

Efficacy and Safety of Heat-Sensitive Moxibustion Combined with Herbal Fumigation for Oxaliplatin-Induced Peripheral Neuropathy: A Single-Center Randomized Controlled Trial

Wen Xu

janiceman0403@163.com

Nanjing University of Chinese Medicine

Xian Zhou

Nanjing University of Chinese Medicine

Yu Zeng

Nanjing Hospital of Traditional Chinese Medicine

Sixuan Han

Nanjing Hospital of Traditional Chinese Medicine

Yanyan Hong

Nanjing Hospital of Traditional Chinese Medicine

Research Article

Keywords: heat-sensitive moxibustion, herbal fumigation and washing, colorectal cancer, oxaliplatin, oxaliplatin-induced peripheral neuropathy, OIPN

Posted Date: September 30th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10625063/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

This study evaluated the clinical efficacy and safety of combining heat-sensitive moxibustion (HSM) with herbal fumigation and washing (HFW) for patients with colorectal cancer (CRC) suffering from oxaliplatin-induced peripheral neuropathy (OIPN), specifically those presenting with the traditional Chinese medicine (TCM) syndrome of *qi* stagnation and blood stasis.

Methods

This single-center randomized controlled trial enrolled 70 patients with CRC complicated by OIPN and *qi* stagnation and blood stasis syndrome who were treated at Nanjing Hospital of Traditional Chinese Medicine from January 9 to June 2026. Participants were randomized 1:1 to a control group or an intervention group, with 35 patients in each group. All participants received standard chemotherapy and routine nursing care. The control group underwent adjunctive HFW, while the intervention group received concurrent HSM in addition to the same HFW. The intervention lasted for two consecutive chemotherapy cycles. The primary outcome was the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Chemotherapy-Induced Peripheral Neuropathy 20 (EORTC QLQ-CIPN20) score. Secondary outcomes included peripheral neuropathy grade according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI-CTCAE v5.0), Numerical Rating Scale (NRS) score, TCM syndrome score, and nerve conduction velocity (NCV). The study protocol was approved by the Ethics Committee of Nanjing Hospital of Traditional Chinese Medicine on January 8, 2026 (approval No. 2026KY006-01), before enrollment of the first participant on January 9, 2026. The trial was retrospectively registered with the International Traditional Medicine Clinical Trial Registry (ITMCTR; registration No. ITMCTR2026001917) on May 22, 2026.

Results

A total of 67 patients were included in the per-protocol analysis, comprising 34 patients in the control group and 33 patients in the intervention group. The estimated cumulative oxaliplatin exposure before enrollment did not differ significantly between groups ($p = 0.981$). After treatment and at 4 weeks after completion of the intervention, the EORTC QLQ-CIPN20 scores were lower in the intervention group than in the control group, with between-group differences of -2.39 points (95% CI: -3.60 to -1.19; $p < 0.001$) and -3.03 points (95% CI: -4.33 to -1.74; $p < 0.001$), respectively. NCI-CTCAE v5.0 neuropathy grade was also less severe in the intervention group at both time points ($p = 0.006$ and $p = 0.028$). After treatment, the TCM syndrome score was lower in the intervention group than in the control group ($p < 0.001$), and motor nerve conduction velocities of the median nerve and common peroneal nerve were higher ($p = 0.016$ and $p = 0.006$). No statistically significant between-group differences were observed in sensory nerve conduction velocities or NRS scores. No serious adverse events occurred in either group.

Conclusion

The adjunctive application of HSM to HFW effectively reduced the short-term overall symptom burden of OIPN and mitigated the severity of peripheral neuropathy in CRC patients with *qi* stagnation and blood stasis syndrome, with no serious adverse events observed. The short-term benefits of this multimodal approach primarily translated into a reduction in neurological symptom burden and functional limitations, rather than providing direct analgesia. This accessible regimen holds promise as an adjunctive, non-pharmacological supportive care strategy in oncology, though larger multicenter trials are warranted to establish its long-term efficacy and clinical significance.

1 Introduction

Colorectal cancer (CRC) is one of the leading gastrointestinal malignancies worldwide in terms of both incidence and mortality (1). Oxaliplatin-containing combination chemotherapy is an important component of postoperative adjuvant therapy and systemic treatment for advanced CRC. It is commonly used in fluoropyrimidine-plus-oxaliplatin regimens and may improve disease-free survival and long-term prognosis in some patients (2). However, while exerting antitumor effects, oxaliplatin may also induce dose-limiting oxaliplatin-induced peripheral neuropathy (OIPN), an important subtype of chemotherapy-induced peripheral neuropathy (CIPN). OIPN is mainly characterized by glove-and-stockings numbness, tingling, hypoesthesia, cold sensitivity, and impaired fine motor function of the extremities. Severe symptoms may affect chemotherapy adherence and quality of life (3). Some patients require chemotherapy dose modification or treatment delay or experience reduced self-care capacity because of persistent numbness, hypoesthesia, and cold-triggered dysesthesia. Non-painful neurological symptoms, in particular, are often insufficiently relieved by analgesic strategies alone.

The pathogenesis of OIPN is multifactorial, involving dorsal root ganglion injury, axonal degeneration, mitochondrial dysfunction, ion-channel abnormalities, and neuroimmune responses (4–6). Consequently, conventional pharmacological interventions remain limited. Commonly used neuromodulatory and symptom-control drugs show interindividual variability in effectiveness, and evidence for pharmacological treatment of painful OIPN is concentrated mainly on duloxetine (7). Therefore, on the basis of standardized antitumor therapy and safety-oriented nursing care, exploration of safe and feasible non-pharmacological interventions has clear value in oncology supportive care.

In traditional Chinese medicine (TCM), chemotherapy-related peripheral neuropathy is generally classified under categories such as *bi* syndrome, blood *bi*, and numbness. Its core pathogenesis is considered to involve toxin-induced collateral damage, cold coagulation and blood stasis, impaired circulation of *qi* and blood, and insufficient nourishment of the extremities (8). Herbal fumigation and washing (HFW) acts on the hands, feet, and symptomatic distal extremities through warm herbal liquid and may warm the meridians, dispel cold, activate blood, unblock the collaterals, promote *qi* movement, and relieve pain. It has been applied in previous intervention studies for OIPN (9, 10).

Heat-sensitive moxibustion (HSM) identifies heat-sensitized responses at acupoints and provides targeted thermal stimulation, with the theoretical effects of warming and unblocking the meridians and harmonizing *qi* and blood (11, 12). Compared with ordinary mild moxibustion, HSM emphasizes heat-sensitive acupoints, propagation of moxibustion sensation, and individualized control of moxibustion dosage. These features may be suitable for peripheral nerve dysfunction characterized by distal numbness, cold pain, and abnormal sensation. Previous studies of HSM combined with finger rehabilitation exercises incorporated EORTC QLQ-CIPN20 and nerve conduction velocity as observation indicators, providing an evaluative pathway for TCM external therapy in CRC patients with OIPN (13). Randomized trials of electroacupuncture for prevention of CIPN have also used patient-reported outcomes and nerve conduction velocity as key outcomes (14).

On the basis of the local external-therapy characteristics of HFW - namely direct external action and warming of the collaterals - and the therapeutic advantages of HSM, including sensitivity-based point selection and activation of channel *qi*, this study used HFW as the base control and evaluated the clinical efficacy and safety of adding HSM in patients with CRC complicated by OIPN and *qi* stagnation and blood stasis syndrome. Given the core pathogenesis of impaired *qi* movement, stasis obstructing the collaterals, and malnourishment of the extremities, we hypothesized that the local warming and unblocking effects of HFW might provide a favorable microenvironment for HSM to activate channel *qi*, and that the combination might produce synergistic benefit. The study evaluated patient-reported outcomes, neuropathy grading, TCM syndrome score, nerve conduction function, oxaliplatin exposure, and safety, with the aim of providing a clinical reference for TCM external supportive therapy in OIPN.

