How to Investigate and Follow Up Undifferentiated Peripheral Inflammatory Arthritis? 3e Initiative 2008–2009: Systematic Reviews and Clinical Algorithm

The 3e (Evidence, Expertise, Exchange) Initiative in Rheumatology is a multinational effort aimed at generating evidence-based recommendations for common clinical problems. It integrates systematically generated evidence with expert opinion of a broad panel of international rheumatologists. Phases I and II of the 3e Initiative addressed, respectively, the management of ankylosing spondylitis and the use of methotrexate in rheumatoid arthritis.

The objective of phase III 2008–2009 was to develop practical recommendations for management of patients with undifferentiated peripheral inflammatory arthritis (UPIA). Patients with UPIA are commonly seen in rheumatology practice and often remain without a specific diagnosis. Their management varies considerably among rheumatologists; there are no widely accepted criteria for diagnosis and no guidance on how to investigate and follow up these patients.

In this international project, experts agreed to label as "undifferentiated" those patients with at least one swollen joint but no clear diagnosis following initial rheumatologic assessment.

The clinical questions were selected by an international expert group of rheumatologists (697 rheumatologists from 17 countries) with interest in arthritis research, and from both academic institutions and private practice. By way of a Delphi process, the group selected the following 9 questions:

- Which differential diagnoses should be considered in inflammatory arthritis? What are the minimal clinical, laboratory, and imaging investigations necessary to confirm and follow up an undifferentiated arthritis, and how often?[1]
- What is the diagnostic and predictive value of demographics (age, gender, race), medical history (e.g., uveitis, scleritis, psoriasis, urethritis, inflammatory bowel disease, early morning stiffness), and physical examination (joint distribution/swollen/duration)? Which elements of history should be done at baseline and repeated at what interval in patients with undifferentiated arthritis?[2]
- What is the diagnostic and predictive value of acute-phase reactant (erythrocyte sedimentation rate, C-reactive protein)? Should they be done at baseline and repeated at what interval in patients with undifferentiated arthritis?[3]
- What is the diagnostic and predictive value of antibodies (cyclic citrullinated peptide, rheumatoid factor, antinuclear antibody)? Should they be done at baseline and repeated at what interval in patients with undifferentiated arthritis?[4]
- What is the diagnostic and predictive value of radiography? Should it be done at baseline and repeated at what interval in patients with undifferentiated arthritis?[5]
- What is the diagnostic and predictive value of the following imaging studies: ultrasound, magnetic resonance imaging. Should they be done at baseline, and repeated at which interval in patients with undifferentiated arthritis?[6]
- What is the diagnostic and predictive value of genetic markers (e.g., HLA-B27, HLA-DR4, shared epitope)?[7]
- What is the contribution of synovial biopsy in UPIA?[8]
- Which clinical assessments of disease activity (e.g., Disease Activity Score, Simplified Disease Activity Score, Simplified Disease Activity Index, Clinical Disease Activity Index) should be done at baseline and repeated at what interval in patients with undifferentiated arthritis?[9]

For each of these questions, a systematic literature review (SLR) was performed by 9 multinational fellows supervised by 5 SLR expert mentors. Following these SLR, international recommendations were formulated by rheumatologists from 16 countries[10].

In addition, an algorithm was created to represent the dynamic nature of this condition. Over time, symptoms of UPIA may resolve or progress into a specific diagnosis and an algorithm can help organize the stepwise approach to decision-making. To this end, after the 9 recommendations were formulated, an expert panel met for a round table discussion with the objective of developing an algorithm for the investigation and followup of UPIA. The algorithm drew on the clinical experience of the consensus panel, the 9 international recommendations, and evidence from the literature[11].

The goal of this supplement is to gather the systematic reviews of these 9 questions in the same volume and to present the algorithm created by the participants. We are very pleased with the enthusiasm and the commitment of the 16 participating countries.

We would like to thank all our experts, the scientific committee members, and the fellows for their collaboration on this ambitious program and for the high-level scientific content of the 3e Initiative on UPIA.

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