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ORIGINAL ARTICLE

The effects of virtual reality-mediated tendon and nerve gliding exercises in the conservative management of carpal tunnel syndrome: a double-blind randomized placebo controlled trial

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ABSTRACT

BACKGROUND: Carpal tunnel syndrome (CTS) is a common condition resulting from compression of the median nerve at the wrist. First-line treatment typically involves conservative management, which commonly includes splinting and gliding exercises. Emerging evidence suggests the potential benefits of using virtual reality (VR) in rehabilitation.
AIM: This study aimed to assess the effects of VR-mediated tendon and nerve gliding exercises on the conservative treatment of CTS, compared to video-assisted (sham virtual) and home-based gliding exercises.
DESIGN: This study was a prospective, double-blind, randomized, placebo controlled interventional trial.
SETTING: The study was conducted in the Department of Physical Medicine and Rehabilitation at a university hospital.
POPULATION: The study included patients with mild to moderate CTS.
METHODS: The study included a total of 54 hands from 33 patients. The participants were randomly allocated into three groups: the VR-mediated group (VG), the sham VR-mediated group (SG), and the control (home-based) group (CG). Both intervention groups engaged in gliding exercises utilizing a Leap Motion Controller-based VR system and instructional videos, under the supervision of a physical therapist. The VR system was activated for the VG and deactivated for the SG. Exercises were performed twice weekly for eight weeks. The CG received a brochure describing the gliding exercises. Primary outcomes were symptom severity measured by the Numerical Rating Scale (NRS) and the Boston Carpal Tunnel Questionnaire (BCTQ), along with nerve conduction studies. Secondary outcomes included muscle strength (hand grip, key pinch), sensory measures (static two-point discrimination, vibration), and quality of life.
RESULTS: Both the VG and SG showed significant improvements in NRS and BCTQ scores compared to the CG in within-group comparisons. Nighttime symptoms improved significantly in the VG compared to the CG in between-group analyses. Electrophysiological findings showed no significant changes.
CONCLUSIONS: An eight-week VR-mediated exercise program may enhance tendon and nerve gliding exercise effectiveness, particularly for nighttime symptoms in CTS patients.
CLINICAL REHABILITATION IMPACT: In the future, challenging exercises requiring time and supervision could be effectively performed through VR, offering an alternative to traditional methods.

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KEY WORDS: Virtual reality; Exercise; Carpal tunnel syndrome; Conservative treatment.

Carpal tunnel syndrome (CTS) is a common entrapment mononeuropathy characterized by sensory and motor deficits in the median nerve distribution in the hand. CTS occurs when the median nerve is compressed as it passes through the carpal tunnel.[1-5]

Early symptoms of CTS include tingling, numbness, or pain in the first three fingers and the radial half of the ring finger.[1, 6] In severe cases, CTS can cause weakness and atrophy in the median-innervated thenar muscles,[1, 7] resulting in limitations in daily activities and job duties and ultimately affecting quality of life.[1-4]

CTS is typically classified as mild, moderate, or severe based on the severity of symptoms, signs, and electrophysiological findings.[1] According to the findings of a systematic review, many authors recommend nonsurgical treatments for mild to moderate CTS, including wrist splints, neurodynamic exercises, therapeutic ultrasound, and steroid injections.[1, 3, 8, 9] Surgical intervention is usually necessary for patients with severe CTS.[8, 9] However, there is conflicting scientific evidence regarding the efficacy of both conservative and surgical treatments.[2]

Wrist splinting and neurodynamic exercises are the most common conservative management options for patients with mild to moderate CTS.[3] There is a growing body of evidence suggesting that median nerve mobilization exercises may be effective in the conservative treatment of CTS.[1, 4, 10-13] It has been suggested that these exercises may decrease adhesion inside the carpal tunnel, reduce carpal tunnel pressure, and increase blood flow to the nerve. Consequently, this provides symptom relief.[1, 3, 11, 14] However, it is crucial to perform these exercises correctly, as improper execution may stretch the median nerve and exacerbate symptoms.[1, 3, 4, 12, 15]

Recently, there has been a rapid emergence of evidence regarding the use of new technologies, such as virtual reality (VR) in rehabilitation medicine.[16, 17] The use of VR in rehabilitation may offer several advantages, including increasing patient motivation, enhancing therapeutic effectiveness by ensuring the correct application of exercises, saving time and cost by reducing the need for supervision, and minimizing contact between patients and health professionals during events like the COVID-19 outbreak.[16-20] In rehabilitation clinics, exercises that are challenging to perform and take time to learn are typically supervised by a physical therapist. However, an exercise program based on VR can facilitate the learning of exercises and ensure their proper application. Numerous studies support the use of VR technologies in neurorehabilitation,[18, 21] but there is limited evidence for its use in rehabilitating other upper extremity disorders such as CTS. Considering the importance of correctly applying neurodynamic exercises, it can be hypothesized that tendon and nerve gliding exercises will be more effective in a virtual environment. The aim of this study was to compare the use of VR-mediated tendon and nerve gliding exercises with sham VR-mediated (video-assisted) or traditional home-based gliding exercise programs in patients with mild to moderate CTS.

