

New Concepts in the Assessment and Treatment of Regional Musculoskeletal Pain and Sports Injury

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During the past decade there have been significant advances in understanding the basic science of musculoskeletal injury and healing. These new concepts alter the approach to injury management and rehabilitation for clinicians managing musculoskeletal conditions. This article examines the most recent advances in the treatment of regional musculoskeletal pain, and muscle and tendon sports injury. Specifically, developments in understanding the pathogenesis of muscle and tendon sports injuries, newer imaging modalities, and updated treatment paradigms and their rationale are reviewed. The purpose of this review is to provide the clinician with new approaches for treating nonsurgical muscle and tendon injuries.

INTRODUCTION

Increased participation in recreational sports has led to an increase in musculoskeletal injuries. In 2001, American Sports Data, Inc. [1] reported that almost 40 million Americans were involved in recreational sports; 7.2 million students participated in high school athletics during the 2005 to 2006 academic year [2]. Among adult Americans age 55 and older, there was a 266% increase in the number who held health club memberships during the years 1987 to 2001 [1].

Of the almost 40 million injury-related emergency department visits annually, approximately 10% are sports related [1]. According to the U.S. Consumer Products Safety Commission, there were approximately 1.4 million injuries among U.S. high school student athletes participating in practices or competitions during the 2005 to 2006 academic year [2,3] and a 54% increase in all sports injuries among people older than 65 years of age from 1990 to 1996 [1]. Furthermore, 80% of all sports injuries involve the musculoskeletal system [4]. These statistics underscore a need to understand soft tissue injuries associated with sports and to review new treatment concepts in regional musculoskeletal pain. As the baby boomers age, the challenge will be to understand age-related changes to the musculoskeletal system and to keep senior athletes active.

TENDINOPATHY

Tendon Structure and Function

Tendons function to store elastic energy and to transmit force between muscle and bone. Tendons have many functions, including the transmission of tensile load, stabilization of joints, absorbing large shocks, and protecting muscles from damage. The tendon midsubstance is a dense, fibrous connective tissue of fiber bundles mostly aligned along the long axis of the tendon. The tendon-bone insertion (enthesis) shows more rounded cells with a gradual transition from tendon to fibrocartilage, then to calcified fibrocartilage, and finally to mineralized bone [5]. Acute injuries occur when a tendon's function is disrupted by events such as sudden loading or excessive force. Chronic injury may be caused by repetitive minor trauma or use.

Acute Tendon Injury

An acute injury is typically caused by a traumatic event that may result in a partial tear or a complete rupture of a tendon. When there is an acute partial tear, an inflammatory reaction

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Table 1. Risk factors for tendinosis

Age	>35 years old
Frequency	>3x/week
Duration	>30 min/session
Intensity	Demanding activity
Gender	Female > Male

may follow. The entire healing sequence, which includes the inflammation, proliferation, and maturation phases, leads to a predictable healing and repair response [6].

Tendinosis

The term tendinosis usually refers to chronic conditions affecting tendons, often as a result of repetitive loading. Histologic examination of the tendon typically shows little or no sign of inflammation. The histopathology of tendinopathy is characterized by angiofibroblastic changes [7,8]. As Barr et al [7] describe, tendinosis reflects structural and/or radiological findings of tendon degeneration. Some authors [6,9,10] have theorized this type of tendon injury represents “failed” healing. Chronic tendon injuries do not heal with the same mechanism as acute injuries. In chronic injuries, the normally neatly arranged, relatively hypocellular extracellular matrix becomes disrupted by an increase in the number of cells. Unlike the acute healing mechanism in which type I collagen is produced, in chronic healing the extracellular matrix produces type III collagen, which is thinner and does not form bundles like type I. This altered structure disrupts the tendon and affects its ability to absorb forces [11,12]. The pain present with tendinopathy appears to be associated with neovascularization and the expression of metalloproteinases [13]. Studies of Achilles and patellar tendinopathies have demonstrated an increase in blood vessels and nerves in damaged tendons. These changes are associated with increased pain and poor function [14,15].

