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Review

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Efficacy of ultrasound-guided perineural injections of the median nerve: A systematic review

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Abstract

Objectives: In this review, we discuss the efficacy of ultrasound (US)-guided versus landmark (LM)-guided median perineurial nerve injections in carpal tunnel syndrome (CTS).

Materials and methods: Initial search of PubMed, Scopus, Web of Science, and Emboss databases using search terms such as "median neuropathy," "ultrasound-guided," and "median nerve injection" from October 1966 to May 2023 yielded 4,172 articles to be screened by one reviewer for eligibility and two reviewers for full-text review. The study quality of the resulting 12 articles was assessed using the Newcastle-Ottawa Scale (NOS) and Revised Cochrane Risk of Bias Tool of Randomized Trials (RoB 2).

Results: All 12 articles reviewed evaluated efficacy of US-guided injections relative to LM-guided injections. Nine studies showed improved outcomes in US-guided injections compared to LM-guided, including improvement in the Boston Carpal Tunnel Syndrome Symptom Severity Scale and Functional Status Scale and improvement in procedural pain and injection pain.

Conclusion: Both US-guided and LM-guided median perineurial nerve injections can improve outcomes in patients with CTS. However, further studies are warranted to assess the accuracy of US-guided median perineurial nerve injections compared to LM-guided to effectively conclude whether one technique is superior to the other.

Keywords: Anatomic landmarks, median nerve injection, median neuropathy, ultrasound-guided.

Carpal tunnel syndrome (CTS) is a common cause of pain, paresthesia, and weakness in the median nerve distribution that can be debilitating. Options for conservative treatment include resting wrist splints and the placement of injectate surrounding the median nerve inside the carpal tunnel. Types of injectates include glucocorticoids and regenerative agents such as 5% dextrose and platelet-rich plasma.[1] These conservative measures can delay or prevent the need for surgical release of the carpal tunnel. Accurate placement of injectate is necessary to provide the most symptomatic relief and to avoid further injury to the median nerve. Current techniques for carpal tunnel injection include the use of landmark (LM) and ultrasound (US) guidance. Anatomic LMs of

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the distal wrist crease and palmaris longus tendon are used during the former technique. With US guidance, the median nerve can be directly visualized to bathe the median nerve within the carpal tunnel both superiorly and inferiorly.

In recent years, US-guided procedures have increasingly become more prevalent as evidenced by many studies and systematic reviews demonstrating its utility.[2-10] However, there is still a lack of literature directly comparing the efficacy of US-guided injections versus other modalities of injection such as LM-guided ones. In this review, we discuss the efficacy of US- and LM-guided median perineurial nerve injections in CTS patients in the light of literature data.

MATERIALS AND METHODS

Search strategy

For our initial search, PubMed, Scopus, Web of Science, and Embase databases were utilized with search terms such as "median neuropathy," "ultrasound-guided," and "median nerve injection." A full list of search terms is included in the supplementary materials. (See Supplementary Table 1). These databases were searched from October 1966 to May 2023. The most recent date of the literature search was June 19, 2023. This search generated 6,345 articles with 2,178 duplicates removed, leaving 4,172 to be screened. Those articles were, then, screened by title and abstract to only include human studies written in English with a comparison intervention using the same injectate, leaving 28 studies for full-text review. After full-text review, 12 articles were unanimously chosen by the first and second authors to ultimately be included in the systematic review (Figure 1).

Assessment of study quality

Each study was evaluated using either the Newcastle-Ottawa Scale (NOS) or the Revised Cochrane Risk of Bias Tool for Randomized Trials

