**Challenges and opportunities in trauma research: study designs and patient-reported outcome measures**
Ochen, Y.

# CHAPTER 6

## Operative treatment versus nonoperative treatment of Achilles tendon ruptures: systematic review and meta-analysis

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(The BMJ)

# Abstract

## Background

The management of acute Achilles tendon ruptures—operative or nonoperative treatment—is much debated. The aim of this study was to compare re-rupture rate, complication rate, and functional outcome after operative versus nonoperative treatment of Achilles tendon ruptures; to compare re-rupture rate after early and late full weight bearing; to evaluate re-rupture rate after functional rehabilitation with early range of motion; and to compare effect estimates from randomized controlled trials and observational studies.

## Methods

The PubMed/Medline, Embase, CENTRAL, and CINAHL databases were last searched on 25 April 2018 for studies comparing operative versus nonoperative treatment of Achilles tendon ruptures. Randomized controlled trials and observational studies reporting on comparison of operative versus nonoperative treatment of acute Achilles tendon ruptures were included. Data extraction was performed independently in pairs, by four reviewers, with the use of a predefined data extraction file. Outcomes were pooled using random effects models and presented as risk difference, risk ratio, or mean difference, with 95% confidence interval.

## Results

29 studies were included—10 randomized controlled trials and 19 observational studies. The 10 trials included 944 (6%) patients, and the 19 observational studies included 14 918 (94%) patients. A significant reduction in re-ruptures was seen after operative treatment (2.3%) compared with nonoperative treatment (3.9%) (risk difference 1.6%; risk ratio 0.43, 95% confidence interval 0.31 to 0.60; $P<0.001$; $I^2=22\%$). Operative treatment resulted in a significantly higher complication rate than nonoperative treatment (4.9% *v* 1.6%; risk difference 3.3%; risk ratio 2.76, 1.84 to 4.13; $P<0.001$; $I^2=45\%$). The main difference in complication rate was attributable to the incidence of infection (2.8%) in the operative group. A similar reduction in re-rupture rate in favor of operative treatment was seen after both early and late full weight bearing. No significant difference in re-rupture rate was seen between operative and nonoperative treatment in studies that used accelerated functional rehabilitation with early range of motion (risk ratio 0.60, 0.26 to 1.37; $P=0.23$; $I^2=0\%$). No difference in effect estimates was seen between randomized controlled trials and observational studies.

## Conclusion

This meta-analysis shows that operative treatment of Achilles tendon ruptures reduces the risk of re-rupture compared with nonoperative treatment. However, re-rupture rates are low and differences between treatment groups are small (risk difference 1.6%). Operative treatment results in a higher risk of other complications (risk difference 3.3%). The final decision on the management of acute Achilles tendon ruptures should be based on patient specific factors and shared decision making. This review emphasizes the potential benefits of adding high quality observational studies in meta-analyses for the evaluation of objective outcome measures after surgical treatment.

## Introduction

Rupture of the Achilles tendon is a frequently encountered injury, with an incidence of 31 per 100 000 per year, and is most common in the young to middle aged active population, with a reported mean age ranging from 37 to 44 years.[1,2] Recent studies indicate that the incidence of Achilles tendon rupture is still increasing owing to a more active older population.[2] Injury of the Achilles tendon can be debilitating because of its role in ambulation and activity, affecting both athletes and non-athletes. The management of acute Achilles tendon ruptures—operative or nonoperative treatment—is much debated.[2]

Several meta-analyses of randomized controlled trials (RCTs) have shown that operative treatment significantly reduces the risk of tendon re-rupture compared with nonoperative treatment, with a reported risk difference in re-rupture rate varying from 5% to 7%.[3-6] However, operative treatment leads to a significant increase in other complications such as infection, deep vein thrombosis, and sural nerve injury, with a reported risk difference varying from 16% to 21%.[3,4,6] The incidence of operative treatment has declined over the past decade as a result of multiple RCTs showing comparable results between operative and nonoperative treatment.[1,2]

A recent systematic review of overlapping meta-analyses evaluated nine meta-analyses that compared operative and nonoperative treatment of Achilles tendon ruptures. The discordance found among the nine meta-analyses indicated that further investigation is warranted as rehabilitation protocols, weight bearing restrictions, and treatment modalities have evolved.[7]

Systematic reviews and meta-analyses of RCTs are considered the highest level of evidence for the evaluation of treatment effects. However, several reports have shown that little evidence exists for significant differences in effect estimates between RCTs and observational studies.[8-11] The addition of observational studies in meta-analyses increases sample size, which could enable the evaluation of small treatment effects and infrequent outcome measures. Furthermore, observational studies might provide insight into a variety of populations and long-term effects compared with the usually highly selected patient populations in RCTs.[12,13] Both RCTs and observational studies are increasingly used in orthopedic trauma meta-analyses for the evaluation of treatment effects.[14-17]

The primary aim of this systematic review and meta-analysis was to compare re-rupture rate, complication rate, and functional outcome after operative versus nonoperative treatment of acute Achilles tendon ruptures. Secondly, we sought to evaluate re-rupture rate after early and late full weight bearing and compare re-rupture rate after functional rehabilitation with early range of motion. Finally, we compared effect estimates obtained from RCTs and observational studies.

## Methods

This systematic review and meta-analysis was performed and reported according to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklists.[18-20] A published protocol for this review does not exist.

### Search strategy and selection criteria

We last searched the PubMed/Medline, Embase, CENTRAL, and CINAHL databases on 25 April 2018 for studies comparing operative versus nonoperative treatment of Achilles tendon ruptures. The search syntax is provided in supplementary Table S1. Duplicate articles were removed. Two reviewers (Y.O., R.H.H.G.) independently screened titles and abstracts for eligibility of identified studies. All published comparative studies, both RCTs and observational studies, reporting on the comparison of operative versus nonoperative treatment of acute Achilles tendon ruptures were eligible for inclusion.

After title and abstract screening, the same two reviewers (Y.O., R.H.H.G.) independently reviewed full text articles. Inclusion criteria were acute Achilles tendon rupture, operative treatment (open or minimally invasive surgery) versus nonoperative treatment (cast immobilization or functional bracing), treatment within four weeks of rupture, age 16 years or older, and reporting of re-rupture rate, complication rate, or functional outcome. Exclusion criteria were delayed presentation (treatment more than four weeks after rupture), treatment for re-rupture, language other than English, no availability of full text article, and letters, meeting proceedings, and case reports. We had no inclusion restrictions based on weight bearing status or functional rehabilitation protocol. Disagreements on eligibility of full text articles were resolved by consensus or by discussion with a third reviewer (R.M.H.). References of included studies were screened, and backwards citation tracking was performed using Web of Science to identify articles not found in the original literature search.

### Data extraction

Four reviewers (Y.O., R.H.H.G., R.M.H., R.B.B.) extracted data independently in pairs, using a predefined data extraction file. The following baseline characteristics were extracted from the included studies: first author, year of publication, study design, country in which the study was performed, study period, number of included patients, operative method, nonoperative method, full weight bearing status, functional rehabilitation protocol, and mean follow-up. Studies reporting on patient cohorts described in previously published articles were excluded or merged.

### Quality assessment

The same four reviewers (Y.O., R.H.H.G., R.M.H., R.B.B.), in pairs, independently assessed the methodological quality of included studies by using the Methodological Index for Non-Randomized Studies (MINORS).[21] The MINORS is a validated instrument for the assessment of methodological quality and clear reporting of non-randomized surgical studies, resulting in a score ranging from 0 to 24 for comparative studies.[21] In this study the assessment of methodological quality resulted in a score ranging from 0 to 24 for RCTs and prospective cohort studies. The methodological quality of retrospective cohort studies resulted in a score ranging from 0 to 18. The MINORS criteria for prospective collection of data, loss to follow-up, and prospective calculation of study size were not applicable to the retrospective cohort studies. Details on the methodological quality assessment are provided in supplementary Table S2. Disagreements were resolved by consensus.

### Primary and secondary outcomes

The primary outcome measure was re-rupture rate after operative or nonoperative treatment. Secondary outcome measures included complication rate, functional outcome scores, return to sporting activity, and return to work after operative or nonoperative treatment. We defined complication rate as the rate of complications other than re-rupture. Complications included reports of wound infection, sural nerve injury, deep vein thrombosis, and pulmonary embolism. Functional outcome scores included the Achilles Tendon Rupture Score (ATRS).[22] We subdivided functional outcome scores according to follow-up, into short term (one year of less) and long-term (more than one year). We defined return to sporting activity as the duration in months before resumption of sports and return to work as the duration in weeks before resuming work. In studies that reported on both open and minimally invasive surgery, we used the combined outcome measures.

## Statistical analysis

We present all continuous variables as mean value with standard deviation or range. We converted continuous variables to mean and standard deviation if sufficient information was available, using the methods described in the Cochrane Handbook for Systematic Reviews of Interventions.[23] We extracted dichotomous variables as absolute number and percentage, pooled them using the Mantel-Haenszel method, and presented them as risk difference and risk ratio with 95% confidence interval. We pooled continuous outcomes by using the inverse variance weighting method and presented them as mean difference with 95% confidence interval. We used random effects models for all analyses. We assessed statistical heterogeneity between studies by visual inspection of forest plots and by the $I^2$ and $\chi^2$ statistics for heterogeneity. We used the overall effect Z test to determine the significance level for treatment effects. All analyses were stratified according to study design—RCTs or observational studies. We assessed difference in effect estimates between the two subgroups as described in the Cochrane Handbook for Systematic Reviews of Interventions.[23] The significance level for difference in effect estimates across the subgroups was determined by the test for subgroup differences. We defined the significance level for treatment effects and differences across the subgroups as a P value below 0.05. We assessed potential publication bias by visual inspection of funnel plots with risk ratio and standard error.[24] We used Review Manager (RevMan, version 5.3.5) for all statistical analyses.[25] We further assessed publication bias with Begg's and Egger's statistical tests using Stata 13.1.

## Primary sensitivity analyses

We did sensitivity analyses for the primary outcome, including studies with an early (four weeks or less) and late (more than four weeks) full weight bearing status after treatment. Studies reporting on both an early and a late full weight bearing cohort were accordingly divided for sensitivity analysis. We did an additional sensitivity analysis for the primary outcome with studies that included an accelerated functional rehabilitation protocol. We defined accelerated functional rehabilitation as the start of early range of motion within three weeks after nonoperative treatment. Rehabilitation with functional bracing systems with successive fixed degrees of plantar flexion, which did not allow for free range of motion, were not considered as accelerated rehabilitation.

### Secondary sensitivity analyses

We did secondary sensitivity analyses for high quality studies and year of study period, regarding re-rupture rate and complication rate. We defined high quality studies as RCTs or prospective cohort studies with a MINORS score of 16 or higher (range 0-24) or retrospective cohort studies with a MINORS score of 12 or higher (range 0-18). We did additional sensitivity analyses with studies that included patients after the study period 2000, to account for the development of new rehabilitation protocols, operative techniques, and nonoperative treatment modalities.

## Results

### Search

Figure 1 shows a flowchart of the literature search and study selection. Full text articles could not be obtained for three studies.[26-28] Four studies reported on patient cohorts described in previously published articles and were excluded or merged with the original studies.[29-32] This resulted in the final inclusion of 29 studies for analyses in this systematic review and meta-analysis—10 RCTs and 19 observational tudies.[33-61]

**Baseline study characteristics**

The 29 studies included 15 862 patients, of whom 9375 were treated operatively and 6487 nonoperatively. The overall weighted mean age was 41 (range 17-86) years, 41 years in the operative group and 44 years in the nonoperative group. Overall, the studies included 11 779 (74%) males. Overall follow-up ranged from 10 to 95 months. Table 1 shows the baseline characteristics for both RCTs and observational studies. In addition, supplementary Table S3 shows the treatment characteristics of all included studies.

The 10 RCTs included 944 (6%) patients; 469 patients were treated operatively and 475 nonoperatively. The weighted mean age was 40 years in both treatment groups, and 779 (83%) males were included. The operative method was open surgery in nine studies and minimally invasive surgery in one study.

