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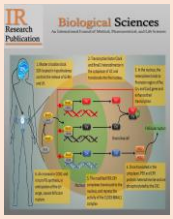

Osteoarthritis: Nutrition and lifestyle intervention

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ABSTRACT

Osteoarthritis (OA) is a chronic and common musculoskeletal disease that affects a significant portion of the population, particularly with age. It is characterized by cartilage degeneration and new bone formation at joint margins, leading to pain and stiffness. Although OA was once considered a passive process of joint wear and tear, it has now been recognized as a metabolically active process. Several factors can contribute to OA, including age, sex, ethnicity, genetic profile, hormonal status, bone mineral density, and lifestyle factors, such as obesity, joint injuries and deformities, sports participation, muscle weakness, and occupational factors. Currently, there is no known cure for OA. OA management focuses on reducing pain and maintaining or improving joint functions. Pharmacological and nonpharmacological treatments are available for OA. Nonpharmacological treatments include exercise, patient education, telephone support, and weight reduction, all of which are safe and effective interventions. However, dietary and lifestyle interventions have received insufficient attention. Therefore, this review aims to highlight the importance of nutritional and lifestyle interventions in the management of OA, particularly knee osteoarthritis.

Introduction

Osteoarthritis (OA) is a major cause of pain and disability among the general population. According to the Australian Burden of Disease Study [1], OA is Australia's tenth leading cause of the disease burden. It is also the fourth most common cause of years lost owing to disability. According to the 1995 National Health Survey,[2] about 6.4% of the Australian population had OA. It is the ninth most prevalent long-term condition reported in Australian patients. According to the 1997 World Health Report up to 40% of people over 70 years of age suffer from OA of the knee. Almost 80% of patients with OA have some degree of movement limitation, and 25% cannot perform activities of daily living.

OA is not a passive joint put-on-and-tear technique, but a metabolically lively technique. Its pathogenesis includes biomechanical and biochemical changes in the cartilage and subchondral bone, destroying cartilage [3] Cartilage is composed of water, collagen, and proteoglycans. Collagen provides energy and proteoglycans deliver distensibility and sufficient hydration. The cells of cartilage (chondrocytes) are responsible for the synthesis and catabolism of the

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extracellular matrix. In healthy cartilage, there's a dynamic balance between cartilage degradation via wear and its production by using chondrocytes [4]. But, this system will become disrupted in OA, mainly to increase degenerative changes inclusive of disruption of the collagen community and depletion of proteoglycans, mainly to the breakdown of cartilage that is followed by means of an abnormal bone-transforming repair system, which leads to the formation of subchondral cysts and osteophytes. The synovial infection produces accelerated levels of cytokines, including interleukin 1 (IL-1) and tumor necrosis factor-alpha (TNF-α), which stimulate metalloproteinase and nitric oxide manufacturing, inducing cartilage degradation. Interleukin 6 (IL-6) in aggregate with mechanical stresses additionally induces cytokine receptors that bind to IL-1 and TNF-α inside the cartilage, inflicting further destruction.

Clinical features

The main symptoms of OA are pain and joint stiffness, which are exacerbated and relieved by exercise and rest, respectively. This may lead to a sedentary lifestyle, depression, and sleep problems, especially in the elderly. The pain can range from poorly localized, asymmetric, and episodic pain in the early course of the disease to an increase in severity and frequency of pain as the disease progresses. Stiffness is common in affected joints. It usually occurs in the morning or after inactivity [5]. Joint crepitus, swelling, inflammation, synovitis, and joint effusion may also be present but swelling, Inflammation, and joint effusion are often observed in more advanced stages of OA. Inflammation, if present, is usually mild and localized to the affected joint. Eventually, joint mobility may be limited, which can lead to joint deformity [6].

Diagnosis

The diagnosis is based on a patient's history of symptoms, physical examination, and radiographic assessment. Physical findings included tenderness on pressure, bony enlargement, crepitus on motion, and a limited range of motion. The radiographic changes associated with OA include joint space narrowing, increased subchondral bone density, and osteophytes' presence [7]. However, the correlation between the clinical presentation of the disease and radiographic changes varies considerably between patients. Some patients with radiographic evidence of advanced joint degeneration have minimal symptoms, whereas others with minimal radiographic changes have severe symptoms. Blood tests are not useful for diagnosis because there are no associated laboratory test abnormalities for OA [8].

Risk factors

The development of OA is due to the interaction of both systemic and local biomechanical factors.8 Systemic factors operate by influencing a person's predisposition to develop the disease, making the cartilage more vulnerable to daily injuries and less likely to repair, whereas local biomechanical factors result in abnormal biomechanical loading at specific joint sites. Once systemic factors are in place, local biomechanical factors then begin to play a role in the joint breakdown [9]. Systemic factors included age, sex, ethnicity, genetic profile, hormonal status, bone mineral density (BMD), and nutritional factors. Although hormonal status, BMD, and nutritional factors are alterable, age, sex, ethnicity, and genetic profile are unchangeable. Local biomechanical factors include obesity, joint injury, and deformity, participation in sports, muscle weakness, and occupational factors. Thus, they are potentially preventable. Ultimately, all these factors will determine the site and severity of OA and can influence either the development of OA or its subsequent progression [10].