Materials and methods

Study design

This prospective, randomized, double-blind, placebo-controlled interventional trial was conducted between April 2021 and May 2023 at the Department of Physical Medicine and Rehabilitation in the Faculty Hospital. The study protocol was approved by the Local Ethics Committee of the Faculty on September 7, 2020 (Decision No. 142688), in accordance with the Declaration of Helsinki. The trial was registered at clinicaltrials.gov (NCT05563909) on October 1, 2022, prior to the start of the study. The study strictly adhered to the CONSORT statement for reporting trials (Figure 1).

Participants

Out of the 57 consecutive patients (representing 85 hands) with clinically suspected CTS referred to our electromyography (EMG) laboratory for electrodiagnostic testing, a total of 33 patients (54 hands) met the eligibility criteria and were included in the study. Prior to enrollment, participants were fully informed about the study's purpose and their right to withdraw at any stage without needing to provide a reason. Additionally, written informed consent was obtained from each patient before their participation in this study.

The demographic characteristics of the participants were comprehensively documented, including age, gender, dominant hand, occupation, underlying diseases, and duration of symptoms, among others. Physical examinations were conducted for each participant, encompassing a range of tests. These included the static two-point discrimination (2-PD) test, timed vibration test, manual muscle testing (MMT) of the abductor pollicis brevis (APB), handgrip and key-pinch strength tests, along with specific provocative clinical tests for CTS. Additionally, all patients underwent a nerve conduction study (NCS) of the upper limbs at baseline.

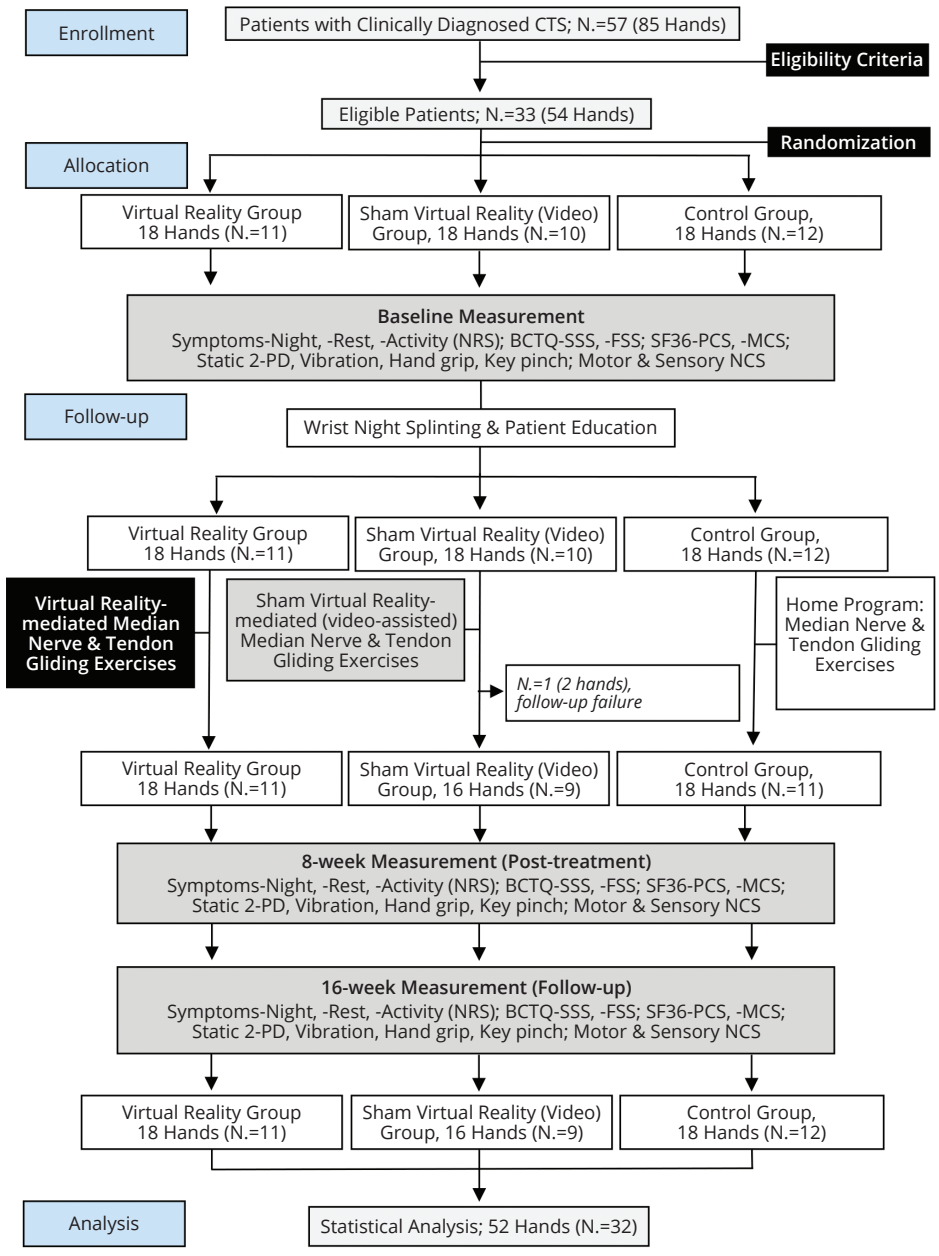

Figure 1.—CONSORT flow diagram of the study.
CTS: carpal tunnel syndrome; NRS: Numeric Rating Scale; BCTQ: Boston Carpal Tunnel Questionnaire; SSS: Symptom Severity Scale; FSS: Functional Status Scale; 2-PD: two-point discrimination; SF-36: Short Form-36; PCS: physical component summary; MCS: mental component summary; NCS: nerve conduction studies.

