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Original article

# Effectiveness of adding pain neuroscience education to telerehabilitation in patients with carpal tunnel syndrome: A randomized controlled trial

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A R T I C L E I N F O

*Keywords:*
Nerve compression syndromes
Telemedicine
Health education
Exercise therapy
Preoperative period

A B S T R A C T

*Background:* Previous studies have shown positive results of pain neuroscience education (PNE) combined with exercise in patients with chronic musculoskeletal disorders. However, the effects of this intervention in patients with carpal tunnel syndrome (CTS) admitted to a telerehabilitation program remain unexplored.
*Objective:* To compare the effectiveness of a 6-week telerehabilitation program based on PNE + exercise versus exercise alone on patient-reported outcomes after treatment and at 6-weeks post-treatment follow-up in patients with CTS awaiting surgery.
*Design:* Randomized controlled trial.
*Methods:* Thirty participants were randomly assigned to the PNE + exercise or exercise-only group. Outcome measures included pain intensity, pain catastrophizing, kinesiophobia, symptom severity, function, symptoms of anxiety and depression, quality of life, self-perception of improvement. Inferential analyses of the data were performed using a two-factor mixed analysis of variance.
*Results:* Twenty-five participants completed the study. A significant time × group interaction with a large effect size was observed for kinesiophobia ($F = 6.67$, $p = 0.005$, $\eta p^2 = 0.225$) and symptom severity ($F = 4.82$, $p = 0.013$, $\eta p^2 = 0.173$). No significant interaction was observed for the other variables ($p > 0.05$). A significant difference in self-perceived improvement was observed in favor of the PNE + exercise group after treatment ($p < 0.05$). Although there were significant and clinically relevant improvements within the PNE + exercise group in pain intensity and catastrophizing, there were no significant differences between the groups.
*Conclusions:* The addition of PNE to a telerehabilitation exercise program showed short-term improvements in kinesiophobia and symptom severity and greater self-perceived improvement in patients with CTS awaiting surgery. This study highlighted the benefits of including PNE in telerehabilitation interventions for patients with CTS.

## 1. Introduction

Carpal tunnel syndrome (CTS) is a frequent cause of disability that occurs when the median nerve is compressed by inflammation or narrowing at the level of the carpal tunnel (Núñez-Cortés et al., 2022). The most common symptoms of CTS are the gradual onset of tingling or numbness in the region of the median nerve and weakness of the thumb (Erickson et al., 2019; Thiese et al., 2014). The severity of symptoms and pain in CTS may be modulated by different psychosocial variables (e.g. catastrophizing, depression and anxiety) (De et al., 2013; Jerosch-Herold

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et al., 2017; Nunez et al., 2010).

Carpal tunnel release is usually indicated in cases where symptoms do not improve after six weeks of non-surgical treatment or for those who have ongoing symptoms or atrophy of the thumb musculature (Chandra et al., 2013; Erickson et al., 2019). Nevertheless, the literature suggests that conservative treatment should be considered as a first-line option before surgery, even in severe cases of CTS (Fernández-de-Las Peñas et al., 2015). Nerve and tendon gliding exercises are often included as part of multimodal treatment to improve function and reduce pain and symptom severity (Fernández-de-Las Peñas et al., 2015; Hamzeh et al., 2021; Horng et al., 2011). In fact, exercise-based physical therapy can produce similar results to surgery in terms of pain and function (Fernández-de-Las Peñas et al., 2015). In addition, encouraging physical activity may be a valuable strategy for reducing pain intensity and depressive symptoms in patients with CTS awaiting surgery (Núñez-Cortés et al., 2023).

The high healthcare demand caused by the COVID-19 pandemic forced many hospitals around the world to suspend elective or non-urgent hand surgeries (Picardo et al., 2021; Toia et al., 2021). Importantly, this situation may lead to increased attention to pharmaceutical alternatives for pain management, particularly opioid treatments (Choe et al., 2023; Karos et al., 2020). In this scenario, the use of telerehabilitation allowed to improve the accessibility of rehabilitation care, offering physiotherapists an accessible and low-cost opportunity to educate patients, improve compliance with therapeutic exercise and monitor patients' progress through remote consultations in musculoskeletal conditions (Turolla et al., 2020; Zhang et al., 2022). Indeed, telerehabilitation has demonstrated some clinical and functional outcomes as effective as face-to-face interventions, making it a good alternative to improve accessibility to rehabilitation care in a context of social distancing (Cifu and Eapen, 2021). However, to our knowledge, telerehabilitation in patients with CTS remains unexplored.

A recent meta-analysis identified depressive symptoms, anxiety and catastrophizing as important predictors of poor postoperative outcomes in patients with CTS (Núñez-Cortés et al., 2021), therefore, these variables should be addressed by clinicians at the preoperative level. In addition, some patients with CTS awaiting surgery during the COVID-19 pandemic may present with high levels of pain, catastrophizing and depressive symptoms, which may be related to a low level of physical activity and a low educational level (Núñez-Cortés et al., 2023). In this context, it is necessary to evaluate the efficacy of preoperative telerehabilitation programs with biopsychosocial approaches aimed at both increasing physical activity levels and providing the knowledge and skills needed to understand pain, in the short term, so that patients can better cope with surgery. Considering that the symptoms of CTS may be modulated by different psychosocial variables (De et al., 2013; Jerosch-Herold et al., 2017; Nunez et al., 2010), the treatment approaches, including telerehabilitation, need to move away from the biomedical bubble (The Lancet, 2018). In this regard, pain neuroscience education (PNE), which aims to facilitate individuals to change their negative beliefs related to pain, could be a promising alternative (Louw et al., 2016; Moseley and Butler, 2015). Recent meta-analyses have concluded that PNE has positive short-term effects in achieving improvements in pain, disability, kinesiophobia, and pain catastrophizing in patients with chronic musculoskeletal disorders, especially when combined with exercise (Siddall et al. (2022); Watson et al. (2019)). Although international clinical guidelines recommend exercise as a key element in the management of chronic musculoskeletal pain (Daenen et al., 2015), exercise combined with PNE in telerehabilitation programs is scarce.

The addition of PNE to an exercise-based telerehabilitation program may be an innovative alternative to reduce kinesiophobia and negative beliefs related to pain (Taulaniemi et al., 2020), improving the physical and mental health of patients with CTS who have not been able to access face-to-face treatment. Therefore, the aim of this study was to compare the effectiveness of a 6-week telerehabilitation program based on PNE plus exercise versus exercise alone on patient-reported outcomes after treatment (week 6) and at six weeks post-treatment follow-up (week 12) in patients with CTS awaiting surgery.

