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REVIEW

FASCIAL TISSUE AND OSTEOARTHRITIS: FROM BIOLOGY TO CLINICAL IMPLICATIONS

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ABSTRACT

Background: Fascia (FA) is a type of connective tissue that forms a network throughout the body which provides mechanical support and transmits forces across the entire body. Emerging research shows that fascia has a significant impact on pain and neuromuscular function in individuals with osteoarthritis (OA). Altered fascial stiffness can contribute to joint dysfunction, reduced mobility, and increased pain levels. The literature has been reviewed regarding myofascial pain in OA and how connective tissues respond to immobilization. However, there does not appear to be an integrated review synthesizing what we know about the biological mechanisms of fascia, including mechano-transduction processes during immobilization, as well as its application to clinical practice for individuals suffering from OA.

Materials and methods: A non-systematic literature search was performed in PubMed according to the SANRA framework. The search terms included fascia, extracellular matrix, connective tissue, innervation, mechanical properties, immobilization, and osteoarthritis. The search results comprised publications written in English from approximately 2009 to 2025, which were subjected to qualitative analysis.

Results: The data indicate that the fascia demonstrates viscoelastic characteristics in response to mechanical loading. Cell–matrix mechanical coupling is further transduced into transcriptional programs through mechanosensitive pathways, including integrins, YAP/TAZ, and Piezo channels. In contrast to this viscoelastic nature, immobilization elicits

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both qualitative and quantitative changes to connective tissue, namely collagen disorganization and hyaluronic acid aggregation, along with decreased sliding potential and impaired innervation, contributing to an increase in stiffness and decrease in range of motion (ROM). Studies utilizing imaging modalities in patients diagnosed with osteoarthritis have shown evidence of increased stiffness of the iliotibial tract on shear wave elastography and thickening of the plantar fascia. There is heterogeneity among patients diagnosed with Osteoarthritis based on the involvement of the fascia, with varying degrees of phenotypic expression. Studies examining the use of manual myofascial therapies have demonstrated a reduction in stiffness and improvement in ROM, with numerous studies reporting short-term benefits. However, these studies also highlight the limitations of their methodology.

Conclusions: The currently available evidence provides preliminary support for the inclusion of interventions targeting the fascia as part of a multifaceted approach to treating OA. The existing body of evidence related to the efficacy of treatments targeting the fascia in the treatment of OA is variable and methodologically limited. Therefore, adequately powered randomized controlled trials involving standardized protocols for assessment, imaging-based assessment of fascial properties, and categorization by osteoarthritis phenotype are required to determine whether treatments directed towards the fascia can provide clinically relevant efficacy in addition to providing information regarding long-term effects.

KEYWORDS

Fascia, extracellular matrix, osteoarthritis, connective tissue, mechanotransduction, myofascial therapy, immobilization

INTRODUCTION

The fascia (FA) is a network of connective tissue sheets that envelops and interconnects muscles, joints, nerves, blood vessels, and organs throughout the body. Together, these soft structures form a three-dimensional mechanical structure formed mainly by fibroblasts and myofibroblasts embedded in an extracellular matrix (ECM)[1-3]. Therefore, the FA is considered a mechanoreactive and highly innervated organ with a sensory function (i.e., proprioception, exteroception, and nociception)[4-6].

The structure of this organization has been proposed to support a tensegrity-based system for force distribution in the body[7,8]. Prolonged immobilization is associated with significant alterations in fascial composition and function[9,10]. Specifically, when muscles are shortened for an extended period, structural alterations in the connective tissue and tendon may occur, including decreased sarcomere numbers, increased amounts of poorly organized peri-and endomyosium, and an increase in hyaluronic acid content within the tissue, leading to an overall increased viscosity in the tissue[11-13].

Understanding fascial properties is relevant to the modern understanding of osteoarthritis (OA), a degenerative joint disease characterized by cartilage loss and breakdown, synovial inflammation, and alterations in joint function[14]. Traditionally considered a cartilage-driven condition, OA is now recognized as a whole-joint disease affecting the cartilage, subchondral bone, synovium, ligaments, capsule, and periarticular soft tissues[14]. Thus, changes in the fascial network may affect joint stability and mechanical loading and contribute to the inflammatory processes involved in disease progression[15,16].

Osteoarthritis (OA) is the most prevalent joint disorder worldwide, affecting over 500 million people globally and representing a leading cause of disability and chronic musculoskeletal pain in older adults[17]. This condition imposes a substantial socioeconomic burden through long-term functional limitations, reduced participation in daily activities, and progressive loss of independence[14].

Given its rich innervation and mechanical continuity, the fascia may contribute to nociception and neuromuscular control, potentially contributing to pain sensitization and motor dysfunction in patients with OA[18]. Moreover, fascial dysregulation may perpetuate a cycle of mechanical overload and chronic inflammation, further worsening joint degeneration[18].

Despite an expanding body of literature on fascia biology and the systemic dimensions of OA, the specific interface between fascial alterations and OA pathophysiology remains incompletely characterized. Previous reviews have addressed the myofascial component of OA pain[18] and connective tissue responses to immobilization[10]. However, a synthesis that integrates fascial biology and mechanotransduction with immobilization as a biological model of altered loading and the clinical context of OA is currently lacking. In the present review, we adopted an expanded anatomical framework that considers the fascia as a continuous system encompassing the superficial fascia, deep fascia, and muscle-associated connective tissue layers (epimysium, perimysium, and endomysium). Within this conceptual scope, this study aims to summarize the current evidence on fascial structure, function, and mechanical properties under physiological and pathological conditions — with a specific focus on immobilization — and to discuss the biological rationale for considering fascia-targeted interventions within multimodal OA rehabilitation.

MATERIALS AND METHODS

This narrative review was conducted in accordance with the recommendations of the Scale for the Assessment of

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Narrative Review Articles (SANRA[19]) and aims to provide an interpretive synthesis of the literature on fascial biology, mechanotransduction, the effects of immobilization on connective tissue, and the potential biological rationale for considering fascia-targeted interventions in osteoarthritis.

A non-systematic literature search was performed in PubMed in November 2025 using combinations of the following terms: fascia, extracellular matrix, connective tissue, innervation, mechanical properties, immobilization, manual therapy, and osteoarthritis. The reference lists of the included studies were screened to identify additional relevant articles. English-language original studies and review articles published primarily between 2009 and 2025 were considered, with selective inclusion of earlier landmark contributions that were conceptually relevant. Given the narrative scope of the review and the heterogeneity of the included literature, no formal eligibility criteria, dual reviewer screening, or formal quality assessments were applied. The authors qualitatively synthesized the data based on the conceptual relevance of fascial biology and its potential implications for OA.

RESULTS

Human fascia anatomy

In this review, the fascia is considered within an expanded anatomical framework that includes the superficial fascia, deep fascia, and muscle-associated connective tissue layers, such as the epimysium, perimysium, and endomysium *(Table 1)*. Although these structures differ in morphology, location, and function, they are anatomically and mechanically interconnected and can be considered components of a continuous fascial system[12,20].

