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Review Article

Conservative and Emerging Rehabilitative Approaches for Knee Osteoarthritis Management

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Abstract

Background: Knee osteoarthritis (OA) involves complex interactions between biological and biomechanical factors that drive joint degeneration. Conservative rehabilitation approaches are standard initial management, but have limited long-term efficacy.

Purpose: To review key aspects of knee OA pathophysiology and emerging therapeutic directions.

Main body: Abnormal loading and altered neuromuscular control disrupt knee joint biomechanics in OA. Inflammation, PAR receptor signaling, and impaired chondrocyte mechanobiology promote cartilage catabolism. Subchondral bone and osteophyte changes also occur. While conservative strategies like gait retraining, proprioceptive exercises, bracing, and core strengthening help reduce symptoms and improve function, intrinsic joint damage eventually limits efficacy. Novel approaches using biologics, regenerative cell therapy, tissue engineering constructs, and nanotechnology aim to repair cartilage and modify disease progression, but require further optimization and testing before clinical implementation.

Conclusion: Addressing both the biomechanical and biological factors contributing to knee OA will be key for developing effective therapies able to halt joint degeneration and restore function.

Keywords: osteoarthritis; knee; biomechanics; inflammation; regeneration; tissue engineering

Background

Knee osteoarthritis (OA) is a highly prevalent joint disease and major cause of chronic disability worldwide. The complex interplay between biological factors and mechanical forces in the pathogenesis of knee OA continues to be elucidated. Dysregulated molecular signaling, inflammatory changes, and altered joint biomechanics disrupt the normal homeostasis of articular cartilage, synovium, and subchondral bone, leading to progressive breakdown of these tissues. As the global burden of knee OA rises with aging populations, there is an increasing need for therapies that can effectively halt or reverse joint degeneration [1]. Conservative rehabilitation approaches remain the standard first-line treatment for knee OA. Protocols aim to address neuromuscular impairments, strengthen muscles, improve range of motion and flexibility, normalize gait mechanics, and reduce excessive joint stresses. However, the intrinsic joint changes of OA often limit the efficacy of conservative management long-term. There is growing interest in novel biological agents, tissue engineering, regenerative cell therapies, and nanotechnology platforms that may modify OA disease progression. However, many emerging approaches remain in early investigation [2]. This review provides a focused update on the key pathophysiological factors underpinning knee OA progression and summarizes both established and innovative therapeutic directions. A greater understanding of how biological and biomechanical elements interact to drive joint degeneration will be instrumental for developing integrated treatment strategies able to durably modify disease and improve long-term outcomes.

II. Knee joint biomechanics

Knee osteoarthritis involves complex changes in joint loading and kinematics that contribute to cartilage breakdown and disability. Advanced

biomechanical analysis provides valuable insights into how altered gait patterns, muscle forces, and contact stresses accelerate degeneration of the tibiofemoral and patellofemoral compartments. Understanding key aspects of knee joint biomechanics is critical for identifying targets for conservative and surgical management of knee OA [3].

Gait Analysis and Ground Reaction Forces

Instrumented 3D gait analysis is an important tool for evaluating knee joint biomechanics. Force plates and motion capture systems quantify ground reaction forces, joint moments, and lower extremity kinematics during walking. Findings include decreased walking speed, reduced knee flexion, prolonged stance phase, and asymmetrical weight bearing in knee OA patients [4].

The first peak of the vertical ground reaction force represents impact loading at heel strike. The second peak corresponds to maximal weight acceptance in stance. Both peaks are attenuated in knee OA gait as a pain avoidance strategy. However, this leads to reduced shock absorption and higher joint stresses. Lateral thrust gait and wide base of support are also common, aimed at reducing knee adduction moments [5].

Gait retraining focused on restoring heel strike, increasing cadence, normalizing sagittal plane ROM, and reducing excessive foot external rotation can help improve knee biomechanics. However, abnormalities often persist due to structural changes [6].

Knee Adduction Moment and Dynamic Joint Loading

The external knee adduction moment, measured via gait analysis, reflects dynamic loading on the medial compartment during stance. It corresponds to the frontal plane lever arm and ground reaction force vector. A higher knee adduction moment is associated with greater severity and progression of medial compartment knee OA. Interventions aim to reduce the adduction moment by laterally shifting the center of mass, decreasing stance time, using gait aids, modifying footwear, and performing muscle strengthening exercises. However, substantial changes in knee biomechanics are difficult to achieve through conservative treatment once structural joint deterioration develops [7, 8].