2 Materials and methods

2.1 General information

This study was a single-center, randomized, controlled, parallel-group add-on clinical trial, prepared with reference to the Consolidated Standards of Reporting Trials (CONSORT) and reporting standards for non-pharmacological intervention trials (15, 16). A total of 70 patients with CRC who were receiving oxaliplatin-containing chemotherapy, had developed OIPN, and met the TCM diagnostic criteria for *qi* stagnation and blood stasis syndrome were enrolled at Nanjing Hospital of Traditional Chinese Medicine from January 9 to June 2026. Patients were randomized 1:1 using a random-number table to the control group or intervention group, with 35 patients in each group. During the study, one patient in the control group withdrew because of a mild adverse event. In the intervention group, one patient withdrew because of a mild adverse event, and one patient withdrew later because of personal factors and disease progression. Finally, 67 patients completed the protocol, including 34 in the control group and 33 in the intervention group.

Baseline data included age, sex, body mass index (BMI), tumor site, tumor-node-metastasis (TNM) stage, baseline chemotherapy regimen, chemotherapy cycles before enrollment, estimated cumulative oxaliplatin dose before enrollment, OIPN grade, Numerical Rating Scale (NRS) score, EORTC QLQ-CIPN20

score, and TCM syndrome score. Baseline chemotherapy regimens were categorized as CAPOX/XELOX, FOLFOX, or other oxaliplatin-containing regimens. Other oxaliplatin-containing regimens referred to regimens that were not classified as CAPOX/XELOX or FOLFOX but still contained oxaliplatin; in the original records, the oxaliplatin dose per cycle in this category was 150–200 mg. The estimated cumulative oxaliplatin dose before enrollment was calculated from the recorded oxaliplatin dose per cycle in the chemotherapy regimen and the number of completed chemotherapy cycles before enrollment, expressed in milligrams. This indicator was used to describe the baseline oxaliplatin exposure level in the two groups, whereas actual dose reduction, treatment delay, or discontinuation should still be verified against physicians' orders and administration records.

The sample size was estimated on the basis of patient-reported OIPN symptom burden. According to previous studies and psychometric validation of EORTC QLQ-CIPN20 (17), the expected between-group difference was approximately 5.0 points, with a standard deviation of approximately 6.0 points. With a two-sided alpha of 0.05 and 80% power ($\beta = 0.20$), approximately 25 patients were required in each group. Allowing for an approximately 20% dropout rate and considering stable estimation of the primary and key secondary outcomes, the final target sample size was set at 35 patients per group, for a total of 70 patients. Participant protection, informed consent, and ethical review were conducted in accordance with applicable Chinese regulations and the ethical principles of the Declaration of Helsinki. The study protocol (version 1.0, dated November 4, 2025) was approved by the Ethics Committee of Nanjing Hospital of Traditional Chinese Medicine on January 8, 2026 (approval No. 2026KY006-01). The first participant provided written informed consent and was enrolled on January 9, 2026. No participant was consented, randomized, or treated before ethical approval was granted, and all participants provided written informed consent before any study-specific intervention. The trial was retrospectively registered with the International Traditional Medicine Clinical Trial Registry (ITMCTR; registration No. ITMCTR2026001917) on May 22, 2026.

2.2 Randomization, allocation concealment, and blinding

The random sequence was generated by a random-number table and kept by an independent researcher who was not directly involved in recruitment, treatment implementation, or outcome assessment. Allocation results were placed in opaque sealed envelopes sequentially numbered according to enrollment order. After screening, informed consent, and baseline assessment were completed, the study coordinator opened the envelopes in sequence and assigned participants to groups. The envelopes remained sealed before opening, and allocation results were not disclosed to patients, treatment providers, or outcome assessors before completion of baseline assessment, thereby reducing selection bias.

Because HSM and HFW are procedural external therapies, complete blinding of participants and treatment providers was not feasible. Outcome assessors and statisticians remained blinded to group assignment until data locking and completion of analysis. Scale assessment, neuroelectrophysiological testing, and data entry followed standardized procedures. Personnel implementing non-pharmacological interventions received standardized training. The treatment process recorded actual treatment sessions,

treatment-course completion, reasons for interruption or discontinuation, and adverse events to evaluate intervention adherence and implementation consistency.

2.3 Diagnostic criteria

Western medical diagnosis was based on the Chinese Guidelines for Diagnosis and Treatment of Colorectal Cancer (2023 edition) and expert consensus on chemotherapy-induced peripheral neuropathy (1, 3). OIPN grading used the National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI-CTCAE v5.0) criteria for peripheral sensory neuropathy and peripheral motor neuropathy (18). When a participant had both sensory and motor neuropathy manifestations, the higher grade was recorded as the overall OIPN grade. TCM syndrome differentiation was based on the Guidelines for Clinical Research of New Chinese Medicines (trial edition) and technical specifications for TCM nursing (19, 20), and participants were diagnosed as having *qi* stagnation and blood stasis syndrome. Main manifestations included distal numbness, tingling, fixed pain, cold hands and feet, and heaviness of the limbs; the tongue was purple-dark or had petechiae or ecchymosis, and the pulse was wiry and choppy.

2.4 Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) age 18–80 years; (2) pathological or cytological diagnosis of CRC; (3) meeting the TCM diagnostic criteria for *qi* stagnation and blood stasis syndrome; (4) currently receiving an oxaliplatin-containing chemotherapy regimen and scheduled to continue chemotherapy for at least two cycles; (5) occurrence of OIPN with NCI-CTCAE v5.0 grade ≥ 1 ; (6) expected survival ≥ 3 months; (7) clear consciousness and ability to cooperate with scale assessment and neuroelectrophysiological examination; and (8) voluntary participation with signed informed consent.

The exclusion criteria were as follows: (1) peripheral neuropathy not caused by oxaliplatin; (2) comorbid diabetic peripheral neuropathy, autoimmune peripheral neuropathy, brain metastasis, spinal cord compression, or other diseases that could cause neurological dysfunction; (3) severe diseases of the heart, liver, kidney, hematopoietic system, or endocrine system; (4) skin injury, infection, severe scarring, or allergic dermatosis at the treatment site; (5) use within 2 weeks before treatment of mecobalamin, gabapentin, pregabalin, duloxetine, or other drugs that could affect neurological symptom assessment, or receipt of acupuncture, local physiotherapy, or other special therapies that could affect outcome determination; (6) pregnancy or lactation; (7) participation in another clinical study; and (8) poor adherence or inability to complete scale assessment, neuroelectrophysiological testing, or follow-up.

2.5 Discontinuation, elimination, and dropout criteria

Discontinuation criteria were as follows: (1) during the study, disease progression, poor tolerability, or clinical need required switching to a non-oxaliplatin regimen, termination of chemotherapy, or investigator judgment that the participant should not continue the original antitumor treatment; (2) a serious adverse event occurred during intervention and was assessed by the investigator as related to HFW or HSM, making continued participation inappropriate; or (3) OIPN symptoms worsened

substantially and required addition of specific treatments that could affect neurological symptom assessment, such as mecobalamin, thioctic acid, gabapentin, pregabalin, or duloxetine.

