Physiotherapy 121 (2023) 23–36

Systematic review

The effectiveness of high-intensity laser therapy in individuals with neck pain: a systematic review and meta-analysis

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Abstract

Objectives The primary objective of this meta-analysis was to determine whether high-intensity laser therapy (HILT) was effective in improving pain intensity, cervical range of motion (ROM), functional activity, and quality of life (QOL) in individuals with neck pain.
Data sources PubMed, PEDro, Embase, Cochrane Library, Web of Science, and ClinicalTrials.gov were searched from inception to March 26, 2022.
Study selection Randomized controlled trials (RCTs) involving HILT for neck pain were selected.
Data extraction and data synthesis Two raters were independent in data extraction. The methodological quality was evaluated using the PEDro scale, and the level of evidence was assessed using the GRADE system. RevMan5.4 was used for meta-analysis.
Results Eight RCTs were included and their PEDro scores were moderate to high. Compared with placebo, HILT was effective in improving pain intensity (SMD 2.12, 95%CI 1.24 to 3.00; moderate quality evidence), cervical flexion (SMD 1.31, 95%CI 0.27 to 2.35; moderate quality evidence), extension (SMD 1.43, 95%CI 0.24 to 2.63; moderate quality evidence), right lateral flexion (SMD 1.36, 95%CI 0.15 to 2.56; low-quality evidence). There was a trend of better outcome in functional activity after HILT (SMD 1.73, 95%CI −0.05 to 3.54; low quality evidence).
Limitations There was limited information available on QOL.
Conclusion HILT may be considered as an adjunctive treatment modality for neck pain. There was moderate quality evidence that HILT may improve pain intensity and cervical ROM in individuals with neck pain, but there was low quality evidence that HILT was not effective in improving functional activity.

Systematic review registration number PROSPERO CRD42021254078

Contribution of the paper

- HILT has the potential to improve pain intensity and cervical range of motion in the management of neck pain.
- The effect of HILT in improving functional activity for individuals with neck pain is less pronounced
- Evidence on the use of HILT in improving quality of life for individuals with neck pain is limited.

Keywords: Neck pain; Laser therapy; Rehabilitation; Systematic review; Meta-analysis

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https://doi.org/10.1016/j.physio.2023.07.003

Introduction

Neck pain is an increasingly common form of musculoskeletal pain and is characterized by a high frequency of recurrence [1]. Neck pain is one of the major global causes of disability in most countries, leading to decreased work efficiency, poor quality of life (QOL), and increased medical expenses [2]. The risk factors of neck pain include psychosocial and physical risk factors [3]. Non-invasive treatments such as exercises, manipulation, and physical agents have been suggested for the management of neck pain [4–6]; however, the effectiveness of physical agents such as laser therapy for neck pain is still uncertain and controversial.

Laser therapy is a non-invasive and painless physiotherapy modality consisting of low-level laser therapy (LLLT) and high-intensity laser therapy (HILT) while both shared similar photo-biomodulation and anti-inflammatory effects, LLLT (energy output ≤500 mW) reaches superficial tissues only, while HILT (energy output > 500 mW) can reach deeper tissues. In addition, HILT can produce photothermal effects [7,8]. Recently, HILT has been used in the treatment of various diseases, as its photothermal, photochemical, analgesic, and photomechanical effects can increase vein diameter and body surface temperature [9,10], activate cell metabolism at the molecular and cellular levels [11], slow the transmission of pain stimuli and increase the production of morphine-mimetic substances [12], and alter the mechanical forces acting on cells, respectively [13]. HILT has been found effective for reducing pain intensity and improving functional activity in individuals experiencing musculoskeletal disorders, including neck pain [7,14,15]. Alayat et al. [16] reported that HILT effectively reduced pain and increased cervical range of motion (ROM) and functional activity after 6 weeks of treatment.

HILT has unique advantages over other noninvasive physical modalities, such as ultrasound (US) and transcutaneous electrical nerve stimulation (TENS), for the treatment of neck pain. A study [17] comparing the effects of HILT with a combination of TENS and US treatment on neck pain intensity, ROM, and functional activity reported increased efficacy across all outcomes for those receiving HILT. The authors recommended that HILT should be promoted for the treatment of neck pain. As such, it is important to consolidate the research evidence to provide greater clarity on the clinical efficacy of HILT on pain intensity, cervical ROM, functional activity, and QOL in individuals with neck pain.

Three previous reviews [7,14,15] have examined the effects of HILT on musculoskeletal disorders. However, few randomized control trials (RCTs) that were included in these reviews addressed neck pain [7,14,15]. The heterogeneity of the results was high [14] and the outcomes focused solely on pain and functional activity [14,15]. In addition, the level of supporting evidence was low [15]. However, in recent years, more clinical trials investigating the effect of HILT on neck pain have been published. Therefore, the primary objective of this systematic review was to explore the effectiveness of HILT on pain intensity, cervical ROM, functional activity, and QOL in individuals with neck pain (i.e., comparison with placebo, control, or no intervention). The secondary objective was to compare HILT with other physiotherapy interventions.

Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [18] was followed. This research protocol was registered in the PROSPERO database (CRD42021254078).

Research objectives

The research objectives were constructed using the PICO format. The primary research objective was to determine whether HILT (I: intervention) was effective in improving pain intensity, cervical ROM, functional activity, and QOL (O: outcomes) in individuals with neck pain (P: population) compared with no intervention, placebo or attentional control (Comparison). The secondary research objective was to determine whether HILT (I) more effective than other physiotherapy interventions (C) in the treatment of the above outcomes (O) among individuals with neck pain (P).

