

# Acupuncture in Multiple Myeloma Peripheral Neuropathy: A Systematic Review

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**Background:** Peripheral neuropathy (PN) is a prevalent complication of multiple myeloma (MM), due to the disease itself or its treatment. Despite extensive research, the optimal treatment for multiple myeloma peripheral neuropathy (MMPN) remains unclear. Clinical practice has shown the potential efficacy of acupuncture in managing MMPN. This study aimed to conduct a comprehensive analysis of the literature to assess the effectiveness and safety of acupuncture as a treatment for MMPN.

**Methods:** The PubMed, Web of Science, MEDLINE, Cochrane Library, and Embase databases were comprehensively searched from inception to November 1, 2023 to identify relevant studies pertaining to the use of acupuncture to treat MMPN.

**Results:** A total of five studies, encompassing 97 patients diagnosed with drug-related PN, were ultimately included in this analysis. The literature lacks any reports pertaining to the utilization of acupuncture for disease-related PN. ST36, LI4, SP6, and EX-LE-10 were found to be the most frequently chosen acupoints. Following acupuncture treatment, there was a consistent reduction in scores on the Visual Analogue Scale (VAS), Neuropathic Pain Scale (NPS), Brief Pain Inventory-Short Form (BPI-SF), and Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity (FACT/GOG-Ntx) among MMPN patients. The results of Nerve Conduction Velocity (NCV) tests yielded conflicting results. No severe adverse effects were reported.

**Conclusion:** The use of acupuncture for disease-related PN has not been studied to date. Acupuncture is safe for drug-related PN and is helpful for relieving pain. But uncertainty exists regarding the efficacy of this approach because there is substantial heterogeneity with respect to acupuncture treatment regimens, and more high-quality studies on this topic are warranted.

**Keywords:** multiple myeloma peripheral neuropathy, acupuncture, pain, systematic review

## Introduction

Multiple myeloma (MM) is a neoplastic disorder characterized by the proliferation of plasma cells within the bone marrow.<sup>1</sup> Peripheral neuropathy (PN) is a common complication of MM that mainly manifests as sensory neuropathies and motor neuropathies in severe cases.<sup>2</sup> Multiple myeloma peripheral neuropathy (MMPN) can be divided into disease-related PN and drug-related PN. In disease-related PN, sensory modalities may be affected, resulting in axonal sensorimotor neuropathy with a length-dependent pattern of axonal regrowth.<sup>3</sup> Drug-related PN is mainly caused by first-line drugs such as the proteasome inhibitor bortezomib and the immunomodulator thalidomide, which is one of the major challenges in the current drug management of MM.<sup>4</sup> Clinical evaluations suggest that up to 20% of patients with MM develop PN at diagnosis, and up to 75% of patients may develop therapeutic PN during treatment.<sup>5</sup> Among drug-related PNs, the incidence of bortezomib-induced peripheral neuropathy (BIPN) can reach 40%, and the incidence of thalidomide-induced peripheral neuropathy (TIPN) varies greatly, ranging from 25% to 75%.<sup>6</sup>

MMPN has a significant impact on patients' physical and mental health and quality of life. The occurrence and severity of drug-related PN are strongly related to the drug dose.<sup>7</sup> Severe drug-related PN can only control the development of neurotoxicity by adjusting the dose, changing the route of administration, interrupting drugs or

prolonging the interval between chemotherapy, which also reduces the therapeutic effect of the primary disease. Available treatment options for the prevention and treatment of MMPN are limited. Generally, vitamin B drugs are administered to nourish nerves, and painkillers are used to relieve pain, but the effect is not satisfactory. Therefore, an effective treatment method is urgently needed to control the occurrence and development of MMPN. A large amount of medical evidence indicates that acupuncture plays a potential role in relieving cancer pain, and the analgesic effect of acupuncture is one of its most widely accepted effects.<sup>8</sup> Additionally, available studies have suggested that acupuncture is effective in the treatment of diabetic PN and paclitaxel- and oxaliplatin- induced PN,<sup>9,10</sup> suggesting that acupuncture is a useful alternative to relieve symptoms of PN. Previous investigations have shown the synergistic impact of acupuncture and bortezomib on prolonging the survival of mice with MM.<sup>11</sup> Acupuncture has been regarded to have strong potential as an adjunctive therapy for treating MMPN.<sup>12</sup> Several studies have explored the potential clinical implications of using acupuncture to treat MMPN, but no systematic review has examined this topic. The objective of this study was to perform a comprehensive analysis of clinical studies evaluating the efficacy and safety of acupuncture in patients with MMPN and to offer a systematic perspective for clinical practice.

