Pathophysiology of Acute Exercise-Induced Muscular Injury: Clinical Implications

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Abstract: *Acute muscular injury is the most common injury affecting athletes and those participating in exercise. Nearly everyone has experienced soreness after unaccustomed or intense exercise. Clinically, acute strains and delayed-onset muscle soreness are very similar. The purpose of this paper is to review the predisposing factors, mechanisms of injury, structural changes, and biochemical changes associated with these injuries. Laboratory and clinical findings are discussed to help athletic trainers differentiate between the two conditions and to provide a background knowledge for evaluation, prevention, and treatment of exercise-induced muscular injury.*

The musculotendinous unit is the force-generating component of functional movement. However, it is one of the least understood links in human movement and one of the most frequently injured tissues during exercise. Athletic trainers evaluate and treat musculoskeletal injuries daily. This paper provides a review of contemporary literature on the pathophysiology of acute strains and delayed-onset muscle soreness. Predisposing factors and mechanisms of injury are presented to aid the reader in the prevention of muscular injury, while structural and biochemical changes are reviewed for the purpose of evaluation and treatment. By understanding the pathophysiology of exercise-induced muscle injury, we may be better able to prevent, evaluate, and treat these injuries.

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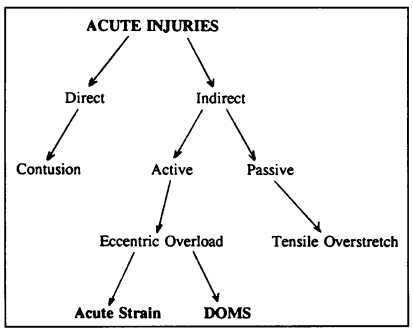
Muscle Injury Classification

Musculoskeletal injuries are very common in both athletes and nonathletes. Although both acute and chronic injuries are seen, we will limit this review to acute muscular injuries. Acute injuries result from: 1) direct trauma, causing a contusion at the point of contact, or 2) indirect trauma, causing a disruption in the myofibers without contact. Indirect injuries may be passive or active. Passive injuries result from a tensile overstretch of the muscle without contraction, whereas active injuries usually result from eccentric overload of the muscles.[28,32,46] These active injuries can be classified as acute strains or exercise-induced muscle soreness (see Figure).

Because most exercise-induced muscular injuries result from active contraction of muscles, our discussion will focus on injuries resulting from eccentric overload: acute strains and exercise-induced soreness. Exercise-induced muscular soreness or delayed-onset muscle soreness (DOMS) may be considered symptoms of injury. DOMS, however, limits performance resulting from decreased motion, decreased force production, and pain[2,14,15,26,48,51,58]; therefore, it is relevant to our discussion of acute exercise-induced muscular injury.



Types of acute muscular injury.

Both acute strains and DOMS usually occur as a result of eccentric overload and structural alteration[26,54] and result in an inflammatory reaction.[56] Although each presents similar clinical symptoms and functional limitations, they should be differentiated to determine proper treatment. For example, acute strains may require rest, whereas DOMS may respond better to stretching and activity.

Clinically, acute muscle strain injuries can be distinguished from DOMS based on the history of the injury. A strain results from a specific episode, is painful, and is easily recognized by the patient as an injury.[28] DOMS, however, usually begins 12 to 48 hours postexercise, with no specific event causing the injury[2,11,63] other than repeated eccentric muscle contraction. In both injuries, palpation, passive stretching, and active movement will cause pain.[28,56] Classification and clinical findings of acute exercise-induced muscular injury are summarized in Table 1.

Acute Strain

Acute muscular strains result from macrotrauma with immediate and direct signs and symptoms.[17,30] Most experimental studies, however, focus on acute muscular strain resulting from passive stretch in animal models. Taylor et al[61] noted that both clinical and experimental strains result from large tensile forces that cause damage to the musculotendinous structure. In a review by Garret,[28] many laboratory studies were identified that were consistent with clinical findings of muscular injury.

Predisposing Factors

Garret[28] suggested three types of muscle that are at possible risk for injury:

Two-joint Muscles. Motion at one joint can place two-joint muscles in a position of increased passive tension. The increased passive tension may lead to an overstretch injury.