Data sources and searches

PubMed, PEDro, Embase, Cochrane Library, Web of Science, and ClinicalTrials.gov were searched from inception to April 20, 2021. The search results were further updated in March 26, 2022. The following medical keywords for the search were “neck pain, neck ache, neckache, cervical pain, cervicalgia, cervicodynia” and “high intensity laser therapy, laser therapy, high power laser therapy, HILT”. The detailed search strategy of the PubMed database is shown in Appendix 1. Other databases were searched using relevant keywords. Furthermore, we manually searched the references of all full-text RCTs to identify any additional RCTs meeting the inclusion criteria.

Selection criteria

To be eligible for inclusion, the RCTs had to include adults with the main clinical symptom of neck pain. To address the primary research objective, the experimental group was HILT alone whereas the comparison group was placebo laser or no intervention; or the experimental group was HILT combined with other treatments, whereas the comparison group was placebo combined with identical other treatments. For addressing the secondary research objective, the experimental group was HILT alone whereas the comparison group was other physiotherapy interventions; or the

experimental group was HILT combined with other treatments, whereas the comparison group was other physiotherapy interventions combined with identical other treatments. The main outcome indicator was at least one of pain intensity, cervical ROM, functional activity, or QOL. RCTs had to be published in English. RCTs were excluded if (1) the participants had a primary diagnosis in addition to neck pain; (2) HILT was not included as a therapy for neck pain; or (3) the full text or accompanying data were not available.

Two researchers (YH. Xie, MX. Liao, F.M.H. Lam et al.) independently used Endnote X9 to ensure no duplicates were included, and then screened the titles and abstracts of the selected RCTs to carefully determine which should be included. The full texts of the RCTs were then evaluated by the same researchers. Any discrepancies between the two researchers were settled by discussion; if a consensus could not be reached, a third independent team member (LR. Liao) made a decision.

Methodological quality assessment

The PEDro (Physiotherapy Evidence Database) scale was used to assess the methodological quality and the risk of bias of all included RCTs. The PEDro scale consists of ten evaluation items, of which eight items assess the risk of bias, and two items assess the completeness of the statistical reporting. According to the total PEDro score, trials were of high quality (low risk of bias) if they scored 6 or more and were of low quality (high risk of bias) if they scored 3 or less [19].

Data extraction

Two authors (YH. Xie, MX. Liao) initially summarized all data independently. A third independent researcher (LR. Liao) settled disagreements by discussion until a consensus was reached. The data extracted were authors, year of publication, patient characteristics, methods of treatment of experimental and control groups, specific HILT treatment parameters, outcomes, main results, and conclusions. When data were not available, we emailed the corresponding author up to three times. If the author did not reply, the data were considered irretrievable.

Data synthesis and analysis

Meta-analysis was only performed for a given outcome if at least two RCTs used the same outcome measure. RevMan software version 5.4 was used for data analysis. Weighted mean differences (WMDs) with 95% confidence intervals (CIs) were calculated for each outcome that was measured by the same assessment tool. Otherwise, standardized mean differences (SMDs) were used. Chi-square and I^2 tests were used to assess the heterogeneity of the data. If $p \geq 0.11$ and $I^2 \leq 50\%$, a fixed effect model was used; otherwise, a random effect model was used[20]. Results were considered statistically significant if p was $< .05$.

For each meta-analysis, the quality of evidence was assessed according to the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) system. The level of evidence was classified as high, moderate, low, and very low. As only RCTs were included in this review, the rating for each level of evidence started with high quality. There were five reasons (risk of bias, imprecision, inconsistency, indirectness of evidence and publication bias) for potentially downgrading the quality of evidence (by one or two levels) [21].

Results

Study selection

Searching of the six databases yielded a total of 1796 RCTs, with 925 remaining after the removal of duplicates. After careful analysis of the titles and/or abstracts of these RCTs, 911 were excluded that did not meet the eligibility criteria. We next read the full texts of the remaining 14 RCTs for further screening. Six RCTs were excluded because we could not retrieve the full-text (n = 3) or because HILT was not used for the laser therapy (n = 3). Finally, eight RCTs [16,17,22–27] were identified as being suitable for systematic review and meta-analysis (Fig. 1).

Methodological quality assessment

The detailed PEDro scores of all included RCTs are shown in Table 1. According to the total PEDro score, the scores of the included RCTs ranged from 4 to 8 points (with a mean of 5.5 and a standard deviation of 1.5). Two RCTs [23,25] were of high quality (low risk of bias) and the remaining RCTs [16,17,22,24,26,27] were of moderate quality (4≤ score ≤6). All trials implemented randomized allocation to groups. 50% of RCTs were unblinded to study participants, 87.5% of RCTs were unblinded to therapists, and 75% of RCTs were unblinded to assessors.

Characteristics of included studies

Participants

Tables 2–3 show the details of the characteristics of all included RCTs [16,17,22–27]. The included RCTs recruited participants diagnosed with cervical spondylosis [17], cervical disc herniation [22], chronic neck pain [16,27],