## Materials and Methods

### Registration and Protocol

This systematic review was conducted in accordance with the PRISMA 2020 checklist,<sup>13</sup> ([Supplementary Table 1](#)), which has been registered on the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY202370046).

### Search Sources and Data Extraction

This systematic review investigated the use of acupuncture as a therapeutic approach for the management of MMPN. The PubMed, Web of Science, MEDLINE, Embase, and Cochrane Library databases were searched using the following terms: (multiple myeloma OR MM) AND (peripheral neuropathy OR PN) AND acupuncture. The databases were searched from their respective inception to November 11, 2023. Only English studies with human participants were included. The inclusion criterion for this study was patients diagnosed with MMPN who had received acupuncture treatment. The exclusion criteria were as follows: animal studies, incomplete or inaccessible data, and data obtained from nonprimary sources. In cases where multiple publications were available for the same study, preference was given to the article containing the most comprehensive information. The personal information includes both general and disease-related information. The outcome indicators included the result of the Visual Analogue Scale (VAS), the Neuropathic Pain Scale (NPS), the Brief Pain Inventory-Short Form (BPI-SF), the Nerve Conduction Velocity (NCV), the Functional Assessment of Cancer Therapy - General (FACT-G), the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity (FACT/GOG-Ntx), proinflammatory and neurotrophic biomarkers, and adverse reaction. Two investigators (C.L. and H.X.) independently retrieved the literatures and extracted the data.

### Quality Assessment

The quality assessment of the case reports, single-arm clinical trials, and randomized controlled trials was conducted utilizing the JBI critical appraisal tool for case report<sup>14</sup> the MINORS tool<sup>15</sup> and the modified Jadad scale,<sup>16</sup> respectively. The literature quality assessment was independently completed by two researchers (C.L. and C.H.) by referring to the relevant literature.

### Data Analysis

Due to the heterogeneity of the data, it was unfeasible to amalgamate them for the purpose of conducting a meta-analysis. Descriptive approaches were employed to analyze the aggregated data. To explore the regularity of acupoint combinations, frequency analysis and association rule analysis were conducted using SPSS Statistics (version 26.0) and SPSS Modeler (version 15.0), respectively. The Apriori algorithm for association rule mining was adopted to analyze the confidence and support of acupoint combinations. The minimum acceptable confidence and support values were

considered for the purpose of pruning the rules. Specifically, a minimum confidence of 100% and a minimum support of 20% were considered. The higher the confidence degree and support values are, the greater the degree of credibility. The acupoint combination network was visualized using Cytoscape (version 3.9.1).

## Results

### Search results and Study Characteristics

A total of 64 studies were initially screened from 5 databases, and 34 studies remained after removing duplicates. The literature was then screened by first reading the title and abstract, and 20 irrelevant studies were excluded. The full texts of the remaining literatures were then searched, and a total of 7 studies went into full-text assessment, of which 1 was excluded because of a lack of complete data,<sup>22</sup> and 1 were excluded because they contained duplicate data.<sup>23</sup> The literature screening process is shown in Figure 1. Ultimately, five studies with a total of 97 patients were included<sup>17-21</sup> (Table 1). There were two single-arm clinical trials,<sup>18,19</sup> one randomized controlled trial,<sup>17</sup> and two case reports.<sup>20,21</sup> In three studies, patients received acupuncture after the discontinuation of bortezomib,<sup>17-19</sup> and in one case report, patients received bortezomib during acupuncture treatment.<sup>20</sup> All patients in the included studies were diagnosed with drug-related PN, and none of the studies reported the use of acupuncture for disease-related PN. Among the five studies, three studies included 95 patients who were diagnosed with drug-related PN of grade  $\geq$  ;<sup>17-19</sup> two of these studies used the CTCAE diagnostic criteria (version 3.0),<sup>17,18</sup> and one study used the NCI-CTC diagnostic criteria (version 4.0).<sup>19</sup> Two studies mentioned only that patients were in a state of BIPN according to neurological exams and electro

