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Effect of Somatosensory Interaction Transcutaneous Electrical Acupoint Stimulation on Cancer-related Fatigue and Immunity

A Randomized Controlled Trial

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Background: This study was intended to evaluate the clinical effect of somatosensory interaction transcutaneous electrical acupoint stimulation (SI-TEAS) on cancer-related fatigue (CRF) and its safety.

Methods: The study protocol had been registered in China Clinical Trial Registration Center with registration number: ChiCTR2100045655. CRF patients were equally divided into SI-TEAS Group, Acupressure Group and Sham Acupressure Group to receive SI-TEAS, acupressure and sham acupressure treatments 5 times a week. The fatigue levels of patients in the 3 groups were measured by the Piper Fatigue Scale during the baseline period and after 4 and 8 weeks (of treatment). The cell immunity of these patients was determined by detecting the T-lymphocyte subsets and NK cells.

Result: Of the 300 participants, 279 have gone through the independent rehabilitation intervention study, including 94 in the SI-TEAS Group, 92 in the Acupressure Group, and 93 in the Sham Acupressure Group. Intergroup comparisons of fatigue degree and cell immunity, namely SI-TEAS Group versus Acupressure Group, Acupressure Group versus Sham Acupressure Group, and SI-TEAS Group versus Sham Acupressure Group, showed that group changes observed during the baseline period and different time points after Week 4 and 8 were statistically different ($P < 0.05$). The SI-TEAS Group had the sharpest decreases in the behavioral, sensory, emotional and cognitive dimensions of fatigue, and the total score, followed by the Acupressure Group, while the Sham Acupressure Group did not show significant changes; the SI-TEAS Group experienced the sharpest increases in the absolute counts of $CD3^+$ T cells, $CD4^+$ T cells, $CD8^+$ T cells, $CD4^+/CD8^+$ T cells, and NK cells, followed by the Acupressure Group, while the Sham Acupressure Group did not show significant changes.

Conclusion: SI-TEAS could significantly relieve the fatigue of CRF patients and improve their cell immunity, which maybe a useful and effective option for reducing CRF in clinical practice.

Key Words: therapy, cancer-related fatigue, TEAS, SI, acupressure, treatment, care

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Cancer-related fatigue (CRF) is one of the most common symptoms of cancer patients, and its incidence rate ranges from 60% to 90%.[1–3] At present, the pathogenesis of CRF remains unclear, and no effective drugs to treat this symptom have been recognized so far.[4,5] Clinical studies showed that nondrug therapy[6] and complementary and alternative therapies,[7] especially acupuncture and acupoint stimulation therapy,[8,9] can significantly relieve CRF. Transcutaneous electrical acupoint stimulation (TEAS) intervention can facilitate neuron regeneration and neurotrophin secretion, increase muscle strength and activity, and improve a variety of accompanying symptoms and quality of life.[10–12] However, TEAS treatment is completely dependent on doctors, and the relevant medical resources are in shortage. Moreover, because the treatment protocols are not universal and because patients have limited self-awareness towards their own condition, recovery can hardly be continued and the treatment is ineffective.[13,14] TEAS studies focus mostly on its effects, while technical innovation in this regard is rarely discussed. The application of somatosensory interaction (SI) in independent rehabilitation with acupoint massage is a new type of sports rehabilitation method.[15,16] It can capture a patient's body movements through somatosensory control equipment, identify and locate acupoints through human-computer interaction, and feedback real-time physiological data during the treatment process to provide possibilities for independent rehabilitation.[17]

The SI-TEAS massage system integrates SI acupoint recognition and location, TEAS, and surface electromyogram (SEMG) signal acquisition. The system, independently developed by Zhejiang Provincial People's Hospital (awarded national software copyright patent, No. 2020SR1236626), consists of a medical care management end, a somatosensory control end, a patient smartphone end, and an acupoint physical therapy end.[18] The overall structure of the SI-TEAS massage system is shown in Figure 1. The specific functions and

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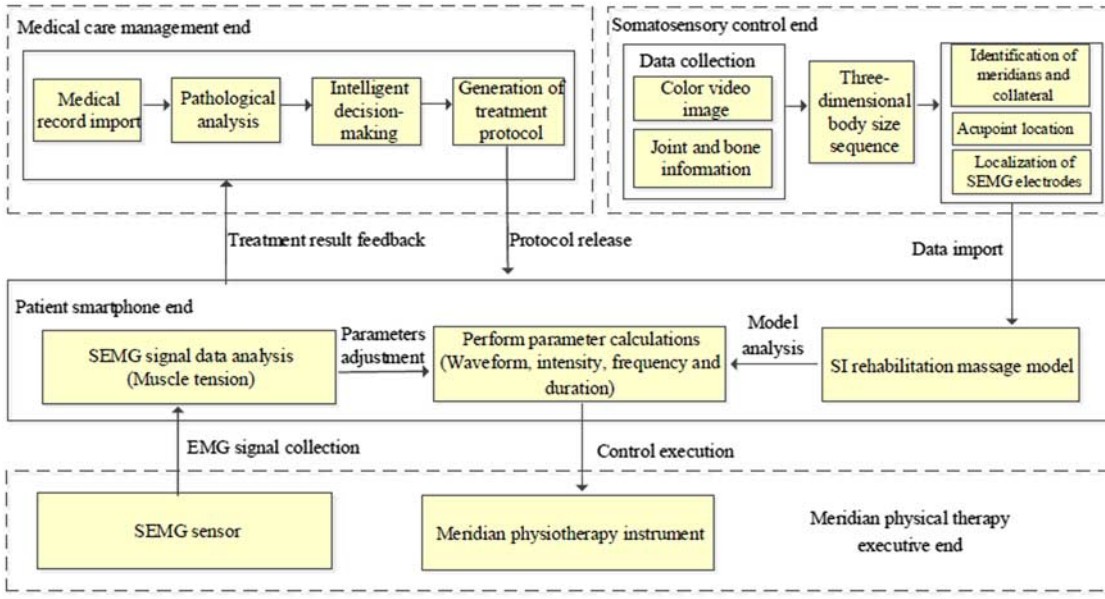

