Ligament Injury and Healing: A Review of Current Clinical Diagnostics and Therapeutics
The Open Rehabilitation Journal
2013; No. 6; pp. 1-20

This article has 203 references

KEY POINTS FROM THIS ARTICLE:

1) “Ligament injuries are among the most common causes of musculoskeletal joint pain and disability encountered in primary practice today.”

2) “Ligament injuries create disruptions in the balance between joint mobility and joint stability, causing abnormal force transmission through the joint, which results in damage to other structures in and around the joint.”

3) “The long-term consequence of non-healed ligament injury is osteoarthritis, the most common joint disorder in the world today.”

4) Ligaments heal through a distinct sequence of cellular events that take place in three consecutive stages:
   A) Acute inflammatory phase
   B) Proliferative or regenerative phase
   C) Tissue remodeling phase

INFLAMMATION PHASE 48-72 hours

PROLIFERATIVE PHASE Several Months

REMODELING PHASE Months to Years

AA) The acute inflammatory phase begins within minutes of injury and continues over the next 48 to 72 hours. Neutrophils, monocytes, and other immune cells migrate to the injured tissue where they ingest and remove debris and damaged cells.

BB) “The proliferative/repair phase begins when immune cells release various growth factors and cytokines. This initiates fibroblast proliferation signals for rebuilding of the ligament tissue matrix.”

CC) “After a few weeks, the proliferative phase merges into the remodeling phase, during which time collagen maturation begins, often lasting for months to as long as years after the initial injury.”
The tissue formed initially appears as disorganized scar tissue. With time, the collagen becomes aligned with the long axis of the ligament during this time; “however, the newly-formed collagen fibrils are abnormal and smaller in diameter than normal ligament tissue.”

“The remodeling phase of ligament repair can continue for many months to years.”

5) Ligament healing “can take months to resolve itself,” and “many ligaments do not regain their normal tensile strength.”

6) MRI and X-rays as diagnostic procedures for ligament injury are inadequate, often leading to “inconclusive or inaccurate readings.”

7) “Ultrasound and digital motion X-ray are able to provide a more detailed image of a ligament’s structure and function.”

8) In ligament healing, “early resumption of activity can stimulate repair and restoration of function and that prolonging rest may actually delay recovery and adversely affect the tissue’s response to repair.”

9) “There is a shift away from the use of steroid injections and nonsteroidal antiinflammatory drugs, as their use has been shown to inhibit the histological, biochemical, and biomechanical properties of ligament healing.”

10) Steroid and nonsteroidal antiinflammatory drugs are “no longer recommended for chronic soft tissue injuries or for acute ligament injuries, except for the shortest possible time, if at all.”

11) Prolotherapy helps resolve ligament injuries of the spine and peripheral joints.

12) Intrinsic ligament injuries occur as a result of improper motion within the joint. [Very Important, as subluxation is improper motion]

13) Extrinsic ligament injuries occur as a result external mechanical factors.

14) Women are ligament dominant; Men are muscle dominant. “Consequently, sprained ligaments occur more frequently in women than in men.”

15) Menstrual cycle hormonal factors may make women more prone to ligament injury.

16) Alterations in the biology and biomechanics of injured ligaments lead to “inadequate healing and tissue formation that is inferior to the tissue it has replaced.” “The incomplete healing and lower integrity of the new ligament tissue results in ligament laxity, predisposing the joint to further injury.”
17) The “cycle of ligament injury and subsequent laxity causes joint instability, which then leads to chronic pain, diminished function, and ultimately, to osteoarthritis (OA) of the affected joint.”

18) “OA remains the long-term consequence of ligament injury and continues to be the most common joint disorder in the world.”

19) Collagen is 75% of the dry weight of ligaments. Type I collagen is 85% of the total collagen within ligaments. “After injury, fibroblasts primarily synthesize type III collagen, not type I collagen.”

