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Reduced Time to Surgery Improves Patient-Reported Outcome After Achilles Tendon Rupture

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Access to the published version may require subscription. Published with permission from: **SAGE Publications** Reduced Time to Surgery Improves Patient-Reported Outcome and decreases the Risk of Adverse Events after Achilles Tendon Rupture

ABSTRACT

Background: Patient outcome after an acute Achilles tendon rupture (ATR) continues to be suboptimal and heterogeneous. Thus, prognostic factors are called for to optimize evidence-based ATR treatment protocols, however, the influence of delayed time from injury to surgery (TTS) on patient outcome after ATR remains largely unknown.

Purpose: To determine whether patient outcomes and adverse events after surgical repair of acute ATR are related to delayed TTS.

Study Design: Cohort study; Level of evidence, 3.

Methods: Two hundred and twenty-eight ATR patients treated with uniform anesthetic and surgical techniques, within 10 days after injury, were retrospectively assessed. TTS depended on a free slot in the operating theatre and neither surgeon nor patient could affect TTS. Patients were assigned into three groups according to trichotomized TTS; short- (<48hours), intermediate- (48-72hours) and long TTS (>72hours). Patient-reported outcome at one-year was assessed using the validated Achilles tendon Total Rupture Score, with scores>80 on a 0-to 100-point scale indicating an overall good outcome. The incidences of adverse events (periand postoperative) and deep venous thrombosis were assessed.

Results: Shorter TTS was significantly associated with increased rate of good outcome and reduced risk of adverse events. Seventy-one percent (95% CI, 60%-83%) of the patients with short TTS attained a good outcome compared to 44% (95% CI, 33%-56%) of the patients

with long TTS (p=.002), and with the intermediate TTS group in between (63%, 95% CI, 47%-78%). The incidence of adverse events was significantly reduced among patients with short TTS 1.4% (95% CI, 1%-4%) as compared to those with intermediate TTS 11% (95% CI, 2%-21%) (p=.035) and to patients with long TTS 14.8% (95% CI, 7%-23%) (p=.003). The risk of sustaining a deep venous thrombosis was not statistically significant different among the three groups (p=.15).

Conclusion: Patients with acute ATR operated on within 48 hours after injury yielded better outcomes and a lower number of adverse events compared to patients operated on after 72 hours. These results conform to evidence-based recommendations from other surgical disciplines and should be used as guidelines for optimizing ATR treatment protocols.

Key terms: Foot, Achilles tendon, Rupture, Time-to-Treatment, Patient Reported Outcome Measures, Postoperative Complications, Venous Thrombosis

What is known about the subject: In other surgical fields, the relation between Time to Surgery and patient outcome has been thoroughly investigated, however there is only one previous study investigating the relation between Time to Surgery and patient outcome after Achilles tendon rupture-surgery.

What this study adds to existing knowledge: This study establishes that a delay of Achilles tendon rupture-surgery may be related to a worse outcome for patients. This finding is in conformity with results of many studies in closely related surgical fields.

INTRODUCTION

The increasing incidence of Achilles tendon ruptures (ATR)^{8,9,19} further stresses the demands of evidence-based treatment protocols to optimize ATR patient care. Discussions for optimizing ATR patient care have mostly focused on whether to treat the patients surgically or conservatively, however, without considering a plausible negative effect of delayed time to surgery (TTS) on patient outcome.

