The Burden of Osteoarthritis: Clinical and Quality-of-Life Issues

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Abstract

Osteoarthritis (OA), the most common form of arthritis, is a potentially devastating joint disease, affecting 27 million US adults. Its pathophysiology is marked by a gradual degenerative process accompanied by low-grade inflammation, and, although there is a strong correlation between age and OA risk, the abnormal changes that occur in the articular cartilage of people with OA differ notably from the typical changes associated with joint aging in several important ways. Risk factors for OA are multiple and span a variety of risk domains, such as lifestyle issues (eg, obesity and engagement in manual labor), genetic predisposition, sex and ethnicity (risk is higher in women and African Americans), and comorbidities.

Clinical outcomes for people with OA typically involve pain, limitations of daily living activities, and overall diminution of quality of life (QOL). The need to evaluate the degree of this burden, as well as to determine treatment approaches and measure their success, requires instruments for measuring QOL. The 2 most commonly used instruments to measure QOL in OA are the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Medical Outcomes Study 36-Item Short-Form Health Survey. Both provide useful global information to the clinician and researcher alike about pain and function in patients with OA, although the WOMAC is more often used in the clinical setting as it is self-administered. A number of other pain and function-specific measures are also available that may provide additional insight into patient status when used in combination with global QOL instruments.

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Osteoarthritis (OA) is the most common form of arthritis, affecting 27 million adults in the United States.[1] OA typically occurs in the hands, knees, spine, and hips, although it may be seen in any of a variety of joints.[2] Clinical diagnosis is based on observed symptoms, radiographic changes, or both, whereas differential diagnosis is normally supported through the use of laboratory studies. Although OA is often characterized as a degenerative disease, low-grade inflammation actually constitutes an important aspect of OA's pathologic process.[3,4]

OA is strongly correlated with aging: the risk of OA increases considerably with each decade after the age of about 45 years.[1] Nevertheless, aging is not inevitably associated with OA. In fact, several pathophysiologic changes that occur in osteoarthritic cartilage differ notably from that associated with age-related changes in cartilage.[5] That said, such age-related changes do play an important role in OA pathogenesis and, at a minimum, predispose individuals to the disease.[6]

Other than increasing age, there are a number of risk factors for OA, including comorbidities both related and unrelated to musculoskeletal conditions.[7] The presence of other joint diseases is the most common musculoskeletal comorbid risk factor, whereas obesity is among the most common nonmusculoskeletal comorbidities associated with OA.[7] Lifestyle variables, such as a history of manual labor and cigarette smoking, as well as sex- and phenotype-related conditions—such as age at menarche and joint hyperlaxity in men—can also play a role in conferring risk of OA.[8] The genetic component of OA risk, while still being studied at present, has been partially elucidated in recent years as genome-wide scan studies have identified genetic variants associated with OA.[9]

Ultimately, it is the burden of suffering experienced by people with OA that is of primary concern, and that burden can be significant. Pain and functional impairment are the key domains of that burden, and taken together they often exert a significant reduction in quality of life (QOL).[10-13] The present review will briefly describe the pathophysiology, prevalence, and typical outcomes of OA before addressing the issue of QOL in OA and the best means in which to measure it.

Pathophysiology of OA

Cartilage remodeling involves balanced interactions of synthesis

and degradation to achieve homeostasis of the extracellular matrix (ECM).[14] In OA this process becomes unbalanced, leading to pathologic changes in the affected joint.[15] The articular cartilage cells, chrondocytes, are responsible for maintaining homeostasis of the ECM by producing its major components, collagen and proteoglycan, in response to deterioration. Changes in the chrondocytes are associated with abnormal anabolic and catabolic activities as well as abnormal proliferation and apoptosis.

In the early stages of OA, loosening of the collagen network as well as proteoglycan loss occur in the upper cartilage zones and may still, at that point, be reversible.[15] Over time, these changes occur within deeper cartilage zones, reducing the elasticity of the cartilage and making a return to homeostasis increasingly difficult to achieve. Chrondocyte senescence—which is associated with increasing age—also appears to play a part in a reduced capacity for cartilage repair and contributes to OA progression.[16]

Recent data support the notion that changes in subchondral bone are also a factor in cartilage degradation.[17] The subchondral bone, which is in immediate proximity of cartilage, may contribute to cytokines, growth factors, and prostaglandins escalating—perhaps initiating—the degenerative process.

Prevalence and Incidence of OA

Collecting prevalence data from multiple sources, including the Third National Health and Nutrition Examination Survey (NHANES III), the Framingham Osteoarthritis Study, and the Johnston County Osteoarthritis Project, the National Arthritis Data Workgroup arrived at a prevalence figure for 2005 of 26.9 million US adults (aged ≥25 years) with some form of OA.[1] This constitutes a growth of approximately 6 million cases from 1995, more than a one-fourth increase in just 10 years. This likely reflects, in part, an aging of the US population, although increases in other related factors, such as obesity, as well as increases in methods of OA detection, may play a role in this observed prevalence.

