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Autologous platelets have no effect on the healing of human Achilles tendon ruptures: a randomized single-blind study

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Abstract

Background

Several animal studies have shown that local application of platelet-rich plasma (PRP) stimulates tendon repair. Preliminary results from a retrospective case series have shown faster return to sports.

Hypothesis

Autologous PRP stimulates healing of acute Achilles tendon ruptures.

Study design

Randomized, controlled single-blind clinical trial.

Methods

Thirty patients were recruited consecutively. During surgery, tantalum beads were implanted in the Achilles tendon proximal and distal to the rupture. Before final skin suture, randomization was performed and 16 patients were injected with 10 mL PRP whereas 14 were not. The PRP had at least 10 times higher platelet concentration than in the peripheral blood of the patients. Using 3D radiographs (radiostereometry; RSA), the distance between the beads was measured at 7, 19, and 52 weeks while the patient resisted different dorsal flexion moments over the ankle joint. The tendon strain per load could therefore be estimated. Double examinations showed high reproducibility. An estimate of e-modulus was calculated using callus dimensions in CT examinations. At 1 year, functional outcome including the heel-raise index and Achilles Tendon Total Rupture Score (ATRS) was evaluated. The primary effect variables were e-modulus at 7 weeks and heel-raise index at 1 year.

Results

The mechanical variables showed a large degree of variation between subjects that could not be explained by measuring error. In the PRP group, the e-modulus was 13% higher than in the controls at 7 weeks (95% CI -11 to 38). At 19 weeks, the difference was 2% lower (95% CI -

29 to 25). At 52 weeks there was no significant difference in heel-raise index between groups. The ATRS score was, however, lower in the PRP group (p = 0.02), suggesting that PRP had a detrimental effect. There was a correlation between the e-modulus at 7 weeks and at 19 weeks and the heel-raise index at 52 weeks ($r^2 = 0.21$, p = 0.02 and $r^2 = 0.27$, p = 0.005,

respectively).

Conclusions

The results suggest that PRP is not useful for treatment of Achilles tendon ruptures. There was a correlation between early e-modulus and late clinical results, which confirms that the variation in e-modulus provides biologically relevant information, although the correlation was weaker than in previous studies. However, it is unclear how early biomechanics is connected with late clinical results.

Clinical relevance

PRP therapy has become popular in sports medicine but it may not always be efficacious.

What is known about this subject

Case series and animal experimental data suggest that a single dose of PRP stimulates tendon healing, but there have not been any randomized trials.

What this study adds to existing knowledge

This is the first randomized trial on the subject. The results appear to exclude any dramatic positive effect and they possibly suggest a negative effect on the functional 1-year result.

Key Terms: Achilles tendon; Platelet; PRP; Tendon healing; Biomechanics;

Radiostereometry (RSA).

Introduction

Healing after a Achilles tendon rupture is a slow process. Many different treatment methods have been tried to improve tendon healing, with the aim of minimizing the risk of re-rupture and shortening the time until the patient can return to the level of activity before injury. Re-rupture of the healing Achilles tendon can occur late, even 6 months after injury ⁹. In animal experiments, it has been possible to improve the tendon healing process both with mechanical loading^{1 2} and pharmacological treatment²⁶. Another possibility is to use platelet-rich plasma (PRP) ^{17, 25}. 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 ⁸, 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 ²⁴ when injected locally. In rabbit Achilles tendons, increased vascularity and better tissue organization have been found ¹¹. Moreover, one clinical study comparing PRP treated patients with historical controls has indicated that peroperative PRP treatment allows earlier return to sports ¹⁷. This 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, two 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 ⁵. However, a randomized, double-blind placebo-controlled clinical trial involving 54 tendinosis patients failed to show any beneficial effects on clinical outcome ⁶. 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 tendon¹⁸ .We also found that an estimate of 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 one-year follow-up. We have now used this method to measure the early mechanical properties of the healing tendon in a randomized trial, in order 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, as they appeared to be relevant and reasonably sensitive in a previous patient series¹⁸.