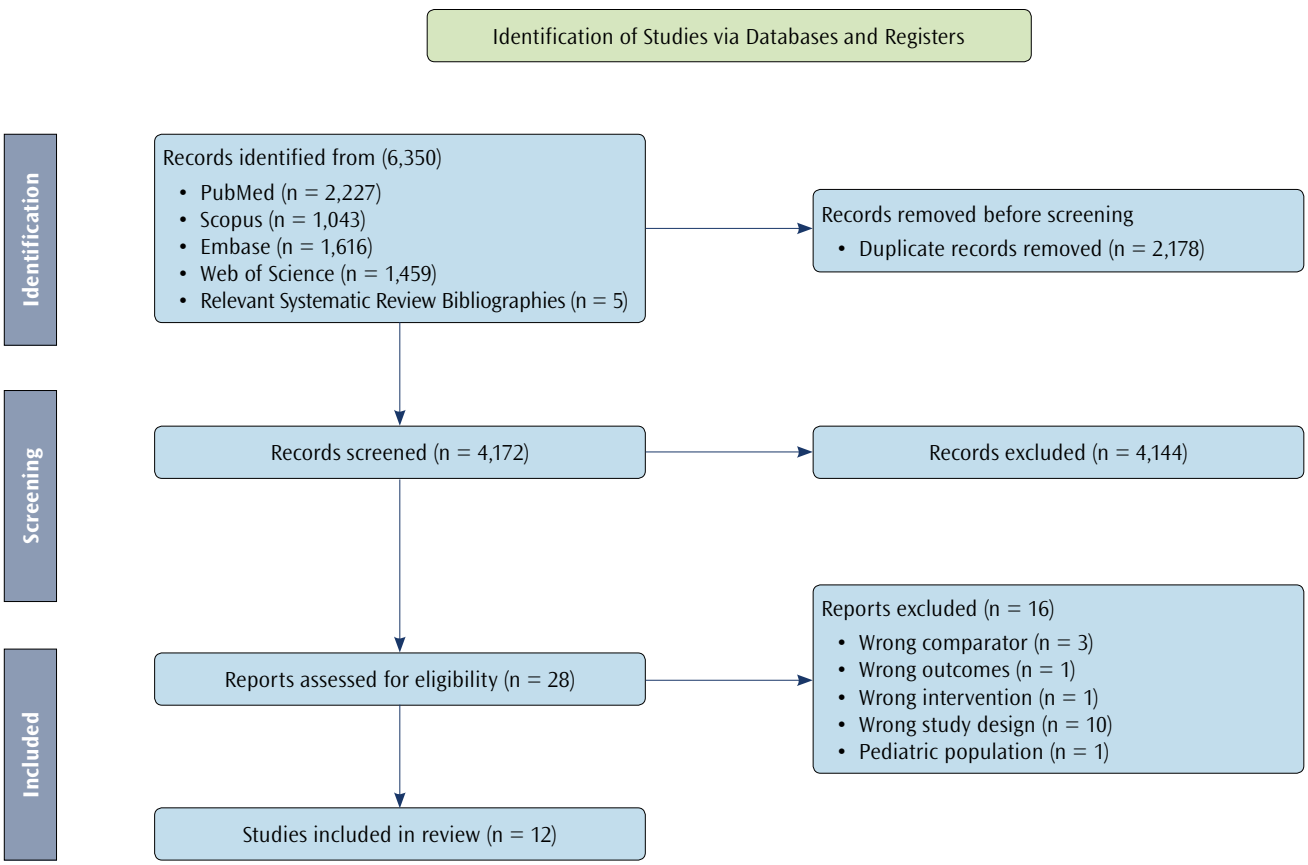


Figure 1. Flow diagram.

(RoB 2). The NOS assesses cohort and case control studies in terms of selection bias, comparability, and exposure/outcome by assigning points to each criterion with a maximum score of nine points indicating low risk of bias. The RoB 2 assesses randomized trials based on factors involved in the randomization process, study intervention, missing outcome data, measurement of outcome, selection of reported result. A grade of high risk of bias in any category results in an overall high risk of bias.

RESULTS

Overview

All 12 of the studies included in this review compared the efficacy of US-guided injections to LM-guided injections (Table 1). Nine of the studies were randomized clinical trials, two were cohort studies, and one was case control. Injection location varied where one study compared US in-plane and US out-of-plane injections relative to LM.[7] Follow-up time ranged from 12 weeks to one year. Due to the nature of the intervention, most of the studies had difficulty with blinding, thereby resulting in an increased risk of bias (Table 2a). Some of the studies were single-blind, while others were double-blind. Objective measurements to evaluate efficacy included the Boston Carpal Tunnel Syndrome Questionnaire (BCTQ), Visual Analog Scale (VAS), electrodiagnostics, and rate of retreatment following steroid injection. As there was heterogeneity in the studies, designs, and outcomes, A particular caution was exercised regarding the generalizability of our results.

Risk of bias assessment

Of the 12 studies, three were observational and assessed using the NOS. All the studies lost at least one point in comparability for lack of blinding of the participants. The study by Omar et al.[9] and Dabees[2] lost a point for inadequate follow up period. The study by Evers et al.[4] lost a point for ascertainment of exposure and imbalance in LM-guided and US-guided groups.[4] The other nine studies were assessed by the RoB 2, and all but one study was found to have high risk of bias. The summary of these evaluations is given in Tables 2a and b.

Median perineurial nerve injection efficacy

Of the 12 studies included in this review, nine showed improved outcomes in US-guided injections compared to LM-guided. Dabees,[2] Karaahmet et al.,[6] Lee et al.,[7] and Rayegani et al.[10] found a statistically significant difference in improvement of US-guided relative to LM-guided injections for the BCTQ Symptom Severity Scale (SSS) and Functional Status Scale (FSS). Dabees[2] found US-guided improved BCTQ-SSS and -FSS by 86.66% (p = 0.002) compared to LM-guided 53.33% (p = 0.252). Karaahmet et al.[6] found BCTQ-SSS change after treatment 17.1 for US-guided and 7.9 for LM-guided (p = 0.001) and BCTQ-FSS change after treatment 12.0 for US-guided and 5.0 for LM-guided (p < 0.001). Lee et al.[7] found significant changes for BCTQ-SSS LM-guided (20.18; p<0.05), US in-plane (12.18; p<0.05), and US out-of-plane (17.41; p < 0.05) and for BCTQ-FSS LM-guided (10.18; p < 0.05), US-in plane (8.76; p < 0.05), and US-out of plane (10.18; p < 0.05). Rayegani et al.[10] observed an improvement in BCTQ-FSS US ulnar in-plane (12.15; p = 0.023), US midline in-plane (12.63; p = 0.019), and LM-guided (14.74; p = 0.000). Dabees[2] found significant improvement of US-guided injections relative to LM-guided in terms of reduction in diameter of median nerve (US 92.31%, LM-guided 40% chi-square 7.304; p = 0.007), normal echogenicity of median nerve (US 100%, LM-guided 57.14% chi-square 6.107; p = 0.013), and return of normal thickness of flexor retinaculum (US-guided 83.33%, LM-guided 37.50% chi-square 3.13; p = 0.044). The retrospective cohort study by Evers et al.[4] found that a higher percentage of LM-guided injections required retreatment and eventual surgery compared to US-guided injections with an odds ratio of retreatment of US-guided compared to LM-guided within one year of 0.45. Makhlouf et al.[8] reported a significant improvement of US-guided relative to LM-guided in pain at two weeks (p = 0.014), reduction in pain from baseline (p = 0.028), pain from baseline at six months (p=0.001), duration of therapeutic effect (p = 0.001), time to next procedure (p = 0.035), needle introduction procedural pain (p = 0.02), and injection pain (p = 0.001).