Age and gender

OA prevalence of OA is based on age and sex. OA increases with age, and women have a higher prevalence of OA than men. Before 50 years of age, men have a higher prevalence than women; however, after 50 years, women have a greater prevalence and incidence of OA than men. The sex difference in prevalence increased with age. Incidence and prevalence of OA then level off or decline in both genders at about 80 years.9 The aging process increases the propensity for osteoarthritis through cartilage calcification, reduced chondrocyte function, reduced joint proprioception, and increased laxity around the joints [11].

Obesity

Obesity is the strongest modifiable risk factor of OA. Literature has shown that being overweight is strongly and positively associated with the development of knee OA [12–13]. Moreover, being overweight increases the risk of progression of knee OA [14,15]. However, the increased risk of knee OA among overweight persons is greater in women than in men. The relationship between obesity and hip OA is inconsistent. Some studies show no relationship [16–18]. They do reveal that the load on the hip with excess weight is substantially lower than the load on the knee. Obesity may act by increasing mechanical stress in weight-bearing joints and increases the risk of developing progressive OA [19].

Bone-mineral density

An inverse relationship between osteoporosis and OA has been discovered, in which persons with osteoporosis have a decreased occurrence of OA, and persons with OA have a reduced occurrence of osteoporosis. Cross-sectional studies have linked OA with high bone density [20]. In the Study of Osteoporotic Fractures,{21} women with hip OA had an 8% to 12% increase in bone density compared to women without OA. Women with knee OA also appear to have relatively high bone density [22]. Furthermore, a study found that women with knee OA maintained or increased their bone-mineral density over 3 years of follow-up when compared with women without knee OA [23]. However, although high bone-mineral density increases the risk for the development of OA, it may be a protective factor for the progression of established OA mainly due to its effect on reducing the risk of joint space loss [24].

Hormones

The high incidence of OA in women after age 50, which is about the age of menopause, suggests that estrogen loss may play a role in causing the disease.6 However, the literature regarding hormone replacement therapy and OA is contradictory [25]. Several studies have reported a reduction in the risk of knee and hip OA with hormone-replacement therapy (HRT) [26–30]. All five studies demonstrated an inverse relationship between HRT and OA prevalence. Moreover, the incidence of knee and hip OA is significantly reduced among long-term users in both the Framingham Study and the Study of Osteoporotic Fractures. In contradiction, HRT leads to higher bone density, which increases the risk of knee and hip OA. Studies have also reported a positive association between OA and estrogen use [31]. This indirect effect of estrogen may counteract the protective effect of estrogen on OA, as suggested by other studies. These conflicting reports suggest the need for additional research to elucidate the mechanisms involved.

Occupational factors

A systematic review of occupational risk factors and knee and hip OA was published in 1997 [32]. Of the 123 studies conducted on risk factors for OA, 17 provided a comparison group and related OA to occupational factors. This review has the following conclusion: (1) a consistently positive relationship exists between occupational exposure and knee OA in men, (2) the evidence suggesting a relationship between knee OA and occupational exposure in women was inconclusive, (3) a consistently positive but weak relationship exists between occupational exposure and hip OA in men, and there is a significant relationship between occupational kneeling and osteoarthritis. From 1994 onwards, five studies were identified [33]. The characteristics of these studies are listed in **Table 1**. Three studies concerned the knee, one concerned the hip, and one concerned both joints. Four studies were case-control studies and one was a cross-sectional study. The results of these studies demonstrate a positive association between several physical activities with joint exposure and OA. However, the results differed somewhat between the sexes. Two studies found that kneeling and squatting were risk factors for knee OA in men [34]. Climbing stairs was found to be a risk factor for knee OA in men in two studies. For women, one study found that kneeling, squatting, and walking were risk factors for knee OA. Climbing stairs was also found to be a risk factor for knee OA in women in three studies. Two studies found that lifting heavy objects was a risk factor for knee OA in both men and women [35,36]. Two studies found that floor layers, construction workers, forestry workers, and farmers were more likely to develop knee OA. One study found that climbing stairs was a risk factor in men and lifting heavy objects was a risk factor in women. Another study found that lifting heavy objects was also a risk factor and that sitting was a protective factor in women [37]. The results of these studies provide further evidence to support the role of occupational physical activities in the occurrence and progression of OA.

Sports participation and trauma

Participation in certain competitive sports increases the risk of OA. Sports activities that demand high-intensity, acute, and direct joint impact as a result of contact with other participants, playing surfaces, or equipment can increase the risk of OA, such as football and soccer. Men with a history of knee injury are 5–6 times more likely to develop OA.OA develops at a younger age and is likely to lead to lengthy disability and unemployment.

