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Extracorporeal shock wave therapy in cubital tunnel syndrome: A pilot study

Yu-Ping Shen *MD*, Yin-Yin Wu *MD*, Heng-Yi Chu *MD*, Tsung-Ying Li *MD*, Liang-Cheng Chen *MD MS*, Yung-Tsan Wu *MD*

Department of Physical Medicine and Rehabilitation, Tri-Service General Hospital, School of Medicine, National Defense Medical Center, Taipei, Taiwan, Republic of China.

Abstract

Objectives: To investigate the clinical therapeutic effect of extracorporeal shock wave therapy in the treatment of cubital tunnel syndrome. *Methods:* Seven patients (10 elbows) with moderate cubital tunnel syndrome participated in this study. Three sessions of radial extracorporeal shock wave therapy (2,000 shots, 4 Bar, 5 Hz) (once a week) were administered to the ulnar nerve at the proximal cubital tunnel region. The primary and secondary outcomes were assessed using the Visual Analog Scale (VAS) and the shortened Disabilities of the Arm, Shoulder and Hand questionnaire (Quick DASH), respectively, at the 4th, 8th, and 12th week, following the 3rd session of shock wave therapy. *Results:* The VAS and Quick DASH scores demonstrated improvements at all follow-up time points, in all treated elbows. The mean VAS and Quick DASH score improved from 4.7±0.3(mean±SE) to2.2±0.2 and 16.6±2.1to 6.8±1.6 respectively during 12 weeks follow up (all p <0.01).
Conclusion: This pilot study revealed the safety and efficacy of extracorporeal shock wave therapy in patients with moderate cubital tunnel syndrome.

Keywords: Cubital tunnel syndrome; ulnar neuropathy; extracorporeal shock wave therapy; disability

INTRODUCTION

Cubital tunnel syndrome (CuTS) is the second most common peripheral nerve entrapment syndrome. The pathophysiology of CuTS results from compression of the ulnar nerve at the cubital tunnel due to increasing traction of the ulnar nerve over the elbow.[1] The etiologic factors include constricting fascial bands, soft-tissue hypertrophy (synovium), space occupied lesions (cyst, hematoma or tumor), bony abnormalities (cubitus valgus, bone spurs), or elbow flexion with ulnar nerve subluxation.[2]

The clinical symptoms of CuTS include numbness, tingling, pain in the 5th finger, and ulnar half of the 4th finger. Furthermore, hand weakness, clumsiness, or atrophy of the intrinsic muscles of the hand occur in patients with moderate to severe CuTS.[3] McGowan stratified the severity of CuTS into three grades based on the symptoms: grade I (mild, intermittent, and purely sensory); grade 2 (moderate and persistent, including weakness); grade 3 (severe, including paresis and muscle atrophy).[4]

CuTS can be managed by conservative and surgical therapy. Conservative treatments include physical therapy, anti-inflammatory medication, avoidance of direct pressure to the medial aspect of the elbow, usage of a nighttime elbow towel orthosis to prevent elbow flexion beyond 50 degrees, and nerve gliding exercises.[5,6] Dallon *et al*. reported that 42% of mild cases and 34% of moderate cases demonstrated improvement after 6 months of conservative treatment.[7] In another study, although a better outcome (80%) and lower recurrence (5%) were noted in mild cases, only 38% and 40% of moderate and severe cases, respectively, showed improvement after one year of conservative treatment.[8] Severe cases and patients failing to respond to conservative treatments are indicated for surgery. However, surgical concerns include complications such as poor wound healing, infection, neuroma formation, and nerve injury.[1] Therefore, an effective and safe conservative treatment for CuTS is needed, especially in moderate to severe cases.

