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Concluding remarks

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Conclusion

This second workshop on hand osteoarthritis (OA), held in Boston, U.S.A. in May 1999, was most stimulating. Hand OA is a frequent, serious and crippling disease. Much still remains to be done with regard to the establishment of its diagnosis, clinical evaluation and treatment. The main objective of the meeting was to continue the dialogue initiated at the first workshop held in 1994, and to allow for constructive debate on the epidemiological, clinical, imaging and therapeutic aspects of research. A number of excellent presentations were made and intensive discussions covering several major areas of clinical interest were held.

Session 1: Epidemiology, genetics and risk factors

The first session focused on epidemiology, genetics and risk factors. The most recent studies published on these topics were reviewed. They provided useful insight into the role of a number of factors involved in the ethiopathogenesis and progression of the disease. The hand is a common site of peripheral joint involvement in OA. Although often underestimated as a cause of disability, it is also an important indicator of a systemic tendency to OA, which may involve weight-bearing joints such as hips and knees. There seems to be no obvious consensus at this time regarding the definition of hand OA and generalized OA. The topography of affected joints as well as the threshold number of affected joints used in defining generalized OA remain unidentified. The site and number of joints involved in fulfilling an accepted definition lacks clarity. Also remaining unclear is the role of symptoms versus structural changes. Such a definition is highly variable from one classification to another. Although the definition of hand OA, particularly for epidemiological studies, has undergone reassessment and revision over the last few years, it still remains a problem. A number of the existing classifications are confusing. The balance between criteria, including clinical symptoms, and anatomical X-ray changes remains to be determined. The inclusion or exclusion of metacarpophalangeal (MCP) and carpometacarpal (CMC) joints vary from one classification to another and should be standardized. There is still debate on whether the erosive form of hand OA should be considered a different disease. There was a general agreement that the definition of hand OA should be made on population-based studies.

A number of epidemiological studies suggest that genetic factors are likely to play an important role in the etiopathogenesis of hand OA. For instance, the greater concordance for hand OA in monozygotic than in dizygotic twins, and the substantial increase in the risk of hand OA in first-degree relatives of these patients provide a strong rationale for a search of the genes involved. The study of the role of genetic factors in this disease is complicated by many factors, including case definition, other risk factors, latence of phenotype expression, difficult access to other members of the family, as well as the absence of a valid definition of the disease *per se*. The ongoing work on the role of genetics in hand OA is most important and should soon provide new insights into the pathogenesis of hand OA.

An agreement was reached on the most common risk factors associated with hand OA. These included age, gender, family, obesity and physical activity/trauma. Age is a well-known and strong risk factor, not only for hand OA but also for all joint sites. It is possible that some risk factors may act by bringing the development of OA forward rather than having specific mechanisms of causation or prevention. There was also an agreement that female gender results in a predisposition to OA at all sites except at the hip. The exact reasons remain unclear. Obesity is a strong risk factor for development of knee OA in women but its association with hand OA remains controversial, with the possible exception of an increased risk of first CMC joint OA.

One important aspect of hand OA is that it often occurs in women around the time of menopause. However, the exact role of sex hormones in this disease is still a controversial issue. The possible influence of hormone replacement therapy (HRT) on the incidence and progression of hand OA is still uncertain. Hormone replacement therapy remains a likely protective risk factor based on studies for hip and knee OA. The data for hand OA are sparse. A large epidemiologic prospective cross-sectional study done on menopausal women with hand OA showed no differences in the characteristics of hand OA between patients who did not receive HRT, whatever the symptom activity. HRT did not seem to influence the severity or the symptom activity of hand OA.

Physical activity/trauma seems to have only modest effects on the prevalence and incidence of hand OA. These factors may be of more importance in the first CMC joints

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and on the dominant hand, on which there are greater mechanical forces. However, the question remains whether the very frequent symmetry of hand sites implies genetic or constitutional cause rather than mechanical factors.

It was agreed that more studies were needed to achieve a more comprehensive understanding of all of the risk factors associated with hand OA. This seems true for almost all of the topics that have been under previous discussion. Recent studies have demonstrated the need for a better definition of the disease in order to make substantial progress in defining the role of genetic and other factors in hand OA. Moreover, the criteria on which such a definition will be based should be very clearly defined, whether they are to be anatomical, functional, symptom-based, etc. We also need to measure and quantify the symptoms and severity of the disease better.

Session 2: Clinical aspects

The workshop was highly productive in reviewing several clinical aspects of hand OA. The importance of the clinical relevance of hand OA was stressed by study reports showing not only its very high prevalence, but also that a large number of these patients present substantial symptoms, which increase with age.

Although very common, a disease such as hand OA has been the subject of a limited number of clinical trials aimed at determining the effectiveness of drug treatment on symptoms and/or progression of structural changes. This disease deserves to be the subject of further therapeutic trials. The demand for treatment is high, and it might not be possible to extrapolate results of trials from other joints such as hip and knee OA to hand OA, which often progress differently. Today there are a number of specific and sensitive tools and assessment methods that allow the hand to be considered a valuable 'model' to study treatments for OA. These tools and methods provide acceptable accuracy leading to conclusive results. Among the different tools available to study the impact of hand OA on patients' health, those exploring function are of particular importance. Moreover, their sensitivity to assess changes over time would be of prime importance, particularly in the context of clinical study. For this purpose, both the functional index of hand OA (FIHOA) and the pain assessment on a visual analog scale (VAS) have been demonstrated through trials to be valid and useful. The wish was expressed that these different methodologies be validated through an international consensus meeting.