Muscle weakness

Quadriceps muscle weakness is common in patients with knee OA. It is generally thought to be the result of disuse and atrophy as a result of minimal use of the painful limb. However, in patients with knee OA who have no joint pain and whose quadriceps muscle mass is not diminished, quadriceps weakness can be evident, even if the quadriceps muscle mass is normal or increased.

Genetics and ethnicity

Table 1. Assessment of occupational and osteoarthritis treatment.

Assessment Criteria	Treatment Options
Severity of symptoms	- Non-pharmacological interventions (e.g., exercise, physical therapy) - Medications (e.g., nonsteroidal anti-inflammatory drugs, analgesics) - Injections (e.g., corticosteroids, hyaluronic acid) - Surgical interventions (e.g., joint replacement)
Functional limitations	- Assistive devices (e.g., braces, splints) - Occupational therapy - Pain management techniques (e.g., heat/cold therapy, transcutaneous electrical nerve stimulation)
Work-related factors	- Ergonomic modifications (e.g., adjustable workstations, proper lifting techniques) - Job accommodations (e.g., reduced workload, modified duties) - Vocational rehabilitation
Disease progression	- Regular monitoring and follow-up - Treatment adjustments as necessary - Referral to specialists (e.g., rheumatologist, orthopedic surgeon)
Patient preferences	- Shared decision-making with the patient - Considering individual goals and priorities - Tailoring treatment approach accordingly

There are many genes linked to OA, and parents of children with early-onset OA are at a higher risk of developing it. Twin studies suggest that there is a strong genetic susceptibility to the disease. OA is more common in Europeans than in Asians, and hand OA is more common in European women than in women of Afro-Caribbean descent.

Nutritional factors: vitamin supplements

There are multiple mechanisms through which nutrients can affect the initiation or progression of OA. Various nutritional factors may influence OA in at least four ways: protection from excessive oxidative damage, modulation of the inflammatory response, cellular differentiation, and biological actions related to bone and collagen synthesis.38 Antioxidants, including vitamins A, C, and E, have been identified as having a potential for antioxidant activity in OA. Vitamin D may also play an important role in OA through bone mineralization, cellular differentiation, and proprioception responses. There have been very few studies of nutritional factors in OA and none have demonstrated any influence on incident knee OA [38].

There is no protective association between dietary or supplemental retinal or β-carotene on either incident OA or progression of OA reported in the literature. In the longitudinal Framingham Knee OA Cohort Study threefold reduction in risk of OA progression was observed in participants in the middle tertile (adjusted OR = 0.3, 95% confidence interval [95% CI] 0.1–0.8) and highest tertile (adjusted OR = 0.3, 95% CI 0.1–0.6) of vitamin C intake. Participants in the highest tertile of vitamin C intake also had a reduced risk of developing knee pain (adjusted OR = 0.3,95% CI 0.1–0.8) during the study. A reduction in the risk of OA progression was also observed for β-carotene (adjusted OR = 0.4, 95% CI 0.2–0.9) and vitamin E intake (adjusted OR = 0.7, 95% CI 0.3–1.6) but was less consistent, in that the β-carotene association diminished substantially after adjustment for vitamin C, and the vitamin E effect was seen only in men. However, no significant association was observed between incident knee OA and vitamin C [39].

Again, in the Longitudinal Framingham Knee OA Cohort Study, the risk for progression of knee OA increased from threefold to fourfold for participants in the middle and lower tertile for both vitamin D intake (odds ratio for the lower compared with the upper tertile, 4.0 [95% CI,1.4–11.6]) and serum levels of vitamin D (odds ratio for the lower compared with the upper tertile,2.9 [CI, 1.0–8.2]). However, no effect was observed for vitamin D status on the risk of incident knee OA. The authors concluded that low serum concentration and low intake of vitamin D both seem to be associated with an increase in the risk of knee OA progression [40]. A few years later, Lane and colleagues found a threefold increase in the risk of incident hip OA in participant subjects in the middle (odds ratio [OR] 3.21, 95% CI 1.06, 9.68) and lowest (OR 3.34, 95% CI 1.13, 9.86) tertile for serum level of 25-vitamin D, providing further evidence that vitamin D status may protect against osteoarthritis [41]. Vitamin D deficiency is an independent predictor of falls in older people and is linked to fragility fractures [42]. There have been few clinical studies on vitamin E activity in patients with OA. A study randomly assigned 29 OA patients to treatment with either tocopherol 600 mg/d for 10 d or a placebo [43]. The authors found that 52% of those receiving vitamin E had a significant reduction in pain compared to 4% of those receiving a placebo. Unfortunately, nutritional modalities are underutilized in management algorithms. Several large and well-designed clinical nutritional studies are required to determine the mechanisms involved.

Management

There is no known cure for OA. The dreams of OA management are in particular discount on pain, preservation or improvement of joint function, and universal development in a health-associated fine of life [44]. OA control consists of an aggregate of non-pharmacological, pharmacological, and Complementary therapies.