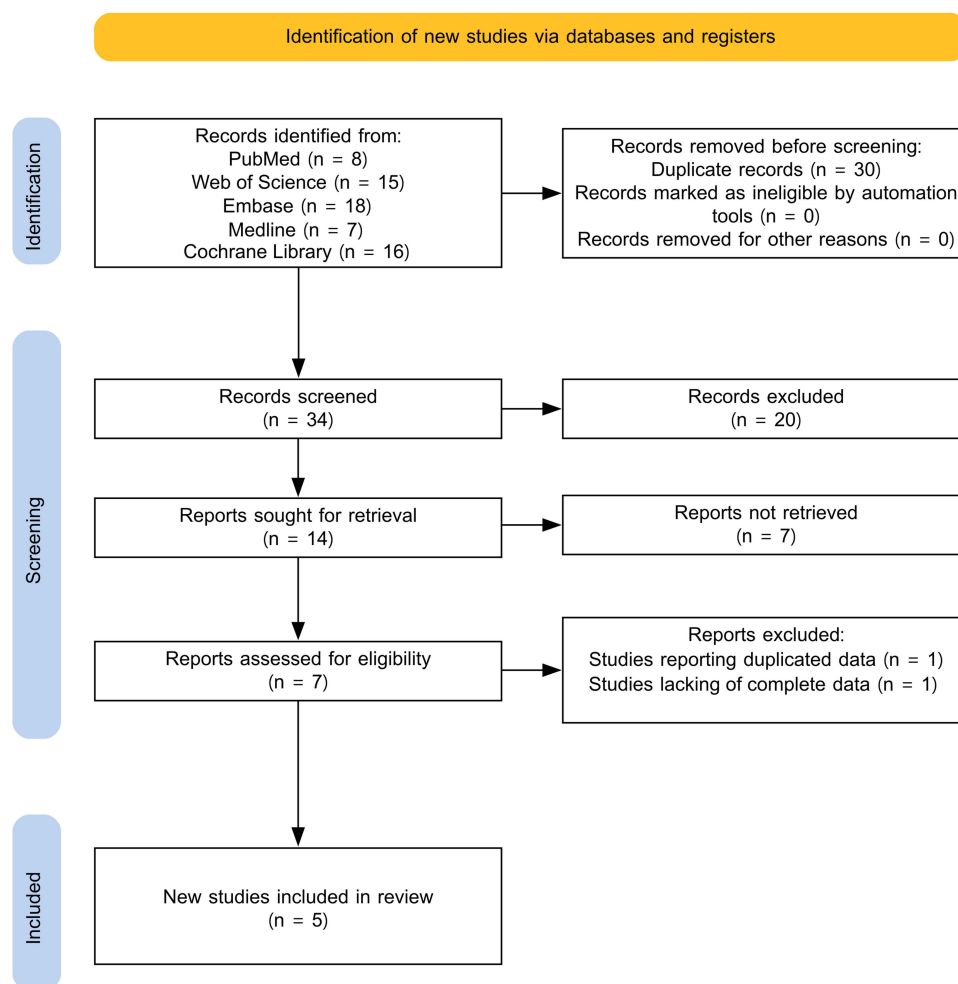


Figure 1 Flow chart of literature screening.

