

OMERACT Workshop: Repair of Structural Damage in Rheumatoid Arthritis

DÉSIRÉE M. van der HEIJDE, JOHN T. SHARP, ROLF RAU, and VIBEKE STRAND, on behalf of the Subcommittee on Healing of Erosions of the OMERACT Imaging Committee

ABSTRACT. This article describes the process and results of a workshop aimed at reviewing data on repair of structural damage collected by the OMERACT Subcommittee on Healing of Erosions and at defining a priority list for the subsequent research agenda. (*J Rheumatol* 2003;30:1108-9)

Key Indexing Terms:

HEALING

REPAIR

EROSIONS

RHEUMATOID ARTHRITIS

The aim of the workshop was to review data collected by the OMERACT Subcommittee on Healing and to develop a list of priorities for the research agenda. A general introduction was given by D. van der Heijde. She first introduced the terms healing and repair. The term healing is loaded with emotion and has different meanings for different persons. This led to extensive discussions in the subcommittee and to the proposal to prefer the term repair. During the workshop both terms were used interchangeably and at the end people were asked to vote for their preferred term.

A second issue that had to be made clear for the audience at the outset was that this workshop would deal only with healing of erosions. As far as we know, repair of cartilage is presently not possible.

There are several reasons why it would be important to find out if healing can occur. First, it would provide significant pathophysiological information. Second, the hypothesis is that repair can be present only if there is complete absence of inflammation. So if healing occurs, this would be a proof of total absence of inflammation. Third, several drugs have now been registered for slowing radiographic progression. The presence of healing could be a differentiation between drugs.

Finally, healing is in fact only relevant if it is in relation to the final outcome of the patient. Therefore we need to answer the question of whether patients with features of repair are doing better compared to patients with no progression of structural damage but without signs of repair. "Doing better" can be defined in many ways: quality of life, physical function, joint replacements, disability pension, etc.

From the University Hospital Maastricht, Maastricht, The Netherlands; University of Washington, Seattle, Washington, USA; Evangelisches Fachkrankenhaus Ratingen, Ratingen, Germany; and Stanford University, Palo Alto, California, USA.

D. van der Heijde, MD, PhD, Professor of Rheumatology, University Hospital Maastricht; J.T. Sharp, MD, Professor of Rheumatology, University of Washington; R. Rau, MD, Professor of Rheumatology, Evangelisches Fachkrankenhaus Ratingen; V. Strand, MD, Clinical Professor of Immunology, Stanford University.

Address reprint requests to Dr. D. van der Heijde, Department of Rheumatology, University Hospital Maastricht, PO Box 5800, 6202 AZ Maastricht, The Netherlands. E-mail: dhe@sint.azm.nl

There remain several outstanding issues. How long does the period of followup need to be before healing can be seen on plain films? Is this different for various drugs? Is it different in early versus late disease?

The opening of the workshop was followed by a presentation on the background of healing by J. Sharp. He started with a quote from a senior rheumatologist, S. Krane, "Erosions can heal, but do they?" Subsequently, he showed evidence from healing processes in animal models, periodontal disease, a patient with psoriatic arthritis, and a patient with gout. He also stated that to seriously propose that healing is a true phenomenon, we must agree on the definition of healing. There are several features described in the literature that would be related to healing. These are sclerosis, cortication, filling-in of erosions, and remodeling and restoration to normal shape. However, it is not known how specific or prevalent these features are. It is not known how frequently healing phenomena occur. There are several case histories in the literature. R. Rau presented several examples of radiographic films of patients, with several followup films throughout the years that show healing. Another indication that healing might be real is the negative scores in trials with new therapeutic agents. The question is, however, do negative scores represent repair? Possibly, but they are due at least in part to measurement error. This issue was further elaborated in the next presentation by D. van der Heijde. The smallest detectable difference (SDD) is an important tool in reducing the likelihood that measurement error accounts for negative scores. Only negative scores greater than the SDD would imply a high probability of repair. However, this would not work in early rheumatoid arthritis. Patients with just one or 2 erosions are perhaps even more likely to show healing, but the healing cannot be picked up, as the SDD is usually greater. Moreover, the SDD is a specific research tool and not applicable in the followup of individual patients in office practise.

