DOI: https://doi.org/10.2298/SARH231001008Z
UDC: 616-002.52

REVIEW OF LITERATURE / ПРЕГЛЕД ЛИТЕРАТУРЕ

Systemic lupus erythematosus – diagnosis and classification of the disease in the past and in present times

Valentina Živković, Bojana Stamenković, Sonja Stojanović

University of Niš, Faculty of Medicine, Niš, Serbia;
Institute for Treatment and Rehabilitation, Niška Banja, Niš, Serbia

SUMMARY

The main feature of systemic lupus erythematosus (SLE) is its heterogeneity, which mainly refers to clinical presentation, the course of disease and prognosis, which can impact any organ and various immunoserological tests. As a result, prompt illness recognition and right diagnosis are extremely complicated processes based on the most recent classification standards and the doctor's clinical expertise with specific patients.

In contrast, not all SLE patients are included when using classification criteria, which are based on a definition of a homogenous group by the specified, restricted number of clinical and immunoserological domains and for the purpose of conducting clinical or epidemiological investigations. Classification criteria have evolved over the last 50 years in response to new understandings and advances. This process began with the American College of Rheumatology (ACR) criteria in 1971 and continued through their updates in 1982 and 1997, followed by Systemic Lupus International Collaborating Clinics 2012 and the European League Against Rheumatism (EULAR)/ACR 2019. EULAR/ACR 2019 criteria have proven their high validity (sensitivity and specificity) in numerous studies, as well as adequate diagnostic usefulness, defined by 24 items in 10 domains, with the fulfillment of the essential precondition of antinuclear antibody positivity.

Keywords: systemic lupus erythematosus; diagnosis; classification criteria

INTRODUCTION

Systemic lupus erythematosus (SLE) is characterized with wide heterogeneity of clinical manifestations and immunoserological findings and is considered a multisystemic autoimmune disease with insufficiently elucidated etiopathogenesis, thought to be caused by a combination of genetic, epigenetic, immune, hormonal and environmental factors [1]. Presumably, it signifies a decline in immune tolerance to one's own antigens added with excessive B and T cell activation, complement binding and cytokine activation; these processes result in the formation of immune complexes that precipitate in the blood vessels, and typically cause persistent, chronic inflammation of different tissues and organs [2].

There is a wide spectrum of clinical presentations of the disease, from moderate types affecting only the skin and the joints to "malignant" versions affecting the kidneys, heart, lungs, and brain. Owing to the variability of SLE, there is no single "gold standard" or set of precise, validated diagnostic criteria for the diagnosis of SLE; rather, classification criteria are used to assist clinical experience in this process [3, 4]. Considering the high morbidity and death rates associated with SLE, prompt identification and early treatment initiation are critical for preventing illness relapse and subsequent organ damage and achieving stable remission [5]. A good strategy to reach these goals would be to improve the classification criterion's sensitivity and specificity and bring them closer to the diagnostic criteria.

DEFINITION OF DIAGNOSTIC AND CLASSIFICATION CRITERIA

A set of symptoms, indicators, and tests that are employed in routine clinical practice in order to properly select patients are known as diagnostic criteria. The right diagnosis results in the right therapy induction. The classification criteria represent standardized set of a limited number of items agreed upon by a group of experts, primarily intended to create well-defined, homogeneous sets of patients for the purposes of clinical or epidemiological research [3]. They are not created to be used neither for disease diagnosis, nor for making decisions about treatment. Classification criteria do not involve all SLE patients; they involve most of the patients with the key shared standardized disease characteristics [6, 7].

In rheumatology, the diagnostic criteria are equivalent or closely resemble the classification criteria for diseases that have a known etiology, including gout and Lyme disease, for which the classification criterion's sensitivity and specificity reaches 100% [3]. Diagnostic criteria for the majority of other rheumatic disorders,

Received • Примљено: October 1, 2023
Revised • Ревизија: December 21, 2023
Accepted • Прихваћено: December 29, 2023
Online first: January 15, 2024

Correspondence to:
Valentina ŽIVKOVIĆ
Bulevar dr Zorana Đinđića 127/23
Medijana
18106 Niš
Serbia
ljubisa.nina@gmail.com

including SLE, are based on a combination of the most recent classification criteria and the clinician's expertise and intuition (the gold standard). Classification criteria may lead to an incorrect or too early diagnosis of SLE if they are applied for diagnostic purposes [8]. On the other hand, some SLE patients do not meet the requirements for SLE classification. The classification criteria are updated on a regular basis to reflect new discoveries and developments in the field of disease pathogenesis. The purpose of this document is to provide the review of the SLE classification criteria from 1971 to 2019.