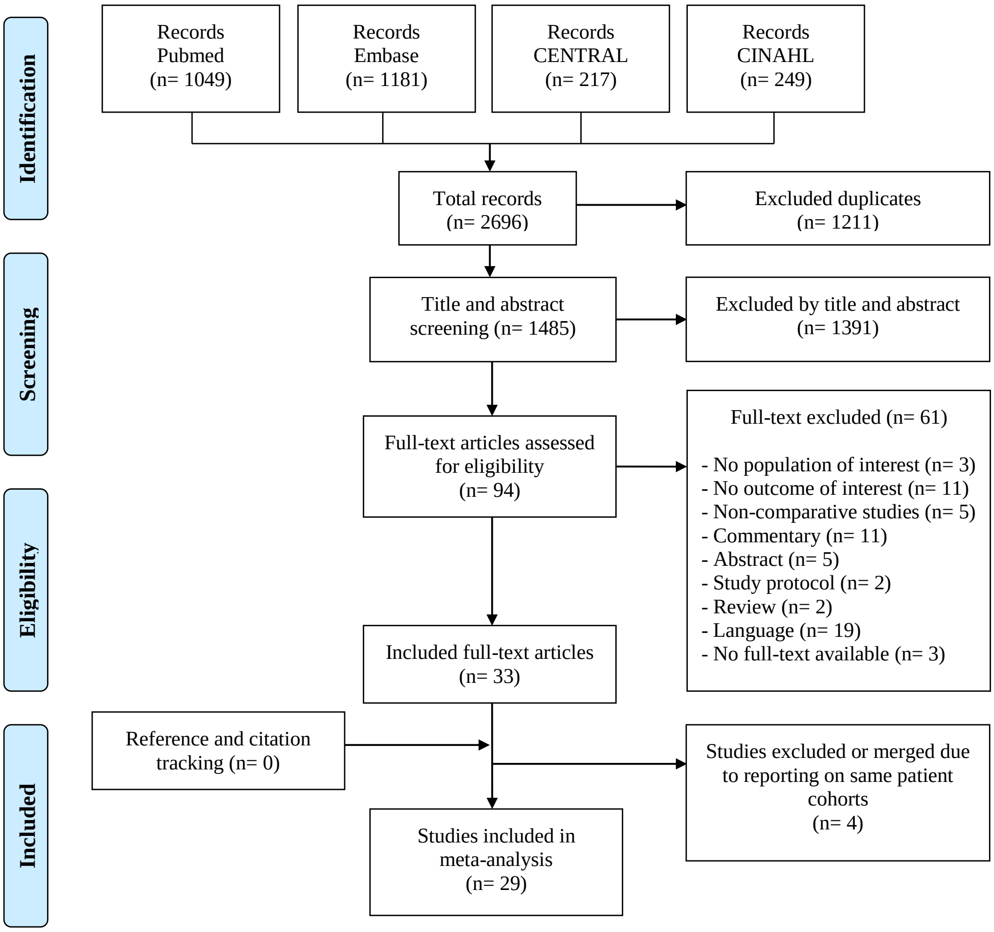


**Figure 1.** PRISMA flow diagram representing the search and selection of studies comparing operative versus nonoperative treatment of Achilles tendon ruptures.

The 19 observational studies—three prospective and 16 retrospective cohort studies—included 14 918 (94%) patients. Operative treatment was performed in 8906 patients, and 6012 were treated nonoperatively. The weighted mean age in the studies was 42 (range 17-86) years, 40 years in the operative group and 44 years in the nonoperative group, and 11 000 (74%) patients were male. The operative method was open surgery in nine studies, unclear in four studies, and a combination of open and minimally invasive surgery in six studies.

## Quality assessment

The overall mean MINORS score was 14.3 (SD 5.2; range 5-23). The mean MINORS score for the RCTs was 20.3 (2.6; 16-23). The mean MINORS score for the observational studies was 11.2 (2.8; 5-16), 14 (2; 12-16) for the prospective cohort studies and 10.6 (2.6; 5-15) for the retrospective cohort studies. The details and distribution of MINORS scores are provided in supplementary Table S4.

**Table 1.** Baseline characteristics of included studies in a meta-analysis of Achilles tendon ruptures

| Study | Year | Study period | Design | Country | Overall number | Number | | Age (years, SD or range) | | Gender (female/male) | | FU (months, SD or range) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **RCTs** | | | | | | OP | NON | OP | NON | OP | NON | OP | NON |
| Cetti et al. | 1993 | 1982-1984 | RCT | Denmark | 111 | 56 | 55 | 37.2 (21-62) | 37.8 (21-65) | 9/47 | 10/45 | 12 | 12 |
| Keating et al. | 2011 | 2000-2004 | RCT | United Kingdom | 80 | 39 | 41 | 41.2 (27-59) | 39.5 (21-58) | 11/28 | 9/32 | 12 | 12 |
| Lantto et al. | 2016 | 2009-2013 | RCT | Finland | 60 | 32 | 28 | 40 (27-57) | 39 (28-60) | 2/30 | 3/25 | 18 | 18 |
| Metz et al. | 2008 | 2004-2005 | RCT | Netherlands | 83 | 42 | 41 | 40 (23-63) | 41 (25-62) | 11/31 | 6/35 | 12 | 12 |
| Möller et al. | 2001 | 1995-1997 | RCT | Sweden | 112 | 59 | 53 | 39.6 (21-63) | 38.5 (26-59) | 8/51 | 5/48 | 24 | 24 |
| Nilsson-Helander et al. | 2010 | 2004-2007 | RCT | Sweden | 97 | 49 | 48 | 40.9 (8.8) | 41.2 (9.5) | 9/40 | 9/39 | 12 | 12 |
| Nistor et al. | 1981 | 1973-1977 | RCT | Sweden | 107 | 46 | 61 | Overall 41 (21-77) | | Overall 11/96 | | Overall 30 (12-60) | |
| Olsson et al. | 2013 | 2009-2010 | RCT | Sweden | 100 | 49 | 51 | 39.8 (8.9) | 39.5 (9.7) | 10/39 | 4/47 | 12 | 12 |
| Twaddle et al. | 2007 | 1997-2002 | RCT | New Zealand | 50 | 25 | 25 | 41.8 | 40.3 | 6/14* | 8/14* | 12 | 12 |
| Willits et al. | 2010 | 2000-2005 | RCT | Canada | 144 | 72 | 72 | 39.7 (11) | 41.1 (8.0) | 13/59 | 13/59 | 24 | 24 |
| **Observational studies** | | | | | | | | | | | | | |
| Bergkvist et al. | 2012 | 2002-2006 | RCS | Sweden | 487 | 220 | 267 | 43 (11) | 47 (14) | Overall 78/409 | | Overall 43 (12-97) | |
| Carden et al. | 1987 | 1969-1981 | RCS | United Kingdom | 71 | 35 | 36 | 42.7 (26-68) | 43 (22-70) | 10/26 | 12/25 | 48 (12-204) | 64 (12-120) |
| Costa et al. | 2006 | 2001-2002 | PCS | United Kingdom | 96 | 48 | 48 | 42 (28-69) | 53 (21-79) | 7/40* | 16/32 | 12 | 12 |
| Cukelj et al. | 2015 | 1998-2013 | RCS | Croatia | 90 | 60 | 30 | 34.8 (4.7 | 35.1 (4.7) | 9/51 | 9/21 | Overall 12 | |
| Ebinesan et al. | 2008 | 2001-2003 | RCS | United Kingdom | 63 | 51 | 12 | 44.8 | 52.1 | 14/37 | 6/6 | N/A | |
| Fahlström et al. | 1998 | 1990-1994 | RCS | Sweden | 31 | 22 | 9 | 34.6 (23-50) | 39.4 (28-51) | Overall 4/27 | | Overall 39 (16-67) | |
| Grubor et al. | 2012 | 2003-2010 | RCS | Bosnia | 42 | 34 | 8 | N/A | | Overall 5/37 | | Overall 12 | |
| Gwynne-Jones et al. | 2011 | 1999-2008 | RCS | New Zealand | 363 | 143 | 220 | 37.4 | 40.9 | 59/84 | 107/113 | N/A | |
| Jaakkola et al. | 2001 | 1985-1999 | RCS | United States | 73 | 35 | 38 | 37.3 (25-64) | 38.0 (21-62) | 3/32 | 6/32 | 43 | 54 |
| Jackson et al. | 2013 | 2002-2008 | PCS | United Kingdom | 80 | 29 | 51 | 37 (24-55) | 47 (27-80) | 3/26 | 16/35 | N/A | |
| Kotnis et al. | 2006 | 2000-2005 | PCS | United Kingdom | 125 | 67 | 58 | 41.0 (26-80) | 43.9 (26-85) | 19/48 | 18/40 | 12 | 12 |
| Lim et al. | 2017 | N/A | RCS | New Zealand | 200 | 99 | 101 | 40.1 | 42 | 21/41* | 32/38* | Overall 78 (24-156) | |
| Miller et al. | 2005 | 1990-1996 | RCS | United Kingdom | 172 | 140 | 32 | 45 | 49 | 23/117 | 11/21 | Overall 95 (53) | |
| Nestorson et al. | 2000 | 1992-1997 | RCS | Sweden | 24 | 14 | 10 | 72 (65-79) | 71 (65-86) | 3/11 | 1/9 | Overall 39 (13-65) | |
| Rajasekar et al. | 2005 | 1997-2001 | RCS | United Kingdom | 35 | 21 | 14 | N/A | | Overall 10/25 | | Overall 24 (9-48) | |
| Renninger et al. | 2016 | 2011-2014 | RCS | United States | 57 | 27 | 30 | 32.3 (25-40) | 29.7 (23-44) | 0/27 | 0/30 | Overall 10 | |
| Van der Linden et al. | 2004 | 1990-2001 | RCS | Netherlands | 292 | 212 | 80 | 37 (9.4) | 42 (12) | 58/154 | 21/59 | Overall 72 (36) | |
| Wang et al. | 2015 | 2007-2011 | RCS | United States | 12570 | 7625 | 4945 | N/A | | 1514/6111 | 1737/3208 | N/A | |
| Weber et al. | 2003 | 1993-1998 | RCS | Switzerland | 47 | 24 | 23 | 38 (28-51) | 39 (17-55) | 4/13* | 8/15 | 49 (30-79) | 23 (12-42) |

OP|NON operative/nonoperative; SD standard deviation; FU follow-up; N/A not available; RCT randomized controlled trial; PCS prospective cohort study; RCS retrospective cohort study; * ratio may not add up to total number of patients due to loss to follow-up

## Primary outcome measure

### Re-rupture rate

Re-rupture rate was reported in all 29 studies. The overall pooled effect showed that operative treatment was associated with a significant reduction in re-rupture rate compared with nonoperative treatment (risk ratio 0.43, 95% confidence interval 0.31 to 0.60; $P<0.001$; $I^2=22\%$) (Figure 2). The pooled effect of RCTs showed a risk ratio of 0.40 (0.24 to 0.69; $P<0.001$; $I^2=0\%$). The pooled effect of observational studies showed a risk ratio of 0.42 (0.28 to 0.64; $P<0.001$; $I^2=31\%$). Re-rupture occurred in 2.3% of patients after operative treatment compared with 3.9% after nonoperative treatment (risk difference 1.6%). We found no significant difference in effect estimates from RCTs and observational studies (test for subgroup differences: $P=0.91$; $I^2=0\%$). There was no visual asymmetry in the funnel plot (supplementary Figure S1). The Begg rank correlation test ($P=0.66$) and Egger linear regression test ($P=0.16$) indicated no evidence of publication bias.

## Secondary outcome measures

### Complication rate

Complication rate was reported in 26 (90%) studies—10 RCTs and 16 observational studies. The overall pooled effect showed a risk ratio of 2.76 (1.84 to 4.13; $P<0.001$; $I^2=45\%$) in favor of nonoperative treatment compared with operative treatment (Figure 3). The pooled effect of RCTs showed a risk ratio of 3.26 (1.26 to 8.41; $P=0.01$; $I^2=74\%$). The pooled effect of observational studies showed a risk ratio of 2.93 (2.28 to 3.75; $P<0.001$; $I^2=0\%$). The incidence of complications was 4.9% after operative treatment compared with 1.6% after nonoperative treatment (risk difference 3.3%). Table 2 shows the classification and incidence of complications. The main complication after operative treatment was infection, which occurred in 2.8% of patients. The main complication after nonoperative treatment was deep vein thrombosis, which occurred in 1.2% of patients compared with 1.0% after operative treatment. We found no significant difference between effect estimates from RCTs and observational studies (test for subgroup differences: $P=0.83$; $I^2=0\%$). There was no visual asymmetry in the funnel plot (supplementary Figure S2). The Begg rank correlation test ($P=0.50$) and Egger linear regression test ($P=0.11$) indicated no evidence of publication bias.

