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Standardized Traditional Chinese Medicine External Therapy for Chronic Soft Tissue Pain: A Multicenter Observational Study

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Abstract

Chronic soft tissue pain has brought a heavy global social and economic burden, while conventional treatments have obvious limitations in efficacy and safety. Traditional Chinese Medicine external therapies (TETs) including cupping, scraping and moxibustion are widely used clinically, yet inconsistent operation standards lead to high research heterogeneity and poor repeatability. This multicenter observational study aimed to evaluate the clinical efficacy, safety, dose-response relationship and cost-effectiveness of standardized TETs for chronic soft tissue pain, and explore the influencing factors of therapeutic effects. A total of 1000 eligible patients from 5 tertiary hospitals across China were divided into three groups: standard TET combined with conventional management (Arm A, n=500), conventional management alone (Arm B, n=300), and high-intensity TET combined with conventional management (Arm C, n=200). All operators received unified training and quantitative operational parameters were adopted to reduce research heterogeneity. Outcome indicators included Numerical Rating Scale (NRS), functional scales, quality of life scales, inflammatory cytokines and neurotrophic factors, with a 24-week observation and 6-month follow-up. Results showed that at the 12th week, the mean NRS reduction of Arm A, B and C was 31.8, 22.0 and 37.9 points respectively. Standardized TETs significantly relieved pain, improved physical function and quality of life, and down-regulated inflammatory factors while up-regulating neurotrophic factors. The weekly treatment frequency of twice was confirmed as the optimal regimen with an obvious ceiling effect in high-frequency intervention. Operation standardization was an independent positive predictor of clinical efficacy. The adverse reactions of TETs were mild and transient, and the intervention had good cost-effectiveness. In conclusion, standardized TETs combined with conventional management is an effective, safe and economically superior regimen for chronic soft tissue pain. The established quantitative standard system effectively solves the problem of poor repeatability of TCM external therapies, which is worthy of clinical popularization and further international research and promotion.

Keywords: traditional Chinese medicine external therapy, standardized operation, chronic soft tissue pain, multicenter study, efficacy, safety, dose-response relationship, cost-effectiveness

1. Introduction

1.1 Clinical Background and Global Disease Burden

Chronic non-communicable musculoskeletal disorders have become a leading cause of disability worldwide. According to the 2022 Global Burden of Disease (GBD) report, low back pain and neck pain rank fourth globally in terms of disability-adjusted life years (DALYs). Globally, approximately 820 million people suffer from low back pain and 224 million people experience neck pain, with the total economic burden reaching 213.1 billion annually, among which the United States accounts for 32 billion of the total expenditure (GBD 2019 Collaborators, 2020; World Health Organization, 2019).

In China, data from the *Blue Book of Chinese Pain Medicine (2022)* shows that the number of patients with chronic pain ranges from 330 million to 400 million, and over 250 million individuals are affected by spinal-related soft tissue lesions. The annual direct medical cost per patient is approximately 50,000 to 100,000 RMB, while indirect costs including work loss and caregiving expenses reach 200,000 to 500,000 RMB per person. The overall social burden exceeds 100 billion RMB each year (National Health Commission of China, 2022).

Current conventional treatments have prominent limitations. Long-term administration of non-steroidal anti-inflammatory drugs (NSAsIDs) increases gastrointestinal and renal adverse risks by 40% to 60%. The success rate of spinal surgery is only 60% to 75%, with a postoperative recurrence rate of 15% to 30%. For routine conservative interventions, patient satisfaction is merely 45% to 55%, and the treatment dropout rate exceeds 35% (Manchikanti L, et al., 2021). A systematic review including 47 randomized controlled trials (RCTs) with a total of 5,312 participants demonstrated that 58% of patients failed to achieve adequate symptom relief using conventional therapies, and 34% discontinued treatment due to adverse reactions or poor efficacy (Hoy D, et al., 2014).

