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Dates: Received: 12 January, 2016; Accepted: 06 February, 2016; Published: 08 February, 2016

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www.peertechz.com

ISSN: 2455-5487

Keywords: Shoulder; Rotator cuff; Tendinopathy; Laser therapy

Review Article

The Efficacy of Laser Therapy for Rotator Cuff Tendinopathy: A Systematic Review and Meta-Analysis

Abstract

Objective: To perform a systematic review and meta-analysis on the efficacy of laser therapy (LT) for rotator cuff (RC) tendinopathy in adults.

Methods: A literature search was conducted in four databases for randomized controlled trials (RCTs) published until May 2014, comparing the efficacy of LT to any other intervention. RCTs' characteristics were extracted using a standardized form and the risk of bias was evaluated using the Cochrane Risk of Bias tool. Data were summarized qualitatively or quantitatively (meta-analysis).

Results: Thirteen RCTs, with moderate mean methodological score (66.4%± 10.0), were included. It was concluded that LT may provide short-term pain relief of minimally significant clinical importance compared to placebo (sham LT), ultrasound therapy, or clinical recommendations alone. In terms of self-reported function and shoulder range of motion (ROM), evidence was inconclusive. When compared to an exercise program, LT was not deemed to have superior effects on pain, function or shoulder ROM. LT in conjunction with exercise was not superior to exercise alone with respect to pain, function and shoulder ROM.

Conclusion: Low to moderate grade evidence supports that LT may reduce pain in the short term in adults with RC tendinopathy, while its effects on function and ROM are not supported. Until more high quality evidence demonstrates clearly the efficacy of LT, clinicians should use LT cautiously and in the sole objective of alleviating pain in the short-term.

Introduction

Shoulder pain is one of the most common reasons for consultation in primary care [1] and its prevalence varies from 7 to 26% in the general population [2]. Rotator cuff (RC) tendinopathy accounts for 69% to 75% of shoulder pain cases [2]. RC tendinopathy is an inclusive term used to describe a pathology of the RC tendons [3], that encompasses other diagnostics such as impingement syndrome, subacromial bursitis, and long head of the biceps tendinopathy [4]. It can result in important functional limitations and in time away from work in workers populations [5]. The etiology of RC tendinopathy has been described as multifactorial and may be related to a combination of both intrinsic and extrinsic causes [6]. Intrinsic causes that contribute to rotator cuff tendon degeneration are related to alterations in its biology, mechanical properties, morphology and vascularity [6]. Extrinsic mechanisms that can contribute to the development of RC tendinopathy by reducing the subacromial space include anatomic variants of the acromion, alterations in scapular or humeral kinematics, postural abnormalities, deficits in the performance of rotator cuff and scapular muscles or decreased flexibility of shoulder soft tissue structures [6].

Multiple rehabilitations modalities exist to treat RC tendinopathy, such as exercise, manual therapy, or electrotherapy. For many of these interventions commonly used in clinics, evidence regarding their efficacy or the magnitude of treatment effects that may be expected is scarce [7]. Laser therapy (LT) is an electrotherapy modality that has been used for decades by physiotherapists despite scarce evidence regarding its efficacy. Based on indirect evidence from animal tendon studies, LT is believed to decrease inflammation, increase angiogenesis, increase fibroblast activity leading to increased collagen production, increase tensile strength and decrease pain [8,9]. A recent review of systematic reviews was published on the effectiveness of conservative interventions for adults with RC tendinopathy, including LT. The authors concluded that the evidence did not support the effectiveness of LT compared to other interventions [10]. However, this review did not include all the available evidence on the efficacy of LT modality in individuals suffering from RC tendinopathy and its conclusions were only qualitative as it was based on previous systematic reviews evaluating evidence published until 2008. Another systematic review on the efficacy of LT for all types of tendinopathies, that included 3 RCTs specific to RC tendinopathy was recently published and concluded

that conflicting evidence exists for the effectiveness of LT in the treatment of all type of tendinopathies; the authors did not make specific conclusions for RC tendinopathy [11]. According to the authors, LT can potentially be effective in terms of pain relief in treating tendinopathy when recommended dosages are used. In fact, one of their conclusions was that adequate recommended laser dosage was not always used in the included studies (low level LT: 8 joules for a wavelength of 780 to 820 nm and 4 joules for a wavelength of 904 nm are recommended) [11], possibly impeding therapeutic treatment effect. A Cochrane systematic review published in 2003 concluded that LT was effective in individuals suffering from shoulder adhesive capsulitis but not in a population suffering from RC tendinopathy [12]. Since the original publication, this review has not been updated. There is therefore a need to gather and to evaluate new evidence regarding the effectiveness of LT specifically for RC tendinopathy. The aim of the present study was to conduct a systematic review and meta-analysis on the effectiveness of LT to treat adults suffering from RC tendinopathy.

Methods

Literature search and study identification

Two evaluators conducted an electronic literature search on Pubmed, CINAHL, Embase and PEDro databases, using a combination of keywords and MESH terms (Figure 1). All databases

were searched from their date of inception to May 2014. Reference lists of all retrieved studies and previous reviews on the subject were searched for further relevant studies.

Data extraction and quality assessment

Study selection: The title and abstract of each article were reviewed by two evaluators to determine eligibility. Pair of raters then independently reviewed each article to determine whether it met the following inclusion criteria: 1-participants suffered from RC tendinopathy or other related diagnostics such as impingement syndrome, long head of the biceps tendinopathy or subacromial bursitis; 2-adult population (≥ 18 years old); 3-at least one of the intervention under study was LT either low level or high level; 4-study design was a randomized controlled trial (RCT); 5-The article was written in English or French. LT could be compared to any other therapeutic modality or to a placebo. The outcomes of interest included patient reported outcomes such as pain, function, health-related quality of life, as well as performance-based outcomes such as shoulder range of motion (ROM) and muscle strength; no studies were however excluded on the basis of specified outcomes measures. Studies that included participants with shoulder pain were eligible as long as it could be determined that the majority of the study participants were suffering from RC tendinopathy. Articles were excluded if they included participants with RC full thickness tear or