Another point raised is that a total score for the entire patient is usually presented. This might not be the optimal way to show repair. Perhaps for purposes of healing a presentation based on the joints would be more appropriate.

On the other hand this approach might introduce new difficulties: what would the conclusion be for a patient who showed deterioration in a few joints and improvement in other joints? A decision should also be taken about whether specific features of healing in combination with a smaller erosion would be necessary to define repair. Or, the other way around, whether specific features such as sclerosis with the same erosion size would be sufficient to decide there is healing?

J. Sharp presented the 2 studies performed by the subcommittee, which are described in detail elsewhere in this issue¹. The most important conclusion was that repair indeed occurs. However, experts were unable to recognize specific features of healing. It was discussed that this may be due to lack of training, to the absence of specificity of these features, or to the selection of the cases included in the studies. Suggestions were made to have additional training with the aid of an atlas specifying the features of repair.

Several research questions remain. First, it is not clear whether a separate scoring method is needed to assess healing or whether we could rely on negative scores using existing scoring methods. The scores could be expressed with respect both to the patient and to the joint.

Another research area would be the relationship between healing and final outcome. Moreover, the hypothesis that repair occurs only in patients (joints) in complete remission is worth testing. The audience also suggested further research with synovial biopsies and magnetic resonance imaging to detect the presence of synovitis and relate this to healing.

Based on the discussions during the workshop, several questions were formulated. These were introduced in the OMERACT plenary session. The first question dealt with terminology. Seventy-five percent of the audience preferred the term repair over healing. Based on the data presented again, 75% of the people accept that repair can appear (8% do not). The question of whether it is relevant to study if we

can rely on negative scores using existing methods or whether we need an additional method to assess repair was answered positively by 78% of the audience, 14% considered it was not relevant, and 8% did not know. Opinion was divided on the question of whether it is relevant and feasible to assess the relationship between repair and serial synovial biopsies. Twenty-eight percent answered yes, 49% no, and 23% did not know. In particular, persons familiar with performing synovial biopsies were much in favor of doing such research. It was noted that difficulty might occur in the correct selection of patients, given the probable low prevalence of repair. Further research on the relationship between repair and magnetic resonance imaging was judged relevant and feasible by 75% of the audience, and not so by 9%. A similar pattern was seen for the relationship between repair and clinical correlates (78% yes, 11% no). Of note, research on the prevalence of repair was judged relevant (89%). Finally, the audience was asked to identify which research question should be addressed first (once it is apparent how to assess repair). Most votes favored investigating the prevalence of repair (40%), followed by the relationship with MRI (25%), and with clinical correlates (22%). Only a few people ranked the relationship with synovial biopsies as the primary research goal (8%).

The Subcommittee on Repair will continue with the suggested research field: initially with the extra training, followed by the development of a method to assess repair in relation to existing scoring methods. After this method has been validated, the research questions outlined above can be addressed.

REFERENCE

1. Sharp JT, van der Heijde D, Boers M, et al. Repair of erosions in rheumatoid arthritis does occur. Results from 2 studies by the OMERACT Subcommittee on Healing of Erosions. *J Rheumatol* 2003;30:1102-7.

Papers presented at the OMERACT 6 Conference,
Gold Coast, Queensland, Australia, April 11–14, 2002.

- Part 1: Patient Perspectives and Economics
- Part 2: Imaging (Repair) and MCID/Low Disease Activity State
- Part 3: Magnetic Resonance Imaging
- Part 4: Outcome Measures for Clinical Trials: Systemic Sclerosis and Osteoarthritis

Parts 3 and 4 will appear in the June and July issues of *The Journal*.