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REVIEW
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The Role of Fascia in Myofascial Pain Syndrome: A Look at Cinderella Tissue

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ABSTRACT

The word "myofascia" refers to the interwoven, indivisible nature of the web of connective tissue (fascia) that surrounds muscle tissue (myo-). The "myo" component of myofascial pain syndrome (MPS) has been covered very well, but the same cannot be said for the "fascial" component. In this article, fascia and its relationship with MPS are discussed.

Keywords: Chronic pain, fascia, myofascial pain, physical medicine and rehabilitation

Introduction

Physiatrists treat various musculoskeletal disorders, emphasizing the importance of understanding their pathophysiology. The fascia, a component of the connective tissues and musculoskeletal system in the human body, could be the key structure and concept needed to understand the processes of various dysfunctions.

Myofascial pain syndrome (MPS) was first described by Simons et al. (1). MPS is a very comprehensive and well-expressed definition. This expression is a term that includes both the muscles and fascia (2). There is no single branch of medicine that deals with muscles, and this has caused muscles to be ignored for years. This being the case, Travel referred to muscles as an orphan organ of medicine in one of his articles (3,4). Musculoskeletal problems and myofascial pain are common conditions that all physicians regularly observe in their daily practice. It is important to be able to detect this disease and be aware of the various treatment options available. The word "myofascia" refers to the interwoven, indivisible nature of the web of connective tissue (fascia) that surrounds muscle tissue (myo-). The "myo" component of MPS has been covered very well, but the same cannot be said for the "fascial" component. Understanding the relationship between deep fascia and epimysium has made fascia a treatment target in MPS treatment (5).

Fascia has been largely neglected in conventional medicine over the past several years, and its contribution to many areas of biomechanics and physiology has been overlooked (6). The first reason for this is the inadequacy of imaging methods that evaluate the fascia. X-rays have traditionally been used to objectively check bones, whereas electromyography is used to study muscles. However, accurately measuring changes in

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fascial tissues in living organisms is challenging. The second reason fascial tissue has been neglected for many years is the dissection method preferred by anatomists. Examining the tissues by dissecting them has made it difficult to evaluate the fascia as a whole. We can determine the number of bones and muscles in the human body, but this is not possible for the fascia. The fascial tissue is a complex structure composed of interconnected bags, string-like condensations, and pockets inside pockets, all linked by septa and layers of connective tissue. Digital modeling using 3D computer systems is necessary to uncover such a network structure. We shall gain further knowledge about fascia in the upcoming years (7). This review aims to provide an understanding of MPS from the perspective of fascia and the fascial system, the importance of which has begun to be understood in recent years.

Definition

The term fascia is frequently used in anatomical contexts, although its precise definition has proved challenging to comprehend. Many anatomical texts have been written about the facia anatomy. However, most anatomy professionals consider fascia only as connective tissue that fills empty spaces in the body (8). In 1983, the International Committee on Anatomical Nomenclature created a system of classification for all structures made of connective tissue. Different definitions have also been provided over the years by the Federative International Committee on Anatomical Terminology in 1998, the British edition of Gray's Anatomy in 2008, and the Fascia Research Congress in 2012. Various perspectives were presented during the 4th International Fascia Research Congress in Washington DC in 2015 (9). Well-known experts in fascial medicine and research presented and discussed the most recent findings in their fields. Finally, a consensus anatomic definition of the fascia was reached: *"…Fascia is a sheath, a sheet, or any other dissectible aggregations of connective tissue that forms beneath the skin to attach, enclose, and separate muscles and other internal organs."*

The functional definition of the fascial system is determined as follows. The fascial system is a three-dimensional network of soft, collagen-rich, loose, and dense fibrous connective tissues that spread throughout the body. The structure consists of multiple components including adipose tissue, adventitia, aponeuroses, deep and superficial fasciae, epineurium, joint capsules, ligaments, membranes, meninges, myofascial expansions, periosteum, retinacula, septa, tendons, visceral fasciae, and all intramuscular and intermuscular connective tissues, encompassing the endo-, peri-, and epimysium. The fascial system surrounds, interweaves, and penetrates all organs, muscles, bones, and nerve fibers, providing the body with a functional framework that enables the coordination of all body systems (9,10).