## 2. Methods

### 2.1. Participants and design

A randomized controlled trial (RCT) with two parallel groups was performed. Participants with a diagnosis of CTS awaiting surgery in two hospitals of the Chilean public health system (Hospital Clínico la Florida and Hospital Provincia Cordillera), who were invited to participate between January and June 2022, were candidates for the present study. The inclusion criteria were: i) age between 18 and 60 years; ii) medical diagnosis of moderate or severe CTS in accordance with the clinical practice guidelines of the Academy of Orthopaedic Physical Therapy and the Academy of Hand and Upper Extremities Physical Therapy (i.e. history, physical examination and tests/measurements) (Erickson et al., 2019); iii) symptoms of at least three months duration, iv) unilateral or bilateral symptoms; v) availability of a smartphone with Internet access, and agreement to participate in the study. Exclusion criteria were: inability to understand instructions, neurological conditions of the central nervous system (e.g. stroke, spinal cord injury), patients on treatment with alternative therapies, previous participation in a telerehabilitation program, and previous surgery on the affected upper limb. All participants were informed about the objective and procedures of the research and gave written informed consent to participate in the study. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the South East Metropolitan Health Service (ID: CEC-08-04/RAD-03), Santiago de Chile. The study was registered on ClinicalTrials.gov (NCT05184413) and adheres to the CONSORT Statement (Moher et al., 2012).

### 2.2. Randomization and allocation

After receiving the surgical waiting list from a physician not involved in the study in each hospital, the investigator involved in the recruitment process randomly contacted potential participants by telephone. The first 30 participants who agreed to participate and met the selection criteria were randomized following a simple randomization procedure using the Randomization software (www.randomization.com). A 1:1 allocation ratio to a PNE + exercise group or to an exercise-only group was considered. The randomization sequence was determined prior to the start of the baseline assessments and was known only to an external research assistant who had no access to participant characteristics and was not involved in the assessment or study intervention. Allocation remained concealed and stored in the cloud until the end of the intervention and collection of all study data. When a participant was enrolled in the study, the external research assistant informed the therapist of the assigned intervention group.

### 2.3. Telerehabilitation program

The telerehabilitation program was conducted using a smartphone videoconferencing method via WhatsApp™ and lasted 6 weeks. Both groups received three telerehabilitation sessions supervised by physiotherapists every 15 days. In the first session, all participants received an individual self-managed exercise program (see below). The PNE + exercise group also received three individual PNE sessions before each exercise session (on the same day). Participants in the study did not have to stop taking any pain medication at the time of the study.

### 2.4. Exercise program

The type and amount of exercises were the same for both groups. The exercise was multicomponent and included aerobic exercise (Hoffman and Hoffman, 2007), digital flexor tendon gliding (Horng et al., 2011), neurodynamic home exercises (Hamzeh et al., 2021), and self-stretching (Shem et al., 2020). Each participant received printed material with the different types of exercises and videos of the execution of each exercise as reinforcement. The exercise program and the characteristics of each exercise are shown in Fig. 1 and Table 1, respectively. In the first videoconference, the physiotherapist demonstrated the exercises and corrected each participant to ensure correct technique and to check that the participants were confident to perform the exercises independently at home. Each participant received on the day of the initial assessment a folder with printed material with the different types of exercises and a sheet to record compliance and prescription of each exercise. Participants were instructed to perform each exercise three days a week for 6 weeks, with a 48-h interval between each session. Each exercise session lasted approximately 30 min. A total of 18 exercise sessions were performed (15 self-managed and 3 supervised). Supervization of the exercises was performed every 15 days. In case of bilateral symptoms, participants were instructed to perform the exercises with both upper extremities.

### 2.5. Pain neuroscience education

The PNE + exercise group additionally received three individual 40-min PNE sessions every 15 days for 6 weeks, via WhatsApp™ video conferencing. The intervention was performed by a physiotherapist with seven years of clinical experience and training in PNE (Butler and Lorimer Moseley, 2013). Participants were instructed to be in a room with no distractions for the videoconferencing session. In addition, audiovisual material was sent between each session (i.e., two videos with examples and metaphors, 6 min each) to reinforce the key contents of the PNE. The total duration of the intervention was 132 min (120 min of synchronous pain education and 12 min of asynchronous material). The key concepts addressed during the online sessions are presented in Table 1. At the end of the last session, as feedback, a multiple-choice and true/false questionnaire was used to assess perceived knowledge and self-management skills. This assessment has not yet been validated and was suggested by Ziegler et al. (available in the Supplementary Material) to motivate patients/participants to learn (Ziegler et al., 2022). For evaluation purposes in our study, the percentage of correct answers was reported.

