

Association Between Clinical and Imaging Outcomes After Therapeutic Loading Exercise in Patients Diagnosed With Achilles or Patellar Tendinopathy at Short- and Long-Term Follow-up: A Systematic Review

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Abstract

Objective: To determine the association between clinical and imaging outcomes after therapeutic loading exercise in Achilles tendinopathy (AT) and patellar tendinopathy (PT) populations at both short- and long-term follow-up. **Data Sources:** The PUBMED and EMBASE databases were searched (up to June 2017) to identify articles that meet the inclusion criteria: (1) patients diagnosed with AT (insertional or midportion) or PT; (2) rehabilitation based on therapeutic loading exercise; and (3) assessment of clinical outcomes and tendon structure using an imaging modality. **Main Results:** Two independent reviewers screened 2894 search results, identifying 21 suitable studies. According to the studies included in this review, clinical results showed significant improvements for patients with AT and PT after eccentric exercise (ECC) and heavy slow resistance (HSR) at short- and long-term follow-up. Imaging outcomes were not consistent. Moderate-to-strong evidence for patients with AT suggested an association between clinical outcomes and imaging outcomes (tendon thickness and tendon neovascularization) after ECC at long-term follow-up. For patients with PT, there was moderate evidence supporting an association between clinical outcomes (questionnaire score and pain) and imaging (tendon thickness and tendon neovascularization) after ECC at short-term follow-up. For both the AT and PT groups, there was moderate evidence for an association between clinical outcomes and tendon thickness and neovascularization after HSR exercise. Results related to the HSR exercise should be interpreted with caution because of the small number of studies.

Conclusions: Based on the findings of the present review, the use of imaging outcomes as a complementary examination to the clinical assessment was confirmed. Overall, an improvement in clinical outcomes seems to be associated with a reduction in tendon thickness and tendon neovascularization. Clinicians should be aware that during the interpretation of the imaging outcomes, factors such as tendinopathy location, exercise modality performed, and a follow-up period should be considered.

Key Words: rehabilitation, tendon structure, Achilles tendon, jumper's knee, pain

(*Clin J Sport Med* 2020;30:390–403)

INTRODUCTION

Tendinopathies of the Achilles and patellar tendons are common conditions characterized by a combination of pain, swelling (diffuse or localized), and impaired performance.¹ This condition affects athletes in several types of sports activities. Prevalence of Achilles tendinopathy (AT) among runners reaches 36%² and prevalence of patellar tendinopathy (PT) among volleyball players is 14% for recreational

players and 45% for elite players.^{3,4} People who do not participate in sports can also be affected.^{4,5} In the management of AT and PT, conservative treatment is frequently the first choice of clinicians.^{6,7} A common intervention used to treat patients diagnosed with AT or PT is exercise.^{6–9} Different therapeutic loading exercises (eccentric exercise [ECC], heavy slow resistance [HSR], and isometric exercise [ISO]) are used to increase the loading capacity of the muscle–tendon unit.⁷

To assess the result of therapeutic loading exercises, clinicians often use clinical examination in combination with imaging techniques. As they are simple and can be performed at low cost, clinical outcomes such as questionnaires and pain scales are often used in trials to measure clinical changes.^{10–13} Imaging examination is also performed to verify changes in tendon structure. Several imaging modalities can be used to assess tendon disorders, with magnetic resonance imaging (MRI) and ultrasound (US) as the preferred ones.¹⁴ The advantage of MRI is that it provides a three-dimensional image of the tendon with excellent soft-tissue contrast, whereas US/Doppler shows tendon abnormalities and the presence/absence of neovascularization, and is frequently used because of widespread availability and cost-effectiveness.¹⁴

Submitted for publication November 24, 2017; accepted April 29, 2018.

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L. M. Rabello is supported by CNPq, National Council for Scientific and Technological Development, Brazil. The remaining authors report no conflicts of interest.

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<http://dx.doi.org/10.1097/JSM.0000000000000624>

Despite the use of both clinical and imaging outcomes, the relation between these measures is not clear yet. So far, authors have observed that patients improve clinically^{15,16} but stated that there is no literature to support observable structural change as an explanation for the response to loading exercise,¹⁵ except for some findings supporting the association after HSR exercise. New imaging techniques and exercise protocols have emerged in recent years, resulting in an increase of the number of clinical studies investigating the effect of load on clinical outcome and tendon structure. This warrants a new overview of available literature. Moreover, the growth in number of studies enables us to separately investigate the results of AT and PT, which seems necessary because of different population characteristics and different responses to exercise rehabilitation,¹⁵ as well as the results at different follow-up periods (short- and long-term).¹⁷

Hence, the purpose of this systematic review was to determine the association between clinical and imaging outcomes after therapeutic loading exercise in AT and PT populations at both short- and long-term follow-up.

METHODS

Search Strategy

Articles were searched using the EMBASE and PUBMED databases up to June 2017. The search strategy is listed in Table 1. The search was complemented by including papers found on the citation track. No restrictions were placed on publication date, and articles were limited to the English language.

Inclusion Criteria

The included articles assessed the effectiveness of a therapeutic loading exercise program for the treatment of Achilles (insertional or noninsertional) or PT by assessing clinical

outcomes and tendon structure using an imaging modality. Therapeutic exercise was defined as “the systematic performance or execution of planned physical movements, postures, or activities intended to enable the patients to remediate or prevent impairments, enhance function, reduce risk, optimize overall health, and enhance fitness and well-being.”¹⁸ The exercise program needed to follow a structured protocol and the training dose (frequency, duration, and type of contraction) had to be described. Articles were eligible for inclusion if they described randomized controlled trials (RCTs), non-RCTs, or cohort studies in a human population.

