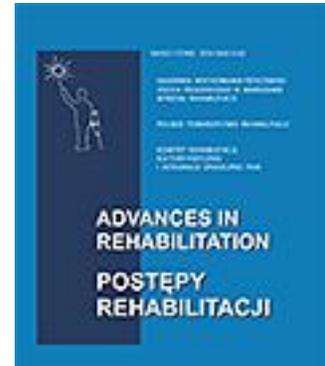


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Reviews

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Effectiveness of high-intensity laser therapy added to a physical therapy program for the treatment of myofascial pain syndrome. A systematic review and meta-analysis

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Abstract

High-intensity laser therapy (HILT) has been incorporated last years as a new resource for musculoskeletal pain management, although studies that support it in Myofascial pain syndrome (MFPS) are limited. This systematic review (SR) aimed to determine the effectiveness of HILT as a therapeutic resource for myofascial pain management. Randomized clinical trials (RCTs) were searched in PubMed, Web of Science, Scopus, Cinahl, Science Direct, and PEDro databases on April 30,2022. The selection criteria included RCTs that compared HILT added to a physical therapy program to a program without HILT, considering as the main outcome pain reduction and secondary results improvement in range of motion or disability in adults with MFPS. Three studies met the eligibility criteria and were included for analysis. The risk of bias was assessed using the Cochrane Rob2 tool, and a meta-analysis was conducted removing one low-quality study. RCTs reported a pain decrease for HILT ($p < 0.01$), and the meta-analysis revealed a mean difference of -1.90 cm (CI 95% = $-2.58, -1.22$) for the visual analog scale (0–10 cm) after four weeks, with a pooled effect in favor of HILT ($p < 0.01$). Although the RCTs individually document improvements in range of motion (ROM) ($p < 0.05$). RCTs show that HILT is effective in reducing pain but not in improving the range of motion in MFPS patients. However, even though the combined analgesic effect is significant, it would not have sufficient clinical relevance. The development of new RCTs is suggested to confirm or improve these results.

Keywords: phototherapy, laser therapy, trigger points, myofascial pain syndromes, high intensity laser therapy

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Introduction

Musculoskeletal pain is one of the leading causes of disability in the world, affecting the quality of life of the adult population, and increasing demands for health care [1]. It has been estimated that one in five adults present musculoskeletal pain, and that between 35 and 65% of people will suffer some type of musculoskeletal disorder at some point in their lives, with incidence increasing with age [2-4].

The International Association for the Study of Pain (IASP) considers myofascial pain syndrome (MFPS) to lie within the category of musculoskeletal pain. MFPS affects the myofascial tissue and presents characteristic tender spots called myofascial trigger points (MTrPs) [5]. MTrPs are identified clinically through palpation and are perceived as muscle nodules within taut muscle bands. MTrPs can reproduce patterns of referred pain and motor and autonomic dysfunctions when they are stimulated [6,7]. MFPS occurs as a result of sarcomere contractures caused by excessive acetylcholine release, a situation that produces local ischemia, changes in pH, and activation of nociceptors [6,7]. These can be caused by direct factors, such as trauma, microtrauma and overuse, or indirect factors, such as nutritional disturbances, sleep disorders, metabolic problems or stress [8]. These factors translate into increased muscle tone, facilitating the appearance of MTrPs, with consequent nociceptor activation and inflammatory mediator release in the affected muscles [8,9]. MFPS also accompanies other musculoskeletal conditions that affect the cervical, lumbar, and shoulder regions, producing regional pain [7].

One technique currently used in physical therapy for connective tissue repair, wound healing and pain management is laser therapy [10-12]. A laser is generated by exciting a medium formed of atoms with free electrons, i.e. stimulated radiation emission, resulting in the emission of coherent light from the visible (commonly red) or infrared spectra [12,13]. As laser energy is absorbed by chromophores (light photo-acceptors) such as water molecules, hemoglobin and melanin, treatment can result in biological effects in tissues where these are present (Grotthus Draper's law) [13].

Therapeutic laser devices have been classified into two types: class IIIb or low-level laser therapy (LILT), and class IV or high-intensity laser therapy (HILT), with the division depending on the output emission power, i.e. lower or higher than 500 milliwatts [12-14].

LILT has non-thermal and shallow effects (3 to 4 centimeters) and is employed to favor or inhibit biological processes (photobiomodulation) depending on the dose of energy delivered (Arndt-Schultz law) [11,12]. HILT was designed as a new resource for musculoskeletal pain management [13,14]. It is characterized by more diffuse and less concentrated emission than LILT, which allows it to reach average depths of 10 to 12cm where it can elicit thermal and photochemical effects [13]. HILT demonstrates greater penetration than LILT, and can stimulate larger areas, favoring the delivery of more energy in less time [13–15].

Currently, LILT is used in physical therapy for musculoskeletal disorders [16–18]. In contrast, HILT is supported for musculoskeletal pain management, including myofascial pain leading to analgesia and increased local circulation. However, few studies have supported its efficacy as a resource in MFPS management [8,13–15,19]. Therefore, the objective of this systematic review with meta-analysis was to evaluate the effectiveness of HILT in a physical therapy program for the treatment of myofascial pain.

Materials and methods

Study design

This systematic review (SR) was developed and reported accordingly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [20]. This SR was registered in the International SR Prospective Registry (PROSPERO) of the National Institute for Health Research (NIHR). The assigned registration number was CRD42022330292.

The researchers used the acronym PICO to structure the research question (participants, intervention, comparison, and outcome). The search algorithm for the electronic databases was structured with the following criteria: adults with MFPS diagnosis, patients receiving HILT intervention with or without any physical therapy treatment (such as physical agents, therapeutic exercise, manual therapy, etc.): the intervention was compared with physical therapy treatments with or without HILT sham applications; the intervention was performed as part of a rehabilitation program for MFPS treatment that evaluated changes in pain intensity as the main outcome, as well as improvements in the range of motion (ROM) or disability changes (measured with disability questionnaires such as Disability Arm, Shoulder

and Hand, Neck Disability Index, Oswestry Disability Index, or other similar), if reported by the articles.

