Effect of Radial Shock Wave Therapy for Carpal Tunnel Syndrome: A Prospective Randomized, Double-Blind, Placebo-Controlled Trial

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ABSTRACT: Three recent studies demonstrated the positive effect of extracorporeal shock wave therapy (ESWT) for treating carpal tunnel syndrome (CTS). However, none have entirely proved the effects of ESWT on CTS because all studies had a small sample size and lacked a placebo-controlled design. Moreover, radial ESWT (rESWT) has not been used to treat CTS. We conducted a prospective randomized, controlled, double-blinded study to assess the effect of rESWT for treating CTS. Thirty-four enrolled patients (40 wrists) were randomized into intervention and control groups (20 wrists in each). Participants in the intervention group underwent three sessions of rESWT with nightly splinting, whereas those in the control group underwent sham rESWT with nightly splinting. The primary outcome was visual analog scale (VAS), whereas the secondary outcomes included the Boston Carpal Tunnel Syndrome Questionnaire (BCTQ), cross-sectional area (CSA) of the median nerve, sensory nerve conduction velocity of the median nerve, and finger pinch strength. Evaluations were performed before treatment and at 1, 4, 8, and 12 weeks after the third rESWT session. A significantly greater improvement in the VAS, BCTQ scores, and CSA of the median nerve was noted in the intervention group throughout the study as compared to the control group (except for BCTQ severity at week 12 and CSA at weeks 1 and 4) ($p < 0.05$). This is the first study to assess rESWT in a randomized placebo-controlled trial and demonstrate that rESWT is a safe and effective method for relieving pain and disability in patients with CTS. © 2015 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 34:977–984, 2016.

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Carpal tunnel syndrome (CTS) is the most common peripheral entrapment neuropathy involving the compression of the median nerve in the carpal tunnel. The average prevalence of CTS in the entire population is 3–4%, and it is predominantly observed in females (7% female and 1% male).[1] CTS is characterized by numbness, tingling, pain, or a burning sensation of at least two of the three digits supplied by the median nerve, although thenar muscle atrophy can also occur in the later stages.[2]

The risk factors for CTS include repetitive wrist stress, obesity, and pregnancy, whereas secondary causes include lesions within the carpal tunnel, metabolic causes, and infection.[2] Unlike other progressive diseases, CTS is characterized by remission and recurrence; hence, its prognosis is often uncertain. Although there are many conservative forms of management, such as wrist splint, steroid injections, and therapeutic ultrasound, their effectiveness is typically insignificant or short-lived.[3] Moreover, Gerritsen et al.[4] revealed a failure rate of 69% for wrist splinting in patients with CTS after a 12-month follow-up period. Moreover, 60–70% of conservatively treated patients with CTS remained symptomatic after 18 months.[5]

Extracorporeal shock waves (ESWs) are defined as a sequence of acoustic pulses characterized by a high peak pressure (100 MPa), fast pressure increase (<10 ns), short duration (10 μs), and an energy density of 0.003–0.89 mJ/mm^2.[6] Different studies have demonstrated the efficacy of ESW therapy (ESWT) for treating various musculoskeletal disorders, such as chronic tendinopathies, calcific tendinitis of the shoulder, lateral epicondylitis, and plantar fasciitis.[6,7] A radial ESW—a pneumatically generated type of shock wave—has low-to-medium energy compared with a traditional focused ESW. These unfocussed shock waves disperse eccentrically from the applicator tip without focusing the energy at a targeted spot, and hence, its penetrative depth is obviously lesser than focused ESWs (up to 3 cm vs. 12 cm).[8] A recent systematic review and meta-analysis reported that the potential advantages of radial ESW therapy (rESWT) over traditional focused ESW therapy (fESWT) in patients with plantar fasciitis includes a larger treatment area, lesser need for specific focusing, no requirement for additional local anesthesia, and low cost.[9]

The effect of ESWT on peripheral nerves has recently received a greater amount of attention. Nearly complete degeneration of the intracutaneous nerve fibers was observed 2, 4, and 7 days after the application of low-energy ESWT to rat skin. Reinnervation occurs 2 weeks after treatment and reaches a non-significant difference.[10] Takahashi et al.[11] also reported similar findings and revealed that multiple low-energy ESWT sessions provided a longer-lasting effect. Hausner et al.[12] reported that low-energy ESWT could induce significant recovery of nerve regeneration, nerve conduction velocity (NCV), and