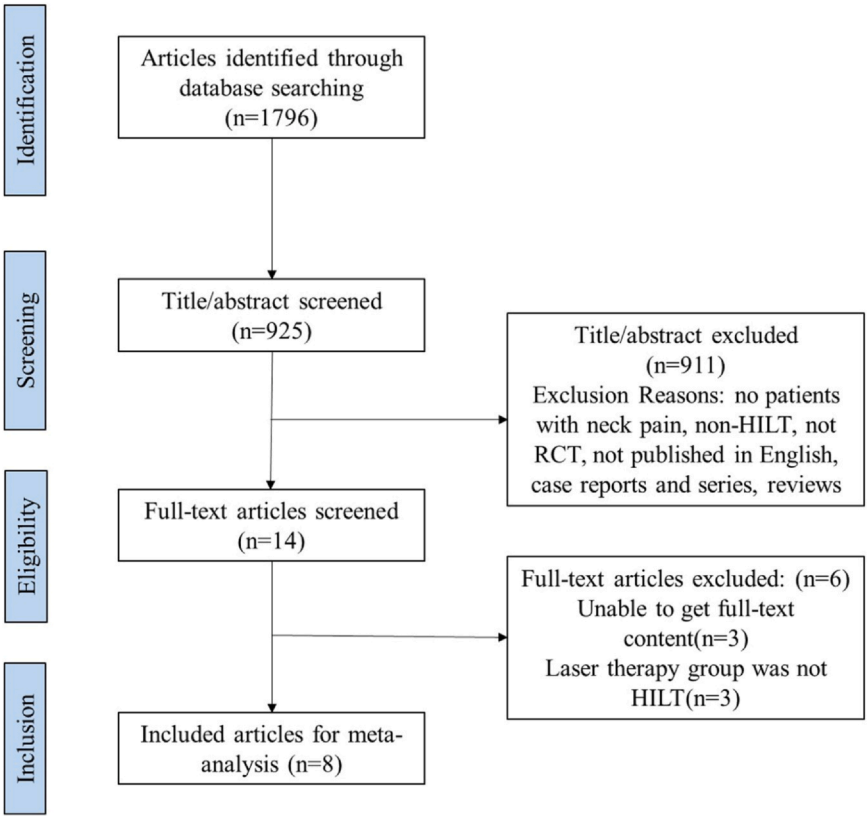

Fig. 1. Flow chart indicating the screening and searching process. HILT: high-intensity laser therapy, RCT: randomized controlled trial.

Table 1
PEDro quality scores of the included studies.

Criterion	Venosa et al. [17]	Alayat et al. [16]	Yilmaz et al. [22]	Dundar et al. [23]	Haładaj et al. [24]	Alayat et al. [25]	Abu Shady et al. [26]	Kenareh et al. [27]
Eligibility criteria	No	Yes	No	Yes	Yes	No	Yes	Yes
Random allocation	1	1	1	1	1	1	1	1
Concealed allocation	0	0	0	1	0	0	1	1
Baseline comparability	1	1	1	1	1	1	1	1
Blinded subjects	0	0	0	1	0	1	1	1
Blinded therapists	0	0	0	0	0	1	0	0
Blinded assessors	0	0	0	1	0	1	0	0
Adequate follow-up	0	0	1	1	0	0	0	0
Intention-to-treat analysis	0	0	0	0	0	0	0	0
Between-group comparisons	1	1	1	1	1	1	1	1
Point estimates and variability	1	1	1	1	1	1	1	1
Total PEDro score	4	4	5	8	4	7	6	6

cervical radicular syndrome [24,26], myofascial pain syndrome of the trapezius [23] or cervical myofascial pain syndrome [25]. They comprised a total of 603 (311 in the experimental group, 292 in the control group; 364 women and 239 men) individuals with neck pain who ranged from 23 to 69 years of age.

Table 2
Characteristics of all included randomized controlled trials.

First Author (years)	Experimental group	Control group	Participants		Outcomes	Main results
			Disease (duration of disease)	Total sample size (N)/ Age (years)/ Sex (F/M)		
Venosa [17]	HILT and exercise	US, TENS, and exercise	cervical spondylosis (> 6 months)	N = 84 (E 42, C 42) Age:34–69 Sex: F 52, M 32	(1) cervical ROM (flexion, extension, and lateral flexion) (2) VAS (3) NDI	(1) After treatment, ROM ↑, VAS and NDI scores ↓ in both groups($p < 0.05$). (2) ROM ↑, VAS and NDI scores ↓ of HILT group was greater than control group($p < 0.05$).
Alayat [16]	HILT and exercise	placebo and exercise	chronic neck pain (> 4 months)	N = 60 (E 30, C 30) Age: 31–40 Sex: F=0, M=60	(1) active ROM (flexion, extension, lateral flexion and rotation) (2) VAS (3) NDI	(1) After treatment, ROM ↑, VAS and NDI scores ↓ in both groups($p < 0.05$). (2) ROM ↑, and VAS scores ↓ was greater in HILT group than that in control group($p < 0.05$), but similar effect in NDI scores.
Yilmaz [22]	HILT and exercise	US, TENS, and exercise	cervical disc herniation (≥3 months)	N = 40 (E 20, C 20) Age: 30–48 Sex: F 22, M 18	(1) active ROM (flexion, extension, lateral flexion and rotation) (2) VAS (3) NPADS	(1) After treatment, ROM ↑, VAS and NPADS scores ↓ in both groups ($p < 0.05$). (2) Similar effect in ROM, VAS, NPADS scores was found between the two groups ($p > 0.05$).
Dundar [23]	HILT and exercise	placebo and exercise	MPS of the trapezius muscle (> 4 months)	N = 75 (E 38, C 37) Age: 26–53 Sex: F 75, M 0	(1) active ROM (flexion, extension, lateral flexion and rotation) (2) VAS (3) NDI (4) SF-36	(1) Improvement in all outcome indexes at weeks 4 and 12 in both groups($p < 0.05$). (2) Improvement in the NDI, VAS, and several subparts of the SF-36 were better in HILT group than that in control group ($p < 0.05$), while the other indexes showed no significant differences between two groups($p > 0.05$).
Haładaj [24]	HILT	traction therapy	cervical radicular syndrome	N = 174 (E 86, C 88) Age: 45.5 (mean) Sex: F 114, M 60	(1) active ROM (flexion, extension, lateral flexion and rotation) (2) VAS (3) NDI	(1) After treatment, ROM ↑, VAS and NPADS scores ↓ in both groups ($p < 0.05$), (2) Similar effect at weeks 4 and 12 between two groups ($p > 0.05$). (3) Greater effects with the HILT group after 12 weeks ($p < 0.05$).
Alayat [25]	HILT, PPRT, and exercise	placebo, PPRT and exercise	cervical MPS	N = 50 (E 25, C 25) Age: 23–33 Sex: F 26, M 34	(1) cervical ROM (flexion, extension, lateral flexion and rotation) (2) VAS (3) PPT	(1) Significant improvement in CROM, PPT, and VAS post-treatment in both groups ($p < 0.05$). (2) HILT group had a more significant effect ($p < 0.05$).
Abu Shady [26]	GroupB: HILT, IR, and IT GroupC: HILT, NDM, IR, and IT	GroupA: NDM, IR, and IT	cervical radiculopathy (> 6 months)	N = 60 (groupA=20, groupB=20, groupC=20) Age: 27–34 Sex: F 32, M 28	(1) cervical ROM (flexion, extension, lateral flexion and rotation) (2) VAS (3) NDI (4) hand grip strength	(1) After treatment, hand grip strength and ROM ↑, VAS and NDI scores ↓ in three groups ($p < 0.05$). (2) Group B and group C had a more significant effect than group A, while group C showed the most significant improvement ($p < 0.05$).