Elimination and dropout criteria were as follows: (1) intervention adherence < 80% (adherence = actual completed intervention sessions/planned intervention sessions x 100%); (2) failure to complete the primary outcome assessment as required, or missing follow-up data affecting efficacy judgment; (3) voluntary withdrawal because of personal preference, scheduling conflicts, or loss to follow-up; or (4) discovery after enrollment that inclusion or exclusion criteria were not met or that an important protocol violation had occurred.

2.6 Interventions

Both groups received standardized chemotherapy and routine oncology nursing care. Routine care included chemotherapy-related health education, warmth preservation of the extremities, avoidance of cold stimulation, fall-risk assessment, observation of pain and numbness symptoms, dietary guidance, psychological support, and nursing care for chemotherapy-related adverse reactions.

On the basis of routine care, the control group received HFW. The prescription was formulated according to the principles of warming the meridians, dispelling cold, activating blood, unblocking the collaterals, promoting *qi* movement, and relieving pain. It included *Lycopodium Herba*, raw *Artemisia argyi* leaves, *Impatiens balsamina* L., vinegar-processed *Olibanum*, vinegar-processed *Myrrha*, *Angelicae Sinensis Radix*, prepared *Pheretima*, *Cinnamomi Ramulus*, *Carthami Flos*, *Lonicerae Japonicae Flos*, *Paeoniae Radix Rubra*, vinegar-processed *Corydalis Rhizoma*, *Saposhnikovia Radix*, raw *Pollen Typhae*, *Zanthoxyli Pericarpium*, and *Campsis Flos*. The temperature of the herbal liquid was confirmed by an electronic thermometer and controlled at 37–41°C. The hands, feet, and symptomatic distal extremities were fumigated and washed for 30 min once daily. Five consecutive days constituted one treatment course, and the intervention continued for two chemotherapy cycles. Actual treatment sessions, skin reactions, and reasons for interruption or discontinuation were recorded. HFW was implemented by oncology nurses or TCM external-therapy nurses who had received standardized training, either in the ward or treatment area, following a standard operating procedure. Patients did not determine the herbal-liquid temperature or adjust treatment duration by themselves.

In addition to the control intervention, the intervention group received HSM. Main acupoints included Hegu (LI4), Neiguan (PC6), Zusanli (ST36), Sanyinjiao (SP6), Taixi (KI3), and Yongquan (KI1), with exploration of heat-sensitive acupoints near symptomatic distal regions; the main acupoints are illustrated in Fig. 1. Individualized moxibustion points were determined by responses such as penetrating heat, expanding heat, transmitting heat, distal heat sensation despite absence of local heat, deep heat sensation, or local soreness and distension. The moxa sticks used were pure moxa sticks (Jiangsu Kangmei Pharmaceutical Co., Ltd.; National Drug Approval No. Z32020253; specification: 25 g per stick, length 20–21 cm, diameter 1.9–2.1 cm; main component: moxa floss). The moxa stick was kept approximately 2–3 cm from the skin. Each session lasted 30 to 60 minutes and was terminated based on patient tolerance, attenuation of the moxibustion sensation, or the disappearance of the heat-

sensitive response. Treatment was performed once daily for 5 consecutive days as one course and continued for two chemotherapy cycles (11, 12). HSM was delivered by uniformly trained and qualified medical or nursing personnel with clinical experience in TCM external therapy or acupuncture-related procedures. During treatment, the patient's moxibustion sensation, skin color, and systemic responses were continuously monitored. The research team established a predefined management plan for local skin adverse reactions. When marked redness, pruritus, or burning discomfort occurred, the intervention was suspended and local observation was performed; adverse events were recorded when necessary, and investigators assessed whether treatment could continue. Interventions in both groups were implemented by uniformly trained medical or nursing personnel with TCM external-therapy or acupuncture-related experience according to standardized operating procedures.

2.7 Outcome measures

The primary outcome was the EORTC QLQ-CIPN20 score after treatment. Key secondary outcomes included NCI-CTCAE v5.0 peripheral neuropathy grade, NRS score, TCM syndrome score, and nerve conduction velocity. The exposure descriptive indicator was estimated cumulative oxaliplatin dose before enrollment. Safety outcomes included adverse events such as skin redness, pruritus, blistering, burn, dizziness, palpitations, and moxibustion syncope.

Assessment time points included before treatment (T0), after completion of the two-cycle intervention (T1), and follow-up visit (T2). T1 was defined as the study assessment after completion of all interventions in the second chemotherapy cycle. T2 was defined as the follow-up visit 4 weeks after completion of all interventions, with an allowed window of ± 7 days, based on the actual visit date. EORTC QLQ-CIPN20 is a 20-item quality-of-life questionnaire developed by the European Organization for Research and Treatment of Cancer for chemotherapy-induced peripheral neuropathy. It is used mainly to assess OIPN-related symptom burden and functional limitation. Each item is scored on a 1–4 scale. In this study, the raw total score of the 20 items was used as the primary analytic indicator, with a theoretical range of 20–80; higher scores indicate greater OIPN-related symptom burden or more substantial functional limitation (21–23).

Neuroelectrophysiological testing was performed using an electromyography/evoked-potential instrument (Shanghai Bendi Medical Instrument Co., Ltd.; model 9031A070). Based on previous neuroconductive-function evaluation pathways in TCM external-therapy studies and the tendency for OIPN to involve distal upper and lower extremities, the following measures were assessed: motor nerve conduction velocity (MCV) of the median nerve, sensory nerve conduction velocity (SCV) of the median nerve, MCV of the common peroneal nerve, and SCV of the superficial peroneal nerve.

Neuroelectrophysiological examination followed a standardized procedure. For each participant, the tested side was kept consistent before and after treatment, and the examination time, tested side, and environmental conditions were checked against study records to reduce the effects of thermal stimulation and ambient temperature on nerve conduction velocity measurement.

2.8 Statistical analysis

Statistical analyses were performed using SPSS 27.0. The primary efficacy analysis used the per-protocol set (PPS; 34 patients in the control group and 33 in the intervention group). Safety analysis included participants who actually received the intervention (safety set, SS; 35 patients in the control group and 35 in the intervention group). This study did not perform missing-value imputation or intention-to-treat/full analysis set (ITT/FAS) analysis; the related implications are addressed in the limitations. Continuous data conforming to a normal distribution are expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$). Within-group pre-post comparisons used paired-sample t tests, and between-group comparisons used independent-sample t tests. For the primary continuous outcomes, between-group differences and 95% confidence intervals are also reported. Non-normally distributed data are expressed as median (P25, P75) and analyzed using rank-sum tests. Count data are expressed as n (%) and analyzed using the chi-square test or Fisher's exact test. Ranked data were analyzed using the Mann-Whitney U test. Multiple secondary outcomes and nerve conduction velocity indicators were exploratory analyses and were not adjusted for multiple comparisons; therefore, positive findings should be interpreted cautiously. A p-value < 0.05 was considered statistically significant. The study flow diagram is shown in Fig. 2.

3 Results

3.1 Baseline characteristics

A total of 70 patients were randomized, with 35 patients in the control group and 35 in the intervention group. During treatment, one patient in the control group withdrew because of a mild adverse event. In the intervention group, one patient withdrew because of a mild adverse event, and one patient later withdrew because of personal factors and disease progression. Finally, 67 patients completed the protocol, including 34 patients in the control group and 33 in the intervention group. Table 1 is based on the PPS analysis. The sex distribution was 20 men and 14 women in the control group and 18 men and 15 women in the intervention group. Before treatment, age, sex, BMI, tumor site, TNM stage, baseline chemotherapy regimen, chemotherapy cycles before enrollment, estimated cumulative oxaliplatin dose before enrollment, OIPN grade, NRS score, EORTC QLQ-CIPN20 score, and TCM syndrome score did not differ significantly between groups ($p > 0.05$), indicating that baseline characteristics were comparable between the two per-protocol groups.