Exhibiting an adverse effect of delayed TTS on patient outcome has been shown to be a common denominator in several orthopedic fields with studies examining both long-term TTS (weeks-months), including rotator cuff tears⁷, meniscal and chondral injuries^{3, 13} and short-term TTS (days) where the adverse effect of prolonged TTS predominantly has been shown in studies on hip fractures.^{12, 18, 21, 25} In hip fracture surgery today, it is recommended not to delay TTS more than 48 hours after admission as an increase in mortality and both minor complications (e.g. post-operative infections) and major complications (e.g. venous thromboembolism) are seen with prolonged delay of surgery.^{14, 18, 21, 25}

Patient outcome after an ATR in regard to subjective and functional outcome is very variable between patients, the risk of deep venous thrombosis (DVT) is high and influencing factors explaining this variety on outcome are still not fully understood.^{4, 5} In contrast, however, the relationships between delayed TTS, complications and patient outcome after ATR are mostly unknown.¹⁷

The purpose of this retrospective cohort was, therefore, to assess TTS in relation to complications and to validated patient-reported outcome one year after surgery. We hypothesized that delayed TTS may negatively affect patient outcome after surgical repair of an ATR and increase the rate of complications such as DVT and adverse events such as infections, surgical complications and re-operations.

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MATERIAL AND METHODS

Ethical approval was obtained from the Regional Ethical Review Committees in Sweden (Dnr: 2013/1791-31/3, 2009/2079-31/2) and the study was listed in clinicaltrials.gov.

Patients

Two-hundred and forty-five patients who had undergone surgery following acute ATR-injury were retrospectively included from two prospectively designed randomized control trials (RCTs) by Domeij-Arverud et al and Valkering et al.^{6, 23} The RCTs investigated different post-operative rehabilitation protocols during the first two post-operative weeks as compared to plaster cast, further described below in the post-operative treament section. These RCTs used identical protocols regarding inclusion criteria, exclusion criteria, anaesthesia and surgical technique. Both RCTs solely examined ATR-patients who had undergone surgery following their injury and there were no control-groups with patients receiving non-operative treatment. Written consent was collected from all patients in both RCTs at study inclusion. Patient inclusion and follow up is described in Figure 1 and patient characteristics are described in Table 1.

Patients who had sustained an acute unilateral rupture at the midsubstance level of the Achilles tendon, and received surgery within 10 days from injury, were eligible for inclusion. Exclusion criteria were: current anticoagulation treatment (including high dose acetylsalicylic acid), known kidney failure, heart failure with pitting edema, thrombophlebitis, thromboembolic event during the previous three months, known malignancy, hemophilia, pregnancy, other surgery during the previous month, inability to follow instructions or planned follow-up at another hospital.

Time to surgery (TTS)

Patients were acutely planned for surgery, but had to wait for a free slot in the operation theater. Neither the patient nor the surgeon could affect the time from ATR injury to surgery. Time to surgery (TTS), i.e. the time from ATR injury to start of the surgical procedure, was calculated by using the time-point at which the patient sustained the injury as described in the patient journal, as well as the starting time point of the surgery as registered in the computerized operation report. Two-hundred and twenty-eight patients with valid TTS received surgery at a major hospital in Sweden. The TTS variable was trichotomized according to the 48-hour time point chosen from other studies, ^{20, 21, 25} plus an additional practical 24-hour cycle, resulting in the 72-hour time point, which is an important biological phase in tendon healing. ² Patients were assigned into the three groups as follows; TTS < 48 hours ("Short"), 48-72 hours ("Intermediate"), TTS > 72 hours ("Long"). Following ATR-surgery, patients were randomized to three different post-operative treatments which is further described below.^{6, 23} Minor surgical complications, re-ruptures and post-operative infections were summarized as adverse events. At two and six weeks post-operatively, the patients were examined for post-operative infections and additionally screened for deep venous thrombosis in the operated leg. At the twelve-month follow-up, patient reported outcome was assessed by use of the validated Achilles tendon Total Rupture Score (ATRS) questionnaire. ¹⁵

Time to Surgery (TTS) and patient characteristics

Among the patient characteristics (sex, age and BMI), only sex was statistically significant associated with TTS (R=.15, p=.023), however, sex was not statistically significant correlated to any of the outcome variables (p>.05).

Surgical procedure

The surgical procedure was performed on an outpatient basis using uniform anesthetic and surgical techniques²² as part of a standardized protocol for anesthesia and surgery, which was used in both RCTs^{6, 23} from which the patients in this study were selected.