| Study or Subgroup | Operative Events | Operative Total | Nonoperative Events | Nonoperative Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| **1.1.1 RCTs** | | | | | | |
| Cetti et al. 1993 | 3 | 56 | 8 | 55 | 5.1% | 0.37 [0.10, 1.32] |
| Keating et al. 2011 | 2 | 39 | 4 | 41 | 3.4% | 0.53 [0.10, 2.71] |
| Lantto et al. 2016 | 1 | 32 | 4 | 28 | 2.1% | 0.22 [0.03, 1.84] |
| Metz et al. 2008 | 3 | 42 | 5 | 41 | 4.5% | 0.59 [0.15, 2.29] |
| Möller et al. 2001 | 1 | 59 | 11 | 53 | 2.4% | 0.08 [0.01, 0.61] |
| Nilsson-Helander et al. 2010 | 2 | 49 | 6 | 48 | 3.7% | 0.33 [0.07, 1.54] |
| Nistor et al. 1981 | 2 | 46 | 5 | 61 | 3.5% | 0.53 [0.11, 2.61] |
| Olsson et al. 2013 | 0 | 49 | 5 | 51 | 1.2% | 0.09 [0.01, 1.67] |
| Twaddle et al. 2007 | 2 | 25 | 1 | 25 | 1.8% | 2.00 [0.19, 20.67] |
| Willits et al. 2010 | 2 | 72 | 3 | 72 | 3.0% | 0.67 [0.11, 3.87] |
| **Subtotal (95% CI)** | | **469** | | **475** | **30.7%** | **0.40 [0.24, 0.69]** |
| Total events | 18 | | 52 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 6.66, df = 9 (P = 0.67); I² = 0% | | | | | | |
| Test for overall effect: Z = 3.28 (P = 0.001) | | | | | | |
| **1.1.2 Observational studies** | | | | | | |
| Bergkvist et al. 2012 | 6 | 220 | 19 | 267 | 8.2% | 0.38 [0.16, 0.94] |
| Carden et al. 1987 | 0 | 35 | 0 | 36 | | Not estimable |
| Costa et al. 2006 | 2 | 48 | 2 | 48 | 2.6% | 1.00 [0.15, 6.81] |
| Cukelj et al. 2015 | 0 | 60 | 3 | 30 | 1.2% | 0.07 [0.00, 1.36] |
| Ebinesan et al. 2008 | 1 | 51 | 1 | 12 | 1.4% | 0.24 [0.02, 3.50] |
| Fahlström et al. 1998 | 0 | 22 | 2 | 9 | 1.2% | 0.09 [0.00, 1.65] |
| Grubor et al. 2012 | 3 | 34 | 4 | 8 | 5.0% | 0.18 [0.05, 0.64] |
| Gwynne-Jones et al. 2011 | 2 | 143 | 19 | 220 | 4.2% | 0.16 [0.04, 0.68] |
| Jaakkola et al. 2001 | 0 | 35 | 3 | 38 | 1.2% | 0.15 [0.01, 2.89] |
| Jackson et al. 2013 | 1 | 29 | 2 | 51 | 1.8% | 0.88 [0.08, 9.28] |
| Kotnis et al. 2006 | 1 | 67 | 2 | 58 | 1.7% | 0.43 [0.04, 4.65] |
| Lim et al. 2017 | 2 | 99 | 6 | 101 | 3.6% | 0.34 [0.07, 1.64] |
| Miller et al. 2005 | 6 | 140 | 3 | 32 | 4.7% | 0.46 [0.12, 1.73] |
| Nestorson et al. 2000 | 1 | 14 | 4 | 10 | 2.3% | 0.18 [0.02, 1.37] |
| Rajasekar et al. 2005 | 0 | 21 | 1 | 14 | 1.0% | 0.23 [0.01, 5.21] |
| Renninger et al. 2016 | 1 | 27 | 2 | 30 | 1.8% | 0.56 [0.05, 5.79] |
| Van der Linden et al. 2004 | 10 | 212 | 4 | 80 | 6.0% | 0.94 [0.30, 2.92] |
| Wang et al. 2015 | 160 | 7625 | 119 | 4945 | 19.4% | 0.87 [0.69, 1.10] |
| Weber et al. 2003 | 1 | 24 | 4 | 23 | 2.2% | 0.24 [0.03, 1.99] |
| **Subtotal (95% CI)** | | **8906** | | **6012** | **69.3%** | **0.42 [0.28, 0.64]** |
| Total events | 197 | | 200 | | | |
| Heterogeneity: Tau² = 0.19; Chi² = 24.53, df = 17 (P = 0.11); I² = 31% | | | | | | |
| Test for overall effect: Z = 3.98 (P < 0.0001) | | | | | | |
| **Total (95% CI)** | | **9375** | | **6487** | **100.0%** | **0.43 [0.31, 0.60]** |
| Total events | 215 | | 252 | | | |
| Heterogeneity: Tau² = 0.13; Chi² = 34.64, df = 27 (P = 0.15); I² = 22% | | | | | | |
| Test for overall effect: Z = 5.04 (P < 0.00001) | | | | | | |
| Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.91), I² = 0% | | | | | | |

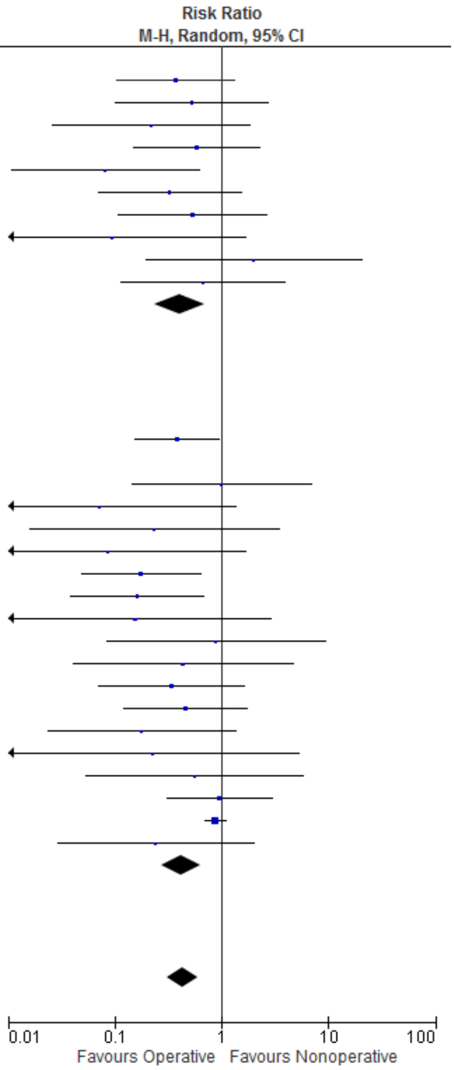


**Figure 2.** Forest plot of re-rupture rate in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.

## Functional outcome

Short term functional outcome assessed according to the ATRS score was reported in three (10%) studies. Nilsson-Helander et al reported a median ATRS score of 75 (range 31-100) in the operative group and 90 (31-100) in the nonoperative group.[58] Olsson et al reported a mean ATRS score of 82 (SD 20) in the operative group compared with 80 (23) in the nonoperative group.[59] In both RCTs, the differences found were non-significant. The observational study by Jackson et al reported a statistical significant difference in median ATRS score—94 (range 23-100) in the operative group and 84 (25-100) in the nonoperative group.[34]

Long-term functional outcome using the ATRS score was assessed in two observational studies. Bergkvist et al reported a mean ATRS score of 83 (SD 19) in the operative group and 78 (22) in

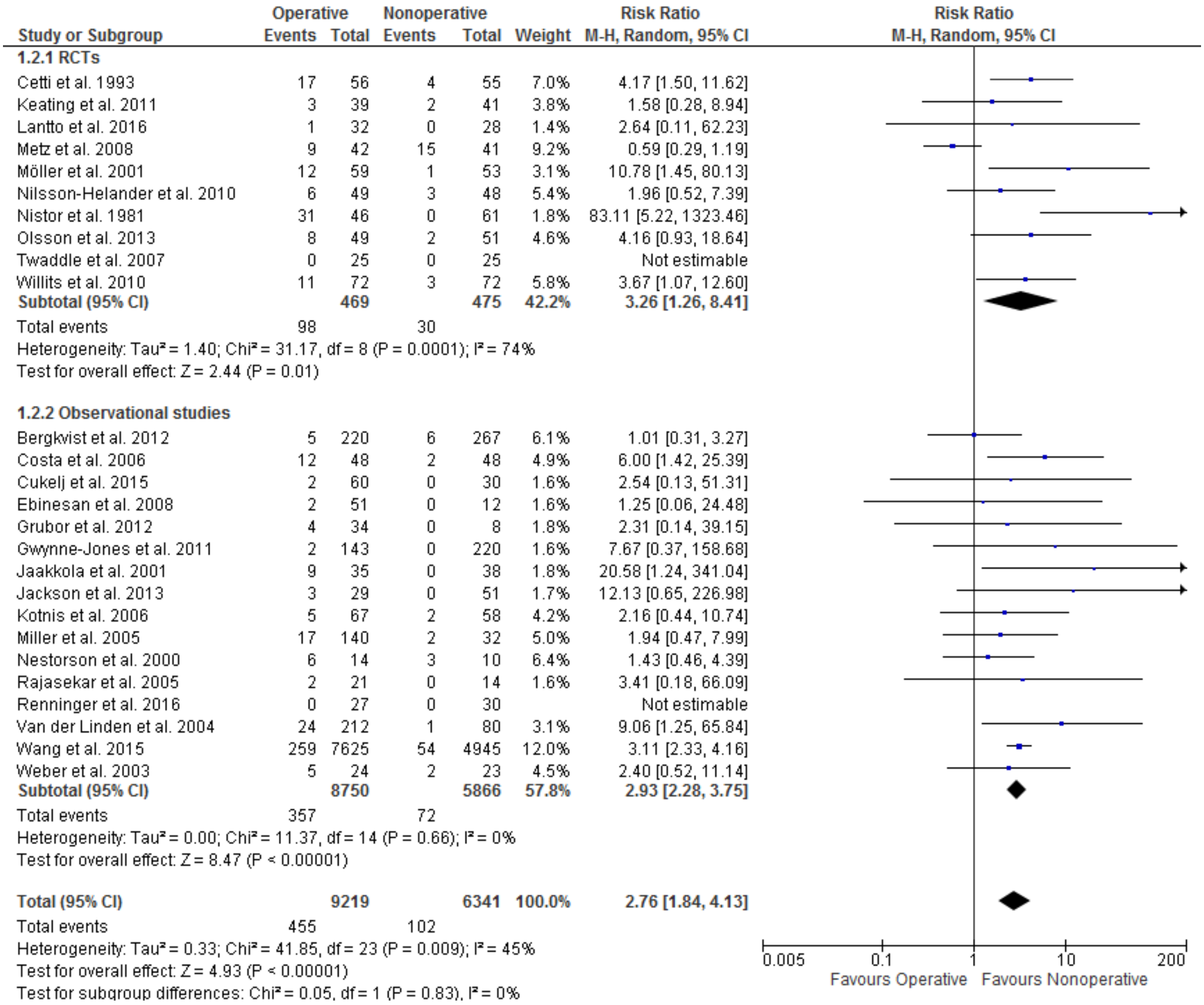


**Figure 3.** Forest plot of complication rate in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.

the nonoperative group.[36] Lim et al reported a mean ATRS score of 85 in both groups.[44] No significant difference was found in either study. We did not pool functional outcome data owing to a wide variety in ATSR score reports and insufficient information to convert data. Descriptive details on functional outcome measures are provided in supplementary Table S5.

**Table 2.** Complications of included studies in a meta-analysis of Achilles tendon ruptures

| Complication classification | Operative (n) | Incidence (%) | Nonoperative (n) | Incidence (%) |
|---|---|---|---|---|
| Pulmonary embolism | 2 | 0.02 | 2 | 0.03 |
| Deep vein thrombosis | 89 | 0.97 | 74 | 1.17 |
| Wound/skin infection | 258 | 2.80 | 1 | 0.02 |
| Sural nerve injury | 39 | 0.42 | 5 | 0.08 |
| Chronic pain | 3 | 0.03 | 2 | 0.03 |
| Scar/skin adhesion | 35 | 0.38 | 15 | 0.24 |
| Wound dehiscence | 8 | 0.09 | 0 | 0 |
| NP/other | 21 | 0.23 | 3 | 0.05 |
| **Total** | **455** | **4.94** | **102** | **1.61** |

NP not specified; n number

## Return to sports and work

Return to sports was reported by four (14%) studies—one RCT and three observational studies (supplementary Table S5). The mean time varied between six and nine months after operative treatment and between six and eight months after nonoperative treatment. We could not pool data on return to sports in a meta-analysis, as only one study reported a mean and standard deviation.

Return to work was reported in nine (31%) studies—four RCTs and five observational studies (supplementary Table S5). The outcome data of six studies could not be pooled owing to insufficient reporting of information. The pooled effect estimates of three studies—two RCTs and one observational study—showed no significant mean difference between operative and nonoperative treatment groups (supplementary Figure S3).

## Primary sensitivity analysis

## Weight bearing status

Early (four weeks or less) weight bearing status was reported in nine (31%) studies—five RCTs and four observational studies. The overall pooled effect showed a significant reduction in re-rupture rate after operative treatment compared with nonoperative treatment in the early (four weeks or less) full weight bearing studies (risk ratio 0.49, 0.26 to 0.93; $P=0.03$; $I^2=9\%$) (supplementary Figure S4). Late (more than four weeks) weight bearing status was reported in 15 (52%) studies—four RCTs and 11 observational studies. The overall pooled effect of the late (more than four weeks) full weight bearing studies also showed a significant reduction in re-rupture rate in favor of operative treatment (risk ratio 0.33, 0.21 to 0.50; $P<0.001$; $I^2=0\%$) (supplementary Figure S5).

## Accelerated functional rehabilitation

Accelerated functional rehabilitation with early range of motion was performed in six (21%) studies—three RCTs and three observational studies. The overall pooled effect showed no significant difference between operative and nonoperative treatment regarding re-rupture rate (risk ratio 0.60, 0.26 to 1.37; $P=0.23$; $I^2=0\%$) (Figure 4).

