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Early E-modulus of healing Achilles tendons correlates with late function.

Similar results with or without surgery

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Abstract

Non-operative treatment of Achilles tendon ruptures is associated with an increased risk of rerupture. We hypothesized that this is due to inferior mechanical properties during an early phase of healing, and performed a randomized trial, using a new method to measure the mechanical properties. Tantalum markers were inserted in the tendon stumps, and tendon strain at different loadings was measured by stereo-radiography (RSA) at 3, 7 and 19 weeks and 18 months after injury. 30 patients were randomized to operative or non-operative treatment. The primary out-come variable was an estimate for the modulus of elasticity at 7 weeks. Strain per force, cross-sectional area and tendon elongation were also measured. The functional outcome variable was the Heel-Raise index after 18 months. There was no difference in the mean modulus of elasticity or other mechanical or functional variables between operative and non-operative treatments at any time-point, but strain per force at 7 and 19 weeks had significantly larger variation in the non-operative group. This group therefore might contain more outliers with poor healing. The modulus of elasticity at 7 weeks correlated with the Heel-Raise index after 18 months in both treatment groups ($r^2=0.75$; $p=0.0001$). This correlation is an intriguing finding.

Introduction

Despite decades of debate, we still have no consensus about the appropriate treatment of acute Achilles tendon ruptures (Bhandari et al., 2002; Khan et al., 2005). Operative treatment with many variations and non-operative treatment are evenly supported in the literature (Aktas et al., 2009; Gigante et al., 2008; Lynch, 2004; Moller et al., 2001; Nistor, 1981). Postoperative methods are also numerous, and in recent studies early mobilisation has become popular because of its favourable effects on tendon healing (Enwemeka et al., Mortensen et al., 1999; Suchak et al., 2008). In animal studies locally applied platelet concentrates have accelerated tendon healing (Aspenberg et al., 2004), and similar results are reported with different growth and differentiation factors (Forsslund et al., 2003; Forsslund et al., 2003; Virchenko et al., 2004).

The criteria for treatment success have to be based on functional outcome and complications (Pajala et al., 2002). Functional results and complication rates often have a low statistical power for comparisons of different treatments. Moreover, they do not give information about the properties of the healing tendon at a given time point during the healing process. Healing of a tendon depends on early factors, such as type of injury, type of surgery and individual repair capacity. It also depends on late factors, such as rehabilitation programs or the patients' motivation for training. A useful measure of early results would make it possible to study the early factors separately.

In a pilot study, we used Roentgen stereophotogrammetric analysis (RSA) (Selvik, 1990) with simultaneous mechanical loading to describe the mechanical properties of a healing Achilles tendon. We found that an estimate for the modulus of elasticity during early stages of healing correlated with the late functional outcome (Schepull et al., 2007). We found that an estimate for the modulus of elasticity during early healing correlated with the late functional outcome.

According to a meta-analysis, non-operatively treated tendons have a higher risk of re-rupture than operatively treated ones (Khan et al., 2005). We speculated that this difference would be caused by inferior mechanical properties in the non-operatively treated tendons at early stages of healing. The specific hypothesis for this study was that the modulus of elasticity at the time of plaster removal (7 weeks) would be lower in the non-operatively treated group than in the operatively treated one.

Methods

All patients between 18 and 65 years presenting with an acute rupture of the Achilles tendon at our hospital were asked to participate. Exclusion criteria were diabetes mellitus, history of cancer, lung or heart diseases and rheumatoid arthritis. Between May 2005 and April 2007 we included 30 consecutive patients (5 women). Two patients refused to participate. All patients were injured during sports or sports related activities.

Randomization was done using sealed envelopes. Patients consented in writing and the study was revised and approved by the Regional Ethics Committee.

Operative treatment

Patients randomized to operative treatment were operated within 5 days after injury.

Operation was performed in local anaesthesia using an open technique with a dorso-medial approach. We adapted both tendon ends with a resorbable suture (Vicryl size 1) using the single loop Kessler technique. We implanted 2 tantalum beads (size 0.8 mm) in the distal part of the tendon, and 2 tantalum beads in the proximal part. We then closed the paratenon and sutured the skin with a resorbable intracutaneous suture. A short leg cast was applied with the foot in equinus position.