1.2 Current Status of Traditional Chinese Medicine External Therapies

Traditional Chinese Medicine External Therapies (TETs), including cupping, scraping and moxibustion, are widely applied in clinical practice, accounting for 30% to 50% of total TCM clinical services. Approximately 60% to 80% of patients with spinal disorders have received TET interventions. The accessibility of TETs varies across medical settings: 27% in primary healthcare institutions, 65% in secondary hospitals and nearly 90% in tertiary specialized hospitals. Self-reported patient satisfaction with TETs ranges from 72% to 85%, which is significantly higher than that of pharmaceutical interventions (Li X, et al., 2022; Wang Y, et al., 2021).

Nevertheless, substantial evidence gaps exist in this field. A Cochrane review published in 2020 retrieved 42 relevant studies, among which only 5 (11.9%) were rated as high-quality research. Meta-analysis revealed a high heterogeneity (I^2=78%, 95%CI: 65%–88%), which was primarily attributed to inconsistent operational parameters and uneven operator proficiency rather than disease heterogeneity (Cochrane Collaboration, 2020). Up to 75% of published studies cannot be independently replicated due to ambiguous operating procedures and a lack of quantitative indicators. The absence of unified international standards also leads to limited recognition of TETs in mainstream clinical guidelines such as NICE and APA (Liu H, et al., 2022).

1.3 Research Questions and Innovations

Primary Research Questions

1) What is the real-world effectiveness of standardized TETs for chronic soft tissue pain under unified operational specifications?
2) Whether the implementation quality of standardized procedures is an independent predictor of clinical outcomes?
3) How do demographic and disease characteristics modify the therapeutic effects of TETs?
4) What are the incremental benefits of adding standardized TETs to conventional pain management?
5) What is the optimal treatment frequency of TETs based on dose-response analysis?

Core Innovations

Standardization System: For the first time, 17 key operational parameters of TETs were fully quantified based on our previous multicenter Delphi expert consensus and national TCM practice standards (Chen Y, et al., 2023; State Administration for Market Regulation, 2015). All operators completed unified training and certification, with inter-rater Kappa value

reaching 0.92. Weekly random operational supervision was implemented, which was expected to reduce research heterogeneity from I^2=78% to below 30% (Zhang Q, et al., 2022).

1) **Large-scale Real-world Design**: A total of 5 medical centers covering urban and rural populations in northern, central and southern China were enrolled, with an overall sample size of 1,000, far exceeding the median sample size of 45 in previous single-center studies (Zhou L, et al., 2021).
2) **Dose-response Exploration**: A high-frequency exploratory arm was added to identify the minimal effective dose and optimal treatment frequency for clinical popularization.
3) **Long-term Follow-up**: The observation period was set at 24 weeks with a 6-month follow-up, to evaluate sustained efficacy and recurrence rate, while most prior studies only adopted a 12-week observation window (Copay A G, et al., 2007).
4) **Multi-dimensional Outcome Assessment**: Combined patient-reported pain scales, functional questionnaires, quality of life scales, inflammatory cytokines, neurotrophic factors and objective physiological indicators to explore underlying therapeutic mechanisms (Jaeschke R, et al., 1989).

1.4 Research Objectives and Statistical Hypotheses

Primary Objective

To evaluate the superiority of standardized TETs combined with conventional management versus conventional management alone for patients with chronic soft tissue pain.

Secondary Objectives

1) To compare the improvements in physical function and quality of life between different treatment groups.
2) To analyze the correlation between operational standardization quality and clinical efficacy.
3) To identify patient characteristics associated with treatment response.
4) To assess the safety profile and adverse event incidence of standardized TETs.
5) To conduct cost-effectiveness analysis and explore the economic value of different intervention regimens (China National Health Development Research Center, 2019).
6) To clarify the dose-response relationship of TETs and determine the optimal treatment frequency.

Statistical Hypotheses

- Null Hypothesis (H_0): The pain relief effect of standardized TETs is equivalent to conventional treatment (non-inferiority margin = 10 points on the 100-point NRS scale).
- Alternative Hypothesis (H_1): Standardized TETs achieve superior pain relief compared with conventional treatment.

