OMERACT/OARSI Initiative to Define States of Severity and Indication for Joint Replacement in Hip and Knee Osteoarthritis

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ABSTRACT. ***Objective.*** Time to theoretical indication of joint replacement surgery has been proposed as a primary outcome for potential structure-modifying interventions for osteoarthritis (OA). The objectives of this OMERACT/OARSI Working Group were to identify pain, physical function, and structure states that represent the progression from early to late disease for individuals with OA of the hip and knee, and to create a composite measure of these 3 domains to define states of OA severity and a surrogate measure of "need for joint replacement surgery."

Methods. For pain, focus groups and one-on-one interviews were used. For function, Rasch analysis was performed on existing indices — the Hip Dysfunction and Osteoarthritis Outcome Score (HOOS) and the Knee injury and Osteoarthritis Outcome Score (KOOS), each of which subsumes the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) questions. For structure, a comparison of existing indices (Kellgren-Lawrence, OARSI stages, and joint space width) was performed for the hip and the knee.

Results. For pain, key features of pain that are most distressing to people with OA from early to late disease were identified. For function, the reduction of the number of items based on the existing indices continues. For structure, the analysis is also ongoing.

Conclusion. Preliminary results were presented at OMERACT 8; the final objective will be to combine the 3 domains (pain, function, and structure) and to create a composite index that could define states of severity and "need for total joint replacement," which could be used to evaluate treatment response to disease-modifying drugs in OA clinical trials. (J Rheumatol 2007;34:1432–5)

Key Indexing Terms:
OSTEOARTHRITIS SEVERITY PAIN FUNCTION
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Osteoarthritis (OA) is a major cause of disability worldwide. Pain and physical disability significantly reduce independence and quality of life and result in significant economic burden in both direct healthcare costs and indirect costs associated with disability[1].

Interest has grown among the scientific community, pharmaceutical companies, and regulatory agencies in the development of drugs that might influence the natural history of OA by preventing, retarding, or reversing cartilage breakdown. These so-called disease-modifying OA drugs should be evaluated using primary outcomes that reflect the disease's natural history. Structural variables, particularly minimal joint space width on plain radiographs, are considered the most appropriate primary outcome measure. However, it would be useful to identify a valid dichotomous outcome variable that would reflect the natural history of OA. In particular, at OMERACT 7, candidacy for total joint replacement (TJR) was discussed as a "hard" outcome measure[2]. Limitations exist, however, in the use of such an outcome, in particular because of variability in the decision to perform surgery[2]. It would be of interest to obtain a modified outcome measure derived from "time to surgery," but avoiding some of its limitations. An alternative is "theoretical time to fulfil the criteria for surgery." This type of "surrogate hard endpoint" is widely used in other specialties. For example, treatments for heart failure are evaluated based on time to heart transplantation. However, the main limitation for OA trials is that no consensus exists regarding when TJR should be proposed.

Thus, an international working group was created following OMERACT 7 in 2004, under the auspices of recognized international organizations, OMERACT (Outcome Measures in Clinical Trials), and OARSI (Osteoarthritis Research Society International), to evaluate the issues related to severity of hip and knee OA. The objective of the working group was to create a composite index that could define states of OA severity. This surrogate marker could then be used to evaluate treatment response to disease-modifying drugs in OA clinical trials. This work is continuing; this report describes the methodology used by the working group.

METHODS

A. Choice of domains and tools defining severity and important in the decision to implement surgery

During a meeting in Paris in December 2004, the members of the working group discussed which domains are essential in defining severity and in deciding to refer a patient for TJR. Based upon their expertise and on an extensive literature review[2], the following 3 domains were selected: pain, functional status, and structural damage.

For each domain, one or several tools must be selected or created. The objectives of the working group were thus to select or create relevant tools, then to develop pain, physical function, and structure states that represent the progression from early to late disease for individuals with OA of the hip and knee.

B. Measurement of pain in individuals with hip or knee OA

Despite the importance of pain in OA, little is known about the quality and characteristics of OA pain, or how these change over time as the disease progresses, which may lead to TJR. Studies have evaluated the effectiveness of pharmacological[3,4] and exercise interventions[5,6] for relieving pain and improving function, but these studies present short-term outcomes and do not provide a sense of the course of pain and disability. Understanding the states of progression of hip and knee OA is critical for providing improved definition of eligibility criteria for clinical trials, for defining criteria for TJR, and for evaluating outcomes in interventional studies.

The objective of the pain group was to develop a series of 5–6 "pain states" that represent the evolution of pain in individuals with hip and knee OA from early to late disease.

Research design and methods

A 2-part study was performed in individuals with a range of levels of severity of hip and/or knee OA, across 6 centers. Focus groups and one-on-one interviews have been used.

Patient selection. English-speaking men and women with OA, aged 40+ years, who experienced pain on 15 or more days of the month were invited to participate.

Focus groups. Format and methodology of the focus groups were standardized. Separate sets of focus groups were conducted in people with mild, moderate, and severe disease and in individuals with hip versus knee OA. Each focus group, comprising up to 8 participants, used a "funnel approach," starting with broad open-ended questions and then increasingly focused on more specific issues. Proceedings of focus groups were audiotaped and transcribed verbatim. Content analysis was performed independently by 2 of the researchers to identify distinct themes.

