Tendon and ligament: basic science, injury and repair

Kalpesh Parmar

Abstract

Tendons and ligaments share many similar features in structure and function. They are load-bearing structures, with tendons transmitting forces from muscle to bone and ligaments transmitting forces from bone to bone. They have specialized zones (at the myotendinous junction for tendons and at the insertion to bone for both), which manage stress loading at these specific areas. They both have a hierarchical physical structure, mainly composed of type I collagen, and both elongate with a typical stress–strain pattern. Injury to both tendons and ligaments is followed by the same pattern of healing phases and can take up to two years to remodel back to a normal structure. The major cell type is the tenocyte (specialised fibroblast) in both tendons and ligaments. They are found within an extracellular matrix. Tendinopathy causes pain and swelling within tendons. Inflammatory cells and myxoid degeneration are characteristic features, with angiogenesis and small fibre nerve growth also seen. The causes are multifactorial and brought together by several hypotheses.

Keywords anatomy; basic science; injury; ligament; repair; tendinopathy; tendon

Tendon and ligament anatomy

There are specialized areas of tendon and ligament at their attachments. The attachment of tendons and ligaments to bone is termed the enthesis, whilst the attachment of tendon to muscle is termed the myotendinous junction.

There are two types of enthesis; fibrous and fibrocartilaginous. In a fibrous enthesis the tendon or ligament attaches directly to bone (such as the deltoid tendon attachment to the humerus); in a fibrocartilaginous enthesis, there are transitional zones – uncalcified fibrocartilage, calcified fibrocartilage and bone (such as is seen in the Achilles tendon). The enthesis dissipates stress at the junction between the relatively soft tendon and the hard bone and thereby reduces peak stress. The myotendinous junction is a highly specialised region where collagen fibrils are inserted deep into recesses formed by myocytes. This arrangement allows transmission of tension forces across the tendon and muscle interface.[1]

Tendons are composed mainly of water and type 1 (85%) collagen, arranged in hierarchical levels of complexity (Figure 1).

Other types of collagen are present at the enthesis, as well around blood vessels. Around major tendon bundles, as well as around the whole tendon itself, there is a thin reticular connective tissue called the epitenon. This transmits lymphatic and blood vessels as well as nerve fibres. Tendon sheaths are found where tendons bend sharply around bone (such as the tibialis posterior around the medial malleolus). The sheath contains synovial fluid to aid movement and reduce friction. The Achilles and patellar tendons have a 'false sheaths' termed the paratenon, which is a condensation of surrounding connective tissue.[2] The functions of this are to allow vascularization of the epitenon, reduce friction and facilitate free movement.

Tendons come in various shapes and sizes. Some have shallow groves on their surface and others are divided into slips (e.g. the obturator internus). The largest tendon is the Achilles tendon. As a general rule, extensor tendons are flatter than flexor tendons, which tend to be round or oval. The extensor tendons, by being flat and having fibrous interconnections, reduce the risk of subluxation as they pass over convex structures such as the metacarpophalangeal and interphalangeal joints when flexing the fingers. The longest tendons are those of the hands and feet and, as well as having an effect on movement, have biomechanical properties related to their length and course that need to be taken into account. Strategic placement of tendons means they acts as effective pulleys - an example would the Achilles tendon using the superior tuberosity of the calcaneus as a pulley to maximize the change in the tendon moment arm as the foot moves from dorsiflexion and plantar flexion.[2]

The extracellular matrix (ECM) surrounds collagen and tendon cells. It is composed of a mixture of proteoglycans, glycoproteins, elastin and various other inorganic molecules (such as calcium, copper and manganese). The ECM binds together fibrils of the collagen fibres in a parallel alignment to allow gliding of the fibrils on movement and diffusion of water soluble molecules.[1]

The major cell type in tendons is the tenocyte. These are specialized fibroblasts, arranged longitudinally around collagen fibrils and are responsible for the secretion of the ECM. Tendons and tendon cells respond to mechanical load. The tenocytes upregulate collagen synthesis when subjected to tensional forces; this occurs through a complex communication system involving gap junctions and neighbouring cells.[2]

