

Autoantibodies at the Center of (sub)Classification-Issues of Detection-Reply

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Letters

COMMENT & RESPONSE

In Reply In their Letter, Vulsteke et al highlight an unmet need: the harmonization of myositis specific autoantibody (MSA) detection. We recently showed that patients with myositis can be classified into 4 homogeneous subgroups¹ and that MSA plays a major role in predicting patients will be in a specific subset. As mentioned by Vulsteke et al, our study did not include a control group of patients with noninflammatory myopathies. This was because our primary aim was to identify homogeneous subgroups of patients with myositis using unsupervised statistical methods based on a complete data set (with no missing data) comprising, among others, MSA. Furthermore, MSAs are now validated diagnostic criteria for immune-mediated necrotizing myopathies² and have been recently recognized as diagnostic criteria for dermatomyositis (239th European NeuroMuscular Center International Workshop, Amsterdam, December 14-16, 2018). In the American College of Rheumatology/European League Against Rheumatism diagnostic criteria for myositis,³ the presence of anti-Jo1 antibody is the item assigned with the heaviest weighted score, but the weakness of this criterium is that no other MSAs were considered.3

Thus, MSAs are crucial for diagnosing and classifying myositis. Vulsteke et al emphasize the necessity of determining the list of MSAs that could be considered. This implies that the chosen MSA must be representative of homogeneous subgroups of patients with characteristic phenotypes. Vulsteke et al discuss the place of the most recently identified MSA, the anti-FHL1 antibody. Nevertheless, the anti-FHL1 antibody has not been associated with a particular subset of patients with myositis. Anti-FHL1 seropositivity appears more often as a marker of myositis severity. In addition, integrating a new MSA for diagnostic and classification criteria will need reproducible observations from different studies involving diverse populations. This is not yet the case for anti-FHL1.

The next point highlighted by Vulsteke et al is associated with the reliability of the methods used routinely for MSA detection. This is a tricky point because he and others have already demonstrated different sensitivity and specificity between immunoassays.⁵ In addition, up to 10% of healthy controls have a positive result for MSA using commercial immunoassays. 5 This suggests the possibility of falsepositive results or that MSA can appear before the onset of myositis as, for example, antibodies against cyclic citrullinated peptide predict the development of rheumatoid arthritis. 6 To answer these points, international efforts are now in progress to try to harmonize the detection of MSA. In addition to the characteristics of the detection tests that will be used (eg, antigen sources, method of detection, or positivity threshold) another point that must be considered is the selection of the screened population. As for the detection of antineutrophil cytoplasmic antibodies, a gating strategy based on clinical and biological manifestations could improve the diagnostic performance. Here, to limit the risk of false positivity, the results of MSA must be combined with other clinical, biological, and morphological (muscle imaging and/or pathology) items of myositis diagnostic criteria.

Another reason for considering MSAs as a classification tool is that they are usually mutually exclusive. Vulsteke et al indicated the possibility of dual positivity in some cases. Nevertheless, this situation remains rare, occurring in 0.5% of myositis cases. In addition to the already mentioned possibility of false-positive results, these double seropositivities must be interpreted after considering other clinical, pathological, and biological parameters.

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- 1. Mariampillai K, Granger B, Amelin D, et al. Development of a new classification system for idiopathic inflammatory myopathies based on clinical manifestations and myositis-specific autoantibodies. *JAMA Neurol.* 2018;75(12): 1528-1537. doi:10.1001/jamaneurol.2018.2598
- 2. Allenbach Y, Mammen AL, Benveniste O, Stenzel W; Immune-Mediated Necrotizing Myopathies Working Group. 224th ENMC International Workshop: Clinico-sero-pathological classification of immune-mediated necrotizing myopathies Zandvoort, The Netherlands, 14-16 October 2016. *Neuromuscul Disord*. 2018;28(1):87-99. doi:10.1016/j.nmd.2017.09.016
- 3. Lundberg IE, Tjärnlund A, Bottai M, et al; International Myositis Classification Criteria Project Consortium, the Euromyositis Register, and the Juvenile Dermatomyositis Cohort Biomarker Study and Repository (UK and Ireland). 2017 European League Against Rheumatism/ American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. Arthritis Rheumatol. 2017;69(12):2271-2282. doi:10.1002/art.40320
- 4. Albrecht I, Wick C, Hallgren Å, et al. Development of autoantibodies against muscle-specific FHL1 in severe inflammatory myopathies. *J Clin Invest*. 2015;125 (12):4612-4624. doi:10.1172/JCI81031
- **5.** Damoiseaux J, Vulsteke J-B, Tseng C-W, et al. Autoantibodies in idiopathic inflammatory myopathies: clinical associations and laboratory evaluation by mono- and multispecific immunoassays [published online January 11, 2019]. *Autoimmun Rev.* doi:10.1016/j.autrev.2018.10.004
- **6**. Rantapää-Dahlqvist S, de Jong BAW, Berglin E, et al. Antibodies against cyclic citrullinated peptide and IgA rheumatoid factor predict the development of rheumatoid arthritis. *Arthritis Rheum*. 2003;48(10):2741-2749. doi:10.1002/art. 11223