Tendon: Principles of Healing and Repair

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Abstract

Tendon stores, releases, and dissipates energy to efficiently transmit contractile forces from muscle to bone. Tendon injury is exceedingly common, with the spectrum ranging from chronic tendinopathy to acute tendon rupture. Tendon generally develops according to three main steps: collagen fibrillogenesis, linear growth, and lateral growth. In the setting of injury, it also repairs and regenerates in three overlapping steps (inflammation, proliferation, and remodeling) with tendon-specific durations. Acute injury to the flexor and extensor tendons of the hand are of particular clinical importance to plastic surgeons, with tendon-specific treatment guided by the general principle of minimum protective immobilization followed by hand therapy to overcome potential adhesions. Thorough knowledge of the underlying biomechanical principles of tendon healing is required to provide optimal care to patients presenting with tendon injury.

Keywords
- tendon healing
- tendon repair
- tendon inflammation

Tendon has chiefly a mechanical part to play at the intersection of muscle and bone, directly transmitting contractile forces while dissolving stress that would otherwise concentrate should muscle interface directly with bone.[1,2] It stores, releases, and dissipates energy to efficiently maintain the joint-loading cycle while protecting adjacent tissues.[1] Nonetheless, tendinous injuries are exceedingly common, with 50% of musculoskeletal injuries recorded in the United States involving tendinous or ligamentous injury and 10% of people (50% of runners) experiencing Achilles tendinopathy by age of 45.[1,3] While tendon rupture usually corresponds to an acute incident, evidence suggests that chronic degenerative changes are usually present and contribute to the rupture.[4] Thus, it is crucial to consider tendon healing in the context of its development, regeneration, and of the histologic changes that reflect its long-term degeneration.

Tendon Anatomy and Classification

A firm grasp of hand and tendon anatomy is the backbone of a productive hand surgery practice. Mechanically, a functional, mature tendon is a highly hierarchical connective tissue composed of ensheathed fascicles of collagen (mainly type I) fibrils aligned with intervening fibroblasts. The tendon's outermost capsule is the epitenon, while its individual fascicles are contained in the endotenon. Paratenon overlies the epitenon in regions where no sheaths exist. All of these encapsulating structures are composed of connective tissue and provide most of the tendon's blood, nerve, and lymphatic supply.[5,6]

Macroscopically, a tendon should be conceptualized in thirds, each with different features and blood supply: the proximal myotendinous junction (MTJ), the distal osteotendinous junction (OTJ), and the central third or belly. The MTJ consists of tendinous collagen fibrils interfacing with myocyte processes and is most vulnerable to injury by tear. A tendon attaches to bone at the OTJ, which is segmented into four zones: dense connective tissue, uncalcified fibrocartilage, calcified fibrocartilage, and bone.[7] Vascularization to each third varies by tendon type. The OTJ and MTJ are largely supplied by an intrinsic system, with periosteal vessels and vessels from the muscle extending into the tendon fibrils.

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The extrinsic system supplies blood through the paratenon or through the synovial sheath via vincula, which are connective tissue bands bridging tendon to bone and containing tiny blood vessels.[8]

Muscular, cutaneous, and peritendinous nerve trunks innervate tendon, though few nerve fibers actually enter tendon proper, instead terminating on its surface as nerve endings.[8] Golgi tendon bodies are myelinated fiber nerve endings functioning as mechanoreceptors capable of detecting changes in tension or pressure—stretch receptors. They occur most frequently at the MTJ.[9] Unmyelinated parasympathetic and sympathetic nerve fiber endings function as nociceptors capable of transmitting and sensing pain.[10]

Three to seven vincula supply each flexor tendon (flexor digitorum superficialis [FDS] and flexor digitorum profundus [FDP]) in the human hand.[11] There are two triangular fibrous bands called vincula brevia in each finger, one connecting the FDS tendon to the proximal interphalangeal joint/P1 head and one connecting the FDP tendon to the distal interphalangeal (DIP) joint/P2 head. There are two longer and more slender bands in each finger called vincula longa, one connecting the FDS tendon to the base of P1 and one connecting the FDP and FDS tendons distal to Camper's chiasm.[11] Tension, friction, and compression can compromise tendon vascularity, which also decreases with age.[12]

Both flexor and extensor tendon lacerations are described by anatomical location. Anatomically, flexor tendon injuries can be classified by affected zone, with zones labeled one to five, distal to proximal. Zone 1 extends from FDP insertion to FDS insertion—FDP avulsion injuries, also known as jersey finger, in this zone are described using the Leddy–Packer classification.[13,14] Zone 2 spans the FDS insertion to the A1 pulley. Zone 3 is from the distal palmar crease to the carpal tunnel. The carpal tunnel constitutes Zone 4, while Zone 5 spans the wrist to the forearm. Extensor injuries are similarly categorized by affected zone, ranging from Zone 1 at the DIP, the disruption of which causes mallet fingers, to Zone 9 encompassing most of the upper forearm.[15]

