Classification/diagnostic criteria for GCA/PMR

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ABSTRACT

Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are two common rheumatic diseases occurring in middle-aged and older persons. Their cause is unknown and in neither is there a single specific diagnostic test. As a result a combination of findings is needed for their diagnosis. The American College of Rheumatology has established criteria for the classification of GCA using two methods. These criteria are best used in research studies involving patients with a diagnosis of vasculitis. One method is based on the so-called traditional format. In this method the patient with vasculitis is classified as GCA if he/ she manifests any 3 among the list of 5 criteria selected. The second method, the tree format or recursive partitioning method, starts with the clinical finding that best separates patients with GCA from others with vasculitis and then uses other criteria successively to point to a final decision regarding the presence or absence of GCA. Diagnostic criteria for GCA have not been formulated. Diagnostic criteria have been established for PMR by analysis of a series of patients, but in practice most rheumatologists use criteria established informally by consensus.

Giant cell arteritis

Giant cell arteritis (GCA) is a member of a complex group of vasculitic diseases that are linked by the presence of necrotizing inflammatory lesions in blood vessels (1). Arteries and other blood vessels of differing sizes and locations in the body may be affected, resulting a broad range of clinical and laboratory findings. The etiology of GCA is not known and its pathogenesis is only beginning to be understood (2-4). The same is true for other forms of vasculitis (5). The causes are likely to be diverse among the vasculitides and possibly even in a single form. Most workers interested in vasculitis agree that there are a number of distinct clinical diseases among the vasculitides, even though in many instances these different forms of vasculitis have overlapping findings. The courses and outcomes of these syndromes vary greatly. Even in patients with one form of vasculitis such as GCA there is a great variation in severity and duration. These findings have made it difficult to accurately define these syndromes and to diagnosis individual patients. Biopsies containing vasculitic lesions confirm the presence of arteritis but by themselves do not necessarily define a specific disease (6). Furthermore, biopsy is a sampling procedure and may miss an involved vascular segment or provide an incomplete picture of the pathology. In occasional cases biopsy is not feasible. Therefore, the diagnosis of a specific form of vasculitis such as GCA depends on the presence of a combination of clinical findings.

The difference between classification and diagnostic criteria is sometimes difficult to understand (7, 8). Both separate patients with the disease in question from others. To some degree the difference depends on the control groups. In the American College of Rheumatology vasculitis criteria studies, all 1,000 patients had vasculitis so the criteria are best used to separate one form of vasculitis from another (9). Thus, these are classification criteria, not diagnostic criteria. The latter separate a given patient from patients with vasculitis as well as other diseases. The ACR studies did not include patients with other diseases. In addition, many tend to forget that with classification criteria there are always misclassified patients, an event that clinicians do not want to happen in the examination of an individual person.

In general terms there are several types of criteria that might be useful in the clinical evaluation of individual patients or the study of a vasculitis such as GCA (8-10). These types are diagnostic criteria (which separate a patient or group of patients from others), classification criteria (which separate a patient or group

of patients from certain others, or into subsets), status criteria (ranking patients by the presence or degree of active disease, the severity, or the presence and degree of tissue damage), prognostic criteria (separate patients with a good or poor outcome), and outcome criteria (separate patients by death, disability or cost).

In addition, a number of methods for the development of these criteria have been developed. The most common are the consensus method (a group of experts agree on a criteria set), the traditional format, (choose X number from a total list of Y criteria), linear discriminant function (weighted criteria are added together and a result above a certain value classifies the patient), logistic regression (natural logarithm formula applied to weighted criteria to derive a value that separates the patients), recursive partitioning (a computer program decides the criteria in sequence that best separate patients with a disease from those without it and a classification tree is formed), and artificial neural networks (a computer program evaluates all combinations of findings in a complex way to separate patients).

In all these methods, a set of patients is first identified who have the disease in question such as GCA (the "gold standard"). If there is no absolute definitive test, the diagnosis may have to be made by expert opinion. This may sound somewhat circular, perhaps, but no other way has been developed. For each patient the values for a variable number of clinical and laboratory findings (criteria) are determined and recorded on data sheets. These known findings are then analyzed by the method chosen, such as the traditional format, and the most sensitive and specific criteria are selected to include as the final result. In the second part of the study, the accuracy of the classification rule is tested on an additional set of cases with the same and different diagnoses. The aim is to develop an accurate way to classify new cases when certain clinical findings are known but not the diagnosis, or to assign a patient to a category when some other clinical parameter (such as prognosis) is being assessed. The criteria developed can then be used

according to their defined purpose. If they are used in other settings, the results may do well or are likely to show an apparently lower accuracy with invalid results (11, 12). It is important to remember that classification or diagnostic criteria that are developed for use in the clinical setting need to be straightforward and simple - otherwise they are unlikely to be widely adopted. At some time in the future, when computers are more pervasive and used by all clinicians in the ordinary practice of medicine, more complex methods may be more readily accepted.

The use of Likelihood Ratio Computations could probably be applied to diagnostic or classification studies (13). The name itself constitutes an advantage. It tells the clinician that the result is a probability, not a certainty, as some with a poor understanding of classification criteria think the result should be.

The ACR criteria for the classification of GCA were formed by comparing the symptoms and findings of 214 patients with a diagnosis of GCA with the clinical findings of 593 patients with other forms of vasculitis (9). In a patient with vasculitis, the finding of 3 of the following 5 criteria was associated with a 94% sensitivity and 91% specificity for the diagnosis of GCA:

- Age greater than or equal to 50 years at the time of disease onset;
- Localized headache of new onset;
- Tenderness or decreased pulse of the temporal artery;
- ESR > 50 mm/hr (Westergren);
- Biopsy which includes an artery, and reveals a necrotizing arteritis with a predominance of mononuclear cells or a granulomatous process with multinucleated giant cells.

If an elevated ESR is excluded, but scalp tenderness and claudication of the jaw, tongue, or with deglutition are added as criteria, the sensitivity for classification is 95% with a specificity of 91%.

Standardized criteria order our investigations of diseases at all levels. They help us to focus our objectives in clinical research. They can enhance the identification of important clinical differences and disease subsets that may im-

prove our understanding of the disease. The process of disease definition needs to be an ongoing process with updates and revisions as we learn more about the diseases.

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