

ABSTRACT: Tenotomy is a commonly encountered clinical entity, whether traumatic or iatrogenic. This article reviews the response of skeletal muscle to tenotomy. The changes are subdivided into molecular, architectural, and functional categories. Architectural disruption of the muscle includes myofiber disorganization, central core necrosis, Z-line streaming, fibrosis of fibers and Golgi tendon organs, changes in sarcomere number, and alterations in the number of membrane particles. Molecular changes include transient changes in myosin heavy chain composition and expression of neural cell adhesion molecule (NCAM). Functionally, tenotomized muscle produces decreased maximum tetanic and twitch tension. Alterations in normal skeletal muscle structure and function are clinically applicable to the understanding of pathological states that follow tendon rupture and iatrogenic tenotomy.

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SKELETAL MUSCLE RESPONSE TO TENOTOMY

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The word "tenotomy," as used in the surgical literature, indicates surgical division of a tendon for relief of a deformity that is caused by congenital or acquired shortening of a muscle. Loss of tendon continuity applies to surgical manipulation, trauma, and degenerative musculoskeletal diseases.⁵⁹ There are vast clinical implications of the changes that occur both in muscles and tendons after tenotomy. Although numerous studies have detailed biochemical and architectural properties of tendons after tenotomy and these results have been incorporated into the clinical realm, little information is available regarding the biological and mechanical response of muscles to surgical tenotomy and to traumatic tendon injury. This has clinical implications in the fields of orthopedics, ophthalmology, and general surgery. By studying the response of muscle to therapeutic

and traumatic tenotomy, a better understanding of skeletal muscle function and response to injury is achieved. In addition, new methods of intervention on muscle's healing response may be investigated, leading to accelerated recovery from surgery and healing after injuries.

There are numerous examples of tendon injuries that lead to debilitation. These include rotator cuff rupture, Achilles tendon injury, flexor or extensor tendon laceration in the hand, and patellar tendon rupture. Additionally, surgical tenotomy is widely used in ophthalmology for realignment of the optic axis.⁵⁶ Tenotomy is commonly performed in foot and ankle surgery for treatment of hallux valgus, in hand surgery for tendon transfers and treatment of mallet finger,¹⁵ in sports medicine for treatment of tendinitis,⁴⁵ in the treatment of rheumatologic diseases such as hamstring tenotomy for hemophilic arthropathy of the knee, in pediatric orthopedics for correction of deformities in cerebral palsy,^{20,53} and in traumatology for the management of compartment syndrome contractures.³³ Thus, it is important to understand the effects of tenotomy on skeletal muscle both acutely, immediately after the surgery,

Abbreviations: CCD, central core disease; DMD, Duchenne muscular dystrophy; EDL, extensor digitorum longus; EMG, electromyographic; MHC, myosin heavy chain; MLC, myosin light chain; NCAM, neural cell adhesion molecule; P₀, maximum tetanic tension

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as well as in the long term, after the muscle has had the chance to adapt to its new environment. The purpose of this review is to highlight several basic studies of skeletal muscle tenotomy and to suggest their clinical implications.

TENOTOMY EFFECTS ON MUSCLE

The immediate effects of tenotomy or tendon rupture on muscle are straightforward. Because normal muscles are typically under resting tension, there is an immediate decrease in the tension across the muscle as well as sarcomere shortening after the muscle loses one of its attachments. Additionally, the specialized neural sensors are affected with respect to the length and tension information that they receive and relay (see below).

Tenotomy Decreases Muscle Mass and Force-Generation Capacity. Tenotomy, studied across a wide range of species, results in decreased muscle mass (Table 1). The specific effect of tenotomy depends both on the species and on the muscle studied. For example, in the rat soleus muscle, 12 days after tenotomy, muscle mass decreased by approximately 50% compared to a normal muscle.^{16,37,40} It has been shown, in general, that the antigravity muscles (composed primarily of slow fibers) atrophy to a greater extent than their antagonists (composed primarily of fast fibers). Additionally, tenotomy leads to greater atrophy of the slow-twitch fibers in cat gastrocnemius and soleus.³⁰ Calcium-activated neutral proteases are upregulated after tenotomy in the rat soleus, reaching the maximum level at 1 week. This time course corresponds to maximum muscle fiber disorganization. These enzymes may be involved in the degenerative events that occur in tenotomized myofibers.⁸

In contrast to the relatively rapid response of the rat soleus muscle, atrophy of the rabbit soleus muscle does not reach a significant level until 4 weeks post-tenotomy.¹⁰ In the rabbit model, reformation of a distal attachment of the muscle to either the tendon stump or surrounding connective tissue with subsequent application of tension decreases atrophy and improves maximum tension production, a measure of muscle strength.^{65,66}

Tenotomy, with intact innervation, leads to several changes in muscle contractile function. Buller and Lewis completely tenotomized all muscles surrounding the rabbit ankle and showed significantly decreased twitch tensions in the tenotomized group (Table 1) to approximately 5–10% of the control

values within only 3 weeks.¹⁶ Additionally, they noted an increase in the speed of muscle contraction, which they attributed to conversion of slow fibers to fast fibers. This is similar to the conversion of slow fibers to fast fibers that occurs with other decreased-use models, such as spinal cord injury⁴⁶ or hindlimb suspension.^{13,63}

Active tenotomy is defined as tenotomy of a muscle while it is undergoing active contraction. Passive tenotomy is tenotomy of a muscle while at rest. Tsai et al. hypothesized that active tenotomy would be more injurious to muscle based on a more violent release of tension. In the rabbit extensor digitorum longus muscle (EDL), they compared active to passive tenotomy over 3 weeks to determine whether active contraction during a tenotomy (simulating traumatic rupture) would lead to greater muscle injury. They found that, after 1 week, the active tenotomy group produced lower maximum tetanic tension compared to passive tenotomy, possibly indicating greater damage to the contractile elements (Fig. 1). By 21 days, however, the active tenotomy group had recovered to a significantly greater degree than the passive tenotomy group.⁶⁶ They hypothesized that the active tenotomy initially caused a greater muscle injury leading to a greater regenerative response, allowing more complete restoration of the contractile function.

