Advances in the healing of flexor tendon injuries

Douglas M. Sammer, MD[1]; Kevin C. Chung, MD, MS[2]

1. Department of Plastic Surgery, UT Southwestern Medical Center, Dallas, Texas, and
2. Division of Plastic Surgery, University of Michigan Health System, Ann Arbor, Michigan

Reprint requests:
Assistant Professor D. M. Sammer, MD,
Department of Plastic Surgery, UT
Southwestern Medical Center, 1801
Inwood Road, Dallas, TX 75390, USA.
Tel: (214) 645-3188;
Fax: (214) 645 3105;
Email:
Douglas.Sammer@UTSouthwestern.edu

ABSTRACT

The intrasynovial flexor tendons of the hand are critical for normal hand function. Injury to these tendons can result in absent finger flexion, and a subsequent loss of overall hand function. The surgical techniques used to repair these tendons have improved in the past few decades, as have the postoperative rehabilitation protocols. In spite of these advances, intrasynovial flexor tendon repairs continue to be plagued by postoperative scar formation, which limits tendon gliding and prevents a full functional recovery. This paper describes the current challenges of flexor tendon repair, and evaluates the most recent advances and strategies for achieving an excellent functional outcome.

The anatomy, physiology, and biomechanics of the intrasynovial flexor tendons of the hand are unique in creating distinctive challenges for successful tendon healing. The goal of flexor tendon repair in the hand is not simply to achieve healing but also to restore tendon gliding to achieve functional finger motion. Healing after flexor tendon repair can be readily accomplished with finger immobilization. However, if the digit is immobilized until tendon healing occurs, the tendon will become adherent to the surrounding tissue that finger motion is lost. On the other hand, early active movement after tendon repair allows the tendon to heal with fewer adhesions but risks tendon rupture.

Tendons heal through a combination of two distinct mechanisms: extrinsic and intrinsic tendon healing. Both mechanisms follow the schema of healing that is common to many tissue types, which includes an inflammatory period of 48–72 hours, fibroblast proliferation, and collagen production lasting 3–4 weeks, followed finally by a period of remodeling, involving collagen cross-linking, reduction of type III collagen, and reorientation of collagen fibers. Extrinsic healing is characterized by the rapid influx of fibroblasts from peritendinous tissue that promote adhesions between the tendon and surrounding tissue. In contrast, intrinsic healing occurs via fibroblasts originating from the endotenon and the tendon itself without adhesion formation, ultimately resulting in greater strength at the repair site, and is facilitated by early mobilization.

In spite of advances in surgical technique and postoperative rehabilitation protocols, the goal of successful tendon healing without adhesions is difficult to achieve. Patients and surgeons continue to struggle with postoperative issues such as loss of motion and tendon rupture. Because of this, numerous strategies for optimizing flexor tendon healing have been studied in the clinical and laboratory settings. In general, these strategies are aimed at four areas. These include (1) rehabilitation protocols, (2) surgical technique and suture material, (3) surface modification and adhesion barriers, and (4) delivery of growth factors.

REHABILITATION

Multiple studies have showed that early controlled motion after flexor tendon repair in the hand results in improved motion.[1–8] A multitude of early motion rehabilitation protocols has been described[9–19] and can be divided into early active and early passive motion protocols. The goal of both types of rehabilitation is to initiate a protected movement of the repaired tendon within the tendon sheath, thereby promoting primary tendon healing and limiting adhesion formation. Unfortunately, although there are hundreds of clinical studies that evaluate the outcomes of different rehabilitation protocols, until recently, there has not been one randomized comparative trial.[20] In 2010, Trumble and colleagues published a prospective randomized clinical trial comparing early active (place and hold) with early passive motion.[21] The study showed better finger range of motion in patients who received the early active rehabilitation protocol, with no increase in tendon rupture rate.