As a general rule, a tendon has a vascular supply which is quantitatively considerably less than that of muscle (which gives it its characteristic white appearance).[2] The blood supply is from three different sites: the myotendinous junction; the osteotendinous junction and the tendon sheath. The main supply comes from the tendon sheath, from where a rich vascular network penetrates deep into the tendon. The muscle supplies the tendon with vascular branches in its proximal portion. The osteotendinous junction contributes a limited blood supply, being restricted to the insertion site itself.[1] The vessels are small and thin walled; blood flow varies depending on exercise levels and can be captured on Doppler ultrasound at varying degrees of loading. Tendons can have areas of poor vascularization. These are particularly seen where tendons cross bone (e.g. in the peroneus longus and tibialis posterior tendons). Angiogenesis seems to be restrained at these sites due to inhibitory factors being secreted from cells (such as endostatin – an inhibitor of angiogenesis).[2]

The nerve supply to tendons is mainly sensory. Nerve branches originate from cutaneous, muscular and peritendinous nerves, mainly terminating in the paratenon/tendon sheath.

Kalpesh Parmar *MBChB MRCSEd MSpMed MSc Med USS FFSEM (UK)*
Consultant in Sports and Exercise Medicine, London Sports Orthopaedics, UK. Conflicts of interest: none declared.

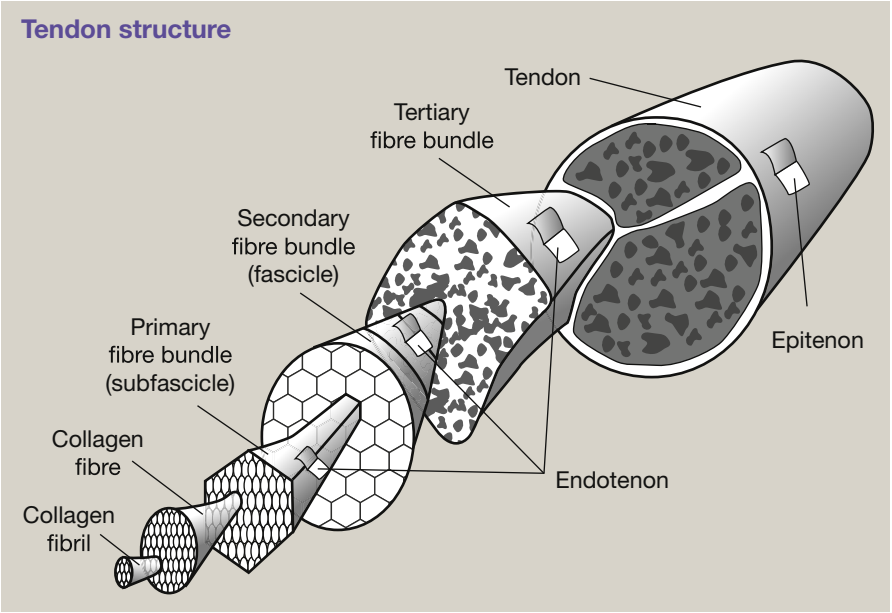

Figure 1 Schematic diagram of tendon in cross-section. Collagen fibrils are bundled into fascicles containing vessels, lymphatics and nerves. The fascicles are grouped together, surrounded by epitenon, and form the gross structure of the tendon, which is further enclosed by paratenon.[3]

Some nerve fibres enter the tendon itself and follow the vascular network into the body of the tendon. These nerves act as Golgi-type organs, mainly located at the myotendinous junction. They detect changes in pressure and pain (with associated neurotransmitters glutamate, acetylcholine and substance P).[1] Nerves can grow into damaged or ruptured tendons in association with blood vessels; this tends to correlate with areas of tendon pain. There is a degree of neuronal plasticity whereby tendon loading can cause involution of the initial ingrowth of nerves into a damaged tendon.[2]

Tendons can elastically recoil after a stretching force is removed. This is functionally related to 'crimps' within the tendon fibrils. When stretched, a tendon reduces the number of crimp zones; recoil of tendon fibrils then occurs on removing the stretch, generating force.[2]

