

Editorial

Osteoarthritis the Killer Hiding in Plain Sight

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EDITORIAL

It is widely known and accepted that osteoarthritis (OA) is very common, and occurs with increasing frequency with advancing age. Estimates from 2005 surmised that 27 million Americans suffered from clinically diagnosed osteoarthritis [1]. Using less stringent criteria, it was estimated that 50 million Americans reported doctor diagnosed arthritis, the vast bulk of which would be OA [2]. The incidence in weight bearing joints such as the knee clearly increases with age, ranging from 13.8% of adults over the age of 26, to 37.4% of adults over the age of 60 [2,3]. In fact, the lifetime risk of osteoarthritis of the knee alone is strikingly high 40% in men and 47% in women [4]. These facts alone should establish osteoarthritis as a major public health concern, but yet OA receives surprisingly little public attention compared to other health issues.

COST AND DISABILITY

Osteoarthritis has been shown in several studies to increase the overall cost of healthcare compared to matched controls [5-7]. For men, this has been estimated at \$4740 per year and even worse for women at \$6212 per year, with an estimated overall impact to healthcare costs of \$185 billion due to the high prevalence of the disease [6-7]. Indirect costs are also substantial with the significant increase in sick days and lost productivity in workers with OA, as well as dramatic 8 fold increase in the chances of reduced work activity [8].

Perhaps not as well known is that osteoarthritis is most common cause of disability amongst adults in the United States, and has been for over 15 years. Functional limitations were linked to arthritis in 17.5% of patients with a disability, and degenerative back issues in another 16.5%. These numbers are each more than heart disease (7.8%), diabetes (3.4%), and lung diseases (4.7%) combined [9]. This problem is not just limited to seniors, with 3.4-15% of working age (18-64) Americans limited by arthritis at work [10]. This study does not take into account the current economic climate and the increasing number of senior citizens remaining in the work force, or the numbers would be even larger.

OBESITY

Superimposed on these issues is the growing obesity epidemic that we are facing. At the same time our world appears to be growing smaller, its inhabitants are growing larger, with

an estimated 1.45 billion people overweight [11]. This is true not only with adults, but also with a recent doubling of childhood obesity. In 1990 when the CDC began the BRFSS to track state by state obesity levels, no states had over 15 % obesity rates, and 10 states had less than 10%. By 2010, no state had less than 20% obesity, and 36 had over 30% [12,13].

With obesity being a well-recognized risk factor for the development of osteoarthritis in weight bearing joints, this portends a future osteoarthritis epidemic as well [14,15]. As the overweight baby boomers get older, it is estimated that by 2030 67 million Americans will be suffering from arthritis, and that number is probably conservative [16,17]. The economic fallout from both lost productivity in the workforce and skyrocketing costs to an already overtaxed healthcare system could be a disaster in the making.

ADIPOSE TISSUE IN OA

It is also becoming apparent that fat plays a much bigger role in osteoarthritis than just its mass and physical force on weight bearing joints. Multiple studies have implicated fatty tissue derived paracrine hormones (adipokines) such as leptin and adiponectin as being players in the biochemical destruction of cartilage [18,24]. Patients with osteoarthritis have higher circulating levels of adipokines, but the predominant effects seem to be at the local level, where large number of inflammatory cells reside in the stromal layers of fat deposits [18]. The infrapatellar fat pad in patients with osteoarthritis of the knee has been shown to have increased adipokine production [19]. Adipokines are also significantly increased in knee osteoarthritis, in cartilage, chondrocytes, and synovial fluid, and more importantly they have been correlated with disease severity [20-24]. Even in osteoarthritis of the hand, where weight is not the issue, obesity has been linked with increased disease progression associated with decreased protective adiponectin levels [25].

Studies have also shown that the presence of metabolic syndrome increase the chances of osteoarthritis significantly over obese patients without the full syndrome, with a "dose effect" based on the number of components present [26,27]. One recent study of women with a mean age of 47 showed a risk of knee OA of 4.7 in normal weight, 12.8% in obese women, and 23.2% in obese women with metabolic syndrome [28]. Taken together, all of this information suggests strong parallels between the well-known impact of metabolic syndrome on producing damage in the

vascular system (atherosclerosis) and perhaps similar damage to joint cartilage and surrounding structures (osteoarthritis).

CHRONIC PAIN AND OBESITY

We are also recognizing that central nervous system factors play an important role in osteoarthritis pain [29,32]. Osteoarthritis has traditionally been thought of as pure model of mechanical or degenerative pain, but the reality is much more complicated. Numerous studies have shown that the degree of radiographic severity is not well correlated with pain or function scores, suggesting that the mechanical defect is not the most important determinant of pain [29,33-34]. Central sensitization and central nervous system involvement, once thought to be only the domain of fibromyalgia, have been established as major components of osteoarthritis pain.