Table 1. Summary of included studies

No.	Study	Objective	Design	Country	Age in Years (range)	Eligibility Criteria	Number of cases and controls	Results
1	Chen et al.,[11] 2018	To compare 6 month outcomes of US guided *vs.* LM-guided injection in CTS patients	Double-blind randomized controlled trial	Taiwan	US-guided (mean, SD) = 51.09 ± 10.09	Inclusion criteria: (1) age 18-80 years; (2) ≥2 of the following symptoms: nocturnal paresthesia; symptomatic relief after shaking hands; pain or paresthesia when hand gripping; or sensory symptoms over thumb, index, middle, or part of ring fingers; (3) symptom duration ≥1 month; (4) mild to moderate CTS Exclusion criteria: (1) symptomatic CTS due to DM, TD, CKD (2) absence of median motor and sensory response in electrodiagnostic tests; (3) muscle atrophy of APB; (4) traumatic nerve injury; (5) peripheral polyneuropathy; (6) previous surgery or local CSI affected wrists; (7) pregnancy; (8) cognitive impairment or other psychiatric disorders; (9) inability to complete 6-month follow-up	US-guided = 22 wrists LM-guided = 17 wrists	US guided change *vs.* LM-guided change from baseline to 6 months Semmes-Weinstein Monofilament Test **1 month 0.71 ($p < 0.01$)** 3 months 0.21 6 months -0.11 **Group *p*-value 0.031** **Time *p*-value < 0.001** **Group-time p-value 0.004** Grip Strength Group *p*-value 0.108 Time *p*-value 0.006 Group-time *p*-value 0.753 Lateral pinch strength Group *p*-value 0.643 **Time *p*-value 0.012** Group-time *p*-value 0.421 Symptom Severity Scale Group *p*-value 0.211 **Time *p*-value 0.001** Group-time *p*-value 0.893 Functional Status Scale Group *p*-value 0.191 **Time *p*-value < 0.001** Group-time *p*-value 0.936 Visual Analog Scale Group *p*-value 0.363 **Time *p*-value < 0.001** Group-time *p*-value 0.944 Distal motor latency Group *p*-value 0.565 **Time *p*-value < 0.001** Group-time *p*-value 0.183 Compound muscle action potential Group *p*-value 0.583 Time *p*-value 0.065 Group-time *p*-value 0.898 Sensory distal latency, peak Group *p*-value 0.167 Time *p*-value 0.006 Group-time *p*-value 0.781 Sensory distal latency, onset Group *p*-value 0.123 **Time *p*-value 0.001** Group-time *p*-value 0.083 Sensory nerve conduction velocity Group *p*-value 0.424 **Time *p*-value 0.004** Group-time *p*-value 0.038 Sensory nerve action potential amplitude Group *p*-value 0.845 Time *p*-value 0.111 Group-time *p*-value 0.723 Digit4 comparison study Group *p*-value 0.921 **Time *p*-value < 0.001** **Group-time *p*-value 0.046**
2	Dabees[2] 2015	To evaluate role of ultrasound guided steroid injection in treatment of carpal tunnel syndrome	Prospective comparative study	Egypt	Age range = 20–60 years Mean age = 40 years	Inclusion criteria: Patients with idiopathic CTS diagnosed by clinical examination, electrophysiological study, and ultrasound. Patients with mild to moderate symptoms of carpal tunnel syndrome, who failed responding to other methods of treatment and / or those refused surgery Exclusion criteria: Male and female patients with parkinsonism, traumatic nerve injury, previous steroid injection in the same wrists and other causes of neuropathy	Total cases = 30 US-guided cases = 15 LM-guided cases = 15 26 females 4 males	Improvement after Steroid Injection Symptomatic Severity and Functional Evaluation by BCTQ **US-guided 86.66% $p = 0.002$** LM-guided 53.33% $p = 0.252$ Reduced diameter median nerve **US-guided 92.31%** LM-guided 40% **Chi square 7.304 ($p = 0.007$)** Normal echogenicity median nerve **US-guided 100%** LM-guided 57.14% **Chi square 6.107 ($p = 0.013$)** Relieved flattening and return to normal axis US-guided 66.67% LM-guided 50% Chi square 0.194 ($p = 0.659$) Returned of normal thickness of FR **US-guided 83.33%** LM-guided 37.50% **Chi square 3.13 ($p = 0.044$)**