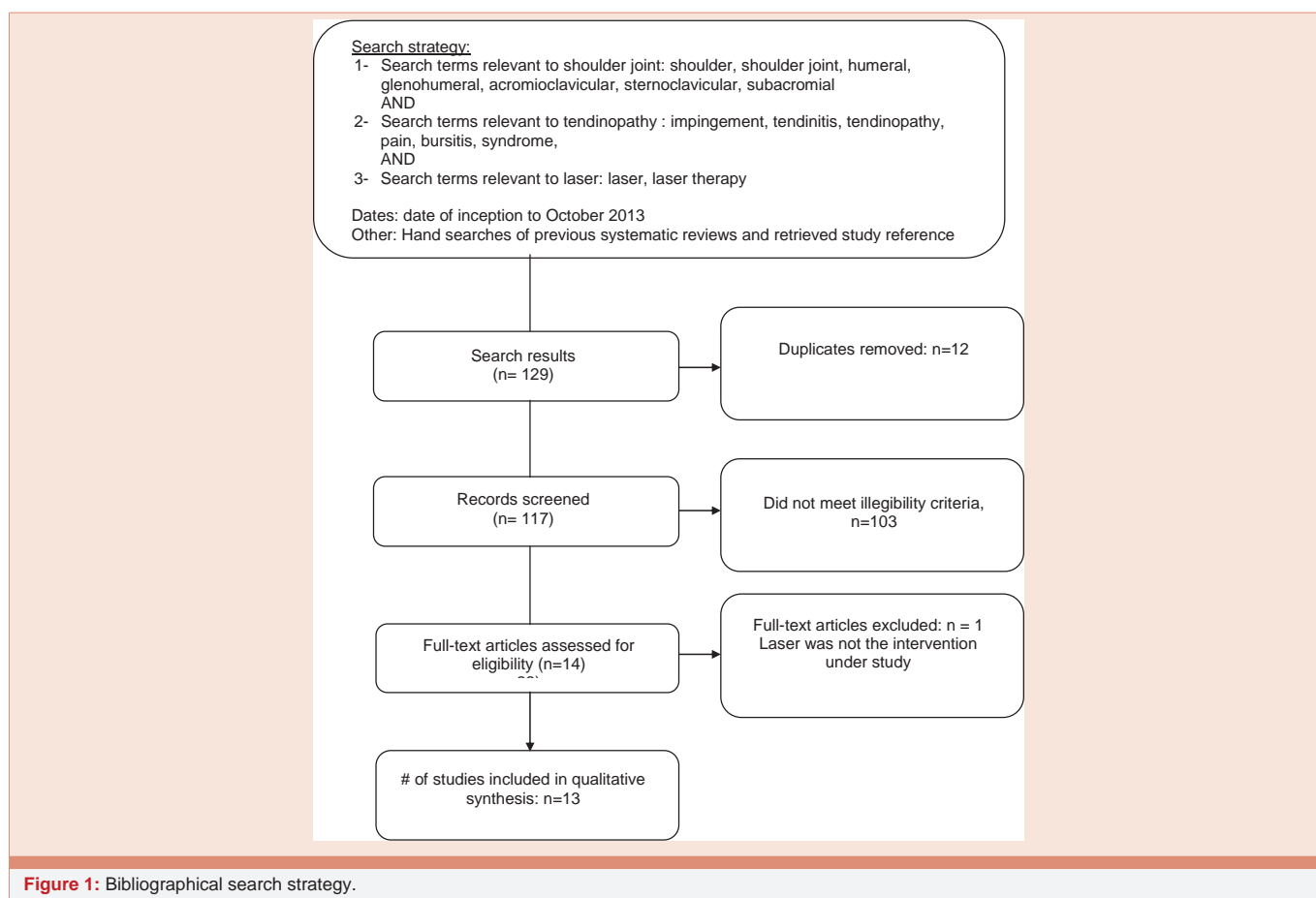


Figure 1: Bibliographical search strategy.

with postsurgical conditions.

Data extraction: Characteristics of the included studies were extracted by one evaluator using a standardized form. The relevant details for LT and control interventions including the LT parameters, type of control intervention, average number and frequency of treatment visits, and co-interventions were collected. The descriptive information for the patient population such as number of patients, country where the trial was conducted, age, and sex, occupation, and presence of comorbidities were also extracted. Finally, outcome data were collected for patient reported outcomes and performance-based outcomes (follow-up period and main results).

Risk of bias tool: The risk of bias of the included studies was appraised with the Cochrane risk of bias tool [13]. Six methodological domains were appraised separately: sequence generation, allocation concealment, blinding (participants, provider and assessor), incomplete outcome data, selective outcome data reporting, and other sources of bias. The assessment of each item was done regarding its risk of potential bias: “yes” indicated low risk of bias, “no” indicated high risk of bias, and “unclear” indicated an unclear or unknown risk of bias, based on the information provided in the paper [13]. For each methodological item, we assigned a score of 2 if a low risk of bias was present, a score of 1 if the risk of bias was unclear or unknown, and a score of 0 if a high risk of bias was found to be present and we calculated a total score (out of 16) to give an overview of the methodological quality and risk of bias of each included RCT.

Data analyses: After the independent evaluation of each study, pair of raters met to compare ratings and resolve disparities. A structured consensus approach was used that involved: 1-re-review of the manuscripts; 2- discussion of the adherence to standards; and 3- use of an independent third evaluator if consensus was not achieved. Pre-consensus inter-rater agreement on individual methodological items was calculated with weighted kappa and inter-rater reliability of the total methodological scores was assessed with an intra-class correlation coefficient (ICC). There was no formal mechanism to exclude studies on the basis of quality, but studies were rank ordered in terms of risk of bias and the risk of bias was considered in the recommendations/conclusions. The studies that used similar interventions, outcome measures and follow-up periods were identified, and results were pooled into meta-analyses. Analyses

were performed using Review Manager (version 5.2) of the Cochrane Collaboration [13]. Mean differences (MD) or standardized mean differences (SMD) with 95% confidence intervals (CIs) were calculated. To determine the degree of heterogeneity, testing was conducted using the I² measure. To pool data, we considered that a I²<60% was acceptable [14]. Because the overall number of studies included in the meta-analysis was small and true effect sizes varied between studies, random effect models were used. Funnel plots were not generated because of the small number of trials included for each analysis. Statistical significance was considered at p<0.05 [14]. When included studies could not be pooled, a qualitative review of the evidence was performed. Minimal clinically important difference was used to assess the clinical efficacy of the interventions of concerns in this review.

Results

Description and findings of included studies

The literature search led to the initial identification of 14 RCTs (Figure 1). One study was however excluded because LT was not the main treatment under study [15]. Therefore, 13 publications met the inclusion criteria and were included (Table 1).

All included studies compared the effectiveness of LT either alone or in combination with other modalities to various interventions such as oral non-steroidal anti-inflammatory drugs (NSAIDs), exercise, ultrasound, or a placebo. One study compared LT to a control group receiving only advice and to a group receiving ultrasonography [16], two studies compared LT to a placebo [17,18], five studies compared active LT and exercise to sham LT and exercise [19-23], one study compared LT to ultrasound [24], one study compared high intensity LT to ultrasound [25], two studies compared the added effect of LT to exercise [24,26], and two RCTs compared multiple rehabilitation modalities with or without LT as the main treatment under study [27,28].

Efficacy of laser therapy compared to placebo or control: One study (n=36) compared LT to advice (information on posture and shoulder movements to avoid) given by a health professional [16]. A greater proportion of participants reported pain relief (90%) in the LT group compared to the advice group (50%) and inter-group comparison reached statistical significance (p<0.01). Moreover, LT

Table 1: Characteristics of included studies.

First author, year of publication	Participants-Diagnostic-Mean age-Gender	Description of treatment	Number of participants	Follow-up period (days)	Outcomes measures	Main results	Risk of bias score (/16)
Laser therapy vs. placebo or control							
Saunders, 2003	Adults with supraspinatus tendinosis (>4 weeks) diagnosed with empty can test Mean age: 56.5 years Gender: Male: 19 Female: 17	Laser therapy (820 nm, 50 mW, 30J/cm ²) for 3 minutes, 3x/week for 3 weeks (Lt)	12	21	Proportion of participants experiencing pain reduction at the end of treatment	Lt: 90% Co: 50% Us: 58% Inter-group comparison: p<0.01	9
		Control Group (advice) (Co)	12		Pain and disability diary based on Oswestry low back pain questionnaire	Lt Vs. Co: p<0.05 in favour of Lt	
		Ultrasound (1.5 W/cm ² , 1 MHz for 6 minutes, 3x/week for 3 weeks (Us))	12			Us Vs. Co: p≥0.05	

