Published in final edited form as:

Arthritis Care Res (Hoboken). 2017 July ; 69(7): 1060–1065. doi:10.1002/acr.23108.

Effectiveness of Ultrasound-Guided compared to Blind Steroid Injections in the Treatment of Carpal Tunnel Syndrome

Stefanie Evers, M.D.^{1,3}, Andrew J. Bryan, M.D.¹, Thomas L. Sanders, M.D.¹, Ruud W. Selles, Ph.D.^{3,4}, Russell Gelfman, M.D.², and Peter C. Amadio, M.D.¹

¹Department of Orthopedic surgery, Mayo clinic, Rochester, MN, United States ²Department of Physical Medicine and Rehabilitation, Mayo clinic, Rochester, MN, United States ³Department of Plastic, Reconstructive and Hand surgery, Erasmus Medical Center, Rotterdam, the Netherlands ⁴Department of Rehabilitation Medicine, Erasmus Medical Center, Rotterdam, the Netherlands

Abstract

Background—The aim of this study was to compare the effectiveness of ultrasound-guided injections to blind injections in the treatment of carpal tunnel syndrome (CTS) in a large community-based cohort.

Methods—This study evaluated residents of Olmsted County, MN, USA, treated with a corticosteroid injection for CTS between 2001 and 2010. The proportion of patients receiving retreatment and the duration of retreatment-free survival between blind and ultrasound-guided injections were compared. Propensity score matching was used to control for confounding by indication.

Results—In the matched dataset consisting of 234 (out of 600) hands treated with a blind injection and 87 (out of 89) ultrasound-guided injection cases, ultrasound guidance was associated with a reduced hazard of retreatment (hazard ratio, 0.59; 95% confidence interval [CI], 0.37 - 0.93). In addition, ultrasound guidance was associated with 55% reduced odds of retreatment within one year compared to blind injections (adjusted odds ratio, 0.45; 95% CI, 0.24 - 0.83).

Conclusion—This study indicates that ultrasound-guided injections are more effective in comparison to blind injections in the treatment of CTS.

Introduction

Corticosteroid injection is frequently used to treat carpal tunnel syndrome (CTS) and is effective in reducing symptoms (1). However, there is only strong evidence for benefits of steroid injection in the short term and about half of the patients require further treatment

Corresponding author contact information: Stefanie Evers, Tendon and Soft Tissue Biology Laboratory, Mayo Clinic, Rochester, 200 1st St. SW, Rochester, MN 55905, Phone: (507) 538-1717, Fax: (507) 284-539, evers.stefanie@mayo.edu.

None of the authors have any commercial associations that might pose or create a conflict of interest with information presented in the submitted manuscript. None of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay and direct, funds to Mayo Clinic or any other charitable or nonprofit organization with which the authors are affiliated or associated. This study was funded by a grant from NIH/NIAMS (AR62613, R01AG034676) and funds provided by the Mayo Foundation for Medical Education and Research.

within one year (1, 2). Injections into the carpal tunnel are commonly performed palpation-guided using anatomical landmarks (3–7). While the most common techniques have been described as being safe and reliable (5–7), this ‘blind’ intervention does not provide certainty on whether the injected steroid is adequately placed in the carpal tunnel. Moreover, cadaveric studies have indicated that there is wide variability of injectate distribution following carpal tunnel injection (8, 9). Misplaced injectates or injectates that cannot distribute freely within the carpal tunnel will likely result in residual symptoms or early recurrence of symptoms.

Ultrasound, a nonionizing and relatively inexpensive imaging tool, may improve the accuracy and consequently the efficacy of the injection in CTS (10). It may allow physicians to place the needle tip and injectate closer to the median nerve, without damaging the surrounding tissue or the median nerve itself. The few studies that have investigated ultrasound guidance for injections in CTS (11–13), generally indicate that ultrasound-guided injections result in better symptom relief and increased therapeutic duration compared to non-ultrasound-guided injections. However, these studies were limited by small sample sizes and short-term follow-up. Therefore, the purpose of this study was to compare the effectiveness of ultrasound-guided injections to palpation-guided injections in patients with CTS in a large community-based cohort over a longer period of follow-up.

Methods

Data collection

This retrospective study evaluated residents of Olmsted County, MN, USA, treated with a corticosteroid injection for CTS between 2001 and 2010. Subjects were identified using the resources of the Rochester Epidemiology Project (14) with selection based on a Current Procedural Terminology (CPT) code for diagnosis of carpal tunnel syndrome (ICD-9 354.0) and carpal tunnel injection (CPT 20526). Subjects were followed through their medical record until 2014.