Table 1. Continued

No.	Study	Objective	Design	Country	Age in Years (range)	Eligibility Criteria	Number of cases and controls	Results
3	Eslamian et al.[3] 2017	Compare clinical and electrodiagnostic efficacy of US-guided versus LM-guided steroid injections in patient with CTS	Randomized Clinical Trial	Iran	US-guided, mean ± SE 54.52 ± 2.05 LM-guided, mean ± SE 49.33 ± 1.82	Inclusion criteria: Primary moderate idiopathic CTS with a clinical and electrodiagnostic conformation of CTS, as well as: (1) hand numbness and tingling or pain in the distribution of the median nerve, (2) nocturnal worsening of the symptoms, (3) positive Tinel and/or Phalen sign, (4) the desire of the participant to have a corticosteroid injection Exclusion criteria: (1) thenar atrophy, (2) prior carpal tunnel decompressive surgery, (3) previous corticosteroid injection of CTS in the preceding 6 months, (4) polyneuropathy as documented on nerve conduction studies, (5) the presence of infection or skin lesion at the site of injection, (6) severe CTS in EMG presenting with Fib/PSW in median innervated hand muscles, (7) low-amplitude median CMAP <2 mV, (8) active cervical radiculopathy confirmed with electrodiagnosis or MRI study, (9) history of wrist fracture, and (10) refusal of informed consent or inability to participate in follow-ups	US-guided cases = 30 LM-guided = 30	Clinical and Functional Evaluations Mean ± SE BCTQ symptom: US-guided baseline 3.03 ± 0.13 **US-guided week 12 1.63 ± 0.10 ($p < 0.001$)** LM-guided baseline 3.39 ± 0.11 **LM-guided week 12 1.95 ± 0.15 ($p < 0.001$)** US-guided *vs.* LM-guided improvement $p = 0.798$ BCTQ function: US-guided baseline 2.68 ± 0.13 **US-guided week 12 1.54 ± 0.97 ($p < 0.001$)** LM-guided baseline 2.68 ± 0.11 **LM-guided week 12 1.61 ± 0.12 ($p < 0.001$)** US-guided *vs.* LM-guided improvement $p = 0.645$ BCTQ total: US-guided baseline 2.86 ± 0.12 **US-guided week 12 1.58 ± 0.09 ($p < 0.001$)** LM-guided baseline-3.08 ± 0.10 **LM-guided week 12 1.80 ± 0.13 ($p < 0.001$)** US-guided *vs.* LM-guided improvement $p = 0.299$ SNAP amplitude: US-guided baseline 17.2 ± 1.64 US- guided week 12 18.56 ± 1.09 ($p = 0.194$) LM-guided baseline 15.86 ± 0.18 **LM-guided week 12 21.79 ± 1.93 ($p < 0.001$)** **US-guided *vs.* LM-guided improvement $p = 0.003$**
4	Evers et al.[4] 2017	Compare effectiveness of US-guided injections to LM-guided injections in treatment of CTS	Retrospective Cohort Study	United States	LM-guided group (mean, SD) = 50 ± 14 US-guided group (mean, SD) = 50 ± 15	Inclusion criteria: Current Procedural Terminology (CPT) code for diagnosis of carpal tunnel syndrome (ICD-9 354.0) and carpal tunnel injection (CPT-20526). Patients with an age of 21–80, diagnosis of carpal tunnel syndrome and a follow-up of at least one year after initial injection were included in the study. Exclusion criteria: Patients were excluded if they received surgical carpal tunnel release prior to injection	Total cases = 533, 689 hands US-guided cases = 89 hands LM-guided cases = 600 hands	Retreatment: US-55% LM-72% Eventual surgery: US-44% LM-64% **Retreatment- free survival US group HR 0.59 (95% CI 0.37–0.93)** **OR retreatment within one year US group compared to LM group: 0.45 (95% CI 0.24–0.83)**
5	Karaahmet et al.[6] 2017	Compare effectiveness of US- guided injection *vs.* LM-guided injection of corticosteroids for carpal tunnel syndrome	Prospective Randomized Clinical Trial	Turkey	LM-guided group (mean, SD) = 61.5 ± 10.3 US-guided group (mean, SD) = 59.4 ± 12.4	Inclusion criteria: Patients who presented to the physical medicine and rehabilitation outpatient clinic and were treated with a steroid injection using US-guided versus LM-guided techniques for severe CTS. Patients with severe idiopathic CTS according to clinical diagnosis and a validated CTS electrophysiological severity scale were included in this study. All patients had complaints of paresthesia and/or numbness along the median nerve distribution area of the hand with nocturnal worsening. Exclusion criteria: Patients with systemic diseases such as inflammatory rheumatic disease, diabetes mellitus, thyroid disease, history of CTS surgery, or peripheral nerve lesion of the forearm were excluded from the study.	Total cases = 31 US-guided cases = 15 LM-guided cases = 16	Boston Symptom Severity Scale (BSSS) change after treatment: **US-17.1 ± 8.6** **LM-7.9 ± 6.7** **p = 0.001** Functional Status Scale (FSS) change after treatment: **US-12.0 ± 4.7** **LM-5.0 ± 5.6** **$p < 0.001$** SNAP change after treatment **US-3.9 ± 5.3** **LM-12.1 ± 14.7** **$p = 0.022$** SNCV change after treatment **US-6.8 ± 10.8** **LM-13.3 ± 12.5** **$p = 0.008$** DML change after treatment US-1.2 ± 0.7 LM-1.3 ± 0.9 $p = 0.079$ CMAP change after treatment US-0.9 ± 1.3 LM-1.7 ± 1.9 $p = 0.101$ Cross sectional area median nerve US guided pre-treatment 0.18 ± 0.04 US guided post-treatment 0.15 ± 0.05