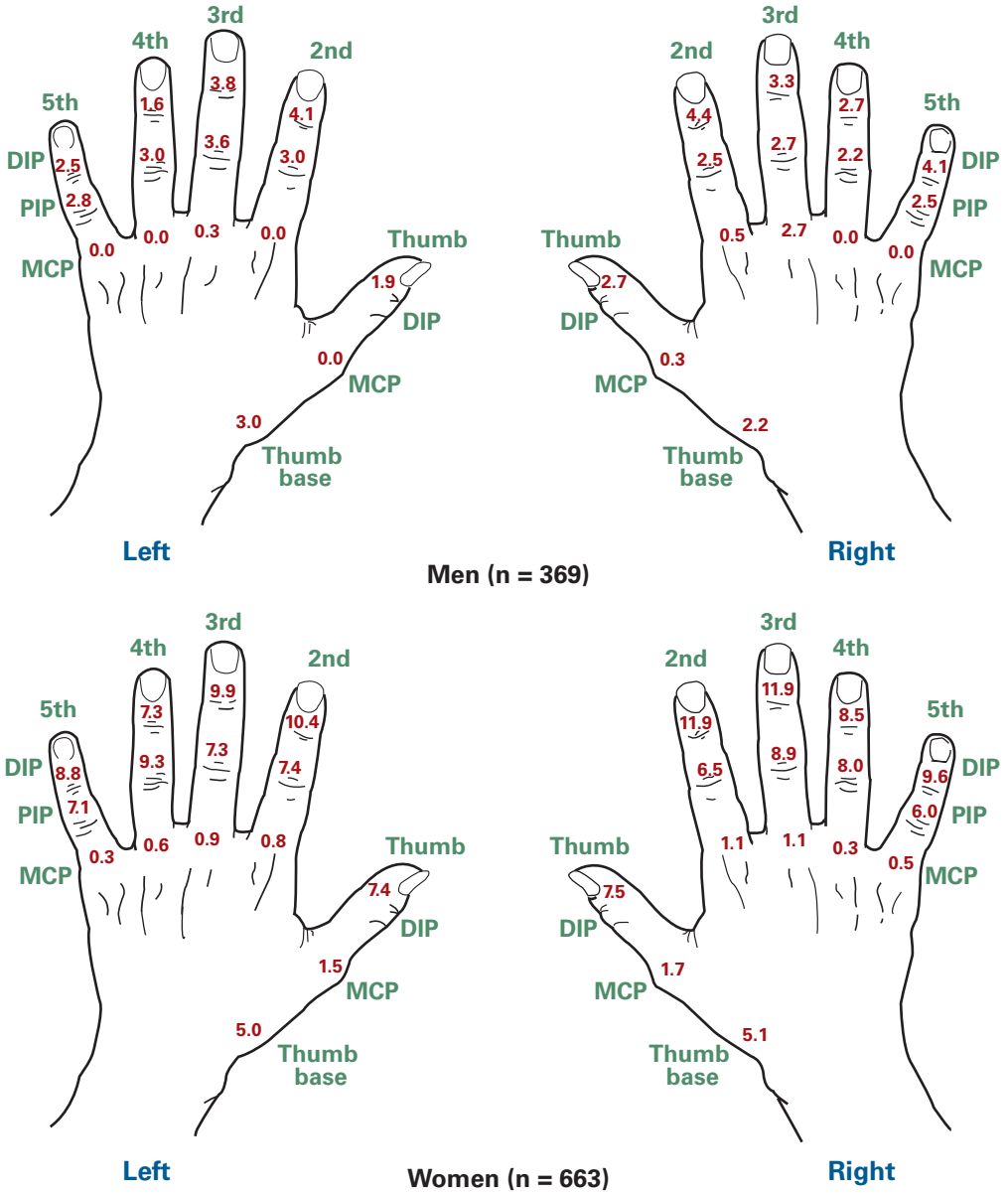
Nevertheless, the prevalence of OA does increase dramatically with age. Data from the Framingham study showed that the prevalence of knee OA nearly doubled in patients aged 45 years or older compared with those 26 years or older.[1] The proportion of women with OA also increases relative to men as age increases. Whereas the Framingham study found that 4.9% of women at least 26 years of age had knee OA compared with 4.6% of men, the gap increased to 7.2% versus 5.9%, respectively, in the 45 years or older group. This gap was replicated in the Johnston County study, although a higher rate of knee OA for both men and women aged 45 years or older was observed.[1] In that study, the rate of knee OA was 18.7% for women compared with 13.5% for men. The Johnston County study further observed a higher rate of hip OA in women 45 years or older (9.3%) compared with men in the same age group (8.7%).