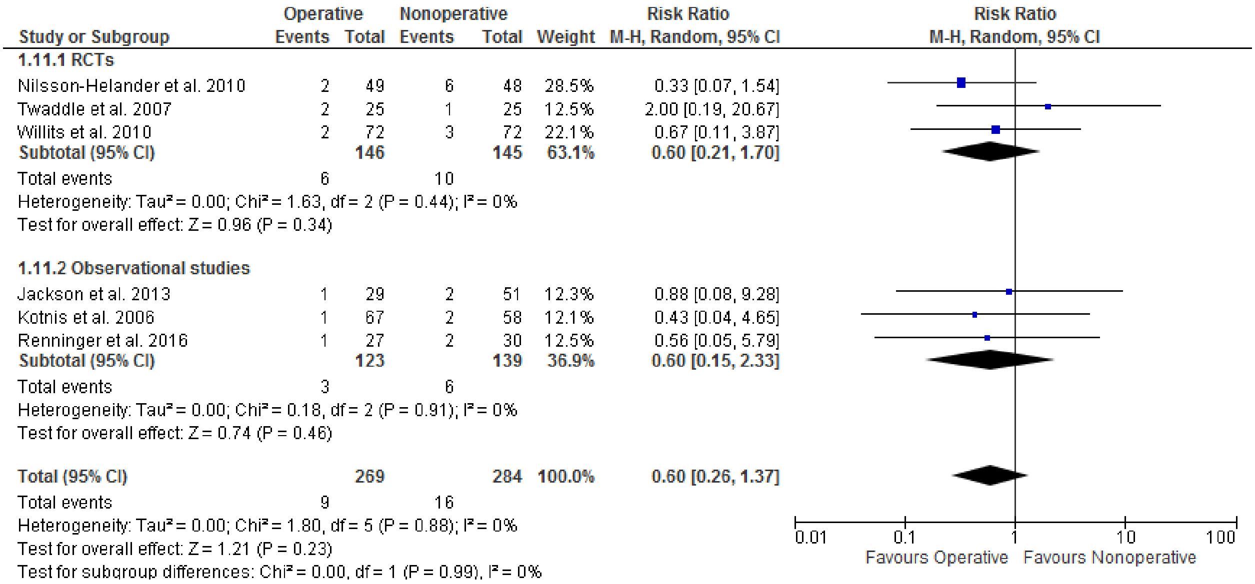


**Figure 4.** Forest plot of re-rupture rate in studies that included accelerated functional rehabilitation in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.

## Secondary sensitivity analyses

Table 3 shows the results of the secondary sensitivity analyses. Re-rupture rate was reported in 17 (59%) high quality studies—10 RCTs and seven observational studies. The overall pooled effect showed that operative treatment was associated with a significant reduction in re-rupture rate compared with nonoperative treatment (risk difference 5.1%; risk ratio 0.44, 0.30 to 0.64; P<0.001; $I^2$=0%) (supplementary Figure S6). Re-rupture rate was reported in 14 studies (48%) with a study period after the year 2000—six RCTs and eight observational studies. The overall pooled effect showed a significant reduction in re-rupture rate after operative treatment compared with nonoperative treatment (risk difference 0.9%; risk ratio 0.59, 0.42 to 0.83; P=0.002; $I^2$=10%) (supplementary Figure S7).

**Table 3**. Secondary sensitivity analyses of included studies in a meta-analysis of Achilles tendon ruptures

| | **Re-rupture** | | | | | |
|---|---|---|---|---|---|---|
| | n | RD | RR | 95% CI | p-value | $I^2$ |
| All studies | 29 | 1.6% | 0.43 | 0.31 to 0.60 | <0.001 | 22% |
| High-quality studies | 17 | 5.1% | 0.44 | 0.30 to 0.64 | <0.001 | 0% |
| Study period (≥ 2000) | 14 | 0.9% | 0.59 | 0.42 to 0.83 | 0.002 | 10% |
| | **Complication** | | | | | |
| All studies | 26 | 3.3% | 2.76 | 1.84 to 4.13 | <0.001 | 45% |
| High-quality studies | 16 | 8.8% | 2.72 | 1.44 to 5.12 | 0.002 | 62% |
| Study period (≥ 2000) | 14 | 2.4% | 2.15 | 1.28 to 3.60 | 0.004 | 52% |

n number of studies; RD risk difference; RR risk ratio; 95% CI confidence interval; $I^2$ heterogeneity

Complication rate was reported in 16 (55%) high quality studies—10 RCTs and six observational studies. The overall pooled effect showed a risk ratio of 2.72 (1.44 to 5.12; P=0.002; $I^2$=62%) in favor of nonoperative treatment compared with operative treatment (risk difference 8.8%) (supplementary Figure S8). Complication rate was reported in 14 (48%) studies with a study period after the year 2000—six RCTs and eight observational studies. The overall pooled effect showed a risk ratio of 2.15 (1.28 to 3.60; P=0.004; $I^2$=52%) in favor of nonoperative treatment compared with operative treatment (risk difference 2.4%) (supplementary Figure S9).

## Discussion

This systematic review and meta-analysis, including both RCTs and observational studies, compared outcomes after operative versus nonoperative treatment of acute Achilles tendon ruptures. The pooled effect estimate showed that operative treatment was associated with a significant reduction in re-rupture rate compared with nonoperative treatment. However, operative treatment resulted in a significantly higher rate of other complications. Sensitivity analyses showed a similar reduction in re-rupture rate after both early and late full weight bearing in favor of operative treatment compared with nonoperative treatment. However, we found no significant difference in re-rupture rate if accelerated functional rehabilitation with early range of motion was used. Sensitivity analyses with high quality studies and studies with a study period after the year 2000 also showed operative treatment to be associated with a significant reduction in re-rupture rate but a higher risk of other complications. We found no significant difference in effect estimates from RCTs and observational studies, for either re-rupture rate or complication rate.

Operative treatment reduces the risk of re-rupture compared with nonoperative treatment, but it also results in a higher risk of other complications. These findings are in accordance with those of previous meta-analyses.[3,4,6] Our review included 10 RCTs with a total of 944 patients, which resulted in an increased number of patients available for analyses, thus exceeding previous meta-analyses. Furthermore, the inclusion of observational studies resulted in an additional 14 918 patients for analyses. The previous meta-analyses reported a risk difference in re-rupture rate varying from 5% to 7% and a risk difference of other complications varying from 16% to 21%.[3-6] However, with the addition of observational studies, this review shows that differences between treatment groups are small, with a risk difference in re-rupture rate of 1.6% and a risk difference of 3.3% for other complications.

Functional outcome measures included the ATRS score, return to sports, and return to work. The ATRS score is the most commonly used patient reported instrument to evaluate limitations after treatment for an acute Achilles tendon rupture.[2] ATRS scores were not pooled in this study, but most studies showed no significant difference in ATRS score between the operative and nonoperative treatment groups. Resumption of sports was reported by only four studies; the results indicate no difference between operative treatment (six to nine months) and nonoperative treatment (six to eight months). The pooled effect of return to work showed no significant difference between treatment groups. Wilkins et al pooled return to work data from four studies and also found no statistical significant difference.[5] Soroceanu et al reported a statistically significant difference with the pooled data from four studies; operatively treated patients returned to work 19 days earlier than nonoperatively treated patients (P=0.0014).[6] Wilkins et al included return to work data in their pooled results from the studies by Nistor et al and Cetti et al.[5,52,57] In our study, we did not use the return to work data from these two studies owing to reporting of mean and range and the absence of standard deviations. Soroceanu et al also included the study by Cetti et al, as well as the study by Majewski et al,[6,52,62] which we excluded as it was in a language other than English. However, both our meta-analysis and the studies by Wilkins et al and Soroceanu et al are limited by the number of included patients in the return to work subgroup analyses.[5,6] Unfortunately, accurate comparison of functional outcome measures remains difficult owing to differences in protocols, patient oriented outcome measures, duration of follow-up, and presentation of data.

We found a lower re-rupture rate after both early and late full weight bearing in favor of operative treatment; this is in contrast to a previous meta-analysis by Van der Eng et al,[63] which found no difference in re-rupture rate. The previous meta-analysis could be limited by the number of included patients in the subgroup analyses. In our review, with the addition of observational studies, sensitivity analysis showed a significant difference in re-rupture rate after both early and late full weight bearing in favor of operative treatment. However, regardless of re-rupture rate, timing of weight bearing might influence other outcome measures as shown in different lower extremity injuries. De Boer et al found that early weight bearing regimens did not negatively affect functional outcome after treatment for displaced intra-articular calcaneal fractures.[64] Previously, Smeeing et al showed that early weight bearing tended to accelerate return to work and daily activities compared with late weight bearing, after internal fixation of ankle fractures.[65] Eliasson et al evaluated tendon elongation, mechanical properties, and functional outcomes during the first 12 months after operative treatment of acute Achilles tendon ruptures.[66] However, they found that different rehabilitation regimens did not affect the outcome measures. Further research could focus on the effect of early weight bearing and long-term functional outcome after treatment of Achilles tendon ruptures.

Soroceanu et al found no significant difference in re-rupture rate in their subgroup analysis if functional rehabilitation with early range of motion was used (risk difference 1.7%; P=0.45).[6] However, they did not define the specific inclusion criteria and definition of early range of motion and functional rehabilitation. Unfortunately, evaluation of the effect of accelerated functional rehabilitation remains difficult owing to use of a wide variety of definitions and protocols. Our review found no significant difference in re-rupture rate if accelerated functional rehabilitation with early range of motion within three weeks was used after nonoperative treatment. These findings indicate that nonoperative management is acceptable for acute Achilles tendon ruptures, if patients are instructed and monitored according to a standardized rehabilitation protocol. However, both our review and the study by Soroceanu et al could be limited by the number of included patients in the subgroup analyses.[6]

The sensitivity analyses including high quality studies resulted in similar risk ratios and significance levels for re-rupture and complication rate. The results showed a risk difference of 5.1% for re-rupture rate, comparable to previous results of meta-analyses of RCTs alone. However, the risk difference of other complications (8.8%) in the high-quality sensitivity analysis was still considerably lower than in previous reports. This difference in other complications could be attributable to the inclusion of studies with both open and minimally invasive surgical techniques. The complication sensitivity analysis with high quality studies included one RCT with minimally invasive surgery and three observational studies that included both open and minimally invasive surgery. A meta-analysis by Yang et al,[67] including five RCTs and four cohort studies, found a significantly lower rate of deep infection with percutaneous treatment (0.6%) than with open treatment (3.6%) (P=0.04). However, the authors reported no significant difference in the rate of re-rupture between percutaneous and open treatment.[67]

The sensitivity analyses including studies with a study period after the year 2000 showed similar risk ratios and significance levels regarding re-rupture and complication rate. However, the risk differences between treatment groups were smaller than in all other analyses. The study period sensitivity analyses included one RCT with minimally invasive surgery and four observational studies that included both open and minimally invasive surgery. These findings might indicate an overall reduction in complications after treatment of Achilles tendon ruptures due to the development of new rehabilitation protocols and operative techniques, regardless the use of operative or nonoperative treatment. However, it should be noted that both the level of high-quality studies and the study period were arbitrarily chosen.

We found no difference in pooled effect estimates from RCTs and observational studies. This is in line with previous reports showing that differences in effect estimates between RCTs and observational studies are small.[8,9,11,13,15,17] Observational studies, however, have also been associated with an overestimation of treatment effects compared with RCTs.[68,69] Hemkens et al assessed the difference in treatment effect estimates for mortality between observational studies and RCTs.[69] They evaluated 16 observational studies and 36 subsequent RCTs investigating the same clinical questions. Overall, observational studies significantly overestimated the effects of treatment compared with RCTs.[69] This overestimation of treatment effects could be explained by the effects of bias and confounding in observational studies.[70] However, overestimates by observational studies could also be explained by the potential selection bias in RCTs. RCTs require strict conditions such as selection of participants, inclusion/exclusion criteria, randomization method, and outcome measurements. The patient population in daily clinical practice can differ from the often highly selected patient populations in RCTs, which could be the reason for the discrepancy between treatment effects.[71,72] Nevertheless, observational studies increase sample size, which could lead to the evaluation of small treatment effects and infrequent outcome measures. Furthermore, the addition of observational studies might provide insight into a variety of populations and long-term effects. These results could improve the representation of daily clinical practice, with various levels of surgical experience and differences in operative techniques, provided that confounding has been adequately addressed.[12,13] In this meta-analysis, pooled effect estimates obtained from RCTs and observational studies were similar. Several orthopedic trauma meta-analyses including both RCTs and observational studies have shown high quality observational studies to result in similar treatment effects to RCTs.[15-17] These findings indicate that the effect of potentially unmeasured confounding in high quality observational studies seems relatively small, emphasizing the possible benefits of combining different study designs for the evaluation of objective outcome measures after surgical treatment.