Tibiofemoral and Patellofemoral Kinematics

Knee OA involves kinematic changes and contact stress abnormalities in both the tibiofemoral and patellofemoral joints. Altered tibiofemoral kinematics include decreased internal rotation with knee flexion as well as paradoxical anterior sliding of the femur on the tibia. This disrupts optimal joint congruency through the range of motion. Patellofemoral OA is also common. It involves inferior patellar tilt, reduced patellar mobility, and altered patellar tracking, especially in early knee flexion. This leads to increased patellofemoral contact pressures, particularly with activities like stair ambulation. Improving soft tissue flexibility, patellar mobilization, quadriceps strengthening, and movement pattern retraining can help optimize patellofemoral and tibiofemoral mechanics. However, structural changes still limit normal joint excursion long-term [9-11].

Flexion/Extension ROM and Concentric Quad Strength

Knee OA involves reduced flexion/extension ROM, commonly entering a painful stiff arc between 20-50˚ flexion. This corresponds to reduced knee excursion in midstance to terminal swing during gait. A flexed knee posture is adopted to avoid loading the joint near full extension. Concentric quadriceps strength is also diminished, despite muscle hypertrophy in early OA. The rectus femoris is particularly prone to weakness and atrophy. This impairs shock absorption and acceleration of the limb. Eccentric quad strength may be better maintained to control knee flexion. Stretching, ROM exercises, patellar mobilization, and progressive quadriceps strengthening help counteract these impairments. Maximizing knee ROM is key for normal gait, while improving quad strength reduces joint stresses [12-14].

Proprioception and Postural Stability

Proprioceptive deficits and poor postural control are common complaints in knee OA, which increase fall risk. Reduced knee position sense, altered somatosensory input, and impaired reflex response times are evident. Proprioceptive and balance exercises are recommended, including knee joint repositioning, dynamic standing balance activities, and use of unstable surfaces. This helps maximize sensory input and motor responses around the knee. However, OA-related structural damage still impacts overall function [15-17].

Innovations in Motion Capture and Musculoskeletal Modeling

Advanced motion capture tools offer greater insight into in-vivo knee joint biomechanics. Dynamic stereo radiography tracks bony movement through activity. Biplanar videoradiography also assesses kinematics via low-dose x-ray. Musculoskeletal modeling analyzes muscle and joint contact forces noninvasively. OpenSim software uses 3D motion data, EMG, and optimization algorithms to estimate knee contact patterns. This helps target interventions to specific loading abnormalities [18-20].

III. Trunk and lower limb biomechanics

Biomechanical factors play an important role in the development and progression of knee OA. Abnormal joint loading and altered gait mechanics can accelerate cartilage breakdown and joint degeneration. Furthermore, impairments in trunk and lower limb muscle function can disrupt normal movement patterns and increase mechanical stress on the knee joint. An understanding of trunk and lower limb biomechanics is crucial for identifying risk factors, guiding treatment, and optimizing function in individuals with knee OA [21, 22].

Core Stability and Lumbar Posture

Core stability refers to the ability to control the position and motion of the trunk and pelvis during functional activities. It depends on motor control and muscular capacity of the abdominals, back extensors, gluteals, and other core musculature. Impaired core stability is associated with knee OA and can manifest as poor lumbar posture, altered pelvic tilt, and inefficient muscle recruitment patterns. Individuals with knee OA often exhibit a flexed lumbar posture, increased anterior pelvic tilt, and overactivation of the erector spinae muscles. This disrupts the optimal alignment of the pelvis over the femur and tibia, altering forces at the knee joint. Excessive anterior pelvic tilt allows the femur to internally rotate and adduct, increasing lateral compression of the joint. Flexed lumbar posture also causes abnormal flexion moments at the knee during gait. Core strengthening exercises that target the transverse abdominis, multifidus, and pelvic floor muscles are recommended to improve spine and pelvic stability in knee OA patients. This helps restore neutral alignment, enhance shock absorption, and reduce abnormal stresses on the knee joint during weightbearing activities [23-25].

