

Ultrasonography Predictive Factors of Response to Local Steroid Injection in Patients with Carpal Tunnel Syndrome

Abstract

Background: The aim of this study is to determine the predictive value of ultrasonography for results of local steroid injection in patients with carpal tunnel syndrome (CTS). **Materials and Methods:** This prospective cohort study was conducted during a 1-year period in outpatient clinics of rehabilitation and physical medicine including 35 patients with moderate and severe CTS who receive ultrasonography-guided local steroid injection. The Boston self-assessment questionnaire and electrodiagnosis parameters were recorded at baseline, 1 month, and 3 months after therapy. We also recorded the baseline ultrasonography parameters to determine the predictors of outcome. **Results:** The sensory severity score and functional status scale along with electrodiagnosis parameters decreased significantly at 1 month ($P < 0.001$) and remained unchanged after 3 months. Volar bulging was negatively associated with sensory nerve action potential latency ($r = -0.392$; $P = 0.020$). Cross-sectional area (CSA) of maximal swelling (MS; $r = 0.409$; $P = 0.015$), CSA at 2-cm of MS ($r = 0.563$; $P < 0.001$), and CSA at 12-cm of MS ($r = 0.521$; $P = 0.001$) correlated positively with compound muscle action potential (CMAP) amplitude while maximal swelling/12-cm MS ratio ($r = -0.439$; $P = 0.008$) and maximal swelling/2-cm MS ratio ($r = -0.342$; $P = 0.045$) correlated negatively. CSA at 12-cm of MS also correlated positively with CMAP amplitude nerve conduction velocity ($r = 0.436$; $P = 0.010$). **Conclusion:** Volar bulging, CSA of maximal swelling, CSA of MS at 2-cm, and CSA of MS at 12-cm are among the ultrasonographic predictors of response to local steroid injection in patients with CTS.

Keywords: Carpal tunnel syndrome, local steroid therapy, prediction, ultrasonography

Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment syndrome of peripheral nerve caused by the impairment of the median nerve due to compression as it passes through the carpal tunnel. The syndrome is diagnosed clinically according to the sign and symptoms and the physical examination.^[1] The diagnosis is confirmed by the electrophysiologic studies including nerve conduction and electromyography.^[2] However, the lack of accuracy in diagnosis has been mentioned as one the most common causes of treatment failure.^[3] The treatment options for CTS include conservative management and the surgical decompression of the median nerve. The nonoperative options for treatment of CTS include local corticosteroids injection, oral corticosteroids, knight orthosis, and physical therapy.^[1,4] It has been demonstrated that local injection of steroids is associated with significant relieving of symptoms at

10 weeks and reducing the rate of surgery 1 year after treatment.^[5,6] However, surgery remains the best therapeutic option for patients with CTS with good response rate and low recurrence rate.

Recently, ultrasonography has been used to evaluate the carpal tunnel anatomy for a better diagnosis as well as evaluation of response to therapy.^[7,8] Increased cross-sectional area (CSA) at the level of the pisiform bone, increased swelling ratio, increased flattening ratio at the level of the hook of hamate, and the presence of palmar bowing (posteroanterior replacement of the palmar flexor retinaculum) have been shown to be associated with CTS.^[7,8] Some authors have also utilized the ultrasonography to predict the outcome after local steroid injection.^[9,10] It has been demonstrated that the therapeutic success of local steroid injection is mainly associated with the finding of power Doppler signal.^[9] The initial median nerve swelling and its

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ratio have also been presented as a predictor of response after steroid injection. Despite the current evidence, data regarding the ultrasonographic predictors of response to steroid injection therapy in patient with CTS are scarce. Thus, the aim of the current study was to determine the ultrasonographic predictors of response to local steroid injection in patients with CTS.

Materials and Methods

Study population

This was a prospective cohort study being performed during a 1-year period from March 2014 to March 2015 in rehabilitation and physical medicine outpatient clinics of Isfahan University of Medical Sciences. We have included adult patients (>18 years) diagnosed with moderate to severe CTS referring to our clinics for management. Diagnosis of CTS was according to the clinical signs and symptoms of CTS and confirmation by nerve conduction studies (NCSs) (electrodiagnosis). The CTS was graded from mild to severe according to Sucher^[11] based on electrodiagnosis. We only included those with moderate and severe CTS who wanted to receive local steroid injections for treatment. We excluded those who had underlining disease attributable with CTS including diabetes mellitus, thyroid dysfunction, tumor, traumatic nerve damage, fractures of the distal radius, and pregnancy. Those with conditions affecting the outcome of therapy such as cervical disc herniation, fibromyalgia, mucopolysaccharides, and simultaneous neuropathy were also excluded. Previous local steroid injection in the affected wrist and upper extremity surgery on the wrist were among the exclusion criteria. Those with advanced and prolonged CTS leading to severe thenar muscle atrophy and motor weakness were also excluded from the study. The study protocol was approved by the Medical Ethics Committee and the Institutional Review Board of Isfahan University of Medical Sciences. All the patients provided their informed written consents before inclusion in the study.