England, et al., 1989	Adults with either supraspinatus or bicipital tendonitis lasting for at least 4 weeks Mean age: 48 years Gender: Male: 15 Female: 15	Laser therapy (904 nm, 3 mW, 4000 Hz) for 5 minutes 3 times a week for 2 weeks (Lt) Placebo-dummy laser (PI) Naproxen sodium 550 mg BID for 2 weeks (Na)	10 10 10	14	Difference in medians for overall pain assessed with a 10 cm VAS between Lt and Na groups at the end of treatment Difference between medians for self-perceived benefit assessed with a 10 cm VAS between Lt and PI: 1.pain 2.stiffness 3.function 4.movement Difference in medians in shoulder active range of motion(°) between Lt and PI groups for: 1.Flexion 2.Abduction 3.Extension	2.0 cm (95% CI 1.0 to 3.5) 1. 2.5 cm (95% CI 2.0 to 3.0) 2. 1.0 cm (95% CI 0 to 3.0) 3. 1.5 cm (95% CI -0.01 cm, to 3.9) 4. 2.0 cm (95% CI 1.0 to 4.0) 1. 10.0° (95% CI 0 to 20.0) 2. 15.0° (95% CI 5.0 to 30.0) 3. 20.0° (95% CI 10.0 to 40.0)	9
Saunders, 1995	Adults (35-65 years) diagnosed with supraspinatus tendinitis Mean age: 50.25 years Gender: Male: 12 Female: 12	Infrared laser (820 nm, 40 mW, 5000 Hz, 30 J/cm ² , for 3 minutes. (Lt) Placebo-dummy laser (PI) 3 times a week for 3 weeks	12 12	21	Mean improvement measured with a 10 cm VAS in: 1.Pain 2.Tenderness 3.Muscle force	1. Inter-group comparison: p<0.05 in favour of Lt (No pre-post comparison presented) 2. Lt: p<0.05 for pre-post treatment comparison PI: p≥0.05 pre-post treatment comparison Inter-group comparison: p<0.05 3. Lt: p<0.001 pre-post treatment comparison PI: p≥0.05 pre-post treatment (No inter-group comparison presented)	12
Laser therapy with exercise vs. exercise alone or compared to another intervention							
Vecchio, et al., 1993	Adults (17-77 years) with rotator cuff tendinitis with a painful arc of abduction and painful isometric abduction, external or internal rotations Mean age: 54.4 years Gender: Male: 10 Female: 15	Continuous irradiation laser (830 nm, 30 mW) for 10 minutes, 2 times a week for 8 weeks (Lt) Placebo-dummy laser (PI) Both groups had an exercise program instructed by a physiotherapist	19 16	56	Pain at rest assessed with a 10 cm VAS at: 1.Baseline 2.4 weeks 3.8 weeks Pain during movement assessed with a 10 cm VAS at: 1.Baseline 2.4 weeks 3.8 weeks	1.Lt: 6.9 ± 0.5, PI: 5.3 ± 0.7 p=0.09 2.Lt: 3.4 ± 0.8, PI: 2.1 ± 0.9 p=0.21 3.Lt: 4.4 ± 0.9, PI: 3.2 ± 1.2 p=0.50 1.Lt: 6.2 ± 0.6, PI: 4.9 ± 0.7 p=0.14 2.Lt: 2.7 ± 0.8, PI: 1.2 ± 1.0 p=0.24 3.Lt: 3.6 ± 0.9, PI: 1.8 ± 1.2 p=0.34	12



					<p>Pain at night assessed with a 10 cm VAS at: 1. Baseline 2.4 weeks 3.8 weeks</p> <p>Overall self-perceived function assessed with a 10 cm VAS at: 1. Baseline 2.4 weeks 3.8 weeks</p> <p>Global score for shoulder range of motion (x36)^{° 1} : 1. Baseline 2.4 weeks 3.8 weeks</p>	<p>1.Lt: 6.0 ± 0.6, PI: 4.1 ± 0.8 <i>p</i>=0.08 2.Lt: 2.2 ± 0.6, PI: 1.4 ± 0.6 <i>p</i>=0.33 3.Lt: 3.9 ± 0.7, PI: 2.2 ± 1.0 <i>p</i>=0.30</p> <p>1.Lt: 6.5 ± 0.6, PI: 5.7 ± 0.6 <i>p</i>=0.34 2.Lt: 2.9 ± 0.6, PI: 2.0 ± 0.8 <i>p</i>=0.36 3.Lt: 3.6 ± 0.9, PI: 2.9 ± 1.1 <i>p</i>=0.7</p> <p>1. Lt: 2.2 ± 0.3, PI: 2.3 ± 0.4 <i>p</i>=0.81 2. Lt: -0.8 ± 0.2, PI: -0.5 ± 0.3 <i>p</i>=0.44 3. Lt: -1.5 ± 0.3, PI: -0.8 ± 0.5 <i>p</i>=0.23</p>	
Bingöl, et al., 2005	<p>Adults with shoulder pain for the last 3 months(10 cm VAS score ≥ 3) and who reported pain aggravation with movement</p> <p>Mean age: 60.5 years Gender: Male: 9 Female: 31</p>	<p>Laser (904nm, 50W 2000 Hz, 2.98J/cm²) 5 minutes for 10 sessions for 2 weeks(Lt)</p> <p>Placebo-dummy laser (PI)</p> <p>Both groups performed supervised exercise program for 15 minutes, 10 session for a 2 week duration</p>	20	14	<p>Mean change in overall pain assessed pre-post treatment with a 100 mm VAS</p> <p>Mean change in shoulder active and passive range of motion (°) pre-post treatment (abduction, flexion, extension, internal rotation, external rotation and adduction)</p>	<p>Lt: 28.3 ± 47.9 <i>p</i> = 0.554 PI: 12.8 ± 37.7 <i>p</i> = 0.775 <i>Inter-group comparison:</i> <i>p</i>=0.373</p> <p>Passive extension: Lt: 7.41 ± 11.61 <i>p</i>=0.017 PI: 0.73 ± 9.13 <i>p</i>=0.854 <i>Inter-group comparison:</i> <i>p</i>=0.029 None of the other movement showed significant inter-group differences</p>	12
Yeldan, et al., 2009	<p>Adults suffering from subacromial impingement syndrome (positive Neer's test, positive Hawkin's test, pain with active shoulder elevation, pain with isometric resisted abduction)</p> <p>Mean age: 55.18 years Gender: Male: 13 Female: 47</p>	<p>Laser (Lt) (904 nm , 27.5W, 2000 Hz,) for 8 minutes</p> <p>Placebo-dummy laser (PI)</p> <p>Each group had an exercise program (15-30 min, 2x/day)</p>	34	21	<p>Mean change in pain assessed with a 10 cm VAS 1. Rest 2. Night 3. During activity</p>	<p>1. Lt: -1.5 ± 2.1 <i>p</i> = 0.01 PI: -2.0 ± 2.5 <i>p</i> = 0.01 <i>Inter-group comparison:</i> <i>p</i>=0.30 2. La: -2.9 ± 2.0 <i>p</i>=0.00 PI: -3.1 ± 2.8 <i>p</i>=0.00 <i>Inter-group comparison:</i> <i>p</i>=0.79 3. Lt: -2.2 ± 1.8 <i>p</i>=0.000 PI: -2.2 ± 2.1 <i>p</i>=0.000 <i>Inter-group comparison:</i> <i>p</i>=0.94</p>	12

					Mean change in DASH score (%)	Lt: -12.1 ± 11.6 <i>p</i> =0.00 PI: -16.3 ± 13.4 <i>p</i> =0.00. <i>Inter-group comparison p</i> =0.26	
					Mean change in Constant-Murley Score (%)	Lt: 11.5 ± 10.7 <i>p</i> =0.00 PI: 14.5 ± 12.9 <i>p</i> =0.00 <i>Inter-group comparison: p</i> = 0.40	
					Mean change in SDQ score (%)	Lt: -25.5 ± 17.6 <i>p</i> =0.00 PI: -30.3 ± 31.0 <i>p</i> =0.00 <i>Inter-group comparison: p</i> =0.71	
Dogan, et al., 2010	Adults with subacromial impingement syndrome (detailed physical examination and MRI Mean age: 53.6 ± 11.3 years Gender: Male: 19 Female: 33	Laser therapy (850 nm, 100 mV, 5 j/cm ²) for 5-6 minute(1x/day, 5 times a week, total 14 sessions) (Lt) Placebo-dummy laser (PI) Both groups received coldpack therapy (10 min) and an exercise program	30 22	21	Overall pain assessed with a 10 cm VAS pre-post treatment SPADI total mean score (%) pre-post treatment Mean shoulder range of motion (°) (flexion, abduction, internal rotation, external rotation, extension and adduction)	Lt: 7.16 ± 1.64 and 3.76 ± 1.45 <i>p</i> =0.000 PI: 7.59 ± 1.76 and 4.63 ± 2.10 <i>p</i> =0.000 <i>Inter-group comparison: p</i> =0.216 Lt: 64.39 ± 23.65 and 44.32 ± 2.80 <i>p</i> =0.000 PI: 62.63 ± 16.58 and 36.39 ± 20.53 <i>p</i> =0.000 <i>Inter-group comparison: p</i> =0.201 No significant differences between groups in mean change in shoulder range of motion	12
Abrisham et al., 2011	Adults suffering from RC tendinopathy with positive Hawkins-Kennedy, Jobe and Speed tests. Mean age: 51.7 years Gender: Male: 30 Female: 50	Laser therapy (890 nm, 2-4 J/cm ²) for 6 minutes, 10 sessions for 2 weeks (Lt) Placebo group (PI) All participants had a supervised and home exercise program	40 40	14	Mean difference of overall pain assessed with VAS (0-10) pre-post treatment Mean difference in shoulder ROM (°): 1.Active flexion 2.Passive flexion 3.Active abduction 4.Passive abduction 5.Active external rotation 6.Passive external rotation	Lt: 4.4 ± 1.2 <i>p</i> =0.000 PI: 2.9 ± 1.1 <i>p</i> =0.000 (No inter-group comparison reported) 1.Lt: 43.1 ± 2.5, PI: 24.5 ± 2.4 Inter-group comparison: <i>p</i> =0.000 2.Lt: 50.2 ± 3.0, PI: 29.1 ± 3.0 Inter-group comparison: <i>p</i> =0.000 3.Lt: 43.1 ± 2.2, PI: 25.2 ± 5.7 Inter-group comparison: <i>p</i> = 0.000 4. Lt: 43.2 ± 2.5, PI: 29.1 ± 3.1 Inter-group comparison: <i>p</i> =0.000 5. Lt: 18.6 ± 1.9, PI: 14.9 ± 1.6 Inter-group comparison: <i>p</i> = 0.000	12