Tenotomy Causes Alterations in Sarcomeres and Supporting Structures. Tenotomy leads to an increase in the connective tissue content of a muscle.⁴⁰ Within 1 week of tenotomy in rat soleus and gastrocnemius muscles, a qualitative increase in both the epimysial and perimysial connective tissue layers was seen (Figs. 2, 3). By 3 weeks after tenotomy, the volume density of connective tissue had increased by a factor of 10, with a greater increase in the soleus muscle compared to the gastrocnemius. In parallel to the connective tissue increase, there was a loss in the number of capillaries. By 3 weeks post-tenotomy, only 47% of the soleus capillaries remained. The capillary effect was more pronounced in the soleus compared to the gastrocnemius.

Tenotomy also plays a role in the organization of sarcomeres in series within a muscle. It has been demonstrated that tenotomy of the proximal and distal tendons of rat soleus muscle not only leads to muscle belly shortening, as expected, but that this shortening is distributed to the sarcomeres in such a way that they shorten proportionally from an average length of 2.6 μm to 1.8 μm .^{5,6} It was further shown that over the course of the following 4 weeks, sarco-

Table 1. Summary of experimental tenotomy studies.*

| Ref. no. | Model and species | Procedure | Endpoint | Measured results | Conclusions |
|----------|------------------------------|------------------------------|--|--|---|
| 37 | Rat soleus and gastrocnemius | Achilles tenotomy | 4–120 days | MHC distribution | Shift in proportion of fast fiber types (temporary). No embryonic myosin expression in tenotomized muscle. |
| 71 | Rat soleus | Proximal and distal tenotomy | 5 days | Histology, transmission EM, energy dispersive X-ray microanalysis | Cores found in type 1 fibers after tenotomy; significant increase in Na ⁺ and Cl [−] concentration. Decreased K ⁺ and S content in tenotomized fibers. |
| 8 | Rat soleus | Achilles tenotomy | 3,5,7,14,21 and 42 days | Calcium protease activity | Maximal protease activity within 1 week after tenotomy. Persistent activity at 2–3 weeks. Return to baseline by 6 weeks. |
| 38 | Rabbit EDL | Active and passive tenotomy | 1,7,21 days | NCAM expression | Molecular changes occur within 24 h. |
| 6 | Rat gastrocnemius and EDL | Passive tenotomy | 1 day, 1,2,4 weeks | Sarcomere lengths and light microscopy | After 1 day, decreased average sarcomere length. Central core fibers found after 1 week in gastrocnemius but not EDL. |
| 7 | Rat soleus | Proximal and distal tenotomy | 2 days–6 weeks | Light and electron microscopy | Central cores after tenotomy formed by addition of newly formed myofibrils at the periphery of the myofiber. |
| 58 | Rat soleus | Tenotomy | 1–4 weeks | Light and electron microscopy | Central core necrosis, Z-band streaming, and nemaline rods observed. |
| 3 | Rat soleus | Proximal and distal tenotomy | 1,2,3,4,6 weeks after tenotomy | Light and histochemistry | Central core necrosis seen in all three fiber types. |
| 2 | Rat soleus | Proximal and distal tenotomy | 1,2,3,4,5,6,7 days after tenotomy | Light and electron microscopy | Segmental necrosis at fiber ends. Peripheral zone of central core fibers consists of normal muscle cross-striations and central zone with the interruption of striation pattern. |
| 4 | Rat soleus | Proximal and distal tenotomy | 1 week after tenotomy | Freeze fracture | Decrease in number of intramembranous particles. |
| 5 | Rat soleus | Proximal and distal tenotomy | 1 day and 4 weeks after tenotomy | Light microscopy | Muscle bellies and sarcomere length shortened after 1 day. After 4 weeks, muscle bellies remain shortened, but sarcomere lengths return to normal. |
| 10 | Rabbit soleus | Tenotomy and immobilization | 4 weeks after tenotomy | Muscle mass, length, fiber type and area, density, tetanic force, rate of force generation | Achilles tenotomy resulted in a 20% decreased and 50% drop in P ₀ after 2 weeks. Tenotomy and immobilization resulted in a 90% drop in P ₀ . Small beneficial effect of electrical stimulation. |
| 40 | Rat soleus and gastrocnemius | Tenotomy and immobilization | 1,2, and 3 weeks | Density of capillaries and connective tissue by scanning EM | Increased endomysial and perimysial layers and decreased capillary density. |
| 41 | Rat soleus and gastrocnemius | Tenotomy and immobilization | 1,2, and 3 weeks | Number of muscle spindles, Golgi tendon organs, and intrafusal fibers; diameter of intrafusal fibers | Diameter of intrafusal fibers increased after 1 week and then decreased after 3 weeks. Spindle and Golgi capsules thickened nearly two-fold 3 weeks post-tenotomy. |
| 39 | Various human muscles | Spontaneous tendon rupture | 1 day to 6 months after tendon rupture | Light microscopy, histochemistry, and electron microscopy | Decreased SDH and CPK activity. Decreased number of type 1 fibers. Disruption and disorientation of myofibrils; Z-line streaming and disorganization. Enlarged mitochondria and sarcoplasmic reticulum dilatation. |
| 42 | Rat soleus | Achilles tenotomy | 24 h–40 days | Light and electron microscopy | Nerve input is necessary for the development of central cores and nemaline rods. Lesions prevented by sciatic neurotomy or cordotomy. |