Table 1. Continued

No.	Study	Objective	Design	Country	Age in Years (range)	Eligibility Criteria	Number of cases and controls	Results
6	Lee et al.[7] 2014	Evaluate degree of symptom improvement and change of electrophysiological and ultrasonographic findings after US-guided steroid injection using in-plane ulnar approach in CTS	Prospective randomized single-blind clinical trial	South Korea	In-plane ulnar approach injection group (mean, SD) = 55.2 ± 13.2 Out-plane injection group (mean, SD) = 52.6 ± 11.6 LM-guided (mean, SD) = 50.3 ± 9.6	Inclusion criteria: Patients with mild to moderate idiopathic CTS with a neurophysiological confirmation were included in this study. Mild and moderate CTS were defined as slowing of the sensory conduction velocity and/or abnormal distal motor latency according to a validated CTS electrophysiological severity scale. We investigated outpatients with idiopathic CTS diagnosed by physical examination and electrodiagnosis. All patients had complaints of paresthesia or numbness in the median nerve distribution area of the hand with nocturnal worsening for a period of at least 3 months. Exclusion criteria: Symptomatic CTS because of diabetes, thyroid disease or rheumatic disease, age < 18 years, pregnancy, previous treatment of CTS, previous fracture or deformities at the wrist, cervical radiculopathy, and other polyneuropathy	Total cases = 44 patients, 75 hands In-plane ulnar approach injection group = 15 patients, 26 hands Out-plane injection group = 14 patients, 24 hands LM-guided = 15 patients, 25 hands	DML after 12 weeks LM-guided 4.68 ± 2.08 **US in-plane 4.08 ± 0.78 (p < 0.05 *vs.* baseline)** US out of plane 4.71 ± 1.48 CMAP LM-guided 11.09 ± 4.97 **US in-plane 14.50 ± 4.57 (p < 0.05 *vs.* baseline)** **US out of plane 13.31 ± 5.01 (p < 0.05 *vs.* baseline)** SDL2 LM-guided 4.08 ± 1.67 **US in- plane 4.18 ± 1.12 (p < 0.05 vs. baseline)** **US out of plane 3.98 ± 0.67** **(p < 0.05 *vs.* baseline)** SNAP2 **LM-guided - 13.03 ± 8.72 (p < 0.05 *vs.* baseline)** **US out of plane - 18.01 ± 8.92 (p < 0.05 *vs.* baseline and 4 weeks)** **US in-plane - 14.21 ± 9.01** **(p < 0.05 *vs.* baseline)** Median to Ulnar Sensory Nerve Distal Latency Ratio LM-guided 1.93 ± 0.87 US out of plane 1.82 ± 0.99 **US in-plane 1.17 ± 0.78 (p < 0.05 *vs.* baseline)** SSS of BCTQ: **LM-guided 20.18 ± 0.78 (p < 0.05 *vs.* baseline)** **US in-plane 12.18 ± 6.63(p < 0.05 *vs.* baseline)** **US out of plane 17.41 ± 5.78** **(p < 0.05 *vs.* baseline and 4 weeks)** FSS of BCTQ: **LM-guided 10.18 ± 7.14 (p < 0.05 *vs.* baseline)** **US in-plane 8.76 ± 3.86 (p < 0.05 *vs.* baseline)** **US out of plane 10.18 ± 6.88** **(p < 0.05 *vs.* baseline)**
7	Makhlouf et al.[8] 2014	To evaluate whether sonographic needle guidance affects outcomes of corticosteroid injection for symptomatic carpal	Randomized Controlled Trial	United States	LM-guided group (mean, SD) = 52.2 ± 9.7 US-guided group (mean, SD) = 45.7 ± 14.8	Inclusion criteria for participants with carpal tunnel syndrome included (1) hand numbness and tingling in the distribution of the median nerve, (2) decreased grip strength, (3) persistent hand pain, (4) nocturnal hand pain, (5) significant pain in the affected hand by 0–10 cm Visual Analogue Pain Sale (VAS) where VAS ≥ 5 cm, (6) positive Tinel's and/or Phalen's sign, (7) failure of splinting and/or hand rest, and (8) the desire of the participant to have a corticosteroid injection Exclusion criteria included (1) thenar atrophy, (2) prior carpal tunnel decompressive surgery, (3) the diagnosis of thoracic outlet syndrome, (4) non-carpal tunnel syndrome polyneuropathy as documented on electromyogram/ nerve con- duction studies, (5) hemorrhagic diathesis, (6) use of warfarin or antiplatelet drugs, (7) the presence of infection, or (8) previous corticosteroid injection into the carpal tunnel in the preceding 6 months.	US-guided cases = 37 LM-guided cases = 40	Pain at 2 weeks (10 cm VAS): LM 3.0 ± 3.3 cm US 1.1 ± 1.7 cm **63.3% difference *p* = 0.014** Reduction in pain from baseline (10 cm VAS) LM 4.4 ± 2.7 cm *p* < 0.001 US 6.1 ± 2.3 cm *p* < 0.001 **38.6% difference *p* = 0.028** Pain at 6 months (10 cm VAS): LM 6.1 ± 2.8 cm US 3.1 ± 3.1 cm **49.1% difference *p* = 0.001** Duration of therapeutic effect (months): LM 3.1 ± 2.0 US 5.3 ± 1.3 **71.0% *p* = 0.001** Time to next procedure (months) (reinjection or referral to surgery): LM 7.0 ± 3.2 US 9.1 ± 3.1 **30.0% difference *p* = 0.035** Needle Introduction Procedural Pain (VAS) LM 4.7 ± 2.6 US 3.1 ± 2.1 **34% difference *p* = 0.02** Injection Pain LM 3.5 ± 3.9 US 0.8 ± 1.3 **77.1% difference *p* = 0.001**