CTS diagnosis

In this study, the diagnosis of CTS was determined based on a combination of clinical and electrophysiological findings. The criteria for diagnosing CTS included the following: 1) the presence of at least one characteristic symptom such as numbness, tingling, and/or pain in the distribution of the median nerve in the hand (1st, 2nd, and 3rd digits, and the lateral part of the 4th digit), this could include symptoms that awaken the patient at night or pain radiating from the wrist to the shoulder; 2) the presence of at least one positive clinical sign including Tinel's, Phalen's, reverse Phalen's, and carpal compression tests; 3) the presence of at least one specific electrophysiological finding such as median distal motor latency (DML) greater than or equal to 4.0 ms, median sensory nerve conduction velocity (NCV) lower than or equal to 40 ms/s, or a fourth digit to wrist median *versus* ulnar

sensory nerve action potential peak latency difference exceeding 0.4 ms.[2, 22, 23]

Inclusion and exclusion criteria

The inclusion criteria were patients diagnosed with CTS aged between 18 and 65 years. The exclusion criteria were as follows: presence of muscle weakness (MMT<5) or atrophy in the thenar muscles, pregnancy, history of carpal tunnel release surgery, prior steroid injection into the carpal tunnel, previous trauma or surgery in the hand/wrist region, prior physical therapy within the past six months, presence of metabolic disease, such as diabetes mellitus or thyroid disease, rheumatic diseases, including rheumatoid arthritis, autoimmune disease, renal failure, peripheral polyneuropathy, specific musculoskeletal diseases, such as cervical radiculopathy and tenosynovitis, and lack of cooperation.

Randomization and blinding

The physical therapist (B.O.), responsible for administering treatments, randomly assigned eligible participants (hands) into three groups using a computer-generated sequence, applying a 1:1 equal allocation ratio. The groups were the VR-mediated exercise group (VG, N.=18), the video-assisted (sham VR) exercise group (SG, N.=18), and the traditional home-based exercise (control) group (CG, N.=18). Participants with bilateral CTS were assigned to the same group. To maintain the integrity of the study, all participants were kept blind to their group assignments. To ensure objectivity in the measurements, the same investigator (B.S. for clinical assessments and S.A. for electrophysiological examinations) conducted all baseline, post-treatment, and follow-up evaluations. These investigators were not informed about the group allocations of the participants, maintaining blinding throughout the trial.

Intervention

At the beginning of the study, all participants in the three groups were provided with comprehensive information about CTS, including its definition, epidemiology, risk factors, etiopathogenesis, clinical symptoms and signs, differential diagnosis, and treatment options, with an emphasis on tendon and nerve gliding exercises. They were also instructed to wear a wrist night splint for eight weeks and advised not to use any other treatment methods or medications during the study.

Participants in the VG practiced tendon and nerve gliding exercises using the Leap Motion Controller (LMC)-based VR system. The LMC, an optical hand tracking module, was connected to a desktop computer in the therapy room. It displayed a virtual hand image on the left side of the screen that corresponded to the participants' real-time hand movements. The right side of the screen showed instructional videos for the gliding exercises (Figure 2). In contrast, participants in the SG (Sham-VR or video-assisted) performed tendon and nerve gliding exercises similar to those in the VG. However, they exercised in front of the turned-off LMC device.

Exercise sessions

The exercise sessions were conducted by the physical therapist (B.O.), who was not involved in outcome assessments. Participants in both VG and SG participated in an eight-week exercise program consisting of median nerve and tendon gliding exercises. Each therapy session for the VG and SG included two types of exercises. The first type was nerve gliding exercises, which were performed in six positions: 1) fingers and thumb in flexion, wrist in neutral, grasp; 2) fingers and thumb extended, wrist in neutral; 3) wrist and fingers extended, thumb in neutral; 4) fingers, thumb, and wrist extended; 5) same as the fourth position with the forearm in supination; 6) same as the fifth position with gentle stretching of the thumb by the other hand. The second type was tendon gliding exercises, which were conducted in five positions: 1) all finger joints in the neutral position, straight; 2) metacarpophalangeal (MCP) joints at 90° flexion, proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints in the neutral, table-top; 3) MCP and PIP joints in full flexion, DIP joints in the neutral, straight fist; 4) PIP and DIP joints in full flexion, MCP joints in the neutral, hook fist; 5) all finger joints in full flexion, full fist.[24]

Participants were instructed to hold each exercise position for seven seconds. Each series included six nerve gliding exercises and five tendon gliding exercises, done in two sets of ten repetitions each, with a 15-second rest interval between series. The exercise sessions, which were conducted twice a week for eight weeks, lasted about 30 minutes each. Attendance was closely monitored and recorded for the VG and SG during the eight-week period. Additionally, participants in these groups were encouraged to practice the exercises at home twice a day.

