Research Paper

The Effects of Radial Extra Corporeal Shock Wave and Low-power Laser Therapies on Clinical and Electrophysiological Parameters in Moderate Carpal Tunnel Syndrome: A Blinded Randomized Control Trial

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ABSTRACT

Objectives: Carpal tunnel syndrome (CTS) is a common peripheral entrapment neuropathy with squeezing of the median nerve and the patient is unable to function properly. There are different physiotherapy interventions for the management of these patients and recently, shock wave therapy and low-power laser (LPL) have been widely used, but there is no strong evidence comparing the effect of shock wave therapy and LLLT. Therefore, this trial was designed to compare the effect of extracorporeal shock wave therapy (ESWT), LPL, and routine interventions on clinical outcomes and electrophysiological parameters in patients with moderate CTS.

Methods: Fifty-four patients were randomly assigned to the control (routine interventions), ESWT, and LPL therapy groups. All participants received transcutaneous electrical nerve stimulation (TENS) therapeutic ultrasound, hot pack, mobilization, and stretching for ten sessions over two weeks. Additionally, the ESWT group received radial ESWT in four sessions, and the LPL therapy group received laser in ten sessions. The primary outcomes were pain (assessed by the visual analog scale), function (assessed using the Boston questionnaire (BQ)), hand grip, and finger pinch strength. Secondary outcomes were electrophysiological parameters (distal motor and sensory latency and nerve conduction velocity (NCV) of the median nerve.

Results: Time group interactions were significant for pain, the symptom severity subscale of BQ, finger pinch, and hand grip strength ($P<0.001$). Significant improvements were seen in clinical and sensory latency and motor NCV of the median nerve ($P<0.05$). The ESWT group experienced significant improvements with a large effect size in pain, function, and finger pinch strength compared to the control group ($P<0.01$). Additionally, the LPL therapy group showed significant changes in the function and finger pinch and hand grip strength compared to the control group. There were no significant differences between the LPL therapy and ESWT groups except for pain in favor of the ESWT group. No significant differences were found among the three groups in electrophysiological parameters ($P>0.05$).

Discussion: Although laser therapy increased the efficacy of routine interventions, it seems adding ESWT to the routine treatment may be superior for the management of moderate CTS patients.

Keywords:
Carpal tunnel syndrome, Extracorporeal shock wave therapy, Low-power laser, Surface electromyography, Visual analogue scale, Boston carpal tunnel questionnaire

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Highlights

• Low-power laser and shock wave therapies had positive effects on pain reduction, grip and pinch strength, and function in carpal tunnel patients.

• Low-power laser and shock wave therapies had a positive effect on sensory latency and motor nerve conduction velocity of the median nerve

• There were no significant differences between the low-level laser therapy (LLLT) therapy and extracorporeal shock wave therapy (ESWT) groups except for pain in favor of the ESWT group.

• The two interventions had the same effect on electrophysiological parameters.

Plain Language Summary

Compression on the wrist tunnel leads to pain, numbness, and tingling sensation or falling objects from the hand in severe cases. Nonsurgical methods can help improve the signs and symptoms in early diagnosis. Recently, using shock wave therapy and low-level laser therapy (LLLT) has been very attractive in these patients, but there are not many studies comparing the effects of these methods. In this study, we assessed the effect of adding LLLT or shock wave therapy to exercise, mobilization, and stretching, on pain, strength, function, and electrophysiological findings. After two weeks of physiotherapy intervention, positive effects were seen on the reduction of pain and the improvement of strength and function. Likewise, nerve impulses revealed recovery after treatment in three groups. Our results detected much improvement in patients who received shock wave therapy based on effect size. Therefore, we can suggest these interventions as perfect methods in the management of moderate patients with carpal tunnel syndrome, particularly the addition of shock wave therapy to routine treatment.

Introduction

Carpal tunnel syndrome (CTS) is a common peripheral neuropathy in the upper extremity resulting from compression and entrapment of the median nerve [1, 2]. It affects up to 5% of the general population with a higher frequency in females [1, 3, 4]. Numbness, tingling, and pain in the three first fingers and the lateral side of the fourth finger, impairment in fine movements and in severe conditions, weakness of hand movements, inability to hold objects, atrophy of thenar muscles, and nocturnal pain are common symptoms and signs [5-8].

CTS is clinically categorized into mild, moderate, severe, and very severe [9]. Evidence suggests that in the early stage, a blockage in venous circulation leads to hyperemic and edematous median nerve. Following blood circulation impairment, demyelination of the median nerve and axonal loss progress [10]. Additionally, there are higher levels of prostaglandin E2, vascular endothelial growth factor, and interleukin-6 in CTS patients [11, 12].