Exclusion Criteria

Systematic reviews, case reports, and abstracts were excluded. Other exclusion criteria were: (a) participants having a history of AT or PT tendon ruptures or other knee or foot injury that might have interfered with the outcome; (b) participants having performed a sport exercise as treatment (eg cycling and running), without therapeutic exercise associated with that; (c) participants who followed with another intervention, such as injections; (d) no image outcome reported; or (e) studies assessing the acute effect of a single set of exercises.

Study Selection

Two authors (L.M.R. and J.Z.) independently screened the titles and abstracts of the articles. If no decision could be made based on title and abstract, the full text was screened. Any disagreements were resolved by a third author (I.v.d.A.-S.). Finally, reference lists of included articles were screened.

Quality Assessment

The methodological quality of the articles was assessed using the Quality Index tool published by Downs and Black¹⁹ for

Database	Search String
PubMed	("Achilles Tendon"[Mesh] OR achilles tend*[tw] OR achillodyn*[tw] OR ((achill*[tw] OR patella*[tw]) AND ("Tendinopathy"[Mesh] OR tendonit*[tw] OR tendinit*[tw] OR tendinos*[tw] OR tendinopath*[tw] OR tendon*[tw]))) AND ("exercise Therapy"[Mesh] OR exercis*[tw] OR sport*[tw] OR ((eccentric[tw] OR resistance[tw] OR conservativ*[tw] OR traditional*[tw] OR reduced[tw] OR rehabilitat*[tw] OR loading [tw] OR load[tw]) AND (treatment[tw] OR treated[tw] OR therap*[tw] OR regimen[tw] OR program*[tw] OR training[tw] OR management[tw] OR protocol*[tw] OR eccentric load*[tw]))) AND ("Diagnostic Imaging"[Mesh] OR imaging[tw] OR ultraso*[tw] OR echogenicit*[tw] OR hyperechogen*[tw] OR hypoechogen*[tw] OR echotyp*[tw] OR Doppler[tw] OR (structural[tw] AND (chang*[tw] OR improv*[tw]))) OR (tendon*[tw] AND (structure[tw] OR thickness[tw] OR swelling[tw])) OR vasculari*[tw] OR neovasculari*[tw] OR neovessels[tw] OR number of vessels[tw] OR tissue characterization[tw] OR "blood flow"[tw] OR microcirculat*[tw] OR filling pressure[tw] OR cross sectional area[tw])) NOT ("Animals"[Mesh] NOT "Humans"[Mesh])
Embase	('Achilles tendon'/exp OR 'achilles tendinitis'/exp OR achillodyn*:ab,ti,de OR ((achill* OR patella*) NEAR/3 (tendino* OR tendini* OR tendon*)):de,ab,de) AND ('kinesiotherapy'/exp OR 'exercise'/exp OR exercis*:ab,ti,de OR sport*:ab,ti,de OR ((eccentric OR resistance OR conservativ* OR traditional* OR reduced OR rehabilitat* OR loading OR load) NEAR/2 (treatment OR treated OR therap* OR regimen OR program* OR training OR management OR protocol* OR eccentric)):ab,ti,de) AND ('diagnostic imaging'/exp OR 'echography'/exp OR 'flow measurement'/exp OR imaging:ab,ti,de OR ultraso*: ab,ti,de OR echogenicit*:ab,ti,de OR hyperechogen*:ab,ti,de OR hypoechogen*:ab,ti,de OR echotyp*: ab,ti,de OR Doppler:ab,ti,de OR (structural NEXT/2 (chang* OR improv*)):ab,ti,de OR (tendon* NEXT/2 (structure OR thickness OR swelling)):ab,ti,de OR vasculari*:ab,ti,de OR neovasculari*:ab,ti,de OR neovessels:ab,ti,de OR 'number of vessels':ab,ti,de OR 'tissue characterization':ab,ti,de OR 'blood flow':ab,ti,de OR microcirculat*:ab,ti,de OR 'filling pressure':ab,ti,de OR 'cross sectional area': ab,ti,de) NOT ('animal'/exp NOT 'human'/exp)

randomized and nonrandomized trials. This tool has a high internal consistency (Kuder–Richardson formula $20 = 0.89$), test–retest reliability ($r = 0.88$) and criterion validity (0.90), and good interrater reliability ($r = 0.75$). The Quality Index tool has 27 items distributed across four domains: reporting (items 1–10), external validity (items 11–13), internal validity (items 14–26), and power (item 27). Twenty-six items were rated either as yes (=1) or no/unable to determine (=0), and 1 item was rated on a 3-point scale (yes = 2, partial = 1, and no = 0). For the present review, checklist item number 27 about sample size calculation was simplified to a score of 0 (no sample size calculation) or 1 (sample size calculation reported). Higher scores indicate a better methodological quality of the study. The following cutoff points have been suggested to categorize articles by quality: excellent (26–28), good (20–25), fair (15–19), and poor (<14).¹⁹ Quality was assessed by two independent authors (L.M.R. and I.v.d.A.-S.), and a consensus meeting was held to resolve discrepancies between the authors. If consensus was not achieved following this meeting, a third author (J.Z.) provided the final judgment.

Data Extraction

One author (L.M.R.) extracted the following information from the included articles using 1 form developed in advance: first author, year of publication, study design, population (physical activities performed before, tendon portion injured, sample size, age, and duration of symptoms), intervention, follow-up period, clinical outcomes measured, and imaging tool performed. The findings for changes on clinical and imaging outcomes were extracted, and the *P* value was presented (when described by the authors). The clinical outcomes were divided into four domains: (1) questionnaires (Victorian Institute of Sport Assessment–Achilles questionnaire [VISA-A], Victorian Institute of Sport Assessment–Patella questionnaire [VISA-P], American Orthopaedic Foot and Ankle Society ankle score [AOFAS], and Short Form-36 [SF-36]); (2) pain measured during rest and activities; (3) performance, including return to sport and activity level; and (4) patient satisfaction with the treatment. The follow-up period was divided into short-term (up to 24 weeks after the beginning of the treatment) and long-term (more than 24 weeks after the beginning of the treatment).