Back Extensor Strength

In addition to core muscles, the back extensor muscles play a key role in maintaining upright posture and stabilizing the trunk. The erector spinae

muscles, particularly the longissimus and iliocostalis, act to extend and laterally flex the spine. Weakness of the back extensors is associated with knee OA and exacerbates postural dysfunction. Individuals with knee OA often have poor back extensor strength due to age-related sarcopenia, disuse, and pain avoidance behaviors. This contributes to inefficient eccentric control of trunk flexion moments during gait, resulting in greater impact loading at the knee joint. Strengthening exercises for the back extensors, such as prone extensions, bridges, and bird dogs, can help reinforce proper lumbar posture and alignment. Improving back extensor strength reduces abnormal flexion moments and medial compartment loading in knee OA patients [26, 27].

Hip Abductor Strength

The hip abductor muscles, including the gluteus medius and minimus, are critical for stabilization of the pelvis and lower extremity during gait. Weakness of the hip abductors is a predominant impairment associated with knee OA. It leads to an unstable pelvis and lateral trunk lean over the stance limb, increasing the knee adduction moment. Individuals with knee OA often have gluteal muscle atrophy and hip abductor weakness on the affected side. This allows the pelvis to excessively drop toward the contralateral limb during single-leg stance, causing dynamic knee valgus and increased load on the medial compartment. Strengthening exercises for the hip abductors such as clamshells, side steps, and resistance band walks help improve pelvic stability and normalize the position of the knee during gait [28, 29].

Pelvic Biomechanics

Alterations in pelvic kinematics and muscle recruitment patterns are frequently noted in knee OA patients. Excessive anterior pelvic tilt, internal rotation of the hip, and dynamic knee valgus are common gait deviations. These disrupt the optimal alignment of the hip, knee, and ankle joints. Abnormal pelvic motion is both a consequence and contributor to muscle weakness around the hip. Gluteus maximus weakness promotes anterior pelvic tilt, while gluteus medius weakness allows uncontrolled pelvic drop toward the contralateral limb during gait. Targeted strengthening of the hip abductors, extensors, and external rotators helps control pelvic motion, improving lower extremity alignment and reducing knee joint stresses [30-32].

Trunk Lean and Posture

Excessive lateral trunk lean over the stance limb is a compensation adopted by many knee OA patients to reduce load on the affected side. However, this leads to an asymmetrical gait pattern and may accelerate degeneration. Ipsilateral trunk lean shifts the body's center of mass away from the affected knee, decreasing the external knee adduction moment. However, it also causes lateral flexion of the spine and pelvis toward the contralateral side. This disrupts normal hip abduction mechanics, often worsening dynamic knee valgus. Improving core stability, back extensor strength, and hip abductor function helps reduce excessive trunk lean in knee OA patients. Cueing upright posture and symmetrical weight shifting also helps retrain proper gait mechanics. However, moderate trunk lean may still be used as a protective strategy in severe medial compartment OA [33-35].

Compensatory Gait Patterns

Individuals with knee OA adopt various compensatory gait patterns to reduce loading on the affected joint. Common adaptations include reduced walking speed, shortened stride length, increased stance time, toe-out gait, lateral trunk lean, and medial thrust gait. While these patterns temporarily decrease joint stresses, they exacerbate muscle weakness over time. A slow, abbreviated gait allows avoidance of knee flexion and quadriceps recruitment. Prolonged stance time on the contralateral limb increases hip abductor demands. Toe-out gait laterally displaces the center of pressure, increasing compensatory trunk lean. Each pattern further disrupts normal lower extremity mechanics. Gait retraining focused on restoring heel strike, cadence, stride length, and symmetry can help correct maladaptive patterns in knee OA. Improving strength, flexibility, and conditioning also allows patients to walk with less compensation. However, some adaptations may be retained in severe knee OA despite rehabilitation [36, 37].