Its etiology is often multifactorial, but repetitive and excessive movements of wrist and hand, heavy lifting, vibration, pregnancy, obesity, and diseases, such as rheumatoid arthritis and diabetes mellitus affect the development of CTS [1, 2].

Physical examination, special clinical tests, and electrodiagnostic examination are used to diagnose CTS [10, 13]. Positive Phalen's maneuver and Tinel's tests, longer latency, and slower conduction velocity have been found in patients [4].

The FUNCTION and quality of life are affected by CTS; therefore, management and treatment of patients are very important. Most patients with mild-to-moderate disease respond to conservative interventions, while in severe cases, surgery is recommended [10, 14].

Anti-inflammatory drugs, therapeutic ultrasound, electrical stimulation, tendon gliding, mobilization techniques, and wrist splinting are common non-surgical interventions [8, 15]. Two other popular treatments are low-power laser (LPL) therapy and extracorporeal shock wave therapy (ESWT). Although the mechanisms of LPL and ESW histologically vary, they have anti-inflammatory and analgesic effects. Additionally, it has been theorized that LPL can increase ATP production and cellular respiration, and results in improving blood circulation and moving waste products away from the concentration area [8, 10, 14]. In addition to anti-inflammatory and analgesic effects, ESWT can lead to tissue remodeling and re-innervation of nerves by generating acoustic waves in tissue and increasing the metabolic rate of tissues [2, 5, 7].

Extensive research has investigated the effects of LPL and ESWT alone or with other common treatments in CTS patients with controversial results [1, 2, 5, 10, 14, 16]. However, there are not many studies comparing the effects of these methods and, also comparing the effects of routine treatments (ultrasound (US), transcutaneous electrical nerve stimulation (TENS), heat, mobilization, and stretching), LPL, and ESWT on the median sensory and motor distal latency and motor nerve conduction velocity (NCV) of the median nerve. One of the methods for the diagnosis of CTS is electrophysiological finding [10, 14]. Therefore, we decided to assess and compare the effect of LPL and ESWT along with common treatment because of the wide use of these modalities. Finding the modality with the superior effect is useful for choosing the best intervention in the future because of the knowledge gap in this way.

Materials and Methods

This double-blind randomized controlled trial was conducted on 54 patients with moderate CTS visiting the physiotherapy clinic of the Tehran University of Medical Sciences from June 2020 to February 2022.

Having numbness, tingling, pain in the first three fingers and lateral side of the fourth finger, nocturnal pain, weakness in hand movements, positive Tinel's percussion test or Phalen's maneuver test were used for the diagnosis of CTS [5-8]. Then, eligible participants were re-assessed by an electrophysiologist physician to verify CTS. Maximum normal values of distal motor and sensory latency of the median nerve are 4.2 and 3.6 ms, respectively [17, 18]. Thus, patients with sensory distal latency of more than 3.6 ms with normal motor latency were categorized as mild CTS. However, patients with a sensory distal latency of more than 3.6 ms and motor latency longer than 4.2 were categorized as moderate CTS [17, 18].

Subjects were excluded if they had thenar muscles atrophy, lack of sensory and motor responses of median nerve, wrist and hand fractures or operation, cervical radiculopathy, carpal tunnel corticosteroid injection in the last six months, and also pregnant and diabetics and those receiving conservative treatments within two weeks [8, 9, 19, 20].

Randomization, allocation concealment, and blinding

A random number generator [21] was used to allocate eligible participants to groups A, B, and C (block size=6, number of blocks=9). The control group (group A) received routine interventions, group B received routine interventions plus LPL, and group C received routine interventions plus ESWT.

The patients' outcome assessor and the person who analyzed the outcomes were blinded to details of treatment protocols. All interventions were performed by a physical therapist who was not blinded.

Sample size

G*power software, version 3.1.9.2, was used to calculate the sample size. Based on studies by Haghighat et al. [22] and Paoloni et al. [23], repeated measures ANOVA with an effect size of 0.25, a significant level of 0.05, power of 80%, drop out of 15%, a total of 18 patients was estimated for each group.

Primary outcomes

Pain intensity was assessed by visual analog scale (VAS) as a valid and simple tool [24, 25]. The participants were asked to determine the pain level of their wrist and hand from zero (no pain) to ten (severe pain).

Function was assessed by the valid and reliable Persian version of the Boston carpal tunnel syndrome questionnaire (BQ) [23, 24]. This questionnaire has two subscales: symptom severity subscale (SSS=11 items) and functional status subscale (FSS=8 items). The SSS evaluates pain, numbness, tingling, and difficulty in grasping small objects. A five-point Likert scale is used (normal, slight, medium, severe, and very serious) to score items of this subscale. The FSS assesses the hand function during daily activities using a five-point Likert scale (no difficulty, little difficulty, moderate difficulty, intense difficulty, and unable to perform the activity). Each item of both subscales is scored from one to five and the sum of the included items is the total score.

