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Review Article

Are Osteoarthritis Inflammation and Its Related Sensorimotor Interactions Both Noteworthy and Modifiable Key Players?

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Abstract

Joints are sensitive structures whose qualitative and quantitative components depend not only on the harmonious interactions of hormones, enzymes, vitamins, minerals and protein, but also on the stresses put upon them by function as well as their intrinsic and extrinsic neuromotor environments, activity and integrity. This paper reviews some recent pathological insights regarding the synovial joint's lining and its immune cellular responses that indicate when traumatized may evoke a possible unstoppable cascade of inflammation and possible cartilage destruction unless abated in a timely way. One essential movement correlate that may especially fail to limit the spread of osteoarthritis inflammation and its oftentimes severe repercussions, namely muscle dysfunction is specifically discussed. Based on what is known we argue in favor of its possible untapped utility in efforts to reverse or mitigate post traumatic arthritis, especially in the face of persistent mechanical impacts.

Keywords: Inflammation; Joint; Muscle; Osteoarthritis; Pain; Proprioception; Treatment

Introduction

Today, in terms of prevalence rates, osteoarthritis a worldwide debilitating musculoskeletal condition affecting joint mobility is found to impact vast numbers of older adults and increasingly younger adults, despite years of study devoted to its prevention and intervention opportunities [1,2]. Indeed, as of 2025 it appears safe to say most osteoarthritis treatments have shown less than optimally desired outcomes and a limited ability to reverse the condition. Some moreover, may in fact pose a risk for incurring further health challenges and progressive disease worsening unless addressed strategically and insightfully, for example excess exercise applied to an inflamed joint may prove detrimental rather than therapeutic especially in the case of repeated muscle damage in the case of eccentric and stretching exercises [3,4].

How an osteoarthritis condition is managed is however of utmost importance because the degree of desired outcomes even in the face of joint replacement surgery is predicted by pre surgical joint and health status. This is especially relevant in the case of the oftentimes reported spread of osteoarthritis pain to other joints and the onset or development of a perpetual vicious pain state termed central sensitization that can have an adverse downstream effect on functional mobility and anatomical associated structures such as muscle fibers, fascia associated joint nerve supply and networks, lymphatics and blood vessels even in the face of intervention [4-6].

Another possible barrier to progress is that despite its potential for mitigation, osteoarthritis is commonly defined as a non-inflammatory disease wherein chronic destruction of the articular cartilage lining of the joint secondary to micro and macro injury prevail, but where both patients as well as providers may fail to appreciate both its pro-inflammatory and anti-inflammatory inherent biological underpinnings and possible opportunities for healing [7]. Its biological correlates also appear to have been poorly studied to date [8].

It is also apparent that osteoarthritis continues to be associated with age, even though modifiable lifestyle, neural and behavioral factors-are now known to be of high as well as of utmost deterministic salience.

Physical and other allied health therapists are increasingly seen as the key interventionists in this regard, as they are skilled at evaluating, planning and treating osteoarthritis cases with limited or absent joint range of movement secondary to diverse painful musculoskeletal disease manifestations as well as those with joint instability. Their basic aim in this regard is to prevent or reduce modifiable risk factors and restore or improve optimal functional status and avoid the 'spread' of the disease to other joints and possible comorbid health conditions that impair healing such as diabetes. Examples of what has been applied at the diseased knee show however that this is not a linear association to any degree. In addition, some physical therapy techniques are however, more popular than others or demanded by today's consumer, even if universally unproven, such as various anti inflammatory injections, exercise recommendations that may not be universally suitable or indicated and treatment guidelines delivered using technology may not prove patient-specific understandable, practical, or obtainable by many older adults. Also, following evidence based practices must remain questionable at best, given the immense limitations here and a failure to appreciate the need for comparative studies and a sound underlying model of practice and a deep appreciation of the degree to which mechanical, inflammatory, neuromuscular or metabolic disturbances can impair joint function independently as well as interactively. Better insights into the nature of the subject's beliefs, social and mental health state are also warranted [9,10].

In this regard the 2023 Eular Conference experts who revised their prior knee osteoarthritis recommendations included two overarching principles and eight evidence-based recommendations including the importance of (1) An individualized, multicomponent management plan; (2) Information, education and self-management; (3) Exercise with adequate tailoring of dosage and progression; (4) Mode of exercise delivery; (5) Maintenance of healthy weight and weight loss; (6) Footwear, walking aids and assistive devices; (7) Work-related advice and (8) Behavior change techniques to improve lifestyle. But no mention of joint pathology perse was discussed and the eight key principles were derived on the basis of a survey with only certain questions and seeming absence of objective or current case presentations [11].

With osteoarthritis problems and costs on the rise perhaps a more nuanced approach to unique attributes of osteoarthritis biology will prove helpful. In particular, an ability to appreciate the disease complexity at multiple levels, not only the degeneration of the cartilage extracellular matrix and generation of bioactive fragments, but how abnormal movement can impact chondrocye membrane receptors, ion channels, signaling pathways and cellular metabolism that in turn lead to extracellular matrix degradation and the generation of bioactive fragments that may impact muscle tone and noxious joint sensory receptors is not universally evidenced [12].

Gelber posits that with regard to knee osteoarthritis although pharmacologic and non-pharmacologic interventions are generally effective at alleviating pain and improving physical function, they do not fundamentally reverse the pathologic and radiographic process of osteoarthritis at this time as is desired [13]. Unfortunately, as the severity of disease increases, the magnitude of pain and functional impairment intensifies and renders it more difficult to relieve pain and restore functionality. However, if one considers current knowledge of cartilage cell biology and the inflammatory associations thereof more carefully, the therapist may well emulate those successes shown in the laboratory when carefully controlled recovery approaches after an injury are put forth.

As noted by Martin, et al., in post-traumatic osteoarthritis, the joint degeneration, pain and dysfunction that develop following joint injury is most directly related to elevated articular surface contact stresses, such as mechanical stresses that exceed the tolerance of the articular surface in one or more synovial joints, or are enacted too slowly to afford joint protection, plus repetitive loading due to incongruity/instability [14].

Purpose

This mini review aimed to summarize and elucidate upon a possible shift in thinking about osteoarthritis as an incurable inevitable life phase. It sought to highlight the known processes that appear to occur readily in post acute traumatic osteoarthritis states as far as the key joint tissues of the synovium and cartilage are concerned and the potential for one or more sensorimotor or proprioceptive pathway deficits to impact deleterious post traumatic synovial joint reactions, neurogenic inflammation and pain. This idea was based on the failure of past interventions to impact osteoarthritis safely and universally to a high degree of

efficacy and new knowledge acknowledging the intricate make up of the moveable or synovial joints and their diverse synovial cell typologies and properties, support tissues and surrounding and intrinsic sensory nerve units and signaling pathways that have diverse oftentimes pathogenic responses to trauma and repeated joint impacts.