Extracorporeal shock wave therapy (ESWT) has been widely used for treating various musculoskeletal disorders including calcific tendonitis, epicondylitis, Achilles tendinopathy, and plantar fasciitis. The proposed biological

Address correspondence to: Dr. Yung-Tsan Wu, MD, Department of Physical Medicine and Rehabilitation, Tri-Service General Hospital, School of Medicine, National Defense Medical Center, No. 325, Sec. 2, Cheng-Kung Road, Neihu District, Taipei, Taiwan, Republic of China. Tel: +886-2-8792-3311, e-mail: crwu98@gmail.com

effects include neurogenesis, angiogenesis, anti-inflammation, production of growth factors, and the activation of progenitor cells and stem cells.[9] Axonal regeneration, proliferation of Schwann cells, and macrophage activation during myelin debris removal in nerve repair have also been described.[9] Recently, ESWT has been proven to be beneficial in carpal tunnel syndrome (CTS).[10-13] However, ESWT in the treatment of CuTS has not been assessed yet. Hence, we conducted a pilot study applying ESWT in patients with moderate CuTS.

METHODS

Participants

We enrolled 7 patients (10 elbows), aged 35-71 years, with a diagnosis of moderate CuTS. The diagnosis was based on clinical symptoms (numbness, tingling, pain in the 5th finger, and the ulnar half of the 4th finger) and electrophysiological studies. Patients' symptoms and signs including motor weakness, had persisted for at least 6 months (McGowan grade 2).[4] The nerve conduction velocity fit the criteria of a relative drop in conduction velocity more than 10 m/s of ulnar motor nerve across the elbow.[2] We excluded patients who had brachial plexus neuropathy, history of elbow trauma or operation, diabetes mellitus, malignancy, coagulopathy, pregnancy, active infection, or implanted pacemakers. All participants provided informed consent for this study. The trial was approved by the institutional review board of Tri-Service General Hospital and registered at ClinicalTrials.gov (number NCT02801461). Additional management during the study period was regulated in the patients.

ESWT intervention

Patients were seated and the target elbow was placed on the table with 40-50 degrees flexion, in a relaxed position. We identified the ulnar nerve proximal to the inlet of the cubital tunnel where swelling of the nerve was observed with Tinel's sign, using ultrasonography (MyLab™ 25Gold, Esaote, Genova, Italy) (Figure 1A).[11] Radial EWST (Pagani Elettronica, Milano, Italy) was administered with 2000 shots, 4 Bar pressure, and 5 Hz frequency by a single physician, using a probe perpendicular to the ulnar nerve (Figure 1B).[11,12] The participants received ESWT weekly for 3 consecutive weeks (total of 3 sessions). All patients tolerated the procedure well, without any analgesic agent.

Outcome measurements

The assessments were performed by a single physician, before treatment, and on the 4th, 8th, and 12th week after the third ESWT session.

Primary outcome

The Visual Analog Scale (VAS) was used to quantify digital pain or paresthesia/dysthesia within one week. The scale ranged from 0 (painless) to 10 (severe pain).[14]

Secondary outcome

The Disabilities of the Arm, Shoulder and Hand questionnaire (DASH) has been widely used to evaluate upper extremity disorders, including CuTS.[15,16] We applied shortened DASH (Quick DASH), which exhibits similar effectiveness as DASH, for assessment.[17] The questionnaire contains an 11-item disability/symptom scale (each with 5 levels of response, ranging from 1 to 5). A higher score means more disability or more severe symptoms.

Data analysis

All the data were statistically analyzed by using the SPSS version 22.0 (SPSS Inc., Chicago, IL,

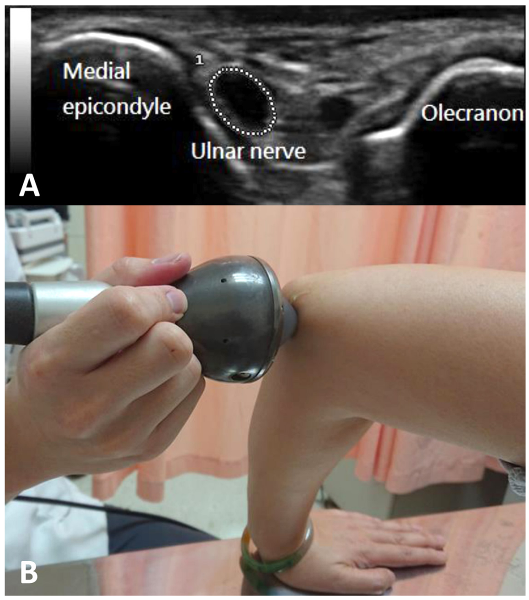

Figure 1. (A) Detection of the swelling of the ulnar nerve (dotted circle) at cubital tunnel using ultrasonography. (B) The patient was seated and the target elbow was placed on the table with 40 to 50 degrees flexion. Radial shock wave therapy was applied with the probe perpendicular to the ulnar nerve.

