

Physical therapy versus radial extracorporeal shock wave therapy in the treatment of carpal tunnel syndrome: A randomized-controlled study

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ABSTRACT

Objectives: This study aims to compare the efficacy of physical therapy (PT) and radial extracorporeal shock wave therapy (rESWT) in the treatment of carpal tunnel syndrome (CTS).

Patients and methods: Between May 2020 and July 2020, a total of 125 wrists of 95 patients (22 males, 73 females; mean age: 54.3±11.3 years; range, 19 to 69 years) with mild-to-moderate CTS were allocated into three groups and evaluated. The control group (Group 1, n=42) was treated with splinting and an exercise program. Group 2 (n=42) was treated with a total of three sessions of rESWT, splinting and an exercise program. Group 3 (n=41) was treated with a total of 15 sessions of PT modalities, splinting, and an exercise program. Each patient was evaluated before, three weeks and 12 weeks after treatment using a Visual Analog Scale (VAS), the Boston Carpal Tunnel Questionnaire (BCTQ), the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale, and electrodiagnostic testing.

Results: The reduction in VAS, BCTQ, LANSS, and improvement in sensory nerve conduction velocity were significantly greater at three and 12 weeks of follow-up in Groups 2 and 3, compared to Group 1 (p<0.001). A greater improvement was observed in all clinical parameters in Group 2, compared to Group 3 (p<0.001).

Conclusion: This is the first study to compare the treatment outcomes of PT and rESWT in the treatment of CTS. The results of this study show that both PT and rESWT are effective in the treatment of CTS; however, rESWT yields superior treatment effects compared to conventional PT. The practicalities of administering rESWT and its efficacy in the treatment of CTS may make it the treatment of choice.

Keywords: Carpal tunnel syndrome, functionality, radial extracorporeal shock wave therapy, pain, physical therapy.

Carpal tunnel syndrome (CTS) is the most common of all entrapment syndromes with a prevalence of 1 to 5%. It describes the compression of the median nerve, as it travels through the carpal tunnel of the wrist, largely resulting in sensory symptoms of paresthesia and pain in the areas of the hand innervated by the nerve. It can also lead to muscle atrophy, loss of motor function, and disability of the hand.^[1] Electrodiagnostic testing is used to make a definite diagnosis. The mainstay of the pathophysiology of CTS includes mechanical damage to the median nerve

due to build-up of pressure in the carpal tunnel and nerve ischemia.^[2] Chronic compression of the median nerve also results in neuronal depolarization and the release of neuropeptides such as substance P and calcitonin-gene-related peptide. These neuropeptides stimulate the release of endothelial nitric oxide, thereby triggering vasodilatation and neurogenic inflammation.^[3]

Management of CTS depends on disease severity. Physical therapy (PT), in particular, is the conventional

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non-surgical treatment of choice in the management of mild-to-moderate CTS, resulting in pain reduction and improved function. Recommended PT modalities include laser, ultrasound (US), and liquid paraffin therapy.^[4] Ultrasound therapy has given satisfactory results in the treatment of mild-to-moderate CTS.^[5] The biophysical effects of US have been shown to trigger nerve regeneration and healing.^[6]

Extracorporeal shock wave therapy (ESWT) is a non-invasive treatment method in which high frequency sound waves are applied to the body.^[7] It can be divided into radial (rESWT) and focused (fESWT) based on the design of the reflector and resultant pressure and energy applied. Animal studies have shown that ESWT, and particularly rESWT, can be successfully used in the treatment of peripheral nerve lesions, improving nerve regeneration and functional activity.^[8,9] Human studies on its uses in the treatment of peripheral neuropathies such as interdigital neuroma, distal symmetric polyneuropathy and CTS have also given promising results.^[10-14] The mechanism of action of ESWT in the treatment of CTS remains largely unknown. However, it is thought that the anti-inflammatory, angiogenic, and neurogenic effects of ESWT encourage tissue regeneration in CTS, thereby reducing the patient's symptoms and promoting an improvement in function.^[15] Moreover, rESWT rather than fESWT may be the better therapeutic option in CTS, as it can be applied to a wider area, incorporating both the median nerve and surrounding tissues.^[16]

Although there are many therapeutic options in the treatment of mild-to-moderate CTS, there is no consensus on the most effective treatment.^[4] Extracorporeal shock wave therapy has become a desirable treatment option in recent years. However, due to small patient numbers in trials to date and a limited number of placebo-controlled studies, the efficacy of this treatment option is still under debate. In the present study, we aimed to compare the efficacy of rESWT to the recommended conventional PT modalities, including therapeutic US, in the treatment of CTS with regards to nociceptive and neuropathic pain, symptom severity and functionality and nerve conduction study outcomes.