Participants in the CG received a brochure with instructions for the tendon and nerve gliding exercises. They

Figure 2.—Example of a supervised exercise session using virtual reality, which includes tendon and nerve gliding exercises. The virtual hand image is displayed on the left side of the screen, while instructional videos are shown on the right side.

were also advised to perform the exercise series, consisting of ten repetitions in two sets, twice a day for eight weeks.

After the post-treatment assessment, all participants in the three groups were instructed to continue performing the exercises at least once a day until the 16-week follow-up assessment. The details of the intervention program for each study group are summarized in Table I.

TABLE I.—*Details of interventions according to the study groups.*

Intervention/content	Dose/intensity	Duration	VG	SG	CG
Splinting					
• Wrist splint	At nights	1- to 8-week	+	+	+
Education					
• About risk factors, etiopathogenesis, clinical feature, and treatment options of CTS	Once	-	+	+	+
Supervised tendon & nerve gliding exercise session					
• VR-mediated	10 repetitions, 2 sets, twice a week	1- to 8-week	+	-	-
• Sham VR-mediated (Video-assisted)	10 repetitions, 2 sets, twice a week	1- to 8-week	-	+	-
Home program					
• Tendon and nerve gliding exercises	10 repetitions, 2 sets, twice a day	1- to 8-week	+	+	+
• Tendon and nerve gliding exercises	10 repetitions, 2 sets, once a day	8- to 16-week	+	+	+

VG: virtual reality group; SG: sham virtual reality group; CG: control group; CTS: carpal tunnel syndrome; VR: virtual reality.

Outcome measures

The primary outcomes of the study were symptom severity, which was measured using the Numerical Rating Scale (NRS), and symptom severity and functional status, which were assessed using the Boston Carpal Tunnel Questionnaire (BCTQ), and NCS. The secondary outcomes included muscle strength (hand grip and key pinch), sensory measures (static 2-PD and timed vibration tests), and health-related quality of life (HRQoL) which were assessed using the Short Form 36 (SF-36).

All electrophysiologic studies were consistently conducted in the same EMG laboratory by a designated investigator (S.A.). Physical examinations for baseline and follow-up assessments were performed by the fourth-year Physical Medicine & Rehabilitation (PM&R) resident (B.S.). Participants completed self-reported questionnaires to provide details on the intensity of their symptoms, functional status, and HRQoL. Those with bilateral CTS filled out separate questionnaires for each hand. Demographic information was collected from all participants at the start of the study. Following the baseline assessment, the intervention program was conducted over an eight-week period. Participants were then reassessed within two weeks of the intervention's conclusion (post-treatment assessment). A final follow-up assessment was performed at 16 weeks.

NRS

Participants were asked to rate the current intensity of their CTS symptoms (including nighttime, resting, and during activity) over the past week using the NRS. The scale ranged from zero, indicating no symptoms, to ten, representing the worst symptoms.[25]

BCTQ

The BCTQ is a specialized questionnaire designed to assess CTS symptoms. It is composed of two subscales: an 11-item symptom severity scale (SSS) and an 8-item functional status scale (FSS). These subscales evaluate the degree of symptom severity and functional impairment on a five-point scale ranging from one (no symptoms or no difficulty) to five (severe symptoms or inability to perform activities). Each subscale's total score is derived by summing the individual scores and dividing by the number of items, with the total score ranging from one to five. A higher score indicates greater symptom severity or functional disability. The BCTQ has been extensively validated and is known for its high reliability and sensitivity to clinical changes in assessing symptoms and function in CTS patients. A post-treatment difference of at least 0.47 points in the BCTQ-SSS score was considered clinically significant.[2, 26-28] The Turkish version's validity and reliability were established by Sezgin *et al.* in 2006.[29]

Electrodiagnostic studies

The NCS, both at baseline and during follow-ups, was conducted by an experienced physiatrist (S.A.) in the EMG laboratory of the department. The same electrodiagnostic device (NIHON KOHDEN Neuropack M1 MEB-9200 EMG Unit) was used for all NCS. The NCS was performed in a quiet, air-conditioned room, using superficial electrodes and following the laboratory's standard protocol. To ensure accuracy, the temperature of the examination room was maintained at 26 °C, and the skin temperature of the hand/forearm was kept at 32 °C.

For sensory NCS, antidromic methods were utilized. A total of 10 sensory nerve action potentials (SNAP) were averaged for each test. The median sensory nerve studies involved stimulating the wrist and recording responses at the index finger, approximately 13 cm distal to the stimulation site. Key measurements included the distal (onset) sensory latency, peak-to-peak amplitude of the SNAP, and sensory NCV for the median nerve. Additionally, the study calculated the difference between median and ulnar sensory latencies at the peak of the SNAP, at a distance of 13 cm from the ring finger.