20) Ligaments are covered by a vascular and cellular layer called the epiligament, which “contains sensory and proprioceptive nerves.” [Important]

21) “When ligaments are strained, the proprioceptive nerves initiate neurological feedback signals that activate muscle contraction around the joint, allowing the body to protect and stabilize the joint after injury.” [Important]

22) Ligament attachment to the periosteum can be traumatized; “recurring stress causes inflammation and often fibrosis.”

23) “As ligament load is increased, more ligament fibers are recruited (straight lines), and the slack in the fibers is removed until the entire ligament tears.”
24) “Creep is defined as the deformation or elongation of a ligament over time under a constant load or stress.”

25) “When ligaments are stretched or elongated past a certain point for a prolonged period of time, they can lose their ability to retain their original shape. When this occurs, the ligament becomes lax and unable to properly support the joint, leading to instability and pain, and eventually to OA of the joint.”

26) Ligaments have an important role as sensory organs involved in ligamento-muscular reflexes, protecting the joint and preventing injury when the ligament and joint are under stress.

27) Ligaments contain mechanoreceptors, providing proprioception and kinesthesia, causing activation or inhibition of muscular activities to protect the joint through neurological reflexes. The muscular activation caused by ligament reflexes provides for the preservation of joint stability.

28) “The injured ligament structure is replaced with tissue that is grossly, histologically, biochemically, and biomechanically similar to scar tissue.” “Even fully remodeled scar tissue remains grossly, microscopically, and functionally different from normal tissues.”

29) “The persisting abnormalities present in the remodeled ligament matrix can have profound implications on joint biomechanics, depending on the functional demands placed on the tissue.”

30) “Since remodeled ligament tissue is morphologically and biomechanically inferior to normal ligament tissue, ligament laxity results, causing functional disability of the affected joint and predisposing other soft tissues in and around the joint to further damage.”

31) Importantly, the abnormal remodeled matrix includes “abnormal innervations.” [Important]

32) The inner layer of the joint capsule has the synovium which produces the synovial fluid. Capsular injury often alters the viscosity of the synovial fluid, causing long-term alteration in joint lubrication and function. Prolonged inflammation further alters the viscosity of the synovial fluid.

33) The “remodeled ligaments are not nearly as good as new.”

34) Abnormal cross-linking of collagen fibrils in repaired ligaments cause weakness and stiffness, “often remaining for months or years after initial injury.”

35) Injured ligaments typically regain only 40% to 80% of their normal strength.
Post injury ligament weakness and joint laxity “causes alterations in the load distribution of the joint, which disrupts the underlying cartilage and bone, causing wear and increasing shear. In time, this leads to osteochondral degeneration or OA.”

“OA begins when one or more ligaments become unstable or lax, and the bones begin to track improperly and put pressure on different areas, resulting in the rubbing of bone on cartilage. This causes the breakdown of cartilage and ultimately leads to deterioration, whereby the joint is reduced to bone on bone, a mechanical problem of the joint that leads to abnormality of the joint’s mechanics.”

“Hypermobility and ligament laxity have become clear risk factors for the prevalence of OA”

“The most important diagnostic tools in treating any bodily injury are the patient’s physical symptoms.”

“One major shortcoming in MRI evaluation of ligaments is that, while it is semi-effective at recognizing major tissue disruptions including complete ligament tears, MRI is unable to detect when ligaments are lax or stretched.” “An injured ligament that has become stretched two or even three times its normal length appears no differently than an uninjured one because MRI only shows soft tissue contrast, not tissue quality.”

Imaging by diagnostic musculoskeletal ultrasound, especially B-mode (brightness mode) sonography, displays the entire physiologic spectrum from active inflammation to resolved fibrosis.

X-rays “pick up certain structural abnormalities that are considered indicative of particular ligament injuries.”