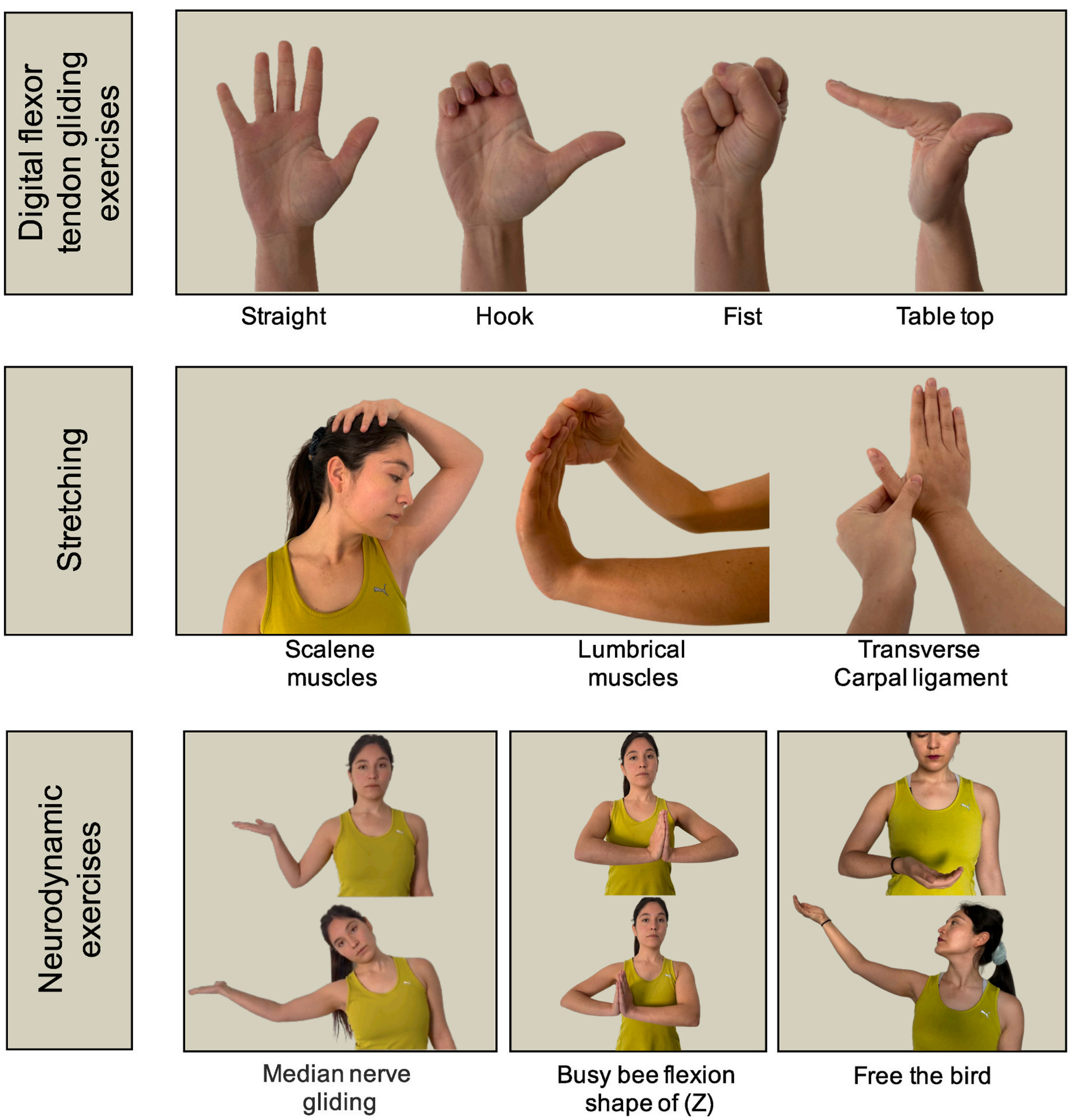


**Fig. 1.** Exercises included in the telerehabilitation program.

**Table 1**
Intervention characteristics.

| INTERVENTIONS | WEEKS 1 | 2 | 3 | 4 | 5 | 6 | CHARACTERISTICS |
|---|---|---|---|---|---|---|---|
| **Brisk walking (all patients)** [a] | | | | | | | |
| 15 min at moderate intensity | ● | ● | | | | | Moderate intensity was determined by the Talk test (i.e. can hold a conversation but not sing). |
| 20 min at moderate intensity | | | ● | ● | | | |
| 25 min at moderate intensity | | | | | ● | ● | |
| **Digital flexor tendon gliding exercises (all patients)** [a] | | | | | | | |
| Straight | ● | ● | ● | ● | ● | ● | Maximum number of repetitions up to a perceived exertion on the Borg CR10 scale of 4/10 (week 1–2), 5/10 (week 3–4) and 6/10 (week 5–6). |
| Hook | ● | ● | ● | ● | ● | ● | |
| Fist | ● | ● | ● | ● | ● | ● | |
| Table top | ● | ● | ● | ● | ● | ● | |
| **Stretching (all patients)** [a] | | | | | | | |
| Scalene muscles | ● | ● | | | | | 45 s 2 times |
| Transverse carpal ligament | | | ● | ● | ● | ● | 30 s 4 times |
| Lumbrical muscles | | | ● | ● | ● | ● | 45 s 2 times |
| **Neurodynamic exercise (all patients)** [a] | | | | | | | |
| Median nerve gliding exercise | ● | ● | | | | | Each exercise included 3 sets of 10 repetitions. |
| Busy bee flexion shape of (Z) exercise | | | ● | ● | | | |
| Free the bird exercise | | | | | ● | ● | |
| **Pain Neuroscience Education (only in experimental group)** | | | | | | | |
| Neurobiology concepts: pain pathways; the synapse; the neuron; pain is a function of the body's alert system. | ● | | | | | | Three synchronous individual sessions of 40 min by interactive videoconference plus asynchronous reinforcement videos between each session (two 6-min videos). Theoretical information was illustrated with images, examples and metaphors (visual support) |
| Examples on "Pain does not always equate to tissue injury". | ● | | | | | | |
| Pain is a nerve sensitivity: concept of central sensitization and pain modulation, i.e., descending nociceptive inhibition and facilitation. | ● | | | | | | |
| Reinforcement videos (asynchronous). | | ● | | | | | |
| Review of content covered in previous sessions; Dispelling common misconceptions about pain. | | | ● | | | | |
| Influencing/sustaining factors: Pain can be positively and negatively influenced by many factors, e.g., influence of stress, emotions, thoughts, quality of sleep and expectations. | | | ● | | | | |
| Examples of neuroplastic changes due to experience and learning. | | | ● | | | | |
| Reinforcement videos (asynchronous). | | | | ● | | | |
| Review of content covered in previous sessions. | | | | | ● | | |
| Concepts related to self-management perception: strategies to help manage pain, e.g., importance of movement and relaxation/breathing techniques. | | | | | ● | | |
| Learning assessment [b] | | | | | ● | | |

[a] Three days a week (self-managed), each session was separated by 48 h. Supervision for reinforcement and adjustment of progressions every 15 days by interactive videoconference via WhatsApp™. Restriction: Pain intensity >4 during exercise, on a numerical pain rating scale (0–10).
[b] A multiple-choice and true/false questionnaire to assess knowledge and perceived self-management skills was used as feedback at the end of the intervention (Available in the previous study by Ziegler et al., 2022).

### 2.6. Usability

At the end of each treatment, all participants completed the System Usability Scale (SUS) to assess their experience with the telerehabilitation system (Jordan et al., 1996), to ensure that both groups perceived the same subjective usability of telerehabilitation. The SUS is a simple 10-item scale that provides an overview of subjective usability evaluations (range, 0–100). Scores between 68 and 80 suggest a "good" useable interactive system and scores above 80 can be considered "excellent" (Bangor et al., 2008).

### 2.7. Clinical outcome measures

The evaluations of the participants were performed by an evaluator from each hospital who was unaware of the group allocation. The physiotherapist who performed the interventions was not involved in the evaluation process. In the first interview, participants completed self-reported information regarding age, sex, duration of CTS (months), educational level (primary, secondary or higher), analgesic intake and minutes of moderate physical activity per week. Participants were assessed before starting treatment (baseline) and reassessed after treatment (week 6) and at six weeks post-treatment follow-up (week 12). If there were symptoms in both hands, the hand with the more severe symptoms was evaluated because it was the hand that was to be operated on. Compliance with the exercise program was assessed by means of a record sheet to be filled out by the patient at home. To define 100% adherence to the exercise program, both the number of sessions completed (out of a total of 18 sessions) and the number of exercises completed within each session were considered.

### 2.8. Pain intensity

The primary outcome measure was pain intensity assessed using the numeric pain rating scale (NPRS) (Dworkin et al., 2005). Participants were asked to rate the average pain intensity during the seven days prior to the assessment on a defined 0 to 10-point scale, where 0 represents "no pain" and 10 is "worst pain imaginable." The minimum clinically important difference (MCID) for this scale is 2 points (Dworkin et al., 2008).