It specifically sought to uncover if efforts to avoid repetitive impacts coupled with efforts to improve overall neuromotor status and joint physiology would prove likely to help avert, obviate or mitigate cartilage attrition due to inflammatory factors such as hypoxia and synovium located biochemical and molecular structure and pathway abnormalities.

Hypothesis

It was anticipated that based on careful evaluations of what is known about the potent influence of joint trauma on inflammatory responses that lead to possible intense bouts of chronic joint pain, a multi pronged stepped approach including sensorimotor rehabilitation can help to overcome the degree of inflammation and pain experienced by many in the face of a joint injury, especially in the post traumatic period and in the context of the aging joint.

Significance

Osteoarthritis is undoubtedly a significant contributor to the global disability burden, with its incidence expected to escalate by 74.9% by 2050 and its enormous impact. It is a realm of endeavor requiring urgent attention in order to tackle this future public health epidemic [9].

Although deemed 'incurable' and a highly disabling progressive destructive disease of the older adult population, both clinical as well as laboratory data imply osteoarthritis may be attenuated or prevented from an inevitable downward spiral of disability and derangement by careful upstream evaluations and early treatment, rather by any age-related wear and tear mechanism. If so, an enormous costly public health burden may be offset, as well as fostering lives of decreased suffering.

One recent idea that appears promising is that osteoarthritis, although viewed as a multifactorial disease that emanates largely from the convergence of both genetic and environmental factors, it that joint degeneration may be influenced by a single unanticipated injury, cumulative repetitive impact and loading effects, joint overuse, fatigue, instability, recurrent injuries and a too rapid a return to functions that provokes inflammation post injury and may be intervened upon with promising effects. Several other risk factors for osteoarthritis that could be prevented include obesity, joint instability and joint malalignment. Alternately, a failure to appreciate any prevailing degree of mitochondrial dysfunction, damage-associated molecular patterns, cytokines, metabolites and crystals in the synovium that can activate synovial cells and mediate synovial inflammation may encourage the downward spiral associated with inflammatory inputs and outputs. This knowledge could however form the basis of more patient specific evaluations, targeted interventions and the development of novel therapeutics [15,16].

That is, current research shows a concerted effort to improve the prevention and management of osteoarthritis in this regard may help avert a host of damaging biological processes and system alterations particularly post injury inflammation [16]. Pinpointing the source of an injury, which could arise from bone or support structure tissue disruptions, cartilage matrix disruptions and swelling, blood-vessel and nerve injuries and curtailing future insults is strongly indicated here to control and resolve any lingering inflammation and with this continuous tissue remodeling processes that may foster recurring joint injuries and a destructive inflammatory cycle [16].

Indeed, although previously neglected as an osteoarthritis disease correlate, it is now entirely plausible to examine whether the ability to slow down or mitigate osteoarthritis disease progression by targeting one or more catabolic or anabolic inflammation attributes is a viable line of inquiry and one worthy of consideration [1]. Researchers are thus clearly continuing their efforts in the quest to unveil new osteoarthritis inflammatory insights plus therapeutic targets that can modify its disabling symptoms and arrest the disease progression and harm attributable to excess pro inflammatory signals and processes of destruction, while also examining repair options.

Methods

To establish insight as to current osteoarthritis inflammatory implications a review extending over the most recent studies published in the last five years [2021-2025] was undertaken as regards the themes of: osteoarthritis, synovial membrane, muscle

and inflammation, plus proprioception as applied to joint injury, pain and derangement. Older articles of note were deemed informative and accepted if they were reports of structural biology and biochemistry. Data bases used were: PUBMED, PubMed Central and Google Scholar.

The review is an abbreviated one however and is not all inclusive nor a meta-analysis or systematic review, but one that strove to carefully examine key trends worthy of future study and clinical consideration, given new diagnostic modes of inquiry and novel questions not yet answered. Peer reviewed laboratory and clinical studies were deemed acceptable. Articles discussing rheumatoid arthritis and invasive approaches such as blood platelet rich plasma injections and surgery, as well as drug and exercise studies were not examined. No specific forms of osteoarthritis were detailed and for more detailed background information, readers can examine prior comprehensive reports as well as 2025 current reports [17-20]. Key topics categorized were those pertaining to osteoarthritis, synovial membrane and joint inflammation, neuromotor aspects of joint function and dysfunction, possible non pharmacologic therapy approaches.

Results

Osteoarthritis

Osteoarthritis, a disabling condition affecting one or more freely moving joints such as the knee joint, commonly fosters progressively intense bouts of pain and disability among many older adults no matter where they reside. Deemed largely incurable, repetitive impact and loading, joint trauma and overuse and recurrent injuries especially in the face of acute injury or chronic disease manifestations may exacerbate the disease, especially with regard to the cartilage lining and its matrix [16].

Although long accepted as an aging syndrome and one that is irreversible, the condition is currently conceived of as having both genetic and environmental underpinnings and arising from intricate interactions among mechanical stresses, inflammatory processes and disruptions in bone and cartilage structure and metabolism [16,21,22]. Indeed, while many older adults do not suffer from this condition, or only incur problems at one joint and not others, repetitive impact loading, joint malalignment, joint instability, overuse and recurrent injuries arguably predispose to some degree of joint degeneration and various degrees of joint inflammation [16,21,23,24].

A major cause of disability worldwide recent research in bone immunology indicates that immune-mediated mechanisms significantly contribute to the progression of osteoarthritis as discussed by Mathieu, et al., [25,26]. These interactions are observed to foster a pro-inflammatory joint microenvironment, thus contributing to cartilage breakdown, persistent synovial membrane inflammation and the sclerosis of subchondral bone [27]. There may also be possible persistent stimulation of joint pain fibers, nerve mechanoreceptors and possible reactionary deficits or abnormalities in afferent input pathways that can alter motor outputs unfavorably and thereby their protective shock absorption functions that play a role in altering the highly vulnerable synovial environment [19,28].

Thus, in addition to age factors, several interrelated pathological processes, including neuroplasticity, nerve damage, joint position sense or movement or vibration sense alterations and sensory disturbances can conceivably foster activation of innate inflammatory pathways and the recruitment of monocytes, lymphocytes and other leukocytes that may all mediate osteoarthritis development and attrition and neuropathic pain [5,21,23]. In addition, subnormal muscle forces can induce the spread of local joint inflammation and pathology to other joints, for example if they provoke falls and falls injuries, which commonly produces a net loss of local tissue proteoglycan in osteoarthritic cartilage and possible bone fractures and thus represents a possible disease modifiable pathway.

