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Conservative Management of Acute Lower Limb Tendinopathies: A Systematic Review

ABSTRACT

Background: Most knowledge regarding conservative management for lower limb tendinopathy (LLT) is for persistent symptoms, with less known about conservative management of acute LLT. Sub-optimal management of acute LLT is detrimental in many regards, not least the likely conversion to persistent symptoms.

Objectives: To synthesise existing literature on conservative management of acute LLTs

Design: Systematic review of relevant literature (PROSPERO (ID: CRD42018117882))

Method: A search was made of multiple databases (MEDLINE, CINAHL & EMBASE) using relevant search terms. Titles, abstracts, and then full texts were filtered to find articles that met the strict inclusion / exclusion criteria. Searching, data extraction, and quality assessment, using GRADE, were done independently by two authors. To understand how the interventions impacted the duration of reported symptoms, results were split into three time points: short term (<4 weeks), medium-term (4-12 weeks) and long-term (>12 weeks).

Results: 13 studies (n=534) met the criteria for inclusion. There was very low level of certainty for the effectiveness of interventions at short-term, medium-term, and long-term follow ups. However, there were large effects seen across a number of different treatments on pain intensity and disability in LLTs.

Conclusions: This review demonstrates that limited evidence currently exists to guide the management of acute lower limb tendinopathy, and the quality of the existing evidence is collectively low. These findings inform the discussion of different treatment options with patients in a shared decision-making process to empower and enable the patient.

Key Words: lower limb, tendinopathy, conservative management, acute

INTRODUCTION

Tendinopathy is a common musculoskeletal condition that refers to tendon-related pain and is associated with a noticeable decrease in activity tolerance (Cook & Purdam, 2009; Scott et al., 2020). Several different tendinopathies affect the lower limb (lower limb tendinopathies (LLT)) and share many pathological and clinical features. For instance, a key factor in the development of LLT is excessive tendon loading, which can either be tensile or compressive in nature (Cook & Purdam, 2009). Tensile loads occur as the tendon participates in energy storage and release via the stretch-shortening cycle, whilst compressive loads occur at the tendon enthesis where the tendon is compressed against a bony prominence (Debenham, Travers, Gibson, Campbell, & Allison, 2016; Grimaldi et al., 2015). LLT examples where compressive loads are evident include gluteal tendinopathy, proximal hamstring tendinopathy and insertional Achilles tendinopathy (Cardoso, Pizzari, Kinsella, Hope, & Cook, 2019).

LLT's affect both athletic and sedentary populations, impacting function and quality of life (Grimaldi et al., 2015; Malliaras, Barton, Reeves, & Langberg, 2013), although some variation exists in the prevalence of tendinopathy (Table 1). For example, patellar tendinopathy is more likely to affect a younger person and gluteal tendinopathy is more likely affect females (Cook et al., 1997; Segal et al., 2007).

Tendinopathy has been classified pathologically as either 1) reactive, 2) dysrepair or 3) degenerative tendinopathy; the former two equivalent to an 'acute' state, and the latter to a persistent state (Cook & Purdam, 2009). The purpose of pathological classification is to guide management choices, by matching treatment to the stage of pathology in attempt to optimise clinical outcomes (Silbernagel, Hanlon, & Sprague, 2020). Acute management of any musculoskeletal injury is important as it influences both short and long term recovery (Bleakley et al., 2010; Lagas et al., 2020). Optimised acute management, often aided by stratification tools, can produce excellent results in terms of generic health benefit, cost savings and reducing the conversion to persistence (Hill et al., 2011). Whilst this has been

observed in other conditions such as non-specific low back pain (Foster et al., 2018; Maher, Underwood, & Buchbinder, 2017) and patellofemoral pain (Crossley et al., 2016), where early management consensus exists, no such guidance exists for LLT management (Vicenzino et al., 2020). Conservative management, with exercise as a cornerstone, is considered the primary management strategy for LLT (Grimaldi et al., 2015; Malliaras, Cook, Purdam, & Rio, 2015; Wilson et al., 2018), but this understanding remains incomplete. Additional treatment options considered for LLT include taping, manual therapy, shockwave therapy and acupuncture. Furthermore, most knowledge regarding conservative management is for persistent LLT, with less known about conservative management of acute LLT. Sub-optimal management of acute LLT is detrimental in many regards, not least the likely conversion to persistent symptoms as demonstrated in Achilles tendinopathy (AT) (Lagas et al., 2020). The aim of this systematic review was to synthesise existing literature on conservative management of acute LLTs; in doing so this review should assist clinicians in making treatment choices and prompt researchers towards future areas of investigation.

MATERIALS AND METHODS

A systematic review was undertaken following a predetermined protocol compliant with the preferred reporting items of review (PRISMA) statement (Moher et al., 2015). The study protocol was prospectively registered and published with PROSPERO (ID: CRD42018117882).

Data Sources and Search Strategy

An electronic search of MEDLINE, CINAHL and EMBASE was undertaken from their inception to January 2020 with search terms developed using PICO (Moher et al., 2015). Searches 1 and 2 were limited to title due to their specific terms, whereas search 3 was limited to full text due to their generic concepts (Table 2). The electronic search was complimented with hand searching of the reference lists of papers identified through full text, with four papers identified. Citation searching of the papers identified was completed and content experts were contacted via e-mail to optimise inclusion of published articles missed in in the preceding search. Two review authors (KM and GS) independently screened studies, firstly by title and abstract, and then by full text for eligibility. Disagreements between reviewers were resolved by discussion and if required, by mediation from a third reviewer (AM) in order to achieve consensus.