Spinal Mobility and Erector Spinae Condition

Loss of spinal mobility and tightness of the erector spinae and surrounding musculature is common in knee OA. Restricted spine flexion, extension, and rotation alters trunk-pelvic coordination and affects lower extremity mobility during gait. Hip range of motion is also limited by impaired spinal mobility, particularly hip extension and internal rotation. This reduces shock absorption at the hip and increases dynamic joint loading at the knee. Tight erector spinae muscles contribute to flexed posture and abnormal anterior pelvic tilt as well. Spinal mobility exercises, soft tissue and manual therapy, and erector spinae stretching and self-myofascial release help address these impairments. Improving spinal mobility allows greater excursion between the thorax and pelvis when walking, taking stress off the lower extremities. Keeping the erector spinae flexible also helps optimize lumbar lordosis and pelvic position [38, 39].

Associated Low Back Pain

Low back pain is frequently present along with knee OA due to shared risk factors, abnormal gait mechanics, and compensatory muscle patterns. Axial skeleton pain inhibits mobility and predisposes to further muscle weakness and joint degeneration. Knee OA patients with low back pain walk slower and demonstrate greater lateral trunk lean compared to those without back pain. They also exhibit weaker hip abductor and back extensor muscles as well as more pronounced lumbar flexion with gait. The presence of back pain accentuates abnormal movement patterns and dysfunction. Treatment should address both the knee OA as well as low back impairments. Core and back strengthening, gait retraining, weight management, and manual therapy help alleviate low back symptoms while also improving biomechanics around the knee. The use of assistive devices such as crutches or canes may also be warranted to reduce excessive joint stresses. A multimodal approach is key for optimal outcomes [40-42].

IV. Molecular mechanisms and histopathology of knee osteoarthritis

Knee osteoarthritis involves complex molecular changes within the articular cartilage, subchondral bone, synovium and other joint tissues. These drive the characteristic histopathological features of OA including cartilage destruction, osteophytes, subchondral sclerosis and synovitis. Understanding the molecular processes underpinning OA pathology provides insight into disease progression and targets for therapy [43].

Synovial Inflammation and PAR Receptor Signaling

Low-grade synovial inflammation is a key feature of knee osteoarthritis as depicted in Table 1. The synovium shows macrophage infiltration, angiogenesis and thickening. Inflammatory cytokines like IL-1β, TNF-α and IL-6 are released, perpetuating cartilage catabolism. Protease-activated receptors (PARs) are elevated in OA synovium and mediate cellular responses to matrix-degrading enzymes. PAR-1 and PAR-2 in particular

contribute to sustained inflammation. Agonism of PAR receptors triggers the production of MMPs, ADAMTS, and other degradative enzymes by synovial fibroblasts and chondrocytes. PAR signaling also drives phenotypic changes in macrophages toward pro-inflammatory M1 polarization. Pharmacological PAR inhibitors demonstrate potential as disease-modifying OA drugs by dampening synovitis and cartilage damage. However, directly targeting upstream cytokine activity may be needed to fully ameliorate inflammation [43-56].

Table 1: Molecular Mediators of Synovial Inflammation in Knee OA.

Mediator	Sources	Effects
IL-1β	Macrophages, synoviocytes	Induces MMPs and ADAMTS, inhibits collagen/aggrecan synthesis
TNF-α	Macrophages, synoviocytes	Activates synovial fibroblasts, upregulates MMPs
IL-6	Macrophages, synoviocytes, chondrocytes	Stimulates inflammatory signaling, joint pain
IL-17	T helper cells	Synergizes with TNF-α to increase inflammation
IL-18	Macrophages, chondrocytes	Induces interferon gamma, IL-1β, TNF-α
PAR-1	Synoviocytes, chondrocytes	Mediates cellular responses to MMPs, ADAMTS
PAR-2	Synoviocytes, chondrocytes	Mediates cellular responses to mast cell tryptase

Cartilage Loading Response and Chondrocyte Mechanobiology

Chondrocytes sense and respond to mechanical loads to maintain healthy cartilage homeostasis. However, abnormal joint loading in OA disrupts chondrocyte mechanobiology, shifting balance toward catabolism. Excessive compressive loading suppresses collagen II/aggrecan synthesis while increasing MMP expression. Reduced dynamic loading also downregulates anabolic activity. Altered chondrocyte signaling through the TGF-β, Wnt/β-catenin, BMP and PI3K/Akt pathways underpins aberrant gene expression changes. Inflammatory cytokines further impair chondrocyte mechanoresponsiveness. IL-1β and TNFα blunt the ability of mechanical stimulus to induce anabolic activation via TGF-β. Load-induced inhibition of NF-κB is also lost. Pharmacological agents aim to restore chondrocyte mechanobiological function by modulating cellular osmolarity, ion channels, and cytoskeletal tension [57-60].