Li, et al., who affirm osteoarthritis is a chronic and degenerative disease marked by inflammation and extracellular matrix degeneration show that contributing to synovial inflammation and cartilage destruction is an orphan nuclear receptor found to mediate inflammatory responses in the cartilage tissue in the face of joint damage [29]. These receptors that are normally quiescent may be mitigated however in the face of carefully targeted sensorimotor rehabilitation strategies, joint protection modalities and education.

Bolander, et al., advocate for efforts in this regard because a failure to regenerate cartilage post trauma may reflect persistent inflammation that continue to induce a cycle of degenerative osteoarthritis damage and many possible diverse mobility

challenges, wherein that small quantity of highly viscous fluid that normally serves as a cartilage lubricant fails to foster adequate nutrition for the cartilage cells [30]. As well, adverse impacts on the nutritive supply of the surrounding joint tendons, bnrsae, tendon sheaths, ligaments, nerves and blood vessels may ensue in addition to parallel declines in cartilage shock absorption capacity [31,32]. In turn, these alterations may forge an increase in pain and a gradual associated fibrosis of the subsynovial tissue and ongoing inflammation sufficient to sensitize surrounding sensory neurons to further pain, joint degeneration, joint swelling and stiffness [21,22].

In particular, repeated mechanical insults may perpetuate prevailing inflammatory processes wherein inherent synovial fibroblasts found to assume distinct functional identities, can drive a wave of pathological joint crosstalk communications that have far reaching and complex catabolic and destructive outcomes [33]. In addition, the lubricating properties of synovial fluid may be undermined, as may cartilage and bone structural status and thus the joint's load bearing capacity [34,35].

Inflammatory Mechanisms

There is no doubt that the histological changes observed in the osteoarthritis synovial membrane generally includes features of an inflammatory "synovitis"; plus a range of abnormalities, such as synovial lining hyperplasia, macrophage and lymphocyte infiltration, neoangiogenesis and fibrosis [36]. This pattern of synovial reaction that varies with disease duration and associated metabolic and structural changes in other joint tissues, is potentially compounded by multiple age associated cellular system declines and as pain evolves, a state of sensitization and/or neuropathic pain, as well as reflex muscle response abnormalities may wane or become subnormal [33].

As proposed by Bolander, et al., there is a strong need for preventing inflammation as well as for treatment applications that can restore the articular cartilage and joint homeostasis as proposed by Liu, et al., [30,33]. Information on how synovial fluid composition may foster pro-regenerative immune cell influences on possible progenitor cells and thereby pain and radiographic disease progression is especially indicated here [15]. Indeed, clinical interventions are likely to fail if attempts to offset hypoxia and that limit the apparent mechano-sensitive synovial pathway of inflammatory metabolic responses are not forthcoming. At the same time, associated alterations in muscle reflex activity and motor memory may foster a host of additionally adverse synovial pro inflammatory reactions [36-38]. Moreover, a failure to abate inflammation commonly tends towards increases in joint effusion and a state of elevated intraarticular pressure that can compress the intracapsular vein. This may be followed by increases in joint outflow resistance and a fall in the regional blood flow of the joint and a state of tissue hypoxia that fosters cartilage degeneration [39].

In short, data indicate that pro-actively targeting inflammation is a potentially potent and salient factor in achieving more profound success in retarding osteoarthritis disease progression and its oftentimes suboptimal impact on therapeutic targets [25,40,41]. Indeed, even if osteoarthritis origins are poorly understood, it appears that synovial joint dysfunction predates destruction of the osteochondral unit cellular and functional alterations. In this regard, the cells of the synovial membrane that may be influenced by cartilage and subchondral bone cleavage fragments and matrix degradation products may induce a cycle of perpetual and progressive joint destruction from apoptotic and necrotic cells and associated molecules that trigger innate immunity and low-grade synovial inflammation [40].

Unsurprisingly, Kofoed, et al., for example implies osteoarthritis is a complex joint disease that cannot be treated simplisitically [42]. This is due to its multiple diverse correlates including inflammation possible joint effusion and muscle inhibition, plus the suboptimal transfer of oxygen across the synovial membrane and synovial fibrosis [43]. Alternately, careful attention to the nature of inherent cartilage matrix synthetic versus degradation pathways and fostering favorable cytokine effects may prove valuable [44-46].

In particular, targeting the molecular basis of joint inflammation, oxidative stress and its complex crosstalk communications between chondrocytes, synoviocytes, osteocytes, sensory nerves and immune cells may help normalize rather exacerbate cytokine production as well as other key inflammatory mediators, such as IL- IL-6, TNF-α and Wnt/β-catenin signaling that may foster synovial hypertrophy [33,45-49].

On the other hand, a lack of insight into the extent of crosstalk between joint tissues such as the synovium and cartilage at the cellular level within the innate immune inflammatory network, especially in the absence of soundly construed therapeutic approaches can predictably influence the perpetual formation and progression of osteoarthritis [50-52]. Others show alterations of cartilage surface or degradation of biomacromolecules within synovial fluid that may increase the wear and tear of the cartilage [15].

Di Carlo, et al., propose a further role for mesenchymal stem/stromal cells recruited in the synovium in the osteoarthritis disease cycle because these cells can stimulate the formation of osteoclasts or bone resporptive cells [53]. Macfarlane, et al., propose inflammation is a potential pain generator and treatment target in osteoarthritis and propose that white blood cells may be implicated in the disease cycle [54]. Moreover, innate immunity processes that originate from the immune receptor Dectin-1 located on macrophages may influence progression of osteoarthritis [55, 56]. However, their differences, impacts and spatial and transcriptional linkage mechanisms with immune cell and cartilage dynamics remain challenging to isolate and should be studied systematically as proposed by Niu, et al., [57].

Joint Proprioception and Sensorimotor Attributes

Although not linked as a risk factor to synovial inflammation, it appears proprioception, an umbrella term encompasses an array of sensitive intrinsic and extrinsic sensors or mechanoreceptors and their neural pathways designed to detect, integrate and transmit information on joint position, movement and stability, must be considered as having a meaningful bearing on movement quality and precision that those muscle based adaptations that are joint protective as well as functional [40]. An intricate system that monitors and impacts muscle contraction magnitude and temporal sequence, locomotion, joint stability and muscle contractile processes is surely a system underpinning almost all life affirming mobility and stability functions. Proprioceptors including diverse sensory receptors and input and output pathways and located in the joint tissues, muscles, central and interneuron spinal pathways may all be vulnerable to insults with far reaching implications for joint and movement status.

As per Salo, an expanding body of knowledge clearly shows a highly complex array of sensorimotor receptors and processes that lie within joint tissues and their muscles and that are paramount in preserving the smooth normal functioning of the motor-skeletal system and in averting the inflammatory response to joint injuries and diseases [58].