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amplitude in rats treated with nerve autografts of the sciatic nerve. The effect was the most remarkable at 8 weeks after the nerve injury, although the effect was not significant or disappeared 12 weeks after surgery, with the exception of conduction velocity. Lee et al.[13] demonstrated that the early application of low-energy ESWT effectively increases functional activity and gait in rats with crushed sciatic nerves. Mense et al.[14] also reported that low-energy ESWT could aid in the rapid regeneration of injured nerve fibers. Recently, rESWT was demonstrated to be beneficial for neuropathic pain in rats with chronic constriction injuries.[15]

On the other hand, a few animal studies have shown that high-energy ESWT resulted in histological damage to the myelin sheath.[16,17] Therefore, the safety of ESWT remains controversial. Subsequently, Wu et al.[18,19] showed that although high-intensity ESWT ($0.49\,mJ/mm^2$) temporarily results in a 60–80% decrease in motor nerve conduction velocity (MNCV) of the sciatic nerves in rats, no significant change is observed in functional activity and the decreased MNCV recovers within 14 days of treatment. Moreover, in that study, low-energy ESWT, which is currently used for musculoskeletal disorders, did not decrease the MNCV, and hence, the authors suggest that the ESWT is harmless to the peripheral nerves.

In recent years, few studies have reported the use of ESWT as an alternative management for treating peripheral neuropathy in humans, including conditions such as interdigital neuroma,[20] stump neuroma,[21] distal symmetric polyneuropathy,[22] and CTS,[23–25] and have yielded positive benefits. However, studies published to date have not entirely proved the effects of ESWT on peripheral neuropathy in the human population because these studies enrolled a small number of patients, lacked a placebo-controlled design, and did not include a long-term follow-up period. Moreover, to our knowledge, rESWT has not been used to treat CTS thus far.

In the present study, we aimed to assess the analgesic effect and prognosis of patients with CTS in the median nerve after receiving rESWT.

METHODS

Study Design

This prospective, randomized, controlled, double-blinded study, with an evidence level of 1, was conducted at a single medical center. Its design was reviewed and approved by the institutional review board of Tri-Service General Hospital. All enrolled subjects provided written informed consent for participation. The study was registered at www.ClinicalTrials.gov (number NCT02218229). Between March 1, 2014 and July 15, 2015, 60 patients diagnosed with CTS were screened for eligibility; of them, 34 were enrolled. These 34 enrolled patients (40 wrists) were block randomized with a 1:1 ratio into two groups by an independent researcher using a computer-generated randomization of study numbers (Microsoft Excel). In the intervention group, participants underwent weekly rESWT for three consecutive weeks, whereas the control group received sham rESWT treatment for the same interval.

To provide fundamental therapeutic care for CTS, the use of a wrist night splint was prescribed for each subject in both groups after the first rESWT. The wrist night splint was firmly fixed in the neutral position to immobilize the affected wrist.[3] Patients were ordered to wear the splint while resting at night and at least 8 h per day during the study period. All procedures were conducted by a single physician. Patients were instructed to avoid any other treatment for CTS-related pain or discomfort, including analgesic agents, injections, and acupuncture, from the initial screening through the study period. They were asked to notify us if they had received any of these therapies.

Inclusion and Exclusion Criteria

Patients who had typical symptoms and signs of CTS, such as a positive Tinel's sign or Phalen's test; numbness/tingling in at least two of the first, second, or third digits; and a CTS diagnosis that was confirmed using an electrophysiological study[26,27] were enrolled in the study. Patients who had conditions mimicking CTS, such as cervical radiculopathy, polyneuropathy, brachial plexopathy, or thoracic outlet syndrome or who had previously undergone wrist surgery or steroid injection for CTS were excluded from the study.

Shock Wave Therapy Intervention

Patients were seated in a relaxed position with their forearm and finger resting on the table. With the palm facing up, the median nerve was identified at the line of the proximal carpal tunnel (pisiform level)[28] by using musculoskeletal ultrasonography (Terason, t3000, Teratech, Massachusetts); the same physician performed the procedures. Physio Shock Wave Therapy (Pagani Elettronica, Milano, Italy) was used for rESWT,[29] and the rESWT site was located on the median nerve. The rESWT was administered with 2,000 shots, at a pressure of four Bar, and a frequency of 5 Hz. The treated area ranged from the pisiform level to 2 cm proximal to the median nerve, with an equal diffusion of 2,000 shots. The probe was oriented perpendicular to the patient's palm and the entire procedure was painless without the additional need for anesthesia or analgesic drugs. The sham control rESWT involved sound but no energy. The patients were discharged without any significant complications such as pain and bleeding.