Patients and methods

All patients between 18 and 60 years of age presenting with an acute rupture of the Achilles tendon (not older than three days) at our hospital were asked to participate in the study after receiving verbal and written information. Exclusion criteria were diabetes mellitus, a history of cancer, 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 one patient refused to participate in the study (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

As 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, and were sent to the Department of Transfusion Medicine at Linköping University Hospital on the day before surgery. One unit of whole blood (450 mL) was collected with citrate-phosphate dextrose (CPD) as anti-coagulant. From this unit of blood, PRP was obtained by double centrifugation according to accredited procedures⁷. 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 16–29 mL) and had a mean concentration of 3,673 (SD 1051) × 10⁹ platelets/mL.

The PRP was stored at 22°C with constant rotation for up to 20 h before use. The swirling phenomenon (reflecting platelet viability) of the PRPs was examined before use ⁴ and found to be well-maintained in all cases.

Operative treatment and randomization

Surgery was done using a conventional open technique with a dorso-medial approach. We used local anesthesia with carbocaine 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. This was the amount that was possible to inject without leakage before skin suture. Then the skin was sutured using a resorbable intracutaneous suture (Monocryl size 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, this cast was replaced with a cast where the ankle was in neutral position, and another 3.5 weeks was allowed to pass. Full weight bearing 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 two weeks. The training program consisted first of mobility exercises, then muscle strength exercises (two and one-legged toe

raises at slow and fast speed) and balance exercises (standing on one leg on different surfaces and wobble boards). Plyometric exercises (simple two-leg jumps) were allowed from week 16 with a progression during the weeks that followed (jumping on one leg in different directions). If the patient could manage 15–20 toe raises, jogging was allowed from week 18. Full activity, including sports, was allowed after approximately 5 months.

Randomization was done using sealed envelopes, with blocks of 6 patients and exchange of a pair of envelopes between the blocks. The patients had earphones with loud music during opening of the envelope and during the injection, in order to conceal the type of treatment. The patients were therefore not aware of whether or not we had injected the platelet concentrate. 16 patients were randomized to the PRP group and 14 patients were randomized to the control group.

Follow-up: mechanical properties

To calculate e-modulus, RSA ²⁰ 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.

RSA

RSA is a method that is frequently used in orthopedic research. It provides the possibility to measure the distance between tantalum beads in 3 dimensions with a high degree of accuracy ³. 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 two planes using extra-corporal calibration markers in a standardized cage.

We performed RSA after 7 weeks (within 15 minutes of cast removal), after 19 weeks (i.e. 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 two follow-ups, the 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 to load it with weights. The pedal pivoted around an axis with an adjustable distance from the posterior aspect of the heel. This allowed estimation of the moment arms from X-rays (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) and 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 X-ray exposures, there was a rest period of 3 minutes. These first two X-ray exposures were used as the control examination. Moreover, these exposures served as preconditioning 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, it can be mentioned here that the testing procedure at 7 weeks led to a strain of 2.0% (SD 0.4). At 19 weeks, the strain was 1.0% (SD 0.7).

A final RSA was done 12 months after surgery. This examination differed slightly from the first two examinations, 7 and 19 weeks after surgery. This time also, the patients had to resist the applied loading for 15 seconds with 3 min intervals, but we increased the force from the baseline 25 N in 100 N increments, with no repetition (i.e. 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 in order 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.

The RSA analysis used 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 talar trochlea as pivot point (pedal point to trochlea center, and trochlea center to center of tendon). This was all done by a technician who was blinded as to patient treatment.

CT

We measured the transverse area at mid-distance between the proximal and distal markers at 7, 19, and 52 weeks using CT. We also determined the position of the beads within the tendon using CT. Beads lying outside the tendon on the CT scans were excluded.

Follow-up: functional outcomes

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

The non-injured side was always tested first. Patients were barefoot during all tests. Passive range of motion in dorsal and plantar flexion was registered with a hand-held goniometer. Calf circumference was measured with a measuring tape, 10 cm below the tibial tuberosity. A reduction in calf circumference indicates muscle atrophy¹², and measurements have shown good test-retest reliability ¹³. The relationship between calf circumference and calf muscle strength and endurance has been shown to be weak ¹². 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 one single-limb toe raise measured in centimeters from the floor to the heel. Heelraise testing has been recommended for evaluation of calf muscle function. The number of heel raises a person can perform is dependent on the height of the heel raise. Thus, we previously created a heel-raise index, defined as the number of heel raises the patient could do multiplied by height of the heel raise, and normalized as a percentage of the other side ¹⁸. Tests that combine the number of heel raises and their height have been found to have good reliability and validity in detecting functional impairments²². As this variable was found to be correlated to e-modulus in a previous study ¹⁹, it was used as the primary functional outcome variable.