FIGURE 1. Overall structure of SI-TEAS Massage System. SI indicates somatosensory interaction. full color online

implementation method of the system are as follows: medical care management end: managing all patients' rehabilitation information, including individual diagnosis and treatment information and rehabilitation schemes. The management process starts with importing information including the patient's basic information, contact information, body mass index, tumor, node, metastases (TNM) stage, menopausal status, and treatment methods. Then, the system makes a scientific analysis on adverse reactions and intelligently recommends a treatment protocol based on the TNM stage as well as the pathologic examination results and surgical data of the patient. Finally, the doctor adjusts the protocol based on his clinical experience and generates an individual acupoint massage intervention plan that suits the patient. Somatosensory control end: instructing the patient to locate meridians and collateral, acupoints, and SEMG electrodes. First, the somatosensory controller collects color video images and joint and bone information of the patient, and generates 3-dimensional body size sequence data. The meridian acupoint grid model is corrected based on the 3-dimensional body size data, and dynamic fittings of the body are completed based on skeleton correspondence. This prepares for real-time collection of body posture information through video. Then, with the SI technology, the patient is instructed to learn basic acupoint massage. Patient smartphone end: managing the patient's individual rehabilitation through acupoint massage. The patient massages herself as instructed by the SI rehabilitation massage model and the waveform, intensity, frequency, and duration of massage intervention automatically set by the system. During the rehabilitation process, the system detects muscle tension data based on the SEMG signal and automatically adjusts the parameters of massage intervention. After the massage intervention is completed, the smartphone end will upload the patient's rehabilitation data to the medical care management end, and the patient may also give feedback to and consult her doctor through voice or text. Acupoint physical therapy end: executing the TEAS massage command given from the smartphone end and tracking acupoint SEMG changes during the TEAS process.

Therefore, this study focus on the typical symptom of CRF in cancer patients and attempts to explore an effective treatment method for CRF by applying the innovative SI-TEAS massage system in personalized and independent acupoint massage intervention, to provide evidence to the clinical treatment and nursing care of CRF.

METHODS

Ethical Approval

This study was a randomized controlled trial design. The study protocol had been registered in China Clinical Trial Registration Center with registration number: ChiCTR2100045655. The study had been approved by the Ethics Committee of Zhejiang Provincial People's Hospital (approval number: 2021QT133). Written informed consents had been obtained from all the participants.

Research Population

Cancer patients treated in the Department of Acupuncture and Oncology of our hospital from March to August 2020 were selected. On the basis of a random number table, the patients were randomly divided into the SI-TEAS Group, the Acupressure Massage (AM) Group, and the Pseudo Acupoint Massage (FAM) Group.

The inclusion criteria for patients were as following: all the subjects were diagnosed as malignant tumors by pathology or cytology; they met the CRF diagnostic criteria specified in the International Classification of Diseases (Version 10) (ICD-10) that included recurrence and duration of fatigue symptoms for over 2 weeks, accompanied by 5 or more other symptoms[19]; they were scored ≥ 4 on the Revised Piper Fatigue Scale (RPFS)[20]; their expected survival time was ≥ 6 months; They were aged 60 years or below; they or their family members were able to use computers and smartphones; they were willing to participate in this study.

The exclusion criteria for patients were as following: suffering from tumor recurrence or metastasis confirmed by clinical and imaging examinations; having severe heart, lung insufficiency or other major primary diseases; having

contraindications to acupoint massage; having a history of mental illness; having severe skin diseases; past participation in other clinical research.

Intervention Method

This study was a randomized controlled trial. On the basis of a random number table, patients were randomly and equally divided into the SI-TEAS Group (strong stimulation), the AM Group (mild stimulation), and the FAM Group (sham stimulation). The researchers used an evaluation tool to evaluate the treatment effects on the patients before the intervention and during the fourth and eighth weeks (of treatment), respectively. The intervention was applied for a total of 8 weeks.

SI-TEAS Group

According to the Chinese national standard *Location of Points* (GB 12346-90), the research team, after making statistical analysis, filtration and adjustments, selected points like Baihui, Taiyang, Dazhui, Zhongwan, Guanyuan, Qihai, Neiguan, Shenmen, Zusanli, Sanyinjiao, and Taixi for the SI-TEAS intervention, based on the physiological characteristics of acupoints and their relevance to the disease,[21,22] while considering the independent rehabilitation demand of the patients, drawing on the existing clinical first-line experience, and combining expert consultations.

