# **Original Article**

# Effect of Electrical Stimulation on Gastrointestinal Symptoms in Lung Cancer Patients during Chemotherapy: A Randomized Controlled Trial

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# ABSTRACT

Objective: The objective was to evaluate the effects of transcutaneous acupoint electric stimulation (TAES) and gastric electrical stimulation (GES) on cancer patients with chemotherapy-induced gastrointestinal (GI) symptoms. Methods: A total of 122 lung cancer patients receiving chemotherapy were assigned randomly to the following two groups: control group (usual care group, n = 61) and intervention group (TAES plus GES, n = 61). TAES involved two acupoints such as Neiguan (PC6) and Zusanli (ST36). GES was performed at gastric pacing sites on the body surface such as the places of projection of gastric antrum and corpus on the body surface. GES was performed on these sites for 14 days continuously (25 min every time, once daily). The effects of TAES and GES on GI symptoms were assessed using the Memorial Symptom Assessment Scale on the day prior to chemotherapy (time point 1) and days 14 (time point 2) and

28 (time point 3) after chemotherapy. **Results:** No significant differences in the demographic and disease-related variables were detected between the two groups. Differences in symptom occurrence and severity at time point 1 were not statistically significant between the two groups (both P > 0.05). At time points 2 and 3, GI symptoms such as loss of appetite, nausea, vomiting, diarrhea, and constipation in the stimulation group had statistically significantly improved compared with the control group (all P < 0.05). **Conclusions:** TAES and GES were efficacious in relieving GI discomfort in lung cancer patients after chemotherapy. TAES combined with GES is a safe and easy-to-use tool to manage GI symptoms in practice.

**Key words:** Chemotherapy, gastric electrical stimulation, gastrointestinal symptoms, lung cancer patients, transcutaneous acupoint electrical stimulation

# Introduction

Lung cancer remains the most common cancer in both men and women in Eastern Asia<sup>[1]</sup> and the principal cause of cancer-related mortality in the world,

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which accounts for over one million deaths annually.<sup>[2]</sup> Chemotherapy remains the main treatment modality for

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the treatment of lung cancer.<sup>[3]</sup> Although chemotherapy can significantly reduce the mortality of lung cancer patients, chemotherapy-induced symptoms are still a major burden for them. Gastrointestinal (GI) symptoms are recognized as one of the most prevalent adverse events of chemotherapy.<sup>[4]</sup> An additional research has shown that the most burdensome symptoms in almost half of the cancer patients are GI symptoms caused by the diseases or treatments such as chemotherapy.<sup>[5,6]</sup>

The most common GI symptoms associated with chemotherapy are lack of appetite, chemotherapy-induced nausea and vomiting (CINV), constipation, and diarrhea.<sup>[7,8]</sup> Researches indicated that almost 80% of cancer patients have nausea, almost 70% of cancer patients have constipation, and over 50% of cancer patients have vomiting and diarrhea during chemotherapy.<sup>[9]</sup> Despite significant antiemetic advances, almost 50% of cancer patients undergoing chemotherapy still experience nausea and vomiting.

Currently, traditional Chinese medicine (TCM) treatment of GI symptoms has been the focus of many studies. With reference to National Comprehensive Cancer Network (NCCN) Guideline for Palliative Care version 1.2020, the interventions for nausea and vomiting include nonpharmacologic therapies such as acupuncture.<sup>[10]</sup> The Oncology Nursing Society has clearly indicated that acupuncture and acupressure are very effective nonpharmacologic interventions for CINV management and should be considered to be incorporated into practice guidelines.<sup>[11]</sup> Transcutaneous acupoint electric stimulation (TAES) incorporates the use of electrodes into traditional Chinese acupoint therapy to stimulate specific acupoints for the purpose of relieving symptoms and rehabilitation. According to TCM channel and collateral theory, acupoints such as Neiguan (PC6) and Zusanli (ST36) can be electrically stimulated to relieve CINV or constipation.<sup>[12]</sup> A study has shown that the electroacupuncture stimulation at PC6 can regulate endocrine level, inhibit gastric acid secretion, and promote the GI motility<sup>[13]</sup> and the electroacupuncture stimulation at ST36 can improve GI motility and promote defecation in humans.<sup>[14]</sup> Multiple acupoint stimulation has been proved to be more effective compared with single acupoint stimulation, especially in regulating the spleen and stomach function and promoting GI motility and thus can relieve certain symptoms such as nausea, vomiting, and constipation. The most commonly used acupoints for relieving GI symptoms are Neiguan and Zusanli.<sup>[15,16]</sup> The effect of two acupoint stimulation on GI symptoms in cancer patients has not been studied yet.

