

REVIEW ARTICLE (META-ANALYSIS)

Ultrasound-Guided Versus Landmark-Guided Local Corticosteroid Injection for Carpal Tunnel Syndrome: A Systematic Review and Meta-Analysis of Randomized Controlled Trials



Arash Babaei-Ghazani, MD,^a Peyman Roomizadeh, MD,^a Bijan Forogh, MD,^a Seyed-Mohammad Moeini-Taba, MD,^a Amin Abedini, MD,^b Mona Kadkhodaie, MD,^a Fateme Jahanjoo, MSc,^c Bina Eftekharsadat, MD^c

From the ^aNeuromusculoskeletal Research Center, Department of Physical Medicine and Rehabilitation, Iran University of Medical Sciences, Tehran; ^bMedical Students Research Center, Isfahan University of Medical Sciences, Isfahan; and ^cPhysical Medicine and Rehabilitation Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Abstract

Objective: To review the literature and assess the comparative effectiveness of ultrasound-guided versus landmark-guided local corticosteroid injections in patients with carpal tunnel syndrome (CTS).

Data Sources: Cochrane Central Register of Controlled Trials, MEDLINE (PubMed), Embase (Ovid), and Web of Science (from inception to February 1, 2017).

Study Selection: Randomized controlled trials (RCTs) comparing ultrasound-guided injection with landmark-guided injection in patients with CTS were included.

Data Extraction: Two authors independently screened abstracts and full texts. The outcomes of interest were Symptom Severity Scale (SSS) and Functional Status Scale (FSS) scores of the Boston Carpal Tunnel Questionnaire and 4 electrodiagnostic parameters, including compound muscle action potential (CMAP), sensory nerve action potential (SNAP), distal motor latency (DML), and distal sensory latency (DSL).

Data Synthesis: Overall, 569 abstracts were retrieved and checked for eligibility; finally, 3 RCTs were included (181 injected hands). Pooled analysis showed that ultrasound-guided injection was more effective in SSS improvement (mean difference [MD], $-.46$; 95% confidence interval [CI], $-.59$ to $-.32$; $P < .00001$), whereas no significant difference was observed between the 2 methods in terms of the FSS (MD, $-.25$; 95% CI, $-.56$ to $.05$; $P = .10$). There were also no statistically significant differences in improvements of CMAP (MD, 1.54 ; 95% CI, 0.01 to 3.07 ; $P = .05$), SNAP (MD, -0.02 ; 95% CI, -6.27 to 6.23 ; $P > .99$), DML (MD, $.05$; 95% CI, $-.30$ to $.39$; $P = .80$), or DSL (MD, $.00$; 95% CI, $-.65$ to $.65$; $P > .99$).

Conclusions: This review suggested that ultrasound-guided injection was more effective than landmark-guided injection in symptom severity improvement in patients with CTS; however, no significant differences were observed in functional status or electrodiagnostic improvements between the 2 methods.

Archives of Physical Medicine and Rehabilitation 2018;99:766-75

© 2017 by the American Congress of Rehabilitation Medicine

Local corticosteroids injection into the carpal tunnel is a widely used treatment for carpal tunnel syndrome (CTS).^{1,2} For decades, clinicians have used various anatomic landmark-guided

techniques for carpal tunnel injection.³⁻⁵ These techniques have been developed with the goal of delivering steroids directly to the carpal tunnel and avoiding median nerve injury during injection. Over recent years, the use of ultrasound guidance for carpal tunnel injection has progressively gained popularity among clinicians. Ultrasound guidance provides real-time and dynamic display of

Disclosures: none.

the carpal tunnel structures, anatomic variations, and position of the needle at the time of injection.⁶ These advantages help the therapist to monitor the injection process and avoid iatrogenic lesions to the median nerve, tendons, and vessels caused by the tip of the needle. Despite these advantages, some authors have argued against the routine use of ultrasound-guided CTS injections in clinical practice. An active debate is currently ongoing in the literature whether ultrasound-guided injection results in better treatment outcomes than the landmark-guided injection.^{7,8}

This uncertainty has been amplified by conflicting results obtained from different trials comparing clinical effectiveness of ultrasound-guided versus landmark-guided injections in patients with CTS.⁹⁻¹¹ In addition, concerns have been raised about the greater treatment costs and increased risk of infection associated with ultrasound-guided CTS injections.⁷

To provide more evidence for clinical decision-making and update the topic, this systematic review and meta-analysis was conducted to consolidate the existing evidence from the relevant randomized controlled trials (RCTs) comparing the effectiveness of ultrasound-guided versus landmark-guided injections on symptom severity, functional status, and electrodiagnostic outcomes in patients with CTS.

Methods

This systematic review closely followed guidelines in the Cochrane Collaboration handbook¹² and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.¹³ Because this study involved secondary analysis of data available in the public databases, it was exempt from ethical review by the ethics committee of Iran University of Medical Sciences.

Sources and search strategy

To obtain material for this study, two authors (P.R. and A.B.-G.) independently conducted a systematic search of 4 electronic databases, including Cochrane Central Register of Controlled Trials, MEDLINE (PubMed), Embase (Ovid), and Web of Science, from inception to February 1, 2017. The purpose of the search was to identify any RCT comparing the effectiveness of ultrasound-guided versus landmark-guided corticosteroid injections in patients with CTS, irrespective of the type of corticosteroid, dose of corticosteroid, size of syringe, and injection technique (proximal/distal or in plane/out of plane). The following keywords, Medical Subject Headings, and Boolean operators were used: “carpal tunnel or carpal tunnel syndrome,” “ultrasound or ultrasonography or sonography or sonographic or

sonographically,” “injection or injections,” “landmark or blind,” “corticosteroids or corticosteroid or steroid or steroids,” “methylprednisolone or triamcinolone,” and “guide or guided.”