The intervention was applied once a day and for 5 days a week. There were 2 courses of treatment, 4 weeks for each. The intervention was applied specifically as follows. Patient management records were documented: nurses entered the collected basic information and disease related information about the patients into the SI acupoint massage system, and medical staff determined an acupoint massage intervention scheme according to the patient's condition. Preliminary guidance: step by step, therapists helped the patients or their family members to understand the *Guide to the Use of Somatosensory Interaction Acupoint Massage System* and related acupoint massage rehabilitation methods; they also provided guidance on how to install the system Application on the patient smartphone end, how to import personal information, how to download the rehabilitation treatment scheme, how to generate specific multimedia information (texts, pictures, videos, etc.) for implementation, and how to communicate with medical staff through voice and text. Massage equipment was lent to the patients, along with instructions for use. SI acupoint massage location: The patient, facing the somatosensory controller, stood at the shooting center of the human body model, and the somatosensory controller captured pictures of her bones and muscles. The pictures were converted into a dynamic simulation model fit with the human body. Key marked points were determined in the model to automatically generate the acupoints in the patient. Faced the somatosensory controller and the computer display screen, the patient followed the system instructions to locate meridians and collateral, to identify acupoints, to learn to identify acupoints in the muscle belly, and to check whether the acupoints and muscle belly were located correctly. Application of acupoint massage: the patients opened the acupoint massage application on their smartphones at home and followed the instructions to put 50×50 mm electrodes against designated acupoint for TEAS acupoint massage. Positive and negative electrodes with a diameter of 10 mm were applied to the muscles at the corresponding acupoints, with a distance of 20 mm between the electrodes. The SEMG signal from the muscles was detected in real time, and the waveform, intensity, frequency, and duration of massage were adjusted dynamically. After the massage was ended, local skin was observed for damaged or swelling. Communication: after the massage was ended, the patients entered feedback in the Application through voice or text to communicate with their doctors and nurses. Monitoring management: the medical staff analyzed and evaluated the massage effect on the patients based on the phased rehabilitation treatment data transmitted from the patients' smartphone Application every week, and adjusted the rehabilitation scheme.

AM Group

The therapists imparted acupoint massage knowledge to patients in the AM Group, distributed independent acupoint massage training materials to them, taught them massage methods and techniques, time, precautions and so on through PPT, and provided practical demonstrations. The AM Group had the same acupoints for the syndromes as the SI-TEAS Group. The patients were supposed to gently press the selected acupoints with their fingertips and turned their fingertips in a clockwise direction while holding on the acupoints to produce sore, numb, swelling, and painful feelings. The massage was applied once per day and 5 times per week, with each acupoint pressed for 3 to 5 minutes and with a frequency of 90 to 120 times per minute. Specialist nurses followed up the patients once per week by phone or WeChat to check the application of massage interventions and answer questions.

FAM Group

The FAM Group followed the same massage method and massage intervention process as the AM Group. The therapists instructed patients in the FAM Group to press 8 to 10 acupoints. The acupoints to be pressed were different from those used in the symptom treatment. All the patients did not realize the irrelevance of these pressed acupoints to the symptom treatment.

Evaluation Indicators

The effects on the CRF patients were evaluated by a selected treatment effect observation system that combined a subjective scale with laboratory examination indicators. The RPFS was selected to evaluate the CRF of the patients. It included a scale from 0 to 10 to evaluate the behavioral, sensory, emotional, and cognitive dimensions of fatigue, plus a total score. The higher the score, the more tired the patient was[23,24] 5 mL fasting venous blood samples were collected from the patients 1 day before the intervention as well as 4 and 8 weeks after the interventions. Immunofluorescence and flow cytometry were used to test the serum T-lymphocyte subsets-related indicators ($CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$) and NK cells[25] to assess the cellular immunity of the patients.

Statistical Method

SPSS 22.0 statistical software was used to analyze the data, and use cases were classified, expressed in percentage, and subject to χ^2 test; the measurement data was expressed as mean ± SD and subject to analysis of variance; a mixed effect model was used to evaluate intergroup differences from baseline to the eighth week, and with time and group as fixed effects, intergroup differences were calculated with a 95% confidence interval (CI) at each time point; all the results were statistically significant, with $P < 0.05$. Absolute count tubes were used to take the absolute counts of cell subsets to further analyze blood cell samples. The absolute counts of lymphocyte subsets were taken according to the accurately quantified fluorescent microspheres in the tubes as standard internal reference.

RESULTS

Patient Inclusion and Characteristics

A total of 300 female breast cancer postoperative patients were included in the study (Fig. 2 for the comprehensive standards for this reporting trial), and 5 cases were excluded at the end of the study. One patient in the SI-TEAS Group was excluded for quitting the second course of treatment after feeling that the symptom was gone after 4 weeks; 2 patients were excluded for not receiving a reexamination after 4 weeks; 3 patients were excluded for not receiving a reexamination after 8 weeks. One patient in the Acupressure Group was excluded for not being obedient and refusing to apply acupoint massage; 2 patients were excluded for not receiving a reexamination after 4 weeks; 3 patients were excluded for not receiving a reexamination after 8 weeks; 2 patients were excluded for incomplete data. Two patients in the Sham Acupressure Group were excluded for not being obedient and refusing to apply acupoint massage; 1 patient was excluded for not receiving a reexamination after 4 weeks; 2 patients were excluded for not receiving a reexamination after 8 weeks; 2 patients were excluded for incomplete data. Finally, 279 cases completed the study, including 94 cases in the SI-TEAS Group, 92 cases in the Acupressure Group, and 93 in the Sham Acupressure Group.

