

Common Musculoskeletal Problems in Primary Care Settings

Module on Osteoarthritis of Knee

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1. Introduction

Osteoarthritis (OA) is the most common form of arthritis. It occurs most frequently in the hands, hips, and knees.¹ Osteoarthritis of knee (OA knee) manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodelling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness.²

OA knee can be divided into two types, primary and secondary. Primary osteoarthritis is articular degeneration without any apparent underlying reason. Secondary osteoarthritis is the consequence of either an abnormal concentration of force across the joint as with post-traumatic causes or abnormal articular cartilage, such as rheumatoid arthritis.³

2. Natural course

With primary OA, the cartilage within a joint begins to break down and the underlying bone begins to change. OA can cause pain, stiffness, and swelling. They typically become more severe, more frequent, and more debilitating over time; some people are no longer able to do daily tasks or work. The rate of progression also varies for each individual.^{1,3}

It is notorious that certain pathologies can lead to rapid progression of osteoarthritis in the affected compartment within a few years, resulting in a painful joint that can only be treated by joint arthroplasty surgery.⁴ These pathologies can be considered as “joint threatening” and include the followings:

- Pathologies resulting in total loss of function of meniscus (e.g. complete root tear of posterior horn of meniscus; full thickness, full width radial tear of meniscus)
- Pathologies resulting in loss of subchondral support of the articular cartilage (e.g. spontaneous osteonecrosis of knee; osteochondritis dissecans)

- Pathologies resulting in loss of congruency of articular cartilage (e.g. displaced intra-articular fracture of distal femur, tibial plateau or patella)
- Pathologies resulting in rapid loss of cartilage (e.g. infection, uncontrolled inflammatory joint disease, etc)

Early detection and prompt treatment of these “joint threatening” pathologies is an important strategy to minimize the need of unnecessary joint replacement surgery in middle-aged subjects.

3. Risk factors of Osteoarthritis of Knee

Multiple risk factors have been linked to OA, several of which are discussed below.

3.1. Non-modifiable risk factors

Age

Age is one of the strongest predictors of OA, with incidence of hand, hip, and OA knee increasing with age, especially after the age of 50 years.⁵⁻⁷

Gender

Female gender is associated with a higher prevalence and severity of OA. A large meta-analysis demonstrated a higher risk of OA prevalence and incidence in women.⁷ In addition, women were found to have more severe OA knee than men, particularly after menopause.^{6,8}

Genetics

OA in all of its forms appears to be strongly genetically determined with approximately 30%-65% of the risk of OA being genetically determined. A recent review on 21 genome-wide associated scan studies has identified 21 independent susceptibility loci for OA.⁹ Twin and family studies suggest that the influence of genetic factors is approximately 40% and 65% in radiographic OA of the hand and knee in women, about 60% for OA of the hip, and approximately 70% for OA of the spine, independent of known environmental or demographic confounding factors.¹⁰

Anatomic factors

Anatomic factors such as joint shape and alignment have been associated with the development of OA. A meta-analysis of high-quality cohort studies of radiographic and magnetic resonance imaging (MRI)-diagnosed OA found that varus or valgus malalignment of the knee joint is an independent risk factor for progression of OA knee.¹¹

3.2. Modifiable risk factors

Obesity

Obesity represents one of the most important risk factors for both the incidence and progression of OA knee.^{12,13} Body mass index (BMI) is shown to be positively associated with the risk of developing OA knee and risk of requiring knee replacement.¹⁴⁻¹⁸ Body weight also influences the severity of the disease, with obese individuals experiencing more severe joint degeneration in the knees.¹³ Approximately 25% of new OA knee cases are related to overweight and obese.¹⁹

Previous knee injury

Previous knee injury is associated with the development of OA.¹⁹⁻²² A meta-analysis has shown that approximately 5% of new OA knee cases are related to a previous knee injury.¹⁹ Previous traumatic knee injury, such as meniscal and cruciate tears, fractures and dislocations, is also a major risk factor for the development of OA knee.²³

Occupation

Certain occupational activities, especially those related to repetitive knee bending, may increase the risk of developing OA knee. Occupation involving vibration, repetitive movement, long hours of kneeling, squatting, and standing have been shown to be associated with an increased risk of developing of OA knee.^{24,25} A British study has revealed that prolonged or repeated knee bending is a risk factor for OA knee, and that risk may be higher in jobs which entail both knee bending and mechanical loading.²⁶

4. Prevention of Osteoarthritis of Knee

To prevent OA knee, individuals should maintain optimal body weight and pay attention to protect their joint to prevent joint injuries (Table 1), e.g. during exercise or playing sports.