Yet proprioceptive capabilities that underpin movement and movement efficiency have been shown to be decreased or altered post joint injury to varying degrees, as well as in cases with osteoarthritis exhibiting joint effusion [59-61]. Moreover, while some surgical procedures seem to restore selected proprioceptive abilities; others do not and deficits may yet persist in influencing the disease trajectory adversely, as well as function especially in the face of ongoing inflammation rather than effusion alone [62-64].

In addition to chronic autoimmune inflammation, related changes of the peripheral nervous system can engender unfavorable energy balances and continuous local joint destruction processes [64]. Salo, reports that in recent times there has been a new and growing appreciation of the major role played by sensory neurons in promoting regional inflammatory responses and that many of the specific neuronal mechanisms and molecules that mediate these reflexes have significance with respect to pain, trauma and regional inflammatory disorders [58].

According to Mathew, et al., swelling, stiffness and pain in osteoarthritis may be influenced by an emergent degree of nociceptor hyperactivity responses and excessive release of inflammatory factors and pain mediators [65]. There may also be extensive remodelling and plasticity of the joint innervation system with subsequent adverse structural, functional and molecular alterations in sensory and autonomic axons wiring. Sprouting and reorganization of sensory and autonomic fibers with the invasion of ectopic branches into surrounding inflamed tissues are associated with the upregulation of pain markers and thereby possible rewiring and sensitization of the joints along with multiple subnormal neuromotor mediated musculoskeletal postural and protective shock absorption deficits.

Cujedko, et al., who sought to determine whether deficient proprioception mediates the association between systemic inflammation and muscle weakness in knee osteoarthritis showed higher erythrocyte sedimentation rates were associated with poor proprioception [66]. Poor proprioception and higher erythrocyte sedimentation rates were associated with muscle weakness

and mediated the association between systemic inflammation and muscle weakness and appear to prevail in late stage knee osteoarthritis [67]. This linkage of proprioception may hence prove a potent mediator of persistent pain, as well as substantial reparative impairments and osteoarthritis function and functional efficiency, acuity and reactive capacity. Studies show for example that osteoarthritis cases with posterior knee cruciate ligament lesions exhibited deficient proprioceptive accuracy that may not improve post surgery in all cases or improve at first, but not in the long term [67,68]. Gayreth, et al., found however that proprioceptive training was effective on pain, joint position sense, range of motion, muscle strength, functionality, physical performance and quality of life in patients with knee osteoarthritis in all radiological stages [69].

Magbi, et al., found persons with hand osteoarthritis had more frequent neglect-like symptoms and were slower and less accurate compared to healthy controls at hand left/right judgments, which was indicative of disrupted working body schema that may have a bearing on hand function and the development and progression of hand osteoarthritis [70]. This implied a possible mechanistic role for proprioception in the osteoarthritis pathogenic cycle and that any deficiency in this regard may have the potential to stimulate premature chondrocyte senescence and cartilage mechanical and chemical insults [71-74]. While strength training and electroacupuncture may improve joint proprioception and help to alleviate rather than promote joint inflammation, a role for low intensity muscle contraction therapy has been advocated for reducing or attenuating joint inflammation and central pain sensitisation [75-78].

However, until more acceptance of these ideas becomes more routine, it appears issues that arise in terms of reactive abnormalities in proprioception such as deficits in extrafusal muscle fiber activation, muscle mass declines, muscle weakness, poor muscle endurance, fatigue associated muscle metabolic alterations, muscle imbalances, muscle protein degradation and ligament destruction may all remain unchecked and potent osteoarthritis inflammation and destruction mediators [79]. As well, there may be permanent changes of the viscoelastic properties of the osteoarthritis joint capsule, joint effusion effects that inhibit optimal muscle reflex responses, as well as cartilage, or bone immune systems impacts and others that tend to persist in the absence of carefully targeted and timely intervention and are commonly not remedied to a high degree by surgery, various anti inflammatory or narcotic drugs, or injections [80-84].

Discussion

Despite more than a century of study and thousands of investigations, it is clear osteoarthritis remains a widespread painful disabling disease and one inducing great suffering. Often associated with a low grade inflammatory response that hastens its severity and progression, even if not universally recognized disruptions in one or more joints are not only the consequence of age, but point strongly to a role for perpetual inflammation of an injured joint or a diseased joint during loading and cartilaginous unloading [48,85,86]. The possible enormous impact of inflammation on sensorimotor control mechanisms and receptor pathways and nerve attrition changes alone even in the case of modest joint pathology clearly has the potential to impact possible inflammatory and adverse degenerative mechanical influences that fail to be abated and provoke or exacerbate cartilage lesions especially if joint loading is repeatedly subnormal [65].

This is despite a rich growing volume of attention to osteoarthritis and its inflammatory implications, including observations indicating many immunogenic responses, plus associated alterations in joint sensory inputs and motor outputs wherein chronic pain appears to represent the interactions of impacts of multiple neural mechanisms that affect immune and structural biology. The lack of importance delegated to muscle that may itself be inflamed and of limited mass may further prove to be an important disease moderator and mediator, even if rarely alluded to. Thus even in the face of cutting-edge cell therapy, immune modulation and molecular targeting strategies, a persistent deficit in any component of the sensorimotor system may fail to help counter synovial based oxidative stress correlates and mechanisms, cartilage nutrition and articular cartilage repair [87-92]. More insightful temporal tracking of osteoarthritis pathology from a holistic and comprehensive perspective that is supported by both personal testimonies as well as objective analyses may further help to point to a window of opportunity for interventions at the cellular level, rather than drugs to curb erosive osteoarthritis inflammation impacts [33]. The multiple systems that may be implicated here, for example metabolic, biological, bone, immunological and neuromuscular factors should be clarified and better classified to enable clinical efficacy decisions in the future [24]. Other risk factors in this regard including occupational related physical activities should be studied as well [22].

As well, elucidating upon how muscle mechanisms and joint inflammation can be better understood relative to cartilage anabolic processes, rather than catabolic processes and how alterations from an inflamed joint can alter spinal cord located neural biology may prove valuable [19,93-96]. Comparing how humans chondrocytes respond to different modalities that are carefully titrated and whether this will impact signaling pathways that foster cartilage viability such as those embedded in proprioceptors, including muscle afferents and efferents also appears worthy of future study [97,98].

