Osteoarthritis

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Abstract

Osteoarthritis (OA) is a chronic disease involving the entire joint, although the main tissue implicated in osteoarthritis is the cartilage. The most common joints affected include the knees, hips, lower back and neck, small joints of the fingers, base of the thumb and big toe. Progressive degeneration, chronic pain, stiffness, joint instability and joint space narrowing are clinical features associated with the condition. Osteoarthritis develops and progresses due to risk factors such as advancing age, female gender, and excessive mechanical stress, affecting mainly weight bearing joints of the knee, hip and spine. Thorough history taking, physical examination for signs and symptoms as well as appropriate imaging examinations and laboratory markers have to be considered during diagnosis and monitoring. The disease pathology is complex and current therapy does not prevent initiation or progression of osteoarthritis. Appropriate management combines non-pharmacological and pharmacological strategies aimed at alleviating symptoms and improving a patients' quality of life.

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Introduction

Arthritis is an umbrella term used for various different arthritic conditions that are chronic, painful and debilitating. Arthritic diseases include six main types: rheumatoid arthritis, juvenile arthritis, psoriatic arthritis, gouty arthritis, ankylosing spondylitis and osteoarthritis.[1] These musculoskeletal disorders contribute significantly to the global disability burden.[2,3] Osteoarthritis, also known as degenerative joint disease or degenerative arthritis is the most common chronic condition of the joints. The joints most commonly affected include the knees, hips, lower back and neck, small joints of the fingers, base of the thumb and big toe.[4] Osteoarthritis occurs mainly later in life,[5] and according to epidemiological studies, affects an estimated 15% of the world population.[2] It is a debilitating progressive disease, affecting 60% of men and 70% of women over the age of 65.[6] The level of disability depends on several factors and the effect that OA has on a given individual does vary.[5]

Pathophysiology of osteoarthritis

Osteoarthritis is a complex, chronic inflammatory disease of synovial joints,[7] involving the articular cartilage, a unique tissue between the ends of bones in the joints.[5,8] Below the cartilage is a layer of bone, the subchondral bone that acts as a shock absorber in weight-bearing joints (e.g. hips and knees). Synovial fluid fills the joint space and contains abundant hyaluronic acid (HA) that acts as a lubricant. In OA patients, hyaluronan is both smaller in size (referring to its molecular weight) and lower in concentration, providing less efficient lubrication. The subchondral bone plate thickens in patients suffering from OA[9,10] causing the joint space to narrow.[11,12]

Recent research eluded that OA involves the entire joint and not only the articular cartilage, as initially thought – refer to Figure 1. A combination of cellular changes and biomechanical stresses cause several secondary changes. The latter include subchondral bone remodelling, formation of osteophytes, development of bone marrow lesions, changes in the synovium, joint capsule, ligaments and periarticular muscles, and meniscal tears and extrusion.[2,13-15] Figure 2 depicts a radiograph of the hip, revealing severe superior migration of the femoral head, subchondral sclerosis, prominent osteophytes, and a large Egger cyst in the superior acetabulum. The femoral head also reflects loss of articular cartilage.[16]