SR selection criteria

The inclusion criteria for the articles comprised the following: (1) randomized clinical trials (RCTs), (2) human studies, (3) articles in English or Spanish language, (4) participants of both sexes older than 18 years, (5) participants with MFPS diagnosis, (6) studies that used HILT alone or in combination with another intervention for MFPS, (7) comparison with another intervention or sham application, and (7) outcome measures as changes in pain intensity, range of motion, or disability. The following were excluded: (I) systematic reviews (SR), case reports, and literature reviews; (II) animal or *in vitro* studies; (III) myofascial pain associated with a neurological or other musculoskeletal disorders; and (IV) studies with incomplete abstracts or texts or not downloaded.

Search strategy

Three researchers (HDB-O, JO-C and RE-L) independently searched the following electronic databases: PubMed, Scopus, Web of Science (WoS), Cinahl, Science Direct, and PEDro to identify potentially eligible randomized clinical trials (RCTs) examining the effectiveness of HILT in the management of MFPS; the last update was performed on April 30, 2022. For the search, keywords from the MeSH dictionary were chosen (Medical Subject Headings). The search terms included "Lasers", "Laser Therapy", "Phototherapy", "High Intensity Laser Therapy", "Class IV laser", "Musculoskeletal Pain", "Myofascial Pain Syndromes" and "Trigger Points" connected through the Boolean terms "OR" and "AND" obtaining the following algorithm: (((("Lasers") OR ("Laser Therapy")) OR ("Phototherapy")) OR ("High Intensity Laser Therapy")) OR ("Class IV laser")) AND (((("Musculoskeletal Pain") OR ("Myofascial Pain Syndromes")) OR ("Trigger Points"))). The filters used were "clinical trial" and "randomized controlled trial".

Searches for each database were downloaded and analyzed with the Rayyan tool developed for the preliminary selection of articles by analyzing abstracts and article titles [21]. First, the article titles and abstracts were searched based on the selection criteria, classifying them into three categories ("included," "perhaps," and "excluded"), and then full

texts of potentially eligible articles were downloaded and reviewed for evaluation. Discrepancies for the “maybe” category were resolved by mediation and discussion with a third author (MA-A). For included trials, objective, participants' demographic data, evaluation sessions, follow-up period, HILT treatment protocol, and outcomes of interest were analyzed independently.

Article quality and risk of bias

Before the risk of bias in the articles was assessed, by reviewing the methodological strengths and weaknesses (internal validity), their quality was estimated based on their score in the PEDro (Physiotherapy Evidence database) [22]. RCTs with scores of less than five were classified as "low quality," while scores greater than or equal to five were considered "high quality".

The risk of bias was assessed with the RoB.2 tool from the Cochrane Collaboration [23,24] according to the following criteria: (1) randomization process bias; (2) bias due to deviations from planned interventions; (3) missing outcome data bias; (4) outcome measurement bias; (5) reported outcome selection bias; and (6) overall bias. The researchers rated each risk of bias criterion as *high* or *low*, or *unclear* where the data provided was not sufficient to decide. The data extraction and quality assessment were performed by three reviewers (HDB-O, JO-C, and RE-L). A third reviewer (MA) was included if there was no consensus. Studies with two or more high risks of bias were considered low quality. Subsequently, box and summary plots were constructed with the Robvis tool (Fig. 2) [25].

Quality of the evidence

The assessments of quality evidence for the main outcomes were carried out with the Grading of Recommendation, Assessment, Development, and Evaluation tool (GRADE), which classifies the quality of the evidence as *high*, *moderate*, *low* or *very low* [26]. The results were summarized using the Guideline Development Tool (GRADEpro, GDT) (<https://www.gradepro.org>) and presented in Table 4.

Results

Search results

The preliminary search in the selected databases yielded a total of 1242 articles (Medline via Pubmed, n = 41; Scopus, n = 327; WoS, n = 185; Cinahl, n = 113; Science Direct, n = 697; and PEDro, n = 2). Subsequently, duplicate articles were resolved, obtaining 679 for analysis. After reviewing the titles and abstracts, eleven articles were obtained in the categories "maybe" and "included" based on the selection criteria. The eleven articles were reviewed, and, after consensus, three studies were kept for review. The main reasons for exclusion consisted of low-intensity laser treatment (LILT) in MFPS or MTrPs treatment (n = 5), the use of HILT in nonspecific chronic neck pain (n = 1), and cervical radiculopathy (n = 2). Figure 1 presents additional information on the search strategy through the PRISMA flowchart [27].