Gastric electrical stimulation (GES) is performed based on normal gastric electrophysiology and has a two-way regulation effect on gastric function. GES utilizes physiological frequency and high energy to entrain gastric slow waves, thus leading to improvement in gastric emptying. A study<sup>[17]</sup> has suggested that GES can exert an effect on the proximal stomach, thus leading to reduced gastric tone and increased gastric motility. A study has indicated that GES can relieve gastroparesis symptoms such as bloating, anorexia, nausea, and vomiting.<sup>[18]</sup> However, there is no evidence to indicate whether GES can play a role in improving chemotherapy-induced GI symptoms.

This study aimed to fill out this gap by investigating the effects of TAES and GES on chemotherapy-induced GI symptoms in lung cancer patients.

# Gastrointestinal symptoms, acupoint stimulation, and gastric electrical stimulation theory

#### **Gastrointestinal symptoms**

GI symptoms are not only a prevalent short-term adverse effect, but also a long-term problem. It has been proved that GI symptoms can increase patient distress and thus result in changes in functional status, treatment failure, depression, and poor quality of life in patients.<sup>[6]</sup> Most GI symptoms have a common pathogenic factor, or one symptom (e.g., nausea) may cause another symptom (vomiting), thus chemotherapy-induced GI symptoms have been more likely to occur in clusters and affect each other, and then negatively affect patient outcomes.<sup>[19]</sup> Cancer patients are commonly advised to take medicines to reduce the side effects of chemotherapy, but they prefer nondrug interventions.<sup>[20]</sup>

#### Acupoint stimulation theory

The Neiguan acupoint (PC6) is generally taken as a key acupoint for treating internal medicine disorders with the following effects: regulating qi; relieving chest stuffiness; normalizing stomach by checking the upward perverted Qi flow; and treating diseases in the chest, spleen, and stomach.<sup>[21]</sup> The Zusanli acupoint (ST36) is an acupoint of stomach meridians of foot Yangming, which is full of qi and blood. This acupoint is always stimulated to regulate the stomach-qi and remove pathogenic factors.<sup>[22]</sup>

#### Gastric electrical stimulation theory

The action mechanism of GES is not clear yet. Some studies suggest that the action mechanism of GES may be as follows: (I) GES may strengthen gastric slow wave activity and improve gastro-electric dysrhythmia, thus increasing gastric contraction and emptying; (II) GES at low and intermediate frequencies can promote the release of acetylcholine from nerve tissue and enhance gastric motility; and (III) the effect of GES may be mediated in part by the vagus nerve. Electrical stimulation can activate the endogenous myenteric nerve plexus and pacemaker cells (interstitial cells of Cajal), thus the gastric motility is increased.<sup>[23-25]</sup> In this study, cutaneous GES was performed.

# Methods

#### **Research design**

A randomized controlled trial design was used in this study. The research assistants collected the results of surveys on the day before chemotherapy (time point 1) and days 14 (time point 2) and day 28 (time point 3) after chemotherapy. The researchers explained the purpose of this study and asked each patient to sign a confidentiality agreement. All patients signed a written informed consent form before randomized assignment. This study was registered on the Chinese Clinical Trial Registry. The registration number of the clinical trial was ChiCTR1800018628.

