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ORIGINAL RESEARCH

Exploring the Rules of Related Parameters in Transcutaneous Electrical Nerve Stimulation for Cancer Pain Based on Data Mining

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ABSTRACT

Introduction: This study aims to investigate the regularity of related parameters in the treatment of cancer pain using transcutaneous electrical nerve stimulation (TENS).
Methods: A comprehensive literature search was conducted in databases such as PubMed, Cochrane Library, Embase, Web of Science, OVID, CNKI, CBM, VIP, and WANNGFANG from inception up to December 2022. A database was established, and data mining techniques were applied to analyze the relevant TENS parameters.
Results: A total of 27 articles were included, encompassing nine current frequencies, four retention times, four treatment frequencies, and two wave types. On the basis of the analysis of parameter association rules, the most closely related parameter combination for clinical TENS in the treatment of cancer pain was a current frequency of 2/100 Hz, a treatment frequency of once a day, a retention time of 30 min, and the dilatational wave. Moreover, the study involved 22 acupuncture points distributed along 13 meridians. According to the analysis of acupuncture point association rules, Hegu (LI04), Zusanli (ST36), and Sanyinjiao (SP06) were the most closely related acupuncture points and could be used in combination for clinical TENS in cancer pain treatment. Furthermore, cluster analysis was conducted on acupuncture points with a frequency ≥ 5, resulting in three categories: the first category included Sanyinjiao (SP06), Zusanli (ST36), Hegu (LI04), Jiaji point, and Neiguan (PC06); the second category included Ashi point; and the third category included Back shu point.
Conclusion: In the treatment of cancer pain using TENS, it is recommended to use a current frequency of 2/100 Hz, a treatment frequency of once a day, a retention time of 30 min, and the dilatational wave. The electrode positions were primarily selected from Ashi point, Back shu point, Sanyinjiao (SP06), Zusanli (ST36), Hegu (LI04), Jiaji point, and Neiguan (PC06) to achieve the best analgesic effect.

Quan-yao Li and Wen-xiao Yang contributed equally to this study.

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Keywords: Transcutaneous electrical nerve stimulation; Cancer; Cancer pain; Data mining; Parameters

Key Summary Points

The use of three-step pain relief drugs for cancer pain treatment can lead to adverse reactions.

Transcutaneous electrical nerve stimulation (TENS) is effective in alleviating cancer pain and has been proven to be safe without adverse reactions. However, the current practice of TENS for cancer pain lacks standardization.

This study employs data mining analysis to explore the relevant parameter rules of TENS in the treatment of cancer pain. It summarizes the principles of acupoint selection to guide clinical treatment of cancer pain with TENS.

Recommended parameters for TENS treatment of cancer pain include a current frequency of 2/100 Hz, a treatment frequency of once a day, a retention time of 30 min, and the use of dilatational wave. Effective electrode positions include Ashi point, Back shu point, Sanyinjiao (SP06), Zusanli (ST36), Hegu (LI04), Jiaji point, and Neiguan (PC06) to achieve optimal analgesic effects. These parameters have been shown to effectively produce the best analgesic effects. Additionally, these findings provide guidance for the design of related clinical studies.

INTRODUCTION

Cancer pain is a common complication of malignant tumors and significantly impacts the quality of life for patients with cancer. Current research reports indicate that approximately 90% of patients with advanced malignant tumors experience varying degrees of cancer pain [1]. The World Health Organization (WHO) has recognized the reduction of cancer pain in patients as a priority in palliative treatment of malignant tumors [2]. Therefore, actively improving the management of cancer pain is of great significance for both the antitumor treatment and the overall quality of life for patients with cancer. Currently, the treatment of cancer pain primarily relies on the three-step cancer pain relief method recommended by the WHO [3], which has shown significant efficacy for patients with moderate to severe pain. However, long-term use of analgesic drugs within this approach can lead to varying degrees of adverse reactions, including drug dependence and addiction [4, 5], which can render patients unable to tolerate the treatment. Studies have shown that over 40% of patients discontinue treatment because of concerns about adverse drug reactions, resulting in the further progression of cancer pain and a loss of control [6–8]. Therefore, actively seeking effective treatments for cancer pain that can alleviate the risk of addiction is an urgent problem in clinical practice.

Transcutaneous electrical nerve stimulation (TENS) is an electrotherapy method that delivers specific low-frequency pulse currents into the human body through the skin to treat pain. It finds wide applications in various treatments, such as acute and chronic pain management and preoperative analgesia [9–11]. The National Comprehensive Cancer Network (NCCN) guidelines for adult cancer pain recommend acupuncture, TENS, and three-step analgesic drugs as the main interventions [12]. Unlike traditional electrical stimulation, which primarily targets motor fibers, TENS predominantly stimulates sensory fibers. Clinical studies have confirmed the significant analgesic effects of TENS in alleviating cancer pain, providing added benefits of safety and efficacy without adverse reactions [13, 14]. However, the application of TENS for cancer pain currently lacks standardization. Instrument parameters (current frequency, wave, retention time, and treatment frequency) and acupoint selection vary for different levels of cancer pain [15], hindering a comprehensive understanding of the role of TENS in cancer pain management. Therefore, this study aims to explore the relevant parameter patterns of TENS in cancer pain treatment through data mining analysis and summarize the principles of acupoint selection. The findings will provide evidence-based guidance for the clinical application of TENS in the management of cancer pain.

MATERIALS AND METHODS

Literature Sources

Search strings with the terms Transcutaneous electrical acupoint stimulation, TEAS, Transcutaneous electrical nerve stimulation, TENS, Electrical stimulation, Electrotherapy, Bioelectrical stimulation, Cancer pain, Cancer-associated pain, Neoplasm-related pain, Oncological pain, Tumor-related pain, Cancer-related Pain, and Neoplasm associated pain were used to identify literature on the treatment of cancer pain by transcutaneous electrical nerve stimulation in the following databases: Pubmed, Cochrane Library, Embase, Web of Science, OVID, CNKI, CBM, VIP, and WANNGFANG. The search was conducted from inception up to December 2022.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Inclusion Criteria

1. Research objects: Patients diagnosed with malignant tumors by cytology or pathology, and experiencing cancer pain, without restrictions on gender, age, race, or tumor types.
2. Study type: Clinical randomized controlled trials.
3. Intervention measures: The control group received conventional analgesics alone, while the treatment group received TENS in addition to conventional analgesics.

Exclusion Criteria

1. Narrative reviews, systematic reviews (meta-analysis), scoping reviews, etc.
2. Basic research involving cell or animal experiments.
3. Literature with duplicated data.
4. Literature with uncertain clinical efficacy.

Database Establishment

Two researchers independently screened the literature on the basis of the aforementioned inclusion and exclusion criteria and cross-checked their screening results. Any disagreements were resolved through discussion with a third researcher. Data meeting the inclusion and exclusion criteria were extracted from the literature and included the article title, publication date, first author's name, and relevant TENS parameters, such as current frequency, retention time, treatment frequency, wave type, and acupuncture points.

Quality Evaluation

The quality of the included literature was assessed using bias risk assessment tools, which included evaluating randomization methods, allocation concealment, single and double-blinding, data integrity, selective reporting of results, and other biases. Each criterion was classified as low risk, unclear, or high risk.

Statistical Analysis

Statistical descriptive analysis of the relevant TENS parameters in the included literature was performed using Excel 2013. The association rules of relevant parameters were analyzed using the Apriori algorithm in SPSS Modeler 18.1 software. Cluster analysis of acupuncture point prescriptions with a frequency ≥ 5 was conducted using the clustering method, and a dendrogram of acupuncture points was generated using SPSS 26.0 software.