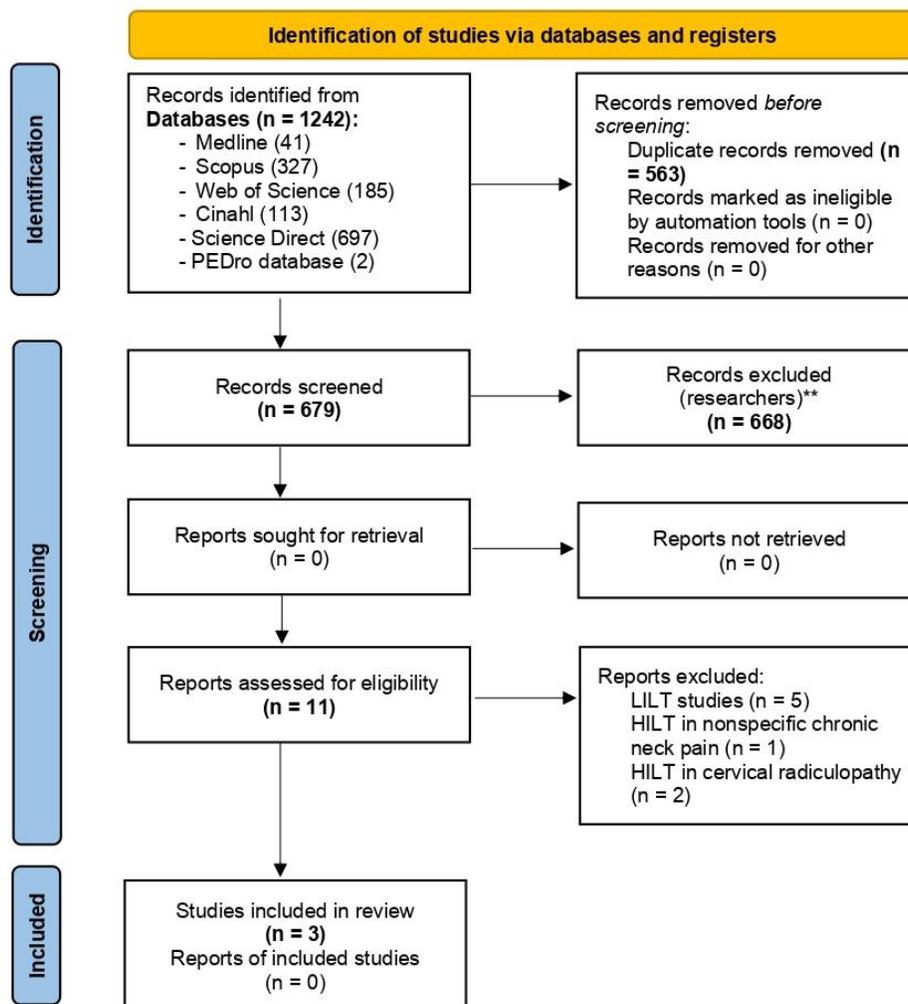


Fig. 1. Flowchart of included studies in accordance with PRISMA 2020 guidelines [27]

PEDro and RoB.2 assessment for individual RCTs

The quality of the RCTs was first assessed based on the PEDro scale score (Tab. 1). The results indicate that 66.6% of the articles (n = 2) demonstrate high quality based on internal validity, with PEDro scores equal to or greater than five [22]. As the study by Ahmed et al. was not in the PEDro database, it was evaluated and scored four points by the researchers [30].

Figure 2 presents the RoB.2 assessment. The randomization process was rated as low risk in 66.7% of the articles [28,29]. The *deviations from intended intervention* bias was evaluated as high risk in one article [30], some concerns in another [29], and low risk of bias in the other [28], i.e. 33.3% for each category. The *missing outcome data* was rated as low risk in two articles, i.e. 66.6% [28,29]. *Measurement of the outcome* bias was rated as low risk for 100% of the articles [28–30]. The *selection of the reported results* bias was assessed as low risk in two articles i.e. 66.6% [28,29]. Lastly, the overall bias was rated at 33.3% for each of high risk, some concerns and low risk [28–30].

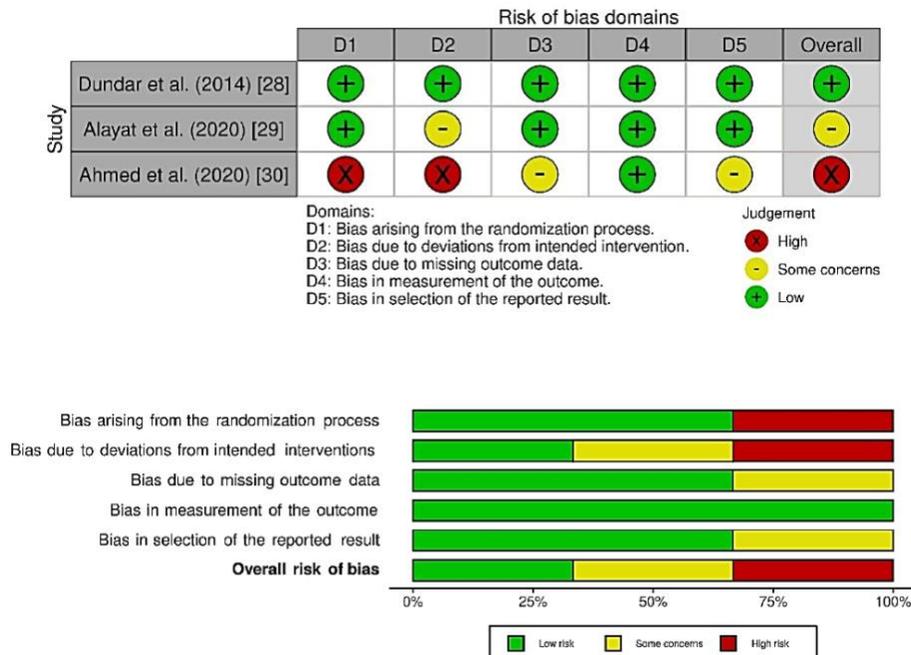


Fig. 2. Risk of bias summary: evaluations about risk of each tested bias as percentages across all included RCTs

Tab. 1. PEDro scale score of the analyzed RCTs

Clinical trial number	Author year of publication	PEDro scale criteria											TOTAL SCORE
		CRITERIA 1	CRITERIA 2	CRITERIA 3	CRITERIA 4	CRITERIA 5	CRITERIA 6	CRITERIA 7	CRITERIA 8	CRITERIA 9	CRITERIA 10	CRITERIA 11	
1	Dundar et al (2014) [28]	1	1	1	1	1	0	1	1	0	1	1	8/10
2	Alayat et al. (2020) [29]	0	1	0	1	1	1	1	0	0	1	1	6/10
3	Ahmed et al. (2020) [30]	1	1	0	1	0	0	0	0	0	1	1	4/10

PEDro (Physiotherapy Evidence Database) scale criteria:

Criteria 1: The selection criteria were specified.

Criteria 2: Subjects were randomized into groups (in a crossover study, subjects were randomized as they received treatments).

Criteria 3: The assignment was hidden.

Criteria 4: The groups were similar at the beginning in relation to the most important prognostic indicators.

Criteria 5: All subjects were blinded.

Criteria 6: All therapists who administered the therapy were blinded.

Criteria 7: All assessors who measured at least one key outcome were blinded.

Criteria 8: Measures of at least one of the key outcomes were obtained from more than 85% of the subjects initially assigned to the groups.

Criteria 9: Results were presented for all subjects who received treatment or were assigned to the control group, or, when this could not be the case, data for at least one key outcome were analyzed by ‘intention to treat’.

Criteria 10: Results of statistical comparisons between groups were reported for at least one key outcome.

Criteria 11: The study provides point and variability measures for at least one key outcome.

RCT characteristics

Table 2 summarizes the selected RCT's characteristics as well as the primary and secondary outcomes of interest. The included trials were published from 2015 to 2020 and conducted in Turkey, Saudi Arabia, and Egypt. The overall population included 176 patients with a mean age of

33.5 years (SD 7.6), divided into 132 women and 44 men. A total of 88 patients received HILT, while another 88 patients were treated with a sham application within a physical therapy program [28,29], or only the physical therapy program [30].

