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To cite: Wang et al.
Ultrasound-Guided Local
Corticosteroid Injection for
Carpal Tunnel Syndrome: An
updated Meta-Analysis of
Randomized Controlled Trials.
Inplasy protocol 202140027.
doi:
10.37766/inplasy2021.4.0027

Received: 06 April 2021

Published: 06 April 2021

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Support: None.

**Review Stage at time of this
submission:** Data analysis.

Conflicts of interest:
None declared.

Ultrasound-Guided Local Corticosteroid Injection for Carpal Tunnel Syndrome: An updated Meta-Analysis of Randomized Controlled Trials

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Review question / Objective: This updated meta-analysis aimed to compare the efficacy and safety of ultrasound-guided (US-guided) versus landmark-guided (LM-guided) local corticosteroid injection for carpal tunnel syndrome (CTS)

Eligibility criteria: The inclusion criteria for eligible articles were as follows: (1) CTS with a clinical diagnosis and neurophysiologic confirmation, (2) RCTs compared the clinical effectiveness of US-guided versus LM-guided (blind) corticosteroid injection, without limitation in the type and dose of corticosteroid, size of syringe, and method of injection, (3) reported at least one of the following outcomes: pain and function parameters, electrophysiological outcomes or adverse events. Publications were excluded if they were: (1) CTS due to trauma or any metabolic disorders (such as thyroid disease, rheumatoid disorders, diabetes mellitus), (2) duplicated manuscripts, letters, reviews, case reports, case series, conference abstracts, in vitro biomechanical studies and animal studies.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 April 2021 and was last updated on 06 April 2021 (registration number INPLASY202140027).

INTRODUCTION

Review question / Objective: This updated meta-analysis aimed to compare the efficacy and safety of ultrasound-guided (US-guided) versus landmark-guided (LM-guided) local corticosteroid injection for carpal tunnel syndrome (CTS).

Condition being studied: Carpal tunnel syndrome (CTS) is the most common nerve entrapment syndrome occurring in the upper limbs, with a prevalence of 36.08 per 10 000 people. Clinical manifestations of CTS manifest as paresthesia, tingling, weakness, and numbness in distribution of median nerve distal to carpal tunnel. Various nonsurgical and surgical strategies

are available to manage CTS. Among them, local corticosteroid injection based on anatomical landmarks was the most classic and frequently used. However, this conventional method cannot visualize the puncture process, which would lead to the damage of crucial surrounding tissues, especially in the case of median nerve anatomic variations. Furthermore, a misplaced injection may result in earlier symptom recurrence. Since these years, US-guided carpal tunnel injection is gaining popularity among clinicians. Compared with the LM-guided approach, US-guided can dynamically display carpal tunnel structures, anatomical variations, and the needle position during injection in real-time, avoiding iatrogenic injury of median nerve, tendon, and vessel. A recent systematic review conducted by Babaei-Ghazani et al. has indicated that US-guided is superior to LM-guided in BCTQs but not in BCTQf and electrophysiological results. However, there are only three RCTs with 181 hands diagnosed as CTS in their meta-analysis, and additional studies have been conducted recently. The purpose of our systematic review and meta-analysis is to update these results.

METHODS

Participant or population: The inclusion criteria for eligible articles were as follows: (1) CTS with a clinical diagnosis and neurophysiologic confirmation, (2) RCTs compared the clinical effectiveness of US-guided versus LM-guided (blind) corticosteroid injection, without limitation in the type and dose of corticosteroid, size of syringe, and method of injection, (3) reported at least one of the following outcomes: pain and function parameters, electrophysiological outcomes or adverse events. Publications were excluded if they were: (1) CTS due to trauma or any metabolic disorders (such as thyroid disease, rheumatoid disorders, diabetes mellitus), (2) duplicated manuscripts, letters, reviews, case reports, case series, conference abstracts, *in vitro* biomechanical studies and animal studies.

Intervention: Corticosteroid injection.

Comparator: LM-guided (blind) corticosteroid injection.

Study designs to be included: randomized controlled trials.