Table 1. Prevention of Osteoarthritis of Knee

1. Maintaining optimal body weight and weight reduction

- Increased body weight can increase the risk of developing OA knee and influence the severity of the disease.¹³⁻¹⁸ Weight loss can prevent the onset of OA knee, relieve symptoms, improve physical function and increase quality of life.¹³ Weight loss can reduce the risk for symptomatic OA knee in women.²⁷

2. Avoid knee injury

- To avoid knee injuries when exercising or playing sports, the National Institute of Arthritis and Musculoskeletal and Skin Diseases recommends the following:²⁸
 - Avoid bending knees past 90 degrees when doing half-knee bends.
 - Avoid twisting knees by keeping feet as flat as possible during stretches.
 - When jumping, land with your knees bent.
 - Do warmup exercises and stretches before vigorous activities such as running and also before less vigorous ones such as golf. Stretch the Achilles tendon, hamstring, and quadriceps areas and hold the positions.
 - Don't bounce.
 - Don't overdo.
 - Cool down following vigorous sports. For example, after a race, walk or walk/jog for 5 minutes so that your pulse comes down gradually.
 - Wear properly fitting shoes that provide shock absorption and stability.
 - Use the softest exercise surface available while running, and avoid running on hard surfaces like asphalt and concrete. Run on flat surfaces. Running uphill may increase the stress on the Achilles tendon and the leg itself.

5. Assessment and Diagnosis of Osteoarthritis of Knee

An initial assessment of people with OA knee should be based on a complete history and physical examination, including ascertaining the effect of OA knee on the person's function, quality of life, occupation, mood, sleep, relationships and leisure activities.^{29,30}

As part of the holistic assessment, patient's knowledge of the disease and treatment alternatives, previous experiences with treatment, and expectations of current treatment should be asked.³¹ Presence of medical co-morbidities, modifiable risk factors and family or social support should be assessed.

Other factors considered as part of the holistic assessment are listed below.³¹

- pain assessment – nature of pain, other sites of pain, self-help strategies, analgesics use, doses, frequency, side effects and current understanding about persistent pain;
- functional capacity – including walking ability, stair climbing, sit-to-stand and balance;
- influence of comorbidities and falls risk;
- modifiable risk factors – e.g. overweight/obesity and joint injury;
- psychological factors – screen for depression, stressors in life and mood;
- social factors – effect of the condition on activities of daily living, relationships, quality of life, and recreational and occupational activities;
- health beliefs and concerns – previous knowledge of OA knee, expectations of treatment and understanding of treatment options, including benefits and harms;
- attitudes to physical activity and exercise – concerns, participation restriction and beliefs; and
- presence of support – concerns and expectations of carers.

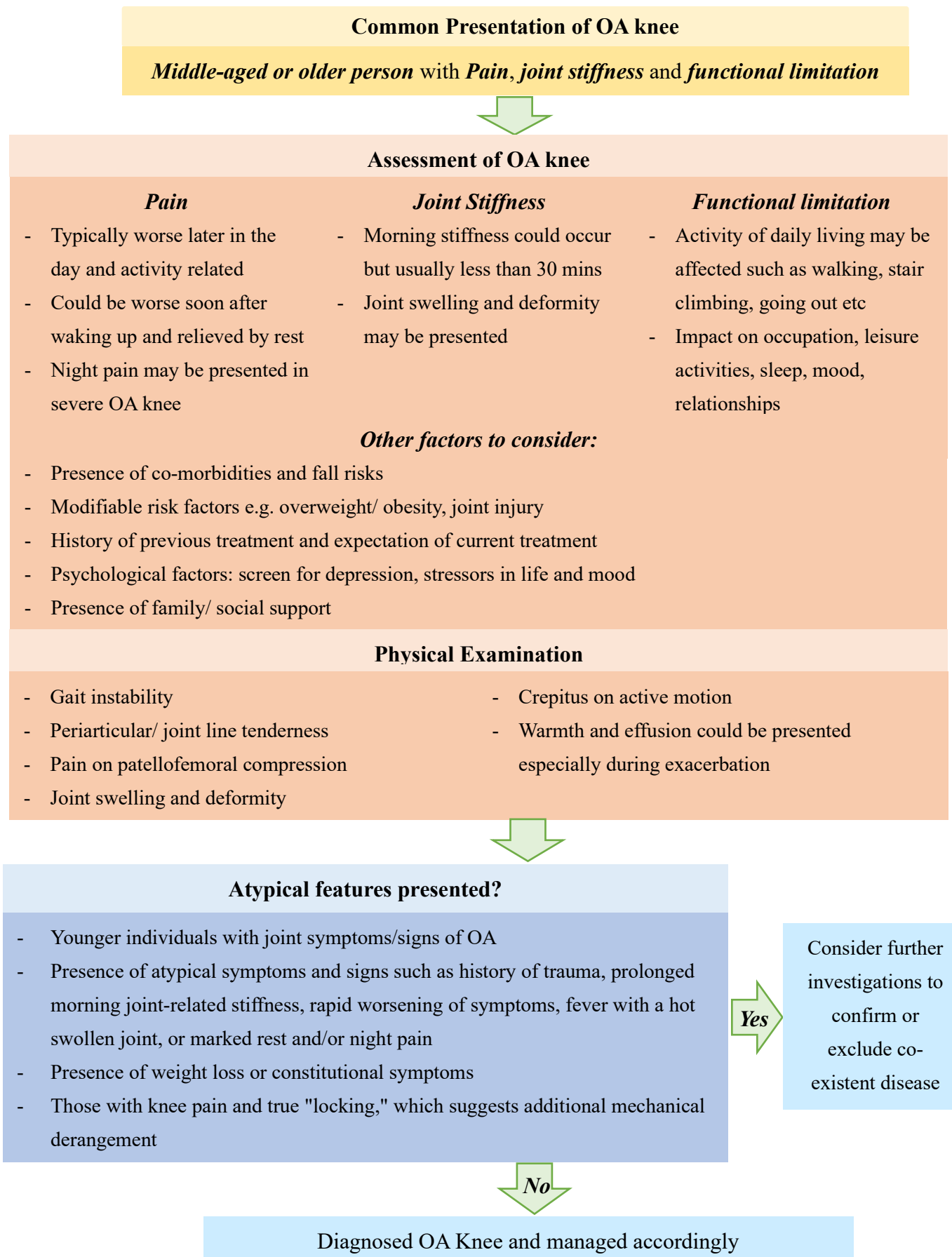
After taking into account these factors and discussing the risks and benefits of treatment options, a personalised management plan can be developed in collaboration with the person.