Inclusion and exclusion criteria

All titles and abstracts of the collected articles were reviewed for relevance without any language restriction independently by the same authors (P.R. and A.B.-G.). Conflicts were resolved through discussion or referral to a third author (B.E.). The criteria for including articles in this review were as follows: (1) study with an RCT design published in a peer-reviewed journal, (2) primary aim to compare the clinical effectiveness of ultrasound-guided versus landmark-guided (blind) corticosteroid carpal tunnel injection in patients with CTS, and (3) study published in full text. Case reports, case series, conference abstracts, observational studies, review articles, letters, and technical reports were excluded from this review. Only the English abstracts of the articles in other languages were studied for eligibility of inclusion. The eligible studies that met the inclusion criteria were imported into EndNote software version X7,⁴ and then duplicates were removed. The reference lists of the included studies were screened for any further relevant articles. Subsequently, 3 RCTs met the inclusion criteria and were included in this meta-analysis.⁹⁻¹¹

Assessment of risk of bias

Two authors (P.R. and A.B.-G.) independently evaluated the risk of bias of each trial. Disagreements were resolved by consensus or consultation with a third author (B.E.) where necessary. The risk of bias of each study was assessed using the Cochrane Collaboration risk of bias tool.¹² The following methodologic domains were evaluated for this purpose: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other potential bias (free of expertise bias). Each criterion was explicitly judged and classified as low risk of bias, high risk of bias, or unclear risk of bias.

Data extraction and outcome measures

After selection of the eligible articles, 2 authors (P.R. and M.K.) extracted data from each study and summarized them into standard data tables designed for this review. The data extracted included the following: (1) details of the study including author, year of publication, location of study, and sample size; (2) demographic characteristics of the study population including mean and SD of age, sex, and body mass index; and (3) characteristics of the CTS of the patients including symptoms duration, symptoms severity, and longest follow-up duration.

Outcome measures

The outcome measures included for this meta-analysis were functional and severity scores of the Boston Carpal Tunnel Syndrome Questionnaire (BCTQ) and 4 electrodiagnostic parameters. The BCTQ is a validated and widely used outcome instrument for CTS in clinical studies, consisting of 2 parts: the Symptom Severity Scale (SSS) (11 questions) and the Functional Status Scale (FSS) (8 questions). All answers are rated from 1 to 5, and the sum of individual scores is divided by the number of items. A higher mean score indicates greater symptoms severity or

List of abbreviations:

BCTQ	Boston Carpal Tunnel Syndrome Questionnaire
CI	confidence interval
CMAP	compound muscle action potential
CTS	carpal tunnel syndrome
DML	distal motor latency
DSL	distal sensory latency
FSS	Functional Status Scale
MD	mean difference
RCT	randomized controlled trial
SNAP	sensory nerve action potential
SSS	Symptom Severity Scale

functional disability.¹⁴ The BCTQ was evaluated in all trials included in this review. With respect to electrodiagnosis outcomes, the common parameters reported were compound muscle action potential (CMAP), sensory nerve action potential (SNAP), distal motor latency (DML), and distal sensory latency (DSL). In this regard, the following outcomes were selected to perform meta-analysis: (1) BCTQ FSS; (2) BCTQ SSS; and (3) 4 electrodiagnostic parameters, including CMAP, SNAP, DML, and DSL.

Data synthesis

Statistical analysis was performed using RevMan version 5.3.^b The means and SDs for all continuous variables were obtained. When not available, they were calculated from other effect estimates and dispersion measures.¹² In particular, for one study¹¹ in which deviation from the mean was reported using SE, the SD was calculated by multiplying the SE in square root of the sample size (ie, $SE \times \sqrt{30}$). Data were analyzed by calculation of the mean differences (MDs) and 95% confidence intervals (CIs) for continuous variables. The statistical heterogeneity of trials was assessed by the Cochrane Q test for heterogeneity and the I^2 test for inconsistency. If $P < .10$ (Q test), the results were considered heterogeneous, and if the I^2 was $\geq 50\%$, the results were considered inconsistent. If the test results for heterogeneity were significant, a random effect model was used. Otherwise, if there was no significant heterogeneity, the fixed effect model was applied. In 2 studies,^{9,11} the SSS and FSS were reported as the mean of all answered items in each scale, whereas in the Lee et al study,¹⁰ the sum of individual items for each scale was reported. Therefore, to obtain mean scores of items in each scale, the means and SDs of the SSS and FSS in the Lee study¹⁰ were divided by 11 (number of SSS items) and 8 (number of FSS items), respectively. In the Lee study,¹⁰ the patients in the ultrasound-guided group were further subdivided into 2 in-plane and out of plane subgroups based on needle approach during ultrasound-guided injection. Because the purpose of the present meta-analysis was not to compare the effectiveness of different injection approaches, an overall estimate of the 2 subgroups was calculated using weighted average and pooled SD. Forest plots were used to present the results from this meta-analysis graphically.

Results

Results of the search and description of studies

Through the database search, a total of 569 studies were identified in the initial evaluation. By screening titles and abstracts of these studies, 564 articles, including duplicates, case reports, case series, retrospective studies, review articles, letters, conference abstracts, meta-analyses, and technical reports, were excluded. Five RCTs^{9-11,15,16} were identified, and their full texts were obtained for further assessment. On further scrutiny, 2 of these 5 RCTs were excluded from the meta-analysis because of the following reasons: in one study¹⁵ the efficacy of ultrasound-guided versus nerve stimulation-guided (but not landmark-guided) injection was compared, and in another study¹⁶ the outcome measures were visual analog scale for pain and costs of treatment. Neither of these were within the scope of this meta-analysis. No additional studies were identified in searching the reference lists of the included articles. The details of the selection process are demonstrated in figure 1. The

characteristics of the 3 included RCTs⁹⁻¹¹ are summarized in table 1. The included studies were published from 2013 to 2015, and all were written in English. The total study sample size was 181 hands with CTS, and the longest follow-up was 12 weeks in all trials. The baseline values of the outcomes and their changes from baseline are demonstrated in table 2.

