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Erosion defined: back to basics

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Abstract

Current classification criteria for rheumatoid arthritis allow its classification on the basis of the presence of erosions, in the absence of other indicators. Nevertheless, definition or quantitation of erosions was lacking. A European task force has now addressed this issue by analysing radiographic erosions in two cohorts of patients with early disease.

Targeted biologic therapies markedly slow the progression of structural damage in rheumatoid arthritis (RA); thus, the presence of bony erosion suggests that had treatment been initiated earlier, joint damage might have been prevented. Some patients with early inflammatory arthritis, the group most likely to benefit from prompt initiation of treatment, are not classified as having RA using the 1987 classification criteria.¹ For this reason, the 2010 American College of rheumatology (ACR)-European League against rheumatism (EULAR) RA classification criteria were developed to diagnose and classify patients with RA.² Because these new criteria were intended to identify patients early in the course of disease, radiographic evidence of erosions was intentionally omitted from them. 'Typical' erosive disease was nevertheless acknowledged as indicative of RA regardless of other criteria, but what constituted clinically significant erosive disease was not defined. Accordingly, a task force was convened by EULAR to address this issue, and the definition of erosive disease upon which they agreed has now been published by van der Heijde *et al.* in *Annals of the Rheumatic Diseases*.³

To understand the need for the new definition of erosive disease, it is instructive to review the process by which the 2010 classification criteria for RA were developed. The working group originally charged with creating them first met in 2007, with the primary aim of facilitating clinical studies of patients with early disease and enabling their inclusion in trials of novel therapeutic agents. Data from one north American and seven European cohorts of patients with early undifferentiated synovitis were analyzed to determine which characteristics might predict subsequent development of RA.⁴ to avoid circular logic, the decision to treat a patient with methotrexate to prevent structural damage was used as a surrogate for diagnosing RA. Anatomic location of swollen and tender joints, levels of acute-phase reactants, and titres of serological biomarkers were the clinical features identified as contributing most to the decision to initiate methotrexate therapy.

During the second phase of this process, the applicability of these clinical features to case histories of actual patients with inflammatory arthritis was collaboratively assessed with the aid of decision-support computer software.⁵ subsequently, the final clinical features agreed upon were grouped into four domains: number and size of involved joints, presence of rheumatoid factor or anti-citrullinated protein antibodies, acute-phase reactant levels, and duration of symptoms. each feature within a domain was then assigned a weighted score of up to 10 to represent the likelihood of its association with the decision to initiate methotrexate therapy, and then summed into a final weighted 0–10 score (higher score indicating greater probability that methotrexate would be initiated). The working group established a cut-off of 6, above which a patient would be classified as having definite RA according to the 2010 criteria.²

As radiographic evidence of bony erosion is a hallmark of established RA, but was intentionally omitted from the classification score to enable inclusion of patients with early disease, the working group determined that “erosions typical for RA” constitute sufficient evidence for patients to be classified as having the disease even with a score <6.² thus, a patient with active synovitis and radiographic evidence of “significant erosive disease” can be diagnosed with RA according to the 2010 criteria without further application of the scoring system.²

“...definition of erosive disease is important to ensure homogeneity...in clinical trials”

The task force convened by EULAR to define “erosions typical for RA”, which consisted of 15 European and 2 American rheumatologists, followed a process similar to that used to develop the 2010 criteria.³ Plain radiographs of both hands and both feet, performed at the baseline visit for early arthritis, were scored by one of two experienced readers using the Sharp–van der Heijde method.⁶ the number of joints demonstrating 1 erosion, defined as a cortical break visible on plain radiograph, was scored, with no data available regarding the number of erosions within individual joints or the presence of erosions in other joints. then, to assess the validity of different cutoffs in the number of erosive joints, their sensitivity and specificity were calculated in patients who scored <6 points using the clinical algorithm at baseline but who were initiated on methotrexate or another DMARD within 1 year of entering into the cohort, or who had inflammatory arthritis that persisted over the subsequent 5 years.

In contrast to the intent of the ACR–EULAR working group that created the 2010 RA classification criteria, for whom the presence of an erosion would suffice to classify a patient with synovitis in at least one joint as having RA, the EULAR task force anticipated that erosions would be used to classify a patient as having RA only if that patient did not fulfil the 2010 criteria on the basis of clinical features. Thus, this task force considered it most important that the definition of erosive disease be highly specific.⁶ although few patients have erosions without fulfilling other clinical criteria, pre-specification of the definition of erosive disease is important to ensure homogeneity in the populations of patients included in clinical trials. using a cut-off of 3 erosive joints yielded specificity >85% in all situations and >90% in all but one; after reviewing this analysis, the task force voted to maximize specificity, even at the expense of sensitivity, and defined a cut-off of 3 erosive joints.³

“...the definition of erosive disease ... fills in a ‘cortical break’ in the 2010 criteria for RA”

An interesting consideration is that, although an inexpensive and commonly available means of assessing bony erosions, plain radiography is one of the least sensitive modalities for detecting them.⁷ ultrasound can reveal subtle cortical disruption and MRI is capable of demonstrating lesions that evolve into bony erosions earlier than would be visible on plain radiographs. Furthermore, high resolution Ct scanning often reveals many more erosions than are evident on plain radiographs. Thus, a patient with inflammatory polyarthritis who has evidence of a single cortical break in one joint on plain radiographs of the hand probably has several erosions that can be identified by other imaging modalities. One might speculate, therefore, that had the number of erosions observed within each joint been taken into account when the plain radiographs were scored, or if a more sensitive imaging modality had been used to assess erosions in the hands and feet of the patients with early inflammatory arthritis, the EULAR task force might have arrived at a cut-off for erosive disease of fewer than three erosive joints to define RA.

Besides defining the characteristics of clinical trial cohorts, what is the clinical significance of detecting bony erosions? their presence reveals a disease process—capable of further destruction—in which activity of osteoclasts at the bone–pannus interface is evident.⁸ this situation prompts aggressive therapeutic intervention with targeted therapies that can markedly suppress bone destruction. Whether a patient has one cortical break or more than

three, evidence of bony erosion is likely to prompt the rheumatologist to initiate a therapeutic intervention.

The 2010 RA classification criteria working group intended that a patient with synovitis in at least one joint and radiographic evidence of bony erosion would be classified as having RA without the need to apply the score-based algorithm. as an alternative, for patients who do not score the requisite 6 points to be classified as having RA on the basis of clinical features, the definition of erosive disease by van der Heijde and colleagues³ fills in a 'cortical break' in the 2010 criteria for RA. Application of this new definition will determine whether it enables early diagnosis of the majority of those patients who might not otherwise meet the 2010 ACR–EULAR classification criteria for RA.

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