Autologous Platelets Have No Effect on the Healing of Human Achilles Tendon Ruptures

A Randomized Single-Blind Study

Thorsten Schepull,* MD, Joanna Kvist,† PhD, RPT, Hanna Normann,† RPT, Marie Trinks,‡ BS, Gösta Berlin,‡ MD, PhD, and Per Aspenberg,*§ MD, PhD

Investigation performed at Linköping University, Linköping, Sweden

Background: Animal studies have shown that local application of platelet-rich plasma (PRP) stimulates tendon repair. Preliminary retrospective case series have shown faster return to sports. Hypothesis: Autologous PRP stimulates healing of acute Achilles tendon ruptures.

Study Design: Randomized controlled trial; Level of evidence, 2.

Methods: Thirty patients were recruited consecutively. During surgery, tantalum beads were implanted in the Achilles tendon proximal and distal to the rupture. Before skin suture, randomization was performed, and 16 patients were injected with 10 mL PRP (10 times higher platelet concentration than peripheral blood) whereas 14 were not. With 3-dimensional radiographs (roentgen stereophotogrammetric analysis; RSA), the distance between the beads was measured at 7, 19, and 52 weeks while the patient resisted different dorsiflexion moments over the ankle joint, thereby estimating tendon strain per load. An estimate of elasticity modulus was calculated using callus dimensions from computed tomography. At 1 year, functional outcome was evaluated, including the heel raise index and Achilles Tendon Total Rupture Score. The primary effect variables were elasticity modulus at 7 weeks and heel raise index at 1 year.

Results: The mechanical variables showed a large degree of variation between patients that could not be explained by measuring error. No significant group differences in elasticity modulus could be shown. There was no significant difference in heel raise index. The Achilles Tendon Total Rupture Score was lower in the PRP group, suggesting a detrimental effect. There was a correlation between the elasticity modulus at 7 and 19 weeks and the heel raise index at 52 weeks.

Conclusion: The results suggest that PRP is not useful for treatment of Achilles tendon ruptures. The variation in elasticity modulus provides biologically relevant information, although it is unclear how early biomechanics is connected to late clinical results.

Keywords: Achilles tendon; platelet; platelet-rich plasma; tendon healing; biomechanics; roentgen stereophotogrammetric analysis

Healing after an Achilles tendon rupture is a slow process. Many treatment methods have been tried to improve tendon healing, with the aim of minimizing the risk of rerupture and shortening the time until the patient can return to the level of activity before injury. Rerupture of the healing Achilles tendon can occur late, even 6 months after injury. In animal experiments, it has been possible to improve the tendon-healing process with mechanical loading and pharmacological treatment. Another possibility is to use platelet-rich plasma (PRP). The physiology of tissue repair and scarring involves the release of a cocktail of bioactive proteins and growth factors from activated platelets. Although the efficacy of PRP in bone healing is debated, some studies have indicated that it may be better suited for stimulation of fibrous tissue repair. Rat models have shown that PRP increases tendon strength when injected locally. Increased vascularity and better tissue organization have been found in rabbit Achilles tendons. However, one clinical study comparing PRP-treated patients with historical controls indicated that preoperative PRP treatment allows earlier return to sports, which has attracted the interest of sports physicians.
especially as small centrifuges and practical kits are available for production of PRP in the physician’s office.

Regarding tendinosis, 2 important studies on PRP treatment have recently been published. Improved mechanical properties were found in a study on horses, where core lesions were treated with PRP, excised, and tested mechanically. However, a randomized double-blind placebo-controlled clinical trial involving 54 tendinosis patients failed to show any beneficial effects on clinical outcome.

In previous studies, we established the use of roentgen stereophotogrammetric analysis (RSA) with simultaneous mechanical loading as a method that can describe the mechanical properties of a healing Achilles tendon. We also found that an estimate of the modulus of elasticity (E-modulus; Young’s modulus, which describes an elastic property of the tissue) during early healing showed a correlation to the functional outcome at the 1-year follow-up. We have now used this method to measure the early mechanical properties of the healing tendon in a randomized trial to determine whether there is any positive effect of PRP on tendon repair. E-modulus at week 7 and the heel raise index at week 52 were chosen as the primary outcome variables because they appeared to be relevant and reasonably sensitive in a previous patient series.

