

# Court-Type Thai Traditional Massage for Patients with Intractable Peripheral Neuropathic Pain: a Randomized Controlled Trial

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## ABSTRACT

**Objective:** Neuropathic pain management involves both pharmacological and non-pharmacological interventions. Despite this, no prior research has demonstrated the efficacy of court-type Thai traditional massage (CTTM) for neuropathic pain relief. This study aimed to investigate the potential benefits of CTTM in alleviating neuropathic pain.

**Materials and Methods:** A preliminary single-blind randomized controlled trial was conducted on 28 participants with peripheral neuropathic pain, who were equally assigned to 2 groups. Both groups received standard drug treatment; however, the intervention group additionally received CTTM and hot herbal compression, while the active control group only received HHC. The adjuvant treatments were administered twice weekly for 4 weeks (V1-V8). A follow-up was conducted 4 weeks posttreatment (V9). Outcome measures were assessed at V1, V4, V8, and V9 using a numerical rating scale and the Thai versions of the Neuropathic Pain Symptom Inventory, the Brief Pain Inventory, and the EQ-5L-5D health questionnaire.

**Results:** The data revealed that the intervention and active control groups had statistically significant differences in their pain intensity scores ( $P < 0.001$ ), total neuropathic pain intensity scores ( $P = 0.001$ ), and utility of health scores ( $P = 0.007$ ) during the follow-up period. When comparing outcomes between V1 and V8, the groups exhibited significant differences in pain reduction ( $P = 0.003$ ) and quality of life ( $P = 0.027$ ).

**Conclusion:** This study provides initial evidence supporting the potential benefits of CTTM in alleviating peripheral neuropathic pain and improving quality of life. Future research should further investigate the application of CTTM in managing peripheral neuropathic pain conditions.

**Keywords:** Complementary therapies; massage; pain intensity; peripheral neuropathic pain; quality of life; randomized controlled trial (Siriraj Med J 2023; 75: 599-611)

## INTRODUCTION

Peripheral neuropathic pain arises from lesions or diseases affecting the somatosensory nervous system.<sup>1</sup> Comprehensive clinical pain assessment of neuropathic pain encompasses severity, characteristics, medication

usage and potential side effects, the impact of mobility and usual activities. For example, chronic low back pain patients with peripheral neuropathic pain were associated with higher disability than the patients without neuropathic pain.<sup>2</sup> A crucial outcome of neuropathic pain

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management is patient-reported pain relief or intensity reduction, individual adverse effects, and utilization of rescue medication. Although numerous drug classes are employed in pharmacological pain treatment, various nonpharmacological strategies are utilized to alleviate pain especially alternative medicine practices such as acupuncture, massage therapy, and behavior modification.<sup>3</sup>

Court-type Thai traditional massage (CTTM), a therapeutic technique that originated in Thailand, aims to facilitate patient healing and rehabilitation. This massage approach is characterized by the application of pressure using fingers and hands along specific massage lines and points on the body. Practitioners manipulate posture and angles to regulate the direction and intensity of pressure during massage.<sup>4</sup>

Several prior clinical trials have investigated the effects of CTTM on pain and psychological conditions. Traditional Thai massage (TTM) reduced spasticity and enhanced limb functions in elderly stroke patients, with results comparable to conventional physical therapy programs.<sup>5</sup> Patients with osteoarthritis experienced increased walking speed and improved quality of life following CTTM treatment.<sup>6</sup> A study comparing the efficacy of CTTM and amitriptyline for chronic tension-type headache patients demonstrated a significant decrease in pain severity.<sup>7</sup> CTTM outperformed topical diclofenac in enhancing the quality of life and shoulder functionality while decreasing pain intensity in patients with frozen shoulders.<sup>8</sup> Furthermore, CTTM effectively alleviated upper trapezius myofascial pain syndrome.<sup>9</sup> The effects of CTTM on electroencephalograms indicated a significant increase relaxation in patients with scapulothoracic syndrome.<sup>10</sup> However, no study has yet examined the efficacy of CTTM in patients with neuropathy. Consequently, the present study aimed to investigate the impacts of CTTM on pain relief, physical and emotional functions, and quality of life in patients with peripheral neuropathic pain.

## MATERIALS AND METHODS

### Study design

This study was a preliminary single-blind, parallel-group, randomized controlled trial. Before the research commenced, it was approved by the Siriraj Institutional Review Board on September 18, 2019 (COA no. Si 649/2019) and registered in the Thai Clinical Trials Registry on August 1, 2021 (TCTR20210801006). Participants with intractable peripheral neuropathic pain were recruited from the pain clinic at Siriraj Hospital. All participants provided informed consent before commencing the study. The total duration of the investigation was 8 weeks.