With the patient in a prone position, local anaesthetics was introduced to the skin, subcutis and peritendinous space. Surgery was initiated using a medial incision over the Achilles tendon followed by a central incision, through fascia cruris and the paratenon. Repair of the Achilles tendon was performed using a modified Kessler suture technique with two 1–0 polydioxanone threads, bringing the stumps of the ruptured Achilles tendon together end-to-end. The paratenon and fascia cruris were closed using a 3–0 Vicryl® suture and the skin was closed using a 3–0 Ethilon® suture. To relieve potential post-operative pain, all patients were prescribed tablets containing paracetamol 500 mg/codeine 30 mg.

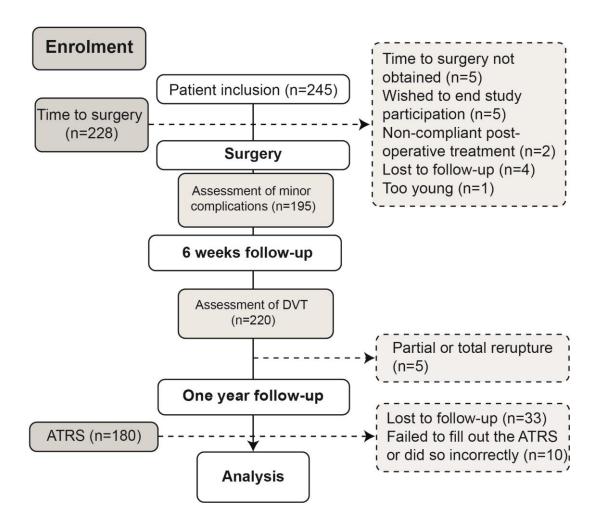


Figure 1 - Patient flowchart. 245 patients suffering unilateral Achilles tendon rupture were included

and then operated on. Abbreviations: ATRS = Achilles tendon Total Rupture Score, DVT = Deep

Venous Thrombosis

	Variable	Short TTS < 48 hours	Intermediate TTS 48 to 72 hours	Long TTS > 72 hours	P-value
		(n = 74)	(n = 49)	(n = 105)	
Patient	TTS, mean (SD), h:m	34:58 (10:28)	64:47 (6:26)	105:15 (34:07)	N/A
characteristics	Sex, n (%), male	60/74 (81)	47/49 (96)	77/105 (73)	.004
	Age, mean (SD), years	39 (7.2)	41 (8.7)	41 (8.5)	.37
	BMI, mean (SD), kg/cm ²	26.4 (3.4)	26.6 (2.7)	25.8 (3.5)	.26
Outcome	ATRS>80, n (%)	45/63 (71)	26/42 (62)	33/75 (44)	.004
variables	Complication n (%)				
	Adverse events	1/69 (1)	5/45 (11)	12/81 (15)	.017
	DVT occurrence	32/73 (44)	29/49 (59)	44/102 (43)	.15

Table 1 – Patient Demographics and outcome

Abbreviations: TTS = Time to Surgery, ATRS = Achilles tendon Total Rupture Score, DVT = Deep Venous Thrombosis, N/A = Not Applicable

Post-operative treatment

The post-operative treatment varied during the first two post-operative weeks due to the two RCTs incorporating partly different post-operative protocols. In the first RCT, patients were post-operatively randomized to either intermittent pneumatic compression (IPC) under a brace (n =69), or immobilization in a plaster cast (n=70).⁶ In the second RCT, patients were post-operatively randomized to either mobilization using an orthosis (n=66), or, immobilization in a plaster cast (n=23)²³. Postoperative treatment was correlated to TTS (R= .34, p= <.001), however, there was no statistically significant correlation between postoperative treatment and any of the outcome variables (p>.2). The lack of impact of the post-operative treatments, used in both RCTs, on patient outcome has also been demonstrated in two previously published studies.^{1, 23}