Architecture of the Fascia

It is crucial to comprehend the fascial system's composition in order to comprehend its architecture and function. It should be noted that fascia is a connective tissue. Fascia layers vary from one another significantly. Each layer is unique in both composition and orientation (11,12). For example, superficial fascia is loosely packed and irregular, whereas deep fascia consists of a well-organized fibrous layer. The classification of the human fascia is schematized in Figure 1.

Superficial Fascia

Superficial fascia is a layer of membranous connective tissue comprising loosely packed intertwined collagen fibers mixed with abundant elastic fibers. It is thicker on the trunk and gradually becomes thinner in the extremities. The retinaculum cutis superficialis, which has thick and vertical collagen septa, connects the superficial fascia to the skin. In addition, it is connected to the deep fascia through the retinaculum cutis profundus, which has loosely oblique and very elastic collagen septa. Deep fat tissue is the region between the superficial fascia and deep fascia, whereas superficial fat tissue is the area between the epidermis and superficial fascia, which contains the superficial retinacula cutis (12). It protects the body against heat loss.

Deep Fascia

Deep fascia is denser than superficial fascia. Collagen bundles are more compact and are regularly arranged. The orientation, composition, and architecture of the deep fascia allow classification as either aponeurotic or epimysial fascia. The deep fascia is more than a tough-barrier structure composed of collagen and elastin. It is a metabolically active

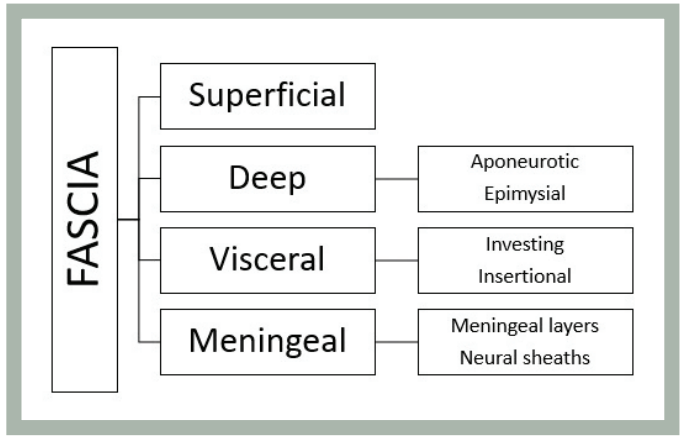

Figure 1. Classification of the human fascia

tissue layer that, in addition to contributing to gliding, also provides protective functions.

The fibrous sheaths that envelop and secure a muscle group or attach a large muscle are known as aponeurotic fascia. The aponeurotic fascia comprises two to three layers of parallel bundles of collagen fibers. Each layer is isolated from the others by a thin layer of loose connective tissue, allowing them to slide over each other independently. This independence gives each layer a distinct impact on the functionality of the tissue.

The epimysial fascia encompasses all thin collagen layers closely attached to the muscle. The epimysical fasciae envelop and stick to the entire muscle and can be a term used to encompass all the intramuscular connective tissue, such as the epimysium, perimysium, and endomysium. Tendons have a compact fibrous structure and can transfer forces between neighboring synergistic muscle fiber bundles, which may be part of the same motor unit. Because of its intimate association with muscle tissue, the epimysial fascia cannot be separated from the muscle. Both epimysial fascia and epimysium proper transmit the force of the muscle to the surrounding areas through myofascial expansions, but they have different thicknesses. The epimysial fascia is thicker (0.5-0.9 mm), whereas the epimysium is thinner (0.1 mm). Both aponeurotic and epimysial fascia transmit the forces of muscle contraction. The perimysium, which surrounds the muscle fiber bundles and continues into the endomysium, which encircles each muscle fiber, is closely related to the epimysium (12). A schematic representation of the fascia from the skin to the muscle is shown in Figure 2.

Connective Tissue

Connective tissue has three main basic components: cells, fibers, and a ground substance (13).