There are various anatomically specialized zones in relation to tendons. Around joint capsules, tendons tend to attach beyond the joint and can blend to the joint capsule, resulting in a common attachment (e.g. as seen in the rotator cuff of the shoulder). Fascial connections of tendons are also seen, especially around bone. Stress dissipation occurs at the enthesis as a result (e.g. as seen at the insertion of the biceps brachii tendon to the bicipital aponeurosis and radial tuberosity). Bursae are closely related to tendons at insertion points e.g. the retrocalcaneal bursa. Fat pads are located close to tendons. Large fat pads are seen adjacent to the Achilles and patellar tendons. They are richly vascularized and innervated. The infrapatellar fat pad (Hoffa's fat pad) has finger-like extensions of fat projecting into the patellar tendon whilst Kager's fat pad moves in and out the of the retrocalcaneal bursa with ankle plantar and dorsiflexion.

Ligaments

Ligaments are short fibrous bands connecting bone or supporting soft tissue structures. They are hierarchically organized and composed mainly of type I collagen fibres (70% dry weight) (Figure 1). They also contain small amounts of elastin, though proportionally more than tendons, and also display a crimp pattern which allows elongation in relation to load. At the insertion into bone, the ligament becomes more flexible and can have either a direct or indirect insertion. Direct insertions are associated with long ligaments inserting into small areas of bone. They comprise of four distinct zones: ligament; unmineralized fibrocartilage; mineralized fibrocartilage and bone. An example is the femoral origin of the anterior cruciate ligament.

Indirect insertions are generally found on short ligaments that insert into a larger area. They connect to bone via Sharpey's fibres — collagen fibres continuous from ligament to bone forming a very strong attachment. An example would be the tibial attachment of the medial collateral ligament.

On application of load, the ligament fibres initially straighten their crimp pattern under relatively small forces (toe phase). As fibrils become uncrimped, the ligament stiffens and then absorbs considerably greater energy from applied force, elongating in a linear fashion until failure occurs (called the yield phase) (Figure 2).[4]

Blood supply to ligaments is via diffusion from synovium and from the extracellular space around the periphery of tendons; in the central part of tendon, there is a complex of vessels passing longitudinally through the ligament.[5] Its importance is for nutrition of the central part of the tendon. Knee ligaments have been found to have proprioceptive and nociceptive nerve endings. The cruciate ligaments accommodate morphologically different sensory nerve endings (Ruffini endings, Pacinian corpuscles, Golgi tendon organ-like endings, and free nerve endings) with different capabilities, providing the central nervous system with information not only about noxious and chemical events but also about characteristics of movements and position-related stretches of these ligaments.[6]

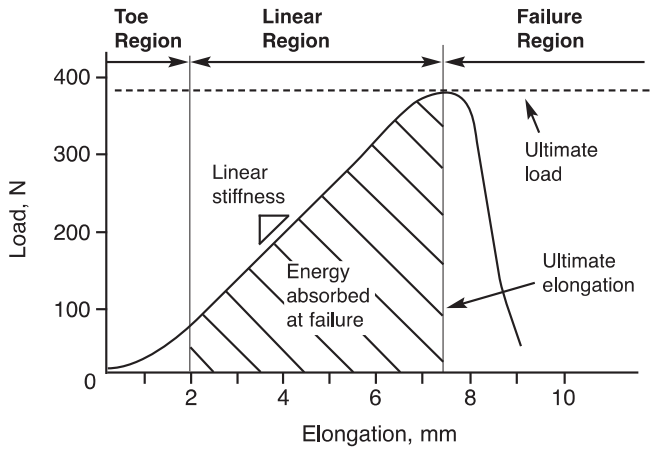

Figure 2 Typical stress–strain curve describing the mechanical properties of the medial collateral ligament of the knee, mid-substance.[4]

Injury to ligaments elicits a healing response. The first phase is the haemorrhagic phase with a haematoma formation around the injured ligament. An inflammatory phase then occurs with the influx of inflammatory cells and monocytes replacing the haematoma with granulation tissue. After around 2 weeks an immature collagen matrix replaces the granulation tissue, with the extracellular matrix in a random configuration in the central part of the ligament. This marks the start of the reparative phase, in the course of which the ligament comes to superficially resemble its pre-injury appearance after several weeks. The last phase is the remodelling phase. Collagen fibres continue to align along the axis of the ligament with maturation of the collagen matrix. This can takes months or even years after the injury.[4]