PATIENTS AND METHODS

All patients between 18 and 60 years of age presenting with an acute rupture of the Achilles tendon (not older than 3 days) at our hospital were asked to participate in the study after receiving oral and written information. Exclusion criteria were diabetes mellitus, a history of cancer or lung or heart diseases, or any other diseases that could compromise the locomotory system. Between September 2007 and April 2008, we included 30 consecutive patients with an Achilles tendon rupture; only 1 patient refused to participate in the study (see Figure 1). All patients were recreational athletes and were injured during sports or sports-related activities. The patients consented in writing, and the study was revised and approved by the Regional Ethics Committee.

Preparation of Platelet Concentrate

Because randomization was planned to take place during surgery, autologous PRP had to be prepared from all 30 patients. All patients were operated on within 5 days of injury; on the day before surgery, all were sent to the Department of Transfusion Medicine at Linköping University Hospital. One unit of whole blood (450 mL) was collected with citrate phosphate dextrose as anticoagulant. From this unit of blood, PRP was obtained by double centrifugation according to accredited procedures. The platelet concentration was measured with the Micros 60 hematology analyzer (ABX Diagnostics, Montpellier, France). The PRP preparations had a mean volume of 21 mL (range, 16 to 29 mL) and a mean concentration of 3678 ± 1061 × 10⁶ platelets per mL.

The PRP was stored at 22°C with constant rotation for up to 20 hours before use. The swirling phenomenon (reflecting platelet viability) of the PRPs was examined before use and found to be well maintained in all cases.

Operative Treatment and Randomization

Surgery was done using a conventional open technique with a dorsomedial approach. We used local anesthesia with Carbocaine (mepivacaine hydrochloride) and adrenaline. The ends of the tendon were adapted 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 of the same size in the proximal part. We then closed the paratenon. Then, a cannula was inserted into the rupture site, and a randomization envelope was opened. In cases where a patient was allocated to PRP treatment, a syringe was filled with 10 mL of autologous PRP (with addition of 1 mL of calcium chloride at 0.25 mmol/mL) and connected to the cannula. About 6 mL of the platelet concentrate was injected into the rupture site—the amount possible to inject without leakage before skin suture. Then the skin was sutured with a resorbable intracutaneous suture (Monocryl 3-0). Finally, the remaining 4 mL was injected transdermally into the rupture site. There was sometimes leakage from the wound, but we estimated it to be no more than 1 mL. No injections were given to control patients. Their platelet concentrate was discarded, but all patients received their own erythrocytes as a transfusion during surgery.

A short-leg cast was applied with the foot in the equinus position. After 3.5 weeks, the cast was replaced with one in which the ankle was in neutral position, and another 3.5 weeks were allowed to pass. Full weightbearing was allowed as tolerated from the beginning. The cast was removed after 7 weeks in total, and the patients were instructed to use shoes with a 2-cm elevation of the heels for another 4 weeks. Physiotherapy started after removal of the cast, and all patients followed the same rehabilitation protocol. All patients received instructions for home training and visited the physiotherapist every 2 weeks. The training program consisted first of mobility exercises, then muscle strength exercises (2- and 1-legged toe raises at slow and fast speed) and balance exercises (standing on 1 leg on different surfaces and wobble boards). Plyometric exercises (simple 2-leg jumps) were allowed from week 16, with a progression during the weeks that followed (jumping on 1 leg in different directions). If the patient could manage 15 to 20 toe raises, jogging was allowed from week 18. Full activity, including sports, was allowed after approximately 5 months.

Randomization was done with sealed envelopes, with blocks of 6 patients, and with one random exchange of a pair of envelopes between the blocks (to preclude investigator deduction of treatment). The patients had earphones...
31 patients with Achilles tendon rupture assessed for eligibility (n = 31)

Refused to participate (n = 1)

Randomized (n = 30)

Allocated to PRP treatment (n = 16)

Lost to follow-up 7 weeks (n = 1) due to infection

Allocated to control group (n = 14)

Lost to follow-up 19 weeks (n = 1) due to rerupture

Primary endpoint

Analyzed at 7 w (n = 15)

Analyzed at 19 w (n = 14)

Analyzed at 52 w (n = 12)

Analyzed at 52 w (n = 14)

Figure 1. CONSORT flow diagram. PRP, platelet-rich plasma; W, weeks.

Follow-up: Mechanical Properties

To calculate E-modulus, RSA was used to measure strain under defined loading, and computed tomography (CT) was used to measure the transverse area of the tendon at the rupture site.