Cell

The metabolic characteristics of biological tissue are provided by the cells. Fibroblasts are the predominant cell type in fascial tissue; they play an important role in mechanotransduction and the secretion of extracellular matrix (ECM) precursors, which preserve the tissue's structural integrity and structure (14). Fibroblasts synthesize collagen fiber types I and III, whereas fasciocytes and hyaluronan (HA)-secreting cells create additional intracellular components, including glycosaminoglycans (GAG). Adipocytes are located in the connective tissue. Fat cells can be categorized as white and brown adipocytes. Adipocytes store energy and serve as crucial insulation, intermediate fillers, and facilitate smooth movement (15).

Fibers

Fibers contribute to the mechanical properties of connective tissue. Fibers can transmit force generated by muscle cells and appear to increase in strength and thickness when subjected to tensile stress. There are two types of fibers in connective tissue: collagen and elastic fibers (16). Collagen is the primary structural protein in connective tissue.

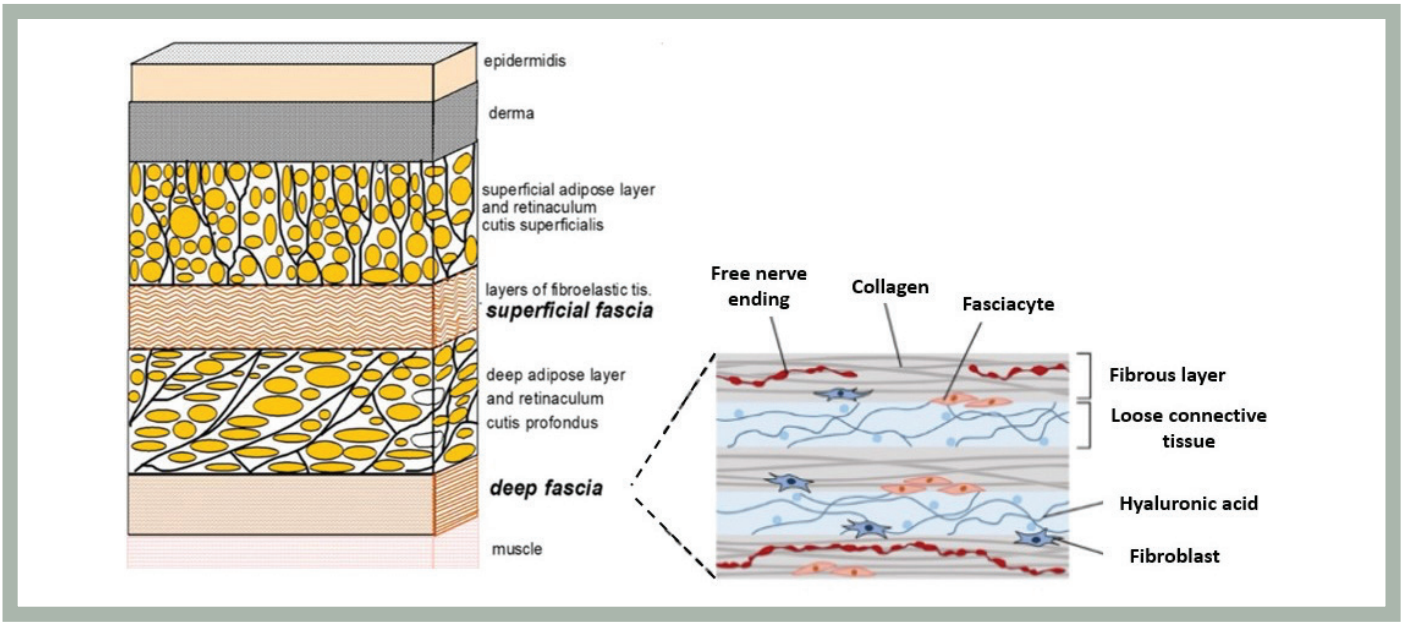

Figure 2. Schematic representation of the fascia from skin to muscle

There are many types of collagen, and almost 90% of the collagen in the muscles is located in the perimysium. Collagen fibers in the deep fascia are aligned parallel to each other, whereas other levels include collagen sequences with varying fiber orientations (17). Elastin fibers are thinner than collagen fibers and form a 3D network around the collagen fibers. Elastin is a protein that gives collagen the ability to stretch and to tolerate tension. Elastic and collagen fibers are not aligned in parallel. They lie on top of each other and/or rotate around each other, thus creating a three-dimensional interactive superstructure and imparting strength and flexibility to the entire tissue matrix (18).