Study protocol

All the patients were first examined, and a detailed history and clinical examination was carried out by the rehabilitation and physical medicine resident and the findings were recorded in the data gathering form. Demographic information and the clinical data were also recorded. All the patients were assessed by electrodiagnosis parameters to confirm the diagnosis. All the electrodiagnosis procedures were performed by the same attending physician. All the patients filled the Boston self-assessment questionnaire (BQ) which was previously translated and validated in Persian.^[12] This questionnaire is consist of two parts: Symptom severity scale (SSS) and functional status scale (FSS). Carpal tunnel ultrasonography was performed by a radiologist who was blind to the clinical and electrodiagnosis findings. All the findings were recorded in the data gathering form.

All the patients received single-dose steroid injection into the carpal tunnel after the diagnostic modalities were performed. Ultrasonographic-guided steroid injection was performed using ulnar-side technique previously described by Smith *et al.*^[13] Accordingly, the wrist was placed at mild dorsiflexion. Using a 26-gauge needle, 20 mg of methylprednisolone acetate (Caspian Pharmaceutical, Tehran, Iran) was injected on the ulnar tendon of palmaris longus muscle with an angle of 30° below flexor retinaculum under guide of ultrasonography. All the patients received cockup wrist splint, nonsteroidal anti-inflammatory drug, and a GABAminergic agent after the injection.

Electrodiagnosis procedure

All the electrodiagnosis procedures were performed by the same attending physician using an electrodiagnostic device. The patient's hand temperature was preserved above 32°C and median motor NCS was performed for recording initial latency and baseline to peak amplitude from active site of abductor pollicis brevis (motor point). Stimulation was done as orthodromic in wrist 8 cm above the data logger site. Median sensory NCS was also performed for recording initial latency and baseline to peak amplitude from third finger (active site) with antidromic stimulation in hand wrist (14 cm above logger site) and in hand palm (7 cm above logger site). The diagnostic criteria and severity grading of CTS were selected according to previously described one.^[11] The electrodiagnosis parameters included sensory nerve action potential (SNAP) and compound muscle action potential (CMAP). For each the amplitude, latency and nerve conduction velocity were recorded.

Wrist ultrasonography

Ultrasound was performed using a high-frequency probe linear and sonography machine by the same radiologist who was blinded to the clinical and electrodiagnosis findings. With the patient in supine position, supinated forearm, and wrist in neutral position, ultrasonography probe was placed vertical to prevent nerve anisotropy and deformation. We measured the median nerve CSA at Pisiform bone (1–2 cm in normal individuals), transverse to anteroposterior diameter ratio of nerve at bone level (<1.4 in normal individuals), volar bulging of the flexor retinaculum (normally <3.1 mm), and the CSA of the median nerve. The CSA was measured at three locations. The three locations of the median nerve ultrasonography parameters included the maximal swelling point (MS) of the median nerve, 2 cm proximal from MS (2MS), and 12 cm proximal from MS (12MS). Following measurement, the CSA was calculated. The CSA of the median nerve was measured by continuous tracing of the nerve circumference, excluding the hyperechoic epineuria rim. The average value was reported based on three measurements. Using the CSAs of MS, 2MS, and 12MS, the CSA ratio of the median nerve was then calculated (MS/12MS, 2MS/12MS).^[14]

Follow-up and measurements

Patients were evaluated 1 and 3 months after the injection. The electrodiagnosis procedure was performed in each follow-up visit and the patients were asked to fill the BQ themselves. The complications were evaluated during follow-up visits and were recorded.

Statistical analysis

To have 80% power to determine the predictive value of ultrasonography parameters for response to local steroid injection with $\alpha = 0.01$ and coefficient equal to 1.96, a minimum number of 33 patients were required for the study. To compensate for nonvaluable patients, we included a total number of 45 patients in the current study. All statistical analyses were carried out utilizing Statistical Package for Social Sciences version 20.0 (SPSS Inc., Chicago, Illinois, USA). Data are reported as mean \pm standard deviation and proportions as appropriate. Repeated measures were used to evaluate the trends in changes of parametric variables. Paired *t*-test was used to compare the severity of symptoms and functional status as well as electrodiagnosis parameters before and after injection. We used Pearson correlation to determine the linear correlation between the initial ultrasound parameters and clinical response of patients (based on symptom severity and FSS). The correlation coefficients were also reported. Two-sided $P < 0.05$ was considered statistically significant.