Nonpharmacological treatment

The nonpharmacological remedy is the important thing for OA control and has to be maintained throughout the remedy length, consistent with the American College of Rheumatology [45]. Those treatment paradigms consist of workout, affected person schooling and guide, weight reduction, mechanical non-pharmacological and complementary treatments must be utilized earlier than the graduation of pharmacological treatment workout has to be the main non-pharmacological intervention for patients with arthritis. Workout is the best and cheaper intervention in OA [46]. The goals of an exercise application are to preserve a variety of movements, muscle power, and well-known health. Therefore, there are three classes of healing exercises: range of movement and versatility workout, muscle conditioning and strengthening exercises, and cardio cardiovascular exercise. Forty-four aerobic sporting events together with swimming, on foot, and water aerobics can improve cardiovascular health, sense of properly-being, and intellectual characteristics, and decrease disability, depression, and tension. Resistance exercising that will increase muscle strength can enhance joint characteristics and mobility. currently, the Yankee Geriatrics Society published suggestions on exercising prescriptions for older adults with OA pain [47] protection of quadriceps electricity is critical in knee OA. Quadriceps weakness is usually found in knee OA, suggesting that the weakness may be because of muscle dysfunction and that a weak spot may be a dangerous issue for ailment progression [48]. Therefore, a workout directed in the direction of growing quadriceps strength and strengthening the quadriceps muscle mass is useful. a systematic evaluation of randomized managed trials on the effectiveness of exercise remedy in patients with hip or knee OA concluded that workout therapy changed into powerful in these patients [49] 11 trials have been reviewed [50–58]. Ache, self-mentioned incapacity, observed disability in taking walks, and the affected person's worldwide evaluation. impact was used as the outcome measure. The result of the overview demonstrated beneficial brief-term results of exercising therapy in patients with knee OA and, to a lesser quantity, in patients with hip OA (one take a look at). there was a small beneficial effect of workout remedy on each self-pronounced incapacity and discovered incapacity in walking, small-to-mild, useful impact on pain, and mild-to-awesome beneficial effect in step with the affected person's worldwide assessment of impact. however, there were no records available on the lengthy-term effects of exercise remedies. comparison of the effectiveness of different exercise packages remained inconclusive. Recently, several research has verified the effectiveness of exercise therapy for the treatment of OA, and the results of a number of them are quite exciting and worth reviewing [59–64]. The characteristics of these studies were also proven in Desk 10.2. One examine determined that low-intensity biking (40% of heart price reserve (HRR) for 10 weeks turned into as powerful as high-intensity biking (70% of HRR) in enhancing features and gait, reducing pain, and growing cardio capacity in older subjects cycling did no longer increase acute ache in either group. some other stud randomly allocated aged sufferers (suggest age,73 years) with knee OA to a revolutionary, domestic-based exercise application, consisting of resistance and strengthening, or to a managed software of range-of-movement sports without resistance all businesses were given general dosing of NSAIDs and allowed to avoid analgesia using paracetamol. Even though both groups stepped forward from baseline at some stage in the 8-week study, those in the progressive exercise program using common items at home showed a greater reduction in activity-related pain and greater improvement in mobility and walking measures. There appears to be a beneficial short-term effect of exercise therapy in patients with a knee. OA, and to a lesser extent in patients with hip OA. Further research is needed to study the long-term effectiveness of exercise therapy, the effectiveness of exercise therapy in patients with hip OA, and to compare the effectiveness of different exercise programs.49 Patient education is important for patients with OA and their families so that they develop an understanding of the disease and how to avoid major disability by slowing disease progression. Psychological support is essential.65 Patient education has been shown in randomized controlled trials to be cost-effective and associated with reduced pain and improved quality of life [65–71] shows the characteristics of randomized controlled trials on patient education in the management of OA. A meta-analysis comparing the effects of patient-education interventions and NSAIDs treatment on pain and functional disability in patients with OA identified ten controlled trials [72].

The authors concluded that patient education provided additional benefits that were 20%–30% as great as the effects of NSAID treatments for pain relief in OA. The Arthritis Foundation Self-Management Program is one such program. These