Among the different risk factors associated with OA, mechanical factors seem to be of particular relevance to hand OA. A report presented at the workshop demonstrated that men with high maximal grip strength had an increased risk of OA in proximal interphalangeal (PIP), MCP and thumb-base joints. Women with high maximal grip strength had an increased risk of developing OA in MCP joints and a modest increase in risk for OA in the thumb base. No association was found between maximal grip strength and incident distal interphalangeal (DIP) OA in men or women.

Although several studies have been conducted on epidemiology, genetics, clinical and radiological presentations of hand OA, conversely, only a limited number of therapeutic studies in hand OA were found. The existing published data on hand OA raises numerous questions and gives very few answers with regard to the evaluation of therapeutic agents mainly because of several methodological limitations. Based on those findings a number of recommendations seems appropriate, including that a consensus needs to be reached on diagnosing hand OA, the definitions of the disease, its severity and symptom activity, and allowing for standardized selection of patients. Primary and secondary evaluation criteria with appropriate, validated, reliable and sensitive tools need to be selected. Moreover, it would be preferable that the present widely accepted guidelines for the conduct of clinical trials in OA be adapted to the need for further specific studies in hand OA.

Session 3: Imaging

This session included three main parts: a review of the radiological assessment methods of hand OA, the scoring system of Verbruggen and Veys, and a special point—how calcified cartilage advances into articular cartilage.

For the moment, the best method for assessing the grade and progression of hand OA is standard radiography, provided it is performed separately for each hand. To date, only the posteroanterior frontal view has been used. The X-ray features should be graded separately to assess the extent and course of the disease, and not as a composite index. In hand OA, osteophyte size is the most sensitive indicator of progression in contrast to hip and knee OA, where it is the joint space narrowing (JSN). At the present time, and for long-term trials, either the Kallman or the Verbruggen–Veys grading system could be used. However, whether a combination of both these grading systems would be more reliable and relevant remains to be seen. Atlases were considered critically: a simple diagram of each X-ray feature of every grade of hand joints could become a more reliable tool than the existing radiographic atlases.

The two scoring systems used to assess progression of hand OA were described in detail by Verbruggen and Veys, who conducted a three-year trial. The systems used were: (1) the *anatomical lesion progression system* in OA joints (osteophytes, JSN, subchrondral sclerosis) and (2) the *anatomical phase system*. The latter was able to track the erosive phase that was present or occurred in 40% of patients who were symptomatic at onset and for whom the lesion progression system was not designed and did not work—erosions prevent the interpretation of changes in JSN and in subchondral bone lesions. The erosive phase is followed by a predictable reparative phase. Another criterion was considered: occurrence of new OA X-ray signs in joints that were not involved at baseline. However, this was not observed during the three-year trial.

Using macroradiographs, the advancement of the zone of calcified cartilage, termed a ZCC step, was seen in 64% of 44 hand OA patients and localized in the convex articular surface of half the hand joints. After 18 months, new ZCC steps had formed in about one-third of cases. However, the significance of this curious feature is unknown. These changes are tiny (<0.2 mm), are not associated with JS width reduction, and do not seem to be related to mechanical stress. The hypothesis of a vascular disturbance in microcirculation is debatable.

Session 4: Therapeutic problems

An important question raised during this session was whether the critical review of existing therapeutic trials in

hand OA allows avoidance of past flaws. Besides some classic shortcomings (e.g. definition of a primary assessment criterion), this session addressed some issues more specific to hand OA. (1) Should thumb root (CMC1) OA be assessed together with other joints in hand OA or separately? (2) What is the minimal level of pain on VAS, the minimum number of painful joints, the minimal value of the functional index score for inclusion into a trial for a given patient? (3) What are the most reliable criteria of hand OA activity? (4) What is the best duration of a structure-modifying drug trial? More than 3 years? (5) What is the most reliable radiographic scoring system? A consensus is needed to provide answers to these questions.

Some of the papers presented tried to rough out some solutions. Regarding diagnosis, additional items to the American College of Rheumatology (ACR) criteria are proposed, as well as a limited number of exclusion criteria. Likewise, with regard to the selection of patients, additional criteria are proposed in order to distinguish between 'active' and 'quiescent' hand OA. For example: VAS pain >30 mm, Dreiser's index score >5–6 points. Concerning efficacy assessment, the Dreiser functional index seems more accurate and sensitive to change when completed with the weekly self-assessment of joint pain. The other functional index for hand OA, termed AUSCAN, is not freely available. For structure-modifying drug trials, X-ray features of OA scored according to one of the existing methods are probably more reliable when conducted over three years, using strict inclusion criteria. Combining these results with symptoms is strongly desirable.

The following issues concerning clinical trials are still awaiting answers and obviously indicate the need for more studies. Which functional index to use? Use daily or weekly questionnaires or tracking flares and their duration? Which scoring system is the best for long-term structure-modifying drug trials? And what does 'long-term' mean? How to choose between a 2 (minimal) or a 5 (maximal) year duration, or an intermediate span? We realize that the scientific requirements are endless. However, we have to start somewhere.