The differences between the 3 groups in terms of sex, age, marriage, education, tumor type, TNM staging, and treatment method were not statistically significant (all $P > 0.05$), indicating that they were comparable in the baseline characteristics. See Table 1 for details.

Comparison in Fatigue Dimensional and Immunity Changes at Different Time Points

Table 2 and Figure 3 provided changes in the scores in each fatigue dimension and the total scores of the 3 treatment groups after the fourth and eighth weeks compared with the baseline period. Judging from the mixed linear model, a clear downward trend could be observed in all the fatigue dimensional scores and the total score of patients in the SI-TEAS Group after 4 and 8 weeks of intervention. The same trend could be

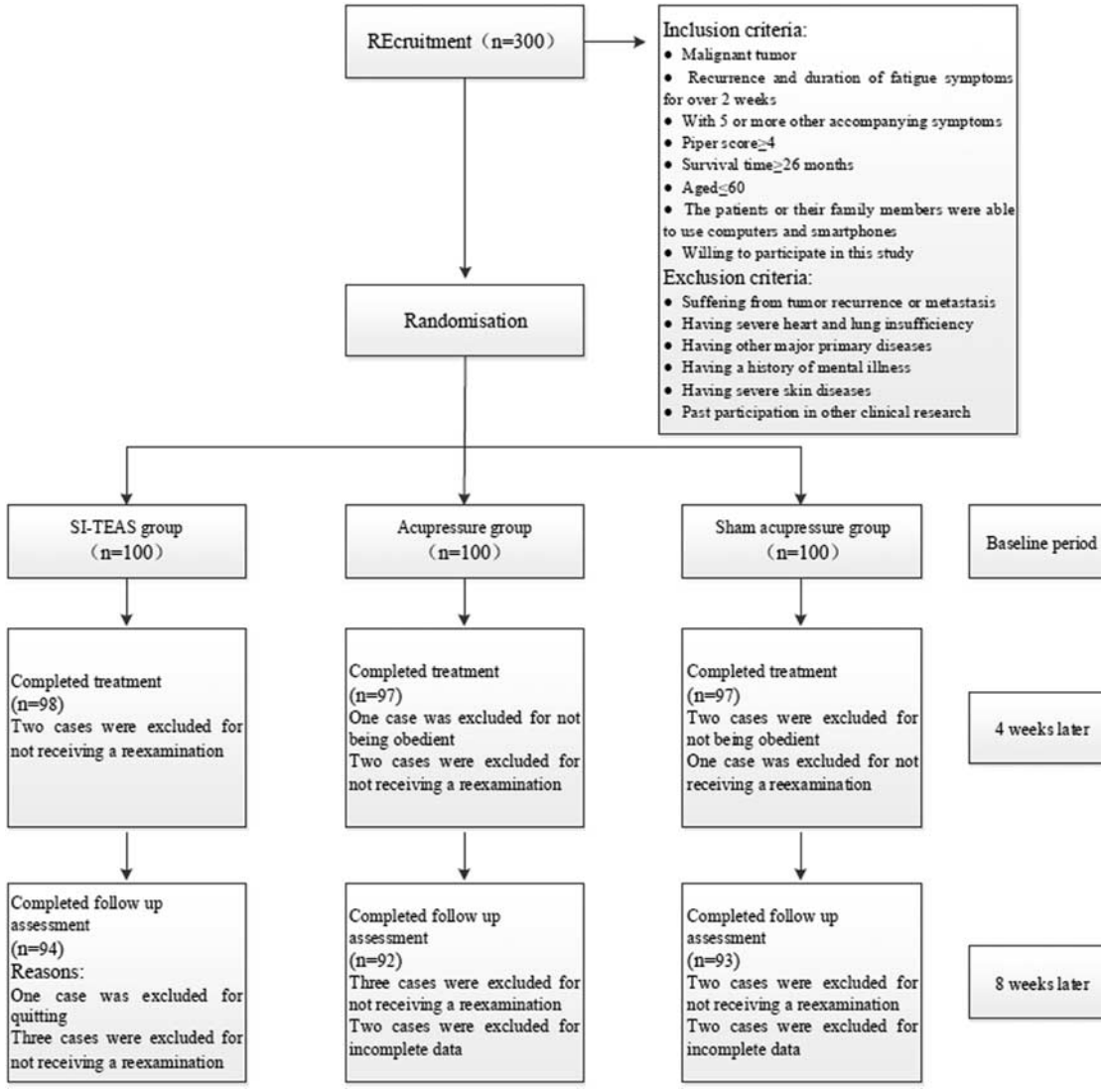

FIGURE 2. The Consolidated Standards for Reporting Trials (CONSORT) diagram.

