Review

Osteoarthritis year 2012 in review: clinical

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Introduction

Osteoarthritis (OA) is the most common form of arthritis, and is a major cause of morbidity, activity limitation, physical disability, excess health care utilization and reduced health-related quality of life, especially in people aged 45 and above. OA can be considered as a disease defined by characteristic structural alterations of the joint, including focal degradation of articular cartilage and remodeling of subchondral bone with the formation of osteophytes at the joint margins, as well as an illness defined by a person's symptoms, including pain, fatigue, mood alterations and sleep disturbance. Symptomatic hip and knee OA have been shown to be associated with excess all-cause mortality.

Epidemiologic and clinical research in OA continues to focus on analytic and descriptive epidemiology, and the role of both nonpharmacologic and pharmacologic therapies in the management of OA, respectively. This review highlights selected articles in these areas published in the peer-reviewed literature during the period from September 2011 through March 2012. The updated 2012 American College of Rheumatology recommendations for the management of hand, hip and knee OA were published in April 2012; they are cited here because of relevance to readers but are not reviewed in detail in this manuscript.

Methods

The primary literature search was conducted using PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) with the search terms “osteoarthritis [ti] AND clinical [All Fields]” and the following limits activated: humans, English language, all adult 19+ years, published between September 1, 2011 and March 31, 2012. This search identified 113 articles. A secondary literature search was then conducted with the search terms “osteoarthritis [ti] AND hand”, “osteoarthritis [ti] AND hip”, and “osteoarthritis [ti] AND knee”, with the same limits; these searches identified a total of 40, 71 and 208 articles, respectively.

The titles of all articles were reviewed in order to refine the topic area; articles in the topic areas of biology, biomarkers, genetics and genomics, imaging, and rehabilitation and outcomes were excluded from further review as they are covered by other authors in this issue.

Individual articles were selected for discussion in this manuscript at the sole discretion of the author.

Results

Epidemiology

Haugen and colleagues reported on the descriptive epidemiology of hand OA in the Framingham Study. Hand OA was defined as one or more joints with Kellgren–Lawrence (KL) grade 2 or higher changes. The age-standardized prevalence of hand OA was only modestly higher in women (44.2%) than men (37.7%), whereas...
the age-standardized prevalence of symptomatic hand OA was much higher in women than men (15.9% vs 8.2%) as was that of erosive OA (9.9% vs 3.3%). The crude incidence of hand OA over 9-year follow-up was similar in women and men, whereas the vast majority of both women and men with hand OA at baseline showed progression during follow-up. Development of erosive disease occurred mainly in those with nonerosive disease at baseline, and was more frequent in women (17.3%) than men (9.6%). These findings further support the observation that erosive OA is part of the spectrum of hand OA and not a separate entity.

The effect of case definition of OA was explored in a meta-analysis by Pereira and colleagues. These authors performed a systematic review of studies of OA incidence and prevalence from 1995 through 2011 and fully analyzed 72 articles that reported descriptive epidemiology of hand, hip and/or knee OA. Radiographic definitions were most commonly used for classification with symptomatic and self-reported status less common in descending order. Based on radiographic criteria, prevalence was highest for hand OA and lowest for hip OA; however, there was considerable heterogeneity of prevalence estimates across studies. Furthermore, while there were no differences in summary prevalence estimates by gender for hand and hip OA, there was a significantly greater prevalence of radiographic knee OA among women compared to men. Similar patterns of results were noted using other case definitions; however, overall estimates were lowest using the self-reported case definitions at all sites except for knee OA in men. The authors concluded that method of case definition needs to be considered when comparing results of descriptive epidemiologic studies of OA.

Another method of case definition is the use of hand photographs. The technique of hand photography for assessing OA was initially introduced by Acheson and colleagues over 40 years ago in the New Haven Study of Joint Diseases and used by Hirsch and colleagues in the Women’s Health and Aging Study some 20 years ago. Jonsson and colleagues have now demonstrated the reliability and validity of high quality digital photographs of the hands for the diagnosis of hand OA in 381 elderly subjects enrolled in the AGES-Reykjavik Study.