Table 1. Continued

| Ref. no. | Model and species | Procedure | Endpoint | Measured results | Conclusions |
|----------|------------------------------------|---|---|---|--|
| 16 | Rabbit soleus | Tenotomy of dorsiflexors | 17 to 85 days | Twitch tension and isometric recordings | Shortened contraction time with no conversion from slow to fast muscle fibers. |
| 19 | Human Achilles tendon ruptures | Achilles tendon repair patients | Measurements taken at 1,2,3,6,12,24, and 52 weeks | Distance between ends of the tendon; ROM, and plantar flexion strength | Mobile cast postoperatively, increased ROM and plantarflexion strength, and decreased tendon elongation and scar formation. |
| 35 | Rat soleus, gastrocnemius, EDL, TA | Tenotomy followed by dorsal root sectioning | Muscles studied 3 and 7 days after tenotomy | Muscle shortening and contracture after tenotomy or tenotomy and deafferentation | Tenotomy alone caused greater rate of atrophy than tenotomy combined with deafferentation. Atrophy more rapid in plantar flexors than dorsiflexors. |
| 47 | Human Achilles tendon ruptures | Achilles tendon repair followed by early range of motion | Follow-up at 6 weeks and 3,6,12, and 24 months | Pain evaluation, functional deficit, and return to sports | Suture technique provides rigid and stable fixation that allows early range of motion, strengthening, and functional rehabilitation leading to minimal plantar flexion strength deficit. |
| 49 | Mouse soleus | Achilles tenotomy and/or tibial nerve section | 1,3,5,7,14 days | Length and mass of soleus muscle after tenotomy and/or denervation | Muscle atrophy 24 h after tenotomy. Simultaneous tenotomy and denervation afforded a temporary delay in atrophy for 2 days. By 7 days, there was equal atrophy in the experimental groups. |
| 64 | Human Achilles tendon ruptures | Achilles tendon repaired and postop motion | Follow-up ranged 14–56 months | Clinical evaluation, functional, testing and strength testing | No increased risk of rerupture and good return of plantar flexion strength when treating Achilles tendon repairs with early range of motion. |
| 52 | Rabbit soleus and peroneus longus | Tenotomy of tendons crossing ankle and/or sciatic neurotomy | 3 days to 3 months | SDH activity, fiber size and type, histology | Denervation decreased SDH activity. Tenotomy caused degenerative changes in soleus but not peroneus. Denervation prevented degenerative changes. |
| 36 | Rabbit gastrocnemius | Achilles tenotomy | 9 days to 20 months | Muscle spindle spontaneous sensory activity and histology of medial head of gastrocnemius | Spindles react to muscle stretch with increased discharge frequency & by post-excitatory inhibition on removal of stretch. Preservation of muscle spindle structure and tendon organs due to shortening of muscle. |
| 67 | Rabbit soleus and TA | EMG during reflex and active movement | 1,2 days, 6 weeks, 3 months | EMG activity | TA shows continuous EMG activity for 2 weeks after tenotomy while soleus activity ceases immediately. |
| 66 | Rabbit EDL | Active or passive tenotomy | 1,7,21 days | Maximum tetanic tension | After active tenotomy, maximum tension drops below that of passive tenotomy at 1 and 7 days. By 21 days, active tenotomy produces higher maximum tension than passive tenotomy. |

*CPK, creatine phosphokinase; EDL, extensor digitorum longus; EMG, electromyogram; MHC, myosin heavy chain; NCAM, neural cell adhesion molecule; P_{max} , maximum tetanic tension; ROM, range of motion; SDH, succinate dehydrogenase activity; TA, tibialis anterior.

mere length returned to normal as the fibers decreased serial sarcomere number. This suggests that the reduction of sarcomeres in series was made in order to optimize the contractile function of each sarcomere. If this is true, it would be analogous to studies of immobilization in which sarcomere length returns to optimal by changing sarcomere num-

ber.^{62,70} Baker sought to explain the mechanism of sarcomere removal and noted preferential fiber necrosis in both the peripheral ends of the proximally and distally tenotomized rat soleus with a significant infiltration by inflammatory phagocytic cells, lysosomes, and autophagic granules within 1 day after tenotomy.² This was termed “segmental necrosis.”