Table 2 (*Continued*)

First Author (years)	Experimental group	Control group	Participants		Outcomes	Main results
			Disease (duration of disease)	Total sample size (N)/ Age (years)/ Sex (F/M)		
Kenareh [27]	HILT and exercise	US and exercise	non-specific neck pain (≥ 6 months)	N = 60 (E 30, C 30) Age: 26–53 Sex: F 43, M 17	(1) VAS (2) NDI (3) NPADS (4) BQN	(1) After treatment, significant improvement in VAS, NDI, NPADS and BQN in both groups ($p < 0.05$). (2) The effect of HILT group was significantly higher than US group ($P < 0.05$).

RCT: randomized controlled trial; E: experimental group; C: control group; CNP: chronic neck pain; M: male; F: female MPS: myofascial pain syndrome; MTrPs: myofascial trigger points; HILT: high-intensity laser therapy; TENS: transcutaneous nerve stimulation; US: ultrasound; PPRT: progressive pressure release technique; NDM: neurodynamic mobilization; IR: infrared radiation; IT: interferential treatment; VAS: visual analog scale; ROM: range of motion; NDI: neck disability index; SF-36: short-form 36 health survey; NPADS: neck pain and disability scale; PPT: pressure pain threshold; BQN: bournemouth questionnaire for neck pain.

Interventions

Six RCTs [16,17,22,23,25,27] delivered HILT plus exercise as the experimental group, and the remaining two RCTs delivered HILT alone [24] or HILT in combination with neurodynamic mobilization/infrared radiation/interferential treatment [26]. The control group were placebo plus exercise [16,23,25], ultrasound (US)/transcutaneous electrical nerve stimulation (TENS) = plus exercise [17,22,27], cervical traction therapy [24], or neurodynamic mobilization/infrared radiation/interferential treatment [26]. The duration of treatment ranged from 2 to 6 weeks.

Outcome measures

The outcomes were pain intensity, cervical ROM, functional activity, and QOL. All of the studies [16,17,22–27] used the visual analogue scale (VAS) to assess pain intensity. Six RCTs [16,17,23,24,26,27] evaluated neck functional activity using the Neck Disability Index (NDI) and two RCTs [22,27] used the Neck Pain and Disability Scale. One RCTs [23] assessed QOL using the 36-Item Short Form Health Survey (SF-36).

HILT parameters

Six RCTs [16,17,22,23,25,26] used neodymium: yttrium–aluminum–garnet laser instruments, and two RCTs [24,27] did not report their laser source. The laser wavelength used in six RCTs was 1064 nm [16,17,22,23,25,26], while one RCT [24] reported a HILT wavelength of 980 nm. In terms of treatment protocols, all RCTs [16,17,22–27] used manual scanning and divided the laser treatments into two or three stages. A single session of HILT involved an irradiation time of 8–30 min, and the duration of the treatment program ranged from 2 to 6 weeks. The power, frequency, energy density, total energy dose, and treatment area were different across all of the included RCTs [16,17,22–27]. Details of the HILT protocols used are listed in Table 3.

Effect of HILT on pain intensity

All included RCTs [16,17,22–27] used the VAS to evaluate the pain intensity, but due to the difference in nature of the comparison groups between trials, only those trials that compared HILT with placebo were used for meta-analysis (4 trials, 225 participants) [16,23,25,26]. The results showed that HILT led to large improvement in pain intensity compared with placebo (SMD 2.12, 95%CI 1.24–3.00, $p < 0.05$; Fig. 2). The quality of evidence, as assessed by GRADE, was moderate (Table 4).

Two studies compared HILT with US combined with TENS. Venosa et al. [17] found greater reduction in pain intensity after HILT, but Yilmaz et al. [22] reported that both groups had similar results. Kenareh et al. [27]

Table 3
Characteristics of HILT parameters.

