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Review

Osteoarthritis year in review 2015: clinical

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SUMMARY

The purpose of this review is to highlight clinical research in osteoarthritis (OA). A literature search was conducted using PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) with the search terms "osteoarthritis [All Fields] AND treatment [All Fields]" and the following limits activated: humans, English language, all adult 19+ years, published between April 1, 2014 and April 1, 2015. A second literature search was then conducted with the search terms "osteoarthritis [All Fields] AND epidemiology [All Fields]", with the same limits. Reports of surgical outcome, case series, surgical technique, tissue sample or culture studies, trial protocols, and pilot studies were excluded. Of 1523, 150 were considered relevant. Among epidemiologic and observational clinical studies, themes included physical activity, early knee OA, and confidence/instability/falls. Symptom outcomes of pharmacologic treatments were reported for methotrexate, adalimumab, anti-nerve growth factor monoclonal antibodies, strontium ranelate, bisphosphonates, glucosamine, and chondroitin sulfate, and structural outcomes of pharmacologic treatments for strontium ranelate, recombinant human fibroblast growth factor 18, and glucosamine and chondroitin sulfate. Symptom outcomes of non-pharmacologic interventions were reported for: neuromuscular exercise, quadriceps strengthening, weight reduction and maintenance, TENS, therapeutic ultrasound, stepped care strategies, cognitive behavior therapy for sleep disturbance, acupuncture, gait modification, booster physical therapy, a web-based therapeutic exercise resource center for knee OA; hip physical therapy for hip OA; and joint protection and hand exercises for hand OA. Structure outcomes of non-pharmacologic interventions were reported for patellofemoral bracing.

Introduction

This is an important era in the clinical investigation of osteoarthritis (OA); a confluence of advances positions investigators to accelerate the pace of work and gains in knowledge. Towards this mission, an annual review can help to organize the large amount of work accomplished in the past year, a particularly useful task for a field as broad and heterogeneous as clinical OA. While some themes emerged, a number of studies did not fall into a theme *per se*. The OARSI definition of OA is: "a disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodeling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness" (http://oarsi.org/research/standardization-osteoarthritis-definitions).

Among the most important concepts that emerged in this annual review of the literature is continued and further appreciation of stage of pre-disease or disease and clinical phenotype, both in terms of prognosis and suitability and likelihood of success of specific interventions. The ultimate goal of intervention that delays disease and disability progression in this heterogeneous condition will necessitate clear delineation of the phenotypes and disease stages that are encompassed by the label of OA. In recognition of this, OARSI has made the following call:

New specific and sensitive disease endpoints are critically needed to alleviate roadblocks to development of disease modifying therapeutics for OA. A key step in this process is the development of standardized definitions of OA. Standardization of OA definitions would aid communication across the field and help advance drug development for OA and research by achieving consensus on globally recognized

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definitions of disease and globally recognized standards for classifying the disease. We anticipate that these definitions could facilitate communication about the disease among industry and non-industry researchers, regulatory agencies, funding agencies, third party payers, and patients.

We further anticipate that these definitions would be maintained by OARSI and be subjected to regular refinement as new scientific advances demand. Definitions proposed are not intended to distinguish an OA patient uniquely from patients with other forms of arthritis; but rather, they are intended to provide definitions of the disease process that supersede the many and varied OA phenotypes, to spur scientific advances, and facilitate communication with regulatory agencies. The draft definitions can be viewed as the building blocks for defining OA phenotypes. We fully acknowledge that these building blocks are likely most applicable to knee and hip OA, possibly helpful for hand OA, but will require modification for spine OA. (http://oarsi.org/research/standardization-osteoarthritis-definitions)

The purpose of the current review is to highlight clinical research in OA, particularly in the realms of epidemiology, observational clinical studies, pharmacologic treatment, and non-pharmacologic interventions and strategies. Although an attempt to summarize clinical research in OA in the past year is valuable, it must be emphasized that this is a narrative review and that it is not feasible to summarize all of the important findings of each of these papers.