The superficial fascia is located within the subcutaneous tissue, a few millimeters below the skin, and is composed of loosely arranged collagen fibers, elastic fibers, adipose tissue, vessels, and nerves[21,22]. In addition to its structural role, the superficial fascia contributes to exteroception, thermoregulation, lymphatic and venous

Fascial component	Structural composition	Anatomical location	Innervation	Main functions
Superficial fascia	Loosely arranged collagen fibres (mainly types I and III), elastic fibres, adipocytes, vessels, nerves, and loose connective tissue; variable thickness depending on body region	Located within the subcutaneous tissue, a few millimetres below the skin, more developed in some body regions and along specific surfaces	Free nerve endings, Ruffini-like and Pacinian-like corpuscles, sympathetic fibres associated with vessels and connective tissue	Exteroception, thermoregulation, pain perception, support of lymphatic and venous flow, and mechanical coupling between skin and deeper tissues
Deep fascia	Dense regular connective tissue is organized in two or three collagen-rich layers, often separated by loose connective tissue rich in hyaluronan, and may receive muscular expansions.	Located beneath the hypodermis and above or around the muscles, it includes specialized structures such as the paratendon, periosteum, and neurovascular sheaths.	Free nerve endings, Ruffini-like and Pacinian-like corpuscles, sensory and autonomic fibres	Force transmission, proprioception, nociception, intermuscular coordination, compartmental organisation, and support of gliding between adjacent tissue planes
Epimysium	Collagen-rich connective tissue layer surrounding the whole muscle; contains multiple fibre orientations and ECM rich in hyaluronan at interfaces	Envelops the external surface of skeletal muscle and interfaces with the deep fascia and the perimysial network	Associated with muscle spindles, intramuscular nerves, and vessels; contributes to sensory and mechanical integration	Mechanical linkage between muscle and surrounding fascia, lateral force transmission, support of muscle shape and gliding of the muscle belly
Perimysium	The connective tissue network is composed mainly of collagen types I and III, organized in multidirectional lamellae around fascicles.	Surrounds and separates muscle fascicles within skeletal muscle	Closely associated with vascular and neural branches supplying fascicles	Organisation of muscle fascicles, transmission of forces between fibres and fascicles, support of intramuscular vessels and nerves, and contribution to passive muscle stiffness
Endomysium	Delicate connective tissue network surrounding individual muscle fibres; rich in collagen type IV and basement membrane-associated components	Located around each myofiber, forming the finest connective tissue compartment of skeletal muscle	Closely related to capillaries and terminal neural elements within the muscle	Structural support of individual fibres, local force transmission, coupling between myofibers and ECM, and contribution to microenvironmental homeostasis

Table 1. *Main anatomical and functional features of fascial system components. The table summarizes the structural composition, anatomical location, sensory organization, and functional role of the superficial fascia, deep fascia, and muscle-associated connective tissue layers within an expanded fascial framework. Adapted from the sources cited in this section.*

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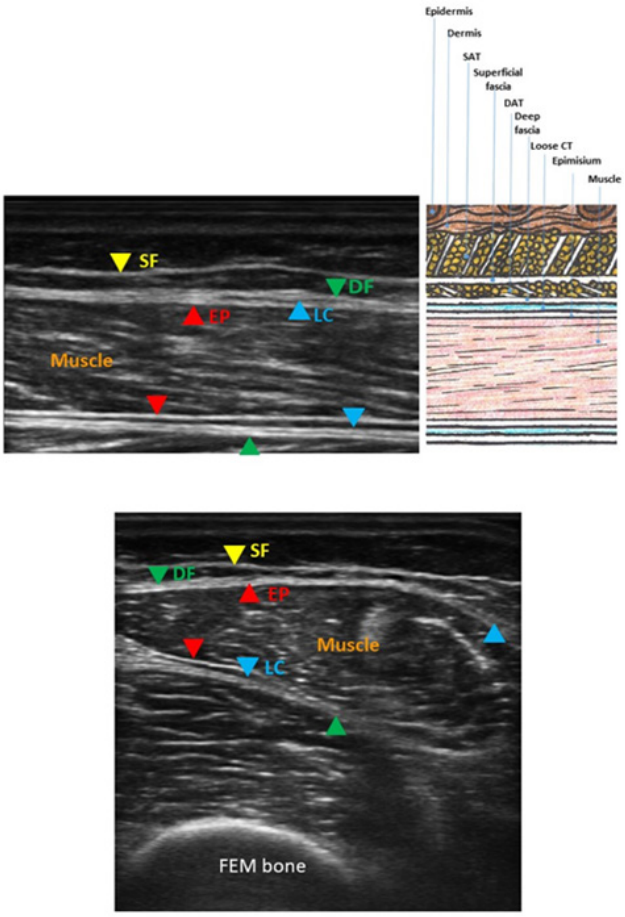


Figure 1. *Ultrasound image of a portion of the rectus femoris muscle in healthy participants. Top: longitudinal section; bottom: transverse section. SF (yellow) superficial fascia, DF (green) deep fascia, EP (red) epimysium fascia, LC (blue) loose connective tissue, rich in hyaluronic acid, located between deep fascia layers and between deep fascia and epimysium. Muscle (orange) portion of the rectus femoris muscle and FEM bone (white) femoral bone.*

Abbreviations: DAT, deep adipose tissue; SAT, superficial adipose tissue.

support, and pain perception[21,22]. The deep fascia is a more organized connective tissue structure located beneath the hypodermis and is typically composed of dense collagen layers separated by loose connective tissue rich in hyaluronan, which facilitates gliding between adjacent planes[23-25]. The deep fascia also includes functionally specialized structures, such as the paratendon, periosteum, and neurovascular sheaths, and is involved in force transmission, proprioception, and mechanical coordination between the muscles and joints[26] *(Fig. 1)*.

Muscle-associated connective tissue is organized into epimysium, perimysium, and endomysium[23,27]. The epimysium surrounds the entire muscle, the perimysium organizes the muscle fibers into fascicles, and the endomysium surrounds individual muscle fibers. These layers are structurally continuous and contribute not only to the integrity of the skeletal muscle but also to lateral force transmission, viscoelastic behavior, and embedding of intramuscular nerves and vessels[23,26-28]. Therefore, the mechanical behavior of the musculoskeletal system, in addition to its elastic behavior, can be influenced by both the contractile elements and the properties and organization of the connective tissue within each skeletal muscle[26,29].

Given that there are various definitions of “fascia” in the literature, it will be helpful to define the difference between true fascia (or fascia proper) and the various forms of connective tissue associated with muscles. Nonetheless, the concept of a fascial continuum can help one understand how changes in the connective tissue in a particular area may impact the regional movement mechanics of tissues and their gliding, as well as their associated neuromuscular functions.