However, it is important to rule out other possible differential diagnosis, including

- life threatening and limb threatening condition (e.g. infection, malignancies and locally aggressive musculoskeletal tumour, etc); and
- joint threatening condition⁴ (e.g. pathologies leading to rapid progression of underlying OA, such as root tear of meniscus; full thickness, full width radial tear of meniscus; spontaneous osteonecrosis of knee, etc)

Algorithm for the assessment of OA knee is shown in Figure 1.

Figure 1. Algorithm for assessment of Osteoarthritis of Knee



5.1. Clinical signs and symptoms of Osteoarthritis of Knee

The primary symptoms of OA knee are joint pain, stiffness, and functional limitation. Symptoms usually present in a middle-aged or older person. Other manifestations in patients with OA knee include sequelae such as muscle weakness, poor balance and joint deformity.³¹

Pain is typically worse later in the day but can also be worse in the morning soon after waking up and relieved by rest.^{32,33} There may also be night pain in severe OA knee that can interfere with sleep.

OA knee can cause morning stiffness, but it usually lasts for less than 30 minutes, unlike rheumatoid arthritis.^{34,35} There may be joint swelling and tenderness, with or without crepitation. Deformity may be presented in severe OA knee.³³ Reduced range of motion (both active and passive movement) mainly results from marginal osteophytes and capsular thickening, but synovial hyperplasia and effusion may also contribute.

Instability in gait may occur. Giving way or buckling is a common symptom in OA knee. It is predominantly a sign of muscle weakness with subsequent altered patellar tracking (with lateral patellar subluxation) but it may also associate with true joint instability.

5.2. Diagnosis of Osteoarthritis of Knee

OA knee can be diagnosed clinically.

The typical diagnosis of OA knee can be made clinically, without requiring further investigations if a person^{30,31,36-39}

- is aged 45 years or older;
- has activity-related joint pain;
- has morning stiffness that lasts less than 30 minutes;
- has crepitus on active motion; and
- has no detectable warmth¹.

¹ Warmth and effusion can also be present in OA knee, especially during exacerbation.

Additional features that may be present include³⁹

- deformity: varus deformity (less commonly valgus for the knee);
- gait instability;
- periarticular or joint-line tenderness; or
- pain on patellofemoral compression.

5.3. Investigations

Due to the absence of strong evidence, routine imaging is generally not recommended if the patient presents with a typical clinical presentation.^{30,36,40} Appropriate laboratory investigations and imaging could be considered subject to clinical situation, especially for patients with atypical clinical presentation.^{30,31,33,36} The differential diagnosis includes gout, pseudogout, trauma and septic arthritis, etc.³³

Characteristic features of OA including marginal osteophytes, joint space narrowing, subchondral sclerosis, and cysts.^{41,42} However, radiographic changes in OA are often correlate poorly with symptoms. Also, radiographic OA is a common incidental asymptomatic finding in older people.^{43,44}

Other investigation (e.g. MRI) may be considered if the diagnosis is in doubt and there is clinical suspicion, especially if the patient is relatively young or if the symptoms occur after significant knee injury.³⁵ Structural changes demonstrated on MRI are also detected in asymptomatic knees in a large population study.⁴⁵ The purpose of MRI is to identify joint threatening pathologies (e.g. complete root tear or complete radial tear of meniscus, osteochondritis dissecans) at an early stage to minimize the chance of premature development of end-stage arthritis of knee in a relatively young adult.

Additional laboratory tests (e.g. erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor, synovial fluid aspirate for crystal confirmation,) may be required to confirm or exclude co-existent inflammatory disease in people with suggestive symptoms or signs.