Interventions

The landmark-guided carpal tunnel injection in all trials was performed by placing the needle proximal to the distal wrist crease and ulnar to the palmaris longus tendon. The ultrasound-guided carpal tunnel injection technique was in-plane in the Eslamian et al study,¹¹ out of plane in the Ustün et al study,⁹ and both in-plane and out of plane in the Lee et al study.¹⁰ The dose and type of glucocorticoid was 40mg of methylprednisolone in the Eslamian¹¹ and Ustün⁹ studies, and 40mg of triamcinolone in the Lee¹⁰ study.

Risk of bias in included studies

The results of the risk of bias assessment are presented in figure 2. Only the trial by Eslamian¹¹ provided underlying sample size calculation, whereas the remaining 2 trials^{9,10} did not justify the number of included patients. The randomization method was described in the Eslamian¹¹ and Ustün⁹ trials adequately, but Lee¹⁰ did not clearly describe the process of random allocation. None of the trials blinded the therapist because it was not applicable because of the study designs. Also, none of the trials specified whether treatment allocation was concealed. The Eslamian¹¹ and Ustün⁹ trials adequately blinded the outcome assessor, whereas the Lee trial,¹⁰ although reported to be single-blinded, did not provide any details about blinding of outcome assessor or participants. The number of participants completing the study was adequately reported in all trials. Lee¹⁰ and Ustün⁹ did not report data about MDs in the SSS and FSS. No other potential sources of bias were identified in the Eslamian trial¹¹ because a single physician performed all ultrasound-guided injections and a different physician performed landmark-guided injections in this study. However, in the remaining 2 trials, it was not specified whether a single physician performed injections. This may bias the estimates of treatment effects because the expertise of different physicians may not be equal. Finally, in the Lee trial,¹⁰ the baseline similarity between the 2 intervention groups was not evaluated statistically.

Efficacy of ultrasound-guided injection versus landmark-guided injection

Change in SSS

All 3 trials,⁹⁻¹¹ including 181 analyzed hands, provided data on symptom severity improvement 12 weeks after injections. A heterogeneity test showed no significant heterogeneity among studies ($I^2 = 0\%$, $P = .58$); therefore, the fixed effect model was used to pool the data. The overall estimate suggested that the ultrasound-guided injection was more effective than the landmark-guided injection in reducing SSS score (MD, $-.46$; 95% CI, $-.59$ to $-.32$; $P < .0001$) (fig 3A).

Change in FSS

All 3 trials,⁹⁻¹¹ including 181 analyzed hands, provided data on function improvement at 12 weeks after treatment. There was no