Ground Substance

The ground substance is composed of water and GAGs, which contribute viscosity and plasticity to the tissues. The ground substance itself is a gel-like material including an extrafibrillar matrix, but no collagen or elastin fibers. Collagen and elastin fibers create a 3D network, while the basic substance surrounds and fills the spaces. GAGs are long-chain polysaccharides attached to the core protein of proteoglycans. Various GAG groups have been recognized. The most prevalent compounds are HA, chondroitin sulfate, dermatan sulfate, and heparan sulfate (19).

HA is the most common found GAG in loose connective tissue. HA provides moisture to the skin and facilitates the movement of muscles, tendons, and fascia against each other. HA acts primarily as a lubricant, maintaining normal tissue viscosity and allowing fascial layers to glide over each other (20). HA is widely distributed in the musculoskeletal system, particularly in the spaces between the layers of the aponeurotic fascia, muscles and deep fascia, loose connective tissue that envelops muscle bundles, and intramuscular fascial layers. Furthermore, the perivascular and perineural areas are important for HA. In particular, in the perivascular area around veins and the perineural area surrounding nerves, HA is required to provide appropriate gliding of these structures. Insufficient gliding carries the risk of nerve compression and vascular occlusion (20). Temperature, chemical elements, and pressure can modulate the chemical properties of HA.

Innervation

Proprioceptors, also referred to as mechanoreceptors, are the primary sensory receptors in the musculoskeletal system. Mechanoreceptors are integrated into the fascial system. Research has demonstrated the significance of mechanoreceptors in the layers of fascia, particularly in the highly innervated superficial layers of deep fascia. The facial layers contain free nerve endings and Ruffini and Pacinian corpuscles. The number of free nerve endings, which can also detect temperature, mechanical stimuli, and nociception, is considerably higher than that of other mechanoreceptors (21). The activation of nerve receptors within the fascia may be altered by the viscoelasticity of the tissue. These mechanoreceptors participate in the responses triggered by the viscoelasticity of the surrounding tissue. The dynamic response of mechanoreceptors is shaped by the viscoelasticity of the fascial tissue and HA. Because of the deterioration in the structure of HA and the increase in the densification viscosity, the normal gliding and lubricating effect decreases (21).

Imaging Technique

Another situation that makes understanding the fascial system difficult is the limitation of imaging methods. While bone tissue is evaluated by direct radiography, muscle tissue is evaluated by methods such as EMG. Until recently, there was no imaging method to evaluate the fascial system. Innovations in advanced evaluation technologies, such as tissue imaging, have made it possible to analyze variations in fascial behavior with greater clarity. The fascia can be visualized via computed tomography, magnetic resonance imaging, and ultrasound (US). US is also an advantageous method because it allows both static and dynamic evaluation of fascia (22). There are heterogeneities in fascial measurement protocols with US regarding the selected axis, probe position, and number of measurements taken. Additionally, patient body position also affected fascial thickness and stiffness, further limiting comparisons between studies. Nonetheless, limited studies suggest that US measurements of fascial thickness may have acceptable reliability (23). Ultrasonographic images of the superficial and deep fascia and their location within and under the skin are shown in Figure 3.

A relatively novel imaging method that can be used to assess fascia is elastography. Fascial elasticity was first qualitatively evaluated using axial strain elastography (ASE). Because ASE measurements are user-dependent, shear wave elastography has emerged as a viable objective addition to US and clinical evaluation in the assessment of fascial elasticity in the diagnosis of fascial pathologies (24). Figure 4 shows an example of elastography showing the fascia.