Muscles Contracting Eccentrically. Functional activities in exercise require both concentric and eccentric contractions. Muscular strains are considered to result most often from eccentric contrac-

Table 1.—Clinical Manifestations of Exercise-Induced Muscular Injury

Evaluation	Acute Strain	DOMS
History	One specific episode	Unaccustomed/intense exercise
Structures involved	Musculotendinous junction	Muscle and connective tissue
Muscle contractions	Eccentric	Eccentric
Pain	Immediate, localized	Delayed, diffuse, dull ache
Palpation	Point tenderness, ± defect	Point tenderness, no defect
Swelling	±	±
Stretching	Painful	Painful
Weakness	Yes	Yes
Active movement	Painful	Painful

tions[28,32,57,66] because higher specific tensions produced in eccentric exercise lead to myofiber overload injury.[2,58,61] Eccentric contractions are common in the deceleration phase of activity.

Muscles With a Higher Percentage of Type II Fibers. These fast-twitch muscles create greater speed of contraction which may predispose a muscle to injury. Because most of the muscle action involved with running and sprinting is eccentric, muscle strains most often occur in sprinters or "speed athletes."

Arnheim[4] noted that the muscles with the highest incidence of strains in sports are the hamstrings, gastrocnemius, quadriceps, hip flexors, hip adductors, erector spinae, deltoid, and rotator cuff. In addition, he stated that a fault in the reciprocal coordination of the agonist and antagonist muscles may cause muscular strain. Knapic et al[43] reported that flexibility imbalances between agonists and antagonists may predispose athletes to injury. Interestingly, however, the flexible sides were most likely to be injured.

Previously injured muscle may also be more vulnerable to reinjury.[30] Jonhagen et al[41] reported that sprinters with recent hamstring injuries had tighter and weaker hamstrings than uninjured sprinters, although it was not known if this finding was a cause or a result of injury. Inadequate rehabilitation may not restore full strength, flexibility, and endurance to the involved tissues before return to activity. Subsequently, muscle weakness, tightness, and fatigue may predispose muscle to injury.[24,28]

Stretching and warmup before exercise have been advocated to prevent muscular injury[6,60,64] on the assumption that cold or tight muscles[23] might predispose one to muscular strain. Few experimental studies exist supporting these claims. However, inadequate warm-up exercises have been shown to be associated with muscle strains.[37] Increased tissue temperatures of 1°C[53] and 4°C[60] allowed greater elongation of the muscle before failure. Similarly, Noonan et al[50] reported that warm muscles (40°C) were less stiff than cold (25°C) muscles and required greater length to fail, offering experimental data to support warm-up as an aid in injury prevention and enhanced performance.

Mechanism of Injury

Acute muscular strains usually result from a specific event of macrotrauma.[17,30] A strain may involve the muscle itself or adjacent tissue, such as fascia or tendon.[4] The severity of the injury is in direct relation to the forces placed upon the muscle.[45] Mechanically, an acute strain may be caused by an abnormal muscular contraction,[4] a response to high specific tensions,[2] or forcible stretching of a muscle while it is active.[28] Each of these mechanisms is related to eccentric contraction, in which sufficient tensile forces develop to cause irreversible changes in the structure of the musculotendinous unit.[61]

Prevention of Acute Strains

Prevention of acute muscular strains should begin with adequate preseason screening of flexibility and strength balances in major joints such as the knee, shoulder, and ankle. Evaluation of previous muscle injuries should be performed to assess flexibility, strength, endurance, and proprioception. Preseason and in-season conditioning of muscle groups is also vital for prevention. Adequate agonist/antagonist ratios for strength and flexibility should be attained for major muscle groups, including quadriceps/hamstrings, shoulder internal rotators/external rotators, ankle dorsiflexors/plantarflexors, and abdominals/paraspinals. Muscles must be strengthened in the mode in which they are used functionally; ie, eccentric muscles should be strengthened eccentrically.