Subchondral Bone Changes and Osteophyte Formation

Subchondral bone sclerosis, bone marrow lesions and osteophyte formation reflect altered bone metabolism in knee OA. Subchondral osteoblasts show hypertrophic differentiation and upregulation of MMPs/ADAMTS, perpetuating cartilage degradation. RANKL expression promotes subchondral osteoclastogenesis, contributing to bone lesions. Wnt/β-catenin signaling in subchondral precursors drives osteophyte development at joint margins. Local TGF-β and BMP activity also stimulate uncontrolled osteophyte growth. Sclerostin antibody treatment reduces osteophytosis in animal models by regulating Wnt signaling, while bisphosphonates like zoledronate inhibit bone resorption. Anti-resorptives may delay OA progression by preventing subchondral changes and bone loss. However, effects on cartilage warrant further study. Targeting Wnt/β-catenin signaling also shows potential to slow osteophyte formation and synovial fibroblast activation [61-63].

V. Conservative management approaches

Conservative management is the cornerstone of knee osteoarthritis treatment focused on reducing pain, improving function, and delaying disease progression as depicted in Table 2. Evidence-based rehabilitation strategies aim to address impairments in strength, flexibility, alignment, and neuromotor control. Although not disease-modifying, personalized conservative approaches remain the mainstay of initial OA management.

Individualized Movement Pattern Retraining

Altered movement strategies and muscle activation patterns underlie many biomechanical abnormalities in knee OA. Retraining functional movement is an important corrective approach. Proximal kinetic chain exercises address core and hip stability to improve lumbopelvic control. Distal exercises target foot mechanics, ankle mobility, and knee alignment. The aim is to engrain proper mechanics during gait, sit to stand, and other activities. Real-time biofeedback through video and mirror gait analysis helps patients self-correct posture and movement dysfunctions. Verbal, tactile, and visual cueing facilitates long-term motor pattern changes. However, compensations may persist without concomitant muscle strengthening [64, 65].

Proprioceptive and Balance Exercises

Proprioceptive and balance training is recommended to improve neuromuscular control in knee OA. Protocols incorporate activities like single leg standing, dynamic balance on unstable surfaces, and joint repositioning tasks. Balance challenges are progressed by altering base of support, vision, and adding cognitive tasks. The aim is to enhance strength, proprioception, and reactive responses. Evidence indicates modest improvements in postural sway, balance confidence, and physical function. Proprioceptive deficits may still exist long-term, requiring ongoing balance exercise. But this training helps reduce fall risk and build compensatory strategies. Combining with strength, gait, and ROM exercises optimizes outcomes [66, 67].

Functional Knee Bracing and Taping

Knee braces and taping techniques aim to provide external joint support, enhance proprioception, and improve alignment. Evidence for clinical efficacy remains mixed. Braces with variable stiffness seek to unload damaged compartments by directing forces laterally or medially. Patellofemoral braces also offload forces through the retinaculum. Small benefits for pain, symptoms, and function have been demonstrated. Taping techniques similarly guide patellar tracking and knee kinematics. Specialized movement pattern taping uses neuromuscular facilitation to enhance firing of weakened muscles. This shows promise for short-term pain relief and improved muscle activation. Compliance is a major limitation for braces and taping. Combining with exercise and gait retraining optimizes outcomes. Long-term benefits are unlikely with bracing or taping alone due to knee OA progression [68, 69].

Trunk Muscle Strengthening Protocols

Trunk muscle dysfunction contributes to abnormal knee loading. Weak core muscles lead to compensatory movement patterns. Therefore, trunk and hip exercises are a key component of knee OA rehabilitation. Transverse abdominis and multifidus training improves lumbar spine stability. Gluteal strengthening enhances pelvic control during gait. Targeting the back extensors also corrects flexed posture. A stable lumbopelvic region allows lower extremity muscles to function more optimally. Low-level evidence indicates modest benefits from core training for pain and function in knee OA. Core stability programs also help reduce low back pain commonly associated with knee OA. They are an important adjunct to knee-focused strengthening [70, 71].