Outcome Measurements

A single physician, who was blinded to the randomization, performed all of the measurements. The evaluation was performed before treatment as well as on the 1st, 4th, 8th, and 12th week after the third rESWT session.

Primary Outcome

Visual Analog Scale (VAS)

The VAS was used to quantify digital pain and paresthesia within the last week, and its scale ranged from 0 (no pain) to 10 (extremely severe pain).[30]

Secondary Outcome

(1) Boston Carpal Tunnel Syndrome Questionnaire (BCTQ): The BCTQ is the most commonly used questionnaire in clinical studies for evaluating the symptom severity and functional status of patients with CTS.[31] The symptom severity subscale has 11 questions scored from one point

(mildest) to five points (most severe), whereas the functional status subscale has eight questions scored from one point (no difficulty with activity) to five points (cannot perform the activity at all).

(2) Cross-sectional area (CSA): The CSA of the median nerve was measured at the proximal inlet of the carpal tunnel (level with the pisiform bone) by the same physician.[27,28] Patients held their wrists in the neutral position with their palms facing upwards and fingers in a semi-extended position. The CSA was measured three times, and the mean value was used for the analysis. The ultrasonographic evaluation of the CSA in the median nerve showed high sensitivity (89%) and specificity (83%) for the diagnosis of CTS.[28]

(3) Sensory nerve conduction velocity (SNCV): The antidromic sensory NCV (SNCV) of the median nerve was measured in all the subjects according to the protocol reported by the American Academy of Neurology with Sierra Wave (Cadwell Laboratories, Kennewick, WA).[26] All examinations were performed by the same physician in the same room at 25°C. Skin temperature on the hand and wrist was maintained at 32.0–34.0°C. The active and reference ring electrodes were placed over the second proximal and distal interphalangeal joints. The median nerve was stimulated at the wrist between the palmaris longus and flexor carpi radialis tendon at a distance of approximately 14 cm from the active electrode. All of the parameters were measured three times and the mean value was used for the analysis.

(4) Finger pinch: Finger pinch strength was measured using a Jamar dynamometer (Fabrication Enterprises Inc., NY). Patients were instructed to sit with their shoulders adducted and neutrally rotated, with their elbows flexed at 90°. The forearms and wrists were maintained in the neutral position for the palmar pinch.[27,32] The finger pinch was performed three times, and the mean value was used for the analysis.

Sample Size

To avoid a type II error, a preliminary power analysis (power, 0.8; $\alpha = 0.05$; effect size, 0.45) was used to determine an appropriate sample size (found to be 17) for each group for this study.

Data Analysis

Statistical analyses were performed using IBM SPSS Statistics Version 22 (Asia Analytics Taiwan Ltd., Taipei, Taiwan). Demographic data were analyzed by the Mann–Whitney *U*-test for continuous data and the χ^2 test for categorical data. The data at various follow-up points were analyzed using repeated-measures analysis of variance followed by post hoc tests. The differences between groups were investigated using the Mann–Whitney *U*-test. All statistical tests were two-tailed, and statistical significance was set at $p < 0.05$.

RESULTS

A total of 34 patients completed the study and both groups equally consisted of 20 wrists (see Fig. 1 for the participant enrollment flow diagram). The baseline demographic and clinical characteristics of the study population are summarized in Table 1, and there were no significant differences between the groups. Table 2 presents the VAS scores, BCTQ scores, finger pinch test results, SNCV values, and CSA measurements of the median nerve before and after treatment. A significant improvement in all measured parameters ($p < 0.05$) was noted in both groups at all observed time points as compared to the pretreatment data (except for BCTQ function at weeks 8 and 12 in the control group).