Contributing factors in the development of chronic tendinopathy include the age of the individual and the frequency, duration, and intensity of the action in which the individual participates (Table 1). As individuals age, their tendons lose strength, elasticity, and the ability to repair. In young athletes, there appears to have been an increase in the incidence of overuse injuries as training regimens have intensified and extended year round [16]; more aggressive training regimens may not provide sufficient time for microtrauma to repair itself [17].

Multiple factors may contribute to the development of tendinosis. Although overuse is a key factor [18-20], deficiencies in muscle strength, flexibility, or joint stability may also contribute [6]. Appropriate sports-specific conditioning, proper nutrition, rest, and appropriate rehabilitation may decrease the incidence of overuse injury [16]. Biomechanical and intrinsic factors also contribute to chronic tendon injuries. For example, a volleyball player who has decreased ankle dorsiflexion will experience greater ground forces when landing after jumping because of the decreased ability

to absorb the transmitted force [20]. Table 2 lists different etiologies of tendinopathy.

The use of imaging modalities, such as magnetic resonance imaging (MRI) and ultrasound (US), to diagnose tendinosis can expedite treatment of the condition and possibly allow the patient to return to normal activity more quickly. In addition, understanding the staging systems and pain phases in tendinosis (Table 3) can assist physicians in diagnosis and treatment [21].

Enthesopathy

Entheses, which are commonly known as insertion sites—osteotendinous or osteoligamentous junctions—are prone to overuse injuries. The entire concept of an enthesis organ is relatively new in musculoskeletal research. Benjamin et al [22] have spent more than 20 years researching and developing the concept of the enthesis organ. The enthesis organ is a collection of related tissues at or near the enthesis. It is a metabolically active and richly innervated collection of structures.

Fifty percent of athletic injuries involve tendinous insertions [23]. Alterations in mechanical factors can cause abnormal amounts of stress across the muscle, bone, and the ligament/tendon unit. Injuries can result if a muscle becomes fatigued after exercise, resulting in enthesopathy [22]. One example of the role of biomechanical factors contributing to enthesopathy is the patellar tendon mechanism. Andriacchi and Birac [24] report that jogging results in greater stress on the anterior muscles (quadriceps femoris) than on the posterior muscles (hamstring muscle complex, gastrocnemius, and soleus) of the leg. The resulting imbalance can contribute to developing patellar enthesopathy.

MUSCLE INJURY AND PAIN

Acute Muscle Strain

Acute muscle strains typically present as sudden onset of localized pain during a physically demanding activity. Injury can occur because of a sudden overload or muscle incoordination. For example, pain may occur during the transition from an eccentric contraction (eg, the downward movement of a dumbbell in a biceps curl) to a concentric contraction (eg, the upward movement of a dumbbell in a biceps curl).

Table 2. Etiology of tendinopathy

Types	Examples
Overuse	Running Jumping
Intrinsic factors	Genetics, eg, tenascin-C gene (Mokone) Estrogen Type V collagen (Mokone)
Extrinsic factors	Biomechanical Factors Alteration of muscle-tendon unit

Table 3. Staging systems and pain phases of tendinosis (21)

Pathologic Stages	Phases of Pain
I Temporary irritation	I Mild pain after exercise (<24 hours)
II Permanent tendinosis	II Pain after exercise (>48 hours), resolves with warm-up
III Permanent tendinosis, >50% tendon cross section	III Pain with exercise, does not alter activity
IV Partial or total rupture of tendon	IV Pain with exercise, alters activity
	V Pain with heavy ADL
	VI Intermittent rest pain does not disturb sleep. Pain with light ADL
	VII Constant rest pain and pain that disturbs sleep

ADL = activities of daily living.

Chronic Muscle Strain

Chronic muscle overuse injuries are common. According to DiFiori [25], between 30% and 50% of all sports-related injuries in adolescents are attributable to overuse. Risk factors for recurrent or chronic muscle strains are listed in Table 4 [26].

The pathogenesis of chronic muscle pain is an area of active research [7]. Chronic regional muscle pain or myofascial pain syndrome is attributed to myofascial trigger points (MTrPs) in skeletal muscle alone or in combination with other pain generators [27,28]. A MTrP is a localized area of tenderness and hyperirritability in the muscle, tendons, and ligaments, and is associated with a characteristic referral pattern [29]. According to Shah et al [30], the pain associated with MTrPs is a common cause of nonarticular musculoskeletal pain. Simons et al [31] theorize that pain associated with MTrPs comes from a hypersensitive nodule in a taut band of skeletal muscle, which may have previously sustained injury.

