
Article

Modern Approaches to Early Diagnosis of Knee Osteoarthritis and Optimization of Treatment Tactics

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Abstract: Knee osteoarthritis is a leading cause of pain, disability, and reduced quality of life worldwide, and its burden is rising with population aging and obesity. Most patients are diagnosed at advanced stages, when structural damage is largely irreversible. Conventional radiography detects KOA only after considerable cartilage loss, and there is no consensus on a standardized algorithm for identifying early disease or on treatment strategies tailored to disease stage and patient phenotype. This review analyzed recent clinical guidelines and peer-reviewed studies on clinical assessment, imaging radiography, ultrasonography, and biochemical markers of cartilage and bone turnover, together with pharmacological, non-pharmacological, and surgical treatment approaches. Early KOA can be identified through combined clinical evaluation and sensitive imaging; MRI and ultrasonography reveal cartilage, synovial, and meniscal changes before radiographic signs appear, while biomarkers show promise as adjuncts. Core treatment includes patient education, structured exercise, and weight management, supplemented by topical or oral analgesics and intra-articular therapies. Arthroplasty is reserved for advanced disease. A stage-based, individualized strategy that integrates early multimodal diagnosis with timely conservative treatment may slow progression, reduce pain, and delay surgery. Prospective trials are needed to validate diagnostic algorithms and compare treatment effectiveness.

Keywords: knee osteoarthritis, early diagnosis, MRI, ultrasonography, biomarkers, treatment optimization



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Introduction

Osteoarthritis is the most common degenerative joint disease and a leading cause of chronic pain, mobility limitation, and loss of independence in adults. According to the Global Burden of Disease estimates, about 595 million people were living with OA in 2020, and the knee was the most frequently affected joint, with roughly 365 million cases [1]. Population aging, rising obesity, and sports- and occupation-related joint injuries are expected to increase this burden further, placing growing demands on health systems and on patients' quality of life. Knee osteoarthritis is now understood as a disease of the whole joint rather than of cartilage alone. Progressive degradation of articular cartilage occurs together with subchondral bone remodeling, osteophyte formation, synovial inflammation, and meniscal and ligamentous changes. Because pain and functional limitation usually appear only after these processes are well established, diagnosis is often made late, at a stage when structural damage is largely irreversible and therapeutic options are limited mainly to symptom control and, eventually, joint replacement.

Diagnosis in routine practice still relies heavily on clinical examination and plain radiography graded by the Kellgren–Lawrence scale [2]. Radiographs, however, show cartilage

loss only indirectly through joint space narrowing and cannot reliably detect early changes in cartilage, synovium, or bone marrow. In response, the concept of early KOA has emerged, and proposed classification criteria combine symptoms, clinical findings, and advanced imaging such as MRI to identify patients before radiographic disease develops [3]. Ultrasonography, MRI, and biochemical markers of cartilage and bone turnover are being studied as complementary tools, but their diagnostic thresholds, availability, and cost-effectiveness have not been standardized.

Treatment strategies face a parallel problem. Current guidelines recommend a stepwise, largely conservative approach: patient education, structured exercise, weight reduction, and pharmacological options such as topical and oral anti-inflammatory drugs and intra-articular injections, with surgery reserved for advanced disease [4]. Yet no intervention has been proven to modify the course of the disease, evidence for several injectable therapies remains inconsistent, and treatment is rarely matched to disease stage or patient phenotype. As a result, the potential benefit of acting during the early window, when the process may still be slowed, is underused.

Therefore, a critical synthesis of modern diagnostic approaches for early KOA and of treatment tactics adapted to disease stage is needed. The aim of this article is to review current methods of early diagnosis, evaluate the evidence for conservative and other treatment options, and propose an optimized, individualized, stage-based management strategy.[5]

Knee osteoarthritis is a leading cause of chronic pain, mobility limitation, and functional impairment among adults worldwide. According to the Global Burden of Disease study, over 595 million people were living with osteoarthritis globally, with more than 374.7 million cases involving the knee joint [6]. Driven by population aging, the rising prevalence of obesity, and joint injuries, the burden of knee osteoarthritis is projected to increase by 74.9% by 2050. In modern rheumatology and orthopedics, KOA is recognized as a disease of the entire joint rather than an isolated degradation of articular cartilage. Progressive cartilage breakdown occurs alongside subchondral bone remodeling, osteophyte formation, synovial inflammation, and meniscal and ligamentous alterations [7]. In routine clinical practice, diagnosis relies heavily on physical examination and plain radiography graded by the Kellgren–Lawrence scale [8]. However, conventional radiographs detect cartilage loss only indirectly through joint space narrowing and fail to identify structural alterations during the initial stages. Consequently, the concept of "Early KOA" has emerged, establishing criteria to identify structural and clinical changes before radiographic features manifest [9].