A comparison of the two groups indicated a significantly greater improvement in the VAS and BCTQ scores in intervention group throughout the study (except for the BCTQ severity at week 12, $p = 0.171$) (Table 3). Although a greater increase in SNCV and CSA of the median nerve was noted in the intervention group as compared to that in the control group at the observed time points, the differences were not significant, except for CSA at weeks 8 and 12 (Table 3). Moreover, differences in the improvement in finger pinch results were similar between groups ($p > 0.05$). No serious side effects or complications were observed in either group. No patient received additional medication or any other treatment during the course of the study.

DISCUSSION

To our knowledge, the present study is the first prospective randomized, double-blind, placebo-controlled study to investigate the benefit of rESWT for treating CTS. Compared to the control group, the rESWT intervention group showed significantly reduced pain and disability and decreased CSA of the median nerve at least 12 weeks after treatment.

In recent years, a few animal studies have shown that low-energy ESWT directly focusing on the nerve tissue positively affects reinnervation and functional improvement without any obvious weakness or side effects.[10–15] Although high-intensity ESWT can damage the nerve tissues, recent studies have shown that this therapy is harmless to the peripheral nerves, because the temporary decreases in MNCV values recover within 14 days, without any significant weakness or functional impairment.[18,19] Moreover, high-energy ESWT is rarely used to treat musculoskeletal disorders, but is used for the treatment of delayed fracture in clinical practice. To date, no published neurological complications from ESWT have been reported in the literature. Our study did not observe any decrease in SNCV or functional activity, and confirmed that rESWT is a safe strategy for treating CTS.

Fridman et al.[20] initially performed a small randomized placebo-controlled double-blind study to investigate the effects of ESWT in patients with interdigital neuroma in 2009. Twelve weeks after treatment, 69% patients of the ESWT group ($n = 9$) had VAS scores <3 ($p < 0.0001$) and only 40% of the sham group ($n = 4$) achieved similar pain relief ($p = 0.1218$). Subsequent studies have shown that

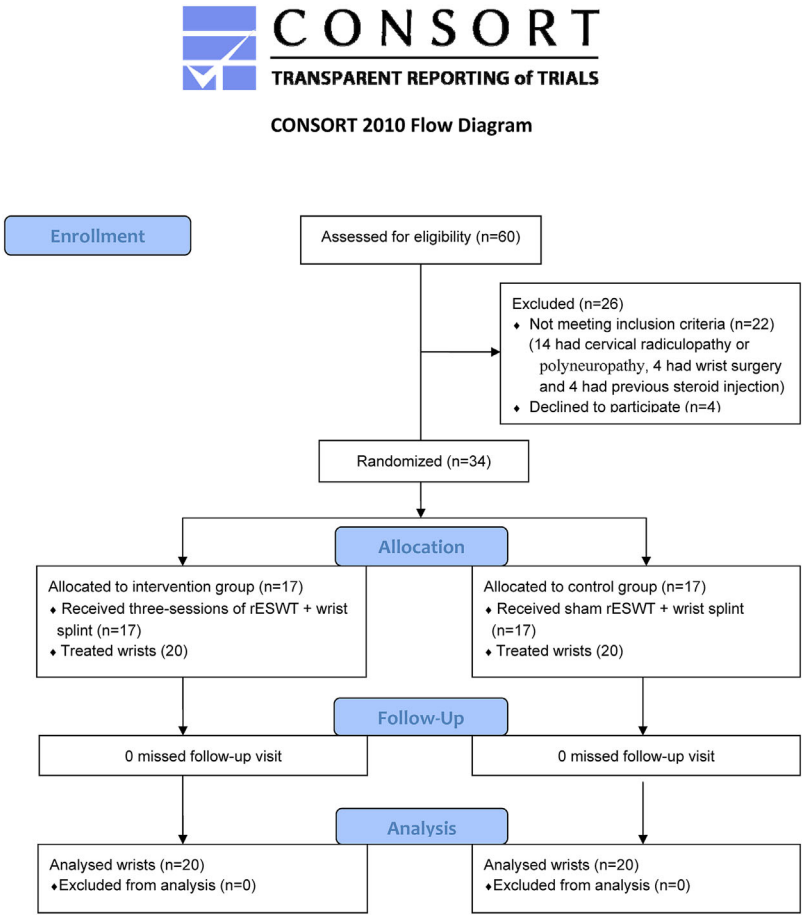

Figure 1. Study flow diagram.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Participants