In important new research [31-33], some authors describe a method to measure the local biochemical milieu of the trigger point. With their method, they found the region around MTrPs is associated with an abnormal local biochemical milieu. Specifically, bradykinin, 5-hydroxytryptamine (serotonin), hydrogen ions, cytokines, catecholamines, neuropeptides, and prostaglandins are released from damaged muscle tissue and bind to pain receptors (nociceptors), which become sensitized and lead to localized pain and tenderness. When nerves in muscle tissue are continuously activated, central sensitization of dorsal horn neurons occurs [32,33]. The longer these molecules are present, the more likely the pain and tenderness will continue [34].

MTrPs may become activated (acutely or in a sustained fashion) from muscle overload. When muscle is in a shortened position, a latent MTrP can convert to an active MTrP. An active MTrP in one area can induce an MTrP in a distant site. From a histological perspective, this phenomenon is the result of muscle fibers having a number of contractions forming "knots." Forces between fibers then potentially cause stress on adjacent muscle fibers, leading to multiple MTrPs. MTrPs are commonly found in the postural muscles of the neck, shoulder, and pelvic girdles. Specific muscles include the upper trapezius, scalene, sternocleidomastoid, levator scapulae, and quadratus lumborum [34].

Shah's explanation of biochemical changes further elucidates the reasons for referred pain and local tenderness from

MTrPs. The works of Shah et al [30], Curatolo et al [34] and Simons [35] works provide the most up-to-date information in regard to the pathogenesis of MTrPs. This research provides the clinicians with the background for etiology of MTrPs, which enables clinicians to better diagnose and treat chronic and overuse muscular injuries. Specifically, in chronic muscle pain and sports injury, the clinician should consider treatment of the local injury as well as pharmacologic treatment of the sensitized central nervous system.

NEWER TECHNIQUES FOR MUSCULOSKELETAL IMAGING

One of the most exciting areas of change and progress in the diagnosis and treatment of sports injuries includes the expanding use of imaging with MRI and musculoskeletal US, particularly for soft tissue injuries.

MRI

MRI has been described as the "most versatile and robust of all radiographic methods for examining injured athletes" [36]. Micheo et al [37] highlighted that this technology allows for direct visualization of bone and soft tissue structures. The different sequences permit the evaluation of multiple tissues such as bone, bone marrow, hyaline cartilage, menisci, ligaments, and tendons [38].

MRI is also very helpful in diagnosing the severity of bony stress injuries. For example, the MRI grading system for tibial stress injuries is divided into 4 categories. Grade 1 is considered mild-to-moderate periosteal edema on short tau inversion recovery imaging without marrow changes. Grade 2 is moderate-to-severe periosteal edema with marrow changes on T2-weighted images. Grade 3 includes 2 or more marrow changes on T1-weighted imaging. Grade 4 reveals a visible fracture line visible [39,40]. Additionally, MRIs are useful in grading the severity of ligament and tendon injuries.

Table 4. Muscle strain recurrence factors

Fatigue
Insufficient warm-up
History of previous injury
Muscle tightness
Decreased agonist/antagonist strength ratio

Magnetic Resonance Elastography (MRE)

MRE is a noninvasive technique used to measure the stiffness of biological tissues. The technique uses standard MRI equipment with a gradient-coupled vibration that causes shear waves. Because stiffer tissue has longer wavelengths, shear waves are used to calculate the stiffness of the tissue. Chen et al [41] reported the use of MRE in successfully identifying and quantifying myofascial taut bands. Although MRE is currently a research tool, it may have future application as a diagnostic tool that objectively measures the presence or absence of MTrPs.