For analysis of force development during gait and vertical jump, we used the CODA motion analysis system, version mpx30 (Charnwood Dynamics Ltd., Rothley, Leicestershire, UK) together with a force plate (Kistler Holding AG, Winterthur, Switzerland) that was built in the floor. During gait analysis, the patients were unaware of the location of the plate and were asked to walk with normal gait pattern between two parallel lines on the floor. For vertical jumping, the patients were instructed to stand on the force plate, jump as high as possible on one leg, and land on the force plate on the same leg. Maximal force during toe-off phase at vertical jump and level walking was registered. Time in the air was analyzed for the vertical jump. Three measurements were carried out for each task and each leg, and a mean value was used in the analysis. The vertical jump was performed only at the one-year follow-up. This test has shown good test-retest reliability ²¹.

All patients also filled in and returned the form for the validated Achilles tendon acute rupture score (ATRS) ¹⁶. ATRS has been shown to have good validity, reliability, and sensitivity for limitations related to symptoms during various activities in individuals who have had total ruptures of the Achilles tendon.

Statistics

This study was designed to test the hypothesis that treatment with platelet concentrate would improve mechanical properties of the healing Achilles tendon. The primary outcome variable was e-modulus at the time of cast removal. Other mechanical properties at this and other time points were secondary variables.

A second goal was to test the hypothesis that PRP treatment influences the functional outcome. For this, we used a heel-raise index at one 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 is correlated to mechanical variables at an early time point ¹⁸ Other functional outcomes were regarded as descriptive.

Statistical analysis of mechanical data was performed with Student's t-test and simple linear regression analysis using SPSS software version 17. Group differences are further described by use of the 95% confidence interval for the difference between group means. For example, in Table 1, Min -11 in the row for e-modulus at 7 weeks means that more than 11% reduction of the modulus by PRP treatment could be excluded with 95% 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, as this would give a power of 80% to find a difference of slightly above one 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 them suffered a re-rupture 2 months after removal of the cast. The measurements from this patient at 7 weeks were still included, but data after the re-rupture were excluded. The re-rupture was treated non-operatively 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, as they were outside the tendon substance on CT examination. However, because two beads were always inserted on either side of the rupture, the other bead could be used and no patient had to be excluded due to malpositioning of tantalum beads.

One patient in the control group was unable to resist the 150-N weight at 7 weeks, due to 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 three months. This was not cause for exclusion from the study. However, we have also 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 one year, and in one case the RSA X-rays at one 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 analysed for 15 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% (95% CI -13 to 38) higher with PRP treatment than in the controls. 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).

The mean transverse area of all patients doubled from 7 to 19 weeks (Table 3, Figure 3). This accounted for the entire reduction in strain per force, as the modulus was unchanged (Table 3, Figure 4). Even at one year, the transverse area was greater than at the time of plaster removal.

Functional outcomes

At the six-month follow-up, 2 patients (one in the PRP group and one in the control group) were unable to do a heel raise of more than 5 cm, and they were therefore excluded from the endurance test. Heel-raise index could not be calculated for these patients.

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 to range of motion and level walking. At the 12-month follow-up, heel-raise endurance, heel-raise height, heel-raise index, and peak force at toe-off had all increased

significantly (p < 0.05). Still, compared to the non-injured 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 also remained significant when the two patients with DVT were excluded.

Correlation between mechanical and functional variables

The e-modulus of all tendons at 7 weeks and at 19 weeks showed a weak but significant correlation with heel-raise index ($r^2 = 0.21$, p = 0.02 and $r^2 = 0.27$, p = 0.005, respectively). There was also a correlation between strain per force at both 7 weeks and 19 weeks and heel-raise index ($r^2 = 0.19$, p = 0.02 and $r^2 = 0.16$, p = 0.04, respectively). There was no correlation between transverse area at 7 weeks and at 19 weeks and heel-raise index. At 52 weeks, there was a correlation between e-modulus and heel-raise index ($r^2 = 0.32$, p = 0.003). There was a negative correlation between transverse area and heel-raise index ($r^2 = 0.15$, p = 0.04). Strain per force showed no such correlation.