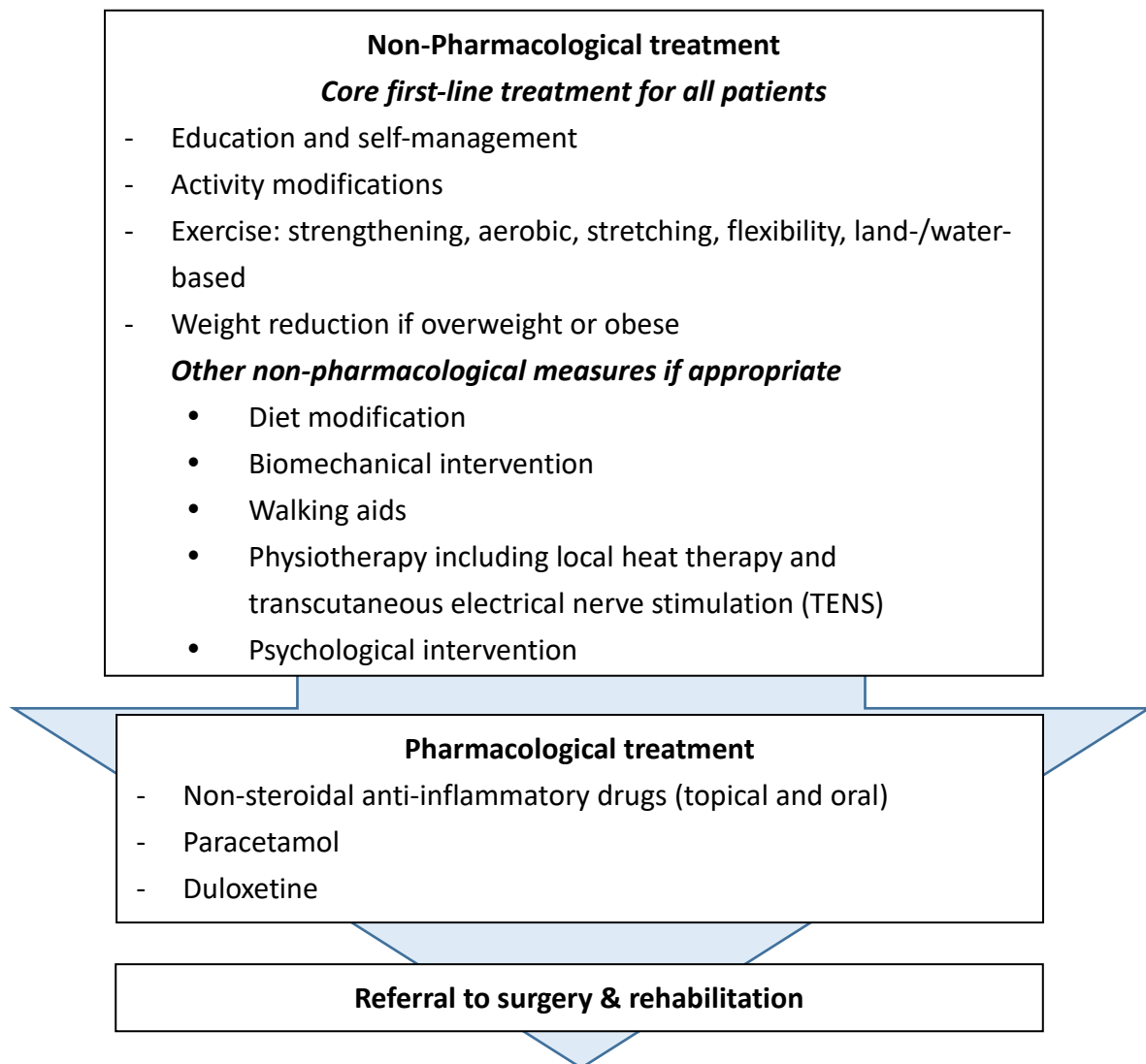
Appropriate imaging and laboratory investigations should be carried out in

- younger individuals (at or below 45-year old);
- history of significant injury;
- those with knee pain and true "locking," which suggests additional mechanical derangement
- presence of atypical symptoms and signs such as prolonged morning joint-related stiffness, rapid worsening of symptoms, the presence of fever with a hot swollen joint, or marked rest and/or night pain;^{30,31} or
- presence of weight loss or constitutional symptoms.

6. Management of Osteoarthritis of Knee

The goals of OA management in primary care are to minimize pain, optimize function, and targeting modifiable risk factors for disease progression. Appropriate interventions of OA knee should include a combination of non-pharmacologic and pharmacological treatment modalities.

