malar/maculopapular rash, proteinuria, low C3 and C4, antinuclear antibodies (ANA) and immunologic disorder being the strongest SLE predictors. Our model produced SLE risk probabilities (depending on the combination of features) correlating positively with disease severity and organ damage, and allowing the unbiased classification of a validation cohort into diagnostic certainty levels (unlikely, possible, likely, definite SLE) based on the likelihood of SLE against other diagnoses. Operating the model as binary (lupus/not-lupus), we noted excellent accuracy (94.8%) for identifying SLE, and high sensitivity for early disease (93.8%), nephritis (97.9%), neuropsychiatric (91.8%) and severe lupus requiring immunosuppressives/biologics (96.4%). This was converted into a scoring system, whereby a score >7 has 94.2% accuracy.

**Conclusions** We have developed and validated an accurate, clinician-friendly algorithm based on classical disease features for early SLE diagnosis and treatment to improve patient outcomes.

**INTRODUCTION**

Diagnosis of systemic lupus erythematosus (SLE) can be challenging and delayed by several months or years,4,5 resulting in increased patient uncertainty, referrals and healthcare utilisation.4 Delays in diagnosis and treatment initiation have been linked to increased flares and organ dysfunction.4,6 SLE diagnosis often relies on the acumen of physicians and is typically elicited by the presence of ‘high-yield’ features or multiple, although less-specific findings. Due to absence of diagnostic criteria, classification criteria, developed to facilitate the inclusion of homogeneous disease populations in clinical
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studies,7 are commonly used as a diagnostic aid. The Systemic Lupus International Collaborating Clinics (SLICC)8 and European League Against Rheumatism/American College of Rheumatology (EULAR/ACR)9 10 criteria enable the earlier classification of increased number of patients.11 Moreover, the EULAR/ACR 2019 criteria achieve the highest combination of sensitivity and specificity.9 11 Improved classification has not remedied the challenge for diagnosis especially at early stages.11 12

Artificial intelligence tools based on machine learning (ML) are increasingly used to manage difficult medical tasks. Such models can be trained from different kinds of medical or biological data.13 14 ML has been used for the molecular classification of inflammatory myositis15 and rheumatoid arthritis,16 for predicting mortality,17 response to biological agents18 and disease activity,19 whereas less effort has been directed towards diagnosis.20 21 Building robust computational models that avoid excess complexity represents an important challenge.14 22

Herein, we applied ML on panels of clinical features aiming to construct a model that can accurately detect SLE against competing rheumatologic conditions. We used a discovery cohort of patients with SLE or control diseases to train two standard ML algorithms, namely, the Random Forests (RF) the Least Absolute Shrinkage and Selection Operator (LASSO) followed by Logistic Regression (LR). RF is a non-linear method with high complexity and thus, less explainable, whereas the LR is a linear method supporting simpler, more clinically interpretable results.23 The best model selected by internal cross-validation (CV) was further evaluated in an independent validation cohort. Through this process, we developed a novel, simple Least Absolute Shrinkage and Selection Operator-logistic regression (LASSO-LR) model of variably weighted, standard clinical features that can produce individualised SLE risk probabilities alike clinical diagnostic reasoning. Our model had excellent accuracy for SLE, including early and severe forms of the disease, therefore it could represent a useful clinical tool.

METHODS

Discovery and validation cohorts
We used data from the Rheumatology Clinics at the University Hospital of Heraklion and the ‘Attikon’ University Hospital, Athens. Both centres have established SLE registries and use homogenised, structured forms for collecting clinical characteristics (including classification criteria), use of treatments and disease outcomes.11 24–26 We included patients diagnosed during 01/2005-06/2019 with SLE or miscellaneous control rheumatological diseases that are relevant to the differential diagnosis of lupus (online supplemental table S1) by consultant rheumatologists with ≥5 years clinical practice. A randomly selected discovery cohort of 401 patients with SLE and 401 controls were used to construct, train and compare the ML models. The balanced (1:1) ratio of SLE and controls helps to minimise any predictive modeling biases. An external validation cohort of consecutively registered 512 patients with SLE and 143 controls was used to provide an unbiased estimate of the diagnostic accuracy of the best model. The study was approved by the local ethics committees.