						6. Lt: 22.5 ± 2.1, Pl: 15.3 ± 1.8 Inter-group comparison: p = 0.000	
Otadi, et al., 2012	Adults with shoulder tendonitis diagnosed by MRI or CT scan Mean age: 48.7 years Gender: Male: 0 Female: 42	Laser therapy (830 nm, 30 mW, 1J/cm ²) + ultrasound (Lt) Ultrasound for 5 minute (1 mHz 1W/cm ²) (Us) 3 times a week for 10 weeks Both group performed an exercise program (2x/day)	21 23	84	% participants greatly or much improved on overall pain Mean difference in Constant- Murley score from baseline to 4 weeks (%)	1. Lt: 42.1%, Us: 14.3%, p<0.001 Lt: 19.2 (95%CI: 10.3 to 28.2) Us: 30.0 (95%CI: 24.01 to 35.89) Mean difference: 10.71% (95%CI: -21.09 to 0.34 to, p=0.043	10
Laser therapy vs. ultrasound							
Santamanto, et al., 2009	Adults with subacromial impingement syndrome diagnosed by MRI or ultrasonography Mean age: 54.1± 9 years Gender: Male: 28 Female: 42	High-intensity laser therapy (1064 nm, 6 W, 760 mJ/cm ²) 10 min, 5 days/week for 2 weeks (Hi) Ultrasound (1 MHz, 2W/cm ² , effective radiating head area: 4.6 cm ²) 5x/week for 2 weeks (Ul)	35 35	14	Mean difference in overall pain assessed with a 10 cm VAS Mean change in Constant-Murley Score (%) Mean change in Simple Shoulder Test (%)	Hi: 3.8 (95%CI: 3.3 to 4.4) Ul: 2.2 (95% CI: 1.9 to 2.4) <i>Inter-group comparison: p<0.001</i> Hi: -12.7 (95%CI: -13.9 to -11.4) Ul: -9.0 (95%CI: -10.0 to -8.1) <i>Inter-group comparison: p=0.03</i> Hi: -2.5 (95%CI: -2.9 to -2.1) Ul: -1.8 (95%CI: -2.0 to -1.6) <i>Inter-group comparison: p=0.06</i>	14
Calis, et al., 2011	Adults (18-65 years) with subacromial impingement syndrome diagnosed by MRI Mean age: 49.2 years Gender: Male: 17 Female: 35	Laser therapy (904 nm, 6 mW, 3 mHz, 1 J/cm ²) for 2 minutes daily (Lt) Ultrasound (1.5 W/cm ² , 3 MHz) for 5 minutes daily (Ul) Exercise program only (X's) Lt and Ul group also received an exercise program	21 15 16	15	Pain assessed with a 10 cm VAS pre and post treatment: 1.At rest 2.At night 3.During movement Constant-Murley Score (%) pre and post treatment	1. Lt: 4.0 ± 3.5 and 2.6 ± 2.3 p=0.01 Ul: 3.6 ± 2.5 and 2.2 ± 2.1 p=0.01 X's: 4.7 ± 2.5 and 4.0 ± 2.7 p=0.04 <i>Inter-group comparison: p=0.10</i> 2.Lt: 6.4 ± 3.00 and 3.7 ± 2.9 p=0.003 Ul: 7.0 ± 1.1 and 3.7 ± 2.2 p=0.001 X's: 6.1 ± 2.5 and 4.8 ± 2.7 p=0.009 <i>Inter-group comparison: p=0.35</i> 3.Lt: 5.9 ± 2.1 and 3.7 ± 2.4 p=0.001 Ul: 6.7 ± 1.5 and 4.2 ± 2.3 p=0.001 X's: 6.4 ± 1.3 and 5.5 ± 1.9 p=0.013 <i>Inter-group comparison: p=0.07</i> Lt: 56.2 ± 15.5 and 64.6 ± 16.2 p=0.001 Ul: 52.0 ± 9.9 and 62.9 ± 6.9 p=0.001 X's: 48.4 ± 14.6 and	6



					Shoulder range of motion (°) pre and post treatment (flexion, abduction, internal rotation and external rotation)	56.3 ± 13.1 p=0.001 Inter-group comparison: p=0.13 No significant differences between groups for all shoulder movements	
Laser therapy vs. exercise							
Bal, et al., 2009	Adults (18-70 years) with subacromial impingement syndrome lasting from 6 week to 6 months with shoulder pain, positive Neer and Hawkins-Kennedy signs, and a positive subacromial injection test (10 mL of 1% lignocaine) Mean age: 52.4 years Gender: Male:12 Female:28	Ga-As laser therapy (904 nm, 5500 Hz, 27W 1.6 J, 16.5 mW/cm ²) for 10 minutes, 5x/week for 2 weeks (Lt) combined with 12 week comprehensive home exercise program with application of hot/cold packs	22	84	Median night pain assessed with a 100 mm VAS (IQR) 1. Mean change at 2 weeks 2. Mean change at 12 weeks Median SPADI total score (%) 1. Mean change at 2 weeks 2. Mean change at 12 weeks Median UCLA Shoulder Score (0-35) (IQR) 1. At 2 weeks 2. At 12 weeks	1. Lt: -22.7 ± 24.36, X's: -21.7 ± 19.21 Inter-group comparison: p=0.659 2. Lt: -54.7 ± 24.68, X's: -31.5 ± 27.77 Inter-group comparison: p=0.008 1. Lt -16.2 ± 17.7 p≥0.05 X's: -23.2 ± 17.1 p<0.01 Inter-group comparison: p=0.213 2. Lt: -32.7 ± 18.6 X's: -37.2 ± 21.3 No inter-group comparison presented 1. Lt: 26 (5) X's: 25 (4.7) 2. Lt: 33 (4.2) X's: 29 (6) Inter-group comparison: p≥0.05	9
Laser therapy in conjunction with other interventions vs. other type of interventions							
Eslamian, et al., 2011	Adults with RC tendinopathy with 2 out of 5 diagnostic tests: painful arc syndrome, impingement, Kennedy-Hawkins or supraspinatus tests. Mean age: 50.18 years Gender: Male: 24 Female: 26	LT (830 nm, 100 mW, 4J/cm ² for 5 min) + superficial hot therapy + US + TENS + exercise program I (Lt) Superficial hot therapy + US + TENS + exercise program (Co) 3x/week for 10 sessions	25	42	Mean change in overall pain score assessed with a 10 cm VAS pre-post treatment Mean change in SDQ score (%) pre and post treatment Shoulder ROM (°) before and after treatment (active abduction, passive abduction and active external rotation)	Lt: -4.16 ± 1.93 p<0.001 Co: -2.68 ± 2.70 p=0.001 Inter-group comparison: p=0.031 Lt: -9.06 ± 5.53 p<0.001 Co: -5.88 ± 4.40 p<0.001 Inter-group comparison p=0.029 No significant differences between groups for all movements	11
<p>BID: 2x/day; VAS: Visual Analogue Scale; US: Ultrasound; 95% CI: 95% Confidence Interval; DASH: Disability of the Arm, Shoulder and Hand questionnaire (0-100, a lower score indicates a better status)</p> <p>Constant- Murley (0-100, a higher score indicates a better status); SDQ: Shoulder Disability Questionnaire. (0-100, A lower score indicates a better status); MRI: Magnetic Resonance Imaging; SPADI: Shoulder Pain and Disability Index (0-100, a lower score indicates a better status); CT: Computed Tomography; UCLA: University of California-Los Angeles shoulder score (0-100, a lower score indicates a better status); IQR: Inter-Quartile Range; TENS: Transcutaneous Electrical Neuro-Stimulation</p>							

