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ADVANCES IN THE UNDERSTANDING OF OSTEOARTHRITIS

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ABSTRACT
Joint instability creates a clinical and economic burden in the health care system. Injuries and disorders that directly damage the joint structure or lead to joint instability are highly associated with osteoarthritis (OA). Thus, understanding the physiology of joint stability and the mechanisms of joint instability-induced OA is of clinical significance. Discusses the structure and function of major joint tissues, including periarticular muscles, which play a significant role in joint stability. The mechanisms of ligament injury-associated joint instability of these joints. mThese advances may lead to new opportunities for clinical intervention in the prevention and early treatment of OA.

KEYWORDS: Osteoarthritis, joint stability, joint instability, joint injury, ligament injury, Radiographs, X-ray.

INTRODUCTION

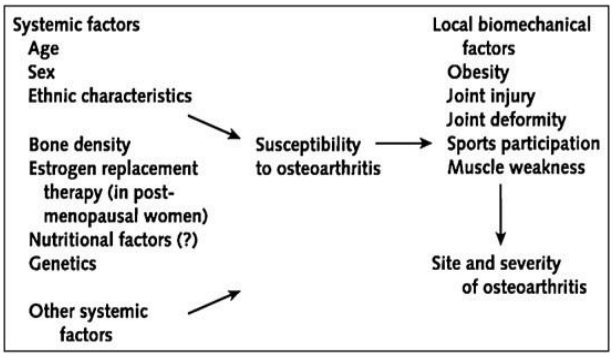
Osteoarthritis (OA) is the most common articular disease worldwide; its high prevalence entails significant costs to society .Direct costs of osteoarthritis include clinician visits, medications, and surgical intervention, indirect cost is the time lost from work.[1]

The aim of this work is to demonstrate the advances in etiopathogenesis, clinical assessment and management of osteoarthritis.

The World Health Organization (WHO) figures of worldwide estimates are that 9.6% of men and 18% of women aged more than 60 years have symptomatic OA. The prevalence of OA increases with age because the condition is not reversible. Men are affected more often than women among those aged less than 45 years, whereas women are affected more frequently among those aged more than 55 years.[2]

Risk factors for osteoarthritis

OA has a multifactorial etiology and can be considered the product of interplay between systemic and local factors.



Risk factors for osteoarthritis.

Pathogenesis of Osteoarthritis

OA has no common pathophysiologic pathway, but only a final common end stage. The inflammatory changes in OA are secondary and are caused by particulate and soluble breakdown products of cartilage and bone. OA should not be considered to be a degenerative joint disease as the cells of the cartilage and bone are normal and, if the high levels of intra-articular stress are reduced, can restore the damaged tissue to normal. The common mechanical factor underlying OA is a pathologic increase in intra-articular stress. Excessive loading of a joint, causes bone to fracture, rather than fracturing the cartilage. In contrast, sub-fracture impulsive loads cause micro-injury of the subchondral bone and articular cartilage that may exceed the ability of the joint to repair the damage.[3]

Ageing and osteoarthritis

Apparently, OA is not simply a wear and tear process but a process depending on biological ageing. Articular cartilage is optimized to maximally support fitness during the reproductive period of individuals. Many theories have been proposed to explain the correlation between aging and primary osteoarthritis. All these theories are based on the assumption that OA originates in the articular cartilage.[4]

These include

1) Wear and tear.
2) Changes in the cartilage matrix.
3) RAGE receptor driven processes.
4) Reactive oxygen species.
5) Loss of growth factor responsiveness.
6) Chondrocyte apoptosis.
7) Mutations and inborn errors.
8) Changes in subchondral bone.
9) Changes in muscle.
10) Changes in tendons.