Myofascial Meridians

The effect of muscles is traditionally defined as the movement of a muscle on two bone structures, rather than carrying the load of the body. Nonetheless, some estimates

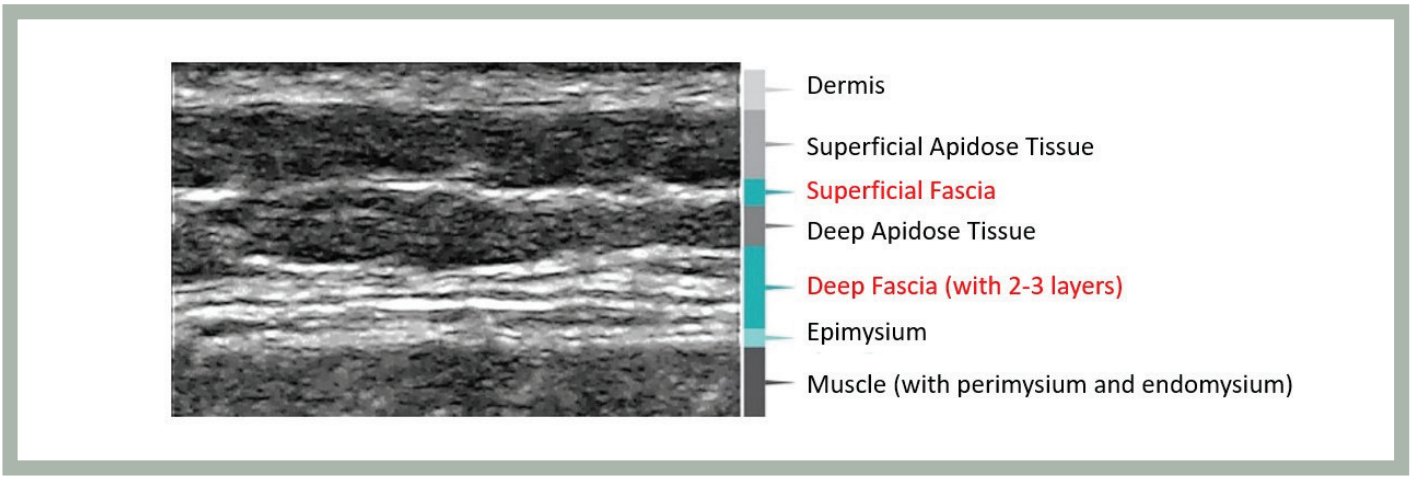

Figure 3. Understanding the fascial anatomy

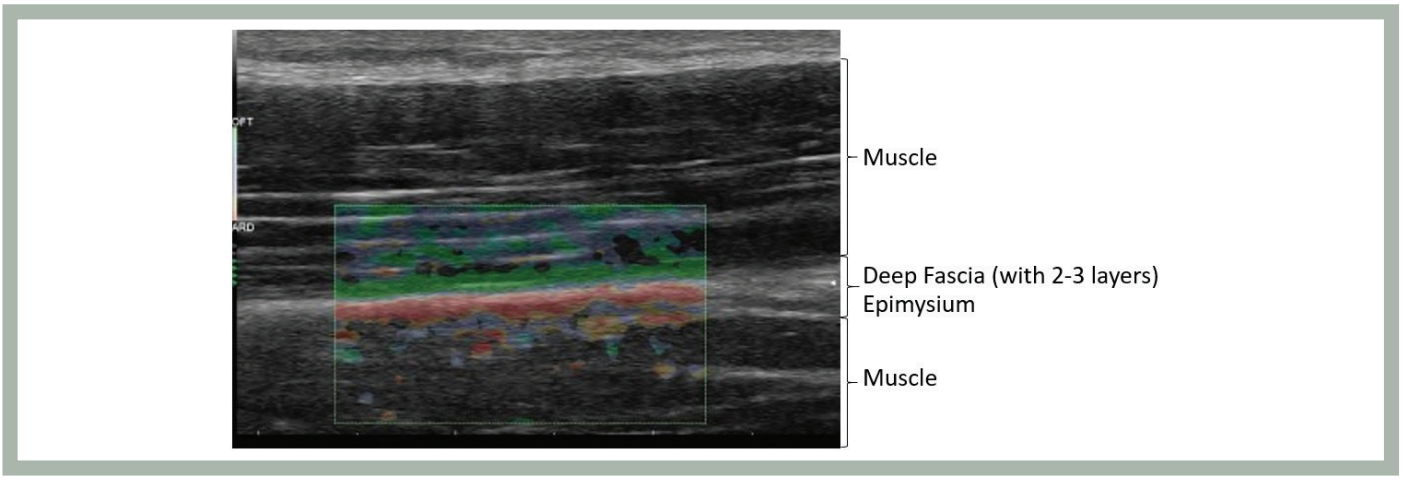

Figure 4. An example of elastography showing deep fascia

claim that 30% of the muscle contractile force is communicated to the perimuscular fascial elements and 70% is delivered to the bone (25).