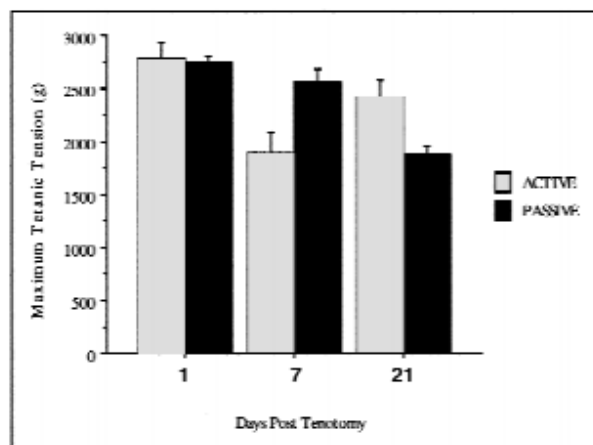


FIGURE 1. After active and passive tenotomy, there is initially a greater decline in maximum tetanic tension in the active group at 7 days, with improved recovery by 21 days, possibly indicating a greater regenerative response. From Tsai et al.⁶⁶

The necrotic portion of the muscle fiber was seen in continuity with the more normal part of the fiber, which was located toward the mid-belly. He hypothesized that this represented a key event leading to sarcomere number reorganization after tenotomy.

Theoretically, the muscle architecture probably plays a role in the degree of sarcomere reorganization. Fibers that are parallel to the long axis of the fiber (low pennation angle) have the greater relative shortening and greater degree of remodeling compared to those fibers with more oblique orientations (high penetration angle). The change in sarcomere number may represent a general theme of skeletal muscle. Sarcomere number is a plastic value that

adapts to the new muscle environment. While this is a logical hypothesis based on the literature, the extent to which such adaptations are characteristic of muscle is yet to be determined.

Tenotomy Causes Alterations in Muscle Fiber Fine Structure. Structural changes that appear in tenotomized muscle involve the basic structure of the fibers themselves. Central muscle fiber cores are a classic pathological sign in histological sections. Central core disease (CCD) and nemaline myopathy are two of the most common of the congenital myopathies in patients who often present as a "floppy infant."^{17,48} In the tenotomy literature, the term central core was originally used to describe the central fiber disorganization seen at the light and electron microscopic level. Further work since that time has separated the pathological entities of central cores

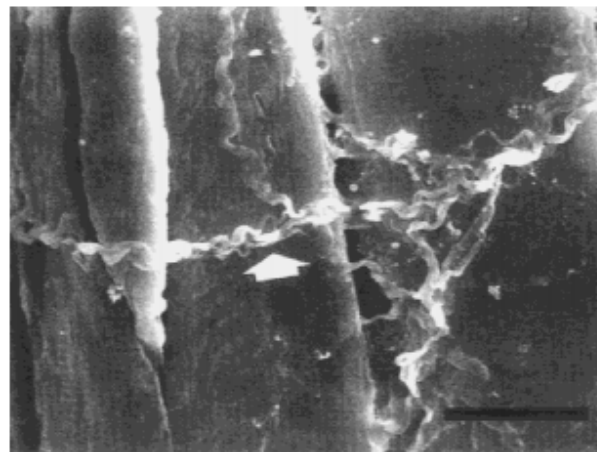


FIGURE 2. In normal muscle, a few delicate collagen fibers (arrow) are seen with minimal connective tissue by SEM. Bar = 10 μ m. From Josza et al.⁴⁰

from that of target fibers. Target fibers are fibers consisting of three zones: a central zone with decreased oxidative capacity analogous to the central core in CCD, an intermediate zone of increased oxidative enzyme activity, and a peripheral zone consisting of normal muscle microscopic structure. The target fiber is brought about by denervation and reinnervation. According to De Coster et al., they are demonstrated when the "trophic influence of the nervous system" is interrupted.²³ Central cores can be multiple in the same fiber and can extend along the entire length of the fiber whereas targets are usually central and localized within the fiber.^{17,23,29} Histological changes have been demonstrated in tenotomized muscle in both the cat and rat, initially

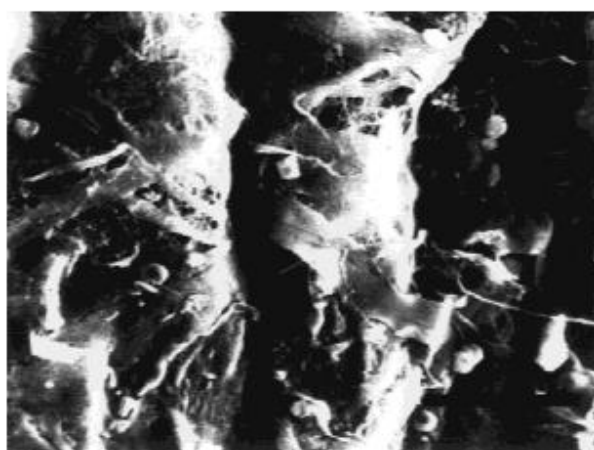


FIGURE 3. In the soleus, 3 weeks post-tenotomy, there is a dense connective tissue envelope separating the muscle fibers. Bar = 10 μ m. From Josza et al.⁴⁰

described as central cores.^{17,30} At the light microscopic level, these regions consisted of a peripheral normal region and a central region of disorganized myofibrils.² They were seen in tenotomized rat muscle within 7 days.⁵⁸ Most of these fibers lost their myosin ATPase and succinate dehydrogenase activity within the cores, indicating not only structural but also metabolic derangement. Although the specific function of these fibers was not explicitly measured, given the inability to generate force using myosin cross-bridges and the lack of oxidative capacity, it can be expected that the function of these fibers is compromised. The so-called cores as described in the early tenotomy literature represent target fibers based on the mechanism of their formation and their microscopic appearance. According to De Reuck et al., target fiber formation can be inhibited by performing simultaneous neurectomy in the rat gastrocnemius model, suggesting the need for muscle activation in order to manifest these histological and structural changes.²⁴⁻²⁶