In particular, a parallel role for age and disease associated muscle mass declines and muscle fat mass excesses that may increase osteoarthritis risk and perpetuate inflammation should not be ignored [99]. In addition, the specific role of muscle inflammation in its own right cannot be ignored and may be amenable to a combined treatment approach of distraction followed by exercise [100,101]. Those with poor position sense and signs of obesity who may have poor muscle endurance and those with depression should be specifically targeted and with an expected favorable set of results [102-104]. In the interim researchers can help to expand upon our understandings and examine the exact mechanisms involved in the transition of synovial fibroblasts into a myofibroblast-like phenotype that drives fibrosis and which presently may serve as key drivers or humoral mediators that maintain inflammatory processes, including the release of proteases and cytokines that cause cartilage and bone destruction, calcification of articular cartilage and painful joint symptoms [105-109]. By contrast, careful stimulation of synovial fibroblasts that may exert reparative and protective effects on chondrocytes of cases with osteoarthritis by promoting cell proliferation, inhibiting inflammation and stabilizing cellular structures, may potentially mitigate the progression of cartilage lesions in these patients [110].

Until then, there can be no doubt a high degree of suffering among the older adult osteoarthritis population along with an immense global burden [111,112] will prevail and will possibly be related to past or present synovial joint tissue inflammatory and signaling pathways that accompany osteoarthritis and the degree to which neuromotor influences fail or function to protect one or more joints. Coupled with this is patient education that reinforces dangers of excess loading, stressful endeavors, fatigue and excess narcotic usage.

Conclusion

Despite the limitations of this brief overview of the literature implicating inflammatory and signaling pathways disruptions observed in osteoarthritis, we believe there is growing supportive data as regards possible.

1. Increases in the osteoarthritis burden over time in the face of unrestricted mechanical damage and inflammation, obscure pathogenic understandings and a weak education and joint protection focus, irrespective of age
2. Sensorimotor mechanisms that fail to mediate joint protection can initiate or foster joint damage, neuropathic pain and limited tissue healing and recovery potential in their own right and should be sought routinely and treated accordingly
3. Carefully tailored and targeted interventions that do not provoke joint stress, muscle fatigue, or joint and/or muscle effusion, but being mindful to avoid kinesiophobia-as applied earlier rather than later may foster a favorable change in the osteoarthritis synovial microenvironment and its multiple disease relevant molecular and motor control pathways
4. The prevention of harmful mechanical stimuli that can evoke extensive inflammatory molecular interactions alongside a role for sensorimotor rehabilitation and periodic assessments of the disease processes may prove especially fruitful at all ages and stages of osteoarthritis pathology
5. Further basic and clinical research to highlight the role of the neural system in the osteoarthritic inflammation and pain production cycle is strongly indicated
6. Modifying or preventing post traumatic osteoarthritis appears plausible

In the interim, mechanisms that may be amenable to modification include alterations in overall immune responses, apoptosis, pyroptosis and metabolic programming that may all play a pivotal role in the disease progression especially in the face of unrestrained mechanical insults.

Realm of Possible Non Pharmacologic Anti-inflammatory Interventions

- Avoidance of kinesiophobia [113]
- Avoidance of exercise fatigue [114]
- Compression sleeves
- Distraction [101]

- Education
- Electroacupuncture
- Electrical muscle stimulation
- EULAR recommendations [11]
- Exercises to build strength, endurance, balance [117]
- Foot wear, shoes, in soles as indicated
- Ice or cold therapy
- Low intensity ultrasound [71]
- Obesity prevention/control [115,117]
- Proprioceptive neuromuscular rehabilitation [69,116]
- Rest
- Splints and braces
- Stress reduction
- Taping [117]

Conflict of Interests

The authors declare no conflict of interest.

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References

1. Siddiq MAB, Oo WM, Hunter DJ. New therapeutic strategies in osteoarthritis. Jt Bone Spine. 2024;91(6):105739.
2. Courties A, Kouki I, Soliman N. Osteoarthritis year in review 2024: Epidemiology and therapy. Osteoarthritis Cartilage. 2024;32(11):1397-404.
3. Han H, Ro DH, Han HS. Overall compilation of adverse effects of non-steroidal anti-inflammatory drugs: S hypothesis-free systematic investigation using a nationwide cohort study. Front Pharmacol. 2025;16:1539328.
4. Dessem D, Ambalavanar R, Evancho M. Eccentric muscle contraction and stretching evoke mechanical hyperalgesia and modulate CGRP and P2X(3) expression in a functionally relevant manner. Pain. 2010;149(2):284-95.
5. Syx D, Tran PB, Miller RE. Peripheral mechanisms contributing to osteoarthritis pain. Curr Rheumatol Rep. 2018;20:1-1.
6. Sikdar S, Srbely J, Shah J. A model for personalized diagnostics for non-specific low back pain: The role of the myofascial unit. Front Pain Res (Lausanne). 2023;4:1237802.
7. Shawl M, Geetha T, Burnett D. Omega-3 supplementation and its effects on osteoarthritis. Nutrients. 2024;16(11):1650.
8. Jenei-Lanzl Z, Zaucke F. Osteoarthritis year in review 2024: Biology. Osteoarthritis Cartilage. 2025;33(1):58-66.
9. Zhu S, Qu W, He C. Evaluation and management of knee osteoarthritis. J Evid Based Med. 2024;17(3):675-87.
10. Abramoff B, Caldera FE. Osteoarthritis: Pathology, diagnosis and treatment options. Med Clin North Am. 2020;104(2):293-311.
11. Moseng T, Vlieland TP, Battista S. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis: 2023 update. Ann Rheum Dis. 2024;83(6):730-740.
12. Marks R. Osteoarthritis and articular cartilage: biomechanics and novel treatment paradigms. Adv Aging Res. 2014;3;297-309.
13. Gelber AC. Knee osteoarthritis. Ann Intern Med. 2024;177(9):ITC129-44.
14. Martin JA, Anderson DD, Goetz JE. Complementary models reveal cellular responses to contact stresses that contribute to post-traumatic osteoarthritis. J Orthop Res. 2017;35(3):515-23.
15. Sanchez-Lopez E, Coras R. Synovial inflammation in osteoarthritis progression. Nat Rev Rheumatol. 2022;18;5:258-75.
16. Haubruck P, Pinto MM, Moradi B. Monocytes, macrophages and their potential niches in synovial joints - therapeutic targets in post-traumatic osteoarthritis? Front Immunol. 2021;12:763702.
17. Ur Rehman S, Iqbal S, Shahid MU. Cartilage: Structure, function and the pathogenesis of osteoarthritis. In Advancements in Synovial Joint Science-Structure, Function and Beyond 2024 Jan 23. IntechOpen.
18. Marks R. Osteoarthritis and proprioception: What does the literature reveal? Int J Orthop. 2017;4(5):826-36.