#### Patients

The sample size was calculated using the formula by Chow *et al.*<sup>[26]</sup> according to the difference in the proportion of the two groups. We referred to the estimated incidence rate of nausea (66.9%) in the intervention group in our previous study, with the incidence rate of control group as 87.2%, with a type I error  $\alpha$  of 0.05, and 95% power (1 -  $\beta$ ), thus 105 participants were the calculated sample size. When considering 10% nonresponse rate, the final sample size was initially determined to be 116. The sample size was calculated according to the incidence rates of GI symptoms (lack of appetite, nausea, vomiting, constipation, and diarrhea) in our previous study; the sample size calculated according to the incidence rate of nausea was highest and was therefore selected as the final sample size.

#### **Settings**

All participants were recruited among the inpatients of Hunan Cancer Hospital in Changsha from December 2017 to March 2018. Patients were selected based on the following inclusion criteria: (I) patients diagnosed with lung cancer; (II) patients aged 18-80 years; (III) patients receiving the first cycle of chemotherapy after definite diagnosis; (IV) patients with normal functions of the main organs (such as liver, kidney, and heart); (V) patients expected to survive for >3 months; (VI) patients who had a Karnofsky performance status (KPS) score of 60 points; (VII) patients who signed informed consent form; and (VIII) patients who were able to understand and speak Mandarin Chinese. Patients who were pregnant and mentally ill or used a cardiac pacemaker were excluded from the study. The patients were treated free of charge, and they received no additional financial rewards. In order to reduce patients' dropout rate, we answered our patients' questions about this study and treatment in time. In addition, toothpastes, toothbrushes, and towels were handed out to patients after filling out questionnaires on day 28.

#### Intervention

Usual nursing care included physical exercise guidance, dietary modifications, and health consultation and medication instructions. GI–1 middle/low-frequency therapeutic apparatus (Beijing Simailaifu Medical Equipment Technology Co. Ltd., Beijing, China) was used for transcutaneous acupoint electrical stimulation and GES. The authors did not have any financial relationship with the company that sponsored this study.

#### Procedures

Trainings in relation to the acupoint positioning method and the intensity and frequency of electrical stimulation at two acupoints such as Neiguan (PC6) and Zusanli (ST36) and at the places of projection of the gastric antrum and corpus on the body surface were provided by clinical specialists in TCM and gastroenterological surgery. These two acupoints were positioned based on the anatomical locations of acupoints in Table 1 and Figures 1, 2.<sup>[27]</sup> GES electrodes were placed according to gastric pacing position

Table 1: Location of acupoints for the transcutaneous acupointelectrical stimulation and gastric electrical stimulationelectrodes						
Location						
Located on the palmar side of the forearm. 2 cun above the transverse crease of the wrist						
Sitting with the knee flexed. 1 cun below tibial tuberosity outside the inferior border						
2-4 cm away from the midpoint of the straight line between xiphoid and umbilicus at the right side						
3-5 cm away from the midpoint of the straight line between xiphoid and umbilicus at the left side and 1 cm away from the midpoint at the left side						

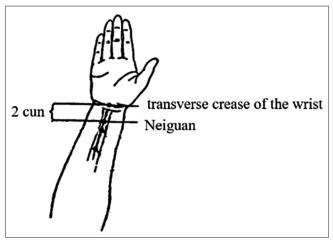


Figure 1: Neiguan location

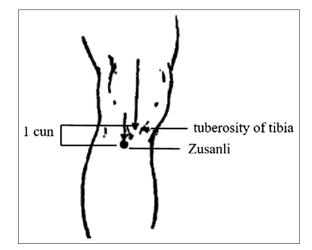


Figure 2: Zusanli location

as shown in Table 1 and Figure 3.<sup>[28]</sup> The gastric pacing position is projection points of the gastric antrum and gastric corpus on the body surface.

TAES and GES were performed for 25 min daily for 14 days. Electrodes were placed on bilateral acupoints PC6 and ST36, and then the GI–1 apparatus was connected, subsequently 2 kHz modulated medium frequency current and 1–150 Hz modulation frequency were used for stimulation. The positive and negative electrodes for use in gastric pacing were placed to projection points of the gastric antrum and gastric corpus on the body surface for 10 Hz modulation frequency with 50 ms pulse width. Each stimulation was performed for 25 min.