Cellular components of fascia

The major cellular components of the fascial tissue system are fibroblasts and myofibroblasts embedded in the extracellular matrix (ECM). Other cell types also contribute to maintaining homeostasis and promoting sliding along the fascial plane[30,31].

Fibroblasts and myofibroblasts

Fibroblasts are the principal cells of all forms of connective tissue and play a primary role in the synthesis, maintenance, and remodeling of the ECM[4,32,33]. Fibroblasts, in conjunction with integrins and other surface receptors, can sense mechanical forces in their environment due to the ECM and adjust matrix synthesis and organize the tissue appropriately[32,33]. Therefore, fibroblast function is closely associated with mechanotransduction and connective tissue adaptability to loading conditions *(Fig. 2)*.

Myofibroblasts exhibit a contractile phenotype that is intermediate between fibroblasts and smooth muscle

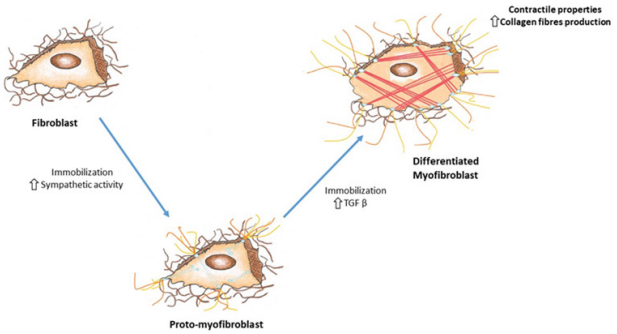


Figure 2. *Schematic representation of fibroblast-to-myofibroblast differentiation. Mechanical stimuli, cytokines (including TGF-β), and environmental factors promote the transition of fibroblasts into myofibroblasts. This process is characterized by the expression of alpha-smooth muscle actin (α-SMA), increased cytoskeletal organization, and enhanced contractility. Myofibroblasts establish connections with the extracellular matrix through integrin-mediated adhesion complexes, contributing to tissue remodeling and increased stiffness.*

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cells[31,34,35]. Their differentiation is promoted by multiple endogenous and exogenous stimuli, among which mechanical loading and transforming growth factor-beta (TGF-β) are considered particularly relevant[34-37]. The transition toward a myofibroblast phenotype is characterized by the de novo expression of alpha-smooth muscle actin and the development of actin stress fibers connected to the surrounding ECM *(Fig. 2)* through adhesion complexes containing integrins and fibronectin[34,36]. These structures allow bidirectional force transmission between the cell and matrix, supporting the role of myofibroblasts in tissue remodeling and regulation of connective tissue tension[34,36,38].

Although the in vivo contribution of myofibroblasts to fascial stiffness remains incompletely defined, increased myofibroblast activity has been associated with fibrotic remodeling and ECM deposition[31,34]. Experimental evidence also suggests that changes in autonomic activity, local pH, cytokine signaling, and persistent mechanical stress may modulate myofibroblast behavior[31,36]. Accordingly, myofibroblasts may represent one of the cellular mechanisms through which chronic loading alterations contribute to long-term changes in the stiffness of connective tissue. Importantly, the myofibroblast phenotype is at least partially reversible: in reduced mechanical tension and modified microenvironmental cues, myofibroblasts may undergo apoptosis or de-differentiate, which has implications for both the persistence and potential reversibility of connective tissue stiffening[34].

Fasciacytes

Fasciacytes are described as fibroblast-like in terms of morphology, but they specifically produce high levels of hyaluronic acid, which contributes to the ability of the fascia to glide[39]. Morphologically, fasciacytes differ from classic fibroblasts; their nuclei are more rounded *(Fig. 3)*, and there is less extension of the cytoplasm. Fasciacytes also reside primarily where dense fibrous connective tissue meets loose connective tissue[39]. Fibroblasts primarily function in controlling the non-cellular matrix formed by collagen and elastin, while fasciacytes are considered to be much more active in the loose connective tissue compartment of the extracellular matrix *(Fig. 3)*, especially when hyaluronic acid-rich areas allow for slippage between layers[39,40]. However, their precise functional relevance in vivo remains unclear.

Telocytes

Telocytes are interstitial connective tissue cells characterized by small cell bodies and long cytoplasmic extensions called telopodes[41]. They form an extensive three-dimensional communication network and are implicated in tissue repair, remodeling, intercellular signaling, and immune regulation[41,42]. Their specific roles in fascial physiology and pathology have not yet been clearly established; however, they may contribute to local tissue homeostasis and intercellular communication within the fascial microenvironment.

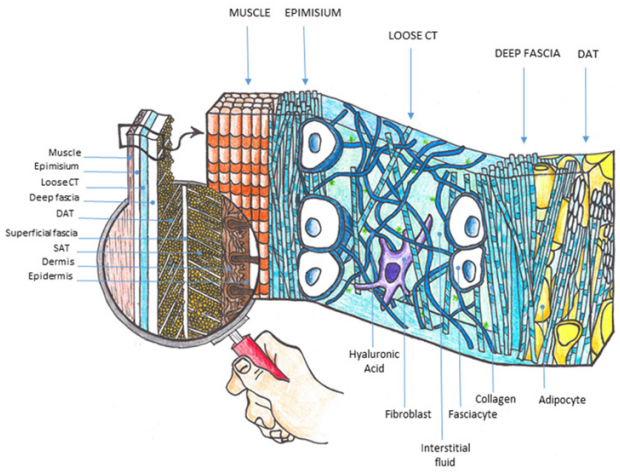


Figure 3. *Organization of the extracellular matrix in fascial tissue. The figure illustrates the arrangement of collagen fibers, elastic fibers, hyaluronan-rich loose connective tissue, and interstitial fluid within the fascial system. These components contribute to tissue viscoelasticity, hydration, and interlayer gliding, thereby enabling efficient force transmission and adaptation to mechanical loading.*

Extracellular matrix

The extracellular matrix (ECM) is a highly dynamic and mechanically active component of the fascial tissue. The components include collagen fibers *(Fig. 3)*, elastic fibers, proteoglycans *(Table 2)*, glycoproteins, hyaluronic acid, and interstitial fluid. These components create a supramolecular network that supports tissue integrity, transmits force, and modulates mechanobiology at the local level[6,43,44].

The ECM plays a critical role in maintaining structural continuity within the skeletal muscle and its connective tissue by providing physical connections among myofibers, blood vessels, and nerves. The ECM is essential for the transmission of mechanical forces through these tissues and their organization[6,23,27]. Additionally, the ECM interacts directly with the sarcolemma, cytoskeleton, and nucleus of cells, indicating that it is not simply a passive scaffold but an active regulator of cell function and tissue adaptation[43,45]. Cell-matrix mechanical coupling is further transduced into transcriptional programs through mechanosensitive pathways, such as the YAP/TAZ axis, which links matrix stiffness to cell phenotype and ECM remodeling[46]. Because of the responsiveness of ECM composition and hydration to various biological and mechanical stimuli, alterations in ECM organization can influence the viscoelastic properties, sliding resistance, and stiffness of tissues[27,43].