Warmup and stretching before activity are thought to prevent muscular strains. Smith[55] offers an excellent review of the literature supporting the efficacy of this practice. Active warmup such as jogging or biking should be performed before specific muscle stretching with emphasis on muscles at risk for strain, including two-joint muscles and those with high percentages of fast-twitch fibers (hamstrings, gastrocnemius, quadriceps, biceps), and muscles with high incidence of strain (hip flexors, hip adductors, erector spinae, rotator cuff). Muscles which contract eccentrically or decelerate in functional high-speed activities, such as the posterior rotator cuff in throwing athletes or the hamstrings in sprinters should be stretched for 15 to 20 seconds[6,8,62] and repeated four times.[62] Static stretching in combination with passive heating may be more effective than passive heating alone.[38]

Structural Changes

The most vulnerable site for an indirect strain injury is just distal to the musculotendinous junction or the tendon-bone junction[5,28–31,61]; therefore, knowledge of musculoskeletal surface anatomy and palpation skill is important. Pain, swelling, deformity, and point tenderness may be localized over the musculotendinous junction immediately after injury. Tendons themselves are very resilient to injury and are rarely injured acutely. Tendons will pull away from a bone, a bone will break, or a muscle will tear before tendons are injured.[4] However, in contrast to the musculotendinous junction, tendons are more susceptible to microtrauma.[30]

A muscle strain may be partial or complete, depending on the amount and degree of fiber disruption within the muscle.[28] Strains can be classified by three degrees: first degree, a minute separation of muscle fibers; second degree, partial tearing of some fibers; and third degree, a complete rupture or tendinous avulsion. While full-thickness tears do occur, partial or incomplete tears or strains are more common[30] and are clinically characterized by focal pain and swelling.[28] A palpable defect such as a bulge or gap in the muscle may be found in a complete or partial tear. Disruptions in the fibers cause biochemical changes both from direct injury to the fibers and from the inflammatory reaction.

Biochemical Changes

Serum creatine kinase (CK) and lactate dehydrogenase (LDH) enzyme levels are used to indirectly assess muscle damage following eccentric exercise.[1,2,12,14–16,26,47,48,54,58] In addition to the release of these biochemical markers, all acute strains undergo similar inflammatory reactions. Acute inflammation is the fundamental reaction designed to protect, localize, and remove injurious agents from the body in preparation for healing and repair.[4] Chemical mediators are present in acute muscular strain, as with any inflammation. These include: histamine, serotonin, bradykinin, and prostaglandin.[4] These chemicals increase the capillary membrane permeability, change blood vessel diameter, and stimulate pain receptors. Edema results from an accumulation of proteins and transudate in the interstitial space. This accumulation is a result of increased capillary membrane permeability secondary to the chemical mediators. Therefore, the characteristic swelling, heat, redness, and pain of inflammation are due to biochemical changes[4] caused by the chemical mediators. Nikolaou et al[49] noted an inflammatory reaction and edema at 1 to 2 days after a stretch-induced muscular injury. The acute phase of inflammation lasts up to 3 to 4 days after the initial injury[4] unless the tissue continues to be traumatized, as is commonly seen when injured athletes return to activity too soon or are progressed too rapidly. Proliferation of fibroblasts, increased collagen production, and degradation of mature collagen have an overall weakening effect on the tissue; therefore, efforts to stretch the tissue perpetuate the irritation and progressive limitation,[42] leading to chronic muscle strains.

As the inflammatory phase subsides, repair begins and lasts for 2 to 3 weeks. The repair phase is characterized by capillary growth and fibroblast activity to form immature collagen. This immature collagen is easily injured if overstressed; however, proper growth and alignment can be stimulated with appropriate tensile loading in the line of normal stresses.[42] The final stage of healing is maturation and remodeling of collagen, occurring from 2 to 3 weeks after onset until there is pain-free functional use of the muscle.[42] If the healing fibers are not properly stressed, the fibers adhere to surrounding tissue and form a restricting scar which is resilient to remodeling.

Treatment of Acute Strains

The key to returning any injured athlete to competition safely is to provide an optimal environment for healing and to progress the patient according to: 1) the severity of the injury, 2) the natural healing process of the body, and 3) the response of the tissue to new demands. Treatment goals for any soft-tissue injury must take the natural healing process into consideration. The overall goal is to assist the body with its natural healing process. The body must go through each stage with any soft tissue injury; therefore, the athletic trainer must not return the athlete to activity too soon. Two to three weeks of restricted activity may be a minimum to allow for collagen formation and prevent reinjury in all soft-tissue injuries.