A qualitative analysis of the data was performed because of its heterogeneity. The levels of evidence were used according to the recommendations made by van Tulder et al²⁰:

1. Strong evidence (+ + + or – – –): consistent findings among high-quality studies ($n \geq 2$).
2. Moderate evidence (+ + or – –): consistent findings between multiple low-quality studies and/or within 1 high-quality study.
3. Limited evidence (+ or –): 1 low-quality study.
4. Conflicting evidence (+/–): inconsistent findings among multiple studies.
5. No evidence: no studies.

Regarding the results of the association between clinical and imaging outcomes, we define an association between outcomes when both measures improved significantly. In cases where statistical tests were not applied, it was considered an association when both measures showed improvement.

RESULTS

Article Selection

The search in PubMed resulted in 1323 articles and the search in Embase in 1571 articles. After excluding duplicates (706 articles) and irrelevant articles based on titles and abstract screening 31 articles remained, another 11 of which were excluded after reading the full text. The reference lists of the included articles were manually checked and 1 additional article was identified, leaving a final yield of 21 articles. Figure 1 shows a flowchart of the selection process.

Methodological Quality

The quality assessment scores of the AT and PT studies ranged from 9 to 25 and 15 to 20, respectively. The quality assessment results for each of the four domains (reporting, external validity, internal validity, and power) are shown in Table 2.

Study Characteristics

The included articles described 13 RCTs,^{10,17,21–31} seven cohort studies,^{12,32–37} and 1 pilot study.³⁸ Eighteen studies investigated the effect of exercise on AT and three studies investigated the effect of exercise on PT. Two different exercise programs were investigated in the articles included, ECC exercise and HSR exercise. As described before, four main clinical outcomes were identified: questionnaires, pain (visual analogue scale [VAS]), patient performance, and patient satisfaction. The imaging tools used to assess Achilles tendon were US, ultrasound tissue characterization (UTC), and MRI, whereas US and MRI were used to assess the patellar tendon. The studies in the AT population included outcomes on short- and long-term follow-up, whereas the studies investigating patients with PT included only short-term follow-up. Detailed information about the study characteristics is shown in Table 3.

Participant Characteristics

Achilles Tendinopathy Studies

The AT studies included a total of 468 participants (ECC: 446 and HSR: 22), of which 63% was men, and a mean age of 42.4 years. Of the 18 studies included, 16 evaluated participants with only midportion symptoms^{10,21–23,25–29,32–38} and 2 included patients diagnosed with midportion and insertional symptoms.^{17,24} Because of this inclusion methodology of the studies, it was not possible to perform separate analysis of both groups, insertional and midportion AT. In 8 studies, the subjects were involved in a sport activity,^{10,17,23–25,27,29,32} 6 studies recruited mixed subjects with idiopathic and sport-related injuries^{21,26,28,33,34,37} and 4 studies did not report whether participants were involved in a sport activity.^{22,35,36,38} Fifty percent of the studies included subjects who were allowed to perform sport activities during the rehabilitation program.

Patellar Tendinopathy Studies

The PT studies included 49 male participants (ECC: 28 and HSR: 21) with a mean age of 37.5 years, and most of the subjects presented chronic PT. All the participants included in

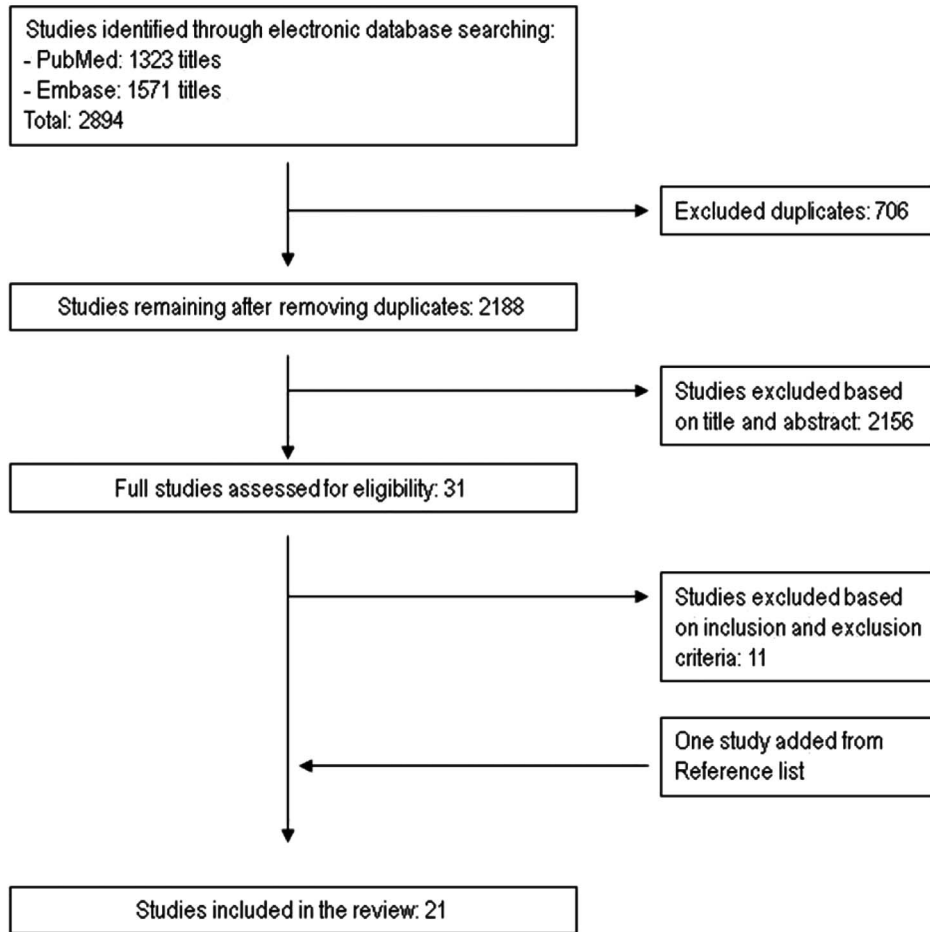


Figure 1. Study inclusion flowchart.