Results

Overall, we included 45 patients with moderate and severe CTS receiving single local steroid injection. During the study, 3 patients underwent surgery and 7 patients were lost to follow-up. Thus, the total number of patients included in the final analysis was 35. The mean age of the patients was 47.9 ± 9.7 (ranging from 30 to 65) years. There were 27 (77.1%) women and 8 (22.9%) men among the participants. At baseline, 29 (82.9%) patients suffered from moderate and 6 (17.1%) from severe CTS. Table 1 summarizes the trend in changes of clinical and electrodiagnosis parameters from baseline to 3 months after the steroid injection. We found that the FSS ($P < 0.001$) and SSS ($P < 0.001$) improved significantly after 1 month and the effects lasted for 3 months. In the same way, all the electrodiagnosis parameters improved significantly after a month and lasted for 3 months except for SNAP latency which remained unchanged [Table 1]. The severity grading of CTS according to electrodiagnosis parameters decreased significantly after 1 month of therapy which remained unchanged after 3 months [Table 2].

We performed a correlation analysis to determine the ultrasonographic predictors of response to steroid therapy in these patients. We found that none of the ultrasonographic parameters had correlation with clinical outcome measures including SSS and FSS [Table 3]. However, we found that volar bulging was negatively associated with SNAP

Table 1: Trend of changes of clinical, electrodiagnosis, and ultrasonographic parameters in 35 patients with moderate and severe carpal tunnel syndrome receiving local steroid injection from baseline to 3-month follow-up

Parameters	Baseline	1 month	3 months	P
SSS	2.96 \pm 0.89	1.49 \pm 0.40*	1.40 \pm 0.57 [§]	<0.001
FSS	2.67 \pm 0.78	1.42 \pm 0.43*	1.39 \pm 0.55 [§]	<0.001
SNAP latency (ms)	4.50 \pm 1.58	4.35 \pm 0.92	4.42 \pm 0.56	0.436
SNAP amplitude (μ V)	12.09 \pm 8.4	16.12 \pm 8.50*	16.28 \pm 7.58 [§]	<0.001
SNAP NCV (mm/ms)	23.80 \pm 9.9	29.50 \pm 0.2*	30.22 \pm 7.09 [§]	<0.001
CMAP latency (ms)	5.30 \pm 0.91	4.81 \pm 0.68*	4.66 \pm 0.50 [§]	<0.001
CMAP amplitude (mV)	5.79 \pm 1.30	6.90 \pm 1.33*	7.00 \pm 1.17 [§]	<0.001
CMAP NCV (mm/ms)	52.72 \pm 4.7	54.33 \pm 4.16*	54.43 \pm 3.56 [§]	<0.001
T/AP ratio	2.95 \pm 0.6	-	-	-
Volar bulging (mm)	3.93 \pm 1.36	-	-	-
CSA of MS (mm ²)	14.61 \pm 3.0	-	-	-
CSA at 2MS (mm ²)	7.29 \pm 1.97	-	-	-
CSA at 12MS (mm ²)	4.74 \pm 1.40	-	-	-
MS/12MS	3.17 \pm 0.72	-	-	-
2MS/12MS	1.56 \pm 0.27	-	-	-
MS/2MS	2.09 \pm 0.52	-	-	-

*Statistically significant difference when compared to baseline using paired *t*-test ($P < 0.05$), [§]Statistically significant difference when compared to baseline using paired *t*-test ($P < 0.05$). CMAP: Compound muscle action potential, CSA: Cross-sectional area, FSS: Functional status scale, MS: Maximal swelling point, NCV: Nerve conduction velocity, SNAP: Sensory nerve action potential, SSS: Symptom severity scale, T/AP: Transverse to anteroposterior, 2MS: 12 cm proximal from MS, 12MS: 12 cm proximal from MS

latency ($r = -0.392$; $P = 0.020$). CSA of MS ($r = 0.409$; $P = 0.015$) CSA at 2MS ($r = 0.563$; $P < 0.001$), CSA at 12MS ($r = 0.521$; $P = 0.001$) were all correlated positively with CMAP amplitude while MS/12MS ratio ($r = -0.439$; $P = 0.008$) and MS/2MS ratio ($r = -0.342$; $P = 0.045$) correlated negatively with that [Table 4]. CSA at 12MS also correlated positively with CMAP NCV ($r = 0.436$; $P = 0.010$). No complication regarding the steroid injection was recorded.