While the term myofascia refers to the muscle fibers embedded in the fascia, the myofascial chain can be defined as a series of interconnected nerve and muscle pathways. According to this concept, fascia can be viewed as specific traction patterns throughout the body that distribute tension, facilitate movement, and provide stability throughout the body. This theory has helped them discover how two or more distant structures in the body affect each other. Myofascial meridians are anatomical identifiers that are usually defined as continuous bands of fascial tissue that run throughout the body. The term "meridian," in particular, is one of several terminologies used by leading fascia researchers today. However, there are also those who use different terminology. For example, Myers (26), a leading fascia researcher, used the term "trains" to classify these fascia vectors. Terms such as trains, meridians, lines, and chains can be used interchangeably and generally mean the same thing (26). Myers (26) defined 12 myofascial meridians that connect distant parts of the body through fascial tissues. Accordingly, the basic rule for selecting the components of a meridian is a direct linear connection between two muscles (5,26). Proximal and distal fascial connections among different muscles can affect their function. These linkages are known as myofascial chains, which may assist in clarifying referred pain and dysfunction in distant anatomical systems. The significance of myofascial chains was emphasized in a 2016 systematic review. Accordingly, it was concluded that "most skeletal muscles are directly attached to connective tissue" for the three myofascial chains (superficial posterior line, posterior functional line, anterior functional line) (26). The soft tissue components of the included myofascial chains are given in Table 1. Different theories on meridians have been developed by evaluating the cellular and global responses created on

Table 1. Soft tissue components of the included myofascial chains

Myofascial meridians	Soft tissue components
Superficial back line	Plantar fascia Achilles tendon/M. gastrocnemius Hamstrings Sacrotuberous ligament Lumbar fascia/erector spinae
Superficial front line	Toe extensors, M. tibialis anterior, anterior crural department Subpatellar tendon M. rectus femoris/quadriceps M. rectus abdominis M. sternalis/sternocondral fascia M. sternocleidomastoideus
Back functional line	M. vastus lateralis M. gluteus maximus Lumbar fascia M. latissimus dorsi
Front functional line	M. adductor longus M. rectus abdominis M. pectoralis major
Spiral line	Lumbar/erector spinae Sacrotuberous ligament M. biceps femoris M. peroneus longus M. tibialis anterior M. tensor fasciae latae, iliotibial tract M. obliquus abdominis internus/externus M. serratus anterior M. rhomboideus major/minor M. splenius capitis/cervicis
Lateral line	M. peroneus longus/brevis, lateral crural compartment Iliotibial tract M. tensor fasciae latae M. gluteus maximus M. obliquus abdominis internus/externus M. splenius capitis/M. sternocleidomastoideus

the fascia by mechanical stimuli during movement. Some of these theories include piezoelectric effect, viscoelasticity, and mechanoconduction.

Role of Fascia in Myofascial Pain Syndrome

MPS, a common regional pain syndrome, is a clinical disease with sensory-motor and autonomic components. MPS is a soft tissue and muscle-based condition that is often associated with the presence of myofascial trigger points (TP). The clinical symptoms of MPS can occur in acute and chronic forms. Conditions such as previous trauma, poor ergonomics during repetitive activity, psychological factors, structural changes in the spine, hypothyroidism, and vitamin deficiencies are among the important risk factors (27,28). MPS is a common disease and is usually diagnosed through history and physical examination (28,29).