The observation that the OA gap increases between men and women as they age is consistent with incidence data from the Framingham Osteoarthritis Study focusing on individuals aged 63 to 91 years (mean age, 70.8 years).[18] Among these older subjects, the age-adjusted relative risk (RR) of women experiencing radiographically determined knee OA compared with men was 1.79 (95% confidence interval [CI], 1.08-2.94).[18] Symptomatic knee OA was almost twice as likely (RR, 1.96; 95% CI, 1.01-3.82) for women compared with men.[18] Estimates of the rate of increase for knee OA in women was approximately 2% per year for radiographically determined disease.[18] Prevalence data regarding hand OA in more than 1000 study subjects aged 71 to 100 years from the original Framingham study (years analyzed: 1992-1993) again found a much higher rate of disease in women (26.2%) compared with men (13.4%). The **Figure** shows the distribution of OA symptoms at various joints in the hands for both men and women.[19]

Ethnicity also plays a role in OA risk. According to prevalence data from NHANES III (1991-1994), radiographic knee OA was observed in 17.7% of African American participants aged 60 years or older compared with 14.8% of Mexican American and 11.9% of white participants in the same age group (both differences $P < .01$).[20] Of note, the dual elevated risk of being both African American and female was observed with a prevalence of radiographic knee OA of 60.2% (95% CI, 52.8-67.5).[20]

Finally, with regard to the distribution of OA across its 3 most common sites—hands, knees, and

■ **Figure.** Prevalence of Symptomatic Hand Osteoarthritis Among People ≥71 Years of Age in the Framingham Study 1992-1993



DIP indicates distal interphalangeal; MCP, metacarpophalangeal; PIP, proximal interphalangeal.

hips—incidence data from a large health maintenance organization database showed that for every 100,000 person-years, the incidence of knee OA occurred 240 times compared with 100 times for hand OA and 88 for hip OA.[21]

Clinical Outcomes in OA

The burden that befalls people with OA is enormous both in terms of reduced function and the experience of pain, not to mention their considerable sequelae. An analysis of a compilation of various surveys (including NHANES III), databases (including the National Hospital Discharge Database), disease registers, and epidemiologic studies found that OA was the seventh leading cause of disability in women and the twelfth leading cause in men.[22] Among people 65 to 74 years of age, OA was found to be the fifth largest cause of disability,

ahead of dementia, diabetes, prostate cancer, and breast cancer.[22] These data are consistent with those from the Framingham study, which found that among older (mean age ~74 years) study participants, knee OA, taken alone, represented 1 of the 4 largest causes of disability along with heart disease, depression, and stroke.[13] A significant proportion of the patient population in the Framingham study with knee OA were unable to perform a variety of activities of daily living, such as heavy home chores (34% disabled), walking 1 mile (31%), stair climbing (10%), and grocery shopping (10%).[13] In fact, the ability to walk 1 mile or to undertake light housekeeping was notably more restricted among those with knee OA compared with matched patients with heart disease.[13]

It is interesting to note that the burden of OA in terms of functional deficits can affect areas beyond the immediate OA loci. For example, an analysis of participants in the Johnston County Osteoarthritis Project with joint-specific hand symptoms found that not only did they experience significant deterioration in performance-based functional status overall—as might be expected—but that the disability extended beyond that which one would intuitively associate with hand OA. People with hand OA symptoms in this study experienced significant deterioration in performing both upper- *and* lower-extremity tasks.[11] These results were based on both a self-report instrument (the Health Assessment Questionnaire [HAQ] Disability Index) as well as performance-based functional measures (timed "5 chair stands" and gait measured over an 8-foot walking course).[11]

A separate analysis of participants in the Johnston County Osteoarthritis Project found that having knee OA, and the severity of knee pain in particular, was associated with a high degree of functional impairment.[12] Even mild knee pain was strongly associated with disability in performing 16 of the 20 upper- and lower-extremity tasks included in the HAQ disability index.[12] For those with moderate-to-severe pain, significant disability was observed with all 20 tasks in the HAQ index (all $P < .001$).[12]

The common presence of comorbidities within the OA patient population exerts additional deleterious effects on both physical functioning and pain.[10,23]