TABLE 1. The Comparison on the Characteristics of Participants

Item	SI-TEAS Group (n = 94), n (%)	Acupressure Group (n = 92), n (%)	Sham Acupressure Group (n = 93), n (%)	*P*
Sex				0.461
Male	42 (44.68)	49 (53.26)	48 (51.61)	
Female	52 (55.32)	43 (47.74)	45 (48.39)	
Age (mean ± SD) (y)	47.46 ± 6.42	46.72 ± 7.52	47.40 ± 6.56	0.717
Marriage				0.215
Single	5 (5.32)	11 (11.96)	4 (4.30)	
Married	81 (86.17)	72 (78.26)	83 (89.25)	
Divorced/widowed	8 (8.51)	9 (9.78)	6 (6.45)	
Education				0.061
Senior high school and below	45 (47.87)	33 (35.87)	49 (52.69)	
College and above	49 (52.13)	59 (64.13)	44 (47.31)	
Tumor type				0.094
Head and neck cancer	9 (9.57)	13 (14.13)	15 (16.13)	
Breast cancer	24 (25.53)	10 (10.87)	29 (31.18)	
Lung cancer	11 (11.70)	19 (20.65)	8 (8.60)	
Liver cancer	12 (12.77)	14 (15.22)	13 (13.98)	
Gastric cancer	12 (12.77)	13 (14.13)	7 (7.53)	
Intestinal cancer	13 (13.83)	11 (11.96)	8 (8.60)	
Cervical cancer	9 (9.57)	6 (6.52)	10 (10.75)	
Others	4 (4.26)	6 (6.52)	3 (3.23)	
TNM Staging				0.348
Stage I	18 (19.15)	18 (19.57)	9 (9.68)	
Stage II	31 (32.98)	36 (39.13)	36 (38.71)	
Stage III	32 (34.04)	31 (33.70)	38 (40.86)	
Stage IV	13 (13.83)	7 (7.61)	10 (10.75)	
Treatment method				
Surgery	71 (75.53)	76 (82.61)	81 (87.10)	0.119
Chemotherapy	61 (64.89)	63 (68.48)	67 (72.04)	0.575
Radiotherapy	28 (29.79)	32 (34.78)	43 (46.24)	0.058
Immunity	20 (21.28)	19 (20.65)	21 (22.58)	0.948
Targeted	5 (5.32)	5 (5.43)	7 (7.53)	0.778
Others	21 (22.34)	16 (17.39)	23 (24.73)	0.464

SI-TEAS indicates somatosensory interaction transcutaneous electrical acupoint stimulation; TNM, tumor, node, metastases.

observed in the Acupressure Group. However, no clear changes could be observed in the Sham Acupressure Group.

Intergroup comparison of the behavioral, sensory, emotional, and cognitive dimensions of fatigue and the total score showed that the SI-TEAS Group and the Acupressure Group had statistically different changes at each time point after the fourth and eighth weeks (all $P < 0.05$). The Acupressure Group and the Sham Acupressure Group had statistically different changes at each time point after the fourth and eighth weeks (all $P < 0.05$). The SI-TEAS Group and the Sham Acupressure Group had statistically different changes at each time point after the fourth and eighth weeks (all $P < 0.05$).

Table 2 and Figure 4 have showed the intergroup changes in the absolute counts of T-lymphocyte subsets and NK cells after the fourth and eighth weeks compared with the baseline period. Judging from the mixed linear model, a clear upward trend could be observed in the absolute counts of T-lymphocyte subsets and NK cells of the SI-TEAS Group after 4 and 8 weeks of intervention. The same clear upward trend could be observed in the Acupressure Group. However, no clear changes could be observed in the Sham Acupressure Group.

Intergroup comparison of the absolute counts of $CD3^+$ T cells, $CD4^+$ T cells, $CD8^+$ T cells, $CD4^+/CD8^+$ T cells, and NK cells showed that the SI-TEAS Group and the Acupressure Group had statistically different changes at each time point after the fourth and eighth weeks (95% CI: 102.90,170.97 and 135.43,184.12 for $CD3^+$; 95% CI: 52.68,91.16 and 142.46,176.91 for $CD4^+$; 95% CI: 28.80,47.87 and 71.78,89.71 for $CD8^+$; 95% CI: 24.72,45.09 and 75.47,98.86, $P < 0.001$ for NK; 95% CI: 0.01,0.05, $P < 0.01$ and 0.04,0.07, $P < 0.001$ for $CD4^+/CD8^+$). The Acupressure Group and the Sham Acupressure Group had statistically different changes at each time point after the fourth and eighth weeks (95% CI: 45.23,113.48 and 223.85,282.67 for $CD3^+$; 95% CI: 85.26,123.84 and 202.31,236.85 for $CD4^+$; 95% CI: 40.07,59.20 and 101.72,119.69 for $CD8^+$; 95% CI: 0.06,0.10 and 0.11,0.13 for $CD4^+/CD8^+$; 95% CI: 45.98,66.41 and 108.93,132.39, $P < 0.001$ for NK). The SI-TEAS Group and the Sham Acupressure Group had statistically different changes at each time point after the fourth and eighth weeks (95% CI: 182.34,250.23 and 393.76,442.32 for $CD3^+$; 95% CI: 157.28,195.65 and 362.09,396.44 for $CD4^+$; 95% CI: 78.46,97.48 and 182.51,200.39 for $CD8^+$; 95% CI: 0.09,0.12 and 0.16,0.18 for $CD4^+/CD8^+$; 95% CI: 80.94,101.26 and 196.16,219.49, $P < 0.001$ for NK).