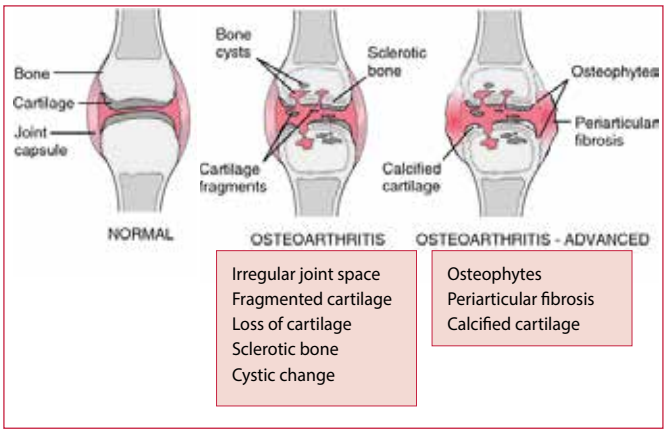

Figure 1. Joint involvement in OA

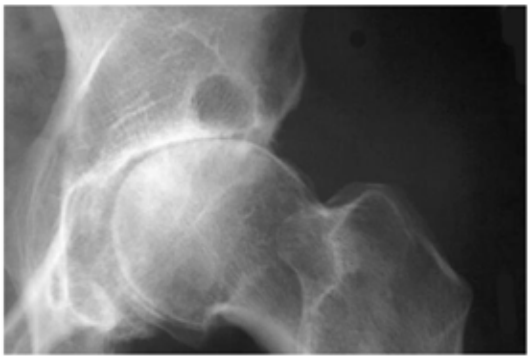

Figure 2. OA of the hip[16]

Cartilage is the main tissue afflicted by OA.[17] Chondrocytes are the only cells found in healthy cartilage and are responsible for the production and maintenance of the cartilage over the lifetime of an individual.[18] During the progression of OA, chondrocytes actively remodel the extracellular matrix (ECM) of cartilage under inflammatory conditions – the latter due to wear and tear or trauma. In the presence of inflammation, the disease progresses further due to changes in the biomechanical environment of chondrocytes, brought about by alteration of the ECM. The changes in ECM composition and structure, further prevent mesenchymal stem cells (that migrate from bone marrow) to partake in the repair process by inhibiting their chondrogenic differentiation. The continuous interplay between changes in ECM and changes in cellular function under inflammation, drives the pathology of this chronic degenerative joint disease.[18] Figure 3 depicts this interplay.

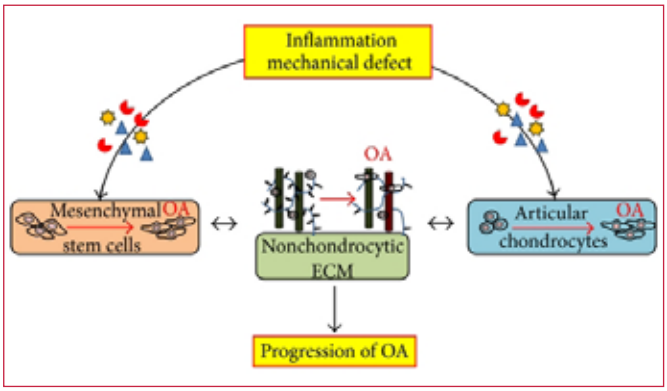

Figure 3. Changes in ECM of cartilage during inflammation[17]

Aetiology and risk factors of osteoarthritis

Idiopathic OA is the most common form of arthritis[6] as the root cause of the disease is unknown.[7] The development and progression of OA is multifactorial, precipitating from interplay between various risk factors:[4,15,19, 20-24]

- Advancing age – incidence of OA does increase with age, although not a definite consequence of aging.
- Female gender – women after menopause are more susceptible to knee arthritis because of an increasing level of osteocalcin and bone resorption.[25,26]

Osteocalcin is a noncollagenous protein hormone found in bone and dentin, also known as bone gamma-carboxyglutamic acid-containing protein (BGLAP)

- High bone density
- Reduced muscle strength
- Malalignment of joints
- Excessive mechanical stress
- Obesity
- Sports and other trauma to the joints

The normal joint is well adapted to withstand physiological loads, but abnormal loading can increase the risk of OA. Trauma, heavy manual labour, and obesity all carry an increased risk of OA:

- Workers in certain occupations, such as coal miners, dockyard workers, and farmers have an increased risk of hip and knee OA
- Obesity is a well-established risk factor in the development of knee OA