The mechanism of sarcomere structural reorganization that follows tenotomy and the formation of the central cores themselves is poorly understood. Baker showed that normal muscle fibers (Fig. 4) begin to show morphological changes within 1 day after tenotomy, including mitochondrial swelling and Z-line dissolution.² Using electron microscopy, he showed that myofibrils along the entire length of the fiber underwent destruction. His findings indicated that the peripheral normal region of the central core fibers was actually the region of new myofibril proliferation. In this respect, fiber rebuilding recapitulated the developmental process.⁴⁴ Nemaline rods

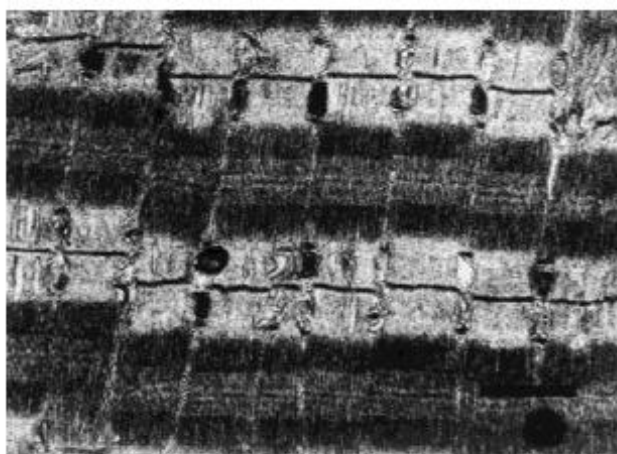


FIGURE 4. Electron micrograph of control skeletal muscle demonstrating linear arrangement of Z-bands. Bar = 1 μ m.

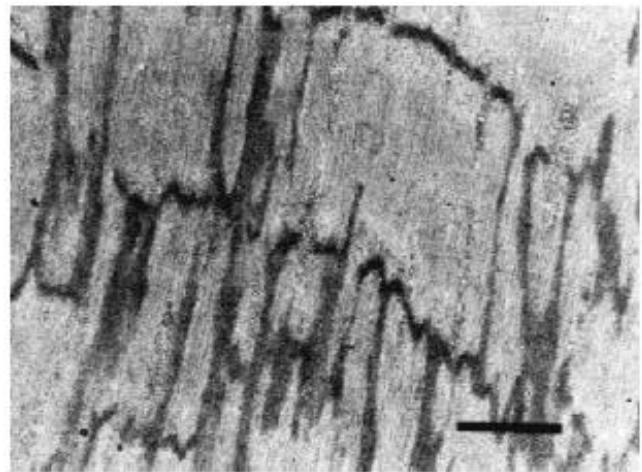


FIGURE 5. Z-band streaming in tenotomized rat soleus muscle. Bar = 1 μ m. From Shafiq et al.⁵⁸

are characteristic findings in nemaline myopathy, a myopathy of either sporadic or autosomal inheritance.^{31,54} These structures are ascribed to excessive collections of Z-band components. These same nemaline rods have been demonstrated in animal models of tenotomy.⁵⁵ Other structural changes in tenotomized muscle include mitochondrial degeneration with autophagic vacuoles and Z-band streaming (Fig. 5). As early as 1 day after tenotomy, there is swelling of the sarcoplasmic reticulum, especially the terminal cisternae. Based on these results, Baker hypothesized that these changes are analogous to those seen in Duchenne muscular dystrophy (DMD).⁴

Of interest to many investigators are the molecular factors responsible for changes in muscle structure and function. Baker used the freeze-fracture technique to examine the membrane morphological

response to tenotomy in rats 1 week after soleus tenotomy.⁴ Previous studies on DMD muscle showed a decrease in intramembranous particles on both the cytoplasmic and external faces of the freeze fracture specimens.⁵⁷ The authors speculated that the decrease in intramembranous particles affected membrane permeability, which may have lead to the degenerative changes observed. Wróblewski and Edström performed X-ray microanalysis to quantify the amounts of sodium, chloride, and potassium within central core fibers after tenotomy in rats (Fig. 6).⁷¹ In the core fibers studied, they found increased sodium, increased chloride, and decreased potassium compared to contralateral controls. This was attributed to an inability of the plasma membrane to maintain normal ionic electrochemical gradients. A

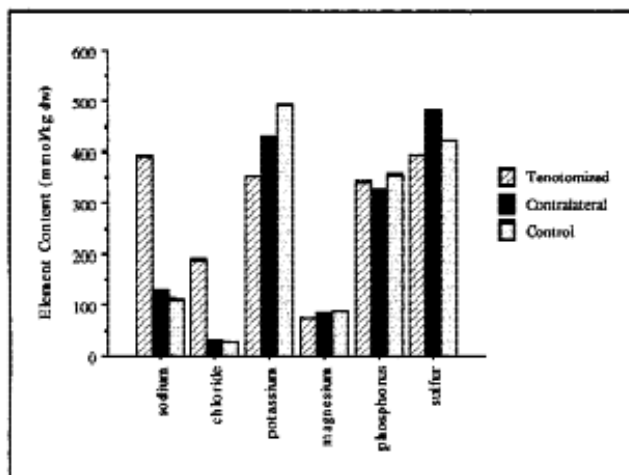


FIGURE 6. Bar graphs of the content of elements as determined by X-ray microanalysis in the soleus muscle fibers after tenotomy compared with contralateral nontenotomized soleus and soleus from normal rats. From Wróblewski and Edström.⁷¹

change in sodium and potassium of the same magnitude has been reported in human myopathic muscle, including myotonic dystrophy and myotubular myopathy.²⁸

Tenotomy Causes Alterations in Myosin Heavy Chain Expression.