Several potential limitations in this review need to be considered. Firstly, results might be influenced by missing articles. However, in addition to the extensive electronic database search, funnel plots did not indicate evidence for publication bias. Three studies could not be obtained in full text, but these articles were all published before 1996.[2,6,27,28] Secondly, the methodological quality of included studies was assessed by the MINORS criteria, which do not differentiate between randomized and non-randomized studies. However, the MINORS criteria were externally validated using RCTs and are able to distinguish adequately between study designs, as well-designed randomized trials score higher than well designed non-randomized studies.[21] The incidence of complications could be affected by the use of different treatment protocols. Five studies mentioned the use of prophylaxis for deep vein thrombosis.[51,53,56,58,59] However, descriptions were not comprehensive and the duration and types of prophylaxis varied widely. Finally, sensitivity analyses for the evaluation of weight bearing status and accelerated rehabilitation were performed using data from both RCTs and observational studies. However, the primary analysis showed no significant difference in effect estimates between the two study designs in terms of re-rupture rate.

Operative treatment of acute Achilles tendon ruptures reduces the risk of re-rupture compared with nonoperative treatment, although the incidence of re-ruptures is low and differences are small (2.3% v 3.9%). Operative treatment results in a higher risk of other complications compared with nonoperative treatment, mostly attributable to the increased risk of infection. Nonoperative treatment might be the preferred treatment for acute Achilles tendon rupture, owing to the higher risk of other complications after operative treatment and the relative small benefit in re-rupture rate. However, patient specific factors should always be taken into consideration and patients should be counselled about the incidence of complications.

Unfortunately, comparison of the literature remains difficult owing to a wide variety of rehabilitation protocols, weight bearing restrictions, treatment modalities, patient oriented outcome measures, and duration of follow-up. The discordance among studies makes comparisons between treatment modalities difficult, indicating a substantial need for further research. We suggest future research to focus on the effect of comorbidities on the success of treatment for Achilles tendon rupture. Studies could compare outcomes according to different age groups and evaluate effects in a variety of populations such as in patients with immunosuppression, diabetes mellitus, increased body mass index, neuropathy, peripheral vascular disease, and dermatological disorders. Furthermore, future studies should strive to determine the optimal treatment for acute Achilles tendon ruptures on the basis of patients' expectations. Operative treatment is associated with complications inherent to the treatment itself, such as infection. However, athletic people may prefer operative treatment to enhance and expedite their outcomes, whereas a sedentary person with limited functional outcome expectations may prefer nonoperative treatment.[3] We believe that more data are needed for the development of a shared decision making algorithm to guide surgeons and physicians regarding the most appropriate treatment option for each individual patient.

## Conclusion

In this meta-analysis, operative treatment of acute Achilles tendon ruptures reduced the risk of re-rupture compared with nonoperative treatment. However, re-rupture rates are low and differences between treatment groups are small, with a risk difference of 1.6%. Operative treatment results in a higher risk of other complications, with a risk difference of 3.3%, mostly due to the increased risk of infection. Patients should be counselled about complications, and the final decision for operative or nonoperative management should be based on patient specific factors and shared decision making. Further research is needed for the development of a shared decision-making algorithm. Moreover, this review emphasizes the potential benefits of adding high quality observational studies in meta-analyses to complement RCTs for the evaluation of objective outcome measures after surgical treatments.

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# Supplementary materials to Chapter 6

**Table S1.** Search syntax performed last on April 25th, 2018

| Database | Syntax |
|---|---|
| PubMed/MEDLINE (n= 1049) | ((((((((((achilles tendon[MeSH Terms]) OR achilles tendon[Title/Abstract]) OR achill*[Title/Abstract]) OR tendoachill*[Title/Abstract]) OR calcaneal*[Title/Abstract]) OR calcanean*[Title/Abstract]) OR calcaneus[Title/Abstract])) AND ((((((rupture[MeSH Terms]) OR Tendon Injuries[MeSH Terms]) OR ruptu*[Title/Abstract]) OR injur*[Title/Abstract]) OR lesion*[Title/Abstract]) OR tear*[Title/Abstract])))) AND (((((((((((((surgical procedures, operative[MeSH Terms]) OR orthopedics[MeSH Terms]) OR surg*[Title/Abstract]) OR operat*[Title/Abstract]) OR orthop*[Title/Abstract]) OR kessler[Title/Abstract]) OR bunnell[Title/Abstract]) OR krackow[Title/Abstract]) OR ma and griffit[Title/Abstract]) OR achillon[Title/Abstract]) OR tenolig[Title/Abstract]) OR dresden[Title/Abstract]) OR percuta*[Title/Abstract]))) AND (((((((((((((((((Conservative Treatment[MeSH Terms]) OR physical therapy modalities[MeSH Terms]) OR conservative[Title/Abstract]) OR conventional[Title/Abstract]) OR non-operative[Title/Abstract]) OR non operative[Title/Abstract]) OR nonoperative[Title/Abstract]) OR non-surgical[Title/Abstract]) OR non surgical[Title/Abstract]) OR nonsurgical[Title/Abstract]) OR cast*[Title/Abstract]) OR brace*[Title/Abstract]) OR splint*[Title/Abstract]) OR boot*[Title/Abstract]) OR bandage*[Title/Abstract]) OR tape[Title/Abstract]) OR taping[Title/Abstract])) |
| Embase (n= 1181) | ('achilles tendon rupture'/de OR (('achilles tendon'/exp OR 'achilles tendon':ab,ti OR 'achill*':ab,ti OR 'tendoachill*':ab,ti OR 'calcanean*':ab,ti OR 'calcaneus':ab,ti) AND ('rupture'/de OR 'tendon injury'/de OR 'injur*':ab,ti OR 'ruptu*':ab,ti OR 'lesion*':ab,ti OR 'tear*':ab,ti))) AND (('surgery'/de OR 'orthopedic surgery'/de OR 'surg*':ab,ti OR 'operat*':ab,ti OR 'orthop*':ab,ti OR 'kessler':ab,ti OR 'bunnell':ab,ti OR 'krackow':ab,ti OR 'griffit':ab,ti OR 'achillon':ab,ti OR 'tenolig':ab,ti OR 'dresden':ab,ti OR 'percuta*':ab,ti) AND ('conservative treatment'/de OR 'conservative':ab,ti OR 'conventional':ab,ti OR 'non-operative':ab,ti OR 'non operative':ab,ti OR 'nonoperative':ab,ti OR 'non-surgical':ab,ti OR 'non surgical':ab,ti OR 'nonsurgical':ab,ti OR 'cast*':ab,ti OR 'brace*':ab,ti OR 'splint*':ab,ti OR 'boot*':ab,ti OR 'bandage*':ab,ti OR 'tape':ab,ti OR 'taping':ab,ti)) |
| CENTRAL (n= 217) | (Achilles AND rupture) |
| CINAHL (n= 249) | (((MH achilles tendon OR TI achilles tendon OR AB achilles tendon OR TI achill* OR AB achill* OR TI tendoachill* OR AB tendoachill* OR TI calcaneal* OR AB calcaneal* OR TI calcanean* OR AB calcanean* OR TI calcaneus OR AB calcaneus) AND (MH rupture OR MH tendon injuries OR TI rupt* OR AB rupt* OR TI injur* OR AB injur* OR TI lesion* OR AB lesion* OR TI tear* OR AB tear*)) AND ((MH surgical procedures, operative OR MH orthopedics OR TI surg* OR AB surg* OR TI operat* OR AB operat* OR TI orthop* OR AB orthop* OR TI kessler OR AB kessler OR TI bunnell OR AB bunnell OR TI krackow OR AB krackow OR TI ma and griffit OR AB ma and griffit OR TI achillon OR AB achillon OR TI tenolig OR AB tenolig OR TI dresden OR AB dresden OR TI percuta* OR AB percuta*) AND (MH Conservative Treatment OR MH physical therapy modalities OR TI conservative OR AB conservative OR TI conventional OR AB conventional OR TI non-operative OR AB non-operative OR TI non operative OR AB non operative OR TI nonoperative OR AB nonoperative OR TI non-surgical OR AB non-surgical OR TI non surgical OR AB non surgical OR TI nonsurgical OR AB nonsurgical OR TI cast* OR AB cast* OR TI brace* OR AB brace* OR TI splint* OR AB splint* OR TI boot* OR AB boot* OR TI bandage* OR AB bandage* OR TI tape OR AB tape OR TI taping OR AB taping)) |

**Table S2.** Quality assessment according to the MINORS criteria in a meta-analysis of Achilles tendon ruptures

| Criteria | Reported and adequate (2) | Reported but inadequate (1) | Not reported (0) |
|---|---|---|---|
| Clearly stated aim | Aim including outcomes reported | Aim reported without outcomes | Not reported |
| Inclusion consecutive patients | Inclusion/exclusion criteria reported | Unclear description inclusion/exclusion criteria | Not reported |
| Prospective collection data | Prospective | Not applicable | Not applicable |
| Appropriate endpoints | Appropriate endpoints to aim study | Endpoints not appropriate to aim study | Not reported |
| Unbiased assessment | Blinded evaluation of outcomes | Reason not blinding stated | Not reported |
| Appropriate follow-up | ≥ 1 year | < 1 year | Not reported |
| Loss to follow-up < 5% | ≤ 5% | > 5% | Not applicable |
| Prospective calculation study size | Prospective power-analysis performed | Prospective calculation without power-analysis | Not applicable |
| Adequate control group | Operative versus nonoperative treatment | Not applicable | Not applicable |
| Contemporary groups | Study/control group managed during same period | Study/control not managed during same period | Not reported |
| Baseline equivalence groups | Baseline characteristics described and comparable | Baseline characteristics not comparable | Not reported |
| Adequate statistical analyses | Statistical analysis described including type of analyses | Inadequate description statistical analysis | Not reported |

Items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The overall score ranging from 0 to 24 for comparative studies

**Table S3.** Treatment characteristics of included studies in a meta-analysis of Achilles tendon ruptures

| Study | Year | Overall number | Number OP | Number NON | Operative method | Operative suture technique | Nonoperative treatment | Duration (weeks) nonoperative | Accelerated fun. Rehab | Weightbearing ≤ 4 weeks |
|---|---|---|---|---|---|---|---|---|---|---|
| **RCTs** | | | | | | | | | | |
| Cetti et al. | 1993 | 111 | 56 | 55 | Open | Bunnell | Cast | 8 | No | No |
| Keating et al. | 2011 | 80 | 39 | 41 | Open | Kessler | Cast | 10 | No | No |
| Lantto et al. | 2016 | 60 | 32 | 28 | Open | Krackow | Cast/orthosis | 7 | No | Yes |
| Metz et al. | 2008 | 83 | 42 | 41 | MI | Bunnell | Cast/brace | 7 | No | Yes |
| Möller et al. | 2001 | 112 | 59 | 53 | Open | Kessler | Cast | 8 | No | Yes |
| Nilsson-Helander et al. | 2010 | 97 | 49 | 48 | Open | Kessler | Cast/brace | 8 | Yes | No |
| Nistor et al. | 1981 | 107 | 46 | 61 | Open | Bunnell | Cast | 8 | N/A | N/A |
| Olsson et al. | 2013 | 100 | 49 | 51 | Open | Kessler | Brace | 8 | No | Yes |
| Twaddle et al. | 2007 | 50 | 25 | 25 | Open | Krackow | Cast/orthosis | 8 | Yes | No |
| Willits et al. | 2010 | 144 | 72 | 72 | Open | Krackow | Brace | 8 | Yes | Yes |
| **Observational studies** | | | | | | | | | | |
| Bergkvist et al. | 2012 | 487 | 220 | 267 | N/A | N/A | Brace | 8 | N/A | No |
| Carden et al. | 1987 | 71 | 35 | 36 | Open | End-to-end | Cast | 8 | N/A | No |
| Costa et al. | 2006 | 96 | 48 | 48 | Open | End-to-end | Cast/orthosis | 12 | No | Both |
| Cukelj et al. | 2015 | 90 | 60 | 30 | Open/MI (n=30/30) | Lindholm/Ma-Griffith | Cast | 8 | N/A | No |
| Ebinesan et al. | 2008 | 63 | 51 | 12 | Open/MI (n=20/31) | Krackow/Percutaneous | Cast | 6-8 | No | No |
| Fahlström et al. | 1998 | 31 | 22 | 9 | N/A | N/A | Cast | N/A | N/A | N/A |
| Grubor et al. | 2012 | 42 | 34 | 8 | Open/MI (n=15/19) | Lindholm/Ma-Griffith | Cast | 10 | No | No |
| Gwynne-Jones et al. | 2011 | 363 | 143 | 220 | Open | Kessler | Cast | 8 | No | No |
| Jaakkola et al. | 2001 | 73 | 35 | 38 | Open | Bunnell | Cast | 8-10 | No | No |
| Jackson et al. | 2013 | 80 | 29 | 51 | Open | Kessler | Boot | 8 | Yes | Yes |
| Kotnis et al. | 2006 | 125 | 67 | 58 | Open/MI (n=37/30) | N/A | Cast | 8 | Yes | No |
| Lim et al. | 2017 | 200 | 99 | 101 | Open | Kessler | Cast/boot | 8 | No | No |
| Miller et al. | 2005 | 172 | 140 | 32 | Open/MI (n=86/54) | Kessler/Percutaneous | Cast | 6 | No | No |
| Nestorson et al. | 2000 | 24 | 14 | 10 | N/A | End-to-end | Cast/brace | 8 | N/A | N/A |
| Rajasekar et al. | 2005 | 35 | 21 | 14 | Open | Kessler | Cast | 10-13 | No | No |
| Renninger et al. | 2016 | 57 | 27 | 30 | Open/MI (N/A) | N/A | N/A | N/A | Yes | N/A |
| Van der Linden et al. | 2004 | 292 | 212 | 80 | Open | Bunnell | Cast | 12 | N/A | Yes |
| Wang et al. | 2015 | 12570 | 7625 | 4945 | N/A | N/A | N/A | N/A | No | N/A |
| Weber et al. | 2003 | 47 | 24 | 23 | Open | Kessler | Boot | 12 | No | Yes |