Finger pinch and hand grip strength were measured, by finger and hand grip dynamometer, respectively [7, 26, 27]. The participants sit on comfortable chairs with their shoulders in adduction position, elbows in 90 flexion, and forearms in neutral position with affected wrists in 20° to 30° extension. Each participant performed the finger pinch and hand grip three times, and the mean value of repetitions was used for analysis. The primary outcomes were measured at baseline, after the treatment, and after one-week follow-up.

Secondary outcomes

Before electrophysiological evaluations, the examiner measured the skin temperature. If the temperature was less than 32°C, the skin was warmed by a hot pack.

Median sensory nerve action potential (SNAP) was recorded antiheroically by placing an active ring and reference electrodes on the third finger, and the median nerve was stimulated 14 cm proximal of the recording electrode between the flexor carpi radialis and palmaris longus tendon. For recording distal latency of compound motor action potential (CMAP) and motor conduction velocity, the active electrode was placed on the abductor pollicis brevis, and the median nerve was stimulated 8 cm proximal to the recording site. The reference electrode was fixed on the distal of the thumb. The normal value of median nerve motor conduction velocity is 57 m/sec. A supra-maximal stimulation was used for recording SNAP and CMAP latency of the median nerve (Figure 1). The latency was measured in ms [19]. The secondary outcomes were measured at baseline and after the treatment.

Routine treatment protocol

All patients received routine interventions in ten sessions for two weeks, including transcutaneous electrical nerve stimulation (TENS) (multi stimulator 710 p, Novin, Iran), therapeutic ultrasound (US 210 p, Novin, Iran), hot pack, mobilization, and stretching.

In the beginning, a hot pack was used for 5 min on the carpal tunnel. TENS was applied in the conventional mode for 15 min with a frequency of 100 Hz and pulse duration of 80 ms, and electrodes covered carpal tunnel and hand palm [20].

Intermittent ultrasound with an intensity of 1 Watt/cm^2 and a frequency of 1 MHz was applied to the carpal tunnel with a circular moving probe for 5 min [20].

Mobilization of carpal bones includes dorsal-palmar glide at the radiocarpal joint and distraction in mid carpal joint. For mobilizing the radiocarpal joint, participants were asked to place their forearm on the table and the therapist fixed the distal radioulnar joint with one hand, and the other hand was used to mobilize the proximal row of carpal bones in dorsal and palmar directions to increase flexion and extension of the wrist, receptively. For mid carpal distraction, the stabilizing hand was placed on diastral row of carpal bones, and the mobilizing hand distracted the proximal row [28].

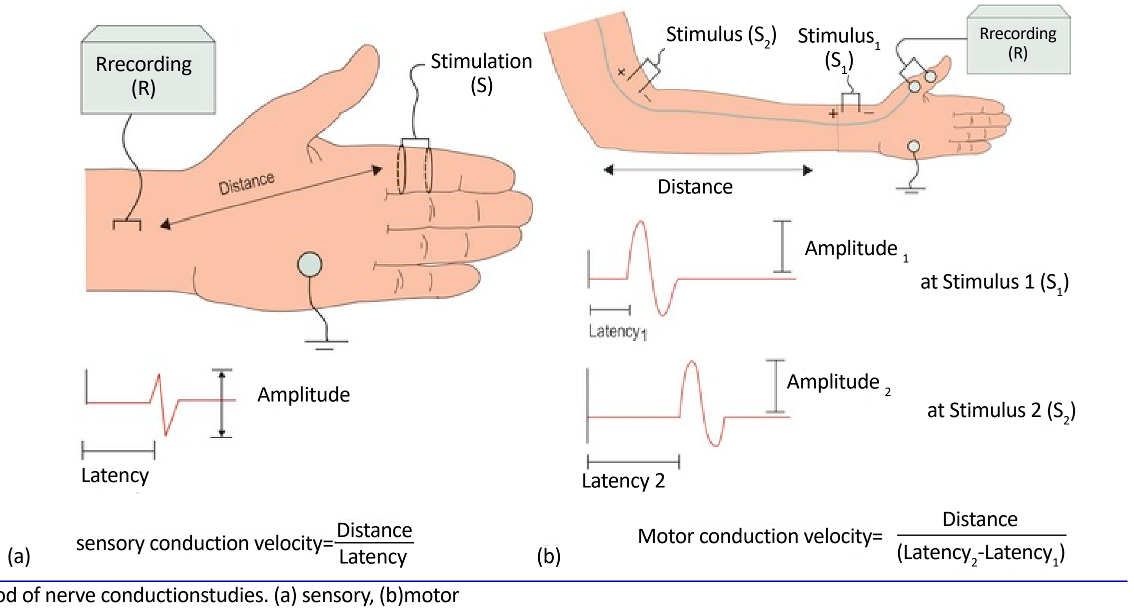

Figure 1. Motor and sensory nerve conduction study

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S: Stimulation site, R: Recording site.