**Table 1** The Basic Characteristics of the Included Studies

Author, Year	The Type of Clinical Research	Number of Patients Received Acupuncture Treatment (n)	Prior Therapy	Time After Discontinuation of Bortezomib	Diagnostic Criteria	Grade of Peripheral Neuropathy, n	Outcome Indicator	Adverse Effects	Quality
Xiaoyan Han, 2017 <sup>17</sup>	Randomized controlled trial	49	N/R	Three months	CTCAE (version 3.0)	Grade 2, 20 Grade 3, 25 Grade 4, 4	VAS; FACT/GOG-Ntx; NCV	Reported	Low
M Kay Garcia, 2014 <sup>18</sup>	Single-arm clinical trial	19	All patients received bortezomib and 3 of them received thalidomide.	Median time were 9.8 months (range, 0.75–41.5).	CTCAE (version 3.0)	Grade 2, 13 Grade 3, 6	FACT/GOG-Ntx; NCV; FACT-G; BPI-SF	N/R	Medium
Ting Bao, 2014 <sup>19</sup>	Single-arm clinical trial	27	All patients received bortezomib, 12 of them on maintenance lenalidomide.	Median time were 19 months (range, 1–83).	NCI-CTC (version 4.0)	Grade 2, 12 Grade 3, 14 Grade 4, 1	NPS; FACT/GOG-Ntx; NCV; Biomarker	Reported	Medium
Sibel Mandiroglu, 2015 <sup>20</sup>	Case report	1	Patients received bortezomib.	Bortezomib treatment was continued during the acupuncture treatment.	N/R	Reported	High VAS	Reported	High
Ting Bao, 2011 <sup>21</sup>	Case report	1	Electroneurophysiological test Patients received bortezomib and dexamethasone, then underwent autologous peripheral blood stem cell transplantation.	N/R	NPS Neurological exam	N/R	High VAS	Reported	High

**Abbreviations:** N/R, Not reported; VAS, Visual Analogue Scale; NPS, Neuropathic Pain Scale; BPI-SF, Brief Pain Inventory-Short Form; NCV, Nerve Conduction Velocity; FACT/GOG-Ntx, Functional Assessment of Cancer Therapy/ Gynecologic Oncology Group-Neurotoxicity; FACT-G, Functional Assessment of Cancer Therapy- General.

neurophysiological tests.<sup>20,21</sup> To evaluate the efficacy of acupuncture, the VAS was used in two studies,<sup>17,21</sup> the NPS was used in two studies,<sup>19,20</sup> the BPI-SF was used in one study,<sup>18</sup> the NCV test was used in three studies,<sup>17–19</sup> the FACT-G was used in one study,<sup>18</sup> the FACT/GOG-Ntx was used in three studies,<sup>17–19</sup> and proinflammatory and neurotrophic biomarkers were assessed in one study.<sup>19</sup> Four studies reported whether there were adverse reactions.<sup>17,19–21</sup>

Two case reports<sup>20,21</sup> were evaluated as having high methodological quality in accordance with the JBI critical appraisal tool for case report ([Supplementary Table 2](#)). The MINORS tool was used to assess the quality of two single-arm clinical trials;<sup>18,19</sup> these trials were found to be of medium quality ([Supplementary Table 3](#)). The quality of randomized controlled trials<sup>17</sup> was evaluated using the modified Jadad scale these trials were found to be of low-quality ([Supplementary Table 4](#)).

## Summary of Intervention

The details of the acupuncture treatment methods used are summarized in [Table 2](#). In two single-arm clinical trials<sup>18,19</sup> and two case reports,<sup>20,21</sup> patients received synergistic symptomatic treatment involving acupuncture. In a randomized controlled trial,<sup>17</sup> patients in the treatment group received acupuncture combined with methylcobalamin, and patients in the control group received only methylcobalamin. Four studies used body acupuncture,<sup>17,18,20,21</sup> and only one study used a combination of auricular acupuncture plus body acupuncture<sup>19</sup> ([Figure 2a](#)). Among the studies that used body acupuncture, one used electroacupuncture,<sup>18</sup> and the other used manual acupuncture.

The acupoints utilized in auricular acupuncture included shen men, point zero, and two supplementary acupoints where the electrodermal signal was observed.<sup>19</sup> ST36, LI4, SP6 and EX-LE-10 were the most-frequently used acupoints for body acupuncture ([Figure 2b](#)). According to the results of association rule mining, the SP6-ST36 combination (support value: 60%, confidence value: 100%), LI4- EX-LE-10 combination (support value: 40%, confidence value: 100%), and SP6-ST36-LI4 combination (support value: 40%, confidence value: 100%) were the core acupoint combinations ([Figure 2c](#) and [Supplementary Table 5](#)).

