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Epidemiology of Osteoarthritis: Literature Update

Ernest R. Vina[a,b] and **C. Kent Kwoh**[a,b]

[a]Division of Rheumatology, Department of Medicine, University of Arizona, Tucson, Arizona, USA

[b]Arthritis Center, University of Arizona, Tucson, Arizona, USA

Abstract

Purpose of review—The purpose of this review is to highlight recent studies of osteoarthritis epidemiology, including research on prevalence, disease impact, and potential risk factors.

Recent findings—Osteoarthritis (OA) is highly prevalent in the US and around the globe. It is a leading cause of disability and can negatively impact people's physical and mental well-being. Healthcare resources and costs associated with managing the disease can be substantial. There is increasing evidence that there are different OA phenotypes that reflect different mechanisms of the disease. Various person-level risk factors are recognized, including sociodemographic characteristics (e.g., female gender, African-American race), genetic predispositions, obesity, diet-related factors, and high bone density/mass. Joint-level risk factors include specific bone/joint shapes, thigh flexor muscle weakness, joint malalignment, participation in certain occupational/sports activities, and joint injury. Recent studies have enhanced our understanding of pre-radiographic lesions associated with OA.

Summary—Application of these new findings may allow us to develop innovative strategies and novel therapies with the purpose of preventing new disease onset and minimizing disease progression.

Keywords

epidemiology; osteoarthritis; impact; phenotypes; risk factors

INTRODUCTION

A number of reviews on the epidemiology of osteoarthritis (OA) have been conducted in the past decade [1–5]. This review highlights new research findings since the middle of 2016. Similar to the other reviews [1–3,5], we will begin by presenting recent data on disease prevalence. We will then discuss recent findings on the impact of OA and the disease's distinct phenotypes. Finally, we will describe new information concerning systemic- and local-level risk factors associated with OA development and/or progression.

Correspondence to: Ernest R. Vina, MD, MS, University of Arizona Arthritis Center, 1501 N. Campbell Ave., PO Box 245093, Tucson, AZ 85724-5093, USA. Tel.#: (520) 626-4206. Fax #: (520) 626-2587. evina@email.arizona.edu.

Conflicts of Interest

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PREVALENCE

The estimated prevalence and incidence of OA vary depending on the definition of OA, the specific joint(s) being evaluated, and the population being studied [1–3]. Using data from the National Health Interview Survey, it was recently estimated that 14 million people in the US have symptomatic knee OA (KOA), including >3 million racial/ethnic minorities [6]. Notably, more than half those with KOA are <65 years of age. Recent cohort and community-based studies have also measured the prevalence of OA of different joints in various communities in South America [7,8], Asia [9–11], and the Middle East [12].

IMPACT OF OSTEOARTHRITIS

OA is a well-known cause of disability around the globe [13]. In a large cohort study of Mexican Americans, the number of activities of daily living impairments was 1.12-1.35 times greater among those with OA, compared to those without it [14]. In a nationwide survey conducted in Korea, the estimated years lived with disability was exceptionally high among elderly males (836 per 10,0000) and females (3039 per 10,0000) with OA [15]. In a population-based study in Sweden, the greater risk for sick leave or disability among those working in female- or male-dominated job sectors was attributed to KOA [16].

Besides affecting people's physical health, OA may also negatively impact people's mental health. Data from the Osteoarthritis Initiative (OAI) study demonstrated that those with lower limb OA had greater odds of developing depressive symptoms than those without the disease [17]. OA was also associated with greater odds of suicidal ideation [18]. Another study found a strong relationship between OA and perceived memory loss that was partially mediated by sleep and mood impairments [19].

There is also increasing evidence that OA is a risk factor for cardiovascular disease development. A meta-analysis found that the risk of myocardial infarction was significantly increased in OA and other types of arthritis [20]. Other studies similarly linked coronary heart disease with OA [21,22]. In parallel, the Chingford Cohort study found an increased risk of cardiovascular disease-specific and all-cause mortality among women with symptomatic KOA compared to women without signs/symptoms of OA [23]. Interestingly, there was no relationship found between hand OA and mortality risk. A Swedish study reported no increased mortality in patients with knee and hip OA compared to the general population [24].