Each technique was performed ten times per session with 10 seconds of rest and 5 seconds of rest between repetitions.

Additionally, participants were instructed to perform self-stretching of carpal ligaments four times a day for two weeks. They were trained to extend their wrists by contralateral hand up to 90 degrees to stretch carpal ligaments [29].

Routine treatment plus ESWT group: In addition to routine treatment, this group received radial ESWT using a shockwave device (90 G, Novin, Iran) two times per week for two consecutive weeks. Participants were asked to sit on a chair with their forearms in the supine position and elbows in 90° flexion on the table. The approximate location of the median nerve was identified between flexor carpi radialis and palmaris longus tendons, and then, coupling gel was applied to the carpal tunnel. Shock waves with 900 shocks and 4 bar pressure with a frequency of 15 Hz were applied perpendicular to the carpal tunnel on the median nerve [1].

Routine treatment plus LPL group: This group received routine treatment plus LPL (Gallium arsenide laser, 860 B, Novin, Iran) with a wavelength of 775 nm, frequency of 6500 Hz, and intensity of 7 J/cm^2 on the carpal tunnel between the distal crease and Kaplan-cardinal line, 5 min per session, five sessions per week for two consecutive weeks [8].

Data analysis

SPSS software, version 22 was used to perform analyses. Normal distribution was checked by the Kolmogorov-Smirnov test. One-way ANOVA was used to compare continuous demographic variables and outcomes at baseline. Categorical variables were compared among groups by a chi-square test. Interaction of time (baseline, after the treatment, and after follow-up)×group (control, ESWT, and LPLT) was assessed by two-way repeated measures ANOVA. Within-group comparisons were made by repeated measures ANOVA. The Bonferroni test was used for post-hoc analyses. Cohen's d effect size was used for magnitude analysis of differences (<0.19 (trivial zone), 0.2< Cohen's d<0.49 (small efficacy), 0.5< medium efficacy <0.79 (medium efficacy), and >0.8 (large efficacy) [30].

Results

The baseline characteristics of patients and the mean values of primary and secondary outcomes are summarized in Tables 1 and 2.

The results of two-way repeated measures ANOVA revealed that time group interactions were significant for pain (F=2.69, P=0.042), SSS of BQ (F=3.57, P=0.019), finger pinch strength (F=2.66, P=0.048), and hand grip strength (F=3.11, P=0.033), while no statistical significance was found for FSS of BQ (F=1.12, P=0.345).

Pain

Between-group comparisons showed that after treatment, pain intensity significantly was lower in the EWST group compared to the control (P<0.001) and LPL groups (P=0.001), while after follow-up, only the difference between the ESWT and control group was statistically significant (P=0.015) (Table 3). Cohen's d effect size also confirmed a high efficacy of EWST in reducing pain compared to other interventions (effect size >08). The magnitude of the difference in pain intensity between the control and LPL therapy group was in the medium range in favor of the LPL therapy group (effect size=-0.66) without statistically significant difference (P=0.157) (Table 3).

Function

One-way ANOVA/ANCOVA results showed significant differences among groups in SSS and FSS of the BQ. Post-hoc analyses revealed that the ESWT group had lower scores in both subscales of the BQ [SSS: P=0.003, FSS: P=0.001] and after the follow-up [SSS: P<0.001, FSS: P=0.005] than the control group, and based on Cohen's d effect size, these differences were large (Table 3).

Additionally, there were statistical differences between the LPL therapy and the control groups in the BQ scores. After the treatment (SSS: P=0.013, FSS: P=0.011) and follow-up [SSS: P<0.001, FSS: P=0.011), the LPL therapy group showed lower scores in both subscales of the BQ (SSS: P<0.001, FSS: P=0.011) compared to the control group. Cohen's d confirmed the high efficacy of the combination of routine interventions with LPL compared to routine treatment in improving function.

The ESWT and LPL therapy groups showed no significant difference in subscales of the BQ (P>0.05) (Table 3).