Assessment of deep venous thrombosis (DVT)

At two and six weeks post-operatively, all patients were screened for DVT in the operated leg by unilateral compression duplex ultrasound. Two experienced ultrasonographists, blinded to the treatment regimens, performed all the compression duplex ultrasound using a Philips CX 50 ultrasound machine (Philips Medical Systems, Andover, MA, USA). The standard procedure included evaluation of all deep proximal and distal veins, including muscle veins, as well as v. saphena magna. The criteria for DVT diagnosis and the diagnostic procedure have been described earlier. ^{6, 11} Proximal DVT was defined as a thrombosis that involved the popliteal vein or any more proximal veins, with or without involvement of the calf veins. Briefly, the DVT diagnosis was based on a transversal ultrasound compression test of the blood vessel, and assessment of blood flow in the veins by color Doppler flow.

Assessment of adverse events

An adverse event was noted if the patient exhibited any of the following: peri-operative complications, post-operative infections at two or six weeks' follow-up or a rerupture at any time during the year following surgery. The rate of each of the complications presented above was low and they were therefore collapsed to one factor.

Patient-reported Outcome Measures (PROMs)

Patients answered the validated Achilles tendon Total Rupture score questionnaire (ATRS, Swedish, version 6) at the twelve-month follow-up appointment in order to determine the patient's degree of symptoms. ATRS includes ten specific questions (scored from 0 to 10, 10 indicating no limitations). The maximal total score of the ATRS is 100, signifying the best possible outcome. A score of ATRS >80 was considered as an overall good subjective outcome.

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Statistical analysis

All data were entered in SPSS (IBM SPSS, Version 24.0. Armonk, NY, USA). The variables were summarized with standard descriptive statistics such as mean, standard deviation and frequency. Group differences were described with p-values and 95% CI. All variables were checked for skewness. Correlations between different variables and outcome were expressed as Pearson's correlations coefficients. Non-parametric Spearman's rank correlation was used if a distribution was severely skewed. Comparisons between groups were performed using Pearson's chi square test for categorical variables and one-way anova for continuous variables. The level of significance was $\leq 5\%$ (two tailed) for all analyses.

RESULTS

Patient-reported outcome

We found that the prevalence of good subjective outcome (ATRS>80) at one year after ATR differed statistically significant among the three TTS-groups (p = .004; Table 1), with the best outcome in the group with short TTS. A good subjective outcome was observed in 71% (45/63) (95% CI, 60% to 83%) of patients with short TTS (<48h), which was a significantly higher rate compared to patients with long TTS (>72h), where a good subjective outcome was seen in only 44% of patients (34/77) (95% CI, 33% to 56%) (p=.002). The patients with intermediate TTS (48-72h) were in-between the two other groups with a good subjective outcome observed in 63% (25/40) (95% CI, 47% to 78%) of the cases (Figure 2).

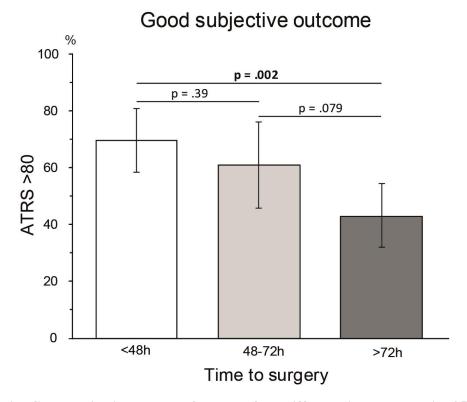


Figure 2 – Good subjective outcome for each of the different time groups with 95% CI.

The risk of exhibiting an adverse event differed significantly among the three TTS -groups (p=.017; Table 1), with the highest prevalence in the long TTS group. Among patients with short TTS, 1.4% (1/69) exhibited an adverse event (95% CI, 1% to 4%), which was significantly less compared to the group with intermediate TTS (p=.035), where patients exhibited 11.1% (5/45) adverse events (95% CI, 2% to 21%), and also significantly less than the group with long TTS (p=.003), where 14.8% (12/81) of patients exhibited an adverse event (95% CI, 7% to 23%) (Figure 3).