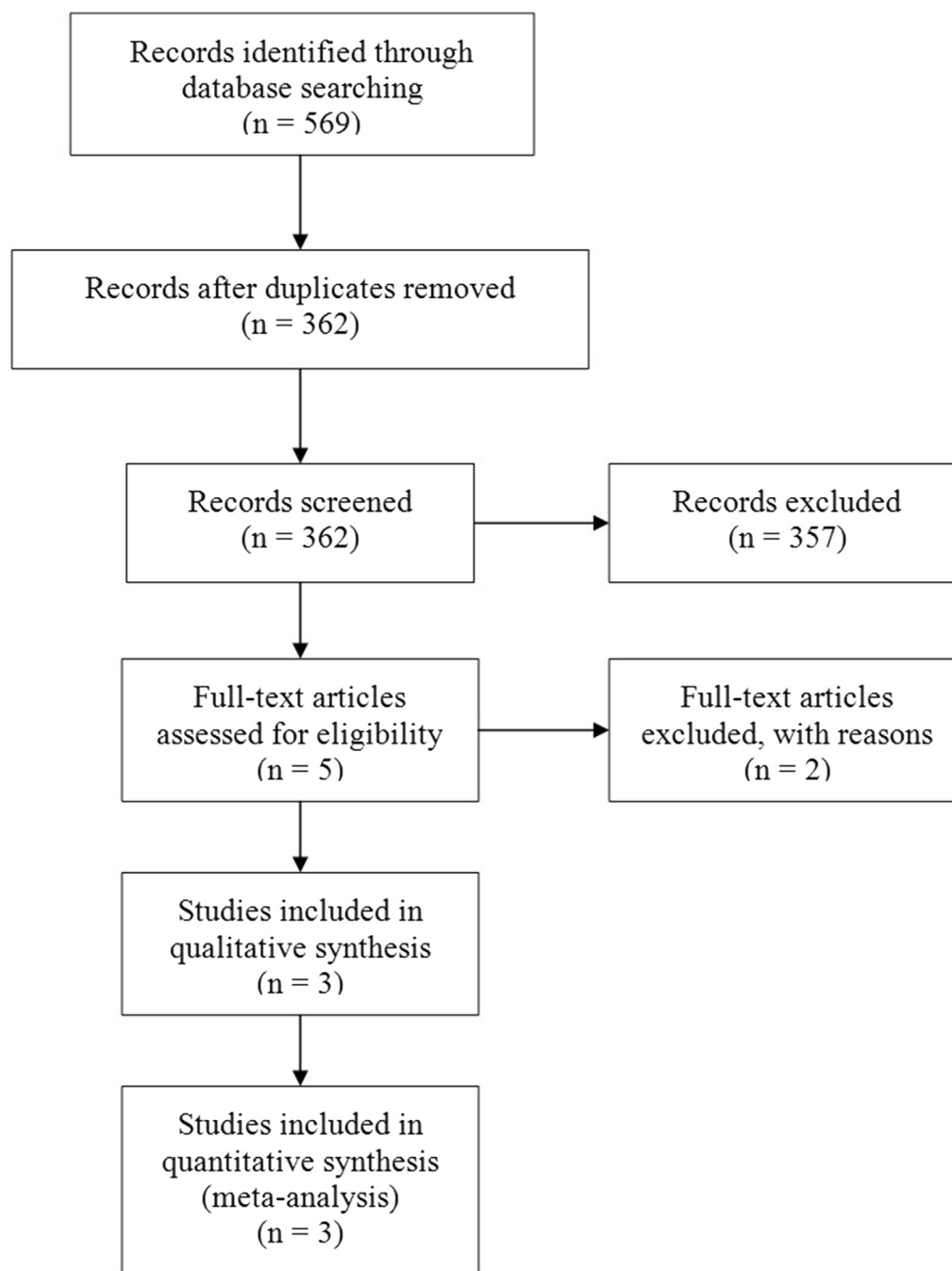


Fig 1 Flow diagram for selection of RCTs included in the meta-analysis.

heterogeneity between studies ($I^2=0\%$, $P=.45$), and the fixed effect model was used. A pooled analysis on FSS improvement revealed that the difference between the 2 groups was not statistically significant (MD, $-.25$; 95% CI, $-.56$ to $.05$; $P=.10$) (fig 3B).

Change in electrodiagnostic parameters

Two trials,^{10,11} including 135 analyzed hands, evaluated improvements in electrodiagnostic parameters after treatments. Pooled analyses on data from these studies suggested no

significant differences in improvements of motor/sensory action potentials and latencies between the 2 injection methods. In details, there was no significant heterogeneity among the studies for CMAP ($I^2=50\%$, $P=.16$), and the fixed effects model was used. The overall estimates indicated no significant difference between the 2 injection methods in improving CMAP (MD, 1.54 ; 95% CI, $0.01-3.07$; $P=.05$) (fig 4A). With respect to SNAP, a heterogeneity test revealed a significant heterogeneity among the studies ($I^2=77\%$, $P=.04$); therefore, the random effect model was used. The overall estimates indicated no significant difference between the 2 injection methods (MD, -0.02 ; 95% CI, -6.27 to

Table 1 Characteristics of the included studies

Author, Country (Year)	Study Design	No. of Patients	No. of Hands	Age (y)	Sex (F:M)	Symptom Duration (mo)	Symptom Severity Based on EDS	Baseline FSS Score	Baseline SSS Score	Longest Follow-Up Duration (wk)	Study Outcomes
Ustün et al, ⁹ Turkey (2013)	RCT	US-G: 23 LM-G: 23 Total: 46	US-G: 23 LM-G: 23 Total: 46	US-G: 45.9±10.4 LM-G: 42.7±11.3 Total: 44	US-G: 19:4 LM-G: 22:1 Total: 41:5	US-G: 16.7±10.6 LM-G: 10.1±10.1 Total: NA	Moderate to severe	US-G: 2.4±0.7 LM-G: 2.6±1.0 Total: NA	US-G: 2.6±0.6 LM-G: 2.3±0.6 Total: NA	12	BCTQ, EDS
Lee et al, ¹⁰ Korea (2014)	RCT	US-G (in-plane): 15 US-G (out of plane): 14 LM-G: 15 Total: 44	US-G (in-plane): 26 US-G (out of plane): 24 LM-G: 25 Total: 75	US-G (in-plane): 55.2±13.2 US-G (out of plane): 52.6±11.6 LM-G: 50.3±9.6 Total: NA	US-G (in-plane): 14:1 US-G (out of plane): 14:0 LM-G: 13:2 Total: 41:3	US-G (in-plane): 8.9±2.2 US-G (out of plane): 9.4±3.6 LM-G: 7.6±2.9 Total: NA	Mild to moderate	US-G (in-plane): 13.2±6.3 US-G (out of plane): 14.0±7.0 LM-G: 12.1±5.7 Total: NA	US-G (in-plane): 29.5±7.8 US-G (out of plane): 28.3±7.0 LM-G: 30.21±8.14 Total: NA	12	BCTQ, EDS, CSA, FR
Eslamian et al, ¹¹ Iran (2017)	RCT	US-G: 27 LM-G: 20 Total: 47	US-G: 30 LM-G: 30 Total: 60	US-G: 54.5±2.0* LM-G: 49.3±1.8* Total: NA	US-G: 25:2 LM-G: 20:0 Total: 45:2	US-G: NA LM-G: NA Total: NA	40 moderate, 7 moderate to severe	US-G: 2.6±0.1* LM-G: 2.6±0.1* Total: NA	US-G: 3.0±0.1* LM-G: 3.3±0.1* Total: NA	12	BCTQ, EDS

NOTE. Data are presented as n, mean ± SD, or as otherwise indicated.

Abbreviations: CSA, cross-sectional area; EDS, electrodiagnostic study; F, female; FR, flattening ratio; LM-G, landmark-guided; M, male; NA, not available; US-G, ultrasound-guided.

* Presented as mean ± SE.