### 2.9. Pain catastrophizing

The Pain Catastrophizing Scale (PCS) was used to measure catastrophic thinking in response to pain through 13 statements with four possible options, from 1 "not at all" to 4 "all the time" (Sullivan et al., 1995). Higher scores (range, 0–52) indicate greater pain catastrophizing. The Spanish version of the PCS has shown adequate internal consistency and test-retest reliability (García Campayo et al., 2008). The minimum detectable change (MDC) of the PCS is 10.45 points (García

Campayo et al., 2008).

### 2.10. Kinesiophobia

The Spanish version of the Tampa Scale for Kinesiophobia-11 (TSK-11) was used to measure fear of movement (Gómez-Pérez et al., 2011). The TSK-11 has demonstrated acceptable consistency and validity (Gómez-Pérez et al., 2011). Total scores range from 11 to 44, with higher values representing worse outcome (i.e. greater interference of pain with fear avoidance behavior). The MDC for the TSK-11 is 5.6 points in people with chronic pain(Hapidou et al., 2012).

### 2.11. Severity of symptoms and function

The Boston Carpal Tunnel Questionnaire (BCTQ) measures self-reported functional status (BCTQ-FS) and severity of symptoms (BCTQ-SSS) (Levine et al., 1993). The BCTQ-SSS consists of 11 questions, each question provides 5 response choices, from 1 (no symptoms) to 5 (most severe/often). The BCTQ-FS includes 8 questions assessing difficulty with daily tasks. These responses are also scored on a 5-point scale (1–5). The MCID has been determined to be 0.74 points for the function subscale and 1.14 points for the symptom severity subscale (Kim and Jeon, 2013).

### 2.12. Mental health

The Hospital Anxiety and Depression Scale (HADS) was used to assess mental health using two 0–21 point subscales (anxiety and depression) (Zigmond and Snaith, 1983). The score is obtained by summing the items of each subscale, with higher values representing a worse outcome. A score of 0–7 is considered normal, 8–10 is considered a possible case and ≥11 indicates a probable clinical case of anxiety or depression (Zigmond and Snaith, 1983). The MCID is 1.67 points for the anxiety subscale and 1.85 for the depression subscale (Lemay et al., 2019).

### 2.13. Quality of life

The EuroQol5-dimensions (EQ-5D) was used as a self-assessed health-related quality of life questionnaire (EuroQol Group, 1990). The EQ-5D essentially consists of two pages: First, the EQ-5D description system, which provides a single index value for health status where a score of 1 represents "perfect health", 0 is a health state equivalent to death and values below 0 represent "worse than death" states. Second, a visual analogue scale (EQ-VAS) numbered from 0 "the worst health you can imagine" to 100 "the best health you can imagine".

### 2.14. Self-perception of improvement

The Patient Global Impression of Change Scale (PGICS) consists of two subscales, one categorical and one quantitative (Perrot and Lantéri-Minet, 2019). The categorical scale is a 7-point verbal scale with the following options: i) "very much improved", ii) "much improved", ii) "minimally improved", iv) "no change", v) "worse", vi) "much worse", and vii) "very much worse". The categories "very much improved" and "much improved" are considered a clinically significant improvement (Perrot and Lantéri-Minet, 2019). The quantitative scale consists of a line from 0 to 10, where 0 = much better and 10 = much worse.

### 2.15. Sample size calculation

An a priori sample size calculation was performed in G*Power software (version 3.1, Universität Düsseldorf, Germany) using the fixed effects ANOVA statistical test. An effect size of $f = 0.685$ was estimated based on a previous study on the effectiveness of PNE, which found a between-group difference greater than the MCID of 2 points on the NPRS with a large effect size ($d = 1.37$) (Bodes Pardo et al., 2018). The effect size transformation was performed with an online calculator (Lenhard and Lenhard, 2017). With α err prob = 0.05 and power (β-1 err prob) = 0.8, a total of 24 patients were required. The sample size was increased by 20% to account for potential dropouts during the follow-up period. The resulting sample size was 30 participants.

### 2.16. Statistical methods

Statistical analysis was performed with SPSS version 22.0 (IBM Corporation, Armonk, NY, USA). The normality of the data was tested using the Shapiro-Wilk test. Mean ± standard deviation (SD) or median and interquartile range (IQR) values were calculated for continuous data according to parametric or nonparametric distribution, respectively. The significance level was set at 0.05 for all statistical analyses.

Baseline differences between groups were compared using the Chi-square test for distributions of categorical variables and the independent *t*-test for continuous variables. If the data did not have a normal distribution, the Mann Whitney *U* test was used. The mean difference (MD) between groups was calculated with a 95% confidence interval (95% CI). Inferential analyses of the data were performed using a two-factor mixed analysis of variance (ANOVA): i) a between-subjects factor with two categories (two treatment groups); ii) a within-subject factor with three categories (three measures of time). When a significant interaction between factors was found, the simple mean effect (one-way ANOVA for each group) and simple pairwise comparisons (unpaired *t*-test between the two groups) were used. The chi-square test and independent *t*-test were used to explore differences between groups for the categorical and continuous PGICS, respectively, at each time measurement. Differences between usability and adherence at the end of treatment were tested with the independent *t*-test or Mann Whitney *U* test according to the distribution. The partial eta squared ($\eta p^2$) values were calculated as a measure of the effect size and the results were interpreted as small (>0.01), medium (>0.06) and large (>0.14) (Cohen, 2013).

## 3. Results

Twenty-five participants completed the study and their data were used in the final analyses (Fig. 2). No significant differences were observed between the PNE + exercise group and the exercise group before starting the intervention (Table 2). The mean usability of the interaction system for telerehabilitation was "excellent" in both groups (SUS score >80). No significant differences were observed between groups ($p > 0.05$) (Table 3). Compliance with the telerehabilitation program was over 80% in both groups, with no significant differences ($p > 0.05$) (Table 3). In the PNE + exercise group, the assessment of learning after pain education was 88% (IQR = 19) for the assessment of knowledge of key concepts and 100% (IQR = 17) for perceived self-management (Table S1).

### 3.1. Pain intensity

The ANOVA model indicated a significant main effect of the time factor ($F = 3.52$, $p = 0.038$, $\eta p^2 = 0.133$) but not of the group factor ($p > 0.05$). There was no significant time × group interaction ($F = 1.81$, $p = 0.174$, $\eta p^2 = 0.073$). Significant and clinically relevant differences in NPRS were observed at week 6 in the PNE + exercise group (MD: 2.0 points, 95% CI: 3.8 to −0.2). The exercise group showed no improvement at any time point (Table 4).

