The disease markers that will aid arthritis research

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A combination of biochemical and MRI markers will allow improved measurement of osteoarthritis (OA) progression. The biomarkers, described in BioMed Central's open access journal *Arthritis Research and Therapy*, will be useful for the design and interpretation of trials of new disease modifying drugs.

Erik Dam, from Nordic Bioscience, Denmark, worked with a team of researchers to develop and evaluate the markers. He said, "Presently, there is no disease-modifying OA drug with a consistent, documented effect despite several clinical attempts in late stage phases. We believe that effective therapies could be demonstrated, if tools were available that allow identification of rapid progressors for inclusion in trials. With this in mind, we investigated whether combinations of biochemical and MRI-based biomarkers might improve diagnosis and prognosis of knee osteoarthritis".

Dam and his colleagues included 159 subjects in their trial. After exclusions, a total of 287 knees were measured. At baseline and after 21 months, biochemical (urinary collagen type II C-telopeptide fragment, CTX-II) and MRI-based markers were quantified. MRI markers included cartilage volume, thickness, area, roughness, homogeneity, and curvature in the medial tibio-femoral compartment. Joint space width, the presently accepted marker for population selection in clinical studies, was measured from radiographs. According to Dam, "The best individual diagnostic marker was cartilage roughness and the best individual prognostic marker was homogeneity. The aggregate cartilage

longevity marker (combining CTX-II, volume, area, thickness, congruity, roughness, and homogeneity) performed very well both diagnostically and prognostically - and superior to the individual biochemical and MRI markers. We attribute this to the combination of markers with complementary information about cartilage quantity (e.g. volume), quality (e.g. homogeneity), and breakdown (CTX-II) that together allow superior diagnosis/prognosis".

The proposed aggregate marker methodology may have a direct impact on the design of clinical studies. The researchers claim, "By allowing the selection of a high risk population, the study sample size can be lowered while still improving the chance of a positive study outcome. This should facilitate the development of effective drugs".

More information: Identification of progressors in osteoarthritis by combining biochemical and MRI-based markers, Erik B Dam, Marco Loog, Claus Christiansen, Inger Byrjalsen, Jenny Folkesson, Mads Nielsen, Arish A Qazi, Paola C Pettersen, Patrick Garnero and Morten A Karsdal, *Arthritis Research & Therapy* (in press), arthritis-research.com/

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