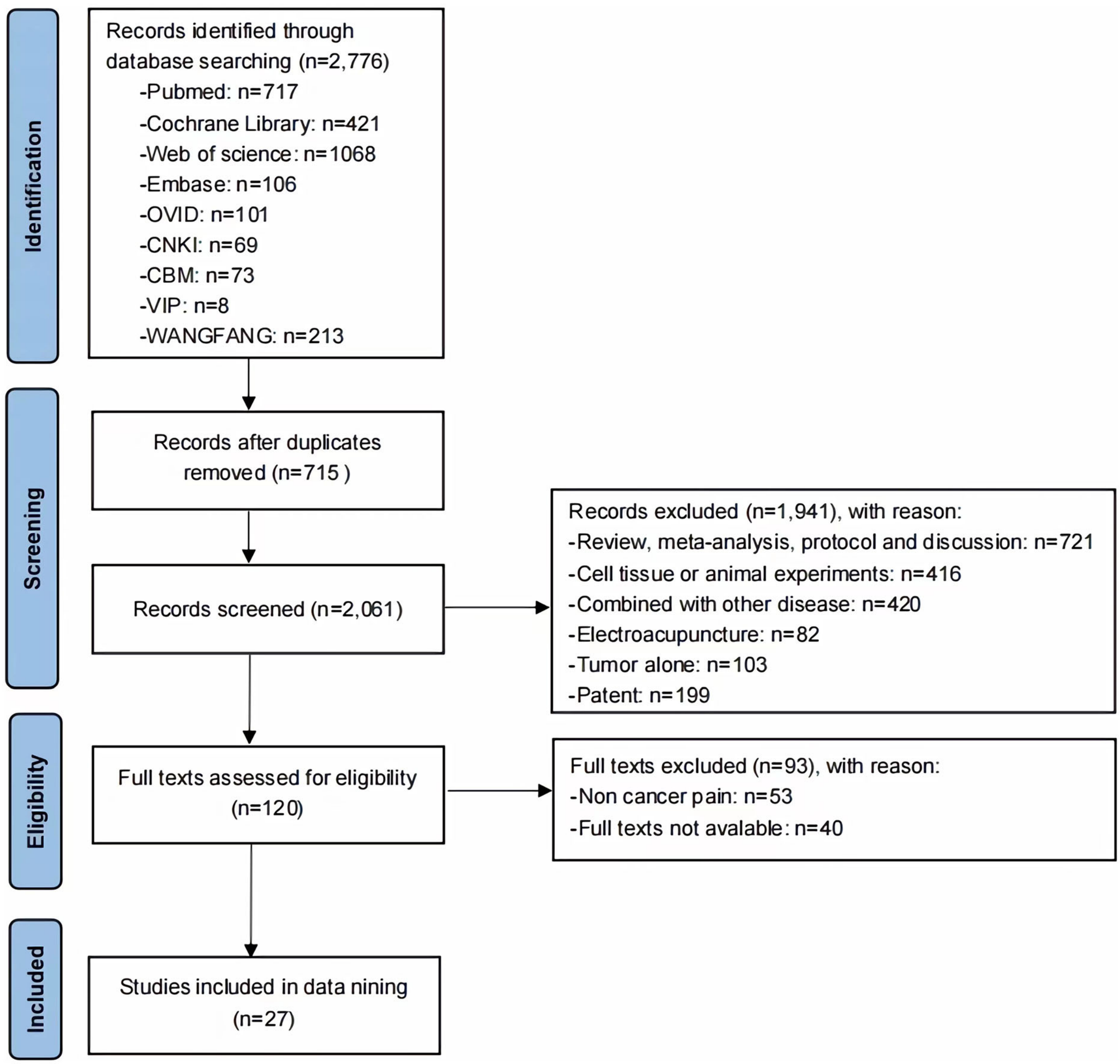

Fig. 1 Flowchart

RESULTS

Literature Retrieval Results

Following the retrieval strategy, a total of 2776 articles were retrieved. NoteExpress 3.6.0 was utilized to organize the literature, resulting in the identification and exclusion of 715 duplicate or repetitive publications. Subsequently, the remaining literature underwent further screening, and 1941 articles were excluded on the basis of their titles and abstracts. Finally, a comprehensive assessment of the full texts of the remaining 120 articles was conducted, and 27 articles were ultimately included in the analysis (Fig. 1, Table 1).

Among the 27 included articles, 22 articles [16–20, 23–38, 41] reported randomized assignments, while 5 articles [9, 21, 22, 39, 40] did not specify the assignment scheme. Three articles [19, 20, 37] mentioned assignment concealment. Eight articles [17, 18, 20, 34–37, 39] incorporated blinding methods. The data from all 27 articles were complete, and there

Table 1 Basic features of the included literature

Number	Included literature	Retention time (min)	Frequency of current (Hz)	Wave	Frequency of treatment
1	Wang (2021) [16]	30	2/100	Not mentioned	Once a day
2	Du (2019) [17]	30	2/100	Dilatational wave	Once a day
3	He (2019) [18]	30	2/100	Not mentioned	Twice a day
4	Liu (2018) [19]	30	2/100	Dilatational wave	Twice a day
5	Bao (2016) [20]	30	2/100	Dilatational wave	Twice a day
6	He (2012) [21]	30	Not mentioned	Dilatational wave	Once a day
7	Wang (2011) [22]	30	2/100	Dilatational wave	Twice a day
8	Zhang (2019) [23]	30	Not mentioned	Dilatational wave	Once a day
9	Deng (2017) [24]	Not mentioned	Not mentioned	Not mentioned	Not mentioned
10	Wu (2017) [25]	Not mentioned	Not mentioned	Not mentioned	Not mentioned
11	Wang (2016) [26]	20	5–100	Not mentioned	Once a day
12	Li (2016) [27]	30	2/100	Dilatational wave	Once a day
13	Weng (2015) [28]	30	2/100	Dilatational wave	Once a day
14	Li (2015) [29]	30	2/100	Dilatational wave	Once a day
15	Li (2014) [30]	30	2/100	Dilatational wave	Once a day
16	Chen (2002) [31]	30	2/100	Not mentioned	Once a day
17	Pu (2021) [32]	30	5–100	Not mentioned	Twice a day
18	Nakano (2020) [33]	30	100	Not mentioned	Once a day
19	Siemens (2020) [34]	30	100	Continuous wave	Once a day
20	Lee (2019) [35]	30	125	Continuous wave	Once a week
21	Loh (2015) [9]	30	120	Continuous wave	Once a day

Table 1 continued

Number	Included literature	Retention time (min)	Frequency of current (Hz)	Wave	Frequency of treatment
22	He (2021) [36]	30	2/100	Not mentioned	Twice a day
23	Chou (2021) [37]	20	10/80	Dilatational wave	Once a day
24	Zhang (2016) [38]	30	2/100	Dilatational wave	Twice a day
25	Schleder (2017) [39]	40	10–200	Not mentioned	Once a day
26	Sampaio (2016) [40]	30	10/130	Not mentioned	Once a day
27	Bennett (2010) [41]	60	80	Not mentioned	Twice a week

were no selective reporting results or other biases (Figs. 2 and 3).

Frequency of Current

Frequency of current was mentioned in 23 studies, encompassing nine different frequencies. Among these frequencies, three accounted for more than 5%, listed in descending order of rate of occurrence: 2/100 Hz (56.52%), 100 Hz (8.70%), and 5–100 Hz (8.70%). The overall frequency involvement was 73.91% (Table 2, Fig. 4).

Retention Time

Retention time was mentioned in 25 studies, involving four different retention times. These times, listed in descending order of frequency, were 30 min (84.00%), 20 min (8.00%), 40 min (4.00%), and 60 min (4.00%) (Table 3, Fig. 5).

Frequency of Treatment

Frequency of treatment was reported in 25 studies, encompassing four different treatment frequencies. The frequencies, listed in descending order of rate of occurrence, were once a day (64.00%), twice a day (28.00%), once a week (4.00%), and twice a week (4.00%) (Table 4, Fig. 6).

Wave Frequency

Wave frequency was mentioned in 15 studies, involving two types of waves. These waves, listed in descending order of frequency, were dilatational wave (80.00%) and continuous wave (20.00%) (Table 5).

Analysis of Parameter Association Rules

Using the Apriori algorithm, we analyzed the association rules among the four parameters mentioned above. The minimum support was set to 15, the minimum confidence was set to 80, and the maximum number of preceding items was 2. The results revealed a total of 13 association rules. Notably, the current frequency of 2/100 Hz, treatment frequency of once a day, retention time of 30 min, and utilization of dilatational wave were found to have the closest relationship. This combination of parameters can be considered a classic approach

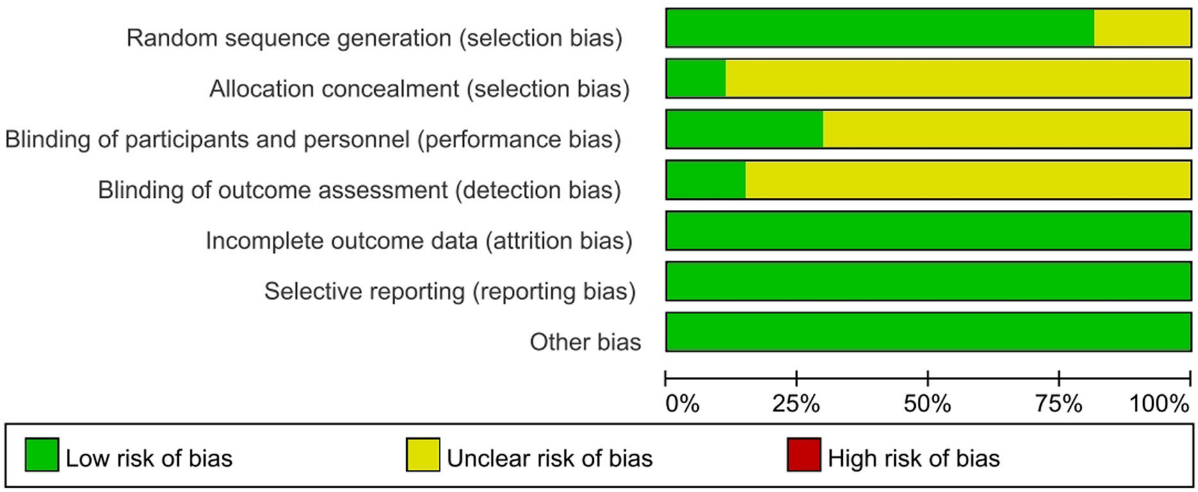

Fig. 2 Risk of bias graph

for the clinical treatment of cancer pain using TENS (Table 6, Fig. 7).