Table 1
Baseline characteristics of the two groups.

Variable	Control group (n = 34)	Intervention group (n = 33)	p-value
Age, years	63.97 ± 9.03	63.91 ± 9.62	0.979
BMI, kg/m ²	23.32 ± 1.96	23.87 ± 1.74	0.231
Sex			0.807
Male	20 (58.8)	18 (54.5)	
Female	14 (41.2)	15 (45.5)	
Tumor site			0.373
Colon	21 (61.8)	16 (48.5)	
Rectum	13 (38.2)	16 (48.5)	
Rectosigmoid junction	0 (0.0)	1 (3.0)	
TNM stage			0.585
Stage II	5 (14.7)	8 (24.2)	
Stage III	15 (44.1)	14 (42.4)	
Stage IV	14 (41.2)	11 (33.3)	
Baseline chemotherapy regimen			0.097
CAPOX/XELOX	25 (73.5)	23 (69.7)	
FOLFOX	9 (26.5)	6 (18.2)	
Other oxaliplatin-containing regimen	0 (0.0)	4 (12.1)	
Chemotherapy cycles before enrollment, cycles	3.26 ± 0.93	3.21 ± 0.89	0.814
Estimated cumulative oxaliplatin dose before enrollment, mg	601.47 ± 222.34	602.73 ± 212.78	0.981
OIPN grade (baseline)			0.934
Grade 1	22 (64.7)	21 (63.6)	
Grade 2	12 (35.3)	12 (36.4)	
Grade 3	0 (0.0)	0 (0.0)	

Note: This table is based on the PPS analysis. Continuous data are expressed as $\bar{x} \pm s$, and count data as n (%). Between-group comparisons used independent-sample t tests for continuous data and chi-square or Fisher exact tests for count data. Baseline chemotherapy regimens were categorized as CAPOX/XELOX, FOLFOX, or other oxaliplatin-containing regimens.

Variable	Control group (n = 34)	Intervention group (n = 33)	p-value
NRS score, points	4.35 ± 0.81	4.39 ± 1.12	0.864
EORTC QLQ-CIPN20 score, points	41.21 ± 3.08	40.94 ± 3.59	0.745
TCM syndrome score, points	19.15 ± 2.52	18.79 ± 3.39	0.624
Note: This table is based on the PPS analysis. Continuous data are expressed as $\bar{x} \pm s$, and count data as n (%). Between-group comparisons used independent-sample t tests for continuous data and chi-square or Fisher exact tests for count data. Baseline chemotherapy regimens were categorized as CAPOX/XELOX, FOLFOX, or other oxaliplatin-containing regimens.			

3.2 NCI-CTCAE v5.0 peripheral neuropathy grades before and after treatment

After treatment and at the 4-week follow-up after completion of all interventions, OIPN grade severity was lower in the intervention group than in the control group ($p = 0.006$ and $p = 0.028$, respectively). The distribution of peripheral neuropathy grades at each assessment time point is presented in Table 2.

Table 2
NCI-CTCAE v5.0 peripheral neuropathy grades before and after treatment.

Time point	Group	Grade 0	Grade 1	Grade 2	Grade 3	Statistic	p-value
Baseline	Control group	0	22	12	0	—	—
Baseline	Intervention group	0	21	12	0		
Post-treatment	Control group	5	21	8	0	752.0	0.006
Post-treatment	Intervention group	12	20	1	0		
Follow-up	Control group	6	19	9	0	718.5	0.028
Follow-up	Intervention group	12	18	3	0		
Note: Values are numbers of patients. Between-group comparisons after treatment and at follow-up used the Mann-Whitney U test.							

3.3 Symptom scores and EORTC QLQ-CIPN20 scores before and after treatment

After treatment, EORTC QLQ-CIPN20 scores were 36.00 ± 2.73 in the control group and 33.61 ± 2.15 in the intervention group. At the 4-week follow-up after completion of all interventions, scores were 36.97 ± 2.88 and 33.94 ± 2.40 , respectively. Scores were lower in the intervention group at both time points. The

between-group differences were – 2.39 points (95% CI: -3.60 to -1.19; $p < 0.001$) and – 3.03 points (95% CI: -4.33 to -1.74; $p < 0.001$), respectively. Although statistically significant, the absolute between-group differences were smaller than the expected 5.0-point difference used for sample-size estimation. After treatment, the TCM syndrome score was lower in the intervention group than in the control group ($p < 0.001$). No statistically significant between-group differences were observed in NRS scores after treatment or at follow-up ($p = 0.789$ and $p = 0.862$). The detailed results for NRS, EORTC QLQ-CIPN20, and TCM syndrome scores are presented in Table 3.

Table 3
NRS, EORTC QLQ-CIPN20, and TCM syndrome scores before and after treatment.

Outcome	Time point	Control group (n = 34)	Intervention group (n = 33)	p-value	Between-group difference (95% CI)
NRS	Baseline	4.35 ± 0.81	4.39 ± 1.12	—	—
NRS	Post-treatment	3.29 ± 0.97	3.36 ± 1.14	0.789	0.07 (-0.45, 0.59)
NRS	Follow-up	3.35 ± 1.07	3.30 ± 1.26	0.862	-0.05 (-0.62, 0.52)
EORTC QLQ-CIPN20 score	Baseline	41.21 ± 3.08	40.94 ± 3.59	—	—
EORTC QLQ-CIPN20 score	Post-treatment	36.00 ± 2.73	33.61 ± 2.15	< 0.001	-2.39 (-3.60, -1.19)
EORTC QLQ-CIPN20 score	Follow-up	36.97 ± 2.88	33.94 ± 2.40	< 0.001	-3.03 (-4.33, -1.74)
TCM syndrome score	Baseline	19.15 ± 2.52	18.79 ± 3.39	—	—
TCM syndrome score	Post-treatment	10.32 ± 2.60	7.97 ± 1.93	< 0.001	-2.35 (-3.47, -1.23)

Note: Lower NRS, TCM syndrome, and EORTC QLQ-CIPN20 scores indicate lower symptom burden or fewer functional limitations. Between-group differences were calculated as intervention group minus control group. Baseline values are presented as baseline characteristics; between-group differences and 95% CIs are therefore not listed for baseline.

3.4 Nerve conduction velocity before and after treatment

After treatment, median nerve MCV and common peroneal nerve MCV were higher in the intervention group than in the control group ($p = 0.016$ and $p = 0.006$, respectively). No statistically significant between-group differences were observed in median nerve SCV or superficial peroneal nerve SCV. The nerve conduction velocity results are presented in Table 4.

Table 4
Nerve conduction velocity before and after treatment ($\bar{x} \pm s$, m/s).

Outcome	Time point	Control group (n = 34)	Intervention group (n = 33)	p-value
Median nerve MCV	Baseline	54.97 $\pm$ 3.87	55.32 $\pm$ 3.08	0.682
Median nerve MCV	Post-treatment	55.01 $\pm$ 4.67	57.49 $\pm$ 3.45	0.016
Median nerve SCV	Baseline	54.10 $\pm$ 3.99	54.08 $\pm$ 4.01	0.979
Median nerve SCV	Post-treatment	54.32 $\pm$ 4.92	56.14 $\pm$ 4.07	0.105
Common peroneal nerve MCV	Baseline	45.27 $\pm$ 3.55	45.92 $\pm$ 2.74	0.402
Common peroneal nerve MCV	Post-treatment	45.96 $\pm$ 4.24	48.62 $\pm$ 3.30	0.006
Superficial peroneal nerve SCV	Baseline	43.42 $\pm$ 4.65	43.24 $\pm$ 3.43	0.857
Superficial peroneal nerve SCV	Post-treatment	44.48 $\pm$ 5.38	44.68 $\pm$ 4.38	0.871
Note: MCV, motor nerve conduction velocity; SCV, sensory nerve conduction velocity.				