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. Patients were excluded if they received surgical carpal tunnel release prior to injection. Study data were collected and managed by three physicians (SE, AB, TS) using Research Electronic Data Capture (REDCap)(15). Data were collected independently and for inter-rater agreement between reviewers Cohen’s kappa coefficients were calculated for a subset of the cases. Cohen’s kappa was 0.845 for our primary outcome measure (16). Any discrepancies between the information extracted by the three reviewers were resolved through discussion.

Data collection included the following patient factors: age, gender, diagnosis of primary carpal tunnel syndrome and laterality, and the presence of pregnancy, diabetes mellitus, rheumatoid arthritis, peripheral neuropathy, cervical radiculopathy or other comorbidities such as previous trauma to the affected hand or wrist, Kienbock’s disease, or volar ganglion cyst. The severity of CTS was assessed using available EMG data, classified in the following categories; normal, mild, moderate and severe, by a neurologist or physiatrist. For reports not mentioning severity, the reviewers scored severity based on the classification of Stevens

(17). Treatment-specific characteristics included volume of injection, type and concentration of steroid and the use of ultrasound guidance. To compare the effective dose of the steroids, we converted the concentration of each steroid to the equivalent of Triamcinolone using a conversion table of the relative potency of steroids (18), since Triamcinolone was the most common type of steroid in our cohort. We also collected information about any injections and surgical interventions following the initial injection.

Outcome measurements

The outcome measure in this study was ‘failure’ of injection, defined as either a second injection or surgical carpal tunnel release that was performed within one year after the initial injection. Additionally a survival analysis was performed to compare the duration of retreatment-free survival by initial treatment groups.

Statistical analysis

Propensity score matching was used to control for confounding by indication (19). The propensity score (PS) was defined as the likelihood of receiving a blind injection or an ultrasound-guided injection based on baseline characteristics. The following covariates were included in the model: age, gender, EMG severity, pregnancy related CTS, comorbidities such as rheumatoid arthritis, diabetes mellitus, neuropathy, and ‘other’ comorbidities.

The propensity scores were used to match blind injection cases to ultrasound-guided injection cases on a one-to-three basis using nearest-neighbor matching with a tolerance width of 0.2 SD of the logit of the propensity score. A one-to-three ratio, as compared to a one-to-one ratio, was used to maximize statistical power because our sample had many more non-ultrasound-guided subjects. Significance testing and a comparison of the standardized mean differences were performed to assess whether the balance in baseline characteristics improved. Standardized mean differences were calculated using the formulas for continuous covariates and dichotomous variables described by Austin et al. (20). The unmatched subjects were excluded from further analyses and the remaining subjects were treated as independent samples, because the theory behind propensity score matching implies that only within groups of subjects with similar propensity scores, the distributions of the covariates will be similar, not within the individual pairs (21, 22).

Kaplan-Meier survival curves were plotted for each treatment group separately to evaluate the unadjusted effect of ultrasound guidance and a log-rank was performed to compare the long term outcome of the two treatment groups. Adjusted time to retreatment was tested using a cox mixed effects model, with a random subject effect to account for the correlation between outcomes of hands in bilateral cases and adjustment for volume of injection, effective dose of injection and any baseline characteristic with standard mean difference greater than 10% after matching. Proportional hazard assumptions were tested using a cox.zph test.

The effect of ultrasound guidance on retreatment within one year was estimated by fitting a logistic model applied to the PS-matched dataset using generalized estimating equations with robust variance estimator and an exchangeable structure for the working correlation matrix. This approach allows adjustment for bilateral cases. In this multivariable model we

also adjusted for volume of injection, effective dose of injection and any baseline characteristic with a standardized mean difference greater than 10% after matching (23). In addition, the number needed to treat (NNT) was calculated using the following formula; $NNT = (1 - (PEER * (1 - OR))) / ((1 - PEER) * (PEER) * (1 - OR))$, whereas PEER stands for 'Patient Expected Event Rate'.

A p-value of < 0.05 was considered statistically significant and the statistical analyses and propensity score matching were performed using R (version 3.2.4-revised) with survival package (version 2.38-3) and package 'coxme' version (2.2-5), IBM SPSS Statistics, Version 22.0 (IBM Corp., Armonk, N.Y.) and the Thoemmes algorithm (24) (version 3.04).

Results

Patient selection and baseline characteristics

A total of 756 subjects with CTS diagnosis and a CTS injection within the specified time window were identified. Among the 756 subjects, 232 patients had bilateral CTS resulting in a total of 988 treated hands (Figure 1). Cases with an injection volume greater than 4 mL were excluded from the analysis, since 4 mL was the maximum amount used in the ultrasound-guided injection group. We excluded 186 injections with a volume greater than 4 mL and 97 cases in which information about volume or effective dose of injection was missing, since all missing data was found to be random. After exclusion of another 16 cases that had less than 1 year follow-up due to death or relocation, the dataset consisted of 533 eligible subjects (689 hands), of which 89 were ultrasound-guided cases.