### 3.2. Pain catastrophizing

The ANOVA model indicated a significant main effect of the time factor ($F = 9.43$, $p < 0.001$, $\eta p^2 = 0.291$) but not of the group factor ($p > 0.05$). There was no significant time × group interaction ($F = 2.27$, $p = 0.115$, $\eta p^2 = 0.090$). Significant and clinically relevant differences from baseline were observed in PCS at week 6 (MD: 13.2 points 95%CI: 21.4

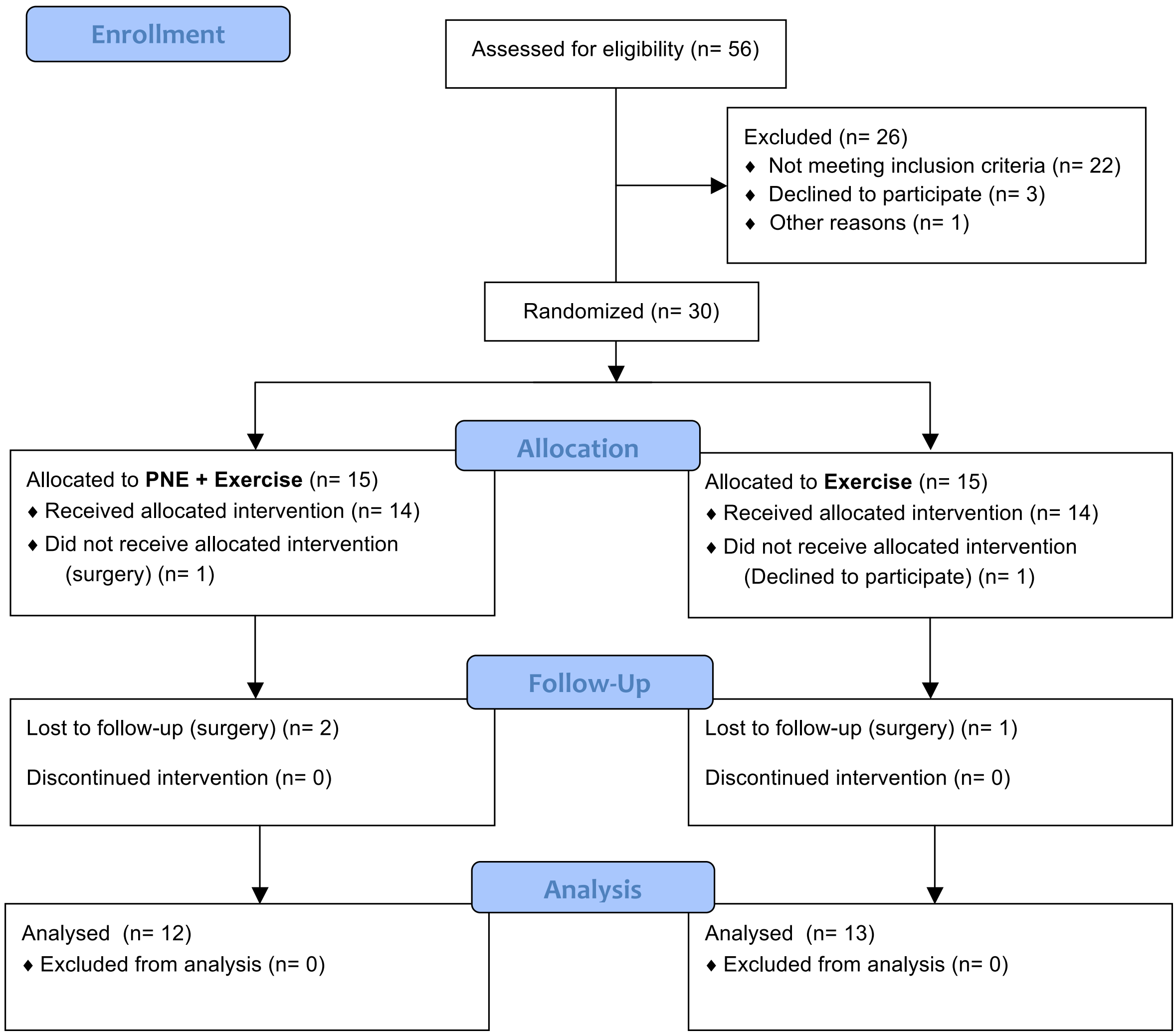


**Fig. 2.** CONSORT flowchart for the selection of participants.
Note: PNE, Pain Neuroscience Education.

to −4.9) and week 12 (MD: 8.8 points, 95%CI: 17.1 to −0.4) in the PNE + exercise group. The exercise group showed no improvement at any time point (Table 4).

### 3.3. *Kinesiophobia*

The ANOVA model indicated a significant main effect of the time factor ($F = 6.65$, $p = 0.003$, $\eta p^2 = 0.221$) and on the group factor ($F = 5.41$, $p = 0.022$, $\eta p^2 = 0.074$). Additionally, a significant time × group interaction with a large effect size was observed ($F = 6.67$, $p = 0.005$, $\eta p^2 = 0.225$). Significant and clinically relevant differences from baseline were observed in TSK-11 at week 6 (MD: 6.1 points 95%CI: 10.3 to −1.8) and week 12 (MD: 7.7 points, 95%CI: 12.8 to −2.4) in the PNE + exercise group. The exercise group showed no improvement at any time point (Table 4). At weeks 6 and 12, the mean between-group difference in TSK-11 was −5.2 points [95% CI: 9.7 to −0.6; $p = 0.028$] and −5.7 points [95% CI: 10.8 to −0.5; $p = 0.034$], respectively.

### 3.4. *Function*

The ANOVA model indicated a significant main effect of the time factor ($F = 5.02$, $p = 0.014$, $\eta p^2 = 0.179$) but not of the group factor ($p > 0.05$). There was no significant time × group interaction ($F = 1.25$, $p = 0.296$, $\eta p^2 = 0.051$). Significant differences from baseline were observed in BCTQ-FS at week 6 in the PNE + exercise group (MD: 0.7 points, 95% CI: 1.2 to −0.1) but the improvement was not sustained at the 12-week follow-up. The exercise group showed no improvement at any time point (Table 4).

### 3.5. *Severity of symptoms*

The ANOVA model indicated a significant main effect of the time factor ($F = 11.32$, $p = 0.003$, $\eta p^2 = 0.330$). In addition, a significant time × group interaction with a large effect size was observed ($F = 4.82$, $p = 0.013$, $\eta p^2 = 0.173$). Significant differences from baseline were observed in BCTQ-SSS at week 6 (MD: 0.9 points 95%CI: 1.4 to −0.4) and week 12 (MD: 0.6 points, 95%CI: 1.0 to −0.2) in the PNE + exercise group. The exercise group showed no improvement at any time point (Table 4).