OP|NON operative/nonoperative; N/A not available; MI minimally invasive; n number; Fun. Rehab functional rehabilitation

**Table S4.** Quality assessment of included studies in a meta-analysis of Achilles tendon ruptures

| **MINORS criteria** | **RCTs** Cetti et al. 1993 | Keating et al. 2011 | Lantto et al. 2016 | Metz et al. 2008 | Möller et al. 2001 | Nilsson-Helander et al. 2010 | Nistor et al. 1981 | Olsson et al. 2013 | Twaddle et al. 2007 | Willits et al. 2010 |
|---|---|---|---|---|---|---|---|---|---|---|
| Clearly stated aim | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Inclusion consecutive patients | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 |
| Prospective collection of data | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Appropriate endpoints | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Unbiased assessment endpoints | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| Appropriate follow-up | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 |
| Loss to follow-up < 5% | 0 | 2 | 2 | 2 | 2 | 0 | 0 | 2 | 0 | 0 |
| Prospective calculation size | 0 | 2 | 2 | 2 | 0 | 2 | 0 | 2 | 2 | 2 |
| Adequate control group | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Contemporary groups | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Baseline equivalence of groups | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 1 | 2 |
| Adequate statistical analysis | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 |
| **Total MINORS score** | **16** | **23** | **22** | **22** | **20** | **21** | **16** | **23** | **19** | **21** |

| **MINORS criteria** | **Observational studies** Bergkvist et al. 2012 | Carden et al. 1987 | Costa et al. 2006 | Cukelj et al. 2015 | Ebinesan et al. 2008 | Fahlström et al. 1998 | Grubor et al. 2012 | Gwynne-Jones et al. 2011 | Jaakkola et al. 2001 | Jackson et al. 2013 | Kotnis et al. 2006 | Lim et al. 2017 | Miller et al. 2005 | Nestorson et al. 2000 | Rajasekar et al. 2005 | Renninger et al. 2016 | Van der Linden et al. 2004 | Wang et al. 2015 | Weber et al. 2003 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clearly stated aim | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 |
| Inclusion consecutive patients | 2 | 0 | 0 | 0 | 2 | 1 | 0 | 2 | 2 | 2 | 2 | 1 | 2 | 1 | 2 | 2 | 2 | 1 | 2 |
| Prospective collection of data | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Appropriate endpoints | 2 | 1 | 2 | 1 | 2 | 1 | 1 | 2 | 1 | 2 | 1 | 2 | 2 | 1 | 1 | 2 | 2 | 1 | 1 |
| Unbiased assessment endpoints | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| Appropriate follow-up | 2 | 2 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 2 | 2 | 0 | 1 | 0 | 0 | 0 | 1 |
| Loss to follow-up < 5% | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Prospective calculation size | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Adequate control group | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Contemporary groups | 2 | 2 | 2 | 1 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 1 | 1 | 1 | 0 | 1 |
| Baseline equivalence of groups | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 2 | 2 | 2 | 0 | 2 | 1 | 0 | 1 |
| Adequate statistical analysis | 1 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 1 | 0 | 2 | 2 | 2 | 2 |
| **Total MINORS score** | **14** | **10** | **14** | **7** | **9** | **11** | **5** | **10** | **11** | **12** | **16** | **13** | **15** | **10** | **9** | **13** | **13** | **8** | **12** |

Items are scored 0 (not reported/ not applicable), 1 (reported but inadequate) or 2 (reported and adequate). The overall score ranging from 0 to 24 for comparative studies

**Table S5.** Outcome measures of included studies in a meta-analysis of Achilles tendon ruptures

| Study | Re-rupture n (%) | | Complication n (%) | | ATRS ≤ 1 year (mean, SD or range) | | ATRS > 1 year (mean, SD or range) | | Return sports (months, SD or range) | | Return work (weeks, SD or range) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **RCTs** | **OP** | **NON** | **OP** | **NON** | **OP** | **NON** | **OP** | **NON** | **OP** | **NON** | **OP** | **NON** |
| Cetti et al. 1993 | 3 (5) | 8 (15) | 17 (30) | 4 (7) | N/A | | N/A | | N/A | | 6.2 (0.5-19) | 8.0 (0-52) |
| Keating et al. 2011 | 2 (5) | 4 (10) | 3 (8) | 2 (5) | N/A | | N/A | | 7.8 (3-12) | 8.0 (4-12) | N/A | |
| Lantto et al. 2016 | 1 (3) | 4 (14) | 1 (3) | 0 | N/A | | N/A | | N/A | | N/A | |
| Metz et al. 2008 | 3 (7) | 5 (12) | 9 (21) | 15 (37) | N/A | | N/A | | N/A | | 8.4 (12) | 15.4 (16) |
| Möller et al. 2001 | 1 (2) | 11 (21) | 12 (20) | 1 (2) | N/A | | N/A | | N/A | | 8 (7) | 11 (8) |
| Nilsson-Helander et al. 2010 | 2 (4) | 6 (13) | 6 (12) | 3 (6) | 75 (31-100)* | 90 (31-100)* | N/A | | N/A | | N/A | |
| Nistor et al. 1981 | 2 (4) | 5 (8) | 31 (67) | 0 | N/A | | N/A | | N/A | | 13 (0-30) | 9 (0-44) |
| Olsson et al. 2013 | 0 | 5 (10) | 8 (16) | 2 (4) | 82 (20) | 80 (23) | N/A | | N/A | | N/A | |
| Twaddle et al. 2007 | 2 (8) | 1 (4) | 0 | 0 | N/A | | N/A | | N/A | | N/A | |
| Willits et al. 2010 | 2 (3) | 3 (4) | 11 (15) | 3 (4) | N/A | | N/A | | N/A | | N/A | |
| **Observational studies** | | | | | | | | | | | | |
| Bergkvist et al. 2012 | 6 (3) | 19 (7) | 5 (2) | 6 (2) | N/A | | 83 (19) | 78 (22) | N/A | | N/A | |
| Carden et al. 1987 | 0 | 0 | N/A | | N/A | | N/A | | 8.9 (1.0) | 6.5 (0.7) | 8.5 (1) | 5.4 (1) |
| Costa et al. 2006 | 2 (4) | 2 (4) | 12 (25) | 2 (4) | N/A | | N/A | | N/A | | N/A | |
| Cukelj et al. 2015 | 0 | 3 (10) | 2 (3) | 0 | N/A | | N/A | | N/A | | N/A | |
| Ebinesan et al. 2008 | 1 (2) | 1 (8) | 2 (4) | 0 | N/A | | N/A | | N/A | | N/A | |
| Fahlström et al. 1998 | 0 | 2 (22) | N/A | | N/A | | N/A | | N/A | | 7 (0-13) | 11 (0-26) |
| Grubor et al. 2012 | 3 (9) | 4 (50) | 4 (12) | 0 | N/A | | N/A | | N/A | | N/A | |
| Gwynne-Jones et al. 2011 | 2 (1) | 19 (9) | 2 (1) | 0 | N/A | | N/A | | N/A | | N/A | |
| Jaakkola et al. 2001 | 0 | 3 (8) | 9 (26) | 0 | N/A | | N/A | | N/A | | N/A | |
| Jackson et al. 2013 | 1 (3) | 2 (4) | 3 (10) | 0 | 94 (23-100)* | 84 (25-100)* | N/A | | N/A | | N/A | |
| Kotnis et al. 2006 | 1 (1) | 2 (3) | 5 (7) | 2 (3) | N/A | | N/A | | N/A | | N/A | |
| Lim et al. 2017 | 2 (2) | 6 (6) | N/A | | N/A | | 84.8 | 85.3 | N/A | | N/A | |
| Miller et al. 2005 | 6 (4) | 3 (9) | 17 (12) | 2 (6) | N/A | | N/A | | 8.0 | 7.5 | 10.3 | 10.4 |
| Nestorson et al. 2000 | 1 (7) | 4 (40) | 6 (43) | 3 (30) | N/A | | N/A | | N/A | | N/A | |
| Rajasekar et al. 2005 | 0 | 1 (7) | 2 (10) | 0 | N/A | | N/A | | N/A | | N/A | |
| Renninger et al. 2016 | 1 (4) | 2 (7) | 0 | 0 | N/A | | N/A | | N/A | | 29 (13-52) | 35 (21-70) |
| Van der Linden et al. 2004 | 10 (5) | 4 (5) | 24 (11) | 1 (1) | N/A | | N/A | | N/A | | N/A | |
| Wang et al. 2015 | 160 (2) | 119 (2) | 259 (3) | 54 (1) | N/A | | N/A | | N/A | | N/A | |
| Weber et al. 2003 | 1 (5) | 4 (17) | 5 (21) | 2 (9) | N/A | | N/A | | 5.7 | 5.5 | 6 (1-12) | 4 (0-12) |

OP|NON operative/nonoperative; n number; SD standard deviation; N/A not available; ATRS Achilles Tendon Rupture Score; * median

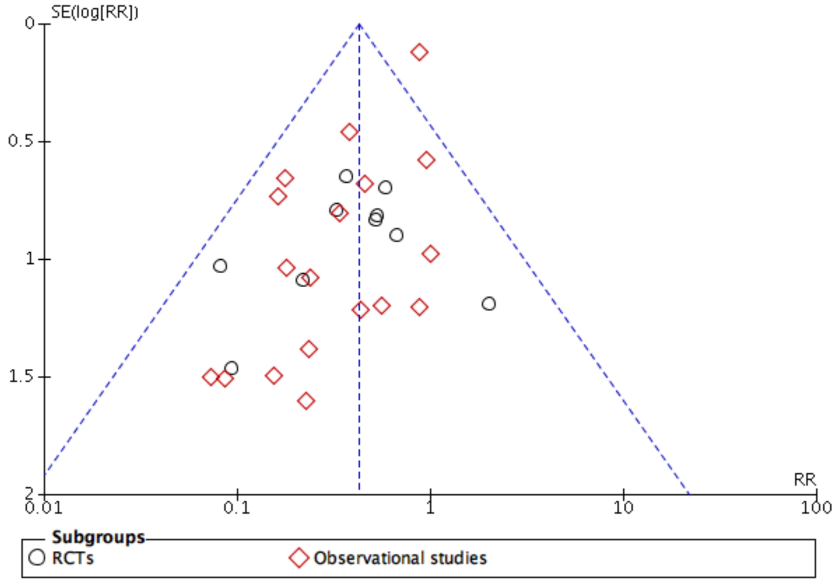


**Figure S1.** Funnel plot of re-rupture rate in a meta-analysis of Achilles tendon ruptures (RR risk ratio; SE standard error).

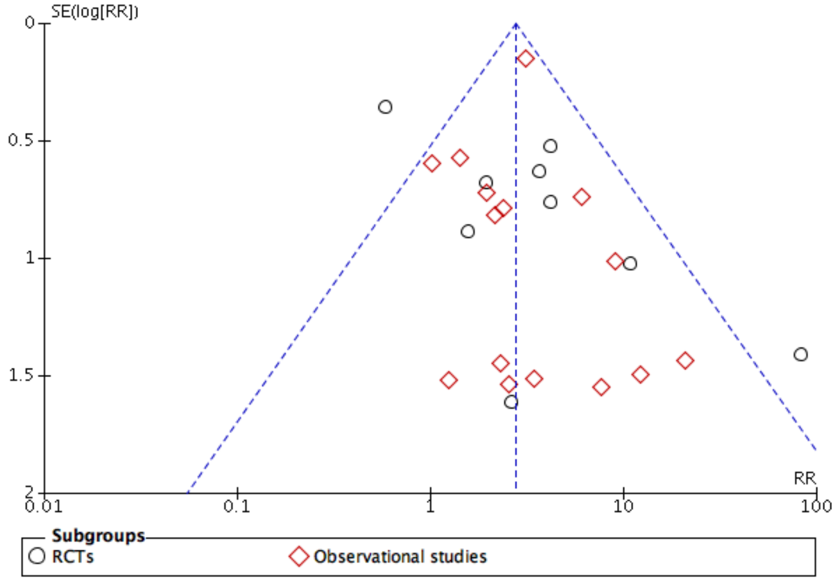


**Figure S2.** Funnel plot of complication rate in a meta-analysis of Achilles tendon ruptures (RR risk ratio; SE standard error).

