NEW CLASSIFICATION CRITERIA FOR SLE

PhD., Associate Professor of faculty therapy Usmanova D. N.,
Assistant Yuldasheva S. L.
Master of degree Amirmuhammadov U. A.,
Master of degree Ulmasov Sh.N.,
Andizhan State medical institute

Abstract. Classification criteria are essential for science, defining a group of patients sufficiently homogenous to make meaningful clinical trials and translational studies possible. Beyond this, however, useful classification criteria will shape our concept of the disease. This was definitely true for the 1982 SLE classification criteria system of the American College of Rheumatology (ACR), with 11 criteria, at least four of which had to be positive for classification [1]. In 1997, these criteria were amended to include two of the three current standard tests for anti-phospholipid antibodies, namely anti-cardiolipin antibodies and lupus anticoagulant [2]. At the same time, the LE cell phenomenon was released into history. Further progress led to an increase in information pertinent to SLE classification. Prominent examples were routine measurement of serum complement levels [3] and renal biopsy having become the standard approach for managing patients with (suspected) lupus nephritis [6]. While useful, the ACR criteria did not keep up with better understanding of the clinical manifestations and laboratory findings in SLE . This prompted the need for new SLE classification criteria.

Keywords: Systemic lupus erythematosus, classification criteria, diagnosis, autoantibodies, lupus nephritis

НОВЫЕ КЛАССИФИКАЦИОННЫЕ КРИТЕРИИ СКВ

К.м.н., доцент Усманова Д. Н.
Ассистент Юлдашева С. Л.
Магистр Амирмухаммадов У. А.
Магистр Улмасов Ш. Н.
Андижанский государственный медицинский институт

Keywords: Systemic lupus erythematosus, classification criteria, diagnosis, autoantibodies, lupus nephritis

Аннотация. Критерии классификации важны для науки, определяя группу пациентов, достаточно однородную, чтобы сделать возможными значимые клинические испытания и трансляционные исследования. Помимо этого, однако, полезные критерии классификации будут формировать наше представление о болезни. Это определенно верно для системы критериев классификации СКВ 1982 года Американского колледжа ревматологов (ACR) с 11 критериями, по крайней мере четыре из которых должны были быть положительными для классификации [1]. В 1997 г. в эти критерии были внесены поправки, включившие два из трех существующих стандартных тестов на антифосфолипидные антитела, а именно антикардиолипиновые антитела и волчаночный антикоагулянт [2]. В то же время феномен LE клеток был выпущен в историю. Дальнейший прогресс привел к увеличению информации, относящейся к классификации СКВ. Яркими примерами являются рутинное измерение уровня комплемента в сыворотке [3] и биопсия почки, ставшая стандартным подходом к лечению пациентов с (подозрением на) волчаночным нефритом [6]. Несмотря на свою полезность, критерии ACR не соответствовали лучшему пониманию клинических проявлений и лабораторных данных при СКВ. Это вызвало необходимость в новых критериях классификации СКВ.

Ключевые слова: системная красная волчанка, классификационные критерии, диагностика, аутоантитела, волчаночный нефрит.

The EULAR/ACR criteria project defined increasing specificity to the high level of the revised ACR criteria, while still increasing sensitivity, as the main statistical goal .Throughout the EULAR/ACR classification criteria project, decisions in doubt were made in favor of specificity, even if they threatened to reduce sensitivity. This approach was successful ,with the specificity of the revised ACR criteria reached in the derivation cohort (96% vs 95%) and in the validation cohort (93% vs 93%). This was due to several steps taken. From the first draft proposal, one step accordingly was to take ANA out of the specific criteria items and to reposition the ANA test to an entry criterion [6], as discussed later. Lymphopenia, another lower specificity item, was eliminated by the external experts in the nominal group technique (NGT) exercise [5]. Defining domains, within which only the highest-ranking item was counted [2], was another step towards higher specificity. Less obvious, a strategic decision had significant impact on the specificity of the criteria. Most features of SLE are mimicked by other conditions. The ACR criteria system had therefore already defined exclusion criteria for seizures, psychosis and thrombocytopenia [1]. The SLICC criteria defined exclusions for a total of 10 items [6]. Even this list of exclusions was not complete. Instead of a list, for the EULAR/ACR criteria, one attribution rule that limits the items taken into account for SLE to those not more likely explained by another condition [4] replaces individual exclusions. This is in line with what clinicians do in their daily routine. It may, however, need more experience and can cause problems when calculating EULAR/ACR classification criteria performance from older databases that do not contain such information. Basically though, researchers should never count a classification criterion as “SLE” if they know it is due to another condition. SLE by nature is a systemic autoimmune disease [3]. For classification criteria (or diagnosis, for that matter), SLE without findings in the autoimmune serology therefore is a potentially dangerous construct. This was also