### Participants

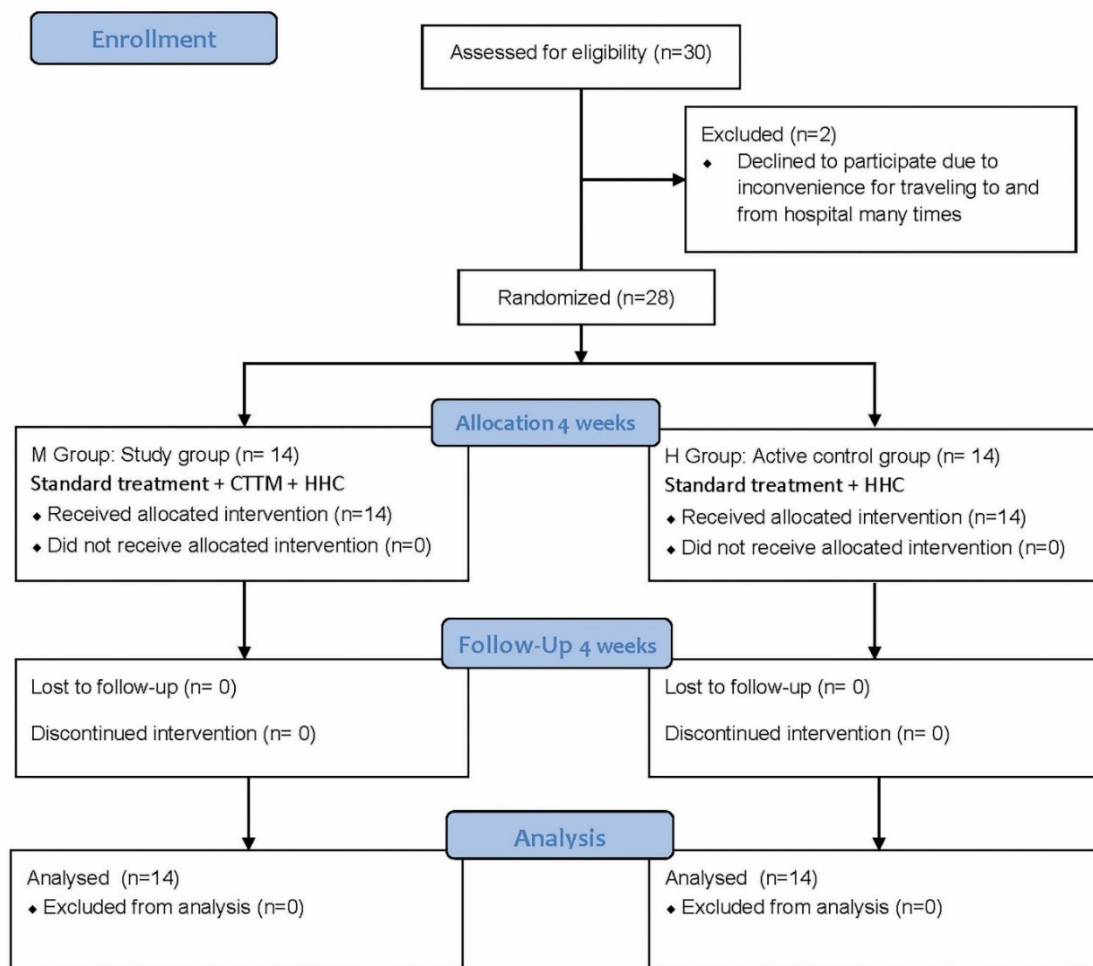
The inclusion criteria for this study required patients to be over 18 years of age and diagnosed with peripheral neuropathic pain by the grading system for neuropathic pain diagnosis.<sup>11</sup> Additionally, patients were required to present with Neuropathic Pain Questionnaire 4 (DN4)<sup>12</sup> scores  $\geq 4$  and numerical rating scale (NRS) pain scores  $\geq 4$  at recruitment. Before study participation, patients' treatment progress during the preceding 3 months had to be stable, and they needed to be able to visit Siriraj Hospital at least twice a week. Exclusion criteria encompassed patients with surgery planned within 3 months, a history of uncontrollable psychiatric disorders, open wounds in the painful area, addiction to alcohol or drugs, pregnancy, or any contraindications specified in this study, such as a fever exceeding 38.5 °C or skin disease on the affected area. The research and participant assignments were conducted at the Ayurved Applied Thai Traditional Medicine Clinic.

The criteria for the withdrawal of participants from the study were 1) voluntary withdrawal at any time due to inability to comply with study requirements or other reasons (e.g., experiencing side effects), 2) physician-advised withdrawal for a patient's health or well-being, and 3) loss to follow-up.

### Interventions

The intervention ("M") group received standard neuropathic pain treatment and twice-weekly adjuvant treatment with CTTM and hot herbal compression (HHC) for 4 weeks. The active control ("H") group received standard treatment and twice-weekly HHC for 4 weeks. The treatment phase spanned the first to the eighth visits (V1-V8). A follow-up was conducted at the ninth visit (V9), held 4 weeks after the conclusion of treatment. A consort diagram of the study is depicted in Fig 1. Four applied traditional Thai massage (ATTM) practitioners with over 5 years of experience administering the interventions. The pressure the ATTMs could exert with their hands was determined to ensure that there would be consistent pressure levels across treatments. Each participant group was assigned 2 ATTM practitioners, who alternately treated the patients in their assigned groups throughout the study.

**The CTTM treatments** were categorized into 2 distinct massage patterns targeting the upper and lower extremity areas, corresponding to the patients' s pain locations. The first pattern focused on the upper extremity region, encompassing the upper back and upper limbs. The second pattern addressed the lower extremity region (the lower back and lower limbs). The duration of the



**Fig 1.** CONSORT diagram of the study

Participants were randomly divided into 2 groups by the randomization method. (1) Study group (M group): received treatment according to the standard neuropathic pain protocol plus adjuvant treatment (court-type Thai traditional massage [CTTM] and hot herbal compress [HHC] twice a week for 4 weeks). (2) Active control group (H group): treated according to the standard neuropathic pain protocol and HHC twice a week for 4 weeks. Allocation was a treatment phase of twice weekly (V1-V8); follow-up occurred after a 4-week rest period at the end of treatment (V9).

massage treatment was about 45 minutes. Both groups received HHC following the same patterns for about 15 minutes. Fig 2 illustrates the massage lines and points utilized in each pattern.

**The compression balls** utilized in the HHC were specially produced by the Ayurved Siriraj Manufacturing Unit of Herbal Medicine and Products, adhering to good manufacturing practice guidelines. The primary ingredients of the dry balls were *Zingiber montanum* (Koenig) Link ex Dietr., *Curcuma longa* Linn., *Curcuma zedoaria* (Berg) Roscoe., *Cymbopogon citratus* (De ex Nees) Stapf., and borneol, along with other components, amounting to a total of 150 grams per piece. Before application on patients, the balls were heated to a temperature of 43 to 45 °C.