One-on-one interviews. A modification of Ruta's Patient Generated Index (PGI)[7] was used to assess the priorities and concerns of individuals living with hip or knee OA pain, and the varying weights and values that they attach to their concerns. The PGI consists of 3 parts:

Part 1 — Participants identify aspects of their OA pain that they consider most distressing.

Part 2 — Participants are asked to rate how far they are *currently* from their ideal in each of the chosen areas on a 7-point Likert scale.

Part 3 — Participants weigh the relative importance of the different areas for their overall quality of life.

Content analysis was performed to identify consistent responses and trends over time (from early to late disease) in the pain/symptom elements identified as most distressing. The information obtained will be overlaid on that from the focus groups.

Creation of pain states for OA. A list of key descriptors of the pain/symptom experience along the course of OA was derived. This information will be used to generate a new pain/symptom measure for OA. The psychometric properties of this new measure will be assessed, along with its reliability and validity, against existing measures (e.g., WOMAC), prior to being incorporated into a composite measure for OA.

C. Physical function in hip and knee OA

The objective of the function group was to develop physical function states that represent the progression of physical disability from early to late disease for individuals with OA of the hip and knee.

Research design and methods

OA-specific measures such as the Western Ontario and McMaster University Osteoarthritis Index (WOMAC)[8,9], Hip Dysfunction and Osteoarthritis Outcome Score (HOOS)[10], and Knee injury and Osteoarthritis Outcome Score (KOOS)[11] are commonly used self-reported measures. However, the physical subscales (function in daily living and function in sports and recreational activities) are too long for defining states based on physical function for our purposes. Hence, the first objective was to use Rasch analysis to define a short measure of physical function, 5–8 items.

This study used existing Canadian, US, and European anonymized HOOS, KOOS, and WOMAC data. The first stage of the analysis was to confirm unidimensionality of the WOMAC physical and HOOS and KOOS activities of daily living function and sport/recreation function subscales using principal component analysis.

The partial credit model[12] of the Rasch model was used for data analysis. The criteria for retaining items were that the items fit the Rasch model, represent the range of severity (i.e. logit values in the range of 2.0 to –2.0), and are invariant (i.e., are free from differential item functioning) by age, sex, culture, and severity as evaluated by differential item function. Differential item functioning by age, sex, culture, and hip versus knee was evaluated graphically and by comparing the item difficulty (logits) between groups. Items demonstrating statistically significant differential item functioning were excluded. In order to achieve the most parsimonious measure, the remaining items were reduced with the goal of maintaining the range of difficulty of the items while eliminating redundant items.

The next stage was to compare how the scores from the short physical measures relate to the long form scores. Subject scores on the short and long forms of the pooled data were evaluated by correlation methods.

This work forms the basis for the development of physical states, which will be defined by the hierarchical, interval-level items in the short measure. These states will be developed from an abridged version of patient-relevant measures of physical function that are accepted standards for reporting physical functioning in OA.

D. Determining structure severity states for hip and knee OA

The objective was to evaluate previously validated measures of joint damage, including radiographic grading systems: joint space narrowing (JSN) measurement on radiograph, the Kellgren-Lawrence (KL) classification, and the OARSI JSN atlas as well as features on joint examination such as range of motion.

Methods

Radiographic grading systems. Following a training session, hip and knee radiographs are obtained from existing databases and are evaluated by 2 observers. For each radiograph, the KL and the OARSI JSN stages are obtained, and the minimal joint space width is calculated. The joint space width is then categorized according to Croft and Lane (hip), or with thresholds established using the median and quartiles of the distribution obtained (knee). The measurement properties of each of the 3 methods are being determined. The final tool will be chosen according to its conformity with the OMERACT filter (feasibility, truth, discriminant capacity). Here, feasibility is not an issue. For truth, in addition to inter- and intra-observer reliability, construct validity is determined through correlation with pain and function scores, criterion validity is determined by the ability of the score to predict subsequent joint replace-

ment, and for discriminant capacity, sensitivity to change or responsiveness is assessed using the standardized response mean.

RESULTS

Preliminary results of pain focus groups, Rasch analyses of WOMAC/KOOS data, and an assessment of the reliability, validity and responsiveness of radiographic scoring systems for OA were presented.

The main points of the meeting at OMERACT 8 included presentation of the preliminary results, and discussions of future steps. The group aimed for final results for each domain around December 2006. Validation of the new tools will begin as soon as they are finalized (all tools will have to pass the OMERACT filter), followed by translation of the tools into other languages.

DISCUSSION

Little work has been performed up to now on the methodological issues of defining severity states in OA. This working group, under the aegis of OMERACT and OARSI, is developing pain, physical function and structure states that represent the progression from early to late disease for individuals with OA of the hip and knee.

Full results should be available in 2007 with subsequent discussion of the creation of a composite scoring system for OA. The working group will also endeavor to coordinate this project with other projects in these same areas. Then the aim is to define 4 to 6 severity states for each tool. The final objective is to combine the 3 domains, pain, function and structure, to create a composite index that could define states of severity. "Theoretical need for TJR" will then be defined as some of the severity states. This should provide a valid endpoint for trials of disease-modifying drugs OA.

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