Collagen fibers

Collagen is the major structural protein of the ECM and is essential for maintaining tissue integrity and load-bearing function[27,47]. Different collagen types contribute

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Molecule/ system	Category	Main biological role	Relationship with fascial mechanics and cell behavior	Response to loading/ immobilization
Fibronectin	ECM glycoprotein	Cell adhesion, migration, matrix assembly, wound repair	Connects ECM components to integrin receptors and the cytoskeleton, contributing to mechanotransduction and tissue remodelling	May increase during tissue remodelling and reduced loading; involved in fibrotic responses
Laminins	Basement membrane glycoproteins	Structural organisation of basement membrane, cell adhesion, differentiation, and migration	contributes to the coupling between myofibers and the surrounding ECM, helping to maintain structural integrity at the cell–matrix interface.	Generally more stable; less clearly responsive to exercise than other matrix molecules
Tenascin	ECM glycoprotein	Matrix remodelling, modulation of cell adhesion, response to tissue stress	It modulates fibronectin–integrin interactions and is associated with tissue adaptation under altered mechanical conditions.	Typically increases in response to mechanical stress, injury, or inflammation
Decorin	Small leucine-rich proteoglycan	Regulation of collagen fibrillogenesis and ECM organisation; modulation of growth factor activity	Influences collagen fiber assembly and may regulate tissue stiffness and remodeling through interactions with TGF-β	May be altered during connective tissue remodelling and fibrosis
Integrin-based adhesion system	Transmembrane receptor complex	Bidirectional cell–ECM signaling, force sensing, mechanotransduction	Links ECM molecules such as fibronectin to the intracellular cytoskeleton, enabling conversion of mechanical stimuli into cellular responses	Reduced loading may impair normal cell–matrix signalling, and altered integrin signalling is associated with remodelling and detachment phenomena.
Hyaluronan-rich loose connective matrix	Glycosaminoglycan - rich ECM compartment	Hydration, lubrication, interlayer gliding, and regulation of tissue viscosity	Critical for sliding between adjacent fascial layers and for adaptation to movement	Immobilization may increase viscosity and molecular aggregation, impairing gliding and contributing to densification of the powder.

Table 2. *Major extracellular matrix molecules involved in fascial structure, mechanotransduction, and remodeling. The table summarizes the selected ECM components and adhesion systems relevant to tissue organization, cell–matrix signaling, and loading-dependent remodeling.*

to distinct aspects of connective tissue organization. Types I and III are predominant in interstitial connective tissues and are involved in force transmission and tensile resistance, whereas types IV and VI are associated with the basement membrane and are closely related to the myofiber surface[23,47]. Through these different structural roles, collagen contributes to force transfer, stability, and mechanical coupling between cellular and extracellular compartments[27,48].

Elastic fibers

Elastic fibers consist of an elastin core surrounded by microfibrils and are responsible for tissue extensibility and recoil[49]. Their mechanical resilience contributes to the capacity of connective tissue to undergo deformation and return to its original configuration after unloading. Because elastic fibers have limited regenerative potential in adult tissues, structural damage or degradation may have long-lasting effects on tissue mechanics[49].

Hyaluronan

Hyaluronic acid is the primary unsulfated glycosaminoglycan in the extracellular matrix that provides the majority of the water-holding space within an area and is responsible for both lubrication and layer-to-layer gliding[50,51]. Hyaluronic acid is primarily found in loose connective tissues between different layers of the fascia and at the fascial-muscle junction *(Fig. 3)*[39,50,51], which helps facilitate sliding and adaptability to movement. Hyaluronic acid-rich areas are particularly important for the autonomous functioning of the fascial planes. Impairments in the gliding functions of hyaluronic acid due to changes in its concentration, molecular aggregates, or viscosity result in the densification and stiffening of these areas[50,51].

Proteoglycans and glycoproteins

Proteoglycans and glycoproteins *(Table 2)* are essential regulators of ECM architecture, cell adhesion, and mechanotransduction[33,52,53]. Molecules such as

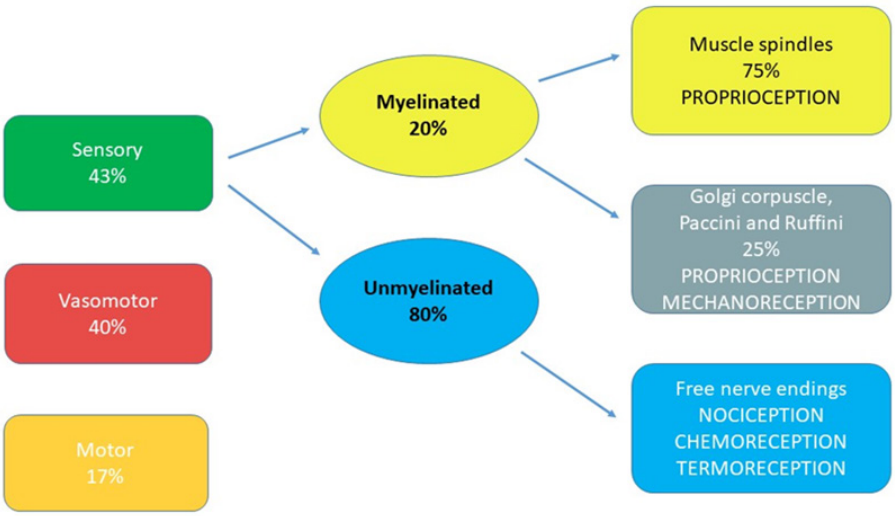


Figure 4. *A summary of the peripheral nerves composition.*

fibronectin, laminins, tenascin, decorin, and integrin-associated adhesion systems contribute to the structural organization of the matrix and cell-extracellular matrix (ECM) signaling[43,44,52]. These molecules are also sensitive to physical loading and disuse, indicating that ECM remodeling is influenced not only by injury or inflammation but also by changes in habitual movement and mechanical stimulation[54].

Interstitial fluid and matrix hydration

Fascial tissues, particularly their loose connective tissue components, are rich in interstitial fluid[6]. Matrix hydration is strongly influenced by hyaluronan and other charged ECM molecules that regulate water retention and local osmotic behavior. Changes in water content, ion concentration, and pH can alter ECM viscosity and viscoelastic behavior, thereby affecting gliding between tissue layers and mechanical stiffness[3,50,54]. In particular, reduced pH has been shown to increase hyaluronan viscosity, a mechanism that may contribute to connective tissue densification and altered musculoskeletal function[53].

Fascia innervation

Fascial tissues are increasingly recognized as richly innervated sensory structures *(Fig. 4)* with potential relevance to proprioception, nociception, and autonomic regulation[55-62]. Immunohistochemical studies have indicated that both the superficial and deep fascia contain free nerve endings, encapsulated receptors, and autonomic fibers, although the density and functional distribution of these elements vary according to the anatomical location and tissue type[55,56,59-62].