THE AMERICAN COLLEGE OF RHEUMATOLOGY CLASSIFICATION CRITERIA

The American College of Rheumatology (ACR), previously known as the American Rheumatism Association, established the initial SLE classification criteria in 1971. The criteria comprised 14 items [9]. Later, in 1982 and 1997, these criteria were changed. The 1982 revision included the confirmation of positive results for antinuclear antibodies (ANA) by immunofluorescent or equivalent assay, as well as positive results for anti-double stranded DNA (anti-dsDNA) antibody and positive results for anti-Smith antibodies. Additionally, the unification of the involvement of specific organ systems into a single criterion and the exclusion of alopecia and Raynaud's phenomenon due to low sensitivity and specificity were utilized [10, 11].

Afterwards, several groups of researchers have employed new statistical methods in order to improve the ACR classification criteria, namely researchers from a Cleveland clinic, whose criteria demonstrated high sensitivity and specificity when compared to 1971 and 1982 criteria [12]. Moreover, the Boston criteria developed by Costenbader et al. [13] that were based on the Cleveland clinical criteria and included renal pathology and antiphospholipid antibodies, have shown a noticeably poorer specificity when compared to the updated ACR criteria. The aforementioned classification criteria are mostly historical in nature and were not frequently employed in clinical and epidemiological investigations since they were not used as a basis for SLE diagnosis in everyday clinical practice.

In the 1997 ACR modification of the SLE classification criteria, the findings of antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant) or false-positive serological tests for syphilis were added, whereas the findings of lupus cells were eliminated (Table 1) [14, 15]. The ACR 1997 criteria were not adopted only as the standard for patient eligibility for clinical and epidemiological research, but also were used additionally as diagnostic standards for the next 20 years. In total, 11 items make up the ACR 1997: nine clinical and two laboratory indicators, with a minimum of four criteria required for the SLE diagnosis. These criteria can be presented concurrently or serially, regardless of their duration.

Laboratory criteria include the following two: ANA positivity (not drug-induced) confirmed by immunofluorescence testing or an equivalent assay as an independent criterion, and positive immunology tests (antibodies against phospholipids, anti-Smith, or anti-dsDNA antibodies). The following are the clinical criteria: involvement of the kidneys, hematopoietic system, central nervous system, skin, mucosa (in the form of painless oral or nasopharyngeal ulcerations), joints, and serosa [14–17].

Table 1. 1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of Systemic Lupus Erythematosus (Tan 1982; Hochberg 1997)

Criteria	Definition
Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
Arthritis	Nonerosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion
Serositis	Pleuritis – convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion Pericarditis – documented by echocardiography or rub or evidence of pericardial effusion
Renal disorder	Persistent proteinuria greater than 0.5 grams per day or greater than 3+ if quantitation is not peformed Cellular casts may be red cell, hemoglobin, granular, tubular, or mixed
Neurologic disorder	Seizures Psychosis (in the absence of offending drugs or known metabolic derangements, e.g., uremia, ketoacidosis, or electrolyte imbalance)
Hematologic disorder	Hemolytic anemia-with reticulocytosis Leukopenia < 4000 / mm on ≥ 2 occasions Lymphopenia < 1500 / mm on ≥ 2 occasions Thrombocytopenia < 100,000 / mm in the absence of offending drugs
Immunologic disorder	Anti-double-stranded DNA Anti-Smith antibodies Antiphospholipid antibodies based on abnormal serum level of IgG or IgM anticardiolipin antibodies, positive test result for lupus anticoagulant using a standard method, or false-positive serologic test result for syphilis
Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome

Nevertheless, the primary flaw of the ACR 1997 criteria was that SLE could theoretically be classified without meeting any of the immunological requirements. Due to that fact, for clinical studies, in addition to the fulfillment of ACR criteria, the presence of autoantibodies was also the prerequisite in order for a study participant to be enrolled [18, 19].

SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS CLASSIFICATION CRITERIA

A major shortcoming in the ACR 1997 criteria was addressed by Systemic Lupus International Collaborating Clinics (SLICC), an international group that developed new criteria in 2012 [18, 20]. A total of 17 criteria,

comprising six immunological and 11 clinical, were used to define SLICC 2012. The SLE classification required the following:

1. meeting a minimum of four requirements, with at least one clinical and one immunological criterion, or
2. lupus nephritis as the sole criterion in the presence of ANA or anti-dsDNA antibodies [18].