Gait Retraining and Activity Modification

Altering gait mechanics and impact forces through ambulation aids, footwear, and activity modification strategies helps reduce knee joint loading. However, compliance is a major limitation. Gait retraining focused on posture, increasing cadence, normalizing hip and knee motion, and reducing trunk sway shows promise. Canes and lateral wedge insoles aim to shift the center of mass medially to decrease the knee adduction moment. Activity guidelines promote low-impact exercise while limiting repetitive climbing and deep knee bending. Small reductions in knee adduction moment and improvements in pain and function have been demonstrated. However, clinical effects are modest since gait is dictated largely by structural joint changes [72, 73].

Table 2: Conservative Management Approaches for Knee OA.

Strategy	Methods	Evidence for Efficacy
Exercise	Strengthening, aerobic exercise, balance training	Well-supported for pain relief, function
Weight loss	Dietary changes, physical activity	Significant benefit if ≥5% weight loss
Bracing	Unloader braces, patellofemoral braces	Small benefits for symptoms and function
Taping	Kinesiotaping, facilitative movement taping	Short-term pain relief, improved muscle function
Activity modification	Reducing repetitive impact, stair climbing	Less loading but long-term compliance issues
Gait aids	Canes, walkers, lateral wedge insoles	Modest biomechanical effects, pain relief

VI. Emerging therapies

While conservative management remains the foundation of knee OA treatment, various novel therapeutic approaches aim to repair joint damage and slow disease progression as depicted in Table 3. These emerging technologies target cartilage regeneration, modulation of inflammation, and restoration of joint biomechanics. However, most remain in early phases of research.

Biologics like Platelet-Rich Plasma

Platelet-rich plasma (PRP) contains concentrated autologous growth factors and cytokines from platelets that stimulate healing. Multiple PRP formulations are being studied for knee OA via intra-articular injection. PRP aims to drive anabolic processes in cartilage while suppressing inflammation. Growth factors like TGF-β, IGF-1, and PDGF upregulate extracellular matrix synthesis. Anti-inflammatory cytokines like IL-1ra also counteract inflammatory mediators. Small trials demonstrate potential symptom relief and functional improvement at 6-12 months post-injection. However, optimal PRP formulations and mechanisms of action are unclear. High quality studies with isotope-labeling and MRI outcomes are needed to determine effects on actual joint structure [74-76].

Tissue Engineering for Cartilage Repair

Tissue engineering seeks to regenerate hyaline-like cartilage using scaffolds, cells, and biological cues. Scaffolds provide 3D structure for cell growth, while growth factors stimulate matrix production. Stem cells, chondrocytes, and chondroprogenitors are studied cell sources to generate neo-cartilage tissue in scaffolds. Hydrogels, nanofibers, and decellularized extracellular matrix serve as potential biomaterials. Products are implanted into cartilage defects or engineered into total joint replacements. Preclinical data is promising, but few products are approved for clinical use. Significant challenges remain for translating benchtop concepts into effective OA therapies. Optimal scaffold properties, cell sourcing, and biomechanical durability require further research [77, 78].

Regenerative Medicine Using Stem Cells

Adult mesenchymal stem cells (MSCs) offer regenerative potential for OA cartilage defects. Bone marrow, synovial tissue, and adipose tissue provide autologous MSCs for transplantation. Allogeneic MSCs from healthy donors are also being studied. MSCs secrete paracrine signaling molecules that modulate inflammation and enhance tissue repair. Intra-articular injection aims to slow OA progression, while implantation into lesions stimulates focal cartilage regeneration. Early clinical outcomes provide mixed results. Some improvement in pain and function is noted, but minimal cartilage thickening on imaging. Vast research is underway to enhance MSC potency via preconditioning in bioreactors and combinatorial scaffolds. Standardization of cell processing and dosing is also needed [79-87].