Acupoint Frequency

A total of 22 acupuncture points were analyzed, resulting in a total count of 90 acupoints. Among these, seven acupuncture points had a frequency ≥ 5%. Listed in descending order, they were Zusanli (ST36) (17.78%), Ashi point (13.33%), Hegu (LI04) (12.22%), Sanyinjiao (SP06) (10.00%), Back shu point (8.89%), Jiaji point (5.56%), and Neiguan (PC06) (5.56%). The overall frequency involvement was 73.33% (Table 7).

Meridian Tropism of Acupoints

The analysis included a total of 22 acupoints distributed among 13 meridians. Six meridians had a frequency of at least 10%. In descending order, these meridians were the Foot Yangming Stomach Meridian (18.89%), Ashi Point (13.33%), the Foot Taiyang Bladder Meridian (12.22%), the Hand Yangming Large Intestine Meridian (12.22%), the Hand Jueyin Pericardium Meridian (10.00%), and the Foot Taiyin Spleen Meridian (10.00%). The overall frequency involvement was 76.67% (Table 8).

Analysis of Association Rules of Acupoints

Using the Apriori algorithm to analyze the association rules of acupoints, with a minimum support of 15, minimum confidence of 80, and a maximum number of preceding items of 2, a total of 13 association rules were derived. Among these rules, Hegu (LI04), Zusanli (ST36), and Sanyinjiao (SP06) were found to have the closest relationship. This combination of acupoints can be considered a classic approach in the clinical practice of TENS for treating cancer pain (Table 9, Fig. 8).

Cluster Analysis of Acupoints

Cluster analyses were performed on the acupoints with a frequency ≥ 5% using SPSS software. The results categorized the acupuncture points into three groups. The first category consisted of Sanyinjiao (SP06), Zusanli (ST36), Hegu (LI04), Jiaji point, and Neiguan (PC06). The second category included the Ashi point, while the third category comprised the Back shu point (Fig. 9).

DISCUSSION

Cancer pain, occurring during the development and treatment of malignant tumors, is a

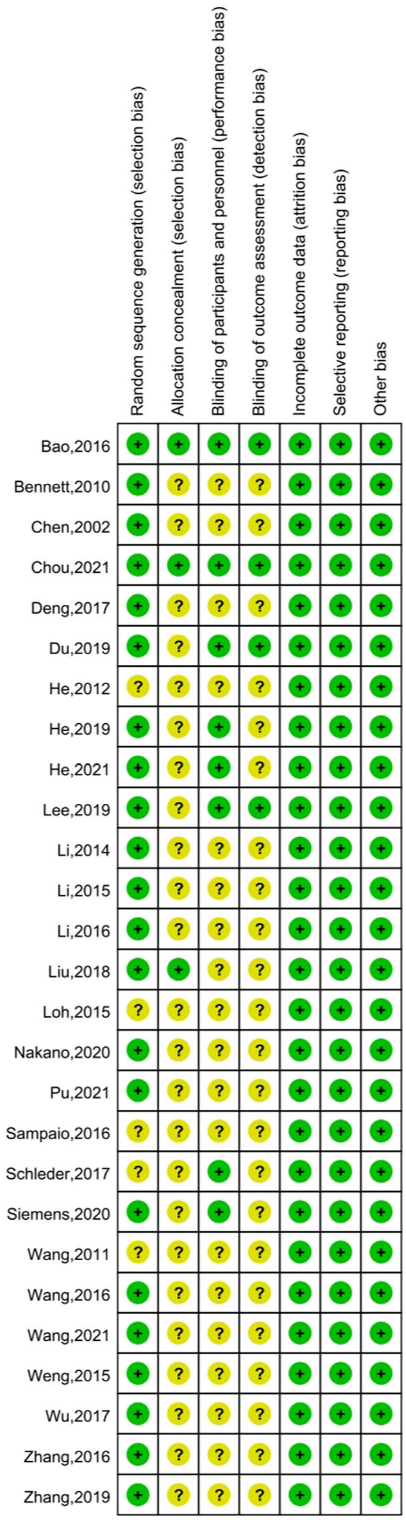

Fig. 3 Risk of bias summary

Table 2 Frequency of current

Number	Frequency of current (Hz)	Count	Frequency (%)
1	2/100	13	56.52
2	100	2	8.70
3	5–100	2	8.70
4	10/130	1	4.35
5	10/80	1	4.35
6	10–200	1	4.35
7	120	1	4.35
8	125	1	4.35
9	80	1	4.35

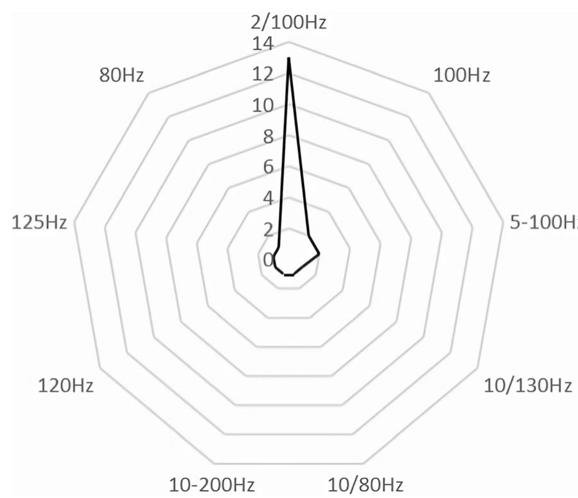

Fig. 4 Frequency of current radar diagram

Table 3 Retention time

Number	Retention time (min)	Count	Frequency (%)
1	30	21	84.00
2	20	2	8.00
3	40	1	4.00
4	60	1	4.00

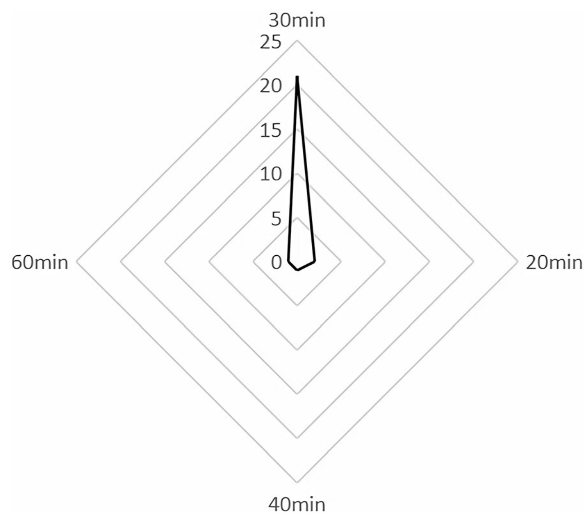

Fig. 5 Retention time radar diagram

Table 4 Frequency of treatment

Number	Frequency of treatment	Count	Frequency (%)
1	Once a day	16	64.00
2	Twice a day	7	28.00
3	Once a week	1	4.00
4	Twice a week	1	4.00

common complication among patients with cancer. The underlying causes of this condition include stimulation of the body's inflammatory response, compression of vital tissues or nerve damage by the tumor leading to neuropathic pain, tumor infiltration and metastasis resulting in bone destruction, and pain caused by anti-tumor treatments. Furthermore, radiotherapy can induce radiation fibrosis, which directly compresses nerves and hinders microvascular flow, causing abnormal nerve function. Nerve tissue compression and damage also contribute to central sensitization and pain [20, 42].

TENS, a non-invasive intervention, has been extensively utilized for diagnosing and treating various acute and chronic pain conditions, demonstrating notable clinical efficacy. TENS has shown particular advantages in the management of cancer pain [18, 43]. Lee et al. [35] applied TENS to patients with cancer undergoing radiotherapy and observed a significant improvement in rest pain related to acute oral mucositis, whereas its effect on motion pain was not significant. Bennett et al. [41] found that TENS can alleviate motion pain in patients with cancer bone metastases.