Myosin is the molecular motor that powers contraction in skeletal muscle. Myosin is the key protein in fiber type determination. It has a vital role in muscle function as a result of its interaction with actin. Each myosin molecule chain contains six subunits, two heavy chains (MHC) and four myosin light chains (MLC). The heavy chains have important functional significance as they are related to the maximum muscle fiber speed of contraction.¹⁴ Many muscles are a mosaic of these fibers, whereas others are predominately slow or fast. The fiber type system was initially based on laboratory observations of twitch time, peak torque, and degree of fatigability, and content of oxidative enzymes. With newer techniques such as immunohistochemistry, gel electrophoresis, and molecular biology, more definitive analysis of muscle fiber type is now available. Additionally, various species and specific muscles have variable fiber typing, based on MHC isoforms. Much of the tenotomy literature precedes many of these newer techniques and thus fibers are simply divided into slow, (type I) or fast, (type 2) fibers.^{16,58,67} As mentioned earlier, the soleus, a classic postural muscle, is composed largely of slow fibers, whereas the gastrocnemius muscle consists primarily of fast fibers. In addition, myosins expressed during em-

bryogenesis and in the neonatal period are also expressed during muscle regeneration. During traumatic injuries, toxin injection, and local anesthetic infusion, muscle fibers are destroyed, leading to formation of new fibers that express developmental myosins as they regenerate.²² These developmental myosins are also commonly expressed after denervation injury to muscle. The effect of tenotomy compared to denervation alone on the expression of myosins has been studied in rat muscle.³⁷ The total MHC content, slow and fast MHC, embryonic MHC, and muscle mass were measured. Total soleus MHC content decreased to 15% of control values 10 days after tenotomy. The gastrocnemius seemed more resistant and only decreased its total MHC to 70% of control values. There was only a transient shift between various MHC isoforms but no long-term changes were noted (Figs. 7,8). In the active and passive tenotomy model described by Tsai et al.,⁶⁶ tenotomy did not bring about any expression of embryonic myosins, commonly expressed after denervation injury or traumatic injury, nor was any fiber type change noted based on immunohistochemistry.^{1,38}

Relationship between Tenotomy and Innervation.

The effect of tenotomy on neural function is complex, involving both the efferent and afferent pathways. Tenotomy was traditionally used as a method for simulating immobilization of muscle,²² but, as mentioned earlier, this is probably not a straightforward comparison since the magnitude and the du-

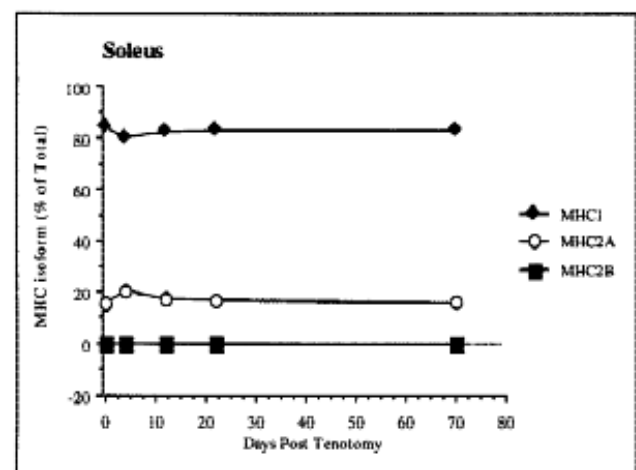


FIGURE 7. SDS-PAGE quantification of myosin heavy-chain composition at various time periods after tenotomy of the rat soleus. From Jakubiec-Puka et al.³⁷

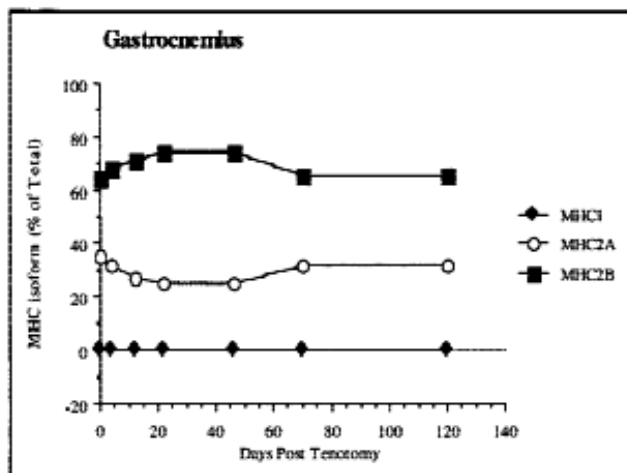


FIGURE 8. SDS-PAGE quantification of myosin heavy-chain composition at various time periods after tenotomy of the rat gastrocnemius. From Jakubiec-Puka et al.³⁷

ration of muscle unloading are not explicitly known. Electromyographic (EMG) activity is reportedly decreased or absent in animal tenotomy models.⁶⁷ The specific muscle and its physiological role leads to variable changes in response to tenotomy. Vrbová showed that the soleus, a postural muscle, sustains marked alteration in its EMG profile whereas tibialis anterior, a phasic muscle, maintains its EMG profile after tenotomy. Interestingly, within 1 day after spinal cord section, no reflex activity can be elicited in the soleus, whereas the tibialis anterior maintains its reflex activity on EMG analysis.⁶⁷ This may represent an inability of the muscle to be reflexly activated or may truly represent decreased neural drive to the muscle itself.