DISCUSSION

CRF involves very complex neurophysiological processes and is closely related to neurotransmitters at different levels in the central nervous system.[26,27] The results of this study showed that compared with the AM Group and the FAM Group, the SI-TEAS Group had the greatest changes in fatigue and immunity after 4 and 8 weeks of intervention, which confirmed significant intervention effects; in contrast, although the AM Group experienced similar relief in their fatigue symptom, their overall improvement was lower than that of the SI-TEAS Group; the application of sham acupressure had no

TABLE 2. Intergroup Comparison in Different Fatigue Dimensions and Immunity at Different Time Points

	Baseline Visit			Week 4 Visit				Week 8 Visit			
	Mean (SD)			Mean (SD)				Mean (SD)			
Variable	SI-TEAS Group (n = 94)	Acupressure Group (n = 92)	Sham Acupressure Group(n = 93)	SI-TEAS Group (n = 94)	Acupressure Group (n = 92)	Sham Acupressure Group (n = 93)	95% CI*	SI-TEAS Group (n = 94)	Acupressure Group (n = 92)	Sham Acupressure Group (n = 93)	95% CI*
RPFS											
Behavioral	6.61 (0.81)	6.79 (1.33)	6.92 (1.04)	5.21 (0.78)	5.76 (1.36)	6.89 (1.03)	(−0.86,−0.24)† (−1.45,−0.82)‡ (−2.00,−1.38)§	3.59 (0.77)	4.59 (1.35)	6.93 (1.05)	(−1.31,−0.69)† (−2.65,−2.02)‡ (−3.65,−3.03)§
Sensory	6.99 (0.69)	6.74 (1.31)	6.70 (1.13)	4.92 (0.75)	6.28 (1.34)	6.63 (1.14)	(−1.68,−1.04)† (−0.67,0.03)‡ (−2.03,−1.39)§	2.81 (0.70)	5.20 (1.41)	6.65 (1.14)	(−2.72,−2.08)† (−1.77,−1.12)‡ (−4.16,−3.52)§
Emotional	6.76 (1.21)	6.73 (0.86)	7.02 (1.10)	4.91 (1.18)	5.70 (0.90)	6.96 (1.16)	(−1.07,−0.44)† (−1.62,−0.99)‡ (−2.37,−1.74)§	2.80 (1.18)	4.36 (0.92)	6.97 (1.12)	(−1.87,−1.25)† (−2.93,−2.30)‡ (−4.49,−3.87)§
Cognitive	6.88 (1.20)	6.72 (1.21)	6.80 (1.09)	4.88 (1.16)	5.70 (1.24)	6.76 (1.13)	(−1.17,−0.49)† (−1.41,−0.73)‡ (−2.23,−1.55)§	2.75 (1.13)	4.39 (1.29)	6.73 (1.16)	(−1.98,−1.29)† (−2.69,−1.99)‡ (−4.32,−3.63)§
Total score	6.83 (0.60)	6.76 (0.56)	6.87 (0.59)	4.99 (0.58)	5.87 (0.56)	6.82 (0.58)	(−1.04,−0.71)† (−1.12,−0.79)‡ (−2.00,−1.67)§	3.00 (0.58)	4.64 (0.54)	6.83 (0.58)	(−1.80,−1.48)† (−2.35,−2.02)‡ (−3.99,−3.66)§
Lymphocyte subsets											
$CD3^+$	840.97 (135.18)	847.01 (119.47)	817.72 (126.45)	1137.62 (98.59)	1000.69 (117.98)	821.33 (134.55)	(102.90,170.97)† (45.23,113.48)‡ (182.34,250.23)§	1347.29 (58.17)	1187.51 (62.84)	829.25 (118.34)	(135.43,184.12)† (223.85,282.67)‡ (393.76,442.32)§
$CD4^+$	512.04 (56.93)	521.39 (60.87)	505.09 (65.39)	685.73 (61.10)	613.82 (67.45)	509.27 (71.04)	(52.68,91.16)† (85.26,123.84)‡ (157.28,195.65)§	882.38 (58.98)	722.70 (58.86)	503.12 (61.11)	(142.46,176.91)† (202.31,236.85)‡ (362.09,396.44)§
$CD8^+$	332.57 (30.53)	336.38 (29.57)	330.17 (32.21)	421.09 (32.23)	382.75 (31.77)	333.12 (35.00)	(28.80,47.87)† (40.07,59.20)‡ (78.46,97.48)§	521.27 (30.68)	440.52 (31.28)	329.82 (31.16)	(71.78,89.71)† (101.72,119.69)‡ (182.51,200.39)§
$CD4^+/CD8^+$	1.54 (0.07)	1.55 (0.08)	1.53 (0.07)	1.63 (0.03)	1.60 (0.06)	1.52 (0.09)	(0.01,0.05)† (0.06,0.10)‡ (0.09,0.12)§	1.69 (0.04)	1.64 (0.03)	1.52 (0.06)	(0.04,0.07)† (0.11,0.13)‡ (0.16,0.18)§
NK	282.69 (30.74)	286.75 (29.82)	280.23 (32.39)	372.94 (32.03)	338.03 (38.38)	283.63 (37.25)	(24.72,45.09)† (45.98,66.41)‡ (80.94,101.26)§	487.47 (32.25)	400.30 (54.12)	279.65 (31.22)	(75.47,98.86)† (108.93,132.39)‡ (196.16,219.49)§

*Derived from a linear mixed model.
†SI-TEAS Group versus Acupressure Group.
‡Acupressure Group versus Sham Acupressure Group.
§SI-TEAS Group versus Sham Acupressure Group.
RPFS indicates Revised Piper Fatigue Scale; SI-TEAS, somatosensory interaction transcutaneous electrical acupoint stimulation.