the studies were involved in sports activities. All the included studies allowed subjects to perform sports activities during the rehabilitation program. An overview of all the included articles is shown in Table 3.

Clinical Outcomes

Achilles Tendinopathy

Eccentric Exercise

At short-term follow-up, there was strong evidence that questionnaire scores^{10,21,22,24,27-29,32,34} and pain^{10,17,21-24,26-29,33} improved and moderate evidence that performance^{10,33,37} increased. At long-term follow-up, there was moderate evidence that questionnaire score,^{10,25,28,38} pain,^{10,17,26,28,35,36} and patient performance^{10,26,28} improved, and that patients were satisfied with the treatment.^{10,17,35,36}

Heavy Slow Resistance Exercise

Based on 1 study,¹⁰ there was moderate evidence that questionnaire score, pain, and patient performance improved at short- and long-term follow-up. There was moderate evidence that patients were satisfied with the treatment at short- and long-term follow-up.

Patellar Tendinopathy

Eccentric Exercise

There was moderate evidence that questionnaire score^{12,30} and pain¹² improved at short-term follow-up. There was moderate evidence that patients were not satisfied with the treatment at short- and long-term follow-up.¹²

Heavy Slow Resistance Exercise

At short-term follow-up, there was moderate evidence that questionnaire score^{12,31} and pain^{12,31} improved. At long-term follow-up, there was moderate evidence that there was no change in questionnaire score¹² and pain.¹² Moderate evidence suggests that patients were satisfied at short- and long-term follow-up.¹²

Imaging Outcomes

Achilles Tendinopathy

Eccentric Exercise

There was strong evidence that there was no change in tendon thickness at short-term follow-up.^{17,21,22,28,29,32} There was moderate evidence of increased tendon volume^{32,37} and

TABLE 2. Scores of the Quality Assessment List

Reference	Reporting (Max = 11)	External Validity (Max = 3)	Internal Validity		Power (Max = 1)	Total (Max = 28)	Article Quality
			Bias (Max = 7)	Confounding (Max = 6)			
AT							
Boesen et al (2017)	10	3	6	5	1	25	Good
Tshehaie et al (2017)	9	2	5	4	0	20	Good
Balius et al (2016)	10	3	5	4	0	22	Good
Beyer et al (2015)	10	1	5	6	1	23	Good
Gärdin et al (2013)	8	0	3	2	0	13	Poor
Horstmann et al (2013)	10	0	6	4	1	21	Good
Ram et al (2013)	10	1	5	0	1	17	Fair
de Vos et al (2012)	9	0	4	2	1	16	Fair
De Jonge et al (2010)	8	1	4	4	0	17	Fair
Gärdin et al (2010)	7	0	4	2	0	13	Poor
Richards et al (2010)	6	1	4	1	0	12	Poor
De Vos et al (2007)	9	1	6	4	0	20	Good
Petersen et al (2007)	9	0	2	3	0	14	Fair
Rompe et al (2007)	9	0	4	5	0	18	Fair
Nørregaard et al (2007)	9	0	5	1	0	15	Fair
Ohberg and Alfredson (2004)	5	0	3	1	0	9	Poor
Ohberg et al (2004)	7	0	1	1	0	9	Poor
Shalabi et al (2004)	7	0	4	2	0	13	Poor
PT							
Biernat et al (2014)	9	0	4	2	0	15	Fair
Kongsgaard et al (2010)	9	0	5	1	0	15	Fair
Kongsgaard et al (2009)	7	1	6	5	1	20	Good

decreased tendon cross-sectional area (CSA).³² At long-term follow-up, there was moderate evidence of reduced tendon neovascularization.^{10,35,38}

Heavy Slow Resistance Exercise

Based on 1 study,¹⁰ there was moderate evidence of reduced tendon thickness and tendon neovascularization at short- and long-term follow-up.

Patellar Tendinopathy

Imaging outcomes were measured at short-term follow-up.

Eccentric Exercise

There was moderate evidence suggesting that there was no change in tendon thickness.¹² There was moderate evidence that tendon CSA increased.¹²

Heavy Slow Resistance Exercise

There was moderate evidence that tendon thickness decreased¹² and tendon CSA did not change.^{12,31} The description of clinical and imaging outcomes is shown in Table 4.

Association Between Clinical and Imaging Outcomes

Achilles Tendinopathy

The results of the association between clinical outcomes and imaging outcomes after ECC exercise at short-term follow-

up strongly suggest that an improvement in patient performance and patient satisfaction was associated with reduced tendon neovascularization. There was also strong evidence supporting the association between patient satisfaction and reduced tendon thickness. At long-term follow-up, there was moderate evidence suggesting that a reduction in tendon thickness, tendon abnormalities, and tendon neovascularization was associated with improved clinical outcomes such as pain, performance, and patient satisfaction. All the associations, at short- and at long-term follow-up, are shown in Table 5.