Table 1. Continued

No.	Study	Objective	Design	Country	Age in Years (range)	Eligibility Criteria	Number of cases and controls	Results
8	Omar et al.[9] 2018	Compare clinical outcomes of US-guided injection *vs.* LM-guided for management of CTS	Prospective comparative study	Egypt	LM-guided group (mean, SD, range) = 35.8 ± 8.6, 25–60 US-guided group (mean, SD, range) = 34.9 ± 6.6, 25–45	Inclusion criteria: Patients diagnosed both clinically and electro-physiologically with carpal tunnel syndrome were included. Mononeuropathy at wrist with prolonged distal latency, that does not have evidence of axonal involvement in electrophysiologic studies were considered and disease duration not exceeding a year. Exclusion criteria: Patients with history of previous carpal tunnel surgery, patients known to have CTS due to systemic illness and/ or connective tissue disease.	US-guided cases = 15 LM-guided cases = 15	BCTQ-SSS after treatment: **LM-13% normal, 40% minimal, 34% mild, 13% moderate $p = 0.05$** **US-40% normal, 34% minimal, 26% mild $p = 0.03$** US *vs.* LM $p = 0.24$ BCTQ-FSS after treatment: **LM-13% normal, 40% minimal, 34% mild, 13% moderate $p = 0.05$** **US-40% normal, 34% minimal, 26% mild $p = 0.03$** NCS: **LM-6% normal, 6% minimal, 86% mild $p < 0.0001$** **US-26% normal, 60% minimal, 13% mild $p < 0.0001$** Cross Sectional Area **LM-6% normal, 53% mild, 40% moderate $p < 0.0001$** **US-46% normal, 53% mild $p = 0.005$** Flattening Ratio **LM-73% low, 26% high $p < 0.0001$** **US-low 100% $p < 0.0001$**
9	Rayegani et al.[10] 2019	To investigate value of US on improving efficacy of local triamcinolone injection	Single-blinded randomized parallel trial	Iran	Ulnar In-Plane (mean, SD) = 54.39 ± 9.3 US-Midline In-Plane (mean, SD) = 54.56 ± 9.6 LM-Guided (mean, SD) = 54.04 ± 10.3	Inclusion criteria: Patients who presented or referred with CTS symptoms to electrodiagnosis (EDX) clinic of Shohada-e-Tajrish hospital. The diagnosis, as well as the severity grade, was confirmed using EDX Exclusion criteria: pregnancy, severe CTS grade in EDX or thenar atrophy, history of diabetes mellitus, rheumatoid arthritis or thyroid disorders, prior relevant surgery or hand trauma, any local injection in the wrist during the last 6 months, and active cervical radiculopathy or other peripheral neuropathies in the upper extremity	Ulnar In-Plane cases = 26 US-Midline In-Plane cases = 27 LM-Guided cases = 23	VAS after treatment: **US (ulnar in-plane)-2.41 ± 1.79 $p = 0.009$** **US (midline in-plane)-2.8 ± 2.04 $p = 0.001$** **LM-3.04 ± 1.98 $p = 0.023$** Pain-free grip strength: **US (ulnar in-plane)-28.67 ± 10.41 $p = 0.001$** **US (midline in-plane)-25.37 ± 9.12 $p = 0.000$** **LM-28.59 ± 12.7 $p = 0.000$** BCTQ-SSS: US (ulnar in-plane)-16.35 ± 6.21 $p = 0.542$ US (midline in-plane)-18.81 ± 7.99 $p = 0.089$ LM-21.7 ± 10.47 $p = 0.20$ BCTQ-FSS: **US (ulnar in-plane)-12.15 ± 5.28 $p = 0.023$** **US (midline in-plane)-12.63 ± 4.03 $p = 0.019$** **LM-14.74 ± 7.58 $p = 0.000$** CSA: US (ulnar in-plane)-0.163 ± 0.15 $p = 0.777$ **US (midline in-plane)-0.128 ± 0.02 $p = 0.000$** LM-0.131 ± 0.03 $p = 0.374$ SNAP amp: **US (ulnar in-plane)-29.53 ± 10.77 $p = 0.000$** **US (midline in-plane)-27.88 ± 11.53 $p = 0.000$** **LM-28.62 ± 8.57 $p = 0.000$** SNAP lat: **US (ulnar in-plane)-4.14 ± 0.47 $p = 0.000$** **US (midline in-plane)-4.17 ± 0.49 $p = 0.000$** **LM-4.12 ± 0.54 $p = 0.000$** CMAP amp: **US (ulnar in-plane)-7.66 ± 2.33 $p = 0.000$** **US (midline in-plane)-7.18 ± 1.63 $p = 0.000$** **LM-6.85 ± 1.93 $p = 0.000$** CMAP lat: US (ulnar in-plane)-4.35 ± 0.57 US (midline in-plane)-4.35 ± 0.56 LM-4.32 ± 0.66 NCV: **US (ulnar in-plane)-53.6 ± 4.51 $p = 0.004$** **US (midline in-plane)-54.74 ± 5.74 $p = 0.000$** **LM-56.47 ± 6.05 $p = 0.001$**