Eligibility Criteria

Population

In alignment with our operating definition of acute tendinopathy, studies that included participants with symptom duration greater than three months were excluded (Cook & Purdam, 2009; Rowe et al., 2012). The review included participants over the age of sixteen (Malliaras et al., 2015) with a diagnosis of gluteal tendinopathy (GT), proximal hamstring tendinopathy (PHT), adductor tendinopathy, iliotibial band syndrome (ITBS), patellar

tendinopathy (PT), Achilles tendinopathy or plantar fasciopathy (PF). Diagnosis needed to be made by clinical assessment with the minimum diagnostic criteria being pain provoked by loading of the tendon with preserved range of motion (Cook, Rio, Purdam, & Docking, 2016; Malliaras et al., 2013; Rowe et al., 2012; Visnes & Bahr, 2007). Studies investigating surgical or injection procedures were excluded.

Outcome Measures

Any self-reported measures associated with pain intensity or disability were included. Studies that used no self-reported measures were excluded.

Study Design

To maximise the return from the search, studies were eligible for inclusion if they were randomised controlled trials (RCTs), non-randomised controlled trials (non-RCTs), case-control studies, case-series studies or case studies examining the effect of conservative management of acute tendinopathy. Narrative reviews, editorials or other opinion-based publications were excluded (Malliaras et al., 2013; Mallows, Debenham, Walker, & Littlewood, 2016).

Language

Only studies published in the English language were included.

Risk of Bias

Risk of bias assessment of the included studies was undertaken by two review authors (KM and GS) using the Cochrane Risk of Bias (RoB) 2.0 tool and the Risk of Bias In Non-Randomised Studies of Intervention (ROBINS-I) assessment tool (Higgins et al., 2011; Sterne et al., 2016). If disagreement arose between authors, a third author (AM) was consulted. In regard to the RoB 2.0 tool, studies were assessed based on the following domains: 1) sequence generation, 2) allocation concealment, 3) blinding, 4) incomplete outcome data, 5) selective outcome reporting, and 6) other sources of bias. Studies

assessed via the ROBINS-I assessment tool were evaluated against the following domains; 1) bias due to confounding, 2) bias in selection of participants, 3) bias in classification of interventions, 4) bias due to deviations from intended interventions, 4) bias due to missing data, 5) bias in measurement of outcomes, and 6) bias in selection of the reported result.

Data Extraction

All data was extracted independently by two reviewers (KM and GS) using a pre-determined data extraction form. Data included study design, participant characteristics, sample size, intervention, duration of symptoms, baseline and follow up data at each timepoint for outcomes of interest, within group comparison(s), between group comparison(s), conclusion, and limitations. There were no discrepancies and hence, no disagreement between reviewers.

Data Synthesis

There was considerable heterogeneity regarding study design, populations and measures used within the included studies. Therefore, a qualitative synthesis was employed to report these data, completed using an analytic technique based on developing key concepts from the studies and then translating findings from one study into another (Walsh & Downe, 2005). Themes were progressively more refined until a consensus was reached as to core themes which were discussed alongside quantitative data. Qualitative synthesis was informed by the risk of bias assessment, and the assessment of the overall certainty of findings.

Primary outcomes were presented as mean and standard deviation at the time points of interest. Rate of improvement for pain intensity and disability per intervention were reported by measuring the treatment effect, the within-group change from baseline, as completed in previous LLT review (Murphy et al., 2018). The treatment effect was compared against the minimally clinical important differences (MCID) for the appropriate outcome measure. To understand how the interventions impacted the duration of reported symptoms, results were

split into three time points: short term (<4 weeks), medium-term (4-12 weeks) and long-term (>12 weeks). Within-group effect sizes were reported for each study at each of the time points of interest. Between-group effect sizes were reported when statistically significant differences were reported in the study.

Assessment of the Overall Certainty of Findings

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach involves making an overall judgement of the certainty of the body of evidence based on the overall risk of bias, consistency of results, directness of the evidence and publication bias (Guyatt et al., 2009). GRADE was calculated for the above time points and completed by authors AM and PM.

RESULTS

Study Selection

Figure 1 represents the results of the study identification process. Once additional records were identified and duplicates removed, 2502 articles were identified. After title and abstract screening, 63 articles were considered for full text review. Finally, after applying the inclusion and exclusion criteria of this review, 16 articles were included for risk of bias assessment.

Study Characteristics

Of the 16 included studies (Table 3), six studies assessed PT; four trials were RCTs (da Cunha, Dias, Santos, & Lopes, 2012; Rio et al., 2017a; Wilson, Sevier, Helfst, Honing, & Thomann, 2000; Young, Cook, Purdam, Kiss, & Alfredson, 2005), one was a randomised cross-over study (Rio et al., 2015), and the final trial was a case series (Rio, Purdam, Girdwood, & Cook, 2017b). Five studies assessed PF utilising an RCT design (Ghafoor, Ahmad, & Gondal, 2016; Hyland, Lichtman, Webber-Gaffney, & Cohen, 2006; Ordahan, Turkoglu, Karahan, & Akkurt, 2017; Rahbar et al., 2018; Rompe, Cacchio, Furia, Weil, & Maffulli, 2010). Four studies assessed AT; two were RCTs (Kishmishian, Richards, & Selfe, 2019; Tumilty, Baxter, McDonough, & Hurley, 2012), one was a case study (Mccormack, 2012) and the final one was a case series (Maquirriain & Kokalj, 2014). One observational cohort study assessed ITBS (Beers, Ryan, Kasubuchi, Fraser, & Taunton, 2008) and no studies were identified for PHT or GT. Study characteristics are described in Table 6. Studies included a total of 534 participants, all of whom were recruited from the general population other than those in the Rio *et al* (2017a), Rio *et al* (2017b), Rio *et al* (2015), and Young *et al* (2005)(Young et al., 2005) studies, who recruited jumping athletes. Two studies

stated the mean duration of the intervention groups, 3.6 weeks, 3.9 weeks (Rompe et al., 2010) and 6 weeks (Mccormack, 2012). Two studies inclusion criteria for symptom duration were 1-3 months (Rahbar et al., 2018) and less than two weeks (Maquirriain & Kokalj, 2014). Four studies included participants within an athletic season (Rio et al., 2015, 2017a, 2017b; Young et al., 2005). 8 studies did not state the mean duration of symptoms per intervention group (Beers et al., 2008; da Cunha et al., 2012; Ghafoor et al., 2016; Hyland et al., 2006; Kishmishian et al., 2019; Ordahan et al., 2017; Tumilty et al., 2012; Wilson et al., 2000).