Temporal trends in knee OA in the United States were examined using data from several rounds of the National Health and Nutrition Examination Survey (NHANES) conducted over a 30-year period and examination cycles of the Framingham Osteoarthritis Study conducted over a 20-year period. These authors reported a significant increase in frequency of age-adjusted frequent knee pain and symptomatic radiographic knee OA that was only partially explained by changes in body mass index (BMI). While they did not offer explanations for this increase in knee pain, they did suggest that it may be related to the increase in the rate of total knee arthroplasties being performed in the US as well as several European countries.

A systematic review of observational epidemiologic studies confirmed that knee injury was a major risk factor for the development of knee OA and that this result was consistent across study design, gender, type of knee injury and method of case definition of knee OA. These results support public health recommendations by the Arthritis Foundation and Centers for Disease Control and Prevention focusing on primary prevention of knee OA through reducing the incidence of major knee injuries.

Treatment

Nonpharmacologic modalities

Weight loss. Weight reduction is recommended for the management of patients with symptomatic lower limb OA by all major rheumatology professional societies. Another randomized controlled trial, conducted over 52-weeks in 96 Danish patients with symptomatic radiographic knee OA, found that weight loss accomplished through an intensive low calorie diet was associated with a significant reduction in knee pain, as measured by the Western Ontario MacMaster Osteoarthritis Index (WOMAC), but not function, as measured by both the WOMAC and Health Assessment Questionnaire. Furthermore, the mean improvement in knee pain (7.2 units on a 0–100 normalized scale) was less than the minimal clinically important difference of 10 units and the proportion of subjects having a substantial (≥50 percent) improvement in pain did not differ significantly between the groups. The authors did not assess potential effects of weight loss on structure modification as they did not obtain follow-up knee radiographs at end of study.

Bariatric surgery is used as part of an overall weight management strategy in morbidly obese (BMI ≥ 35 kg/m²) patients and results in not only weight loss but also improvement in comorbidities including type 2 diabetes mellitus and hypertension. Gill and colleagues reported the results of a systematic review to determine whether weight loss following bariatric surgery was associated with improvement in pain in patients with hip or knee OA. They identified six studies, five case series and one case–control study; there were no randomized controlled trials comparing bariatric surgery to intensive dietary weight loss strategies. They concluded that, despite the relative paucity of high quality evidence, the data supported an association between weight loss following bariatric surgery and improvement in hip and knee pain.

Pinto and colleagues concluded that there was only limited evidence for the cost-effectiveness of nonpharmacologic, nonsurgical interventions, including weight loss, for the management of hip and/or knee OA. These authors stressed the need for high-quality economic evaluations in order to demonstrate value for these nonpharmacologic interventions. Such a study of bariatric surgery should include assessment of not only OA-related outcomes but also effects of the interventions on comorbidities, including type 2 diabetes, hypertension and cardiovascular disease, and the need for concomitant therapies.

Pharmacologic therapies

Complementary and alternative medicine (CAM). Lapanne and colleagues analyzed baseline data from the Osteoarthritis Initiative and reported that almost one-half of subjects with radiographic tibiofemoral knee OA reported using one or more types of CAM; furthermore, nearly one-half of these subjects used CAM in combination with conventional therapies. The most common type of CAM therapy used was nutritional supplements, including chondroitin sulfate and glucosamine. The study was limited by its cross-sectional design and no conclusions could be made about the efficacy or safety of CAM therapy.

Chondroitin sulfate and glucosamine sulfate are registered as pharmacologic therapies in some countries in Europe and considered slow-acting, symptomatic drugs for osteoarthritis (SySOAs); however, despite published recommendations supporting their use, there remains controversy about their efficacy for treating OA. Gabay and colleagues reported results of a 6-month, randomized, controlled trial of chondroitin sulfate in 162 patients with symptomatic radiographic hand OA. Patients allocated to receive chondroitin sulfate at a dose of 800 mg/day had significantly greater improvement in global assessment of hand pain and self-reported hand function, as measured by the Dreiser index, than those allocated to receive placebo; there was no evidence of effect modification by presence of erosive OA and no difference is frequency of reported adverse events.

