Osteoarthritis is a serious disease

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Received and accepted on September 20, 2019.

Clin Exp Rheumatol 2019; 37 (Suppl. 120): S3-S6.

Key words: osteoarthritis, incidence, prevalence, cost of illness, disability, morbidity

ABSTRACT

Osteoarthritis (OA) is the most common form of arthritis, affecting 1 in 3 people over age 65 and women more so than men. The prevalence of OA is rising due, in part, to the increasing prevalence of OA risk factors, including obesity, physical inactivity, and joint injury. OA-related joint pain causes functional limitations, poor sleep, fatigue, depressed mood and loss of independence. Compared to age and sex-matched peers, OA patients incur higher out of pocket health-related expenditures and substantial costs due to lost productivity. Most people with OA (59–87%) have at least one other chronic condition, especially cardiometabolic conditions. Symptomatic OA may impair the ability of people with cardiometabolic conditions to exercise and lose weight, resulting in increased risk for poor outcomes. People with OA and other chonic conditions are less likely to receive a diagnosis or recommended treatment. Further, in these individuals the most effective and safest treatment is physical activity/exercise coupled with self-management strategies, which is only moderately effective. Given the already high, and growing, burden of OA, enhanced effort is required to identify better – more effective and safe – treatments for the majority of people with OA who are living with other chronic conditions.

OA is highly prevalent

Osteoarthritis (OA) is the most common form of arthritis (1, 2), affecting 1 in 3 people over age 65 (3) and women more so than men (1). OA typically affects the hips, knees, hands, feet and spine, with a high prevalence of polyarticular involvement. Data from the US Osteoarthritis Initiative (OAI) and the Multicenter OA Study (MOST) studies showed that 80% of individuals with bilateral knee pain had remote site pain, including low back pain (4-6). It is estimated that 242 million people are living with symptomatic hip and/or knee OA (3.8% of the population worldwide; 2.3% men and 4.5% women), but the total burden of disease due to OA is unknown.

The prevalence of OA is rising, due at least in part to the increasing prevalence of OA risk factors, including obesity, physical inactivity, and joint injury. Globally, all-age obesity increased by 26% from 2000 to 2013; by 2014 39% of adults aged 18+ years were overweight (BMI 25 to 29 kg/m^2; >1.9 billion adults) & 13% were obese (BMI≥ 35 kg/m^2; >600 million people). Approximately 23% of adults aged 18+ years performed insufficient physical activity in 2010 (20% men and 27% women). The proportions were even higher in high-income countries: 26% men and 35% women. From 2000 to 2013, the proportion with low physical activity increased 20% (1, 2).

Physical inactivity is associated with muscle weakness, which is also a risk factor for OA. Finally, the past few decades have seen an increase in participation in youth sports/recreational activity in all ages, which has resulted in increased rates of joint injury, *e.g.* meniscal and anterior cruciate ligament tears. However, these factors do not fully explain the exponential rise in prevalence indicating that other factors, yet unexplained, are contributing (7).

Burden of illness due to OA

Recent evidence indicates that the disease burden due to OA is similar to that of rheumatoid arthritis (RA) (8, 9), as a benchmark for severe arthritis. OA accounts for 2.4% of all years lived with disability (YLD) (1, 10). Between 1990 and 2013, a 75% increase was seen in OA-related YLDs worldwide such that currently, OA is the third most rapidly rising condition associate with disability after diabetes and dementia (10).

OA is characterised by structural changes at the level of the joint (the

Competing interests: none declared.

disease) and symptoms and disability at the level of the individual (the illness). OA-related joint pain, especially knee OA (11), causes functional limitations (12), poor quality sleep, fatigue (13, 14), depressed mood (15, 16), loss of independence (12) and is the primary indication for joint replacement surgery (15, 17-20).