Intervention

Several different conservative interventions were identified. Nine examined exercise (isotonic, isometric, eccentric, and stretching) (Beers et al., 2008; da Cunha et al., 2012; Hyland et al., 2006; Mccormack, 2012; Rio et al., 2015, 2017a, 2017b; Rompe et al., 2010; Wilson et al., 2000; Young et al., 2005), five examined a form of electrotherapy (extracorporeal shockwave therapy (ESWT), radial shockwave therapy (RSWT), low level laser therapy, and placebo low level laser therapy) (Ghafoor et al., 2016; Ordahan et al., 2017; Rahbar et al., 2018; Rompe et al., 2010; Tumilty et al., 2012), three examined manual therapy (mobilisation, and ASTYM) (Ghafoor et al., 2016; McCormack, 2012; Wilson et al., 2000), three examined dry needling or acupuncture (Ghafoor et al., 2016; Kishmishian et al., 2019; Rahbar et al., 2018) two examined taping (Hyland et al., 2006; Ordahan et al., 2017) and one examined NSAIDs (Maquirriain & Kokalj, 2014).

<u>Risk of Bias in Included Studies</u>

The risk of bias of included studies is summarised in Figure 2 and Table 4 for the 11 RCTs, and the 5 non-RCTs, respectively. Seven RCTs were assigned “high risk”, three RCTs were assigned “some concerns” and one RCT was assigned “low risk”. Five non-RCTs were assessed by the ROBINS-I tool. Three studies were assigned “low risk”, one study assigned “moderate risk”, and one study assigned “critical risk”.

Quality of the Body of Evidence

The quality of the body of evidence was assessed as per the GRADE approach. There was very low level of certainty for the effectiveness of interventions at short-term, medium-term, and long-term follow ups (Table 5).

Rate of Improvement

Pain Intensity

Five studies presented raw data for improvement in pain intensity (Figure 3) (Ghafoor et al., 2016; Hyland et al., 2006; Kishmishian et al., 2019; Ordahan et al., 2017; Rahbar et al., 2018). Given that the Minimum Clinically Important Difference (MCID) for Numerical Pain Rating Scale (NPRS) and Visual Analogue Scale (VAS) are 2 (Michener, Snyder, & Leggin, 2011) and 1.4 (Tashjian, Deloach, Porucznik, & Powell, 2009), respectively, four interventions (stretching (Hyland et al., 2006), shockwave therapy (Ordahan et al., 2017; Rahbar et al., 2018), taping (Hyland et al., 2006; Ordahan et al., 2017), and dry needling (Rahbar et al., 2018) achieved the required MCID at the short-term follow up for PF and three interventions: shockwave therapy (Ordahan et al., 2017; Rahbar et al., 2018), taping (Hyland et al., 2006; Ordahan et al., 2017), and dry needling (Rahbar et al., 2018) achieved the required MCID at medium-term follow up for PF.

Two interventions: non-steroidal anti-inflammatory drugs (NSAIDs) (Maquirriain & Kokalj, 2014) & acupuncture (Kishmishian et al., 2019) achieved the required MCID at the short-term follow up for AT. Two interventions: manual therapy (Ghafoor et al., 2016) & acupuncture (Kishmishian et al., 2019) achieved the MCID at the medium-term follow up.

Disability

From the AT population, enough data existed to present rate of improvement for disability (Figure 4). All four interventions: acupuncture (Kishmishian et al., 2019), sham acupuncture (Kishmishian et al., 2019), low level laser therapy (Tumilty et al., 2012) and placebo low level

laser therapy (Tumilty et al., 2012) improved disability within 4-weeks (as measured by the Victorian Institute of Sport Assessment-Achilles Questionnaire (VISA-A)), after which improvements plateaued (MCID for VISA-A is 16 points (Macdermid & Silbernagel, 2015)). Two interventions: low level laser therapy (Tumilty et al., 2012) & placebo low level laser therapy (Tumilty et al., 2012) achieved the MCID at short-term, medium-term and long-term follow ups. One intervention, acupuncture (Kishmishian et al., 2019) achieved the MCID at short-term and medium-term follow up.

Data Synthesis

The extracted data for the domains of pain intensity and disability have been presented in Tables 6, 7 and 8 for short-term (<4 weeks), medium-term (4-12 weeks), and long-term (>12 weeks) follow-up, respectively. Cohen's *d* and magnitude of effect size are presented for statistically significant results unless specified.

Short-term Follow Up (<4 weeks)

Eight studies (five RCTs (Hyland et al., 2006; Kishmishian et al., 2019; Rahbar et al., 2018; Rio et al., 2017a; Tumilty et al., 2012), two observational studies (Maquirriain & Kokalj, 2014; Rio et al., 2017b) and one randomised cross-over trial (Rio et al., 2015)) provide very low certainty for the effect of conservative management within four weeks. In the context of this low certainty, four interventions: stretching (Hyland et al., 2006), taping (Hyland et al., 2006), shockwave therapy (Rahbar et al., 2018), and dry needling (Rahbar et al., 2018) demonstrated large effect for reducing pain intensity in PF within 4 weeks (Table 7). Two interventions: shockwave therapy (Rahbar et al., 2018) & dry needling (Rahbar et al., 2018)) demonstrated large effect for improving disability in PF. Two interventions: NSAID (Maquirriain & Kokalj, 2014) & acupuncture (Kishmishian et al., 2019) demonstrated large effect for reducing pain in AT and 1 intervention, acupuncture (Kishmishian et al., 2019) demonstrated large effect for improving disability in AT. One intervention, isometric exercise

(Rio et al., 2017a)) demonstrated large effect for reducing pain and improving disability in PT.