Inflammatory Phase. Effective management of muscular strains begins at the time of injury. Care for acute injuries must be initiated as quickly as possible with rest, ice, compression, and elevation (RICE) for at least 48 hours. Cold slows the inflammatory process and decreases pain and muscle spasm; compression and elevation reduce edema. An ice bag wrapped with an elastic wrap, elevation, and crutches may be used. Rest protects the injured tissue; however, immobilization may be detrimental to healing and the uninjured tissue. As the inflammation subsides, pain-free, passive range of motion (ROM) and gentle joint mobilization should be initiated to maintain soft-tissue and joint integrity. Gentle, pain-free, submaximal isometric muscle sets may be used at multiple angles to maintain strength and keep the developing scar tissue mobile. Aggressive stretching and strengthening is contraindicated. Any increase in pain, swelling, warmth, or redness indicates a proliferation of the inflammatory phase which should be treated only with RICE. Modalities for pain and edema such as electrical stimulation and pulsed ultrasound should be used during both the inflammatory and repair phases.

Repair Phase. The inflammatory and repair phases overlap during the first week after injury. As the inflammation subsides, the athlete may attempt too much activity too soon. This prolongs the inflammatory phase and leads to chronic muscle strain. However, as collagen is laid down, it must be appropriately stressed in the normal lines of tension. This is a critical "turning point" in the treatment of muscle injuries and may be the most important stage for the trainer or therapist in any rehabilitation. Signs of inflammation (pain, swelling, redness, warmth) are used to determine whether the tissues are being overstressed with activity. The rehabilitation program must be constantly evaluated. Frequency, intensity, and duration of exercises are altered to allow for healing and to prevent inflammation for the next 1 to 2 weeks. Cold in the form of cryostretch or cryokinetics (see Ref. 44) may be beneficial initially to allow for pain-free exercise to aid in the formation of the scar tissue. Heat in the form of warm whirlpools, moist heat, or ultrasound is used to promote capillary growth and increase ROM. Contrast baths may be most beneficial during this period. Gentle, pain-free stretching and pain-free submaximal isometrics can be incorporated into contract-relax techniques to help align collagen fibers. These exercises are progressed to active ROM for the agonist. Active or resistive motion of the antagonist or contralateral extremity may also be incorporated. Finally, a cardiovascular conditioning program should be incorporated for any athlete not capable of full athletic participation.

Maturation and Remodeling Phase. As collagen matures, it requires tension in the line of normal stresses to remodel properly. Clinically, this stage presents at about 2 to 3 weeks after injury and is characterized by: 1) the absence of inflammation, 2) full, pain-free ROM, and 3) pain after tissue resistance, which is felt with passive ROM.[42] The athlete is progressed as tolerated with limited participation in his/her sport. Rehabilitation includes more vigorous stretching, closed- and open-chain strengthening, cardiovascular training, and sport-specific activities. It is vital to remember that muscles must be stressed and overloaded in the manner in which they are used functionally, following the principle of specificity. Type of contraction (eccentric vs concentric), metabolism (aerobic vs anaerobic), and functional pattern (diagonal vs cardinal plane) should be specific to the activity in which they are used. Eccentric exercise is functional in most athletic activities, develops greater tension than concentric exercise, and may be more comfortable in the early stages of rehabilitation.[7] Eccentric contraction may be performed against manual, isotonic, isokinetic, or elastic resistance. Massage, aquatic therapy, and plyometrics are beneficial to any soft-tissue treatment. Proprioceptive and endurance training are used in the advanced stages of rehabilitation. Modalities before and after activity may be beneficial as well. An elastic or neoprene wrap with a felt pad directly over the injury site provides warmth and compression. After the athlete has regained full, pain-free active ROM and over 90% strength bilaterally, full participation is allowed. Maintenance programs should be independent and individualized to avoid any dysfunctional adaptation or compensation.

