

**Literature Review**

**The effectiveness of high-intensity interval training as a treatment option in symptomatic knee osteoarthritis**

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**ABSTRACT**

One of the most often musculoskeletal disorders in adults is osteoarthritis, which occurs due to degenerative processes in the joints, through wear and tear mechanism, especially in the articular cartilage. The treatment options for osteoarthritis are classified into symptomatic therapy and disease modification therapy. However, many people who suffer from osteoarthritis have limitations in their daily activities, thus preventing them from modifying their lifestyles. Many types of exercise exist, yet the best exercise for symptomatic osteoarthritis hasn't been found. In daily practices, Moderate Intensity Continuous Training (MICT) is the most recommended and the type of exercise commonly performed by patients with OA because MICT has a range of cardiovascular health benefits and maintains body weight. However, MICT may not provide enough stimulus to increase lower muscle mass and strength, articular changes that might contribute to the pain, stiffness, and functional limitations seen in patients with knee OA. Some new studies found that High-Intensity Interval Training (HIIT) is more efficient than MICT as a classic exercise after six to eight weeks of exercise. HIIT in symptomatic osteoarthritis can significantly improve a patient's fitness, visceral fats, and symptoms. HIIT can be a treatment option in resolving symptomatic knee osteoarthritis.

**Keywords:** high-intensity interval training, HIIT, osteoarthritis, exercise, treatment options  
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## INTRODUCTION

One of the most often musculoskeletal disorders in adults is osteoarthritis. The global prevalence of osteoarthritis is 16%, and the incidence is 203 per 10,000 people each year of knee osteoarthritis.<sup>1</sup> These incidence increase as the age increased. According to the United Nations, 703 million people aged 65 years or more are having this condition in the world. The United Nations also predicted that by 2050, the population of these numbers would double, reaching about 1.5 billion people.<sup>2</sup> These will make osteoarthritis a disease of concern as osteoarthritis will be a burden for the patient.

Osteoarthritis occurs due to degenerative processes in the joints, through wear and tear mechanism, especially in the articular cartilage. Osteoarthritis may be idiopathic and may be secondary to genetics (Col2 defect), overload (obesity, dysplasia, femoral acetabular impingement), or trauma. The pathologic changes in osteoarthritis include focal area loss of articular cartilage within a synovial joint, sclerosis, and some degree of changes in joint tissues. Osteoarthritis occurs in the most commonly used joints, such as knees, hips, fingers, and the lower region of the spine. The most frequent symptoms complained are pain, stiffness, and movement disorders. Limited movement is the most common symptom found; as many as 80% and 25% of osteoarthritis sufferers said that they could not return to their daily activities. The resulting movement limitations certainly interfere with the quality of life of most people suffering from osteoarthritis.<sup>3,4</sup>

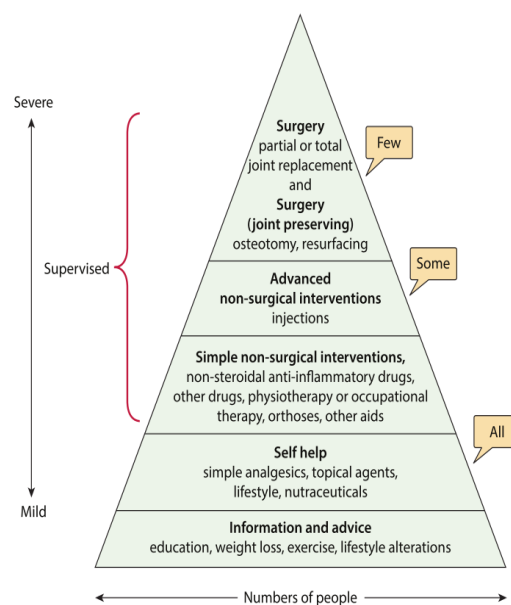
The treatment modality for osteoarthritis is classified into symptomatic therapy and disease modification therapy. Symptomatic therapy itself consists of non-operative and operative treatments. The first-line treatment for symptomatic osteoarthritis is lifestyle adjustment, such as weight loss and exercise. However, many people who suffer from osteoarthritis have limitations in their daily activities preventing them from modifying their lifestyles. Many types of exercise exist, yet the best exercise for symptomatic osteoarthritis hasn't been found. This review will discuss high-intensity interval training as a treatment modality in symptomatic knee osteoarthritis.