In the median motor NCS, the recording electrode was placed over the APB muscle. Stimulation of the median nerve was performed at the wrist (6 cm proximal to the recording electrode) and the elbow. The measurements taken included DML, compound muscle action potential amplitude (base-to-peak), and motor NCV in the forearm segment.

Muscle strength

Handgrip strength, measured in kilograms, was assessed using a portable Jamar hydraulic hand dynamometer (Model 5030 J1, Sammons Preston Rolyan, Bolingbrook, IL, USA). Key-pinch strength, recorded in kilopascals, was evaluated using a Jamar pinch dynamometer (Model 5030 J1, Sammons Preston Rolyan, Bolingbrook, IL, USA). Participants were instructed to squeeze the dynamometer as forcefully as possible while seated. The mean value of three consecutive attempts was recorded for each participant.[2]

Sensory measures

Sensory measures are crucial for assessing the function of the median nerve. A sensory test used in this study was the static 2-PD test, which evaluates the ability to distinguish two closely spaced points on the skin. Participants

were asked to identify the number of points touching the pulp of the index finger. Additionally, the timed vibration test was employed, involving the application of a 256 cps tuning fork to the index finger pulp while the participant was seated. The mean value of three consecutive tests was calculated for each sensory outcome.[6]

HRQoL

The Short Form 36 (SF-36) questionnaire, a widely recognized self-administered tool, was used to assess HRQoL. This 36-item questionnaire includes eight subscales: physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. Additionally, it features two summary scales: the physical component summary (PCS) and the mental component summary (MCS).[30, 31] In our study, we preferred to use the summary score (PCS and MCS) instead of the eight subscales. This decision was made to streamline the statistical analysis by reducing the number of comparisons. After recoding the responses, the relevant items were used to calculate scores for each of the eight subscales. These subscale scores range from 0 to 100, where higher scores indicate a better quality of life in the respective domain. The reliability and validity of the SF-36 in the Turkish population have been previously established.[32]

Statistical analysis

The sample size for the study was determined based on the anticipated clinically relevant improvement in the BCTQ-SSS, which is a primary outcome measure. This improvement was assessed from baseline to the 8-week post-treatment and 16-week follow-up periods. Drawing on effect sizes from previous studies (0.47),[3, 33] we aimed to achieve 80% statistical power at a significance level of 0.05. Based on these parameters, a minimum of 17 hands per group was required. We used G*Power software, version 3.1.9.7, to calculate the optimal sample size and power. To account for potential participant withdrawal, a total of 54 hands (18 hands per group) were included in the study.

The normality of the data distribution was assessed using the Shapiro-Wilk Test. Given the non-normal distribution of most variables at baseline and/or follow-up, as well as the small sample sizes, non-parametric tests were preferred for data analysis to minimize any interpretation bias.

Descriptive statistics were presented as the mean (standard deviation) and median (range). The homogeneity of baseline variables across the three groups was evaluated using the Kruskal-Wallis Test and the Chi-square Test.

For within-group analysis, changes were assessed using the Friedman Test for three dependent variables and the Wilcoxon signed-rank test for two dependent variables. Differences between baseline and post-treatment/follow-up values for each outcome were calculated and compared across groups using the Kruskal-Wallis Test. Pairwise comparisons were conducted using the Mann-Whitney U Test, with the significance level adjusted to 0.017 *via* the Bonferroni correction (P value=0.05/number of pairwise comparisons). Dichotomous variables between groups were analyzed using the Kruskal-Wallis and Chi-square Tests. Effect sizes were estimated using Cohen's d value, based on the calculated z-values. A P value of <0.05 was considered statistically significant. All analyses were performed using SPSS software, version 21.0 for Windows (Statistical Package for the Social Sciences, Chicago, IL, USA).

Results

As summarized in the study's flow chart (Figure 1), of the 33 participants (54 hands) initially included, one participant (two hands) from the SG was excluded due to non-participation in post-treatment and follow-up assessments. Therefore, this participant's data were not included in the final statistical analysis. Consequently, the per-protocol analysis was conducted on the remaining 32 participants (52 hands) who completed the trial according to the study protocol. The compliance rate for the tendon and nerve gliding exercise program was 90% in the interventional groups.

The demographic and clinical characteristics of the participants at baseline are summarized in Table II. The average age of the participants was 51.3±7.9 years, ranging from 34 to 64 years. A significant majority (84.9%) were women, and 87.9% were married. About 58% of the participants were housewives. The average duration of symptoms reported was approximately 12 years, with the majority (77.2%) experiencing bilateral symptoms. There were no significant differences between the three groups in terms of gender, age, Body Mass Index, marital status, education level, occupation, hand dominance, affected limb, or duration of symptoms. However, baseline assessment revealed significant differences among the groups in the BCTQ-SSS, PCS, hand-grip strength, and DML values (refer to Supplementary Digital Material 1: Supplementary Table I, Supplementary Table II).