The limitations of plain radiography in early KOA necessitate the integration of sensitive imaging modalities. Magnetic Resonance Imaging enables the detection of early cartilage fibrillation, synovitis, meniscal tears, and bone marrow lesions years before radiographic changes appear [10]. Ultrasonography serves as an accessible, point-of-care alternative for evaluating synovial hyperplasia, joint effusion, and early osteophytosis. Additionally, biochemical markers of cartilage and bone turnover—such as type II collagen degradation products, cartilage oligomeric matrix protein (COMP), and inflammatory cytokines—are being investigated as complementary tools for monitoring disease activity. However, standardized diagnostic thresholds and the cost-effectiveness of these biomarkers and advanced imaging techniques remain to be fully established [11]. Automated image analysis using artificial intelligence and deep neural networks represents an emerging avenue for enhancing diagnostic precision.

Current clinical practice guidelines unanimously recommend non-pharmacological core therapies as the first-line management strategy for KOA [5, 6]. Patient education, structured exercise regimens, and weight reduction are essential components across all stages of the disease. A body weight reduction of 5–10% significantly reduces mechanical joint loading and decreases systemic levels of pro-inflammatory cytokines. Recent clinical data demonstrate that intensive lifestyle modifications combined with modern pharmacotherapeutic weight-loss agents can slow cartilage loss and alleviate joint pain. Concurrently, therapeutic exercise strengthens the quadriceps musculature and enhances dynamic joint stability.

Systemic and topical nonsteroidal anti-inflammatory drugs (NSAIDs) remain the first-line pharmacological options for symptomatic relief [12]. However, systemic NSAID use is frequently constrained by gastrointestinal, renal, and cardiovascular safety risks during long-term administration. Intra-articular (IA) injections are widely utilized as localized adjuncts. IA

corticosteroids provide rapid, short-term relief during acute inflammatory flares and synovitis. Hyaluronic acid injections aim to restore the viscoelastic properties of synovial fluid, whereas autologous platelet-rich plasma and mesenchymal stem cell therapies are under active investigation for their potential regenerative effects [13]. Nevertheless, robust high-level evidence supporting disease-modifying outcomes for intra-articular therapies remains inconclusive.

When conservative measures fail to provide adequate relief and structural joint damage reaches an advanced stage Kellgren–Lawrence grades III–IV, surgical intervention is considered. Total knee arthroplasty is the established, highly effective surgical standard for relieving severe pain and restoring joint function. Conversely, joint-preserving surgical procedures—such as corrective osteotomy and arthroscopic lavage—have more circumscribed indications in early-to-moderate KOA. Timely, stage-appropriate conservative management during early disease can effectively delay the clinical necessity for total joint replacement.

Critical synthesis of current literature highlights several persistent gaps in KOA management, including the absence of a globally validated, consensus-based diagnostic algorithm for early KOA, limited integration of biochemical markers and MRI-based phenotyping into routine clinical workflows, and a lack of stage-specific, phenotype-driven treatment protocols tailored to individual patient profiles. Future prospective randomized controlled trials are required to validate early diagnostic criteria and demonstrate the long-term clinical efficacy of early multimodal conservative interventions.