Roentgen Stereophotogrammetria Analysis. RSA is a frequently used method in orthopaedic research. It provides the possibility to measure the distance between tantalum beads in 3 dimensions and with a high degree of accuracy. A change in position (e.g., ankle flexion) does not influence the measurements if the tissue is not deformed. During RSA, simultaneous radiographs are taken in 2 planes using extracorporeal calibration markers in a standardized cage.

We performed RSA after 7 weeks (within 15 minutes of cast removal), after 19 weeks (12 weeks after cast removal), and after 52 weeks (12 months). We used the same protocol at the first 2 follow-ups and a slightly different protocol at the last follow-up. At the first 2 follow-ups, the patients sat on an examination table with the foot in
a specially designed frame and with 8° of plantar flexion. The frame allowed us to apply a pedal to the forefoot and load it with weights. The pedal pivoted around an axis with an adjustable distance from the posterior aspect of the heel, which allowed estimation of the moment arms from radiographs (see below). The patients were then asked to keep the foot in position and to resist the dorsal flexion moment derived from the pedal during loading. The first force applied to the pedal was 25 N and the second was 150 N. The 25-N loading was intended to provide a baseline value (a reasonable relaxation of the dorsal flexor muscles), whereas 150 N was the main loading (loading sufficient to produce strain). The patients had to resist the force for 15 seconds before the radiographs were taken; thereafter, the weight was immediately removed. Between all exposures, there was a rest period of 3 minutes. These first 2 exposures were used as the control examination. Moreover, they served as pre-conditioning loading of the Achilles tendon. After another 3-minute rest, the main examination was performed, again with 25 N and 150 N. Where not otherwise stated, all results refer to the second/main examination. Strain-per-force values (assuming a linear relationship) were calculated with correction for the lever arms of the forefoot and the calcaneus and are expressed as a percentage per 100 N of tendon force.

For descriptive reasons, the testing procedure at 7 weeks led to a strain of 2.0% ± 0.4%. At 19 weeks, the strain was 1.0% ± 0.7%.

A final RSA was done 12 months after surgery. This examination differed slightly from the first 2 examinations, 7 and 19 weeks after surgery. Also at this time, the patients had to resist the applied loading for 15 seconds with 3-minute intervals, but we increased the force from the baseline 25 N in 100-N increments, with no repetition (ie, the forces were 25, 125, 225, 325, and 425 N). Strain per force was now calculated from the slope of the regression lines for all measurements. During the course of the study, we omitted the measurements with 125 N and 325 N to reduce exposure to radiation.

The 4 beads were numbered from proximal to distal (Figure 2). The change in distance between beads 2 and 3 at the second/main loading with 25 N was the value used for analysis.

In addition to the above, single unloaded RSA examinations were performed with the leg in plaster, shortly after change from the equinus position to the normal position at 3.5 weeks and immediately before cast removal at 7 weeks. This was done to measure creep.

The RSA analysis was based on the UmRSA 4.1 system (RSA Biomedical, Umea, Sweden). Simultaneous exposures were done using a calibration plate designed for RSA of the hip. Rigid bodies were not calculated. We used the RSA software to calculate distances between 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 CT lateral radiographs, with the center of the talus trochlea as pivot point (pedal point to trochlea center, trochlea center to center of tendon).

Follow-up: Functional Outcomes

The first 20 consecutive patients underwent functional examination 6 months after surgery, and all patients but 1 were examined at the 1-year follow-up. All patients were examined by a physiotherapist who was blinded to treatment and had not seen the patients before. The patients were still blinded regarding their treatment.

The noninjured side was always tested first. Patients were barefoot during all tests. Passive range of motion in dorsal and plantar flexion was registered with a handheld goniometer. Calf circumference was measured with a measuring tape, 10 cm below the tibial tuberosity. A reduction in calf circumference indicates muscle atrophy, and measurements have shown good test-retest reliability. The relationship between calf circumference and calf muscle strength and endurance has been shown to be weak. Still, measurement of calf circumference is one of the most common evaluation methods after Achilles tendon ruptures. Muscle performance was evaluated with maximal number of single-limb toe raises (cadence, 30 raises per minute; height of the heel should be at least 5 cm from the floor) and maximal height of 1 single-limb toe raise, measured in centimeters from the floor to the heel. Heel raise testing has been recommended for evaluation of calf muscle function. The number of heel raises that a person can perform depends on the height of the heel raise. Thus, we created a heel raise index, defined as the number of heel raises that the patient could do, multiplied by height of the heel raise and normalized as a percentage of the other side. Tests that combine the number of heel raises and their height have been found to have good reliability and validity in detecting functional impairments. Because this variable was correlated to E-modulus in a previous study, it was used as the primary functional outcome variable.