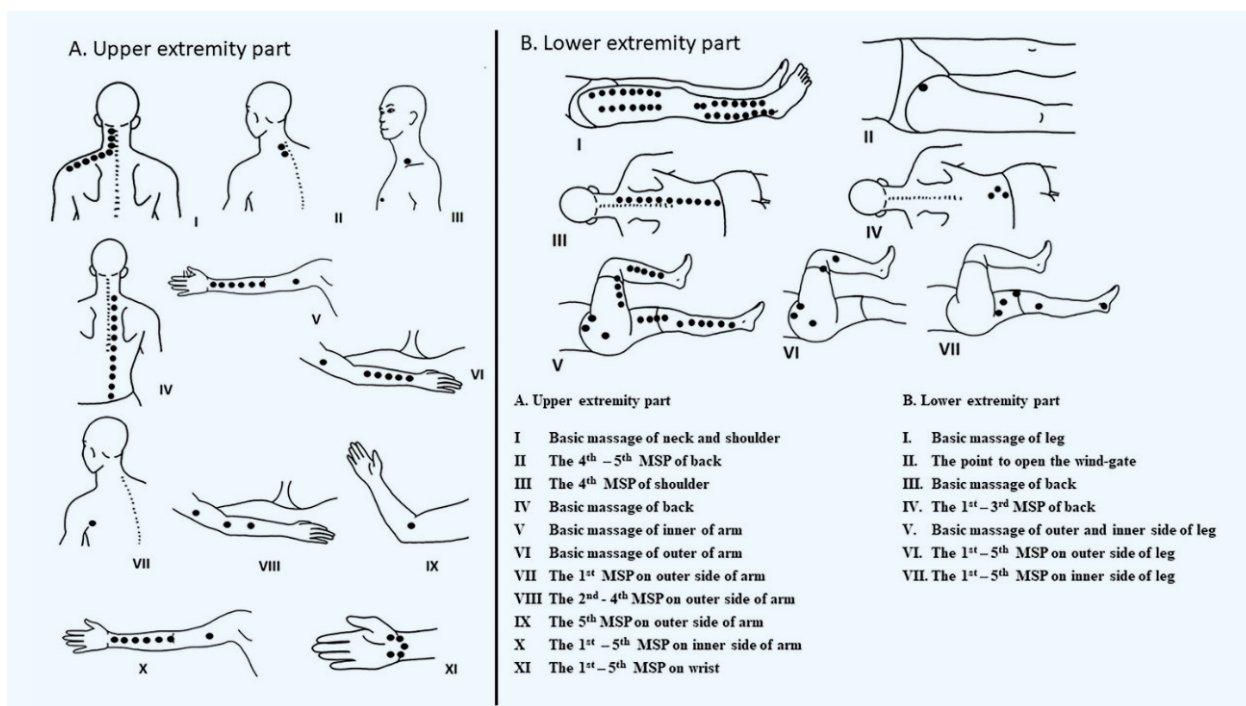
### Measured outcomes

The primary outcome was pain intensity reduction. It was assessed with numerical rating scales (NRS)<sup>13,14</sup>

and the Thai versions of the Neuropathic Pain Symptom Inventory (NPSI-T).<sup>15</sup> Pain severity was measured 4 times (at V1, V4, V8, and V9) as an average in the past 24 hours. The NRS of pain severity was also assessed before and after each treatment session. The secondary outcomes were pain-related interferences and the patients's quality of life. This was self-assessed with the Brief Pain Inventory (BPI-T) and EQ-5D-5L at V1, V4, V8, and V9.

NRS is the 11-point scale asking participants to select a number from 0 to 10 that best represents their pain intensity, with 0 meaning "no pain at all" and 10 meaning "pain as bad as it could be." The participant's NRS score is the number they select.

The NPSI-T is a self-assessment tool with 12 items (Q1-Q12). Total intensity pain scores range from 0 to 100 and are the sum of the scores for each item other than Q4 and Q7. Subgroups of NPSI are divided into 5 clinical domains and calculated following questions: superficial spontaneous pain (Q1), deep spontaneous



**Fig 2.** The basic court-type Thai traditional massage line and point and the major signal point of massage in the M group

pain  $([Q2+Q3]/2)$ , paroxysmal pain  $([Q5+Q6]/2)$ , evoked pain  $([Q8+Q9+Q10]/3)$ , and paresthesia/dysesthesia  $([Q11+Q12]/2)$ . The study demonstrated the validity and reliability of the NPSI-T for assessing neuropathic pain in Thai patients.<sup>14</sup>

The *BPI-T* is a self-report measure used to rapidly assess the severity of pain and its impact on functioning. It is a reliable and valid instrument for assessing chronic pain.<sup>16,17</sup> The *BPI-T* has 9 items to evaluate the severity of pain and the effect of this pain on daily functioning. By using a 0 to 10 scale, our patients were asked to rate 1) their worst, least, average, and current pain intensity, 2) the perceived effectiveness of their current treatments, 3) the degree to which pain interferes with general activities, mood, walking ability, normal work, relationships with people, sleep, and enjoyment of life.

The *EQ-5D-5L* is a quality-of-life assessment tool recommended by the EuroQol Group as the preferred method for evaluating utility. For Thailand, these coefficients were studied by interviewing sample comprising 1,207 people and health-related quality of life measurement property testing and its preference-based score in the Thai population.<sup>18</sup> In a comparison of the Thai *EQ-5D-5L* and *EQ-5D-3L* value sets, the *EQ-5D-5L* scored higher.<sup>19</sup> The first part of the *EQ-5D-5L* assessment encompasses 5 health dimensions: mobility, self-care, usual activities, pain, and anxiety. Each dimension features 5 severity levels, ranging from “no problem” to “extreme problem.” The second part consists of directly evaluating health

status via the Visual Analog Scale (*EQ-VAS*), with scores from 0 to 100 (0 representing the worst health state and 100 representing the best health state). The utility score is based on the responses in the first section, using a country-specific utility score table that reflects the person’s preference regarding their health. The score ranges from 0 to 1, with 0 meaning death and 1 meaning perfect health.<sup>18</sup>

**Sample size and randomization**

*Sample size calculation:* The establishment of the sample size for testing two independent means was based on an n4Studie calculation and derived from a pilot study with a sample size of 10. The size for each group was determined to be 25. An adjustment was then made for interim analysis (N per group = 25 \* 1.11 = 27.75), with the resulting sample size rounded to 28.