Sensory outflow from the cat gastrocnemius as measured by electromyography increases after tenotomy.³⁶ There is an increase in the amplitude of monosynaptic reflex as a result of stimulation of the afferent nerve of the tenotomized muscle.^{11,12,43} Degenerative changes are less severe in animals with interruption of sensory outflow from the tenotomized muscle.^{35,49} This could mean that neural activity may in some way be responsible for these events.

The occurrence of central fiber degeneration and formation of nemaline rods requires intact innervation in the rat soleus. According to Karpati et al., the absence of innervation brought about by cordotomy or sciatic neuropathy leads only to muscle atrophy.⁴² However, according to De Reuck, the formation of target fibers after tenotomy could be inhibited in the rat gastrocnemius by performing concurrent neurotomy.²⁴ It may be that subsequent

neural stimulation of an already shortened muscle leads to these changes or that the neural input has some trophic influence on the involved muscle fibers. Afferent pathways are probably very important in the degenerative effects of tenotomy. Cat soleus muscles immobilized in a shortened position, simulating tenotomy, underwent equal atrophy regardless of cordotomy or deafferentation.²⁷ Dorsal root section decreased the degree of tenotomy-induced atrophy in rat soleus, indicating that some abnormality in the afferent pathways may play a role in the etiology of muscle atrophy.⁴²

The presence of changes in the afferent outflow from muscle has been demonstrated using both physiological and histological studies. Coordination is affected by the output of Golgi tendon organs and muscle spindle receptors. They respond to both active contractions and passive stretch of muscle. Muscle spindle length is decreased in length in tenotomized muscle.³⁶ Tenotomized muscle has also been shown to have increased stretch sensitivity, indicating possible alteration in the output from muscle spindle receptors and Golgi tendon organs.⁷² The shortened state of tenotomized muscle does not fully explain these alterations in receptor output. Józsa et al. demonstrated that there is decreased periaxial space as well as fibrosis of the capsules of both muscle spindles and of Golgi tendon organs, with some receptors becoming completely fibrosed. They hypothesized that the changes in elasticity and fluid content result in diminished responses to periorgan pressure changes required for activation.⁴¹

Nerve-Muscle Communication after Tenotomy.

Neural cell adhesion molecule (NCAM) was expressed in the rabbit EDL within 1 day after both active and passive tenotomy.³⁸ NCAM is a cell-surface molecule that is involved in embryogenesis with the establishment of muscle-nerve and nerve-nerve connections.³² It is also expressed on the surface of denervated muscle cells²¹ and regenerating muscle cells.¹⁸ It is expressed neither in necrotic nor degenerating muscle fibers. NCAM has been used as a model to quantify muscle injury by determining the percentage of cells expressing the molecule.^{50,51} The expression of NCAM in the rabbit model may represent molecular evidence of denervation as well as regeneration after atrophy within tenotomized muscle or may simply represent acute shock to the neuromuscular junction that accompanies dramatic unloading with possible functional disruption of the neuromuscular junction. In a different model of muscle injury, eccentric contraction injury, Warren

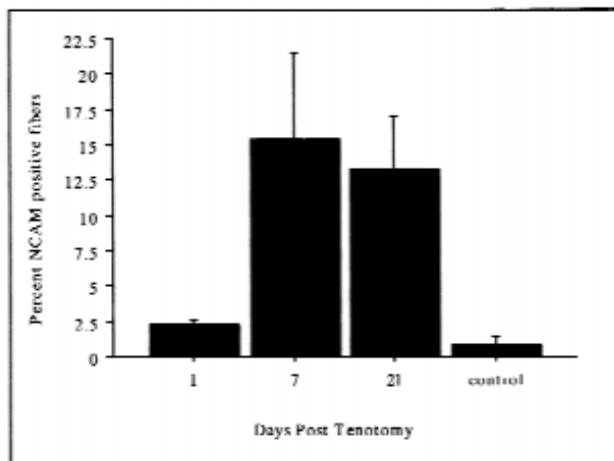


FIGURE 9. NCAM expression increases within 1 day after tenotomy in rabbit EDL muscle with further increases by 7 and 21 days. From Jamali et al.³⁸

et al. demonstrated changes typically associated with denervation in mechanically injured muscle. They reported a 79% increase in acetylcholine receptor level within 3 days after eccentric injury, which is analogous to that seen in a "transiently denervated muscle."⁶⁸ The acute changes seen with tenotomy within 1 day as well as the expression of NCAM in this time course may represent similar early chemical alterations in the muscle (Fig. 9).