Measuring QOL in OA

The necessity of measuring QOL arises from a need to understand its impact on OA patients in order to guide decision making—to determine how and what interventions are appropriate—in the management of the disease. Measuring QOL further allows clinicians the opportunity to determine the efficacy of a given intervention. Numerous instruments are currently available for measuring different aspects of QOL in the OA patient, including those that measure general QOL, functional capacities, the experience of pain, and psychological dimensions of QOL. The most commonly used instrument specific to OA is the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). WOMAC is a 24-item self-report questionnaire that addresses joint pain, stiffness, and loss of function related to OA of the knee and hip.[24-26] Since its initial validation, WOMAC has been widely used in clinical trials, and has been repeatedly shown to provide utility as a measure of patient QOL, response to treatment, prediction of treatment outcomes, as well as sensitivity to minimal perceptible clinical improvement.[24,27-30] An electronic touch-screen version of the WOMAC (the e-WOMAC) has shown similar responsiveness to the paper version in OA patients.[31]

The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) provides an 8-scale evaluation of physical and mental QOL based on 36 questions. Although the SF-36 is not specific to OA, it is, like WOMAC, widely used to guide OA treatment in clinical trials, being fairly sensitive to minimal perceptible clinical improvement.[24,27-29,32] A more OA-specific instrument, the SF-36 Arthritis-Specific Health Index, was developed to better target the OA patient population, but to date has not been widely adopted.[33,34]

Although both the WOMAC and SF-36 instruments function relatively well in assessing various QOL domains in OA, WOMAC may be more responsive than the SF-36 instrument to detecting changes in function.[24] In fact, the validity of both instruments has been challenged.[35] Although it should be noted that WOMAC is widely accepted for its ability to measure pain and functional deficits in OA, Stratford et al have questioned its validity in measuring pain.[35] According to their analysis, the factors that comprise pain evaluation are not valid, while they state that the pain scale as a whole is not internally consistent.[35] The authors suggest

Table. Individual Functional Performance Measures

Test	Instructions	Measurement
Timed "Up & Go"	Patient is sitting in an armchair with his/her back up against the chair back. A piece of tape is placed 3 m from the chair. On the signal "go," the patient gets up, walks to the tape line, turns around, walks back to the chair, and sits down again using a normal walking pace.	Time from "go" to return to sitting position
Six-Minute Walk	Patient walks unaided and alone for a period of 6 minutes on a flat surface, not a bike or treadmill nor oval or circular track. Phrases used when speaking to patients should be standardized. Encouragement is allowed as long as it is always the same from one patient to the next.	Distance walked in 6 minutes
Stair Measure	On the signal "go," patient ascends and descends 9 stairs, step height 20 cm, at a comfortable pace.	Time from "go" to return to initial position
Fast Self-Paced Walk	Patient is instructed to walk a 20-m indoor course (eg, hallway) as quickly as possible without overexertion, twice.	Time elapsed for two 20-m lengths excluding the turn

something other than pain is being measured by the "pain" portion of WOMAC.

The SF-36, apart from its lesser responsiveness to functional assessment, as already noted, has also been faulted as an inadequate instrument in the rehabilitation setting. The primary complaint has to do with questions in the SF-36 that assume the subject is living in a fairly normal environment—engaged in social and work activities as well as housework—none of which may apply to patients in a rehabilitation facility.[36]

Similar to WOMAC, but unlike the SF-36, the Stanford HAQ is a self-report instrument; it was first developed in 1978 to measure disability in rheumatic diseases, and exists in a modified version (MSHAQ).[37] Although it is still widely used in patients with musculoskeletal diseases, the HAQ tends to be applied more to rheumatoid arthritis than OA. The advantage of instruments such as WOMAC and the HAQ, in the clinical setting, is that as self-administered instruments, they are both simple to complete and require little time expenditure on the part of the clinical staff. The SF-36, in contrast, requires administration by a clinician, which at least partly explains why the SF-36 is more frequently used in clinical trials than in physicians' offices.

WOMAC, the SF-36, and HAQ all represent integrated instruments aimed at bringing together multiple QOL-related domains in order to arrive at a global view of patient status; however, there are specific tests available that allow for more targeted functional and pain measurement. For example, the visual analog scale for pain is widely known and used, as are such functional measures as the Stair Measure, the Fast Self-Paced Walk Test, the Timed "Up & Go" Test, the Six-Minute Walk Test, range-of-motion tests, and the Knee Society clinical rating system[38,39] (Table). These specific testing modalities may provide useful additional information in the clinical setting, particularly in combination with global instruments, to help physicians make treatment decisions. Some authors have suggested that clinical decision making should routinely utilize these specific functional tests, observing that global QOL tests when used in isolation are not sufficiently reliable indicators to guide treatment decision making.[38,40]

In summary, a great deal is now known about OA epidemiology and pathophysiology, as well as the anticipated disease course. Such information provides an opportunity to both target disease prevention as well as to define therapeutic approaches to decrease disease morbidity. Meaningful therapeutic responses are more effectively delineated when based on reproducible functional QOL measures.

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