Based on Zi Wu Liu Zhu theory, acupoint stimulation combined with gastric pacing should be performed in lung cancer patients between 9:00 and 11:00 a.m. or 11:00 a.m. and 13:00 p.m. every day. The optimal stimulation intensity was regulated by individual maximum tolerance every day. The electrical stimulation was appropriate when the patient had mild acupuncture needle sensation and warm sensation at the places where the electrodes were placed, and then the patients gradually adapted to current stimulation. The intensity of the stimulating current was indicated in the electronic medical record at every treatment. The patients were also informed of each acupoint stimulation session, involving stimulation date, frequency, and intensity. After each session, the patients made an appointment for the next session.

The second time point (day 14) was determined because of the intervention period. In addition, a cycle was defined as 28 days in all patients receiving chemotherapy regimens, thus we selected day 28 as the third time point to measure whether electrical stimulation had long-term effect on GI symptoms.

#### Measures

The general information of patients such as age, gender, education, marital status, and occupation and the

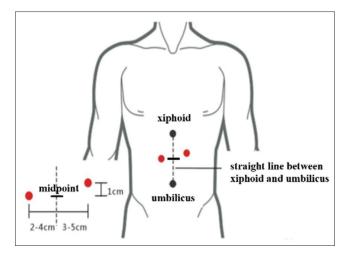


Figure 3: Gastric pacing position

disease-related data such as stage, type of chemotherapy, antiemetic regimen, and the Karnofsky performance status (KPS) score were measured, and GI symptoms were assessed using the Memorial Symptom Assessment Scale (MSAS), which reflected the incidence rate, severity, and distress of GI symptoms.

MSAS is a 32-item, multidimensional patient-rated scale that has been developed to assess common cancer-induced physical and psychological symptom.<sup>[29]</sup> Twenty-four symptoms are evaluated with regard to frequency, severity, and distress, while only eight symptoms are evaluated with regard to severity and distress.<sup>[30]</sup> In the scale, symptoms are recorded as present or absent. If the symptoms are present, their frequency and severity are recorded using a 4-point rating scale (1–4), or the distress status is recorded using a 5-point rating scale (0-4) during the previous 1 week. Higher scores indicate higher frequency, severity, and distress of symptoms. If there is no incidence of one symptom, the score of that symptom is 0. If one symptom is present, the symptom score is the total average score within the rating scale.<sup>[31]</sup> MSAS includes Physical Symptom Subscale Score (PHYS), Psychological Symptom Subscale Score (PSYCH), and Global Distress Index (GDI). PHYS score is the total average score for 12 symptoms such as lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth, nausea, vomiting, taste change, weight loss, feeling bloated, and dizziness. The PSYCH is an average of the total of all scores for six symptoms such as worrying, sadness, nervousness, difficulty sleep, feeling irritable, and difficult to concentrate. GDI is the average frequency of four psychological symptoms (feeling sad, worrying, feeling irritable, and nervous) and the distress related to six physical symptoms (appetite loss, lack of energy, pain, feeling drowsy, constipation, and dry mouth). Total MSAS score is the average of symptom scores for all the 32 symptoms.<sup>[32]</sup> MSAS has demonstrated good validity and reliability in many countries,<sup>[29-31]</sup> and it has been translated into Chinese and applied to measure the statuses of multidimensional symptoms of cancer survivors.<sup>[33]</sup> The reliability of subscales and total Cronbach's alpha coefficients of Chinese version of MSAS range from 0.79 to 0.87.

#### Statistical analysis

SPSS 22.0 (StataCorp, College Station, TX, USA) was used for statistical analyses. Demographic data, baseline characteristics, and incidence rates of GI complications were analyzed using descriptive statistical analysis, and the results were expressed as mean and percentage. Chi-squared test was used to compare demographic data between two groups. Repeated-measures analysis of variance and *t*-test were used to analyze the effectiveness of interventions. P <0.05 was considered statistically significant.