One study investigated the effect of HSR exercise in patients diagnosed with AT, showing moderate evidence that a reduction in tendon thickness and tendon neovascularization was associated with improved clinical outcomes (function and pain) at short- and at long-term follow-up.¹⁰

Patellar Tendinopathy

All the articles included in this systematic review observed the effect of loading exercise on patients diagnosed with PT at short-term follow-up. One article additionally measured the effect of loading exercise on long-term follow-up, but at that follow-up moment, only clinical outcomes were assessed.¹²

There was moderate evidence supporting the association of a reduction in tendon thickness and tendon neovascularization with improved pain and function for both ECC and HSR exercise. Furthermore, after HSR exercise, tendon thickness and tendon neovascularization were also associated with

TABLE 3. Characteristics of the Included Articles										
References	Design	Site of Pathology	Population			Follow-up	Imaging Examination	Imaging Outcome	Clinical Outcome	Therapeutic Loading Exercise
			Sample Size (Male: Female)	Mean Age	Pain Duration (mo)					
AT										
Boesen et al (2017)	RCT	Midportion	19:0	40.9 (6.6)	30.8 (37.4)	6, 12, and 24 wk	US	Tendon thickness	VISA-A, pain (VAS), patient satisfaction, and performance	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
								Tendon neovascularization		
Tshehaie et al (2017)	Cohort	Midportion	8:12	46 (9.5)	9	24 wk	MRI	Tendon volume	VISA-A	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
								Tendon CSA		
								Tendon thickness		
								Intratendinous signal		
Balius et al (2016)	RCT	Midportion	15:04	38.9 (6.6)	>3 mo.	6 and 12 wk	US	Tendon thickness	VISA-A, pain (VAS)	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
Beyer et al (2015)	RCT	Midportion	18:07	48 (2)	19 (5)	12 and 52 wk	US (GS and CD)	Tendon thickness	VISA-A, pain (VAS), level of activity, patient satisfaction	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
			14:08	48 (2)	17 (3)			Tendon neovascularization		HSR exercise—12 wk, 3× wk (# reps decreased, load increased p/wk). Used resistance equipment in fitness center.
Gärdin et al (2013)	Cohort	Midportion	14:06	51	31	12 wk	MRI	Intratendinous signal	Pain and performance	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
Horstmann et al (2013)	RCT	Midportion	10:09	45.7 (8.5)	>6 mo	12 wk	US (GS)	Tendon abnormalities	Pain (palpation)	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
Ram et al (2013)	RCT	Midportion	9:11	49.2 (9.07)	>3 mo.	12 wk	US (GS and CD)	Tendon neovascularization	VISA-A, pain (VAS) and patient satisfaction	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
		Insertional						Tendon appearance		

TABLE 3. Characteristics of the Included Articles (Continued)

References	Design	Site of Pathology	Population			Follow-up	Imaging Examination	Imaging Outcome	Clinical Outcome	Therapeutic Loading Exercise
			Sample Size (Male: Female)	Mean Age	Pain Duration (mo)					
de Vos et al (2012)	Cohort	Midportion	10:15	46 (9.5)	36	2, 8, 16, and 24 wk	UTC	Tendon echo types	VISA-A	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
de Jonge et al (2010)	RCT	Midportion	37:26	44.6 (7.9)	30.7 (50.8)	12 mo	US	Tendon neovascularization	VISA-A and patient satisfaction	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
Gärdin et al (2010)	RCT	Midportion	16:08	49	12	29–58 mo	MRI	Tendon volume	Pain and performance	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
								Intratendinous signal		
Richards et al (2010)	Pilot	Midportion	5:04	47	NR	12 mo	US (GS and CD) MRI	Tendon thickness	VISA-A	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
								Tendon neovascularization		
de Vos et al (2007)	RCT	Midportion	37:26	44.6 (7.9)	30.7 (50.8)	12 wk	US	Tendon neovascularization	VISA-A, patient satisfaction	ECC exercise—12, 2× day (180 reps/day), rec. Alfredson
Petersen et al (2007)	RCT	Midportion	23:14	42.1 (11)	7.1 (2.6)	6 and 12 wk postintervention	US (GS)	Tendon thickness	AOFAS, SF-36, pain (VAS), performance	ECC exercise—12 wk, 3× day (270 reps/day)
Rompe et al (2007)	RCT	Midportion	9:16	48.1 (9.9)	10.9 (7.7)	4 mo	US (GS)	Tendon thickness	VISA-A, pain, and patient satisfaction	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
Nørregaard et al (2007)	RCT	Midportion	20:21	41 (2)	26 (9)	12 wk and 12 mo	US (GS)	Tendon thickness	Pain and patient satisfaction	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
		Insertional								
Öhberg and Alfredson (2004)	Cohort	Midportion	22:08	48	NR	3–48 mo	US (GS and CD)	Tendon abnormalities	Pain and patient satisfaction	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson
								Tendon neovascularization		

TABLE 3. Characteristics of the Included Articles (Continued)