Epidemiology of Tendon Injury

The dramatic increase in tendon injuries in recent decades is attributable in large part to a population-level shift toward active living. Interestingly, despite being the strongest tendon in the human body, the Achilles tendon is injured more frequently than any other, succumbing to tensional forces created by repetitive movements in strenuous sporting activity.[16] Of particular interest to plastic surgeons, hand injuries represent up to 20% of all injuries treated in emergency departments, with 55 and 93% of patients, respectively, treated for short-superficial or short-deep hand lacerations experiencing concomitant tendon injury. For reference, tendinous hand injury was found to be 23 times more common than scaphoid fractures.[6,17]

A higher propensity for tendinous hand injury has been reported in men as compared with women—a finding largely attributed to gender-related activities.[17–19] A higher incidence of extensor tendon injuries (as compared with flexor tendon injuries) and of injuries to the index finger has been reported compared with other digits.[17] Importantly, flexor tendon injury occurs most frequently in Zone 2 with the profundus tendon to the small finger identified as the most common flexor tendon injured.[17,20]

Development and Structure of Healthy Tendon

While tissue-specific checkpoints govern fibrillogenesis throughout the body, tendon generally develops according to three main steps: (1) tendon collagen fibrillogenesis, (2) linear growth, and (3) lateral growth.[1,21,22] The first step consists of immature fibril formation by extracellular assembly of collagen molecules. In the second step, the fibril intermediates attach end-to-end and attain mechanical/lengthwise maturity. Large diameter fibrils spawn in the third step as a result of side-to-side attachment of multiple long fibrils.[22] Though tendon in its mature form is approximately 70% collagen I, other regulatory molecules are essential as they underpin tissue-specific fibrillogenesis. For example, it is known from animal models that prominent expression of collagen III may be related to smaller fibril diameter and suppressed lateral growth of collagen I. The opposite is thought to be true about dermatan sulfate or chondroitin proteoglycan side chains, which are thought to be associated with larger diameter fibrils.[23–25]

Acute and Chronic Changes in Tendon Injury

While extreme exercise, concomitant loading, aging, and oxidative stress are recognized as physical and biological factors that engender tendinopathy, the exact pathogenesis of tendinopathy is poorly defined. For years, the accepted model of tendinopathy was one of tendinitis, or inflammation. More recent histopathological studies have identified tendinosis (chronic degeneration), as the culprit in most cases of tendinopathy.[26–30] It is responsible for the symptoms of pain, decreased strength, and impairment in activities of daily living commonly attributed to tendinitis. The affected region in tendinosis exhibits structural and cellular changes relative to unaffected tissue. While healthy tendon is characterized by parallel, wavy, clearly defined bundles of collagen, diseased tissue is recognizable by its lack of alignment or demarcation between neighboring bundles and its increased diameter.[31] On a cellular level, tendinosis is characterized by neovascularization, hypercellularity, and atypical fibroblast proliferation.[32] Tenocytes capable of producing collagen change shape, with their nuclei exhibiting signs of fibrocartilaginous metaplasia.[33,34] Biomechanically, tendinosis predisposes tendon to rupture.[4]

Similar features have been observed in senescent tendon. Aging decreases tenoblast volume and plasmalemmal surface density, increases the nucleus-to-cytoplasm ratio, and suppresses protein synthesis.[1] Collectively, these features contribute to decreased collagen turnover, characterized by thicker collagen fibers with greater variability in fiber diameter. The activity of lysol oxidase, an enzyme essential

for collagen production, decreases, which in turn increases nonreducible collagen cross-linking.[1,35] Biomechanically, this impedes capacity to withstand loading and increases stiffness.[1]

In the setting of acute intrasynovial flexor tendon injury, disruption of the tissue surrounding the lacerated tendon compound the severity of injury. Leakage of synovial fluid from within the digital sheath causes tendon starvation, slowing the repair process. This occurs through absolute synovial fluid loss, but also through disruption of the pressure distribution crucial to the process of imbibition by which tendon gets most of its nutrients.[36] It follows logically that injury to the tendon blood supply itself also hinders tendon healing in the acute setting. Importantly, as surgical apposition of the two ends of an injured tendon remains the gold standard for tendon injury treatment, one must be mindful to limit intraoperative trauma, which is additive to the severity of the original injury.