### 3.6. *Mental health*

The ANOVA model indicated a non-significant main effect of the time factor and group factor in both subscales ($p > 0.05$). Additionally, a non-significant time × group interaction was observed for both subscales (anxiety: $F = 1.50$, $p = 0.235$, $\eta p^2 = 0.061$; depression: $F = 1.29$, $p = 0.286$, $\eta p^2 = 0.053$). Clinically relevant improvements in both subscales of the HADS were observed at week 6 in the PNE + exercise group, but the improvement was not sustained at the 12-week follow-up. The exercise group showed no improvement at any time point (Table 4).

**Table 2**
Baseline comparison between groups.

| Characteristics | PNE + Exercise (n = 12) | Exercise (n = 13) | Valor-p |
|---|---|---|---|
| Age (years) | 45.9 ± 7.5 | 43.6 ± 8.1 | 0.469 |
| Female gender (%) | 91.7% | 92.3% | 0.740 |
| BMI (kg/m$^2$) | 29.7 ± 5.2 | 33.3 ± 7.3 | 0.177 |
| Duration of CTS (months) | 36 (51) | 43 (45) | 0.810 |
| Symptom distribution | | | |
| Bilateral symptoms | 33.3% | 30.8% | 0.891 |
| Unilateral symptoms | 66.7% | 69.2% | |
| Educational level (%) | | | |
| Primary | 41.7% | 53.8% | 0.418 |
| Secondary/Higher | 58.3% | 46.2% | |
| Physical Activity (minutes) | 37.5 (150) | 45 (165) | 0.810 |
| Patients taking analgesics (%) | 50% | 69% | 0.327 |
| NPRS (0–10) | 6.8 ± 1.9 | 5.8 ± 2.1 | 0.234 |
| PCS (0–52) | 25.5 ± 11.8 | 26.4 ± 15.9 | 0.866 |
| TSK-11 (0–44) | 31.1 ± 5.6 | 29.4 ± 4.3 | 0.404 |
| BCTQ-FS (0–5) | 3.0 ± 0.6 | 3.1 ± 0.5 | 0.769 |
| BCTQ-SSS (0–5) | 3.4 ± 0.7 | 3.0 ± 0.5 | 0.059 |
| HADS-A (0–21) | 10.4 ± 4.2 | 9.5 ± 4.3 | 0.580 |
| HADS-D (0–21) | 7.5 ± 4.4 | 5.7 ± 3.9 | 0.284 |
| EQ5D (0–1) | 0.5 ± 0.2 | 0.6 ± 0.2 | 0.424 |
| EQVAS (0–100) | 56.3 ± 13.9 | 57.2 ± 16.4 | 0.883 |

Data are expressed as mean ± SD or median (interquartile range).
Abbreviations: BMI, Body Mass Index; BCTQ-FS, Boston Carpal Tunnel Questionnaire-Functional Scale; BCTQ-SSS, Boston Carpal Tunnel Questionnaire-Symptom Severity Scale; EQ5D, EuroQuol 5D; EQVAS, EuroQuol Visual Analog Scale; HADS, Hospital Anxiety and Depression Scale (-A, anxiety, -D, depression); NPRS, numeric pain rating scale; PCS, Pain Catastrophizing Scale; PNE, Pain Neuroscience Education; TSK-11,Tampa Scale for.

**Table 3**
Comparison between groups for impression of change, usability and adherence.

| Outcome | PNE + TE (n = 12) | TE (n = 13) | Valor-p | Effect size |
|---|---|---|---|---|
| **Week 6 (after treatment)** | | | | |
| PGIC (0–10) | 3.1 ± 1.6 | 4.3 ± 1.1 | **0.037*** | 0.893 |
| PGIC (% "very much improved" or "much improved") | 66.7 | 23.1 | **0.028*** | 1.050 |
| SUS (0–100) | 83.8 ± 10.7 | 81.2 ± 8.6 | 0.508 | 0.270 |
| Adherence (%) | 84.0 (7.5) | 92.0 (27.5) | 0.406 | 0.153 |
| **Week 12 (follow-up)** | | | | |
| PGIC (0–10) | 3.7 ± 2.7 | 3.8 ± 2.2 | 0.857 | 0.073 |
| PGIC (% "very much improved" or "much improved") | 50 | 38.5 | 0.561 | 0.259 |

Data are expressed as mean ± SD or median (interquartile range).
Abbreviation: SUS, System Usability Scale; PNE, Pain Neuroscience Education; PGIC, Patients' Global Impression of Chang scale; TE, Therapeutic Exercise. The parametric (d) and nonparametric (r) effect size of d and r can be interpreted as follows: d = 0.2 and r = 0.1, small; d = 0.5 and r = 0.3, medium; d = 0.8 and r = 0.5, large, respectively. Bold type denotes statistically significant differences.

### 3.7. *Quality of life*

The ANOVA model indicated a non-significant main effect of the time factor in both subscales ($p > 0.05$). Only a significant main effect of the group factor on the EQ-VAS was observed ($F = 5.56$, $p = 0.021$, $\eta p^2 = 0.075$), but a non-significant time × group interaction was observed for both EQ-5D ($F = 1.47$, $p = 0.240$, $\eta p^2 = 0.060$) and EQ-VAS ($F = 2.93$, $p = 0.063$, $\eta p^2 = 0.113$) (Table 4). At week 12, a mean difference between groups of 15.7 points [95% CI: 3.57 to 27.85, $p = 0.013$] was obtained on the EQ-VAS.

### 3.8. *Self-perception of improvement*

Significant differences were observed in favor of the PNE + exercise group after treatment on the continuous subscale (0–10) of the PGICS (3.1 ± 1.6 vs 4.3 ± 1.1, $p = 0.037$, ES = 0.893). Furthermore, on the categorical subscale, 66.7% of patients in the PNE + exercise group reported clinically significant improvement (i.e. categories "very much improved" and "much improved"), compared to 23.1% in the exercise group (chi-square = 4.812, $p = 0.023$). No significant differences were observed between groups at week 12 ($p > 0.05$) (Table 3).

## 4. Discussion

This RCT compared two telerehabilitation programs, combined treatment with PNE + exercise versus isolated exercise in patients with CTS awaiting surgery in two hospitals of the Chilean public health system. Overall, the proposed interactive system for telerehabilitation had excellent usability and adherence was over 80% in both groups. Our results showed that a combined PNE + exercise program was more effective than exercise alone in reducing kinesiophobia and symptom severity. In addition, self-perceived improvement was greater in the PNE + exercise group compared to that of the exercise-only group at the end of treatment. In the last decade there have been an increasing number of systematic reviews and meta-analyses on telerehabilitation. To date, the available systematic reviews on the effects of PNE have not included RCTs in patients with CTS in a telerehabilitation setting (Bülow et al., 2021; Louw et al., 2016; Moseley and Butler, 2015; Siddall et al., 2022; Tegner et al., 2018; Watson et al., 2019; Wood and Hendrick, 2019). This study is therefore a novelty in this field.