Parameter	Venosa et al. [17]	Alayat et al. [16]	Yilmaz et al. [22]	Dundar et al. [23]	Haładaj et al. [24]	Alayat et al. [25]	Abu Shady et al. [26]	Kenareh et al. [27]
Instrument	Nd:YAG laser HIRO®3 device (ASA, Arcugnano, Vicenza, Italy)	Nd:YAG laser HIRO®3 device (ASA, Arcugnano, Vicenza, Italy)	Nd:YAG laser (BTL brand 6000 series,United Kingdom)	Nd:YAG laser (HIRO®3.0; ASA laser, Arcugnano, Italy)	not available	Nd:YAG laser HIRO®3 device (ASA, Arcugnano, Vicenza, Italy)	Nd:YAG laser HIRO®3 device (ASA, Arcugnano, Vicenza, Italy)	VELAS II-15B device (Wuhan Gigaa Optronics Technology, China)
Wavelength (nm)	1064	1064	1064	1064	980	1064	1064	not available
Continuous/ Pulse	Pulse	Pulse	Pulse	Pulse	phase1: pulse phase2: continuous	Pulse	Pulse	not available
Power(W)	Peak 3000	Peak 3000	8 (peak 3000)	Peak 3000	phase1:600 mW phase2:300 mW	Peak 3000 Average 10.5	Peak 3000	phase1: 10 phase2: 7
Frequency (Hz)	10–40	10–40	25	10–40	25	15	10–40	25
Treatment protocol	phase1: fast manual scanning; phase2: fixed (8 trigger points); phase3: slow manual scanning	phase1: fast manual scanning; phase2: fixed (8 trigger points); phase3: slow manual scanning	manual scanning	phase1: fast manual scanning (100 cm² per 30 s); phase2: fixed (6 trigger points); phase3: slow manual scanning (100 cm² per 60 s)	manual scanning	perpendicularly to the predetermined trigger points in four phases	manual scanning performed longitudinally & transversely and perpendicular to the treated area	manual scanning
Total energy dose(J)	phase1: 1000/cm^2; phase2: 200; phase3:850	phase1: 1025; phase2: 200; phase3:1025	1850	phase1: 500; phase2: 60; phase3:500	phase1: 195; phase2:1250	phase1: 10/point phase2: 12.5/point phase3: 12.5/point phase4: 15/point	not available	not available
Energy Density (mJ/cm²)	510–1780 mJ/cm²	phase1: 360 and 510; phase2: 510; phase3: 360 and 510	5 J/cm²	phase1: 360,410,510; phase2:610; phase3: 360,410,510	phase1: 5 J/cm²; phase2:50 J/cm²	phase1: 510/point phase2: 610/point phase3: 710/point phase4: 810/point	510–1780	phase1: 15 J/cm²; phase2:100 J/cm²
Treatment area	the posterior neck on the paraspinal area, interscapular area, trapezius, sternocleidomastoid muscles bilaterally, and eight trigger points	the paraspinal area, upper back, interscapular area, trapezius and sternocleidomastoid muscles, and posterior and lateral shoulder areas. and eight trigger points	the bilateral paraspinal muscles, internal sides of the scapula, the upper trapezius and the neck region	the bilateral trapezius muscles, six trigger points over the trapezius muscle	the transverse processes of each of the cervical vertebrae, and muscles from the C_4 to T_4	at least 8 trigger points	the para-spinal area on the neck posterior aspect, upper back, inter-scapular area, trapezius, sternocleidomastoid muscles, and posterior & lateral shoulder areas.	not available

Table 3 (*Continued*)

Parameter	Venosa et al. [17]	Alayat et al. [16]	Yilmaz et al. [22]	Dundar et al. [23]	Haładaj et al. [24]	Alayat et al. [25]	Abu Shady et al. [26]	Kenareh et al. [27]
Irradiation Time	30 mins	15 mins	15 mins	15 mins	phase1:3.5 mins; phase2:6.5 mins	phase1: 7 s/point phase2: 7 s/point phase3: 6 s/point phase4: 6 s/point	15 mins	phase1: 3 mins; phase2: 6 mins
Frequency and (duration)	2 sessions/week (6 weeks)	2 sessions/week (6 weeks)	5 sessions/week (4 weeks)	15 sessions (3 weeks)	5 sessions/week (2 weeks)	3 sessions/week (4 weeks)	3 sessions/week (4 weeks)	10 sessions (2 weeks)

Nd:YAG: neodymium-doped yttrium aluminum garnet

compared HILT with US, and found that HILT led to was greater improvement in pain intensity. Haladaj et al. [24] compared HILT with traction therapy, and found that effect on pain intensity was similar at weeks 4 and 12 but HILT induced greater treatment effect after 12 weeks.

Effect of HILT on cervical ROM

Seven RCTs [16,17,22–26] examined the effects of HILT on cervical ROM. Compared with the placebo group, our meta-analysis involving of four RCTs [16,23,25,26] (225 participants) showed that HILT was effective in improving cervical flexion (SMD 1.31, 95%CI 0.27 to 2.35, $p < 0.05$; moderate quality evidence) (Fig. 3 and Table 4), extension (SMD 1.43, 95%CI 0.24 to 2.63, $p < 0.05$; moderate quality evidence) (Fig. 3 and Table 4), and right lateral flexion (SMD 1.36, 95%CI 0.15 to 2.56, $p < 0.05$; low quality evidence) (Fig. 3 and Table 4). However, there were no significant effects of HILT on left lateral flexion, right rotation, and left rotation between the two groups (low quality evidence) (Fig. 3 and Table 4).

HILT was compared with US combined with TENS in Venosa et al. [17] and Yilmaz et al. [22]. Superior effect of HILT on improving ROM was only found in the former study. Finally, Haladaj et al. [24] found that HILT was not more effective than traction therapy in improving cervical ROM at weeks 4 and 12 but was more superior after 12 weeks.

Effect of HILT on functional activity

Six RCTs [16,17,23,24,26,27] used the NDI to evaluate the functional activity. Compared with the placebo group, our meta-analysis of three RCTs [16,23,26] involving 175 participants revealed a trend of positive outcome for the HILT group (SMD 1.73, 95%CI −0.05 to 3.54, $p > 0.05$; low quality evidence) (Fig. 4 and Table 4). As indicated by the confidence intervals, there was a small chance that the placebo group had better outcome.

Compared with US combined with TENS, the decrease in NDI scores of the HILT group was greater in the study by Venosa et al. [17]. Kenareh et al. [27] found that HILT was more effective than US in functional activity. Haladaj et al. [24] showed that HILT and traction therapy had similar effect on functional activity at weeks 4 and 12 but the former had greater treatment effect after 12 weeks.