Positional MRI (pMRI)

It has been suggested that pMRI is more sensitive and specific than traditional MRI for viewing disorders such as spondylolysis, spondylolisthesis, or disk herniation [42]. Because the signs and symptoms of low back pain may be postural-related and because anatomical structures change in position, it may be useful to obtain MRIs in the flexed and extended position [42,43]. In a comparison of weight-bearing or upright positioning for pMRI to supine positioning, 52% of patients demonstrate abnormalities on pMRI not seen on supine MRI [44]. Another study by Kuwazawa et al [45] measured the cross-sectional area of the cervical spinal cord at each disc level in supine and erect pMRI and found posture-dependent differences of the cross-sectional area [45]. This finding may allow earlier diagnosis of the cause of the structural changes associated with cervical myelopathy. In addition, the authors of a Swiss study [46] concluded that pMRI more frequently demonstrates minor neural compromise in the lumbar spine than conventional MR imaging.

Traditional MRI is quite sensitive but not very specific for back pain, ie, many patients with abnormal MRIs have no symptoms [47]. Increasing the sensitivity of MRI through the use of pMRI may cause a further loss in specificity. Therefore, further study to determine the role of pMRI in the clinical setting is required.

Magnetic Resonance Arthrography (MRA)

MRA is a highly sensitive and specific method of imaging intraarticular anatomy and pathology, especially at the shoulder, hip, and elbow [48-50]. MRA evaluates capsuloligamentous structures, small chondral defects, and loose bodies. Most commonly, it is performed in the shoulder and hip because it may more accurately identify labral tears [49]. In the ankle, MRA improves the sensitivity for detection of ligament tears [51]. A study in 2004 [50] evaluated the diagnostic accuracy of MRA compared with traditional MRI for hip intraarticular pathology and found MRA was more sensitive than MRI. However, there were also more false-positive results.

Musculoskeletal Ultrasound (US)

Musculoskeletal US is a newer diagnostic tool that is changing the approach to diagnosis and treatment. A recent review

on musculoskeletal US by Smith and Finoff [52] describes the ability of US to diagnose an array of pathology, including tendinosis, tendon tears, nerve entrapments, muscle strains, ligament sprains, and joint effusions. In 2008 Park et al [53] evaluated the diagnostic value of US for medial epicondyle pain. Clinical diagnosis was compared with US findings. The results revealed that the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of US for clinical medial epicondyle pain was greater than 91% in all categories. Therefore, US should be considered as an initial imaging method for evaluating medial epicondyle pain when imaging is needed [53].

Musculoskeletal US has also been used to detect acute changes immediately after a competition. Detection of the earliest signs of inflammation after an event might be useful as a strategy for preventing more serious or chronic injuries. The authors of a 2007 study [54] investigated the acute changes in the biceps tendon of patients after high-intensity wheelchair activity. The subjects who had more playing time showed a larger increase in tendon diameter, or a greater amount of edema. Thus, the authors concluded that this could be the first sign of overuse injury. With the increased use of US in the United States, this trend may expand.

Doppler US uses reflected sound waves to evaluate flow in blood vessels. In 2006 a study [55] was conducted to determine the degree of Achilles tendinopathy in badminton players that experienced Achilles pain requiring medication. Thirty-four Achilles tendons in 26 players, 18 on the dominant side and 16 on the nondominant side, were analyzed. Before a badminton match, color Doppler flow was not present in 16% of players in either tendon. After the match, all players had some color Doppler flow in one or both tendons. In another study [56], authors examined the Doppler US neovascularization score before and after treatment. Although the authors [56] concluded that there was no significant correlation between neovascularization score and clinical severity at baseline, there were various graded levels of neovascularization present in symptomatic tendons. These 2 studies could lead one to theorize that repeated stress upon the Achilles tendon creates neovascularization.

There is a growing list of conditions for which US examination is becoming a preferred imaging technique. In Europe, for example, US is preferred for imaging tendinopathies involving the hamstring, groin, ankle, patella, Achilles, rotator cuff, elbow, and wrist [57]. Table 5 outlines the benefits of musculoskeletal US based on the tissue type [57]. Additionally, musculoskeletal US can be used for diagnosing dynamic conditions (such as tendon subluxations or shoulder impingement) because structures can be visualized during provocative dynamic maneuvers.

In addition to diagnostic use, US can be used to guide injections for treatment. Smith and Hurdle [58] concluded that US guidance in the physiatric office can be timely, effective, and safe for performing hip intraarticular injections. Additionally, injection via US has been studied in intraarticular trapeziometacarpal injections in frozen cadaveric hand specimens [59], in the piriformis for buttock pain [60,61], and knee and hip joints for osteoarthritis pain [62].