“Cineradiography such as Digital Motion X-ray (DMX) has been used as a means of visualizing the moving joint under radiography or fluoroscopy. DMX is able to spot ligament damage that static films and MRI miss and shows limitations of certain motions of the joint, providing the clinician with insight into the functionality of particular ligaments. Although it can be used to observe the motion of any mobile joint, DMX is particularly useful in diagnosing upper cervical ligament injury, especially in the case of C1-C2 vertebral segments which have no discs.”

“Ligament healing is slow and often incomplete.”

“Joint laxity caused by ligament injury improves slowly over a period of 6 weeks to a year, after which a large percentage of patients still have objective mechanical laxity and subjective joint instability.”

Early controlled resumption of activity after injury enhances regeneration and improves matrix organization and strength.
47) “Immobilizing a joint with a ligament injury can cause detrimental side effects, such as synovial adhesions, an increase in collagen degradation and a subsequent decrease in collagen synthesis, and a greater percentage of disorganized collagen fibrils.”

48) “According to the most recent systematic reviews on research into soft tissue injuries in humans, no controlled studies appear to favor immobilization for the treatment of ligament injuries.”

49) “Carefully controlled exercise plans promote healing of injured ligaments. Motion itself causes an increase in blood flow to the affected joint, providing the damaged tissue of the ligament with nutrients and metabolites necessary for its repair and healing.”

50) “Mobilization for the treatment of soft tissue damage has also been found to decrease muscle atrophy, osteoporosis, adhesions, and joint stiffness following injury.”

51) NSAIDs are potentially deleterious to soft tissue healing. NSAIDS inhibit ligament healing and “lead to impaired mechanical strength.”

52) “NSAIDs are no longer recommended for chronic soft tissue (ligament) injuries, and their use is cautioned in athletes who have ligament injuries. In the case of acute ligament injuries, NSAIDs should be used for the shortest period of time possible, if used at all.”

53) Corticosteroid injections “inhibit the histological, biochemical, and biomechanical properties of ligament healing.” Corticosteroid injections into injured ligaments have an adverse effect on healing; they inhibit fibroblast function and collagen synthesis. Steroid-injected ligaments have smaller cross sectional area and are weaker.

54) “Diet and nutrition have an effect on the body’s homeostasis, including the ligaments and their potential to heal.” A major culprit in the development of OA is the American diet. It causes poor circulation to the microscopic blood vessels that carry oxygen and other nutrients to the joints. “Since the articulating bone and surrounding joint cartilage receive their nourishment and oxygen from both joint capsule fluid and small blood vessels, they become compromised when the supply of blood becomes impaired.”

55) Vitamins and minerals help provide the body with energy and promote tissue repair.

56) “After ligaments have been surgically repaired or reconstructed, they remain weaker than the original ligaments and are unable to hold the same tensile load.”
Prolotherapy (proliferative therapy, regenerative injection therapy and platelet rich plasma) involves the injection of small amounts of proliferant solutions (hypertonic dextrose, sodium morrhuate, platelet rich plasma) into ligaments and tendons at the painful enthesis (attachment site to bone), as well as at trigger points and adjacent joint to accelerate healing. Prolotherapy enhances the inflammatory healing response.

“Prolotherapy injections are given to the articular ligaments of the entire spine, pelvis and peripheral joints to tighten unstable joints.”

“Ligament healing is often slow and incomplete, as is the joint laxity caused by ligament injury which shows improvement gradually over a period of six weeks to a year after injury.” Yet, “objective mechanical laxity and subjective joint instability are still observed in a large percentage of patients.”

To improve the quality of ligament healing after injury or surgery, controlled motion “can stimulate repair and restoration of function, and that treatment of ligament injuries with prolonged rest may actually delay recovery and adversely affect the tissue’s ability to repair itself.”

“The histological, biochemical, and biomechanical properties of ligament healing are inhibited by the use of steroid injections and NSAIDs.” “NSAIDS are no longer recommended for chronic soft tissue injuries.”