Effect of HILT on QOL

Only one RCT [23] reported the effect of HILT on QOL. Both the HILT and placebo groups induced similar improvements on total SF-36 score for QOL. However, more improvement in the specific subsections of the SF-36 (i.e., physical function, role-physical function, bodily pain, general health, social functioning, and role-emotional

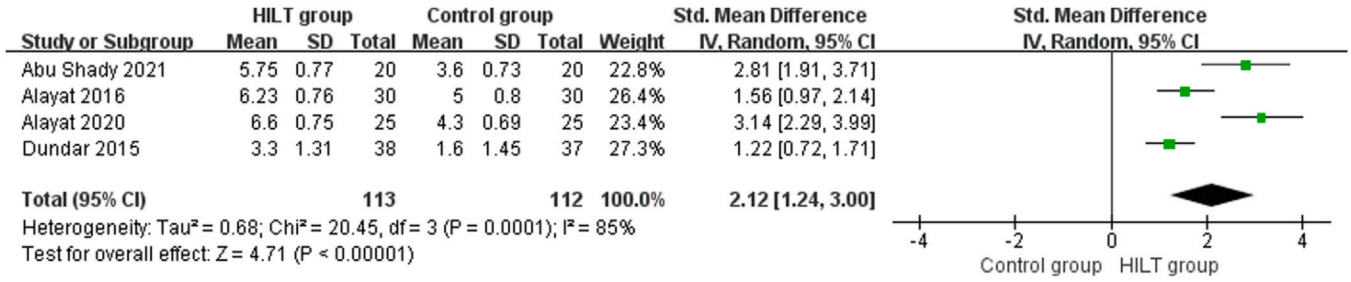

Fig. 2. Forest plot results for meta-analysis (weighted mean difference and 95% CI) of HILT on pain intensity compared with placebo. HILT: high-intensity laser therapy.

problems) was found in the HILT group compared with the placebo group.

Adverse effects

No adverse effects were reported in any of the RCTs [16,17,22–27] included in this systematic review.

Discussion

The primary objective of this meta-analysis was to determine whether HILT was effective in improving pain intensity, cervical ROM, functional activity and QOL in individuals with neck pain. Given the large variability in the treatment involved in the comparison groups across studies, meta-analysis was only possible for those trials that compared HILT with placebo. The results of meta-analysis showed that compared with placebo, HILT led to significant reduction in pain intensity and increase in cervical ROM (flexion, extension, right lateral flexion) among individuals with neck pain, but not left lateral flexion and rotation, and functional activity.

Effect of HILT on pain intensity

Our results suggested that HILT reduced pain intensity in individuals with neck pain compared with placebo. This finding was consistent with the findings of two previous systematic reviews [14,15] which showed that HILT was more effective than the control group in relieving pain in the neck area, according to their subgroup analysis by treatment regions.

Currently, the exact mechanisms underlying the pain-relieving effect induced by HILT are still inconclusive. Several potential mechanisms have been proposed. First, HILT has a photothermal effect, which increases blood circulation in local tissues and improves vascular permeability, thereby promoting the absorption of inflammatory substances and the clearance of inflammatory cells. The photothermal effect may make patients feel warmer and more comfortable. These may in turn reduce pain. Second, HILT has a stronger and broader photo-biomodulation effect on local tissues than LLLT. Thus, more adenosine triphosphate (ATP), proteins and other metabolic substances are produced by stimulated cells, thus boosting tissue metabolism [28–30]. Third, the laser may inhibit peripheral nociceptive receptors, slow nociceptive transmission and increase the secretion of pain-relieving substances in the body, thereby increasing pain thresholds [31–33].

Effect of HILT on cervical ROM

This meta-analysis revealed significant improvements in cervical flexion, extension, and right lateral flexion in the HILT group compared with the placebo group. A previous study [34] has reported that limited cervical ROM can occur due to factors such as pain and weak muscle strength. When neck pain is experienced, there is often an abnormal fear of movement that would lead to selective braking of the neck to avoid further aggravation of pain, which in turn results in limited cervical ROM [35]. The analgesic effect induced by HILT may partly explain the improvement in cervical ROM. In addition, the photothermal effect of HILT may also improve deep tissue flexibility, resulting in increased ROM.

Effect of HILT on functional activity

Overall, the effect of HILT on functional activity is not as prominent. This may be due to limited number of studies (n = 3) and a small overall sample size (n = 175) in the analysis [16,23,26]. Upon closer examination, Alayat et al. [16] reported no differences in functional activity between the two groups whereas the other two studies [23,26]

Table 4
Level of evidence by Grading of Recommendations Assessment, Development, and Evaluation (GRADE).

Outcome		Number of participants (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Level of evidence	Absolute Effects (95% CI)
Pain intensity		225(4)	0	-1[a]	0	0	0	Moderate	SMD 2.12 (1.24 to 3)
Cervical ROM	Flexion	225(4)	0	-1[a]	0	0	0	Moderate	SMD 1.31 (0.27 to 2.35)
	Extension	225(4)	0	-1[a]	0	0	0	Moderate	SMD 1.43 (0.24 to 2.63)
	Right Lateral Flexion	185(3)	0	-1[a]	0	-1[b]	0	Low	SMD 1.36 (0.15 to 2.56)
	Left Lateral Flexion	185(3)	0	-1[a]	0	-1[b c]	0	Low	SMD 1.04 (−0.21 to 2.28)
	Right Rotation	185(3)	0	-1[a]	0	-1[b c]	0	Low	SMD 1.45 (−0.21 to 3.12)
	Left Rotation	185(3)	0	-1[a]	0	-1[b c]	0	Low	SMD 0.96 (−0.2 to 2.12)
Functional activity		175(3)	0	-1[a]	0	-1[b]	0	Low	SMD 1.73 (−0.07 to 3.54)
Quality of life		75(1)	0	-1[e]	0	-1[b e]	-1[e]	Very low	/

HILT: high-intensity laser therapy; VAS: visual analog scale; NDI: neck disability index; NPADS: neck pain and disability scale; SF-36: short-form 36 health survey; NA: not available; CPT: conventional physical therapy.
[a]High heterogeneity $I^2 \geq 50\%$ in the primary and high methodological quality analysis.
[b]Sample size n < 200.
[c]The 95%CI failed to exclude important benefit.
[d]More than half of the included trials for outcome evaluation had a PEDro score ≤4.
[e]Insufficient studies for meta-analysis.