In studies using body acupuncture, the needle was positioned after de qi. Needle retention for 30 minutes was reported in one study,<sup>17</sup> and that for 20 minutes was reported in three studies.<sup>18–20</sup> Four studies reported the depth of needling: 0.3–1.0 inches,<sup>17</sup> 0.5–1.5 inches,<sup>18</sup> 0.5 inches,<sup>19</sup> and 10–20 mm.<sup>20</sup>

## Efficacy and Safety Assessment

The safety and efficacy of acupuncture for improving pain, neurological function, quality of life, and biomarkers levels in patients with MMPN are summarized in [Table 3](#).

### Improvements in Pain

Pain improvement was assessed using the VAS, NPS, and BPI-SF. The VAS is a commonly used measure for evaluating variations in pain intensity in the area of cancer pain assessment.<sup>24</sup> The NPS is a multifaceted instrument that employs a self-reported visual analogue to delineate levels of pain intensity and its corresponding attributes.<sup>25</sup> The BPI-SF is a self-administered survey utilized to evaluate the magnitude of pain and its influence on patients' daily activities.<sup>26</sup> Higher NPS, VAS and BPI-SF scores indicate worse pain symptoms.

Two studies reported VAS scores. Ting Bao reported that the VAS score of patients decreased from 8/10 to 2/10 after acupuncture treatment.<sup>21</sup> Xiaoyan Han reported that the VAS score significantly decreased in the acupuncture combined with methylcobalamin group compared to that in methylcobalamin group.<sup>17</sup> Two studies reported the results of the NPS. In a case reported by Sibel Mandiroglu, the NPS decreased from 4/10 to 0/10 after acupuncture treatment.<sup>20</sup> Similarly, Ting Bao reported a decrease in the NPS after acupuncture treatment.<sup>19</sup> According to a single-arm clinical trial conducted by M Kay Garcia, the BPI-SF indicated notable improvements in pain severity at all measured time points.<sup>18</sup>

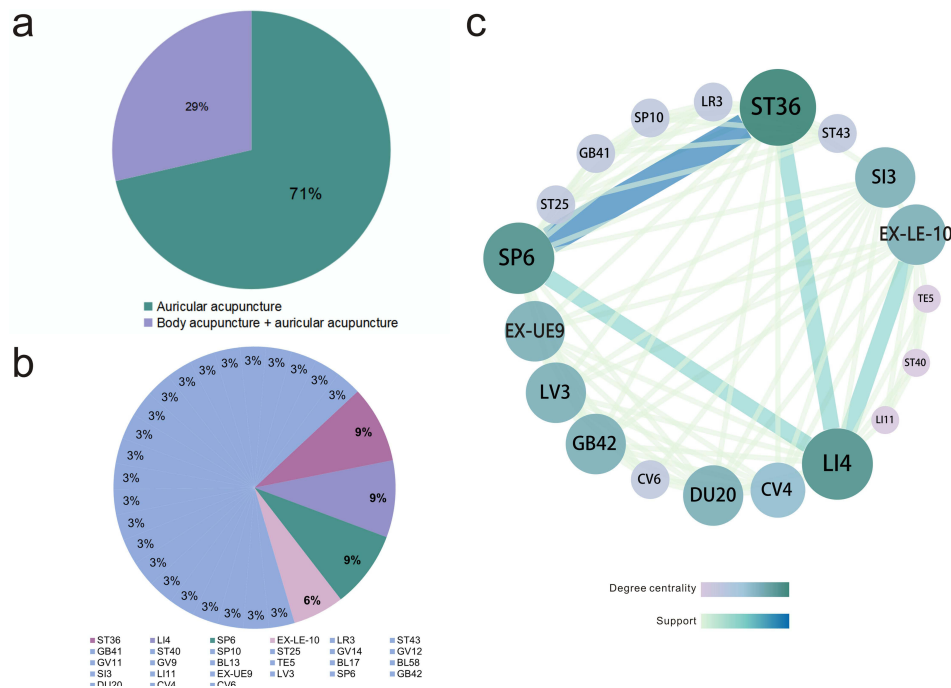
### Neurological Function

Neurological function was measured using the NCV test, which included assessments of motor nerve conduction velocity (MCV) and sensory nerve conduction velocity (SCV). These tests were performed using an electromyography machine.