programs include information about disease processes, medications, and their actions and reactions, together with goal setting for exercises and. pain-management strategies [73]. Telephone support is another cost-effective non-pharmacological approach for patients with OA.45 Telephone support has been shown to benefit in reducing pain and improving functional status without a significant increase in costs. Social support through telephone counseling demonstrated significant improvements in functional status, reduced health care costs, and total health status as measured by the Arthritis Impact Measurement Scales (AIMS), Sickness Impact Profile (SIP), and Life Change Events (LCE) [74–78]. Weight reduction is a crucial method because weight benefit is a crucial modifiable threat to knee OA. The ACR recommendations advise that obese patients with hip or knee OA lose weight. Research has shown that weight loss can gradual development and display improvement in signs of knee OA [79–81]. The Framingham observation proved that modest weight reduction decreased the risk of developing symptomatic knee OA in girls. Eleven in the control of OA, weight discounts must play a key function, as should workout. Pain and incapacity can preclude ordinary exercising; consequently, weight loss can also be carried out through dietetic consultation, food diaries, cognitive behavior amendment, and decreased energy intake. Mechanical aids, along with shock-absorbing footwear, reduce the effect of the load on the knee joint. Proprioception is advanced, pain is reduced by heel wedging, and on-foot sticks can provide safe and functional help to the motion. Unfortunately, there may be the most effective anecdotal and ancient evidence of gain due to the paucity of well-designed research. Physiotherapy and occupational remedy evaluation are encouraged for functional boundaries [82]. Acupuncture is a component of the Chinese healthcare system and can be traced back a minimum of 2000 years. The overall principle of acupuncture is primarily based on the premise that there are patterns of strength flowing through the body that might be crucial for fitness. Acupuncture is thought to correct this imbalance within the float of this energy [83]. The result of a systematic overview eighty-four on the effectiveness of acupuncture as a complementary treatment for OA is inconclusive. The traits of some of the studies [84–90]. If the evidence from randomized controlled trials is considered, a subsequent conclusion may be drawn. Acupuncture is not superior to sham needling (sham needling is the needling of non-acupuncture factors and represents an attempt to discover a credible 'placebo' for acupuncture) in reducing aches from OA. Both methods reduced the number of aches with similar results. This may mean that sham-needling has particular outcomes similar to those of acupuncture, or that both methods are associated with large and similar nonspecific results. A greater recent systematic review of the effectiveness of acupuncture for knee OA identified seven trials. ninety-one of these trials had proven that there was robust evidence that actual acupuncture changed into greater effective than sham acupuncture for knee OA aches. but, from a practical perspective, there was inconclusive evidence that real acupuncture was more effective than sham acupuncture [91] Therefore, there is moderately strong evidence from controlled trials to support the use of acupuncture as adjunctive therapy for OA.

Pharmacological treatment

Pain is the primary symptom of OA, and a couple of medicines are needed to alleviate the pain and enhance its features. In 2000, the Yankee University of Rheumatology (ACR) forty-five and the ECU League of Institutions of Rheumatology (EULAR) [92] published pointers for using pharmacological remedies for hip and knee OA. due to the fact then, an updated systematic assessment, epidemiologic research, and scientific trials were posted. The outcomes of those reviews, studies, and trials boost problems concerning the validity of ACR and EULAR recommendations. Pharmacological treatments include paracetamol, NSAIDs, topical analgesics, COX-2 inhibitors, intra-articular Treatment plans, and surgical treatments. Paracetamol is the favored preliminary treatment, with doses of up to one g four instances a day. It is far more secure and well-tolerated by older companies. Both the ACR and the EULAR guidelines advocate it as preliminary therapy, and many elderly sufferers have commonplace comorbidities that vicinity them at the chance of side effects and drug interactions from other medicines. Paracetamol on the therapeutic dosage stated has a brilliant protection report. It has a slender healing and toxicity variety; therefore, a modest overdose may be associated with hepatic toxicity [93]. Different studies advocate that paracetamol is preferred over nonsteroidal anti-inflammatory drugs (NSAIDs) in treating patients with persistent liver disorders. Paracetamol is thought to inhibit imperative cyclo-oxygenase (COX) with only a vulnerable effect on peripheral prostaglandin synthesis [94,95]. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been found to have equal efficacy to that of paracetamol in most patients. Both the ACR and EULAR recommendations stated that patients with OA who fail to respond to full doses of paracetamol should be considered candidates for NSAIDs [96]. There is good evidence for the efficacy of NSAIDs compared to both paracetamol and placebos in patients with OA. However, there is no consistent evidence suggesting that one NSAID is superior to another in relieving pain in patients with OA [97–99]. Traditional nonselective NSAIDs are associated with