At 3.5 weeks, the cast was removed and a new cast was applied with the ankle in a neutral position for another 3.5 weeks. Full weight bearing was allowed from the beginning. The cast was removed at 7 weeks in total, and the patients were instructed to use shoes with a 2 cm elevation of the heels for another 6 weeks. Physiotherapy started after cast removal, following our previous hospital routines. Full activity, including sports, was allowed after approximately 5 months.

Non-operative treatment

Patients randomized to non-operative treatment were treated immediately in the emergency room. The rupture site was palpated and marked with a permanent marker pen. A short leg cast was then applied with the foot in equinus position. At 3.5 weeks, this cast was removed. Using a special injection needle, 2 tantalum beads 0.8 mm were injected into the distal part of the tendon and 2 beads into the proximal part. We used our earlier marking as reference to distinguish between the proximal and distal tendon stumps. A new cast was applied with the foot in the neutral position for another 3.5 weeks. Also in this group, full weight bearing was allowed. The cast was removed at 7 weeks in total, and after cast removal, these patients followed the same regimen as the operated group, as regards instructions, shoes and physiotherapy.

Follow-up: Mechanical properties

We used Roentgen stereophotogrammetric analysis (RSA) to measure strain under defined loading, and CT and ultrasound to measure the transverse area of the tendon at the rupture site. This allowed calculation of the modulus of elasticity (Young's modulus).

RSA

RSA provides the possibility to measure the distance between tantalum beads in 3 dimensions with high accuracy. A change in position, e.g. ankle flexion, does not influence the measurements if the tendon tissue is not deformed. During RSA, simultaneous radiographs are taken in two planes using extra-corporal calibration markers in a standardized cage.

We performed RSA at 3.5 weeks, 7 weeks (within 48 hours after cast removal), 19 weeks, and 18 months. At 3.5 weeks there was just a single x-ray exposure, taken after the plaster had been changed to a new one in neutral position.

At 7 weeks, 19 weeks and 18 months, RSA-examinations were combined with mechanical loading. Patients sat on an examination table with the foot in a specially designed frame, and with 8 degrees of plantar flexion. The frame allowed us to apply a pedal to the forefoot and load it with weights. The patients were then asked to keep the foot in position and to resist the force of the pedal. The first force applied to the pedal was 25 N and the second was 150 N (Figure 1). The 25 N loading was intended to provide a base-line value (a reasonable relaxation of the dorsal flexor muscles) and 150 N was the main loading (sufficient loading to produce strain). The patients had to resist the force for 15 seconds before the radiographs were taken. Between all x-ray exposures there was a break for 3 minutes. These first two x-ray exposures were used as control examination. Moreover, these exposures served as preconditioning loading of the Achilles tendon. After another 3 minute break, the main examination was performed, again with 25 N and 150 N. When not otherwise stated, all results refer to the second (main) examination. Strain per force values (assuming linear relationship) were calculated with correction for the lever arms of the forefoot and the calcaneus, and are expressed as % per 100 N tendon force.

The 4 beads were numbered from proximal to distal. Elongation between the different times for follow-up was based on the change in distance between the beads 2 and 3 at the second (main) loading with 150 N. We measured the elongation of the tendon during the second cast period (in neutral position) by taking RSA images directly after the cast had been applied at 3.5 weeks and just prior to cast removal at 7 weeks.

For RSA analysis, we used the UmRSA 4.1 system and software to calculate the distances between the single beads. Tendon force was calculated from pedal force. The pedal pivoted around an axis so that the force had a defined loading point in a lateral projection. Lever arms were calculated from lateral radiographs of the CT scan with the centre of the talar trochlea as pivot point.