Monitoring of the patient's response to therapy should also be done on a regular basis. The summary for management of OA knee of different degrees is illustrated in algorithms. (Figure 2)

Figure 2. Summary for management of Osteoarthritis of Knee

6.1. Non-pharmacological treatment

Non-pharmacological treatment comprises core first-line treatment for all patients with OA knee, irrespective of severity, and can be used in combination. It includes education, self-management, exercise, and weight reduction.⁴⁶

6.1.1. Education and self-management

Patients should be fully informed about the etiology of OA knee, risk factors (especially the ones that are modifiable and specific to the patient), and expected prognosis.⁴⁷ Disease progression, investigations (if necessary) and treatment option should be offered to patient. Accurate information, verbal or written, will enhance patient's understanding of the condition and its management, and to counter misconceptions, such as exercise will worsen OA knee.³⁰

Self-management education (Table 2) aims at teaching patients problem-solving skills and involves the concept of self-efficacy, which gives patients confidence in their capacity to carry out a particular behaviour necessary to reach a desired goal. Self-management education can occur through several ways such as face-to-face meetings, group sessions, the Internet, and telephone-based sessions.⁴⁷

Table 2. Practical self-care tips for Osteoarthritis of Knee⁴⁸

Practical self-care tips for patients with OA knee:

1. Maintain an ideal body weight. Minimize excessive weight bearing of knee joint.
2. Avoid carrying heavy objects. Use a trolley if necessary.
3. Avoid prolonged standing or walking. Use a walking aid with appropriate height if required.
4. Avoid putting the knee joint in one position for a long time e.g. sitting on low stool or squatting.
5. Ensure proper balance between work and rest. Watch out for and be mindful of joint pain.
6. Appropriate knee exercise and thigh muscle strengthening exercise can protect the knee joint. Consult a doctor or physiotherapist for advice.

A multidisciplinary exercise programme developed in Hong Kong, incorporating nurse-led education, physiotherapist-led exercises and occupational therapist-led management programme with emphasis on disease coping strategies and fatigue management demonstrated both short term (6 week and 3 month) and mid-term (1 year) improvement in pain control, physical capacity, physical function and quality of life.⁴⁶

6.1.2. Exercise

All patients with OA knee should be counseled on exercise for pain relief and joint protection irrespective of age, radiographic disease severity, pain intensity, functional levels, and comorbidities.³⁰ Exercise should include local muscle strengthening and low impact general aerobic fitness (e.g. walking and cycling, Tai chi, etc).³⁰ A Cochrane review concluded that land-based exercise e.g. Tai Chi, improves knee pain, physical function and quality of life.⁴⁹ Tai Chi improves balance and is associated with a reduced falls risk in older patients with OA knee.⁵⁰

At present, there is no strong evidence on the best prescription of exercise modalities and dosage (i.e. intensity, duration, frequency). However, a meta-analysis studying the safety of long-term physical activity for older adults with knee pain suggested that long-term low impact therapeutic exercise (ranging from 3 months to 30 months), was consistently safe across a broad range of types and intensities of interventions, including stretching exercise, range of motion exercise, muscle strengthening exercise, walking and cycling, Tai chi, balance and agility exercise; with no evidence of serious adverse events, increases in pain, decreases in physical function, progression of structural OA on imaging or increased total knee replacement at group level.⁵¹ A combination of low-impact aerobic fitness training (e.g. walking and cycling) and lower limb strengthening exercises, should be able to address the full spectrum of impairments in most patients with OA knee.

Exercises involving high impact on the joints such as running or jumping are usually discouraged in order to avoid further joint damage, especially in cases of more advanced OA knee although it was not possible to determine the role of running in the pathogenesis knee OA because conflicting results were found in a meta-analysis.⁵²

Aquatic exercise has short-term benefits for function but minor benefits for pain in a review in 2016.⁵³ It may be useful for patients with severe pain and/or poor physical function, whom land-based exercise may not be possible for, due to its better tolerance and lower potential to cause adverse events.

For further details on exercise for patients with OA knee can refer to the link below from Department of Health, Hong Kong:

https://www.chp.gov.hk/archive/epp/files/DoctorsHanbook_ch9.pdf.

6.1.3. *Weight reduction*

Maintaining an ideal body weight is critical to preserve joint structures and improve symptoms. In addition to the mechanical consequences of obesity and overweight to the joint, adipokines released by the adipose tissue such as leptin and adiponectin are directly involved in the inflammatory component of OA and cartilage damage.⁵⁴

Overweight and obesity is a major risk factor for the onset and progression of symptomatic and radiographic OA, and is common among people with OA knee.³⁰ A meta-analysis reported that overweight and obesity increases the risk of developing OA knee around two-fold and five-fold respectively.¹⁷

Evidence has shown that weight reduction may lower the risk of developing symptomatic OA knee and reduced knee pain by over 50% with 10% reduction of body weight.^{27,55} Weight reduction program should be individualized, however, an initial target of 5-10% weight reduction within a six-month period should be reasonable.⁵⁶ Dietary and exercise interventions can be considered first before considering pharmacological or other methods.

Caloric restriction, particularly in older adults, may contribute to the loss of lean mass and lead to muscle weakness and should, therefore, be combined with strengthening exercises to prevent these adverse effects.

6.1.4. *Other non-pharmacological measures*

Other primary non-pharmacological measures for OA knee include diet modification, braces and orthosis, walking aids, local heat therapy, transcutaneous electrical nerve stimulation, manual therapy, pulsed electromagnetic therapy, low level laser therapy, extracorporeal shockwave therapy and psychological intervention. These measures may not have sufficient data to demonstrate efficacy but may reasonably be tried as adjunctive measures for patients after consideration of potential harm, cost and patient preference.