## Osteoarthritis

Osteoarthritis is a disease that results from loss of joint cartilage followed by sclerosis of the associated bones and changes in other joint tissues. Osteoarthritis mainly

involves the synovial joint. This pathology can be seen using imaging of the joints. Kellgren and Lawrence described the first formalized attempts at establishing a radiographic classification scheme for osteoarthritis in 1957. The Kellgren-Lawrence system classifies osteoarthritis on the basis of pathological changes in radiograph that further classifies osteoarthritis into four grades (0 to 4) according to the pathological changes. These pathological changes cause complaints from patients. The emergence of pathological abnormalities in osteoarthritis is caused by various factors, including systemic predisposition and local biomechanical factors. The systemic predispositions for osteoarthritis include genetics, age, gender, diet, and obesity. Meanwhile, local biomechanical factors are abnormalities in joint shape and size, history of trauma, neuromuscular disorders, obesity, and occupational factors.<sup>5</sup>

Chief complaints in patients are pain, joint stiffness, fatigue, sleep disturbances, depression, and disabilities in movement and activities. On physical examination, joint tenderness, swelling around the bones, reduced range of motion, crepitus, and muscle weakness can be found. Symptomatic therapy for osteoarthritis begins with lifestyle modification and topical analgesics that the patient can do independently. If independent treatment cannot treat symptomatic symptoms due to osteoarthritis, patients can visit a doctor for further treatment. In advanced treatment, therapy using NSAIDs, physiotherapy, orthosis aids, injection, and surgery are used.<sup>3,6,7</sup>



**Figure 1.** The pyramid of treatment in symptomatic osteoarthritis.<sup>3</sup>

## The Role of Exercise in Osteoarthritis

Pain in osteoarthritis is a combination of structural changes, peripheral and also central pain processing mechanisms. The neuroplastic changes in the nociceptive system distort the sensory processing in the central nervous system, malfunctioning of descending pain-inhibitory mechanisms, enhanced pain-facilitatory mechanisms, and long-term potentiation of the neural synapses that can amplify pain experiences by the increasing degree, duration, and spatial extent. Osteoarthritis pain may also contribute to systemic factors such as metabolic changes, genetic and psychological. These factors may determine the pain pattern in patients.<sup>8</sup>

A mixed-method review by Michael Hurley *et al.* in 2018 found moderate-quality evidence of exercise in its role as a treatment in symptomatic osteoarthritis. Exercise decreased pain by 6% (95% confidence interval (CI) -9% to -4%, nine studies, 1058 participants), equivalent to reducing pain by 1.25 points from 6.5 to 5.3 on a 0 to 20 scale. Exercise also enhanced the physical function by 5.6 percent (95% CI -7.6% to 2.0%; standardized mean difference (SMD) -0.27, 95% CI -0.37 to -0.17), equivalent to WOMAC Index (Western Ontario and McMaster Universities Osteoarthritis Index) on a 0 to 100 scale from 49.9 to 44.3 (13 studies, 1599 participants). Apart from physical function, the exercise also improve self-efficacy, reduce depression, and improve social function (using the SF-36 scale).<sup>9</sup>

The meta-epidemiological study by Marius Henriksen *et al.* in 2017 also found that exercise has a similar effect to oral analgesics in symptomatic knee osteoarthritis. The goal of their study was to assess the effectiveness of exercise against oral analgesics for pain relief in patients with osteoarthritis of the knee. Their study included 6 Cochrane reviews (four pharmacological and two exercises). Using the analytical method, they found no significant statistical differences between pharmacological and exercise intervention.<sup>10</sup>

Marlene Fransen *et al.* also found some high-quality evidence indicating that land-based exercise provides benefits that last two to six months after treatment, reduced knee pain, and moderate-quality evidence that showed improved physical function in patients with knee osteoarthritis. In their review, fifty-four randomized clinical trial studies searched from five databases up until May 2013 were included. The magnitude of treatment was

considered moderate to small but comparable with non-steroidal anti-inflammatory drugs.<sup>11,12</sup>

