Aggressive Rehabilitation with Nonsurgical Treatment Demonstrates Improved Fatigue Mechanics and Functional Outcomes Following Achilles Tendon Rupture in an Animal Model

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Introduction

Achilles tendon ruptures are devastating injuries that affect 8.3 in 100,000 people yearly.[1] Despite the higher risk for complications and increased costs, operative treatment has historically been believed to provide superior outcomes compared to non-operative treatment in terms of function and re-rupture rates.[2] However, recent studies have suggested that surgical treatment for Achilles ruptures is not necessarily superior.[3,4] To elucidate the basic mechanical and structural mechanisms governing these clinical outcomes, it is necessary to evaluate the role of various surgical and rehabilitation strategies on tendon quality and function in a controlled model system. Therefore, the objective of this study was to investigate the effects of surgical repair and limb immobilization on Achilles healing and ankle joint function following complete tendon transection in a rat model. We hypothesized that surgical treatment and aggressive rehabilitation would result in superior Achilles tendon mechanical, structural, and functional properties following injury.

Methods

Study Design: Sprague Dawley rats (n = 108) received 2 weeks of treadmill exercise training (up to 60 minutes at 10m/min)5 (IACUC approved) prior to surgical removal of the right central plantaris longus tendon and blunt mid-substance transection of the right Achilles tendon. Animals were then randomized into repaired (R) (Modified Kessler approach) (n = 54) or non-repaired (NR) (n = 54) groups, and all hind limbs were immobilized in plantar flexion. These groups were further divided into aggressive (Agg), moderate (Mod), or conservative (Con) rehabilitation (Figure 1). Functional evaluation (n = 18/group) of passive ankle joint range of motion (ROM) and stiffness was completed using a custom torque cell and accelerometer-based device on anesthetized animals.[5] All assays were performed after 6 weeks of healing. Ex vivo Assays: After sacrifice, the Achilles tendon-foot complex was carefully removed en bloc, fine dissected, measured for cross sectional area, and secured in fixtures. Tendons were then loaded at 1N in a PBS bath while a series of sagittal B-mode high frequency ultrasound images (HFUS) were acquired using a 40MHz scanner (Vevo 2100, MS550D; VisualSonics) (n = 10-11/group).[6] Tendons were then mechanically tested and imaged (n = 10-11/group) with a protocol consisting of stress relaxation (6% strain), a low-load dynamic frequency sweep (0.1 to 10 Hz), and fatigue testing (~10-75% of ultimate failure load) at 2Hz using a sinusoidal waveform until failure (Instron Electropuls 3000). Analysis: Functional ankle joint properties (i.e., ankle ROM and stiffness) for both dorsiflexion and plantar flexion were evaluated. Achilles tendon percent relaxation, dynamic modulus, tanδ, toe and linear modulus, hysteresis, cycles to failure, and laxity were computed from mechanical and optical testing data. Echogenicity and collagen fiber alignment were evaluated from the HFUS images for the injury region.[6] Two-way ANOVAs with post hoc Fisher's tests were used to evaluate the

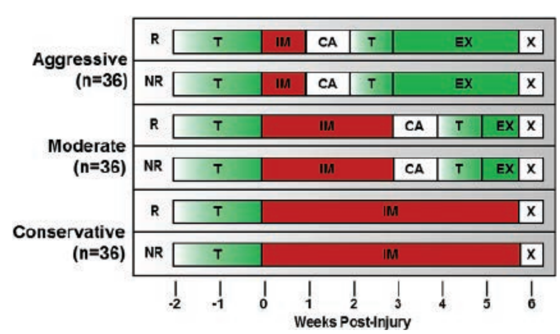

Figure 1. Study Design. Animals were trained for two weeks prior to injury. Following injury, animals were divided into aggressive, moderate, and conservative rehabilitation groups. Definitions: CA- cage activity; T- treadmill training; IM- immobilization; EX- exercise; R- repaired; X- Sacrifice.