*Randomization:* The patients were assigned into 2 groups by a computer-generated program that utilized the block-of-4 randomization method. The sealed envelope method was also employed to maintain anonymity by using assigned numbers.

*Blinding:* A separate ATTM, who was not involved in the treatments and was blinded to the patient groups, conducted treatment evaluations. The practitioner inquired about the participants’ pre- and post-treatment pain levels and checked their vital signs. The ATTM also assessed the patients with the NPSI-T, the *BPI-T*, and the *EQ-5D-5L* health questionnaire at V1, V4, V8, and V9.

## Statistical analyses

Analyses were conducted using IBM SPSS Statistics for Windows, version 22 (IBM Corp, Armonk, NY, USA), with a two-sided  $P$  value of  $\leq .05$  considered statistically significant. Continuous data are reported as the means  $\pm$  standard deviations, while categorical data are presented as percentages (%). Normality analysis was performed using the Shapiro-Wilk test. Comparisons were made with repeated measures ANOVA to compare means within and between groups for NRS, NPSI-T, BPI-T, and EQ-5D-5L. The unpaired t-test was employed to calculate the differences in the mean values at V1 and V8.

## RESULTS

### Study participants

This study involved 28 patients diagnosed with peripheral nerve injury, peripheral nerve compression or radiculopathy with peripheral neuropathic pain. The characteristics of the participants in the M and H groups are presented in Table 1. The 2 groups had no significant differences in their demographic profiles or neuropathic pain baselines (DN4, initial average NRS, level of pain severity, pain duration, and area of pain). Most with the participants were diagnosed of lumbosacral radiculopathy. During eight weeks of the study, all participants were continued the same prescribed gabapentinoids, weak opioids, psychological and physical therapy as prior the study individually.

### Treatment outcomes

#### NRS assessments of pain

Both groups showed a statistically significant decrease in pain severity between before and after each treatment session (Fig 3A). The average NRS pain scores showed significant differences between both groups and within the M group but not the H group, according to repeated measures ANOVA at V1, V4, V8, and V9; which were  $6.3 \pm 1.8$ ,  $3.8 \pm 1.7$ ,  $3.6 \pm 1.8$  and  $4.1 \pm 2.1$  in M group ( $P < 0.001$ ) and  $5.4 \pm 1.6$ ,  $4.5 \pm 1.4$ ,  $5.2 \pm 1.8$  and  $4.2 \pm 2.3$  in H group ( $P = 0.067$ ), respectively (Table 2 and Fig 3B). There was a significant decrease in the M group's average NRS pain scores when comparing V4, V8, and V9 to V1 (Fig 3C). The M group also exhibited a clinically significant decline in pain severity from V1 to V8.

#### Thai version of EQ-5D-5L

The EQ-VAS of EQ-5D-5L displayed no statistically significant difference between groups (Fig 3D). In contrast, the utility score revealed a statistically significant difference between both groups ( $P = 0.007$ ) and within the M group ( $P = 0.004$ ; Table 2 and Fig 3E).

#### BPI-T assessments of pain

The mean BPI-T pain severity scores were compared between groups. The M group exhibited lower pain levels than the H group in the worst and average pain assessments, with statistically significant differences (Table 2, Fig 4A, and Fig 4C). Furthermore, the M group demonstrated differences in average pain levels within the group when comparing V4 and V8 with V1, as well as differences in worst pain levels within the group when comparing V4 with V1. Pain interference in all aspects of the BPI-T showed no difference when comparing between and within groups (Table 2 and Fig 4D - 4J).

#### NPSI-T assessments of pain

NPSI-T is an appropriate tool for assessing neuropathic pain.<sup>15,20</sup> Our study results revealed a significant difference in NPSI-T score reductions between groups and in the M group's total intensity score from V1 to V8. The total intensity pain scores between groups (Fig 4K) demonstrated statistically significant differences ( $P = 0.001$ ). The intensity pain scores of the M group also decreased significantly ( $P = 0.005$ ). Subscores of NPSI-T for all 5 types of pain showed no differences within a group (Table 2 and Fig 4L - 4P).

## DISCUSSION

Although all 28 patients had chronic intractable with peripheral neuropathic pain, and were diagnosed peripheral nerve injury, peripheral nerve compression or radiculopathy with peripheral neuropathic pain. CTTM was found to significantly relieve pain for patients in the M group compared to those in the H group. The results also indicated the difference in the degree of reduction in pain severity levels. The total NPSI-T and utility scores of EQ-5D-5L demonstrated a statistically significant decrease in pain and increased quality of life at V8 in the M group.