Table 2 Outcome variables reported in included trials

Study	Sample Size	BCTQ FSSS			BCTQ SSS			CMAP (mV)			SNAP (μ V)			DML (ms)			DSL (ms)		
		Baseline	After 12wk	<i>P</i>	Baseline Value	After 12wk	<i>P</i>	Baseline Value	After 12wk	<i>P</i>	Baseline Value	After 12wk	<i>P</i>	Baseline Value	After 12wk	<i>P</i>	Baseline Value	After 12wk	<i>P</i>
Ustün et al ⁹																			
US- guided	23	2.4±0.7	1.3±0.4	.001	2.6±0.6	1.30±0.4	.001	7.7±1.8	NA	NA	NA	NA	NA	5.0±1.0	NA	NA	NA	NA	NA
LM- guided	23	2.6±1.0	1.8±1.0	.001	2.3±0.6	1.6±0.7	.001	8.0±1.9	NA	NA	NA	NA	NA	5.23±1.1	NA	NA	NA	NA	NA
Lee et al ¹⁰																			
US- guided (in-plane)	26	13.2±6.3	8.7±3.8	<.05	29.5±7.8	12.1±6.6	<.05	11.9±4.1	14.5±4.5	<.05	12.6±7.8	18.0±8.9	<.05	5.1±1.7	4.0±0.7	<.05	4.9±0.8	3.9±0.6	<.05
US- guided (out of plane)	24	14.0±7.0	10.1±6.8	<.05	28.3±7.0	17.4±5.78	<.05	11.4±5.2	13.3±5.0	<.05	12.1±8.7	14.2±9.0	<.05	5.3±2.0	4.7±1.4	>.05	5.2±1.2	4.1±1.1	<.05
LM-guided group	25	12.1±5.7	10.1±7.1	<.05	30.21±8.14	20.1±0.7	<.05	10.9±5.01	11.0±4.9	>.05	11.8±7.6	13.0±8.7	<.05	4.9±1.8	4.6±2.0	>.05	4.8±1.1	4.0±1.6	>.05
Eslamian et al ¹¹																			
US-guided	30	2.6±0.1	1.5±0.9	<.001	3.0±0.1	1.63±0.10	<.001	9.2±0.6	9.8±0.7	.172	17.2±1.6	18.5±1.0	.194	5.2±0.2	4.7±0.1	.001	4.2±0.2	3.6±0.9	.002
LM-guided	30	2.6±0.1	1.6±0.1	<.001	3.3±0.1	1.95±0.15	<.001	8.4±0.7	9.2±0.7	.068	15.8±0.1	21.7±1.9	<.001	5.3±0.2	4.6±0.1	<.001	4.2±0.2	3.6±0.1	<.001

Abbreviation: NA, not available.

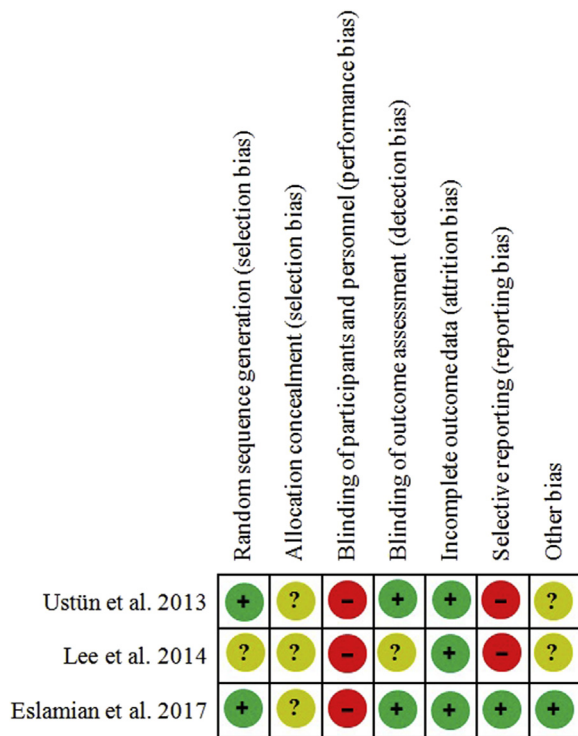


Fig 2 Risk of bias assessment for the RCTs included in the meta-analysis. The items were judged as low risk, unclear risk, or high risk. The + symbol represents low risk of bias; ?, unclear risk of bias; -, high risk of bias.

6.23; $P > .99$) (fig 4B). Finally, there was no significant heterogeneity between studies in terms of DML ($I^2 = 0\%$, $P = .40$) and DSL ($I^2 = 0\%$, $P = .93$); therefore, the fixed effects models were used for both analysis. A pooled analysis showed that the differences between ultrasound-guided and landmark-guided groups were not significant for DML (MD, .05; 95% CI, -.30 to .39;

$P = .80$) (fig 4C) or DSL (MD, .00; 95% CI, -.65 to .65; $P > .99$) (fig 4D).

Adverse events

No serious adverse events were reported in any of the included trials. Only one study¹⁰ reported the number of adverse events in each group. They reported no vessel insult in the ultrasound-guided groups (out of plane and in-plane), 1 median nerve insult in the in-plane group, and 6 median nerve insults in the out of plane group (out of 14 out of plane and 15 in-plane injections). In the landmark-guided group, there were 5 cases with median nerve insult and 2 cases with vessel insult (out of 15 landmark-guided injections). However, they reported the differences in the adverse events between the groups were not statistically significant.

Discussion

There is a plethora of treatment options available for patients with CTS; among them, local corticosteroids injection into the carpal tunnel shows to be effective in mild to moderate CTS.¹⁷⁻¹⁹ The use of ultrasound guidance for CTS injection is increasing among clinicians practicing musculoskeletal medicine. Despite its several advantages, the superiority of ultrasound-guided injections over conventional landmark-guided injections has been a matter of controversy in recent years.^{7,8} A number of trials have been performed with conflicting results; however, the cumulative knowledge gained from the existing evidence needed to be consolidated in a quantitative summary of the results to determine whether ultrasound-guided injections result in better clinical outcomes. In this systematic review and meta-analysis, we incorporated 3 RCTs comparing the effectiveness of ultrasound-guided versus landmark-guided injections on symptom severity, functional status, and motor/sensory action potentials and latencies in patients with CTS. Based on findings of this study, ultrasound-guided injection demonstrated a higher efficacy in improving symptom severity compared with the conventional landmark-guided injection, but no