There was large effect for reducing pain between stretching and control group in PF in favour of the stretching group (Hyland et al., 2006). There was large effect for reducing pain between calcaneal taping and sham taping in PF in favour of the calcaneal taping group (Hyland et al., 2006). Large effect for reducing pain was demonstrated between NSAIDs and control group in favour of NSAIDs in AT (Maquirriain & Kokalj, 2014). There was medium effect for improving disability between low level laser therapy and placebo low level laser therapy in favour of placebo for AT (Tumilty et al., 2012). Two studies demonstrated large effect for reducing pain between isometric and isotonic exercises in favour of isometric exercises in PT (Rio et al., 2015, 2017b).

Medium-term Follow Up (4-12 weeks)

Eleven studies; nine RCTs (da Cunha et al., 2012; Ghafoor et al., 2016; Kishmishian et al., 2019; Ordahan et al., 2017; Rahbar et al., 2018; Rompe et al., 2010; Tumilty et al., 2012; Wilson et al., 2000; Young et al., 2005), one observational study (Beers et al., 2008) and one case study (Mccormack, 2012) provide a very low certainty for the effect of conservative management at medium-term follow up.

In the context of this very low certainty, four interventions: shockwave therapy (Ordahan et al., 2017; Rahbar et al., 2018), taping (Ordahan et al., 2017), manual therapy (Ghafoor et al., 2016) and, dry needling (Rahbar et al., 2018) demonstrated large effect for reducing pain intensity in PF and three interventions: shockwave therapy (Rahbar et al., 2018), manual therapy (Ghafoor et al., 2016), and dry needling (Rahbar et al., 2018) demonstrated large effect for improving disability in PF. One intervention, acupuncture (Kishmishian et al., 2019)) demonstrated large effect for reducing pain intensity in AT, two interventions : low level laser therapy & placebo low level laser therapy (Tumilty et al., 2012) demonstrated

large effect for improving disability in AT and one intervention, isotonic exercise (Beers et al., 2008)) demonstrated large effect for reducing pain intensity in ITBS (Table 8).

One study demonstrated medium effect size for reducing pain intensity and improving disability in favour of dry needling compared to ESWT in PF (Rahbar et al., 2018). One study demonstrated medium effect size for reducing pain intensity and small effect for improving disability in favour of acupuncture compared to sham acupuncture in AT (Kishmishian et al., 2019).

Long-term Follow Up (>12 weeks)

Two RCTs provide very low certainty for the effect of conservative management at long-term follow up. In the context of this very low certainty, two interventions: low level laser therapy & placebo low level laser therapy (Tumilty et al., 2012) demonstrated large effect for reducing pain intensity and improving disability in AT (Table 9). There was no statistically significant difference between any interventions.

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DISCUSSION

The aim of this systematic review was to explore and evaluate conservative management for acute LLT and is the first review of its kind. Overall, there was significant heterogeneity and very low certainty for the effectiveness of conservative management for acute lower limb 340 tendinopathies. Whilst this review does identify data indicating several conservative interventions that demonstrated efficacy, the low level of certainty of these findings indicates that clinicians should consider these interventions with tempered enthusiasm.

There was paucity of high-quality studies investigating effect of conservative management on acute LLTs; 6 studies for PT, 5 for PF, 4 for AT and 1 for ITBS, with no studies found for 345 acute GT or PHT. Further high quality studies, adhering to ICON standards (Rio et al., 2019; Scott et al., 2020; Vicenzino et al., 2020) that assess the effectiveness of conservative interventions are required. Furthermore, based on the literature for similar musculoskeletal disorders (e.g. non-specific low back pain, patellofemoral pain) and persistent LLT, we would value the inclusion of a *"wait-and-see"* approach in these methodologies. Finally, we note 350 that no study used education as an intervention, no outcomes for psychological factors were recorded, and little consideration of cognitive and contextual factors have been made. (Mallows et al., 2016). Given the relevance of these issues to acute and persistent musculoskeletal conditions (Chester, Jerosch-Herold, Lewis, & Shepstone, 2016; Cotchett et

al., 2020; Turner, Malliaras, Goulis, & Mc Auliffe, 2020), there is a clear knowledge-gap in this space for LLT and insights here are likely to have a favourable impact for reducing conversion to persistency from acute LLT.

A variety of interventions achieved the MCID for reducing pain (Figure 2) at the short term follow up for PF and AT and the rate of improvement did not seem to alter depending on whether the intervention was passive or active. Similar response was noted for rate of improvement in disability for AT, with three interventions (low level laser therapy, placebo low level laser therapy & acupuncture) all achieving the MCID at short-term and medium term follow ups. The finding that placebo low level laser therapy performed equally with the experimental groups suggests the benefit from treatment may lay beyond the intended mechanism of the intervention itself. Such uncertainty of effect has been highlighted previously. For instance, in persistent AT, the proposed intention of loading programmes are to address tendon material or mechanical properties, or to correct muscle impairments, yet clinically significant improvements are seen in timeframes inconsistent with these mechanisms (Murphy et al., 2018). It is therefore feasible that improvement in pain and disability within this timeframe may be better explained by factors outside the musculoskeletal system (Bialosky, Bishop, Price, Robinson, & George, 2009).

In the medium and long term, there were a range of interventions demonstrating large effect for reducing pain intensity and improving disability in PF, AT, and ITBS. However, due to the study designs, these large effect sizes may reflect contributions from other confounding factors, such as contextual factors (e.g. patient expectations and beliefs), regression to the mean (Morton & Torgerson, 2003) , spontaneous recovery and the Hawthorne effect (Caneiro, Bunzli, & O'Sullivan, 2020).

A notable intervention absent in the literature is the 'wait-and-see' approach which can control for some of these non-specific effects. Given this absence, we cannot exclude the possibility that the specific type of intervention for acute lower limb tendinopathy is less of a concern, but rather that the named intervention is superior to no intervention at all. This

concept is currently recommended in other acute musculoskeletal conditions, (Crossley et al., 2016; Foster et al., 2018), and is not unprecedented in the tendinopathy literature (Van Der Vlist et al., 2020). However, the outcome of a "*wait-and-*see" approach for acute LLT is uncertain as no studies in this systematic review included this as an intervention.