an increased risk for serious upper gastrointestinal complications, including bleeding and perforation; nephrotoxicity, including acute renal insufficiency; and congestive heart failure and adverse reproductive outcomes [100]. The use of topical analgesics, such as capsaicin cream, is appropriate for persons with mild-to-moderate knee OA pain who do not respond to paracetamol and do not wish to receive systemic therapy. A thin film of capsaicin cream should be applied to symptomatic joints four times daily. To be effective, it generally requires consistent use over time. Topical NSAIDs are used by patients who do not wish to use or cannot tolerate NSAIDs systemically. There is some systemic absorption but no excess risk of upper GI bleeding [101]. Cyclooxygenase-2 (COX-2) inhibitors celecoxib and rofecoxib should be used for patients with OA who are at increased risk of serious upper gastrointestinal complications and where NSAIDs are contraindicated. Both celecoxib and rofecoxib are more effective compared to placebo, and comparable in efficacy to NSAIDs. The results of two large long-term outcome studies, the Celecoxib Long-term Arthritis Safety Study (CLASS) [102] and the Vioxx Gastrointestinal Outcomes Research Study (VIGOR) [103], found that both celecoxib and rofecoxib are associated with a significantly lower risk for symptomatic and complicated gastro duodenal ulcers. These data suggest an advantageous safety profile in comparison to non-selective NSAIDs. Moreover, they appear to be better tolerated at the doses recommended for the treatment of OA, and neither has a significant effect on platelet aggregation or bleeding time. Therefore, they are preferable to non-selective NSAIDs for OA patients with an increased risk of upper gastrointestinal complications. However, as with non-selective NSAIDs, COX-2 inhibitors can cause renal toxicity. [104] An alternative to COX-2 inhibitors is the use of non-selective NSAIDs with gastroprotective agents. Because the adverse upper GI events attributed to NSAIDs in the elderly are dose-dependent, non-selective NSAIDs should be started at low analgesic doses and increased to full anti-inflammatory doses only if lower doses do not provide adequate symptomatic relief. If the patient is at an increased risk of a serious upper GI adverse event, gastroprotective agents should be used even if non-selective NSAIDs are administered at a low dosage. Regular monitoring of elderly patients taking COX-2 inhibitors is necessary for intercurrent illness and comorbidities, and new prescriptions that may reduce the safety of intra-articular therapy, in the form of an injection of corticosteroids, are indicated for acute knee OA pain, especially in patients with signs of joint inflammation and joint effusion. Although it is effective in reducing pain, the effect is short-term. Clinical trials have shown that the improvement of symptoms is marginally better than placebos and usually does not last for more than a few weeks. However, there is a likelihood of infection and joint damage owing to repeated injections. Therefore, no more than four injections should be administered in one year because of the possibility of joint damage. Intra-articular injection of hyaluronan is used only for patients with knee OA. Hyaluronan is a naturally occurring substance in synovial fluid. In patients with OA, there is a reduced concentration of hyaluronan, resulting in low-viscosity synovial fluid and an increase in cartilage loading. Viscous injections are intended to substitute hyaluronan, normally found in the joint. The results of randomized controlled trials suggest superior pain relief to placebos and comparable with, or greater than, that with intra-articular corticosteroid injection but with a longer duration of action. Surgical treatment, such as total joint replacement, is indicated for patients with moderate-to-severe pain and functional impairment who fail to respond to medical therapy. In a study of the outcome of knee replacement, patients reported having significant and persistent relief of pain, improved physical function, and satisfaction for at least 2 to 7 years after surgery [105]. Knee replacement procedures have also been shown to be cost-effective [106,107]. However, the timing of the surgery is important. One study found that subjects with poor functional status at the time of surgery had worse outcomes than those who underwent surgery at an earlier stage [108]. COX-2 Inhibitors. COX-2 inhibitors are contraindicated in patients with OA who are at risk of ischemic heart disease and stroke.

Complementary therapies

McAlindon and Felson have demonstrated that OA subjects whose diets are richer in antioxidants, such as vitamin C, vitamin D, and green tea, have a slower progression of joint space narrowing on x-ray over long-term follow-up [109]. Whether these agents can alleviate the symptoms of arthritis or prevent joint damage remains unclear. However, well-designed prospective randomized controlled studies are needed to understand the mechanisms involved. Omega-3 long-chain polyunsaturated fatty acids (n-3 LC PUFA) dietary supplements have been shown to significantly improve tender joint scores and duration of early-morning stiffness in OA [110,111]. The mechanism involved in n-3 LC PUFA supplementation is based on the fact that dietary n-6 and n-3 fatty acids are the primary modulators of the lipid composition of membrane phospholipids. Fatty acids in the membrane phospholipids are the precursors of prostaglandins and eicosanoids, which are important mediators of inflammation, cytokine synthesis, and cell communication [112]. The modern Western diet contains an excess of n-6 fatty acids and a low level of n-3 fatty acids [113,114]. Supplementation of n-3 LC PUFA in