However, much remains unknown about the relative merits of different flexor tendon rehabilitation protocols. For example, is composite active motion in which the fingers are moved from an extended position to a flexed position under the power of the forearm muscles (such as is used in the Belfast protocol)[17] preferable to active place and hold? Furthermore, many therapists practice a variation of a standard published protocol, such as the timing of advancement within the protocol, when tendon gliding is initiated, when blocking is initiated, when passive extension is initiated, and how edema control is performed. It is unknown what impact these common practice variations have on outcomes. There is a need for large randomized clinical trials designed to answer these questions. It is also important for future trials to be

consistent in their outcome measurements so that subsequent data aggregation and meta-analysis can be performed. Active finger motion and tendon rupture rate are critical outcome measurements. However, many other outcome measurements are also important. In addition to composite active finger motion, individual joint motion and passive motion should be reported. Grip and pinch strength, as well as an objective measure of hand dexterity and overall function such as the Jebsen-Taylor test,[22] should be presented. In addition to objective measures of function, patient-rated outcomes should be a component in any future studies of flexor tendon rehabilitation. These outcomes tools include the Michigan Hand Questionnaire (MHQ), and the disabilities of the arm, shoulder, and hand, which are two well-established instruments that measure patient-rated hand function. The MHQ is particularly useful because it evaluates hand function in multiple domains of hand use and includes a measurement of pain.[23–29] Finally, with the current emphasis on the rising cost of medical care, future studies must also measure the cost-effectiveness of various rehabilitation protocols.

SURGICAL TECHNIQUE/SUTURE MATERIAL

An ideal flexor tendon repair must be strong enough to withstand an early passive or active motion rehabilitation protocol. Furthermore, the repair should be technically straight forward, result in minimal suture burden, and should not adversely affect tendon gliding or healing. Many techniques for flexor tendon repair have been described and studied, including the Kessler, modified Kessler, Tajima-Kessler, Bunnell, Tsuge, Indiana/Strickland, Gelberman, locked cruciate, and many others.[30–40] A number of factors have emerged as being important. The strength of the core repair is proportional to the number of suture strands that cross the repair site.[40] The strength of the repair is also proportional to the suture diameter and to the strength of the suture material itself.[40,41] Locking bites in the core repair reduce failure by suture pullout. Finally, the use of an epitendinous suture decreases gapping at the repair site during loading and increases repair strength by as much as 20%.[41] Based on these findings, most surgeons employ a four-strand core repair using 4-0 or 3-0 suture and use an epitendinous suture.[40]

Recent investigations have explored the potential role of barbed suture in flexor tendon repairs. The barbs on the surface of the suture pierce the tissue at multiple points along the course of the suture, resulting in increased resistance to pullout. Because barbed suture "grasps" the tissue it passes through, tension is distributed along the course of the suture material, and knots are not required. The potential advantage of barbed suture in flexor tendon repair arises from the fact that the repair would be knotless. Standard suture repairs require one or more knots that are placed on the tendon surface or within the repair site, depending upon the repair technique. External knots located on the tendon surface interfere with tendon gliding and can catch on the flexor tendon sheath. Knots within the repair site reduce the contact surface of the tendon ends and might adversely affect tendon healing. A knotless repair would obviate these problems.

Recent cadaveric studies have shown that four-strand barbed suture knotless repairs can have similar biomechanical characteristics to standard knotted four-strand repairs in terms of load to failure and gapping characteristics.[42–44] However, much remains unknown about how barbed suture repairs might perform in vivo. For one, none of these repairs have been studied with cyclical loading, which is a more meaningful and physiologic way to load tendon repairs. Furthermore, no studies have been performed to examine the effect of barbed sutures on tendon gliding or adhesion formation. Finally, because barbed suture is not specifically designed for use in tendons, it is possible that an alternative barb configuration may prove to be superior to the currently available sutures. For example, barb size, angle, density, orientation, and configuration could all be optimized for use in tendon tissue. Future research should be directed toward studying the response of barbed suture knotless repairs to cyclical loading, the effect of barbed suture repairs on tendon gliding resistance and adhesion formation, and on optimizing barb characteristics for use in tendon tissue.

