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Review

Osteoarthritis year in review 2016: clinical

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SUMMARY

Both epidemiologic and clinical research continues to be performed in osteoarthritis (OA). While epidemiologic studies identify risk factors for incident and progressive disease, clinical studies explore the role of both non-pharmacologic and pharmacologic treatments, including oral and intra-articular therapies. We performed a systematic review of the literature using PubMed for the time period between April 1, 2015 to February 22, 2016. Selected publications in the areas of both epidemiology and treatment are reviewed in this article.

Introduction

Osteoarthritis (OA), a disease of articular joints, is the most common form of arthritis. OA is associated with significant morbidity, mortality, physical disability, and increased health care expenditures in middle age and elderly individuals[1,2]. OA results from a number of different etiologies that eventually end with a common phenotype that involves and disrupts all of the tissues within and surrounding the involved joint[3].

Research to identify risk factors for the development and progression of OA aims to develop novel treatments to both prevent and treat painful OA. In the past year, there have been a number of interesting studies that have explored the pathophysiology, epidemiology, and novel treatments for OA.

This manuscript will review a fraction of the recent clinical developments in the field of OA related to epidemiology, as well as both non-pharmacologic and pharmacologic treatments to reduce pain, radiographic progression, and improve function in subjects with OA.

Methods

We performed a primary literature search in PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) using the search terms.

"Osteoarthritis [All Fields] AND Epidemiology [All Fields]" and "Osteoarthritis [All Fields] AND Treatment [All Fields]" with the following limits activated: humans, English language, all adult 19+ years, published between April 1, 2015 and February 22, 2016. The primary and secondary searches identified a total of 629 articles. The titles of all of the articles were reviewed and we excluded case series, studies of surgical techniques, tissue sample or culture studies, clinical trial protocols, abstracts and studies that focused on biology, imaging, biomarkers, genetics and genomics, rehabilitation and surgical outcomes as these are covered by other authors in this issue. After the exclusions, we identified 104 articles which we considered relevant to our focus on epidemiology and clinical studies. Two authors (KS, BLW) reviewed the 104 articles and graded them on importance/relevance and methodology and gave each article a score that was a 1 – if the article was both important and had strong methodology; 2 – if the article was weak in either importance or methodology and 3 – if the article was weak in both importance and methodology. The third author (NEL) reviewed the scoring of the 104 articles and if there were differences in the assessments, the three authors performed a consensus grading. In

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this review, we have included studies that were considered by the authors to be of relatively high quality and have the potential to influence the treatment of OA.

Results

Epidemiology

OA of the knee is a heterogeneous disease, and attempts to define different subgroups or phenotypes may be useful to clinicians to focus the management of these patients. Recently, Knoop *et al.* using data from the osteoarthritis initiative (OAI) cohort defined five phenotypes: a minimal joint disease phenotype, strong muscle phenotype, non-obese and weak muscle phenotype, obese and weak muscle phenotype, and depressive phenotype. These phenotypes were based on four patient characteristics that could be measured in clinical practice and included upper leg strength, body mass index, radiographic OA and depressive mood[4]. The goal of the study by M. van der Esch *et al.* was to validate the previously established phenotypes of knee OA based on similar patient characteristics from the Amsterdam OA cohort (knee OA subjects ($n = 551$), mean age of 61 years). Cluster analysis identified five phenotypes of knee OA patients that included minimal joint disease phenotype, strong muscle strength phenotype, severe radiographic OA phenotype, obese phenotype, and depressed mood phenotype. To a large extent, these results replicated the five phenotypes identified with the OAI cohort and suggest that these phenotypes are stable, valid, and may be clinically relevant: dividing knee OA patients on the basis of four clinical characteristics may allow for personalized care of these patients[5].

Patients with knee OA frequently have knee pain and disability that can lead to a reduction in their quality of life. A systematic meta-analysis was done of cohort studies for risk factor for the onset of knee pain[6]. There were 6554 papers identified and 46 studies were included in the analysis. The independent factors associated with incident knee pain included being overweight based on Body Mass Index (BMI) (25–30 kg/m^2) (pooled OR of 1.98, 95% Confidence Interval (CI): 1.57–2.20), obesity (BMI > 30 kg/m^2) (pooled OR 2.66, 95% CI: 2.15–2.38), female gender (pooled OR 1.68, 95% CI: 0.90–1.87), and previous knee injury (pooled OR 2.83, 95% CI: 1.91–4.19). Hand OA was not significant and smoking was found not to be a significant risk factor or have any protective effect. Population attributable fractions were calculated for knee injury and obesity and 5.1% of incident knee pain subjects resulted from previous injury while 17.3% resulted from obesity and 24.6% from being overweight or obese. These results suggest physicians can identify risk factors and personalize treatment to patients at risk of developing incident knee pain, and also that obesity is and continues to be a significant predictor of incident knee pain.