Clinical Implications and Future Direction

This review found very low certainty for conservative management for acute lower limb tendinopathies, with a large degree of imprecision, inconsistency, indirectness, and high risk of bias being observed at all three time points. Likewise, whilst most interventions had a large effect on pain intensity and disability over a short and medium-term timeframe, only one study assessed both outcomes over a long-term follow up (Tumilty et al., 2012). We speculate that several contextual factors may have influenced these results, and suggest that clinically, the choice of intervention may be less important than the shared-decision making itself to determine which intervention is meaningful to the patient. This process may play a more important role in optimising outcomes.

Strengths and Limitations

This review is the first of its kind to evaluate conservative management for acute LLTs and is relevant to a wide range of conditions. As access to healthcare services increases globally, clinicians are seeing more patients with acute LLT. This review provides these clinicians with an overview on the current evidence regarding conservative management to manage acute LLT and contribute to preventing the conversion to persistency. These findings are robust given the adherence to PRISMA guidelines.

This review highlights several limitations of the evidence base in its entirety. Firstly, very low level of certainty was found at all 3 time points for the different LLTs with only 1 RCT considered "low risk". Given the number of serious methodological issues seen in other studies, this decreased the confidence of the conclusion that can be drawn from those "high risk" studies. Secondly, there was considerable heterogeneity present in the included

studies, particularly regarding the type of intervention, duration of intervention, outcome measured, and length of follow up limiting our ability to meta-analyse and make stronger recommendations (Mc Auliffe, Whiteley, Malliaras, & O'Sullivan, 2019). Thirdly, not all studies gave raw data for their outcomes which reduced the number of studies that could be analysed for effect sizes and rate of improvement. Fourthly, language was restricted to English language, however the research examining this bias is conflicting (Higgins et al., 2019). Finally, we acknowledge that the GRADE approach puts RCT's at an advantage regarding the certainty of the evidence and as several studies were non-randomised trials, this may have reduced the effectiveness of the GRADE approach.

CONCLUSION

This review demonstrates that limited evidence currently exists to guide the management of acute lower limb tendinopathy, and the quality of the existing evidence is collectively low. In the context of this evidence base, this review also demonstrates that a large effect in pain intensity and disability in acute lower limb tendinopathies such as PF, PT, AT & ITBS can be gained via a range of interventions at short and medium-term follow ups. Clinicians should apply these findings in the context of evidence-based practice, informing the discussion of different treatment options with patients in a shared decision-making process. Further research to investigate the effect of "*wait-and-see*" approach is needed as well as understanding beliefs and expectations from people with acute lower limb tendinopathies.

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440 REFERENCE LIST

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TABLES

Table 1 Lower limb tendinopathy diagnostic criteria, prevalence rate and incidence rate

685 *Table 2 Search terms used for database searches*

Search Term			
Tendinopathy	**Diagnostic Criteria**	**PR**	**IR**
Adductor related tendinopathy (ART)	Pain in groin during hip adduction against resistance	1.22	1.13
Gluteal tendinopathy (GT)	Insidious onset of pain and tenderness primarily at the greater trochanter	4.22	3.29
Proximal hamstring tendinopathy (PHT)	Lower gluteal pain reproduced by placing proximal hamstring tendons under compressive and tensile load	N/A	N/A
Patellar tendinopathy (PT)	Pain localised on inferior pole of the patellar & load related pain with demand on knee extensors	1.6	1.6
Achilles tendinopathy (AT)	Mid-portion Achilles tendinopathy; pain and tenderness 2-7cm from insertion onto the calcaneus with diffused or localised swelling	2.35	2.16
Plantar fasciopathy (PF)	Pain located at the anteromedial aspect of the plantar heel during weight bearing	2.44	2.34

IR incidence rate per 1000 person-years; PR, prevalence rate per 1000 person-years (Albers, Zwerver, Diercks, Dekker, & Van den Akker-Scheek, 2016; Goom, Malliaras, Reiman, & Purdam, 2016; Grimaldi et al., 2015; Malliaras et al., 2015; Riel et al., 2017; van Dijk, van Sterkenburg, Wiegerinck, Karlsson, & Maffulli, 2011)

S1	("Greater trochanteric pain syndrome" OR "Trochanteric bursitis" OR "Lateral hip pain" OR "Lateral hip tendin*" OR "Lateral hip tendon*" OR "Glut* tend?n*" OR "Glut* min* tend*" OR "Glut* med* tend*" OR "HIP and bursitis" OR "Iliotibial band" OR "Achilles tend?n*" OR "Tendo achilles" OR "patella* tend?n*" OR "jumper* knee" OR "hamstring tend*" OR "Plantar fasci*" OR "Plantar heel")	Title (TI)
AND		
S2	"Ultrasound" OR "Therapeutic ultrasound" OR "Podiatry" OR "Orthotics" OR "Insoles" OR "Strengthening" OR "Stretching" OR "Eccentric exercise" OR "Concentric exercise" OR "Isometric exercise" OR "Ice" OR "Myofascial release" OR "Soft tissue release" OR "Deep tissue massage" OR "Joint mobilisation" OR "Walking aids" OR "Manual therapy" OR "Pulsed SWD" OR "Pulsed shortwave diathermy" OR "Megapulse" OR "Pulsed electromagnetic energy" OR "Acupuncture" OR "Hydrotherapy" OR "Shockwave" OR "Extracorporeal shockwave therapy" OR "ESWT" OR "Injection" OR "Corticosteroid injection" OR "Steroid injection" OR "NSAID" OR "Drug therapy" OR "Pain relief" OR "Pain control" OR "Non-steroidal anti-inflammatory drugs" OR "Rest" OR "Weight loss" OR "Analgesia" OR "PRP injections" OR "'Platelet rich plasma injections" OR "Autologous blood injections"	Title (TI)