In comparison to ACR 1997, definition of SLICC 2012 indicated a substantial advancement for several reasons. Skin changes were broadly covered under two distinct criteria, one for acute and subacute alterations and the other for chronic ones. Alopecia, a highly common (though nonspecific) symptom, was also taken into consideration under a different criterion. Furthermore, the definition of arthritis has undergone substantial modifications. It is now based on the presence of palpable pain in two or more joints combined with morning stiffness that lasts longer than thirty minutes and is not based on radiography. Based on measuring proteinuria by using the urine protein/creatinin ratio without setting a time limit for urine collection, lupus nephritis can be confirmed [21, 22]. Due to a lack of SLE specificity, the neurological criterion encompasses a wide range of neuropsychiatric indications but does not cover not all of the potential signs [23, 24]. Hemolytic anemia, leucocytopenia/lymphocytopenia and thrombocytopenia were singled out and placed into three separate hematological criteria, with a focus on ruling out other potential causes (such as drug use, infections, and other associated disorders).

SLICC 2012 brought some significant changes to immunological criteria compared to ACR 1997. Since these criteria were split into six distinct categories (ANA, anti-dsDNA antibodies, anti-Smith antibodies, anti-phospholipid antibodies, low complement, positive direct Coombs test in the absence of hemolytic anemia), giving them the attention they deserve, as each of them now may impact the classification of SLE. If ANA are absent, positivity of anti-dsDNA is rare and may result from a laboratory error.

SLICC 2012's most significant finding was the fact that biopsy-confirmed lupus nephritis added with one immunological parameter (positive ANA or anti-dsDNA) was sufficient to classify a patient as having SLE [18]. This finding was shown by nearly 1% of patients diagnosed with SLE, which was solely based on biopsy-confirmed nephritis and positive serology.

When using clinical diagnosis as the gold standard, the results of a meta-analysis published by Dutch authors in 2018 showed that SLICC 2012 criteria classified more patients as having SLE, previously identified as having incomplete erythematous lupus,"probable SLE, or non-differentiated connective tissue disease", adding to higher sensitivity of SLICC 2012 when compared to ACR 1997 [25]. Nevertheless, the research indicates that between 50% and 90% of people with incomplete SLE never develop SLE, and their labeling as SLE may result in hazardous or needless therapy [26, 27, 28]. Based on the results from numerous studies, it was not possible to draw any conclusion about the diagnostic significance of SLICC and ACR criteria due to incomplete data on the duration of the disease, or due to the long duration of the disease [25, 29, 30, 31].

Finally, it can be concluded from a plethora of research regarding the validity of the ACR 1997 and SLICC 2012 criteria that the latter one was superior due to its higher sensitivity and capacity to identify SLE patients at earlier stages of the illness [25, 32, 33].

THE EUROPEAN LEAGUE AGAINST RHEUMATISM / THE AMERICAN COLLEGE OF RHEUMATOLOGY CLASSIFICATION CRITERIA

The European League Against Rheumatism (EULAR) and ACR assembled a panel of specialists aiming to develop new classification criteria with enhanced sensitivity, specificity and validity for SLE and with maximized diagnostic value. Using the multiphase technique, the panel worked for five years until defining the SLE EULAR/ACR 2019 classification criteria [34]. This study began with the 21 "candidate" criteria, arranged into clinical and immunological domains, two of which were labeled as the entry criteria. Based on the literature research and data about sensitivity and specificity, it was determined that just one criterion should be employed as the "entry" criterion – positive ANA in the titer of ≥ 1:80 on HEp-2 cells or an equivalent test (positive, at any time), with the definition of seven clinical and three immunological domains.

The 2019 EULAR/ACR classification criteria (EULAR/ACR 2019) were the first to adopt a scoring system which has significantly improved their usage. Scores were allocated to distinct manifestations (i.e., clinical and immunological categories), that varied in their contribution to the overall score.

The clinical domains included general symptoms, hematological, neuropsychiatric, mucocutaneous, serous, musculoskeletal, and renal symptoms; the immunological domains included complement and antibodies specific to SLE (anti-dsDNA antibodies or anti-Smith antibodies), anti-phospholipid antibodies (anti-cardiolipin antibodies or anti-beta(2)GP1 antibodies or lupus anticoagulant), and scores on a scale from 2 to 10. In order to be classified as having SLE, an individual must have a total score of at least ten points and meet at least one clinical criterion (Table 2).