Currently, the treatment mechanism of TENS is predominantly explained by the gate control theory and the diffuse nociceptive control theory. The gate control theory, proposed by Melzack and Wall [44], postulates a neural regulatory mechanism between spinal dorsal horn glial cells and secondary neuron T cells, which can either facilitate or inhibit sensory nerve impulses from the periphery to the central nervous system, akin to a "gate effect." When TENS generates diverse impulses, it not only reduces the activation of spinal dorsal horn neurons but also inhibits pain transmission at the spinal cord level, decreasing central excitability and effectively closing the gate. Consequently, TENS reduces mechanical and thermal pain, thus achieving analgesia [45–48]. The diffuse nociceptive control theory involves using a noxious stimulus to suppress pain in other regions [49], thereby achieving pain treatment through "treating pain with pain." Studies have indicated a relationship between the analgesic mechanism of TENS and the opioid system [50]. Furthermore, different electrical stimulation frequencies can induce the release of various peptides with differing analgesic effects [51]. Additionally, TENS can relieve pain by regulating cortical blood flow and activating the ascending reticular system of the brainstem [52].

The frequency parameter in TENS plays a vital role in its analgesic effect. Some studies have found that for pain caused by inflammation, high-frequency TENS (100 Hz) exhibits better clinical efficacy compared to low-frequency TENS (2 Hz). However, for pathological pain, low-frequency TENS (2 Hz) yields better clinical outcomes than high-frequency TENS (100 Hz). Regarding cancer pain, there is no significant difference in clinical efficacy between low and high frequencies. Nevertheless, using a combination of 2 Hz and 100 Hz can effectively mitigate tolerance resulting from

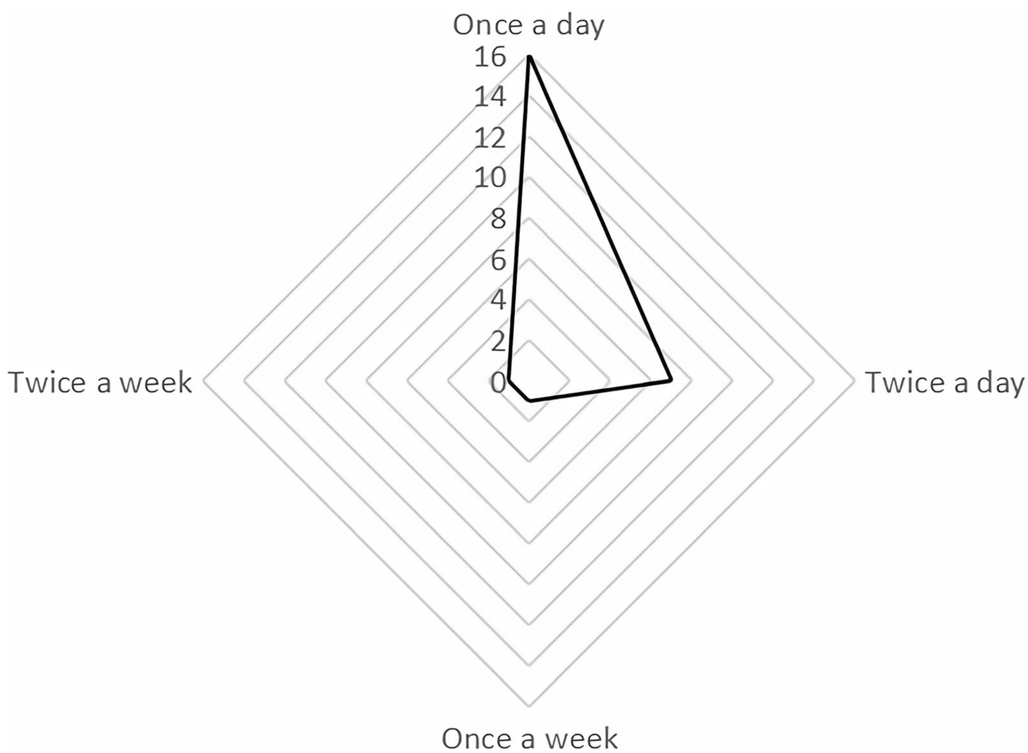

Fig. 6 Frequency of treatment radar diagram

Table 5 Wave frequency

Number	Wave	Count	Frequency (%)
1	Dilatational wave	12	80.00
2	Continuous wave	3	20.00

prolonged stimulation [53, 54]. de Oliveira et al. [55] discovered that TENS low-frequency and high-frequency stimulation increased the levels of endocannabinoids in mouse paws, spinal cords, and dorsolateral gray matter around the aqueduct of the midbrain, effectively alleviating the occurrence and progression of cancer pain. Dailey et al. [56] reported that the use of mixed-frequency (high and low frequency) stimulation can enhance patient tolerance and exhibit a cumulative analgesic effect. Davis et al. [57] also found that the application of both high and low frequencies improves acute pain. Therefore, different current frequencies have distinct neurophysiological mechanisms for analgesia. High-frequency TENS mainly activates Aβ fibers in the superficial subcutaneous layer, regulating spinal cord analgesia, whereas low-frequency TENS predominantly activates Aδ fibers, achieving analgesia by controlling pain [58]. Studies have revealed a close relationship between electrical stimulation and the secretion of opioid peptides in the central nervous system, with different current frequencies leading to the release of different opioid peptides. Specifically, 2 Hz predominantly induces the stimulation of enkephalins and endorphins, while 100 Hz primarily prompts the spinal cord to release dynorphins. Clinical treatment [59] involving alternate stimulation of 2 Hz and 100 Hz significantly enhances the release of enkephalins, endorphins, and dynorphins in the brain and spinal cord, thus elevating the pain threshold, enhancing patient tolerance, and achieving optimal analgesic effects. Consistent with previous studies, the most commonly used current frequency in this study was 2/100 Hz, which is widely employed in clinical practice and effectively alleviates patient pain while increasing their pain threshold.

Table 6 Parameter association rules table

Number	Association rules	Count	Support	Confidence	Lift
1	(Frequency of treatment = Once a day) → (Retention time (min) = 30 min)	16	64	81.25	0.97
2	(Frequency of current (Hz) = 2/100 Hz) → (Retention time (min) = 30 min)	13	52	100.00	1.19
3	(Wave = Dilatational wave) → (Retention time (min) = 30 min)	12	48	91.67	1.09
4	(Wave = Dilatational wave and Retention time (min) = 30 min) → (Frequency of current (Hz) = 2/100 Hz)	11	44	81.82	1.57
5	(Wave = Dilatational wave and Frequency of current (Hz) = 2/100 Hz) → (Retention time (min) = 30 min)	9	36	100.00	1.19
6	(Frequency of treatment = Twice a day) → (Frequency of current (Hz) = 2/100 Hz)	7	28	85.71	1.65
7	(Frequency of treatment = Twice a day) → (Retention time (min) = 30 min)	7	28	100.00	1.19
8	(Frequency of treatment = Twice a day and Retention time (min) = 30 min) → (Frequency of current (Hz) = 2/100 Hz)	7	28	85.71	1.65
9	(Wave = Dilatational wave and Frequency of treatment = Once a day) → (Retention time (min) = 30 min)	7	28	85.71	1.02
10	(Frequency of current (Hz) = 2/100 Hz and Frequency of treatment = Once a day) → (Retention time (min) = 30 min)	7	28	100.00	1.19
11	(Frequency of treatment = Twice a day and Frequency of current (Hz) = 2/100 Hz) → (Retention time (min) = 30 min)	6	24	100.00	1.19
12	(Frequency of treatment = Twice a day and Wave = Dilatational wave) → (Frequency of current (Hz) = 2/100 Hz)	4	16	100.00	1.92
13	(Frequency of treatment = Twice a day and Wave = Dilatational wave) → (Retention time (min) = 30 min)	4	16	100.00	1.19

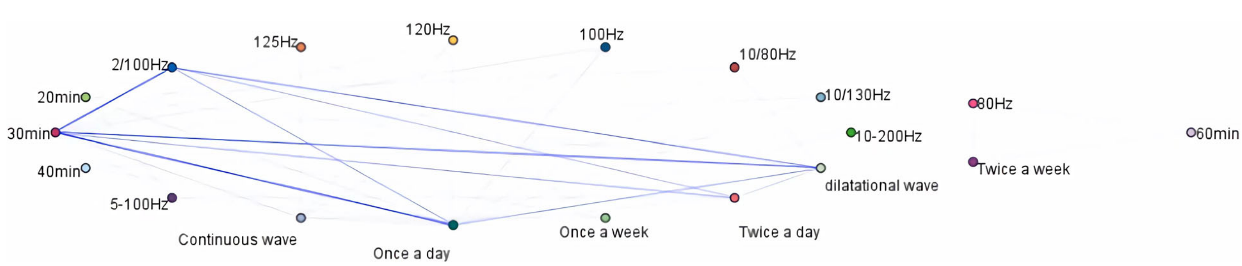

Fig. 7 Network diagram of parameter association rules

In addition to various TENS parameters, treatment retention time and frequency also significantly influence the analgesic effect. Some studies have reported good analgesic effects in approximately 50% of patients with chronic pain after TENS usage for a certain

