Magnetic resonance imaging evidence of bone edema in the wrist and metatarsophalangeal joints was an independent predictor of future development of rheumatoid arthritis in a prospective Danish study of patients with early undifferentiated arthritis.

Incorporating MRI bone edema findings, together with clinical and biochemical parameters, yielded a prediction model that showed unprecedented accuracy in identifying which patients would or would not develop rheumatoid arthritis, Dr. Anne Duer-Jensen of Copenhagen University Hospital at Hvidovre and Copenhagen University Hospital at Glostrup, and her associates reported in Arthritis & Rheumatism (2011;63:2192-202).

The study involved 116 patients with early undifferentiated arthritis, 23% of whom went on to meet American College of Rheumatology 1987 criteria for RA during a median 17 months of follow-up. They were matched with 24 healthy controls. The predi-
tive model had a sensitivity of 81% and a specificity of 82% for progression to RA. Thus, it classified 82% of patients correctly.

That’s a markedly better predictive accuracy than achieved when the investigators applied the published and validated van der Helm-van Mil prediction model to the same study population. The van der Helm-van Mil model (Arthritis Rheum. 2007;56:433-40) had a 60% predictive accuracy.

Major Finding: Incorporating MRI bone edema findings, together with clinical and biochemical parameters, yielded a prediction model that had a sensitivity of 81% and a specificity of 82% for progression to RA.

Data Source: The study involved 24 healthy controls and 116 patients with early undifferentiated arthritis, 23% of whom went on to meet American College of Rheumatology 1987 criteria for RA during a median 17 months of follow-up.

Disclosures: This study was funded by the Danish Rheumatism Foundation and other foundation grants. While Dr. Duer-Jensen reported having no financial conflicts of interest, several of her associates did. Those can be found on the full text of the journal article.

The formula for the current iteration of the prediction model is cumbersome. A simpler version would be welcome.

Toward that end, the investigators tried using MRI bone edema scores for the wrist or MTP joints alone, but they found that it uncontrollably weakened the model’s predictive power.

The next step in this project will be to see how the prediction model performs in other cohorts of patients with early undifferentiated arthritis.

The goal is to develop a tool that enables physicians to extend the current, highly successful early and aggressive treatment strategy for RA into the pre-RA setting.

Panel Urges Revamping of Rheumatology Clinical Trials

BY BRUCE JANCIN
FROM ARTHRITIS & RHEUMATISM

Clinical trials in rheumatoid arthritis that have been done for drug approval fail to address numerous issues critically important to clinical care, according to an American College of Rheumatology task force report.

The group was critical of current clinical trial design and offered half a dozen recommendations for reforms aimed at boosting clinical relevance. The task force also drew up a ranked priority list for the next generation of RA clinical trials, i.e., studies needed to address current major knowledge gaps. Topping this must-have list are trials of induction therapy in early disease.

Induction therapy. The group recommended as an initial practical step a three-armed trial comparing current standard conventional methotrexate monotherapy to methotrexate plus a tumor necrosis factor (TNF) inhibitor versus methotrexate plus a non-TNF inhibitor biologic agent.

This trial should be double-blind and consist of three phases: induction, maintenance therapy, and treatment withdrawal in patients phases: induction, maintenance therapy, and treatment withdrawal in patients.

At present there are essentially no data to guide medication tapering and discontinuation decisions. The panel proposed piggyback tapering trials – with liberal collection of biologic specimens – on the back of current trials and next-generation induction trials.

Active disease despite methotrexate therapy. Roughly 70% of patients with early RA fail to achieve low disease activity on methotrexate monotherapy. There is a need for clinical trials aimed at defining optimal methotrexate dosing strategies, the panel agreed. Beyond that, however, the task force was split on the best way forward.

Some argued that active comparator trials of various add-on therapies in subgroups of animal responders to methotrexate are badly needed now, while others said it makes more sense to hold off until biomarkers can be identified that will help in making individualized treatment decisions based on an agent’s mechanism of action.

The task force didn’t address the issue of how the proposed research agenda will be funded. Of note, however, of 25 experts invited to an ACR conference on clinical trial priorities and design that was held last year, most were from academia, four came from the National Institutes of Health, three were Food and Drug Administration officials, and none were from the pharmaceutical industry.

The task force proposed numerous changes in clinical trial design aimed at yielding results that are more meaningful and clinical rheumatology practice. For example, the group declared that in the current era of proven highly effective RA therapies, placebo-controlled clinical trials have become ethically questionable and should be greatly de-emphasized in favor of active comparator studies.

The task force also raised ethical concerns about the current rule that an assigned therapy must be continued for a prolonged period of follow-up, often 1-2 years, even though modern therapies are expected to bring maximum clinical benefit in 3-6 months.

The panel expressed reservations about the generalizability of clinical trials in RA that are increasingly being conducted in developing countries. The group recommended that when these trials are reported, the investigators should fully describe the study population and assess the generalizability of the findings.

In addition to Dr. O’Dell, the members of the ACR Rheumatoid Arthritis Clinical Trial Investigators Ad Hoc Task Force were co-chair Dr. Michael E. Weinblatt of Brigham and Women’s Hospital, Boston; Dr. Ted R. Mikuls of the University of Nebraska, Omaha; and Dr. Robert A. Colbert of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, Md. Dr. Weinblatt has received consulting fees from Abbott, Amgen, Astellas, AstraZeneca, Biogen Idec, Bristol-Myers Squibb, Centocor, Crescendo, Lilly, Pfizer, and Roche.

THE NEED FOR SUCH BIOMARKERS WAS ‘A RECURRENT THEME THAT PROMINENTLY PERMEATED AND AT TIMES DOMINATED OUR DISCUSSIONS,’ DR. O’DELL

MRI Bone Edema Predicts Rheumatoid Arthritis

BY BRUCE JANCIN
FROM ARTHRITIS & RHEUMATISM

There are essentially no MRI summary scores for bone edema proved to be a significantly more potent predictor of RA than MRI scores for synovitis or erosion.