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Letter

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What should we do about criteria in rheumatology?

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Abstract

Many rheumatological conditions have a clearly understood aetiology and unequivocal clinical and laboratory features, such septic arthritis. However, a significant number of complex conditions do not. There is uncertainty about what actually distinguishes one disease from health or from another similar disease or within a group of diseases, separating one type of condition from another. Adding to the potential confusion are terms such as disease definition. We have been concerned about the way these three terms (classification, diagnosis and definition) have been used interchangeably in medical publications as well as in medical practice and discuss ways to address this issue.

Key words: Criteria, diagnosis, classification, definition.

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Dear Editor,

In light of intense current interest in applying new understanding of disease pathogenesis and new classes of therapies, we are concerned about the way in which three related terms – classification, diagnosis, and definition – are used interchangeably in publications and in medical practice. This confusion has affected efforts to rationalize understanding and therapy, for example in rheumatoid arthritis (RA) and vasculitis, representing two areas of great interest to rheumatologists. Although the term *definition* is used by everyone now and then, in the current controversies regarding diagnosis and classification for rheumatological conditions it lacks added value. In practice, almost all published criteria were designed as classification criteria, not *diagnostic* criteria. *Classification* criteria are developed by comparing patients with one form of the disease with those who have another form, drawn from the same disease set, with due consideration of the mimics to be excluded. Although published classification criteria and disease definitions have disclaimers warning against their use in individual patients for diagnosis, they are commonly employed in this way in clinical practice.

For most rheumatological conditions, we do not understand their aetiology, and there are no "gold standard", unequivocal clinical and laboratory features to distinguish one disease from another or even from normality. This contrasts with diabetes mellitus, defined by an elevated glucose, or hypertension, defined by sustained elevation of blood pressure. In the practice of medicine, between doctor and patient, a *diagnosis* implies a prognosis and a therapeutic plan. Usually, *classification* criteria are more rigorous than *diagnostic* criteria because researchers require homogeneous populations, which can exclude patients from a study because they have atypical manifestations of the disease. However, the new criteria for rheumatoid arthritis[1] redefine RA as 'arthritis that needs to be treated with methotrexate', which will inevitably lead to the inclusion of patients who do not have RA. Therefore, patients in clinical trials are a subset of those with the disease but can also include some who may not actually have it, either due to limitations of the classification system or inappropriate application of criteria. Ultimately this will lead to incorrect diagnosis and treatment of some cases, potentially altering the outcome of the study. The implication is that

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early intervention trials unnecessarily expose some patients to the risks of powerful (and potentially costly) therapy.

In RA, preventing severe disease by early treatment will inevitably treat some cases not destined to get it. RA, which is probably a group of diseases, is considered as a single entity based on the new ACR/EULAR classification criteria.[1] However, there may be a worse outcome and better response to therapy for anticyclic citrullinated peptide antibody (ACPA)-positive patients compared to ACPA-negative patients.[2] Hence improving the classification criteria is a task that will never be complete. Despite the protest that the ACR/EULAR 2010 classification criteria for RA are not meant for diagnosis, in fact by calling the described disease rheumatoid arthritis, the criteria have pre-empted the term rheumatoid arthritis. Fortunately, the criteria define an excellent diagnostic boundary, as long as clinicians expect to discover occasional patients who do not run true to form.

The collection of diseases encompassed by the term vasculitis presents a different conundrum. In systemic vasculitis, the current American College of Rheumatology (ACR) classification criteria[3] for polyarteritis nodosa (PAN) fail to recognise microscopic polyangiitis (MPA), raising the problem that publications relating to patients with PAN are likely to be "contaminated" by the presence of patients with MPA, whose pathogenesis, pattern of disease, and response to treatment are very different from PAN.[4,5] The ACR classification criteria were developed using a large dataset of items observed in patients with 7 different types of vasculitis. This means that at best the criteria can be used to subset or subtype patients who are already known to have vasculitis into their more specific category. However, these same criteria that distinguish one type of vasculitis from another do not necessarily help in distinguishing a patient with a specific form of vasculitis with a condition which may mimic vasculitis such as infection, drug toxicity or cancer. This is mainly because patients with these other "mimic" conditions have not been compared with vasculitis patients in terms of their distinguishing or characteristics at disease onset to determine which are the most discriminating features, and furthermore what strength of certainty can be measured when applying criteria derived in this way. Bruce and Bell[6] showed poor concordance when applying ACR criteria and Chapel Hill *definitions*[7] in 24 patients with primary systemic vasculitis. Revision of the original Chapel Hill consensus definitions is currently underway, but this is data free and consists of improving terms through collective observer experience. Whilst this is valuable, the proof of any such endeavour can only be in the validation of new terms. Linder et al.,[8] recently used an artificial neural network using Chapel Hill definitions and ACR criteria to distinguish GPA from MPA, ultimately applying another *classification* approach, not *diagnostic* criteria as claimed in the publication. We are currently undertaking a study to develop diagnostic criteria and improve existing classification criteria in vasculitis,[9] learning from process used to develop the ACR/EULAR classification criteria for RA. How can we influence the significant stakeholders? We need data-rich analyses of the different disease entities with clear statements on the level of certainty of criteria applied based on comparisons between relevant groups (e.g. between vasculitis and mimic conditions for diagnostic criteria); or between different forms of vasculitis (for classification criteria).

We need clear names of conditions based on rigorous understanding of the underlying pathogenic mechanisms to separate different disease entities which are currently gathered under umbrella terms such as rheumatoid arthritis or vasculitis. Until then, however, we must continue to develop more refined, clinically-based criteria in order to provide more, or in some cases, less certainty, from prospective data collection and analysis.

References

1. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Ann Rheum Dis* 2010;69:1580-8.
2. van der Linden MP, van der Woude D, Ioan-Facsinay A, et al. Value of anti-modified citrullinated vimentin and third-generation anti-cyclic citrullinated peptide compared with second-generation anti-cyclic citrullinated peptide and rheumatoid factor in predicting disease outcome in undifferentiated arthritis and rheumatoid arthritis. *Arthritis Rheum* 2009;60:2232-41.
3. Lightfoot RW Jr, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa. *Arthritis Rheum* 1990;33:1088-93.
4. Henegar C, Pagnoux C, Puéchal X, et al.; French Vasculitis Study Group. A paradigm of diagnostic criteria for polyarteritis nodosa: analysis of a series of 949 patients with vasculitides. *Arthritis Rheum* 2008;58:1528-38.
5. Basu N, Watts R, Bajema I, et al. EULAR points to consider in the development of classification and diagnostic criteria in systemic vasculitis. *Ann Rheum Dis* 2010;69:1744-50.
6. Bruce IN, Bell AL. A comparison of two nomenclature systems for primary systemic vasculitis. *Br J Rheumatol* 1997;36:453-8.
7. Jennette JC, Falk RJ, Andrassy K, et al. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. *Arthritis Rheum* 1994;37:187-92
8. Linder R, Orth I, Hagen EC, van der Woude FJ, Schmitt WH. Differentiation between Wegener's granulomatosis and microscopic polyangiitis by an artificial neural network and by traditional methods. *J Rheumatol* 2011;38:1039-47.
9. Luqmani RA, Suppiah R, Grayson PC, Merkel PA, Watts R. Nomenclature and classification of vasculitis - update on the ACR/EULAR diagnosis and classification of vasculitis study (DCVAS). *Clin Exp Immunol* 2011;164 Suppl 1:11-3.