Table 1 shows the baseline characteristics of the subjects before and after matching and the treatment characteristics of the matched dataset. Before matching, the proportion of patients who had 'normal' EMG-result was significantly greater in the ultrasound-guided group. Additionally, the proportion of patients with rheumatoid arthritis associated CTS was significantly greater in the ultrasound-guided treatment group.

Based on the estimated propensity scores, we were able to match 234 hands treated with a blind injection to 87 ultrasound-guided injection cases.

Comparison between groups

Mean (standard deviation) follow-up period was 7.2 years (± 2.9) for the blind injection group and 5.6 years (± 2.5) for the ultrasound-guided injection group. In the unadjusted Kaplan-Meier curves for retreatment (Figure 2), the difference in retreatment between blind- and ultrasound-guided subjects occurred mainly within the first 1.5 years after initial injection. The log-rank test indicated a significantly better retreatment-free survival curve for the ultrasound-guided group. Multivariable cox mixed effect analysis of retreatment-free survival, showed an adjusted decreased hazard of retreatment in favor of the ultrasound-guided group (hazard ratio, 0.59; 95% confidence interval [CI], 0.37 - 0.93). Within the ultrasound-guided group 55% (N=48/87) received retreatment with eventual surgery in 44% (N=38/87) of the cases. Within the blind injection group retreatment was 72% (N=169/234), with eventual surgery in 64% of the cases (N= 150/234).

As the vast majority of the failures occurred within one year, the odds ratio (OR) of failure within one year was calculated. Binary logistic analysis indicated that, after adjustment for bilateral cases and covariates, ultrasound guidance was associated with 55% reduced odds of retreatment within one year compared to blind injections (adjusted OR, 0.45; 95% CI, 0.24 - 0.83). Since there was still a slight difference in the proportions of 'normal' EMG after matching, we applied additional adjustment for EMG results to this analysis, with similar results. Retreatment within one year was performed in 41% (N=36/87) of the cases within the ultrasound-guided group and 58% (N=135/234) of the cases within the blind injection group. The number needed to treat to prevent one patient from retreatment within one year was five.

Subgroup analysis

Since the majority of the ultrasound-guided injections was performed by a physical medicine and rehabilitation (PMR) physician (Table 2), we realized that specialty of physician might be a confounder in our cohort. Therefore, we also compared the blind and ultrasound-guided injections performed by only the PMR physicians. This subgroup consisted of 60 ultrasound-guided injections and 124 blind injection cases. We found a comparable adjusted odds-ratio of 0.48 (95% CI, 0.23 - 1.00), although not significant in this smaller sample.

Discussion

The purpose of this study was to assess the effectiveness of ultrasound-guided injections compared to blind injections in the treatment of CTS. Our findings, based on a large population-based cohort, indicate that ultrasound-guided injections are more effective in comparison to blind injections. We found that the retreatment-free survival between blind and ultrasound-guided injections was significantly different, in favor of the ultrasound-guided group. In addition, the odds of 'failure' of injection within one year were 55% reduced in the ultrasound-guided group relative to the blind injection group.

Our finding of an improved effectiveness of injections when they are performed under ultrasound-guidance is in line with the results of previous studies. A trial on 46 patients with CTS, randomized to either an ultrasound-guided or blind injection group found significantly 'greater improvement in Boston Carpal Tunnel Questionnaire (BCTQ) symptom severity at 12 weeks follow-up in favor of the ultrasound-guided group (11). In addition, a study on 75 cases of 44 patients with CTS receiving an injection using either one of two different ultrasound-guided approaches or a blind injection found not only a significantly greater improvement in symptoms in one of the ultrasound-guided groups, but also a larger decrease in cross-sectional area of the median nerve and greater improvement in nerve conduction (12). In the present study, we confirm that the previously reported improvement of short-term symptoms can also reduce the number of reinjections or surgery.

While our outcomes are only defined in terms of therapeutic success, there are additional potential benefits of ultrasound guidance. Ultrasound guidance can potentially lead to a decreased risk of median nerve and surrounding tissue damage (6, 10, 25). In addition, a randomized controlled study on the cost-effectiveness of ultrasound-guided injections found

reduced costs for responders in the ultrasound-guided group relative to the blind injection group, due to a reduction in costs of reinjection or referral to surgery (13). Moreover, ultrasound does not only provide real-time visualization of the needle tip, it also provides high-resolution images of all the structures within the carpal tunnel and can therefore contribute to the diagnosis (26).