In addition, OA consumes a substantial amount of healthcare resources and costs. Studies have demonstrated that OA was associated with higher risk of hospitalization and emergency department charges among those who present in the emergency room for other reasons [25,26]. The average direct cost of OA in Canada increased from $577 to $811 per patient/year between 2003-2010, primarily due to joint replacement surgery costs [27]. In the US, the estimated total annual average direct per-patient cost varied from $1,442 to $21,335 (adjusted to 2015 US$ equivalent) [28]. Observed variations in cost were partly attributed to differences in healthcare resource categories measured between claims data and survey data-based studies.

PHENOTYPES

A phenotype can be defined as a combination of disease attributes that describes differences between patients as they relate to distinct outcomes of interest [29]. KOA is a heterogeneous disease with a very complex pathology. There is growing consensus that these differences are due to the existence of different phenotypes that may represent different mechanisms of the disease [4,30,31]. With different phenotypes, clinicians may tailor their disease management [30]. A recent systematic review identified six variables which represent six clinical phenotypes [31]: 1) chronic pain (with prominent central mechanism), 2) inflammation, 3) metabolic syndrome, 4) bone and cartilage metabolism, 5) mechanical overload, and 6) minimal joint disease. The six phenotypes may represent different disease etiologies with the exception of the minimal joint disease phenotype that classifies subjects based on disease progression.

Another systematic review reported on which characteristics are most relevant in distinguishing KOA phenotypes [32]. Clinical phenotypes are the KOA phenotypes most frequently investigated, followed by laboratory and imaging phenotypes (Table 1). Authors of the review concluded that pain sensitization, psychological distress, radiographic severity, body mass index (BMI), muscle strength, inflammation, and comorbidities (especially metabolic syndrome) were most associated with clinically distinct phenotypes. They also reported that gender, metabolic abnormalities, pattern of cartilage damage, and inflammation were most relevant in distinguishing structural phenotypes.

RISK FACTORS: SYSTEMIC

The World Health Organization defines risk factor as any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease [33]. Current evidence on person-level risk factors associated with OA disease development and/or progression follows below.

Sociodemographic

Older age is a well-known risk factor for OA [1–3]. Compared to men, women are more likely to develop hand, foot, and KOA but are less likely to develop cervical spine OA [1]. A new study of incident diagnoses of OA among US service members comparably found that the rates of shoulder and cervical spine OA were higher among men than women [34]. Another found that lower levels of endogenous sex hormones were associated with increased knee effusion-synovitis only in women and not in men with symptomatic OA [35].

Compared to other races, African-Americans are also more likely to develop symptomatic knee and hip OA [2,5]. There are known racial/ethnic differences in radiographic OA features [5]. In a longitudinal study, it was recently discovered that African-American males had higher risk of medial knee joint space width (JSW) loss over time than African-American females and whites [36]. Controlling for other known risk factors for KOA attenuated these differences, however.

Genetic

Approximately 30%-65% of the risk of OA is genetically determined [1,3]. A recent review by Warner *et al* [37] highlighted the main findings from genetic association studies on OA to date. They reported that genome-wide associated scan (GWAS) studies have so far identified 21 independent susceptibility loci for OA. Since this review's publication, the single nucleotide polymorphism (SNP) rs4238326 in the ALDH1A2 gene was linked with KOA risk in a Chinese sample study [38]. This is relevant, as genetic variants within the ALDH1A2 gene was only previously linked with hand OA in European populations [37]. Data from the Chingford study also found that the SNP rs11688000 in the neurokinin 1 receptor gene (TACR1) was associated with decreased risk of symptomatic OA [39].

An issue with conducting genetic association studies for OA is the heterogeneity of phenotypes used. Using endophenotypes, which can be more reliably quantified (e.g., minimum JSW), can help reduce this problem [37,40]. Four distinct loci were recently associated with minimum JSW in a hip OA study [41].