Tendon elongation

The tendons elongated (median 4.5 mm) from 3 weeks to 7 weeks, i.e. between the change of foot position with the cast and cast removal. Elongation of the tendons from 7 to 19 weeks

was median 2.9 mm. From 19 weeks to 52 weeks, it was - 0.4 mm. There was no significant difference between the groups for any time period (Table 6, Figure 5).

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

Error of measurements

In order 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 force; see Methods section) at 7 and 19 weeks. The first and second strain values showed correlations at 7 weeks ($r^2 = 0.54$) and at 19 weeks ($r^2 = 0.94$). Furthermore, we compared the strain between the outer beads (bead 1 and bead 4) with the strain between beads closer to the rupture site (bead 2 and bead 3) in all patients where no beads had to be excluded due to malpositioning. Also here, there was a good correlation at 7 weeks ($r^2 = 0.63$) and at 19 weeks ($r^2 = 0.90$).

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 time period ($r^2 = 0.94$).

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 X-ray examinations at 12 months was reduced after the eleventh

patient to minimize the radiation exposure). The r^2 -value was 0.85 or higher for all but one patient, and the median value was 0.93.

Discussion

This is the first randomized controlled trial in treating 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 confidence interval for the difference between group means precludes that the treatment increased the e-modulus by more than 38%. Moreover, the treatment had a negative effect on the ATRS. As this was not a predetermined primary variable, however, this negative result must be interpreted with caution.

Our results contrast with those of Sanchez et al.¹⁷ who found an earlier return to sports after PRP treatment, compared to 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 in 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 focus on early healing, but use different outcome variables.

The PRP was stored overnight before surgery. However, we checked viability by examining the swirling phenomenon immediately before treatment of the patient, in accordance with blood service routines. It has been shown previously that preparation and one day of storage of PRP lead to release of growth factor from platelets in the order of 20% ¹⁰. 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 prior to 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 together 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 also mechanically loaded²⁴. 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 this will have faded out with time.

This study has also allowed other observations regarding tendon repair. It appears that during the first months of healing, the most important process is callus growth. The 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), this is compensated for by an increase in transverse area. At one year, there was relatively little variation in tendon stiffness, but a larger variation in modulus. This suggests that poor tissue properties were compensated for by a greater transverse area (there was a significant negative correlation between the two). This might explain the negative correlation between transverse area at this time point and heel-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 ^{14-15, 23}, but not with results on the effect of PRP ¹⁷. 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 previously reported that there is a correlation between the e-modulus in particular at the time of plaster removal and function at 18 months ¹⁸. This was the case also 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 Results, the two beads on each side of the rupture site behaved similarly and in a way that is consistent with a homogenous 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 previously reported that the strain (in per cent) is similar regardless of whether the beads close to the rupture or those further away are used for the measurement ¹⁸. 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 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 possibly suggest that it has a negative effect on the functional 1-year result.

Acknowledgements, competing interests

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The authors declare that they have no competing interests

Table 1. Mechanical properties of healing Achilles tendons with autologous platelet (PRP) or control treatment. Mean (SD) and 95% CI for the difference between the group means,

expressed as percentage of control mean

	PRP	Control	95 % CI		
			Lower	Mean	Upper
E-modulus at 7	91 (29)	80 (22)	-11	13	38
weeks (MPa)					
Strain per force at 7	0.7 (0.3)	0.9 (0.2)	-36	-14	8
weeks (% per 100 N)					
Area at 7 weeks	1.54 (0.36)	1.59 (0.35)	-20	-3	14
(cm ²)					
E-modulus at 19	90 (29)	92 (35)	-29	-2	25
weeks (MPa)					
Strain per force at 19	0.4 (0.1)	0.4 (0.5)	-72	-12	47
weeks (% per 100 N)					
Area at 19 weeks	3.24 (65)	3.59 (57)	-23	-10	3
(cm ²)					
E-modulus at 52	239 (69)	260 (98)	-35	-8	19
weeks (MPa)					
Strain per force at 52	0.2 (0.05)	0.2 (0.09)	-34	3	39
weeks (% per 100 N)					
Area at 52 weeks	2.76 (0.70)	2.75 (0.55)	-18	0.4	19
(cm ²)					