The superficial fascia is densely innervated by free nerve endings, Ruffini-like and Pacinian-like corpuscles, and sympathetic fibers associated with blood vessels and surrounding connective tissue[56]. The distribution of these fibers suggests an important role for the superficial fascia in exteroception, thermoregulation, vasomotor regulation, and nociception[26,56,57,61]. In the deep fascia, sensory innervation is abundant and includes both peptidergic and non-peptidergic fibers, with particular relevance to the transmission of proprioceptive and nociceptive signals related to movement[55,59-62]. Free nerve endings in fascial tissues can detect mechanical, chemical, and thermal stimuli[57,62]. Activation of these receptors can be modulated by the tension generated by the load on the fascia and by the pre-load created at the time of muscle contraction, supporting the idea that the fascia contributes to the integration of movement-related sensory information[57]. Fascia may therefore be involved not only in the transmission of nociceptive signals but also in the modulation of motor control and body awareness.

The autonomic component of fascial innervation is of particular interest in this context. Most sympathetic fibers associated with the fascia are located near blood vessels, where they regulate vasoconstriction; however, some sympathetic fibers are also dispersed throughout the connective tissue[56,57]. It has been speculated that sustained sympathetic stimulation may indirectly affect fascial tone through its effects on blood vessels, trophic growth factors, and inflammatory cytokines, with the potential involvement of TGF-β and myofibroblasts[31,57]. However, our understanding of the functional significance of this interaction in vivo is limited.

In summary, the current knowledge provides strong evidence that fascial innervation is both anatomically complex and functionally significant. Changes in fascial properties, such as increased stiffness and reduced sliding capability, may contribute to alterations in pain perception, proprioceptive function, and neuromuscular coordination.

Fascia mechanical properties

The mechanical behavior of fascial tissue is complex and depends on its hierarchical structure, regional anatomy, fiber orientation, hydration state, and loading history[3,28,63,64]. Rather than behaving as a homogeneous material, the fascia shows marked anisotropy and heterogeneity, with mechanical properties that vary according to the anatomical site and direction of loading[25,28,58].

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The viscoelastic properties of fascial tissue are important characteristics. When subjected to a mechanical load, the fascia undergoes deformation that depends on the duration of force application. The stress–strain relationship can be described using two distinct elements: an elastic component and a viscous component. These two elements allow the fascia to act as a shock-absorbing medium that distributes and reduces the amplitude of applied loads through the absorption and dissipation of forces. Fascial hysteresis, load history dependence, and strain-dependent stiffness are important parameters for describing fascial mechanics when subjected to repetitive or constant loads[1,8,63].

The mechanical behavior is also strongly influenced by the collagen architecture. The orientation of collagen fibers across different fascial layers determines how the tissue responds to longitudinal loading, transverse loading, and shear stress[25,28]. In multilayered fascia, this organization enables a combination of tensile resistance and interlayer sliding, which is essential for efficient force transmission and coordination[3,25,28]. Similarly, within muscle-associated connective tissue, differences between longitudinal stiffness and shear behavior reflect the structural specialization of the endomysium, perimysium, and epimysium[23,26-28].

Fascial stiffness is not fixed and may change in response to both short- and long-term stimuli. Short-term changes may be related to alterations in tissue hydration, fluid distribution, and collagen fiber alignment, whereas long-term adaptations may involve ECM remodeling and cellular responses, such as myofibroblast differentiation[3,8,54,63]. These processes likely act in combination and may contribute to changes in tissue gliding, mechanical resistance, and efficiency of movement. At the microscopic level, ECM-cell mechanotransduction pathways, including integrins, focal adhesions and focal adhesion complexes, cytoskeleton remodeling, and matrix viscoelastic characteristics (hydration and poroelastic properties), regulate the transmission of forces and adaptive processes within tissues. Clinical studies using ultrasound imaging in patients with severe acquired brain injuries have shown increases in intramuscular connective tissue in conjunction with abnormal architectural patterns of muscles following long periods of immobilization. This is indicative of changes in the mechanical behavior of the connective tissue associated with the muscle[65] *(Fig. 5)*. While there are differences in the pathophysiology of severe acquired brain injury and osteoarthritis (notably due to the presence of spasticity, denervation, and systemic inflammatory conditions), it provides an example of how prolonged unloading of tissues may result in structural reorganization of the connective tissue associated with the muscle.

The overall contribution of fascial tissues in transmitting and regulating mechanical forces through the musculoskeletal system is significant, as such force transmission influences muscle and movement performance[2,3,7] and influences how muscles work together for coordinated movements. The function of the fascia in a healthy state can also serve as a reference point when examining alterations due to stiffness, disuse, or abnormal motor control.

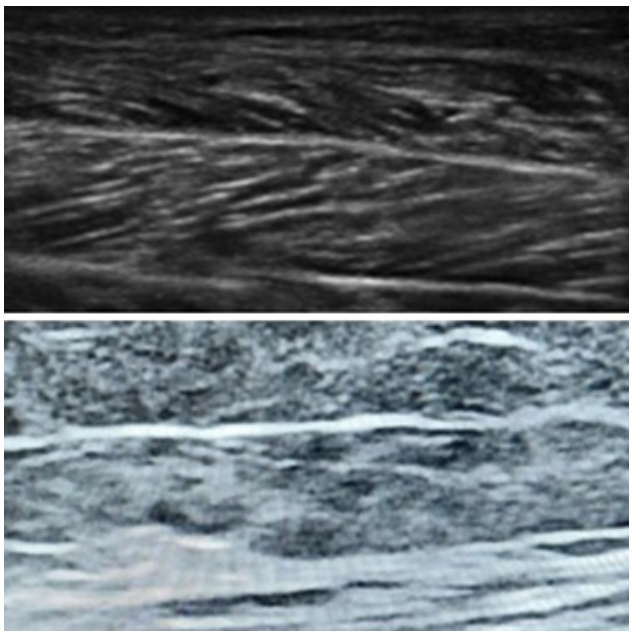


Figure 5. *Ultrasound image of a portion of the medial gemellus muscle in the longitudinal section. Top: Muscle of a healthy subject. Bottom: muscle of the plegic leg of a patient 3 months after neurological injuries. High fibrotic muscle (a marked increase in white area): increase, disorganization, and densification of collagen tissue and remodelling of the ECM matrix.*

Effect of immobilization on fascial tissues

Changes in skeletal muscle and connective tissue have been identified as part of the effects of immobilization on both cellular components of muscle-associated fascia and the extracellular matrix (ECM)[9,10,26,66]. The changes that occur due to immobilization include decreased muscle CSA, increased connective tissue, altered organization of collagen *(Fig. 5)*, decreased capillary density, and impaired sliding within the tissues; all of these changes can lead to an increase in stiffness and impeded motion[11,66,67]. In the context of this review, immobilization is relevant because it represents a biological model of how changing loads can affect fascial structure and function over time. The evidence summarized in the following sections is derived from heterogeneous experimental models, including cast immobilization, denervation, hindlimb suspension, and clinical disuse, which differ in their relative contributions of mechanical unloading, neural input, and systemic factors; this heterogeneity should be considered when interpreting the underlying mechanisms.