Variables and data set preparation
For each patient, demographics, rheumatological disease and date of diagnosis, date of earliest reported occurrence of each of the items from the three classification criteria (ACR 1997,27 SLICC 2012,8 EULAR/ACR 20199 10) and date of last follow-up visit/assessment were extracted. Attribution of the criteria items to SLE or not was arbitrated by rheumatologists (DTB, GKB, AF) using the EULAR/ACR attribution rule.9 10 We used criteria items both in their original version and after deconvolution into subitems (eg, ‘maculopapular rash’ subitem from the EULAR/ACR 2019 ‘acute cutaneous lupus’ criterion). In addition, we monitored a predefined list of non-criteria features (online supplemental table S2). Missing data were eliminated through vigorous charts review and quality control.

Disease subsets and outcomes
Early SLE was defined as duration less than 24 months since diagnosis. Lupus nephritis was determined according to kidney histological findings suggestive of lupus in a patient with compatible clinical and/or serological findings. Neuropsychiatric lupus was diagnosed through multidisciplinary approach9 10 and ascertained by the Italian Study Group attribution model.29 The British Isles Lupus Assessment Group (BILAG) glossary30 was used to classify the severity of manifestations as previously detailed.1 11 Use of immunosuppressive/biologic treatments and the physician global assessment of disease severity were also collected. The date of each item of the SLICC/ACR damage index (SDI)31 was monitored.

Feature selection, model construction and evaluation
We followed two approaches for developing a predictive model for SLE. First, we combined each one of the three classification criteria with additional, non-redundant features from the other two criteria sets and with non-criteria features; second, we developed a de novo model based on clinical variables selected from the three classification criteria and non-criteria features. Univariable LR (online supplemental table S3) was performed in the discovery cohort to determine the association of each individual feature with SLE and correlation analysis (online supplemental table S4) to detect collinearity between features/predictors and assist clinicians in the construction of feature panels. Clinicians (GKB,CA) created 20 panels of features with the aim to introduce alternative feature versions. Each panel was submitted into two ML algorithms for feature selection, namely, RF and LASSO, the latter followed by LR (figure 1). Details are provided in the online supplemental methods.

We performed a 10-fold stratified CV process (division of the dataset into 10 folds of near-equal size without resubstitution) to construct and compare the 40 multivariable models for their predictive capability. Each fold (10%) was used as a test data set to determine the model performance, while the remaining nine folds (90%) were used as the training data set for the model construction. We evaluated the following metrics (averaged from the 10 CV test data sets): sensitivity, specificity, accuracy and area under the receiver operating characteristic curve (AUC-ROC). The model with the highest accuracy was selected as the best to undergo evaluation in the validation cohort.

Statistical analysis
The Kruskal-Wallis analysis of variance was used to compare means and the χ² test to compare proportions. To convert the LASSO-LR model into scoring system, regression coefficients were divided by the smallest coefficient followed by rounding to the nearest 0.5 value. Statistical analyses were performed using the R software (V3.5.1) and SPSS (V25.0). Feature selection and ranking, model construction, evaluation and validation were developed in MATLAB V9.2.
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RESULTS
Combination of the classification criteria with additional features yields modest improvements in diagnostic accuracy for SLE
Classification criteria comprising different collections of clinical and immunological features classify patients with SLE in routine practice with high sensitivity and specificity.\(^{11,32-36}\) We examined whether their combination with additional, non-redundant features can improve their performance. We used a discovery cohort of randomly selected 802 adults with SLE or control rheumatologic diseases (1:1 ratio) to prepare 20 clinically selected panels of classification criteria items (both in their original version and deconvoluted into subitems in the case of composite items) and non-criteria features. Two machine learning methods were applied for feature selection and model construction for each panel: (A) Random Forests (RF) and (B) Least Absolute Shrinkage and Selection Operator (LASSO) followed by logistic regression (LASSO-LR). The best model (highest accuracy in the 10-fold cross-validation process) was further tested in an independent dataset of 512 patients with systemic lupus erythematosus (SLE) and 143 disease controls (validation cohort). AUC, area under the curve; CV, cross-validation; ROC, receiver operating curve.