	Intervention Group ($n = 20$)	Control Group ($n = 20$)	p-Value
Age (year) (SD)	54.70 ± 7.96	57.80 ± 6.51	0.186
Body height (cm)	157.35 ± 7.02	156.28 ± 6.88	0.628
Body weight (kg)	63.39 ± 13.21	62.30 ± 8.81	0.760
Diabetes mellitus (n)	1 (5%)	3 (15%)	0.605
Hypertension (n)	4 (20%)	4 (20%)	1.000
Sex			1.000
Male (n) (%)	2 (10%)	3 (15%)	
Female (n) (%)	18 (90%)	17 (85%)	
Duration (months) (SD)	34.10 ± 33.11	36.10 ± 30.80	0.844
Dominant hand			1.000
Right (n) (%)	19 (95%)	20 (100%)	
Left (n) (%)	1 (5%)	0 (0)	
Lesion site			0.752
Right side (n) (%)	9 (45%)	11 (55%)	
Left side (n) (%)	11 (55%)	9 (45%)	
VAS	6.36 ± 0.87	5.90 ± 1.22	0.178
BCTQs	32.65 ± 7.86	29.95 ± 8.46	0.302
BCTQf	17.70 ± 4.21	16.65 ± 5.03	0.478
CSA (mm^2)	13.69 ± 2.11	12.38 ± 2.62	0.088
SNCV (m/s)	31.81 ± 5.33	30.49 ± 7.28	0.519
FP (kg)	3.30 ± 0.84	3.70 ± 1.59	0.321

VAS, visual analog scale; BCTQ, Boston Carpal Tunnel Syndrome Questionnaire (s, severity and f, function); CSA, cross-sectional area; SNCV, sensory nerve conduction velocity; FP, finger pinch.

Table 2. Outcome Variables in Each Group Before and After Treatment

	Intervention Group ($n = 20$)		Control Group ($n = 20$)	
	Mean ± SD	p-Value	Mean ± SD	p-Value
VAS-Pre	6.36 ± 0.87		5.90 ± 1.22	
VAS Wk1	3.15 ± 0.98	<0.001	4.47 ± 1.05	<0.001
VAS Wk4	2.48 ± 1.00	<0.001	4.12 ± 1.14	<0.001
VAS Wk8	2.77 ± 1.37	<0.001	3.80 ± 1.35	<0.001
VAS Wk12	2.70 ± 1.23	<0.001	3.59 ± 1.27	<0.001
BCTQs-Pre	32.65 ± 7.86		29.95 ± 8.46	
BCTQs Wk1	20.20 ± 5.02	<0.001	23.75 ± 6.76	0.005
BCTQs Wk4	18.90 ± 4.76	<0.001	23.45 ± 7.01	0.009
BCTQs Wk8	17.50 ± 4.11	<0.001	22.00 ± 6.32	0.002
BCTQs Wk12	18.45 ± 4.76	<0.001	19.80 ± 5.04	0.002
BCTQf-Pre	17.70 ± 4.21		16.65 ± 5.03	
BCTQf Wk1	11.75 ± 2.51	<0.001	14.30 ± 4.46	0.021
BCTQf Wk4	10.90 ± 2.81	<0.001	13.70 ± 4.84	0.019
BCTQf Wk8	10.70 ± 2.52	<0.001	13.95 ± 5.48	0.109
BCTQf Wk12	10.60 ± 2.28	<0.001	13.50 ± 5.77	0.107
CSA-Pre (mm^2)	13.69 ± 2.11		12.38 ± 2.62	
CSA Wk1	12.22 ± 2.54	<0.001	11.42 ± 2.20	0.003
CSA Wk4	12.00 ± 2.27	<0.001	11.23 ± 2.31	0.001
CSA Wk8	11.58 ± 2.18	<0.001	11.10 ± 2.25	0.003
CSA Wk12	11.26 ± 2.52	<0.001	10.89 ± 2.05	0.002
SNCV-Pre (m/s)	31.81 ± 5.33		30.49 ± 7.28	
SNCV Wk1	32.50 ± 5.61	1.000	31.85 ± 7.52	0.029
SNCV Wk4	34.04 ± 6.42	0.006	31.98 ± 7.62	0.002
SNCV Wk8	33.92 ± 5.98	0.001	32.15 ± 7.80	0.003
SNCV Wk12	34.92 ± 6.14	<0.001	32.68 ± 8.07	0.002
FP-Pre (kg)	3.30 ± 0.84		3.70 ± 1.59	
FP Wk1	4.19 ± 1.12	<0.001	4.65 ± 1.89	0.001
FP Wk4	4.48 ± 1.24	<0.001	4.95 ± 1.96	<0.001
FP Wk8	4.68 ± 1.17	<0.001	5.28 ± 1.93	<0.001
FP Wk12	5.07 ± 1.53	<0.001	5.44 ± 1.89	<0.001