This is especially true for obese individuals, where pain has been shown to have a larger impact on decrease in function, as well as on worsened quality of life [35]. Pain catastrophizing involves feelings of helplessness regarding pain, ongoing rumination over the pain, and amplified fear of the threat of pain [36]. Catastrophization has been shown to be amplified in obese individuals, leading to decreased physical activity as well as increased binge eating and weight gain [37]. Chronic pain is present in an astounding 52% of obese patients, with central obesity being the strongest risk factor of the components of the metabolic syndrome, with an odds ratio of 1.7 even after controlling for osteoarthritis, insulin resistance, inflammation, and neuropathy [38].

MORTALITY IN OA

It has been well known for a number of years that mortality is significantly increased in patients with rheumatoid arthritis, largely through increased cardiovascular deaths [39,41]. This has been speculated to be due to complications from the effects of chronic inflammation on the vascular system. Because systemic inflammation is lacking in osteoarthritis, it has also been assumed that osteoarthritis would not carry this same risk.

However, several studies in the past have suggested that in fact mortality is increased in patients with osteoarthritis [42,44]. One longitudinal population based study showed an increase in risk of death with increasing number of joints affected by OA, with a hazard ratio of 1.45 for every increase of 3.1 joint groups involved (out of 18 joint groups) [42]. Another study found that in a small group with historical controls, there was increased ischemic heart disease deaths in both RA (1.66 OR) and OA (1.96 OR) compared with siblings of the RA patients (1.05 OR) [44].

A recent longitudinal population based study confirmed this trend of increased mortality in osteoarthritis patients [45]. After a median follow up of 14 years, patients with osteoarthritis had an increased mortality of 1.55 OR compared to the general population, which was even more pronounced for cardiovascular death at 1.71 OR. Patients with a walking disability at baseline had an increased risk of death of 1.93 OR, which when adjusted for age, sex, and comorbidities remained significant at 1.48 OR. Fully adjusted risk of cardiovascular death in the patients with walking disability was even higher at 1.72 OR. Patients with a severe walking limitation had increased risk of death when compared

to those with a disability (1.88 vs 1.31). Thus it does appear that osteoarthritis can in fact be a deadly disease, especially when it results in a big decrease in physical function.

Osteoarthritis can also significantly amplify the risk of mortality in frail elderly individuals [46]. An analysis of Framingham heart study patients showed increased hazard ratio of 2.26 for coronary artery events in patients with symptomatic hand osteoarthritis, and remained significant even when correcting for lower extremity arthritis and difficulty walking [47].

OA AS A CHRONIC DISEASE

When the subject of chronic diseases is brought up, the discussion usually centers on cardiovascular disease, diabetes, COPD, etc., with osteoarthritis rarely entering the discussion. Yet OA is extremely common, causes significant dysfunction and disability, engenders very large public health costs, is expected to increase in prevalence, and increases mortality. That certainly fits the bill as a chronic disease, and one worthy of significant attention.

Osteoarthritis also acts synergistically with other chronic disease to increase morbidity and most likely mortality, as already noted. About 40-60% of people with other chronic diseases also suffer from osteoarthritis, which can be synergistic poorer outcomes due to decreased exercise [48,50]. The presence of arthritis has been shown to increase the risk of activity limitations in patients with other chronic conditions by 1.4-1.6 times [51]. Thus focusing on osteoarthritis as a potential stumbling block to the successful treatment of other health conditions should lead to better outcomes.

However in the limited time frame for doctor patient discussions, arthritis often gets overlooked. Patients perceive osteoarthritis as more disabling than diabetes, hypertension, and heart disease, but physicians have been shown to be more focused the latter [52]. This discordance can lead to dissatisfaction and frustration in the patients, and a less than desired clinical improvement by all [53].

By the same token, patients are often hesitant to follow their physician's advice to exercise out of the unfounded but common fear that they will make their arthritis worse. Kinesiophobia, or fear of movement, is one of the most important limiting factors in patient's activity levels, and has been shown to be more predictive of disability than OA x-ray severity [54,55]. This fear of movement has been shown to be even greater in obese patients, adding insult to injury in their challenges to be more active [56].

TOWARDS SOLUTIONS

So what are we to do? The first step towards getting better is admitting we are facing a big problem. Increased awareness of the size, scope, and morbidity of the arthritis epidemic amongst patients, providers, and policy makers is critical. Understanding the relationship between increased fatty tissue and arthritis, both from a weight and biochemical impact, will help provide more incentive for weight loss. One modeling prediction estimated that reducing obesity levels back to 1998 levels would prevent over 100,000 knee replacements, as well as extend quality adjusted life expectancy by almost 8 million years in the United States alone

[16]. Patients need to grasp that a very modest and achievable 10% loss in weight is a better pain medicine than any pill that they could take. Recognizing the contributions of central chronic pain and fear of movement to the decreased function of patients with osteoarthritis can lead to previously unrecognized avenues for improvement. Clinicians being alert for arthritis as a limiting factor in other chronic health problems can widen the collection net for patients getting better education and treatment. We all need to keep moving, as the book on the benefits of exercise keeps getting thicker every day, as does the contrasting tome of the risks of inactivity. The task ahead may look enormous, but taken one patient at a time, anything is possible.

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