#### **Ethical approval**

This study was approved by the Medical Ethics Committee of the Hunan Cancer Hospital, China (Approval No. 2017 year [12]). The researchers elaborated on the content of the clinical trial, including possible benefits and harms, and then obtained written informed consent forms from all patients. If the results confirmed that the electrical stimulation was effective in patients in the intervention group, the patients in the control group would also undergo the same TAES and GIES treatment as the patients in the intervention group after this study.

#### Results

A total of 130 patients were recruited on a voluntary basis, of whom, 4 patients refused to participate in this study, 2 patients dropped out of this study due to the fact that their personal circumstances were changed, and 2 patients could not tolerate chemotherapy. Ultimately, 122 patients were included in the intervention and control groups, with 61 patients in each group. All patients in the intervention group who underwent electrical stimulation had no adverse events [Figure 4].

#### **Baseline characteristics**

A total of 130 lung cancer patients were invited to participate in this study; 8 patients did not complete the questionnaire, and finally 122 (93.8%) patients were included in the final analysis. The general characteristics of the patients are presented in Table 1. Fifty-nine (48.4%) patients had Stage III lung cancer. Seventy-nine (64.8%) patients were treated with 5-HT<sub>3</sub>RA + NK-1RA + dexamethasone. There were no significant differences in baseline characteristics between the two groups [all P > 0.05, Tables 2 and 3], and there was no significant difference in KPS score between the two groups (P = 0.135).

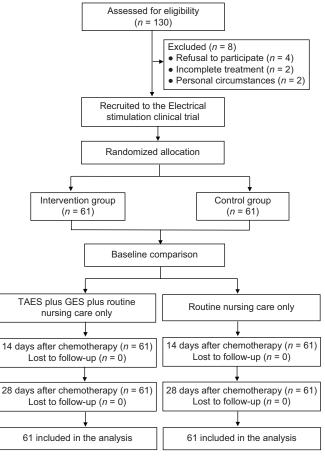


Figure 4: Flowchart of the study

### Effects of transcutaneous acupoint electric stimulation and gastric electrical stimulation on gastrointestinal symptoms

The incidence rates of GI symptoms in 122 patients were detected at time points 1–3. Table 4 illustrates that there were no significant differences in all the GI symptoms between the two groups at time point 1 (P > 0.05). At time point 2, the incidence rates of loss of appetite, nausea, and constipation had significantly decreased in the intervention group compared with that of the control group (P < 0.05). There were significant differences in loss of appetite, nausea, constipation, and diarrhea between the two groups at time point 3 (P < 0.05).

Table 5 shows standard deviation outcome scores and the differences between two groups, time effect, and interaction effect on each GI symptom at time points 1–3. There were statistically significant differences in incidence rates and scores of loss of appetite, nausea, vomiting, and constipation between the two groups. Compared with the baseline data, the severity scores of each GI symptom decreased significantly at time point 3 in the intervention group and increased in the control group (all  $P_{groups} < 0.05$ ). The time effects on loss of appetite, nausea, vomiting, and constipation scores were also significant. There was a

Mao, et al.: Electrical	Stimulation on	Gastrointestinal	Symptoms	in Lung (	Cancer Patients
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Variables	Intervention group ( <i>n</i> =61), <i>n</i> (%)	Control group ( $n=61$ ), $n$ (%)	Chi-squared test	Р
Gender				
Male	44 (72.1)	48 (78.7)	0.707	0.400
Female	17 (27.9)	13 (21.3)		
Education				
Primary	7 (11.5)	5 (8.2)	0.505	0.904
Secondary	20 (32.8)	20 (32.8)		
Bachelor	23 (37.7)	26 (42.6)		
Higher education	11 (18.1)	10 (16.4)		
Marital status				
Unmarried	0	1 (1.6)	1.542	0.673
Married	56 (91.8)	57 (93.4)		
Divorced	2 (3.3)	1 (1.6)		
Widow	3 (4.9)	2 (3.3)		
Occupation				
Full time	17 (27.9)	11 (18.0)	4.052	0.256
Part time	19 (31.1)	14 (23.0)		
Student	6 (9.8)	8 (13.1)		
Others	19 (31.2)	28 (45.9)		
Stage				
II	17 (27.9)	19 (31.1)	0.868ª	0.648
III	32 (52.5)	27 (44.3)		
Others	12 (19.7)	15 (24.6)		
Type of chemotherapy				
EP	34 (55.7)	35 (57.4)	0.298	0.862
NP	25 (41.0)	23 (37.7)		
IP	2 (3.3)	3 (4.9)		
Antiemetic regimen				
5-HT3 RA + NK1RA	12 (19.7)	13 (21.3)	0.376ª	0.829
5-HT3RA + NK1RA + dexamethasone	41 (67.2)	38 (62.3)		
Others	8 (13.1)	10 (16.4)		