Unfortunately, knee OA is under-diagnosed and under-treated, especially in people with other chronic conditions. When knee OA is inadequately treated, people manage by avoiding physical activities, like walking, that exacerbate their pain (21-23). This is problematic as physical activity/exercise is at present the most effective and safe non-surgical treatment for hip and knee OA. Over 50 randomised, controlled trials (RCTs) have shown that physical activity is effective in reducing knee pain, improving function and preventing development of major mobility limitations compared with usual care, with a benefit-to-risk profile greater than any other non-surgical treatment (24-26). Physical activity also reduces excess body weight and thus joint load, joint stiffness, muscle weakness, depressed mood and poor balance, and has positive effects on lipid metabolism, hyperglycaemia and systemic inflammation (27, 28).

Economic burden of OA

In 2003 in the US, the total costs attributable to arthritis and other rheumatic conditions were estimated at approximately $128 billion or 1.2% of the gross domestic product, with direct costs due of $80.8 billion (*i.e.* medical expenditures) and indirect costs of $47.0 billion (*i.e.* lost earnings). In 2010 in the US, nearly 10% of all ambulatory care visits were for a diagnosis of arthritis or other rheumatic conditions; of these, 58% were estimated to be for symptomatic OA (29).

The economic burden due to OA (30) is the result of direct costs to the health care system, indirect costs to individuals living with OA, and the intangible costs of living with a chronic disabling condition, as shown in Table I.

Compared to age and sex-matched peers, OA patients incur higher out of pocket health-related expenditures (30). People with OA also incur substantial costs due to lost productivity, including both absenteeism (days off work) and presenteeism (reduced self-reported productivity at work). Indirect costs due to lost productivity are estimated at $3.4-$13.2 billion/year. Greater OA pain severity is associated with greater health care use, absenteeism and presenteeism, and early retirement (31, 32). As the burden of OA rises globally, so too will the economic burden.

Table I. Factors contributing to the economic burden of osteoarthritis.

Direct costs	Indirect costs	Intangible costs
Costs of surgery	Loss of productivity	Pain and suffering
Hospital resources	Absenteeism	Reduced quality of life
Caregiver time	Premature mortality	Potential depression and anxiety
Pharmacological and non-pharmacological treatment	Disability payments/benefits	
Costs of side effects from treatments		
Research		

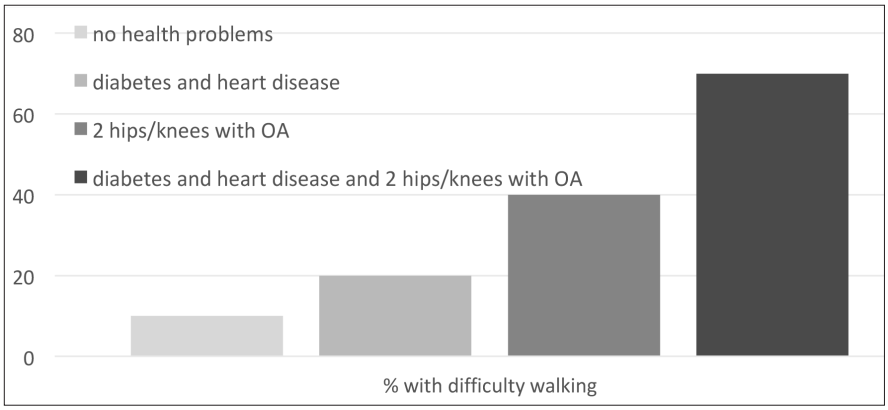

Fig. 1. Predicted probability of difficulty walking for a 60-year-old, middle-income, normal-weight woman (ref. 33).

The contribution of hip and knee OA to walking ability

In an Ontario cohort aged 55+ years (n=18,490), 10% met criteria for hip OA and 15.4% for knee OA and 25.4% reported difficulty walking (33). Using multivariable logistic regression modeling, the number of hips and knees affected by symptomatic OA was the strongest determinant of walking difficulty (controlling for age, sex, income, BMI, hip fracture & chronic medical conditions: hypertension, stroke, neurologic disorders, diabetes, cancer, respiratory diseases, peripheral vascular disease, mental health disorders, dementia). The predicted probability of difficulty walking for a 60-year-old, middle-income, normal-weight woman was 5-10%, 10% with diabetes, and 50% with diabetes and bilateral knee OA (33). (Fig. 1)

Comorbidity in people with OA

Older age, obesity and physical inactivity are risk factors for many chronic conditions. Thus, comorbidity is common among people with OA. It is estimated that 59 to 87% of people with OA have at least one other chronic condition. On average, people with OA have 2.6 moderate-to-severe comorbidities (23) and 31% have five or more other chronic conditions (34-36). In particular, abdominal obesity (increased waist circumference) and metabolic syndrome (obesity, diabetes, hypertension and dyslipidaemia) are more common in people with OA than in control subjects (63% *vs*. 38% and 59% *vs*. 23%, respectively) (35).