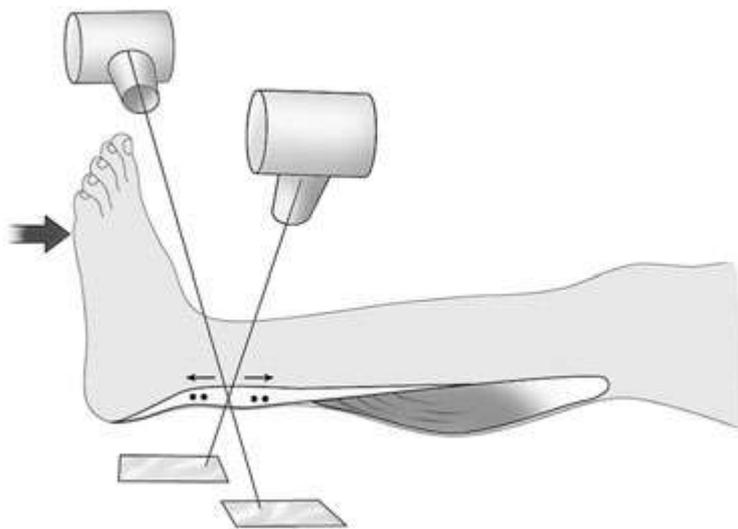


Figure 1. RSA examinations performed at 7 and 19 weeks and 18 months

A final RSA was done aft 18 months. This examination differed slightly from the previous. Also here the patients had to resist the applied loading for 15 seconds with 3 min intervals, but the forces were 25 N, 125 N, 225 N, 325 N and 425 N.

CT and Ultrasound

We measured the transverse (cross-sectional) area at mid-distance between the proximal and distal markers at 7 weeks using CT, and at 19 weeks using ultrasound. CT was used at 7 weeks because we also wanted to determine the position of the beads within the tendon

(Figure 2). Beads lying outside the tendon on the CT-scans were excluded. The ultrasound examination at 19 weeks was performed by one experienced radiologist.

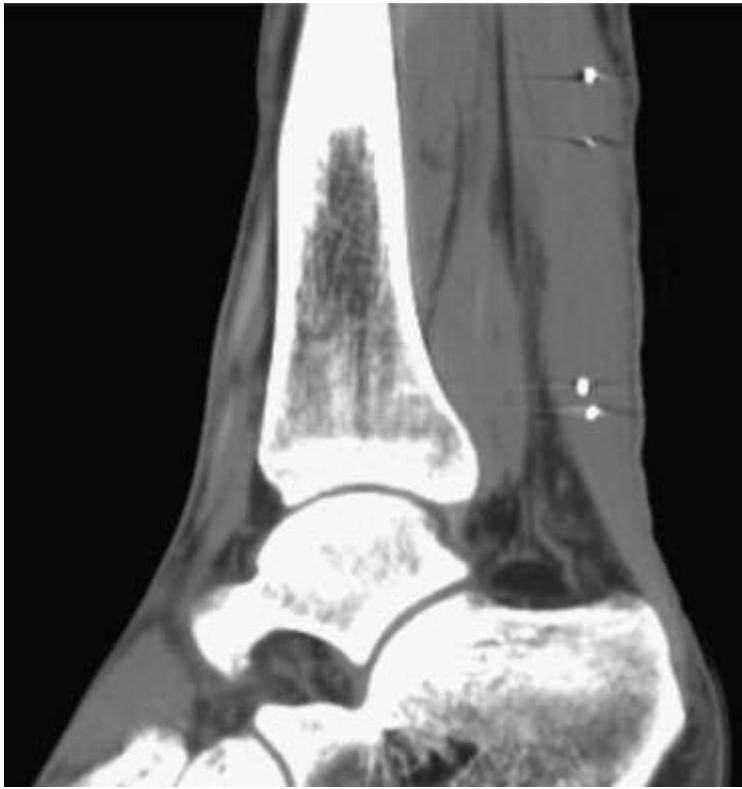


Figure 2. CT examination to confirm correct position of the tantalum beads. The two tantalum markers on each side of the healing rupture appear enlarged due to artefacts.