**Table 2** The Details of the Intervention Protocol

Author	Acupoint	Depth	Needle-Retention Time	Treatment Course	Coadministered Treatment
Xiaoyan Han <sup>17</sup>	LR3, ST43, GB41, SP6, ST36, SP10, ST25, GV14, GV12, GV11, GV9, BL13, BL17, BL58.	0.3–1.0 inches.	Left in place for 30 minutes.	Patients received acupuncture daily for 3 days, then once every alternate day for 10 days as a treatment cycle. Each cycle was repeated every 28 days and the complete treatment included three cycles.	Methylcobalamin
M Kay Garcia <sup>18</sup>	LI4, SI3, EX-UE9, LV3, SP6, GB42, ST36, EX-LE-10, DU 20, CV4, CV6.	0.5–1.5 inches.	Electrical stimulation was applied from LI4 (negative) to SI3 (positive) and from LV3 (negative) to GB42 (positive) at 2–100 Hz for 20 minutes.	Patients received acupuncture 3 times per week for 4 weeks followed by 1 week off (week 5) and then twice per week for 4 more weeks.	For neuropathy symptoms: pregabalin, gabapentin. For pain control: hydrocodone, oxycodone, morphine, hydromorphone.
Ting Bao <sup>19</sup>	Auricular acupoints: shen men, point zero, two additional auricular acupuncture points where electrodermal signal was detected. Body acupoints: LI4, TE5, LI11, ST40, EX-LE-10	0.5 inches.	Left in place for 20 minutes.	Patients received acupuncture 10 times: twice weekly for the first 2 weeks, weekly for 4 weeks, and then biweekly for 4 weeks.	Narcotics, gabapentin, amitriptyline, pregabalin, duloxetine.
Sibel Mandiroglu <sup>20</sup>	ST36, SP6, LI4.	10–20 millimeters.	Left in place for 20 minutes.	Patients received acupuncture 15 times: every other day in the first five treatments and then twice a week.	N/R
Ting Bao, 2011 <sup>21</sup>	LI4, SJ5, LI11, ST40, EX-LE-10.	N/R	N/R	Patients received acupuncture once per week for 6 treatments.	Morphine, oxycodone.

**Abbreviation:** N/R, Not reported.



**Figure 2** The distribution pattern of selected acupoint. (a) Types of selected acupuncture. (b) Frequency of selected acupoints. (c) The combination rules of selected acupoints.

Three studies reported the result of NCV tests. Only one study reported the MCV and SCV (except for the median nerve SCV) were improved in the acupuncture combined with methylcobalamin group compared with the methylcobalamin group.<sup>17</sup> M Kay Garcia reported that no significant changes were detected in NCV tests,<sup>18</sup> and Ting Bao reported that NCV test results did not change between baseline and the end of the study.<sup>19</sup>

### Quality of Life

The assessment of the quality of life of MMPN patients was conducted utilizing the FACT/GOG-Ntx and FACT-G. The FACT/GOG-Ntx subscale, comprises an 11-item neurotoxicity module that supplements the primary quality of life measurement of the FACT-G questionnaire,<sup>27</sup> commonly employed to evaluate chemotherapy-induced peripheral neuropathy (CIPN) in individuals with cancer.<sup>28</sup>

**Table 3** Summary of the Efficacy and Safety Assessments

Author	Pain			Neurological Function	Quality of Life		Adverse Effect
	VAS	NPS	BPI-SF	NCV	FACT/GOG-Ntx	FACT-G	
Xiaoyan Han <sup>17</sup>	Decreased	N/R	N/R	Increased	Decreased	N/R	No adverse effects were reported.
M Kay Garcia <sup>18</sup>	N/R	N/R	Decreased	NS	Decreased	Decreased	N/R
Ting Bao <sup>19</sup>	N/R	Decreased	N/R	NS	Decreased	N/R	No adverse effects were reported.
Sibel Mandiroglu <sup>20</sup>	N/R	Decreased	N/R	N/R	N/R	N/R	No adverse effects were reported.
Ting Bao <sup>21</sup>	Decreased	N/R	N/R	N/R	N/R	N/R	No adverse effects were reported.

**Abbreviations:** N/R, not reported; NS, No significant change; VAS, Visual Analogue Scale; NPS, Neuropathic Pain Scale; BPI-SF, Brief Pain Inventory-Short Form; NCV, Nerve Conduction Velocity; FACT/GOG-Ntx, Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity; FACT-G, Functional Assessment of Cancer Therapy- General; MCV, motor nerve conduction velocity; SCV, sensory nerve conduction velocity.