Impact of OA on comorbid conditions

OA may impair the ability of people with cardiometabolic conditions to exercise and lose weight, which is core to the management of these conditions

(27). In longitudinal cohort studies, hip/knee OA is associated with higher risk for all-cause and CV death, largely due to OA-related difficulty walking (37-40). In an Ontario cohort aged 55+ years (n=18,490), after adjusting for confounders, baseline hip/knee OA predicted a significantly higher risk for CV events; the effect was fully explained by OA-related difficulty walking (39).

Subsequent studies have examined the effect of total joint arthroplasty (TJA) on subsequent CVD events among individuals with symptomatic knee/knee OA. Ravi *et al*. showed (40) that individuals that underwent a TJA were significantly less likely than matched OA controls who did not have TJA to experience a cardiovascular event (hazards ratio 0.56, 95% confidence interval, CI, 0.43 to 0.74, $p<0.001$). Similarly, Lin W-Y *et al*. (41) documented that patients with knee OA who underwent TKA had a lower 3-year cumulative risk of stroke and acute myocardial infarction (AMI) than propensity-score matched controls (adjusted OR for CVD=0.56; 95% CI 0.51–0.61; $p<0.001$).

Among people with symptomatic hip and/or knee OA and concomitant diabetes, difficulty walking has also been shown to predict higher risk of serious diabetes complications (21), and an increased risk for incidence diabetes in those who did not have diabetes at baseline (42). Potential explanations include the influence of OA-related low-grade systemic inflammation on insulin resistance, use of NSAIDs for OA pain, and weight gain and sedentary behaviour due to avoidance of painful activities (27, 28, 43, 44). Thus, OA-related difficulty walking is a clinically relevant and modifiable risk factor for poorer outcomes in other chronic conditions.

Evidence-based management of knee OA

There are no current licensed drugs with proven disease-modifying activity for OA. Thus, management of OA is focused on improving pain, disability and quality of life with non-pharmacologic and pharmacologic therapies. Given the high prevalence of comorbid conditions among people with hip/knee OA, the safest and most effective treatment for hip/knee OA is physical activity/exercise coupled with self-management strategies. All OA treatment guidelines (24, 45, 46) recommend promotion of self-management, healthy weight, and a combination of strengthening and aerobic exercises (47) as core management strategies. When non-surgical therapies fail to control OA symptoms, joint replacement is recommended. However, joint replacement is not a cure for OA; as many as 20–30% of hip and knee replacement recipients report little or no improvement in their OA symptoms and/or dissatisfaction with their surgical results one year after joint replacement (48, 49). As researchers continue to work towards better understanding of the risk factors for poor outcome following hip/knee joint replacement, there remains an urgent need to identify efficacious and effective non-surgical therapies to prevent and treat OA.

Summary

OA is a serious disease. It causes substantial, persistent morbidity from pain, fatigue, sleep disturbance, depression and disability, which has an enormous burden on people's day-to-day functioning and quality of life. The economic burden is substantial and growing. OA poses a major barrier to people's mobility (walking) and thus to achieving sufficient physical activity. Available treatments are only modestly effective, and may be unsafe for use in the context of specific comorbidities such as hypertension or cardiovascular disease. Physical inactivity resulting from inadequately treated OA significantly increases risk for incident and progressive cardiometabolic disease. Public health strategies to address risk factors for hip/knee OA, importantly obesity, physical inactivity and knee injury, in concert with interventions to improve the timely diagnosis and effective management of OA has potential to substantially improve the quality of lives and health outcomes of people with or at risk for OA and reduce the global burden of OA on society.

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