conjunction with a high dietary intake of n-6 fatty acids is not effective in increasing cellular levels of n-3 LCPUFA [115,116]. The key to supplementation is to limit the intake of n-6 fatty acids in the diet so that the n-6 to n-3 balance approaches.There is considerable variation in the activities of prostaglandins and eicosanoids derived from n-6 fatty acids and n-3 LCPUFA. The N-6-derived eicosanoids exhibit proinflammatory activity, potent chemotactic activity, vasodilation, and increased vascular permeability. n-3 LC PUFA-derived prostaglandins and eicosanoids are anti-inflammatory, much less active, and poorly synthesized. Thus, n-3 LC PUFA supplementation can alter the balance of n-6 to n-3 prostaglandins and eicosanoids to produce decreased inflammatory activity [117]. Fish oil supplementation at the rate of 20 to 40 mg/kg body weight/day, in conjunction with a diet low in n-6 PUFA and saturated fat, leads to significant incorporation of N-3 LC PUFA in membrane phospholipids.110 n-3 LCPUFA in membrane phospholipids suppress the production of inflammatory cytokines such as IL-1 and TNF-α, which induce cartilage degradation and destruction. This study suggests the need for further clinical trials on nutritional regimens for OA. A systematic review of randomized controlled trials on the effectiveness of herbal medicines or symptomatic slow-acting drugs for OA (SYSODOA) in the treatment of OA [118]-included 10 trials and 2 systematic reviews of 11 different herbal medicines. The review found promising evidence for the effective use of some herbal preparations in reducing pain and improving mobility, function, and disability in OA. There is moderately strong evidence of the use of capsaicin cream [119,120] to relieve OA symptoms. There is promising evidence for avocado and soybean unsaponifiable (ASU) [121,122]. There is weak evidence for Reumalex, [123] willow bark, [124] common stinging nettle,[125] and the Ayurvedic herbal preparation. Articulin-F [126] However, there is no evidence of clinically significant benefits for ginger extract [127]. “Weak evidence” describes herbs with a single randomized controlled trial with significant results; “promising evidence” describes herbs with two favorable trials; “moderately strong evidence” describes herbs with three or more favorable trials. Capsaicin is derived from hot chili peppers. It is used as a topical analgesic for various conditions that are characterized by pain. The results of a meta-analysis and an RCT120 for the treatment of OA with topically applied capsaicin have shown that capsaicin cream can significantly reduce.Pain associated with OA. Avocado and soybean unsaponifiable (ASU) are extracts of avocado and soya bean made of unsaponifiable fractions of avocado oil and soybean oil. The results of two RCTs showed that ASU could significantly improve hip or knee OA symptoms and reduce NSAID consumption. In addition, there is evidence suggesting that some herbal medicines reduce the consumption of NSAIDs, and the incidence of adverse effects of these herbal medicines is low, suggesting that they are relatively safe. In conclusion, some herbal medicines have proven to be effective and relatively safe for the treatment of OA. Therefore, they may be employed to lower NSAID consumption and thus reduce the adverse effects of NSAIDs, particularly when comorbidities are involved. Glucosamine sulfate and chondroitin sulfate are nutritional supplements available as over-the-counter preparations that are used to relieve musculoskeletal symptoms. Glucosamine is an amino sugar precursor to glycosaminoglycans that form a component of articular cartilage proteoglycans, and chondroitin sulfate is a glycosaminoglycan found in articular cartilage. A meta-analysis and quality assessment of 15 double-blind, randomized, placebo-controlled trials of glucosamine and chondroitin sulfate concluded that these supplements are likely to be effective for the symptomatic management of OA. However, the authors were reluctant to draw any firm conclusions because of insufficient information about the study designs and potential for publication. bias, as most of the trials are industry supported [128]. Characteristics of studies on glucosamine sulfate [129–136] and chondroitin sulfate [137–140]. A systematic review was studied. Sixteen double-blind, randomized controlled trials involving the use of glucosamine for the treatment of OA. This review concludes that glucosamine is effective and safe for OA. All but one of the 13 studies in which glucosamine was compared with placebos proved glucosamine to be superior in pain relief [141]. A recently published randomized, double-blind, placebo-controlled trial [142] is the first long-term study to evaluate the efficacy of glucosamine sulfate on OA. It has been shown that glucosamine has a beneficial effect in retarding degenerative joint changes and improving the symptoms in patients with knee OA. This study followed 212 patients with knee OA for 3 years. They were randomly assigned to receive either 1500 mg of oral glucosamine sulfate or placebo once daily for 3 years. The main outcome measures were joint-space width, assessed by radiographs, and symptoms scored by the.Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index. The 106 patients. receiving glucosamine sulfate had a non-significant mean joint-space loss of 0.06 mm (95% CI,0.22–0.09). The 106 patients receiving placebos had progressive joint-space narrowing, with a mean joint space loss after 3 years of 0.31 mm (95% CI, 0.48–0.13). Symptoms were significantly improved in the glucosamine sulfate group compared with the placebo group, with significant improvements in pain and physical function. The authors concluded that the long-term combined structure-modifying and symptom-modifying effects of glucosamine sulfate suggest that it could. be a disease-modifying