3.5 Safety

No serious adverse events occurred in either group during the study. The safety analysis set included all 70 participants who actually received an intervention. In the control group, skin redness occurred in 2 patients and pruritus in 1 patient, for an overall adverse-event rate of 8.57%. In the intervention group, skin redness occurred in 4 patients and pruritus in 3 patients, for an overall adverse-event rate of 20.00%. The incidence of mild skin reactions was numerically higher in the intervention group, but the overall adverse-event rate did not differ significantly between groups ($p = 0.306$). No blistering, burn, dizziness/palpitations, or moxibustion syncope occurred in either group. One patient in each group withdrew from the study because of local skin pruritus and unwillingness to continue the intervention; symptoms resolved after discontinuation. One additional patient in the intervention group withdrew because of personal factors and disease progression. A detailed comparison of adverse events between the two groups is presented in Table 5.

Table 5
Safety comparison between groups.

Variable	Control group (n = 35)	Intervention group (n = 35)	Statistic	p-value
Skin redness	2 (5.71)	4 (11.43)	Fisher	0.673
Pruritus	1 (2.86)	3 (8.57)	Fisher	0.614
Blister	0 (0.00)	0 (0.00)	Fisher	1.000
Burn	0 (0.00)	0 (0.00)	Fisher	1.000
Dizziness/palpitations	0 (0.00)	0 (0.00)	Fisher	1.000
Moxibustion syncope	0 (0.00)	0 (0.00)	Fisher	1.000
Serious adverse events	0 (0.00)	0 (0.00)	Fisher	1.000
Overall adverse-event rate	3 (8.57)	7 (20.00)	chi-square = 1.050	0.306
Note: Values are n (%). Between-group comparisons used the chi-square test or Fisher exact test.				

4 Discussion

In comprehensive cancer treatment, OIPN is a common dose-limiting toxicity in patients with CRC. It can cause distal numbness, tingling, cold sensitivity, hypoesthesia, and impairment of fine motor function, and it substantially affects quality of life (3). Current modern medical options for prevention and treatment of OIPN remain limited. Duloxetine is used mainly for symptom control in painful OIPN, but its coverage of non-pain symptoms such as numbness, hypoesthesia, and functional limitation is insufficient (7). Therefore, exploration of safe and implementable non-pharmacological supportive-care interventions on the basis of standardized antitumor therapy has practical clinical significance.

This randomized controlled study evaluated the addition of HSM to HFW. The study design used HFW alone as the base external-therapy control and observed whether adding HSM affected overall OIPN symptom burden, neuropathy grade, TCM syndrome score, nerve conduction function, and safety. In the PPS analysis, EORTC QLQ-CIPN20 scores after treatment and at 4 weeks after completion of all interventions were lower in the intervention group than in the control group. NCI-CTCAE v5.0 peripheral neuropathy grade and post-treatment TCM syndrome score also favored the intervention group. These findings suggest that adding HSM to HFW may have short-term effects in reducing OIPN-related symptom burden and improving TCM syndrome manifestations.

It should be emphasized that NRS scores did not show clear between-group differences after treatment or at follow-up. Therefore, this study cannot conclude that adding HSM significantly reduces pain intensity. This negative result may be related to the symptom spectrum of the study population: baseline NRS scores in both groups were approximately 4.3, indicating overall moderate pain, whereas OIPN often

presents more prominently as distal numbness, hypoesthesia, cold-triggered dysesthesia, and impairment of fine motor function. Pain intensity is not necessarily the dominant symptom in all patients. The coexistence of improvements in EORTC QLQ-CIPN20 score and NCI-CTCAE v5.0 grade with negative NRS findings suggests that the short-term effect of the combined regimen may be reflected more in the overall burden of paresthesia, numbness, and functional limitation than in pain reduction alone. Regarding nerve conduction velocity, median nerve MCV and common peroneal nerve MCV showed between-group differences, whereas median nerve SCV and superficial peroneal nerve SCV did not show statistical advantages. Therefore, objective improvement in nerve conduction function should be interpreted cautiously. Overall, the results are best understood as a statistical signal of short-term improvement in symptom burden and grading rather than definitive evidence that adding HSM comprehensively improves pain, nerve conduction function, or overall neurophysiological recovery.

HFW served as the basic local external therapy and warming-collateral intervention in this study. In the prescription, *Lycopodii Herba*, raw *Artemisia argyi* leaves, *Impatiens balsamina* L., *Cinnamomi Ramulus*, and *Zanthoxyli Pericarpium* mainly warm the meridians, dispel cold, relax tendons, and unblock collaterals. *Angelicae Sinensis Radix*, *Carthami Flos*, *Paeoniae Radix Rubra*, and raw *Pollen Typhae* mainly activate blood and resolve stasis. Vinegar-processed *Olibanum*, vinegar-processed *Myrrha*, and vinegar-processed *Corydalis Rhizoma* mainly promote *qi* movement and unblock collaterals. *Lonicerae Japonicae Flos* and *Saposhnikovia Radix* provide additional clearing and wind-dispelling effects. Direct action of the herbal liquid on the hands, feet, and symptomatic distal extremities may improve local circulation through warm stimulation and herbal penetration, thereby relieving numbness, cold hands and feet, and functional limitation. Previous studies of HFW, herbal bathing, and auricular point pressing have also suggested that local external therapies may improve neurotoxic symptoms and clinical manifestations in patients with OIPN (9, 10, 24).

HSM is characterized by first detecting heat-sensitive acupoints and then applying individualized moxibustion according to responses such as penetrating heat, expanding heat, transmitting heat, distal heat sensation, and deep heat sensation. Compared with fixed-acupoint mild moxibustion, HSM emphasizes acupoint sensitization, propagation of moxibustion sensation, and dynamic adjustment of moxibustion dosage, allowing treatment stimulation to match the patient's current meridian response (11, 12). In this study, Hegu (LI4), Neiguan (PC6), Zusanli (ST36), Sanyinjiao (SP6), Taixi (KI3), and Yongquan (KI1) were selected to address distal hand-foot symptoms, spleen-stomach *qi* and blood generation, liver-kidney nourishment, and meridian regulation. Related studies have shown that HSM combined with other TCM external therapies may improve peripheral nerve dysfunction, and acupuncture theory also supports the combined use of meridian-based point selection and local point selection to warm and unblock the meridians and harmonize *qi* and blood (25, 26).

From the perspective of intervention structure, this study did not compare the independent effect of HSM; instead, it evaluated the additional benefit of HSM on the basis of HFW. HFW emphasizes local warming and herbal penetration in the hands and feet, whereas HSM emphasizes stimulation of heat-sensitive points and systemic meridian regulation. The two approaches may be complementary in

improving impaired *qi*-blood movement, promoting peripheral circulation, and reducing abnormal sensory input. Regarding a potential synergistic mechanism, the moist-heat effect of HFW may increase local skin temperature and moisture content, dilate peripheral microvessels, and reduce stratum-corneum barrier resistance, thereby providing a more favorable tissue microenvironment for thermal stimulation and topical herbal effects. On this basis, HSM may transmit thermal stimulation from local to deep and distal regions through heat-sensitive responses such as penetrating, expanding, and transmitting heat, further promoting *qi*-blood movement and peripheral circulation.