Cellular changes induced by immobilization

Reduced movement, prolonged mechanical unloading, hypoxia, and continued low-grade inflammation can

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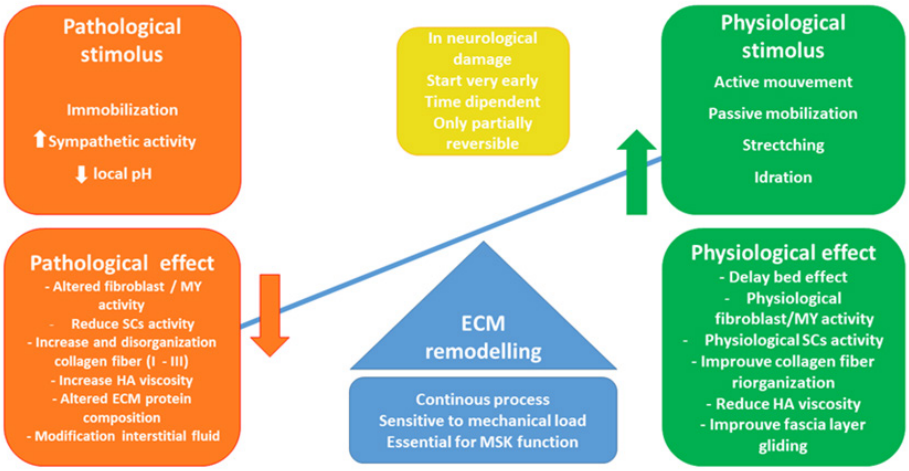


Figure 6. *Connective tissue and ECM remodelling following immobilization.*
Abbreviations: ECM, extracellular matrix; HA, hyaluronic acid; MSK, muscular; MY, myofibroblast; SCs, satellite cells, muscle stem cells.

activate fibroblasts or differentiate myofibroblasts *(Fig. 2)*. A large portion of this is due to TGF-β signaling[34,68,69], which can lead to increased extracellular matrix (ECM) synthesis (including collagen I, fibronectin, tenascin, and other ECM proteins involved in fibrosis and tissue remodeling[68,69]. The degree to which these processes are specific to the fascia, as opposed to muscle-associated connective tissue, is unknown, and most available evidence is derived from studies on muscle-associated connective tissue rather than the fascia itself. However, there appears to be an increase in matrix deposition (and therefore potentially an increase in tissue stiffness and a decrease in mechanical adaptation) in immobilized tissues. Immobilization may also affect satellite cell activity and muscle trophism, contributing to a reduced muscle cross-sectional area and altered tissue mechanical properties[70].

ECM and collagen remodeling

Immobilization, even for short periods, may increase collagen I and III content, particularly in peri- and endomysial areas *(Fig. 6)*, while altering matrix organization and reducing the regularity of the connective tissue network[9,11,26]. These changes are often accompanied by disorganization of the collagen architecture, with consequences for force transmission and tissue compliance[9]. Conversely, controlled stretching and reloading have been shown to promote favorable connective tissue organization and may partially reverse some of the structural changes induced by immobilization[9,10,71,72]. Such effects are thought to depend, at least in part, on the mechanosensitive pathways regulating matrix turnover and muscle–connective tissue interaction[10,73].

Hyaluronan, matrix viscosity, and gliding impairment

Beyond the aforementioned role of hyaluronan in normal fascial gliding, immobilization also impacts the biochemical properties and rheological behaviors of glycosaminoglycan-and hyaluronic acid-rich loose connective tissues[74-77], and thus may impact the ability of hyaluronic acid molecules to be metabolized and exchanged through movements[6], leading to increased molecule aggregations that can increase local viscosity *(Fig. 7)* in the fascia and ultimately limit the motion of gliding between fasciae[6,75,76]. The results of such alterations are likely to include what is referred to as fascial densification. Fascial densification occurs when there is a decrease in the efficiency of gliding between two or more adjacent connective tissue layers owing to increased mechanical resistance[77].

Viscosity can affect how forces are distributed throughout a body; it can limit the amount of adaptation occurring at various joints during movement and can affect the threshold required for mechanoreceptors and nociceptors located in the fascial network to be activated[6]. As with the other mechanisms mentioned above, quantifying this mechanism in vivo is very difficult; however, it serves to link immobilization, reduced tissue gliding, stiffness, and altered sensory feedback.

Vascular and neural consequences of immobilization

Prolonged inactivity has been shown to decrease the number of capillaries within muscles and the way in which muscle fibers are connected by connective tissue, both of which could reduce blood flow to the muscle (which can

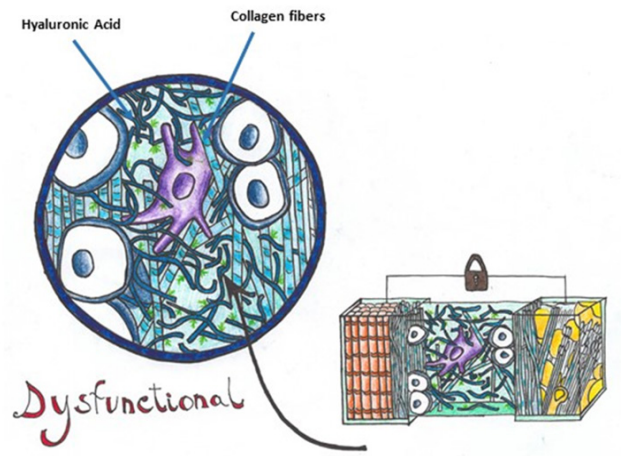


Figure 7. *Graphical summary of ECM alterations due to immobilization. On the left: increased density of hyaluronic acid, increased production and disorganization of collagen fiber.*

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lead to loss of muscle mass)[6,9,26] and result in abnormal changes in the amount or location of nerve receptors that respond to pain (nociceptors) and those that provide information about position and length (proprioceptors) found in abnormal fascia[12,26,62]. Abnormal increases in the density or stiffness of the connective tissue surrounding the muscle fibers can physically restrict the function of the muscle spindles and/or influence the sensory information that reaches the central nervous system from the periphery, thus influencing an individual's ability to feel the location of their body parts during voluntary movements[26,61].

Osteoarthritis and fascia

Osteoarthritis is defined as a chronic and degenerative condition that affects joints throughout their body; with all joint structures being affected over time (cartilage, sub-chondral bone, synovial membrane, etc.)[14,78-81]. Historically, osteoarthritis was referred to as an illness of the cartilage; however, it is currently recognized as a multi-tissue issue where changes in the mechanical characteristics of the tissue, inflammation, composition of the extracellular matrix, and sensorimotor functionality can be factors that contribute to both symptomatology and disability[14,78,79,81]. Within this framework, fascial tissues may be relevant not as primary drivers of OA onset but as potential modulators of pain, stiffness, and movement dysfunction. Fascial alterations may influence tissue gliding, force transmission, proprioceptive signaling, and local nociceptive sensitivity, thereby contributing to the complex symptom profile of OA[12,18,26]. This interpretation is consistent with the concept that non-cartilaginous soft tissues may participate in the mechanical and sensory environments of osteoarthritic joints.