Methodology

This study employs a comprehensive literature-based methodology combining narrative review, comparative synthesis, and stage-specific analytical frameworks to evaluate modern diagnostic modalities and optimize treatment strategies for knee osteoarthritis. Grounded in contemporary epidemiological data, KOA is conceptualized not merely as isolated articular cartilage loss, but as a complex, whole-joint disease characterized by subchondral bone remodeling, synovial inflammation, and structural meniscal alterations. To systematically bridge the gap between initial pathological changes and clinical management, this study establishes a structured framework that links early diagnostic detection directly with individualized, stage-appropriate therapeutic interventions. Traditional clinical practice relies primarily on plain radiography graded by the Kellgren–Lawrence scale. However, conventional radiographs only indirectly indicate cartilage degradation through joint space narrowing, creating a critical knowledge gap where structural damage becomes largely irreversible prior to formal diagnosis. To address this limitation, this review systematically evaluates sensitive imaging techniques—specifically Magnetic Resonance Imaging and Ultrasonography alongside biochemical markers of bone and cartilage turnover, such as type II collagen degradation products and cartilage oligomeric matrix protein. Through comparative diagnostic synthesis, MRI is integrated for its high sensitivity in detecting early cartilage fibrillation, bone marrow lesions, and synovitis, while ultrasonography is incorporated as a point-of-care tool for assessing synovial hyperplasia and early osteophytosis. Furthermore, emerging artificial intelligence models and deep neural network algorithms are analyzed for their capacity to enhance automated grading accuracy. The analytical workflow categorizes diagnostic findings into specific disease phenotypes—mechanical, inflammatory, and metabolic—to map them directly against stage-based therapeutic options. The methodology synthesizes current evidence across three core therapeutic domains: core non-pharmacological interventions evaluating structured exercise, patient education, and lifestyle-driven weight management aimed at a 5–10% weight reduction as baseline foundations; targeted pharmacotherapy and intra-articular interventions assessing topical and systemic NSAIDs alongside intra-articular corticosteroids for acute synovitis, hyaluronic acid for viscosupplementation, and regenerative therapies like platelet-rich plasma and mesenchymal stem cells; and surgical management defining precise thresholds where conservative measures fail and structural degeneration warrants joint-preserving osteotomy or total knee arthroplasty. The synthesis yields an integrated management algorithm demonstrating that early multimodal diagnosis—combining clinical evaluation with MRI and ultrasound sensitivity—enables clinical action during the optimal "early window" before irreversible joint destruction occurs. The primary clinical implication of this approach is a paradigm shift from reactive symptom control to

proactive, stage-based disease management. Tailoring multimodal conservative treatments to specific patient phenotypes reduces pain, slows structural progression, and significantly delays the necessity for invasive joint replacement surgery. Finally, prospective randomized controlled trial frameworks are outlined to further validate these diagnostic thresholds and quantify the long-term cost-effectiveness of early individualized interventions.[14]

Results and Discussion

Synthesis of current clinical and imaging evidence reveals that early multimodal assessment significantly outperforms conventional radiography in identifying knee osteoarthritis before irreversible structural destruction occurs. While plain radiographs graded by the Kellgren–Lawrence scale remain the standard in routine practice, they only detect indirect cartilage loss through joint space narrowing at advanced stages. In contrast, sensitive imaging modalities—specifically Magnetic Resonance Imaging and Ultrasonography successfully capture pre-radiographic structural alterations, including early cartilage fibrillation, bone marrow lesions, synovial hyperplasia, and meniscal micro-tears. When combined with emerging biochemical markers of bone and cartilage turnover, such as type II collagen degradation products and cartilage oligomeric matrix protein, these modalities allow clinicians to identify KOA during an early, potentially modifiable window. Figure 1. Deep theoretical analysis indicates that KOA should be conceptualized not merely as mechanical cartilage wear, but as a complex, whole-joint disease driven by distinct inflammatory, metabolic, and mechanical phenotypes.[15]



Figure 1. Synthesis of current clinical, imaging, and molecular evidence reveals

Synthesis of current clinical, imaging, and molecular evidence reveals that knee osteoarthritis is not merely a consequence of mechanical cartilage wear, but a complex, whole-joint pathobiological disease driven by intricate cellular and molecular shifts (Figure 1). In a healthy human knee, tissue stem cells TSCs dominated by regenerative phenotypes SDF1+, SOX9+, CD146+, CD105+, PDGFRB+, and ACAN+ maintain joint tissue homeostasis. However, aging, obesity, mechanical trauma, and excessive locomotion disrupt this delicate balance, downregulating regenerative TSCs while upregulating osteogenic TSCs NT5E+, ALCAM+, and NGF+ and triggering osteogenic transitions characterized by RUNX2, ASPN, and OGN expression. Concurrently, articular cartilage experiences an expansion of detrimental chondrocytes (MDCs producing MMP13, TNFRSF11B, CCL20, LAMB, and WNT7B, while the synovium undergoes macrophage infiltration—featuring quadruple-positive pro-inflammatory macrophages IL1 β +, IL6+, TNF α +, and iNOS+ alongside pain-associated macrophages P2RX7+, CSF1R+, AIF+, and PTGS2+—coupled with fibroblast expansion. These Figure 2. molecular mechanisms directly drive synovial inflammation, chronic pain, and progressive structural degradation.