Tab. 2. Characteristics of the included RCTs

N°	TITLE	AUTHOR YEAR COUNTRY	Sample size (n) men women mean age (years) ± DE	EG CG	Intervention	HILT Parameters	Sessions	Outcomes (measuring instrument)	Evaluation time
1	Effect of high-intensity laser therapy in the management of myofascial pain syndrome of the trapezius: a double-blind, placebo-controlled study.	Dundar et al. [28] 2015 Turkey	n = 76 men = 0 women = 76 39 ± 12.9	EG = 38 (men: 0; women: 38) CG = 38 (men: 0; women: 38)	EG = HILT + exercise (stretching, ROM and strength exercise) CG = Sham + exercise (stretching, ROM and strength exercise)	Scan and punctual application Wavelength: 1064nm Peak power: 3kW Pulsed emission (duty cycle: 0.1%) Frequency: 10 to 40 Hz Energy density: application in 3 subphases 500 J (manual scan), 60J (point) and 500 J (manual scan).	15 (3 weeks)	Pain (VAS) Cervical ROM (Inclinometer) Disability (NDI) Life quality (SF- 36)	T0: baseline T1: 4 weeks (end of treatment) T2: 12 weeks
2	Pulsed ND:YAG laser combined with progressive pressure release in the treatment of cervical myofascial pain syndrome: a randomized control trial.	Alayat et al. [29] 2020 Saudi Arabia	n = 50 men = 26 women = 24 28.5 ± 5.07	EG = 25 (men: 12; women: 18) CG = 25 (men: 14; women: 16)	EG = HILT + PPRT + exercises (stretching and strength exercises) CG = Sham + PPRT + exercises (stretching and strength exercises)	punctual application Wavelength: 1064nm Peak power: 10.5W Pulsed emission (duty cycle: 0.1%) Energy density: 10, 12.5, and 15 per point	12 (4 weeks)	Pain intensity (VAS) PPT (algometry) Cervical ROM (inclinometer)	T0: baseline T1: 4 weeks (end of treatment)

3	High intensity laser therapy on pain in patients with myofascial trigger points	Ahmed et al. [30] 2020 Egypt	n = 50 men = 18 women = 32 30 ± 5.6	EG = 25 (men: 9; women: 16) CG = 25 (men: 9; women: 16)	EG = HILT + TENS + US + stretching exercise CG = TENS + US + stretching exercise	Punctual application Wavelength: 810nm and 980nm (dual) Peak power: 7W Pulsed emission (duty cycle: 0.1%) Energy density: 20 per point	8 (4 weeks)	Pain intensity (VAS)	T0: baseline T1: 4 weeks (end of treatment)
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Own elaboration.

CG- control group, EG- experimental group, NDI- neck disability index, ND YAG- neodymium-doped yttrium aluminum garnet laser, PPRT- progressive pressure release technique, HILT- high-intensity laser therapy, PPT- pain pressure threshold, TENS- transeletrical nerve stimulation, RCT- randomized controlled trial, ROM- range of movement, SF-36- the 36-Item Short Form Survey, US- therapeutic ultrasound, VAS- visual analog scale, P-value < 0.05*

HILT treatments were performed in all studies on the upper trapezius muscle by spot application to tender points [28–30]. Only one study incorporates a scanning application along the muscle belly into its laser treatment protocol [28]. The treatments were developed between three and four weeks with a frequency of two to three sessions per week until completed, for a total of 8 to 15 treatments. All trials used infrared lasers with a wavelength of 1064 nanometers [29,30] and a mixed wavelength of 980–810 nm [28]. The HILT treatments used a pulsatile emission (duty cycles of 0.1% and 50%) with energy densities ranging between 10 and 60 joules per treatment point. Treatment times for HILT were variable depending on the number of points on the trapezius, with treatments ranging from 2 to 15 minutes. All HILT and control groups received a physical therapy program with cervical muscle stretching exercises. In addition, two studies incorporated muscle strengthening exercises for the neck [28,29].

Other complementary treatments include manual therapy (progressive pressure technique on painful points) [29], transcutaneous electrical nerve stimulation (TENS), and therapeutic ultrasound (US) [30].

Main and secondary outcomes

All studies evaluated changes in pain intensity through a visual analog scale (VAS) [28–30], while two studies described changes in cervical ROM evaluated with an inclinometer [28,29]. The VAS was used in the RCTs to assess pain at rest [28–30], pain on movement [28], and pain on movement [28]. On the other hand, painful pressure threshold (PPT) measurement with algometry can be observed in one study [29], and another clinical trial determined neck disability with the Neck Disability Index (NDI) and quality of life with the SF-36 questionnaire [28]. All studies evaluated these outcomes in two-time points, before treatment and at the end of treatment at week 4 [28–30], while only one study shows a follow-up evaluation for week 12 (two months after treatment) [28]. HILT group information concerning the results and statistical comparisons for pain intensity, cervical ROM, neck disability, and life quality are presented in Table 3. Dundar et al. [28] found the HILT group to display statistically significant improvements in pain intensity scores (VAS) ($p < 0.001$), cervical ROM (grades with inclinometer) ($p < 0.05$), neck disability (percentage) ($p < 0.001$) and all dimensions of SF-36 questionnaire (GH, general health; GMH, general mental health; BP, bodily pain; PF, physical function, RL, role limitations due to physical activities; RLEP, role limitations due to emotional problems, social functioning, and vitality) ($p < 0.05$) at the assessments on week 4 and week 12 after treatment. On the other hand, when comparing the groups, statistically significant differences are observed after weeks 4 and 12 in favor of the HILT group for the following outcomes: pain intensity (at rest, in movement, and night pain) ($p < 0.01$), cervical disability ($p < 0.01$) and SF-36 scores in general health, physical function, bodily pain, role limitations due to physical activities, role limitations due to emotional problems, and social functioning ($p < 0.01$) [28]. However, no significant difference was found between groups regarding cervical ROM grades and SF-36 scores for general mental health and vitality ($p > 0.05$). Similarly, Alayat et al. [29] showed significant improvements in pain intensity (VAS scores), pain pressure threshold (PPT), and overall cervical ROM when the intragroup and intergroup analysis was performed at four weeks after treatment ($p < 0.05$). Lastly, Ahmed et al. [30] report that the HILT group showed statistically significant improvements in VAS scores after four weeks of treatment when compared with the control group at the same time point ($p < 0.001$).