The FACT/GOG-Ntx score was reported in three studies. Xiaoyan Han reported that the FACT/GOG-Ntx score decreased significantly in the acupuncture combined with methylcobalamin group compared to the methylcobalamin group.<sup>17</sup> M Kay Garcia demonstrated that the FACT/GOG-Ntx score decreased significantly between baseline and all subsequent time points.<sup>18</sup> Ting Bao reported that the average FACT/GOG-Ntx score decreased and remained at a low level at the endpoint of treatment, and a decrease in the FACT/GOG-Ntx score was noted for ambulation, manual dexterity, and auditory capabilities, and there was no decrease in overall functionality (joint pain or muscular cramps and weakness).<sup>19</sup>

In a study conducted by M Kay Garcia, the FACT-G score was measured.<sup>18</sup> The findings indicated that acupuncture had a noteworthy temporal effect on the physical well-being scale score, with a notable decrease at the treatment period and during the follow-up. However, no notable improvements were observed in the domains of social/family well-being, emotional well-being, or functional well-being.

### The Expression Levels of Biomarkers

One study<sup>19</sup> reported changes in biomarkers after acupuncture. The biomarkers included eight proinflammatory cytokines, interleukin-6 (IL-6), IL-8, IL-10, IL-17a, macrophage inflammatory protein-1 $\alpha$  (MIP-1 $\alpha$ ), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), vascular endothelial growth factor (VEGF), and insulin-like growth factor-1 (IGF-1), and four neurotrophic factors: nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), and  $\beta$ -endorphin ( $\beta$ -EP). There were no statistically significant alterations in any of the 12 biomarkers.

### Safety Assessment

Four studies reported adverse effects, and no adverse events occurred.<sup>17,19–21</sup>

## Discussion

Proteasome inhibitors and the immunostimulatory greatly improve progression-free and overall survival for MM patients, but TIPN and BIPN have a significant impact on the quality of life of patients, often necessitating the reduction, postponement, or premature discontinuation of effective treatment, which is widely recognized as a major challenge in the management of drug side effects in MM.<sup>29</sup> The American College of Chest Physicians (ACCP) evidence-based clinical practice guide points out that acupuncture as a complementary therapy and adjuvant therapy can effectively control cancer pain and PN.<sup>30</sup> In clinical practice, acupuncture is often used for the empiric treatment of MMPN. The aim of the present study was to systematically evaluate the efficacy and safety of acupuncture in the treatment of MMPN by reviewing the literature. Three studies reported 95 patients who were diagnosed with grade  $\geq 2$  PN,<sup>17–19</sup> and two patients were only diagnosed with BIPN in two case reports.<sup>20,21</sup> Patients in three studies received acupuncture treatment after the discontinuation of bortezomib,<sup>17–19</sup> and in one case report, they received acupuncture treatment during bortezomib treatment,<sup>20</sup> which precluded the reversibility of the effect of acupuncture after the discontinuation of BIPN.

Body acupuncture is the most commonly used technique and was reported in all five included studies. Among the studies that used body acupuncture, one used electroacupuncture.<sup>18</sup> Needle retention for 30 minutes was reported in one study,<sup>17</sup> and 20 minutes was reported in three studies.<sup>18–20</sup> Based on the findings of three studies employing body acupuncture, the placement of needles subsequent to the attainment of de qi, characterized by sensations of numbness, tingling, or warmth at the site of needle insertion, is pivotal for the efficacy of acupuncture. Furthermore, de qi is reported to serve as the fundamental mechanism underlying the sustained analgesic outcomes associated with acupuncture.<sup>31</sup> ST36, LI4, SP6 and EX-LE-10 were the most frequently used, and the SP6-ST36 combination, LI4-EX-LE-10 combination, and SP6-ST36-LI4 combination were the core acupoint combinations for MMPN patients. In previous studies, ST36 and SP6 were the most widely used acupoints for diabetic neuropathy,<sup>32</sup> and LI4 acupressure was effective at decreasing pain and duration of labour.<sup>33</sup> Acupuncture at ST36 has shown clinical benefits in relieving inflammation through mechanisms such as vagus nerve activation, macrophage polarization, and regulation of the MAPK signaling pathway, TLR4/NF- $\kappa$ B signaling, and the cholinergic anti-inflammatory pathway.<sup>34</sup> One study used auricular acupuncture in combination with body acupuncture. The auricular acupuncture acupoints used were shen men, point zero, and 2 additional auricular acupuncture points where the electrodermal signal was detected. According to evidence-based



