Specificity of Systemic Sclerosis Classification Criteria

To the Editor:

As the steering committee of the American College of Rheumatology/European League Against Rheumatism project that developed the 2013 criteria for the classification of systemic sclerosis (SSc)[1,2], we read with interest the publication of Hoffmann-Vold, *et al*[3]. Using data from the Norwegian Systemic Connective Tissue Disease and Vasculitis Registry, Hoffmann-Vold, *et al*'s report clearly supported the new criteria as having excellent sensitivity (96%) for SSc. The study was unique in that the authors had access to a large database of subjects with mixed connective tissue disease (MCTD) that was used to calculate specificity of the criteria for that particular illness. They reported a specificity of 90% for the new criteria.

We would like to make several points about their observations. The SSc classification criteria steering committee and the expert consultants involved in creating the new criteria agreed that the criteria could allow for classification of patients with another rheumatic disease as also having SSc[1,2]. It is well known that several rheumatic diseases may occasionally overlap with each other and the criteria were designed to recognize that fact. When applying the criteria to a patient to be used in an SSc study, it is up to the discretion of the researcher to decide whether patients with overlap features, or who may also meet criteria for other rheumatic diseases, should be included in the study.

MCTD itself is still a somewhat controversial entity[4,5,6,7,8]. Is MCTD a single discrete entity or does it represent a true overlap of several distinct diseases? If a patient labeled as having MCTD meets criteria for SSc, that patient may indeed have the illness we commonly call SSc, but may also have other concomitant conditions. So in that sense, the classification of that patient as having SSc is not an error or a false-positive result.

A second point is that specificity is clearly related to the population used as the comparator. And the predictive value of the criteria is related to the prevalence of the comparator diseases in the particular population from which the study subjects will be chosen. So realistically, if a center with expertise and interest in SSc were enrolling SSc subjects in a study, the prevalence of MCTD, even if it were a distinct disease, would likely be very low in the population from which the subjects were being chosen. Thus, the likelihood that a subject who meets SSc criteria actually has SSc is still very high. If you were to imagine a population of patients in which SSc and MCTD had equal prevalence, if all cases that met criteria were enrolled in an SSc study, only 9.4% of the subjects would have MCTD. And because equal prevalence of these 2 diseases is very unlikely, that would seem to be a maximum misclassification rate.

The last point is that even if MCTD is a discrete illness, a specificity for such a close mimicker of SSc of 90% could indeed be considered excellent. This is certainly in the same range or better than figures for the specificity of other rheumatic disease criteria[9,10,11,12,13,14].

Finally, we are very grateful for this report of Hoffmann-Vold, *et al* because it confirms both the very high sensitivity of the SSc criteria and the very acceptable real-world specificity.

MURRAY BARON, MD, Jewish General Hospital and McGill University, Montreal, Quebec; JANET E. POPE, MD, MPH, St. Joseph's Health Care London and University of Western Ontario, London, Ontario, Canada; FRANK VAN DEN HOOGEN, MD, PhD, St. Maartenskliniek and Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands; DINESH KHANNA, MD, MS, University of Michigan, Ann Arbor, Michigan, USA; JAAP FRANSEN, PhD, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands; SINDHU R. JOHNSON, MD, PhD, Toronto Western Hospital, Mount Sinai Hospital, and University of Toronto, Toronto, Ontario, Canada; MARCO MATUCCI-CERINIC, MD, PhD, University of Florence, Florence, Italy. Address correspondence to Dr. M. Baron, Jewish General Hospital, A-725, Montreal, Quebec H3T 1E2, Canada. E-mail: mbaron@rhu.jgh.mcgill.ca

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