

## Osteoarthritis: Pathophysiology, treatment update and role of exercise

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**Abstract:** Osteoarthritis being common degenerative disorder especially in both sexes of elderly with higher risk among obese, previous injury, developmental disorder & inherited disorder of joints/limbs remains area of focus for researchers, physicians & governments. Diagnosis is straightforward based on history and imaging, but management always remains challenge ranges from preventive through conservative & operative. Financial constrains because of increased life expectancy & more health awareness leading to management by exercise, visco-supplementation, arthroplasties, & rehabilitation services & need to be explored. Established role of exercise preventive as well as therapeutic being a cheaper option is getting popularity & further innovative exercise programs can be designed to get better outcome. The article emphasis on different modalities of osteoarthritis management with some focus on exercise.

**Keywords:** Osteoarthritis, Degenerative disorder, Contributory factor, Exercise, Treatment

Date of Submission: 26-06-2019

Date of acceptance: 13-07-2019

### I. Introduction

Osteoarthritis (OA) is a type of joint disease that results from breakdown of joint cartilage and underlying bone [1].Osteoarthritis is the most common form of arthritis affecting about 237 million people (3.3% of the world population)[2].Among those above 60 years old, about 10% of males and 18% of females are affected [3].It is the cause of about 2% of years lived with disability [4].In Australia about 1.9 million people are affected [5],and in the United States 30 to 53 million people are affected [6].It becomes more common in both sexes as people become older [7].Causes include previous joint injury, abnormal joint or limb development, and inherited factors [7,3].Risk is greater in those who are overweight, have legs of different lengths, or have jobs that result in high levels of joint stress [3].Osteoarthritis is believed to be caused by mechanical stress on the joint and low grade inflammatory process [8].It develops as cartilage is lost and underlying bone is affected.[7].As pain may make it difficult to exercise, muscle loss may occur [3].The most common symptoms are joint pain and stiffness [7].Initially, symptoms may occur only following exercise, but over time they may become content. Most commonly involved joints are those near the ends of the fingers, at the base of the thumb, neck, lower back, knee, and hips [7]. Diagnosis is typically based on signs and symptoms, with medical imaging and other tests occasionally to support or rule out other problems [7].Treatment includes, exercise, efforts to decrease joint stress, support groups, and pain medications[7,9].

### II. Prevalence

Worldwide, as of 2010,approximately 250 million people had osteoarthritis of the knee(3.6% of the population[10].Hip osteoarthritis affects about 0.85 % of the population [10].As of 2004,osteoarthritis globally causes moderate to severe disability in 43.4 million people [11].Together, knee and hip osteoarthritis had ranking for disability globally of 11<sup>th</sup> among 291 disease conditions assessed[11].In the United States as of 2012,Osteoarthritis affected 52.5 million people, approximately 50% of whom were 65 years and or older [6].It is estimated that 80% of the population have radiographic evidence of osteoarthritis by age 65,although 60%of those will have symptoms [12].The rate of osteoarthritis in the United States is forecast to be 78 million (26%) adults by 2040 [6].In the United States, there were approximate 964,000 hospitalization for osteoarthritis in 2011,a rate of 31 stays per 10,000 population[13].With an aggregate cost of \$14.8 billion (\$15,400 per stay),it

was the second to expensive condition in U.S. hospital stays in 2011. By payer, it was the second costly condition billed to Medicare and private insurance [14].

### **III. Contributory Factor**

Damage from mechanical stress with insufficient self-repair by joints is believed to be the primary cause of osteoarthritis [15]. Sources of this stress may include misalignment of bones caused by congenital or pathogenic causes, mechanical injury, excess body weight; loss of strength in the muscles supporting a joint and impairment of peripheral nerves, leading to sudden or uncoordinated movements [15]. However exercise running in the absence of injury, has not been found to increase the risk of knee osteoarthritis [4]. Nor has cracking one's knuckles been found to play a role [16].

**Prominent risk factor** : The development of osteoarthritis is correlated with history of previous joint injury and obesity, especially with respect to knees [17]. Changes in sex hormone levels may play a role in the development of osteoarthritis, as it is more prevalent among post-menopausal women than among men of same age [7,18].

Increased risk of developing knee and hip osteoarthritis was found among those who work with manual handling (e.g. lifting), have physically demanding work, walk at work, and have climbing tasks at work (e.g. climb stairs or ladders). [19]. With hip osteoarthritis in particular, increased risk of development over time was found among those who work in bent or twisted positions [19]. For knee osteoarthritis in particular, increased risk was found among those who work in a kneeling or squatting position, experience heavy lifting in combination with kneeling or squatting posture, and work standing up [19]. Women and men have similar occupational risk for the development of osteoarthritis [19].