Tab. 3. Results and statistical comparisons for pain, ROM, neck disability and life quality of HILT groups in the analyzed RCTs

Study	Outcomes and measurement tools	T0: Baseline mean \pm SD	T1: Evaluation at 4 weeks mean \pm SD	T2: Evaluation at 12 weeks mean \pm SD	p- value intragroup T0-T1	p-value intragroup T0-T2	p-value between groups at T1
Dundar (2014) [28]	Pain at rest (VAS) (cm)	5.9 \pm 1.4	2.7 \pm 1.2	2.6 \pm 1.2	< 0.001*	< 0.001*	< 0.001*
	Pain at movement (VAS) (cm)	6.1 \pm 1.6	3.1 \pm 1.1	3.1 \pm 1.2			
	Pain at night (VAS) (cm)	4.7 \pm 2.7	1.8 \pm 1.4	1.6 \pm 1.5			
	ROM-Cervical flexion(°)	54.7 \pm 9.4	57.2 \pm 8.4	57.4 \pm 8.6	0.002*	0.001*	0.842
	ROM-Cervical extensión (°)	49.3 \pm 7.5	52.1 \pm 7.9	52.2 \pm 8,5	0.003*	0.004*	0.865
	ROM-Right cervical lateral flexion (°)	40.1 \pm 6.7	44.2 \pm 5.7	45.5 \pm 3,8	< 0.001*	< 0.001*	0.462
	ROM-Left cervical lateral flexion(°)	42.4 \pm 6.8	45.6 \pm 6.7	46.4 \pm 6.2			0.413
	ROM-Right cervical rotation (°)	75.3 \pm 7.2	81.4 \pm 8.2	81.5 \pm 7.8			0.785
	ROM-Left cervical rotation (°)	77.4 \pm 6.3	83.1 \pm 7.3	82.9 \pm 7.9			0.612
	Neck disability index (%)	32.6 \pm 6.6	21.1 \pm 6.3	20.3 \pm 6.22	< 0.001*	< 0.001*	< 0.001*
	SF-36,PF-domain	57.7 \pm 12.2	73.5 \pm 11.4	72.9 \pm 13.1	< 0.001*	< 0.001*	< 0.001*
	SF-36,RL-domain	51.7 \pm 20.8	69.8 \pm 15.4	70.5 \pm 11.7			
	SF-36,BP-domain	44.9 \pm 15.6	61.2 \pm 13.7	60.8 \pm 14.7			
	SF-36,GH-domain	51.8 \pm 12.3	68.3 \pm 11.9	69.4 \pm 12.9			
	SF-36,V-domain	48.0 \pm 10.8	54.6 \pm 9.8	55.6 \pm 10.4	0.003*	0.002*	0.467
	SF-36,SF-domain	57.3 \pm 8.9	72.8 \pm 10.6	73.1 \pm 11.3	< 0.001*	< 0.001*	< 0.001*
SF-36,RLEP-domain	48.3 \pm 19.7	65.1 \pm 16.2	66.3 \pm 17.3				
SF-36,GMH-domain	49.1 \pm 9.9	55.7 \pm 9.6	56.3 \pm 8.9	0.005*	0.003*	0.854	
Alayat (2020) [29]	Pain at rest (VAS) (cm)	8.03 \pm 0.72	1.43 \pm 0.773	/	< 0.05*	/	< 0.05*
	Pain pressure threshold(kg/cm2)	1.61 \pm 0.37	2.85 \pm 0.49	/		/	
	ROM - Cervical flexion (°)	47.83 \pm 2.94	59.46 \pm 3.17	/		/	
	ROM - Cervical extension (°)	46.73 \pm 3.54	61.0 \pm 4.1	/		/	
	ROM - Right cervical lateral flexion (°)	30.6 \pm 2.35	41.5 \pm 1.59	/		/	

	ROM - Left cervical lateral flexion (°)	31.96 ± 2.17	42.76 ± 2.92	/		/	
	ROM - Right cervical rotation (°)	48.93 ± 3.08	64.36 ± 2.17	/		/	
	ROM - Left cervical rotation (°)	49.66 ± 2.97	64.03 ± 1.99	/		/	
Ahmed (2020) [30]	Pain at rest (VAS) (cm)	6.68 ± 1.24	2.6 ± 0.7	/	< 0.01*	/	< 0.01*

BP- bodily pain, HILT- high-intensity laser therapy, GH- general health, GMH- general mental health, PF- physical function, RLEP- role limitations due to emotional problems, RL- role limitations due to physical, SF-36- short-form 36 health survey, SF- social functioning, V- vitality, VAS- visual analog scale, p < 0.05*

Main outcome meta-analysis

All studies that included data allowing a meta-analysis for pain intensity at rest after treatment (four weeks), measured with the visual analog scale (VAS), are given in Figure 3 [28–30]. The pooled effect favors the laser groups, even though the confidence interval intersects the line of no effect; i.e. no significant difference was observed. No significant difference in pain intensity (VAS) at rest was found between the experimental groups and controls at four weeks, based on the estimated overall mean difference (mean difference, MD = -1.23 cm; 95% confidence interval, CI = -2.70,0.24; p-value = 0.10); however, considerable heterogeneity was observed between the RCTs ($I^2 = 97\%$, $p < 0.01$).

A subsequent sensitivity analysis excluded the Ahmed et al. [22,24] RCT based on its methodological quality: this metadata excluding the Ahmed study is given in Figure 3. It shows a decrease in heterogeneity ($I^2 = 68\%$, $p = 0.08$), a greater mean difference, and a lower confidence interval that does not intersect the line of no effect, with HILT yielding significantly better results (mean difference, MD = -1.90 cm; 95% confidence interval, CI = -2.58,-1.22; p-value <0.01). However, in the light of the number of studies and the variability in the main outcome when all are included in the analysis, it is unclear whether this mean difference is clinically relevant. It would indicate that to manage pain intensity at rest, HILT would yield significant changes after four weeks compared to another physical therapy intervention, although this should be analyzed with caution as substantial heterogeneity was observed between the studies following the sensitivity analysis.