Table 5. US in soft tissue injuries

Location	Benefit
Muscle	Loss of the normal muscle fibers can be visualized after the first 24 hours.
Muscle-tendon junction	Using dynamic stress at the junction, the operator can visualize partial tears.
Tendon	Can analyze the amount of fluid in tendon sheath, which is increased in tendinopathy. Can detect earlier changes than via MRI. Color Doppler U/S allows for diagnosis of neovascularization and visualization of blood vessels. Direct visualization of split tendons and/or partial tears.
Enthesis	Can evaluate cortical irregularities. Displays increased vascularity.
Ligament	Partial ruptures and neovascularization via repetitive injury can be detected

PHARMACOLOGICAL TREATMENT OF REGIONAL MUSCLE PAIN AND SPORTS INJURY

Nonsteroidal Antiinflammatory Drugs (NSAIDs)

NSAIDs have been a mainstay of treatment of athletic injuries for many years, especially in the acute setting. The benefits of NSAIDs are antiinflammatory, antipyretic, and analgesic properties. Despite these properties, new research has shown that NSAIDs are only mildly effective in relieving the symptoms of most muscle, ligament, and tendon injuries and are potentially deleterious to tissue healing [63]. The use of NSAIDs to treat ligament sprains, deep muscle contusions, and acute tenosynovitis injuries is beneficial, but the recommended use of NSAIDs is for only 5 to 7 days. According to Mehallo et al [63], NSAIDs may be effective in decreasing pain, improving early muscle recovery, and allowing faster return to sport after muscle strain and eccentric muscle injury. However, the potential adverse effects of NSAIDs, which include hypertension, altered renal function, peptic ulceration, and increased rates of myocardial infarction with certain NSAIDs should be considered when one prescribes this type of medication.

Topical Preparations

Topical agents are useful in soft tissue injuries because they are delivered noninvasively in a localized area rather than administered systemically or via injection. Some topical agents, such as capsaicin, lidocaine patches, and salicylates, have been available for some time. One study found a topical NSAID, diclofenac, to be as effective as an oral analgesic in the treatment of lateral epicondylitis and shoulder periarthritides [64].

Although not presently available in the United States, topically applied glyceryl trinitrate (GTN) may be effective in treating chronic tendinopathies [65-67]. The inhibition of nitric oxide leads to decreased collagen content and collagen synthesis via fibroblasts. However, by eliminating this inhibition (ie, stimulating nitric oxide) through the use of GTN, nitric oxide may fuel collagen synthesis [68]. It is hypothesized that reduction in pain is a result of collagen synthesis enhancement [65-67]. Topical GTN therapy (1.25 mg per 24 hours) decreases pain, increases tendon force, improves

functional measures, and improves symptom resolution in Achilles tendinopathy, lateral epicondylitis, and supraspinatus tendinopathy [65-67,69]. Finally, topical GTN has been shown to be effective in decreasing pain in the early stages of rehabilitation for chronic extensor tendinosis at the elbow. A recent study [70] showed topical GTN treatment is not as effective as corticosteroid injections. Further study found that topical GTN did not provide any additional benefit over physical therapy for Achilles tendinopathy [71].

The side effects of GTN include rash and headache, which resolve on discontinuation of treatment. It should not be used concomitantly in patients taking phosphodiesterase inhibitors such as sildenafil because of the risk of causing hypotension. Although studies have provided conflicting results, continued research on the efficacy of this topical agent appears warranted.

Botulinum Toxin Type A (Botox)

Botulinum toxin type A (btxA), or Botox, is a neurotoxin that inhibits the release of the neurotransmitter acetylcholine at the neuromuscular junction and inhibits skeletal muscle contraction. Therapeutic uses of botulinum toxin include a reduction in muscular spasticity, increased function in chronic whiplash-associated disorder, and decreased myofascial pain [72]. Side effects of btxA injections include allergic reactions and permanent muscle and tendon injury. Although current evidence does not support the use of botulinum toxin injections for tendon injuries, studies have shown that intramuscular injection of btxA can provide short-term reduction of local muscle overactivity [73-76]. In one multicenter study [77], 130 subjects with epicondylitis were treated with btxA injections. Repeated follow-up examinations at 2, 6, 12, and 18 weeks revealed increased grip strength and decreased pain in the btxA group [77]. Botulinum toxin type B (Myobloc) is also available in the United States; however, it has not been as widely studied for the treatment of musculoskeletal disorders.