Obesity in adulthood is a well-established risk factor for incident knee OA. Birth weight is known to be associated with a number of chronic diseases including heart disease and low bone mass, but the relation of birth weight to OA has not been largely investigated. Hussain *et al.* reviewed the birth weight and history of premature births in individuals that were over the age of 40 years at the time of a joint arthroplasty through linking it to the Australian Orthopedic Association National Joint Replacement Registry between years 2002–2011[7]. They found that among 75 subjects that underwent joint replacement for OA, low body weight (hazard ratio (HR) was 2.04 (95% CI: 1.11–3.75)) and preterm birth (HR of 2.50 (95% CI: 1.29–4.87)) increased risk for hip arthroplasty after adjustment for known and potential covariates including age, sex, body mass index, education level, hypertension, diabetes mellitus, smoking, and physical activity. Interestingly, no association was found for knee arthroplasty. These results support the concept that risk factors for OA in the knee and hip differ. The role of low birth weight and premature birth in the development of hip OA is worthy of further investigation.

The role of weight in both the development and progression of knee OA has been a topic of investigation this year. Teichtahl *et al.* determined how change in weight influenced tibial cartilage volume as measured by MRI. The investigators evaluated 112 obese subjects and collected weight, questionnaires and performed MRI scans of the knee, at baseline and an average 2.3 years later and found that weight change was associated with change in medial tibial cartilage volume across both weight gain and weight loss; however, this was not observed in the lateral tibial cartilage for either weight gain or weight loss. The change in weight, both loss and gain was also associated with significant changes in Western Ontario McMaster (WOMAC) subscales. These results confirm qualitative observations that weight gain reduces medial tibial cartilage volume and worse knee symptoms while weight loss has the opposite effects[8]. Also, clinicians should continue to work with obese patients to both lose weight and also prevent weight gain as both of these interventions can prevent loss of medial articular cartilage.

The epidemiology of knee and hip OA also includes risk factor identification for joint replacement. There is an increasing interest in the role of vascular disease in OA, as investigations in the Netherlands reported that subjects with knee OA and hand OA progression had more intimal media thickness of the carotid artery compared to controls[9]. Hussain *et al.* asked whether differences in microcirculation might influence the risk of incident knee and hip replacement for OA. The study subjects were studied from the Australian Diabetes, Obesity and Lifestyle Study that had vascular caliber measured with a nonmydriatic digital fundal camera between 1999 and 2000, were ≥40 years when the joint replacement was performed and had a knee replacement between the years of 2002–2011. They reported that 77 subjects underwent a total knee replacement for OA and these subjects had significantly more narrowed retinal arteriolar caliber compared to subjects in the cohort that did not have a knee replacement. For every standard deviation reduction in retinal arteriolar narrowing, the risk of knee replacement risk increased by 25%. The subjects with the narrowest two-thirds of arteriolar caliber had a HR for joint replacement of 2.0 (95% CI: 1.07–3.74) after adjustment for known and potential covariates. These data suggest a link between microcirculation, atherosclerosis and OA suggesting that more research is warranted in this area[10].

Another study on the epidemiology of knee replacement was performed by Wise *et al.* It is common for individuals with knee pain to seek medical attention and in the case of severe knee pain potentially receive a joint replacement. However, knee function has not previously been well characterized as a risk factor for knee joint replacement. The investigators utilized the Multicenter Osteoarthritis Study (MOST), which is an NIH funded observational study of subjects recruited between the ages of 50 and 79 years that either had knee OA or were at high risk of OA. The authors enrolled 2946 subjects and estimated the risk of a knee replacement over 30 months based on functional impairment as measured by WOMAC function subscale. They found that subjects with a high level of functional impairment by WOMAC function score had 15.5 times the risk of undergoing a total knee arthroplasty (TKA) adjusting for covariates, and even after adjusting for knee pain severity the group of subjects with the worst functional impairment had 5.9 times the risk of undergoing a TKA compared with those with the best functional status. Also, the relative risk of TKA at every level of functional impairment was greater for women than for men. This study reminds clinicians to ask their patients with knee pain about knee function and it appears that knee function is a strong predictor of TKA[11].