Table 3: Comparison of baseline values of continuous variables between the two groups (Mean±SD)

Variables	Intervention group (n=61)	Control group ( $n=61$ )	t-test	Р			
Age (years)	$50.66 \pm 9.621$	$50.48 \pm 10.748$	-0.098	0.922			
KPS	$84.92 \pm 6.224$	$86.72 \pm 7.005$	1.503	0.135			
KPS: Karnofsky performance status; SD: Standard deviation							

significant decrease in the severity scores of GI symptom at time points 2 and 3 compared with that of baseline scores (all  $P_{\text{time}} < 0.05$ ). In addition, different GI symptoms caused different levels of distress. In the intervention group, loss of appetite was the most troublesome symptom for patients at time points 1–3. In the control group, nausea was the most troublesome symptom at time points 1 and 3.

#### Discussion

This study evaluated the effects of TAES and GES on GI symptoms in lung cancer patients during chemotherapy. The results showed that the incidence rate and severity of GI symptoms in lung cancer patients increased slightly during chemotherapy, which may be related to the injured GI mucosa,

release of neurotransmitters and inflammatory mediators, and altered sensation caused by chemotherapy. Therefore, the patients may experience a number of GI symptoms.<sup>[6]</sup> It is not easy to improve GI symptoms for cancer patients due to the fact that there is no standard guideline for GI symptom interventions. At present, chemotherapy-induced GI symptoms need to be taken seriously.

This study demonstrated that TAES on Neiguan (PC6) and Zusanli (ST36) combined with GES can be used to reduce the incidence rate, severity, and level of disturbance of GI symptoms. Our findings are similar to those reported in previous literatures. Some studies have proved that the acupoint stimulation has a certain mitigating effect on chemotherapy-induced CINV,<sup>[34]</sup> constipation,<sup>[35]</sup> and diarrhea.<sup>[36]</sup> Another study concluded that GES is effective in improving appetite loss, nausea, and vomiting in gastroparesis patients.<sup>[37]</sup> TAES combined with GES is a value-added intervention besides pharmaceutical management for lung cancer patients. The incidence rates of GI symptoms were compared between two groups, and the results indicated that the electrical stimulation therapy was most effective in reducing nausea symptom, which maybe due to the fact that most patients in this study received combined treatment of multiple antiemetics such as 5-HT<sub>3</sub>RA + NK1RA + dexamethasone

Variables	Groups	Time point 1 (%)	Time point 2 (%)	Time point 3 (%)	
Loss of	Intervention group	73.8	80.3	77.0	
appetite	Control group	83.6	93.4	91.8	
	$\chi^2$	3.335	4.60	9.904	
	Р	0.189	0.032*	0.019*	
Nausea	Intervention group	68.9	77.0	60.7	
	Control group	57.4	96.7	96.7	
	$\chi^2$	1.725	10.358	23.657	
	Р	0.189	0.001**	0.000**	
Vomiting	Intervention group	29.5	24.6	24.6	
	Control group	23.0	24.6	24.6	
	$\chi^2$	0.678	0.000	0.000	
	Р	0.410	1.000	1.000	
Constipation	Intervention group	59.0	47.5	34.4	
	Control group	55.7	65.6	68.9	
	$\chi^2$	0.134	4.037	14.475	
	Р	0.714	0.045*	0.000**	
Diarrhea	Intervention group	11.5	13.1	6.6	
	Control group	11.5	21.3	21.3	
	$\chi^2$	1.438	1.438	5.536	
	Р	0.230	0.230	0.019*	

for parenteral anticancer agents (cisplatin) with a high emetic potential, which were recommended by NCCN Guidelines Version 2.2020 Antiemesis.

