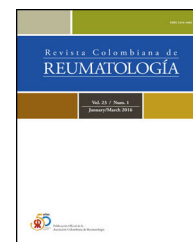




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Editorial

Predictive models and biomarkers in neuropsychiatric systemic lupus erythematosus

Modelos predictivos y biomarcadores en el lupus eritematoso sistémico neuropsiquiátrico



Our editor-in-chief requested me to write an editorial for the current issue of the Journal. This editorial seeks to highlight and review the importance of the article «Clinical and serological predictors of neuropsychiatric manifestations in patients with systemic lupus erythematosus», which will be published in the Journal.

As the time allowed for the preparation of this writing was short, and although I have worked on the subject to do it in a more efficient way, I wanted to help myself with the new tools of artificial intelligence (AI); therefore, this editorial is generated with the help of ChatGPT.

Systemic lupus erythematosus (SLE) is a disease very heterogeneous in its manifestations, including a particularly devastating and also variable form as it is neuropsychiatric SLE (NPSLE), which is characterized by the presence of neurological and psychiatric manifestations. Early detection and adequate treatment of these manifestations are fundamental to improve the quality of life of the patients.¹ In this sense, the predictive models and biomarkers have been widely evaluated and have become promising tools for earlier diagnosis and, possibly in the future, for the implementation of more precise therapeutic strategies.

Predictive models are algorithms or systems that use clinical and biological data to predict the risk of developing a particular disease or complication in susceptible individuals. In the case of NPSLE, predictive models can be used to identify those patients with a higher risk of presenting neuropsychiatric manifestations, which would allow early intervention and a personalized therapeutic approach. These models can be based on a combination of genetic factors, biomarkers, clinical data, and individual characteristics of the patient.

Quevedo et al.,² who use some of the analytical tools for the generation of predictive models, present in their article a decision tree based on clinical characteristics such as non-scarring alopecia and the presence of oral ulcers, together with leukopenia and anti-Ro antibodies, a predictive model for NPSLE with an accuracy of 75.6%, a sensitivity of 57%, a specificity of 86%, a positive predictive value (PPV) of 72% and a negative predictive value (NPV) of 76%.

The article evaluates several analysis tools for the generation of predictive models, and this makes it very valuable, since it motivates readers to understand how the heterogeneity of lupus, with its multiple manifestations, can provide us with elements to be used as variables, which in the predictive models would show associations with certain outcomes, with statistical weight and predictive capacity.

The selection of the tool depends on the specific problem, the type of data, and the objectives of the analysis. It is important, then, to select carefully the tool and apply the appropriate statistical techniques to build accurate and reliable predictive models.

Quevedo et al. evaluate various tools, and at the end they present the data in a decision tree.² Decision trees are graphical representations of decisions and their possible consequences; they are useful for classification and regression tasks. Decision tree models split the data based on different attributes to create branches which ultimately lead to predictions or decisions.³

Statistical methods based on decision trees are considered to be one of the best and most used to analyze complex data. These methods produce predictive tools with high accuracy, stability and ease of interpretation.³

The terminology of the trees is graphical: a T tree has a root that is the top node, and the observations are transmitted along the tree; decisions are made at each of the nodes (also called children) until a terminal or leaf node is reached. Each non-terminal node (also called internal node) contains a question on which a split is based. Each terminal node contains the class label (for a classification problem) or an average response (for a least squares regression problem). The nodes in a tree can also be chance or probability nodes.³

The statistical tools that use these decision trees can be based on the R statistical software, which includes the *Machine Learning R (mlr)* tool, one of the types of artificial intelligence, and packages such as the *Recursive Partitioning (RPART)* and *Random Forest*, to create one of the classifiers.³ These tools are used by Quevedo et al. in their article.²

The serological markers used in this work draw attention, all of them are more related to other manifestations in SLE, but not so specific for NPSLE. The availability of more specific antibodies such as anti-NMDA, anti-ribosomal-P, anti-aquaporin or anti-neuronal,⁴ is very restricted, but it would be interesting to include these markers in future predictive models.

Biomarkers are known to be biological indicators that are used to assess the presence or progression of a disease. In NPSLE, they can provide invaluable information on the activity and severity of neuropsychiatric manifestations. Currently, several potential biomarkers such as certain specific antibodies, inflammatory cytokines, and neuronal growth factors have been identified. Using proteomics, the search for protein biomarkers in serum and cerebrospinal fluid has also been carried out with small groups of patients, but their validation is pending.^{5,6}

The greatest challenge in NPSLE, also evidenced in the article written by Quevedo et al.,² is the variability in the manifestations, since we are referring to 19 syndromes established according to the American College of Rheumatology,⁷ with different possible pathophysiological mechanisms and diverse potential biomarkers.⁸ The prediction could be easier in manifestations that can be explained by antiphospholipid antibodies, such as chorea or ischemic disease of the nervous system, and not for mood swings, headaches or other manifestations with unclear pathophysiology and still without specific biomarkers. For this reason, I consider that the predictive model can be more difficult when the different manifestations are unified and when trying to predict such a broad outcome (see Table 2 of the article of Quevedo et al.²).

The combination of predictive models and biomarkers in the context of NPSLE can have a significant impact on clinical practice and research. The ability to identify the patients at risk of developing neuropsychiatric complications and the use of biomarkers to assess disease activity could allow for earlier and more effective interventions, which in turn could improve the prognosis and quality of life of the patients⁵; how-

ever, it is important to highlight that there are still challenges in the development and implementation of these models and biomarkers in clinical practice. Rigorous validation and additional studies are required to confirm their clinical usefulness and to establish standardized criteria for their use. In addition, is essential to address any potential bias in their development.

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Gloria Vasquez

Rheumatology Section, Department of Internal Medicine, Cellular Immunology and Immunogenetics Group, Faculty of Medicine, Universidad de Antioquia, Medellín, Colombia

E-mail address: glomavas@gmail.com

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