This study's clinical outcomes were based on subjective assessments covering pain severity, quality of life, and pain interference. Although the VAS, NRS, and BPI-PS are widely used, no evidence unequivocally demonstrates their superiority in measuring pain.<sup>21</sup> This study utilized NRS to assess pain severity and pain relief. Previous researches support this approach.<sup>11,13</sup>

#### Evidence of the efficacy of CTTM

A previous study showed a median pain score reduction of 4.5 VAS units using aromatherapy massage for neuropathic pain in diabetic patients.<sup>22</sup> Another study found that neuropathic pain decreased 2 to 4 weeks after using lavender oil in aromatherapy massage without

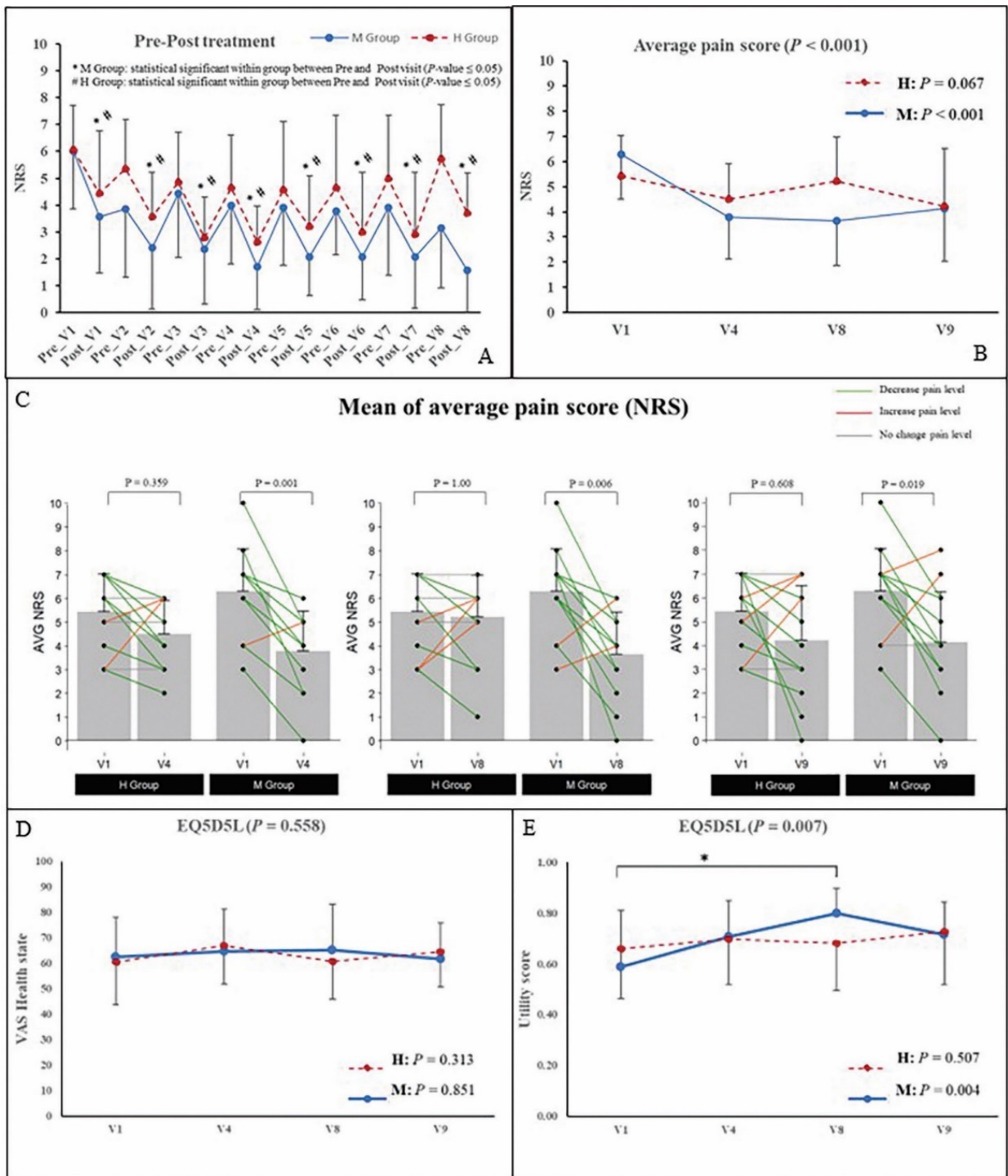
**TABLE 1.** Comparison of demographic data of the participants.

Variable	M group (N = 14)	H group (N = 14)	P
Sex <sup>a</sup> Male	7 (50%)	4 (29%)	0.440
BMI group <sup>a</sup>			
Underweight	0	1 (7%)	0.119
Normal weight	5 (36%)	5 (36%)	
Pre-obesity	3 (21%)	6 (43%)	
Obesity class I	1 (7%)	2 (14%)	
Obesity class II	5 (36%)	0	
Age <sup>b</sup> (years)	58.9 ± 13.8	60.4 ± 15.7	0.781
Age group <sup>a</sup>			
30–60	8 (57%)	6 (43%)	0.450
> 60	6 (43%)	8 (57%)	
Underlying disease			
Diabetes mellitus	1	3	N/A
Hyperlipidemia/heart	4	2	
Gout	0	2	
Thyroid	1	1	
Hypertension	7	6	
DN4 <sup>b</sup>	5.4 ± 1.1	5.1 ± 1.1	0.489
DN4	5 (4,8)	5 (4,7)	N/A
Initial NRS (average pain) <sup>b</sup>	6.3 ± 1.8	5.4 ± 1.6	0.191
Initial pain severity <sup>a</sup>			
Mild (1-3)	1 (7%)	3 (21%)	0.513
Moderate (4-6)	6 (43%)	6 (43%)	
Severe (7-10)	7 (50%)	5 (36%)	
Pain duration <sup>a</sup> (years)			
< 1	2 (14%)	2 (14%)	0.104
1–3	1 (7%)	6 (43%)	
> 3–10	9 (64%)	6 (43%)	
> 10	2 (14%)	0 (0%)	
Area of pain <sup>a</sup>			
Upper extremity	2 (14%)	2 (14%)	0.555
Lower extremity	3 (21%)	5 (36%)	
Lower extremity & lower back	9 (64%)	7 (50%)	
Diagnosis			
Peripheral nerve injury	2 (14%)	1 (7%)	N/A
Peripheral nerve compression	1 (7%)	2 (14%)	
Radiculopathy			
Cervical level	0	2 (14%)	N/A
Lumbosacral level	11 (79%)	9 (64%)	
Drug			
Antidepressants	7	3	N/A
Sodium-channel blockers	2	2	
Gabapentinoids	14	14	
Weak opioids	9	10	
Strong opioids	2	1	
Topical agents (Capsaicin, analgesic)	0	3	

Data are presented as number (%), mean ± SD, or median (min, max)

<sup>a</sup>P values between groups were calculated by the chi-squared test.