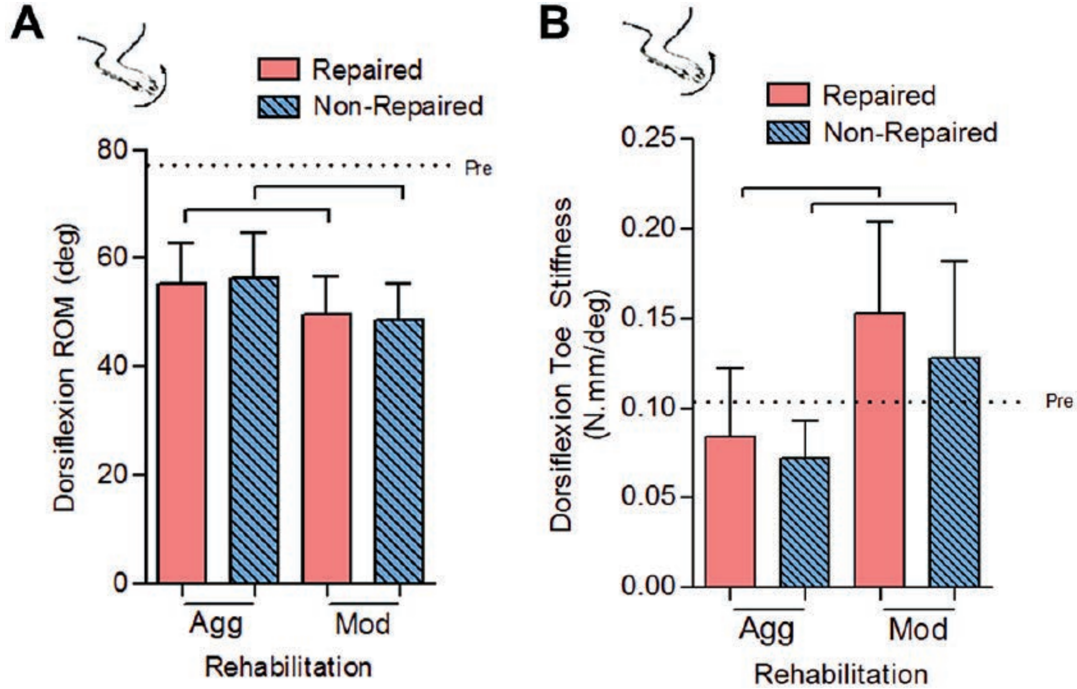

Figure 2. Ankle Joint Range of Motion (ROM) and Stiffness Functional Outcomes. Rehabilitation was a significant factor ($p < 0.05$) on dorsiflexion ROM (A) and toe stiffness (B) after 6-weeks of healing. Data shown as mean ± standard deviation. Lines indicate significant difference ($p < 0.05$). Pre-Surgery values.

effects of surgical treatment and rehabilitation on mechanical, functional, and structural properties.

Results

After 6 weeks of healing, the plantar- (data not shown) and dorsi-flexion ROM was superior in aggressively rehabilitated animals, closer to pre-injury values (Figure 2). Aggressively rehabilitated animals had dorsiflexion toe stiffness values closer to pre-injury values compared to the moderate rehabilitation group. No changes in plantarflexion toe or linear stiffness, or dorsiflexion linear stiffness were observed. Tendon cross sectional area was higher in repaired tendons, and this effect was exacerbated in animals with aggressive rehabilitation. Mechanical property evaluation revealed an increase in the toe modulus in non-repaired aggressively rehabilitated tendons, but no changes in the percent relaxation or dynamic properties. Marked differences in quasi-static linear modulus and fatigue properties were observed (Figure 3) ($p < 0.05$). Specifically, non-repaired tendons with aggressive and moderate rehabilitation had an increased linear modulus and number of cycles to failure (Figure 3) ($p < 0.05$). Additionally, the number of cycles to failure was greatest in the aggressively rehabilitated group. Non-repaired tendons experienced more