PATIENTS AND METHODS

This single-center study, prospective, randomized-controlled study was conducted at Erzurum Regional Training and Research Hospital, Department of Physical Medicine and Rehabilitation (PMR) between May 2020 and July 2020. A total of 121 patients

(156 wrists) presenting with symptoms of CTS for more than three months with physical examination and electrophysiological findings consistent with mild to moderate CTS were screened. Exclusion criteria included the presence of other sensory or motor neuropathies; history of surgery, trauma or fracture of the index hand and wrist; And history of corticosteroid injection or PT of the index wrist within the past three months. Finally, a total of 125 wrists of 95 patients (22 males, 73 females; mean age: 54.3±11.3 years; range, 19 to 69 years) who completed the study were included (Figure 1). A written informed consent was obtained from each patient. The study protocol was approved by the Erzurum Regional Training and Research Hospital Ethics Committee (date/no: 2020/10-106). The study was conducted in accordance with the principles of the Declaration of Helsinki.

All patients were educated on the importance of avoidance of repetitive wrist movements. Occupational risks for the development of CTS were also questioned and discussed. Patients were advised regarding adjustments to work routines, workplace ergonomics and the appropriate use of workplace tools where necessary.

Group allocation

The patients who met the inclusion criteria were block randomized into one of three treatment groups using the Random Allocation Software Program version 1.0 (M. Saghaei, MD., Isfahan, Iran).^[17] Firstly, this software was used to specify the number of groups and to assign a name to each group. The type of randomization was, then, selected. Once the software had assigned each study participant to a group, they were directed to the PT unit accordingly. Patient age, sex, body mass index (BMI), hand affected, time since CTS symptom onset, CTS severity based on electrodiagnostic findings, and comorbidities were recorded.

Interventions

The patients in Group 1 (32 patients, 42 wrists) were treated with splinting of the affected hand at night and a home exercise program. A wrist orthosis which held the wrist in the neutral position was used for splinting at night time for a minimum of 8 h. Each patient was given a home exercise program of wrist range of motion, wrist stretch, wrist isometric strengthening and median nerve glide exercises to be performed daily for the duration of the study; 10 repeats of each exercise, three times daily for three months.

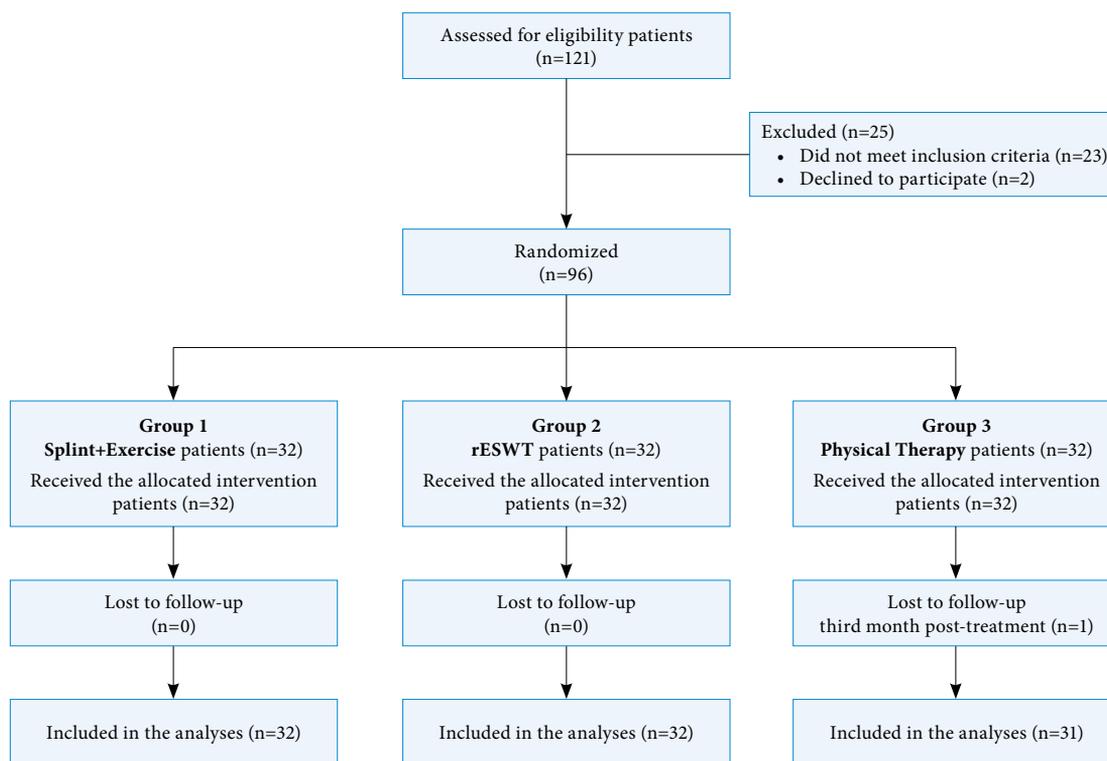


Figure 1. CONSORT diagram depicting flow through the study from recruitment to analysis.

rESWT: Radial extracorporeal shock wave therapy.