Follow-up: Functional outcomes

The patients were examined 18 months after injury by a physiotherapist (JK), who had not previously been involved in the treatment. A number of muscle performance tests were performed, but only the primary variable (heel raise index) is reported here. Heel raise test has been recommended for evaluating calf muscle function (Möller et al., 2005; Schepull et al., 2007; Silbernagel et al., 2009). We previously created a Heel-Raise index, defined as the number of heel raises the patient could do, multiplied with heel raise height, as percentage of the other side (Schepull et al 2007). Patients also filled in the Achilles Tendon Rupture Score (ATRS) form (Nilsson-Helander et al., 2007).

Statistics

This study was designed to test the hypothesis that treatment (operative or non-operative) would influence tendon mechanical properties. The main outcome variable was the modulus of elasticity at the time of cast removal. A second goal was to confirm our previous observation, that mechanical properties shortly after cast removal predict the functional outcome. The predetermined variables for this were the modulus of elasticity at the time of cast removal and the Heel-Raise index at the last follow-up. Levene's test was used to assess equality of variance.

Statistical analysis was performed by Student's t-test and simple linear regression analysis using SPSS, version 17. No power analysis could be performed, due to the lack of previous data.

Results

Values for the modulus of elasticity at 7 weeks were analysed for 11 non-operated and 14 operated patients (see exclusions below).

Mechanical properties: Operative versus non-operative treatment

The mean modulus of elasticity at 7 weeks was 7 % higher in the non-operated group (95 % CI: 40 % higher to 23 % lower). We could not find a difference in any of the mechanical variables between operative and non-operative treatment (Table 1), except that there was significantly higher variation in strain per force in the non-operative group at 7 and 19 weeks (Levene's test $p=0.026$ and $p=0.035$, respectively).

Functional outcomes and correlation with mechanical properties

The Heel-Raise index and the ATRS score at 18 months did not differ between operated ($n=11$) and non-operated ($n=9$) groups. Neither could we detect a correlation between ATRS and the Heel-Raise index, probably because ATRS showed a ceiling effect at 18 months. The median score was 93 (maximum 100); operated 93 (range 84 - 100) and non-operated 95 (range 77 - 100).

The modulus of elasticity at 7 weeks showed a correlation with the Heel-Raise index ($n = 19$; $r^2=0.75$; $p=0.0001$), but not at 19 weeks. Strain per force at 7 weeks ($n = 19$; $r^2=0.37$; $p=0.003$) also correlated with the Heel-Raise index, but not at 19 weeks. The transverse area at 7 and 19 weeks did not correlate with the Heel-Raise index.

Tendon elongation

The tendons elongated from 3 to 7 weeks (median 3.1mm) and from 7 to 19 weeks (median 4.7mm). Between 7 weeks and 18 months we observed a slight shortening of 0.7mm. There was no difference between the operative and the non-operative treatment groups at any time period (Table 2).

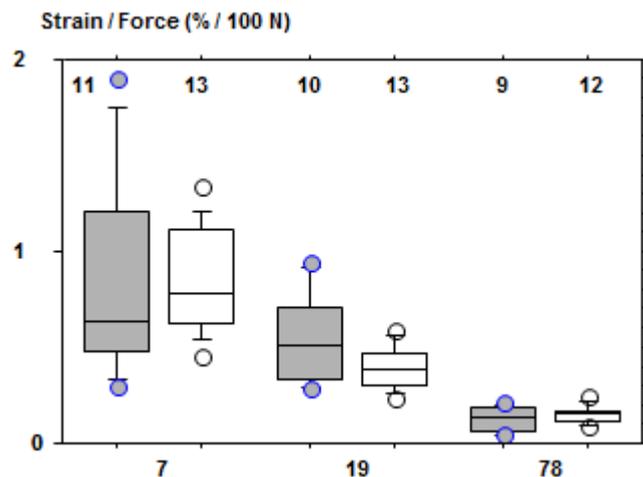


Figure 3. Strain per force (% per 100 N) at 7 and 19 weeks and 18 months post-op. Non-operative treatment grey, and operative white. N for each box is given on top.