Methods

A literature search was conducted using PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) with the search terms "osteoarthritis [All Fields] AND treatment [All Fields]" and the following limits activated: humans, English language, all adult 19+ years, published between April 1, 2014 and April 1, 2015. A second literature search was then conducted with the search terms "osteoarthritis [All Fields] AND epidemiology [All Fields]", with the same limits. These searches were repeated using Embase (http://www.embase.com/). Reports of surgical outcome, case series, surgical technique, tissue sample or culture studies, trial protocols, pilot studies and meeting abstracts were excluded as were reports focusing on imaging, biomarkers, and rehabilitation, as these topics are being summarized within other reviews in this issue. Of 1523 papers identified, 150 were considered relevant.

Results

Papers are described under the heading (below) which corresponds with the primary goal of the reported work. However, some papers could have been included in more than one category. Table I lists all papers falling within a given category.

Epidemiologic and observational clinical studies

Manuscripts are organized into certain themes that emerged (physical activity, early OA, confidence/instability/falls), followed by sections devoted to cross-sectional studies of prevalent knee OA, longitudinal studies dealing with incident knee OA, longitudinal studies dealing with knee OA progression, cross-sectional studies of physical functioning in knee OA, longitudinal studies of physical functioning in knee OA, hip OA, hand OA, foot OA, and pain.

Physical activity

Papers dealing with physical activity reported on the association of activity with incident knee OA and with joint pain and stiffness, factors associated with activity avoidance, impact of sedentary activity, effect of walking on incident function limitation, qualitative analysis of symptom impact on activity, impact of time in light intensity activity on disability outcomes, and association with health-related utility.

In middle-aged women in the Australian Longitudinal Study on Women's Health, physical activity between 47 and 58 years of age was associated with lower risk of joint pain and stiffness nine years later[1]. A qualitative study in Canada characterized consequences of symptoms on physical activity in persons with self-reported knee OA or symptoms[2]. Meeting physical activity guidelines was not associated with incident radiographic or symptomatic knee OA in middle-aged or older adults in the Johnston County Osteoarthritis Project[3]. Knee pain and lower vitality were associated with activity avoidance[4].

Being less sedentary was associated with better function in the Osteoarthritis Initiative, independent of moderate-vigorous physical activity minutes[5]. More walking was associated with a lower risk of incident function limitation in persons with or at higher risk for knee OA in the Multicenter Osteoarthritis Study[6]. Greater daily time in light intensity physical activity was associated with reduced onset and progression of disability in Osteoarthritis Initiative participants[7]. There was a graded association between sedentary behavior and elevated systolic blood pressure, independent of moderate-vigorous physical activity minutes, in persons with or at higher risk for knee OA in the Osteoarthritis Initiative[8]. In another report utilizing the Osteoarthritis Initiative, physical activity level was associated with health-related utility[9].

Early OA

Papers dealing with early OA reported on the first activities to become painful in knee OA, prediction of early knee OA, significance of minor radiographic features, significance of pre-radiographic MRI lesions, and impact of rapid radiographic change in early OA.

In persons without radiographic OA in the Osteoarthritis Initiative, incident radiographic OA was associated with a prior trajectory of increasing knee pain, stiffness, and difficulties with functional tasks; over the 4-year study period there was no change in symptoms in the control knees which did not develop OA[10]. Pain and difficulty with activities associated with higher dynamic loading were associated with longer prodromal phases[10]. In persons with or at higher risk for knee OA in the Osteoarthritis Initiative, knee pain was most likely to first appear during weightbearing activities involving bending, such as using stairs[11]. Questionnaire variables, genetic markers, other-site OA, and biochemical markers added only modestly to prediction of knee OA incidence using age, gender, and body mass index (BMI) in the Rotterdam Study-I; doubtful minor X-ray features strongly predicted future knee OA[12]. In persons Kellgren and Lawrence radiographic grade 0 in both knees in the Osteoarthritis Initiative, baseline cartilage damage, bone marrow lesions, and meniscal tears were associated with persistent symptoms in the next 4 years[13]. In persons with early symptomatic knee OA in the Osteoarthritis Initiative and in the Cohort Hip and Cohort Knee Study, rapid radiological change was associated with worsening of pain and function[14]. Young and active athletes in a study in Qatar had a greater risk of manifesting early OA features[15].

Confidence/instability/falls

The spectrum of knee confidence, instability, and falls emerged as a theme, including manuscripts dealing with factors associated with knee confidence, consequences of knee buckling, fall risk in the setting of OA, the bone mineral density/fracture relationship in OA, and the combined impact of falls and OA on function.

Worse knee confidence was associated with pain, self-reported knee instability, weakness, and varus–valgus motion during gait in