CLINICAL IMPLICATIONS

As mentioned above, tendon injury is a common clinical entity, whether traumatic, degenerative, or surgically induced. Tenotomy results in decreased muscle length and corresponding sarcomere length, a change in the neural output from muscle receptors altering EMG activity. From a clinical standpoint, early tendon repair and mobilization is the best method to avoid pathological changes in the corresponding muscle by restoring the muscle to its original length. The idea of early primary tendon repair and mobilization to permit a smooth gliding surface has become a standard part of management of tendon injuries.^{34,60,61} As knowledge of the changes that take place in tenotomized muscle increases, it is increasingly apparent that the timing of tendon repair is extremely important to prevent these molecular and structural events. Delay in tendon repair may affect the ability to achieve normal length and function as a result of muscle contracture and atrophy. To investigate this, Tsai et al. performed tenotomy of rabbit EDL muscles. Maximum tetanic tension (P_o)

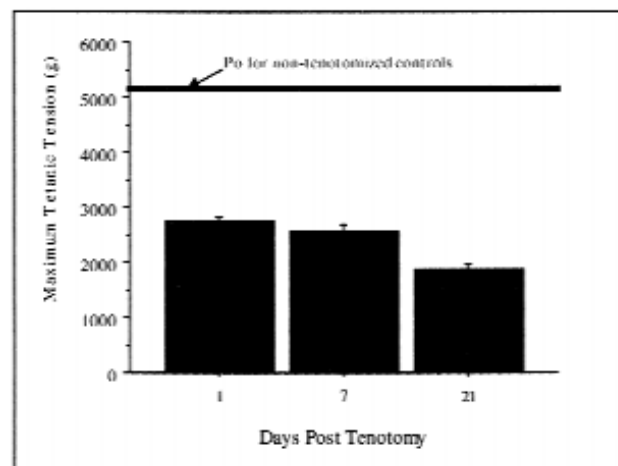


FIGURE 10. Maximum tetanic tension decreases to 50% of normal within 1 day after passive tenotomy, and this trend progresses at 7 days and at 21 days. From Tsai et al.⁶⁶

is a commonly used measure of muscle motor activity and function.^{9,69} Within 1 day after tenotomy, there was a 50% decline in maximum muscle tension production which continued to decrease over the ensuing 3 weeks (Fig. 10). In another experiment, rabbit EDL tendons were cut and then restored to their original length by suturing to the ankle retinaculum at 1 week, a time-course consistent with many flexor tendon repairs after injury. It was found that over the first 3 weeks after the repair, the previously observed decline was averted and maximum tension production increased precipitously by 1 day and then progressively to 21 days after repair, consistent with a regenerative process (Fig. 11). It was expected that

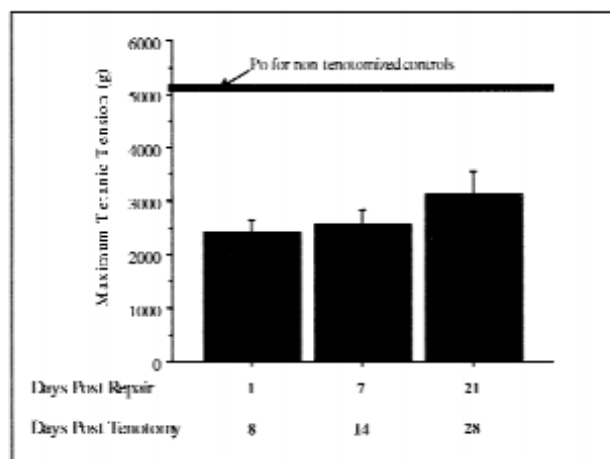


FIGURE 11. After simulated tendon repair, the maximum tetanic tension reverses its trend and instead progressively increases demonstrating the importance of tension in the myotendinous unit. From Tsai et al.⁶⁵

the rabbit muscles would respond by gaining sarcomeres after being pulled out to length. However, there was no change in the sarcomere number or sarcomere length in these groups. These data indicate that in the rabbit EDL, within 1 week, there is no significant change in sarcomere number. This is encouraging from a clinical standpoint, as it validates the 1 week window for performing delayed tendon repair.⁶⁵

Other modalities have also been shown to prevent muscle degeneration after tendon injury. Barry et al., using a rabbit soleus model, performed an Achilles tenotomy in the rabbit. They then maintained the leg immobilized for 2 weeks. After this point, the animals were either removed from the splint or maintained for another 2 weeks. In this "mobilized" group, some animals were treated with electrical stimulation. Thus, they compared the effect of natural recovery from immobilization, followed by natural recovery augmented by electrical stimulation using implanted electrodes attached to a mini-stimulator.¹⁰ In their immobilization groups, they confirmed similar myopathic changes seen with tenotomy, demonstrating decreased fiber area, decreased fiber occupancy per field, increased numbers of transitional and fast fibers, decreased tetanic tension, and increased rate of contraction and relaxation. The time of total immobilization was directly correlated with the degree of the above changes. The stimulation groups showed significant improvement in all of the above parameters compared to the nonstimulated animals. Thus, electrical stimulation may have a clinical role in preventing some of these degenerative changes. Multiple clinical studies have advocated a limited period of immobilization followed by early passive remobilization and early weightbearing after Achilles tendon repairs.^{19,47,64} Cetti et al. demonstrated in a prospective study that plantarflexion strength, gait, range of motion, and patient satisfaction were better after treatment of Achilles tendon rupture with a mobile cast that allowed early limited motion. These studies and others reflect the new awareness of muscle preservation using electrical stimulation, range of motion, and activity to minimize the degeneration and atrophy that accompany tenotomy.

It seems clear that muscle response to tendon injury is an area of interest beyond that of basic science alone. It is a common entity encountered in medical clinics on a daily basis. Whether seen in a patient with a traumatic injury such as a biceps or Achilles tendon rupture or in a postoperative patient recovering from a tendon transfer procedure, there are multiple structural and molecular events at play

within the muscular compartment. With this ongoing research, it is becoming increasingly apparent that long-term atrophy and architectural changes can be averted by early restoration of a point of attachment. This philosophy, combined with the modalities of electrical stimulation and early range of motion, will lead to lower levels of postinjury atrophy and shorter duration of rehabilitation.

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