Table 1. Continued

No.	Study	Objective	Design	Country	Age in Years (range)	Eligibility Criteria	Number of cases and controls	Results
10	Roh et al.[12] 2019	Compare effectiveness and complications of US- guided steroid injections with LM-guided injections for CTS	Prospective Randomized Trial	South Korea	LM-guided group (mean, range) = 55 (37-66) US-guided group (mean, range) = 54 (35-64)	Inclusion criteria: Patients who had been diagnosed with CTS. Patients were eligible if their diagnosis of CTS was based on clinical symptoms and findings on the physical examination with confirmation by nerve conduction studies; if the CTS symptoms did not improve following 2 months of nonsurgical treatment consisting of the use of nonsteroidal anti-inflammatory drugs and orthosis wear; and if they had sufficient cognitive and language function to provide informed consent and complete a self-reported questionnaire. The pertinent history and symptoms included paresthesia and/or pain in at least 2 of the median nerve innervated fingers. Other symptoms included weakness and loss of dexterity of the hand. We conducted physical examinations for sensory loss, decreased thenar muscle strength, Tinel sign, and Phalen test to rein- force the diagnosis. Electrophysiological studies were performed prior to surgery. We used the classification by Bland, 15 which includes 7 grades (grade 0 1⁄4 normal to grade 6 1⁄4 extremely severe) based on conduction velocity and amplitude. We sub- categorized grades 0 and 1 as mild, grades 2 and 3 as moderate, and grades above 3 as severe. Exclusion criteria: previous carpal tunnel surgery in the same hand (or in the opposite hand within 1 year), moderate to severe osteoarthritis pain (defined as numeric rating scale of 4) in the upper extremities, a history of psychiatric disorders, peripheral vascular disease, polyneuropathy, cervical radiculopathy, focal nerve entrapment other than CTS, pregnancy, hypothyroidism, rheumatoid arthritis, or if the surgery was covered by workers' compensation insurance.	US-guided cases = 51 LM-guided cases = 51	BCTQ-SSS (24 weeks): LM-2.2 (0.7) US-2.0 (0.7) $p = 0.17$ BCTQ-FSS (24 weeks): LM-2.1 (0.7) US-2.0 (0.7) $p = 0.47$ Grip strength (24 weeks): LM-25.5 (7.5) US-25.4 (7.4) $p = 0.81$ Surgical treatment: LM-12 US-9
11	Ustün et al.[5] 2013	Compare the efficacy and safety of US-guided vs LM-guided steroid injections in patients with CTS	Single-Blind Randomized Prospective Study	Turkey	Mean age = 44	Inclusion criteria: Primary moderately severe idiopathic CTS with a clinical diagnosis and neurophysiologic confirmation. Moderate CTS was defined as slowing of the sensory conduction velocity and abnormal distal motor latency Exclusion criteria: Patients with underlying metabolic disorders such as diabetes mellitus, previous steroid injection in the same wrist, surgery for CTS on the affected hand, peripheral polyneuropathy, and traumatic nerve injury	US-guided cases = 23 LM-guided cases = 23	BCTQ-SSS (12 weeks): LM-1.67, 0.73 $p = 0.001$ US-1.30, 0.45 $p = 0.001$ US-guided *vs.* LM-guided $p = 0.007$ BCTQ-FSS (12 weeks): LM-1.86, 1.09 $p = 0.001$ US-1.36, 0.49 $p = 0.001$ US-guided *vs.* LM-guided $p = 0.298$
12	Vahdatpour et al.[13] 2019	Evaluate degree of symptom improvement, safety, change in electrophysiological findings after US-guided vs LM-guided steroid injection for treatment of CTS	Randomized Prospective Trial	Iran	LM-guided group (mean, SD) = 47.61 ± 8.30 US-guided group (mean, SD) = 48.14 ± 9.41	Inclusion criteria: (A) subjects with CTS symptoms, demonstrating positive Tinel's sign, Phalen, and compression tests, (B) having moderate-to-severe CTS ac- cording to the electrodiagnostic criteria, (C) surgery refusal, (D) age of older than 18 years, and (E) agreement with corticosteroid injection Exclusion criteria: Pregnancy, secondary CTS due to metabolic disorders such as thyroid disease, diabetes mellitus, rheumatologic disorders, chronic kidney disease, and wrist fractures, a history of corticosteroid injection, and conditions mimicking CTS, such as cervical radiculopathy, brachial plexopathy, polyneuropathy, and thoracic outlet syndrome, a previous wrist surgery, physical or medical therapy in the previous month, thenar muscle atrophy, and patient's refusal to complete the follow-ups	US-guided cases = 29 LM-guided cases = 23	BCTQ-SSS (12 weeks): LM-1.47 ± 0.50 US-1.47 ± 0.62 $p = 0.985$ BCTQ-FSS (12 weeks): LM-1.37 ± 0.53 US-1.39 ± 0.60 $p = 0.585$ SNAP latency (12 weeks): LM-4.05 ± 0.48 US-4.36 ± 0.55 $p = 0.363$ SNAP amplitude (12 weeks): **LM-23.28 ± 9.39** **US-17.56 ± 7.25** **$p = 0.016$** SNAP NCV (12 weeks): **LM-36.79 ± 6.08** **US-30.86 ± 5.14** **$p = 0.010$** CMAP latency (12 weeks): LM-4.33 ± 0.44 US-4.64 ± 0.50 $p = 0.739$ CMAP amplitude (12 weeks): **LM-6.21 ± 1.78** **US-7.01 ± 1.20** **$p = 0.02$**

TD: Thyroid disease; CKD: Chronic kidney disease; DM: Diabetes mellitus; APB: Abductor pollicis brevis; CSI: Corticosteroid injection.