Discussion

Local steroid injection is among the most effective conservative management of CTS being associated with improved clinical and electrodiagnosis parameters.^[5,6] The mechanism of CTS includes pressure over the median nerve through the carpal tunnel, inflammation, swelling,

and finally ischemia. Thus, reducing the inflammation and canal swelling will result in improved symptoms.^[15] Local steroids decrease the inflammation and synovial swelling and thus the subsequent ischemia of the median nerve.^[16,17] Recently, ultrasonography has been introduced in the field of management of CTS.^[9,10,14,17] Ultrasonography-guided injection of local steroids and use of ultrasonography for diagnosis and evaluation of response to therapy are

among these utilizations.^[9,10,17] In the current study, we used ultrasonography for both injection of local steroid and also to predict the response to therapy. We found that ultrasonography-guided injection of local steroid is a safe and feasible approach for the treatment of patients with CTS. In addition we found that ultrasonographic parameters including volar bulging and CAS at different points are good predictors of response to local steroid injection. This could be used for patient selection and outcome prediction in patients with CTS.

Recently, Jeong *et al.*^[10] verified the feasibility of initial parameters of ultrasonography or electromyography for the prediction of effect after steroid injection therapy in patients with CTS. Evaluation of median nerve ultrasonography parameters included measurements taken at the MS, 2MS, and 12MS, and its ratio (MS/12MS, 2MS/12MS). After steroid injection therapy, clinical and electromyographic parameters showed significant improvements at 1 or 6 months after injection, and ultrasonographic parameters showed significant changes in maximal area and area ratio (MS/12MS) of the median nerve. Symptom score improvement showed a positive correlation in the initial 2MS and ratio of 2MS/12MS after 6 months ($P < 0.05$).^[10] We found that both clinical and electrodiagnosis parameters improved significantly after 1 month of therapy and remained unchanged after 3 months. In our study, the volar bulging was negatively associated with SNAP latency indicating that increased volar bulging at baseline will predict poor response to local steroid injection determined by SNAP latency. In the same way, we observed that CSA at MS, 2MS, and 12MS correlated positively with CMAP amplitude demonstrating that these parameters could be considered as good predictors of response to therapy with local steroids. The MS/12MS and MS/2MS ratios correlated negatively with CMAP amplitude grouping them as the negative predictors of response to therapy. Finally, 12MS correlated positively with CMAP NCV, placing it among the good predictors of outcome in patients with moderate to severe CTS. In another study, Guillen Astete *et al.*^[9] demonstrated that finding of power-Doppler signal

Table 2: The changes in grades of carpal tunnel syndrome according to electrodiagnosis at baseline and after 3 months

Parameters	Baseline	1 month	3 months	P
Normal (%)	0	1 (2.9)	2 (5.7) [§]	0.011
Mild (%)	0	6 (17.1)*	6 (17.1) [§]	0.018
Moderate (%)	29 (82.9)	26 (74.3)*	25 (71.4) [§]	0.023
Severe (%)	6 (17.1)	2 (5.7)*	2 (5.7) [§]	0.010

*Statistically significant difference when compared to baseline using paired *t*-test ($P < 0.05$), [§]Statistically significant difference when compared to baseline using paired *t*-test ($P < 0.05$)

Table 3: Correlation analysis of final sensory severity score and functional status scale with baseline ultrasonographic parameters in 35 patients with moderate and severe carpal tunnel syndrome after single injection of steroid

Parameters	SSS		FSS	
	r	P	r	P
T/AP ratio	-0.146	0.403	0.071	0.686
Volar bulging (mm)	-0.102	0.560	-0.019	0.912
CSA of MS (mm ²)	0.101	0.562	0.129	0.460
CSA at 2MS (mm ²)	-0.02	0.989	-0.011	0.950
CSA at 12MS (mm ²)	0.033	0.852	0.050	0.776
MS/12MS	0.025	0.886	0.110	0.530
2MS/12MS	0.034	0.847	-0.056	0.748
MS/2MS	0.091	0.605	0.135	0.440

CSA: Cross-sectional area, FSS: Functional status scale, MS: Maximal swelling point, SSS: Symptom severity scale, T/AP: Transverse to anteroposterior, 2MS: 12 cm proximal from MS, 12MS: 12 cm proximal from MS

Table 4: Correlation analysis of final electrodiagnosis parameters with baseline ultrasonographic parameters in 35 patients with moderate and severe carpal tunnel syndrome after single injection of steroid