Table 3 Study Design per lower limb tendinopathy

	Total	RCT	Cross-Over	Observational Cohort	Case Series
PT	6	4	1	-	1
PF	5	5	-	-	-
AT	4	2	-	-	1
ITBS	1	-	-	1	-

GT	0	-	-	-	-
PHT	0	-	-	-	-

690 *Table 4 Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I)*

Studies	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall
Rio 2015	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Beers 2008	Moderate Risk	Moderate Risk	Moderate Risk	Low Risk	Low Risk	Moderate Risk	Low Risk	Moderate Risk
Maquirriain 2014	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
McCormack 2012	Serious Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Moderate Risk	Critical Risk
Rio 2017b	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk

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Table 5. Level of certainty of interventions across three time points, with Grading of Recommendations Assessment, Development and Evaluation

Outcome by time point	No. of studies	Types of studies	No. of participants	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Level of certainty
Less than 4 weeks	8-studies	5 x randomised control trials 2 x observational studies 1 x randomised cross-over trial	254	Serious (-1)	Serious (-1)	Serious (-1)	Serious (-1)	Undetected	*Very low
4-12 weeks	11-studies	9 x randomised control trials 1 x observational study 1 x case study	414	Serious (-1)	Serious (-1)	Serious (-1)	Serious (-1)	Undetected	**Very low
Longer than 12 weeks	2- studies	2 x randomised control trials	159	Serious (-1)	No	Serious (-1)	No	Undetected	***Very low

**, **, ***Downgraded once for risk of bias, once for inconsistency of results, once for imprecision (small sample size or wide confidence intervals) and once for indirectness (interventions delivered over very short period of time or more frequently than expected)*

700 *Table 6 Study Characteristics*

First Author	No of participants	Intervention	Gender	Mean age (years)	Diagnosis	Duration of symptoms	BMI	Outcome measure: Patient rating of condition	Outcome measure: Pain on activity/loading	Outcome measure: Physical function capacity	Outcome measure: Quality of Life	Outcome measure: Pain over specified timeframe	Outcome measure: Disability	Outcome measure: Function	Data collection: Timelines	Study design
Rahbar et al. 2018 (Rahbar et al., 2018)	72	DN Versus ESW	DN = 10 M, 26 F ESWT = 28 F 8 M	DN = 45.08±9.61 (SD) ESWT = 43.22±9.20 (SD)	PF	> 1 month	DN = 25.10±1.84 (SD) ESWT = 27.62±2.43 (SD)	N/A	N/A	N/A	FFI	Pain Intensity (VAS)	FFI	N/A	(T1) at baseline (T2) at 4-weeks (T3) at 8-weeks	Single-blind, RCT
Rompe et al. 2010 (Rompe et al., 2010)	102	PFSS Versus RSWT	PFSS = 18 M, 36 F RSWT = 18 M, 30 F	PFSS = 53.1 (27-70) RSWT = 49.8 (29-68)	PF	PFSS = mean 3.9 weeks (range 2-6) RSWT = mean 3.6 weeks (range 2-6)	PFSS = 27.2 (20-32) RSWT = 28.3 (22-33)	N/A	N/A	N/A	FFI	N/A	FFI	Patient-Relevant Outcme Measures	(T1) at baseline (T2) at 2-months (T3) at 4-months (T4) at 15-months	Single-blind, RCT
Kishmishian et al. 2019 (Kishmishian et al., 2019)	22	Acupuncture Versus Sham Acupuncture	N/A	N/A	AT	Not Stated	N/A	Global Rating of Change	N/A	N/A	EQ5-D	Pain Intensity (NPRS)	VISA-A	N/A	(T1) baseline (T2) at 2-weeks (T3) at 4-weeks (T4) at 12-weeks	Single-blind, RCT
Young et al. 2005 (Young et al., 2005)	17	EDS Versus TES	13 M, 4 F	27.3±1.8 (SD)	PT	Within Season	N/A	N/A	Pain Intensity during single-leg decline squat (VAS)	N/A	N/A	N/A	VISA- P	N/A	(T1) baseline (T2) at 12-weeks (T3) at 12-months	Single-blind, RCT
da Cunha et al. 2012 (da Cunha et al., 2012)	14	PG Versus WP	PG = 8 M, 2 F WP = 6 M, 1 F	PG = 24.1±8.3 WP = 26±5.9	PT	Not Stated	N/A	N/A	N/A	N/A	N/A	Pain Intensity (VAS)	VISA-P	N/A	(T1) baseline (T2) at 8-weeks (T3) at 12 weeks	Double-blind, RCT
Rio et al. 2015 (Ebonie Rio et al., 2015)	6	Isometric Versus Isotonic	6 M	26.9 (18-40)	PT	Within Season	N/A	N/A	Pain intensity during single-leg decline squat (VAS)	N/A	N/A	N/A	VISA-P	N/A	(T1) baseline (T2) Immediate (T3) at 45 mins	Single-blind, Randomised Cross-over study
Rio et al. 2017a (Ebonie Rio et al., 2017)	20	Isometric Versus Isotonic	Isometric = 9 M, 1 F Isotonic = 9 M, 1 F	N/A	PT	Within Season	Isometric = 29.5±9.59 Isotonic = 29.5±9.88	N/A	Pain intensity during single-leg decline squat (VAS)	N/A	N/A	N/A	VISA-P	N/A	(T1) baseline (T2) at 4-weeks	Single-blind, RCT