Pathology

Osteoarthritic joints have abnormal cartilage and bone, with synovial and capsular lesions. Macroscopically, the most characteristic elements are reduced joint space, formation of osteophytes (protrusions of bone and cartilage) mostly at the margins of joints, and sclerosis of the subchondral bone. These changes are the result of several histologic phases.[5]

- **Edema and microcracks.**
- **Fissuring and pitting.**
- **Erosion.**

Articular cartilage is both aneural and avascular. As such, cartilage is incapable of directly generating pain, inflammation, stiffness, or any of the symptoms that patients with OA typically describe. The relation of cartilage to symptoms in OA is likely through secondary mechanisms such as:

- Exposing the underlying subchondral bone nociceptors.
- Vascular congestion of subchondral bone leading to increased intra-osseous pressure.
- Synovitis secondary to articular cartilage damage with activation of synovial membrane nociceptors.[6]

Classification of Osteoarthritis

OA may be primary idiopathic, affecting one or generalized joints or secondary to trauma or other diseases, such as metabolic, endocrine, and calcium pyrophosphate deposition disease. Primary OA may affect all axial and peripheral joints except the 2nd through 4th metacarpophalang-eal and metatarsophalangeal joints. Secondary OA associated with trauma is isolated to the trauma site, and that associated with other diseases varies according to the specific disease.[7]

Classification of osteoarthritis

<table>
<tr><th colspan="2">Primary (Idiopathic) OA</th></tr>
<tr><td colspan="2">Localized</td></tr>
<tr><td>Hands:
Heberden's andBouchard’s nodes (nodal), Erosive interphalangeal arthritis(non nodal), Carpal-1st metacarpal joint</td><td>Hip:
(a) Eccentric (superior)
(b) Concentric (axial, medial)
(c) Diffuse (coxae senilis)</td></tr>
<tr><td>Spine:
(a) Apophyseal joints
(b) Intervertebral joints (disc)
(c) Spondylosis (osteophytes)
(d) Ligamentous(Forestier's disease,DISH)</td><td>Feet:
Hallux valgus, Hallux rigidus, Contracted (hammer/cockup) toes, talonavicular joint.</td></tr>
<tr><td>Other single sites, e.g. Glenohumeral, tibiotalar,sacroiliac, acromioclavicular, temporomandibular joints.</td><td>Knee:
(1) Medial compartment
(2) Lateral compartment
(3) Patellofemoral compartment</td></tr>
<tr><td colspan="2">Generalized includes three or more areas listed above</td></tr>
<tr><td colspan="2">Secondary OA</td></tr>
<tr><td colspan="2">Trauma: Acute or Chronic (occupational, sports)</td></tr>
<tr><td>Metabolic:
• Ochronosis (alkaptonuria)
• Hemochromatosis
• Wilson's disease
• Gaucher's disease</td><td>Endocrine:
• Acromegaly
• Hyperparathyroidism
• Diabetes mellitus
• Obesity
• Hypothyroidism</td></tr>
<tr><td>Neuropathic:
• Charcot joint</td><td>Endemic:
• Kashin-Beck and Mseleni</td></tr>
<tr><td>Calcium deposition diseases:</td><td>Miscellaneous:</td></tr>
</table>

• CPPD deposition • Apatite arthropathy	• Frostbite • Caissons disease • Hemoglobinopathies
Congenital or developmental: Localized diseases: • Legg-Calve-Perthes syndrome, congenital hip dislocation, slipped femoral capital epiphysis **Mechanical factors:** • Unequal lower extremity length, valgus/varus deformity, hypermobility syndromes **Bone dysplasias:** • Epiphyseal dysplasia, spondyloepiphyseal dysplasia, osteo- onychochondrodystrophy	
Other bone and joint diseases: • **Localized:** Fracture, avascular necrosis, hyperostosis, infection, gout • **Diffuse:** Rheumatoid arthritis, Paget's disease, osteopetrosis, osteochondritis	

Clinical Features

The signs and symptoms characteristic of osteoarthritis in the most frequently affected joints, include:

- *General:* Pain, stiffness, gelling, crepitus, bony enlargement, limited range of motion and malalignment.
- *Hands:* DIPs (Heberden nodes), PIPs (Bouchard nodes), CMC; squaring of the base of the hand; medial and lateral deviation at the DIPs and PIPs.
- *Knees:* Patellofemoral joint symptoms worse on the stairs than on the flat; Varus changes with medial compartment disease, valgus with lateral; Baker's (popliteal) cysts and tenderness of the pes anserine bursa are common.
- *Hips:* Typically groin pain, but may present in the buttocks; less so in the knee or below knee; flexion contractures and Trendelenburg sign may be present
- *Cervical spine:* Local spine pain, muscle spasm, and limited motion (lateral flexion and extension); radicular pain, sensory loss or muscle weakness/atrophy in nerve root distribution; cervical myelopathy with long tract signs, bladder dysfunction.
- *Lumbar spine:* Local pain and muscle spasm, limited extension, buttock pain, worse in the after noon, but not nocturnal; radicular pattern with pain, sensory and motor changes in nerve root distribution; spinal stenosis pattern pain with back/leg pain with standing, walking relieved by sitting.

Diagnosis of Osteoarthritis

Laboratory findings

To date there are no pathognomonic laboratory abnormalities. Blood and urine test results are usually normal, and synovial fluid analysis often yields abnormal but nonspecific results.[8]

Noninvasive biochemical markers in osteoarthritis

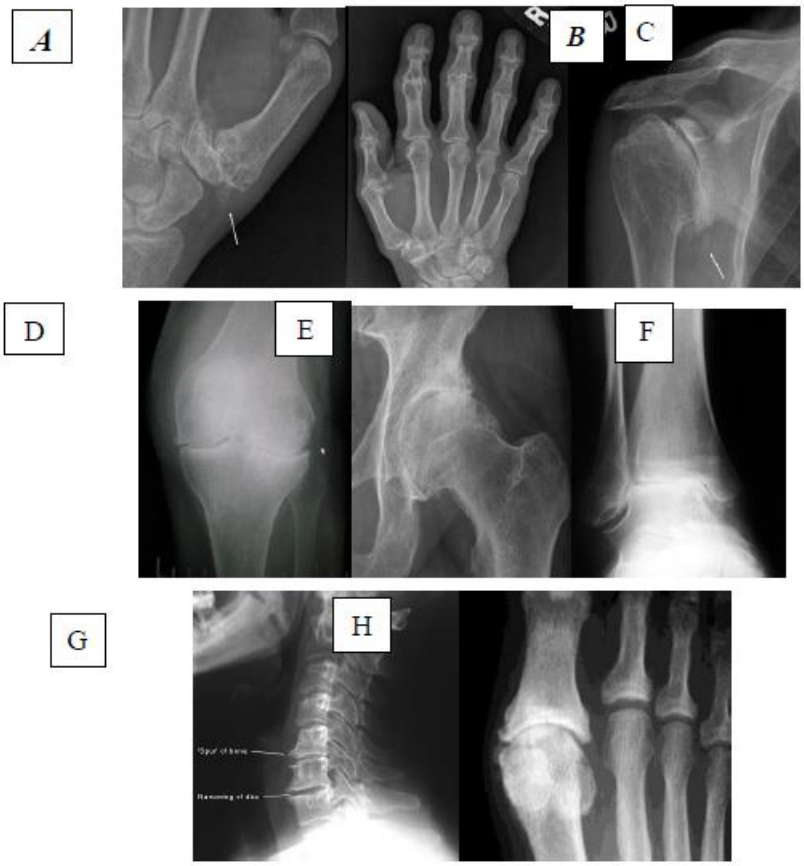
There has been a considerable interest in identifying specific biological markers for bone, cartilage, and synovium tissue turnover which could reflect quantitative and dynamic variations in joint tissue remodeling.[9]

The clinical uses of biological markers in osteoarthritis include

- Early Diagnosis.
- Prediction of progression.
- Monitoring efficacy of disease modifying osteoarthritis treatment**.**