**Less prominent risk factor**: This type of osteoarthritis is caused by other factors but the resulting pathology is the same as for „prominent (primary) osteoarthritis that includes:

a). Alkaptonuria, b). Congenital disorders of the joints c). Diabetes doubles the risk of having a joint replacement due to osteoarthritis and people with diabetes have joint replacements at a younger age than those without diabetes [20]. d). Ehlers-Danlos Syndroms. e). Hemochromatosis and Wilson's disease. f). Inflammatory diseases (such as Perthes diseases) (Lyme disease), and all chronic forms of arthritis (e.g. costochondritis, gout, and rheumatoid arthritis). In gout uric acid crystals cause the cartilage to degenerate at a faster pace. g). Injury to joints or ligaments (such as ACL) as a result of an accident or orthopedic operations. h). Ligamentous deterioration or instability may be a factor. Other: e.g. Marfan syndrome, Obesity, and Joint infection.

### **IV. Pathophysiology**

Osteoarthritis is a degenerative joint disease that may cause gross cartilage loss and morphological damage to other joint tissues, subtler biochemical changes occur in the earliest stages of osteoarthritis progression. The water contents healthy cartilage is finely balanced by compression force driving water out and hydrostatic and osmotic pressure drawing water in [21]. Collagen fibers exert the compressive force, whereas the Gibbs-Donnan effect and cartilage proteoglycan creates osmotic pressure which tends to draw water in [22]. However, during onset of osteoarthritis, the collagen matrix becomes more disorganized and there is decrease in proteoglycan content with in cartilage. The breakdown of collagen fiber results in a net increase in water content [23]. This increase occurs because whilst there is an overall loss of proteoglycans (and thus a decreased osmotic pull). [24]. It is outweighed by a loss of collagen. [23]. Without the protective effect of the proteoglycans, the collagen fibers of the cartilage can become susceptible to degradation and thus exacerbate the degeneration. Inflammation of synovium (joint cavity lining) and the surrounding joint capsule can also occur, though often mild (compared to the synovial inflammation that occurs in rheumatoid arthritis). This can happen as breakdown products from the cartilage are released into the synovial space, and the cells lining the joint attempt to remove them. Other structures within the joints also be affected [25].

The ligament within the joint become thickened and fibrotic and the menisci can become damaged and wear away [26]. Meniscus can be completely absent by the time a person undergoes for joint replacement. New bone outgrowths, called "Spurs" or osteophytes, can form on the margins of the joints, possibly in an attempt to improve the congruence of the articular cartilage surfaces in the absence of the menisci. The subchondral bone volume increases and becomes less mineralized (hypo-mineralization) [27]. All these changes cause problem functioning. The joint in an osteoarthritic joint has been related to thickened synovium [28], and to subchondral bone lesions [28].

## V. Diagnosis

Diagnosis is made with reasonable certainty based on history and clinical examination [29]. X-rays may confirm the diagnosis. The typical changes seen on X-rays include: joint space narrowing, subchondral sclerosis (increased bone formation around the joint), subchondral cyst formation, and osteophytes [30]. Plain films may not correlate with findings on physical examination or with degree of pain [31]. Usually other imaging techniques are not necessary to clinically diagnose osteoarthritis. In 1990, the American College of Rheumatology, using data from a multi-center study developed a set of criteria for the diagnosis of hand osteoarthritis based on hard tissue enlargement and swelling of certain joints [32]. These criteria were found to be 92% sensitive and 98% specific for hand osteoarthritis versus other entities such as rheumatoid arthritis and spondyloarthropathies [33].

**Classification criteria:** A number of classification systems are used for gradation of osteoarthritis that includes:

- a). WOMAC scale, taking into account pain, stiffness and functional limitation [3].
- b). Kellgren-Lawrence grading scale for osteoarthritis of the knee. It uses only fractional radiography features.
- c). Tonnis classification for the hip joint, also using projection radiography features [35].
- d). Knee injury and osteoarthritis Outcome Score (KOOS) and Hip disability and osteoarthritis Outcome Score (HOOS) surveys [36].

Osteoarthritis can be classified into either primary or secondary depending on whether or not there is an identifiable underlying cause. Both primary generalized nodal osteoarthritis and erosive osteoarthritis (EOA, also called inflammatory osteoarthritis) are sub-sets of primary osteoarthritis. EOA is less common and more aggressive inflammatory form of osteoarthritis which often affects the distal interphalangeal joints of the hand and has characteristic articular erosive changes on x-rays [37].