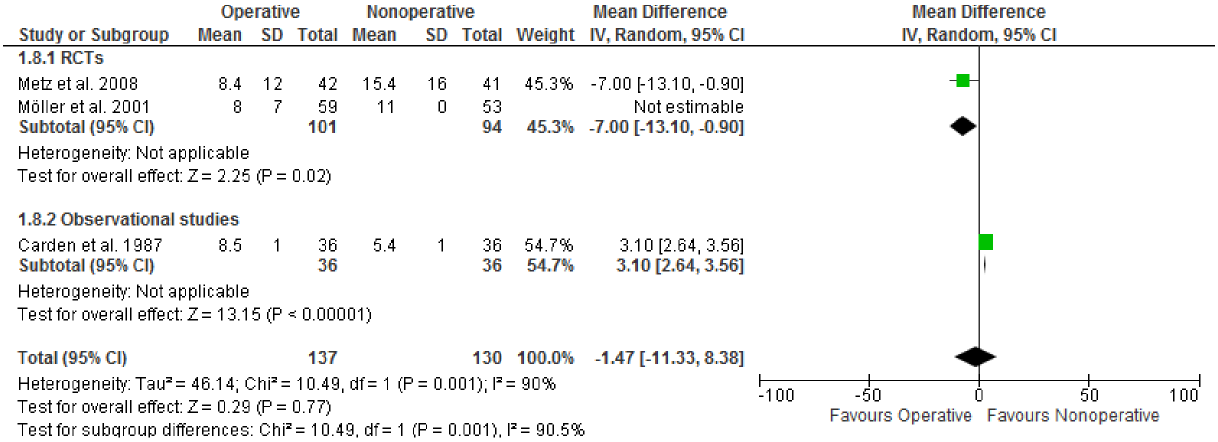


**Figure S3.** Forest plot of return to work in weeks in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.

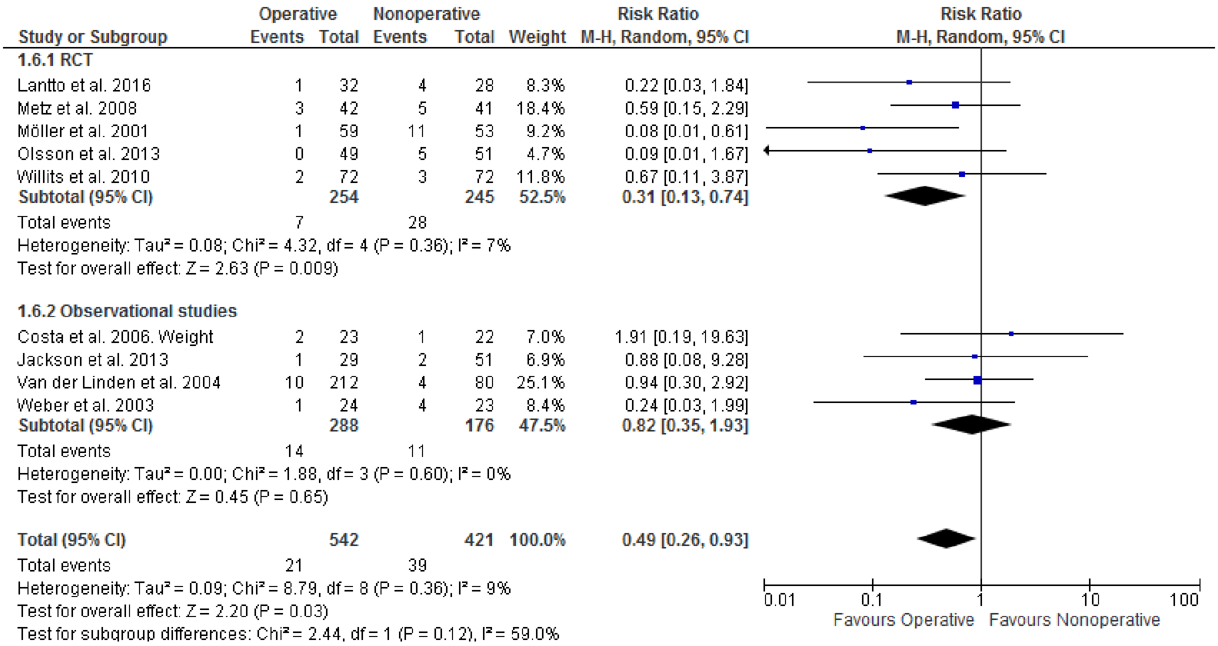


**Figure S4.** Forest plot of re-rupture rate in studies with ≤ 4 weeks full weightbearing in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.

| Study or Subgroup | Operative Events | Operative Total | Nonoperative Events | Nonoperative Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| **1.7.1 RCT** | | | | | | |
| Cetti et al. 1993 | 3 | 56 | 8 | 55 | 11.2% | 0.37 [0.10, 1.32] |
| Keating et al. 2011 | 2 | 39 | 4 | 41 | 6.8% | 0.53 [0.10, 2.71] |
| Nilsson-Helander et al. 2010 | 2 | 49 | 6 | 48 | 7.6% | 0.33 [0.07, 1.54] |
| Twaddle et al. 2007 | 2 | 25 | 1 | 25 | 3.3% | 2.00 [0.19, 20.67] |
| **Subtotal (95% CI)** | | **169** | | **169** | **28.9%** | **0.47 [0.21, 1.04]** |
| Total events | 9 | | 19 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 1.85, df = 3 (P = 0.60); I² = 0% | | | | | | |
| Test for overall effect: Z = 1.86 (P = 0.06) | | | | | | |
| **1.7.2 Observational studies** | | | | | | |
| Bergkvist et al. 2012 | 6 | 220 | 19 | 267 | 22.5% | 0.38 [0.16, 0.94] |
| Carden et al. 1987 | 0 | 35 | 0 | 36 | | Not estimable |
| Costa et al. 2006. Non- weight | 0 | 25 | 1 | 26 | 1.8% | 0.35 [0.01, 8.12] |
| Cukelj et al. 2015 | 0 | 60 | 3 | 30 | 2.1% | 0.07 [0.00, 1.36] |
| Grubor et al. 2012 | 3 | 34 | 4 | 8 | 11.1% | 0.18 [0.05, 0.64] |
| Gwynne-Jones et al. 2011 | 2 | 143 | 19 | 220 | 8.8% | 0.16 [0.04, 0.68] |
| Jaakkola et al. 2001 | 0 | 35 | 3 | 38 | 2.1% | 0.15 [0.01, 2.89] |
| Kotnis et al. 2006 | 1 | 67 | 2 | 58 | 3.2% | 0.43 [0.04, 4.65] |
| Lim et al. 2017 | 2 | 99 | 6 | 101 | 7.3% | 0.34 [0.07, 1.64] |
| Miller et al. 2005 | 6 | 140 | 3 | 32 | 10.3% | 0.46 [0.12, 1.73] |
| Rajasekar et al. 2005 | 0 | 21 | 1 | 14 | 1.9% | 0.23 [0.01, 5.21] |
| **Subtotal (95% CI)** | | **879** | | **830** | **71.1%** | **0.28 [0.17, 0.47]** |
| Total events | 20 | | 61 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 3.26, df = 9 (P = 0.95); I² = 0% | | | | | | |
| Test for overall effect: Z = 4.88 (P < 0.00001) | | | | | | |
| **Total (95% CI)** | | **1048** | | **999** | **100.0%** | **0.33 [0.21, 0.50]** |
| Total events | 29 | | 80 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 6.22, df = 13 (P = 0.94); I² = 0% | | | | | | |
| Test for overall effect: Z = 5.11 (P < 0.00001) | | | | | | |
| Test for subgroup differences: Chi² = 1.12, df = 1 (P = 0.29), I² = 10.8% | | | | | | |

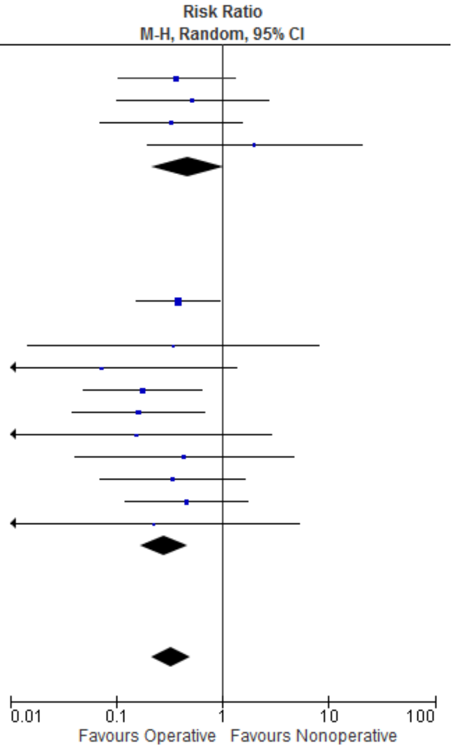


**Figure S5.** Forest plot of re-rupture rate in studies with > 4 weeks full weightbearing in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.

| Study or Subgroup | Operative Events | Operative Total | Nonoperative Events | Nonoperative Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| **1.12.1 RCTs** | | | | | | |
| Cetti et al. 1993 | 3 | 56 | 8 | 55 | 8.8% | 0.37 [0.10, 1.32] |
| Keating et al. 2011 | 2 | 39 | 4 | 41 | 5.3% | 0.53 [0.10, 2.71] |
| Lantto et al. 2016 | 1 | 32 | 4 | 28 | 3.1% | 0.22 [0.03, 1.84] |
| Metz et al. 2008 | 3 | 42 | 5 | 41 | 7.7% | 0.59 [0.15, 2.29] |
| Möller et al. 2001 | 1 | 59 | 11 | 53 | 3.5% | 0.08 [0.01, 0.61] |
| Nilsson-Helander et al. 2010 | 2 | 49 | 6 | 48 | 6.0% | 0.33 [0.07, 1.54] |
| Nistor et al. 1981 | 2 | 46 | 5 | 61 | 5.6% | 0.53 [0.11, 2.61] |
| Olsson et al. 2013 | 0 | 49 | 5 | 51 | 1.7% | 0.09 [0.01, 1.67] |
| Twaddle et al. 2007 | 2 | 25 | 1 | 25 | 2.6% | 2.00 [0.19, 20.67] |
| Willits et al. 2010 | 2 | 72 | 3 | 72 | 4.6% | 0.67 [0.11, 3.87] |
| **Subtotal (95% CI)** | | **469** | | **475** | **49.0%** | **0.40 [0.24, 0.69]** |
| Total events | 18 | | 52 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 6.66, df = 9 (P = 0.67); I² = 0% | | | | | | |
| Test for overall effect: Z = 3.28 (P = 0.001) | | | | | | |
| **1.12.2 Observational studies** | | | | | | |
| Bergkvist et al. 2012 | 6 | 220 | 19 | 267 | 17.6% | 0.38 [0.16, 0.94] |
| Kotnis et al. 2006 | 1 | 67 | 2 | 58 | 2.5% | 0.43 [0.04, 4.65] |
| Lim et al. 2017 | 2 | 99 | 6 | 101 | 5.8% | 0.34 [0.07, 1.64] |
| Miller et al. 2005 | 6 | 140 | 3 | 32 | 8.1% | 0.46 [0.12, 1.73] |
| Renninger et al. 2016 | 1 | 27 | 2 | 30 | 2.6% | 0.56 [0.05, 5.79] |
| Van der Linden et al. 2004 | 10 | 212 | 4 | 80 | 11.2% | 0.94 [0.30, 2.92] |
| Weber et al. 2003 | 1 | 24 | 4 | 23 | 3.2% | 0.24 [0.03, 1.99] |
| **Subtotal (95% CI)** | | **789** | | **591** | **51.0%** | **0.47 [0.28, 0.80]** |
| Total events | 27 | | 40 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 2.24, df = 6 (P = 0.90); I² = 0% | | | | | | |
| Test for overall effect: Z = 2.78 (P = 0.005) | | | | | | |
| **Total (95% CI)** | | **1258** | | **1066** | **100.0%** | **0.44 [0.30, 0.64]** |
| Total events | 45 | | 92 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 9.02, df = 16 (P = 0.91); I² = 0% | | | | | | |
| Test for overall effect: Z = 4.28 (P < 0.0001) | | | | | | |
| Test for subgroup differences: Chi² = 0.16, df = 1 (P = 0.69), I² = 0% | | | | | | |