Rio et al. 2017b (E Rio et al., 2017)	25	Isometric	19 M, 6 F	N/A	PT	Within Season	23.04	N/A	Pain intensity during single-leg decline squat (VAS)	N/A	N/A	N/A	VISA-P	N/A	(T1) baseline (T2) at 1-week (T3) at 2-weeks (T4) at 4-weeks	Case Series
Beers et al. 2008 (Beers et al., 2008)	16	Isotonic	5 M, 11 F	33.7±10.2	ITBS	Not Stated	22.9±2.7	N/A	N/A	Hip Abductor Moments (Dynamometer)	Allan McGavin Health Status Index	Pain Intensity (NRS)	N/A	N/A	(T1) baseline (T2) at 2-weeks (T3) at 4-weeks (T4) at 6-weeks	Cohort Study
Hyland et al. 2006 (Hyland et al., 2006)	41	Taping Versus Stretching Versus Sham Taping Versus Control	Taping = 5 M, 6 F Stretching = 8 M, 2 F Sham Taping = 5 M, 5 F Control = 3 M, 7 F	Taping = 45.5±12.0 Stretching = 34.1±5.9 Sham Taping = 40.4±9.4 Control = 37.6±10.1	PF	Not Stated	Taping = 24.8±4.4 Stretching = 26.3±3.8 Sham Taping = 23.6±1.7 Control = 25.4±4.3	N/A	N/A	N/A	N/A	Pain Intensity (VAS)	N/A	Patient Specific Functional Scale	(T1) baseline (T2) at 3-4 days (T3) at 7 days	Single-blind, RCT
Maquirriain et al. 2014 (Maquirriain & Kokalj, 2014)	28	NSAID	28 M	39.17±10.31	AT	<2 weeks. Mean duration not stated	N/A	N/A	N/A	Leg Stiffness	N/A	Pain Intensity (VAS)	VISA-A	N/A	(T1) baseline (T2) at 8 days	Case Series
Tumilty et al. 2012 (Tumilty et al., 2012)t	40	LLLT Versus Placebo	LLLT = 8 M, 12 F Placebo = 10 M, 10 M	LLLT = 45.6±9.1 Placebo = 46.5±6.4	AT	Not Stated	N/A	N/A	N/A	N/A	N/A	Pain Intensity (NRS)	VISA-A	N/A	(T1) baseline (T2) at 4-weeks (T3) at 12-weeks (T4) at 52-weeks	Double-blind, RCT
Ghafoor et al. 2016 (Ghafoor et al., 2016)	30	MT Versus Ultrasound	MT = 4 M, 11 F Ultrasound = 5 M, 10 F	MT = 45.63±10.81 Ultrasound = 47.14±8.41	PF	Not Stated	MT = 29.76±2.20 Ultrasound = 32.10±1.74	N/A	N/A	N/A	N/A	Pain Intensity (NRS)	FAAM	N/A	(T1) baseline (T2) at 6-weeks	RCT
Ordahan et al. 2017 (Ordahan et al., 2017)	80	ESWT Versus KT	ESWT = 9 M, 28 F KT = 7 M, 26 F	ESWT = 47.8±12.4 KT = 47.7±9.8	PF	Not Stated	ESWT = 32.2±4.9 KT = 31.9±7.2	N/A	N/A	N/A	N/A	Pain Intensity (VAS)	FAOS	N/A	(T1) baseline (T2) at 5-weeks	Single-blind, RCT
Wilson et al. 2000 (Wilson et al., 2000)	20	ASTM Versus Traditional	ASTM = 5 M, 5 F Traditional = 6 M, 4 F	N/A	PT	Not Stated	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Patellofemoral Joint Evaluation Scale	(T1) baseline (T2) at 6-weels	Single-blind, RCT

McCormack 2012 (Mccormack, 2012)	1	ASTM & Eccentric Exercise	1 F	53	AT	6 weeks	N/A	Percentage of Improvement	N/A	N/A	LEFS	Pain Intensity (NRS)	N/A	LEFS	(T1) baseline (T2) at 5-weeks	Case Study

DN, Dry Needling; ESWT, Extracorporeal Shockwave Therapy; F, Female; FAAM, Foot and Ankle Ability Measure; FAOS, Foot and Ankle Outcome Score; FFI, Foot Functional Index; KT, Kinesio Taping; LEFS, Lower Extremity Functional Scale; LLLT, Low Level Laser Therapy; M, Male; MT, Manual Therapy; NRS, Numerical Rating Scale; PFSS, Plantar-Fascia Specific Stretching; PG, Pain Group; RSWT, Radial Shockwave Therapy; VISA-A, Victorian Institute of Sports Assessment- Achilles; VAS, Visual Analogue Scale; VISA-P, Victorian Institute of Sports Assessment- Patellar; WP, Without Pain

Table 7. Effect of Conservative Management on Pain Intensity and Disability in short-term follow up (<4 weeks)

Study	Body Part	Design	Outcome Measure	Follow Up	Intervention	Effect Size	Magnitude	Within Groups *p* value
Pain effect size for follow up ≤ 4 weeks								
Hyland 2006	Plantar Fascia	RCT	VAS (/10)	1 week	Stretching	2.26	Large	<0.001*
					Control	N/A	N/A	-
					Calcaneal Taping	3.09	Large	<0.001*
					Sham Taping	0.38	Small	0.037*
Rahbar 2018	Plantar Fascia	RCT	VAS (/10)	4 weeks	ESWT	1.37	Large	<0.001*
					Dry Needling	1.86	Large	<0.001*
Maquirriain 2014	Achilles	Observational	VAS (/100)	1 week	NSAID	1.29	Large	0.0008*
Tumilty 2012	Achilles	RCT	NPRS (/10)	4 weeks	Low Level Laser Therapy	-	-	Not Significant
					Placebo	0.86	Large	<0.05*
Kishmishian 2019	Achilles	RCT	NPRS (/10)	2 weeks	Acupuncture	0.91	Large	<0.001*
				4 weeks		1.52	Large	<0.001*
				2 weeks	Sham Acupuncture	N/A	N/A	Not Significant
				4 weeks		0.78	Medium	0.002*
Rio 2017a	Patellar	RCT	NPRS (/10)	4 weeks	Isometric	-	-	-
					Isotonic	-	-	-
Rio 2017b	Patellar	Observational	NPRS (/10)	4 weeks	Isometric	0.580†	Large	<0.001*
Rio 2015	Patellar	Randomised Cross-Over	NPRS (/10)	45 minutes	Isometric	4.64	Large	<0.001*
					Isotonic	0.67	Medium	Not Significant
Disability effect size for follow up ≤ 4 weeks								
Hyland 2006	Plantar Fascia	RCT	Patient Specific Functional Scale	1 week	Stretching	N/A	N/A	Not Significant
					Control	N/A	N/A	Not Significant
					Calcaneal Taping	N/A	N/A	Not Significant
					Sham Taping	N/A	N/A	Not Significant
Rahbar 2018	Plantar Fascia	RCT	Foot Function Index	4 weeks	ESWT	1.68	Large	<0.001*
					Dry Needling	1.52	Large	<0.001*
Tumilty 2012	Achilles	RCT	VISA-A	4 weeks	Low Level Laser Therapy	0.77	Medium	<0.05*
					Placebo	0.86	Large	<0.05*
Kishmishian 2019	Achilles	RCT	VISA-A	2 weeks	Acupuncture	0.89	Large	<0.002*
				4 weeks		1.66	Large	<0.001*
				2 weeks	Sham Acupuncture	N/A	N/A	Not Significant
				4 weeks		0.5	Medium	0.016*
Rio 2017b	Patellar	Observational	VISA-P	4 weeks	Isometric	0.568*	Large	<0.001*