Nonsteroidal anti-inflammatory drugs (NSAIDs). Published recommendations continue to support the use of NSAIDs for the...
symptomatic management of patients with OA, although it is suggested that they be used in the lowest dose for the shortest duration possible in order to minimize the occurrence of adverse events. Strand and colleagues reported results of a randomized, double-blind, controlled trial comparing continuous vs intermittent use of celecoxib 200 mg/day for the prevention of ‘flares’ in 858 patients with hip or knee OA. Patients allocated to continuous celecoxib had an almost 50 percent reduction in the rate of ‘flares’ over the 6-month treatment period; this corresponded to approximately two fewer ‘flares’ over the treatment period. Numerous secondary outcomes and results of post-hoc analyses supported the greater efficacy of continuous vs intermittent therapy. Surprisingly, there were no significant differences in adverse events between the groups.

Topical NSAID therapy is recommended for management of hand and knee OA, especially in older patients. Roth and Fuller reported results of an integrated safety analysis of data from over 1,000 patients with hand or knee OA who were enrolled in seven randomized controlled trials of topical diclofenac solution for up to 12 weeks. Dry skin was the most common adverse event in the topical diclofenac group occurring in one-third of subjects; there was no difference in blood pressure or laboratory assessments between the groups.

**Intra-articular therapy.** There were a plethora of publications over this period summarizing results of case series, open-label extension studies and randomized controlled trials of intra-articular hyaluronic preparations for OA. As noted by McNeil, the evidence supporting the efficacy of this treatment modality remains conflicting with heterogeneous results of multiple meta-analyses. I agree with this conclusion.

**Centrally acting agents.** Duloxetine, a serotonin norepinephrine reuptake inhibitor, was approved by the U.S. Food and Drug Administration for the treatment of chronic pain in patients with knee OA in 2010. Frakes and colleagues performed a randomized, double-blind, controlled trial to determine the efficacy and safety of duloxetine as adjunctive therapy when added to optimally dosed background NSAIDs in 524 patients with knee OA with persistent moderate-to-severe knee pain; over three-quarters of patients were taking either ibuprofen or naproxen, with a minority taking meloxicam, celecoxib or diclofenac. Patients allocated to duloxetine had significantly greater improvement in pain, as measured by the Brief Pain Inventory and WOMAC, as well as self-reported function; the OARSI-OMERACT responder criteria was satisfied by almost 70 and 50 percent of duloxetine and placebo-treated patients. Adverse events were more common, as expected, in the duloxetine than placebo-treated patients. The results of this study support the use of duloxetine as adjunctive therapy in knee OA patients with an inadequate response to oral NSAIDs. It would be of interest to see a randomized controlled trial comparing duloxetine and opioid analgesics in this clinical situation.

**Biologic agents.** Monoclonal antibodies are now being explored as biologic agents in patients with OA. Tanezumab is a monoclonal antibody to nerve growth factor that is recommended to the reader. No events of osteonecrosis were reported in this article. Adalimumab is a monoclonal antibody to tumor necrosis factor that is used for the treatment of patients with rheumatoid arthritis and other systemic inflammatory conditions. In an investigator-initiated study, Verbruggen and colleagues examined the structure modifying effect of adalimumab in 60 patients with erosive hand OA. There were no significant differences between treatment groups in either the number of subjects who developed new erosive interphalangeal joints or the number of new erosive interphalangeal joints. There also were no significant differences between groups in symptoms, as measured by the Australian Canadian Osteoarthritis (AUSCAN) index, or grip strength. In exploratory post-hoc analyses, however, the authors did find a significant benefit to adalimumab therapy in subjects who had interphalangeal joints with soft tissue swelling and/or palpable effusion. Adverse events were more common in the adalimumab-treated patients, as expected.

**Emerging agents.** Matthews and Hunter published a comprehensive review of pharmacologic agents in phase II and III development for both symptomatic and structural outcomes in patients with OA that is recommended to the reader.

**Conclusion**

There continues to be publication of many clinical studies in OA. In addition to the articles highlighted above, the reader is referred to the proceedings of an Osteoarthritis Summit and State of the Science held at the Hospital for Special Surgery in June and July 2011, respectively. I agree with this conclusion.

**Author contributions**

Marc Hochberg drafted the article and approved the final version to be published.

**Disclosure statement**

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