was superior to advice in terms of reduction in disabilities ($p < 0.05$) and gain in shoulder muscle force ($p < 0.01$) in the short term [16]. Two RCTs compared LT to a placebo, but because different outcome measures and time points were used, pooling of data was not possible [17,18]. England and colleagues ($n = 30$) reported a statistically significant difference in favour of LT at 2 week follow-up for overall pain score with a mean difference of 2.5 cm (95%CI: 1.0 to 3.5) on a 10 cm VAS scale [17]. In terms of shoulder active range of motion, inter-group comparison reached statistical significance in favour of LT for shoulder flexion and abduction with a mean difference between groups of 20.0° (95%CI: 10.0 to 40.0) and 15.0° (95%CI: 5.0 to 30.0) respectively [17]. The RCT by Saunders et al. ($n = 24$) reported that the proportion of participants who experienced improvement in terms of overall pain at 3 weeks after LT was significantly higher for the LT group compared to the placebo group (80% and 20% respectively, $p < 0.05$). However, in terms of self-perceived overall benefit, inter-group comparison was marginally significant with a mean difference of 1.5 cm in favour of LT (95%CI: -0.01 to 3.9) on a 10 cm VAS [18].

Efficacy of laser therapy compared to oral NSAIDs: The study by England and colleagues also compared LT to oral NSAIDs. In terms of overall pain, inter-group comparison showed a statistically significant difference with a median difference between groups of 2.0 cm on a 10 cm VAS in favour of LT (95%CI: 1.0 to 3.9) at 2-week follow-up [17]. In terms of shoulder ROM: flexion, abduction and extension reached statistical significance for inter-group comparison ($p < 0.001$, $p < 0.005$ and $p < 0.02$ respectively) in favour of LT, but overall self-perceived function was not significantly different between both types of interventions ($p = 0.05$) [17].

Efficacy of laser therapy compared to exercise: Two RCTs ($n = 96$) compared LT to a home exercise program [24,26]. A meta-analysis was conducted for pain at night, 2 weeks after initiation of treatment and revealed no significant differences (10 cm VAS MD: 0.34; 95%CI: -0.83 to 1.51; $p = 0.57$) (Figure 2). The RCT by Calis et al. also compared the efficacy of these two interventions in terms of pain at rest. The exercise group showed greater pain relief with a mean difference in change of 0.71 cm on a 10 cm VAS (inter-group comparison: $p = 0.04$). In terms of pain during movement, pre-post treatment comparison showed significant improvement for both groups; however, inter-group comparison was not statistically

significant ($p \geq 0.05$) [24]. Pre-post treatment comparison showed statistically significant functional improvement on the Constant-Murley Score for both groups, but no significant differences between groups were detected ($p \geq 0.05$). In the study by Bal et al., the authors used the Shoulder Pain And Disability Index (SPADI) and the UCLA Shoulder Score to evaluate function [26]. Both groups reached statistical significance for pre-post treatment comparisons on both scales; however no inter-group comparison was performed by the authors.

Efficacy of laser therapy with exercise compared to exercise alone: Five RCTs compared the efficacy of adding LT to exercise programs where one group received active LT with an exercise program and the other group received a sham LT intervention with the same exercise program [19-23]. Three studies provided data on overall pain and pooling of results was possible 2 or 3 weeks after treatment was initiated [19-21]. A significant overall effect in favour of LT combined with exercise over exercise alone was found (10 cm VAS overall pain MD: 1.38; 95% CI: 0.91 to 1.85) (Figure 3). However, conclusions from the other two RCTs not pooled ($n = 102$) were that, 3 to 6 weeks after the intervention was initiated, LT with exercise was not superior to exercise alone in terms of pain at rest, at night or with movement ($p \geq 0.05$) ($n = 102$) [22,23]. For these two studies, data on pain at night was pooled and the results of this meta-analysis did not show any significant benefit of adding LT to an exercise program (10 cm VAS night pain MD: 0.17; 95%CI -0.41 to 0.75; $p = 0.57$) (Figure 3). Pain at rest was also measured in these two studies, but because of significant heterogeneity, these results were not pooled together ($Tau^2 = 1.03$, $Chi^2 = 3.84$, $df = 1$ ($p = 0.05$); $I^2 = 74\%$). On this specific outcome, conclusion of the two RCTs was that no significant benefit was seen when adding LT to exercise compared to exercise alone ($p \geq 0.05$).

Three studies ($n = 154$) provided data on function with similar assessment time points at 2 to 4 weeks [21-23] and the results of the meta-analysis did not show any significant benefit of adding LT to an exercise program (SMD: -0.21; 95%CI -0.53 to 0.10; $p = 0.19$) (Figure 4).

Four studies also provided data on shoulder active ROM at similar time points (2 to 3 weeks) [19-21,23]. Thus, a meta-analysis was performed with the study by Abrisham et al. removed from

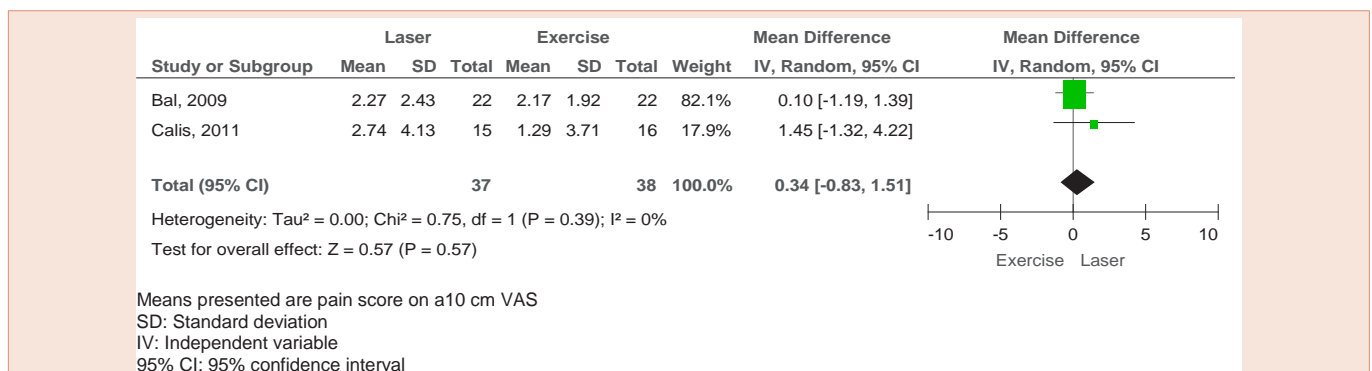


Figure 2: Forest plot of pooled studies comparing laser therapy to exercise alone for change at 2 weeks in pain at night.