**= P>0.05, † = Pearson R Correlation; Extracorporeal Shockwave Therapy; FFI, Foot Functional Index; NPRS, Numerical Pain Rating Scale; NSAID, Non-Steroidal Anti-Inflammatory Drug; VAS, Visual Analogue Scale; VISA-A, Victorian Institute of Sport Assessment – Achilles; VISA-P, Victorian Institute of Sport Assessment - Patellar*

Table 8. Effect of Conservative Management on Pain Intensity and Disability in medium-term follow up (4-12 weeks)

Study	Body Part	Design	Outcome Measure	Follow Up	Intervention	Effect Size	Magnitude	Within Groups *p* value
Pain effect size for follow up 4 < 12 weeks								
Ordahan 2017	Plantar Fascia	RCT	VAS (/100)	5 weeks	ESWT	1.77	Large	0.037*
					Kinesio Taping	1.76	Large	0.036*
Ghafoor 2016	Plantar Fascia	RCT	NPRS (/10)	6 weeks	Manual Therapy	1.93	Large	0.001*
					Ultrasound	N/A	N/A	0.169
Rompe 2010	Plantar Fascia	RCT	FFI Pain Subscale	8 weeks	Stretching	-	-	<0.001*
					RSWT	-	-	Not Significant
Rahbar 2018	Plantar Fascia	RCT	VAS (/10)	8 weeks	ESWT	1.89	Large	<0.001*
					Dry Needling	3	Large	<0.001*
Beers 2018	ITBS	Observational	NPRS (/5)	6 weeks	Isotonic	1.67	Large	-
Kishmishian 2019	Achilles	RCT	NPRS (/10)	12 weeks	Acupuncture	1.25	Large	0.003*
					Sham Acupuncture	0.14	Small	0.016*
Tumilty 2012	Achilles	RCT	NPRS (/10)	12 weeks	Low Level Laser Therapy	0.78	Medium	<0.05*
					Placebo	0.77	Medium	<0.05*
Disability effect size for follow up 4 < 12 weeks								
Ghafoor 2016	Plantar Fascia	RCT	Foot and Ankle Ability Measure	6 weeks	Manual Therapy	0.92	Large	0.001*
					Ultrasound	N/A	N/A	Not Significant
Rahbar 2018	Plantar Fascia	RCT	Foot Function Index	8 weeks	ESWT	2.63	Large	<0.001*
					Dry Needling	2.46	Large	<0.001*
Kishmishian 2019	Achilles	RCT	VISA-A	12 weeks	Acupuncture	1.53	Large	<0.001*
					Sham Acupuncture	0.54	Medium	0.002
Tumilty 2012	Achilles	RCT	VISA-A	12 weeks	Low Level Laser Therapy	0.89	Large	<0.05*
					Placebo	0.93	Large	<0.05*

**= P>0.05; ESWT, Extracorporeal Shockwave Therapy; FFI, Foot Functional Index; NPRS, Numerical Pain Rating Scale; RSWT, Radial Shockwave Therapy; VAS, Visual Analogue Scale; VISA-A, Victorian Institute of Sport Assessment - Achilles*

Table 9. Effect of Conservative Management on Pain Intensity and Disability in long-term follow up (> 12 weeks)

Study	Body Part	Design	Outcome Measure	Follow Up	Intervention	Effect Size	Magnitude	Within Groups *p* value
Pain effect size for follow up >12 weeks								
Tumilty 2012	Achilles	RCT	NPRS (/10)	52 weeks	Low Level Laser Therapy	0.74	Large	<0.05*
					Placebo	0.86	Large	<0.05*
Rompe 2010	Plantar Fascia	RCT	FFI Subscale (/70)	16 weeks	Stretching	-	-	<0.001*
				60 weeks		-	-	Not Significant
				16 weeks	RSWT	-	-	Not Significant
				60 weeks		-	-	Not Significant
Disability effect size for follow up >12 weeks								
Tumilty 2012	Achilles	RCT	VISA-A	52 weeks	Low Level Laser Therapy	0.87	Large	<0.05*
					Placebo	0.9	Large	<0.05*

*= P>0.05; NPRS, Numerical Pain Rating Scale; FFI, Foot Functional Index; RSWT, Radial Shockwave Therapy; VISA-A, Victorian Institute of Sports Assessment

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FIGURE LEGEND

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram of search strategy and study selection process

Figure 2. Risk of Bias 2.0 Assessment

Figure 3. Rate of Improvement for Pain Intensity

Figure 4. Rate of Improvement for Disability (Achilles tendinopathy only)

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