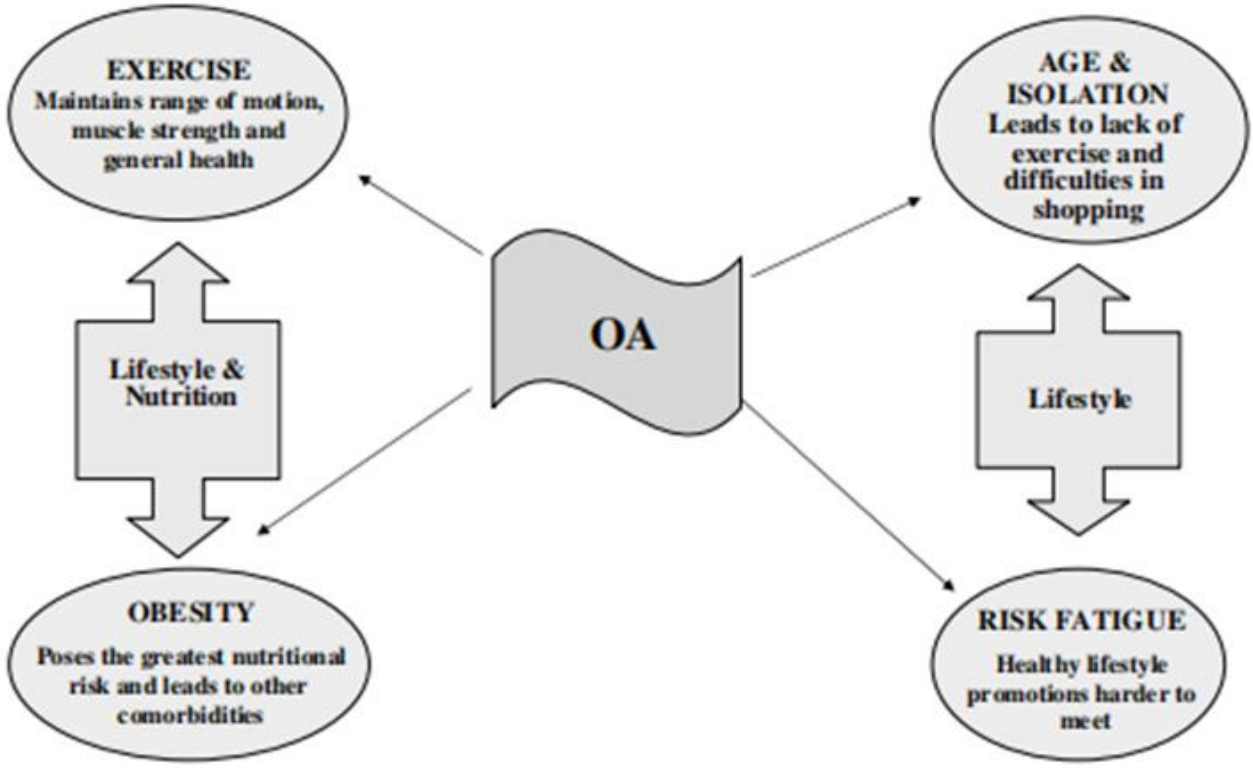

Figure 1. Figure Osteoarthritis impacts, and effects of nutrition and lifestyle. *Credit: Handbook of Nutraceuticals and Functional Foods*

agent in OA. Possible mechanisms of action of glucosamine and chondroitin sulfate include stimulating proteoglycan synthesis in the articular cartilage and inhibiting the enzymes that destroy the cartilage. Therefore, glucosamine may act to relieve symptoms, increase cartilage production, and delay OA progression [143].

Lifestyle and nutritional interventions

The whole picture OA is primarily a condition of an aging, overweight population, and evidence suggests that increased body weight can accelerate the development of OA. The prevalence of OA is likely to increase in Western societies as overweight people and obesity become more common. The association between obesity and the increased incidence of OA has been documented. What is unclear is whether patients with OA are predisposed to obesity due to reduced physical activity or whether obesity contributes to the development of OA. Prospective longitudinal studies have demonstrated that being overweight or obese precedes the development of OA of the knee. In a recent descriptive cross-sectional study, 50% of subjects were obese (BMI >30), and 75% of subjects were assessed as having moderate to high nutritional risk, despite their obesity. This assessment was performed using the Australian Nutrition Screening Initiative (ANSI) tool. Approximately 33% of subjects reported eating alone, changes in eating habits causing weight change in the past 6 months, and 25% indicated that their OA interfered with shopping, preparing and. consuming food. Overweight people and obese are associated with greater risks of high blood pressure, coronary heart disease, type II diabetes mellitus, and some cancers. These comorbidities and the

pharmaceutical load add to the problem of OA in the elderly population. Important aspects of OA management should start with patient education, encouraging a well-balanced diet, weight loss, exercise, social interaction, and referral for routine nutritional assessment and advice [144, 145]. Physical activity levels (PAL) involving joint-specific exercises reduce pain and improve function in patients with knee OA. Exercise can involve joint-specific strength exercise, motion exercise, and general aerobic conditioning, which can be offered in group activities or by a home-based, self-directed program. The effectiveness of home-based exercise for knee OA has been demonstrated, with reduced pain scores and improved function. Aerobic and isokinetic Exercise has been effective in reducing pain and improving gait and function. Health promotion campaigns encourage individuals to increase their PAL, lose weight, lead a healthy lifestyle, and avoid risky behavior. Research suggests that as weight increases, so do the health risks. The promotion of healthy lifestyles and reduction of risky behavior can cause "risk fatigue" by asking too many people in a climate where social trends run contrary to health messages, making compliance more difficult (**Figure 1**} Figure

Osteoarthritis impact and effects of nutrition and lifestyle.

Conclusion

For optimal results, OA management requires a cohesive, multidisciplinary, and individualized approach. Patients need to be involved in their management plan, and as the disease progresses or comorbidities develop, the management plan may need to be revised. These patients may be at risk of poor nutritional health despite being overweight, as obesity often masks the nutritional risk. Weight loss can ameliorate OA symptoms and slow the disease progression. Routine nutritional assessments and dietary advice should be available for all patients with OA. Continued research is needed to evaluate the efficacy of interventions to treat OA, particularly in the older population, which has varied responses to many current treatment paradigms. Osteoarthritis impacts and effects of nutrition and lifestyle.

Contribution of authors

Not applicable

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Conflict of interest

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