Several studies have reported positive effects of PNE on pain, function, and some psychosocial variables in patients with musculoskeletal conditions (Bülow et al., 2021; Louw et al., 2016; Moseley and Butler, 2015; Siddall et al., 2022; Tegner et al., 2018; Watson et al., 2019; Wood and Hendrick, 2019). Some of our results are consistent with the available evidence. For example, Watson et al., 2019 found in their meta-analysis that the effect of PNE treatment for kinesiophobia in adults with chronic musculoskeletal pain was clinically relevant in the short term. Siddall et al., 2022 also found in their meta-analysis that the combination of PNE and exercise resulted in greater improvements in kinesiophobia than exercise

**Table 4**
Outcome measures during the follow-up period and results of the time x group comparative analysis.

| Outcome | Follow-up | PNE + Exercise (n = 12) | | Exercise (n = 13) | | ANOVA Interaction Effect | | |
|---|---|---|---|---|---|---|---|---|
| | | Mean ± SD | Mean within-group difference [95% CI] | Mean ± SD | Mean within-group difference [95% CI] | F | p-value | $\eta^2p$ |
| **NPRS (0–10)** | Baseline | 6.8 ± 1.9 | | 5.8 ± 2.1 | | 1.81 | 0.174 | 0.073 |
| | Week 6 | 4.8 ± 1.7 | −2.0 [-3.8 to −0.2] | 5.5 ± 1.4 | −0.2 [-1.9 to 1.5] | | | |
| | Week 12 | 5.4 ± 2.0 | −1.3 [-3.4 to 0.8] | 4.9 ± 2.5 | −0.9 [-2.8 to 1.2] | | | |
| **PCS (0–52)** | Baseline | 25.5 ± 11.8 | | 26.4 ± 15.9 | | 2.27 | 0.115 | 0.090 |
| | Week 6 | 12.3 ± 6.8 | −13.2 [-21.4 to −4.9] | 22.2 ± 13.8 | −4.2 [-12.2 to 3.6] | | | |
| | Week 12 | 16.8 ± 11.5 | −8.8 [-17.1 to −0.4] | 19.8 ± 15.7 | −6.6 [-14.6 to 1.4] | | | |
| **TSK-11 (0–44)** | Baseline | 31.1 ± 5.6 | | 29.4 ± 4.3 | | 6.67 | **0.005**** | 0.225 |
| | Week 6 | 25.0 ± 5.3 | −6.1 [-10.3 to −1.8] | 30.2 ± 5.7 | 0.8 [-3.3 to 4.8] | | | |
| | Week 12 | 23.4 ± 5.9 | −7.7 [-12.8 to-2.4] | 29.1 ± 6.6 | −0.3 [-5.2 to 4.6] | | | |
| **BCTQ-FS (0–5)** | Baseline | 3.0 ± 0.6 | | 3.1 ± 0.5 | | 1.25 | 0.296 | 0.051 |
| | Week 6 | 2.3 ± 0.5 | −0.7 [-1.2 to −0.1] | 2.7 ± 0.7 | −0.4 [-0.8 to 0.2] | | | |
| | Week 12 | 2.7 ± 0.8 | −0.3 [-0.9 to 0.3] | 2.5 ± 0.9 | −0.5 [-1.1 to 0.1] | | | |
| **BCTQ-SSS (0–5)** | Baseline | 3.4 ± 0.7 | | 3.0 ± 0.5 | | 4.82 | **0.013*** | 0.173 |
| | Week 6 | 2.5 ± 0.5 | −0.9 [-1.4 to −0.4] | 2.8 ± 0.7 | −0.2 [-0.6 to 0.3] | | | |
| | Week 12 | 2.8 ± 0.8 | −0.6 [-1.0 to −0.2] | 2.6 ± 0.8 | −0.4 [-0.8 to 0.0] | | | |
| **HADS-A (0–21)** | Baseline | 10.4 ± 4.2 | | 9.5 ± 4.3 | | 1.50 | 0.235 | 0.061 |
| | Week 6 | 8.1 ± 3.8 | −2.3 [-4.5 to −0.2] | 9.2 ± 4.1 | −0.3 [-2.4 to 1.7] | | | |
| | Week 12 | 8.8 ± 5.1 | −1.6 [-3.8 to 0.6] | 8.5 ± 4.8 | −0.9 [-3.0 to 1.2] | | | |
| **HADS-D (0–21)** | Baseline | 7.5 ± 4.4 | | 5.7 ± 3.9 | | 1.29 | 0.286 | 0.053 |
| | Week 6 | 5.2 ± 3.9 | −2.3 [-5.4 to 0.7] | 5.4 ± 3.6 | −0.3 [-3.2 to 2.6] | | | |
| | Week 12 | 6.1 ± 4.5 | −1.4 [-3.7 to 0.8] | 4.5 ± 4.1 | −1.2 [-3.4 to 1.0] | | | |
| **EQ5D (0–1)** | Baseline | 0.51 ± 0.2 | | 0.57 ± 0.2 | | 1.47 | 0.240 | 0.060 |
| | Week 6 | 0.62 ± 0.2 | 0.11 [-0.1 to 0.3] | 0.55 ± 0.2 | −0.02 [-0.2 to 0.2] | | | |
| | Week 12 | 0.61 ± 0.2 | 0.10 [0.0 to 0.2] | 0.56 ± 0.2 | −0.01 [-0.2 to 0.1] | | | |
| **EQVAS (0–100)** | Baseline | 56.3 ± 13.9 | | 57.2 ± 16.4 | | 2.93 | 0.063 | 0.113 |
| | Week 6 | 69.0 ± 10.3 | 13.7 [0.2 to 27.1] | 60.8 ± 16.8 | 3.6 [-9.3 to 16.5] | | | |
| | Week 12 | 70.5 ± 14.8 | 14.3 [0.8 to 27.7] | 55.6 ± 15.9 | −1.5 [-14.1 to 11.3] | | | |

Abbreviations: BCTQ-FS, Boston Carpal Tunnel Questionnaire-Functional Scale; BCTQ-SSS, Boston Carpal Tunnel Questionnaire-Symptom Severity Scale; EQ5D, EuroQuol 5D; EQVAS, EuroQuol Visual Analog Scale; HADS, Hospital Anxiety and Depression Scale (-A, anxiety, -D, depression); NPRS, numeric pain rating scale; PCS, Pain Catastrophizing Scale; PNE, Pain Neuroscience Education; TSK-11, Tampa Scale for Kinesiophobia-11; 95%CI, 95% confidence interval. *Statistically-significant difference ($p < 0.05$); **Statistically-significant difference ($p < 0.01$); Bold type denotes statistically significant differences.

alone in the same population. Based on our results, we confirm that PNE + exercise as a telerehabilitation modality is a useful intervention to reduce fear of movement in patients with CTS. This could be explained by the fact that the aim of a combined therapy is to reconceptualize pain, reducing the threat value and promoting gradual and safe exercise (Louw et al., 2021). On the other hand, there was a significant improvement in symptom severity reduction in favor of the PNE + exercise group compared to exercise alone. However, the intra-group difference in the BCTQ-SSS was not superior to the MCID (Kim and Jeon, 2013). In relation to self-perception of improvement after treatment, 66.7% of participants in the PNE + exercise group considered that they had much improved or very much improved after treatment. In addition, half of the participants maintained this improvement at the 6-week follow-up, which is considered a clinically significant improvement for this variable (Perrot and Lantéri-Minet, 2019).