Table 7 Acupoint frequency

Number	Acupoint	Count	Frequency (%)
1	Zusanli (ST36)	16	17.78
2	Ashi point	12	13.33
3	Hegu (LI04)	11	12.22
4	Sanyinjiao (SP06)	9	10.00
5	Back shu point	8	8.89
6	Jiaji point	5	5.56
7	Neiguan (PC06)	5	5.56

period, while prolonged TENS treatment may lead to patient tolerance and insensitivity to TENS stimulation, resulting in poor analgesic efficacy [60, 61]. Animal experiments have supported these findings. For patients undergoing long-term TENS treatment, it is recommended to use TENS with modulated waves, which induce rhythmic muscle contractions and effectively reduce patient adaptability and tolerance [62]. Chesterton et al. [63] reported that 30 min is the optimal analgesic duration, which, in combination with different frequencies and intensities, achieves optimal hypoalgesic effects. Katirci Kirmaci et al. [64] also found that electrical stimulation once daily for 30 min can reduce pain, enhance functional capacity, and improve the quality of life. The results of this study indicated that the commonly adopted treatment retention time in clinical practice is once daily for 30 min, combined with the dilatational wave as the optimal treatment parameter. This not only effectively alleviates patient pain but also reduces pain tolerance associated with wave changes, thereby enhancing clinical efficacy.

Based on the findings of this study, the optimal TENS parameters for cancer pain predominantly involve a current frequency of 2/100 Hz, treatment frequency of once daily, treatment retention time of 30 min, and the use of the dilatational wave, which elicits the best analgesic effects. For instance, Du et al. [17] combined TENS with opioids for treating cancer pain caused by bone metastases, utilizing the aforementioned parameter combination. The results demonstrated that the combination of TENS and opioids significantly improved cancer pain in patients, reducing opioid dosage and the occurrence of severe pain attacks. Additionally, this combination alleviated adverse reactions, particularly nausea and vomiting. Similarly, Wang et al. [16] employed TENS, low-dose acetaminophen, and oxycodone in patients with bone metastases from lung cancer, employing the aforementioned parameter combination. The study revealed that this combination reduced opiate dosage and facilitated the achievement of a stable blood drug concentration, thus enhancing analgesic effects. Furthermore, the combined therapy significantly reduced the onset of severe pain and improved patients' quality of life. Additionally, Li et al. [27] applied electrical stimulation with the aforementioned parameters for assisting analgesia, observing a significant reduction in pain intensity and improvement in quality of life.

Apart from the aforementioned parameters, TENS electrode placement plays a crucial role in its clinical efficacy. In order to achieve optimal analgesic effects, TENS electrode placement is determined on the basis of the patient's clinical symptoms and TENS type [65]. Traditionally, TENS electrodes are often positioned in the same nerve dermatome as the site of pain. This approach inhibits pain-conducting thin fibers in the same dermatome by activating thick fibers in the corresponding dermatome, thus achieving analgesia [66]. Ekblom et al. [67] compared the efficacy of traditional TENS electrodes placed within and outside the dermatome for alleviating itching and arm pain. The study revealed that TENS placed within the dermatome had notable antipruritic and analgesic effects, whereas TENS placed outside the dermatome did not yield significant improvement. However, a recent study [68] found that TENS distal stimulation could be applied to alleviate pain across a wider range of sites. Distinct from conventional TENS, electrodes are positioned at the painful site, and TENS distal stimulation selects the contralateral homologous site of the pain point, which is far from the pain point but innervated by overlapping spinal cord segments and unrelated extraneural sites

Table 8 Meridian distribution of acupoints

Number	Meridian	Count of acupoints	Count	Frequency (%)
1	The Foot Yangming Stomach Meridian	2	17	18.89
2	Ashi Point	1	12	13.33
3	The Foot Taiyang Bladder Meridian	3	11	12.22
4	The Hand Yangming Large Intestine Meridian	1	11	12.22
5	The Hand Jueyin Pericardium Meridian	2	9	10.00
6	The Foot Taiyin Spleen Meridian	1	9	10.00
7	The Hand Taiyin Lung Meridian	4	6	6.67
8	Extra point (Non-Meridian point)	1	5	5.56
9	Ren Meridian	2	4	4.44
10	The Hand Shaoyang Sanjiao Meridian	2	3	3.33
11	The Foot Jueyin Liver Meridian	1	1	1.11
12	The Foot Shaoyang Gallbladder Meridian	1	1	1.11
13	The Hand Shao Yin Heart Meridian	1	1	1.11

Table 9 Acupoint association rules table

Number	Association rules	Count	Support	Confidence	Lift
8	(Hegu (LI04)) → (Zusanli (ST36))	11	40.74	90.91	1.53
4	(Sanyinjiao (SP06)) → (Zusanli (ST36))	9	33.33	100.00	1.69
7	(Sanyinjiao (SP06) and Hegu (LI04)) → (Zusanli (ST36))	7	25.93	100.00	1.69
1	(Neiguan (PC06)) → (Zusanli (ST36))	5	18.52	100.00	1.69
2	(Jiaji point) → (Hegu (LI04))	5	18.52	100.00	2.45
3	(Jiaji point) → (Zusanli (ST36))	5	18.52	100.00	1.69
5	(Jiaji point and (Hegu (LI04)) → (Zusanli (ST36))	5	18.52	100.00	1.69
6	(Jiaji point and (Zusanli (ST36)) → (Hegu (LI04))	5	18.52	100.00	2.45
9	(Neiguan (PC06)) → (Hegu (LI04))	5	18.52	80.00	1.96
10	(Jiaji point) → (Sanyinjiao (SP06))	5	18.52	80.00	2.40
11	(Neiguan (PC06) and Zusanli (ST36)) → (Hegu (LI04))	5	18.52	80.00	1.96
12	(Jiaji point and (Hegu (LI04)) → (Sanyinjiao (SP06))	5	18.52	80.00	2.40
13	(Jiaji point and (Zusanli (ST36)) → (Sanyinjiao (SP06))	5	18.52	80.00	2.40