Loading of tendons during exercise promotes tendon remodelling. The process involves both degradation and, immediately after exercise, synthesis of collagen. There is also a breakdown of the ECM catalysed by metalloproteinases, suggested to play a part in tendon adaptation. There is an observed increase in collagen production from an increased number of tendon-derived progenitor cells. Increasing age and the female gender are intrinsic factors whilst lack of exercise, smoking, obesity and high cholesterol are associated with tendon degradation rather than adaptation.[7]

The enthesis

The enthesis is sometimes termed the osteotendinous and osteoligamentous junction. Stress concentrations at the hard-soft tissue interface make the enthesis vulnerable to acute and overuse injury and rheumatological conditions including seronegative spondyloarthropathies such as ankylosing spondylitis.

Many tendons and ligaments attach obliquely to bone. The 'enthesis organ' is a collection of related tissues near the enthesis helping to dissipate stress. The Achilles tendon is a good example with its attachment to the calcaneus. There is an osteotendinous junction with prominent fibrocartilage, a sesamoid fibrocartilage near the deep surface of the tendon and a periosteal fibrocartilage covering the calcaneus. Kager's fat has a wedge-shaped tip of fat protruding into the retrocalcaneal bursa during plantar flexion. The above structures work together in dissipating stress at the enthesis.[4]

All fibrocartilages associated with entheses are avascular under normal circumstances. Vascularity at the enthesis occurs as a result of the influence of vascular endothelial growth factor (VEGF) and endostatin. Adipose tissue around the enthesis contains nerves and blood vessels which could play a role in proprioception.[4]

Tendinopathy

Tendinopathy is characterized by prolonged pain and swelling of a tendon and is mainly a degenerative process (tendinosis). Characteristic findings are: non-acute inflammatory cells, myxoid degeneration and an increase in ground substance. There are also an increased number of tenocyte nuclei, lipid vacuoles and hypoxia with angiogenesis and small nerve ingrowth. This reflects a failure of the tendon repair process. At the level of the tendon sheath/paratenon, the pathology is termed tenosynovitis/paratendinopathy.[8]

Causes of tendinopathy are multifactorial, with altered mechanical loading being the most important factor. Fatigue of collagen fibrils makes tendons susceptible to pathological changes. The amount of tensile stress needed to cause microscopic tendon damage is around 4–8% with complete failure of the tendon occurring at over 12%. Common tendinopathies include the Achilles and patellar tendons in the lower limb and the lateral epicondyle of the elbow in the upper limb.[8] Currently there are three hypotheses for tendon degeneration: mechanical overuse; vascularization and ageing. Repetitive tensile loading causes micro-tears within the tendon leading to growth factor release and vascular ingrowth. Necrotic capillaries contribute to vascular compromise causing hypoxia and subsequent degeneration.[1]

Tendon cells and the ECM control tendon healing. Following tendon injury, tissue inflammation, cell proliferation and ECM remodelling occur. The inflammatory stage begins with the formation of a haematoma. Pro-inflammatory cytokines and fibroblasts start the healing process with angiogenesis occurring, forming a vascular network sufficient to stabilize the injury in the initial stages. The next stage is the proliferation stage. ECM proteoglycans and collagens (mainly type III) are synthesized by fibroblasts and arranged randomly. Increased cellularity and water absorption also occur. The last stage, the remodelling stage, begins around 6–8 weeks after the injury and takes 1–2 years to complete, depending on the age of the patient and condition of the tendon. Consolidation occurs with a decrease in cellularity and matrix production and replacement of type III with type I collagen, causing the tendon to become more fibrous. Collagen fibres start to organise longitudinally, restoring tendon stiffness and tensile strength. After 10 weeks, the maturation stage occurs with an increase in collagen fibre cross-linking.

Conclusion

Tendon and ligament share many structural features and are specially adapted to transmit forces in the musculoskeletal system whilst providing sensory feedback to the neural system. The nerve and blood supply support these functions and the metabolic demands of the tissue are low. However this means that the

process of healing and remodelling are relatively slow, following a pathway similar to fracture healing. Care has to be taken in the rehabilitation after injury to promote the progress and maturity of healing without risking structural failure. ◆

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