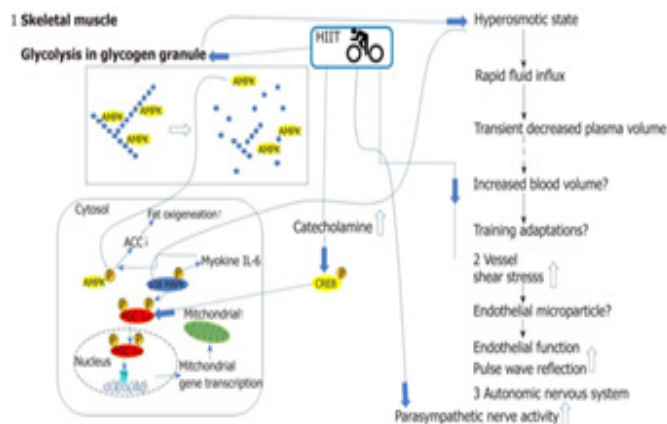
A multicenter prospective cohort study, held by Alex N. Bastick *et al.* in 2016, involved 705 participants with knee osteoarthritis and completed a 5-year follow-up. They found that high BMI, low level of education, one or more comorbidities, high activity limitation scores and joint space tenderness were associated with more pain at first presentation and pain progression.<sup>13</sup> Education, weight loss, exercise, lifestyle modification, and analgesics (over the counter and topical) remain the first-line treatment modality in symptomatic osteoarthritis. Exercise as one of the first-line treatments helps the patient strengthen the muscles around the joint and reduces body weight so that the load on the joints is reduced.<sup>3,14</sup> Some studies that we found also conclude that exercise might offer the same benefit as analgesics.

## High Intensity Interval Training

According to the American College of Sports Medicine, High-Intensity Interval Training, which is commonly called HIIT, is performed at 80% to 95% of a person's estimated maximum heart rate and followed by recovery period of at least equal to the work period, which is performed at 40% to 50% of a person's estimated maximum heart rate. HIIT can easily be modified for all people, including those who have special conditions. HIIT can be performed on all types of exercise: cycling, swimming, running, and other exercises. HIIT provides the same benefits with continuous endurance workouts but with a shorter time to work out. HIIT burns more calories after the workout, which is called excess post-exercise oxygen consumption (EPOC). EPOC occurs within 2 hours after an exercise bout where the body restores itself to pre-exercise levels and uses more energy. EPOC burns about 6 to 15% more calories than the overall workout energy expenditure.<sup>15-17</sup>

Interval Training can be classified as HIIT and sprint interval training (SIT). SIT intensity is about 3.5-fold of maximum oxygen consumption (350% VO<sub>2</sub>max) and has been deemed adaptable only to young, healthy people. Some studies use a specific ratio of exercise to recovery period to improve the body's different energy systems. For example, a balance of 1:1 might be a 3-minute high-intensity training, followed by a 3-minute recovery period. While, SIT exerciser does about 30 seconds of 'sprint' or near full-out effort, followed by a

more extended recovery period, 4 to 4.5 minutes of recovery. This combination of exercises can be repeated 3 to 5 times.<sup>15,18</sup>



**Figure 2.** Metabolic and cardiovascular effects activated by HIIT.<sup>19</sup>

In multiple randomized clinical trials, HIIT shows advantages in various aspects, including skeletal muscles, risk factors, vasculature, respiration, autonomic function, cardiac function, exercise capacity, inflammation, quality of life, physiological markers as VO<sub>2</sub>peak, and endothelial function compared to MICT. HIIT increases glycolysis in skeletal muscle and catecholamine level leading to an increase in the shear stress in the vessel and an increase in the autonomic nerve activity. This low-glycogen state leads to the phosphorylation and activation of peroxisome proliferator-activated receptor  $\gamma$  coactivator 1- $\alpha$  (PGC-1 $\alpha$ ). On the other hand, the increase in catecholamine increases the fat metabolism and activation of cAMP response element-binding protein (CREB). One of the CREB targets is PGC-1 $\alpha$ . The increase in PGC-1 $\alpha$  will increase the mRNA and protein of the mitochondrial oxygenation enzyme and, finally, improvement in physical fitness (aerobic capacity).<sup>19–22</sup>

### High - Intensity Interval Training in Symptomatic Knee Osteoarthritis

Some studies show that HIIT is more efficient than MICT as a classic osteoarthritis exercise after six to eight weeks of exercise. Continuous training such as MICT is training in one period without having time to rest. Continuous training involves aerobic training such as jogging, cycling, swimming, or rowing. MICT generally consists of aerobic exercise at 64–76% peak heart rate. In daily practice, MICT is the most recommended and commonly performed type of exercise by patients with OA because

MICT has cardiovascular health benefits and maintains body weight.<sup>23–25</sup>

On the other hand, HIIT secretes more catecholamine, epinephrine, norepinephrine, and growth hormone than MICT, promoting more fat metabolism although fat burning mechanisms are multifactorial, such as diet and lifestyle. HIIT also indicates superior improvement in VO<sub>2</sub>max and lactate threshold than MICT. Improved VO<sub>2</sub>max is caused by the increase in systolic volume, cardiac output, and peripheral vasodilatation through NO metabolism. Increased lactate threshold causing someone to train for a longer period, so that there is an increase in his performance. HIIT shows a greater expression of glucose transporter 4 (GLUT4), which can be found in adipose tissue and striated muscle (skeletal and cardiac). It means that HIIT can reduce blood sugar and increase insulin sensitivity. Compared to MICT, HIIT also increases the mitochondrial content of skeletal muscle.<sup>26–28</sup>