underlined by the phase II belimumab trials that found success in serologically active SLE patients only [3]. Accordingly, the SLICC criteria for SLE classification demand at least one of six immunological criteria [8], as listed in Table 1. Moreover, a histology compatible with lupus nephritis is sufficient for classification only if accompanied by positive ANA or anti-dsDNA-antibodies. In the EULAR/ACR criteria this principle is taken one step further in making positive ANA an obligatory entry criterion [5]. Antibodies to nuclear acids and their binding proteins are a hallmark of SLE, and all these usually lead to positive ANA [3]. Accordingly, ANA have very high sensitivity for SLE, but limited specificity, given their occurrence in other connective tissue diseases, all sorts of autoimmune disease, and even in healthy individuals. Behaving differently from all other items made ANA less suitable as a specific item, but omitting it would have deprived the criteria of an important concept.While ANA as an obligatory entry criterion makes classification impossible for any SLE patient who never had positive ANA, this decision is based on data showing that truly and persistently ANA-negative SLE is an uncommon situation [5]. Missing this small subset of patients would still be a problem for diagnosis, but not so much for classification. To limit a negative impact, in addition to complying with the old principle that criteria items are counted also historically and with no need to occur simultaneously, a low titer of ≥1:80 was chosen from the systematic literature search and meta-regression analysis [1] and alternative test systems are accepted [6]. However, ANA-negative SLE definitely exists, reaching 6.2% in the SLICC inception cohort [3], and was also reported in biopsy proven lupus nephritis [3], which might exclude a lupus nephritis subset from clinical trials.Serving as scientific tools and as blueprints for better studying SLE, SLE classification criteria have evolved from the 1982 and 1997 revised ACR criteria to the SLICC and, most recently, EULAR/ACR 2019 criteria. Each built on the previous sets by adding new information, trying to maintain feasibility at the same time. The EULAR/ACR criteria have excellent statistical performance for classification. The excellent sensitivity of the SLICC criteria and broad representation of SLE symptoms remain clinically important.

espite differences in structure and statistical performance, the EULAR/ACR and SLICC criteria agree on the importance of both immunological and clinical findings, on the high impact of lupus nephritis by histology, and on most clinical items.

References

1. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; 25: 1271–1277.

2. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997; 40: 172

3. Mosca M, Tani C, Aringer M, Bombardieri S, Boumpas D, Brey R et al. European League Against Rheumatism recommendations for monitoring patients with systemic lupus erythematosus in clinical practice and in observational studies. *Ann Rheum Dis* 2010; 69: 1269–1274.

4. Gladman DD, Ibanez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. *J Rheumatol* 2002; 29: 288–291.

5. Vitali C, Bencivelli W, Isenberg DA, Smolen JS, Snaith ML, Sciuto M et al. Disease activity in systemic lupus erythematosus: report of the Consensus Study Group of the European Workshop for Rheumatology Research. I. A descriptive analysis of 704 European lupus patients. European Consensus Study Group for Disease Activity in SLE. *Clin Exp Rheumatol* 1992; 10: 527–539.

6. Bertsias GK, Tektonidou M, Amoura Z, Aringer M, Bajema I, Berden JH et al. Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA)

recommendations for the management of adult and paediatric lupus nephritis. *Ann Rheum Dis* 2012; 71:1771–1782.