From a modern neurophysiological perspective, moderate and targeted thermal stimulation may alter the subjective perception of numbness, cold sensitivity, and tingling by modulating the thresholds of peripheral nerve-ending receptors, enhancing local blood perfusion, and desensitizing aberrant sensory inputs. However, these mechanisms remain hypothetical and require further validation using microcirculatory and neuroelectrophysiological indicators. HSM also emphasizes dynamic adjustment of treatment sites and moxibustion dosage according to patient feedback, which is consistent with patient-centered and individualized nursing concepts and may enhance patient engagement and adherence to non-pharmacological interventions. Therefore, the effect of the combined regimen is best understood as a composite intervention effect involving local moist-heat external therapy, heat-sensitive acupoint stimulation, active patient feedback, and nursing support. Consistent with the logic of acupuncture and electroacupuncture studies that use peripheral stimulation to regulate nerve function, this combined TCM external-therapy approach may serve as a supplementary supportive-care option for OIPN (27, 28). Previous clinical studies of TCM for prevention and treatment of oxaliplatin neurotoxicity have also suggested that integrated TCM interventions may be important adjuncts for OIPN supportive care (29).

The nerve conduction velocity results provide objective reference information for efficacy evaluation. PPS analysis showed that post-treatment median nerve MCV and common peroneal nerve MCV were higher in the intervention group than in the control group, whereas median nerve SCV and superficial peroneal nerve SCV showed no clear between-group differences. These results suggest that the effect of the combined intervention on nerve conduction function may not be uniform, and it would be inappropriate to infer that a stable overall nerve-repair effect has been established. It is noteworthy that improvements in patient-reported outcomes were not synchronized with most nerve conduction indicators. OIPN involves dorsal root ganglion injury, axonal degeneration, and myelin damage, and structural nerve repair usually requires a longer period. Because the intervention period in this study covered only two chemotherapy cycles, early efficacy may have reflected modulation of symptom perception, local circulation, or abnormal sensory input rather than structural regeneration within a short time. Future studies should further evaluate these findings in relation to cumulative oxaliplatin dose, baseline nerve function, and individual risk stratification (30).

EORTC QLQ-CIPN20 is a CIPN-specific patient-reported outcome measure (PROM) with favorable measurement properties. It captures numbness, tingling, paresthesia, and related functional limitations from the patient's subjective perspective. This study used the scale to evaluate overall OIPN symptom burden, and the intervention group had lower scores after treatment and at follow-up. This result was

consistent with improvements in NCI-CTCAE v5.0 grade and TCM syndrome score, suggesting that HSM combined with HFW may reduce neurotoxicity symptoms at the patient-perceived level. However, the sample size was limited, and the absolute between-group differences after treatment and at follow-up were small and lower than the expected difference used in sample-size estimation. Therefore, these findings are best interpreted as a statistical signal of short-term reduction in symptom burden; their practical clinical value requires further validation in larger samples and with longer follow-up. EORTC QLQ-CIPN20 includes sensory, motor, and autonomic items, and different dimensions may not be equally sensitive to oxaliplatin neurotoxicity. Subsequent studies may perform sensory, motor, and autonomic subscale analyses to assess dimension-specific efficacy more precisely.

From the perspective of clinical nursing application, both HFW and HSM are external therapies with relatively low dependence on equipment. They can be standardized through training and implemented in oncology wards or TCM nursing outpatient clinics. The main implementation costs of the regimen are herbal-liquid preparation, nursing operation time, skin-safety monitoring, and adherence management; the regimen does not depend on expensive instruments. For OIPN patients whose main symptoms are numbness, cold sensitivity, and paresthesia, and for whom pharmacological options are limited, the combined external-therapy approach may have advantages in accessibility and patient acceptance. If multicenter studies are conducted in the future, recording nursing time per session, patient satisfaction, feasibility of home continuation, and cost-effectiveness will help evaluate its implementation value in routine oncology supportive nursing.

This study has several limitations. First, it was a single-center study with a small sample size. Because of the procedural features of TCM external therapy, complete blinding of participants and treatment providers was not feasible, so implementation bias and subjective outcome-assessment bias may remain. Although outcome assessors and statisticians did not participate in treatment implementation and were kept from group information as much as possible, related bias cannot be fully excluded. NCI-CTCAE grading was performed by uniformly trained clinical researchers, but subjective judgment differences may still exist when distinguishing mild subjective sensory abnormalities or the boundary between grade 1 and grade 2. In individual cases, changes in NCI-CTCAE v5.0 grade were not fully consistent with changes in patient-reported outcome scales, suggesting that future studies should strengthen source-document verification, grading review, and control of inter-rater consistency. Second, this study did not include sham moxibustion or placebo control, and the intervention group had additional treatment time and therapeutic contact compared with the control group. Therefore, placebo effects, expectation effects, and extra nursing attention cannot be fully excluded as contributors to patient-reported outcomes. Third, the intervention period covered only two chemotherapy cycles, and follow-up lasted 4 weeks after completion of all interventions, making it difficult to adequately evaluate long-term structural nerve repair and sustained safety. Future studies should collect longer follow-up data to confirm durable benefits and delayed safety events longitudinally. Fourth, the cumulative oxaliplatin dose before enrollment was estimated mainly from protocol-recorded per-cycle doses and completed chemotherapy cycles, and it cannot fully substitute for actual administration records. Future studies should further correct exposure using actual administered dose, dose reductions, treatment

delays, and discontinuation data. Fifth, this study mainly used PPS analysis and did not perform ITT/FAS analysis or missing-value imputation, which may have overestimated the intervention effect to some extent. Sixth, multiple nerve conduction velocity indicators and secondary outcomes were not adjusted for multiple comparisons, and positive results should be interpreted cautiously. Seventh, although the between-group differences in EORTC QLQ-CIPN20 were statistically significant, the absolute differences were small, and the minimal clinically important difference and practical clinical value require further verification.

5 Conclusion

Compared with HFW alone, the adjunctive application of HSM showed short-term statistical signals of reduced overall symptom burden, lower peripheral neuropathy grade severity, and improved TCM syndrome score in patients with CRC complicated by OIPN, without observed serious adverse events. The short-term benefits of this multimodal regimen primarily translated into reductions in neurological symptom burden and functional limitations, rather than direct analgesic effects. Among nerve conduction velocities, only median nerve MCV and common peroneal nerve MCV showed between-group differences, suggesting that early neuroelectrophysiological improvement was not uniform. This accessible regimen holds promise as an adjunctive, non-pharmacological supportive care strategy in oncology. Because this study was limited by its single-center design, small sample size, PPS analysis, and short follow-up, multicenter, larger-sample, registered prospective studies are needed to establish its long-term efficacy, cost-effectiveness, and clinical implementation value.

Declarations

Author Contribution

W.X.: Conceptualization, methodology, investigation, data curation, formal analysis, and writing—original draft. X.Z.: Investigation, participant recruitment, intervention implementation, and data collection. Y.Z.: Data curation, formal analysis, and interpretation of the results. S.H.: Investigation, intervention implementation, outcome assessment, and data collection. Y.H.: Supervision, methodology, project administration, and writing—review and editing. All authors reviewed and approved the final manuscript.