Table 2a. Quality Assessment using the Revised Cochrane Risk-of-Bias Tool for Randomized Trials

Articles	Domain 1	Domain 2[1]	Domain 2[2]	Domain 3	Domain 4	Domain 5	Assessment
Chen et al.[13] 2018	Low risk	High risk	Low risk	High risk	Low risk	High risk	High risk
Eslamian et al.[3] 2017	Some concerns	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Karaahmet et al.[6] 2017	Some concerns	High risk	High risk	Low risk	Some concerns	Low risk	High risk
Lee et al.[7] 2014	High risk	High risk	Low risk	Low risk	Low risk	Low risk	High risk
Makhlouf et al.[8] 2014	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk
Rayegani et al.[10] 2019	High risk	High risk	Low risk	Low risk	Low risk	Low risk	High risk
Roh et al.[9] 2019	High risk	High risk	Low risk	Some concerns	Low risk	Low risk	High risk
Ustun et al.[5] 2013	High risk	Some concerns	Low risk	Low risk	Low risk	Low risk	High risk
Vahdatpour et al.[12] 2019	High risk	High risk	High risk	Some concerns	Low risk	Low risk	High risk

Table 2b. Quality assessment using the Newcastle-Ottawa Quality Assessment scale of included studies

	Selection				Comparability	Outcome/exposure			Total score
Articles	1	1	1	1	2	1	1	1	
Dabees[2] 2015 (cohort)	1	1	1	1	1	1	0	1	7
Evers et al.[4] 2017 (case control)	1	1	1	1	1	0	1	1	7
Omar et al.[9] 2018 (cohort)	1	1	1	0	0	1	0	1	5

On the other hand, studies by Chen et al.,[11] Eslamian et al.,[3] Roh et al.,[12] and Vahdatpour et al.[13] did not show significant difference in efficacy between US-guided and LM-guided injections. The study by Chen et al.[11] compared sensation, grip strength, lateral pinch strength, BCTQ-SSS and -FSS VAS, as well as multiple electromyographic (EMG) factors between US- and LM-guided injections in terms of time and interaction between injection group and time. There was not statistically significant improvement with US-guided intervention over time relative to LM-guided in terms of BCTQ-SSS (p=0.893), -FSS (p=0.936), and VAS (p=0.944). That being said, there was statistically significant improvement in all the above variables relative to time suggesting that both US-guided and LM-guided interventions improve symptoms and function related to median nerve injury over time. Similarly, the study by Omar et al.[9] showed an improvement in the BCTQ-SSS and BCTQ-FSS, nerve conduction studies, and cross-sectional area of the median nerve from steroid injections, but did not show statistically significant differences between US-guided and LM-guided injections. Studies including EMG/nerve conduction velocity data had inconsistent results that did not clearly show statistically significant superiority of US-guided relative to LM-guided injections.[3,6,7,10,11,13]

DISCUSSION

The primary objective of this systematic review was to assess the efficacy of US-versus LM-guided injection of the median nerve. The majority of the studies suggest that efficacy of outcomes in US-guided placement of injectate for the median nerve are increased, compared to LM-guided injections for patients with CTS.[2-10] Although many of the studies showed a statistically significant improvement of CTS with LM-guided injections, the magnitude of improvement was greater in the US-guided group.[2,4-10]

Other important variables to consider that affect the outcomes of each intervention type are those related to patient experience and proficiency of the injector. Makhlouf et al.[8] reported that US-guided injections were associated with reduced procedural pain and reduced overall healthcare costs. Such factors are critical for individual patient care and well-being. Furthermore, the study by Evers et al.[4] showed that the specialty and proficiency of the physician performing the intervention

was another variable that could ultimately affect patient outcomes. In that patient population, 69% of US-guided injections were performed by physical medicine and rehabilitation physicians, 26% by rheumatologists, 3% by orthopedic surgeons, and 1% by radiologists.[4] This finding indicates that the training of the physician likely influences both their injection technique and overall proficiency. Therefore, more emphasis should be placed on training for physicians performing these interventions given the steep learning curve.

Utilizing US in evaluating and treating CTS and other musculoskeletal injuries can help quickly rule out other dangerous etiologies with similar presentations. Furthermore, it can help the provider performing the intervention to better understand patients' individual anatomy both to evaluate the etiology of injury and to guide potential intervention. This guidance would also include clinical decision-making as to which injectate needs to be used for that patient/condition. Yet, the spectrum of carpal tunnel injection is quite broad. Overall, US is a tool which can prioritize patient safety and well-being through more proficient use.

Nonetheless, there are certain limitations that should be noted. This review included studies with high risk of bias as assessed by RoB 2. Due to the nature of the procedure, patients were not blind to the intervention being conducted with US- versus LM-guidance. This risk of bias is exacerbated by the measurement of intervention efficacy by questionnaires completed by the patient and small sample sizes. Since we did not perform a meta-analysis, our study relies on qualitative data from studies that carry a high risk of bias.

In conclusion, both US- guided and LM-guided injections can improve symptoms and functional status of patients with CTS. However, further studies are warranted to assess the accuracy of US-guided median perineurial nerve injections compared to LM-guided to effectively conclude whether one technique is superior to the other. Future directions for assessing accuracy should include prospective US-guided versus LM-guided steroid injections.

Declaration of Conflicting Interests

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Author Contributions

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Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

AI Disclosure

The authors declare that artificial intelligence (AI) tools were not used, or were used solely for language editing, and had no role in data analysis, interpretation, or the formulation of conclusions. All scientific content, data interpretation, and conclusions are the sole responsibility of the authors. The authors further confirm that AI tools were not used to generate, fabricate, or 'hallucinate' references, and that all references have been carefully verified for accuracy.

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