The patients in Group 2 (32 patients, 42 wrists) were treated with splinting of the affected wrist at night, a home exercise program similar to that of group one and a total of three sessions of rESWT at a frequency of one session per week using the Masterpuls® mp200 radial shock wave therapy system (Elite-Storz Medical AG, Kreuzlingen, Switzerland). The rESWT at a pressure of 4 bars, a frequency of 5 Hz and 2,000 impulses in total was applied 2 cm proximal to the median nerve, with the probe directed towards the palm, diffusely over the pisiform.

The patients in Group 3 (32 patients, 42 wrists) were treated with splinting of the affected wrist at night, a home exercise program similar to that of Groups 1 and 2 and 20 min of liquid paraffin treatment of the hand, therapeutic intermittent US (1.5 Watt/cm²) applied to the volar surface of the wrist for 5 min and 20 min of transcutaneous electrical nerve stimulation (TENS) on five consecutive days of the week for a total of 15 sessions over three weeks.

All pre- and post-study evaluations were performed by a single PMR specialist blind to the patient allocation. The randomization of patients was performed by a second PMR specialist. The PT was

conducted by a single experienced physiotherapist. All data analysis was conducted by a PMR specialist blind to the treatment provided. Study participants were contacted by telephone every two weeks to ensure compliance to the use of wrist splints and exercise program. In addition, compliance to treatment was also questioned at the first and third month of follow-up appointments.

Outcome measures

All patients were evaluated prior to commencement of treatment and at three weeks and three months post treatment using the following outcome measures:

1. *Visual Analog Scale (VAS) for wrist and hand pain severity:* The VAS provides a subjective, visual linear pain score from 0 to 10 cm scored by the patient where 0 cm is no pain.
2. *Boston Carpal Tunnel Questionnaire (BCTQ):* This questionnaire measures symptom severity (BCTQs) and functional outcome (BCTQf) specific to CTS using a scale for each. The BCTQs is determined using 11 questions each with five answers to choose from scored from 1 to 5 giving a BCTQs total out of 55. The

higher the score, the greater the symptom severity. The BCTQf questions the difficulty of eight functional activities scored from 1 to 5 giving a BCTQf total out of 40. The higher the score, the worse the functional capacity.^[18]

3. *Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale*: LANSS is a bedside test used to differentiate between nociceptive and neuropathic pain. The first part of the LANSS consists of five questions on neuropathic pain (maximum score of 16). The second part is a physical examination performed by the physician to elicit neuropathic pain. A final test score of ≥ 12 indicates neuropathic pain; a score of < 12 signifies nociceptive pain with a sensitivity of 83% and a specificity of 87%.^[19,20]

Electrophysiological testing

Standard upper normal limit values used in electrodiagnostic testing in the electroneuromyography (ENMG) laboratory of the PMR department were as follows: (i) Median nerve sensory distal latency ≤ 3.6 ms. (ii) Difference between median and ulnar nerve sensory distal latency < 0.4 ms. (iii) Median nerve distal motor latency 8 cm from thenar muscle upper ≤ 4.3 ms.

Cases in which sensory nerve conduction alone was altered were accepted as mild CTS, cases in which both sensory nerve conduction and distal motor latency were affected were deemed moderate CTS. Cases in which sensory, and in some cases motor response, was unobtainable and the motor latency was prolonged were accepted as severe CTS^[21,22] and were excluded from the study.

Statistical analysis

The sample size of the study was calculated using the NCSS-PASS 2020 software (NCSS LLC, UT, USA). A 30% change in BCTQ was used to determine the sample size based on a 5% margin of error and a confidence level of 95% (effect size = 1.0). A sample size of 24 patients per group was required to achieve a statistical and clinical difference among the three groups. Considering possible dropout, 121 patients were assessed for eligibility and 25 of them were excluded. The effect size calculator for one-way analysis of variance (ANOVA) was used to detect differences in the outcome measures among groups.

Statistical analysis was performed using the SPSS for Windows version 17.0 software (SPSS Inc.,

Chicago, IL, USA). Descriptive data were expressed in mean \pm standard deviation (SD) for normally distributed variables and in median (min-max) for non-normally distributed variables. Categorical variables were expressed in number and frequency. The normal distribution and homogeneity of variables were evaluated using histogram graphs and the one-sample Kolmogorov-Smirnov test. The chi-square test was used to compare the distribution of nominal variables among the groups. The one-way ANOVA test was used to compare the group values of parametric data and the Kruskal-Wallis test for non-parametric data. Changes in within group scores were evaluated using the Friedman test, inter-group scores were analyzed using the ANOVA with the repeated measures test. Bonferroni corrected p values were calculated and used in the post-hoc pairwise comparisons. For the Friedman variance analysis, the Wilcoxon test was used for post-hoc paired comparisons and for the Kruskal-Wallis variance analysis the Mann-Whitney U test was used. A p value of < 0.05 was considered statistically significant.