Figure 1  Schematic overview of the methodology for developing a machine learning-based diagnostic model for SLE. We used a discovery cohort of randomly selected 802 adults with SLE or control rheumatologic diseases (1:1 ratio) to prepare 20 clinically selected panels of classification criteria items (both in their original version and deconvoluted into subitems in the case of composite items) and non-criteria features. Two machine learning methods were applied for feature selection and model construction for each panel: (A) Random Forests (RF) and (B) Least Absolute Shrinkage and Selection Operator (LASSO) followed by logistic regression (LASSO-LR). The best model (highest accuracy in the 10-fold cross-validation process) was further tested in an independent dataset of 512 patients with systemic lupus erythematosus (SLE) and 143 disease controls (validation cohort). AUC, area under the curve; CV, cross-validation; ROC, receiver operating curve.
A de novo-constructed LR model has superior performance for SLE diagnosis

We next sought to develop a novel statistical algorithm by integrating individual items from the classification criteria and additional non-criteria manifestations. Feature selection was performed either embedded in RF or prior to the model construction phase, with LR based on LASSO-LR. An important difference between these two methods is that if several highly correlated variables are predictive, LASSO may select one or a few while RF may use all of them. The best model in the discovery cohort 10-fold CV runs was a LASSO-LR model of 14 clinical parameters (hereafter referred to as ‘SLERPI’: SLE Risk Probability Index) (online supplemental table S5).

The model parameters included features from all three sets of classification criteria and ILD as a single non-criteria feature. Autoimmune thrombocytopenia or haemolytic anaemia, malar or maculopapular rash, low C3 and C4, proteinuria (all defined according to the EULAR/ACR 2019 criteria), ANA and the ACR 1997 immunological disorder (modified to include anti-β2-glycoprotein antibodies) had the strongest positive association with SLE (figure 2A, online supplemental figure S1). Using a validation cohort of 512 clinically diagnosed patients with SLE and 143 disease controls to confirm our model, we noted excellent ability to discriminate true positive (SLE) versus false positive (control) cases with an area under the ROC curve (AUC) of 0.981 (figure 2B).

The new LR model enables SLE risk stratification into distinct diagnostic certainty levels

To determine how our model could be used in clinical practice, we applied the LR equation to generate SLE risk probabilities ranging 0%–100%, depending on the combination of features/predictors. We reasoned that different ranges of probabilities correspond to varying diagnostic certainty levels alike clinical thinking. For this, we calculated the SLE risk probabilities for all patients in the discovery cohort followed by unsupervised k-means clustering to detect unbiased risk probabilities partitions. Following merging of the closely related clusters C and D (online supplemental figure S2), we obtained four groups of increasing risk probability bins (0%–14%, 15%–43%, 44%–86%, 87%–100%).

Next, we used the validation cohort to determine the proportion of actual SLE and control patients captured within each predicted SLE risk group (figure 3A). Results were averaged from randomly generated, non-overlapping patient subsets (seven subsets each containing 73 or 74 patients with SLE, two subsets containing 71 and 72 disease controls). We confirmed the high discriminating capacity of our model as the majority of actual SLE and control patients captured within each risk probability bin had high, medium, or low accuracy, respectively (figure 3B).

The SLERPI has high accuracy for detecting SLE including patients with early disease and severe disease requiring potent treatment

In addition to continuous risk prediction, binary outcome models (disease of interest is present or absent) are most helpful in decision-making. We used the discovery cohort for the unbiased definition of the model probability cut-off to separate SLE versus other rheumatological diseases. On the maximal Youden’s statistics, the 50% risk probability threshold was chosen (online supplemental figure S4A-C). At this threshold, the SLERPI demonstrated high sensitivity (95.1%), specificity (93.7%) and accuracy (94.8%, corrected to 93.9% based on an expected 3:17 ratio of SLE: controls in real-life setting) in the total validation cohort (figure 4A, online supplemental figure S5A). When tested against the control subset with undifferentiated connective tissue disease (n=56), the model specificity was 91.1%. We further determined the model discriminative ability in disease subsets of clinical relevance such as early SLE, lupus nephritis, neuropsychiatric SLE(NPSLE) and severe disease due to lower prevalence of British Isles Lupus Assessment Group (BILAG) A manifestations and organ damage (online supplemental figure S3A-B).