For analysis of force development during gait and vertical jump, we used the CODA mpx30 motion analysis.
TABLE 1
Mechanical Properties of Healing Achilles Tendons With Autologous Platelet-Rich Plasma (PRP) or Control Treatment

<table>
<thead>
<tr>
<th></th>
<th>PRP</th>
<th>Control</th>
<th></th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower</td>
<td>Mean</td>
<td>Upper</td>
<td></td>
</tr>
<tr>
<td>E-modulus, MPa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 weeks</td>
<td>91 ± 29</td>
<td>80 ± 22</td>
<td>-11</td>
<td>13</td>
</tr>
<tr>
<td>19 weeks</td>
<td>90 ± 29</td>
<td>80 ± 35</td>
<td>-29</td>
<td>-2</td>
</tr>
<tr>
<td>52 weeks</td>
<td>235 ± 69</td>
<td>280 ± 88</td>
<td>-35</td>
<td>-8</td>
</tr>
<tr>
<td>Strain per force, % per 100 N</td>
<td>0.7 ± 0.3</td>
<td>0.9 ± 0.2</td>
<td>-38</td>
<td>-14</td>
</tr>
<tr>
<td>7 weeks</td>
<td>0.4 ± 0.1</td>
<td>0.4 ± 0.5</td>
<td>-73</td>
<td>-12</td>
</tr>
<tr>
<td>19 weeks</td>
<td>0.2 ± 0.05</td>
<td>0.2 ± 0.09</td>
<td>-34</td>
<td>3</td>
</tr>
<tr>
<td>52 weeks</td>
<td>1.54 ± 0.36</td>
<td>1.59 ± 0.36</td>
<td>-20</td>
<td>-8</td>
</tr>
<tr>
<td>Area, cm²</td>
<td>3.24 ± 0.65</td>
<td>3.59 ± 0.67</td>
<td>-23</td>
<td>-10</td>
</tr>
<tr>
<td>7 weeks</td>
<td>2.75 ± 0.70</td>
<td>2.75 ± 0.55</td>
<td>-18</td>
<td>0.4</td>
</tr>
</tbody>
</table>

*Mean ± SD and 95% confidence interval for the difference between the group means, expressed as percentage of control mean.

TABLE 2
Characteristics of Patients With Autologous Platelet-Rich Plasma (PRP) or Control Treatment

<table>
<thead>
<tr>
<th></th>
<th>Age, y</th>
<th>Sex, M:F</th>
<th>Roentgen Stereophotogrammetric Analysis, n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>3.5 Weeks</td>
</tr>
<tr>
<td>PRP</td>
<td>39.8 ± 6.2</td>
<td>13:3</td>
<td>15</td>
</tr>
<tr>
<td>Control</td>
<td>39.4 ± 8.3</td>
<td>11:3</td>
<td>14</td>
</tr>
</tbody>
</table>

A second goal was to test the hypothesis that PRP treatment influences the functional outcome. For this, we used a heel raise index at 1 year as the primary variable, but we also studied the ATRS. The choice of heel raise index was based on our previous observation that it correlated with mechanical variables at an early time point. Other functional outcomes were regarded as descriptive.

Statistical analysis of the data was performed with the t test and simple linear regression analysis using SPSS 17 (SPSS Inc, Chicago, IL). Group differences were further described by 95% confidence interval (CI) for the difference between group means. For example, in Table 1, -11 in the row for E-modulus at 7 weeks means that more than a 11% reduction of the modulus by PRP treatment could be excluded with 97.5% confidence. Functional data were analyzed using the Mann-Whitney test.

No a priori power analysis could be performed, because there was no information available about how large a difference in E-modulus would be clinically relevant. We therefore chose 2 groups of 15 patients because this gave a power of 80% to find a difference of slightly above 1 standard deviation.