<sup>b</sup>P values between groups were calculated by unpaired t-test.



**Fig 3A.** Comparison of the NRS pain scores before and after treatment sessions within groups by paired t-test for sessions V1 through V8.

\* Statistical significance within the M group, comparing before and after each treatment session ( $P < 0.05$ ).

# Statistical significance within the H group, comparing before and after each treatment session ( $P < 0.05$ ).

**Fig 3B.** Average NRS pain score over 24 hours

**Fig 3C.** Average NRS pain score over 24 hours, comparing V4, V8, and V9 with V1 between and within groups by mixed bar chart and line chart, to show the trends for each time and patient group.

**Fig 3D.** Comparison of the mean differences within groups and between groups at V1, V4, V8, and V9 of VAS health state of EQ 5D 5L

**Fig 3E.** Comparison of the mean differences within groups and between groups at V1, V4, V8, and V9 of utility score of EQ 5D 5L.

\* $P < 0.05$  indicates statistical significance within the M group.

**TABLE 2.** Comparison within groups and between groups at V1, V4, V8, and V9.

Parameters	GR	Mean ± SD				P <sup>a</sup>		Diff V1-V8	95% CI		P <sup>b</sup>
		V1	V4	V8	V9	Within Group	Between Group		Lower	Upper	
NRS	M	6.29 ± 1.77	3.79 ± 1.67	3.64 ± 1.78	4.14 ± 2.11	<b>&lt; 0.001</b>	<b>&lt; 0.001</b>	2.64*	0.70	4.59	<b>0.003</b>
	H	5.43 ± 1.60	4.50 ± 1.40	5.21 ± 1.76	4.21 ± 2.29	0.067		0.21	-1.10	1.52	
NPSI-T Total	M	25.21 ± 15.41	17.14 ± 14.87	15.07 ± 9.97	17.64 ± 7.78	<b>0.005</b>	<b>0.001</b>	10.14*	1.12	19.16	0.403
	H	28.57 ± 15.02	19.43 ± 11.92	21.64 ± 11.63	13.49 ± 13.49	0.081		6.93	-0.60	14.46	
NPSI-T Superficial	M	1.50 ± 2.68	0.79 ± 2.01	0.79 ± 2.08	0.64 ± 1.74	0.294	0.184	0.71	-0.86	2.29	0.819
	H	2.71 ± 2.89	1.71 ± 2.76	1.79 ± 2.72	1.79 ± 3.12	0.563		0.93	-1.47	3.33	
NPSI-T Deep	M	3.32 ± 2.01	2.32 ± 2.36	1.93 ± 2.29	2.68 ± 1.68	0.135	<b>0.029</b>	1.39	-0.32	3.11	0.838
	H	4.43 ± 3.00	2.71 ± 2.64	3.21 ± 1.31	3.18 ± 2.64	0.189		1.21	-0.84	3.27	
NPSI-T Paroxysmal	M	2.54 ± 2.72	1.57 ± 2.50	1.43 ± 1.65	1.50 ± 1.65	0.158	<b>0.033</b>	1.11	-0.66	2.87	0.791
	H	2.57 ± 2.27	1.46 ± 2.60	1.25 ± 1.77	2.32 ± 2.87	0.179		1.32	-0.44	3.08	
NPSI-T Evoked	M	2.17 ± 2.34	1.43 ± 1.92	1.67 ± 2.09	1.74 ± 2.12	0.335	0.080	0.50	-1.15	2.15	0.389
	H	2.33 ± 2.24	1.90 ± 1.60	2.36 ± 1.79	1.00 ± 1.23	0.099		-0.02	-0.87	0.83	
NPSI-T Paresthesia	M	2.75 ± 2.29	2.14 ± 2.53	1.29 ± 1.22	1.71 ± 1.82	0.189	0.197	1.46	-0.05	2.98	0.293
	H	2.43 ± 2.91	1.82 ± 2.22	1.93 ± 1.63	1.89 ± 2.78	0.803		0.50	-1.84	2.84	
EQ 5D 5L Utility score	M	0.587 ± 0.224	0.709 ± 0.142	0.798 ± 0.100	0.716 ± 0.128	<b>0.004</b>	<b>0.007</b>	-0.211*	-0.411	-0.011	<b>0.027</b>
	H	0.660 ± 0.196	0.699 ± 0.179	0.682 ± 0.187	0.728 ± 0.208	0.507		-0.022	-0.173	0.130	
EQ 5D 5L VAS health state	M	62.43 ± 15.75	64.64 ± 16.58	65.36 ± 17.92	61.79 ± 14.22	0.851	0.558	-2.93	-16.24	10.38	0.635
	H	60.43 ± 16.65	67.14 ± 15.41	60.71 ± 14.91	64.64 ± 13.79	0.313		-0.29	-10.97	10.40	
BPI-T worst	M	7.50 ± 1.61	5.36 ± 2.450	5.93 ± 2.09	6.36 ± 1.50	<b>0.018</b>	<b>0.004</b>	1.57	-0.08	3.22	0.356
	H	7.07 ± 1.77	6.14 ± 1.29	6.29 ± 1.82	5.64 ± 2.79	0.123		0.79	-0.87	2.44	
BPI-T least	M	3.14 ± 0.52	3.00 ± 0.54	2.79 ± 0.48	2.57 ± 0.47	0.669	0.219	0.36	-1.30	2.01	0.730
	H	3.93 ± 0.52	3.00 ± 0.50	3.86 ± 0.53	2.93 ± 0.74	0.162		0.07	-1.58	1.73	