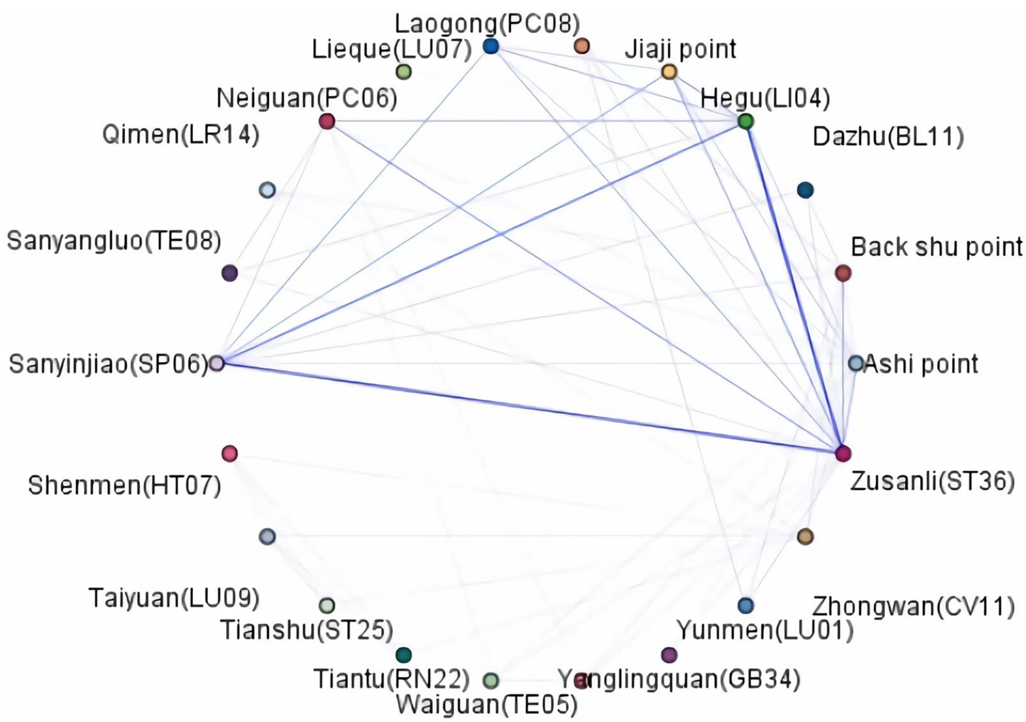

Fig. 8 Network diagram of acupoint association rules

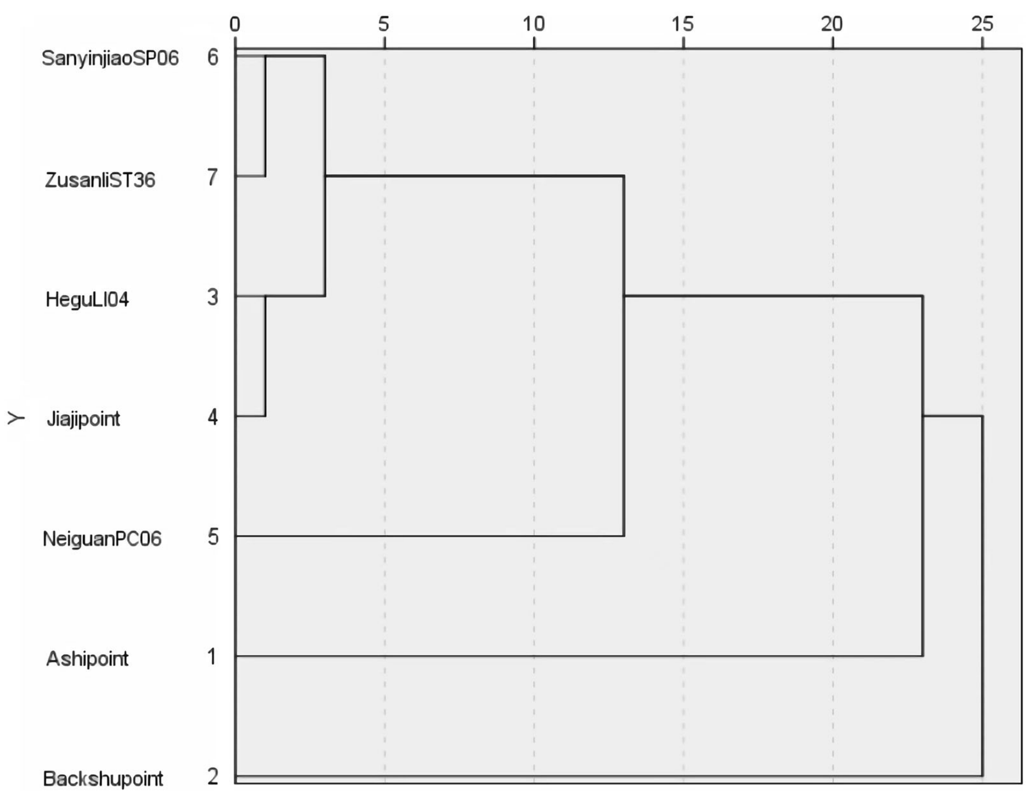

Fig. 9 Cluster analysis of acupoints

[69]. Currently, the positioning of traditional TENS electrodes remains controversial. Cheing et al. [70] positioned electrodes in non-acupoint areas near or around the Quchi (LI11) to verify the analgesic effects of AL-TENS within and outside the dermatome. The comparison revealed that acupoints exhibited better analgesic effects than non-acupoints, albeit without significant differences. Consequently, in clinical practice, the selection of TENS electrode placement remains inconclusive.

The findings of this study suggest that TENS electrode placement primarily focuses on tender points and corresponding acupoints. According to traditional Chinese medicine, cancer pain can be classified under the category of "pain syndrome" based on specific symptoms, often manifested as pain at a specific location. Ashi points, also known as tender points, lack a fixed name or location and represent acupoints or lesion sites serving as operative sites [71]. Modern research has indicated that Ashi points are caused by aseptic inflammation following injury, wherein chemical stimulation from inflammation induces pain, resulting in muscle tension and contracture, ultimately leading to tenderness points [72]. Some studies have confirmed that acting on Ashi points can relieve spastic soft tissues, improve local blood circulation, and promote the reduction of local inflammatory pain, ultimately increasing the release of analgesic substances such as β-endorphin and achieving analgesic effects [73, 74]. On the basis of the results of this study, Ashi points play a crucial role in TENS electrode placement. Therefore, in clinical practice, it is necessary to select the corresponding tender point as the electrode placement site on the basis of the patient's tumor type and pain location, thereby achieving optimal therapeutic effects. Additionally, the study results revealed a higher frequency of Back Shu point usage, which belongs to the Foot Taiyang Bladder Meridian. This meridian includes multiple acupoints corresponding to various viscera. When a specific organ is diseased, the corresponding Back Shu point exhibits a reaction. Therefore, the Back Shu point can serve as a reaction point for disease treatment. Treating a particular organ by targeting its corresponding Back Shu point not only facilitates meridian unblocking but also regulates meridian blood flow, promoting blood movement and disease treatment. Modern research has demonstrated that acting on the Back Shu point can significantly alleviate patient pain symptoms and reduce serum inflammatory cytokine levels [75]. Similarly, Jiaji points were frequently used in this study, and their function is essentially the same as Back Shu points. Hegu (LI04), Zusanli (ST36), and Sanyinjiao (SP06) were frequently used as well and exhibited an intimate association according to association rule analysis. This combination can be considered a classic compatibility combination. When TENS is employed to treat cancer pain, these acupoints can serve as optimal electrode placement locations. Traditional Chinese medicine attributes pain syndrome to "pain caused by poor blood circulation" and "pain caused by lack of nutrition." By acting on Hegu (LI04), Zusanli (ST36), and Sanyinjiao (SP06) through TENS, blood nourishment, circulation promotion, and pain relief can be achieved, thereby treating the disease. Modern research has found significant analgesic effects by employing TENS to treat cancer pain at Hegu (LI04) and Zusanli (ST36), markedly reducing patient pain [21].

This study has certain limitations including the risk of bias due to the limited sample size and the poor quality of the literature. In order to enhance the reliability of the findings, future research should consider conducting large-scale multicenter clinical randomized controlled trials. Furthermore, it is important to explore more specific TENS parameter schemes tailored to different types and degrees of tumors and cancer pain in order to provide better guidance for clinical practice.

CONCLUSION

TENS, as a form of electrical stimulation in modern medicine, offers several advantages including safety, effectiveness, simplicity, and non-addictiveness. It has shown significant improvements in relieving cancer pain, reducing the need for analgesics, and minimizing the occurrence of adverse reactions. TENS represents a promising approach for treating cancer pain by integrating both traditional Chinese medicine and Western medicine. On the basis of the literature analysis conducted in this study, optimal parameters for TENS treatment of cancer pain include a current frequency of 2/100 Hz, a treatment frequency of once a day, and a retention time of 30 min. Additionally, the use of a dilatational wave and targeting specific acupoints such as Ashi point, Back shu point, Sanyinjiao (SP06), Zusanli (ST36), Hegu (LI04), Jiaji point, and Neiguan (PC06) can effectively enhance the analgesic effect of TENS.

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Conflict of Interest. All authors (Quan-yao Li, Wen-xiao Yang, Li-qiu Yao, Hong Chen, Zhen-rui Li, Ya-bin Gong and Jun Shi) confirm that they have no conflicts of interest to disclose.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES

1. He Y, Liu Y, May BH, et al. Effectiveness of acupuncture for cancer pain: protocol for an umbrella review and meta-analyses of controlled trials. BMJ Open. 2017;7(12):e018494. https://doi.org/10.1136/bmjopen-2017-018494.

2. National Health Commission of the People's Republic of China. Guidelines for diagnosis and treatment of cancer pain (2018 edition). J Clin Oncol. 2018;23(10):937–44.

3. Turk DC, Dworkin RH, Burke LB, et al. Developing patient-reported outcome measures for pain clinical trials: IMMPACT recommendations. Pain. 2006;125(3):208–15. https://doi.org/10.1016/j.pain.2006.09.028.

4. Højsted J, Sjøgren P. Addiction to opioids in chronic pain patients: a literature review. Eur J Pain.

2007;11(5):490–518. https://doi.org/10.1016/j.ejpain.2006.08.004.

5. Yuan CP, Chen L. Analysis of the current clinical use of opioid preparations in cancer pain patients both domestically and internationally. Anti Infect Pharm. 2015;12(03):330–2.

6. Yu M, Wang HW, Wang WP, et al. Multicenter study on traditional Chinese medicine analgesic plaster combined with morphine in treatment of moderate and severe cancer pain. Chin J New Drugs Clin Remed. 2015;34(8):617–21. https://doi.org/10.14109/j.cnki.xyylc.2015.08.012.

7. Li Q, Luo J. Research progress in the treatment of chronic moderate and severe cancer pain with opioids. Chin J Pain Med. 2011;17(2):116–9. https://doi.org/10.3969/j.issn.1006-9852.2011.02.010.

8. Guo XZ, Song LP. Correlations between serum tumor markers and bone metastases degree in patients with prostate cancer. Chin Gener Pract. 2015;18(8):903–905,910. https://doi.org/10.3969/J.iSSn.1007-9572.2015.08.011.