One non-operated patient showed an extreme elongation from 7 to 19 weeks (31 mm) and also from 19 weeks to 18 months (another 22 mm). We checked this result by analyzing the other pair of tantalum beads and found similar values, indicating that this elongation value is not a measuring error. This patient had a venous thrombosis, and also the lowest modulus of elasticity and the lowest Heel-Raise index of all patients. He also had a poor ATRS result. In spite of this patient, we could not detect any significant correlation between elongation over time and functional outcome at 18 months.

Error of measurements

In order to control our settings of measurements and confirm that the beads were placed correctly, and were not loose within the tendon, we made double examinations (repetition of RSA 25 N and 150 N force, see METHODS) at 7 and 19 weeks. The first and the second strain

values showed a good correlation at 7 weeks ($r^2=0.80$) and at 19 weeks ($r^2=0.70$).

Furthermore, we compared the strain between the outer beads (bead 1 and bead 4) with the beads closer to the rupture site (bead 2 and bead 3), in all patients where no beads had to be excluded due to malpositioning (results of 24 patients used). Also here, there was a good correlation at 7 ($r^2=0.93$) and 19 weeks ($r^2=0.93$).

At the 18 months follow-up, a regression was calculated between tensile load and strain based on 5 paired values for each the 21 patients available. The r^2 - value was 0.86 or higher for all but 2 patients, and the median was 0.93.

Complications and exclusions

There were no complications related to the tantalum beads or the measurement procedure. Four patients were excluded. One patient did not want to participate in the follow-up. Three patients (all in the non-operated group) were excluded because the CT examination showed that 2 beads were positioned outside of the tendon tissue. One non-operated patient did not turn up for CT or ultrasound examination, so for him, the modulus of elasticity could not be calculated. One patient in the non-operated group had a rerupture 4 weeks after cast removal. Data from that time-point and onwards were excluded. Ultrasound showed that the second rupture was not in the same area as the first rupture, but more proximal. This patient was again treated non-operatively, with a cast in equinus position for 4 weeks and in the neutral position for another 4 weeks. Despite the rerupture, the patient was satisfied with his function after rehabilitation. One patient did not come to the follow-up RSA examination at 18 months.

One patient was unable to resist the 150 N at 7 weeks and was tested with a 100 N weight instead. At the later examinations, there was no such problem. Four patients (all non-

operated) with pain in the calf muscles after change or removal of the cast were sent for ultrasound examination, and in all patients a deep vein thrombosis was discovered. These patients were treated with warfarin for three months. This was not cause for exclusion from the study, but one of the patients was excluded because of poor bead placement, and one did not have data for transverse area (as reported above).

Discussion

Our results for mechanical properties did not show any difference between operative and non-operative treatment, except that there was a significantly higher variation in strain per force in the non-operative group during the first months. This higher variation indicates that a few patients may have poor mechanical properties and probably a greater risk for rerupture, whereas the majority has tendons that heal as well as the operated ones. Although the difference in variation was found both at 7 and 19 weeks, and variance comparison is compulsory in the statistics package, the difference was not a primary hypothesis, and should be interpreted with caution.

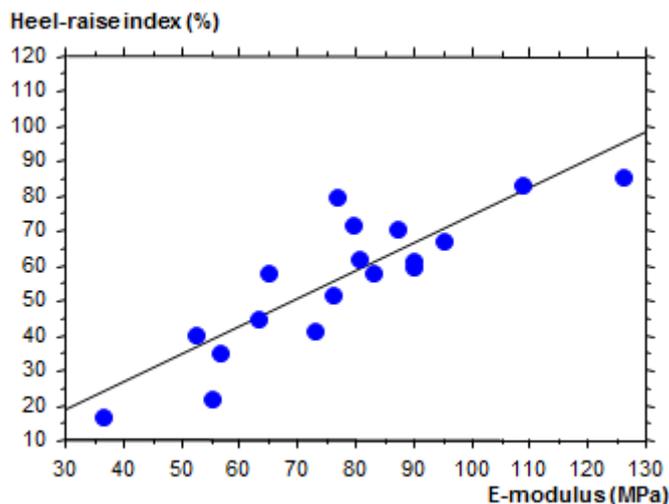


Figure 4. Correlation between the e-modulus (MPa) at 7 weeks and the Heel-Raise index (%) at 18 months.