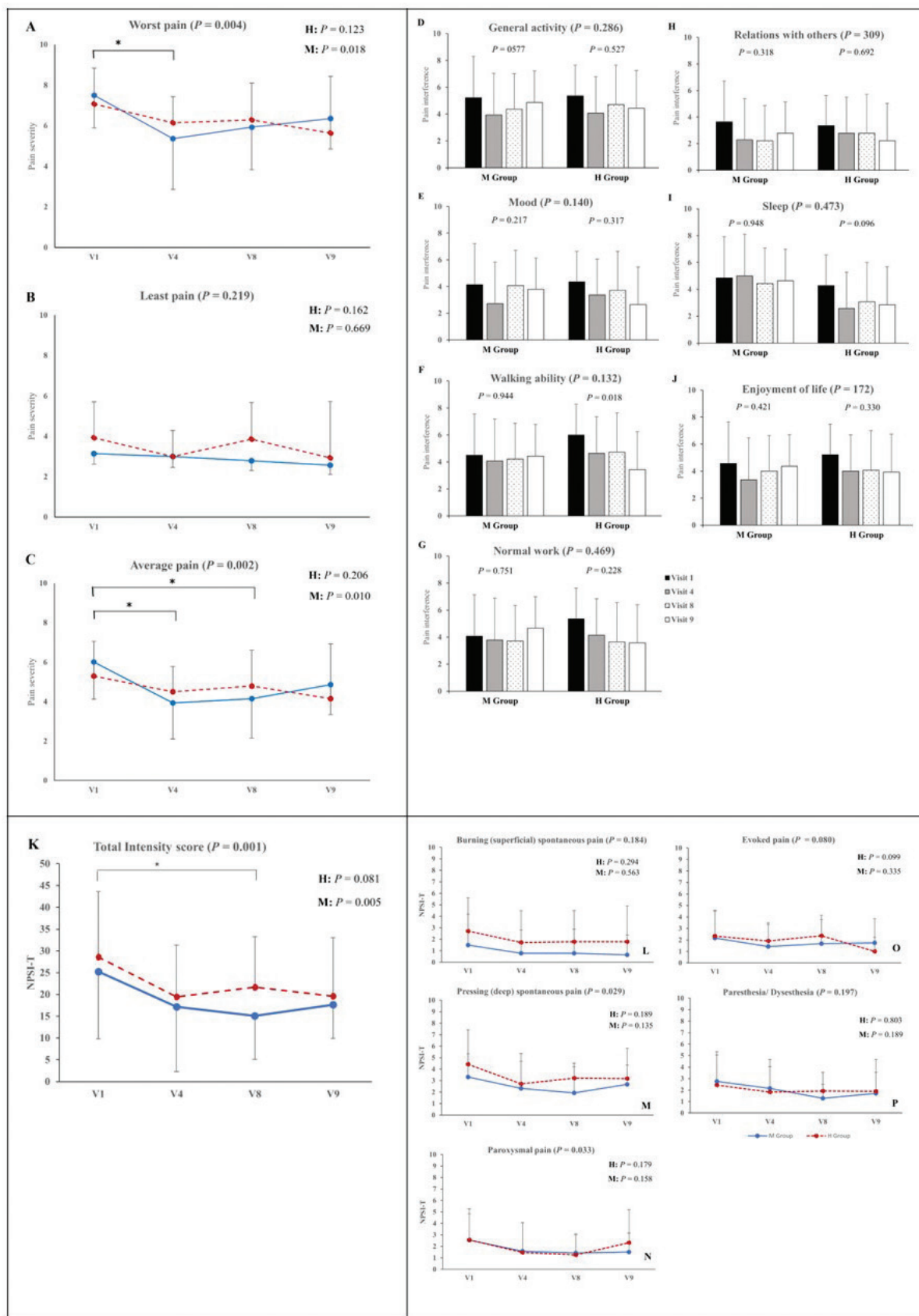


**TABLE 2.** Comparison within groups and between groups at V1, V4, V8, and V9. (Continue)

Parameters	GR	Mean ± SD				<i>P</i> <sup>a</sup>		Diff V1-V8	95% CI		<i>P</i> <sup>b</sup>
		V1	V4	V8	V9	Within Group	Between Group		Lower	Upper	
BPI-T average	M	6.00 ± 1.88	3.93 ± 1.82	4.14 ± 1.99	4.86 ± 1.51	<b>0.010</b>	<b>0.002</b>	1.86*	0.117	3.60	0.127
	H	5.29 ± 1.68	4.50 ± 1.40	4.79 ± 1.76	4.14 ± 2.28	0.206		0.50	-1.24	2.24	
BPI-T activity	M	5.21 ± 3.07	3.93 ± 3.10	4.36 ± 2.65	4.86 ± 2.35	0.577	0.286	0.86	-1.95	3.66	0.879
	H	5.36 ± 2.27	4.07 ± 2.70	4.71 ± 2.92	4.43 ± 2.82	0.527		0.64	-2.16	3.45	
BPI-T mood	M	4.14 ± 2.68	2.71 ± 3.00	4.07 ± 3.05	3.79 ± 3.12	0.217	0.140	0.07	-2.34	2.48	0.637
	H	4.36 ± 2.68	3.36 ± 3.08	3.71 ± 2.87	2.64 ± 3.50	0.317		0.64	-1.77	3.06	
BPI-T walking	M	4.50 ± 3.25	4.07 ± 3.63	4.21 ± 3.53	4.43 ± 2.47	0.944	0.132	0.29	-2.02	2.59	0.390
	H	6.00 ± 2.00	4.64 ± 2.95	4.71 ± 2.92	3.43 ± 3.67	0.018		1.29	-1.02	3.59	
BPI-T normal work	M	4.07 ± 2.97	3.79 ± 3.58	3.71 ± 3.41	4.64 ± 2.73	0.751	0.469	0.36	-2.19	2.91	0.292
	H	5.36 ± 2.37	4.14 ± 3.42	3.64 ± 2.41	3.57 ± 3.03	0.228		1.71	-0.83	4.26	
BPI-T relations	M	3.64 ± 3.79	2.29 ± 2.79	2.21 ± 2.42	2.79 ± 3.07	0.318	0.309	1.43	-1.19	4.05	0.515
	H	3.36 ± 2.92	2.79 ± 2.97	2.79 ± 2.61	2.21 ± 3.07	0.692		0.57	-2.05	3.19	
BPI-T sleep	M	4.86 ± 3.63	5.00 ± 3.19	4.43 ± 2.85	4.64 ± 3.63	0.948	0.473	0.43	-2.04	2.90	0.526
	H	4.29 ± 2.76	2.57 ± 2.74	3.07 ± 2.56	2.86 ± 3.28	0.096		1.21	-1.25	3.68	
BPI-T enjoyment	M	4.57 ± 2.98	3.36 ± 2.87	4.00 ± 2.80	4.36 ± 2.71	0.421	0.172	0.57	-1.69	2.84	0.615
	H	2.46 ± 2.99	4.00 ± 2.56	4.07 ± 3.02	3.93 ± 2.98	0.330		1.14	-1.12	3.41	