9. Loh J, Gulati A. The use of transcutaneous electrical nerve stimulation (TENS) in a major cancer center for the treatment of severe cancer-related pain and associated disability. Pain Med. 2015;16(6):1204–10. https://doi.org/10.1111/pme.12038.

10. Lisón JF, Amer-Cuenca JJ, Piquer-Martí S, et al. Transcutaneous nerve stimulation for pain relief during office hysteroscopy: a randomized controlled trial. Obstet Gynecol. 2017;129(2):363–70. https://doi.org/10.1097/AOG.0000000000001842.

11. Ferreira AP, Costa DR, Oliveira AI, et al. Short-term transcutaneous electrical nerve stimulation reduces pain and improves the masticatory muscle activity in temporomandibular disorder patients: a randomized controlled trial. J Appl Oral Sci. 2017;25(2):112–20. https://doi.org/10.1590/1678-77572016-0173.

12. Shan WQ, Hu KW, Gu K, et al. Interpretation of the National Comprehensive Cancer Network clinical practice guidelines for adult cancer pain. Chin J Clin. 2022;50(01):30–2.

13. Li J, Ding JY, Huang J. Curative effects and costs of oxycontin combined with bio-electric stimulation therapy in treatment of moderate or severe cancer pain. Chin Gener Pract. 2014;17(3):325–7. https://doi.org/10.3969/j.issn.1007-9572.2014.03.021.

14. Bao GA, Zhou J, Yang DH, et al. Preliminary analysis of common parameters for acupuncture treatment of cancer pain. Shanghai J Acupunct Moxibust. 2017;36(2):236–41. https://doi.org/10.13460/j.issn.1005-0957.2017.02.0236.

15. Bennett MI. Mechanism-based cancer-pain therapy. Pain. 2017;158(Suppl 1):S74–8. https://doi.org/10.1097/j.pain.0000000000000825.

16. Wang H, Liu XJ, Ma YH. Clinical observation of transcutaneous electrical nerve stimulation combined with low-dose paracetamol oxycodone on the pain of non-small cell lung cancer bone metastasis. Chin Med Front. 2021;13(01):60–4.

17. Du WB, Bao GA, Shen FX, et al. Clinical efficacy observation of transcutaneous electrical nerve stimulation therapy as adjuvant treatment of opioid analgesia incomplete bone metastases cancer pain. Chin Gener Pract Med. 2019;22(32):3997–4001.

18. He LH, Long XA, Shi JJ, et al. Observation on the effect of transcutaneous electrical nerve stimulation in the treatment of pancreatic cancer pain. Guangdong Med. 2019;40(13):1904–7. https://doi.org/10.13820/j.cnki.gdyx.20184939.

19. Liu Y. Effect and safety evaluation of percutaneous acupoint electrical stimulation combined with three-step analgesia against moderate and severe cancer pain. Zhejiang Univ Chin Med. 2018;1:1–43.

20. Bao GA. Evaluation of analgesic efficacy and advantages of percutaneous nerve electrical stimulation combined with triple step pain relief in the treatment of moderate to severe cancer pain. Zhejiang Univ Tradit Chin Med. 2016;6:1–66.

21. He L. Clinical observation on 13 cases of cancer pain treated with percutaneous acupoint electrical stimulation. Hebei Tradit Chin Med. 2012;34(6):882–4.

22. Wang CY, Fang JQ. Percutaneous acupoint electrical stimulation for cancer pain. Zhejiang J Tradit Chin Med. 2011;46(12):899.

23. Zhang JZ, Li XP, Tang Y, et al. Effect of auricular point pressure seed method combined with acupoint electrophysiology on cancer pain of digestive system. J Hunan Univ Tradit Chin Med. 2019;39(02):241–4.

24. Deng Y, Zhuo XF, Peng JJ, et al. Effect of oxycodone hydrochloride sustained-release tablets combined with bioelectric stimulation on neuropathic cancer pain. J North Sichuan Med Coll. 2017;32(01):30–2.

25. Wu WT, Wang F, Qian Y. The clinical effect of the treatment of combining traditional Chinese and western medicine treatment of moderately severe pain. Chin J Tradit Chin Med. 2017;35(02):492–4.

https://doi.org/10.13193/j.iSSN.1673-7717,2017.02.065.

26. Wang PS. Analysis of different analgesic regimens for moderate and severe cancer pain patients with poor analgesic effect of morphine. Southwest Defense Med. 2016;26(10):1176–8.

27. Li XM, Xiao WH, Zhao HX, et al. Randomized controlled study of HANS assisted analgesia in opioid-tolerant cancer pain patients. Chin J Pain Med. 2016;22(05):364–9.

28. Weng MH, Yu YJ. Effect of oxycodone hydrochloride sustained-release tablets combined with bioelectric stimulation on moderate and severe cancer pain. Health Res. 2015;35(05):562–3+565.

29. Li QH, Zheng W, Liu ZQ. Study on the effect and medical cost of oxycodone hydrochloride sustained-release tablets combined with bioelectric stimulation in the treatment of moderate and severe cancer pain patients. J Pract Cancer. 2015;30(06):922–4.

30. Li J, Ding JJ, Huang J. Effect and cost analysis of oxycodone hydrochloride sustained-release tablets combined with bioelectric stimulation in the treatment of moderate and severe cancer pain. Chin J Gener Med. 2014;17(03):325–7.

31. Chen LL, Hu HQ, Shen AX, et al. Effect of electrical stimulation on patients with cancer pain. Zhejiang J Integr Tradit Chin Western Med. 2002;08:57.

32. Pu JC, Huang HY, Zheng SL. Nursing value of traditional Chinese medicine nursing intervention combined with percutaneous acupoint electrical stimulation for patients with advanced lung cancer with bone metastasis pain. Chin Cancer Clin Rehabil. 2021;28(10):1243–6. https://doi.org/10.13455/j.carolcarrollnkicjcor.2021.10.24.

33. Nakano J, Ishii K, Fukushima T, et al. Effects of transcutaneous electrical nerve stimulation on physical symptoms in advanced cancer patients receiving palliative care. Int J Rehabil Res. 2020;43(1):62–8. https://doi.org/10.1097/MRR.0000000000000386.

34. Siemens W, Boehlke C, Bennett MI, et al. Transcutaneous electrical nerve stimulation for advanced cancer pain inpatients in specialist palliative care-a blinded, randomized, sham-controlled pilot crossover trial. Support Care Cancer. 2020;28(11):5323–33. https://doi.org/10.1007/s00520-020-05370-8.

35. Lee JE, Anderson CM, Perkhounkova Y, et al. Transcutaneous electrical nerve stimulation reduces resting pain in head and neck cancer patients: a randomized and placebo-controlled double-blind pilot study. Cancer Nurs. 2019;42(3):218–28. https://doi.org/10.1097/NCC.0000000000000594.

36. He L, Tan K, Lin X, et al. Multicenter, randomized, double-blind, controlled trial of transcutaneous electrical nerve stimulation for pancreatic cancer related pain. Medicine (Baltimore). 2021;100(5):e23748. https://doi.org/10.1097/MD.0000000000023748.

37. Chou YH, Yeh ML, Huang TS, et al. Acupoint stimulation improves pain and quality of life in head and neck cancer patients with chemoradiotherapy: a randomized controlled trial. Asia Pac J Oncol Nurs. 2021;9(1):61–8. https://doi.org/10.1016/j.apjon.2021.11.002. (Erratum in Asia Pac J Oncol Nurs. 2023;10(4):100208).

38. Zhang H, Huang WF, Hou LL, et al. Effect of traditional Chinese medicine nursing intervention combined with percutaneous acupoint electrical stimulation on advanced lung cancer patients with bone metastasis pain. J Guiyang College Tradit Chin Med. 2016;38(4):85–9. https://doi.org/10.16588/j.carolcarrollnkiissn1002-1108.2016.04.023.

39. Schleder JC, Verner FA, Mauda L, et al. The transcutaneous electrical nerve stimulation of variable frequency intensity has a longer-lasting analgesic action than the burst transcutaneous electrical nerve stimulation in cancer pain. Revista Dor. 2017;18(4):316–20. https://doi.org/10.5935/1806-0013.20170122.

40. Sampaio LR, de Resende MA, Pereira LSM. Effect of transcutaneous electrical nerve stimulation on vertebral metastatic bone pain of breast cancer patients: single case experimental study. Rev Dor São Paulo. 2016;17(2):81–7. https://doi.org/10.5935/1806-0013.20160020.

41. Bennett MI, Johnson MI, Brown SR, et al. Feasibility study of transcutaneous electrical nerve stimulation (TENS) for cancer bone pain. J Pain. 2010;11(4):351–9. https://doi.org/10.1016/j.jpain.2009.08.002.

42. Chwistek M. Recent advances in understanding and managing cancer pain. F1000Res. 2017;6:945. https://doi.org/10.12688/f1000research.10817.1.