Antidepressants

Antidepressants are used to control neuropathic and regional musculoskeletal pain because they modulate serotonin and norepinephrine. Neurochemical abnormalities that contrib-

ute to pain in patients with these symptoms can be positively altered as the result of the effects of antidepressant medications on the cholinergic, histaminergic, and adrenergic pathways [78]. Tricyclic antidepressants such as amitriptyline, nortriptyline, and desipramine are effective for tension-type headaches, fibromyalgia, and pain associated with muscle spasms. Selective serotonin reuptake inhibitors, specifically fluoxetine, have been proven effective in the treatment of fibromyalgia [28,79]. In addition, recent studies on the use of balanced dual-reuptake inhibitors (serotonin and norepinephrine), such as venlafaxine, milnacipran, and duloxetine, for the treatment of fibromyalgia demonstrate improvements in pain and may have applications in chronic regional muscle pain [76,80-83].

Anticonvulsants

Anticonvulsants such as zonisamide, carbamazepine, lamotrigine, and gabapentin (neuropathic pain antagonists) are used for neuropathic pain control. However, these medications have not been approved for these uses by the Food and Drug Administration, and their use for pain is considered off-label use. A related medication, pregabalin, has recently been approved for the treatment of fibromyalgia. One might extrapolate that pregabalin would modulate pain in chronic regional muscle pain; however, this application has not been studied directly.

Tramadol

Tramadol, a central analgesic, is used for pain control and provides a weak opioid mu-receptor agonist and a reuptake inhibitor of norepinephrine and serotonin. Tramadol is the only analgesic that has evidence to support its use in fibromyalgia [84]. Tramadol's multimodal effect has demonstrated efficacy in nociceptive and neuropathic pain.

NONPHARMACOLOGICAL TREATMENT

Extracorporeal Shock Wave Therapy (ESWT)

ESWT is a newer, nonpharmacological treatment for tendinopathies. ESWT involves generating shock waves external to the body and focusing them on a specific internal area or structure. This type of treatment has been used for disrupting kidney stones (lithotripsy) for more than 20 years. In treating tendonopathies, the microtrauma of the repeated shock wave creates neovascularization to the affected area which, in turn, promotes tissue healing. In the United States, ESWT is the only modality approved by the Food and Drug Administration for treatment of plantar fasciitis with associated calcaneal osteophytes, and lateral epicondylitis. Recent studies show that ESWT has been effective in treating chronic insertional Achilles tendinopathy [85] and chronic patellar tendinopa-

thy [86]. In 2005, a study [87] analyzing the effects of ESWT on rotator cuff calcific tendonitis showed significant improvement based on visual analog scores and significant reduction in calcification.

Eccentric Exercise

The goal of any rehabilitation program is to restore function in the shortest amount of time. For soft tissue injuries, especially chronic tendinopathies, eccentric (lengthening) exercise has been used for a number of years [8,88,89]. Progression is based on the absence of pain at each exercise intensity level.

In a long-term study in Scandinavia, researchers analyzed the effects of eccentric exercises compared with stretching exercises in patients with achillodynia, which is defined as pain caused by inflammation of the Achilles tendon [93]. Patients were randomly assigned to one of these daily exercise regimens for a 3-month period. Symptoms were evaluated by the degree of tendon tenderness when palpated, US, a pain questionnaire based on a modified version of the knee injury and osteoarthritis outcome score on knee injuries, and a global assessment of improvement. Follow-up was performed at 3, 6, 9, and 12 weeks and one year. Patients in both groups reported significant improvement after 3 weeks. Symptoms gradually improved during subsequent follow-up visits. The authors concluded that although there were improvements in symptoms in both groups at one year, it was unclear whether improvements were spontaneous or to the result of the prescribed exercise regimens. However, patients who experienced a greater degree of achillodynia in the first 3 months had slightly greater improvements with eccentric exercising [90]. Additional studies [91,92] reveal patients had decreased pain after participating in eccentric exercise programs. For example, patients with patellar tendinopathy had decreased pain after performing eccentric exercises using a decline board.