19. Schaible HG, Grubb BD. Afferent and spinal mechanisms of joint pain. Pain. 1993;55(1):5-4.
20. Van den Bosch MH, Blom AB, van der Kraan PM. Inflammation in osteoarthritis: Our view on its presence and involvement in disease development over the years. Osteoarthritis Cartilage. 2024;32(4):355-64.
21. Grässel S, Muschter D. Peripheral nerve fibers and their neurotransmitters in osteoarthritis pathology. Int J Molecular Sci. 2017;18(5):931.
22. Duong V, Shaheed CA, Ferreira ML. Risk factors for the development of knee osteoarthritis across the lifespan: A systematic review and meta-analysis. Osteoarthritis Cartilage. 2025:S1063-4584(25)00860-X.
23. Griffin TM, Scanzello CR. Innate inflammation and synovial macrophages in osteoarthritis pathophysiology. Clin Exp Rheumatol. 2019;37(5):57-63.
24. Karim A, Hussain MA, Ahmad F. Predictors of osteoarthritis in older Europeans: insights from the SHARE Survey. Musculoskeletal Care. 2025;23(2):e70093.
25. Kloppenburg M, Namane M, Cicuttini F. Osteoarthritis. Lancet. 2025;405(10472):71-85.
26. Mathieu S, Courties A, Mathy C; GO-PAIN network. Features and management of osteoarthritis from the perspective of individuals with osteoarthritis: A systematic review of qualitative studies. Osteoarthr Cartil Open. 2025;7(2):100590.
27. Hu K, Song M, Song T, Jia X, Song Y. Osteoimmunology in osteoarthritis: unraveling the interplay of immunity, inflammation and joint degeneration. J Inflammation Res. 2025:4121-42.
28. Mansfield CJ, Culiver A, Briggs M. The effects of knee osteoarthritis on neural activity during a motor task: A scoping systematic review. Gait and Posture. 2022;96:221-35.
29. Li J, Zhang Y, Gan X. Blocking the LRH-1/LCN2 axis by ML-180, an LRH-1 inverse agonist, ameliorates osteoarthritis via inhibiting the MAPK pathway. Biochem Pharmacol. 2025:116922.
30. Bolander J, Moviglia Brandolina MT. The synovial environment steers cartilage deterioration and regeneration. Sci Adv. 2023;9(16):eade4645.
31. Chung CB, Boucher R, Resnick D. MR imaging of synovial disorders of the knee. Semin Musculoskelet Radiol. 2009;13;4:303-25.
32. Scanzello CR, Goldring SR. The role of synovitis in osteoarthritis pathogenesis. Bone. 2012;51;2:249-57.
33. Liu S, Zhang G, Li N. The interplay of aging and PANoptosis in osteoarthritis pathogenesis: Implications for novel therapeutic strategies. J Inflamm Res. 2025;18:1951-67.
34. Bhattaram P, Chandrasekharan U. The joint synovium: A critical determinant of articular cartilage fate in inflammatory joint diseases. Semin Cell Dev Biol. 2017;62:86-93.
35. Knights AJ, Farrell EC, Ellis OM. Synovial fibroblasts assume distinct functional identities and secrete R-spondin 2 in osteoarthritis. Ann Rheum Dis. 2023;82(2):272-82.
36. Wijesinghe SN, Ditchfield C, Flynn S. Immunomodulation and fibroblast dynamics driving nociceptive joint pain within inflammatory synovium: Unravelling mechanisms for therapeutic advancements in osteoarthritis. Osteoarthritis Cartilage. 2024.
37. Stücker S, Koßlowksi F, Buchholz A. CPP-calcification of articular cartilage is associated with elevated cytokine levels in synovial fluid. Front Cell Dev Biol. 2025;13:1535530.
38. Svalastoga E, Kiaer T. Oxygen consumption, diffusing capacity and blood flow of the synovial membrane in osteoarthritic rabbit knee joints. Acta Vet Scand. 1989;30(2):121-12.
39. Svalastoga E, Grønlund J. Experimental osteoarthritis in the rabbit. III. Acute osteoarthritis: subchondral $P0_2$ and oxygen consumption and diffusion capacity in the synovial membrane. Acta Vet Scand. 1985;26(3):340-51.
40. Semenistaja S, Skuja S, Kadisa A, Groma V. Healthy and osteoarthritis-affected joints facing the cellular crosstalk. Int J Mol Sci. 2023;24(4):4120.
41. Kofoed H. Synovitis causes hypoxia and acidity in synovial fluid and subchondral bone. Injury. 1986;17(6):391-4.
42. Zhang L, Li M, Li X. Characteristics of sensory innervation in synovium of rats within different knee osteoarthritis models and the correlation between synovial fibrosis and hyperalgesia. J Adv Res. 2021;35:141-51.
43. Meng C, Chen S, Liu Q. Therapeutic potential of CHI3L1 in osteoarthritis: Inhibition of cartilage matrix degradation and inflammation through TLR4-MAPK-STAT1 pathway. Int Immunopharmacol. 2025 ;156:114684.
44. Konteles V, Papathanasiou I, Tzetis M. Synovial fibroblast extracellular vesicles induce inflammation via delivering mir-21-5p in osteoarthritis. Cells. 2025;14(7):519.
45. Giorgino R, Albano D, Fusco S. Knee osteoarthritis: Epidemiology, pathogenesis and mesenchymal stem cells: What else is