RESULTS

Patient characteristics are given in Table 2. There were no complications related to the tantalum beads or the mechanical stress of the measurement procedure. Two patients had to be excluded from the PRP group. One of...
Transverse Area and Modulus of Elasticity Over Time in the Platelet-Rich Plasma (PRP) and Control Groups: Mean ± SD

<table>
<thead>
<tr>
<th>Transverse Area</th>
<th>7 Weeks</th>
<th>19 Weeks</th>
<th>52 Weeks</th>
<th>E-modulus</th>
<th>7 Weeks</th>
<th>19 Weeks</th>
<th>52 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRP</td>
<td>155 ± 36</td>
<td>323 ± 66</td>
<td>276 ± 70</td>
<td>90 ± 29</td>
<td>90 ± 29</td>
<td>239 ± 69</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>169 ± 36</td>
<td>369 ± 67</td>
<td>270 ± 56</td>
<td>80 ± 22</td>
<td>92 ± 36</td>
<td>237 ± 97</td>
<td></td>
</tr>
</tbody>
</table>

them suffered a rerupture 2 months after removal of the cast. The measurements from this patient at 7 weeks were still included, but data after the rerupture were excluded. The rerupture was treated nonoperatively with a cast in equinus position for 4 weeks and in the neutral position for another 4 weeks. The other patient who was excluded suffered a deep infection that was treated with antibiotics. The data obtained from mechanical testing of this patient were excluded. Single tantalum beads from 5 patients were excluded because they were outside the tendon substance on CT examination. However, because 2 beads were always inserted on either side of the rupture, the other bead could be used, and no patient had to be excluded because of malpositioning of tantalum beads.

One patient in the control group was unable to resist the 150-N weight at 7 weeks because of pain in the operated area and was tested with a 100-N weight instead. At the later examinations, there was no such problem. One patient in each group had a deep vein thrombosis diagnosed by ultrasound. These patients were treated with warfarin for 3 months. This was not cause for exclusion from the study. However, we analyzed the data after excluding them, and there was no difference in the results, which might otherwise have influenced the conclusions (unpublished results). One patient did not want to participate in the RSA examination after 1 year, and in one case, the RSA radiographs at 1 year did not show the proximal 2 tantalum beads, which meant exclusion of the results.

In total, values for E-modulus at 7 weeks were available and analyzed for 18 PRP patients and 14 control patients. At 19 weeks, there were 14 PRP patients and 14 control patients, and at 52 weeks there were 12 PRP patients and 14 controls. The functional outcome at 6 months was assessed in 10 PRP patients and 10 control patients, and at 52 weeks it was assessed in 15 PRP patients and 14 control patients.

Mechanical Properties

The primary variable—E-modulus at 7 weeks—was 13% higher (95% CI, -11 to 38) with PRP treatment than with the control treatment. At 19 weeks, the E-modulus was reduced by 2% in the PRP group (95% CI, -29 to 25). There were no significant differences between PRP and control results regarding any of the mechanical variables or transverse area at any time point. There were no significant differences either in means or in variances (Table 1).

Functional Outcomes

At the 6-month follow-up, 2 patients (1 in the PRP group and 1 in the control group) were unable to do a heel raise of more than 5 cm; therefore, they were excluded from the endurance test. Heel raise index could not be calculated for these patients.
TABLE 4
Functional Outcome in All Patients, With P Values for Side Differencesa

<table>
<thead>
<tr>
<th>6 Months (n, 20)</th>
<th>1 Year (n, 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
</tr>
<tr>
<td>Dorsal flexion, deg</td>
<td>4 ± 5</td>
</tr>
<tr>
<td>Plantar flexion, deg</td>
<td>4 ± 5</td>
</tr>
<tr>
<td>Calf circumference, % cm</td>
<td>96 ± 3</td>
</tr>
<tr>
<td>Heel raise index, %</td>
<td>64 ± 16</td>
</tr>
<tr>
<td>Peak force at gait, % N</td>
<td>96 ± 4</td>
</tr>
<tr>
<td>Peak force at vertical jump, % N</td>
<td>96 ± 6</td>
</tr>
<tr>
<td>Vertical jump, % seconds</td>
<td>91 ± 9</td>
</tr>
</tbody>
</table>

aRange of motion in degrees is expressed as difference from the noninjured leg. The other variables are presented as the ratio between the injured and noninjured leg.