Another study [90], has shown that an eccentric exercise rehabilitative program is most effective in "overuse" injuries, eg, in treating Achilles tendinosis in runners. There are typically 5 steps in an eccentric exercise program for chronic tendinopathies: warm-up, stretching, eccentric exercise, repeat stretching, and icing. According to Curwin and Stanish [89], patients using this type of exercise program will experience relief of pain and/or regain function within 6 to 14 weeks. More research is needed to understand the clinical effectiveness of prescribing eccentric exercise over other treatments in the management of tendinopathies.

Injections

Platelet-Rich Plasma (PRP) Therapy. A newly developed therapy for treating soft-tissue injuries is PRP therapy. PRP is obtained by special centrifugation of the patient's own blood. The centrifugation process is used to separate platelets from the rest of the patient's blood, thus creating a concentrated platelet-rich medium 4 to 8 times the normal platelet

concentrations. This medium can then be injected into the symptomatic area. Growth factors mediate the biological processes necessary for soft-tissue repair in muscles, tendons, and ligaments after acute, traumatic, or overuse injury. Presumably, PRP may be an effective method for tissue repair because platelets contain growth factors (including insulin-like growth factor-1, basic fibroblast growth factor, platelet-derived growth factor, epidermal growth factor, vascular endothelial growth factor, transforming growth factor- α -1) that are released upon injection at the injury site.

Preliminary results are promising in terms of earlier return to competition after muscle and particularly tendon injury. Mishra and Pavelko [93] published a study on PRP and lateral epicondylitis. A total of 140 patients with chronic elbow tendinosis that were considering surgery were enrolled in the study. Those patients in whom conservative therapy failed were split into 2 groups. One group was to receive injections of PRP, whereas the other group was to receive injections of bupivacaine. Results were very promising; there was a 60% improvement in the PRP group compared with only a 16% improvement in the bupivacaine group. Additionally, at 6 months the PRP group reported an 81% improvement [93,94].

In addition, a study from the surgical field [95] involving athletes evaluated the effectiveness of using PRP after surgical repair of the Achilles tendon. The study revealed that injured athletes who were given the PRP returned to running more quickly and had increased cross-sectional areas of their repaired tendons than those who were not given the therapy. Finally, an animal study found that mechanical loading had a synergistic effect with PRP injection in rats in Achilles tendon repair [96]. Although PRP injections appear to be useful, they should be combined with an appropriate rehabilitation program to provide controlled loading of the musculotendinous unit.

Prolotherapy. Prolotherapy is an injection therapy used to treat chronic ligament, joint capsule, fascial, and tendinous injuries. Prolotherapy involves injecting a proliferative agent (such as hypertonic dextrose, phenol, or sodium morrhuate) at painful entheses to strengthen them via induction of fibroblast proliferation and collagen synthesis, resulting in hypertrophy of the ligament [97]. Some authors [98] have referred to this technique as regenerative injection therapy because growth factor modulation is involved at the cellular level.

Studies have examined the frequency, concentration of solution, and the type of solution to be used as a proliferative agent. Reeves and Hassanein [99] found that 10% dextrose solution injected every 2 months during a 6-month period was very effective in reducing pain and improving range of motion in patients with osteoarthritis of the fingers. Similar benefits were seen with this solution for treatment of knee osteoarthritis and anterior cruciate ligament laxity, with reduced pain and swelling and improved knee flexion [100]. Evidence of radiographic improvement was seen at 1 year [97,100]. In a study by Topol [101], 12.5% dextrose solution

with 0.5% lidocaine solution was injected every 4 weeks in rugby and soccer players with groin pain until resolution of pain, with favorable results.

Studies of the efficacy of prolotherapy for treatment of low back pain show mixed and inconclusive results. Some of the earlier studies, including Ongley et al [102], in which 12.5% dextrose/12.5% glycerin/1.25% phenol in 0.25% lidocaine were injected, and Schwartz [103], in which 5% sodium morrhuate and 1% lidocaine were injected, found that these combinations improved pain and reduced disability ratings. However, more recent studies have failed to replicate these results. At this point, the evidence for the use of prolotherapy in low back pain is insufficient to recommend this as a stand-alone treatment. Evidence supports the use of prolotherapy in combination with spinal manipulation [104].