RESULTS

In this study, 42 wrists were evaluated in each of Groups 1 and Group 2, and 41 in Group 3, as one patient in this group could not be reached at three months of follow-up. There were no missed PT sessions in Group 3.

The mean overall BMI was 25.6 ± 3.4 kg/m²; the BMI in the rESWT group (Group 2) was (26.9 ± 4.9 kg/m²) and significantly higher than that of the other groups ($p = 0.034$). The mean time since symptom onset was 10.5 ± 8.7 months with no significant difference among the groups. Ninety-seven (77.6%) were cases of mild and 28 (22.4%) were cases of moderate CTS. There was no significant inter-group difference in sex, CTS severity, side affected, and comorbidities (Table 1). In total, 11 patients worked with their hands for a living. Two were dairy farmers, seven worked at a desk, one produced handcrafts, and one worked with drills. There was no significant difference in the number of patients working with their hands among the treatment groups.

In all three treatment groups, there was a statistically significant decrease in VAS, BCTQs, BCTQf, and LANSS at three weeks and three months after treatment ($p < 0.001$) and a significant increase in sensory nerve conduction velocity (SNCV) ($p < 0.001$) (Table 2). There was no significant difference among

TABLE 1 Demographic and clinical data													
	Splint+Exercise Group (n=42)			rESWT Group (n=42)			Physical Therapy Group (n=41)			Total (n=125)		p	
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	n	%		
Age (year)			55.8±11.3			53.8±11.8			53.4±10.9			54.3±11.3	0.250*
BMI (kg/m ²)			25.0±1.9			26.9±4.9			24.9±2.0			25.6±3.4	0.034*
Symptom duration (month)			9.5±7.9			11.4±11.1			10.6±6.7			10.5±8.7	0.520*
Sex													0.552**
Female	32	73.19		34	80.95		29	70.73		95	73.00		
Male	10	23.81		8	19.05		12	29.37		30	24.00		
CTS severity													0.864**
Mild	32	73.19		32	76.19		33	80.49		97	77.6		
Moderate	10	23.81		10	23.81		8	19.51		28	22.40		
Lesion site													0.398**
Right	28	66.67		26	61.90		31	75.61		85	68.00		
Left	14	33.33		16	38.10		10	24.39		40	32.00		
Co-morbidities													0.123**
None	23	54.76		26	61.90		29	70.73		78	62.40		
DM	12	28.57		9	21.83		6	14.63		27	21.60		
Hypothyroidism	5	11.90		2	4.76		6	14.63		13	10.40		
RA	2	4.76		2	4.76		0	0.00		4	3.20		
DM+Hypothyroidism	0	0.00		3	7.14		0	0.00		3	2.40		

rESWT: Radial extracorporeal shock wave therapy; SD: Standard deviation; BMI: Body mass index; CTS: Carpal tunnel syndrome; DM: Diabetes mellitus; RA: Rheumatoid arthritis; * Kruskal-Wallis test; ** Chi-square test.

TABLE 2
Intra-group and inter-group evaluation of VAS, BCTQs, BCTQf scores, and SNCV values