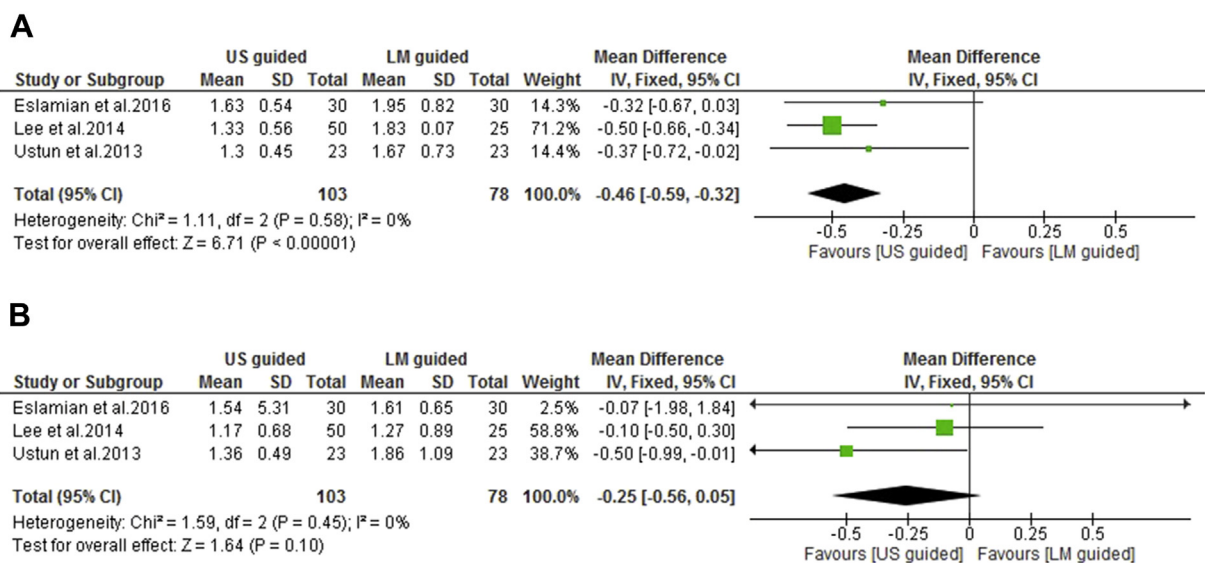
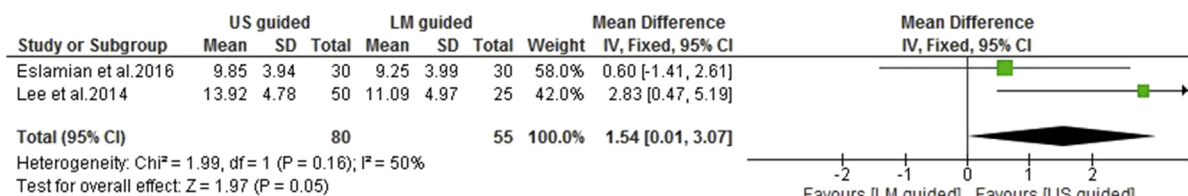
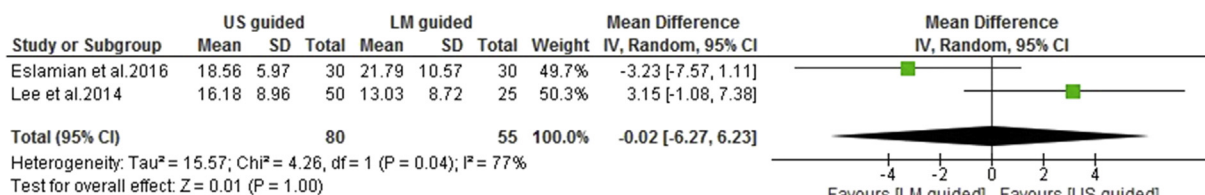


Fig 3 Forest plots of comparison between the ultrasound-guided injection group and landmark-guided injection group: (A) SSS improvement in 12 weeks, and (B) FSS improvement in 12 weeks. Abbreviations: LM, landmark-guided injection group; US, ultrasound-guided injection group; IV, inverse variance weighting.

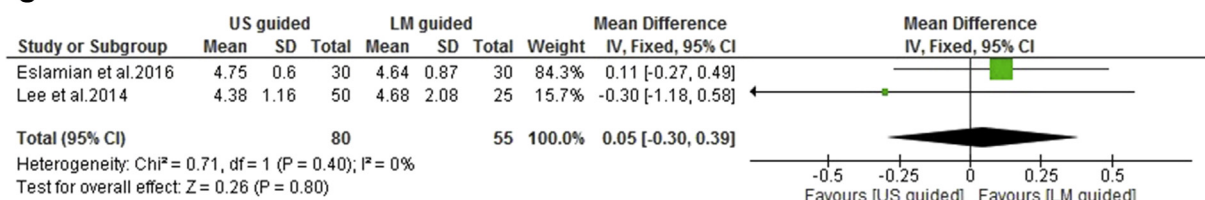
A



B



C



D

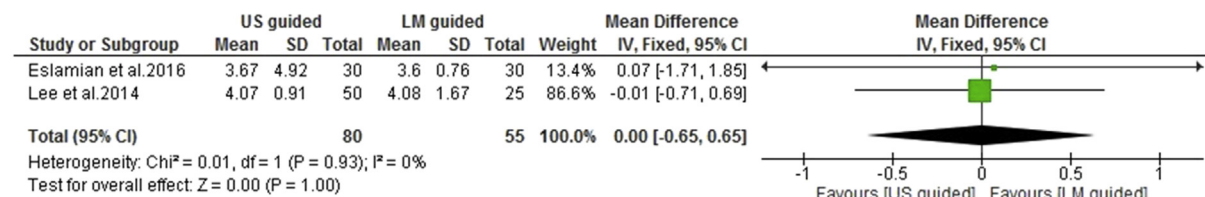


Fig 4 Forest plots of comparison between the ultrasound-guided injection group and landmark-guided injection group: (A) CMAP improvement in 12 weeks; (B) SNAP improvement in 12 weeks; (C) DML improvement in 12 weeks; and (D) DSL improvement in 12 weeks. Abbreviations: LM, landmark-guided injection group; US, ultrasound-guided injection group; IV, inverse variance weighting.

significant differences were noted in functional status or electrodiagnostic improvements between the 2 methods.