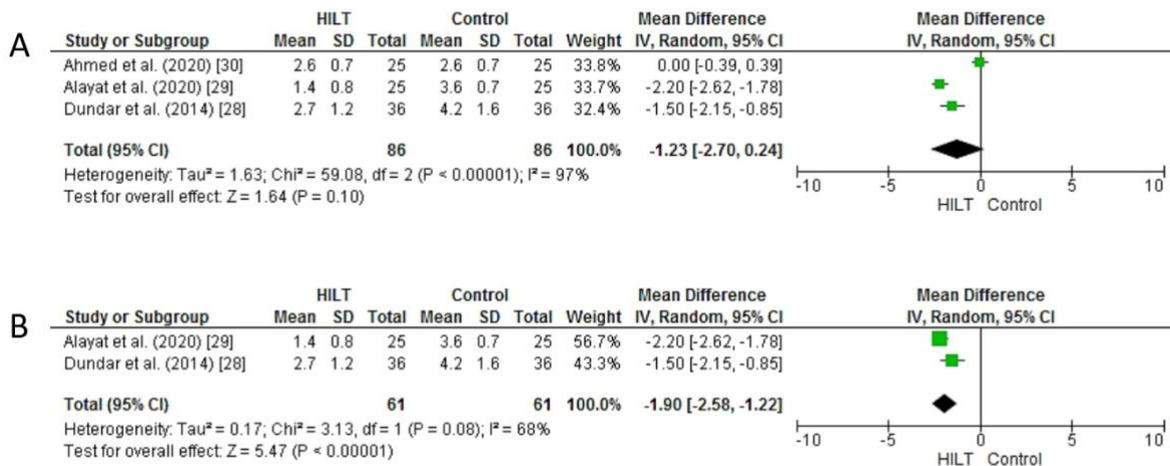


Fig. 3. Forest plot for pain intensity at rest comparison after four weeks, measured with the visual analog scale (VAS). (A) meta-analysis using all RCTs, (B) meta-analysis removing studies with a high risk of bias

Moreover, the quantitative analysis for secondary outcomes, such as ROM of cervical spine (grades) at four weeks (end of treatment), was only reported for the Dundar and Alayat studies, and considerable heterogeneity was observed when performing the meta-analysis (Fig. 4): cervical flexion, $I^2 = 92\%$, $p < 0.01$; cervical extension, $I^2 = 95\%$, $p < 0.01$; cervical right lateral flexion, $I^2 = 87\%$, $p < 0.01$; cervical left lateral flexion, $I^2 = 86\%$, $p < 0.01$; cervical right rotation, $I^2 = 94\%$, $p < 0.01$; cervical left rotation, $I^2 = 93\%$, $p < 0.01$ [31].

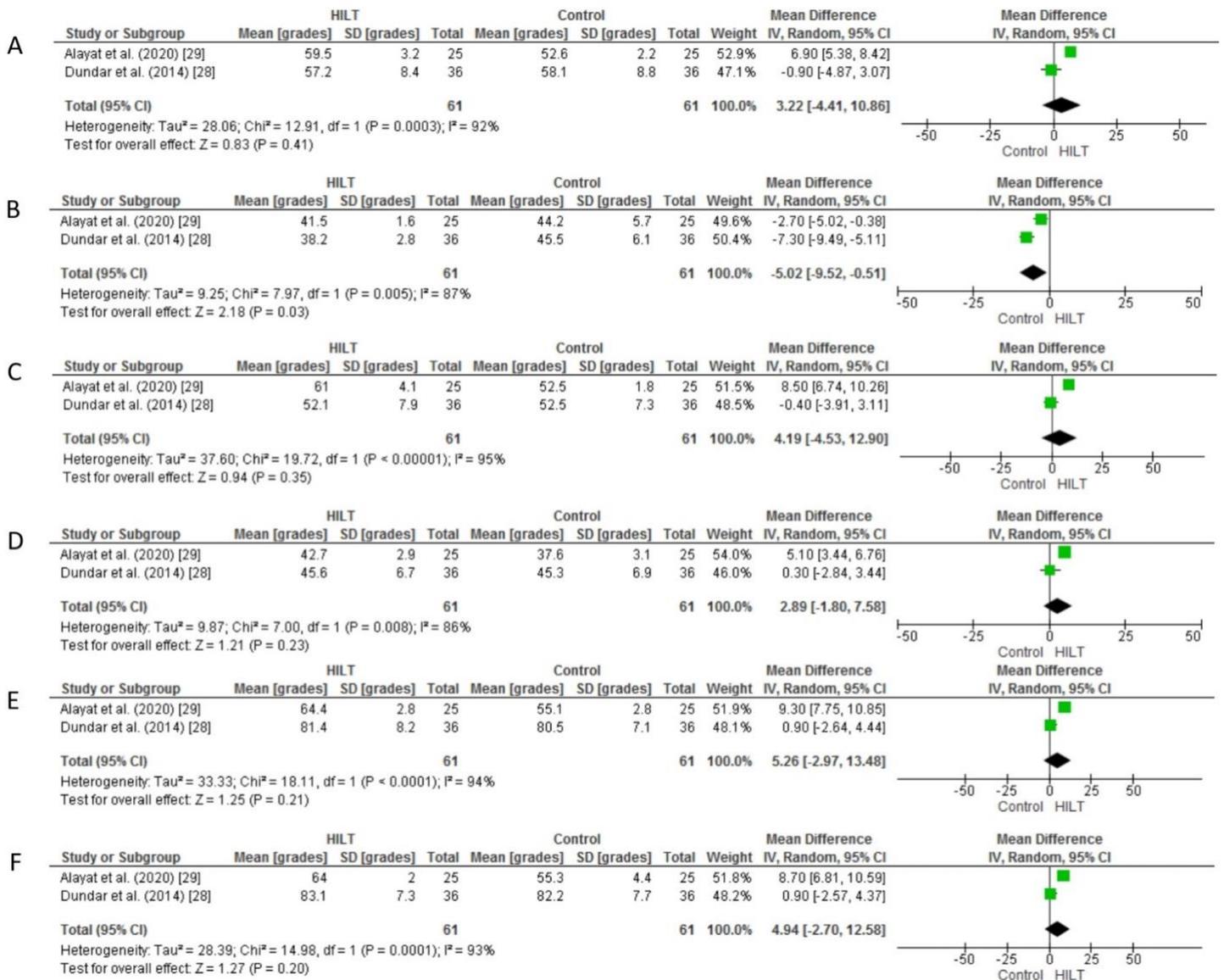


Fig. 4. Forest plot for a range of movement comparison after 4 weeks measured in grades: (A) cervical flexion; (B) cervical extension; (C) cervical right side-bending; (D) cervical left side-bending; (E) cervical right rotation; (F) cervical left rotation

The pooled effect for cervical ROM is in favor of the HILT groups, even though the confidence interval intersects the line of no effect. However, it is observed that cervical right side-bending was better in the control groups, showing a statistically significant overall mean difference at four weeks, albeit with high heterogeneity (I² = 87%; MD = 5.23°; 95% confidence interval, CI = 9.52,0.51; p-value = 0.03).