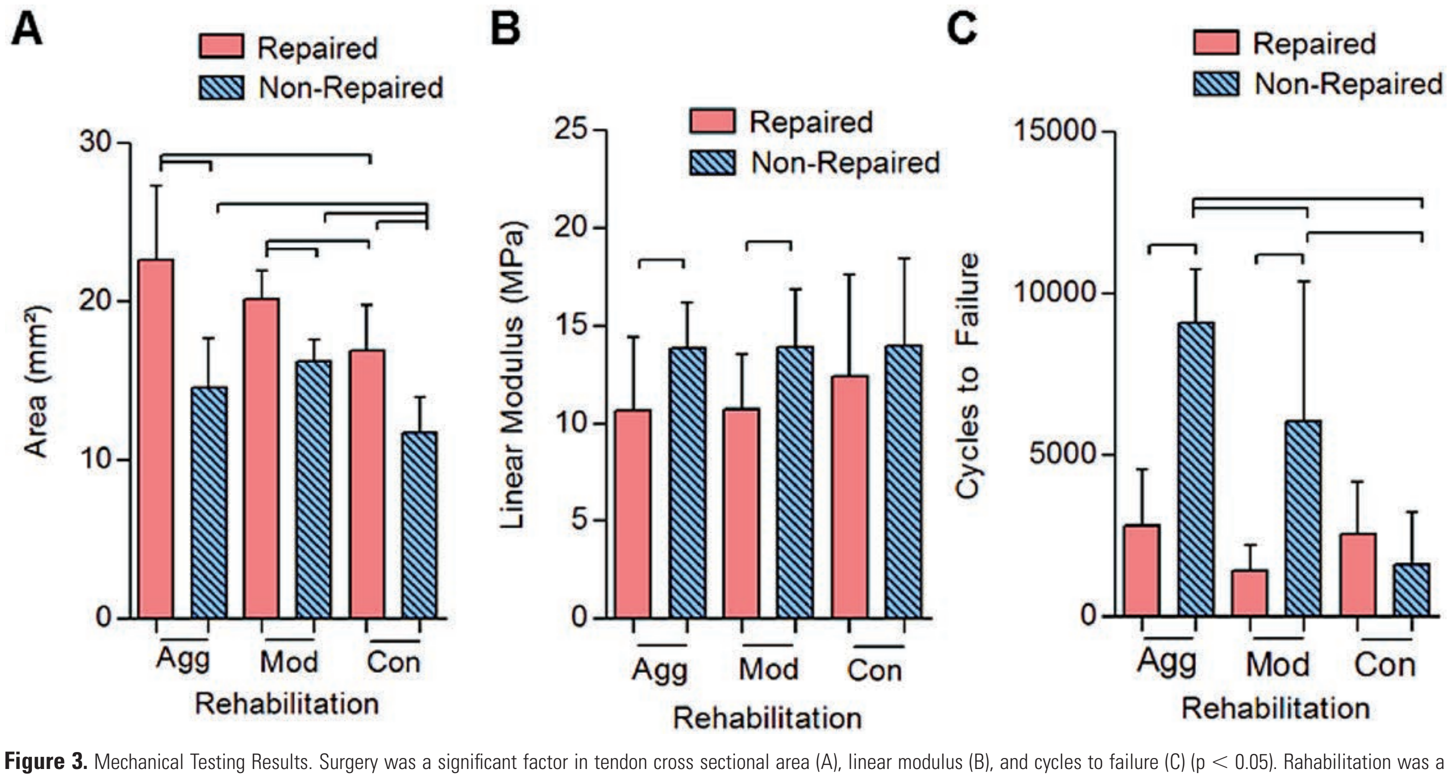

Figure 3. Mechanical Testing Results. Surgery was a significant factor in tendon cross sectional area (A), linear modulus (B), and cycles to failure (C) ($p < 0.05$). Rahabilitation was a significant factor I ntendon cross sectional area and cycles to failure (A,C) ($p < 0.05$). Data shown as mean ± standard deviation. Lines indicate significant differences ($p < 0.05$).

laxity through 5% fatigue life compared to repaired tendons in aggressive and moderate rehabilitation, and transitioned to the secondary phase of fatigue life earlier ($p < 0.05$) (data not shown). Ultrasound evaluation revealed an effect of rehabilitation, but not surgical treatment type, on increased matrix echogenicity, a surrogate measure of fiber density, and alignment ($p < 0.05$) (data not shown).

Discussion

Achilles tendon healing following a variety of common clinical treatment methods was evaluated after 6 weeks of healing in a rat model. We discovered a mechanism whereby non-repaired tendon fatigue properties had marked improvements in the number of cycles to failure. This work suggests the functional and mechanical benefits of aggressive rehabilitation on Achilles tendon healing following a variety of treatment paradigms.[7] Ultrasound evaluation showed promise to detect changes in healing capacity between groups with different rehabilitation strategies. Although the conservative rehabilitated tendons had higher echogenicity and alignment compared to other groups, they also had lower cross sectional area, which likely limited the capacity of the more aligned tendon to withstand fatigue loading. Future work will relate organizational measures from HFUS to tendon fatigue mechanical properties. Additional ongoing studies will evaluate the long-term effects of these treatment and rehabilitation paradigms.

Significance

This study demonstrates that aggressive rehabilitation with nonsurgical management leads to improved tendon fatigue mechanics and ankle function after 6 weeks of healing in this rat Achilles tendon injury model. Ultrasound evaluation showed promise to detect changes in healing capacity between groups.

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References

1. Suchak AA *et al.,* *FAI*, 26(11) 932-6. (2005).
2. Freedman BR *et al.,* *MLTJ*, 4(2) 245-255. (2014).
3. *AAOS Guidelines for Achilles Tendon Repair*, (2009).
4. Soroceanu *et al.,* *JBJS* 94(23):2136-43. (2012).
5. Peltz CD *et al.,* *JOR* 28(7): 841-5. (2010).
6. Riggin CN *et al.,* *JBiomech Eng*, 136(2):21-29. (2014).
7. Olsson N, *et al.,* *AJSM*, 41(12):2867-76. (2013).