Ethics and transparency statement

This study was conducted in accordance with the Declaration of Helsinki and the requirements of ethical review for life science and medical research involving human subjects in China. It was approved by the Ethics Committee of Nanjing Hospital of Traditional Chinese Medicine (approval No. 2026KY006-01), and all participants provided written informed consent. Data sharing statement: subject to ethical approval, protection of participant privacy, and data de-identification requirements, de-identified data and statistical analysis materials supporting the main conclusions of this article may be made available by the corresponding author upon reasonable request. Conflict of interest statement: the authors declare

no conflicts of interest related to this study. Funding and role of the funder: this study was supported by Nanjing Hospital of Traditional Chinese Medicine.

References

1. National Health Commission of the People's Republic of China. Chinese guidelines for diagnosis and treatment of colorectal cancer (2023 edition). *Chinese Journal of Surgery*. 2023;61(8):561–585. [in Chinese].
2. Andre T, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. *New England Journal of Medicine*. 2004;350(23):2343–2351.
3. Cancer Supportive Therapy Committee of the China Anti-Cancer Association; Clinical Chemotherapy Committee of the China Anti-Cancer Association. Chinese expert consensus on diagnosis and treatment of chemotherapy-induced peripheral neuropathy (2022 edition). *Chinese Journal of Oncology*. 2022;44(9):928–934. [in Chinese].
4. Staff NP, Grisold A, Grisold W, et al. Chemotherapy-induced peripheral neuropathy: a current review. *Annals of Neurology*. 2017;81(6):772–781.
5. Chen ZY, Liu L, Yao SN, et al. Toxic mechanisms of chemotherapy-induced peripheral neuropathy and strategies for prevention and treatment with traditional Chinese medicine. *Chinese Traditional and Herbal Drugs*. 2026;57(6):2356–2367. [in Chinese].
6. Flatters SJL, Dougherty PM, Colvin LA. Clinical and preclinical perspectives on chemotherapy-induced peripheral neuropathy (CIPN): a narrative review. *British Journal of Anaesthesia*. 2017;119(4):737–749.
7. Loprinzi CL, Lacchetti C, Bleeker J, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: ASCO guideline update. *Journal of Clinical Oncology*. 2020;38(28):3325–3348.
8. Zhou Y, Tian NJ, Zhao WX, et al. Clinical observation of Danggui Sini Decoction combined with Shentong Zhuyu Decoction and moxibustion for peripheral neuropathy after chemotherapy. *Liaoning Journal of Traditional Chinese Medicine*. 2025;52(6):143–147. [in Chinese].
9. Zhao J. Clinical observation of herbal bathing combined with intradermal needling for chemotherapy-induced peripheral neuropathy. Changsha: Hunan University of Chinese Medicine; 2025. [dissertation, in Chinese].
10. Han Y. Observation on the efficacy of herbal fumigation and washing for peripheral neuropathy caused by oxaliplatin-containing regimens. Urumqi: Xinjiang Medical University; 2017. [dissertation, in Chinese].
11. Xie DY, Chen YQ, Li QL, et al. Clinical safety operation experience of Chen Rixin heat-sensitive moxibustion. *China Journal of Traditional Chinese Medicine and Pharmacy*. 2020;35(4):1869–1871. [in Chinese].

12. Chen RX. Heat-sensitive moxibustion: inheritance, innovation, and development of moxibustion in traditional Chinese medicine. *Chinese Acupuncture & Moxibustion*. 2023;43(4):483–488. [in Chinese].
13. Zeng YY, Yang L, Xu T, et al. Heat-sensitive moxibustion combined with finger rehabilitation exercises for prevention and treatment of peripheral neuropathy after chemotherapy in 48 patients with colorectal cancer. *Fujian Journal of Traditional Chinese Medicine*. 2026. [online ahead of print, in Chinese].
14. Yao Y, Zhang XP, Ge RJ, et al. Electroacupuncture for prevention of chemotherapy-induced peripheral neuropathy: a randomized controlled trial. *Chinese Acupuncture & Moxibustion*. 2024;44(12):1388–1394. [in Chinese].
15. Schulz KF, Altman DG, Moher D, et al. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:c332.
16. Boutron I, Moher D, Altman DG, et al. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Annals of Internal Medicine*. 2008;148(4):295–309.
17. Yeo F, Ng CC, Loh KWJ, et al. Minimal clinically important difference of the EORTC QLQ-CIPN20 for worsening peripheral neuropathy in patients receiving neurotoxic chemotherapy. *Supportive Care in Cancer*. 2019;27(12):4753–4762.
18. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. 2017.
19. Zheng XY. Guidelines for Clinical Research of New Chinese Medicines (trial edition). Beijing: China Medical Science Press; 2002. [in Chinese].
20. China Association of Chinese Medicine. Routine technical operating procedures for TCM nursing. Beijing: China Press of Traditional Chinese Medicine; 2006. [in Chinese].
21. Molassiotis A, Cheng HL, Lopez V, et al. Are we mis-estimating chemotherapy-induced peripheral neuropathy? Analysis of assessment methodologies from a prospective, multinational, longitudinal cohort study of patients receiving neurotoxic chemotherapy. *BMC Cancer*. 2019;19(1):132.
22. Postma TJ, Aaronson NK, Heimans JJ, et al. The development of an EORTC quality of life questionnaire to assess chemotherapy-induced peripheral neuropathy: the QLQ-CIPN20. *European Journal of Cancer*. 2005;41(8):1135–1139.
23. Li T, Park SB, Battaglini E, et al. Assessing chemotherapy-induced peripheral neuropathy with patient reported outcome measures: a systematic review of measurement properties and considerations for future use. *Quality of Life Research*. 2022;31(11):3091–3107.
24. Ma XJ, Shi HX, He WW, et al. Clinical efficacy of herbal fumigation and washing combined with auricular point pressing for chemotherapy-induced peripheral neuropathy. *Medical Practice*. 2025;7:75–78. [in Chinese].
25. Hu SH, Liu M, Liu YR, et al. Clinical study of TCM directional drug penetration combined with heat-sensitive moxibustion for diabetic peripheral neuropathy. *Modern Chinese Medicine*. 2026;46(1):23–

27. [in Chinese].
26. Shi XM. Acupuncture and Moxibustion. 3rd ed. Beijing: China Press of Traditional Chinese Medicine; 2017:145–146. [in Chinese].
27. Bao T, Seidman AD, Piulson L, et al. A phase IIA trial of acupuncture to reduce chemotherapy-induced peripheral neuropathy severity during neoadjuvant or adjuvant weekly paclitaxel chemotherapy in breast cancer patients. *European Journal of Cancer*. 2018;101:12–19.
28. Huang MC, Chang SC, Liao WL, et al. Acupuncture may help to prevent chemotherapy-induced peripheral neuropathy: a randomized, sham-controlled, single-blind study. *The Oncologist*. 2023;28(6):538–548.
29. Ma J, Wei GL, Zhu LJ, et al. Multicenter randomized double-blind controlled clinical study of modified Huangqi Guizhi Wuwu formula granules for prevention and treatment of oxaliplatin neurotoxicity. *Modernization of Traditional Chinese Medicine and Materia Medica-World Science and Technology*. 2019;21(7):1495–1504. [in Chinese].
30. Wei XQ, Lin JR, Ye F, et al. Construction and application of a risk prediction model for oxaliplatin-induced peripheral neuropathy. *Journal of Modern Medicine & Health*. 2022;38(9):1479–1482. [in Chinese].