**Differential diagnosis:** Related pathologies whose names may be confused with osteoarthritis include pseudoarthrosis. This is derived from the Greek roots pseudo, meaning “false” and arthr- meaning joint, together with the ending-osis used for disorders. Radiographic diagnosis results in diagnosis of a fracture arthritis within a joint, which is not to be confused with osteoarthritis which is degenerative pathology affecting a high incidence of distal phalangeal joints of female patients. A polished ivory like appearance may also develop on the bones of the affected joints reflecting change called eburnation [38].

## VI. Treatment

Lifestyle modification (such as weight loss and exercise) and analgesics are the mainstays of treatment. Acetaminophen (also known as paracetamol) is recommended first line with NSAIDs being used as add on therapy only if pain relief is not sufficient [39]. This is due to relative greater safety of acetaminophen [39]. For overweight people, weight loss may be an important factor [40]. Patient education has been shown to be helpful in the self-management of arthritis [40]. It decreases pain, improves function, reduces stiffness and fatigue, and reduces medical usage [40]. Patient education can provide on average 20% pain relief when compared to NSAIDs alone in patients with hip osteoarthritis [40].

**Role and benefits of exercise:** Light to moderate exercise may be beneficial with respect to pain and function in those with osteoarthritis of knee and hip [41]. These exercises should occur at least three times per week [42]. While some evidence supports certain physical therapies, evidence for a combined program is limited [43]. Providing clear advice, making exercises enjoyable, and reassuring people about the importance of doing exercises may lead to greater benefit and more participation [44]. There is not enough evidence to determine the effectiveness of massage therapy [45]. The evidence for manual therapy is inconclusive [46]. Functional, gait, and balance training have been recommended to address impairments of position sense, balance, and strength for individuals with lower extremity arthritis as these can contribute to higher rates of falls in older individuals [47]. For people with hand osteoarthritis exercise may provide small benefits for improving hand function, reducing pain, and relieving finger joint stiffness [48].

Lateral wedge insoles and neutral insoles do not appear to be useful in osteoarthritis of the knee [49]. Knee braces may help [50], but their usefulness has also been disputed [51]. For pain management heat can be used to relieve stiffness, and cold can relieve muscle spasm and pain [52]. Among people with hip and knee osteoarthritis exercise in water may reduce pain and disability, and increase quality of life in the short term [53]. Also therapeutic exercise programs such as aerobic and walking reduce pain and improve physical functioning for up to 6 months after the end of the program for people with knee osteoarthritis [54].

**Oral medication:** The pain medication paracetamol (acetaminophen) is the first line treatment for osteoarthritis [39]. However, a 2015 review found that acetaminophen to only have a small short term benefit with some laboratory concern of liver inflammation [55]. For mild to moderate symptoms effectiveness of acetaminophen is similar to non-steroidal anti-inflammatory drugs (NSAIDs) such as a naproxen, though for more severe symptoms NSAIDs may be more effective [39]. NSAIDs are associated with greater side-effects such as gastrointestinal bleeding [39]. Another class of NSAIDs, COX-2 selective inhibitors (such as celecoxib) are equally effective when compared to nonselective NSAIDs, and have lower rates of adverse gastrointestinal effects, but higher rates of cardiovascular disease such as myocardial infarction [56]. They are more expensive than non-specific NSAIDs [57]. Benefits and risks varies in individuals and need consideration when making treatment decisions [58], and further research comparing NSAIDs and COX-2 selective inhibitors is needed [59]. NSAIDs applied topically are effective for a small number of people [60]. The COX-2 selective inhibitor rofecoxib was removed from the market in 2004, as cardiovascular events were associated with long term use [61].

Failure to achieve desired pain relief in osteoarthritis after 2 weeks should trigger reassessment of dosage and pain medication [62]. Opioids by mouth, including weak opioids such as tramadol and stronger opioids are also often prescribed. Their appropriateness is uncertain, and opioids are recommended only when first line therapies have failed or contraindicated [61]. This is due to their small benefit and relatively large risks of side effects [63]. Oral steroids are not recommended in the treatment of osteoarthritis [64]. Use of antibiotic doxycycline orally for treating osteoarthritis is not associated with clinical improvements in function or joint pain [65]. Any potential benefit related to the potential for doxycycline therapy to address the narrowing of the joint space is not clear, and benefit is outweighed by the potential harm from side effects [65].