Eligibility criteria: The inclusion criteria for eligible articles were as follows: (1) CTS with a clinical diagnosis and neurophysiologic confirmation, (2) RCTs compared the clinical effectiveness of US-guided versus LM-guided (blind) corticosteroid injection, without limitation in the type and dose of corticosteroid, size of syringe, and method of injection, (3) reported at least one of the following outcomes: pain and function parameters, electrophysiological outcomes or adverse events. Publications were excluded if they were: (1) CTS due to trauma or any metabolic disorders (such as thyroid disease, rheumatoid disorders, diabetes mellitus), (2) duplicated manuscripts, letters, reviews, case reports, case series, conference abstracts, *in vitro* biomechanical studies and animal studies.

Information sources: To identify relevant RCTs addressing US-guided local corticosteroid injection for patients with CTS, two authors (W.H.C and Z.Y.) independently conducted a systematic search of electronic databases including Pubmed, Embase, and Cochrane Library from inception to December 25, 2020. The search terms for the study object: 'Carpal Tunnel Syndrome [Mesh]' OR 'Carpal Tunnel Syndrome*' OR 'Syndrome*, Carpal Tunnel' OR 'Amyotrophy, Thenar, Of Carpal Origin' OR 'Median Neuropathy, Carpal Tunnel' OR 'Compression Neuropathy, Carpal Tunnel' OR 'Entrapment Neuropathy, Carpal Tunnel'. The intervention's search terms: 'Ultrasonography, Interventional [Mesh]' OR 'ultrasound-guided' OR 'Ultrasound, Interventional' OR 'Interventional Ultrasound' OR 'Interventional Ultrasonography' OR 'sonographic' OR 'Entrapment Neuropathy, Carpal Tunnel'. We also checked the reference lists of all including articles to

avoid any initially omitted studies. There was no publication language and population limitation during the systematic review.

Main outcome(s): The outcome measures included in this meta-analysis were evaluated using clinical and electrophysiological parameters. Clinical parameters for evaluation of pain and function in CTS were BCTQ(30), which contains 2 distinct scales, the Symptom Severity Scale (BCTQs) (11 questions) and the Functional Status Scale (BCTQf) (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 score indicates more severe symptoms or poorer function. Electrophysiological outcomes, including DML, SDL, CAMP, SNAP, and SNCV, and adverse events were also recorded.

Quality assessment / Risk of bias analysis: The RCTs' methodological quality was assessed independently by D. C. and W. H. Y. using the Cochrane Collaboration's Risk of Bias Tool. High-quality was defined as a score of $\geq 50\%$ (i.e., a "yes" score on $\geq 50\%$ of the criteria) on the methodological quality assessment. Any discrepancies of data extraction and quality assessment were settled by discussing a third independent author (W. H. C.)

Strategy of data synthesis: This meta-analysis was conducted with Review Manager 5.3 software (Cochrane Collaboration, Oxford, UK). Continuous data were calculated through the mean difference (MD) or standardized mean difference (SMD) with 95% CI. We calculated risk ratio (RR) with 95% CI to evaluate the adverse events. Heterogeneity across studies was assessed using Cochran Q and I² test.⁽³¹⁾ The random effects model was used if the heterogeneity test showed statistical significance (I² >50%, p<0.1); otherwise, a random-effects model was adopted. Sensitive analysis or subgroup analysis was used to investigate the source of heterogeneity. Publication bias was assessed statistically by Stata 12.0 (Egger's test).

Subgroup analysis: In the ultrasound-guided group, the in-plane technique and out-plane procedure

Sensitivity analysis: The sensitivity analysis was performed by omitting each study in turn to assess the stability of the results. The results of sensitivity analysis of BCTQs, DML, SNAP, SNCV were not materially differentiated compared with those of the original analysis.

Country(ies) involved: China.

Keywords: Meta-analysis, Ultrasound-Guided, Local corticosteroid injection, Carpal tunnel syndrome.

Contributions of each author:

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Author 3 - Hongyu Wei.

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