The application of ultrasound in the field of musculoskeletal disorders has expanded enormously during the last decade. The real-time imaging capability of the ultrasound provides a rapid and noninvasive technique for dynamic evaluation of joints, ligaments, tendons, and peripheral nerves. Moreover, ultrasonography is relatively low cost, nonionizing, and portable, which can conveniently be used by clinicians in their offices. These features have made ultrasound an ideal imaging modality for diagnosis of a myriad of musculoskeletal conditions.²⁰⁻²² Beyond diagnostics, ultrasound is a useful tool for guiding musculoskeletal interventions, including joint aspirations, injections, and nerve blocks.^{23,24} Ultrasound guidance for injection of CTS allows monitoring the progress of the needle into the carpal tunnel and avoiding lesions to the critical structures (eg, median nerve, radial artery, ulnar neurovascular bundle).^{4,6} The earliest report of application of ultrasound guidance for carpal tunnel injection was

published in 2002 by Grassi et al,²⁵ where the authors used a high frequency (13-MHz) linear transducer to provide ultrasound guidance for injection of a 50-year-old-man with CTS secondary to rheumatoid arthritis. Since then, there have been significant technologic advancements in the equipment, which have improved its image quality and availability. These improvements have made carpal tunnel ultrasonography more feasible for clinicians.

Recently, a relevant systematic review was conducted by Chen et al,²⁶ who performed pairwise meta-analysis (direct comparison) and network meta-analysis (combination of direct and indirect comparison) on relevant RCTs to evaluate the clinical efficacy of 4 commonly used CTS injection approaches (ultrasound-guided: in-plane and out of plane; landmark-guided: proximal to flexor crease and distal to flexor crease). In line with our findings, their pairwise meta-analysis indicated superiority of the ultrasound-guided in-plane approach in improvement of symptom severity (SSS), but the differences in functional status (FSS) improvement were not significant. However, in network meta-analysis, the

pooled estimates of SSS and FSS improvements favored the ultrasound-guided in-plane approach compared with the other injection approaches. Nevertheless, their study included trials published prior to May 2015; therefore, they did not include Eslamian et al,¹¹ a recently published high-quality trial with relatively low risk of bias in our assessment, which failed to demonstrate a significant difference in BCTQ results and electrodiagnostic parameters between ultrasound-guided and landmark-guided injections. In addition, contrary to our meta-analysis, Chen et al²⁶ did not provide data on the pooled effect size of different injection approaches on electrodiagnostic parameters. Therefore, to our knowledge, our study is the first meta-analysis to date which has compared the efficacy of ultrasound-guided and landmark-guided injection approaches on electrodiagnostic variables.

The first population-based, longitudinal cohort study comparing the effectiveness of ultrasound-guided and landmark-guided corticosteroid injection in CTS was published by Evers et al,²⁷ who found that the hazard of retreatment was significantly lower in patients treated with ultrasound-guided injection compared with patients treated with landmark-guided injection. In detail, among patients treated with ultrasound-guided injection, 55% (48/87) needed retreatment, with eventual surgery in 44% (38/87). The corresponding figure for patients treated with landmark-guided injection was significantly higher; 72% (169/234) of the patients received retreatment, with eventual surgery in 64% (150/234). Besides, the odds ratio of treatment failure within 1 year was 55% lower in the ultrasound-guided group in comparison with the landmark-guided group. In another study conducted by Makhlof et al,¹⁶ the cost-effectiveness of ultrasound-guided versus landmark-guided CTS injection was evaluated. Although the cost of the procedure for ultrasound-guided injection was higher than landmark-guided injection, the authors reported significant reduction in cost of treatment for responders in the ultrasound-guided group because of reductions in costs of retreatment and referral to surgery. In particular, ultrasound-guided CTS injection in a hospital outpatient setting resulted in 59.3% reduction in the cost per responder per year. However, cost per patient per year was significantly increased for an outpatient in a physician's office. Beside cost-effectiveness analysis, they also reported that ultrasound-guided injection was associated with lower procedural pain, longer therapeutic duration, and greater reduction in pain scores from the baseline (visual analog scale score) compared with the landmark-guided injection.¹⁶

Study limitations

In this study, a rigorous and extensive literature search was conducted to present an up-to-date review of the literature. However, the findings of this study must be interpreted in view of its limitations. The main limitation of this study is the small sample size available for analysis, which may decrease the statistical power. As a consequence, the results of this meta-analysis should be interpreted with caution. Another limitation is related to the quality of the included studies. All the included trials suffered from lack of blind design and lack of adequate allocation concealment. However, because of the nature of the interventions, it was not possible to blind the therapist and patients. In addition, the included trials had a relatively short duration of follow-up (up to 3 months). At the present time, there is a relative paucity of high-quality studies on this topic. Further studies, with larger

groups of patients and longer follow-ups, are warranted to achieve more reliable results.

Conclusions

There is a paucity of research comparing the efficacy of ultrasound-guided versus landmark-guided injection for patients with CTS. This review suggested that ultrasound-guided injection was more effective than landmark-guided injection in symptom severity improvement in patients with CTS; however, no significant differences were noted in functional status or electrodiagnostic improvement between the 2 methods.

Suppliers

- a. EndNote software version X7; Thomson Reuters.
- b. RevMan version 5.3; The Cochrane Collaboration.

Keywords

Carpal tunnel syndrome; Conservative treatment; Injections; Meta-analysis [publication type]; Rehabilitation; Review [publication type]; Ultrasonography

Corresponding author

Bina Eftekharsadat, MD, Department of Physical Medicine and Rehabilitation, Firozgar hospital, Valieasr square, Tehran, Iran. *E-mail address:* binasadat@yahoo.com.