Clinical and electrophysiological outcomes

The within-group and between-group comparisons for all clinical outcomes at baseline, post-treatment, and follow-

TABLE II.—*Baseline demographic characteristics of participants and homogeneity of variables between the three groups.*

		VG (N. hand=18) (N. participant=11)	SG (N. hand=18) (N. participant=10)	CG (N. hand=18) (N. participant=12)	P
Age (years)	Mean (SD)	52.8 (7.3)	51.1 (6.8)	50.9 (9.5)	0.511†
	Median (min-max)	53.0 (34-63)	49.0 (40-62)	51.0 (37-64)	
BMI (kg/m2)	Mean (SD)	28.0 (3.8)	28.2 (3.4)	28.9 (3.8)	0.703†
	Median (min-max)	26.1 (24.1-35.4)	28.0 (21.8-35.4)	28.5 (22.6-35.5)	
Symptom duration (months)	Mean (SD)	15.2 (14.1)	6.6 (4.6)	12.7 (12.0)	0.100†
	Median (min-max)	12.0 (3-60)	6.0 (1-12)	12.0 (1-36)	
		n (%)	N. (%)	N. (%)	
Gender	Female	9 (81.8)	8 (80.0)	11 (91.7)	0.706††
	Male	2 (18.2)	2 (20.0)	1 (8.3)	
Hand dominance	Right	11 (100.0)	9 (90.0)	12 (100.0)	0.305††
	Left	0 (0.0)	1 (10.0)	0 (0.0)	
Affected limb	Unilateral	4 (36.4)	2 (20.0)	6 (50.0)	0.346††
	Bilateral	7 (63.6)	8 (80.0)	6 (50.0)	
Marital status	Single	2 (18.2)	0 (0.0)	2 (16.7)	0.369††
	Married	9 (81.8)	10 (100.0)	10 (83.3)	
Education level	≤ Primary school	4 (36.4)	5 (50.0)	4 (33.3)	0.806††
	Junior high school	0 (00.0)	1 (10.0)	2 (16.7)	
	High school	4 (36.4)	2 (20.0)	4 (33.3)	
	≥ University	3 (27.3)	2 (20.0)	2 (16.7)	
Job	Housewife	4 (36.4)	7 (70.0)	8 (57.6)	0.516††
	Civil servant	2 (18.2)	2 (20.0)	2 (16.7)	
	Physical worker	4 (36.4)	1 (10.0)	1 (8.3)	
	Retired	1 (9.1)	0 (0.0)	1 (8.3)	

VG: virtual reality group; SG: sham virtual reality group; CG: control group; SD: standard deviation.
†Kruskal-Wallis Test (α=0.05); ††χ^2 Test (α=0.05).

up are detailed in Supplementary Table I and Supplementary Table II. The VG and SG showed significant reductions in nighttime symptoms severity, with the VG experiencing larger decreases (-2.6 and -3.5 points) compared to the SG (-1.6 and -2.8 points) and CG (-0.8 and -1.3 points). In the between-group comparison, a significant difference was observed among the three groups at both post-treatment (P=0.001) and follow-up (P=0.003). Further analysis with the Bonferroni correction highlighted significant reductions in nighttime symptom severity in both the VG (P=0.001, d=1.23) and SG (P=0.010, d=0.96) at post-treatment, as well as in the VG (P=0.002, d=1.19) at follow-up, compared to the CG.

Regarding vibration perception time, the VG demonstrated greater improvements (increases of 5.6 and 6.0 seconds) compared to the SG (increases of 4.3 and 5.0 seconds) and the CG (increases of 1.7 and 2.2 seconds) at post-treatment and follow-up, respectively. In the between-group comparison, significant differences were found at both post-treatment (P=0.028) and follow-up (P=0.031). Pairwise comparisons with Bonferroni correction revealed that the increase in vibration perception time was significantly more pronounced in the VG at both post-treatment (P=0.008, d=0.96) and follow-up (P=0.007, d=0.98) compared to the CG.

There was a decrease in both the BCTQ-SSS and BCTQ-FSS scores post-treatment across all three groups. However, these changes did not reach statistical significance in between-group comparisons. Likewise, improvements were noted in the PCS and MCS of the SF-36, 2-PD, handgrip strength, and key-pinch strength scores in both the post-treatment and follow-up assessments within each group. Yet, these differences were not statistically significant in the between-group comparisons (P>0.05), as detailed in Supplementary Table I.

There was no significant change detected in the NCS values either in post-treatment or in follow-up examinations except for the median-ulnar fourth finger peak latency (please refer to Supplementary Digital Material 1: Supplementary Table II).

Discussion

The primary objective of this study was to assess the efficacy of VR-mediated tendon and nerve gliding exercises compared to traditional home-based exercises for patients

with CTS. Our findings, based on between-group comparisons, indicate that the VR-mediated exercises were more effective in alleviating nighttime symptoms and improving vibration perception time than both video-assisted and traditional home-based exercises. While significant improvements were observed in the within-group comparisons for both the VG and SG, the between-group comparisons did not reveal significant enhancements in other clinical outcomes. These outcomes include symptom severity and functional status as assessed by BCTQ, as well as sensory and motor examination parameters such as 2-PD and muscle strength (hand grip, key pinch). Additionally, no significant differences were found in HRQoL as measured by the SF-36 summary scales or in electrophysiological findings when comparing the results between groups.