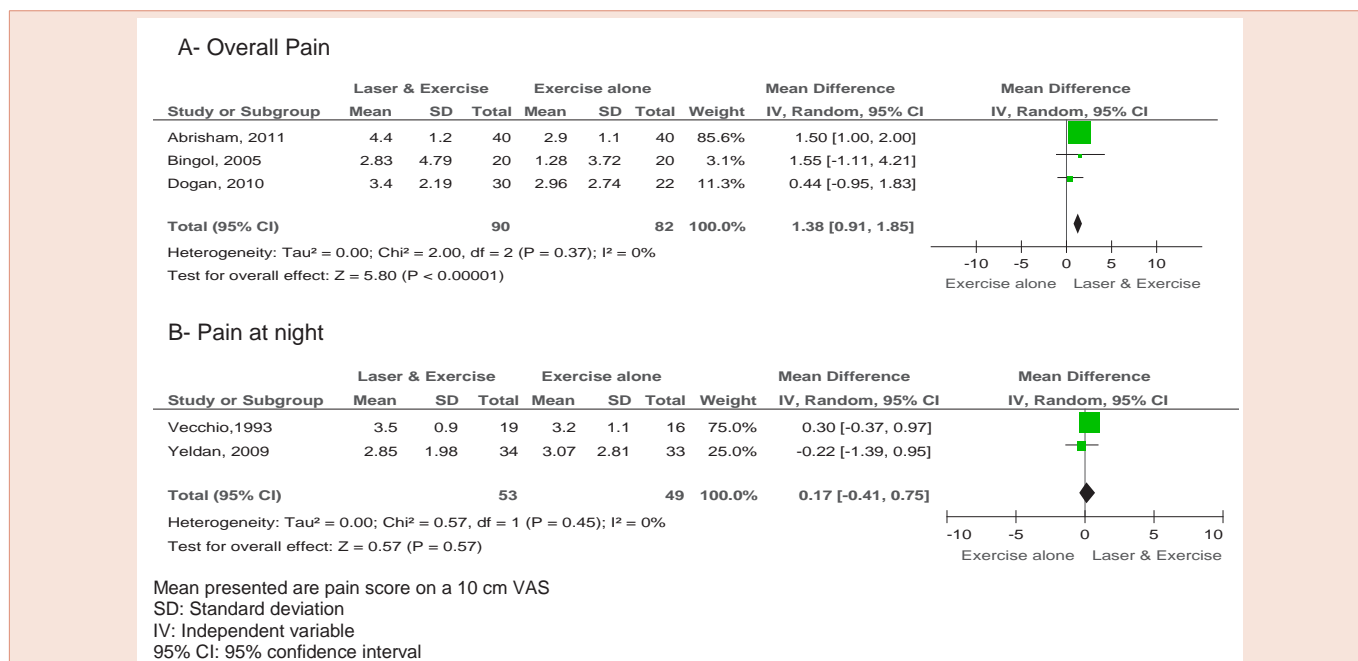


Figure 3: Forest plot of pooled studies comparing laser therapy with exercise to exercise alone for change at 2 to 3 weeks in overall pain (A) and in pain at night (B).

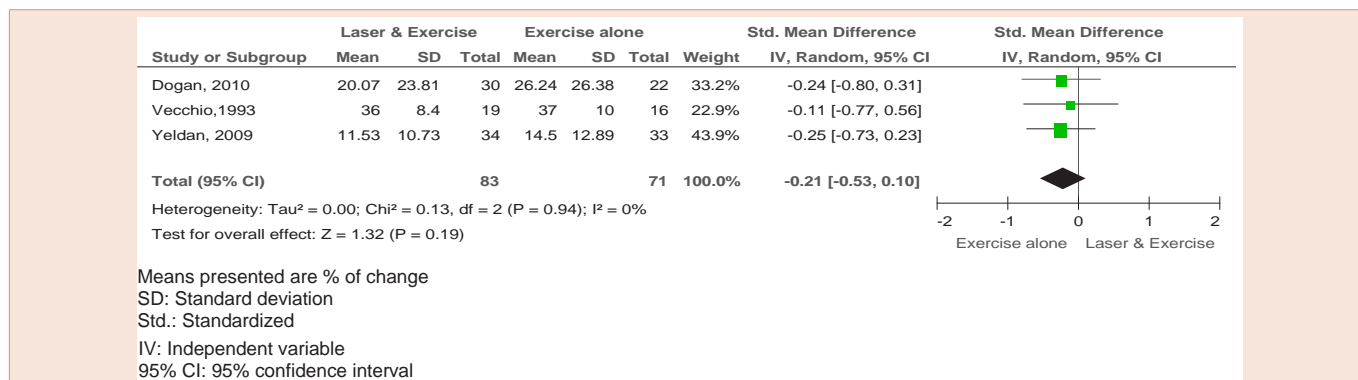


Figure 4: Forest plot of pooled studies comparing laser therapy and exercise alone compared to exercise alone for change at 2 to 4 weeks in self-reported function.

the analysis for shoulder range of motion in flexion, abduction and internal rotation because of significant heterogeneity (I² > 60%) [19]. The overall results (n= 159), revealed a significant effect at 2 to 3 weeks in favour of LT combined with exercise in terms of gain in external rotation (MD: 3.53°; 95%CI: 2.39 to 4.67; p<0.00001), but not for other shoulder movements (p≥0.05) (Figure 5) [20,21,23].

Efficacy of laser therapy with exercise compared to ultrasound with exercise: The study by Otadi et al., (n=44) compared the efficacy of a combined intervention of ultrasound and exercise to LT and exercise [28]. Both groups improved (p<0.001 in pre-post treatment comparisons) in terms of overall pain and shoulder tenderness [28]. No inter-group comparisons were performed for these two outcomes. A greater proportion of participants receiving LT and exercise reported improvement (100%) compared to those who received ultrasound with exercise (75%) (p<0.001) [28]. Function was assessed

using the Constant-Murley Score. Both groups reached statistical significance for pre-post treatment comparison (p<0.001) and inter-group comparison showed a statistically significant difference in favour of the combination of ultrasound and exercise with a mean change between groups of 10.71% (95%CI: 0.34 to -21.09, p=0.043).

Efficacy of LT compared to ultrasound: Calis and colleagues (n=52) compared a group receiving LT to another group receiving ultrasound and reported statistically significant differences for pre-post treatment comparisons in both groups in terms of pain at rest (p=0.01 for each group), pain during movement (p=0.001 for each group) and pain at night (p= 0.003 for the LT group and p=0.001 for the ultrasound group) 2 weeks after treatment initiation [24]. However, between group comparisons did not reach statistical significance (p≥0.05) [24]. In the study by Saunders (n=36) a greater number of participants in the LT group experienced pain relief compared to the