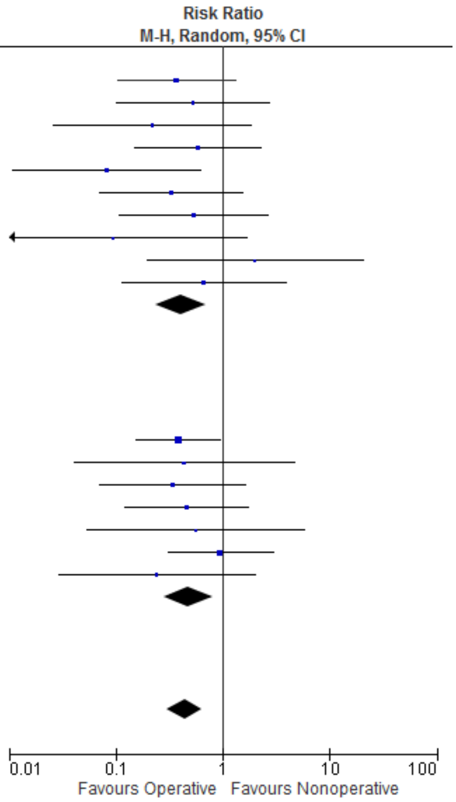


**Figure S6.** Forest plot of re-rupture rate in high-quality studies in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.

| Study or Subgroup | Operative Events | Operative Total | Nonoperative Events | Nonoperative Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| **1.13.1 RCTs** | | | | | | |
| Keating et al. 2011 | 2 | 39 | 4 | 41 | 3.9% | 0.53 [0.10, 2.71] |
| Lantto et al. 2016 | 1 | 32 | 4 | 28 | 2.4% | 0.22 [0.03, 1.84] |
| Metz et al. 2008 | 3 | 42 | 5 | 41 | 5.5% | 0.59 [0.15, 2.29] |
| Nilsson-Helander et al. 2010 | 2 | 49 | 6 | 48 | 4.4% | 0.33 [0.07, 1.54] |
| Olsson et al. 2013 | 0 | 49 | 5 | 51 | 1.3% | 0.09 [0.01, 1.67] |
| Willits et al. 2010 | 2 | 72 | 3 | 72 | 3.4% | 0.67 [0.11, 3.87] |
| **Subtotal (95% CI)** | | **283** | | **281** | **21.0%** | **0.42 [0.20, 0.85]** |
| Total events | 10 | | 27 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 2.14, df = 5 (P = 0.83); I² = 0% | | | | | | |
| Test for overall effect: Z = 2.42 (P = 0.02) | | | | | | |
| **1.13.2 Observational studies** | | | | | | |
| Bergkvist et al. 2012 | 6 | 220 | 19 | 267 | 11.5% | 0.38 [0.16, 0.94] |
| Costa et al. 2006 | 2 | 48 | 2 | 48 | 2.9% | 1.00 [0.15, 6.81] |
| Ebinesan et al. 2008 | 1 | 51 | 1 | 12 | 1.5% | 0.24 [0.02, 3.50] |
| Grubor et al. 2012 | 3 | 34 | 4 | 8 | 6.2% | 0.18 [0.05, 0.64] |
| Jackson et al. 2013 | 1 | 29 | 2 | 51 | 2.0% | 0.88 [0.08, 9.28] |
| Kotnis et al. 2006 | 1 | 67 | 2 | 58 | 1.9% | 0.43 [0.04, 4.65] |
| Renninger et al. 2016 | 1 | 27 | 2 | 30 | 2.0% | 0.56 [0.05, 5.79] |
| Wang et al. 2015 | 160 | 7625 | 119 | 4945 | 51.0% | 0.87 [0.69, 1.10] |
| **Subtotal (95% CI)** | | **8101** | | **5419** | **79.0%** | **0.56 [0.34, 0.94]** |
| Total events | 175 | | 151 | | | |
| Heterogeneity: Tau² = 0.13; Chi² = 9.56, df = 7 (P = 0.21); I² = 27% | | | | | | |
| Test for overall effect: Z = 2.21 (P = 0.03) | | | | | | |
| **Total (95% CI)** | | **8384** | | **5700** | **100.0%** | **0.59 [0.42, 0.83]** |
| Total events | 185 | | 178 | | | |
| Heterogeneity: Tau² = 0.04; Chi² = 14.39, df = 13 (P = 0.35); I² = 10% | | | | | | |
| Test for overall effect: Z = 3.07 (P = 0.002) | | | | | | |
| Test for subgroup differences: Chi² = 0.47, df = 1 (P = 0.49), I² = 0% | | | | | | |

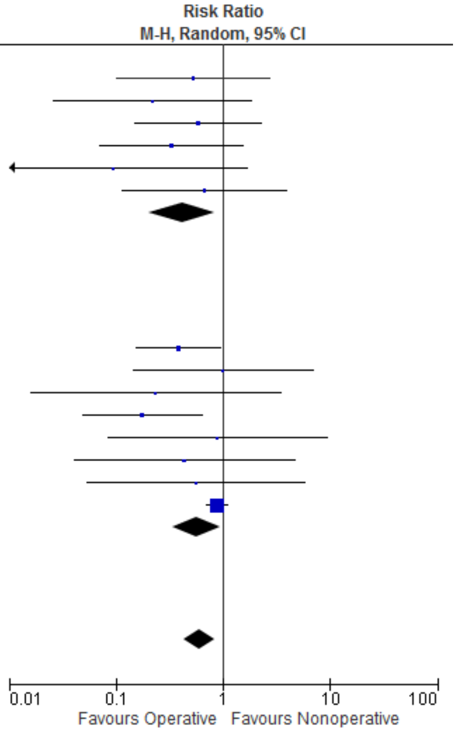


**Figure S7.** Forest plot of re-rupture rate in studies with a study period after the year 2000 in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.

| Study or Subgroup | Operative Events | Operative Total | Nonoperative Events | Nonoperative Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| **1.16.1 RCTs** | | | | | | |
| Cetti et al. 1993 | 17 | 56 | 4 | 55 | 9.5% | 4.17 [1.50, 11.62] |
| Keating et al. 2011 | 3 | 39 | 2 | 41 | 6.5% | 1.58 [0.28, 8.94] |
| Lantto et al. 2016 | 1 | 32 | 0 | 28 | 3.0% | 2.64 [0.11, 62.23] |
| Metz et al. 2008 | 9 | 42 | 15 | 41 | 11.0% | 0.59 [0.29, 1.19] |
| Möller et al. 2001 | 12 | 59 | 1 | 53 | 5.6% | 10.78 [1.45, 80.13] |
| Nilsson-Helander et al. 2010 | 6 | 49 | 3 | 48 | 8.1% | 1.96 [0.52, 7.39] |
| Nistor et al. 1981 | 31 | 46 | 0 | 61 | 3.7% | 83.11 [5.22, 1323.46] |
| Olsson et al. 2013 | 8 | 49 | 2 | 51 | 7.4% | 4.16 [0.93, 18.64] |
| Twaddle et al. 2007 | 0 | 25 | 0 | 25 | | Not estimable |
| Willits et al. 2010 | 11 | 72 | 3 | 72 | 8.6% | 3.67 [1.07, 12.60] |
| **Subtotal (95% CI)** | | **469** | | **475** | **63.5%** | **3.26 [1.26, 8.41]** |
| Total events | 98 | | 30 | | | |
| Heterogeneity: Tau² = 1.40; Chi² = 31.17, df = 8 (P = 0.0001); I² = 74% | | | | | | |
| Test for overall effect: Z = 2.44 (P = 0.01) | | | | | | |
| **1.16.2 Observational studies** | | | | | | |
| Bergkvist et al. 2012 | 5 | 220 | 6 | 267 | 8.8% | 1.01 [0.31, 3.27] |
| Kotnis et al. 2006 | 5 | 67 | 2 | 58 | 7.0% | 2.16 [0.44, 10.74] |
| Miller et al. 2005 | 17 | 140 | 2 | 32 | 7.8% | 1.94 [0.47, 7.99] |
| Renninger et al. 2016 | 0 | 27 | 0 | 30 | | Not estimable |
| Van der Linden et al. 2004 | 24 | 212 | 1 | 80 | 5.7% | 9.06 [1.25, 65.84] |
| Weber et al. 2003 | 5 | 24 | 2 | 23 | 7.3% | 2.40 [0.52, 11.14] |
| **Subtotal (95% CI)** | | **690** | | **490** | **36.5%** | **1.98 [1.03, 3.84]** |
| Total events | 56 | | 13 | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 3.92, df = 4 (P = 0.42); I² = 0% | | | | | | |
| Test for overall effect: Z = 2.03 (P = 0.04) | | | | | | |
| **Total (95% CI)** | | **1159** | | **965** | **100.0%** | **2.72 [1.44, 5.12]** |
| Total events | 154 | | 43 | | | |
| Heterogeneity: Tau² = 0.82; Chi² = 34.50, df = 13 (P = 0.001); I² = 62% | | | | | | |
| Test for overall effect: Z = 3.09 (P = 0.002) | | | | | | |
| Test for subgroup differences: Chi² = 0.71, df = 1 (P = 0.40), I² = 0% | | | | | | |

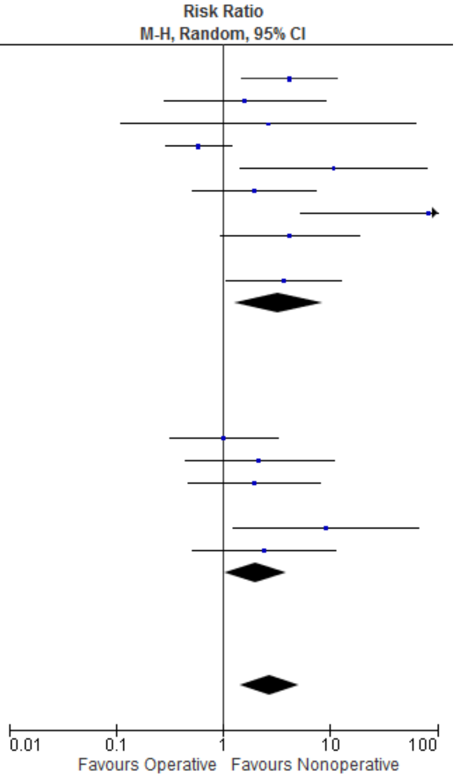


**Figure S8.** Forest plot of complication rate in high-quality studies in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.

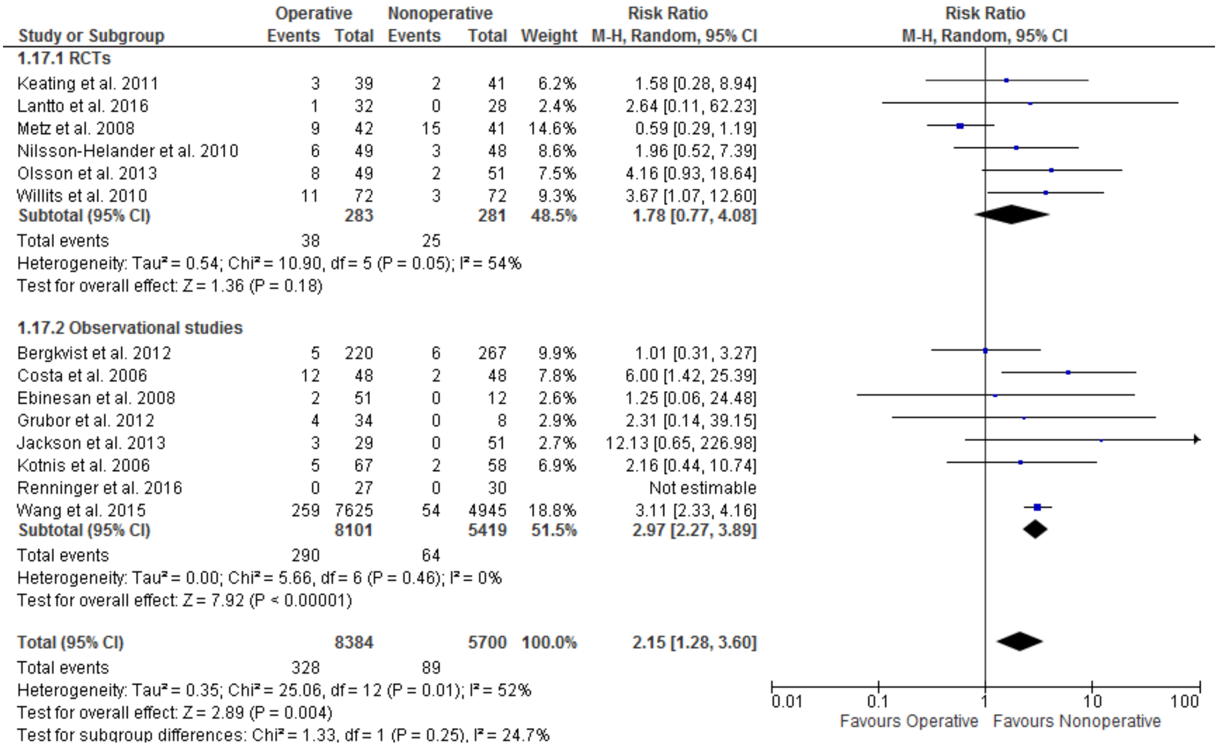


**Figure S9.** Forest plot of complication rate in studies with a study period after the year 2000 in a meta-analysis of Achilles tendon ruptures. M-H, Mantel-Haenszel.