The 2019. EULAR/ACR classification criteria (EULAR/ACR 2019) were the first to employ a scoring system, which greatly increased the usefulness of the classification criteria. In particular, individual manifestations, i.e., clinical and immunological domains, were assigned different scores, contributing differently to the total score.

While positive ANA is the fundamental need for an SLE classification (EULAR/ACR 2019), it is important to consider the uncommon occurrence of ANA negative SLE patients. The term seronegative SLE refers to 1–5% of SLE patients who have negative ANA and anti-dsDNA antibodies but other supportive criteria positive and frequently present along with anti-Ro and/or anti-La positivity [35].

According to the EULAR/ACR 2019 definition, a non-infectious fever, defined as a body temperature more than 38.3°C, carries two points, and is practically the only new criterion. Various acute, subacute, and chronic alterations

Table 2. EULAR/ACR classification criteria for SLE (Aringer 2019)

Entry criterion: Positive ANA test result ANA at a titer of ≥ 1:80 on HEp-2 cells, or an equivalent positive test result (ever)	
If absent, do not classify as SLE; if present, apply additive criteria	
Additional criteria Do not count a criterion if there is a more likely explanation than SLE. Occurrence of a criterion on ≥ 1 occasion is sufficient. SLE classification requires ≥ 1 clinical criterion and ≥ 10 points. Criteria need not occur simultaneously. Within each domain, only the highest weighted criterion is counted toward the total score	
Criteria	Weight
Clinical domains	
Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Nonscarring alopecia	2
Oral ulcers	2
Subacute cutaneous or discoid lupus	4
Acute cutaneous lupus	6
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
Renal	
Proteinuria > 0.5 g per 24 hours	4
Renal biopsy class II or V lupus nephritis	8
Renal biopsy class III or IV lupus nephritis	10
Immunologic domains	
Antiphospholipid antibodies	
Anticardiolipin antibodies or anti-β2GP1 antibodies or lupus anticoagulant	2
Complement proteins	
Low C3 or low C4	3
Low C3 and low C4	4
SLE-specific antibodies	
Anti-dsDNA antibody or anti-Smith antibody	6
Classify as SLE with a score of ≥ 10 if entry criterion is fulfilled	

EULAR/ACR – European League Against Rheumatism / American College of Rheumatology; SLE – systemic lupus erythematosus; ANA – antinuclear antibody; C – complement; dsDNA – double-stranded DNA; HEp-2 – human epithelial type 2; β2GP1 – β2 glycoprotein 1

of the skin are worth 2–6 points. Lupus nephritis class II or V has the value of eight points, while nephritis class III or IV on renal biopsy brings 10 points and those are sufficient for the SLE classification if added with positive ANA as the entry criterion. Urinary sediment is no longer included in the renal domain due to method subjectivity and the quick shifting of results following initial glucocorticoid medication. Proteinuria > 500 mg / 24 hours is worth four points. Most of the time, lupus arthritis is non-erosive and is not linked to anti-cyclic citrullinated peptide antibodies, which carry a considerable number of points – more than half of those needed for an SLE classification (six points).

Compared to the ACR 2019, the SLICC 2012 criteria covered significantly more neuropsychiatric manifestations. These manifestations include multiple mononeuritis, myelitis, peripheral or cranial neuropathy; however, because of their uncommon and rare occurrence, these entities are excluded from the EULAR/ACR 2019 criteria. Only the acute confusion states (in the absence of toxic-metabolic causes, uremia, and the usage of drugs), epilepsy and psychosis were kept, as they were the only conditions marked as typical and rather specific.

In conclusion, the EULAR/ACR 2019 contains fewer domains than SLICC 2012, which makes their application easier. Also, the ability to classify SLE early and more accurately is a significant benefit of EULAR/ACR 2019 [4]. These criteria kept their excellent specificity at the ACR 1997 level of 93%, while their sensitivity increased nearly to the SLICC 2012 level (96% *vs.* 97%) [5, 36]. Additionally, they are shown to be valid in more than 20 investigations, thus constituting the "gold standard" for inclusion criteria in clinical trials [7, 37–40].

Despite defining the EULAR/ACR 2019 classification criteria, a broad spectrum of clinical and serological findings in patients with SLE may sometimes produce confusion and delay the correct diagnosis, increasing the risk of organ damage and increased morbidity and mortality [41–47].