Some limitations of our study should be considered. Amongst clinicians there is not only little consensus with regard to the value of ultrasound guidance of injections into the carpal tunnel, but also with regard to almost all aspects of therapeutic injections in carpal tunnel syndrome, including volume of injection and type and concentration of steroid. This was also reflected in our dataset and resulted in exclusion of a subset of the cases. Although we were able to adjust for the remaining differences in treatment characteristics, a standardized type and volume of the corticosteroid would have been preferable. Another limitation of our study is the exclusion of about 7% of potential cases because the patients had not authorized the use of their medical records for research (14). In addition, a limitation of the study design is the lack of blinding. As a result, the use of ultrasound-guidance may have affected the patients' perception of injection effect, especially as objective measures such as post injection electrodiagnostic testing were not available for analysis.

A strength of the present study is the use of propensity score matching to account for imbalances in observed variables. However, this method cannot account for possible hidden confounding factors. The suggested higher effectiveness of ultrasound-guided injections may depend on the experience of the physician and we cannot rule out that specialty of physician was a confounder. In addition, the physicians in our cohort used different techniques for both types of interventions. Different techniques of ultrasound guidance in carpal tunnel injections have been described (12, 27, 28) and since the study by Lee et al. suggests that one technique may be more efficient than the other, this may have influenced the outcome.

The present study suggests that ultrasound-guided injections are more effective compared to blind injections in the treatment of carpal tunnel syndrome. This outcome warrants further study, for example in a well-designed randomized trial with a well-defined type of steroid and injection volume, using a standardized technique.

Acknowledgments

This study was made possible using the resources of the Rochester Epidemiology Project, which is supported by the National Institute on Aging of the National Institutes of Health under Award Number R01AG034676. The project was additionally supported by NIH/NCRR Colorado CTSI Grant Number UL1 RR025780 and Mayo Foundation.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Significance and Innovations

- This study suggests that corticosteroid injections in the treatment of carpal tunnel syndrome (CTS), the most common entrapment neuropathy, are more effective with the use of ultrasound guidance.
- This is the first study assessing the effectiveness of ultrasound-guidance in the treatment of CTS in a large population based cohort over a longer period of follow-up.
- With the use of propensity score matching the level of evidence for this study is three.

Figure 1.

Figure 2.
Kaplan-Meier curves.

Table 1

Baseline characteristics before and after matching and treatment characteristics after matching.

Characteristic	All subjects				Matched subjects			
	Blind injection (n=600)	US-guided injection (n=89)	Standardized differences	p	Blind injection (n=234)	US-guided injection (n=87)	Standardized differences	p
<i>Demographics</i>								
Female (%)	72	78	0.139	.24	73	77	0.092	.43
Age, mean yr (SD)	50 (14)	50 (15)	0.067	.37	50 (15)	50 (15)	0.006	.93
<i>EMG severity (%)</i>								
Mild	29	18	0.262	.03	17	18	0.034	.79
Moderate	40	36	0.082	.52	40	37	0.007	.58
Severe	6	7	0.105	.83	8	7	0.031	.81
Normal	9	19	0.304	.00	14	17	0.100	.42
Unknown	17	20	0.090	.41	21	21	0.017	.90
<i>Comorbidities (%)</i>								
Diabetes Mellitus	9	6	0.114	.29	7	6	0.041	.63
Rheumatoid Arthritis	6	19	0.401	.00	13	17	0.112	.31
Peripheral neuropathy/Radiculopathy	6	3	0.145	.34	5	3	0.102	.63
Other	3	0	0.249	.09	0	0	NA	NA
Pregnancy induced CTS (%)	3	0	0.249	.11	0	0	NA	NA
<i>Treatment characteristics</i>								
Volume of injection, mean mL (SD)					3.1 (0.7)	2.6 (0.7)	0.689	.08
Effective dose (mg) (%)								.08
< 30					29	16	0.315	
40					24	25	0.023	
60					44	57	0.262	
80					2	1	0.082	

US= ultrasound, SD= standard deviation

Note: continuous variables were tested using an independent sample T-test. Proportions were tested using chi-square test.

Table 2

Proportion of ultrasound-guided and blind injections subdivided by specialty of physician in matched dataset.

Physician specialty	Blind injection (%)	Ultrasound-guided injection (%)
Orthopedic surgery	37	3
Plastic surgery	3	0
Physical medicine and rehabilitation	53	69
Family medicine	1	0
Rheumatology	5	26
Internal medicine	0.4	0
Radiology	0	1