USA). The repeated-measures ANOVA followed by Bonferroni post hoc test and Wilcoxon singed-rank test were used for data at various follow-up. All statistical tests were two-tailed and a p-value less than 0.05 was considered as statistically significant.

RESULTS

The mean age of the participants was 47.9 years. Three among them had bilateral CuTS (Table 1). Post-treatment, VAS decreased significantly in all treated elbows at all follow-up time points (all $p < 0.01$). The mean VAS score at baseline was 4.7±0.3 (mean±SE), and improved to 2.9±0.3, 2.5±0.3, and 2.2±0.2, at the 4^{th}, 8^{th}, and 12^{th} week post-ESWT, respectively (Table 2 and Figure 2). The Quick DASH score also decreased in all cases with time; the mean point before management was 16.6±2.1 and decreased to 11.7±2.5, 7.5±1.3, and 6.8±1.6 at the 4^{th}, 8^{th}, and 12^{th}week post-treatment, respectively (Table 2 and Figure 2, all $p < 0.01$). No patient exhibited complications or required additional management during the study.

DISCUSSION

To our knowledge, this is the first pilot study to assess the therapeutic effect of ESWT in patients with CuTS. The results showed significant improvement of symptoms and disability in all cases during the 12 weeks of follow-up.

The mechanism of ESWT in promoting regeneration of peripheral nerves is unclear. Enhanced regeneration and functional recovery of injured nerves treated by ESWT have been observed in animal studies.[18,19] The biological mechanisms underlying these effects include activation of integrin-extracellular matrix coupling, rising proliferation of Schwann cells, enhanced macrophage activity, and molecular changes in neuron related expression of activating transcription factor 3 (ATF-3) and growth-associated phosphoprotein 43 (GAP-43).[9]

Previous studies have also reported analgesic effects of ESWT, potentially contributing to symptom relief in peripheral neuropathy. ESWT can induce production of nitric oxide (NO) inhibiting NF-ϰB activation, and suppress inflammatory responses.[9,10,20,21] NO can also directly impede pain conduction by opening potassium channels and reducing calcium influx into nerve cells, resulting in hyperpolarization.[10,22] The anti-inflammatory action may also reduce swelling of the soft tissue surrounding the ulnar nerve and decrease the pressure in the cubital

Table 1: General data of study subjects

Case no.	Age (year)	Sex	Lesion side	Duration (month)	VAS				Quick-DASH			
					Baseline	4^{th} week	8^{th} week	12^{th} week	Baseline	4^{th} week	8^{th} week	12^{th} week
1	67.0	Female	Right	120	5	4	4	3	11.36	11.36	9.09	5.68
2	32.0	Male	Left	30	4	3	3	2	11.36	5.68	5.68	4.55
3	40.0	Female	Right	24	5	2	2	2	15.9	6.82	5.68	4.55
4	40.0	Female	Left	24	4	2	2	2	11.36	2.27	4.55	4.55
5	49.0	Female	Left	15	6	2	2	1	13.64	4.55	4.55	2.27
6	35.0	Female	Right	6	5	2	2	2	13.64	9.09	2.27	2.27
7	35.0	Female	Left	6	4	3	2	2	11.36	9.09	4.55	2.27
8	71.0	Male	Left	6	6	5	4	4	22.73	22.73	13.64	11.36
9	55.0	Female	Right	24	4	3	2	2	27.5	22.5	12.5	15
10	55.0	Female	Left	24	4	3	2	2	27.5	22.5	12.5	15
Mean	**47.9**			**27.9**	**4.7**	**2.9**	**2.5**	**2.2**	**16.64**	**11.66**	**7.50**	**6.75**

VAS=Visual analog scale; DASH=Disabilities of the Arm, Shoulder and Hand questionnaire.