- Genetic predisposition – a study of monozygotic twins aged 48 to 70 years, having identical genes, showed 65% influence of genetic factors in developing osteoarthritis.[27] Between 39% and 65% of osteoarthritis in the general population can be attributed to genetic factors.[25]
- Meniscus deficient knees – the prevalence of OA seems to be high among former athletes from team and individual sports when compared to the general population and other occupational sectors.[28]
- Childhood hip disorders e.g. acetabular dysplasia, congenital hip dislocation, epiphysiolysis (abnormal separation of an epiphysis from the bone shaft), and Legg-Calve'-Perthes (a disorder initiated by a disruption of blood flow to the head of the femur) have been implicated in the development of early onset OA of the hip.
- Coxa valga (a deformity of the hip) with acetabular dysplasia.
- Degeneration of the acetabular rim triggered by femoroacetabular impingement (the ball shaped femoral head rubs abnormally or does not permit a normal range of motion in the acetabular socket).

Clinical presentation of osteoarthritis

The main clinical symptoms of osteoarthritis are chronic pain, stiffness, joint instability and joint space narrowing (seen radiographically).[22] Exertion exacerbates the pain associated with osteoarthritis, and may recur following rest. Joint stiffness may occur during morning hours, lasting up to 30 minutes. Locking or instability of joints may also be present.[23] Table I depicts the different signs and symptoms depending on the joints affected.

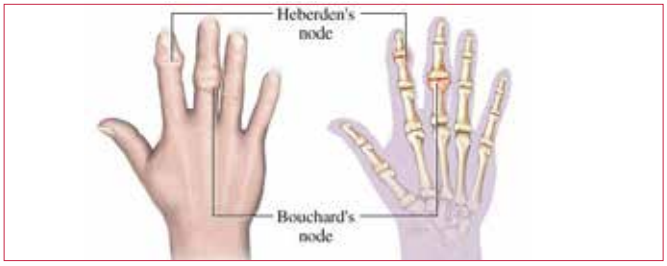

Figure 4. Bony swellings due to OA

Table I. Signs and symptoms of osteoarthritis[23,29]

Joints affected	Signs and symptoms
Hand	Heberden nodes (Fig. 4) at distal interphalangeal joints Bouchard's nodes (Fig. 4) at proximal interphalangeal joints Osteophytes at first metacarpal joint give characteristic square appearance to hands Tenderness over carpometacarpal joint of the thumb
Hip	Pain in groin during weight lifting exercises Stiffness, pronounced following activity Pain in gluteal region Limited joint movement, especially internal rotation
Knee	Pain associated with climbing stairs Transient joint effusion Lateral instability Genu varum (outward bowing of the knees, bandi-leg) Popliteal cyst (Baker's cyst – Fig. 5) Crepitus associated with range of motion
Foot	Usually involves the first metatarsal-phalangeal joint Pain on ambulation Hallux rigidus (Fig. 6) – a limitation to normal movements of flexion and extension Hallux valgus (bunion – Fig. 7) – a deformity of the first metatarsophalangeal joint
Spine	Typical lumbar involvement at L3 and L4 Paraesthesia Loss of sensation at lower extremities Motor weakness from compression of nerve root Loss of reflexes Pseudoclaudication from spinal stenosis
Shoulder	Limited range of motion, especially external rotation Crepitus associated with range of motion