reported that HILT group was more effective in improving functional activity than placebo group. The discrepancies in results may be related to the difference in treatment dosage. The penetration and absorption of laser in biological tissues depends mainly on the treatment dose, which in turn is influenced by the distance from the skin to the damaged tissue, the treatment area and the frequency of HILT sessions [36,37]. A treatment frequency of two sessions weekly was used in Alayat et al. [16] whereas the other two studies involved more frequent treatment sessions (three sessions weekly [26] and five sessions weekly [23]). It is worth mentioning that two included RCTs [17,27] found HILT in combination with exercise induced greater improvement in functional activity than the control group. Furthermore, Haladaj et al. [24] indicated that HILT alone had greater improvement in functional activity after 12 weeks compared with traction therapy alone. Further research is required to examine the effects of HILT on functional activity.

Effect of HILT on QOL

Evidence on the use of HILT to improve QOL is limited, as the result is derived from one RCT only [23]. Although this study found positive effect of HILT on specific aspects of QOL, more research is required to determine the effects of HILT on QOL in individuals with neck pain.

Comparisons with other physiotherapy interventions

HILT was compared with US [27] and traction [24], but the result was based on one study only and no solid conclusion can be made. Although two studies [17,22] compared HILT with US plus TENS, conflicting results were reported. More research is needed to determine the relative effectiveness of HILT and other physiotherapy interventions in the treatment of people with neck pain.

Study limitations

There are a number of limitations to this systematic review and meta-analysis. First, the risk of bias on blinding of therapists/assessors may be high, mainly because of 88% of included RCTs were unblinded to therapists and 75% of included RCTs were unblinded to assessors. Second, there was high heterogeneity in participant conditions and key HILT parameters among the included RCTs [16,17,22–27]. Future studies should attempt identify the optimal treatment parameters/dose of HILT for neck pain. Third, including only RCTs published in English may have excluded potentially useful articles. Finally, long-term follow-up data were not available. Further research is warranted to assess the retention of treatment effect induced by HILT.

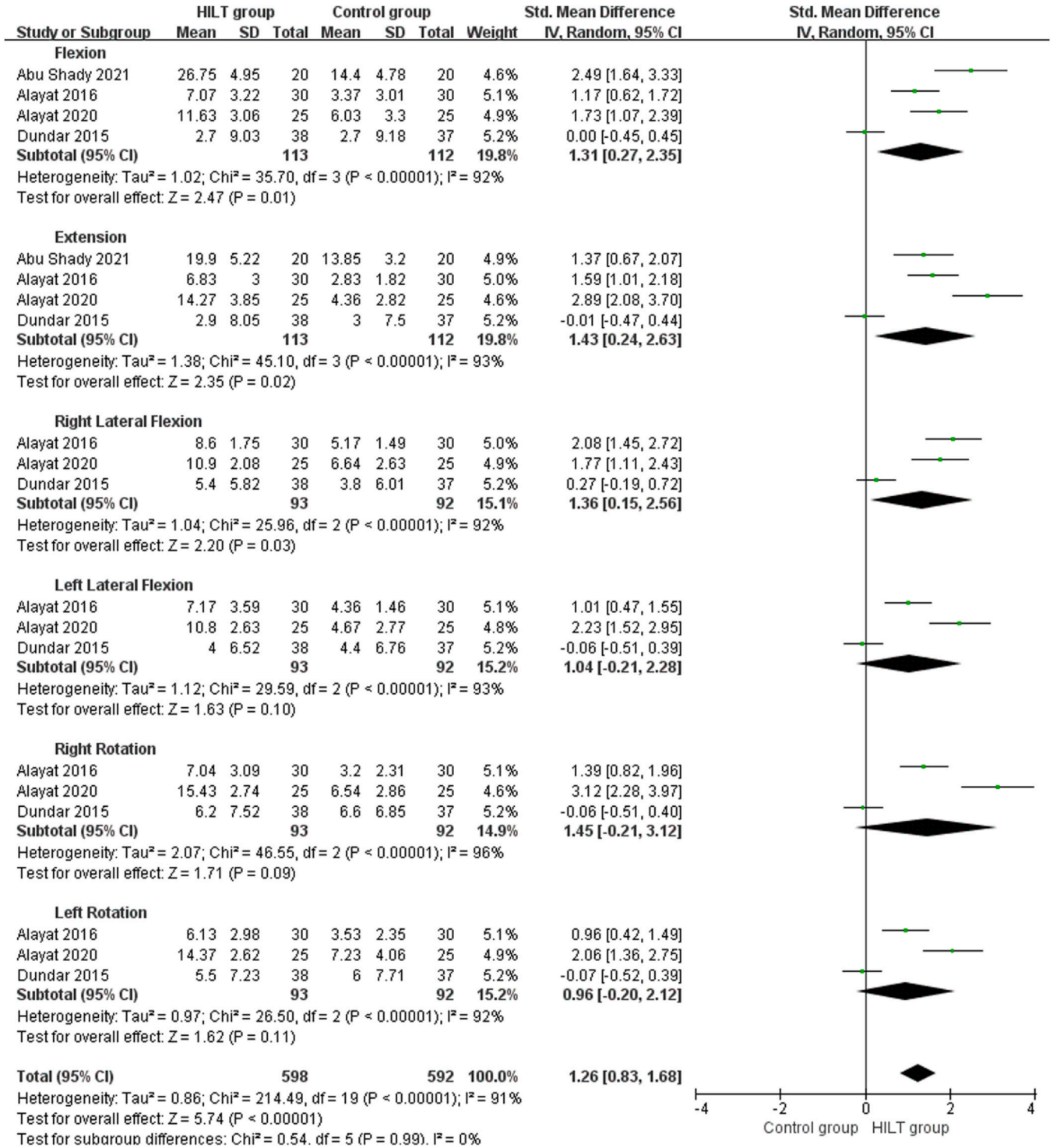

Fig. 3. Forest plot results for meta-analysis (weighted mean difference and 95% CI) of HILT on cervical range of motion compared with placebo. HILT: high-intensity laser therapy.