Beyond this whole-joint perspective, OA is a clinically and biologically heterogeneous disease. A systematic review[82] identified six recurrent phenotypes of knee OA: chronic pain, inflammatory, metabolic syndrome, bone and cartilage metabolism, mechanical overload, and minimal joint disease. This heterogeneity implies that fascial involvement is unlikely to be uniform across patients, although direct studies stratifying fascial findings by OA phenotype are lacking. Recent evidence further suggests that poor core stability is associated with knee OA progression, reinforcing the relevance of biomechanical and functional phenotyping[83].

Mechanical loading is central to cartilage homeostasis and connective tissue adaptation[48,79,81]. Conversely, immobilization and reduced movement are associated with the loss of cartilage volume, narrowing of joint spaces, reduced proteoglycan content, and impaired matrix turnover[48]. Experimental and clinical observations indicate that active and passive movements may support glycosaminoglycan content and proteoglycan synthesis, whereas cyclic loading appears to favor more physiological cartilage structure and function[48,81]. Regarding the fascial system, immobilization induces qualitative and quantitative changes, including increased collagen content, altered ECM composition, reduced gliding, and impaired neuromuscular signaling[6,9,26]. These changes may contribute to increased stiffness, reduced ROM, altered force transmission, and functional limitations. Therefore, immobilization can be considered a relevant biological framework for understanding how altered loading may influence fascial properties and, in turn, potentially aggravate pain and movement dysfunction in osteoarthritis *(Fig. 8)*. In line with this functional perspective, a recent randomized trial in patients with knee OA reported improved walking speed after supervised clinic-based or home-based exercise, although postural control measures did not significantly change[84].

Taken together, these observations describe converging lines of evidence, rather than an established causal model. OA-related pain and movement limitation may favor connective tissue changes through reduced activity and altered loading; conversely, fascial alterations, such

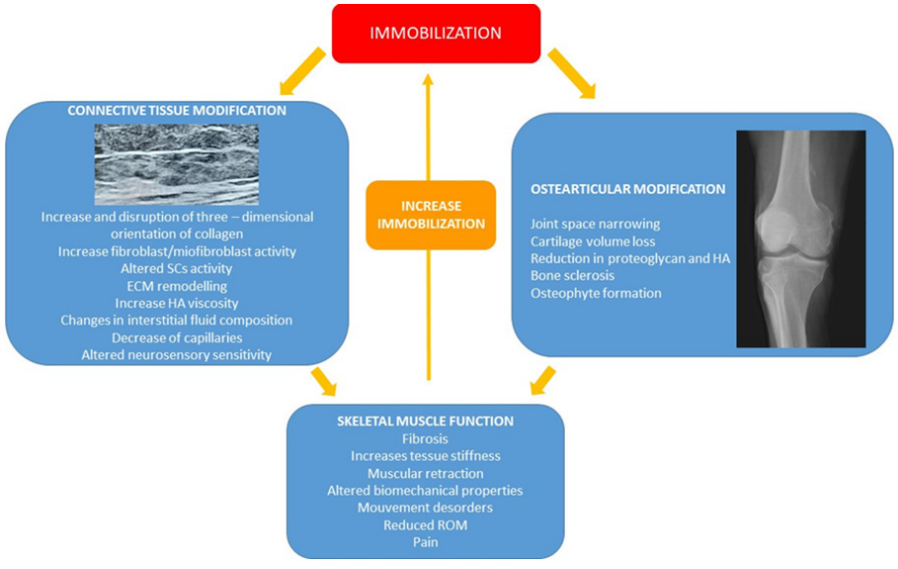


Figure 8. *Effects of immobilization on connective tissue, osteoarticular system, and skeletal muscle function.*
Abbreviations: ECM, extracellular matrix; HA, hyaluronic acid; SCs satellite cells; ROM, range of movement.

as increased stiffness, reduced gliding, and altered sensory input, may reinforce pain persistence and motor dysfunction[18]. The causal direction in individual patients cannot be inferred from the current cross-sectional data; however, this framework may help explain why symptoms do not always match structural joint damage.

These findings represent a convergence of different types of evidence that are not yet part of a single established model to account for the cause and effect. It is possible that decreased physical activity (reduced loading) and associated connective tissue changes could lead to chronic pain and movement limitations. It is also likely that changes in the fascia (increased stiffness, loss of sliding ability, and altered sensation) could contribute to continued pain and limitations in motor function[18]. While we cannot establish causality using our present cross-sectional data regarding individual patient's patterns of behavior or their responses to OA, this conceptual framework may provide some insight into why patients with symptoms related to OA do not consistently show structural joint damage.

These clinical findings support the use of interventions targeting the fascia (myofascial release, instrument-assisted soft tissue mobilization, stretching) as part of a multimodal approach to treat knee osteoarthritis (OA). Systematic review articles on manual therapy for knee OA report some temporary improvements in both pain and function, but there is considerable variability based on methodological quality, and very little data exist on the potential long-term effects of manual therapy[85,86]. While this body of evidence does not currently provide enough support for making definitive claims regarding the effectiveness of a specific treatment, it also supports the need to consider all aspects of an individual's anatomy, including their fascial characteristics, when assessing how to address joint pathology, muscle dysfunction, abnormal movement patterns, and pain.

DISCUSSION

The mechanically responsive nature of the fascia allows it to exhibit viscoelastic behavior and adjust its mechanical characteristics according to different loading conditions[20]. These methods are used to alter the viscoelastic properties of the fascia and promote the health of the musculoskeletal system. These include active movement, passive mobilization, stretching, various types of manual myofascial treatments, and other interventions designed to target specific areas[13]. In contrast, there has been little investigation into the pathophysiological relationship between the mechanical characteristics of the fascia and osteoarthritis. While current studies suggest that the fascia may be involved in the production of symptoms or disruption of normal movements associated with osteoarthritis, this could provide a physiological basis for myofascial-based treatment approaches. This interpretation is consistent with the modern understanding of OA as a multi-articulation disorder affecting not only the cartilage and subchondral bone but also the periarticular soft tissues, along with the biomechanical and sensory interactions between these two groups[87,88].

In patients with OA, increased fascial stiffness has been hypothesized to contribute to a reduced range of motion (ROM), altered motor recruitment, and myofascial pain features[18,89]. In this context, myofascial stiffness may represent one of the factors associated with pain, reduced ROM, and muscle weakness in OA patients[18]. This hypothesis is biologically plausible in light of emerging evidence that ECM alterations in OA are not confined to cartilage but also affect non-cartilaginous soft tissues, where changes in composition and architecture may influence tissue mechanobiology and symptom persistence[90].