**Local application:** There are several NSAIDs available for local (topical) use, including diclofenac. A Cochrane review from 2016 concluded the reasonably reliable evidence is available only for use of local application of diclofenac and ketoprofen in people aged over 40 years with painful knee arthritis [66]. Transdermal opioid pain medications are not typically recommended in the treatment of osteoarthritis [63]. The use of topical capsaicin to treat osteoarthritis is controversial, as some reviews found benefit, while others did not [67,68].

**Injectable drugs:** Joint injection of glucocorticoids (such as hydrocortisone) leads to short term pain relief that may last a few weeks and few months [69]. Injections of hyaluronic acid have not produced improvement compared to placebo for knee arthritis [70], but increased the risk of further pain [70]. A 2015 Cochrane review found that intra-articular corticosteroid injections of knee did not benefit quality of life and had no effect on knee joint space; clinical effects one to six weeks after injection could not be determined clearly due to poor study quality [71]. Another 2015 study reported negative effects of intra-articular corticosteroids injections at higher doses [72], and a 2017, trial showed reduction in cartilage thickness with intra-articular triamcinolone every 12 weeks for 2 years compared to placebo [73]. A 2018 study found that intra-articular triamcinolone is associated with an increased in intraocular pressure [74].

**Surgical intervention:** If the impact of symptoms of osteoarthritis on quality of life is significant and more conservative management is ineffective, joint replacement surgery or resurfacing may be recommended. Evidence supports joint replacement for both knees and hips as it is both clinically effective and cost-effective [75,76]. Surgery to transfer articular cartilage from non-weight-bearing area to the damaged area is one possible procedure that has some success, but there are problems getting the transferred cartilage to integrate well with the existing cartilage at transfer site [77]. Osteotomy may be useful in people with knee osteoarthritis, but has not been well studied and it is unclear whether it is more effective than non-surgical treatment or other types of surgery [78]. Arthroscopic surgery is largely not recommended, as it does not improve outcomes in knee osteoarthritis and may result in harm [79,80]. For people who have shoulder osteoarthritis and do not respond to pharmaceutical approaches, surgical options include a shoulder hemiarthroplasty (replacing a part of the joint), and total shoulder arthroplasty (replacing the joint) [81].

**Glucosamine and Chondroitin:** The effectiveness of glucosamine is controversial [82]. Reviews found it to be equal or slightly better than placebo [83,84]. A difference may exist between glucosamine sulfate and glucosamine hydrochloride, with glucosamine sulfate showing a benefit and glucosamine hydrochloride not [85]. The evidence for glucosamine sulfate having an effect on osteoarthritis progression is somewhat unclear and if present likely modest [86]. The Osteoarthritis Research Society International recommends that glucosamine be discontinued if no

effect is observed after six months [87], and the National Institute of Health and Care Excellence no longer recommends its use [88]. The European Society for Clinical and Economic Aspects of osteoporosis and Osteoarthritis (ESCEO) recommends glucosamine and chondroitin sulfate for knee osteoarthritis [89]. Its use as a therapy for osteoarthritis is usually safe [90].

**Complimentary medicine and Acupuncture:** Avocado-soybean unsaponifiables (ASU) is an extract made from avocado oil and soybean oil. It does not appear to improve or maintain the health of joints [91]. A few high-quality studies of Boswelliaserrata show consistent, but small improvements in pain and function [91]. Curcumin, phytodolor and s-adenosyl methionine (SAME) may be effective in improving the pain [92,67,45,]. There is little evidence to supporting benefits for some supplements, including the Ayurveda herbal and Chinese herbal preparations, fish liver oil, ginger; Russian oil, omega 3 fatty acids; vitamins A,C,E, and D, collagen and willow bark. There is insufficient evidence to make recommendation about the safety and efficacy of these preparations [67]. While acupuncture leads to improvements in pain relief, this improvement is small and may be of questionable importance [93]. Waiting list-controlled trials for peripheral joint osteoarthritis do show clinically relevant benefits, but these may be due to placebo effects [94]. Acupuncture does not produce long term benefit [95].

## VII. Conclusion

Osteoarthritis is the most common type of arthritis affecting large population worldwide, with high hospitalization cost for osteoarthritis an average \$15,400 per stay. Change in lifestyle e.g. weight loss and exercise, and treatment with analgesics are the treatment of choice. Exercise plays an important role in prevention and therapy of osteoarthritis.

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HM.Iftikhar" .Osteoarthritis: pathophysiology, treatment update and role of exercise"IOSR  
Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 7, 2019, pp  
65 -72.