TABLE 5
Functional Outcome in the Platelet-Rich Plasma (PRP) and Control Groupsa, b

<table>
<thead>
<tr>
<th>6 Months (n, 20)</th>
<th>1 Year (n, 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PRP</td>
</tr>
<tr>
<td>Dorsal flexion, deg</td>
<td>6.5 ± 5</td>
</tr>
<tr>
<td>Plantar flexion, deg</td>
<td>4.5 ± 6</td>
</tr>
<tr>
<td>Calf circumference, % cm</td>
<td>96 ± 3</td>
</tr>
<tr>
<td>Heel raise index, %</td>
<td>60 ± 14</td>
</tr>
<tr>
<td>Peak force at gait, % N</td>
<td>96 ± 5</td>
</tr>
<tr>
<td>Peak force at vertical jump, % N</td>
<td>89 ± 11</td>
</tr>
<tr>
<td>Vertical jump, % seconds</td>
<td>62: 59-70</td>
</tr>
</tbody>
</table>

aRange of motion in degrees is expressed as the difference from the noninjured leg. The other variables are presented as the ratio between the injured limb and the noninjured limb.

bAchilles Tendon Total Rupture Score, presented as median with interquartile range.

Significant deficits in function of the injured leg were found in all variables 6 months after rupture (Table 4). The largest deficiency was found for the more demanding activities (heel raises) compared with range of motion and level walking. At the 12-month follow-up, heel raise index and peak force at toe-off had increased significantly (P < .05). Still, compared with the noninjured leg, the injured leg had inferior function in all variables except peak force development during toe-off in gait and vertical jumping (Table 4).

Our main variable for functional outcome—heel raise index at 12 months—was not significantly different between the treatment groups, and no other significant difference in function could be found between the groups, except for plantar flexion at 12 months (Table 5). The ATRS at 12 months was lower (inferior function) for the PRP patients than for the controls (Table 5). This difference remained significant when the 2 patients with deep vein thrombosis were excluded.

Correlation Between Mechanical and Functional Variables

The E-modulus of all tendons at 7 and 19 weeks showed a weak but significant correlation with heel raise index (respectively, r² = .21, P = .02; r² = .27, P = .005). There was also a correlation between strain per force at 7 and 19 weeks and heel raise index (respectively, r² = .19, P = .02; r² = .16, P = .04). There was no correlation between transverse area at 7 and 19 weeks and heel raise index. At 52 weeks, there was a correlation between E-modulus and heel raise index (r² = .32, P = .003). There was a negative correlation between transverse area and heel raise index (r² = .15, P = .04). Strain per force showed no such correlation.

Tendon Elongation

The tendons elongated (median, 4.5 mm) from 3 to 7 weeks (ie, between the change of foot position with the cast and cast removal). Elongation of the tendons from 7 to 19 weeks was 2.9 mm (median). From 19 weeks to 52 weeks, it was −0.4 mm. There was no significant difference between the groups for any period (Table 6, Figure 5).

One patient showed a marked elongation (21 mm) from 19 to 52 weeks. He also had the lowest heel raise index percentage after 1 year (only 17%). This patient was in the control group. Reanalysis after excluding him made no difference to the statistical significance of the ATRS results.
TABLE 6

Elongation Over Time in the PRP and Control Groups: Median ± SD

<table>
<thead>
<tr>
<th></th>
<th>3.5 to 7 Weeks</th>
<th>7 to 19 Weeks</th>
<th>19 to 52 Weeks</th>
<th>7 to 52 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRP</td>
<td>4.72 ± 3.55</td>
<td>2.96 ± 4.73</td>
<td>0.13 ± 3.32</td>
<td>2.08 ± 12.74</td>
</tr>
<tr>
<td>Control</td>
<td>4.20 ± 2.83</td>
<td>2.48 ± 7.69</td>
<td>-0.58 ± 8.96</td>
<td>1.77 ± 9.96</td>
</tr>
</tbody>
</table>

Figure 5. Elongation over time.

Error of Measurements

To control our settings of measurements and to confirm that the beads were placed correctly and that they were not loose within the tendon, we performed double examinations (repetition of RSA, 25 N and 150 N) at 7 and 19 weeks. The first and second strain values showed correlations at 7 weeks ($r^2 = .54$) and 19 weeks ($r^2 = .94$). Furthermore, we compared the strain between the outer beads (beads 1 and 4) with the strain between beads closer to the rupture site (beads 2 and 3) in all patients where no beads had to be excluded because of malpositioning. Also here, there was a good correlation at 7 weeks ($r^2 = .63$) and 19 weeks ($r^2 = .90$).