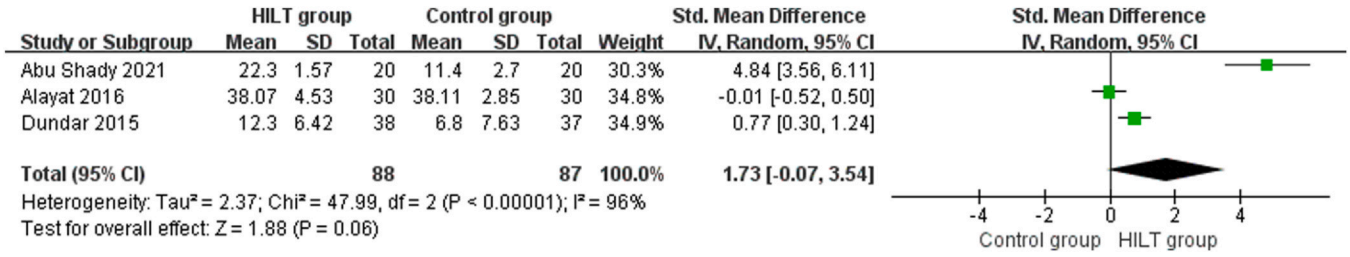

Fig. 4. Forest plot results for meta-analysis (weighted mean difference and 95% CI) of HILT on functional activity compared with placebo. HILT: high-intensity laser therapy.

Conclusion

In summary, HILT may be considered as an adjunctive treatment modality for individuals with neck pain. This meta-analysis showed moderate-quality evidence that HILT may improve pain intensity and cervical ROM in individuals with neck pain. Low quality evidence showed that HILT had a tendency to improve functional activity. The effect of HILT on QOL was examined in one study only. Future studies are needed to identify optimal HILT treatment protocol for reducing neck pain in various conditions, and the retention of treatment effects.

Author contributions

The idea for the study was conceived and designed by Linrong Liao and Yuhua Xie. The literature search was performed by Yueming Gu and Manxia Liao. The data analysis was performed by Yuhua Xie, Manxia Liao and W.C.Hewith.A.Fernando. Yuhua Xie wrote the first draft of manuscript. Yuhua Xie, Freddy MH Lam, Linrong Liao and Marco Y. C. Pang revised all drafts.

Acknowledgements

None.
Ethical approval: Not required.

Funding: This study was supported by the Dongguan Science and Technology of Social Development Program (Grant no. 20221800905692), China; and the Talent Development Foundation of the Dongguan First Affiliated Hospital of Guangdong Medical University (Grant no. GCC2022004), China.

Conflicts of interest

All authors have no conflicts of interest to declare.

Appendix 1. Search strategy for PubMed – move to online supplementary information

#	Searches	Results
1	"single-blind method"[Mesh] OR "double-blind method"[Mesh] OR "randomized controlled trial* "[Mesh] OR "controlled clinical trial* "[Mesh] OR "clinical trial* "[Mesh]	544,632
2	"random*" [Text Word] OR allocation [Text Word] OR "random allocation"[Text Word] OR placebo [Text Word] OR "single blind" [Text Word] OR "double blind" [Text Word] OR "randomized controlled trial* "[Text Word] OR RCT [Text Word]	16,77,299
3	"randomized controlled Trial" [Publication Type] OR "clinical trial" [Publication Type]	928,970
4	1 OR 2 OR 3	2,118,745
5	"neck"[Title/Abstract] OR "cervical"[Title/Abstract] OR "atlanto axial joint"[Title/Abstract] OR "atlanto occipital joint"[Title/Abstract]	452,613
6	neck pain [Mesh]	7871
7	neck pain* [Title/Abstract] OR neck ache* [Title/Abstract] OR Cervicalgia* [Title/Abstract] OR Cervicodynia* [Title/Abstract] OR Neckache [Title/Abstract] OR Cervical Pain [Title/Abstract]	7330
8	"sprain* "[Title/Abstract] OR "strain* "[Title/Abstract] OR "cervicogenic headache"[Title/Abstract] OR "cervicocranial syndrome"[Title/Abstract] OR "cervicobrachial syndrome"[Title/Abstract] OR "cervical spondylosis"[Title/Abstract] OR "cervical myelopathy"[Title/Abstract] OR "cervical radiculopathy"[Title/Abstract] OR "cervical disc disorder* "[Title/Abstract] OR "spinal instability"[Title/Abstract] OR "whiplash"[Title/Abstract]	801,975
9	5 OR 6 OR 7 OR 8	1,261,898
10	laser therapy [Mesh]	64,525
11	laser Therapy[Title/Abstract] OR therapy, laser[Title/Abstract] OR laser irradiation [Title/Abstract] OR laser biostimulation[Title/Abstract] OR laser phototherapy[Title/Abstract]	472

#	Searches	Results
12	phototherapy [Mesh]	48,545
13	phototherapy[Title/Abstract] OR photoradiation therapy[Title/Abstract] OR therapy, photoradiation[Title/Abstract] OR light therapy[Title/Abstract] OR therapy, light[Title/Abstract]	11,688
14	high-intensity laser therapy [Title/Abstract] OR high intensity laser therapy [Title/Abstract] OR high power laser therapy [Title/Abstract] OR high-power laser therapy [Title/Abstract] OR HILT[Title/Abstract] OR Nd: YAG [Title/Abstract] OR high-power laser irradiation [Title/Abstract] OR high power laser irradiation[Title/Abstract]	12,986
15	10 OR 11 OR 12 OR 13 OR 14	121,283
16	4 AND 9 AND 15	621

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