Several studies have found that movement-based interventions, either through active movement or manual myofascial mobilization, can increase mobility and range of motion (ROM) in individuals diagnosed with OA[91-93]. Furthermore, manual myofascial treatments have been identified as having an impact on reducing pain and improving function in patients with various types of musculoskeletal pain conditions. The strength of the body of evidence supporting this statement varies from low to moderate[92,93]. As such, existing research supports a potential role for myofascial interventions in a clinical setting but clearly identifies the need to be cautious when interpreting their effectiveness. This is especially important to do so because most high-quality clinical practice guidelines developed to identify best practices for managing the hip and knee report consistent recommendations for the use of education, exercise, and weight management as primary interventions. However, the same clinical practice guidelines vary significantly regarding the strength of the recommendations for adjunctive approaches[88,94]. Recent evidence also supports the relevance of fascia stretching and myofascial/manual approaches in related musculoskeletal conditions, including cervicothoracic fascia stretching in elderly women and manual or instrument-assisted treatment for myofascial pain[72,95]. In plantar fasciopathy, J-stroke myofascial release showed greater improvements than foam rolling across pain- and function-related outcomes[96].

Movement seems to be a key factor in maintaining the homeostasis of the fascia and reducing stiffness[20,97]. Continuous passive movement and static stretching at or below the individual's pain-free range appear to increase the elastic properties of tissues, diminish the inflammatory response, and inhibit profibrotic signal transduction, that is TGF-beta mediated myofibroblast activity[74,97]. This suggests that a gentle mechanical loading, which does not cause injury, could potentially influence fascial stiffness and inhibit fibrosis development, especially when there has been prolonged immobility. This is consistent with the study by Youssef et al. on cervicothoracic fascia stretching and thoracic mobility in elderly women[72].

Myofascial Release Techniques have been suggested to modify the mechanical properties of fascia through improved tissue mobility, reduced viscosity, reduced densification, and decreased stiffness[12,20]. The mechanisms for these effects may include the reversal of hyaluronan aggregation, possibly due to local changes in temperature[6,13], restoration of gliding between fascial layers; modification of interstitial fluid dynamics; realignment of collagen fibers[1,64], and modulation of activity of fibroblasts. Additional effects on sensory input and proprioceptive processing have also been hypothesized to occur[91].

The focus on this area is likely to be the most important when relating it to proprioception. Both Di Laura Frattura et al.[98] and Knoop et al.[99], have suggested that loss of proprioception could lead to or result from degeneration due to osteoarthritis in the knee. Loss of proprioception can potentially occur as a result of microdamage in intra- and extra-articular structures, which then causes problems for receptor integrity and afferent signaling pathways[99]. Additionally, Di Laura[98] found that patients who underwent arthroplasty continued to experience functional proprioceptive deficits. There are also examples of the importance of addressing proprioceptive function in treating low back pain through evidence-based musculoskeletal treatment practices[100,101].

Clinical trials have shown improvements in the range of motion and pain in patients with knee OA who have received manual myofascial release treatment[102]. Additionally, studies have demonstrated that combination exercise programs, including manual myofascial release, improve flexibility of soft tissues, patellar alignment, and decrease pain in individuals diagnosed with knee OA[103]. Recently, a randomized controlled trial was conducted to evaluate whether Iliotibial Band Manual Myofascial Release (ITB-MMFR) applied after valgus correction exercises improved outcomes better than manual myofascial release alone in patients diagnosed with grade II knee OA. The results showed statistically significant improvement in pain, rom, balance, and quality of life for those receiving both treatments compared to the group receiving only the manual myofascial release, suggesting that myofascial treatment is potentially most effective as part of a comprehensive exercise-based program of care for these patients[104].

Simultaneously, the interpretation of manual and myofascial therapies for OA requires caution. A recent systematic review found that clinical trials of manual therapy for knee OA were predominantly positioned toward the efficacy at the end of the efficacy-effectiveness spectrum, and only a small proportion of studies were judged to be at low risk of bias[105]. In parallel, a 2024 systematic review and meta-analysis concluded that manual therapy may reduce pain and appears safe in knee OA. However, the certainty of evidence remains constrained by methodological limitations and study heterogeneity[106]. In particular, the inherent difficulties in blinding manual treatments and the variable quality of sham or active comparators in available trials may contribute to placebo and expectation effects that are difficult to isolate from specific treatment mechanisms.

Limitations

The present review has several limitations. First, this narrative review was conducted according to the SANRA framework, reflecting the heterogeneous nature of the available literature on fascia and OA. Second, much of the cited evidence derives from studies on fascia in non-OA contexts, immobilization models, or chronic musculoskeletal pain other than OA, which limits the direct transferability of the conclusions. Third, imaging studies that specifically characterize fascial properties in OA populations are few, with small samples and variable methodologies. Finally, the available trials of manual myofascial interventions are heterogeneous in protocol, short-term in outcome assessment, and limited in blinding, which constrains the strength of any treatment recommendation.

Overall, the available literature supports the hypothesis that manual myofascial treatment, either alone or in combination with other interventions, may contribute to pain reduction, improved ROM, and better function in patients with OA[18]. However, the current evidence remains heterogeneous and does not justify strong therapeutic conclusions. In particular, differences in study design, treatment protocols, sample size, and follow-up duration limit the comparability of the available findings[105,106]. Accordingly, myofascial treatment should be considered a potentially useful adjunct within a multimodal rehabilitation strategy rather than a replacement for established first-line OA care[87,88,94]. Further high-quality studies with larger sample sizes, better-defined treatment protocols, and longer follow-ups are needed to clarify the short- and long-term efficacy of manual myofascial treatment in OA and to identify the patient subgroups that are most likely to benefit.

CONCLUSION

Fascia is becoming more widely acknowledged as a dynamic connective tissue that has biomechanical, inflammatory and sensory implications to the symptoms of OA. Alterations in the structural and functional characteristics of the fascia, particularly post-immobilization, may contribute to reduced range of motion, increased pain, and stiffness, thereby providing evidence to support a potential role for the fascia in the modulation of symptomology associated with OA. Understanding how the fascia interacts with muscles and articulating structures on a biological level will assist in linking tissue-specific mechanisms to the diverse clinical phenotypes of OA. Although there is currently some preliminary evidence supporting movement-based treatments and manual myofascial therapies as additional components to standard

physical therapy rehabilitation for patients suffering from OA, due to the heterogeneity and methodological limitations inherent to existing literature, future studies are warranted-namely, randomized trials of sufficient power employing standardized treatment protocols, image-based outcomes assessing specific fascial characteristics (i.e., thickness via ultrasound and/or shear wave elastography), and stratified by OA phenotype—to provide adequate evidence prior to recommending fascia-directed treatments as anything other than adjunctive therapy to multimodal OA management.

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