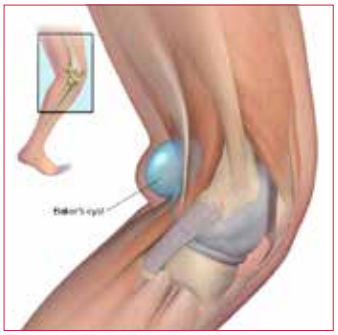

Figure 5. A Baker's cyst

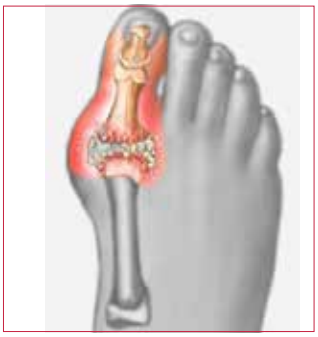

Figure 6. Hallux rigidus

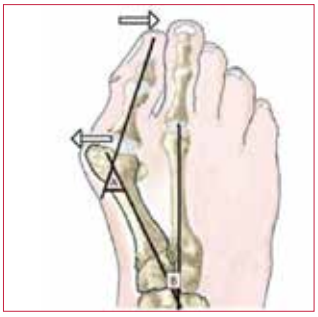

Figure 7. Hallux valgus

Diagnosis

Osteoarthritis is one of the most common, costly and disabling forms of joint disease, and far more common than rheumatoid arthritis. The latter is an autoimmune disease that does not only affect the small joints, but also presents with extra-articular manifestations e.g. anaemia and cardiovascular diseases. Figure 8 depicts the differences between these two diseases.

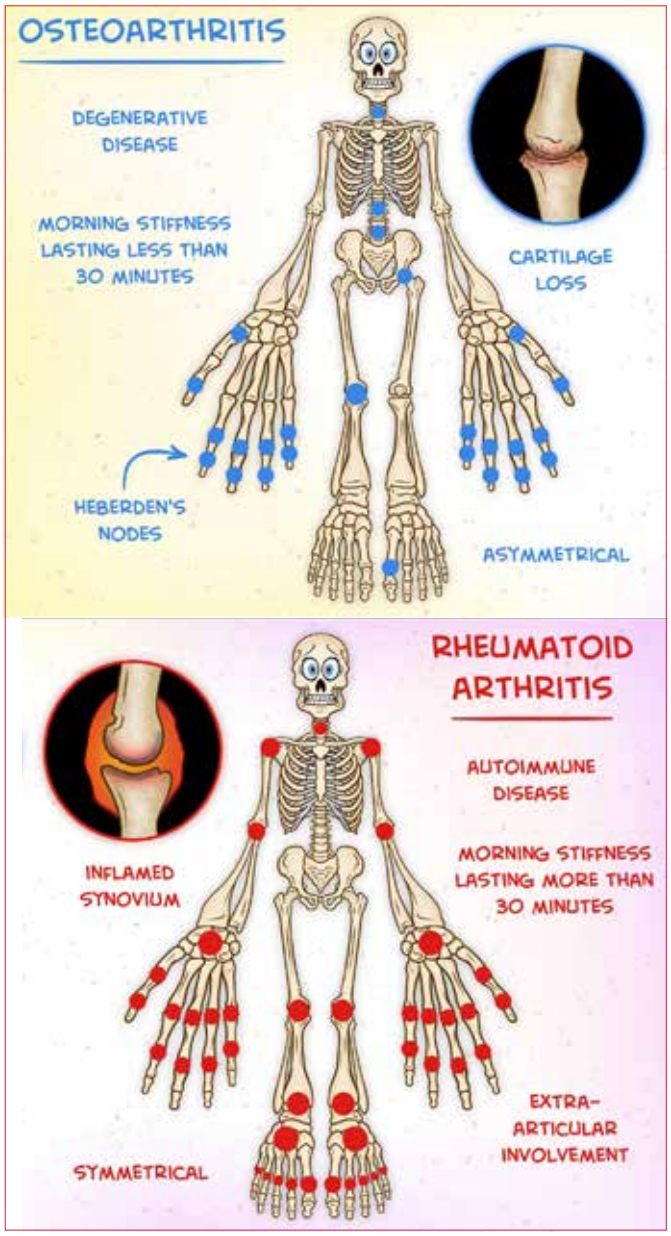

Figure 8. Osteoarthritis *vs* rheumatoid arthritis

Diagnosis of OA has been widely based on clinical features, imaging examinations and laboratory findings.[15,20, 22-24] The American Geriatrics Society has provided clinical guidelines that have guided diagnostic practice in osteoarthritis.[30,31] The clinical approach takes into consideration thorough history taking and physical examination for signs and symptoms. Imaging examinations used diagnostically, to help establish prognosis and monitor effects of therapy, include radiography, computed tomography, positron tomography, ultrasonography and magnetic resonance imaging.[32]