These pathobiological alterations manifest across four distinct clinical and radiographic stages of KOA progression (Figure 2).

Stage 1 Early Stage features microstructural cartilage changes and subclinical synovial inflammation that remain undetectable on conventional radiographs, yet can be successfully identified prior to structural collapse using sensitive modalities such as Magnetic Resonance Imaging and ultrasonography. Stage 2 Mild Stage exhibits early cartilage thinning and minimal joint space narrowing. Stage 3 Moderate Stage is characterized by substantial cartilage loss, clear osteophyte formation, and subchondral sclerosis. Finally, Stage 4 (Severe Stage) presents advanced joint degeneration with complete cartilage disappearance, bone-on-bone friction, and severe structural deformity requiring surgical intervention.

From a practical perspective, recognizing the "early window" during Stages 1 and 2 is critical for shifting management from reactive end-stage treatment to proactive, stage-specific disease modification. Core non-pharmacological interventions—including patient education, structured quadriceps-strengthening exercise programs, and targeted weight management aimed at a 5–10% reduction in body weight—substantially decrease mechanical joint loading and systemic inflammatory cytokine levels. Symptomatic control can be optimized via localized intra-articular therapies, such as corticosteroids for acute inflammatory flares and hyaluronic acid for viscosupplementation, while regenerative options like platelet-rich plasma and mesenchymal stem cells hold potential for mitigating osteogenic transitions in early phases. Conversely, in advanced Stages 3 and 4, conservative measures yield limited efficacy, shifting the clinical threshold toward total knee arthroplasty.

Despite these insights, critical knowledge gaps persist, notably the absence of universally standardized diagnostic thresholds for early-stage KOA, the fragmented clinical integration of biochemical biomarkers, and the unclear long-term disease-modifying efficacy of intra-articular and regenerative therapies. Furthermore, automated diagnostic grading algorithms require extensive external validation across diverse patient cohorts. To bridge these gaps, future research must prioritize multi-center, prospective randomized controlled trials designed to validate stage-specific diagnostic criteria, evaluate phenotype-driven conservative management protocols, and determine the long-term cost-effectiveness of early interventions. Advancing both theoretical frameworks and practical clinical applications will ultimately transform KOA management into a precise, preventive discipline.

CONCLUSION

This study provides a comprehensive synthesis of modern approaches to early diagnosis and the optimization of treatment management for knee osteoarthritis. The findings convincingly demonstrate that KOA is not merely the mechanical wear and tear of articular cartilage, but a complex pathobiological process involving the entire joint complex. On a cellular and molecular level, disease progression is driven by an imbalance in tissue stem cells characterized by the

downregulation of regenerative TSCs, the activation of osteogenic cells, the expansion of detrimental chondrocytes, and synovial macrophage infiltration that triggers persistent inflammation and chronic pain. From a clinical perspective, conventional radiography fails to capture these pathophysiological shifts during early phases, detecting only indirect signs of established cartilage destruction. Incorporating highly sensitive imaging modalities—specifically Magnetic Resonance Imaging and Ultrasonography—alongside specific biochemical markers enables the accurate identification of KOA at Stages 1 and 2, within the critical "early window of opportunity". This diagnostic shift facilitates a transition from reactive symptom management to proactive, stage-specific, and individualized disease modification. Timely implementation of multimodal conservative strategies, including targeted lifestyle modifications, 5–10% weight reduction, structured exercise therapy, and localized intra-articular treatments, significantly alleviates inflammation, decelerates structural joint degradation, and effectively delays the clinical necessity for radical total joint replacement. The primary academic and practical implication of this research is the urgent need to establish and standardize globally recognized diagnostic algorithms for early KOA, as well as to integrate phenotype-driven treatment protocols into routine clinical workflows. Future prospective randomized controlled trials should focus on validating molecular biomarkers and evaluating the long-term clinical and cost-effectiveness of early multimodal conservative interventions.

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