The pathophysiology of CTS remains not fully understood, but it is commonly believed that mechanical compression and local ischemia in the carpal tunnel contribute to the condition. This compression and ischemia are thought to lead to edema and inflammation, subsequently causing intraneural fibrosis and demyelination in the median nerve.[34, 35]

One of the conservative methods for treating CTS involves performing tendon and nerve gliding exercises. These exercises include specific movements and stretches that facilitate the optimal motion of nerves and tendons within the carpal tunnel. They are believed to reduce nerve adhesion, disperse noxious fluids, activate endogenous analgesic neural pathways, increase neural vascularity, and enhance axonal transport, thereby contributing to symptom relief and nerve function improvement.[1, 14, 36-40]

Various clinical trials have explored the effects of tendon and nerve gliding exercises in patients with CTS, comparing them with other treatment modalities. However, the debate regarding the effectiveness of these exercises as a conservative treatment option remains unresolved[36] While some studies, such as one by Bialosky *et al.*,[41] have found these exercises to be ineffective in treating CTS, reporting no significant difference between real and sham neurodynamic techniques in terms of pain reduction, other studies present contrasting viewpoints.[3, 4, 13, 33, 39, 42] For instance, study by Wolny and Linek,[14] among others, suggest that these techniques have clinical significance in reducing symptom severity and improving functional status.

Additionally, several authors who have conducted systematic reviews and meta-analyses on the effectiveness of gliding exercises in CTS treatment have suggested that, despite the current lack of strong evidence, these exercises may still be beneficial as part of a conservative treatment approach, especially when combined with other therapeutic methods.[5, 10, 11, 34, 38, 40, 43] They have emphasized the need for high-quality research to definitively confirm the effectiveness of these exercises. In a systematic review, Núñez de Arenas-Arroyo *et al.* found no clinically significant benefit from neurodynamic techniques when pooling data from various trials with different control treatments.[44] This contrasts with the findings of a more recent systematic review by Zaheer and Ahmed, which evaluated the effectiveness of neurodynamic modulation in patients with mild-to-moderate CTS. Their conclusion was that these techniques not only reduced symptom severity and median motor latency but also improved functional status and median nerve conduction velocity.[45] The inconsistent findings in the literature are thought to arise from methodological concerns in research, such as the utilization of different neuromodulation techniques with varying levels of intensity and potential biases in randomized controlled trials.[5, 36]

The correct positioning of the wrist and adjacent joints, such as the elbow, MCP, and interphalangeal joints, is believed to be critical during tendon and nerve gliding exercises for CTS. Proper alignment and movement are essential for minimizing strain on the median nerve at the wrist and maximizing the gliding of median nerve and tendons through the carpal tunnel. Conversely, incorrect movements during these exercises can lead to overstretching of muscles, tendons, and the median nerve, potentially worsening the condition.[1, 3, 4, 12, 15] Given these considerations, the primary objective of our study was to explore whether the use of VR technology during tendon and nerve gliding exercises could help ensure proper wrist and joint positioning.

As technology continues to advance, VR-mediated therapy is increasingly being used, particularly in the field of neurological rehabilitation. Emerging evidence suggests that VR offers substantial benefits over traditional therapy methods. However, there has been a lack of research exploring the application of VR technology in conducting nerve and tendon gliding exercises for CTS patients. Therefore, the primary objective of our study is to investigate the potential advantages of integrating VR into nerve and tendon gliding exercise therapy. By utilizing VR, our goal is to enhance the effectiveness of these exercises through visual feedback, which helps ensure that patients perform the movements correctly. Additionally, we anticipate that the interactive and engaging nature of VR will improve patient participation and adherence to the treatment regimen.[16, 17, 19-21, 46, 47]

Considering the within-group comparison results of

this study, we can conclude that significant improvements were observed in all three groups regarding the severity of nighttime, activity, and resting symptoms associated with CTS, as measured by the NRS. Additionally, improvements in BCTQ-SSS scores were noted in the VG and the SG, compared to the CG. A noteworthy enhancement in BCTQ-FSS scores was also seen in both the VG and SG, which was not observed in the CG.

From the between-group comparisons, a notable finding was the significant reduction (by 2.6 points) in the severity of nighttime symptoms after the 8-week VR-mediated tendon and nerve gliding exercises. In the context of conservative treatments for CTS, a two-point decrease in NRS scores is considered a clinically significant change.[48] Although the primary outcome of this study was the BCTQ-SSS score, any reduction in nighttime symptoms is clinically significant. This is particularly relevant as CTS patients frequently report disruptions in sleep due to numbness, tingling, and pain, which often lead to waking up at night. Thus, relieving these nighttime symptoms is a significant clinical achievement in the treatment of CTS.