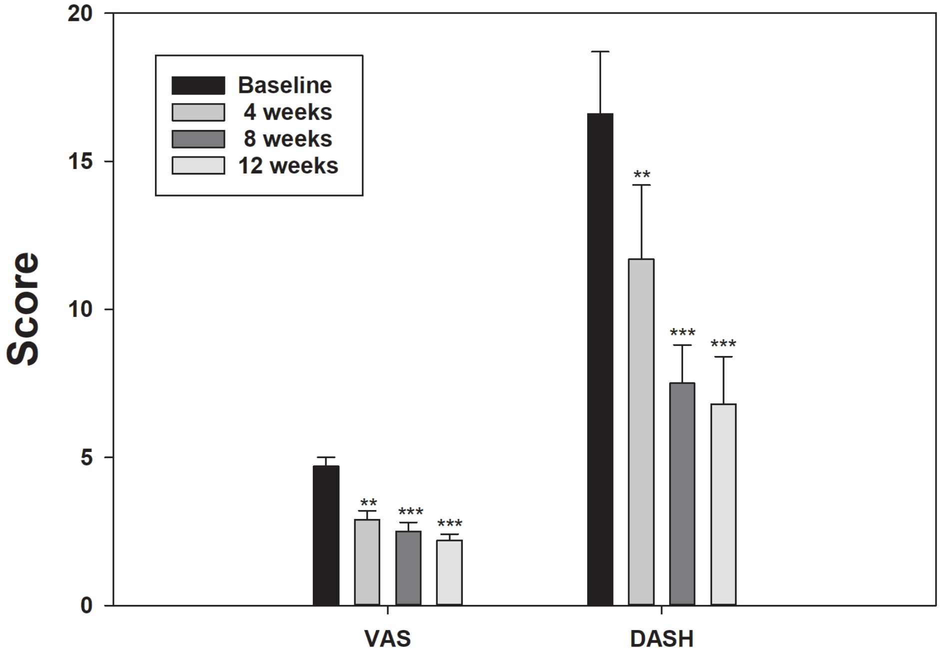

Figure 2. Visual analog scale (VAS) and shortened Disabilities of the Arm, Shoulder and Hand questionnaire (Quick DASH) scores at baseline, and 4th, 8th, and 12th week of follow-up. Compared to baseline, significant improvements on both scales were noted at all follow-up timepoints (all p<0.01).
** p<0.01, ***p<0.001.

tunnel.[10] Moreover, ESWT may contribute to the reduction of calcitonin gene-related peptide (related to transmission of pain).[23] ESWT also inactivates the C fibers and increases activity within the descending inhibitory pathways from the brain stem that modulate gate-control of pain. Additionally, ESWT may promote angiogenesis by upregulating stromal-derived factor 1 (SDF-1), vascular endothelial growth factor (VEGF), and its receptor Flt-1. These effects may improve tissue perfusion, thus, contributing to the clinical benefits[24,25], as nerve ischemia caused by compression and stretching, may occur in CuTS.[3]

In clinical practice, ESWT has been used for treating CTS. Seok *et al*. first reported significant symptom relief and functional improvement at the 1st and 3rd month post-treatment with one session of ESWT.[10] Consequently, other studies also confirmed beneficial effects at 3 to 6-months post-ESWT, for mild to moderate CTS, compared to nutraceutical treatment[13], ultrasound[26], or night orthosis.[27] Wu *et al*. also demonstrated the therapeutic and cumulative effects of ESWT has for mild-to-moderate CTS.[11,12]

Although encouraging effects of ESWT in CTS have been reported, the therapeutic effects of ESWT in CuTS had not been examined in detail, prior to this pilot study. This is due to several differences between the pathophysiology of CTS and CuTS. First, in addition to direct compression of the ulnar nerve through the cubital tunnel, traction of the nerve and decrease of cubital tunnel space resulting from elbow flexion also play an important role in the development of CuTS.[3] However, the incidence of constant elbow flexion is less frequent and repetitive in patients with CuTS than CTS, in their daily activities. Hence, the spontaneous recovery and predictive

Table 2: Outcome measures at baseline and 12-week follow-up

	Baseline (mean±SE)	4 weeks (mean±SE)	8 weeks (mean±SE)	12 weeks (mean±SE)
VAS	4.7±0.3	2.9±0.3**	2.5±0.3***	2.2±0.2***
DASH	16.6±2.1	11.7±2.5**	7.5±1.3***	6.8±1.6***