Pre, pretreatment; SD, standard deviation; VAS, visual analog scale; BCTQ, Boston Carpal Tunnel Syndrome Questionnaire (s, severity and f, function); CSA, cross-sectional area; SNCV, sensory nerve conduction velocity; FP, finger pinch; WK, week.

low-energy ESWT is superior to conventional therapy in patients with stump neuroma.[21] In their pilot study, Lohse–Busch et al.[22] found that the pain intensity of patients with distal symmetric polyneuropathy decreased from 100% to 2.6% after six sessions of ESWT treatment that were performed three times a week, but subsequently increased to 45.7% after 8 weeks.

Seok et al.[23] administered one session of fESWT to treat patients with CTS and compared the results to those after corticosteroid injection ($n = 15$ vs. $n = 16$, respectively). Significant reductions in the VAS and BCTQ scores at 1 and 3 months after treatment were observed in both groups. Unlike the corticosteroid injection group, mild improvement in nerve conduction parameters was noted in the fESWT group, although the difference was not significant. They concluded that ESWT can be as useful as corticosteroid injection for relieving the symptoms of CTS. Paoloni et al.[24] also reported that patients with mild-to-moderate CTS might experience pain relief and increased functionality after three sessions of fESWT alone, as compared to ultrasound and cryo-ultrasound therapy ($n = 12$ vs. $n = 13$ vs. $n = 17$, respectively), and that the effect persisted for 3 months after the end of treatment. Notarnicola et al.[25] performed a randomized controlled trial that showed at least a 6-month effect on pain, BCTQ scores, and electrodiagnostic results after three sessions of fESWT combined with splint or nerve/tendon-gliding exercise compared with that observed after a nutraceutical combination of *Echinacea angustifolia*, α-lipoic acid, conjugated linoleic acid, and quercetin (perinerv) in patients with CTS ($n = 34$ vs. $n = 26$, respectively). However, the above human studies enrolled small numbers of patients and lacked placebo groups or were not blinded. Hence, the placebo effect could not be completely excluded in these studies. The results of the present study confirm the results of the above-mentioned studies, and the effects persisted for at least 12 weeks after the third rESWT session. However, we did not observe a significant increase in SNCV after an additional three rESWT sessions compared with

Table 3. Changes in the Outcome Variables From Baseline to 1, 4, 8, and 12 Weeks After Treatment in the Intervention Group and the Control Group

	Intervention Group ($n = 20$)	Control Group ($n = 20$)	
Difference	Mean Difference ± SD	Mean Difference ± SD	p-Value
VAS-Pre			
VAS Wk1	−3.22 ± 0.90	−1.44 ± 1.05	<0.001
VAS Wk4	−3.89 ± 1.23	−1.79 ± 1.19	<0.001
VAS Wk8	−3.59 ± 1.49	−2.10 ± 1.44	0.003
VAS Wk12	−3.67 ± 1.47	−2.32 ± 1.47	0.006
BCTQs-Pre			
BCTQs Wk1	−12.45 ± 8.97	−6.20 ± 6.65	0.017
BCTQs Wk4	−13.75 ± 7.83	−6.50 ± 7.42	0.005
BCTQs Wk8	−15.15 ± 8.58	−7.95 ± 7.76	0.008
BCTQs Wk12	−14.20 ± 8.67	−10.15 ± 9.67	0.171
BCTQf-Pre			
BCTQf Wk1	−5.95 ± 3.62	−2.35 ± 2.96	0.001
BCTQf Wk4	−6.80 ± 3.83	−2.95 ± 3.66	0.002
BCTQf Wk8	−7.00 ± 3.77	−2.70 ± 4.28	0.002
BCTQf Wk12	−7.10 ± 3.60	−3.15 ± 4.98	0.007
CSA-Pre (mm^2)			
CSA Wk1	−1.48 ± 0.80	−0.96 ± 0.96	0.070
CSA Wk4	−1.69 ± 0.87	−1.15 ± 1.09	0.090
CSA Wk8	−2.11 ± 1.22	−1.28 ± 1.28	0.041
CSA Wk12	−2.43 ± 1.37	−1.49 ± 1.46	0.043
SNCV-Pre (m/s)			
SNCV Wk1	0.69 ± 2.69	1.36 ± 1.78	0.362
SNCV Wk4	2.24 ± 2.45	1.49 ± 1.43	0.246
SNCV Wk8	2.11 ± 1.86	1.65 ± 1.66	0.418
SNCV Wk12	3.12 ± 2.49	2.19 ± 2.10	0.212
FP-Pre (kg)			
FP Wk1	0.90 ± 0.68	0.95 ± 0.89	0.852
FP Wk4	1.18 ± 0.78	1.25 ± 0.97	0.811
FP Wk8	1.39 ± 0.71	1.58 ± 1.02	0.505
FP Wk12	1.77 ± 1.01	1.74 ± 1.08	0.912