Laboratory indication of chronic inflammatory changes, with production of pro-inflammatory cytokines, is apparent during early development of osteoarthritis. Increases in circulating levels of C-reactive protein (CRP), interleukin (IL)-6 and IL-4, and tumour necrosis factor alpha (TNF-α) have been linked to OA and used as possible biomarkers. Interleukin-6 and IL-4 identify radiologically

severe osteoarthritis with low-grade inflammation.[24,33] Chemotactic cytokine ligands and chemokine (C–C motif) receptor 2-expressing cells appear to be increased during joint injury and osteoarthritis.[22,33] Other inflammatory cytokines, such as IL-1b and TNF-α, may be used to indicate degenerative events in cartilage. Elevated serum concentrations of cartilage oligomeric matrix protein (COMP) is another biomarker proposed to have potential use diagnostically.[24]

Management of osteoarthritis

Due to poor understanding of the disease pathology, no current treatment can prevent either initiation or progression of OA.[17] Osteoarthritis cannot be cured,[4] and appropriate management includes a combination of non-pharmacological and pharmacological measures with the ultimate goal to alleviate pain and improve functional status.[16]

Non-pharmacological management

Daily use of the joints actually preserves rather than "wears out" articular cartilage and inadequate use is the commonest cause of cartilage degeneration, as noted more than 50 years ago! An OA-patient should agree to manage themselves by ensuring positive behavioural changes e.g. exercise, weight loss, and use of suitable footwear (including those with shock-absorbing properties).[19] Physical activity, e.g. walking, can reduce pain and help to maintain (or attain) a healthy weight. Excess weight adds additional stress to weight-bearing joints and by losing weight, it can reduce OA pain and limit further joint damage. Strengthening exercises build muscle around the OA-affected joints – this can ease the burden on the affected joints. Exercise also improves joint flexibility and reduces joint stiffness. Gentle stretching of joints can further improve flexibility, decrease stiffness and lessen pain.[4] Other non-pharmacological interventions include patient education, occupational therapy, and heat and cold therapies.[4,16]

Pharmacological management

Analgesics e.g. paracetamol are indicated for mild to moderate OA pain without apparent inflammation. Should the pain relief be insufficient or the clinical presentation of OA is inflammatory, a nonsteroidal anti-inflammatory medicine (NSAID) can be added to the regimen. A topical NSAID preparation can be particularly useful in patients who are at increased risk for adverse events with systemic NSAIDs. Patients with an elevated risk for gastrointestinal toxicity can be managed with a selective cyclooxygenase (COX)-2 inhibitor e.g. celecoxib. Should a patient's pain be highly resistant, tramadol is another option. Judicious use of narcotics e.g. oxycodone and paracetamol with codeine, is reserved for patients presenting with severe OA.[16] Other pharmacological therapy to reduce pain and inflammation includes intra-articular injections of corticosteroid or sodium hyaluronate (also referred to as viscosupplementation e.g. hyaluronan). In patients with OA of the knee, these injections can reduce pain as soon as one week post-injection and last, on average, four to six weeks.[16] Intra-articular corticosteroid injections should be considered as an adjunct to core treatments for the relief of moderate to severe pain in people with OA.[19]

Patients with OA who experience joint symptoms that have a substantial impact on their quality of life and are refractory to non-surgical interventions are considered for referral for surgery.[19]

Conclusion

Effective management of OA is multimodal and involves the participation of both the patient and a multidisciplinary healthcare team. Patient education plays a pivotal role in the success of therapy. Pharmacotherapy must be supported by relevant strengthening physical activity and weight reduction measures to conserve joint integrity. Occupational therapy, and surgical interventions as a last resort, form an important part of the treatment regimen to ensure a better quality of life for the patient.

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