6.1.4.1. Diet modification

Diet modification mainly alleviates symptoms or progression of OA knee by providing an anti-inflammatory environment for knee tissues via encountering reactive oxygen species or modulating hormone-like eicosanoids, and provides nutrients that are important in regulation of bone metabolism. Postulated mechanisms for the above two pathways have been well-suggested in literature,⁵⁷⁻⁶⁸ although strong evidence from systematic literature review or meta-analyses are scarce due to study difficulty.

Some suggestions on principles of diet modification are provided below:

- replace total and saturated fat with mono-unsaturated fat and poly-unsaturated fat;⁵⁷
- decrease ratio of n-6 to n-3 fatty acids in habitual diet;⁵⁸
- include cholesterol-lowering dietary strategies (e.g. plant sterol,⁵⁹ viscous fibre,⁶⁰ tree nuts)⁶¹ for patients with raised blood cholesterol level;⁶²
- increase intake of dietary antioxidants;⁶³
- maintain vitamin D status with regular sun exposure (i.e. 5 to 15 minutes on face, hands and arms, two to three times a week during summer, longer during winter)^{62,64,66} and adequate intake of vitamin K (such as green-leaf vegetables, kiwi fruits, dried prunes, and green-leaf vegetables including spinach, kale and broccoli),⁶⁵ and
- eating a Mediterranean diet can help reduce inflammation in people with osteoarthritis and protect against weight gain.^{67,68}

Some examples on food recommendation for patients with OA knee are listed in Table 3.

Table 3. Examples on food recommendation for patients with OA knee

Food Recommended:

- nuts and seeds
- fatty fish with mono-saturated fat or poly-unsaturated fat (such as salmon, tuna and sardine)
- plant-based oil, except coconut and palm oil
- different coloured fruits and vegetables (such as kiwi)
- green-leaf vegetables (such as spinach, kale and broccoli)
- whole grains
- dried prunes

Food NOT Recommended:

- red meat
- poultry skin
- cheese
- butter and cream
- baked goods (such as cakes and croissants)
- highly processed food items (such as luncheon meat, sausages, coconut/palm oil and coconut milk)

Clinicians may refer patients to a dietitian for more information or in-depth consultations.

6.1.4.2. Knee orthosis or knee braces

Knee braces are widely available for purchase in the market. Varus unloading braces realign the tibiofemoral joint by providing a varus-directed force that aims to reduce valgus malalignment in those with lateral tibiofemoral compartment OA knee while valgus unloading braces reduce varus malalignment in those with medial tibiofemoral compartment OA knee. Patellofemoral braces aim to realign patellar position for those with patellofemoral OA knee.

There is no conclusive evidence on the effects of braces on pain or physical function in people with OA knee.^{31,69} Besides, low compliance of using knee brace was reported due to lack of symptomatic relief, brace discomfort, poor fit, and skin irritation.⁷⁰ Still, it can be considered for selected patients after balancing the benefits and risk of bracing.

6.1.4.3. Insoles and other specialized footwear

Insoles and other specialized footwear have been designed with the aim to reduce stress on osteoarthritic knee compartments and potentially slow disease progression. However, the data in support of these devices suggest limited clinical benefit overall.^{31,71}

6.1.4.4. *Walking aids*

Walking stick (cane) in the contralateral hand (unaffected side) could be considered,^{30,31} especially for patients with

- significant mobility impairment due to OA;
- balance impairments;
- history of falls; and /or
- moderate to severe pain resistant to other treatment options.

6.1.4.5. *Local heat therapy*

Superficial heat can be applied via the use of hot packs or hot water bottles. Heat therapy is aimed to relieve muscle tension and soreness, and improve blood flow. However, there are no robust clinical trials evaluating its effectiveness. Given that heat therapy is cheap and easily available, it may be appropriate to offer local heat therapy as an adjunctive treatment. Patient should be warned about the risk of burn and heat therapy may not be suitable for patient with compromised sensation.³¹

6.1.4.6. *Transcutaneous electrical nerve stimulation (TENS)*

TENS uses low voltage electric current delivered through electrodes fixed to the skin to affect peripheral nerve activity (neuromodulation) as a mechanism to modify nociception and the experience of pain. However, data on the efficacy of TENS in OA are conflicting.⁷²

6.1.4.7. *Manual therapy*

Manual therapy consists of maneuvers applied with manual force from the skilled hands-on techniques to the patient's body to improve joint mobility and/or relieve pain. A systematic review showed there was effect on improving pain, stiffness and physical function but the heterogeneity of the studies were moderate to high.⁷³

6.1.4.8. *Pulsed electromagnetic therapy*

Pulsed electromagnetic therapy is the application of pulsed electromagnetic fields to the body. The treatment could temporarily trigger an increase in pain and discomfort. A systematic review showed there was effect on improving physical function but not pain and stiffness.⁷⁴ The long term data is lacking.

6.1.4.9. *Low level laser therapy*

A systematic review showed there was effect on improving physical function and pain up to 12 weeks and the results were more prominent if using the recommended dosage at 4–8 J with 785–860 nm wavelength and at 1–3 J with 904 nm wavelength per treatment spot.⁷⁵ However, the long term data is lacking.