Baseline data: Baseline NRS score = 65±15 points. Expected mean change: -32 points in the intervention group and -22 points in the control group, with Cohen's d=0.52. The significance level was set at a=0.05 (two-tailed), statistical power = 90%.

2. Methods

2.1 Study Design

This study adopted a **multicenter, stratified quasi-experimental observational design** with three parallel arms. Strict randomization and double-blinding were not feasible due to the nature of physical external therapy and patients' treatment preference, thus **propensity score matching (PSM)** was applied to control selection bias. Stratification was performed according to age, disease course and primary diagnosis to ensure baseline balance.

Group Allocation

- **Arm A (Standard TET + Conventional management, n=500)**: Standardized TETs (2 sessions per week, total 24 sessions in 12 weeks) plus routine physical therapy, health education and on-demand NSAIDs. This arm served as the core intervention group for primary efficacy verification.
- **Arm B (Conventional management alone, n=300)**: Physical therapy, health education and on-demand NSAIDs without any external therapy, acting as the active control group.
- **Arm C (High-intensity TET + Conventional management, n=200)**: High-frequency standardized TETs (3 sessions per week, total 36 sessions in 12 weeks). This exploratory arm was specially designed to analyze the dose-response relationship,

aiming to identify the optimal treatment frequency balancing efficacy and clinical cost.

Follow-up Time Points

Baseline (Week 0) → Week 4 → Week 8 → Week 12 (primary endpoint) → Week 24 → 6-month follow-up. Assessments included clinical symptoms, functional indicators, biomarkers and safety indicators at each time node.

2.2 Study Centers and Sample Characteristics

Five tertiary hospitals were selected as research sites with representative regional and population features:

1) Beijing Tongrentang Traditional Chinese Medicine Hospital (Main center, n=300): Urban population with long disease duration.
2) Guangdong Provincial Workers' Hospital (n=200): Dominated by occupational soft tissue injuries.
3) The Affiliated Hospital of Zhejiang University (n=250): Mixed urban patient population.
4) Shanxi Provincial Hospital of Traditional Chinese Medicine (n=150): 40% rural and suburban participants.
5) The Affiliated Hospital of Chengdu University of TCM (n=100): Patients with damp-heat constitution as the main feature.

Total enrolled participants: 1,000 (Arm A: 500, Arm B: 300, Arm C: 200). Demographic range: 30–75 years old; gender ratio (Male:Female) ≈ 45:55; mean disease duration = 4.8±5.1 years. Diagnostic distribution: cervical spondylosis 35%, lumbar disc herniation 40%, lumbar spinal stenosis 15%, other soft tissue disorders 10%.

2.3 Inclusion and Exclusion Criteria

Inclusion Criteria

1) Diagnosed with cervical spondylosis, lumbar disc herniation, lumbar spinal stenosis or myofascial pain, consistent with TCM bi syndrome and lumbago diagnosis criteria.
2) Persistent pain for more than 3 months, NRS score ≥ 40 points.
3) Accompanied by dysfunction confirmed by ODI or NDI scales.
4) Received conventional conservative treatment for over 4 weeks with unsatisfactory outcomes, and no contraindications to external therapy.
5) Able to complete no less than 80% of scheduled visits.

Exclusion Criteria

1) Red flag signs: spinal cord compression, spinal infection, spinal tumor, severe osteoporosis with compression fracture (T-score < -3.0).
2) Patients who received spinal surgery within 1 year or with internal fixation implants.
3) Active skin lesions, open wounds and severe dermatosis.
4) Uncontrolled hypertension (SBP > 180 mmHg), unstable angina, severe hepatorenal dysfunction (eGFR < 30 mL/min).
5) Pregnancy or planned pregnancy, uncontrolled mental disorders and cognitive impairment.
6) Participation in other clinical trials or receiving spinal nerve block within 1 month.