Parameters	SNAP latency		SNAP amplitude		SNAP NCV		CMAP latency		CMAP amplitude		CMAP NCV	
	r	P	r	P	r	P	r	P	r	P	r	P
T/AP ratio	-0.061	0.726	0.139	0.426	0.026	0.887	-0.017	0.923	0.240	0.165	0.268	0.126
Volar bulging (mm)	-0.392	0.020	0.071	0.685	-0.072	0.680	-0.243	0.160	0.026	0.881	0.117	0.511
CSA of MS (mm ²)	-0.197	0.257	0.169	0.331	0.104	0.552	0.123	0.482	0.409	0.015	0.219	0.213
CSA at 2MS (mm ²)	-0.124	0.477	0.188	0.280	0.171	0.326	-0.193	0.267	0.563	<0.001	0.436	0.010
CSA at 12MS (mm ²)	-0.199	0.252	0.113	0.517	0.119	0.496	-0.041	0.814	0.521	0.001	0.329	0.057
MS/12MS	0.181	0.299	0.040	0.820	-0.021	0.902	0.071	0.685	-0.439	0.008	-0.146	0.410
2MS/12MS	0.178	0.306	0.023	0.894	-0.013	0.942	-0.159	0.362	-0.083	0.637	0.083	0.640
MS/2MS	0.042	0.811	-0.068	0.699	-0.118	0.498	0.239	0.168	-0.342	0.045	-0.196	0.267

CMAP: Compound muscle action potential, CSA: Cross-sectional area, MS: Maximal swelling point, NCV: Nerve conduction velocity, SNAP: Sensory nerve action potential, T/AP: Transverse to anteroposterior, 2MS: 12 cm proximal from MS, 12MS: 12 cm proximal from MS

in carpal tunnel is the most important predictor of response to local steroid injection.

In the current study, the improvement occurred during the 1st month of injection and lasted up to 3 months. It demonstrates that local steroid injection provides initial response in 1 month and lasts for at least for 2 months. Similarly, Jeong *et al.*^[10] reported the initial response occur in 1 month and last for 6 months. Atroshi *et al.*^[5] performed a large randomized clinical trial investigating the role of local steroid injection in the treatment of moderate to severe CTS. They found that improvement in CTS symptom severity scores at 10 weeks was greater in patients who received 80 mg of methylprednisolone and 40 mg of methylprednisolone than in those who received placebo, but there were no significant differences at 1 year. The 1-year rates of surgery were 73%, 81%, and 92% in the 80-mg methylprednisolone, 40-mg methylprednisolone, and placebo groups, respectively. Compared with patients who received placebo, those who received 80 mg of methylprednisolone were less likely to have surgery. With time to surgery incorporated, both 80- and 40-mg methylprednisolone groups had lower likelihood of surgery. Thus, it could be concluded that methylprednisolone injections for CTS have significant benefits in relieving symptoms at 10 weeks and reducing the rate of surgery 1 year after treatment, but the rate of surgery does not decrease after 1 year.^[5]

Recently, many authors have emphasized on the role of ultrasound in diagnosis of CTS.^[14,18] Ultrasonography is a noninvasive and inexpensive and accessible modality that could be used not only for diagnosis but also for predicting the outcome.^[9,10,14,18] Results of the current study indicate that ultrasonography could be used as a useful tool for evaluating and predicting steroid response. A wide range of CTS assessment parameters has been introduced for diagnosis of CTS. Nerve CSA at the level of the proximal pisiform bone and proximal part of the pronator quadratus muscle, the presence of a “notch” sign and “inverted notch” sign, compression site, echogenicity and echotexture of the median nerve proximally to the compression site, evidence of increased vascularity of the median nerve above the compression site in a power Doppler examination and the movability of the median nerve in the carpal tunnel are among the parameters that are being currently used for assessing the CTS.^[19,20]

We note some limitation to the current study. First, the sample size population was small and thus the power of the study was calculated to be 80%. Although acceptable, larger studies are required to determine the ultrasonographic predictive factors of CTS. Second, we did not perform the ultrasonography in follow-up visits. These data are required to determine the changes in ultrasonography parameters in response to therapy. The short follow-up period of the study was also among the weak points of the study.

Further studies are required including these parameters in follow-up. Taken all together, this is among the first studies that provide the predictive factors of response to local steroid injection utilizing ultrasonography.

Conclusion

Volar bulging, CSA at MS, CSA at 2MS, and CSA at 12MS are among the ultrasonographic predictors of response to local steroid injection in patients with CTS.

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Conflicts of interest

There are no conflicts of interest.

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