MICT may not provide enough stimulus to increase lower muscle mass and strength, articular changes, which might contribute to pain, stiffness, and functional limitations seen in patients with knee OA, like HIIT. This can be caused by a plateau period after doing MICT for a long period. A study by Martin J. MacInnis and Martin J. Gibala showed a greater change in mitochondrial protein in type II muscle fiber which is more stimulated in HIIT compared to MICT. However, both groups showed significant benefits in health-related quality of life, but the HIIT group showed greater functional performances.<sup>28</sup>

A study held by Ballesta-Garcia *et al.* compared HIIT in the circuit program with MICT. The 30-second sit-to-stand test was used to measure lower limb strength (STS-30). Participants sat with their feet on the floor and their hands on the opposite shoulder. They were given 30 seconds to stand and sit as many times as they could. This test was carried out only once. The gait was assessed using the timed up and test (TUG). The clock began ticking when the instructor said, “Go,” and ended when the participant returned to their original place. The participants was given a timed trial and the test was performed twice. HIIT in-circuit program shows a better result in STS-30 and TUG.<sup>29</sup>

There are two types of HIIT that can be applied, the first one is aquatic treadmill, and the last one is home-based cycling. Compared to home-based cycling, aquatic HIIT is superior because aquatic environment can reduce knee



joint loading, resulting in immediate and long-term reduction in joint pain. However, the aquatic HIIT is quite expensive and must be supervised in order to obtain maximum benefit. The alternative option for patients with OA is home-based cycling HIIT, which may be done at home by people with knee OA without supervision.<sup>18,30</sup>

One study showed aquatic HIIT increased pain relief after each session of training (ES=1.39) and after six weeks of training (ES=0.64), also increased gait and balance in patients with OA. Although increased pain relief and balance are multifactorial, they are most certainly related to the increase in muscle strength and gain. Increased lower muscle strength in adults with chronic knee pain will improve gait and balance. This study also showed a control group that performed a land treadmill, but the group couldn't reach HIIT because of load-elicited pain.<sup>30,31</sup>

In six weeks of a twice-weekly high-intensity interval of cycle training also shows metabolic changes, which can be seen from the reducing acylcarnitine. Acylcarnitine plays a key role in regulating lipid and sugar metabolism. Change in acylcarnitine is related to many diseases, such as type I and type II diabetes mellitus, coronary artery disease, heart failure, and dementia. In six weeks of HIIT, the reduction of acylcarnitine gives beneficial improvements, including improved skeletal fatty acid oxidation and mitochondrial function. OA pain and function improvements are related to a greater concentration of citrulline, nitric oxide, and creatine. Citrulline promotes exercise tolerance, nitric oxide promotes vasodilatory activity, improves blood delivery to the muscle cells, and creatine provides an energy source. HIIT also shows reduction in amino acids concentration, methionine, phenylalanine, and tyrosine, which can be considered as an increase in protein synthesis to induce biosynthesis of muscle. These metabolic changes are followed by improvement in the ventilatory threshold, representing the aerobic capacity of the skeletal muscle. In addition, HIIT shows a big reduction in visceral fat and fat mass.<sup>18,32</sup>

## CONCLUSION

Osteoarthritis is a disease that results from loss of joint cartilage followed by sclerosis of the associated bones and changes in other joint tissues characterized by pain, joint stiffness, fatigue, sleep disturbances, depression, and disabilities in movement and activities. Symptomatic therapy for osteoarthritis begins with lifestyle modification, most notably with exercise. MICT is the most

recommended and popular exercise for patients with symptomatic osteoarthritis. Still, MICT cannot provide enough stimulus to grow lower muscle mass and strength and to decrease visceral fat like HIIT. Other benefits of HIIT are time-effective and EPOC effect, which can burn more calories after training. Two forms of HIIT can be applied for patients with OA, aquatic and cycling. Six to eight weeks of HIIT in symptomatic osteoarthritis can significantly improve a patient's fitness, visceral fats, and symptoms. HIIT can be a treatment modality in resolving symptomatic knee osteoarthritis. According to patient's and physician's preferences, this finding may provide a wider exercise choice in treating osteoarthritis.

## Disclosure

The authors report no conflicts of interest in this work.

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