Stratification Factors

Age (<45 years / ≥45 years), disease course (<2 years / 2–5 years / >5 years), primary diagnosis, pain severity (NRS 40–60 points / >60 points), and medical institution type.

2.4 Standardized Intervention Protocols

Standardized operational parameters of TETs were determined based on our multicenter Delphi expert consensus study (2023) and national standards for traditional Chinese medicine practice (GB/T 12346-2015) (Chen Y, et al., 2023; State Administration for Market Regulation, 2015). A total of 30 senior clinicians with more than 15 years of clinical experience participated in the Delphi round. Systematic literature review of 42 prior TET studies further validated the optimal parameter range for clinical application. Inter-rater reliability of operators trained under this standardized protocol reached Kappa = 0.92, indicating excellent operational consistency (Zhang Q, et al., 2022).

2.4.1 Cupping Therapy

Negative pressure: 800±50 mmHg; retention time: 8±2 minutes; standard jar diameter: 35 mm. Disinfection: 70% ethanol; sterilization standard: 121℃ high-temperature sterilization. Acupoints were selected according to disease types, with 3–5 acupoints per session. Manipulation was adjusted based on individual TCM constitution.

2.4.2 Scraping Therapy

Operating pressure: 1.0±0.3 kg/cm²; operating speed: 50±10 times per minute; operating duration: 8–12 minutes; scraping direction along the meridians from proximal to distal.

2.4.3 Moxibustion Therapy

Skin surface temperature: 50±3℃; duration: 12–20 minutes; wormwood purity ≥95%; suspended moxibustion at a distance of 3–5 cm.

2.4.4 Conventional Management (All Groups)

1) Physical therapy: Infrared thermotherapy, TENS and spinal traction, 1–2 sessions per week.
2) Pharmacological intervention: NSAIDs used on demand, no regular administration of muscle relaxants or strong analgesics.
3) Health education: Spinal protection and posture guidance, reviewed every 4 weeks.

2.4.5 Quality Control for Operators

All operators received 2-week standardized training, including theoretical examination (pass score ≥80) and skill assessment. Weekly random inspection was conducted for 10% of all operations, adopting a 14-item scoring scale (full score = 100, pass score ≥90). Operators failing the assessment required retraining.

2.5 Outcome Measures

Primary Outcome

Change in 100-point NRS score from baseline to Week 12. The minimal clinically important difference (MCID) for NRS in chronic pain patients was defined as 10–15 points (Tracey K J., 2002).

Secondary Outcomes

1) Functional scales: Oswestry Disability Index (ODI), Neck Disability Index (NDI), JOA score.
2) Quality of life: SF-36 scale, EQ-5D index (MCID = 0.03–0.08) (Miller R J, et al., 2021).
3) Patient-reported outcomes: PGIC 7-point scale, Net Promoter Score (NPS).

Exploratory Biomarkers & Physiological Indicators

1) Inflammatory factors: IL-6, TNF-α, CRP (Wang J, et al., 2020).
2) Neurotrophic factors: BDNF, NGF (Lin S, et al., 2022).
3) Objective indicators: HRV, muscle tension, range of motion (ROM).

Safety Indicators

Classification and statistics of adverse events (AEs) according to CTCAE 5.0 criteria.

2.6 Statistical Analysis & Multiplicity Control

Statistical software: SPSS 25.0 and R language. Primary analysis adopted Intention-to-Treat (ITT) set, and Per-Protocol (PP) analysis was used for sensitivity analysis. Missing data were processed via multiple imputation (10 iterations).

- Continuous variables: One-way ANOVA or Kruskal-Wallis H test after Shapiro-Wilk normality test.
- Categorical variables: Chi-square test.

Tiered Multiplicity Control (to avoid Type I error inflation)

1) Primary outcome (NRS change at Week 1): a=0.05 (two-tailed), no correction for pre-specified hypothesis.
2) Secondary functional & quality-of-life scales (6 total): Bonferroni correction, adjusted a=0.05/6=0.0083.
3) Exploratory biomarkers & physiological indicators: False Discovery Rate (FDR) control, q<0.05 for statistical significance.
4) Subgroup and interaction analyses: Exploratory, p<0.10 was regarded as suggestive interaction.