Herbal and Traditional Chinese Medicine

Natural supplements like glucosamine, chondroitin, curcumin and avocado-soybean unsaponifiables have long been used to alleviate OA symptoms with mild effects. Herbal formulas from traditional Chinese medicine are also being investigated. Anti-inflammatory herbs like Tripterygium wilfordii hook F (TwHF) show potential to reduce OA joint swelling and pain. However, gastrointestinal and liver side effects may limit use. Traditional medicine protocols also incorporate acupuncture, cupping, and massage. Robust clinical trials are lacking to support most supplements and herbs for OA. Safe, standardized dosing of natural products remains a challenge. But secondary OA prevention through circadian rhythm balance, diet, and lifestyle modification is a focus of ongoing integrative medicine research [88-93].

Artificial Intelligence Applications

Artificial intelligence and machine learning are emerging areas with utility for OA diagnosis and management. Algorithms analyze clinical data and imaging to detect joint degeneration and predict outcomes. Computer vision systems automate knee OA severity grading on plain films and MRI. Predictive analytics integrate diverse data like biomarkers, genetics, and

biomechanics to forecast OA progression. Digital coaching apps provide personalized rehabilitation guidance. AI has potential to enhance OA clinical decision-making and monitoring. However, limitations around data bias, opaque algorithms, and overdependence on technology require consideration. Seamless integration into clinical workflow is necessary for practical adoption of AI tools [94-96].

Nanotechnology and Nano-Biosensors

Nanomaterials and nano-biosensors aim to enable minimally invasive diagnosis and targeted OA therapy. Injectable nanocarriers provide controlled intra-articular drug delivery. Multi-functional nanoparticles also allow co-delivery of therapeutic agents. Nano-biosensors implanted in the joint detect early molecular changes and wirelessly transmit data to external receivers. Nanomaterial-coated implants enhance tribological properties to reduce wear. Osteochondral scaffold constructs incorporate nanotopography to optimize cell growth. The nanomedicine field for OA is still nascent but rapidly evolving. While initial results seem promising, extensive toxicology and clinical testing is required prior to mainstream clinical adoption of nanotechnology. Interdisciplinary collaboration will be key to realizing potential benefits while ensuring safety [97-99].

Table 3: Emerging Knee OA Therapies and Current Status.

Therapy	Description	Current Status
PRP	Concentrated autologous growth factors	Early clinical testing
MSCs	Mesenchymal stem cells	Early clinical testing
Tissue engineering	Scaffolds, cells, biological factors	Preclinical development
Curcumin	Anti-inflammatory herbal supplement	Early clinical testing
AI analytics	Imaging analysis, predicting outcomes	Validation of algorithms
Nanocarriers	Injectable joints drug delivery	Preclinical development

Conclusion

Knee osteoarthritis is a complex degenerative disease driven by multiple interacting biological and biomechanical factors. Abnormal joint mechanics, inflammation, and altered tissue metabolism contribute to cartilage breakdown, subchondral bone changes, osteophytosis, and pain. Conservative rehabilitation approaches continue to be a mainstay of OA management by addressing neuromuscular and biomechanical impairments. However, intrinsic joint damage often limits the efficacy of conservative treatment long-term. Emerging biologics, tissue engineering, regenerative medicine, and nanotechnology aim to modify OA disease progression, but robust clinical evidence for these novel therapies remains limited. Further research is critically needed to develop therapies that can effectively repair joint damage and slow progression of knee osteoarthritis.

Recommendations

There is a need for continued research into disease-modifying OA drugs that can counteract inflammation and restore normal cartilage and bone metabolism. Local delivery methods should be explored to target bioactive agents directly to the joint. Regenerative medicine techniques warrant further optimization in terms of scaffold properties, cell sources, growth factors, and biomechanical durability before clinical adoption. Conservative rehabilitation protocols should incorporate gait retraining using real-time biofeedback and be individualized based on each patient's specific movement impairments. Activity guidelines and exercise recommendations should be tailored to the severity and structural progression of knee OA. Ultimately, a combination approach of anti-inflammatory and regenerative drugs along with personalized rehabilitation may provide the greatest long-term impact on slowing disease progression and improving joint health in knee osteoarthritis.

List of abbreviations

OA - osteoarthritis

PAR - protease-activated receptor

PRP - platelet-rich plasma

MSC - mesenchymal stem cell

MMP - matrix metalloproteinase

ADAMTS - A Disintegrin and Metalloproteinase with Thrombospondin Motifs

IGF-1 - insulin-like growth factor 1

PDGF - platelet derived growth factor

TwHF - Tripterygium wilfordii hook F

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