	Splint+Exercise Group (n=42)			rESWT Group (n=42)			Physical Therapy Group (n=41)			p* value	Effect size
	Mean±SD	Median	25 th -75 th Percentile	Mean±SD	Median	25 th -75 th Percentile	Mean±SD	Median	25 th -75 th Percentile		
VAS baseline	6.7±1.1	7.00	6.00-7.00	6.5±1.4	6.00	6.00-7.00	6.7±0.8	7.00	6.00-7.00	<0.001	
VAS 3 rd week	6.0±1.0	6.00	5.00-7.00	2.7±1.0	2.00	2.00-3.00	4.5±0.7	4.00	4.00-5.00		0.86
VAS 3 rd month	5.6±0.9	5.00	5.00-6.00	2.5±0.9	3.00	2.00-3.00	3.9±0.7	4.00	3.00-4.00		0.78
p value**		<0.001			<0.001			<0.001			
BCTQs baseline	32.4±9.1	29.00	28.00-40.00	31.7±9.3	32.00	25.00-33.00	31.8±6.0	30.00	29.00-33.00	<0.001	
BCTQs 3 rd week	29.7±9.1	28.00	25.00-38.00	17.2±7.1	15.00	11.00-21.00	24.8±5.5	25.00	20.00-25.00		1.81
BCTQs 3 rd month	27.4±8.4	25.00	22.00-34.00	14.2±5.0	12.00	11.00-15.00	21.0±6.4	20.00	17.00-22.00		1.84
p value**		<0.001			<0.001			<0.001			
BCTQf baseline	21.8±5.6	18.00	18.00-25.00	20.8±9.0	17.00	16.00-24.00	20.2±6.8	18.00	15.00-24.00	<0.001	
BCTQf 3 rd week	18.7±5.2	18.00	14.00-21.00	11.7±5.2	10.00	8.00-12.00	14.9±5.0	15.00	11.00-16.00		1.18
BCTQf 3 rd month	18.1±4.5	18.00	16.00-20.00	10.3±4.4	9.00	8.00-10.00	13.6±4.6	12.00	10.00-15.00		1.20
p value**		<0.001			<0.001			<0.001			
LANSS baseline	15.9±1.8	15.00	15.00-17.00	16.1±5.6	15.00	12.00-19.00	15.3±4.4	14.00	12.00-14.00	<0.001	
LANSS 3 rd week	15.0±2.2	15.00	13.00-16.00	10.5±4.1	11.00	5.00-14.00	12.2±3.0	11.00	10.00-12.00		1.02
LANSS 3 rd month	14.5±2.2	14.00	13.00-15.00	9.2±4.0	9.00	5.00-13.00	11.1±3.3	11.00	8.00-12.00		1.06
p value**		<0.001			<0.001			<0.001			
SNCV baseline	31.5±2.1	31.00	31.00-33.00	31.9±1.8	32.50	30.60-33.20	33.0±3.3	32.50	32.00-34.00	<0.001	
SNCV 3 rd week	32.3±2.3	32.00	31.90-34.00	34.2±1.4	34.70	33.70-34.90	34.1±2.5	33.80	32.30-34.70		0.76
SNCV 3 rd month	32.7±2.3	32.80	32.50-34.00	35.6±2.0	35.10	34.70-36.60	34.8±2.7	34.90	33.00-35.50		0.82
p value**		<0.001			<0.001			<0.001			

rESWT: Radial extracorporeal shock wave therapy; SD: Standard deviation; VAS: Visual Analog Scale; BCTQs: Boston Carpal Tunnel Questionnaire severity; BCTQf: Boston Carpal Tunnel Questionnaire functional; LANSS: Leeds Assessment of Neuropathic Symptoms and Signs; SNCV: Sensory nerve conduction velocity; * ANOVA with repeated measures; ** Friedman test.

the groups in terms of the distribution of patients with neuropathic and nociceptive pain according to the LANSS (p=0.261).

When the inter-group outcome values were analyzed, the reduction in VAS, BCTQs, BCTQf, and LANSS and increase in nerve conduction velocity were significantly higher in both Groups 2 and 3, compared to Group 1 (p<0.001). Additionally, improvement in all parameters was significantly greater in Group 2, compared to Group 3 (Table 2) (p<0.001) at three weeks and three months after treatment. There were no side effects of treatments in either group (Table 3).

In the analysis of all study participants, there was no correlation between CTS severity and change in VAS (p=0.614, r=0.046), BCTQs (p=0.943, r=0.006), BCTQf (p=0.567, r=0.052), LANSS (p=0.387, r=-0.078), and SNCV (p=0.673, r=-0.038) at three months of follow-up. In the ESWT group, there was a greater improvement in VAS (p=0.006) and BCTQf (p=0.012) in those with moderate CTS at three months of follow-up. There was no significant correlation between CTS severity and the outcome measures in Groups 1 and 3.

DISCUSSION

Carpal tunnel syndrome is the term used to describe the neuropathic signs and symptoms which occur as a result of the entrapment of the median nerve, as it passes through the carpal tunnel. Physical therapy is an established treatment option in the management of mild-to-moderate CTS. This is the first prospective randomized control study comparing the efficacy of conventional PT to rESWT in the treatment of CTS with regards to hand pain and function. The results of this study showed that both rESWT and PT significantly reduced nociceptive pain and other neurogenic symptoms of CTS, and improved function compared to conservative treatment. This improvement was more pronounced in those receiving rESWT. These findings were also supported by the improvement in SNCV, which is a more objective outcome measure.