There was a correlation between the percentage change in distance between beads 2 and 3 over time from 7 to 52 weeks (elongation) and the percentage change in distance for beads 1 and 4 over the same period ($r^2 = .94$).

At the 12-month follow-up, a regression coefficient was calculated between tensile load and strain. The regression was based on 5 paired values for 11 patients and 3 paired values for 15 patients (the number of radiographic examinations at 12 months was reduced after the 11th patient to minimize the radiation exposure). The $r^2$ value was .85 or higher for all but 1 patient; the median value was .93.

DISCUSSION

This is the first randomized controlled trial to treat Achilles tendon ruptures with PRP. We were unable to show any beneficial effect of the PRP treatment on Achilles tendon healing after rupture. A small to moderate effect cannot be excluded, but the CI for the difference between groups precludes that the treatment increased the E-modulus by more than 38%. Moreover, the treatment had a negative effect on the ATRS. Because this was not a predetermined primary variable, this negative result must be interpreted with caution.

Our results contrast those of Sanchez et al, who found earlier return to sports after PRP treatment, compared with historical controls. The studies differ in that Sanchez et al coagulated the PRP in vitro before introducing it into the wound. The platelet concentration in their study was about 3 times higher than the patient's peripheral blood, which is common in studies on PRP. In our study, the volume that was introduced was similar, but the platelet concentration was about 17 times that in the patient's peripheral blood. Both studies focused on early healing but used different outcome variables.

The PRP was stored overnight before surgery. However, we checked platelet viability by examining the swirling phenomenon immediately before treatment of the patient, in accordance with blood service routines. It has been shown that preparation and 1 day of storage of PRP lead to release of growth factor from platelets in the order of 20%. However, the high number of platelets injected in our study makes it unlikely that the lack of effect was caused by low growth factor content, taking into account even a small wound leakage and growth factor release before injection. It therefore seems that PRP treatment is of little value for stimulating tendon repair under the conditions used in our study.

It is possible that the platelets would be efficacious under other conditions, such as after nonoperative treatment or with mechanical loading. Indeed, many surgeons now allow postoperative loading. In rat experiments, it has been shown that platelets enhance tendon repair only if the tendons are mechanically loaded. However, rats and humans differ in many ways. In this case, the most important difference might be size. In the rat, which is relatively small, a large surface area of tissue is exposed to the single drop of injected PRP in relation to the hematoma volume, which the cells from this surface have to replace with new tissue. In humans, larger spaces have to be filled with new tissue, and the relation between volume and area is less favorable. This also takes a longer time so that whatever effects the platelets initially had, the risk is higher that they will have faded with time.

This study allowed other observations regarding tendon repair. It appears that during the first months of healing, the most important process is callus growth.
transverse area doubled from 7 to 19 weeks, but we could not demonstrate any improvement in mechanical tissue properties (E-modulus) at 19 weeks. This was seen first at 1 year.

During later phases of healing, it appears that if the healing has failed to provide good building material (high E-modulus), then it is compensated for by an increase in transverse area. At 1 year, there was relatively little variation in tendon stiffness but a larger variation in modulus, which suggests that poor tissue properties were compensated for by a greater transverse area (there was a significant negative correlation between the 2 variables) and which might explain the negative correlation between transverse area at this time point and heal raise index.

Function had not been restored 12 months after surgical treatment of Achilles tendon rupture. Some improvement was seen between the 6- and 12-month follow-ups. Treatment with PRP made no difference to the functional outcome. Despite this, the patients had a normal gait pattern, and the self-reported function was relatively good. These results are in agreement with the results of previous studies on functional outcome after Achilles tendon rupture but not with results on the effect of PRP. The divergence between the functional outcome and the patient's self-rated function suggests that the disability does not limit the patient in everyday activities. Even so, it may pose a risk of new injuries.

We have reported that there is a correlation between the E-modulus at the time of plaster removal and function at 18 months. This was the case in the present study, although the correlation was weaker, probably because functional measurements were performed earlier (at 12 months instead of 18). It is unclear why the properties of early tendon tissue should be related to late muscle function. However, the relation confirms the relevance of mechanical measurements at the time of plaster removal.