*Significant difference compared to baseline (p<0.05), ** (p<0.01), ***(p<0.001).

outcome in CuTS are usually better than in CTS. Second, the perineural structures comprising the cubital tunnel such as Osborne's ligament, medial collateral ligament, and medial epicondyle of the humerus are relatively hard, with less "cushions" like tendons in the carpal tunnel. Therefore, ESWT can reduce swelling of flexor tendons within the carpal tunnel contributing to greater decompression of the median nerve compared to that in CuTS.[10] In addition to anatomical differences, different mechanisms of pathogenesis may contribute to the different therapeutic results observed due to ESWT in CuTS and CTS. The present pilot study has demonstrated similar therapeutic effects of ESWT in CuTS as CTS.

Limited effects of conservative treatments, including orthoses, towel wrapping, patient education, and work modification for moderate to severe CuTS have been reported.[3,7,8] We included patients with moderate severity and all of them showed improvement without complications, following 3 sessions of ESWT. The proportions are much more than the natural spontaneous recovery rates of about 50%.[3] No sham control was used in this pilot study. (The inclusion of a sham group was thought to be unacceptable to the patients before the therapeutic effect of ESWT for CuTS was confirmed.) However, all patients were symptomatic for at least 6 months (mean 27.9 months), and spontaneous remission of symptoms could mostly be ignored in these chronic cases. Moreover, we can find the most significant improvement in the first month after treatment. Hence, the effect of spontaneous recovery was considered to be small and the effect could be mainly attributable to ESWT. On the other hand, most patients in our study were newly diagnosed with CuTS. Hence, the potential for spontaneous remission still existed in these patients because they may have paid more attention to the pathophysiology of CuTS. Furthermore, placebo effect resulting from ESWT could also partially contribute to the therapeutic effect, especially in the initial days. Nevertheless, the placebo effect alone can hardly explain the significant improvement lasting at least 12 weeks. Despite the above considerations, the therapeutic effects of ESWT for CuTS in our study may still be overestimated and a well-designed randomized controlled trial is recommended in the future.

Some objective measurements, such as electrophysiological and ultrasonographic assessments, are good diagnostic tools, and may be used to assess the severity of CuTS. However, the relationship between these parameters and clinical outcomes in follow-ups is controversial. Indeed, Nathan *et al*.[28] and Gavin *et al*.[29] found that electrophysiological parameters are not consistently correlated with clinical improvements. Duetzmann *et al*.[30] reported that the cross-sectional area of the ulnar nerve did not correlate with the clinical outcomes after surgical decompression. The results of the study by Alblas *et al*.[31] also supported the aforementioned findings. Therefore, we did not apply these evaluations in our follow-up. Although it is valuable to measure muscle strength for post-treatment follow-up, we monitored the response using the Quick DASH score, which partially reflect the muscle strength in daily activities. Izawa *et al*.[32] had noted that DASH scores correlated negatively with muscle strength. However, it would have been more beneficial if we had tested muscle strength directly. This pilot study mainly focused on the clinical subjective outcomes and the feasibility of the therapy for a future trial. Further studies involving muscle strength, electrophysiological, and ultrasonographic evaluations are needed for a more comprehensive assessment.

There are several limitations of this study. First, the number of cases in this pilot study is relatively small with only moderate CuTS. It does not represent the entire patient population. Further studies on patients with different grades of CuTS and larger sample size is suggested. Second, the follow-up duration is relatively short. Longer follow-up will be necessary to determine the long-term effects of ESWT. Significant improvement of the VAS and quick DASH scores by week 12 continued to be observed. Therefore, we believe the beneficial effects could persist beyond 12 weeks if longer follow-up periods were conducted. Third, spontaneous recovery and placebo effects of ESWT cannot be completely ruled out because there was no sham control group. Finally, it would be preferable to evaluate some objective parameters, such as electrophysiological and ultrasonographic features and muscle strength measurement, for a more comprehensive follow-up in the future study.

In conclusion, this pilot study revealed that ESWT is a safe, non-invasive, and novel treatment to ease pain and improve disability in patients with moderate CuTS. Further well-designed studies are needed to validate these findings.

DISCLOSURE

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Conflicts of interest: None

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