SURFACE MODIFICATION/ADHESION BARRIERS

The goal of both tendon surface modification and adhesion barriers is to improve gliding. Surface modification involves applying a substance to the surface of the repaired tendon in order to alter the physical properties of the tendon to make it glide more smoothly. Adhesion barriers refer to physical or chemical barriers that are applied to the tendon in an attempt to minimize adhesion formation. Numerous physical barriers to adhesion formation have been studied, including the application of silicone, polyethylene membranes, alumina shields, polytetrafluoroethylene, and polyhydroxyethylmethacrylate membranes.[45–51] None of these have been successful enough to be used clinically. Other investigators have focused on chemical barriers to adhesion formation, including corticosteroids, 5-flurouracil, alginate, or other substances.[52–61] None of these chemical barriers to adhesion formation have been found to be applicable clinically, usually due to the short duration of effect or because of an adverse effect on tendon healing. Other investigators are currently focusing on modifying the tendon surface in such a way as to improve gliding during the rehabilitation period, as opposed to attempting to directly reduce adhesion formation. Hyaluronic acid, a glucosaminoglycan, combined with gelatin and lubricin, a glycoprotein, has been used to modify the surface of tendons in a canine model of flexor tendon repair.[62] The work of flexion was decreased in treated tendons. However, repair site strength was also decreased. It is not known what substance, if any, can be applied topically to the repaired tendon to reduce adhesion formation or to promote gliding. The key problems appear to be that many substances that promote gliding or decrease adhesion formation fail to persist long enough to be clinically effective and that many of the substances also adversely affect tendon healing. Future research is likely to focus on improving the half life or durability of these substances and on protecting the repair site from the effects of the substance.

DELIVERY OF GROWTH FACTORS

A major focus of recent tendon healing research is on interventions that alter the molecular milieu of the healing tendon, by adding or modulating growth factors in an attempt to augment healing. The temporal, spatial, and quantitative expression of cytokines as well as their roles and interactions

during the healing of flexor tendons is extremely complex and is not well understood. Some of the cytokines that have been found to play central roles in flexor tendon healing include platelet-derived growth factor BB (PDGF-BB), beta-fibroblast growth factor (β-FGF), transforming growth factor beta, and bone morphogenic proteins 12, 13, and 14 (BMP 12, 13, 14). Several methods for delivering cytokines to the repair site have been devised, including fabricated biologic delivery systems, the introduction of stem cells (with or without gene transfer), adenoviral vectors, the use of platelet rich plasma, and others. Bone marrow-derived stromal cells (BMSCs) have been implanted between the lacerated ends of repaired tendons in an in vitro model and have shown increased maximal strength and stiffness compared with controls.[63] The introduction of BMP 12, 13, 14, or β-FGF to a tendon repair site by adenovirus-mediated gene transfer or other means has been shown to augment tendon healing in in vivo animal models as well.[64–67] PDGF-BB has been shown to increase collagen production in an in vivo canine model, when introduced using a collagen patch interposed at the repair site, and has been shown to increase remodeling as well as improve the structural and biomechanical properties of healing tendons.[68–70] A more sophisticated delivery system for PDGF-BB has been fabricated, which employs heparin binding to control the release of PDGF-BB over time.[71] The use of platelet-rich plasma (PRP) has been investigated as well. Although it does not seem to augment tendon healing alone, PRP was found to enhance the effects of a BMSC-seeded collagen patch in an in vitro.[72] Finally, synovial tissue (synovium), which is present and readily accessible during flexor tendon repair, is a source of cells and cytokines. In a canine tendon explant culture model, a synovial patch interposed at the repair site was shown to result in increased repair strength compared with controls.[73]

All of these interventions are in the early stages of investigation and are not ready for clinical application at this time. Many questions remain unanswered. Which cytokines, in what combination, at what time, and at what concentration should be delivered to the repair site? What is the ideal delivery device or method: adenoviral vector, fabricated patch, stem cells (adipose or bone marrow derived, autologous or allogeneic), or other? In addition, the in vivo effects in humans on tendon healing, tendon gliding, inflammation, and adhesion formation are completely unknown.

In conclusion, the goal of flexor tendon repair in the hand is to achieve tendon healing without adhesion formation, resulting in a healed tendon that glides freely within the flexor tendon sheath. In an effort to augment tendon healing and/or minimize adhesion formation, investigations are underway in multiple arenas, including rehabilitation protocols, surgical technique and suture material, surface modification and adhesion barriers, and the delivery of growth factors. Further study is required. Many of the important questions and measurements for quantifying answers to those questions have been discussed.

ACKNOWLEDGMENT

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