Furthermore, our study revealed that VR-mediated tendon and nerve gliding exercises had a significantly greater impact on enhancing vibration perception time compared to both video-assisted and traditional exercises. It is well established that these large myelinated fibers are more susceptible to the effects of compression and ischemia, which are characteristic of nerve entrapment neuropathies like CTS.[49] The observed improvement in vibration perception time among participants undergoing VR-mediated treatment is an important finding. It is possible that these exercises, facilitated by VR technology, may have specific benefits in restoring or improving certain nerve functions that are compromised in CTS.

In interpreting the notable improvements observed in this study, it is crucial to consider two key influencing factors. First, the superiority noted in the intervention groups may partly be attributed to the unique environment in which the gliding exercises were conducted. The exercises were performed in the VR and/or video-mediated environment, under the guidance of a physiotherapist. This immersive and interactive setting could have enhanced the effectiveness of the exercises compared to the CG. Secondly, it is important to note that all participants were instructed to use a night wrist splint throughout the study, in conjunction with performing the tendon and nerve gliding exercises. While this concurrent use of a night splint may have contributed to the overall improvements, we believe that the tendon and nerve gliding exercises played a more significant role. This belief is supported by findings from a recent systematic review investigating the effectiveness of night splints in patients with CTS. The review concluded that night splints led only to minimal improvements in symptoms.[7, 36] Therefore, it is likely that the combination of gliding exercises and night splint usage together contributed a significant portion of the overall improvement in nighttime symptoms observed in our study. The distinct contribution of each intervention, however, requires further exploration in future research.

In our study, we observed a discrepancy in the effects of intervention on various symptoms associated with CTS. Although we found a significant decrease in the severity of nighttime symptoms as measured by the NRS, this was not the case for symptoms related to activity and rest. As anticipated, the BCTQ-SSS scores, which include both daytime and nighttime symptoms, did not exhibit a significant reduction in between-group comparisons.

The results of our study revealed no significant changes in electrophysiological parameters. We hypothesize that the lack of significant change in electrophysiological findings could be attributed to the fact that nerve conduction values were not severely impaired at baseline in the majority of participants. Moreover, it's possible that alterations in nerve conduction values might require a longer duration to manifest, suggesting that the follow-up period of our study may not have been sufficiently lengthy to detect these potential changes. Additionally, the observed reduction in symptoms following neurodynamic techniques, as reported in our study, might be attributed to factors other than direct improvements in median nerve function. One such factor could be a decrease in mechanosensitivity of the nerve. This perspective aligns with the notion that neurodynamic techniques can modulate pain perception through mechanisms that do not necessarily correlate with immediate changes in nerve conduction properties.[5, 14, 36]

In our study, we did not observe any significant changes in the quality of life among participants, as measured by the SF-36. This may be because the SF-36 is a generic quality of life assessment tool, rather than one specifically designed for a particular disease or region. The broad scope of the SF-36 could potentially limit its sensitivity to detect subtle changes specific to CTS patients.

Lastly, no significant differences were found between the groups in terms of muscle strength. This outcome could be related to the baseline characteristics of the study population. The participants in our study had mild to moderate CTS and did not exhibit significant weakness at the beginning of the study. As a result, the potential for ob-

serving significant improvements in muscle strength was likely limited given the initial levels of muscle function.[50]

Strengths and limitations of the study

There were several limitations in our study that should be considered when interpreting the results. Firstly, the sample size was small, which may have limited our ability to detect statistically significant differences, especially when comparing the groups. Secondly, the patients included in the study had been experiencing symptoms of CTS for a long duration, which could have potentially reduced the effectiveness of the gliding exercises. Lastly, the fact that participants in all three groups performed nerve gliding exercises in a variety of ways and used splints according to the protocol throughout the study may have obscured the potential benefits we expected to see with VR-mediated exercises, as hypothesized.

Despite these limitations, our study had several strengths. Firstly, it is the first study to investigate the effectiveness of median nerve and tendon gliding exercises using VR-mediated exercise therapy in patients with CTS. Moreover, both VR- and sham VR-mediated training sessions were supervised by the investigator, which minimized training variability. Lastly, the study employed a combination of self-reports (such as NRS, BCTQ, and SF-36) and objective assessment tools (NCS), enabling us to identify any potential effects of the implemented interventions.

Conclusions

An eight-week VR-mediated exercise program may be able to improve the nighttime symptoms of CTS. However, additional research is required to confirm these findings with a larger sample size and a longer period of follow-up. Furthermore, challenging exercises that require a significant amount of learning and supervision may be able to be performed using VR in the future rather than traditional methods.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions
Sina Arman, Ahmet Kivanc Menekseoglu, and Baran Sezgin contributed to the conceptualization, design of the study, provision of patients and materials, programming and software development, and designing computer programs; Sina Arman, Baran Sezgin, and Burhan Ozgur were involved in collecting data; Sina Arman conducted statistical and qualitative analysis, writing and drafting the manuscript, as well as visualization and data presentation. Sina Arman, Nalan Capan, and Aydan Oral contributed to project administration, supervision, validation, reviewing, and critically revising the manuscript. All authors have read and approved the final version of the manuscript.

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