ST36 on the stomach meridian is commonly stimulated to relieve spleen-deficiency syndrome. The theory of TCM holds that chemotherapy agents can disturb qi and blood of the human body and impair the normal function of zang-fu organs, especially the spleen and stomach, which may be manifested as nausea, vomiting, and poor appetite. The major therapeutic principles are soothing the liver-qi stagnation, regulating the stomach-qi, and removing the dampness.<sup>[38]</sup> The combined stimulation of two acupoints can regulate the gi of middle jiao, enhance the body resistance, and prevent or relieve nausea and vomiting. Therefore, TAES acupoints such as Neiguan and Zusanli can improve GI symptoms. Chen proved that acupoint stimulation such as electroacupuncture and acupressure can reduce chemotherapy-related toxicities, especially GI symptoms (e.g., nausea, vomiting, and diarrhea), and increase chemotherapeutic efficacy.<sup>[39]</sup>

GES can enhance the excitability of the GI system, and it can also inhibit the initiation of abnormal activity. GES may accelerate the conduction velocity of the slow wave, promote the coupling of the slow waves, and coordinate the mechanical-electrical coupling after the meal.<sup>[40]</sup> GES was originally developed for strengthening and regulating gastric slow waves. One method of stimulation is termed gastric pacing, by

Variables	Groups	Time point 1	Time point 2	Time point 3	F <sub>time</sub>	P <sub>time</sub>	F <sub>groups</sub>	Pgroups	F <sub>interaction</sub>	<b>P</b> <sub>interaction</sub>
Loss of appetite										
Symptom	Intervention group	$1.31 \pm 1.01$	$1.30 \pm 0.86$	$0.90 \pm 0.60$	8.00	0.000	10.62	0.001	13.04	0.000
severity	Control group	$1.08 \pm 0.84$	$1.62 \pm 0.99$	$1.75 \pm 1.03$						
Symptom	Intervention group	$1.08 \pm 0.84$	$1.33 \pm 0.87$	$1.05 \pm 0.72$	13.07	0.000	8.032	0.005	9.209	0.000
distress	Control group	$1.25 \pm 0.91$	$1.66 \pm 0.98$	$1.77 \pm 1.02$						
Constipation										
Symptom	Intervention group	$0.90 \pm 0.91$	$0.64 \pm 0.71$	$0.43 \pm 0.64$	4.188	0.016	5.89	0.017	13.80	0.000
severity	Control group	$0.85 \pm 0.91$	$1.05 \pm 0.92$	$0.98 \pm 0.79$						
Symptom	Intervention group	$0.95 \pm 0.94$	$0.72 {\pm} 0.78$	$0.36 \pm 0.55$	3.65	0.028	6.31	0.013	24.62	0.000
distress	Control group	$0.85 \pm 0.91$	$1.08 \pm 1.01$	$1.15 \pm 0.95$						
Diarrhea										
Symptom	Intervention group	$0.11 \pm 0.32$	$0.13 \pm 0.34$	$0.07 {\pm} 0.25$	3.97	0.020	4.03	0.047	9.44	0.000
severity	Control group	$0.13 \pm 0.39$	$0.23 \pm 0.46$	$0.38 \pm 0.76$						
Symptom	Intervention group	$0.13 \pm 0.39$	$0.16 \pm 0.45$	$0.05 \pm 0.22$	3.18	0.043	4.65	0.033	8.06	0.000
distress	Control group	$0.15 \pm 0.44$	$0.31 \pm 0.65$	$0.41 \pm 0.80$						
Nausea										
Symptom	Intervention group	$0.89 \pm 0.76$	$1.08 \pm 0.76$	$0.69 \pm 0.62$	3.33	0.037	39.31	0.000	8.71	0.000
severity	Control group	$1.46 \pm 0.57$	$1.49 \pm 0.62$	$1.59 \pm 0.69$						
Symptom	Intervention group	$1.10 \pm 0.83$	$1.18 \pm 0.90$	$0.64 \pm 0.68$	4.08	0.018	32.13	0.000	28.08	0.000
distress	Control group	$1.51 \pm 0.60$	$1.57 \pm 0.62$	$1.79 \pm 0.71$						
Vomiting										
Symptom	Intervention group	$0.41 \pm 0.82$	$0.33 \pm 0.63$	$0.26 \pm 0.51$	6.61	0.002	4.77	0.031	17.14	0.000
severity	Control group	$0.30 \pm 0.56$	$0.69 \pm 1.18$	$0.92 \pm 1.23$						
Symptom	Intervention group	$0.43 \pm 0.85$	$0.34 \pm 0.66$	$0.30 \pm 0.56$	7.55	0.001	4.50	0.036	16.70	0.000
distress	Control group	$0.31 \pm 0.62$	$0.72 \pm 1.24$	$0.97 \pm 1.30$						