Figures

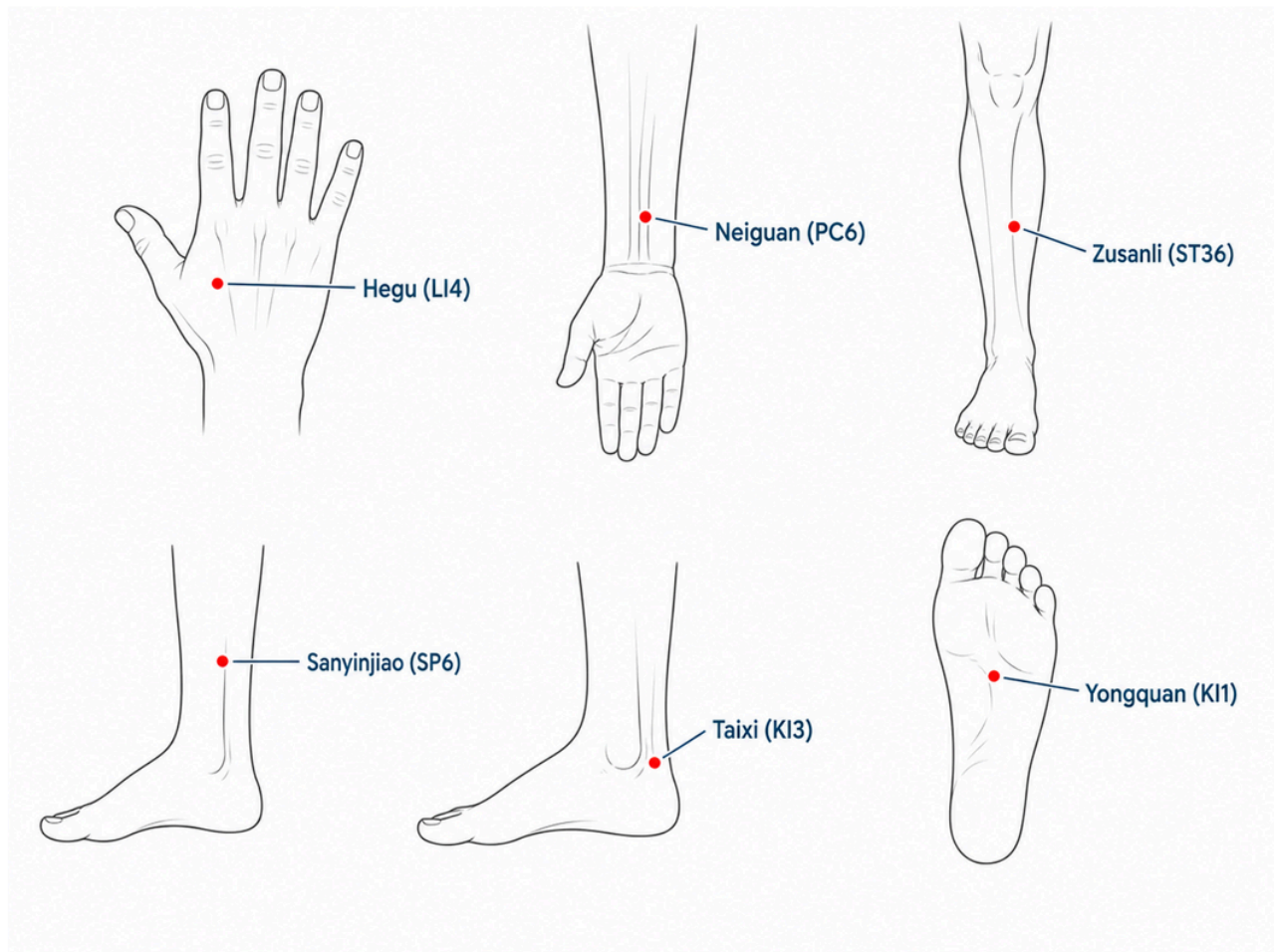


Figure 1

Main acupoints for HSM in the intervention group. The main acupoints included Hegu (LI4), Neiguan (PC6), Zusanli (ST36), Sanyinjiao (SP6), Taixi (KI3), and Yongquan (KI1). In practice, heat-sensitive acupoints were explored near the symptomatic distal extremities.

Technical Route of the Study

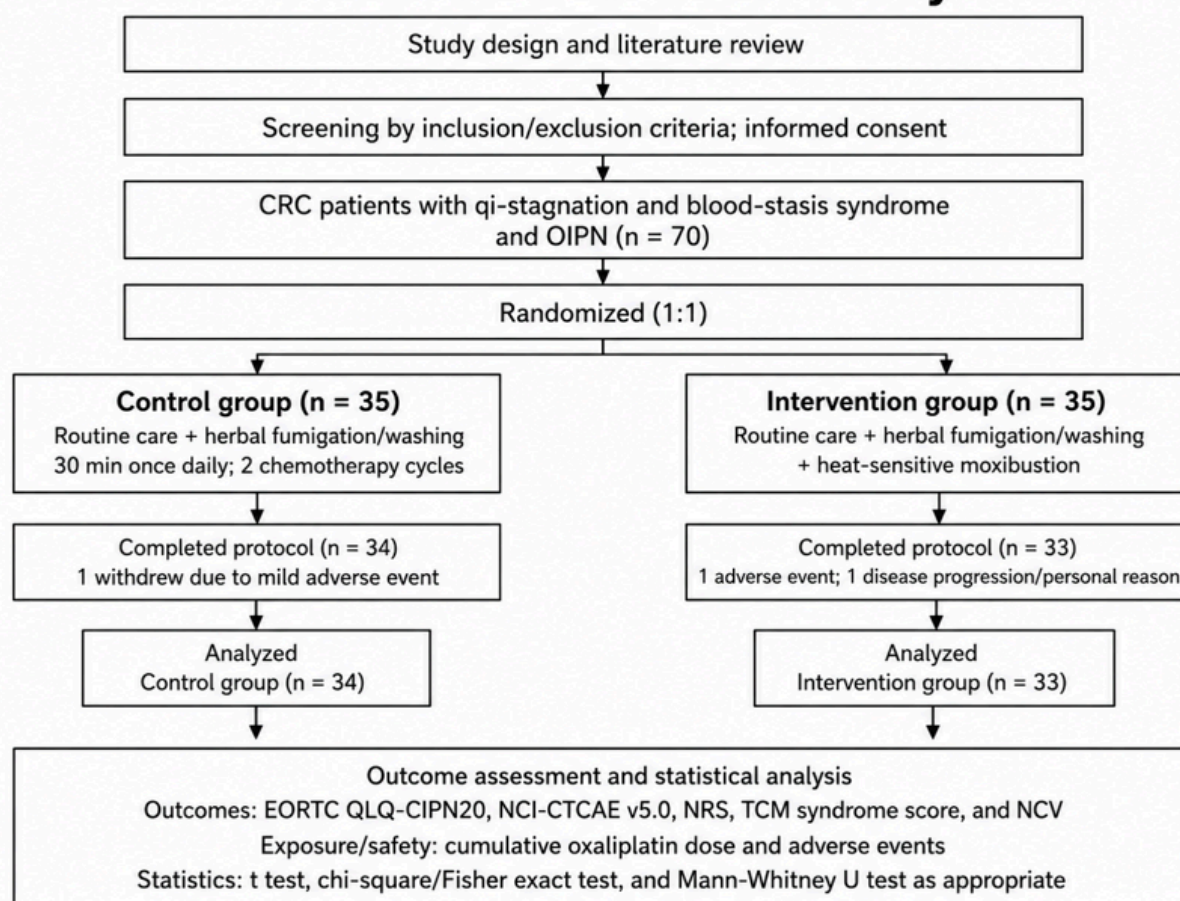


Figure 2

Study flow diagram.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [RawData8.5.xlsx](#)