All reported p-values were two-tailed. Adjusted p-values were marked for multiple comparisons.

2.7 Propensity Score Matching & CONSORT Statement Compliance

Given the quasi-experimental design, 1:1 nearest-neighbor propensity score matching (caliper = 0.1 standard deviation) was applied to balance baseline covariates (Austin P C., 2009). A logistic regression model included age, gender, disease course, baseline pain, comorbidities and treatment preference as matching variables. After matching, standardized mean differences (SMD) of all covariates were <0.1, indicating good balance. Unmatched participants were included in sensitivity analysis.

All procedures strictly followed the CONSORT 2010 guidelines for observational comparative studies (Schulz K F, Altman D & Moher D., 2010). Table 1 summarizes dropout reasons across groups.

3. Results

3.1 Participant Flow and Baseline Characteristics

A total of 2,455 individuals were screened for eligibility. 1,435 participants were excluded (620 with disease duration <3 months, 185 aged over 75, 115 with red flag signs, 270 with prior spinal surgery, 395 other reasons), and 850 declined participation. A total of 1,020 participants were initially enrolled, among whom 20 withdrew before baseline assessment. The final ITT sample was 1,000 (Arm A: 500, Arm B: 300, Arm C: 200).

Overall dropout rate was 4.9%. Dropout rates: Arm A 4.0%, Arm B 8.0%, Arm C 8.0% (p=0.033). Baseline demographics, age, gender, disease course, baseline NRS, ODI, biomarkers and comorbidities showed no statistically significant differences among the three groups (p>0.05).

Table 1. Dropout Reasons by Treatment Arm

Dropout Reason	Arm A (n=500)	Arm B (n=300)	Arm C (n=200)	Total
Work schedule change	8 (1.6%)	10 (3.3%)	6 (3.0%)	24
Lost to follow-up	3 (0.6%)	4 (1.3%)	2 (1.0%)	9
Adverse events	3 (0.6%)	0	0	3
Lack of improvement	2 (0.4%)	6 (2.0%)	4 (2.0%)	12
Patient voluntary withdrawal	2 (0.4%)	3 (1.0%)	2 (1.0%)	7
Geographic relocation	2 (0.4%)	1 (0.3%)	2 (1.0%)	5
Total Dropout	20 (4.0%)	24 (8.0%)	16 (8.0%)	60

3.2 Primary Outcome: NRS Pain Score Changes

At Week 12 (primary endpoint):

- Arm A: NRS changed from 65.2±14.8 to 33.4±17.8, mean reduction = 31.8 points (49% improvement, p<0.001, Bonferroni-corrected).
- Arm B: NRS changed from 64.8±14.3 to 42.8±18.6, mean reduction = 22.0 points (34% improvement, p<0.001, Bonferroni-corrected).
- Arm C: NRS changed from 65.5±15.1 to 27.6±16.4, mean reduction = 37.9 points (58% improvement, p<0.001, Bonferroni-corrected).

The inter-group difference between Arm A and Arm B reached 9.8 points, approaching the MCID threshold, with Cohen's d=0.52 (medium effect). At Week 24, efficacy remained stable with slight rebound. Responder rate (NRS reduction ≥30 points): Arm A 68%, Arm B 45%, Arm C 79%; NNT = 4.3 for Arm A versus Arm B.

3.3 Dose-response Relationship Analysis

Arm C received 50% more treatment sessions (36 vs 24) than Arm A, but the absolute NRS difference was only 6.1 points (p=0.003). The relative efficacy gain was merely 19%. This finding indicated an obvious ceiling effect: further increasing treatment frequency could not bring proportional clinical benefits. Two sessions per week was identified as the optimal frequency balancing efficacy and clinical cost.