MPS has historically been described as a muscle syndrome, and the contribution of the fascia to MPS has not been sufficiently emphasized. Research conducted recently has found that there are various pathologies in the deep fascia. The basis of fascial pathologies is based on changes in HA. The primary etiology of MPS is prolonged muscle contraction due to repetitive activity. Furthermore, MPS may result from a mismatch in the energy requirements and consumption of muscle tissue and neuromuscular dysfunction (30).

During normal muscle contraction, blood flow through the low-pressure capillary bed is temporarily blocked.

When the muscles relax, normal blood flow resumes. When muscles are constantly in a state of low contraction, intramuscular pressure impairs oxygen diffusion into the muscle and fascia and inhibits oxidative metabolism (31). Chronic hypoxia resulting from capillary occlusion causes lactic acid accumulation, reducing the local pH. Decreased pH leads to the association of HA chains and contributes to the "densification" of the fascia. Stecco et al. (32) suggested that overuse of muscle increases the polymerization of HA and therefore increases viscosity. This may alter local biomechanics by preventing the normal "gliding" of the muscle within the loose connective tissue (32). It has been shown that levels of bradykinin, substance P, serotonin, inflammatory cytokines, and calcitonin gene-related peptides, which contribute to nociception, increase in and around myofascial TPs. It is thought that the release of these mediators is associated with local tissue hypoxia and low pH (10).

Superficial and deep fascia, which are rich in free nerve terminals (Aδ and C), may play an important role in the development of MPS in addition to muscle-related fascial layers such as epimysium, perimysium, and endomysium. The deep fascia is located near the muscle surface and is divided by a transition zone of loose connective tissue. As mentioned before, deep fascia consists of multiple fibrous layers that can slide over each other along thin interfaces of loose connective tissue. The change in the HA chains that fill between the fibrous layers of the deep fascia causes the fascia to thicken and the interfascial slip to decrease (33). The rationale for treating myofascial pain should focus on reducing viscosity by disrupting HA chains.

Fascia-related Treatments

There are many effective treatment options that can be applied to treat MPS, but this article will briefly discuss treatments that target the fascia. With the understanding of the importance of deep fascia for referred pain mechanisms, fascial tissue has become a target in treatment. An important goal of fascia-related pain treatment is to reverse changes in HA. Increased temperature and local alkalization reverse the aggregation of HA fragments. The 3D structure of the HA chains, consisting of intermolecular and intramolecular water bridges, gradually deteriorates when the temperature is increased above 40 °C. Exactly at this temperature, there is a change in the viscosity of the HA solutions. This reduction in viscosity can restore normal gliding and normalize the activation of mechanoreceptors in that area. Manipulation, massage therapy, and osteopathic applications of muscles and their associated fascia increase the local temperature of the tissue (34).

In addition, local anesthetics, dextrose, saline, and dry needling are commonly used injection methods for treating myofascial TPs. These procedures can be performed blindly by manual palpation or with the use of US guidance (10,35). These injection applications are also used to treat deep fascia. When planning fascia injections, it is almost mandatory to use US guidance during administration. Hydrodissection is the process of injecting fluid to dissect the deep fascia under US guidance. Hydrodissection is also used to release nerve compression and treat tendinopathy. Unlike a classic TP injection, an interfascial injection, a larger volume of fluid is injected between the fascial layers. This procedure must be performed under US guidance (36). The mechanism of improvement for interfascial injections is still unknown; however, it is thought to cause changes in ECM viscosity or nociceptor stimulation within the fascia. Myofascial release techniques, manual therapy, extracorporeal shock wave therapy, superficial or deep heat, cannabidiol, and acupuncture applications are also used for treating fascial disorders (10,37).

Conclusion

Recent information has revealed that the fascia is involved in musculoskeletal function and myofascial pain. Understanding the physiology and pathophysiology of the fascial system; knowing myofascial chains and connections will be crucial for the development of appropriate techniques for fascial imaging and for further research targeting the fascial system in MPSs.

Ethics

Authorship Contributions

Concept: M.T.Y., B.T.D., Design: M.T.Y., B.T.D., Data Collection or Processing: M.T.Y., B.T.D., Analysis or Interpretation: M.T.Y., B.T.D., Literature Search: M.T.Y., B.T.D., Writing: M.T.Y., B.T.D.

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