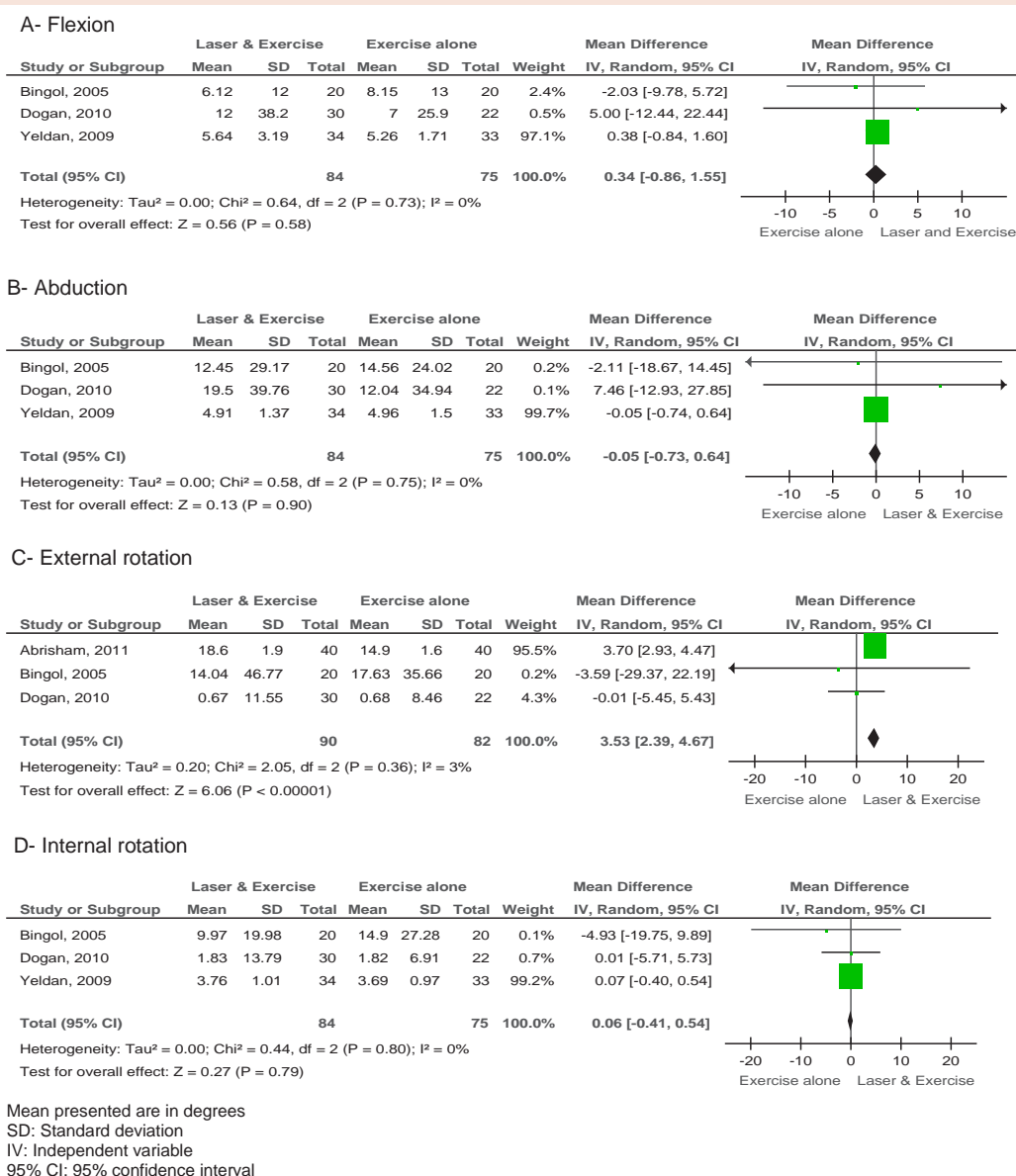


Figure 5: Forest plot of pooled studies comparing laser therapy and exercise compared to exercise alone for change at 2 to 3 weeks in shoulder range of motion in flexion (A), abduction (B), external rotation(C) and internal rotation(D).

ultrasound group at 3 weeks (90% and 58% respectively, p<0.01). In terms of function measured with the Constant-Murley Score, both groups showed significant improvement after 2 weeks, but no intervention was superior (p=0.13) [24]. In the study by Saunders et al., inter-group comparison did not reach statistical significance (p≥0.05) for the pain and disability questionnaire based on a modified version of the Oswestry low back pain questionnaire [16].

One trial (n=70) evaluated high level LT compared to ultrasound [25]. Both groups showed statistically significant differences for pre-post treatment comparison in terms of overall pain (p<0.001) and high level LT was found superior to ultrasound in inter-group comparison for overall pain on a 10 cm VAS (MD: 3.8 cm; 95%CI: 3.3

to 4.4) [25]. Regarding function, measured with the Constant-Murley Score, pre-post treatment comparison reached statistical significance for both groups with a mean difference of -12.69% (95%CI -13.94 to -11.43) for the high level LT group and -9.03% (95%CI: -9.96 to -8.10) for the ultrasound group. Inter-group comparison showed superiority in favour of high level LT (p=0.03) [25].

Efficacy of LT in conjunction with other interventions compared to other type of interventions: The study by Eslamian et al. (n=50) compared the efficacy of a combined intervention (superficial hot therapy, ultrasound, TENS and an exercise program) with or without LT [27]. The authors used a VAS at baseline and at 6 weeks to measure overall pain. Inter-group comparison reached



statistical significance in favour of the combined intervention with LT with a mean change of -4.16 ± 1.93 cm on a 10 cm VAS compared to -2.68 ± 2.7 cm for the group without LT ($p=0.031$) [27]. Using the Shoulder Disability Questionnaire to assess function, the authors found statistically significant differences for pre-post treatment comparisons and inter-group comparison as well, in favour of the combined intervention group including LT (mean changes: $-9.06\% \pm 5.53$ for the LT group and $-5.88\% \pm 4.4$ for the combined intervention group without LT; $p=0.029$) [27].

Methodological quality of included studies

Mean score for the methodological quality of the included studies reached $66.4\% \pm 10.0\%$ indicating moderate methodological quality of the studies. Six trials had a methodological score equal or over 75% (Table 1). In terms of reviewers agreement on the methodological quality of included studies, the intra-class correlation coefficient for overall methodological scores between reviewers was 0.97 (95%CI: 0.90 to 0.99) and the inter-rater agreement for each items of the risk of bias scale ranged from moderate to perfect agreement ($\kappa=0.42$ to 1.0).

All studies lacked some relevant information on the appraised methodological criteria, particularly on allocation concealment and selective reporting [16-20,22,23,27]. Eight studies reported their allocation sequence generation (Table 2) [16,19-21,23-25,27] and five studies reported the procedure for allocation concealment [21,24-26,28]. The blinding procedures were adequately presented in nine studies [18-23,25,27,28]. Incomplete outcome data reporting was scored as high or of unknown risk of bias in two studies [24,28]. Selective outcome reporting was present in all studies, and was mainly associated with the fact that the research protocols were unavailable [16-28]. Other sources of bias were scored as unclear in twelve studies [16-24,26-28].

One study included participants with shoulder pain [20], whereas all other studies included participants suffering from RC tendinopathy. Ten studies (77%) included participants with chronic shoulder tendinopathy, while three studies did not specify the mean duration of symptoms of the participants [19,27,28]. All studies reported the laser parameters and only one study used high-intensity laser, whereas the 12 other studies used low-level laser. Twelve studies (92%) used a VAS as the assessment tool to evaluate pain outcomes, making it the most common outcome [16,17,19-28]. Functional outcome measures were used in twelve studies [16,17,19,21-28]. Four studies had a medium-term follow-up (6 to 12 weeks) [22,26-28], while the others trials followed the participants for only 2 to 3 weeks [16-21,23-25].

Discussion

The aim of this review was to assess the current literature regarding the efficacy of LT for adults suffering from RC tendinopathy. Thirteen studies were included and the methodological quality of the majority of trials was moderate with an average of $66.4\% \pm 10.0\%$.

Based on low level evidence, LT may be effective in reducing overall pain in the short term for adults suffering from RC tendinopathy when compared to a placebo or advice with results that showed clinically

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants	Blinding of personnel/provider	Blinding of outcome assessor	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Abrisham, 2011	+	?	+	?	+	+	?	?
Bal, 2009	-	+	-	?	+	+	?	?
Bingol, 2005	+	?	+	?	+	+	?	?
Calis, 2011	+	+	-	-	-	-	?	?
Dogan, 2010	+	+	+	-	+	+	?	?
England, 1989	?	?	?	-	+	+	?	?
Eslamian, 2011	+	?	+	-	+	+	?	?
Otadi, 2012	?	+	+	-	+	?	?	?
Santamanto, 2009	+	+	+	?	+	+	?	-
Saunders, 1995	?	?	+	-	+	+	?	?
Saunders, 2003	+	?	-	-	+	+	?	?
Vecchio, 1993	?	?	+	+	+	+	?	?
Yeldan, 2009	+	?	+	-	+	+	?	?

Table 2: Methodological assessment of the included studies using the risk of bias tool of the Cochrane collaboration.

important differences. Evidences are unclear concerning the efficacy of LT when compared to ultrasound therapy for pain reduction in terms of clinical significance. However, evidences are inconclusive in terms of self-reported function or shoulder ROM. There is low level evidence that LT is not superior to exercise for pain reduction or for improvement in self-reported function. Based on moderate level evidence, adding LT to an exercise program or to ultrasound does not provide any clinically important benefit compared to exercise or ultrasound alone, in terms of pain, self-reported function or shoulder ROM (Table 3).

More specifically, three RCTs of low to moderate quality evaluated the effect of LT compared to a placebo or to advice [16-18]. All three studies showed statistically significant and clinically important differences in terms of reduction of pain in the short term as the minimal clinically important difference for pain in shoulder patients is considered to be 1.4 cm on a 10 cm VAS [29]. For other outcomes such as function or ROM, studies used non-validated tools or information on measurement procedures was incomplete,

Table 3: Summary table of evidence for the efficacy of laser therapy (LT) for rotator cuff tendinopathy.