A common nontraumatic pathology of hand tendons is proliferative extensor tenosynovitis of the wrist, a condition well-documented in patients diagnosed with rheumatoid arthritis. It is characterized by pain and limited range of motion localizing to the fourth extensor compartment and can lead to tendon rupture.[37] In the context of rheumatoid arthritis, the proliferation is due to synovial tissue hypertrophy, inflammation, and fluid production. Histologically, the pathology infiltrates the tendon proper and exhibits fibrinous adhesions, a feature also observed in tendon healing from acute or chronic traumatic injury.[37]

Repair and Regeneration

Similar to fibrillogenesis, tendon regeneration can be distilled down to three overlapping steps: (1) inflammation, (2) proliferation, and (3) remodeling.[1] The inflammatory stage lasts approximately 48 hours and consists of erythrocyte, leukocyte, endothelial chemoattractant, and platelet infiltration. At this point, the role of macrophages is to consume the necrotic tissue. The proliferative stage is characterized by macrophage and tenocyte-directed synthesis of new, less durable collagen III, the predominant tendon tissue. The tenocytes in this second stage primarily proliferate in the epitenon. The proliferative phase occurs for a period of 7 to 21 days. The third stage begins months after the initial injury, can last longer than 12 months, and involves extracellular matrix alignment and collagen I synthesis replacing the collagen III. Collagen fibers undergo maturation and reorient themselves parallel to the direction of mechanical stress. However, the regenerated tissue has a scar-like appearance and is biomechanically inferior to the original healthy tendon.[38–40]

The three phases of tendon healing occur through a combination of extrinsic and intrinsic mechanisms.[36] The extrinsic mechanism involves inflammatory cells and fibroblasts infiltrating from surrounding tissue, whereas in the intrinsic mechanism, these cells originate from the tendon and epitenon. The extrinsic mechanism predominates earlier in the healing process while the intrinsic mechanism can be delayed, sometimes for days. This difference is attributable to the synovium's enhanced inflammatory and proliferative capacity as compared with the tendon proper.[36] Importantly, extrinsic-predominant healing is associated with larger tendon diameter, increased collagen disorganization, and consequently a propensity to adhere to peritendinous tissue (tendon adhesions). On the other hand, intrinsic healing constitutes the basis upon which early active range of motion protocols are made possible. Thus, through a mix of meticulous surgical technique and early rehabilitation, treatment teams seek to activate the intrinsic pathway rather than the extrinsic pathway. In practice, the goal of treatment is to identify the minimum amount of motion to avoid scarring and tethering to nearby tissue while avoiding jeopardizing the repair site.

From a surgical repair standpoint, it is generally accepted that repair strength is proportionate to the number of strands spanning the repair site, with traditional repair techniques including Tajima and Kessler (two sutures across the repair site) becoming less popular in favor of techniques with four to eight strands across the repair site and a running epitenon stitch.[1] While there is controversy on the use of braided sutures over monofilament in certain repairs such as rotator cuff repairs, monofilament is preferred in the flexor tendons of the hand as it generates less friction and tendon deformity than braided sutures.[41–44]

Other factors that affect tenorrhaphy strength include suture caliber, position ("locked" vs. "grasping"), material, and degree of gap formation across the apposition site.[45] While surgeons largely opt for 3–0 over 4–0 suture in tendon repair due to its tensile strength, this preference comes at the cost of a more traumatic repair process that may further delay healing.[45] Further, while locked sutures confer the added benefit of better mechanical load distribution (as compared with grasping sutures), the position of the knot relative to the repair site has been shown to have little impact on repair strength.[45] Knots external to the repair site may interfere with adjacent structures while knots on the repair site increase the overall diameter of the repair.[45] Regardless, it is important to note that circumferential sutures have proven to be mainly useful as additive—for orientation purposes—to core tendon suture.

Practical Approach for Surgeons

For surgeons to achieve an optimal tendon repair, an appropriate balance between durable tendon repair against excessive adhesion formation must be achieved. Careful selection of the appropriate repair technique and timely rehabilitation has the potential to significantly improve treatment outcomes.

As mentioned previously, tendon repair strength is derived from the number of strands crossing the repair site and from the suture caliber.[46] Further, locked and epitendinous sutures provide more biomechanical leverage. In flexor tendon injury repair, the A2 and A4 pulleys can be vented to ease gliding across the system—this has been associated with better functional recovery.[47] Due to the fact that

prolonged tendon immobilization has been associated with significant repair strength, but increased risk of adhesion formation, pyramidal rehabilitation protocols, whereby range of motion exercises with progressive loading are incorporated to limit adhesion formation, are gaining traction.[47]

When tendon repair rehabilitation protocols across injuries to all zones were compared, no significant difference between active and passive movement protocols was found. Duran protocols, involving controlled passive motion, resulted in the fewest postoperative tendon ruptures (2.3%).[48] Another study found passive range of motion protocols to be associated with fewer tendon ruptures, but greater decrease in range of motion as compared with active motion protocols.[49] The most appropriate postoperative rehabilitation program remains a controversial subject, and each protocol should be personalized based on the type of injury characteristics, surgical technique, and postoperative patient compliance.

Conclusion

Tendon injury is an exceedingly common presentation to emergency departments, making it one of the conditions most frequently treated by plastic surgeons. Factors such as age, mechanism of injury, time to repair, and physical exam findings play critical roles in determining the optimal method of management and postoperative rehabilitation. Hand surgeon familiarity with the subtleties of tendon healing is thus essential to ensure favorable long-term outcomes.

Conflict of Interest
None declared.

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