In contrast to these findings, most systematic reviews report improvements in pain or function with PNE in patients with chronic musculoskeletal pain (Bülow et al., 2021; Louw et al., 2016; Moseley and Butler, 2015; Siddall et al., 2022; Tegner et al., 2018; Watson et al., 2019; Wood and Hendrick, 2019). For example, Malfliet et al. (2018) conclude in a multicenter RCT that combined treatment including PNE appears to be more effective than conventional physical therapy in improving pain and disability, among other outcomes. In fibromyalgia patients, Amer-Cuenca et al. (2020) found that higher doses of PNE (270 min) produced greater improvements in pain intensity than lower doses of PNE (90 min). In our study, 120 min of PNE were delivered by videoconference plus 12 min of reinforcement videos. With this in mind, higher doses of PNE may have improved the results of our study. Additionally, our sample included patients with severe CTS awaiting surgical intervention, most of whom had been symptomatic for longer than 30 months (Table 1). Because of COVID-19, most patients did not have access to timely treatment with a biopsychosocial approach, which may have increased uncertainty and sources of pain-related threat (Karos et al., 2020). In addition, patients in the PNE + exercise group had a mean HADS score above the cutoff point on both subscales (ie, ≥8 points), indicating high levels of anxiety or depression in our sample (Table 1) (Zigmond and Snaith, 1983). Both of these factors may negatively influence the prognosis of physical functioning after rehabilitation (Tseli et al., 2019). All of these factors suggest that our study population may be a group with higher levels of vulnerability in various domains. This may also explain why the exercise-only group did not achieve positive results, despite the literature claiming that exercise-based physical therapy produces improvements in symptoms and function in patients with CTS (Fernández-de-Las Peñas et al., 2015; Hamzeh et al., 2021; Horng et al., 2011). Therefore, future studies should investigate the efficacy of telerehabilitation combined with the support of an interdisciplinary team (i.e., psychologist, occupational therapist, and social worker).

On the other hand, our study showed no significant improvement in the levels of catastrophizing in the PNE + exercise group compared to the exercise group. Nevertheless, it is relevant to mention that in the PNE + exercise group an improvement above the MCD (i.e. above 10.45) was obtained on the PCS at week 6 (García Campayo et al., 2008). This improvement was not sustained at the 12-week assessment, indicating that a greater number of sessions may be necessary to demonstrate stronger results. In terms of symptoms of depression and anxiety, our study also showed no significant differences when comparing the two treatments. Although the MCID of 1.85 and 1.67 points for the depression and anxiety subscales of the HADS were exceeded in the PNE + exercise group (Lemay et al., 2019), this improvement was also not sustained at the week 12 follow-up. In contrast to our results, Chimenti et al. (2023) and Barrenengoa-Cuadra et al. (2021), who also considered higher doses of pain education in the treatment of patients with chronic pain, found greater benefits for catastrophizing and mental health, respectively. Future research should explore the dose-response of PNE to guide clinicians in developing telerehabilitation interventions to find the optimal duration of intervention.

### 4.1. Implications for clinical practice

This study highlights that in this new era of telemedicine, researchers and clinicians should explore biopsychosocial treatment approaches, including PNE, to improve telerehabilitation interventions. The reduction of kinesiophobia following pain education combined with exercise may be a key factor in determining changes in disability and analgesic use in the medium to long term (Murillo et al., 2023). Additionally, clinically relevant improvements in catastrophizing and anxiety symptoms immediately after PNE should also be considered by surgeons, as both variables are important predictors of poor outcomes after surgery (Núñez-Cortés et al., 2021). Therefore, it would be interesting to coordinate surgery in patients with CTS immediately after completion of the 6-week pain education combined with exercise and to evaluate the long-term efficacy of the intervention. Future studies should also consider combining PNE with interdisciplinary and multimodal treatments (e.g. cognitive behavioral therapy and mindfulness), which have shown promise for these variables in other painful conditions such as fibromyalgia (Serrat et al., 2021). Furthermore, these interventions should be tailored to account for social determinants of health (e.g., education level) (Núñez-Cortés et al., 2023) and the diverse cultural backgrounds of patients (Reis et al., 2022).

### 4.2. Strengths and limitations

The novel and useful guidance on how telerehabilitation can improve its effectiveness when combined with PNE is the main strength of our study. In addition, our research provides additional information in the context of non-North American/Western European countries on digital support for patients with persistent pain, specifically on the effectiveness of a low-cost telerehabilitation programme focusing on biopsychosocial aspects. On the other hand, our results should be interpreted taking into account the following limitations. 1) The absence of a control group that did not receive any intervention did not allow the results of the two groups to be compared with the natural history of CTS. Ethical considerations make it difficult to allocate patients with persistent symptoms to a non-intervention group; 2) The effect of the intervention was only assessed preoperatively. Therefore, future RCTs are needed to know both the postoperative and long-term effects of the intervention; 3) Due to the nature of the intervention, it was not possible to blind the patients about PNE. Also, the influence of treatment expectations was not assessed, which may be relevant as patients were candidates for surgery to resolve their symptoms; 4) Although the sample size was calculated, a larger sample could increase the precision, generalizability, and statistical power of their study. Future multicenter studies are needed to corroborate these findings and to address the cultural aspects of pain (Reis et al., 2022).

## 5. Conclusions

The addition of PNE to a telerehabilitation exercise program showed short-term improvements in kinesiophobia and symptom severity and greater self-perceived improvement in patients with CTS awaiting surgery. Although there were significant and clinically relevant improvements within the PNE + exercise group in pain intensity and catastrophizing, there were no significant differences between the groups. This study highlighted the benefits of including PNE in telerehabilitation interventions.

## Ethics

All study procedures were approved by the Ethics Committee of the South East Metropolitan Health Service (ID: CEC-08-04/RAD-03).

## Protocol register

ClinicalTrials.gov (NCT05184413).

## Declarations of competing interest

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.msksp.2023.102835.

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