Treatment	Number of studies	Total number of participants and follow-up period	Pooled effect	Conclusions	Quality of evidence
LT Vs. Placebo or a Control intervention	3	84 14 to 21 days	Pooling of results was not possible	LT may provide short term pain relief, but evidences are inconclusive for self-reported function and ROM	Low Evidence
LT Vs. Exercise alone	2	114 2 to 12 weeks	Pain at night: MD for a 10 cm VAS: 0.34 (95%CI: -0.83 to 1.51; p = 0.57) Pooling of results was not possible for overall pain, pain at rest, self-reported function and shoulder ROM	LT does not seem to provide greater improvement in terms of pain relief, self-reported function and shoulder ROM compared to exercise alone	Low evidence
Laser therapy Vs. Ultrasound	3	142 2 to 3 weeks	Pooling of results was not possible	LT may provide short term pain relief but evidence are inconclusive for self-reported function and shoulder ROM	Low evidence
LT with Exercise Vs. Exercise alone or another intervention	6	318 2 to 12 weeks	Overall pain: MD for a 10 cm VAS: 1.38 (95%CI: 0.91 to 1.85; p<0.00001) in favour of Lt with exercise Pain at night: MD for a 10 cm VAS: 0.17 (95% CI -0.41 to 0.75; p=0.57) Self-reported function: SMD :-0.21 (95% CI -0.53 to 0.10; p=0.19) Shoulder range of motion in external rotation: MD: 3.53 (95% CI 2.39 to 4.67; p< 0.00001) Results for flexion, abduction and internal rotation were pooled but none of them showed statistical significance	There is no added benefit of laser therapy combined with exercise compared to exercise alone in terms of pain reduction, improvement of self-reported function and gains in shoulder ROM. Pooled significant differences measured are not clinically important for overall pain and shoulder external rotation.	Moderate evidence

LT: Laser Therapy; ROM: Range Of Motion; MD: Mean Difference; VAS: Visual Analogue Scale; CI: Confidence Interval; SMD: Standard Mean Difference

therefore making it difficult to formally conclude on the efficacy of LT for these outcomes [16,18]. Compared to ultrasound, results from two moderate to high quality studies, indicate that LT seems to provide a greater reduction in pain [16,25], but in another low quality study this effect was not observed [24]. None of the three studies reported improvement in terms of self-reported function or shoulder ROM [16,24,25]. Results from two low quality RCTs revealed that LT is not superior to exercise for pain relief, self-reported function and shoulder ROM. Although statistically significant and clinically important differences were seen for LT, those differences were not significantly different from gains observed following the exercise program alone. Based on 6 RCTs of low to moderate quality, our results indicate that there is moderate evidence that LT with exercise does not provide any added benefit compared to exercise alone or to exercise with ultrasound. In terms of overall pain, these same studies show a statistically significant overall treatment effect (MD: 1.38 cm; 95%CI: 0.91 to 1.85) but it was just below the minimal clinically important difference of 1.4 cm [29]. When we compared LT with exercise to exercise alone or to exercise with ultrasound, a significant overall treatment effect was seen in terms of shoulder ROM, particularly for external rotation (MD: 3.53; 95% CI: 2.39 to 4.67) but again, it was below the minimal clinically important difference of 18° for external rotation [30]. No other statistically significant or clinically important differences were seen for other shoulder movements. For pain at night and self-reported function, no significant overall treatment effects were detected. It is difficult to draw firm conclusions on the superiority of LT when compared to NSAIDs, as only one study of poor quality was included in this review [17]. Likewise, the use of multiple interventions (ultrasound, TENS

and exercises) with or without LT was only evaluated in one moderate quality study and it is therefore premature to draw any conclusion on the superiority of LT combined to this rehabilitation program [27].

Overall, our results tend to demonstrate that LT used alone may provide short-term pain relief in adults suffering from RC tendinopathy. The treatment effect appears to be small, but of minimally significant clinical importance. One of the assumptions is that LT modulates cyclo-oxygenase-2 expression and therefore promotes an inflammatory response that may lead to a reduction in pain [31].

The present findings have implications for clinicians and suggest that the clinical approach of RC tendinopathy could include LT for the purpose of pain relief in the short-term. But the present results also indicate that for function or ROM, LT may not provide any benefit and may not be the optimal approach to promote complete recovery of RC tendinopathy. Other rehabilitation interventions should initially be used with patients with RC, as exercise therapy presents strong evidence for its efficacy, not only in pain reduction, but also in improvements of function and shoulder impairments (ROM and strength) [4,32].

Our results and conclusions are similar to those of a recent systematic review published on the conservative management of Achilles tendinopathy. Authors concluded that there is moderate evidence that LT may provide improvement in terms of pain and shorten recovery time in individuals suffering from Achilles tendinopathy [33]. A systematic review done by the Cochrane Collaboration however, concluded that LT was an efficacious intervention in individuals suffering from capsulitis but not for those



suffering from RC tendinopathy [7]. The authors' conclusions were based on only 4 of the 13 RCTs included in this review. Another review by Andres et al. reported substantial heterogeneity in effectiveness of LT for all types of tendinopathies and recommended that more high quality RCTs were needed to fully conclude on the efficacy of LT [34]. The authors based their conclusions on 2 RCTs included in this review and did not make specific recommendation regarding RC tendinopathy.

More high quality RCTs are indeed needed to fully conclude on the effectiveness of LT for RC tendinopathy. The methodological quality of the included studies varied and often patients could use co-interventions that were not systematically monitored, such as paracetamol or NSAIDs [17,20,24,27]. Of note, the duration of treatment was short and follow-ups were also short (2 to 12 weeks). Only three studies had a follow-up period of 8 weeks or more [22,26,28]. The dose and precise LT parameters used may have influenced overall treatment LT effects. Although dose somewhat varied between studies, nine out of twelve studies used parameters recommended by the World Laser Therapy Association for low-level LT [35]. In three studies [19,27,28], laser parameters were below the recommended dose of 8 joules for a wavelength of 780 to 820 nm and of 4 joules for a wavelength of 904 nm [35]. Still, removing these three studies of our analyses would not have changed our present conclusions. One study evaluated the effect of high level LT and to our knowledge, no recommended parameters have been published for high level LT.

Strengths and limitations of the review

One strength of this review is the detailed literature search that was conducted in the databases that contained the greatest volume of the scientific literature on this topic. We included exclusively RCTs. The methodological tool used to appraise the quality of the included studies (Cochrane risk of bias assessment tool) is a well-known, validated tool and the concordance between the evaluators in our review was very high. Despite the fact that the reviewers used this tool, there can be some discrepancy in the interpretation and in the scoring, for example, on the blinding item. Pooling of results was not always possible, but we were able to summarize evidence concerning the efficacy of LT in individuals suffering from RC tendinopathy despite the fact that there was an heterogeneity across studies.

Conclusions

Low level evidence exists that LT may provide short term pain relief of minimally significant clinical importance when compared to placebo (sham LT), clinical recommendations (adequate posture and shoulder movements to avoid) or ultrasound, but has no documented effect on self-reported function or performance-based outcomes such as ROM. There is low level evidence that LT is not superior to exercise for pain reduction or for improvement in self-reported function. Based on moderate level evidence, adding LT to an exercise program or to ultrasound does not provide any clinically important benefit compared to exercise or ultrasound alone. Until more high quality evidence demonstrate benefits of LT, clinicians should use this modality cautiously and in the sole objective of alleviating pain in the short-term as other rehabilitation interventions, such as

exercise therapy, present stronger evidence of efficacy, not only in pain reduction, but also in improvement of function and shoulder impairments (ROM and strength).

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Citation: Boudreault J, Desmeules F, Roy JS, Dionne CE, Frémont P, et al. (2016) The Efficacy of Laser Therapy for Rotator Cuff Tendinopathy: A Systematic Review and Meta-Analysis. *J Nov Physiother Phys Rehabil* 3(1): 001-015. DOI: 10.17352/2455-5487.000029