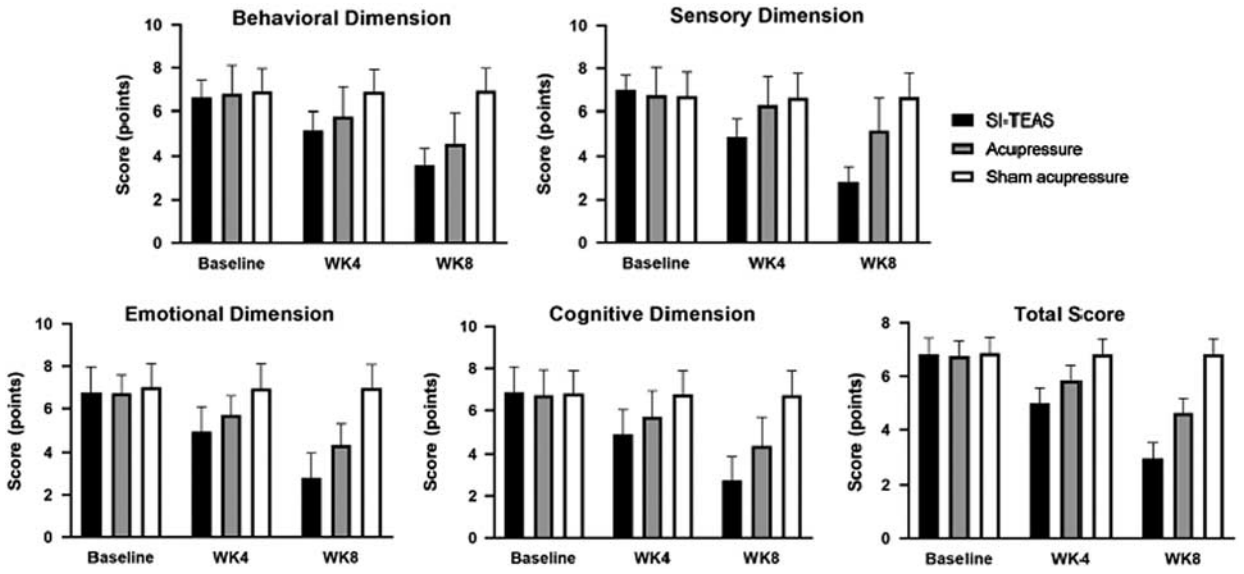

FIGURE 3. Comparison of cancer-related fatigue patients in the 3 groups in piper score during the baseline period and after 4 and 8 weeks of intervention.

clinical efficacy on the fatigue and immunity of the CRF patients. The occurrence of fatigue is closely related to the growth of cancer cells and decreases in the inflammatory factors and in the hemoglobin level of the body itself.[28–31] This study explored the mechanism of a physical therapy on fatigue and cellular immunity. TEAS intervention can facilitate the release of endorphins and enkephalins from the brain to regulate the nervous, endocrine, and immune systems[11,32] bidirectionally. Hou et al[33] applied TEAS to lung cancer patients after chemotherapy, and their CRF was effectively alleviated. This finding was consistent with the results of this study.

According to the traditional Chinese medicine philosophy, CRF is a kind of "consumptive disease" or "asthenic disease." The pathogenesis of CRF can be summarized as damaged viscera and constitution caused by a struggle between the vital energy and the pathogenic factor. The patient's vital energy and blood lose harmony and are mixed by excess and deficiency syndromes, of which the latter dominates.[34] Therefore, the treatment should try to tonify the kidney to regenerate bone marrow and to replenish vital energy and blood. Activating blood circulation to dissipate blood stasis is fundamental to the treatment. As a new acupuncture technique, TEAS can simultaneously exert electrical and acupoint stimulation to promote the alleviation and relief of fatigue symptoms.[35–37] The selected acupoint combination in this study can regulate regulate the vitality to direct the qi, replenish qi to invigorate the spleen, and tonify the kidney to arrest spontaneous emission. Baihui, an acupoint on Du channel and confluence of all yang-channels, can clear dizziness and blurred vision and invigorate the brain and vitality; coupled with Taiyang, Shenmen, and Neiguan, it