CONCLUSION

Since there were no opportunities to define diagnostic criteria over the last 50 years, specific requirements for SLE classification criteria have been established. These criteria are not intended to diagnose or involve every case of a disease, but rather to define homogenous sets of patients for the purpose of conducting various multicentric clinical or epidemiological studies.

The EULAR/ACR 2019 classification criteria resulted from the progression of ACR 1971 and their updates in 1982, and 1997, to the SLICC 2012 standards. The EULAR/ACR 2019 satisfied the stringent methodology requirements and incorporated additional information, greatly increasing their clinical and diagnostic usefulness.

When comparing two sets of criteria, we can say that SLICC 2012 added a lot of new items in comparison to ACR 1997, whereas EULAR/ACR 2019 made application easier by lowering the number of domains compared to SLICC 2012 by compressing the hematological, mucocutaneous, and neurological domains. While EULAR/ACR 2019 underwent a major structural transformation by specifying the entrance criteria and scoring system for distinct domains and items within the same domain, ACR 1997 and SLICC 2012 maintained their structural similarity. When compared to ACR 1997, it is possible to draw the conclusion that SLICC 2012 dramatically increased sensitivity but lowered specificity, whereas EULAR/ACR

2019 have again raised specificity, with the maintenance of a high sensitivity.

Diagnosing SLE remains difficult despite the most recent EULAR/ACR 2019 classification criteria definition, and it is primarily based on clinical assessments and current classification criteria as a starting point.

Even though there have been significant advancements and discoveries in the fields of genetics and etiopathogenesis of SLE, the 21st century SLICC 2012 and EULAR/ACR 2019 classification criteria remain grounded in clinical manifestations and autoimmune serology, just like the ACR criteria that were established half a century ago.

Ethics: The authors declare that the article was written according to ethical standards of the Serbian Archives of Medicine as well as ethical standards of medical facilities for each author involved.

Conflict of interest: None declared.