medicine, auricular therapy has been demonstrated to be both efficacious and safe in managing cancer-related pain.<sup>35</sup> Furthermore, the combination of auricular therapy and drug therapy has shown superior effectiveness compared to the use of analgesic drugs alone in terms of both alleviating pain and minimizing adverse reactions.<sup>36</sup> Auricular point acupressure has the potential to serve as a cost-effective and efficacious complementary modality for individuals seeking to self-manage chemotherapy-induced neuropathy.<sup>37</sup>

According to the results of the included studies, acupuncture provides appropriate pain relief. A consistent decrease in pain intensity was observed according to the result of VAS, NPS, and BPI-SF results, indicating a significant advantage of acupuncture for MMPN patients experiencing pain. The analgesic efficacy of acupuncture has been demonstrated in animal-based research, whereby the activation of nerves that innervate muscles induces the secretion of neurotransmitters, including endorphin and enkephalin, and these neurotransmitters play a crucial role in modulating the pathways of the spinal cord, midbrain, and hypothalamo-hypophyseal system.<sup>38</sup> These alterations elicit the activation of descending pain pathways and exert a regulatory influence on the limbic system.<sup>39</sup> Additionally, the impact of acupuncture on CIPN can be elucidated through the release of opioid peptides and the mitigation of proinflammatory cytokines, and the anti-inflammatory effect of acupuncture is reported to be a key mechanism.<sup>40</sup> However, in a study by Tingbao,<sup>19</sup> there were no significant changes in any of the proinflammatory cytokines or neurotrophic factors at any time point after acupuncture.

The NCV test evaluates the degree of neural function, and discordant results existed among the included studies. The NCV test results did not significantly change between the baseline assessment and the end of the study in two studies,<sup>18,19</sup> and one study reported that the MCV and SCV results improved.<sup>17</sup> The FACT/GOG-Ntx and FACT-G reflect changes in CIPN patients' quality of life. Three studies reported that the FACT/GOG-Ntx score was decreased after acupuncture.<sup>17–19</sup> According to results reported by Tingbo,<sup>19</sup> enhancements in ambulation, manual dexterity, and auditory capabilities were observed. However, there was no observed improvement in joint pain, muscle cramps, or weakness. M Kay Garcia reported that the FACT-G score improved only on the physical well-being scale.<sup>18</sup> These findings indicated that acupuncture has the potential to relieve pain, restore neurological function, and improve quality of life, but more studies with a larger number of patients are needed to confirm these findings.

Heterogeneity in acupuncture therapy protocols, limitations of study design, differences in settings, and varying proficiencies of the acupuncturists have had an impact on the outcome. Although acupuncture is a relatively safe and empirically used treatment modality, there is a lack of high-quality evidence for the effectiveness of acupuncture with advanced methodology, which limits its popularization in clinical applications. PN was observed as a common clinical manifestation associated with MM or as a complication resulting from oncological treatment. All current research focuses on the BIPN, and the efficacy and safety of acupuncture for treating disease-related PN should be assessed in future studies.

## Conclusion

The above findings indicate that acupuncture has the potential to ameliorate pain and improve quality of life for MMPN patients, but there is a lack of consistent evidence on the efficacy of acupuncture in improving neural function. More randomized controlled trials are needed to validate the efficacy and safety of acupuncture in MMPN. Additionally, the extant studies involved only auricular or body acupuncture, and there is still in the homogeneity for the retention time, depth of the needle, and the treatment course. Effective cases and complete details of treatment should be encouraged to establish comprehensive acupuncture modalities and optimize standard treatment regimens for the treatment of MMPN.

## Data Sharing Statement

The detailed information is available from the corresponding author on reasonable request.

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## Disclosure

The authors have no conflict of interest to disclose.

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