<sup>a</sup>Repeated measures ANOVA and adjustment for multiple comparisons (using the Bonferroni method) were used to calculate the *P* values within and between groups. \* Significant *P* values within groups ≤ 0.05 (compared between V8 and V1).

<sup>b</sup>Unpaired t-test was used to calculate *P* values between groups, with means of difference between V1 and V8.



**Fig 4A-4C.** Pain severity (during the preceding 24 hours), assessed by BPI-T, at V1, V4, V8, and V9.

**Fig 4D-4J.** Pain interference (during the preceding 24 hours), assessed by BPI-T, at V1, V4, V8, and V9.

**Fig 4K.** Total intensity scores of the NPSI-T at V1, V4, V8, and V9

**Fig 4L-4P.** Subscores of the NPSI-T at V1, V4, V8, and V9

*P* values calculated within groups and between groups by repeated measures ANOVA and adjustment for multiple comparisons (using the Bonferroni method).

\* $P < 0.05$  indicates statistical significance within the M group.

side effects.<sup>23</sup> In addition, acupuncture may alleviate neuropathic pain from spinal cord injuries. Acupuncture treatment significantly improved present pain, general pain, pain unpleasantness, and coping compared to baseline values in one study.<sup>24</sup> While evidence for CTTM in neuropathic pain treatment is limited, a systematic review of 13 randomized control trials demonstrated acupuncture's effectiveness in diabetic neuropathy, Bell's palsy, and carpal tunnel syndrome.<sup>25</sup> Some studies also showed that acupuncture and another massage therapy effectively treated neuropathic pain after spinal cord injuries.<sup>26</sup>

CTTM, a deep-pressure massage, lacks previous evidence for neuropathic pain treatment. However, the M group in our investigation experienced continuous reductions and statistically significant decreases in average pain scores for the first two weeks (V4) and apparently sustained to four weeks (V8) in the treatment period. However, the pain score in V9, slightly increased from V8 in the M group, reflecting that CTTM might have only a short-term effect on pain reduction. The massage, therefore, may be considered an adjunctive treatment in refractory peripheral neuropathic pain.

### Potential mechanisms of CTTM for pain relief

Animal model studies have outlined various peripheral and central pathophysiological processes after nerve injury, indicating the basis for neuropathic pain mechanisms. Neural plasticity, involving changes in neuronal function, chemistry, and structure, produces the altered sensitivity characteristics of neuropathic pain.<sup>27,28</sup> Animal studies have demonstrated multiple neuropathic pain mechanisms. Still, these mechanisms may not apply to humans when describing massage effects because pain correlated with patterns and impacts on quality of life are also affected by the biological, emotional, and social perspectives.

CTTM has been found to relieve pain in tension headaches<sup>7</sup> and muscle pain of the neck, shoulder and back<sup>29,30</sup>, decrease spasticity, increase functional ability, and improve the quality of life of elderly stroke patients.<sup>5</sup> Deep massage can stretch muscles, helping to break down subcutaneous adhesions and prevent fibrosis<sup>31</sup>, potentially leading to improved sensory feedback from muscle spindle receptors. Furthermore, the repetitive cutaneous stimulation provided by massage may reduce pain through the gate control theory.<sup>32</sup> Massage manipulation has been shown to result in similar patterns of change in skin temperature and blood flow in the upper and lower extremities.<sup>33,34</sup> CTTM stimulates blood and lymphatic circulation and the sympathetic nervous system by exerting

pressure on the skin and muscles. Consequently, the flow of nutrients to tissues is enhanced, and the excretion of toxins and residual substances within the body improves.<sup>4</sup> Another possible explanation for the pain reduction induced by CTTM involves gate control theory. Under this theory, CTTM stimulates pressure receptors by exerting pressure on the skin and muscles, inhibiting the transmission of pain receptors at the spinal cord or the "gate".<sup>35-37</sup> However, the mechanism of CTTM for relieving peripheral neuropathic pain is still not fully elucidated. Limitations of this study include the relatively small sample size and the considerable variation in participant types and settings.

### CONCLUSION

No prior published review of evidence or protocols on the efficacy and safety of CTTM for treating neuropathic pain exists. This study could serve as a preliminary investigation into the effectiveness of CTTM for adjuvant treatment in relieving pain and improving the quality of life for patients with peripheral neuropathic pain. Future studies should explore the frequency of treatment per month and the use of CTTM to treat specific types of peripheral neuropathic pain.

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### Conflicts of interest

All the authors declare they have no personal or professional conflicts of interest relating to any aspect of this study.

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