References	Design	Site of Pathology	Population			Follow-up	Imaging Examination	Imaging Outcome	Clinical Outcome	Therapeutic Loading Exercise	
			Sample Size (Male: Female)	Mean Age	Pain Duration (mo)						
Öhberg et al (2004)	Cohort	Midportion	19:06	50.4 (9.6)	17.1	1.6–7.75 yr	US (GS)	Tendon thickness	Pain and patient satisfaction	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson	
								Tendon abnormalities			
Shalabi et al (2004)	Cohort	Midportion	16:09	51	18	12 wk	MRI	Tendon volume	Pain and performance	ECC exercise—12 wk, 2× day (180 reps/day), rec. Alfredson	
								Intratendinous signal			
PT											
Biernat et al (2014)	RCT	Patellar tendon	15:00	17.7 (0.7)	NR	12, 24 wk	US (GS and CD)	Neovascularization	VISA-P and performance	ECC exercise—squat on decline board (25 degrees), 3 series of 15 reps 1× day. Unstable surface added in fourth wk.	
Kongsgaard et al (2010)	RCT	Patellar tendon	8:00	32.9 (3.5)	15 (3)	12 wk	MRI	CSA	VISA-P and pain (VAS)	HSR exercise—12 wk, 3× wk, decreasing # reps, 3 bilateral exercises/ session: squat, leg press, and hack squat	
Kongsgaard et al (2009)	Cohort	Patellar tendon	12:00	31.3 (8.3)	18.8 (13)	12 wk	US (GS and CD) MRI	Tendon thickness	VISA-P and pain (VAS)	ECC exercise—12 wk, squat on decline board (25 degrees), 3 series of 15 reps, 2× day.	
								Tendon neovascularization			HSR exercise—12 wk, 3× wk, decreasing # reps, 3 bilateral exercises/ session: squat, leg press, and hack squat
								Tendon CSA			

Alfredson, as recommended by Alfredson et al; AUC, area under the curve; CA, color area; CD, color Doppler; GS, grayscale; NR, not reported; P-CSA, patellar cross-sectional area; SI, signal increase.

TABLE 4. Description of Clinical and Imaging Outcomes

References	Clinical Outcome	Imaging Outcome
AT		
Boesen et al (2017)	Short-term follow-up	Short-term follow-up
	VISA-A: increased significantly ($P < 0.05$)	Tendon thickness: no significant changes
	Pain (VAS) during activity: decreased significantly ($P < 0.05$)	Tendon neovascularization: no significant changes
	Performance: 42% of patients returned to running during the trial period	
	Patient satisfaction: 35% and 42% of patients satisfied with treatment at 12 and 24 wk, respectively	
Tsehaie et al (2017)	Short-term follow-up	Short-term follow-up
	VISA-A: increased significantly ($P = 0.004$)	Tendon thickness: no significant changes ($P = 0.179$)
		Tendon volume: decreased significantly ($P = 0.021$)
		Tendon CSA: decreased significantly ($P = 0.048$)
	Intratendinous signal: no significant changes ($P = 0.591$)	
Balius et al (2016)	Short-term follow-up	Short-term follow-up
	VISA-A: increased significantly ($P = 0.045/P < 0.001$)	Tendon thickness: no significant changes
	Pain (VAS) at rest: decreased significantly ($P = 0.020/P = 0.003$)	Reactive tendinopathy—decreased
	Pain (VAS) during activity: decreased significantly ($P < 0.001/P < 0.001$) (reactive tendinopathy/degenerative tendinopathy)	Degenerative tendinopathy—increased
Beyer et al (2015)	Short- and long-term follow-up	Short- and long-term follow-up
	VISA-A: increased significantly ($P < 0.0001$)	Tendon thickness: decreased significantly ($P < 0.0001$)
	Pain (VAS) during running: decreased significantly ($P < 0.001$)	Tendon neovascularization: decreased significantly ($P < 0.005$)
	Pain (VAS) during heel rises: decreased significantly ($P < 0.001$)	
	Performance: significant effect of time ($P < 0.05$)	
	Patient satisfaction: At 12 wk, 80% and 100% of patients satisfied after ECC and HSR exercises, respectively; at 52 wk, 76% and 96% satisfied.	
Gårdin et al (2013)	Short-term follow-up	Short-term follow-up
	Pain: decreased significantly ($P < 0.01$)	Intratendinous signal: no significant changes
	Performance: improved significantly ($P < 0.01$)	
Horstmann et al (2013)	Short-term follow-up	Short-term follow-up
	Pain (palpation): decreased significantly ($P < 0.05$)	Tendon abnormalities: 42.9% of patients showed improved homogeneity in tendon path
Ram et al (2013)	Short-term follow-up	Short-term follow-up
	VISA-A: score improved (baseline: 58.8 – follow-up: 63.95)	Tendon neovascularization: color Doppler activity increased in 19 patients (of 20)
	Pain (VAS) during tendon loading: decreased (baseline: 43—follow-up: 32.79)	Tendon appearance: no significant changes
	Pain (VAS) during tendon loading: decreased (baseline: 29.6—follow-up: 25.37)	
	Patient satisfaction: 10% of patients satisfied with treatment	
de Vos et al (2012)	Short-term follow-up	Short-term follow-up
	VISA-A: increased significantly ($P = 0.01$ after 24 wk)	Echo-types: echo types I and II decreased w/o significance after 24 wk

TABLE 4. Description of Clinical and Imaging Outcomes (Continued)