43. Robb KA, Newham DJ, Williams JE. Transcutaneous electrical nerve stimulation vs. transcutaneous spinal electroanalgesia for chronic pain associated with breast cancer treatments. J Pain Symptom Manage. 2007;33(4):410–9. https://doi.org/10.1016/j.jpainsymman.2006.09.020.

44. Melzack R, Wall PD. Pain mechanisms: a new theory. Science. 1965;150(3699):971–9. https://doi.org/10.1126/science.150.3699.971.

45. Maeda Y, Lisi TL, Vance CG, et al. Release of GABA and activation of GABA(A) in the spinal cord mediates the effects of TENS in rats. Brain Res. 2007;1136(1):43–50. https://doi.org/10.1016/j.brainres.2006.11.061.

46. Chiu TT, Hui-Chan CW, Chein G. A randomized clinical trial of TENS and exercise for patients with chronic neck pain. Clin Rehabil. 2005;19(8): 850–60. https://doi.org/10.1191/0269215505cr920oa.

47. Peng WW, Tang ZY, Zhang FR, et al. Neurobiological mechanisms of TENS-induced analgesia. Neuroimage. 2019;195:396–408. https://doi.org/10.1016/j.neuroimage.2019.03.077.

48. Lisi TL, Sluka KA. A new electrochemical HPLC method for analysis of enkephalins and endomorphins. J Neurosci Methods. 2006;150(1):74–9. https://doi.org/10.1016/j.jneumeth.2005.06.001.

49. Bannister K, Patel R, Goncalves L, et al. Diffuse noxious inhibitory controls and nerve injury: restoring an imbalance between descending monoamine inhibitions and facilitations. Pain. 2015;156(9):1803–11. https://doi.org/10.1097/j.pain.0000000000000240.

50. Han JS, Chen XH, Sun SL, et al. Effect of low- and high-frequency TENS on Met-enkephalin-Arg-Phe and dynorphin A immunoreactivity in human lumbar CSF. Pain. 1991;47(3):295–8. https://doi.org/10.1016/0304-3959(91)90218-M.

51. Xiang XH, Chen YM, Zhang JM, et al. Low- and high-frequency transcutaneous electrical acupoint stimulation induces different effects on cerebral μ-opioid receptor availability in rhesus monkeys. J Neurosci Res. 2014;92(5):555–63. https://doi.org/10.1002/jnr.23351.

52. Ozüm Ü, Akyol M, Balaban H, et al. Effect of cervical spinal cord electrical stimulation on nitric oxide levels in brain and dermal tissues: an evaluation using by real-time nitric oxide measurement. Acta Neurochir (Wien). 2012;154(9):1641–6. https://doi.org/10.1007/s00701-012-1331-3.

53. Fu TF, Du JY, Chen YT, et al. Efficacy evaluation of interventional electroacupuncture therapy at different times on bone cancer pain in morphine-tolerant rats. J Zhejiang Univ Tradit Chin Med. 2017;41(06):447–53. https://doi.org/10.16466/j.issn1005-5509.2017.06.001.

54. Hamza MA, White PF, Ahmed HE, et al. Effect of the frequency of transcutaneous electrical nerve stimulation on the postoperative opioid analgesic requirement and recovery profile. Anesthesiology. 1999;91(5):1232–8. https://doi.org/10.1097/00000542-199911000-00012.

55. de Oliveira HU, Dos Santos RS, Malta IHS, et al. Investigation of the involvement of the endocannabinoid system in TENS-induced antinociception. J Pain. 2020;21(7–8):820–35. https://doi.org/10.1016/j.jpain.2019.11.009.

56. Dailey DL, Vance CGT, Rakel BA, et al. Transcutaneous electrical nerve stimulation reduces movement-evoked pain and fatigue: a randomized. Controlled Trial Arthritis Rheumatol. 2020;72(5): 824–36. https://doi.org/10.1002/art.41170.

57. Davis S, Olaussen A, Bowles K, et al. Review article: Paramedic pain management of femur fractures in the prehospital setting: a systematic review. Emerg Med Australas. 2021;33:601–9. https://doi.org/10.1111/1742-6723.13793.

58. Tang ZY. Research on the analgesic mechanism of transcutaneous electrical nerve stimulation based on laser-evoked potentials. Southwest University; 2018.

59. Zhai FJ, Han SP, Song TJ, et al. Involvement of opioid peptides in the analgesic effect of spinal cord stimulation in a rat model of neuropathic pain. Neurosci Bull. 2022;38(4):403–16. https://doi.org/10.1007/s12264-022-00844-7.

60. Tousignant-Laflamme Y, Laroche C, Beaulieu C, et al. A randomized trial to determine the duration of analgesia following a 15- and a 30-minute application of acupuncture-like TENS on patients with chronic low back pain. Physiother Theory Pract. 2017;33(5):361–9. https://doi.org/10.1080/09593985.2017.1302540.

61. Moreno-Duarte I, Morse LR, Alam M, et al. Targeted therapies using electrical and magnetic neural stimulation for the treatment of chronic pain in spinal cord injury. Neuroimage. 2014;85(Pt 3): 1003–13. https://doi.org/10.1016/j.neuroimage.2013.05.097.

62. Sato KL, Sanada LS, Rakel BA, et al. Increasing intensity of TENS prevents analgesic tolerance in rats. J Pain. 2012;13(9):884–90. https://doi.org/10.1016/j.jpain.2012.06.004.

63. Chesterton LS, Foster NE, Wright CC, et al. Effects of TENS frequency, intensity and stimulation site parameter manipulation on pressure pain thresholds in healthy human subjects. Pain. 2003;106(1–2):73–80. https://doi.org/10.1016/s0304-3959(03)00292-6.

64. Katirci Kirmaci ZI, Adigüzel H, Gögremis M, et al. The effect of transcutaneous electrical nerve stimulation (TENS) and interferential currents (IFC) on pain, functional capacity, and quality of life in patients with multiple sclerosis: a randomized controlled, single-blinded study. Mult Scler Relat

Disord. 2023;71:104541. https://doi.org/10.1016/j.msard.2023.104541.

65. Gobbo M, Maffiuletti NA, Orizio C, et al. Muscle motor point identification is essential for optimizing neuromuscular electrical stimulation use. J Neuroeng Rehabil. 2014;11:17. https://doi.org/10.1186/1743-0003-11-17.

66. Carbonario F, Matsutani LA, Yuan SL, et al. Effectiveness of high-frequency transcutaneous electrical nerve stimulation at tender points as adjuvant therapy for patients with fibromyalgia. Eur J Phys Rehabil Med. 2013;49(2):197–204.

67. Ekblom A, Hansson P, Fjellner B. The influence of extrasegmental mechanical vibratory stimulation and transcutaneous electrical nerve stimulation on histamine-induced itch. Acta Physiol Scand. 1985;125(3):541–5. https://doi.org/10.1111/j.1748-1716.1985.tb07753.x.

68. Yarnitsky D, Dodick DW, Grosberg BM, et al. Remote electrical neuromodulation (REN) relieves acute migraine: a randomized, double-blind, placebo-controlled, multicenter Trial. Headache. 2019;59(8):1240–52. https://doi.org/10.1111/head.13551.

69. Gozani SN. Remote analgesic effects of conventional transcutaneous electrical nerve stimulation: a scientific and clinical review with a focus on chronic pain. J Pain Res. 2019;12:3185–201. https://doi.org/10.2147/JPR.S226600.

70. Cheing GL, Chan WW. Influence of choice of electrical stimulation site on peripheral neurophysiological and hypoalgesic effects. J Rehabil Med. 2009;41(6):412–7. https://doi.org/10.2340/16501977-0350.

71. Liang FR, Wang H. Acupuncture and moxibustion. Beijing: China Traditional Chinese Medicine Press; 2016.

72. Xu YX, Guo H, Chen GZ. Discussion on the formation of Ashi point and its analgesic mechanism. J Liaoning Univ Tradit Chin Med. 2014;16(6):80–2.

73. Lin ZG, Chen SJ, Chen LH, et al. The analgesic effect of massage and massage on neuropathic pain in rats and its effect on serum, dorsal root ganglion, and substance P in the spinal dorsal horn. Chin J Tradit Chin Med. 2019;37(04):877–80. https://doi.org/10.13193/j.issn.1673-7717.2019.04.024.

74. Ma AQ. Study on the analgesic effect and brain mechanism of the “pain as acupoint” pressing method on rats with brachial plexus injury. Shanghai Univ Tradit Chin Med. 2019. https://doi.org/10.27320/d.cnki.gszyu.2019.000273.

75. Chen J, Qiao HF, Li J, et al. Clinical study on the intervention of cancer pain by moxibustion at Beishu point combined with hydroxycodone sustained-release tablets. Shanxi Tradit Chin Med. 2020;41(01):105–7.