Table 1. Demographic characteristics of the groups

Variables		Mean±SD/No. (%)		
		Control (n=18)	ESWT (n=18)	Low-power Laser (n=18)
Age (year)		37.44±5.96	41.94±9.73	41.78±6.55
Weight (kg)		73.17±11.02	76.21±10.53	80.44±11.26
Height (cm)		164.39±6.92	163.72±7.29	163.83±6.31
BMI (kg/m²)		27.04±3.5	28.51±4.19	30±4.08
Sex	Male	3(16.7)	3(16.7)	2(11.1)
	Female	15(83.3)	15(83.3)	16(89.9)
Unilateral CTS		8(61.5)	6(50)	8(61.5)
Bilateral CTS		5(38.5)	6(50)	5(38.5)
Mild CTS		6(33.3)	6(33.3)	5(27.8)
Moderate CTS		12(66.7)	12(66.7)	13(72.2)

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BMI: Body mass index; CTS: Carpal tunnel syndrome; ESWT: Extracorporeal shock wave therapy; SD: Standard deviation.

Table 2. Mean values of primary and secondary outcomes of the study measured by repeated measurements

Primary Outcomes	Mean±SD								
	Control (n=18)			ESWT (n=18)			Low-power Laser (n=18)		
	T0	T1	T2	T0	T1	T2	T0	T1	T2
Pain	6.7±0.9	3.6±0.5	2.9±0.9	6.2±0.7	2.2±0.8	1.8±0.8	6.4±0.8	3.1±0.7	2.3±1.0
Symptom severity subscale of BQ	37.6±7.9	23.1±6.6	20.5±6.7	36.1±8.2	17.5±4.1	13.6±3.0	39.2±9.1	19.5±5.2	14.9±2.8
Functional status subscale of BQ	26.4±4.7	16.2±3.9	14.1±3.7	24.3±4.7	11.9±2.7	10.7±2.6	24±3.9	12.6±2.3	10.9±1.7
Pinch strength	8.6±2.9	10.9±3.1	10.7±2.3	9.1±3.7	12.8±1.7	12.6±2.3	8.1±2.8	11.7±1.6	12.4±1.9
Grip strength	19.4±5.6	23.4±5.5	23.9±6.8	22.7±5.7	27.7±4.6	28.6±4.5	20.7±5.8	26.3±5.4	29.9±4.9

Secondary Outcomes	Control (n=18)		ESWT (n=18)		Low-power Laser (n=18)	
	T0	T1	T0	T1	T0	T1
Latency-SNAP (ms)	4.12±1.27	3.81±1.30	4.03±0.79	3.84±0.9	4.74±1.80	4.02±0.89
Latency-CMAP (ms)	4.71±1.56	4.59±1.54	4.18±0.91	4.07±0.99	4.29±0.87	4.17±0.84
Motor NCV (m/sec)	56.56±7.48	56.71±6.75	57.53±8.22	58.07±8.09	53.67±10.12	54.07±9.83

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BQ: Boston questionnaire; T0: At baseline; T1: End of treatment period; T2: After follow-up; CMAP: Compound motor action potential; M/sec: Meter/seconds; ms: Millisecond; SNAP: Sensory nerve action potential; ESWT: Extracorporeal shock wave therapy.

Table 3. Results of one-way ANOVA/ANCOVA, post-hoc comparisons, and Cohen's d Effect size with 95% CI of primary outcomes

Primary Outcomes		F	P	Post-hoc Between-group Comparisons Mean Difference (95%CI)			Cohen's d		
				ESWT vs. Control	LPL vs. Control	ESWT vs. LPL	ESWT vs. Control	LPL vs. Control	ESWT vs. LPL
Pain	T1	16.17	<0.001	-1.1 (-1.85 to -.0.61)	-0.38 (-.085 to0.09)	-0.71 (-1.18 to-0.25)	-1.9	-0.66	-1.25
	T2	4.32	0.019	-0.86 (-1.58 to -0.13)	-0.46 (-1.16 to0.24)	-0.4 (-1.09 to 0.3)	-1	-0.54	-0.47
SSS of BQ	T1	7.05	0.002	-4.97 (-8.53 to -1.4)	-4.3 (-7.87 to0.73)	-0.67 (-4.27 to2.93)	-1.58	-1.36	-0.15
	T2	12.88	<0.001	-6.54 (-10.11 to-2.96)	-6.09 (-9.67 to 2.51)	-0.44 (-4.06 to 3.17)	-1.51	-1.41	-0.1
FSS of BQ	T1	8.82	0.0005	-3.47 (-5.6 to -1.35)	-2.64 (-4.77 to -0.5)	-0.84 (-2.92 to 1.25)	-1.36	-1.03	-0.33
	T2	6.7	0.003	-2.63 (-4.6 to-0.67)	-2.42 (-4.39 to0.45)	-0.21 (-2.14 to 1.17)	-1.12	-1	-0.1
Pinch strength	T1	5.07	0.001	1.7 (0.37 to 3.03)	1.03 (-0.3 to 2.37)	0.67 (-0.68 to 2)	1.05	0.64	0.41
	T2	25.1	<0.001	1.65 (0.16 to 3.13)	1.86 (0.38 to 3.35)	-0.22 (- 1.71 to 1.28)	0.92	1.04	-0.12
Grip strength	T1	2.14	0.13	2.23 (-0.83 to 5.29)	2.16 (-0.83 to 5.14)	0.07 (-2.94 to 3.08)	0.61	0.59	0.02
	T2	5.97	0.005	3.06 (-0.9 to 7.03)	5.39 (1.52 to 9.26)	-2.33 (-6.23 to 1.57)	0.65	1.15	0.5