The diagnostic threshold of 50% risk probability may be used for the early detection of the disease in patients who have the combination of positive clinical and immunological findings. Our model can be used to predict the risk of SLE and to guide clinical decision-making. Additionally, the SLERPI model can be used to identify patients with early disease and severe disease requiring potent treatment.
A Least Absolute Shrinkage and Selection Operator-logistic regression (LASSO-LR) model shows high discriminating capacity for SLE against competing rheumatological diseases. (A) A LASSO-LR model comprising of 14 clinical and serological features showed the highest accuracy for SLE in the 10-fold cross-validation runs from the discovery cohort. The plot illustrates the features associated with increased likelihood for SLE as compared with control rheumatological diseases along with the corresponding effect sizes (OR; 95% CI, p value). All model parameters are treated as dichotomous (ie, present=1, absent=0) in the LR equation as follows: F(x)=Intercept + (1.80×mucosal ulcers) + (2.96×synovitis) + (1.83×serositis) + (3.66×immunologic disorder) + (4.42×antinuclear antibodies (ANA)) + (2.13×alopecia) + (2.17×neurologic disorder) + (4.25×malar and/or maculopapular rash) + (2.58×subacute cutaneous lupus erythematosus (SCLE) and/or discoid lupus erythematosus (DLE)) + (1.82×leucopenia) + (6.46×thrombocytopenia and/or autoimmune haemolytic anaemia (AIHA)) + (6.63×low C3 and C4) – (1.45×interstitial lung disease (ILD)); 1 defined according to the ACR 1997 classification criteria, 2 defined according to the ACR 1997 criteria modified to include also positive anti-β2 glycoprotein IgG or IgM antibodies, 3 defined according to the EULAR/ACR 2019 classification criteria, 4 defined according to the SLICC 2012 classification criteria, 5 see online supplemental table S2) for definition. (B) The LASSO-LR model presented in (A) was further evaluated in an external (validation) cohort of patients with 512 patients with SLE and 143 disease controls. The graph represents the receiver operating curve with a calculated area under the curve of 0.981 indicating an excellent capacity of the model to discriminate SLE versus disease controls.
Figure 3  The Least Absolute Shrinkage and Selection Operator-logic regression (LASSO-LR) model can generate SLE risk probabilities, which correspond to distinct diagnostic certainty levels and correlate with disease outcomes. (A) Bar plot representation of the fraction of patients with SLE patients and disease controls (validation cohort) according to increasing bins of predicted SLE risk probabilities (0%–14%, 15%–43%, 44%–86%, 87%–100%) calculated by the LASSO-LR model shown in figure 2. Superimposed are the diagnostic accuracies (blue-coloured) corresponding to the rates of correct classification of disease controls against patients with SLE in the lower two probability bins (0%–14%, 15%–43%), and of patients with SLE against disease controls in the higher two probability bins (44%–86%, 87%–100%). Results are averages (±SD) for patient fractions or 95% CI for the accuracy metric) calculated from randomly generated, non-overlapping subsets of patients with SLE (seven subsets each containing 73 or 74 patients) and disease controls (two subsets containing 71 and 72 patients) from the validation cohort. The majority of control (average 80%) and SLE (average 82%) patients belong to the lowest (0%–14%) and the highest (87%–100%) risk probability groups, respectively. In accordance, accuracy was highest in these two extreme risk groups but dropped in the intermediate ones (15%–43%, 44%–86%). (B) Bar plot representation of the relative proportion of SLE and disease controls (validation cohort) within each SLE risk probability bin (0%–14%, 15%–43%, 44%–86%, 87%–100%). Calculations were made from the non-overlapping subsets of patients with SLE and disease controls as outlined in (A). (C) Positive- and negative-likelihood ratios (LRs) (mean, 95% CI) for the diagnosis of SLE against control diagnoses, according to different SLE risk probability thresholds (>14%, >43%, >86%) applied to the discovery cohort. Calculations were made from the non-overlapping subsets of patients with SLE and disease controls as outlined in (A). The >14% threshold had an average LR+5.0 and LR−0.017, which correspond to a moderate increase when tested positive and a large decrease when tested negative in the likelihood for SLE, respectively. (D) Matrices of SLE risk probabilities based on different combinations of features included in the LASSO-LR diagnostic model. In each scenario, the calculated probability fits to one of the four SLE risk groups corresponding to varying diagnostic certainty levels (unlikely SLE: 0%–14%, possible/cannot rule out SLE: 15%–43%, likely SLE: 44%–86%, definite SLE: 87%–100%). (E) Dot plot analysis of the model-generated SLE risk probabilities according to the severity of disease manifestations (defined based on the BILAG system) and organ damage (SLICC/ACR Damage Index (SDI)). Data were generated from the validation cohort patients with SLE (n=512) and are presented as mean (95% CI). The Kruskal-Wallis (non-parametric) analysis of variance test was performed and two-tailed p values are shown. ANA, antinuclear antibodies; RMDs, rheumatic diseases; SCLE, subacute cutaneous lupus erythematosus; SDI, SLICC/ACR damage index; SLE, systemic lupus erythematosus.
A