Other secondary outcomes such as cervical disability (NDI score) and quality of life (SF-36 score) could not be evaluated by meta-analysis because they were only measured in Dunder et al. [28], however, both outcomes demonstrated statistically significant improvements following HILT treatment (Tab. 3). Table 4 shows the evidence quality according to the GRADE assessment [26]. The evidence of HILT treatment effectiveness based on decrease in pain at rest (VAS) after four weeks was classified as low quality. These results can be influenced by the methodological design of some articles and the heterogeneity of others.

Tab. 4. Evidence quality by GRADE (Grading of recommendation, assessment, development, and evaluation) for adding HILT in a physical therapy program for myofascial pain management at the end of treatment (after four weeks) (outcome: pain intensity at rest)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	be used high intensity laser therapy added to a physical therapy program	a physical therapy program without laser therapy	Relative (95% CI)	Absolute (95% CI)		
Pain intensity at rest (follow-up: mean 4 weeks; assessed with: Visual analogue scale (VAS); Scale from: 0 to 10cm)												
3 [28-30]	Randomized trials	serious ^{a,b,c,d}	serious ^e	not serious ^f	serious ^g	none	88	88	-	MD 1.23cm fewer (2.7 fewer to 0.24 more)	⊕○○○ Very low ^h	Important

CI: confidence interval; MD: mean difference

Explanations

- a. In the study by Ahmed et al., it is unclear whether the assignment of participants to the study groups was done by random and concealed assignment.
- b. Problems with blinding participants or assessors are noted in the Ahmet and Alayat et al., studies, which is acknowledged as a high risk of bias.
- c. The studies do not indicate whether there was blinding of the providers, which is recognized as an unclear risk of bias).
- d. For the Ahmet and Alayat et al. studies, it is unclear whether there was any loss of participants and whether the analysis of results was done on an 'intention to treat' basis which is recognized as unclear risk of bias. The studies do not present a flow diagram according to the CONSORT regulations.
- e. The heterogeneity was judged as very serious because the I2 test showed substantial heterogeneity for all studies (50-100%).
- f. The indirect evidence was assessed not serious because the studies compared directly the interventions and outcomes.
- g. The size of the confidence interval was used as a criterion to assess the imprecision as well as the crossing of the line of no effect.
- h. Quality of evidence. Low: the research gives some indication of the probable effect. However, the probability that the effect is substantially different is high

Discussion

One of the main therapeutic goals in MFPS is pain reduction. Laser treatment has been shown to be effective for managing myofascial pain, and has demonstrated equal or greater efficacy than traditional techniques such as dry needling and ischemic pressure, and new technologies such as extracorporeal shock waves (ECSWT) or percutaneous electrical sensory stimulation (PENS) [6,11,36–38]. In the last decade, HILT equipment has been incorporated into rehabilitation. HILT stands out for its thermal effects, coverage of larger treatment areas, and energy delivery in a shorter time, thus achieving its therapeutic effects more quickly (following Roscoe Bunsen's Reciprocity law) [13–15]. Studies regarding the benefits of LILT in myofascial pain and HILT in musculoskeletal pain provide a theoretical basis for considering high-power lasers as a treatment for MFPS [13–15,38,39].

Hence, the present systematic review was performed to evaluate the effectiveness of HILT in the management of myofascial pain. This effectiveness was assessed through a meta-analysis of the outcomes of interest, *viz.* decreased pain and increased ROM, based on three RCTs. The internal validity of the studies was generally satisfactory, although there were some methodological deficiencies, especially associated with the lack of concealed allocation and blinding of participants and treaters; as such, some were assigned a high or uncertain risk of bias [24]. A quantitative analysis was performed only for pain differences at rest (VAS) and cervical ROM before and after treatment because these outcomes were evaluated in all RCTs by the included RCTs. Only one study included an assessment of the intensity of pain on movement, cervical disability (NDI), and quality of life (SF-36); these were reported in the qualitative synthesis of this review (Tab. 2) [28].

The mean difference indicates a decrease in pain at the end of treatment in favor of HILT but not in ROM; however, these results are subject to high heterogeneity between the studies, and hence should be regarded with caution to avoid underestimation or overestimation. The available evidence for HILT analgesia was found to be low quality due to the heterogeneity of the RCTs and the low clinical relevance of DM, even though the results indicated statistically significant differences in favor of HILT, even after the removal of the lower-quality studies.

No analysis was performed of the quality and evidence recommendations for changes in ROM because the results of the meta-analysis were not statistically significant, due to the high heterogeneity between studies. In addition, no changes were found between results despite the

removal of low-quality studies; however, pain intensity was found to improve [31]. This decision is in line with the recommendations of the editorial board of the Cochrane Review group, which suggests reconsidering the meta-analysis if relevant valid data are missing or if the data are not statistically significant and highly heterogeneous, a situation that occurred for the cervical ROM outcome [32]. No quantitative analysis by subgroups (sex or age) was possible because the studies did not provide enough information in this regard.