new? An update. Int J Mol Sci. 2023;24(7):6405.
46. Takeshita M, Nakamura J, Ohtori S. Sensory innervation and inflammatory cytokines in hypertrophic synovia associated with pain transmission in osteoarthritis of the hip: A case-control study. Rheumatol. 2012;51(10):1790-5.
47. Takase K, McCulloch PC, Yik JHN. Clinical and molecular landscape of post-traumatic osteoarthritis. Connect Tissue Res. 2025:1-7.
48. Rosenberg JH, Rai V, Dilisio MF. Damage-associated molecular patterns in the pathogenesis of osteoarthritis: potentially novel therapeutic Targets. Mol Cell Biochem. 2017;434(1-2):171-9.
49. Hernandez SM, Begum L, Keller LE, Fu Q, Zhang S, Fortier LA. Synovium secretome as a disease-modifying treatment for equine osteoarthritis. Am J Vet Res. 2022;83(10):ajvr.22.05.0082.
50. Liu Y, Lu T, Liu Z. Six macrophage-associated genes in synovium constitute a novel diagnostic signature for osteoarthritis. Front Immunol. 2022;13:936606.
51. Deroyer C, Poulet C, Paulissen G. CEMIP (KIAA1199) regulates inflammation, hyperplasia and fibrosis in osteoarthritis synovial membrane. Cell Mol Life Sci. 2022;79(5):260.
52. DiCarlo M, Teti G, Cerqueni G. Synovium-derived stromal cell-induced osteoclastogenesis: A potential osteoarthritis trigger. Clin Sci. 2019;133(16):1813-24.
53. MacFarlane LA, Arant KR, Kostic AM. Identifying inflammation in knee osteoarthritis: relationship of synovial fluid white blood cell count to effusion-synovitis on magnetic resonance imaging. Arthritis Care Res. 2023;75(8):1783-7.
54. Wang C, Zeng Z, Wang T. Unraveling the spatial and signaling dynamics and splicing kinetics of immune infiltration in osteoarthritis synovium. Front Immunol. 2025;16:1521038.
55. Wu H, Qian Y, Zhu K. Roles of innate immune system and receptor Dectin-1 in synovium and cartilage homeostasis of osteoarthritis. Int J Biol Macromol. 2025:142669.
56. Niu S, Li M, Wang J, Zhong P. Identify the potential target of efferocytosis in knee osteoarthritis synovial tissue: A bioinformatics and machine learning-based study. Front Immunol. 2025;16:1550794.
57. Salo P. The role of joint innervation in the pathogenesis of arthritis. Can J Surg. 1999;42(2):91.
58. Jerosch J, Prymka M. Proprioception and joint stability. Knee Surg Sports Traumatol, Arthroscopy. 1996;4(3):171-9.
59. Sharma L, Pai YC. Impaired proprioception and osteoarthritis. Curr Opin Rheumatol. 1997;9(3):253-8.
60. Cho YR, Hong BY, Lim SH. Effects of joint effusion on proprioception in patients with knee osteoarthritis: A single-blind, randomized controlled clinical trial. Osteoarthritis Cartilage. 2011;19(1):22-8.
61. Van der Esch M, Steultjens M, Harlaar J. Joint proprioception, muscle strength and functional ability in patients with osteoarthritis of the knee. Arthritis Care Res. 2007;57(5):787-93.
62. McNair PJ, Marshall RN, Maguire K. Knee joint effusion and proprioception. Arch Phys Med Rehabil. 1995;76(6):566-8.
63. Pongratz G, Straub RH. Role of peripheral nerve fibres in acute and chronic inflammation in arthritis. Nature Rv Rheumatol. 2013;9(2):117-26.
64. Mathew S, Ashraf S, Shorter S. Neurobiological correlates of rheumatoid arthritis and osteoarthritis: remodelling and plasticity of nociceptive and autonomic innervations in synovial joints. The Neuroscientist. 2024:10738584241293049.
65. Cudejko T, Van der Esch M, Van der Leeden M. Proprioception mediates the association between systemic inflammation and muscle weakness in patients with knee osteoarthritis: results from the Amsterdam Osteoarthritis cohort. J Rehabil Med. 2018;50(1):67.
66. Yang B, Shi J, Zhang H, Zhang K, Yan S. Changes of knee proprioception in patients with knee osteoarthritis undergoing unicompartmental knee arthroplasty. Gait Posture. 2025;120:205-10.
67. Salamanna F, Caravelli S, Marchese L. Proprioception and mechanoreceptors in osteoarthritis: A systematic literature review. J Clin Med. 2023;12(20):6623.
68. Gayretli Atan S, Pehlivan E, Bağçacı S. Evaluation of the effectiveness of proprioceptive training according to radiological stages in patients with knee osteoarthritis. Medicina (Kaunas). 2025;61(3):546.
69. Magni NE, McNair PJ, Rice DA. Sensorimotor performance and function in people with osteoarthritis of the hand: A case-control comparison. Semin Arthritis Rheum. 2018;47(5):676-82.
70. Ilfeld BM, Cao KN, Branson R. Ultrasound neuromodulation (low-intensity focused ultrasound) to treat knee osteoarthritis pain: A randomized, observer- and participant-masked, sham-controlled, human-subjects pilot study. J Ultrasound Med. 2025.
71. Ma Y, Hu T, Liu N. Acupotomy ameliorates KOA related chondrocyte premature senescence through YAP/FOXD1 pathway.

J Pain Res. 2025;18:2011-23.
72. Zhu C, Huang X, Yu J. The clinical efficacy of proprioceptive neuromuscular facilitation technique in the treatment of scapulohumeral periarthritis: A systematic review and meta-analysis. BMC Musculoskelet Disord. 2025;26(1):288.
73. Comino-Suárez N, Jiménez-Tamurejo P, Gutiérrez-Herrera MA. Effect of pulsed electromagnetic field and microwave therapy on pain and physical function in older adults with knee osteoarthritis: A randomized clinical trial. J Geriatr Phys Ther. 2025.
74. Guede-Rojas F, Benavides-Villanueva A, Salgado-González S. Effect of strength training on knee proprioception in patients with knee osteoarthritis: A systematic review and meta-analysis. Sports Med Hlth Sci. 2024;6(2):101-10.
75. Zhu H, Yan XH, Chen S. Mechanism of electroacupuncture in improving cartilage tissue injury in rats with knee osteoarthritis by regulating miR-335-5p expression. Zhen Ci Yan Jiu. 2025;50(3):310-8.
76. Zheng X, Gao S, You H. Electroacupuncture improves motor function of rats with osteoarthritis by alleviating joint inflammation through the Wnt-7B/β-catenin signaling pathway. Nan Fang Yi Ke Da Xue Xue Bao. 2023;43(4):590-6.
77. Ishikawa K, Kajiwara Y, Sakamoto J. Low-intensity muscle contraction exercise following the onset of arthritis improves hyperalgesia via reduction of joint inflammation and central sensitization in the spinal cord in a rat model. Neurosci Letters. 2019;706:18-23.
78. Miller RE, Miller RJ, Malfait AM. Osteoarthritis joint pain: The cytokine connection. Cytokine. 2014;70(2):185-93.
79. Chen DI, Shen J, Zhao W. Osteoarthritis: Toward a comprehensive understanding of pathological mechanism. Bone Res. 2017;5(1):1-3.
80. Pagar KR, Khandbahale SV, Kasar PM. Osteoarthritis: pathophysiology and current treatment modalities. Asian J Pharmaceutical Res. 2019;9(4):289-98.
81. Mills K, Hunt MA, Leigh R, Ferber R. A systematic review and meta-analysis of lower limb neuromuscular alterations associated with knee osteoarthritis during level walking. Clin Biomechanic. 2013;28(7):713-24.
82. Lloyd-Roberts GC. The role of capsular changes in osteoarthritis of the hip joint. J Bone and Jt Surg Brit. 1953;35(4):627-42.
83. Rutherford DJ. Intra-articular pressures and joint mechanics: should we pay attention to effusion in knee osteoarthritis? Med Hypotheses. 2014;83(3):292-5.
84. Mintarjo JA, Poerwanto E, Tedyanto EH. Current non-surgical management of knee osteoarthritis. Cureus. 2023;15(6):e40966.
85. Moulin D, Sellam J, Berenbaum F. The role of the immune system in osteoarthritis: mechanisms, challenges and future directions. Nat Rev Rheumatol. 2025;21(4):221-36.
86. Wang J, Xu S, Chen B. Advances in cell therapy for orthopedic diseases: Bridging immune modulation and regeneration. Front Immunol. 2025;16:1567640.
87. Kuo A, Raboczyj A, Nicholson JR. Significant hindlimb static weight-bearing asymmetry persists for 40-weeks in a longitudinal study in two widely used rat models of surgically induced osteoarthritis knee pain. Front Pharmacol. 2025;16:1560265.
88. Tsukada A, Uekusa Y, Ohta E. Association between synovial ntn4 expression and pain scores and its effects on fibroblasts and sensory neurons in end-stage knee osteoarthritis. Cells. 2025;14(6):395.
89. Ge M, Sun W, Xu T. Multi-omics analysis of synovial tissue and fluid reveals differentially expressed proteins and metabolites in osteoarthritis. J Transl Med. 2025;23(1):285.
90. Janczi T, Böhm B, Fehrl Y. Mechanical forces trigger invasive behavior in synovial fibroblasts through N-cadherin/ADAM15 -dependent modulation of LncRNA H19. Sci Rep. 2025;15(1):9814.
91. Huo Z, Fan C, Li K. Identification and validation of hub m7G-related genes and infiltrating immune cells in osteoarthritis based on integrated computational and bioinformatics analysis. BMC Musculoskelet Disord. 2025;26(1):333.
92. Wu Q, Henry JL. Functional changes in muscle afferent neurones in an osteoarthritis model: implications for impaired proprioceptive performance. PLoS One. 2012;7(5):e36854.
93. Roos EM, Herzog W, Block JA. Muscle weakness, afferent sensory dysfunction and exercise in knee osteoarthritis. Nature Rev Rheumatol. 2011;7(1):57-63.
94. O'Connor BL, Brandt KD. Neurogenic factors in the etiopathogenesis of osteoarthritis. Rheum Dis Clin N Am. 1993;19(3):581-605.
95. Woolf CJ. Central sensitization: Implications for the diagnosis and treatment of pain. Pain. 2011;152(3 Suppl):S2-15.
96. Lee CH, Chen CC. Role of proprioceptors in chronic musculoskeletal pain. Exp Physiol. 2024;109(1):45-54.
97. Moon KM, Kim J, Seong Y. Proprioception, the regulator of motor function. BMB Rep. 2021;54(8):393-402.