6.1.4.10. *Extracorporeal shockwave therapy*

Extracorporeal shockwave therapy contains a sequence of single sound impulses characterized by a high-pressure peak and quick pressure rise in a short duration. Local reactions such as skin reddening and swelling are common. A systematic review showed there was effect on improving physical function and pain at 4 to 12 weeks.⁷⁶ The long term data is lacking.

6.1.4.11. *Psychological interventions*

There is evidence showing that psychological interventions, particularly cognitive behavioural therapy (CBT), result in significant improvements in pain and physical and psychological disability in patients with chronic pain.⁷⁷

It aims at teaching patients to best cope with chronic pain through the modification of pain-related thoughts, behaviours, and emotions. CBT combined with exercise may improve outcomes.

6.2. Pharmacological treatment

Pharmacologic therapy can be started in combination with or after a trial of non-pharmacologic interventions.

6.2.1. *Nonsteroidal anti-inflammatory drugs (NSAIDs)*

NSAIDs are anti-inflammatory and analgesic agents commonly used for OA. It is available in both topical and oral forms. Both topical and oral NSAIDs have similar efficacy and significant benefits over placebo.⁷⁸ Caution should be exercised with use in patients with chronic kidney disease, coronary artery disease and congestive heart failure.

Topical NSAIDS

Topical NSAIDs are strongly recommended by American Academy of Orthopaedic Surgeons (AAOS)⁷⁹ and Osteoarthritis Research Society International (OARSI)⁸⁰ for use in patient with OA knee . Topical NSAIDs have much lower levels of systemic absorption compared to oral NSAIDs and both topical and oral NSAIDs have similar efficacy and significant benefits over placebo. Topical ones have less gastrointestinal risk but a higher risk of dermatological side-effects.⁸¹ A systemic review of randomized controlled trials suggested topical NSAIDs had moderate effect size for improvement in pain.⁸² A trial of topical NSAIDs for a short period for effect and discontinue use if not effective should be reasonable. Clinicians also need to monitor and capture the adverse effects along with its use.

Oral NSAIDS (non-selective and COX-2 selective inhibitors)

In a 2015 meta-analysis of data from 137 randomized trials comparing the efficacy of NSAIDs with other therapies for OA knee, all of the oral NSAIDs examined were found to be more effective for pain reduction when compared with placebo and paracetamol.⁸³ Another large network meta-analysis comparing oral NSAIDs, paracetamol, or placebo for the treatment of pain for either hip or OA knee found that all of the oral NSAIDs included in the analysis improved estimates of pain when compared with placebo or paracetamol.⁸⁴

The potential harms of oral NSAIDs are well recognised, and include gastrointestinal,

renal and cardiovascular adverse effects. Older persons, who are at higher risk for OA, may also be at higher risk of adverse effects from oral NSAIDs, so this class of medication should be used with great caution. Patients should be informed of the potential adverse effects. In order to minimize risk of complications, intermittent short-to mid-term use as required, in the lowest effective dose necessary to control symptoms, should be considered. Co-prescription of a proton-pump inhibitor (PPI) or the use of a COX-2 inhibitor should be considered in people at risk of gastrointestinal adverse effects.^{31,80} Oral NSAIDs are not recommended for use in patients with cardiovascular comorbidities and frailty.⁸⁰

6.2.2. *Paracetamol*

Paracetamol, also known as acetaminophen, is typically used to treat mild-to-moderate pain. Different researches and guidelines from AAOS,⁷⁹ OARSI,⁸⁰ Royal Australian College of General Practitioners (RACGP)³¹ had inconsistent recommendation and conclusion on the use of paracetamol for patients with OA knee. A systemic review of randomized controlled trials (RCTs) suggested that paracetamol has only small, non-clinically meaningful benefits for pain in the short term.⁸⁵ The meta-analysis of paracetamol compared to controls published by AAOS demonstrated a meaningful reduction in pain and improved function with no evidence of confounding heterogeneity.⁷⁹ However, paracetamol is associated with infrequent potential significant harms, both short-term excess dosing and long-term regular use.⁸⁸

Therefore, in people who have not been previously prescribed paracetamol in an appropriate dose, a short-term trial may be considered, with cessation of the drug in those who do not respond.

6.2.3. *Duloxetine*

Duloxetine is a serotonin and norepinephrine reuptake inhibitor (SNRI) with central nervous system activity. Its analgesic efficacy in central pain is presumably related to its influence on descending inhibitory pain pathways. This medication can be considered as a second-line treatment for patients with OA knee with depression and/or widespread pain.⁸⁰ Common adverse effects include constipation, nausea, hyperhidrosis, dizziness, headache etc.