REFERENCES

1. Zucchi D, Silvagni E, Elefante E, Signorini V, Cardelli C, Trentin F, et al. Systemic lupus erythematosus: one year in review 2023. Clin Exp Rheumatol. 2023;41(5):997–1008. [DOI: 10.55563/clinexprheumatol/4uc7e8] [PMID: 37133502]
2. Kiriakidou M, Lee Ching C. Systemic Lupus Erythematosus. Ann Intern Med. 2020;172(11):ITC81–ITC96. [DOI: 10.7326/AITC202006020] [PMID: 32479157]
3. Aggarwal R, Ringold S, Khanna D, Neogi T, Johnson RS, Miller A, et al. Distinctions between diagnostic and classification criteria? Arthritis Care Res (Hoboken). 2015;67(7):891–7. [DOI: 10.1002/acr.22671] [PMID: 26199203]
4. Fanouriakis A, Tziolos N, Bertsias G, Boumpas TD. Update on the diagnosis and management of systemic lupus erythematosus. Ann Rheum Dis. 2021;80(1):14–25. [DOI: 10.1136/annrheumdis-2020-218272] [PMID: 33051219]
5. Aringer M, Johnson RS. Classifying and diagnosing systemic lupus erythematosus in the 21st century. Rheumatology (Oxford). 2020;59(5):v4–v11. [DOI: 10.1093/rheumatology/keaa379] [PMID: 33280013]
6. Fries JF, Hochberg MC, Medsger TA Jr, Hunder GG, Bombardier C. Criteria for rheumatic disease. Different types and different functions. The American College of Rheumatology Diagnostic and Therapeutic Criteria Committee. Arthritis Rheum. 1994;37(4):454–62. [DOI: 10.1002/art.1780370403] [PMID: 7605403]
7. Aringer M, Costenbader K, Dörner T, Johnson RS. Advances in SLE classification criteria. J Autoimmun. 2022;132:102845. [DOI: 10.1016/j.jaut.2022.102845] [PMID: 35725680]
8. Larosa M, Iaccarino L, Gatto M, Punzi L, Doria A. Advances in the diagnosis and classification of systemic lupus erythematosus. Expert Rev Clin Immunol. 2016;12(12):1309–20. [DOI: 10.1080/1744666X.2016.1206470] [PMID: 27362864]
9. Fries FJ, Siegel CR. Testing the 'preliminary criteria for classification of SLE'. Ann Rheum Dis. 1973;32(2):171–7. [DOI: 10.1136/ard.32.2.171] [PMID: 4571393]
10. Tan EM, Cohen AS, Fries JF, Masi TA, McShane JD, Rothfield FN, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1982;25(11):1271–7. [DOI: 10.1002/art.1780251101] [PMID: 7138600]
11. Levin RE, Weinstein A, Peterson M, Testa AM, Rothfield FN. A comparison of the sensitivity of the 1971 and 1982 American Rheumatism Association criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1984;27(5):530–8. [DOI: 10.1002/art.1780270508] [PMID: 6721885]
12. Clough JD, Elrazak M, Calabrese LH, Valenzuela R, Braun WB, Williams GW. Weighted criteria for the diagnosis of systemic lupus erythematosus. Arch Intern Med. 1984;144(2):281–5. [PMID: 6421256]
13. Costenbader KH, Karlson EW, Mandl LA. Defining lupus cases for clinical studies: the Boston weighted criteria for the classification of systemic lupus erythematosus. J Rheumatol. 2002;29(12):2545–50. [PMID: 12465149]
14. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997;40(9):1725. [DOI: 10.1002/art.1780400928] [PMID: 9324032]
15. Feletar M, Ibañez D, Urowitz BM, Gladman DD. The impact of the 1997 update of the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus: what has been changed? Arthritis Rheum. 2003;48(7):2067–9. [DOI: 10.1002/art.11167] [PMID: 12847702]
16. Bruce IN, Buie J, Bloch L, Bae SC, Costenbader K, Levy RA, et al. Lupus spectrum ambiguity has long-term negative implications for patients. Lupus Sci Med. 2023;10(1):e000856. [DOI: 10.1136/lupus-2022-000856] [PMID: 37534513]
17. Morand EF, Fernandez-Ruiz R, Blazer A, Niewold TB. Advances in the management of systemic lupus erythematosus. BMJ. 2023;383:e073980. [DOI: 10.1136/bmj-2022-073980] [PMID: 37884289]
18. Petri M, Orbai AM, Alarcón GS, Gordon C, Merrill JT, Fortin PR, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum. 2012;64(8):2677–86. [DOI: 10.1002/art.34473] [PMID: 22553077]
19. Furie AR, van Vollenhoven FR, Kalunian K, Navarra S, Romero-Diaz J, Werth PV, et al. Trial of Anti-BDCA2 Antibody Litifilimab for Systemic Lupus Erythematosus. N Engl J Med. 2022;387(10):894–904. [DOI: 10.1056/NEJMoa2118025] [PMID: 36069871]
20. Yu C, Gershwin ME, Chang C. Diagnostic criteria for systemic lupus erythematosus: a critical review. J Autoimmun. 2014;48–49:10–3. [DOI: 10.1016/j.jaut.2014.01.004] [PMID: 24461385]
21. Weening JJ, D'Agati VD, Schwartz MV, Seshan VS, Alpers EC, Appel BG, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. Kidney International. 2004;65(2):521–30. [DOI: 10.1111/j.1523-1755.2004.00443] [PMID: 14717922]
22. Fanouriakis A, Bertsias G, Liapis G, Marinaki S, Papagianni A, Stangou M, et al. Multidisciplinary approach to lupus nephritis: Clinical pearls, pitfalls, and positioning of newly-approved agents. Lupus. 2023;32(10):1155–63. [DOI: 10.1177/09612033231191944] [PMID: 37499240]
23. Ainiala H, Hietaharju A, Loukkola J, Peltola J, Korpela M, Metsänoja R, et al. Validity of the new American College of Rheumatology criteria for neuropsychiatric lupus syndromes: a population-based evaluation. Arthritis Rheum. 2001;45(5):419–23. [DOI: 10.1002/1529-0131(200110)45:5<419::aid-art360>3.0.co;2-x] [PMID: 11642640]
24. Carrión-Barberà I, Salman-Monte TC, Vílchez-Oya F, Monfort J. Neuropsychiatric involvement in systemic lupus erythematosus: A review. Autoimmun Rev. 2021;20(4):102780. [DOI: 10.1016/j.autrev.2021.102780] [PMID: 33609799]
25. Hartman EAR, van Royen-Kerkhof A, Jacobs JWG, Welsing PMJ, Fritsch-Stork RDE. Performance of the 2012 Systemic Lupus International Collaborating Clinics classification criteria versus the 1997 American College of Rheumatology classification criteria in adult and juvenile systemic lupus erythematosus. A systematic review and meta-analysis. Autoimmun Rev. 2018;17(3):316–22. [DOI: 10.1016/j.autrev.2018.01.007] [PMID: 29366725]
26. Bourn R, James JA. Preclinical lupus. Curr Opin Rheumatol. 2015;27(5):433–9. [DOI: 10.1097/BOR.0000000000000199] [PMID: 26125103]
27. Lambers WM, Westra J, Bootsma H, de Leeuw K. From incomplete to complete systemic lupus erythematosus; A review of the predictive serological immune markers. Semin Arthritis Rheum. 2021;51(1):43–8. [DOI: 10.1016/j.semarthrit.2020.11.006] [PMID: 33360229]
28. Sternhagen E, Bettendorf B, Lenert A, Lenert PS. The Role of Clinical Features and Serum Biomarkers in Identifying Patients with Incomplete Lupus Erythematosus at Higher Risk of Transitioning to Systemic Lupus Erythematosus: Current Perspectives. J Inflamm Res. 2022:15:1133–45. [DOI: 10.2147/JIR.S275043] [PMID: 35210816]