The double-blind, randomized, placebo-controlled study of Wu et al.^[16] was the first to study the efficacy of rESWT in the treatment of CTS and also demonstrated significant improvements in VAS and BCTQ, while the SNCV of the median nerve remained unchanged. Similarly, a previous study comparing the treatment of 60 CTS patients

TABLE 3
The statistical significance levels (p values) of post-*hoc* comparisons

	Intra-Group (Wilcoxon)																						
	Splint+Exercise-rESWT			Splint+Exercise-Physical Therapy			rESWT-Physical Therapy			Splint+Exercise-rESWT			Splint+Exercise-Physical Therapy			rESWT-Physical Therapy							
	p	Baseline-3 rd week	Baseline-3 rd month	p	Baseline-3 rd week	Baseline-3 rd month	p	Baseline-3 rd week	Baseline-3 rd month	p	Baseline-3 rd week	Baseline-3 rd month	p	Baseline-3 rd week	Baseline-3 rd month	p	Baseline-3 rd week	Baseline-3 rd month	p	Baseline-3 rd week	Baseline-3 rd month	p	
VAS	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
BCTQs	<0.001	0.035	<0.001	0.008	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
BCTQf	<0.001	0.014	<0.001	0.206	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
LANSS	<0.001	0.008	<0.001	0.414	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
SNCV	0.001	0.001	<0.001	0.997	0.001	<0.001	0.001	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.003

rESWT: Radial extracorporeal shock wave therapy; VAS: Visual Analog Scale; BCTQs: Boston Carpal Tunnel Questionnaire severity; BCTQf: Boston Carpal Tunnel Questionnaire functional; LANSS: Leeds Assessment of Neuropathic Symptoms and Signs; SNCV: Sensory nerve conduction velocity.

with fESWT versus placebo showed that fESWT yielded significant and sustained improvement in pain, BCTQ and electrophysiological parameters in the fESWT group over a six-month follow-up period.^[23] More recently, a meta-analysis of six randomized-controlled trials concluded that ESWT used in the treatment of CTS reduced symptoms and improved function and electrophysiological findings.^[24] Although in this meta-analysis, ESWT was not found to be a more effective treatment option compared to corticosteroid therapy, the possible side effects of perineural corticosteroid injection, such as infection, median nerve and tendinous injury, limited its repeated use. In contrast, ESWT has only minor side effects such as transient pain and erythema. In the present study, no side effects of treatment were reported.

The results of this study showed that rESWT combined with splinting and a home exercise program was more effective than splinting and a home exercise program alone. A recent double-blind, placebo-controlled trial by Koçak Ulucaköy et al.^[25] also showed that ESWT accompanied by splinting was superior to placebo and splinting alone in terms of improvements in function and electrophysiological findings. Moreover, Seok and Kim^[26] demonstrated that even a single session of ESWT was at least as effective as a single corticosteroid injection in improving CTS-related symptoms. In the current study, the patients were given a total of three sessions of rESWT over a three-week period. This not only provided homogeneity of treatment duration across the groups, but also aimed to provide a cumulative long lasting nociceptive effect on nerve fibers as described by Takahashi et al.^[27] Not only did nociceptive pain reduce with treatment with ESWT, but neuropathic pain also reduced as shown by the LANSS pain score falling below 12 at three months of follow-up. This was also seen in the PT group. Therefore, ESWT and conventional PT can be used in the treatment of neuropathic pain in CTS.

In this study, the reduction in pain, improvement in function and nerve conduction studies were also significantly greater in the PT group (Group 3), compared to the exercise and splinting group. This may be attributed to the effects of therapeutic US used in Group 3. A previous study by Ebenbichler et al.^[5] showed the benefits of therapeutic US in CTS compared to sham US for as long as six months after treatment. Similarly, Mourad et al.^[28] reported an improvement in a nerve conduction study. Even so,

the efficacy of US in the non-surgical treatments of CTS remains somewhat debatable; while some studies have shown the benefits of US, others maintain that data remains insufficient.^[29]

Although the exact therapeutic mechanism of ESWT in the treatment of entrapment neuropathies has not been well established yet, the main therapeutic effects of ESWT in CTS are anti-inflammatory, analgesic, and neuronal regeneration effects.^[24] The anti-inflammatory effects include decreasing the nitric oxide accumulation in the cell and modulating nuclear factor kappa B activation which, in turn, may prevent the induction of the inflammatory process.^[15] In conventional PT, the anti-inflammatory effects of intermittent US are used. The other non-thermal effects of therapeutic US include cavitation, media motion and standing waves, which may elicit tissue-stimulation.^[5] Comparing the efficacy of ESWT, cryo-US, and US in the treatment of mild-to-moderate CTS, Paoloni et al.^[14] found that pain was significantly more reduced in those who received ESWT three months after treatment. Similarly, in our study, ESWT resulted in a greater improvement in all outcome parameters compared to the PT group, including US and other PT modalities, at three weeks and three months after treatment.