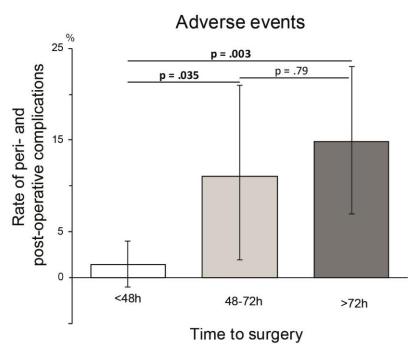


Figure 3 – Adverse events for each of the different time groups with 95% CI.

Deep venous thrombosis (DVT)

The risk of sustaining a DVT was not statistically significant different among the three TTSgroups (Table 1). In the short TTS-group, the incidence of DVT was 43.8% (32/73) (95% CI, 32% to 55%) which was lower compared to the intermediate TTS-group, where 59.2 % (29/49) (95% CI, 45% to 73%) sustained a DVT. In the long TTS-group the DVT-occurrence was 43.1% (44/102) (95% CI, 33% to 53%) (Figure 4).

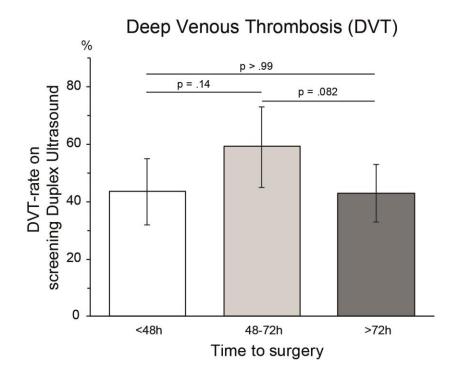


Figure 4 – DVT incidence for each of the different time groups with 95% CI.

DISCUSSION

The results of this study demonstrate for the first time that the timing of surgery in patients with acute Achilles tendon rupture (ATR) has a significant influence on patient-reported outcome at one year post-operatively. We show that reduced time to surgery improves patient-reported outcome and decreases the risk of adverse events after Achilles tendon ruptures.

The most significant finding was to establish a 38% relative reduction (27% absolute reduction) in the number of patients achieving a good subjective outcome when surgery was delayed more than 72 hours as compared to less than 48 hours until surgery. This finding reflected a substantial difference in patient-reported outcome and is corroborated ²⁴ by conclusions from other surgical fields and warrants change in practice guidelines. Such a difference also suggests a new factor underlying the wide variation in ATR patient outcome.

The observed discrepancy in good subjective outcome related to TTS may be partly explained when examining the underlying questions of the validated Achilles tendon Total Rupture score (ATRS) questionnaire. An earlier study has demonstrated that at one year after ATR surgery 44% of the patients experienced limitations due to pain in their limb and 48% of the patients had limitations in walking on uneven surface. ²² It may prove that prolonged TTS diminishes the healing potential of the patient, which may lead to an increased experience of pain. The established worse subjective outcome after more than seventy-two hours' delay may therefore be related to the biology of tendon healing.

After ATR injury the first seventy-two hours are considered the induction phase of tendon healing.² The wound site is infiltrated with blood-derived cells acting as "traffic police",

stopping bleeding, providing immune control, cleaning-up tissue debris and inducing further healing by the release of inflammatory mediators and growth factors. If a second trauma caused by surgery occurs after this induction phase is over there may be a lack of healing inducing factors. Interestingly, human anterior cruciate ligament (ACL)-derived cells obtained during an acute rupture phase exhibit greater healing potential than the cells from a chronic rupture phase.¹⁰ Another factor that has been speculated on in ACL surgery is that delayed TTS may cause retraction of the stumps.¹³ Further studies, however, are needed to conclude on the exact mechanisms underlying the effects of TTS.