98. Wu Q, Xu Z, Ma X. Association of low muscle mass index and sarcopenic obesity with knee osteoarthritis: A systematic review and meta-analysis. J Int Soc Sports Nutr. 2024;21(1):2352393.
99. Drummer DJ, McAdam JS, Seay R. Perioperative assessment of muscle inflammation susceptibility in patients with end-stage osteoarthritis. J Appl Physiol (1985). 2022;132(4):984-94.
100. Liu X, Chen R, Song Z. Exercise following joint distraction inhibits muscle wasting and delays the progression of post-traumatic osteoarthritis in rabbits by activating PGC-1α in skeletal muscle. J Orthop Surg Res. 2024;19(1):325.
101. Cantero-Téllez R, Pérez-Cruzado D, Villafañe JH. The effect of proprioception training on pain intensity in thumb basal joint osteoarthritis: a randomized controlled trial. Int J Environ Res Public Health. 2022;19(6):3592.
102. Saeed Alshahrani M, Reddy RS, Asiri F. Correlation and comparison of quadriceps endurance and knee joint position sense in individuals with and without unilateral knee osteoarthritis. BMC Musculoskelet Disord. 2022;23(1):444.
103. Tarasovs M, Skuja S, Svirskis S. Interconnected pathways: Exploring inflammation, pain and cognitive decline in osteoarthritis. Int J Mol Sci. 2024;25(22):11918.
104. Damerau A, Rosenow E, Alkhoury D. Fibrotic pathways and fibroblast-like synoviocyte phenotypes in osteoarthritis. Front Immunol. 2024;15:1385006.
105. Yang X, Thudium CS, Bay-Jensen AC. Association between markers of synovial inflammation, matrix turnover and symptoms in knee osteoarthritis: A cross-sectional study. Cells. 2021;10(7):1826.
106. Yao Q, Wu X, Tao C. Osteoarthritis: Pathogenic signaling pathways and therapeutic targets. Signal Transduct Target Ther. 2023;8(1):56.
107. Panichi V, Costantini S, Grasso M. Innate immunity and synovitis: Key players in osteoarthritis progression. Int J Mol Sci. 2024;25(22):12082.
108. Stücker S, Koßlowksi F, Buchholz A. CPP-calcification of articular cartilage is associated with elevated cytokine levels in synovial fluid. Front Cell Dev Biol. 2025;13:1535530.
109. Liu Z, Sun Y, Pan J. Single-cell profiling uncovers synovial fibroblast subpopulations associated with chondrocyte injury in osteoarthritis. Front Endocrinol (Lausanne). 2024;15:1479909.
110. Ren JL, Yang J, Hu W. The global burden of osteoarthritis knee: a secondary data analysis of a population-based study. Clin Rheumatol. 2025:1-42.
111. Xu H, Xiao W, Ding C. Global burden of osteoarthritis among postmenopausal women in 204 countries and territories: A systematic analysis for the Global Burden of Disease Study 2021. BMJ Glob Health. 2025;10(3):e017198.
112. Alshehri SHS, Reddy RS, Alshahrani MS. Unraveling the impact of kinesiophobia on proprioception and balance: mediation by pain, mobility and psychological wellbeing in post-total hip replacement recovery. PLoS One. 2024;19(12):e0314627.
113. Hadjisavvas S, Efstathiou MA, Themistocleous IC. Effect of concentric exercise-induced fatigue on proprioception, motor control and performance of the upper limb in handball players. PLoS One. 2024;19(12):e0315103.
114. Gorski T, Casartelli NC, Fitzgerald G. Intramuscular fatty infiltration and its correlation with muscle composition and function in hip osteoarthritis. Skelet Muscle. 2024;14(1):32.
115. Gayretli Atan S, Pehlivan E, Bağçacı S. Evaluation of the effectiveness of proprioceptive training according to radiological stages in patients with knee osteoarthritis. Medicina (Kaunas). 2025;61(3):546.
116. Ghai S, Ghai I, Narciss S. Influence of taping on joint proprioception: A systematic review with between and within group meta-analysis. BMC Musculoskelet Disord. 2024;25(1):480.
117. Ferreira RM, Martins PN, Gonçalves RS. Non-pharmacological and non-surgical interventions to manage patients with knee osteoarthritis: An umbrella review 5-year update. Osteoarthr Cartil Open. 2024;6(3):100497.