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Abbreviations: BQ: Boston questionnaire; CI: Confidence interval; ESWT: Extracorporeal shock wave therapy group; LPL: Low power laser group; T1: End of treatment period; T2: After follow-up.

Table 4. Results of within-group analysis based on the repeated-measures ANOVA

Outcomes	Mean Difference (95% CI) [P]					
	Control Group		ESWT Group		LPL Group	
	T0 vs. T1	T0 vs. T2	T0 vs. T1	T0 vs. T2	T0 vs. T1	T0 vs. T2
Pain	3. 1 [2.7 to 3.5] (<0.001)	3.8 [3.2 to 4.3] (<0.001)	3.9 [3.4 to 4.4] (0.001)	4.3 [3.7 to 5] (0.001)	3.3 [3 to 3.6] (<0.001)	4 [3.5 to 4.6] (<0.001)
SSS of BQ	14.5 [11.9 to 17] (<0.001)	17 [13.6 to 20.5] (0.001)	18.5 [13.9 to 23.1] (0.001)	22.4 [17.2 to 27.7] (0.001)	19.8 [14.9 to 24.7] (<0.001)	24.4 [19 to 29.7] (<0.001)
FSS of BQ	10.2 [9 to 11.4] (<0.001)	12.3 [10.9 to 13.6] (0.001)	12.5 [9.1 to 15.8] (0.001)	13.6 [10.5 to 16.6] (0.001)	11.4 [9.6 to 13.3] (<0.001)	13.2 [11 to 15.4] (<0.001)
Pinch strength	-2.3 [-3.1 to -1.5] (0.001)	-2.1 [-3.3 to -0.9] [0.001)	-3.8 [-5.6 to -1.9] (0.001)	-3.5 [-5.2 to -1.7] (0.001)	-3.6 [-5 to -2.2] (<0.001)	-4.3 [-6.1 to -2.4] (<0.001)
Grip strength	-3.9 [-5.7 to -2.1] (0.001)	-4.4 [-7 to -1.8] (0.001)	-5 [-8.2 to -1.8] (0.002)	-5.9 [-9.3 to -2.4] [0.001)	-5.6 [-8.1 to -3.2] (0.001)	-9.2 [-13.2 to -5.3] (<0.001)
Latency of SNAP (ms)	0.3 [0.6 to 0.55] (0.017)	-	0.19 [0.02 to 0.35] (0.028)	-	0.72 [0.06 to 1.38] (0.035)	-
Latency of CMAP (ms)	0.12 [-0.08 to 0.32] (0.225)	-	0.11 [-0.13 to 0.35] (0.361)	-	0.12 [-0.12 to 0.36] (0.309)	-
Motor NCV (m/sec)	-0.15 [-1.05 to 0.75] (0.728)	-	-0.54 [-1.27 to 0.2] (0.141)	-	-0.39 [-0.73 to -0.06] (0.025)	-

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Abbreviations: BQ: Boston questionnaire; CMAP: Compound motor action potential; CI: Confidence interval; ESWT: Extracorporeal shock wave therapy; LPL: Low power laser group; m/ms: Meter/seconds; Ms: Millisecond; SD: Standard deviation; SNAP: Sensory nerve action potential; T0: At baseline; T1: End of treatment period; T2: After follow-up.

Finger pinch and power grip strength

The one-way ANOVA/ANCOVA results revealed that after the treatment (P=0.008) and follow-up (P=0.025), the mean value of finger pinch strength of the ESWT group statistically was greater than the control group (Table 3). Additionally, after follow-up, the strength of finger pinch (P=0.009) and hand grip (P=0.003) in the

Table 5. Results of one-way ANOVA/ANCOVA, post-hoc comparisons, and Cohen's d effect Size with 95% CI of electrophysiologic parameters