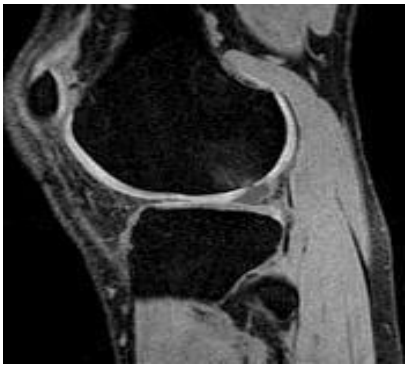
Imaging

Radiographic assessment not only is helpful to diagnose osteoarthritis, but also is useful to establish the severity of joint damage; to monitor disease activity, progression, and response to therapy; and to look for complications of the disorder or the treatment.[10]

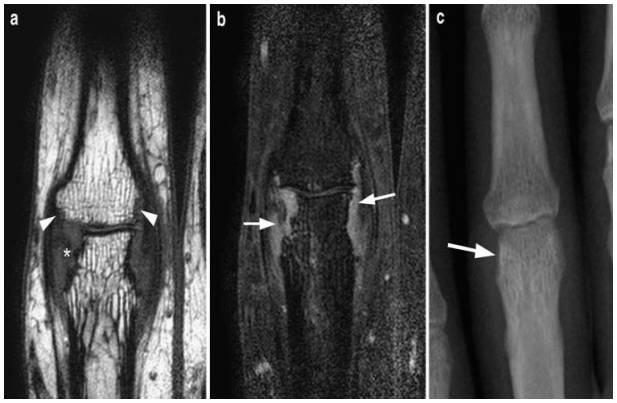


A-H: Radiologic features of osteoarthritis.
Fig. (6): Positioning of the subject for the fixed flexion and Lyon–Schuss radiographs and examples of good and poor alignment of the medial tibial plateau with the X-ray beam.[11]

Magnetic Resonance Imaging (MRI)
MRI is rarely performed to confirm the diagnosis of osteoarthritis, but is sometimes useful to exclude alternative possibilities in a difficult differential diagnosis. All tissues involved in osteoarthritis, including cartilage lesions, fluid effusion, subchondral bone marrow edema, low-grade synovitis, and meniscus or ligament lesions, can be seen by magnetic resonance imaging,MRI is useful for excluding tumor, algoneurodystrophy, or avascular osteonecrosis.[12]



Sagittal 3: Dimensional gradient-echo fat-saturated MRI of the knee reveals full- thickness thinning of the articular cartilage of the lateral femoral condyle posteriorly with underlying degenerative subchondral marrow changes.



Marginal erosions have been recognised as occurring in erosive OA, but have been considered relatively uncommon. OA in MRI may show evidence of erosions even when radiographs indicate a non-erosive form of the disease.[3]

Marginal erosions demonstrated in a proximal interphalangeal (PIP) joint of a 54- year-old woman with osteoarthritis (OA).

Ultrasound
Ultrasound has proved to be more sensitive in detecting bone erosions than conventional radiography in osteoarthritis and other rheumatic disorders. Therefore, it appears to be a promising technique for the diagnosis of

EOA before conventional radiography changes become evident.[14]

Osteoarthritis clinical assessment

One of the instruments widely used to assess pain and disability is the Western Ontario and McMaster Universities (WOMAC) composite index. It is used mainly for the knee. In addition to the WOMAC questionnaire pain subscale, functional disability resulting from knee or hip osteoarthritis is usually evaluated using the WOMAC function subscale, which is a questionnaire of 17 items related to daily activities, and the Lequesne's algofunctional index.[15]

Management of Osteoarthritis

The management of OA can be divided into nonpharmacologic interventions, pharmacologic interventions, and surgical options.

