Biological Augmentation of Flexor Tendon Repair: A Challenging Cellular Landscape

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Editors

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Learning Objectives

- Discuss the epidemiology of flexor tendon injuries
- Review the detailed anatomy of flexor tendons and the clinical presentations of flexor tendon injuries
- Detail the cellular environment of flexor tendons and their healing mechanism
- Evaluate cell and molecular modulation of flexor tendon healing
- Assess pharmacologic treatment methods of flexor tendon injuries

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Advances in surgical technique and rehabilitation have transformed zone II flexor tendon injuries from an inoperable no-man's land to a standard surgical procedure. Despite these advances, many patients develop substantial range of motion–limiting adhesions after primary flexor tendon repair. These suboptimal outcomes may benefit from biologic augmentation or intervention during the flexor tendon healing process. However, there is no consensus biological approach to promote satisfactory flexor tendon healing; we propose that insufficient understanding of the complex cellular milieu in the healing tendon has hindered the development of

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successful therapies. This article reviews recent advances in our understanding of the cellular components of flexor tendon healing and adhesion formation, including resident tendon cells, synovial sheath, macrophages, and bone marrow–derived cells. In addition, it examines molecular approaches that have been used in translational animal models to improve flexor tendon healing and gliding function, with a specific focus on progress made using murine models of healing. This information highlights the importance of understanding and potentially exploiting the heterogeneity of the cellular environment during flexor tendon healing, to define rational therapeutic approaches to improve healing outcomes. *(J Hand Surg Am. 2016;41(1):144–149.*

Key words Flexor tendon, adhesions, cell therapy, tissue engineering.

Approximately 3.5 million injuries to the upper extremity occur annually in the United States, with an incidence of 1,130 injuries per person-years.[1] Of these injuries, 38.4% involve one or more fingers, with the most common mechanism being a laceration. Furthermore, with an incidence of 221/100,000 people per-year, a laceration to the finger or thumb is the most common overall mechanism of injury in the upper extremity encountered in the emergency room setting.[1] Studies have attempted to determine the severity and concomitant injuries to tendons and neurovascular structures. Tuncali et al[2] found that 54.8% of patients with a small laceration (less than 2 to 3 cm) to the hand, wrist, or forearm also had an associated tendon injury, and tendon injuries are more likely to occur with deep lacerations, with 92.5% of deep lacerations resulting in a tendon injury. Of these injuries, a flexor tendon was injured 38.7% of the time (vs extensor tendons 61% of the time) and of those with any tendon injury, the artery and/or nerve was damaged 14.9% of the time. In addition, a 10-year (2001 to 2010) population-based study attempted to describe these injuries by location and injuries to a specific tendon.[3] The authors found 692 tendon injuries over this period, or an incidence of 33.2 per 100,000 person-years. The vast majority of injuries occurred in men (84%), mean age 35.9 years.[3] In agreement with prior studies, flexor tendon injuries were less common than extensor injuries (65% vs 85%, respectively). Flexor tendon injuries occurred most often in zone II ($P < .006$) and the most common injured tendon was the flexor digitorum profundus (FDP) to the index and little fingers (9.1% and 8.5%, respectively); however, this was not significantly different compared with the FDP in other fingers, or relative to the flexor digitorum superficialis (FDS) or the flexor pollicis longus.[3] Thus, although extensor tendon injuries occur more often, injuries to the flexor tendons often occur in zone II, which leads to important implications in their treatment and prognosis.

ANATOMY

Flexor tendon anatomy has been well defined and is beyond the scope of this article. Much of the basic research addressed injuries in zone II, which encompasses the area from the distal palmar crease to the FDS tendon insertion onto the middle phalanx. The annular pulleys are critical to prevent bowstringing of the tendon during flexion, with the A2 and A4 pulleys considered the most critical. Also, emerging evidence suggests that zone II injuries can be further broken down by the tendon location in the distal stump relative to the pulley system, but this may be more for academic purposes because there is no evidence that it has prognostic value.

Zone IIA injury occurs under the A4 pulley, zone IIB under the C1 pulley, zone IIC under the A2 pulley, and zone IID under the A1 pulley. These pulleys are thickening of the flexor tendon sheath, a double-walled synovial lined canal that serves as a source of lubrication for less friction movement of the tendon and a source of nutrients to maintain tendon viability. In addition to the synovial fluid, the tendons are also directly supplied with nutrients via the vinculum, a vascular mesentery that originates from the digital arteries. The FDS and FDP tendons each have 2 vincula that contain vessels for blood supply.

The unique relationship between the FDS and FDP tendons within the flexor sheath and the scarring and adhesions that inevitably occur after repair create a challenge to obtaining predictable outcomes, which makes this an area of consistent interest for both basic science and clinical research.

CLINICAL PICTURE AND DIAGNOSIS

Lacerations of the hand commonly present to the emergency department and a majority of even small lacerations have an associated tendon injury. The crux of a flexor tendon injury diagnosis is the physical examination, which should include careful neurovascular