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Figure 4  The new diagnostic model has high accuracy for systemic lupus erythematosus (SLE) including early and severe disease requiring immunosuppressive or biologic treatment. (A) Confusion matrix of the actual versus predicted cases of patients with SLE (n=512) and disease controls (n=143) in the validation cohort. The LASSO-LR diagnostic model was operated as binary (SLE or not-SLE) by setting the SLE risk probability threshold at ≥50%. Based on the number of true-positive, true-negative, false-positive and false-negative cases, sensitivity, specificity, accuracy, positive- and negative-likelihood ratios are estimated as metrics of the model diagnostic performance. (B) Sensitivity of the LASSO-LR model (operated as binary) for the detection of clinically relevant subsets of SLE including early disease, lupus nephritis, neuropsychiatric lupus, haematological lupus and severe lupus requiring potent immunosuppressive and/or biologic treatment.

clinical SLE, thus resembling clinical reasoning, while attaining a combination of high sensitivity and specificity against alternative rheumatologic diseases. When used as a dichotomous algorithm (SLE-or-not), the SLERPI exhibits high accuracy for SLE, including early and severe/organ-threatening disease forms.

In clinical practice, physicians can elicit the diagnosis of SLE even in the presence of a few high-yield manifestations such as typical malar rash in an individual with anti-DNA autoantibodies. Such decisions reflect a form of human intelligence that develops through clinical experience even with a limited number of patients. Conversely, computational intelligence tools require training on large comprehensive data sets to produce valid results. We used a discovery sample of well-characterised SLE and control patients for unbiased selection of features that contribute most to clinical SLE diagnosis. Patients with SLE with relatively early disease (median duration 4.2 years) and irrespective of the severity of manifestations were included, as compared with developing classification criteria, which typically rely on cases with long-standing disease.

Thrombocytopenia/autoimmune haemolytic anaemia (AIHA), malar rash, proteinuria, ANA, immunological disorder (anti-DNA, anti-Sm, anti-phospholipid antibodies) and combined C3 and C4 hypocomplementemia were the strongest predictors against competing rheumatological diseases. These results are in line with the variably weighted items introduced in the EULAR/ACR 2019 classification criteria, where, for example, thrombocytopenia/AIHA is scored higher than leucopenia and malar rash higher than other rashes.

SLE displays marked phenotypic heterogeneity ranging from systemic to organ-limited/dominant forms. Clinical and immunological features may accrue sequentially in time, thus reflecting an evolving process. Indeed, various terms have been used to describe different patient profiles such as ‘definitive SLE’, ‘probable SLE’, ‘possible SLE’, ‘lupus-like’ or ‘incomplete lupus’. Our model calculates risk probabilities, which correlate with certainty levels for the presence of SLE versus competing rheumatological diseases. Based on unsupervised clustering, we hereby propose a risk probability-based stratification of patients with suspected SLE into ‘unlikely’, ‘possible’ (cannot rule out), ‘likely’ and ‘definitive’ SLE, depending on the type and number of features. This approach resembles diagnostic reasoning especially when encountering a patient for the first time.

Our model can be used not only to exclude (when risk probability is <14%) or confirm (when risk probability exceeds 86%) SLE but also to alert physicians to identify and monitor patients with intermediate probabilities. Similar approaches have been used in other complex diseases.

By operating our model as binary, we achieved very high rates of sensitivity, specificity and accuracy assessed in a validation cohort. Our model can identify SLE under different clinical scenarios such as: (a) lupus autoantibodies concurring with a single clinical feature from a major organ (e.g., thrombocytopenia/AIHA), (b) multiple clinical but no immunological features, (c) limited or non-specific serological features (e.g., ANA) concurring with high-yield clinical manifestations (e.g., malar rash). We noted excellent performance within patient subgroups with early disease, biopsy-proven lupus nephritis, neuropsychiatric disease and severe disease necessitating potent immunosuppressive or biologic therapies.
ML-based tools are increasingly used to simulate human ‘medical reasoning’ and effectively handle complex tasks. Such models can be trained from many different kinds of medical or biological data. Our data sets included well-defined features derived from the three classification criteria, and also non-criteria features often considered by physicians in cases of suspected SLE. ILD was a feature alienating the probability of SLE while favouring alternative rheumatological disease. Integration of additional clinical, laboratory or biological (eg, transcriptome) variables could lead to the development of even more robust models. The fact that our model comprises 14 classical, easily retrieved clinical variables facilitates its clinical implementation.