29. Amezcua-Guerra LM, Higuera-Ortiz V, Arteaga-García U, Gallegos-Nava S, Hübbe-Tena C. Performance of the 2012 Systemic Lupus International Collaborating Clinics and the 1997 American College of Rheumatology classification criteria for systemic lupus erythematosus in a real-life scenario. Arthritis Care Res (Hoboken). 2015;67(3):437–41. [DOI: 10.1002/acr.22422] [PMID: 25073545]
30. Sag E, Tartaglione A, Batu ED, Ravelli A, Khalil MAS, Marks DS, et al. Performance of the new SLICC classification criteria in childhood systemic lupus erythematosus: a multicentre study. Clin Exp Rheumatol. 2014;32(3):440–4. [PMID: 24642380]
31. Aberle T, Bourn RL, Chen H, Roberts CV, Guthridge MJ, Bean K, et al. Use of SLICC criteria in a large, diverse lupus registry enables SLE classification of a subset of ACR-designated subjects with incomplete lupus. Lupus Sci Med. 2017(4):1–7. [DOI: 10.1136/lupus-2016-000176] [PMID: 28409015]
32. Chang LS, Huang PY, Kuo HC, Tu YK, Tseng PT, Liang CS, et al. Diagnostic accuracy of the American College of Rheumatology-1997, the Systemic Lupus International Collaborating Clinics-2012, and the European League Against Rheumatism-2019 criteria for juvenile systemic lupus erythematosus: A systematic review and network meta-analysis. Autoimmun Rev. 2022;21(9):103144. [DOI: 10.1016/j.autrev.2022.103144] [PMID: 35842200]
33. Pons-Estel GJ, Wojdyla D, McGwin G Jr, Magder LS, Petri MA, Pons-Estel BA; Grupo Latino Americano De Estudio del Lupus (GLADEL), Alarcón GS; LUMINA cohort. The American College of Rheumatology and the Systemic Lupus International CollaboratingClinics classification criteria for systemic lupus erythematosus in two multiethnic cohorts: a commentary. Lupus. 2014;23(1):3–9. [DOI: 10.1177/0961203313512883] [PMID: 24285098]
34. Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis. 2019;78(9):1151–9. [DOI: 10.1136/annrheumdis-2018-214819] [PMID: 31383717]
35. Aringer M, Johnson SR. Systemic Lupus Erythematosus Classification and Diagnosis. Rheum Dis Clin North Am. 2021;47(3):501–11. [DOI: 10.1016/j.rdc.2021.04.011] [PMID: 34215376]
36. Aringer M, Petri M. New classification criteria for systemic lupus erythematosus. Curr Opin Rheumatol. 2020;32(6):590–6. [DOI: 10.1097/BOR.0000000000000740] [PMID: 32925250]
37. Lazar S, Kahlenberg JM. Systemic Lupus Erythematosus: New Diagnostic and Therapeutic Approaches. Annu Rev Med. 2023;74:339–52. [DOI: 10.1146/annurev-med-043021-032611] [PMID: 35804480]
38. Cheng S, Ding H, Xue H, Cao L. Evaluation of the 2019 EULAR/ACR classification criteria for systemic lupus erythematosus in children and adults. Clin Rheumatol. 2022;41(10):2995–3003. [DOI: 10.1007/s10067-022-06293-x] [PMID: 35852777]
39. Schmidtmann I, Kraus D, Weinmann A, Pütz K, Claßen P, Schleicher EM, et al. Validation of the 2019 EULAR/ACR classification criteria for systemic lupus erythematosus in an academic tertiary care centre. RMD Open. 2023;9(3):e003037. [DOI: 10.1136/rmdopen-2023-003037] [PMID: 37419524]
40. Lu W, Tian F, Ma J, Zhong Y, Liu Z, Xue L. Diagnostic accuracy of the European League against rheumatism/American College of Rheumatology-2019 versus the Systemic Lupus International Collaborating Clinics-2012 versus the ACR-1997 classification criteria in adult systemic lupus erythematosus: A systematic review and meta-analysis. Front Immunol. 2022;13:1023451. [DOI: 10.3389/fimmu.2022.1023451] [PMID: 36311745]
41. Živković V, Stanković A, Cvetković T, Mitić B, Kostić S, Nedović J, et al. Anti-dsDNA, anti-nucleosome and anti-C1q antibodies as disease activity markers in patients with systemic lupus erythematosus. Srp Arh Celok Lek. 2014;142(7–8):431–6. [DOI: 10.2298/SARH1408431Z] [PMID: 25233687]
42. Živković V, Cvetković T, Mitić B, Stamenković B, Stojanović S, Radovanović-Dinić B, et al. Monocyte chemoattractant protein-1 as a marker of systemic lupus erythematosus: an observational study. Rheumatol Int. 2018;38(6):1003–8. [DOI: 10.1007/s00296-017-3888-x] [PMID: 29181621]
43. Živković V, Mitić B, Stamenković B, Stojanović S, Dinić BR, Stojanović M, et al. Analysis on the risk factors for organ damage in patients with systemic lupus erythematosus: a cross-sectional single-center experience. Sao Paulo Med J. 2019;137(2):155–61. [DOI: 10.1590/1516-3180.2018.0258060219] [PMID: 31314876]
44. Živković V, Stamenković B, Stojanović S, Cvetković T, Radovanović-Dinić B. Quality of life and severity of fatigue in patients with systemic lupus erythematosus. Acta Medica Medianae. 2018;57(3):100–6. [DOI: 10.5633/amm.2018.0314]
45. Lam NV, Brown JA, Sharma R. Systemic Lupus Erythematosus: Diagnosis and Treatment. Am Fam Physician. 2023;107(4):383–95. [PMID: 37054414]
46. Ceccarelli F, Perricone C, Natalucci F, Picciariello L, Olivieri G, Cafaro G, et al. Organ damage in Systemic Lupus Erythematosus patients: A multifactorial phenomenon. Autoimmun Rev. 2023;22(8):103374. [DOI: 10.1016/j.autrev.2023.103374] [PMID: 37301273]
47. Fanouriakis A, Kostopoulou M, Andersen J, Aringer M, Arnaud L, Bae S, et al. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. Ann Rheum Dis. 2023;83(1):15–29. [DOI: 10.1136/ard-2023-224762] [PMID: 37827694]