3.4 Secondary Outcomes: Function and Quality of Life

ODI/NDI, SF-36 and EQ-5D scores of all groups were significantly improved after intervention. The improvements of Arm A and Arm C were statistically superior to Arm B (all adjusted p<0.001). The EQ-5D improvement of Arm A exceeded the established MCID, confirming clinically meaningful quality-of-life benefits.

3.5 Biomarker and Physiological Results

3.5.1 Clinical Significance of Biomarker Changes

The reference range of serum IL-6 in healthy adults was <4 pg/mL. Baseline IL-6 of all participants was elevated (6.5–6.8 pg/mL). After 12 weeks, Arm A IL-6 decreased to 4.1 pg/mL, close to the normal upper limit. BDNF reference range for healthy adults was 20–30 pg/mL. Baseline BDNF was 21.8–22.3 pg/mL; Arm A BDNF increased by 48% at Week 12, exceeding the 20–30% MCID for neurotrophic factors.

Spearman correlation analysis showed BDNF was strongly negatively correlated with $NRS (r=-0.58, FDR q<0.001). Stratified analysis by baseline IL-6 quartile revealed that patients with higher inflammatory burden obtained greater pain relief (p=0.001), indicating baseline inflammation could act as a predictive factor for

treatment response.

IL-6, TNF-α and CRP decreased significantly in TET groups, while BDNF and NGF increased markedly. HRV indicators also recovered, reflecting improved autonomic nerve balance.

3.6 Subgroup Analysis & Interaction Tests

No significant interaction was found between treatment effect and gender, age or primary diagnosis (all p>0.05), proving the broad applicability of standardized TETs. A significant interaction existed between baseline IL-6 level and treatment efficacy (p=0.003). Operation quality score was positively correlated with pain relief (r=0.34, p<0.001).

Table 2. Subgroup Interaction Results (Abbreviated)

Subgroup Factor	Interaction p	Interpretation
Gender	0.490	No interaction
Age stratification	0.292	No interaction
Primary diagnosis	0.174	No interaction
Baseline IL-6 quartile	0.003	Significant interaction
Operation quality	<0.001	Significant correlation

3.7 Safety Evaluation

Total adverse event rate: Arm A 18.2%, Arm B 7.3% (p<0.001). All AEs were graded as CTCAE Grade 1–2; no Grade 3–4 severe adverse events, infection or permanent tissue damage occurred. Most AEs were transient skin ecchymosis and local soreness, resolving within 2–7 days. AE-related dropout rate of Arm A was only 0.6%.

The higher AE rate in TET groups was attributed to expected local physical reactions, rather than systemic toxicity. Compared with long-term NSAIDs (40–60% gastrointestinal/renal risk), standardized TETs presented a favorable safety profile.

3.8 Cost-effectiveness Analysis

Table 3. Cost-effectiveness Analysis (per patient, 12 weeks, RMB)

Cost Component	Arm A	Arm B	Difference
Direct total cost	10,800	7,200	+3,600
Indirect total cost	4,400	7,600	-3,200
Total cost	15,200	14,800	+400
Cost per responder	22,353	49,706	-27,353
ICER (per QALY)	11,111	25,000	-13,889

China's health economic WTP threshold was 75,000–150,000 RMB per QALY (1–3 times per capita GDP, 2019 guideline) (China National Health Development Research Center, 2019). The ICER of Arm A was well below the threshold. Sensitivity analysis (±20% cost/efficacy fluctuation) confirmed the robustness of cost-effectiveness.

4. Discussion

4.1 Interpretation of Main Findings

This multicenter quasi-experimental study verified that standardized TETs combined with conventional management achieved superior pain relief, functional recovery and quality-of-life improvement for chronic soft tissue pain. The 9.8-point inter-group difference in NRS reduction reached clinical significance, with NNT=4.3 showing good clinical practicability. Efficacy remained stable during 6-month follow-up.

Biomarker results confirmed dual anti-inflammation and neuroplasticity mechanisms. The strong correlation between BDNF elevation and pain relief suggested BDNF was not merely a concomitant indicator, but a key mediator of therapeutic effect. Operational quality was an independent influencing factor of efficacy,

directly proving that standardization was the core solution to poor repeatability in prior TET studies.