The second main finding of our study was the establishment of a positive relationship between longer TTS and increased number of adverse events. When it comes to the observed time-dependent increase in e.g. post-operative infections, this may be related to a similar biological explanation as described above. Hence, as the endogenous immune-response declines within seventy-two hours after ATR-injury the risk of infection may increase with TTS.² Our findings are also in line with research from other surgical disciplines. For laparoscopic cholecystectomy, surgery within two days of presentation of acute cholecystitis have been demonstrated to yield the best outcome for patients.²⁴ In the case of e.g. hip fracture surgery, it has been demonstrated how a delay of TTS increases the risk of both complications and mortality.^{16, 18, 21, 25}

The lack of statistically significant difference regarding DVT-occurrence in combination with the non-linear distribution of DVT among the three TTS-groups suggest that other risk factors not fully accounted for in this study are of greater importance than TTS when predicting the prevalence of DVT.

Based on the combined findings of improved outcome and reduced number of complications observed in patients operated on before 72 hours after injury we find it reasonable to propose a recommendation not to delay ATR-surgery more than three days after injury. Since there are no current directions on TTS in ATR patients we suggest a general recommendation to avoid system-related causes to delay ATR surgery and a specific advice to operate within 72 hours. The recommendations proposed were based on patients operated on using open ATR surgery, but should according to basic principles such as biological healing also be applicable to mini-invasive surgery. Our findings also suggest that all ongoing comparisons between non-operative and operative treatments should take TTS into consideration and possibly only compare patients who are operated on within 72 hours after injury.

The results established showing that patients operated on before 48 hours exhibited the best results, imply that it is essential that the perioperative care of ATR patients found suitable for surgery is adequate. The availability of operating rooms and support services needs to be optimized in order to avoid system-related causes of a delay of surgery. These findings also warrant future studies comparing surgically treated ATR patients within 48 hours with patients receiving non-operative treatment.

There is only one earlier publication, with sixty-five patients included, examining TTS on ATR.¹⁷ That study mainly focused on functional outcome at three months and was unable to find any significant differences between patients grouped by TTS. Moreover, the earlier study by Park et.al. did not include assessment of subjective outcome at one year after ATR-surgery. Hence, until further data are available, we suggest the above presented recommendations for surgically treated ATR patients. According to our knowledge, our study is by far the largest ATR cohort, comprising a total of 245 patients, investigating the

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relationship between TTS and patient outcome. Further research must confirm and extend our findings and understanding of TTS after ATR.

In a field where the amount of previous research is limited, our study adds highly relevant results to the current knowledge of how TTS may affect patient outcome. One potential limitation of our study might be that the patients of the different cohorts performed slightly different post-operative rehabilitation protocols. The rehabilitation protocols were, however, considered in the statistical analyses and did not affect the outcome. Another potential limitation would be that patients received different anesthetic- and surgical procedures depending on TTS. However, since the same study protocol, regarding local anesthesia and surgical techniques, were used in both RCTs, we presume all patients received a similar treatment. The strengths of our study are the relatively large sample-size and a meticulous assessment of the time from injury to surgery. One additional advantage in our study was that neither patients nor doctors had any influence on TTS, which was decided by a free slot in the operation theater.

The results of this study warrant prospective randomized trials to corroborate the current findings. However, we consider it unethical to evaluate the influence of a prolonged waiting time for surgery in ATR patients within the context of a randomized controlled trial. Consequently, the best approach would be a cohort study including a large number of prospectively randomized patients, which was done in the present study.

CONCLUSION

Our study established that delayed TTS was associated with poorer patient-reported outcome one year after surgery of an acute ATR. Prolonged TTS was furthermore associated with a higher occurrence of adverse events. Based on these findings we propose not to delay ATRsurgery more than 72 hours.

COMPETING INTERESTS

The authors had no competing interests.

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