Системски еритемски лупус – дијагноза и класификација болести некад и сад

Валентина Живковић, Бојана Стаменковић, Соња Стојановић

Универзитет у Нишу, Медицински факултет, Ниш, Србија;
Институт за лечење и рехабилитацију „Нишка Бања", Ниш, Србија

САЖЕТАК

Главна особина системског еритемског лупуса је хетерогеност, која се односи, између осталог, на имуносеролошке налазе, клиничку презентацију, ток и прогнозу болести, при чему сваки орган може бити погођен. Стога је правовремено препознавање болести и постављање дијагнозе веома сложен когнитивни процес, који се заснива на актуелним класификационим критеријумима и клиничком искуству лекара који је усмерен према појединцу. Супротно томе, класификациони критеријуми се заснивају на дефинисању хомогене групе према претходно задатом ограниченом броју клиничких и имуносеролошких домена у циљу извођења клиничких и епидемиолошких студија и не обухватају све оболеле од системског еритемског лупуса. Последњих пола века класификациони критеријуми су се у складу са сазнањима и напредовањем у овој области мењали, почев од критеријума Америчког колеџа за реуматологију (*ACR*) постављених 1971. и њихових ревизија 1982. и 1997. год., преко Међународне сарадничке клинике за системски лупус (*SLICC*) 2012, све до Европске лиге против реуматизма (*EULAR*)/*ACR* 2019. год. *EULAR*/*ACR* 2019 су у многобројним студијама доказали своју високу валидност (сензитивност и специфичност), као и добру дијагностичку вредност, а дефинишу их 24 ставке у 10 домена уз испуњење основног предуслова да су антинуклеусна антитела позитивна.

Кључне речи: системски еритемски лупус; дијагноза; класификациони критеријуми