Secondary Outcomes	f	P	Post-hoc Between-group Comparisons Mean Difference (95%CI)			Cohen's d		
			ESWT vs. Control	LPL vs. Control	ESWT vs. LPL	ESWT vs. Control	LPL vs. Control	ESWT vs. LPL
Latency of SNAP (ms)	0.66	0.5	0.08 [-0.46 to 0.62]	-0.17 [-0.72 to 0.38]	0.25 [-0.3 to 0.8]	0.12	-0.26	0.38
Latency of CMAP (ms)	0.02	0.9	-0.03 [-0.41 to 0.35]	-0.03 [-0.41 to 0.35]	0.002 [-0.37 to 0.38]	-0.06	-0.07	0.005
Motor NCV (m/sec)	0.54	0.5	0.64 [-0.66 to 1.54]	0.09 [-1.02 to 1.2]	0.35 [-0.77 to 1.47]	0.33	0.06	0.26

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CMAP: Compound motor action potential, CI: Confidence interval; ESWT: Extracorporeal shock wave therapy; LPL: Low power laser group, M/sec: Meter/seconds; Ms: Millisecond; SD: Standard deviation; SNAP: Sensory nerve action potential.

LPL therapy group significantly increased compared to the control group (Table 3). Also, Cohen's d effect size verified the high efficacy of ESWT and LPL therapy in improving finger pinch and hand grip strength (effect size >0.8) (Table 3).

Within-group analyses showed that in all groups, pain finger pinch and hand grip strength and BQ scores significantly improved compared to baseline (Table 4).

Secondary outcome

Based on the one-way ANOVA/ANCOVA results and post-hoc comparisons, no significant differences were found among the groups in electrophysiological parameters (P>0.05) (Table 5). Despite no statistical significance at baseline scores, Cohen's d effect size showed that the LPL therapy and the ESWT were not highly effective in decreasing the SNAP latency and increasing motor NCV, respectively (Table 5). Additionally, within-group analyses showed no significant changes in the latency of CMAP (P>0.05), while after the treatment, all groups showed a significant reduction in the latency of the SNAP, and a significant increase in the motor NCV of the median nerve (P<0.05) (Table 4).

Discussion

This study aimed to compare the effect of routine interventions with adding ESWT or LPLT on clinical and electrophysiological parameters in mild to moderate CTS patients. Our results showed that ESWT and LPL therapy in combination with conventional interventions (heat, TENS, US, mobilization, and stretching) alone improved pain intensity, function, finger pinch, and hand grip strength. However, adding ESWT and LPL therapy to routine interventions caused more improvements in clinical outcomes compared to routine intervention alone. The results also revealed that all interventions significantly reduced the latency of SNAP and increased motor NCV of the median nerve without significant superiority in favor of a specific intervention.

In this study, all participants received heat, TENS, US, mobilization, and stretching with a significant efficacy in improving the outcome of the control group. Therapeutic US because of the reduction of inflammation and TENS due to activating gate control mechanism, can be used for treating CTS patients [9, 31]. Pain improvement was observed in all three groups with preferential effects in favor of the combination of ESWT and usual care with a high effect size.

The results of this study also showed that radial ESWT and LPL combined with routine interventions were more effective than routine interventions alone in improving function without significant differences between the ESWT and LPL groups.

Adding radial ESWT to routine intervention significantly increased the efficacy of the routine interventions with the large effect size. Radial ESWT had no superior effect compared to routine interventions in increasing hand grip strength. No statistical difference was found in the finger pinch and hand grip strength between the LPL and control groups after the end of treatment, while after the follow-up, the finger pinch and hand grip strength considerably increased in the LPL group compared to the control group.

These results seem to be in line with some previous research reporting that ESWT alone or in combination with routine interventions is more effective than routine interventions alone in improving the clinical outcomes of CTS patients. However, due to methodological controversies among the studies, such as the type of intervention received by the control group and different parameters of ESWT, it is difficult to compare the studies.

Saglam et al. [20] found that compared to routine interventions (night splint and home exercises) and physical therapy (night splint and home exercises, therapeutic US group, liquid paraffin, and TENS), the radial ESWT plus routine interventions group experienced significant changes in pain and both subscales of the BQ after a three-week treatment and a 12-week follow-up. Habibzadeh et al. [9] found that radial ESWT with two different application methods (point and sweep) increased the efficacy of routine treatment (including education, TENS, US, rest splint, and vitamin B1). Wu et al. [32] showed that a combination of radial ESWT and night splint is more effective than sham ESWT and night splint in CTS patients. Vahdatpour et al. [33] reported that adding real ESWT increased the efficacy of routine treatment (including night splints, NSAIDs, and vitamin B1). Surprisingly, in another study, Xu et al. reported that after nine and 12-week follow-ups, ESWT significantly decreased pain and scores of BQ compared to injections [5].