Obesity and Metabolic Syndrome

Obesity has long been identified as a risk factor for KOA [1–4]. An updated meta-analysis also showed that increased BMI moderately contributed to increased susceptibility to radiographic and/or clinical hand OA [42]. Although the association between obesity and hip OA had been weak based on previous studies [1,2], a cross-sectional study from Japan [43] and a prospective cohort study from Spain [44] recently found an independent association between weight gain and hip OA diagnosis. Conversely, weight loss has been consistently associated with improved arthritis symptoms in a dose-response manner and slower knee cartilage degeneration in two different study populations [45,46].

Very few previous studies have investigated the relationship between hyperlipidemia and OA [2]. A recent case-control study from the UK demonstrated that hyperlipidemia was in independent risk factor for new onset hand OA [47]. In the Chingford study, higher levels of high-density lipoprotein cholesterol were protective against the incidence of radiographic hand OA [48]. In parallel, use of antilipemic agents (primarily ezetimibe, and excluding statins and fibric acid) was associated with fewer structural and better knee pain changes among OAI participants [49]. Statin use was not associated with reduced risk of consultation or surgery for hip or KOA in a pooled analysis of four cohort studies done in Sweden, however [50].

Examination of the OAI data found an association between higher systolic blood pressure and increased incidence of radiographic KOA [51]. A recent report does not support an association between diabetes mellitus and hand/knee OA [52–54]. There was also no significant association found between metabolic syndrome and radiographic hand OA using Framingham data [55].

Vitamins/Diet

As vitamin D plays a major role in cartilage and bone metabolism, it has been hypothesized that low levels of it may increase OA risk. Previous studies have been conflicting [1–3]. In

the VIDEO study [56–58], patients with vitamin D insufficiency and KOA were randomized to receive either vitamin D3 or placebo. Vitamin D3 supplementation neither slowed progression of joint space narrowing nor did it reduce Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscale scores [56]. After two years, though, effusion synovitis (measured by MRI) remained stable in the vitamin D group but increased in the placebo group [57]. Those with consistently sufficient 25-hydroxyvitamin D levels also had less loss of tibial cartilage volume, less increase in effusion synovitis, and less decrease in physical functioning compared to those with consistently insufficient levels [58].

Research on the role of specific diets in OA has also been active. Using OAI data, high dietary fiber intake was linked to lower risk of developing moderate-severe knee pain over time [59]. Findings from two prospective cohort studies also showed that higher total fiber intake was related to lower risk of symptomatic KOA, but its relation to radiographic KOA was unclear [60]. Another study found that higher soy milk intake was negatively associated with prevalence of radiographic knee osteophytes [61]. Finally, higher adherence to a Mediterranean diet was associated with lower prevalence of clinical and radiographic KOA [62].

Bone Density and Mass

Previous reviews reported that high bone mineral density (BMD) was a risk factor for incidence [3] and prevalence [2] of lower extremity OA. Supplementing these findings, high resolution peripheral quantitative computed tomography tests showed that men with hip joint osteophytes had higher radial trabecular volumetric BMD, while men with hip sclerosis had higher cortical volumetric BMD at the tibia [63]. New evidence suggests that high systemic BMD predates early structural KOA features; higher spine and total hip BMD were recently linked to progression of tibiofemoral cartilage defects as measured by MRI in adults without clinical symptoms [64]. High bone mass was also recently associated with radiographic hand OA findings [65] but not with OA in the TMJ [66].

RISK FACTORS: JOINT-LEVEL

Current evidence on joint-level risk factors associated with OA disease development and/or progression follows below.

Bone/Joint Shape

Bone shape may contribute to the risk of OA as had been previously described primarily in the hip joint [2,3]. Contributing to the body of evidence, a recent population-based OA cohort study in France used 5 measures to describe hip morphology [67]. Among all measures, acetabular index was most strongly associated with the severity and progression of hip OA. In addition, the Rotterdam Study found that those with cam deformity or acetabular dysplasia had double the risk of developing hip OA compared to those without deformity [68].