Each RCT reported pain reduction with HILT when used as part of a physical therapy program with stretching exercises, US, TENS, PPRT, or therapeutic exercises (stretching and strengthening) when compared to the same interventions without HILT or sham HILT applications [28-30]. Pain reduction was documented for different instruments (VAS and PPT) at the end of treatment (four weeks) and follow-up periods (12 weeks), with the HILT-treated groups demonstrating a significantly more favorable outcome. However, the HILT interventions have no clear or explicit effect size in the RCTs, preventing any determination the magnitude of the analgesic response for each study. Nevertheless, HILT demonstrates a consistent pain decrease in MFPS compared with LILT when the same measurement instruments are used; hence, analgesia is achieved when HILT is used as part of physical therapy, compared to LILT with acupuncture, dry needling, PENS or ECSWT [16,36-39]. These findings are in line with recent HILT trials in cervical spondylosis and nonspecific LBP, showing greater analgesia (VAS), improvement in spinal ROM and cervical functionality (NDI) when HILT is combined with therapeutic exercises versus TENS, US, or HILT alone [40,41]. This contrasts with other HILT studies in plantar fasciitis and subacromial impingement that do not report analgesic differences between the same treatments but rather improvements in the HILT groups at the end of treatment [42,43]. Based on these findings, it can be said that HILT intervention is associated with a decrease in pain (intragroup changes); however, it is known how its analgesic effects compare with other interventions, whose effects are unclear. There is clearly a need for further RCTs and systematic reviews with meta-analyses to increase the body of evidence on HILT.

For all RCTs, or only those of better quality, the pooled effect reported in the meta-analysis for pain reduction (mean difference), was found to be -1.23 and -1.90 cm on the VAS scale; this difference was statistically significant and with a large effect size (Cohen's $d > 0.8$). This would represent the typical additional analgesic response that HILT treatments would have over other treatments after three to four weeks of treatment. These results are better than those documented in a previous systematic review with meta-analyses for LILT, indicating a

mean difference of -0.85 in favor of laser [11]. However, both results are lower than the recommended minimally important clinical difference (MCID) for VAS, which suggests a decrease in pain of at least 2.0cm or more [44]. Likewise, it should be noted that the mean difference demonstrates a wide confidence interval, showing a variation of 1.5 cm, resulting in an analgesic response ranging from 0.85 to 2.70. Despite this statistically significant difference revealed by the metaanalysis, this finding probably has little clinical importance.

The metaanalysis showed no significant difference in ROM between groups, although each RCT reported favorable changes at the end of treatment (four weeks) in the HILT groups. This is consistent with studies of HILT in spinal conditions such as cervical spondylosis and low back pain that report improvements in ROM attributed to muscle relaxation due to the photothermal effects of the laser [28,29,41,42]. This again suggests an improvement in ROM with HILT (intragroup), but with no evidence to suggest that it is better than other treatments.

In the qualitative analysis, cervical disability (NDI) and quality of life (SF-36) appear as outcome measures. This is of great value, since it reaffirms the need for physical therapy treatments to recover functional activities and not just focus on deficiencies such as pain, ROM or strength. No metaanalysis of disability outcomes or quality of life was possible as it was only considered in one study [28]. It is recommended that new RCTs incorporate these outcome measures, particularly considering the benefits reported by Dunder [28], and the importance of linking treatments to improvements in functionality, which for patients may be more significant.

A limitation of the RCTs is the diversity of doses used, measured as energy density, which makes it difficult to choose parameters to replicate the treatments with HILT; this was also noted in a systematic review of LILT [8,45]. It is proposed that the dose used by Dunder should be used a reference since this was the best quality trial [28]. In addition, laser therapy should be employed at wavelengths in the infrared range (greater than 760 nanometers) and an energy per painful point of between 20 and 60J [28-30]. These values coincide with the range of energy density reported for LILT, which suggests 12 to 40J should be used to treat MTrPs [8,38,39]. In addition, 500J is recommended for scanning. New RCTs should use a technique combining punctual and scanning applications, as proposed by Dunder [28], since it is possible to cover an entire muscle and its painful points by combining the thermal effects of scanning and the analgesic effects of the punctual technique. Although the HILT applications were mainly oriented to the upper trapezius muscle, a common location of MFPS,

this does not exclude the development of new RCTs using HILT in temporomandibular myofascial pain, spine, or extremities (following the example of LILT) [10,43,46].

Adjunctive treatments for HILT included stretching exercises supplemented with manual therapy (ischemic pressure) or other physical agent modalities such as TENS and US, as reported for LILT [5,8,10]. It is suggested for new RCTs maintain stretching exercises because they are a good complement to the thermal effects of HILT. Likewise, for new RCTs, it is necessary to limit the number of complementary interventions to determine the true analgesic magnitude of HILT, since treatments such as the US or TENS have demonstrated analgesic effectiveness in MFPS [46,47].

In summary, adding HILT to a physiotherapy program reduces the intensity of pain at rest but does not improve the ROM when compared to US, TENS, and/or stretching exercises used without HILT; however, the analgesic benefits are minor. In addition, due to the limited number of RCTs and the methodological shortcomings and heterogeneity of the studies, the quality of evidence for HILT analgesia is low.

Limitations for this SR

This is the first meta-analysis to compare the analgesic effects of HILT on MFPS that tries to give value to the use of new technologies in rehabilitation.. It used a transparent method for evaluating and reporting the evidence based on the PRISMA guidelines and PROSPERO protocol registry.

The researchers highlight the following limitations: Firstly, the search only included six databases and articles in two languages (English and Spanish). As such, it is possible that other trials may have been published in other languages, particularly considering that the studies were conducted in Turkey, Saudi Arabia, and Egypt. Secondly, there was a high degree of statistical heterogeneity between the included studies; hence, only resting pain intensity could be subjected to meta-analysis, without the possibility of assessing other outcome measures such as range of motion or disability. Thirdly, some RCTs demonstrate clear methodological limitations, which may overestimate the HILT intervention. Finally, publication bias could not be assessed given the limited number of RCTs.

Therefore, even though HILT therapy seems to be effective in reducing MFPS when analyzing studies independently, the results should be interpreted with caution, showing the need for the development of new clinical trials.

Conclusion

HILT is a recent resource in physical therapy and has been proposed for the treatment of pain in musculoskeletal disorders, including MFPS. Our findings show that adding HILT to a physiotherapy plan is effective in reducing myofascial pain in the short and long term, although the evidence does not indicate that it is superior to other treatments in this regard, showing a clinically non-significant analgesic effect. Due to the limited number of RCTs and the methodological deficiencies of some of them, the quality of evidence has been assessed as low. These findings support the need for further clinical trials that provide stronger evidence on the efficacy of HILT for myofascial pain treatment incorporating also other functional outcomes.

Conflicts of Interest

The authors declare no conflict of interest.

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