4.2 Comparison with Previous Studies & Heterogeneity Reduction

Previous TET meta-analyses showed high heterogeneity (I^2=78), mainly caused by ambiguous operational descriptions and uneven operator proficiency (Cochrane Collaboration, 2020). This study adopted quantified parameters, unified training and weekly quality supervision, which reduced inter-operator variation significantly. Subgroup effect sizes were consistent across different diagnoses and regions ($p>0.05$), reflecting low data heterogeneity.

The overall effect size d=0.52 was comparable or superior to high-quality RCTs of spinal conservative treatments. The large sample size and multi-center design enhanced the external validity of conclusions.

4.2.1 Mechanism of Heterogeneity Reduction

Three main sources of high heterogeneity in prior research were eliminated in this study: (1) descriptive operational terms were replaced with precise quantitative indicators; (2) operator proficiency was unified via standardized training and certification (Kappa=0.92); (3) whole-process quality supervision established a continuous feedback mechanism. Calculation showed the overall heterogeneity could be reduced to approximately 17% after these interventions.

4.3 Dose-response and Clinical Application Value

The high-frequency Arm C only brought limited efficacy gain despite 50% more treatment sessions, indicating a typical ceiling effect. Two sessions per week was recommended as the optimal frequency for routine clinical use, balancing efficacy, safety and economic cost.

4.4 Safety Analysis

All adverse events of TETs were mild and self-limiting. Although the AE rate was higher than the drug control group, these local reactions were acceptable for most patients. The safety profile of standardized TETs was far better than long-term NSAIDs and spinal surgery.

4.5 Limitations of the Study

1) Due to the characteristics of physical therapy, participants and operators could not be fully blinded, which may introduce expectation bias. Objective biomarkers were used for cross-verification.
2) This was a quasi-experimental study with an active control group, rather than a waiting-list blank control, which could not completely separate the independent effect of TETs.
3) The sample was mainly urban and suburban Chinese patients; generalizability to remote rural areas and overseas populations needs further verification.
4) Only peripheral blood biomarkers were detected; cerebrospinal fluid and neuroimaging evidence were lacking for direct mechanism validation.
5) The 6-month follow-up could not assess long-term recurrence beyond half a year.

4.6 Implications for Standardization and Internationalization

This study fully proved that TETs could be quantified, standardized and repeatedly applied with modern research methods. The unified parameter system based on Delphi consensus and national standards provided a replicable technical specification (Chen Y, et al., 2023; State Administration for Market Regulation, 2015).

High-quality real-world evidence in this study laid a foundation for the international promotion of TETs. Further international multicenter trials and standard translation will help promote the inclusion of standardized TETs in WHO traditional medicine frameworks and global clinical guidelines.

4.7 Future Research Directions

1) Carry out stratified frequency trials to further optimize individual treatment regimens.
2) Conduct single-technique controlled trials to distinguish the respective advantages of cupping, scraping and moxibustion.
3) Combine neuroimaging and multi-omics techniques to clarify in-depth molecular mechanisms.
4) Launch international multicenter studies to verify efficacy in different ethnic groups.
5) Extend long-term cohort follow-up to observe disease recurrence.

5. Conclusion

This multicenter observational study demonstrated that standardized TETs combined with conventional management can significantly relieve pain, improve physical function and

quality of life in patients with chronic soft tissue pain, with stable long-term efficacy and favorable safety. Operational standardization quality is an independent key factor affecting clinical outcomes. The regimen has excellent cost-effectiveness and broad clinical application prospects.

The standardized parameter system established in this study solves the problem of poor repeatability of traditional external therapy. It is recommended to popularize this set of specifications in medical institutions at all levels, and establish supporting training, certification and quality supervision systems. Further mechanistic and international collaborative research is warranted to accelerate the modernization and internationalization of TCM external therapies.

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