Analgesic effects of ESWT involve overstimulating nociceptors, leading to the gate control of pain and blocking of nerve impulses, disrupting some parts of the cell membrane and preventing the stimuli from causing pain. Also, ESWT changes the chemical environment of the area where it is applied and reduces the formation of free radicals, allowing the formation of pain-relieving chemicals.^[30] In general, TENS is thought to activate the descending inhibitory pathways of the brainstem which inhibit the activation of the nociceptive neurons of the spinal cord.^[31] Although there are few studies on the therapeutic effects of TENS in the treatment of CTS, and none comparing ESWT to TENS, in a placebo-controlled trial, TENS was found to be a more effective treatment option compared to placebo.^[32] In another study comparing the clinical effects of TENS to splinting, TENS was not found to be superior.^[33]

Another mechanism of ESWT in the treatment of CTS is its effect on peripheral neuronal regeneration. Nerve regeneration may be induced by accelerating the elimination of the injured axon, increasing Schwann cell proliferation, and increasing axonal

regeneration in animal experiments.^[34] Although the effect of therapeutic US on tissue regeneration is still unclear, it is thought to facilitate recovery in nerve compression by reducing edema and inflammation. Electrophysiological improvement as observed in this study may be explained using these mechanisms.

This is the first study to compare the efficacy of rESWT to conventional PT in the treatment of CTS. The presence of a control group, the sufficient number of study participants, and the evaluation of neuropathic pain as an outcome measure alongside nociceptive pain and function are the strengths of this study. The main limitation of the study is the lack of long-term follow-up results, which is important in determining the efficacy of treatment in a chronic disease such as CTS.

In conclusion, the results of this study show that rESWT and conventional PT can be effectively used to reduce nociceptive and neuropathic pain and improve function in the short term in mild-to-moderate CTS. The rESWT may be preferred over conventional PT owing to its practicalities, such as fewer treatment sessions. Future studies should include a larger patient cohort with a longer follow-up period and a focus on determining the optimal dosage of rESWT required to achieve long-lasting therapeutic efficacy in the treatment of CTS.

Declaration of conflicting interests

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REFERENCES

1. Werner RA, Andary M. Carpal tunnel syndrome: Pathophysiology and clinical neurophysiology. *Clin Neurophysiol* 2002;113:1373-81.
2. MacDermid JC, Wessel J. Clinical diagnosis of carpal tunnel syndrome: A systematic review. *J Hand Ther* 2004;17:309-19.
3. Monacelli G, Rizzo MI, Spagnoli AM, Pardi M, Irace S. The pillar pain in the carpal tunnel's surgery. Neurogenic inflammation? A new therapeutic approach with local anaesthetic. *J Neurosurg Sci* 2008;52:11-5.
4. Martins RS, Siqueira MG. Conservative therapeutic management of carpal tunnel syndrome. *Arq Neuropsiquiatr* 2017;75:819-24.
5. Ebenbichler GR, Resch KL, Nicolakis P, Wiesinger GF, Uhl F, Ghanem AH, et al. Ultrasound treatment for treating the carpal tunnel syndrome: Randomised "sham" controlled trial. *BMJ* 1998;316:731-5.
6. Ostergaard PJ, Meyer MA, Earp BE. Non-operative treatment of carpal tunnel syndrome. *Curr Rev Musculoskelet Med* 2020;13:141-7.
7. Mense S, Hoheisel U. Shock wave treatment improves nerve regeneration in the rat. *Muscle Nerve* 2013;47:702-10.
8. Padua L, Lo Monaco M, Valente EM, Tonali PA. A useful electrophysiologic parameter for diagnosis of carpal tunnel syndrome. *Muscle Nerve* 1996;19:48-53.
9. Lee JH, Kim SG. Effects of extracorporeal shock wave therapy on functional recovery and neurotrophin-3 expression in the spinal cord after crushed sciatic nerve injury in rats. *Ultrasound Med Biol* 2015;41:790-6.
10. Fu M, Cheng H, Li D, Yu X, Ji N, Luo F. Radial shock wave therapy in the treatment of chronic constriction injury model in rats: A preliminary study. *Chin Med J (Engl)* 2014;127:830-4.
11. Fridman R, Cain JD, Weil L Jr. Extracorporeal shockwave therapy for interdigital neuroma: A randomized, placebo-controlled, double-blind trial. *J Am Podiatr Med Assoc* 2009;99:191-3.
12. Lohse-Busch H, Marlinghaus E, Reime U, Möwis U. Focused low-energy extracorporeal shock waves with distally symmetric polyneuropathy (DSPNP): A pilot study. *NeuroRehabilitation* 2014;35:227-33.
13. Huisstede BM, Hoogvliet P, Franke TP, Randsdorp MS, Koes BW. Carpal Tunnel Syndrome: Effectiveness of Physical Therapy and Electrophysical Modalities. An Updated Systematic Review of Randomized Controlled Trials. *Arch Phys Med Rehabil* 2018;99:1623-34.
14. Paoloni M, Tavernese E, Cacchio A, D'orazi V, Ioppolo F, Fini M, et al. Extracorporeal shock wave therapy and ultrasound therapy improve pain and function in patients with carpal tunnel syndrome. A randomized controlled trial. *Eur J Phys Rehabil Med* 2015;51:521-8.
15. Mariotto S, Cavalieri E, Amelio E, Ciampa AR, de Prati AC, Marlinghaus E, et al. Extracorporeal shock waves: From lithotripsy to anti-inflammatory action by NO production. *Nitric Oxide* 2005;12:89-96.
16. Wu YT, Ke MJ, Chou YC, Chang CY, Lin CY, Li TY, et al. Effect of radial shock wave therapy for carpal tunnel syndrome: A prospective randomized, double-blind, placebo-controlled trial. *J Orthop Res* 2016;34:977-84.
17. Saghaei M. Random allocation software for parallel group randomized trials. *BMC Med Res Methodol* 2004;4:26.
18. Sezgin M, Incel NA, Serhan S, Camdeviren H, As I, Erdoğan C. Assessment of symptom severity and functional status in patients with carpal tunnel syndrome: Reliability and functionality of the Turkish version of the Boston Questionnaire. *Disabil Rehabil* 2006;28:1281-5.
19. Levine DW, Simmons BP, Koris MJ, Daltroy LH, Hohl GG, Fossel AH, et al. A self-administered questionnaire for the assessment of severity of symptoms and functional status in carpal tunnel syndrome. *J Bone Joint Surg [Am]* 1993;75:1585-92.
20. Potter J, Higginson IJ, Scadding JW, Quigley C. Identifying neuropathic pain in patients with head and neck cancer: Use of the Leeds Assessment of Neuropathic Symptoms and Signs Scale. *J R Soc Med* 2003;96:379-83.