Nonpharmacologic management of osteoarthritis

Both international published recommendations for knee osteoarthritis: Osteoarthritis Research Society International (OARSI) and the European League Against Rheumatism (EULAR) insist that nonpharmacological approaches for treating osteoarthritis are of major importance,[16] insisted that nonpharmacologic interventions such as weight loss, exercise and orthotics should be an integral part of the management plan for OA.[17]

Nonpharmacologic management of osteoarthritis

Conventional Options

- Patient education.
- Arthritis self-help courses.
- Weight loss.
- Temperature modalities.
- Exercise.
- Orthotics.
- Modified activities of daily living.

Unconventional Options

- Transcutaneous electrical nerve stimulation.
- Pulsed electromagnetic fields.
- Static magnets.
- Acupuncture.
- Spa therapy.
- Yoga.

Pharmacologic management of Osteoarthritis[18]

Once the patient has pursued nonpharmacologic interventions, it is likely that therapy with a drug will be required. The choice of which specific drug or combination treatment to use remains to be individualized (19). Pharmacologic interventions can be subdivided into symptomatic therapy and potential structure or disease-modifying therapy.[20]

Pharmacologic Management of Osteoarthritis.

Topical
• Capsaicin
• Topical nonsteroidal anti-inflammatory drug (NSAID) preparations
Systemic
• Acetaminophen
• Nonselective NSAIDs
• Cyclooxygenase-2 (COX-2)–specific inhibitors
• Tramadol
• Narcotic analgesics
Intra-articular
• Corticosteroids
• Hyaluronic acid derivatives
Nutriceuticals
• Glucosamine
• Chondroitin sulfate
• Ginger extracts
• Avocado and soy unsaponifiable
• Cat's claw
• Shark cartilage
• S-adenosyl methionine
Disease-Modifying Drugs in Osteoarthritis (DMOADs)
• Tetracyclines
• Metalloproteinase or collagenase inhibitors
• Glucosamine
• Diacerein
• Growth factor and cytokine manipulation (interleukin-1 receptor antagonist [IL-1Ra], transforming growth factor-β
• Gene therapy (IL-1Ra, IL-1RII)
• Chondrocyte and stem cell transplantation

Glucosamine and chondroitin sulfate,[21] in a recent study suggested that glucosamine sulfate and chondroitin sulfate may delay the natural radiological progression of OA of the knee. The long-term administration of daily oral glucosamine sulfate at 1,500 mg over a minimal period of 3 years or daily oral chondroitin sulfate at 800 mg over a minimal period of 2 years may retard degenerative processes affecting knee joint cartilage.

Avocado and soy unsaponifiable

Avocado/Soybean unsaponifiable (ASU) are extracts of avocado and soybean which have been identified as agents for the management of OA and joint pain. ASU in combination with Glu and CS demonstrated anti-inflammatory activity, which inhibits the expression of pro-inflammatory mediators and associated molecules.[22]

Gene therapy

It is generally accepted that IL-1 and TNF-alpha are the pivotal cytokines involved in OA physiopathology. Hence, the neutralization of these inflammatory mediators appears to be a logical development for OA therapy. Local delivery of anti-inflammatory cytokines or the in vivo induction of their expression using gene

transfer may provide a novel approach for the treatment of osteoarthritis. The use of this gene under several experimental ex vivo and in vivo conditions could reduce cartilage degradation, and retard the progression of structural changes in osteoarthritis.

Chondrocyte and stem cell transplantation

Increasing incidence of OA and the aging population coupled with insufficient therapeutic choices has led authors to focus on the potential of stem cells as a novel strategy for cartilage repair. Mesenchymal stem cells (MSCs) present themselves as promising, attractive tools for cartilage repair. Tissue engineering and stem cell technologies have established themselves as approved new approaches especially in cartilage and OA research. However, although research with MSCs for cartilage and connective tissue repair has come a long way, it is still only at the beginning of this exciting new journey.[24]

CONCLUSION

As the populations of developed nations age over the next few decades, the need for better understanding of osteoarthritis will continue to grow. Despite an extensive armamentarium and numerous surgical options, osteoarthritis remains incurable, and an improved approach in the treatment of this disease is imperative.

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