We are convinced that there was no migration of tantalum beads in the tendon tissue. As can be seen from the correlations reported in the results, the 2 beads on each side of the rupture site behaved similarly and in a way that is consistent with a homogeneous deformation of the tissue. However, the correlation between values obtained from different beads is less than in our previous study, which is a weakness. We have reported that the strain (in percentage) is similar regardless of whether the beads close to the rupture or further away are used for the measurement. Our data on elongation from one follow-up to the next also indicate that the beads on each side of the rupture site remain in an unchanged position relative to each other.

This study is based on the assumption that healing tendons largely behave in an elastic manner. This is a simplification, which might be problematic. From the first conditioning loading a certain elongation tended to remain to the second, definitive examination. Thus, there may be an element of viscoelasticity. Our use of the term E-modulus must therefore be regarded in the context of an assumption of elastic behavior. This simplification is necessary for practical reasons, and it does not influence our group comparisons.

In conclusion, the present results show that there is no dramatic positive effect of PRP in healing of Achilles tendon rupture, and they possibly suggest that it has a negative effect on the functional 1-year result.

ACKNOWLEDGMENT

We thank Hanna Norrman for performing the functional measurements at the 52-week follow-up.

REFERENCES

Knee Rotational Laxity in a Randomized Comparison of Single- Versus Double-Bundle Anterior Cruciate Ligament Reconstruction

Andrea Hemmerich,† PhD, Willem van der Merwe,* MD, Marijka Batterham,§ PhD, and Christopher L. Vaughan,‡ PhD

Investigation performed at the University of Cape Town, Cape Town, South Africa

Background: While single-bundle anterior cruciate ligament reconstruction reduces anterior-posterior laxity, studies have demonstrated residual rotational instability. Improved pivot-shift results have been shown with the double-bundle graft; however, no study has compared rotational laxity outcome of these surgical techniques in vivo under quantified, isolated torsional loading.

Hypothesis: The anterior cruciate ligament–deficient knee exhibits greater rotational laxity than the contralateral uninjured knee. The double-bundle reconstruction restores rotational joint stability to a greater extent than single-bundle surgery.

Study Design: Controlled laboratory study.

Methods: Rotational laxity of 32 patients with unilateral anterior cruciate ligament injury was assessed in both knees at full extension and 30° of flexion using a magnetic resonance imaging-compatible torsional loading device. Patients were randomly allocated either a single- or double-bundle reconstruction and reassessed 5 months after surgery.

Results: The anterior cruciate ligament-deficient knees demonstrated greater laxity to internal rotational torque in the extended position, but not in the 30° flexed position. No significant differences in rotational laxity were found between single- and double-bundle reconstructions. In extension, excessive internal rotational laxity of injured compared with contralateral knees was reduced by anterior cruciate ligament reconstruction. The single-bundle reconstruction did not affect internal rotation compared with contralateral or preoperative groups. In response to internal rotational torque in the flexed knee position, the double-bundle reconstruction reduced laxity to 10.8° from the pre-operative value of 15.3° (P = .058); postoperative rotation was also significantly less than the contralateral laxity of 16.4° (P = .022).

Conclusion: The ruptured anterior cruciate ligament resulted in increased internal rotational laxity only in the extended position. The single-bundle reconstruction did not affect rotational restraint compared with contralateral or preoperative groups. The double-bundle procedure significantly reduced internal laxity in the flexed position when compared with normal.

Clinical Relevance: As the anterior cruciate ligament is not the primary restraint to rotation, its contribution to joint stability is limited under isolated torsional load. While the double-bundle graft demonstrates superior rotational constraint, this may be excessive for isolated anterior cruciate ligament rupture.

Keywords: in vivo internal-external rotational laxity; anterior cruciate ligament (ACL) reconstruction; single-bundle graft; double-bundle graft; torsional loading

The anterior cruciate ligament (ACL), in addition to its primary role restraining anterior tibial translation, has been shown to contribute to rotational stability of the knee. Conventional surgical techniques adequately restore anterior-posterior (A-P) stability; however, subjective symptoms of "giving-way" and positive pivot-shift test results reveal that rotational laxity often remains. To improve rotational stability outcome, surgical techniques have been modified to reconstruct not just the anteromedial (AM) bundle, but also the posterolateral (PL) bundle of the ACL. Although the single-bundle (SB) technique has been shown to improve knee stability with respect to the injured knee, several biomechanical studies have shown superior functional outcome under anterior and