References	Clinical Outcome	Imaging Outcome
de Jonge et al (2010)	Long-term follow-up	Long-term follow-up
	VISA-A: increased significantly after 1 yr ($P < 0.01$)	Tendon neovascularization: 65% of patients showed some degree of neovascularization at baseline; 71% showed some degree of neovascularization at 1-yr follow-up
	Patient satisfaction: excellent or good in 53.1%.	
Gärden et al (2010)	Long-term follow-up	Long advance term follow-up
	Pain (VAS): decreased significantly ($P < 0.01$)	Tendon volume: decreased without significant changes
	Performance: improved significantly ($P < 0.001$)	Intratendinous signal: decreased
Richards et al (2010)	Long-term follow-up	Long-term follow-up
	VISA-A: scores improved	Tendon thickness: reduced
		Tendon neovascularization: number of neovessels reduced
de Vos et al (2010)	Short-term follow-up	Short-term follow-up
	VISA-A: increased significantly ($P < 0.004$ and $P < 0.001$) patients w/o and w neovascularization at baseline, respectively	Tendon neovascularization: no significant changes (63% of patients showed presence of neovessels at baseline and follow-up)
	Pain (VAS): decreased significantly ($P < 0.005$ and $P < 0.001$) patients w/o and w neovascularization at baseline, respectively	
Petersen et al (2007)	Short- and long-term follow-up	Short- and long-term follow-up
	AOFAS—score improved significantly	Tendon thickness: no significant changes
	SF-36: function and pain improved significantly (short-term)	
Rompe et al (2007)	Pain (VAS) during ADL: decreased significantly	
	Pain (VAS) during walking: decreased significantly	
	Performance: 90% of subjects returned to sports (long-term)	
	Short-term follow-up	Short-term follow-up
	VISA-A: increased significantly ($P < 0.01$)	Tendon thickness: no significant changes
Nørregaard et al (2007)	Pain (load-induced): decreased significantly ($P < 0.01$)	
	Patient satisfaction: 60% of patients were completely recovered or much improved	
	Short- and long-term follow-up	Short-term follow-up
Nørregaard et al (2007)	Pain: decreased significantly ($P < 0.05$)	Tendon thickness: no significant changes
	Patient satisfaction: 23% of patients reported very significant improvement at 12 wk; 91.3% reported very significant improvement or complete cure after 1 yr.	Long-term follow-up
		Tendon thickness: decreased significantly ($P < 0.01$) after 1 yr
Öhberg and Alfredson (2004)	Long-term follow-up	Long-term follow-up
	Pain during load: no pain in 36 of 41 patients.	Tendon neovascularization: 88.8% of tendons showed no remaining neovascularization
	Patient satisfaction: 36 of 41 patients reported good results	Tendon abnormalities: 94.4% of tendons showed more normal tendon structure in US
Öhberg et al (2004)	Long-term follow-up	Long-term follow-up
	Pain: significant improvement	Tendon thickness: decreased significantly ($P < 0.005$)
	Patient satisfaction: 88% of patients satisfied with treatment	Tendon abnormalities: 73% of patients showed normal tendon structure at follow-up

TABLE 4. Description of Clinical and Imaging Outcomes (Continued)

References	Clinical Outcome	Imaging Outcome
Shalabi et al (2004)	Short-term follow-up	Short-term follow-up
	Pain: decreased significantly ($P < 0.01$)	Tendon volume: decreased significantly ($P < 0.05$)
	Performance: improved significantly ($P < 0.001$)	Intratendinous signal: decreased significantly ($P < 0.05$)
	Patient satisfaction	
PT		
Biernat et al (2014)	Short-term follow-up	Short-term follow-up
	VISA-P: increased significantly ($P < 0.05$)	Tendon neovascularization: presence of neovascularization observed in 3 athletes at baseline and 1 athlete at third measurement.
	Performance: no significant changes	Tendon abnormalities: #players with morphological changes decreased from 7 (baseline) to 5 (third measurement)
Kongsgaard et al (2010)	Short-term follow-up	Short-term follow-up
	VISA-P: increased significantly ($P = 0.02$)	Tendon CSA: no significant changes
	Pain (VAS): decreased significantly ($P = 0.008$)	
Kongsgaard et al (2009)	Short-term follow-up	Short-term follow-up
	VISA-P: for both groups, ECC and HSR, increased significantly ($P < 0.01$)	Tendon thickness: decreased significantly from week 0 to week 12 (HSR group) ($P < 0.01$)
	Pain (VAS): for both groups, ECC and HSR, decreased significantly ($P < 0.01$)	Tendon neovascularization: decreased significantly from week 0 to week 12 (HSR group) ($P < 0.01$)
	Patient satisfaction: 42% of patients who performed ECC satisfied; 70% who performed HSR satisfied	Patellar CSA: increased significantly in the ECC group.
	Long-term follow-up	
	VISA-P: no significant changes observed from 0 to 52 wk for both groups	
	Pain (VAS): no significant changes observed from 0 to 52 wk for both groups	
	Patient satisfaction: 22% of patients who performed ECC satisfied; 73% who performed HSR satisfied	

patient satisfaction. All the associations, after ECC and HSR exercises, are shown in Table 6.

DISCUSSION

The aim of this review was to determine the association between clinical and imaging outcome after therapeutic loading exercise in AT and PT populations at both short- and long-term follow-up. Overall, there is moderate evidence for an association between clinical outcomes and tendon thickness and tendon neovascularization in tendinopathy.

An earlier systematic review¹⁶ showed strong evidence to refute the changes in tendon structure as an explanation for response to ECC and moderate evidence for treatment with HSR exercise. However, these investigators did not conduct different analyses for different tendinopathy locations, nor distinguished between short- and long-term follow-up, although different outcomes are likely.¹⁶ In this present review, we indeed observed that at short-term follow-up after ECC exercise, there was an association between clinical outcomes (questionnaire score and pain) and imaging outcomes (tendon thickness and tendon neovascularization) on patients diagnosed with PT, which was not observed on patients diagnosed with AT. There was also an association

between patient satisfaction and imaging outcomes (tendon thickness and tendon neovascularization) among patients with AT, not observed on patients with PT. At long-term follow-up, there was an association between clinical outcomes (questionnaire score, pain, and performance) and imaging outcomes (tendon thickness and tendon neovascularization), which was not observed at short-term follow-up. Moreover, at short-term follow-up, we observed that the clinical and imaging outcomes that were not associated after ECC exercise were associated after HSR exercise.