Delayed-Onset Muscle Soreness

DOMS is commonly seen in patients performing new exercises or in athletes involved in weight-lifting or other eccentric activities. DOMS results from muscle damage[2,11,15,26,58] following eccentric exercise. The onset of DOMS is characterized as a dull, aching pain usually beginning 12 to 48 hours after exercise.[2,11,63] Clarkson et al[15] found that soreness peaks 2 to 3 days following eccentric exercise and subsides linearly within 10 days. In addition to pain, other symptoms include decreased motion and decreased force production.[2,14,15,26,48,51,58,65] Newham and associates,[47] however, reported a decreased force production with electrical stimulation of these muscles, indicating that the soreness itself does not inhibit force production.

Muscles adapt to a single bout of eccentric exercise. This is evidenced by less damage to the muscle after the same exercise months later.[15] The muscle is repaired without any residual dysfunction or scarring and the muscle is often able to resist even greater forces.[12,16,61]

Predisposing Factors

Armstrong[1] suggested two possible causative factors during the initial events of DOMS[2,58]: high tensions and metabolic changes.

High Tensions. High tensions produced during eccentric exercise are more apt to produce myofiber injury than isometric or concentric contractions.

Metabolic Changes. Increased temperature, decreased aerobic capacity, and decreased pH of the muscle may have a role in causing DOMS.

Mechanism of Injury

Exercise that results in the development of soreness is associated with the rapid destruction of muscle tissue.[11,26] The soreness usually results from muscle damage following repetitive eccentric exercise or after the first or second session of a new training program.[2,11,15,22,58] DOMS is also associated with muscle spasm, as evidenced by increased EMG activity.[20,21,46,52] DOMS results primarily from structural muscle damage and microtrauma and may be related to the resultant biochemical changes of the inflammatory process.

Prevention of DOMS

Few studies exist on the prevention of DOMS. Because it is known that eccentric contractions cause muscle damage, DOMS may be prevented with warmup and stretching before and after eccentric or novel exercise. Ideally, DOMS is prevented by avoiding eccentric or unaccustomed exercise. Clinically, this is not possible. Athletes in competition, weight lifters, and patients undergoing early rehabilitation commonly perform eccentric exercise. This eccentric training develops strength to resist further damage.[15] Therefore, specific eccentric training is neccesary for any sport activity to help prevent further damage or injury. Eccentric training sessions should be limited to two per week to allow adequate rest and recovery between sessions. Patients should be educated about the importance and need for eccentric exercises, as well as about the possiblity of DOMS.

Effective prevention of DOMS may begin in the acute stages of treatment before symptoms begin. Prophylactic ibuprofen administered before or immediately after heavy eccentric exercise may decrease the pain associated with DOMS.[34] Yackzan et al[65] found that subjects who received ice massage immediately after eccentric exercise had more ROM 24 hours later than those who did not receive it. Further research is needed on the prevention of DOMS, including the roles of warmup, stretching, and immediate treatment after intense eccentric exercise.

Structural Changes

Structural damage to subcellular components following eccentric exercise has been found by microscopic evaluation.[1,3,11,26,40] High specific tensions seen in eccentric contractions could mechanically disrupt the connective tissue, myofilaments, sarcomere, sarcolemma, or sarcoplasmic reticulum.[1,2,9,10] Friden et al[25,26] found alteration of Z-bands in type II fibers both immediately and 3 days after eccentric exercise.

Damage to the extracellular matrix (ECM, the interface between the myofiber and fascia) following eccentric exercise has been evaluated by Stauber and associates.[58,59] Myofiber and ECM damage result directly from eccentric contractions.[27] Stauber et al[59] reported that eccentric muscle action is related to mechanical shearing at the ECM. These structural changes then cause biochemical changes within the injured tissue.