Recent studies are also exploring the contribution of bone/joint shape in OA development in other joints. In the OAI, changes in bone area and shape of the knee over 24 months among those with mild-to-moderate OA were associated with radiographic and pain progression

over 48 months [69]. In the Tasmanian Older Adult Cohort study, uncommon proximal tibiofibular joint shapes were positively linked to cartilage defects, bone marrow lesions, and osteophytes in the lateral knee compartment [70]. In the Johnston County OA Project, certain ankle morphologies were linked to injury history that could lead to greater predisposition for ankle OA [71].

Muscle Strength

The association between muscle strength and OA may vary depending on the muscles and joints being studied [1–3]. In an examination of anterior cruciate ligament (ACL) injured knees, high thigh muscle cross-sectional area (CSA) and high muscle/fat ratio had a protective effect against KOA prevalence [72]. On the other hand, among OAI subjects without radiographic KOA and with minimal extension strength variability, higher total extensor CSA and vastus medialis CSA were found to increase patellofemoral cartilage loss over time [73]. There was also a strong positive association between extensor-flexor CSA ratio and patellofemoral cartilage deterioration. Similarly, higher knee extensor strength in adolescent men was associated with greater risk of KOA by middle age in a longitudinal study of Swedish registries [74]. However, in a cross-sectional study of hip muscle strength and joints of subjects with hip OA, greater isometric strength of hip and thigh muscle groups was associated with better self-reported physical function [75].

Joint Loads and Alignment

Knee malalignment is a strong predictor of KOA disease progression [1–3]. The association between malalignment and the incidence of KOA is less clear, however [1,2]. More recent studies confirm these assertions [76,77]. In an OAI study, varus thrust (i.e., first appearance/worsening of varus alignment during stance) was associated with KOA progression, but not KOA incidence [77]. In the Multicenter Osteoarthritis Study (MOST), varus thrust increased the odds of worsening medial bone marrow lesions (BMLs) and medial cartilage loss as well as the odds of incident medial BMLs of the knee among those with KOA and those with increased risk of KOA, respectively [78].

Occupation & Sports

Particular repetitive activities inherent in certain occupations (e.g., firefighting, construction work) have long been and continue to be associated with greater risk of OA [1,3,79]. Reports of the associations between sports activities and OA have been conflicting [1,3,80–83] (Table 2). It is also unclear if positive associations are due to sports participation itself or to consequences of injury that occurred with sports participation.

Injury/Surgery

ACL injury, meniscal tear (MT), and direct articular cartilage damage following injury have all been linked to subsequent KOA development [1–3,5]. In a retrospective cohort study, those with ACL tears and lateral MTs had higher risk of developing arthritis and undergoing TKR surgery than those without ACL tears over 10 years [84]. Using a computer simulation model of KOA natural history and management, it was estimated that those with ACL injury

and MT were 2.5 times more likely to develop OA and 4 times more likely to undergo TKR surgery than those without injury [85].

Surgical reconstruction may not necessarily protect those who had sustained these injuries from developing KOA [2]. In the computer simulation model, the estimated cumulative lifetime risk of developing KOA minimally differed between those with ACL tears who were surgically treated vs. those who were not [85]. In another study, having a history of partial meniscectomy was associated with greater risk of incident KOA within a year [86].

Pre-Radiographic Lesions

While previous evidence was sparse [2], new studies have begun focusing on the predictive value of pre-radiographic lesions that may be detected only by MRI.

Synovitis—Effusion and Hoffa synovitis (hyperintensity in the infrapatellar fat pad [IPFP]) were previously associated with the development of incident radiographic KOA [87]. Recently, the Tasmanian cohort study found that baseline IPFP signal score predicted increases in KOA symptoms, tibiofemoral cartilage defects and BMLs, and loss of lateral tibial cartilage volume [88,89]. In the MOST study, Hoffa synovitis was associated with structural damage in the patellofemoral and tibiofemoral joints [90]. Moreover, superolateral Hoffa's fat pad hyperintensity was found to be a local marker of patellofemoral joint structural damage. Change in total synovitis score (from 11 sites) was not found to be related to change in knee pain in a small study of KOA patients, however [91].