Pre, pretreatment; SD, standard deviation; VAS, visual analog scale; BCTQ, Boston Carpal Tunnel Syndrome Questionnaire (s, severity and f, function); CSA, cross-sectional area; SNCV, sensory nerve conduction velocity; FP, finger pinch; WK, week.

splinting alone, even though a greater difference was noted in the intervention group at most of the observed time points (except week 1) (Table 3), which is consistent with the findings of the study by Seok et al.[23] Moreover, a significant decrease in the CSA of the median nerve (mean decreased swelling of the median nerve) was found at weeks 8 and 12 after rESWT as compared with that in the control group. This objective measurement would further verify the benefit of rESWT for treating CTS. Our study is the first to assess rESWT in a randomized placebo-controlled trial.

The true mechanism underlying the effects of neuropathy treated with ESWT remains unknown. Experimental studies have shown that low-energy ESWT stimulates the production of endothelial nitric oxide,[33] angiogenesis,[34,35] and neurogenesis[36,37] via the involvement of the vascular endothelial growth factor. Moreover, ESWT produces anti-inflammatory effects by reducing the levels of calcitonin gene-related peptide.[38] ESWT may also reduce inflammation of the soft tissues around the median nerve, which results in reduced pressure on the median nerve.[23] The latter mechanism could partly explain the results of a study in 2011, which indicated that ESWT resulted in significant long-term reductions of pain, swelling, and redness in patients with pillar pain after carpal tunnel release surgery.[39]

Unlike ESWT in animals, ESWs in humans penetrate the soft tissue and do not "directly" focus on the target nerve, which may yield enhanced safety. However, the superiority of rESWT over fESWT for treating CTS is unclear. One study recommended that rESWT was superior to fESWT for treating plantar fasciitis due to its lower cost and enhanced effectiveness.[9] Furthermore, rESWT is delivered to a larger therapeutic area and has less of a need to specifically focus as compared to fESWT. Hence, rESWT seems to be more suitable for treating CTS since it could be applied to a larger area including the median nerve and its surrounding soft tissues rather than to a small spot. To test this hypothesis,

further well-designed studies have to be performed by direct comparison of the two modalities.

This study has several limitations. First, the mechanism of rESWT for reducing CTS was not evaluated. Second, the number of cases was relatively small. Third, the SNCV of the median nerve alone cannot generate the amount of detail for an electrophysiological study. Fourth, it would be better to follow-up patients for a longer period of time. A significant improvement was noted in BCTQ scores, VAS scores, and CSA of the median nerve by week 12 in the intervention group as compared to that in the control group. Therefore, we believe the effect could continue for more than 12 weeks if the follow-up period is extended. Finally, several questions including the most effective intensity and the appropriate number of ESWT sessions remain unanswered, and further studies need to be conducted in a larger number of patients with multiple strategies to resolve these queries.

In conclusion, our results show that rESWT is a safe, effective, practical, and non-invasive method for relieving pain and disability in patients with CTS and improving ultrasonographic findings. This simple and reproducible procedure is a potentially novel approach for treating CTS. However, further prospective clinical trials are required with a larger sample size and a longer follow-up period.

AUTHORS' CONTRIBUTIONS

All authors contributed the experimental design, data collection and analysis, and editing and approval of the final manuscript.

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