Biochemical Changes

Damage to the sarcolemma and ECM creates an altered chemical environment

Table 2.—Treatment of DOMS

Authors	Treatment	Efficacy
Ciccone et al[13]	Trolamine salicylate phonophoresis	Effective
Denegar et al[18]	TENS	Effective
DeVries[20,21]	Static stretching	Effective
Hasson et al[33]	High speed, voluntary muscle contraction	Effective
Hasson et al[34]	Ibuprofen	Effective
Haynes & Perrin[36]	Topical counterirritant	Effective
Hill & Richardson[39]	Topical trolamine salicylate cream	Effective
Prentice[52]	Static or PNF stretching + cold or heat	Effective
McGlynn et al[46]	Stretching and biofeedback	Reduced EMG, but not pain
Prentice[52]	Heat	Not effective alone
Yaczan et al[65]	Ice massage	Not effective alone
	Continuous ultrasound	Increases pain
Denegar et al[19]	Microcurrent	Not effective, + analgesic effect
Hasson et al[35]	Dexamethasone Iontophoresis	Questionable

within the muscle. The release of proteins and ions into the plasma as a result of inflammation is similar to that found in acute strains.[1,2,59] Increases in these levels indicate damage to the sarcolemma. Elevations of CK, LDH, protein metabolites, and myoglobin have been found in plasma up to 48 hours following eccentric exercise.[2,3,14,54,58,63] These biochemical events occur within the muscle cells themselves and begin approximately 24 hours postexercise,[15] before phagocytic cells enter the injury site.[1] Time-specific clinical events (such as peak soreness at 2 to 3 days) may correspond to the time of increased enzyme levels (such as CK increase at 2 days). While Tiidus[63] reported such a correlation between soreness and enzyme levels, Clarkson et al[15] cautioned against claiming a cause-and-effect relationship based on limited research.

The structural disruption leads to the normal inflammatory response: an increase in chemical mediators such as histamine, bradykinin, prostaglandin, and serotonin,[4] causing pain and swelling. The products of the inflammatory response sensitize free nerve endings in muscle,[11,56] thus increasing soreness. Stauber et al[59] concluded that the DOMS after repeated eccentric muscle action is not because of actual myofiber damage, but more likely results from inflammation.

Treatment of DOMS

Because DOMS results from microtrauma, structural damage in DOMS is not as severe as in acute strains resulting from macrotrauma. The symptoms of DOMS resolve relatively quickly without any residual dysfunction; therefore, DOMS can be treated symptomatically. In any exercise-induced muscular injury, RICE is the ideal immediate treatment to decrease inflammation and pain. However, because DOMS begins at 24 to 48 hours after exercise and peaks at 2 to 3 days after exercise, treatment may not begin immediately after injury.

The goal of treatment of DOMS is to reduce the pain, swelling, inflammation, and muscle spasm. These goals are similar to those in the acute stage of any soft-tissue injury. Several authors have studied the efficacy of these treatments (Table 2). Static or proprioceptive neuromuscular facilitation (PNF) stretching,[20,21,52] high-speed muscular concentrics,[33] nonsteroidal anti-inflammatory drugs (NSAIDs),[34] and topical counterirritants[36,39] have been shown to be effective in reducing pain associated with DOMS. Phonophoresis[13] and transcutaneous electrical nerve stimulation (TENS)[18] may be effective, but the benefits of iontophoresis[35] and biofeedback[46] remain questionable.

Most studies report significant improvement in DOMS with combinations of exercise and modalities. DOMS can be treated symptomatically by reducing the pain, soreness, swelling, and muscle spasm. NSAIDs and topical counterirritants may decrease soreness. Static or PNF stretching in combination with cryotherapy (spray-and-stretch or ice massage) also help to decrease the symptoms of DOMS. In addition, high-speed, rapid concentric muscular contractions may provide relief. Further research is needed on the use of massage, pulsed ultrasound, and electrical stimulation (including TENS, iontophoresis, and microcurrent) in the treatment of DOMS.

Conclusion

Both acute strains and DOMS present similar clinical signs; however, they can be differentiated by history of the injury. While many studies exist on the structural changes and biochemical changes of exercise-induced muscular injury, many questions remain unanswered. The exact changes in human muscle after an acute strain have not been determined. A cause-and-effect relationship for DOMS has not been firmly established. We have reviewed the literature on these acute injuries and provided clinical findings to aid in the care of musculoskeletal injuries. Further research is needed on the causes of these injuries, as well as on effective preventive and treatment techniques to return athletes and patients back to preinjury levels.

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