However, our findings are not in agreement with those of Raissi et al. [19] reporting no superiority in favor of the combination of radial ESWT and wrist splint compared to wrist splint alone. Additionally, Gesslbauer et al. [7] found no significant differences between the real ESWT plus night splint group and the sham ESWT plus night splint group in pain, hand grip strength, and the subscales of the BQ.

The exact physiological mechanism of ESWT in musculoskeletal disorders, such as peripheral neuropathy is not fully understood. It has been suggested that the anti-inflammatory effect of shock waves can be due to the production of nitric oxide (NO) [2, 5]. Mechanical stresses of ESWT stimulate endothelial NO synthesis in inflamed tissues and NO can decrease ongoing inflammation. Reduction of inflammation can release nerve pressure and alleviate symptoms [2, 5].

Improvement of function, finger pinch, and hand grip strength was superior in the LPL group in combination with routine treatments compared to routine treatments alone without a significant difference in pain between these two groups. This finding is consistent with systematic reviews and meta-analyses reporting that the efficacy of LPL therapy is similar to routine interventions in improving pain in mild to moderate CTS patients [16, 34]. Improving hand function and hand grip and finger pinch strength in the LPL therapy group compared to routine treatment could be attributed to the effect of laser on improving the mitochondrial ATP production and cellular oxygen consumption of the affected hand muscles [16, 35].

ESWT was more effective in improving pain after treatment and in follow-up compared to LPL. These effects could be attributed to the higher energy and mechanical effects of shock waves compared to LPL. There was no significant difference between the LPL therapy and ESWT groups in other clinical outcomes.

In our study, the latency of SNAP significantly decreased and motor NCV of the median nerve significantly increased in all groups after the treatment, while no significant reduction was observed in the latency of CMAP. However, no significant difference was found among groups in electrophysiological parameters with a small effect size in favor of LPL and ESWT in decreasing the latency of SNAP and increasing motor NCV. In our study, electrophysiological changes were observed after a two-week treatment, while in most studies, these changes were reported after the follow-up. Previous studies have revealed controversial results about the efficacy of LPL and ESWT in neurophysiological parameters of the median nerve in CTS patients.

Raissi et al. [19] reported a significant decrease in distal motor latency of the median nerve after a 12-week follow-up, while they found no changes in sensory NCV. Habibzadeh et al. [9] found a significant decrease in median sensory and motor distal latency in the ESWT group, while no significant changes were observed in the control group. Xu et al. [5] showed that the ESWT decreased the SNAP and CMAP distal latency of the median nerve, and after a 12-week follow-up, there was a superiority in favor of the injection compared to the ESWT in reducing the SNAP distal latency. Gesslbauer et al. [7] reported that ESWT was effective in decreasing distal motor latency of the median nerve. Sanglam et al. [20] showed that routine interventions, physical therapy, and radial ESWT significantly increased sensory NCV of the median nerve, while between-group comparisons confirmed the superiority of the ESWT. Despite ESWT, studies obviously did not report the positive effects of LPL therapy on improving electrophysiological parameters in CTS patients [8, 10].

Designing a study based on the severity of CTS, comparing these modalities alone or in combination with another electrotherapy agent, long-lasting effect assessment of the intervention, and assessment of these interventions by the US are recommended.

In our study, in addition to the ESWT, the routine treatment and routine treatment plus LPL significantly decreased the sensory distal latency and NCV of the median nerve. It seems possible that these results are due to the anti-inflammatory effects of ESWT, LPL, and therapeutic US. However, it should be mentioned that one of our limitations was the inability in the reliability checking of electrophysiological parameters. These parameters could have been affected by various factors, such as technical errors. Another limitation of our study was short-time follow-up.

Conclusion

Based on the results, routine interventions and a combination of ESWT or LPL with routine interventions were effective in improving clinical outcomes, decreasing sensory latency, and increasing motor NCV of the median nerve in mild to moderate CTS patients. ESWT and LPL were more effective in improving clinical outcomes compared to routine interventions alone, without statistical differences among the groups in electrophysiological parameters. No significant difference was found between the LPL therapy and routine intervention groups in pain. There were no significant differences between ESWT and LPL therapy except for pain. Therefore, it seems that ESWT and LPL are almost equally effective for the treatment of moderate CTS, although based on effect size, the group that received ESWT showed more improvement. Further research with longer follow-ups is required to establish and compare the therapeutic effects of LPL and ESWT.

Ethical Considerations

Compliance with ethical guidelines

The study was approved by the Ethics Committee of Tehran University of Medical Sciences (Code: IR.TUMS.FNM.REC.1399.107) and the study was also registered at the Iranian Registry of Clinical Trials (No.: 20220504054734N1). Before data collection, all eligible participants read and signed the consent form.

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Authors' contributions

All authors contributed equally in preparing of article.

Conflict of interest

The authors declared no conflict of interest.

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