Prolotherapy for lateral epicondylitis, was studied in 24 subjects with refractory lateral elbow pain [105]. The patients were randomly assigned to receive prolotherapy with a mixture of dextrose and sodium morrhuate versus a placebo injection of normal saline. The prolotherapy group improved in extension strength, grip strength, and pain scores, whereas the control group improved in grip strength only when compared with baseline. The clinical improvement in the prolotherapy group was maintained at 52 weeks of follow-up [106]. Prolotherapy may have value in the treatment of chronic enthesopathies, tendinopathies, and osteoarthritis. Continued research into prolotherapy is required to determine what specific agents and protocols are needed to successfully treat patients with this modality.

Steroids. Corticosteroid injections have long been used to treat musculoskeletal disorders [107,108]. Their ability to prevent lysosomal enzyme release and to inhibit the accumulation of neutrophils and the synthesis of inflammatory mediators make them effective antiinflammatory medications. Although steroid injections have been shown to be effective in decreasing inflammation and pain, the extensive review in 2005 by Nichols [109] describe the potential complications of long-term and short-term use of corticosteroids for athletic injuries including an increased risk of tendon ruptures, avascular necrosis, osteonecrosis of femur and hips, and articular cartilage degeneration.

A single corticosteroid injection typically provides mild-to-moderate reduction of pain for up to 6 to 8 weeks. For example, corticosteroid injections are useful in treating the pain associated with tenosynovitis or "trigger finger" [69]. As the result of concerns regarding tendon weakening and rupture, intratendinous corticosteroid injections should be avoided, with injection in the peritendinous area preferred. Similarly, repeated injections should be avoided for the reasons enumerated previously.

An Australian study [110] investigated the efficacy of physiotherapy compared with a "wait-and-see" approach or corticosteroid injections during the course of one year in patients with lateral epicondylitis. The authors concluded that although corticosteroid injections provided superior short-term relief, this type of treatment over time was inferior

to “wait-and-see” strategies or physical therapy. The authors advised most patients with lateral epicondylitis, when given ergonomic advice, that their symptoms will improve over time. In addition, physical therapy is associated with better results than a “wait-and-see” strategy in the short-term and is superior to corticosteroid injections in the long term.

Prolotherapy Versus Corticosteroid Therapy. There are few studies comparing prolotherapy to corticosteroid injection. In principle, these 2 approaches have almost opposite goals and effects. Prolotherapy aims to stimulate cellular proliferation and create temporary inflammation, whereas steroids are intended to reduce inflammation and cellular proliferation. Despite this, both treatments may be advocated for treatment of the same condition, such as lateral epicondylitis. The authors of a small study [111] examined this issue for patients with chronic lateral epicondylitis using a double-blinded methodology. Eighteen subjects were randomized to receive either prolotherapy with dextrose and sodium morrhuate, or injection of 40 mg of depomedrol plus procaine. Primary outcome measurements included visual analog pain scores and disabilities of the arm, shoulder, and hand (ie, DASH) scores. Results favored prolotherapy by a small margin, but larger studies are needed to confirm these findings.

CONCLUSIONS AND AREAS OF FUTURE RESEARCH

Soft-tissue musculoskeletal disorders are common and increasing in frequency as the population of athletically active people ages and younger athletes train year-round in a single sport. Chronic regional muscle pain has recently been found to be associated with biochemical changes in the peripheral nervous system at the area of the trigger point, as well as central nervous system pain transmission and processing. There has been a paradigm shift in the understanding of the pathophysiology of chronic tendinopathy. It is now increasingly clear that inflammation plays less of a role and degeneration a larger one. This finding has led to concern that the commonly used injection of steroids may be of little value in addressing the underlying problem. New musculoskeletal imaging techniques such as musculoskeletal US and MRE may provide the clinician an opportunity to more directly observe the effects of treatments on abnormal musculoskeletal tissue. Finally, the identification of growth factors and creation of therapies based on these factors will likely enhance the ability to facilitate tissue regeneration and healing, ultimately resulting in improved performance.

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