In a meta-analysis of three trials, duloxetine, compared with placebo control, resulted in a greater reduction in pain, improved function and patient-rated impression of improvement.⁸⁷ The use of duloxetine for OA knee adjunctively with NSAIDs would be clinically useful.⁸⁸ However, it is not recommended in patients with gastrointestinal or cardiovascular comorbidities as it has been demonstrated to be associated with higher risk of adverse events.⁸⁰

6.2.4. *Opioids*

In Hong Kong, opioid analgesics are considered if pain relief from paracetamol is inadequate and NSAIDs are contraindicated, ineffective, or poorly tolerated.⁴⁶ However, patients taking opioids have a chance of adverse withdrawal effects that is 4 times higher, and a risk of developing serious side events, including fractures and cardiovascular events, that is 3 times higher.⁴⁶

Due to the relatively high incidence of side effects such as drowsiness, dizziness, and nausea, and the potential to cause harm with long-term use, especially in elderly population, it is better to avoid opioid use in people with OA.

Opioid medications are no longer recommended by AAOS,⁷⁹ OARSI⁸⁰ and RACGP³¹ in view of its poor safety profile.

6.2.5. *Intra-articular steroids*

Intra-articular corticosteroid injections may be useful for symptomatic OA knee, especially where there is a considerable inflammatory component.⁴⁴

Intra-articular glucocorticoid injections should be restricted to patients with moderate to severe pain and contraindications to or failure of other treatment options who are seeking short-term pain relief.^{30,31} Patients should be warned about potential risk of septic arthritis and cartilage damage. It should be noted that septic arthritis should be ruled out and the procedure should be carried out under strict aseptic technique.

Serial injections (every three months) are discouraged and usually not more than three or four times a year as it could result in cartilage or joint damage and increase infection risk. Furthermore, intra-articular injections may increase the risk of peri-operative

infection after total knee replacement and so, it may not be advisable to inject patients who may be candidates for joint replacement procedures within 3 months.⁸⁹

6.2.6. *Intra-articular hyaluronic acid (HA)*

HA is a glycosaminoglycan which is an important component of synovial fluid and articular cartilage. It increases the viscosity of the fluid, and enables it to act as lubricant or shock absorber. While this is a prevalent treatment option, the use of intra-articular HA is not widely recommended due to the lack of robust evidence demonstrating clinically relevant benefits over intraarticular placebo.^{30,79,80,90}

As with all intra-articular injections, septic arthritis should be ruled out and the procedure should be carried out under strict aseptic technique and patients should be warned about potential risk of septic arthritis. It may not be advisable to inject patients who may be candidates for joint replacement procedures within 3 months due to increased risk of peri-operative infection.⁸⁹

6.3. Supplements for Osteoarthritis of Knee

Glucosamine and chondroitin are structural components of cartilage, both are produced naturally in the body. Glucosamine and chondroitin sulfate are available as dietary supplements.

Glucosamine and chondroitin sulfate alone or in combination did not reduce pain effectively in the overall group of patients with OA knee.⁹¹ A strong placebo effect has been demonstrated in the studies involving these dietary supplements. This is well illustrated by the landmark Glucosamine/Chondroitin Intervention Trial (GAIT), in which around 60% of participants experienced at least 20% pain reduction irrespective of whether they received placebo, glucosamine hydrochloride, chondroitin, or the combination of both.⁹¹

Glucosamine and chondroitin are not strongly recommended by major OA guidelines.^{79,90,92}

6.4. Referral to specialist and surgery

Surgery is indicated in patients with OA knee presenting with persistent symptoms, despite an initial attempt of non-operative management.

6.4.1. Options of surgical intervention

6.4.1.1. *Total knee replacement*

Total knee replacement is a very effective treatment for end-stage osteoarthritis of knee in terms of pain relief, and improvement of function and quality of life.

6.4.1.2. *Unicompartmental knee replacement*

Partial knee replacement is effective in managing end-stage osteoarthritis of knee limited to one of the compartments of the knee joint. It is indicated in patients presenting with pain localized in a single compartment (usually medial side) with functional knee ligaments, good range of knee movement and absence of significant deformity.

6.4.1.3. *High tibial osteotomy*

High tibial osteotomy is a surgical option for relatively younger patients with isolated medial compartment osteoarthritis. Patients with autoimmune disease or crystal arthropathy are not suitable. The collateral ligaments have to be functional and the patient should enjoy a good range of knee movement. It is more suitable for patients who are engaged in heavy manual work and those who do not want to have joint replacement too early.

6.4.1.4. *Arthroscopic surgery*

The indication of arthroscopic surgery in end-stage osteoarthritis of knee is limited to patients presenting with symptoms of mechanical locking secondary to loose body or degenerative meniscus tear.³⁰ In a meta-analysis investigating the role of arthroscopic partial meniscectomy as a treatment for osteoarthritis of knee, there is only a small benefit in terms of pain improvement in the arthroscopic surgery group over non-surgical treatment and the effect was limited to 24 months.⁹³

6.4.2. **Referral to specialist**

Patients suffering from end-stage OA knee should be referred to specialist for consideration of total knee arthroplasty.

Early referral to specialist care should be considered if patient presents with:

- significant progressive bone loss or deformity;
- wheelchair bound or bed bound; or
- functional impairment leading to major threat to independence of occupation / performing role.

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