

I-26 OSTEOARTHRITIS BIOLOGY

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Purpose: To review original research papers on the topic of Osteoarthritis (OA) Biology, published in peer-reviewed journals since January 2014.

Methods: A Pubmed Search was conducted using combinations of the terms “osteoarthritis”, “cartilage”, “subchondral bone”, “synovium”, “meniscus”, “joint”, “inflammation”, “pain”, “risk factors”, “ageing”, “obesity”, and “animal models”.

Results: Research continues to focus on the biology of joint tissues, including cartilage, subchondral bone, synovium, meniscus, and increasingly also muscle and nerves. Emerging themes over the past year include: 1) Focus on pathways and mechanisms that may be specific to subtypes of OA and to risk factors such as ageing and obesity; 2) The role of inflammation in different subtypes of OA; 3) Mechanisms of joint pain. Selected *in vitro* and *in vivo* studies of relevance to OA biology will be highlighted.

I-27 CLINICAL

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The purpose of this review is to highlight research in osteoarthritis, particularly in the realms of epidemiology, observational studies, pharmacologic treatment, and non-pharmacologic interventions and strategies. 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 February 10, 2015 (to prepare this abstract; updated search findings will be presented). This search identified 538 articles. A second literature search was then conducted with the search terms “osteoarthritis [All Fields] AND epidemiology [All Fields]”, with the same limits; this search identified a total of 146 articles. Reports of surgical outcome, case series, surgical technique, tissue sample or culture studies, trial protocols, and pilot studies were excluded.

Of 684, 128 were considered relevant. Among epidemiologic and observational studies, themes included: physical activity (e.g., association with incident knee OA, association 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, association with health-related utility); early knee OA, (e.g., first activities to become painful in knee OA, prediction of early knee OA, significance of minor radiographic features, significance of pre-radiographic MRI lesions, impact of rapid radiographic change in early OA); pain (e.g., mechanisms, trajectories, risk profiles); confidence/instability/falls (e.g., fall risk in OA, factors associated with knee confidence, combined impact of falls and OA on function); hand OA (e.g., inflammatory features and hand OA progression, association between MRI-based tissue lesions and progression and erosion development, hand OA and coronary heart disease events, correlates of pain in hand OA, erosive OA as a more severe form of disease, prevalence and burden of CMC OA); foot OA (e.g., prevalence of associated disability, factors associated with 1st MTP OA severity, impact of foot pain on health and function). 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 for strontium ranelate, recombinant human fibroblast growth factor 18, and glucosamine and chondroitin sulfate. Reviews included a Cochrane review of topical rubefacients containing salicylates for chronic conditions and systematic review and network meta-analysis to analyze comparative effectiveness of pharmacologic interventions for knee OA. 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. Additional studies reported on the acute biomechanical effects of lateral wedge insoles. Structure outcomes of non-pharmacologic interventions were reported

for patellofemoral bracing and weight loss. Reviews included meta-analyses of exercise, valgus bracing, ginger, electrical stimulation, and continuous and pulsed ultrasound.

I-28 OSTEOARTHRITIS GENETICS AND GENOMICS: STATUS AND FUTURE PERSPECTIVES

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An overview of the recent progress in genetics of osteoarthritis will be presented and discussed in relation to advances in human genetics studies in general.

Genome-wide SNP association (GWA) studies have been impressively successful at discovering sequence variations that contribute to complex human diseases. Replication of findings in independent sample sets and populations has become the standard practice in GWA studies, greatly minimizing the risk of spurious findings which were common in small scale candidate gene studies. Meta-analysis of GWA studies further capitalize on increased power by analyzing results from several studies together and have dramatically increased the number of loci found to associate with many diseases. The SNPs analyzed in GWA studies are common (until recently) and, therefore, only confer a small risk/effect on the phenotypes. They generally explain only a small portion of the heritability of a disease. Finding, and understanding, the remaining part of the heritability currently represents the main challenge of human genetics. Researchers emphasize whole genome sequencing (WGS) efforts, which offer an opportunity to study all variations in the genome of an individual and to find rare variants of large effect. Other mechanisms are also being studied as contributing factors. This presentation will focus on recent results of GWA, WGS and meta-analyses studies in osteoarthritis. Particular attention will be paid to the importance of sample size, phenotype, replications, collaborations and large scale analyses as illustrated by studies on other human diseases and traits such as height, bone density and diabetes.

I-29 OSTEOARTHRITIS YEAR IN REVIEW: IMAGING

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Purpose: To review recent original research publications related to osteoarthritis and to identify trends and advances.

Methods: Medline/PubMed databases were examined to identify relevant articles. The search terms included “osteoarthritis” combined with “”, and either “radiography”, “MRI”, “ultrasound”, “computed tomography”, or “nuclear medicine.” Articles published, or in Press, between January 2014 and January 2015 were included. Abstracts were reviewed to exclude review articles and case reports.

Results: 471 references were identified (217 human studies). Of the human studies, MRI (144) and radiography (83) were the most common primary modalities in OA studies, while CT (45), ultrasound (17) and nuclear medicine (7) were less commonly used. Most studies are still focused on the knee (131), although increasing numbers of studies are examining the hip (30) and hands (15). Most MRI studies continue to be focused on cartilage, either as the outcome measure, or in the development of improved MRI parametric mapping techniques. Few studies have examined the back (6).

Conclusions: continues to have a major role in osteoarthritis research. Although use of MRI outcomes measures is largely established for epidemiological studies at the knee, the lessons learnt are being steadily translated to other joints such as the hand and hip. Other modalities, such as ultra-sound and CT provide important, complementary information. There remain joint groups with large burden of disease, such as the back, where little work is currently underway.

I-30 SOLUBLE BIOMARKERS; THERE IS TILL A NEED FOR OA BIOMARKERS

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There is still a need for robust and validated biomarkers for preclinical, early clinical and clinical development of novel disease modifying OA drugs (DMOADs) for osteoarthritis (OA). In other words there is still room for more biomarkers that can be used as 1) pharmaco-dynamic and early mode of action biomarkers in *in vitro*, *ex vivo* and *in vivo* models, 2) biomarkers for early identification of efficacy, 3) tools for