using physiologic frequency and high energy to entrain gastric slow waves, leading to improvement of gastric emptying.<sup>[25]</sup> Wendorf *et al.* used GES to reduce severity and incidence rates of nausea and vomiting in patients with gastroparesis and gastroparesis-like syndromes. Lin *et al.*<sup>[41]</sup> reported that chronic GES can dramatically reduce the use of antiemetic medicine, thus improving the quality of life of patients. The organs such as stomach have their own natural pacemakers, and electrical signals they generate can be changed by delivering certain types of electric currents to certain areas of the GI tract.

GI electrical stimulation can normalize gastric dysrhythmia, which resembles the cardiac pacing used in the treatment of cardiac arrhythmia.

Recently, a 3-year clinical study was carried out by Cutts *et al.*,<sup>[42]</sup> and the results showed that GES is superior to standard pharmacological therapies in improving GI symptoms and life quality and reducing medical expenses. A 5-year follow-up study of Abell *et al.* demonstrated that GIES has remarkable effectiveness in improving nausea and vomiting, decreasing the use of parenteral alimentation, and enhancing the life quality of patients.<sup>[43]</sup>

#### Limitations

This study has a few limitations. First, all patients were receiving the first cycle of chemotherapy after diagnosis, but GI symptoms might be worsened during later cycles of chemotherapy. Second, the data were collected only three times during 28 days, which might increase a memory bias and thus affect the study results. In future research, data should be collected more frequently to minimize the potential risk of memory bias. In addition, this study only included lung cancer patients undergoing chemotherapy; more studies are needed to confirm whether the findings of this study can be recommended to cancer patients who receive other forms of treatments such as radiotherapy and surgery. Therefore, in future studies, different cancer diagnoses and treatments should be considered to increase the generalizability of the findings. Finally, appropriate duration of TAES and GES for different patients should be analyzed more precisely in future studies.

#### Implications for oncology nursing

Electrical stimulation is a nonpharmaceutical and easy-to-use tool to manage GI symptom in lung cancer patients receiving chemotherapy. Unlike chemotherapy drugs, electrical stimulation will not cause any side effects. Our study can also provide a standard procedure on intervention (e.g., intervention period) for oncology nurses, which can promote patient satisfaction and life quality in cancer patients.

## Conclusions

TAES and GES can have an effect on GI symptoms. TAES and GES can offer an inexpensive and convenient method for the treatment of lung cancer patients undergoing chemotherapy, which can relieve GI symptoms from day 1 to day 14 during chemotherapy. Future studies should focus on improving the generalizability of promising findings and optimizing study design.

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#### **Conflicts of interest**

The corresponding author, Prof. Yongyi Chen, is the editorial board member of the journal.

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