	Age	Sex	n	n	n	n
	Mean	M / F	RSA 3.5	RSA 7	RSA 19	RSA 52
	(SD)		weeks	weeks	weeks	weeks
PRP	39.8 (6.2)	13 / 3	15	15	14	12
Control	39.4 (8.3)	11/3	14	14	14	14

Table 2. Characteristics of patients with autologous platelet (PRP) or control treatment

Mean	Transverse	Transverse	Transverse	E-modulus	E-modulus	E-modulus
(SD)	area	area	area	7 weeks	19 weeks	52 weeks
	7 weeks	19 weeks	52 weeks			
PRP	155 (36)	323 (65)	276 (70)	90 (29)	90 (29)	239 (69)
Control	159 (35)	359 (57)	270 (55)	80 (22)	92 (35)	237 (97)

Table 3. Transverse area and modulus of elasticity over time in the PRP and control groups

Table 4. Functional outcome in all patients, with p-values for side differences. Results are presented as the ratio between the injured leg and the non-injured leg, expressed as a percentage

	6 months (n = 20)		1 year (n = 29)	
	%	p-value	%	p-value
Dorsal flexion (°)	96	0.001	92	0.002
Plantar flexion (°)	89	0.001	87	< 0.001
Calf circumference (cm)	91	< 0.001	97	< 0.001
Max. no. of toe raises (n)	64	< 0.001	86	0.008
Max. height of a toe raise (cm)	73	< 0.001	79	< 0.001
Heel-raise index *	64	< 0.001	63	< 0.001
Peak force at gait (N)	96	0.001	100	0.369
Peak force at vertical jump (N)			98	0.102
Vertical jump (s)			91	< 0.001

Table 5. Functional outcome in the PRP and control groups. ROM in degrees is expressed as difference from the non-injured leg, with standard deviation. ATRS is presented as median and percentiles. The other variables are presented as the ratio between the injured limb and the non-injured limb, expressed as a percentage

	6 months (n = 20) PRP Control p-			1 year (n = 29) PRP Control p-						
					value			n		value
Dorsal flexion (°)	6.5	(5)	2.5	(4)	0.079	3.0	(5)	2.5	(4)	0.63
Plantar flexion (°)	4.5	(6)	3.5	(3)	0.651	8.0	(5)	3.5	(3)	0.011
Calf circumference (cm)	96	(3)	96	(2)	0.701	96	(5)	97	(2)	0.67
Max. no. of toe raises (n)	63	(33)	68	(15)	0.665	87	(24)	82	(26)	0.585
Max. height of a toe raise (cm)	73	(13)	76	(18)	0.622	78,0	(11)	79,0	(14)	0.845
Heel-raise index *	60	(14)	68	(14)	0.257	69	(23)	67	(27)	0.823
Peak force at gait (N)	95	(5)	98	(2)	0.139	99	(3)	100	(3)	0.881
ATRS	62	(52-70)	89	(52-93)	0.191	78	(75-85)	89	(83-92)	0.014

Median	Elongation	Elongation	Elongation	Elongation
(SD)	3.5–7 weeks	7–19 weeks	19–52 weeks	7–52 weeks
PRP	4.72 (3.65)	2.96 (4.73)	0.18 (4.32)	2.08 (12.74)
group				
Control	4.20 (2.83)	2.48 (7.69)	-0.83 (5.96)	1.77 (9.96)
group				

Table 6. Elongation over time in the PRP and control groups

Legends

Figure 1. Consort flow diagram.

Figure 2. Placement of suture and numbering of marker beads. Beads 2 and 3 were used for

strain measurements and beads 1 and 4 were used as reserve, in case beads 2 or 3 were

incorrectly inserted.

Figure 3. Transverse area over time.

Figure 4. E-modulus over time.

Figure 5. Elongation over time.

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