21. Bennett M. The LANSS Pain Scale: The Leeds assessment of neuropathic symptoms and signs. *Pain* 2001;92:147-57.
22. Rossi S, Giannini F, Passero S, Paradiso C, Battistini N, Cioni R. Sensory neural conduction of median nerve from digits and palm stimulation in carpal tunnel syndrome. *Electroencephalogr Clin Neurophysiol* 1994;93:330-4.
23. Vahdatpour B, Kiyani A, Dehghan F. Effect of extracorporeal shock wave therapy on the treatment of patients with carpal tunnel syndrome. *Adv Biomed Res* 2016;5:120.
24. Kim JC, Jung SH, Lee SU, Lee SY. Effect of extracorporeal shockwave therapy on carpal tunnel syndrome: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 2019;98:e16870.
25. Koçak Ulucaköy R, Yurdakul FG, Bodur H. FRI0689 A conservative treatment option for carpal tunnel syndrome: Extracorporeal shock wave therapy. Prospective, randomized, double blind placebo controlled study. *Annals of the Rheumatic Diseases* 2018;77:863.2-864.
26. Seok H, Kim SH. The effectiveness of extracorporeal shock wave therapy vs. local steroid injection for management of carpal tunnel syndrome: A randomized controlled trial. *Am J Phys Med Rehabil* 2013;92:327-34.
27. Takahashi N, Ohtori S, Saisu T, Moriya H, Wada Y. Second application of low-energy shock waves has a cumulative effect on free nerve endings. *Clin Orthop Relat Res* 2006;443:315-9.
28. Mourad PD, Lazar DA, Curra FP, Mohr BC, Andrus KC, Avellino AM, et al. Ultrasound accelerates functional recovery after peripheral nerve damage. *Neurosurgery* 2001;48:1136-40.
29. Page MJ, O'Connor D, Pitt V, Massy-Westropp N. Therapeutic ultrasound for carpal tunnel syndrome. *Cochrane Database Syst Rev* 2013;2013:CD009601.
30. Speed C. A systematic review of shockwave therapies in soft tissue conditions: Focusing on the evidence. *Br J Sports Med* 2014;48:1538-42.
31. Vance CG, Dailey DL, Rakel BA, Sluka KA. Using TENS for pain control: The state of the evidence. *Pain Manag* 2014;4:197-209.
32. Naeser MA, Hahn KA, Lieberman BE, Branco KF. Carpal tunnel syndrome pain treated with low-level laser and microamperes transcutaneous electric nerve stimulation: A controlled study. *Arch Phys Med Rehabil* 2002;83:978-88.
33. Koca I, Boyaci A, Tutoglu A, Ucar M, Kocaturk O. Assessment of the effectiveness of interferential current therapy and TENS in the management of carpal tunnel syndrome: A randomized controlled study. *Rheumatol Int* 2014;34:1639-45.
34. Hausner T, Nógrádi A. The use of shock waves in peripheral nerve regeneration: New perspectives? *Int Rev Neurobiol* 2013;109:85-98.