Additional studies should prospectively evaluate and independently validate the proposed model to establish its clinical utility and effect on a variety of patient and healthcare outcomes. Notwithstanding, our analysis might provide useful insights towards the possible future development of formal SLE diagnostic criteria, a currently unmet need. To this end, establishing a firm diagnosis and treatment plan still remains at the judgement of experienced physicians.

Our study is limited by its retrospective design and data extraction from medical records; accordingly, some clinical information may have been missed or underestimated. Nonetheless, both centres maintain detailed patient registries and use structured forms for collecting clinical data, which helps to reduce possible information/data completeness bias. Developing a model for early diagnosis should ideally be based on cohorts with very early disease and before the appearance of adverse outcomes, however, it can be challenging to recruit large numbers of such cases. Although we used two state-of-the-art ML approaches, a number of other sophisticated algorithms of higher complexity exist (eg, deep neural networks). Our model also requires validation in additional cohorts of diverse population characteristics (eg, non-Caucasians), including infectious disease controls.

Conclusively, we have developed and evaluated a new, simple and interpretable model for the detection of SLE based on common clinical and serological features. Our model provides risk predictions that correlate with clinical endpoints and support patient probabilistic disease classification of potential clinical relevance. Pending further confirmation of its performance, the SLERPI could assist the early diagnosis and treatment of SLE, including early and severe forms, to improve patient outcomes.

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### Correction note
This article has been corrected since it published Online First. The provenance and peer review statement has been included.

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### Contributors
CA, DN and MN collected data from patient medical charts and also performed data entry. IG designed and implemented the machine learning (ML) methodology, constructed and evaluated the ML models and drafted the relevant methodology sections on feature selection, model construction, evaluation and statistical analysis. AB organised the RedCap database. AR and AF assessed patients enrolled in the study and collected data from patient medical charts. PS and DTB assisted in patient recruitment and critically reviewed the manuscript. GKB conceived and supervised the study, performed statistical analyses and drafted the manuscript.

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### Competing interests
None declared.

### Patient consent for publication
Not required.

### Ethics approval
The study was approved by the Ethics Committee of the University Hospital of Heraklion (protocol number 13960/10-10-2018) and the Ethics Committee of the ‘Attikon’ University Hospital of Athens.

### Provenance and peer review
Not commissioned; externally peer reviewed.

### Data availability statement
Data are available upon reasonable request. Data will be available upon request.

### Supplemental material
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| Table 1 A simple scoring system version of the SLE Risk Probability Index* |
|---------------------------------|---|
| **Feature** | **Score** |
| Malar rash or maculopapular rash† | 3 |
| Subacute cutaneous lupus erythematosus or discoid lupus erythematosus† | 2 |
| Alopecia§ | 1.5 |
| Mucosal ulcers§ | 1 |
| Arthritis§ | 2 |
| Serositis§ | 1.5 |
| Leucopenia<4000/μL (at least once)† | 1.5 |
| Thrombocytopenia or autoimmune haemolytic anaemia† | 4.5 |
| Neurological disorder† | 1.5 |
| Proteinuria>500 mg/24 hour† | 4.5 |
| ANA† | 3 |
| Low C3 and C4† | 2 |
| Immunological disorder (any of: anti-DNA, anti-Sm, anti-phospholipid antibodies¶) | 2.5 |
| Interstitial lung disease** | –1 |

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*| **Feature** | **Score** |
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†Defined as in Aringer et al. 10  
‡Defined as in Hochberg. 27  
§Defined as in Hochberg. 28  
¶Defined as in Hochberg 29 modified to include also positive anti-J2 glycoprotein IgG or IgM or IgA antibodies.  
* Defined as in Hochberg 29.  
** Radiologic features of lung disease suggesting inflammation and fibrosis of the alveoli, distal airways and septal interstitial of the lung, as observed with a high-resolution CT scan of the chest.  
†† When operated at a threshold (sum of individual scores) of >7 (out of a maximum value 30.5), the sensitivity, specificity and accuracy rates are 94.2%, 94.4% and 94.2%, respectively.  
ANA, antinuclear antibodies; SLE, systemic lupus erythematosus.
Systemic lupus erythematosus

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