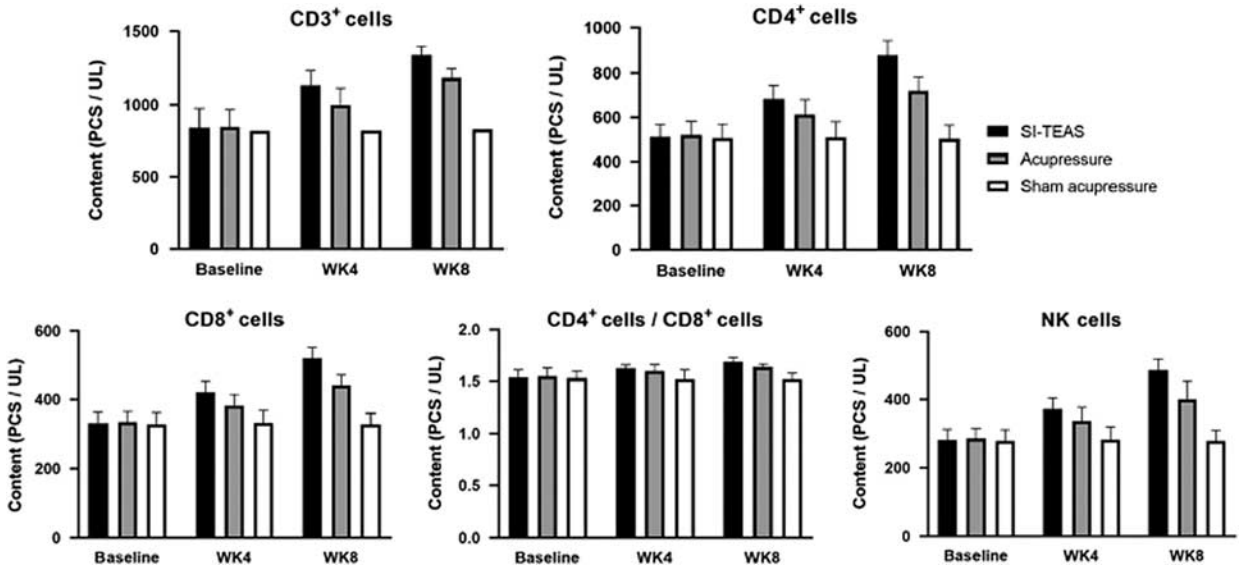

FIGURE 4. Comparison of cancer-related fatigue patients in the 3 groups in the absolute counts of lymphocyte subsets during the baseline period and after 4 and 8 weeks of intervention.

has a spirit-quieting and mind-stabilizing effects; Guanyuan is a confluent acupoint of the Ren channel and three yin channels of foot and, when coupled with Qihai and Dazhui, can reinforce vital energy, nourish yang and enrich essence; Zusanli is a lower confluent acupoint under the stomach and Sanyinjiao is a confluent acupoint of three yin channels of foot.[38–40] The combination of these 2 acupoints, together with Zhongwan, can reinforce qi, nourish blood, and invigorate the spleen and stomach; Taixi is the source acupoint of the kidney meridian which can nourish the kidney and yin and supply vital essence and marrow. The combination of the acupoints above can activate Qi and blood circulation and regulate viscera functions to balance the qi and blood, dredge meridians and qi activity, strengthen the body resistance to eliminate pathogenic factors, and improve immunity and fatigue resistance.[41–43]

TEAS needs to be manually operated step by step. It was difficult for the discharged patients to operate this method. On the one hand, the human acupoints selected were based on empirical evidence and were not accurately located; on the other hand, the empirical treatment protocols varied greatly with individual patients, which made it hard to assess and verify long-term treatment effects.[13,35,44] Previous studies[18,45] have found that the identification and location of acupoints would become much more operable and independent rehabilitation by patients would become easier under the assistance of the SI technology. That study proposed a new physical therapy that combined meridians in the traditional Chinese medicine, SI, and modern electronic technology. During the independent rehabilitation process, the SI-TEAS massage system can integrate body image identification, acupoint location, and massage action recognition to accurately superimpose and reflect the distribution of acupoints in the body and the meridian treatment needs of the patient in real human body projection. The patient's gestures and motion trajectory are tracked in real time, along with visualized rehabilitation goal orientation and dynamic presentation of the motion trajectory. The patient's obedience to instructions for independent rehabilitation is enhanced. As a noninvasive treatment method to activate peripheral nerve fibers with current pulses, the system allows smartphones to control low-frequency pulse currents in a way that stimulates the selected acupoints of the patient, dredges the meridians, activates qi and blood circulation, reconciles yin and yang, and relieves relevant symptoms. It is noninvasive, economical, easy to operate, nondrug, and free from significant adverse effects. At the same time, the system also provides adjustable and controllable intelligent management that excludes human factors and automatically adjusts the frequency, intensity, and waveform of acupoint electrical stimulation through feedback of SEMG signal detection. It provides an automatic external stimulation therapy based on the acupoint theory of traditional Chinese medicine. TEAS studies focus mostly on its effects, while technical innovation in this regard is rarely discussed. This study proposed an innovative approach by combining the SI software system with TEAS to apply acupoint massage. The somatosensory control equipment could capture the patient's body movements and locate acupoints and provide data feedback through human-computer interaction. This approach could not only provide accurate treatment and assess the physiological condition of the patient, but also improve the patient's experience and motivation to receive treatment and provide technical support for subsequent rehabilitation.

However, this study has some limitations. Before the study was started, the research team developed a set of treatment criteria for different stimulation intensities, waveform, and duration to suit the severity of fatigue symptoms, and the patients followed these criteria in choosing appropriate intervention conditions. However, these criteria were not standardized. Moreover, the acupoint massage did not serve as a physiological placebo for the FAM Group because of variations in the selected acupoints. Future studies are expected to further adjust and develop the intervention criteria and the selection of comfort measures for the control group. This study did not comprehensively consider the patient's independent massage restrictions when determining the compatibility of acupoints. Future studies need to consider such restrictions and further explore the best acupoint compatibility. Because of time limitations, the interventions applied in this study were relatively short-term, and the long-term effects need to be further demonstrated. In addition, the subjects of this study were limited to a small group of patients in Hangzhou, China. No detailed assessment of quality of life was made through observation indicators, such as physical health and mental health. Future studies should include an assessment of patients' quality of life and observe safety indicators such as blood routine, liver and kidney functions, and skin reactions, in order to enrich and obtain more scientific research results.

CONCLUSION

As an emerging TCM nursing practice, SI-TEAS has a good short-term effect on treating CRF because it relieve the fatigue of tumor patients and improve their cell immunity. However, this is only a preliminary trial. Large-scale randomized trial studies incorporating appropriately larger sample sizes and longer follow-ups are needed to confirm the findings. In addition, the application effects of SI-TEAS on treating other diseases may also be another interesting topic that warrants further investigations.

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