In studies of patients with hand OA, synovitis was associated with joint tenderness and self-reported hand pain [92,93]. In the Hand Osteoarthritis in Secondary Care (OSTAS) cohort, synovitis was also associated with hand OA radiographic progression [94]. MRI synovitis did not correlate with clinical findings and biological markers of inflammation in a third hand OA study, though [95].

Bone Marrow, Cartilage, and Meniscal Abnormalities—Several new OAI studies have elucidated the relationship of MRI detected abnormalities with KOA risk. In one study, BMLs, cartilage damage, and menisci extrusion were assessed at baseline and 3 years after [96]. Worsening of these MRI lesions was associated with incident radiographic KOA. In a similar study with 7 years of follow-up data, these MRI lesions improved prediction of mild and moderate radiographic KOA development when added to prediction models that only included sociodemographic and patient-reported clinical variables [97]. In a case-control study, worsening of these lesions was more often detected among those who had radiographic and pain progression due to KOA compared to the control group [98]. Finally, BMLs and meniscal extrusion were recently associated with eventual TKR surgery receipt [99].

Other studies have evaluated the association of these pre-radiographic lesions with the risk of other OA types. In the OSTAS study, BMLs did not associate with hand pain in the absence of synovitis [93]. In a different cohort of erosive hand OA patients, BMLs at the proximal and distal joints correlated with examined joint tenderness [92]. BMLs were also linked to radiographic hand OA progression after 2 years in another study [94]. The

Tasmanian cohort study also found that hip cartilage defects were associated with greater pain and radiographic hip OA diagnosis [100].

CONCLUSIONS

OA continues to be a leading cause of morbidity and healthcare cost in the US and around the globe. There may be different OA clinical phenotypes that reflect heterogeneous disease mechanisms. A variety of person-level and joint-level risk factors have been linked to disease development and progression. While many of these risk factors are difficult to change, some may be more amenable to medical and behavioral interventions (e.g., obesity, muscle strength). Recent MRI studies have improved our understanding of MRI-detected damage which precedes radiographic evidence of OA.

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KEY POINTS

- Osteoarthritis (OA) continues to impact the lives of a substantial proportion of adults globally.
- More recent evidence suggests that there are several OA clinical phenotypes that represent different disease mechanisms.
- Person-level risk factors associated with OA include genetic and environmental influences.
- Joint-level risk factors associated with OA include structural abnormalities in bone shape, muscle mass and joint alignment.
- New magnetic resonance imaging studies have begun to allow prediction of radiographic/symptomatic OA development and progression.

Table 1

Osteoarthritis phenotypes and their distinguishing characteristics. Derived from Deveza et al. [32]

Category	Distinguishing Characteristics
Clinical	Pain sensitization profile
	Psychological profile
	Comorbid symptoms profile
	Clinical characteristics
	Knee joint alignment
	Metabolic
	Gait parameters
	Mechanistic factors
Imaging	Knee chondrocalcinosis
	MRI-detected denuded bone areas
	Imaging features and clinical symptoms
	Knee joint compartment (patellofemoral, tibiofemoral)
Laboratory	Biochemical marker patterns
	Inflammatory profile
	Cytokine/chemokine profile (synovial fluid)
	Serum biochemical markers of bone metabolism
	Serum biochemical markers of cartilage metabolism
	Profile of gene expression in peripheral blood leukocytes

Table 2

Recent review studies evaluating the potential association between sports and OA

Study	Activity		Effects
Alentorn-Geli *et al* [81]	•	Running (recreational)	Decreased risk of knee and hip OA
Driban *et al* [82]	•	Soccer	Increased knee OA prevalence
	•	Long-distance running	
	•	Weight lifting	
	•	Wrestling	
Vigdorchik *et al* [83]	•	Soccer	Increased radiographically-confirmed hip OA
	•	Handball	
	•	Track and field	
	•	Hockey	
	•	Long-distance running	No increased risk of radiographically-confirmed hip OA