References

1. Carlson H, Colbert A, Frydl J, Arnall E, Elliot M, Carlson N. Current options for nonsurgical management of carpal tunnel syndrome. *Int J Clin Rheumatol* 2010;5:129-42.
2. Ren YM, Wang XS, Wei ZJ, et al. Efficacy, safety, and cost of surgical versus nonsurgical treatment for carpal tunnel syndrome: a systematic review and meta-analysis. *Medicine (Baltimore)* 2016;95:e4857.
3. Racasan O, Dubert T. The safest location for steroid injection in the treatment of carpal tunnel syndrome. *J Hand Surg Br* 2005;30:412-4.
4. Menge TJ, Rinker EB, Fan KH, Block JJ, Lee DH. Carpal tunnel injections: a novel approach based on wrist width. *J Hand Microsurg* 2016;8:21-6.
5. Kay NR, Marshall PD. A safe, reliable method of carpal tunnel injection. *J Hand Surg Am* 1992;17:1160-1.
6. Smith J, Wisniewski SJ, Finnoff JT, Payne JM. Sonographically guided carpal tunnel injections: the ulnar approach. *J Ultrasound Med* 2008;27:1485-90.
7. Goldberg G, Wollstein R, Chimes GP. Carpal tunnel injection: with or without ultrasound guidance? *PM R* 2011;3:976-81.
8. Lento PH, Strakowski JA. The use of ultrasound in guiding musculoskeletal interventional procedures. *Phys Med Rehabil Clin N Am* 2010;21:559-83.
9. Ustün N, Tok F, Yazgı AE, et al. Ultrasound-guided vs. blind steroid injections in carpal tunnel syndrome: a single-blind randomized prospective study. *Am J Phys Med Rehabil* 2013;92:999-1004.
10. Lee JY, Park Y, Park KD, Lee JK, Lim OK. Effectiveness of ultrasound-guided carpal tunnel injection using in-plane ulnar approach: a prospective, randomized, single-blinded study. *Medicine (Baltimore)* 2014;93:e350.

11. Eslamian F, Eftekharsadat B, Babaei-Ghazani A, Jahanjoo F, Zeinali M. A randomized prospective comparison of ultrasound-guided and landmark-guided steroid injections for carpal tunnel syndrome. *J Clin Neurophysiol* 2017;34:107-13.
12. Higgins J, Green S. *Cochrane handbook for systematic reviews of interventions* version 5.1.0. The Cochrane Collaboration; 2011.
13. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009; 339:b2700.
14. Levine DW, Simmons BP, Koris MJ, et al. A self-administered questionnaire for the assessment of severity of symptoms and functional status in carpal tunnel syndrome. *J Bone Joint Surg Am* 1993; 75:1585-92.
15. Macaire P, Singelyn F, Narchi P, Paqueron X. Ultrasound- or nerve stimulation-guided wrist blocks for carpal tunnel release: a randomized prospective comparative study. *Reg Anesth Pain Med* 2008;33: 363-8.
16. Makhlof T, Emil NS, Sibbitt WL Jr, Fields RA, Bankhurst AD. Outcomes and cost-effectiveness of carpal tunnel injections using sonographic needle guidance. *Clin Rheumatol* 2014;33:849-58.
17. Eftekharsadat B, Babaei-Ghazani A, Habibzadeh A. The efficacy of 100 and 300 mg gabapentin in the treatment of carpal tunnel syndrome. *Iran J Pharm Res* 2015;14:1275-80.
18. Eftekharsadat B, Roomizadeh P, Torabi S, Heshmati-Afshar F, Jahanjoo F, Babaei-Ghazani A. Effectiveness of *Lavendula stoechas* essential oil in treatment of mild to moderate carpal tunnel syndrome: a randomized controlled trial. *J Hand Ther* 2017 Aug 10 [Epub ahead of print].
19. Marshall S, Tardif G, Ashworth N. Local corticosteroid injection for carpal tunnel syndrome. *Cochrane Database Syst Rev* 2007;(2): CD001554.
20. Patil P, Dasgupta B. Role of diagnostic ultrasound in the assessment of musculoskeletal diseases. *Ther Adv Musculoskelet Dis* 2012;4:341-55.
21. Nwawka OK. Update in musculoskeletal ultrasound research. *Sports Health* 2016;8:429-37.
22. Bureau NJ, Ziegler D. Economics of musculoskeletal ultrasound. *Curr Radiol Rep* 2016;4:44.
23. De Muynck M, Parlevliet T, De Cock K, Vanden Bossche L, Vanderstraeten G, Ozcakar L. Musculoskeletal ultrasound for interventional physiatry. *Eur J Phys Rehabil Med* 2012;48:675-87.
24. Joines MM, Motamedi K, Seeger LL, DiFiori JP. Musculoskeletal interventional ultrasound. *Semin Musculoskelet Radiol* 2007;11:192-8.
25. Grassi W, Farina A, Filippucci E, Cervini C. Intralesional therapy in carpal tunnel syndrome: a sonographic-guided approach. *Clin Exp Rheumatol* 2002;20:73-6.
26. Chen PC, Chuang CH, Tu YK, Bai CH, Chen CF, Liaw M. A Bayesian network meta-analysis: comparing the clinical effectiveness of local corticosteroid injections using different treatment strategies for carpal tunnel syndrome. *BMC Musculoskelet Disord* 2015;16:363.
27. Evers S, Bryan AJ, Sanders TL, Selles RW, Gelfman R, Amadio PC. The effectiveness of ultrasound-guided compared to blind steroid injections in the treatment of carpal tunnel syndrome. *Arthritis Care Res (Hoboken)* 2017;69:1060-5.