The observation that the association between clinical and imaging outcomes differed between patients diagnosed with AT and with PT could be a consequence of the different regions of the tendon compromised. Most AT studies (89%) included patients diagnosed with midportion AT, whereas the PT studies included subjects with symptoms at the insertion of the tendon. Previous studies show that there is a difference in function per tendon region: the midportion of the tendon stores elastic energy during lengthening,^{39,40} whereas the insertion of the tendon (entheses) commonly dissipates stress.⁴¹ Corroborating our findings and this difference in function between the Achilles and patellar tendons, a recent study showed that these tendons display different changes in their elastic properties.⁴² On this basis, tendon region and

TABLE 5. Association Between Imaging Outcomes and Clinical Outcomes After ECC and HSR Exercises for Patient Diagnosed With AT, During Short-Term (Left Side of Column) and Long-Term Follow-up (Right Side of Column)

Clinical Outcomes	Imaging Outcomes													
	Tendon Thickness		Tendon Abnormalities		Neovascularization		Tendon Volume		Intratendinous Signal		CSA		Echo Types	
ECC exercise														
Questionnaire score	--	+/–	–	NR	--	+++	++	NR	--	NR	++	NR	–	NR
Pain	--	++	--	++	--	++	+	–	+/–	+				
Performance	+/–	++	NR	NR	+++	++	–	–	+/–	+				
Patient satisfaction	+++	++	+	++	+++	++								
HSR exercise														
Questionnaire	++	++	NR	NR	++	++								
Pain	++	++	NR	NR	++	++								
Performance	++	++	NR	NR	++	++								
Patient satisfaction	++	++	NR	NR	++	++								

*Positive sign (+), existing association between imaging and clinical outcomes; negative sign (–), no association between outcomes; +++ (– – –), strong evidence; ++ (– –), moderate evidence; + (–), limited evidence; +/-, conflicting evidence.
NR, no study reported this association.*

tendon function are factors that should be taken into consideration when investigating the effects of loading exercises on a rehabilitation program.

Another factor that might influence interpretation of the results of the rehabilitation protocol is the follow-up period. According to our review, it seems that the association between clinical outcomes and the changes in Achilles tendon structure are more evident at long-term follow-up after ECC exercise. This result is in agreement with findings of Verrall et al,⁴³ which shows that clinical conditions improve before alteration in tendon morphology. The explanation for this is that after ECC exercise rehabilitation, the tendon develops a higher ability to withstand force and the non-normal adaptation to support the load is no longer needed, which gives time for the tendon to repair.⁴³ Hence, to avoid misinterpretation of the results, the imaging outcomes at short-term follow-up after ECC exercise should be interpreted with caution.

The studies included in this systematic review investigated 2 different exercise modalities, ECC and HSR. Among the included studies on patients diagnosed with AT, there was only one paper that compared the two exercise modalities, finding no significant difference between the therapies. However, patients who performed HSR exercise were more satisfied at short-term follow-up than patients who performed ECC exercise. Among the studies that investigated patients diagnosed with PT, only one compared both exercises, reporting that tendon thickness and tendon neovascularization decreased significantly after HSR exercise and tendon CSA increased significantly after ECC exercise. Differences might be explained by protocol design. Eccentric exercises were performed daily, whereas HSR exercises were performed three times a week. Less frequent exercises could enhance compliance¹⁰ and result in structural changes such as collagen synthesis.¹² It might even be that tendon load (muscle

TABLE 6. Association Between Imaging Outcomes and Clinical Outcomes After ECC and HSR Exercises for Patient Diagnosed With PT During Short-Term Follow-up

Clinical Outcomes	Imaging Outcomes			
	Tendon Thickness	Tendon Abnormalities	Neovascularization	CSA
ECC exercise				
Questionnaire score	++	+	++	NR
Pain	++	NR	++	NR
Performance	NR	–	–	NR
Patient satisfaction	--	NR	--	NR
HSR exercise				
Questionnaire	++	NR	++	–
Pain	++	NR	++	–
Performance	NR	NR	NR	NR
Patient satisfaction	++	NR	++	NR

*Positive sign (+), existing association between imaging and clinical outcomes; negative sign (–), no association between outcomes; +++ (– – –), strong evidence; ++ (– –), moderate evidence; + (–), limited evidence; +/-, conflicting evidence.
NR, no study reported this association.*

contraction intensity) is more important than type of muscular contraction.⁴⁴

To summarize, clinicians who use imaging tools to investigate changes in tendon structure after therapeutic loading exercise in patients diagnosed with AT and PT should be careful when interpreting the imaging findings and take the following into account: (1) tendinopathy location: there are different results for the association between clinical and imaging outcomes for AT and PT populations after ECC exercise; (2) follow-up period: in patients with AT, longer follow-up showed an association between clinical and imaging outcomes; and (3) exercise rehabilitation protocol: on both populations, patients with AT and PT, at short-term follow-up, the clinical outcomes that were not associated with imaging outcomes after ECC exercise were associated after HSR exercise.

Limitations

The results of this review should be interpreted with caution because of the small number of studies, especially for PT. In addition, many of the studies were of poor methodological quality, resulting in low levels of evidence. We recommend that studies investigating the effect of therapeutic loading exercise on tendon structure take all the information requested by the Consort checklist⁴⁵ into consideration at the moment of study designing and reporting. Because this systematic review included only studies that investigated both clinical and imaging outcomes, only ECC and HSR exercises were investigated. The effect of other exercise modalities, such as isometric and eccentric-concentric exercise, needs further investigation that includes both clinical and imaging outcomes.

PERSPECTIVE

Based on the studies included in this review, we suggest that clinicians should consider using imaging outcomes as a complementary examination to the clinical assessment, at the short-term follow-up, as a lack of association between imaging and clinical assessment is found, and especially when using the US. More high-quality research is necessary to investigate the effects of therapeutic loading exercise on clinical and imaging outcomes. In addition, more research is needed to explore the benefits of using new imaging tools such as novel MRI techniques, UTC, and elastography to determine the effect of exercise on tendon structure.

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