Our data suggest that the advantage of surgical treatment would be that it reduces the number of outliers. On the other hand, surgery for Achilles tendon rupture has disadvantages, such as the risk of infections (Lo et al., 1997). If it were possible to identify patients, who are likely to heal less well, the others could be spared the surgery. MRI and ultrasound has been used to examine the status of the ruptured Achilles tendon (Fujikawa et al., 2007). To our knowledge, however, there is no method to identify patients with an increased risk of rerupture.

This study is based on the assumption that the recorded mechanical data are somehow correlated with the risk of rerupture. This appears intuitively reasonable, and is in accordance with unpublished animal data in our laboratory. However, rupture risk may be related to the ability of the healing tendon to absorb mechanical energy. As energy uptake is related to the ability to deform, a high stiffness during early healing is not necessarily an advantage. Moreover, our measurements are based only on elastic properties, and do not consider viscoelasticity. It is possible that differences in such properties between the groups would better explain the risk of rerupture. Due to the low incidence of reruptures, this will be extremely difficult to clarify.

Four patients in the non-operated group were diagnosed with a deep venous thrombosis (DVT). No patient in the operative group showed clinical signs of DVT. In a randomized study of the incidence of DVTs with operative versus non-operative treatment, there was no difference between the groups, both having an incidence as high as 30% (Nilsson-Helander et al., 2009). It is likely that several patients in both groups of our study had undiagnosed DVTs. Because DVTs appear to be common, we did not exclude patients who were diagnosed.

In order to confirm our previous findings of a correlation between early mechanical properties and late functional outcome, the modulus of elasticity and the Heel-Raise index (Schepull et al 2007) were chosen as main outcome variables in the original protocol of this study. The modulus of elasticity and strain per force at 7 weeks showed a correlation with the Heel-Raise index at 18 months. The predictive role of early mechanical properties suggests that if we want to improve results after Achilles tendon rupture, we have to influence early events. However, many factors can't be influenced, such as severity of the injury, tendon pre-injury status or genetic differences.

Elongation of the tendon has been reported to correlate with less favourable functional outcome (Kangas et al., 2007) . We found no correlation between tendon elongation and the Heel-Raise index, but on the other hand, one patient with extreme elongation showed poor clinical results. Probably, a variation in elongation within reasonable limits does not influence the end result.

Perspective

Our results suggest that non-operative and operative treatments provides equal mechanical properties in the healing tendons of most patients. There seems to be a great variation between patients regarding the ability to heal. Patients with a poor healing ability might need surgery. If we could identify those patients preoperatively, these might benefit from tendon suture and the others could possibly be spared surgical treatment.

Acknowledgements, competing interests

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The authors declare that they have no competing interests.

Table 1: Mechanical properties of operated and non-operated Achilles tendon. Mean (SD)

	Operated	Non-Operated
Modulus of elasticity at 7 weeks (MPa)	82.3 (31.0)	87.8 (33.8)
Strain per force at 7 weeks (% per 100 N)	0.8 (0.28)	0.9 (0.55)
Area at 7 weeks (cm ²)	1.62 (0.44)	1.86 (0.49)
Modulus of elasticity at 19 weeks (MPa)	98.0 (24.3)	100.8 (52.6)
Strain per force at 19 weeks (% per 100 N)	0.39 (0.11)	0.54 (0.24)
Area at 19 weeks (cm ²)	2.84 (0.60)	2.42 (0.66)
Strain per force at 18 months (% per 100 N)	0.15 (0.05)	0.13 (0.06)

Table 2: Tendon elongation over time (in mm). One patient with extreme values not included

(described in text).

	3.5 - 7 weeks			7 - 19 weeks			19 - 78 weeks		
	<u>min</u>	<u>median</u>	<u>max</u>	<u>min</u>	<u>median</u>	<u>max</u>	<u>min</u>	<u>median</u>	<u>max</u>
Non OP	-0.2	1.3	5.5	-2.5	1.9	9.9	-3.9	-1.1	0.6
OP	-0.3	3.4	11.9	-2.5	7.2	13.7	-3.1	-0.3	3.9

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