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Original Article

Efficacy of press needle treatment in reducing chemotherapy-induced nausea, vomiting, and retching gastrointestinal cancer patients: A randomized controlled trial

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ABSTRACT

Objective: Chemotherapy-induced nausea and vomiting (CINV) and retching often pose challenges in managing patients with gastrointestinal cancer. This randomized controlled trial sought to evaluate the effectiveness of press needle therapy in mitigating CINV and retching following chemotherapy.

Methods: Two hundred patients with gastrointestinal cancer undergoing folinic acid, fluorouracil, and oxaliplatin (FOLFOX) chemotherapy were randomly assigned to either the press needle group or the control group. The control group received 5-hydroxytryptamine-3 (5-HT3) antagonists and dexamethasone 30 min before chemotherapy, followed by dexamethasone on days 2 and 3 after chemotherapy. In contrast, the press needle group received press needle treatment 30 min prior to chemotherapy. The primary outcome was the Index of Nausea, Vomiting, and Retching (INVR), assessed at seven time points: before chemotherapy and at 12, 24, 36, 48, 60, and 72 h post-chemotherapy.

Results: All patients completed their respective treatments, and no significant adverse effects related to press needle treatment (such as skin allergies, acupoint infections, headaches, or dizziness) were reported. A two-way repeated-measures analysis of variance (ANOVA) revealed significant differences in INVR scores between the two groups ($P < 0.05$). Further analysis with a *t*-test indicated that INVR scores in the press needle treatment group were significantly lower than those in the control group at 12, 24, and 36 hours after chemotherapy ($P < 0.05$), with no significant difference observed thereafter.

Conclusions: Press needle treatment effectively alleviated nausea, vomiting, and retching in patients with gastrointestinal cancer undergoing chemotherapy. It represents a safe, efficient, and convenient complement to preventive treatment with 5-HT3 antagonists.

Trial registration: Chinese Clinical Trial Registry (No. ChiCTR1900024554).

Introduction

Chemotherapy-induced nausea and vomiting (CINV) and retching are common side effects of most antineoplastic drugs, with an incidence rate as high as 75%.[1] Nausea is an unpleasant sensation experienced at the back of the throat and epigastrium that may or may not result in the expulsion of materials from the stomach. Vomiting involves the forceful upward expulsion of contents from the stomach. Retching is an attempt to expel stomach contents without actually bringing anything up.[2] CINV and retching often occur several days after chemotherapy.[3] It can significantly affect the health-related quality of life and nutritional status of patients and may reduce treatment compliance, leading to treatment delay or termination.[3,4] Therefore, the prevention and treatment of CINV and retching are essential for improving the quality of life and treatment efficacy in patients.

Modern medicine suggests that CINV and retching are complex processes involving neural pathways, neurotransmitters, and receptors.[5] CINV receptors are distributed in the posterior area of the medulla oblongata and are found at the end of the vagus nerve near the chromaffin cells of the intestine. The afferent nerve transmits the signal to the brainstem for vomiting reflex processing and then transmits the outgoing signal to different organs and tissues to induce nausea, vomiting, and retching.[6] Antitumor drugs can cause nausea, vomiting, and retching reflexes through two pathways: peripheral and central.[7] In general,

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nausea, vomiting, and retching occur within 24 h of administering antitumor drugs in the peripheral pathway, usually presenting as acute nausea, vomiting, and retching (0–24 h). The central pathway is mainly located in the brain, and nausea and vomiting usually occur 24 h after administering antitumor drugs, usually manifesting as drug-induced delayed nausea, vomiting, and retching (25–120 h).[8] Drugs used to prevent nausea and vomiting include dopamine receptor antagonists, 5-hydroxytryptamine-3 (5-HT3) receptor antagonists, and neurokinin-1 receptor antagonists, which mainly block one type of receptor but cannot completely block different types of nausea, vomiting, and retching.[9]

The National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (2022 Edition) state that a serotonin-3 receptor antagonist combined with dexamethasone is the mainstream treatment for CINV and retching; however, 30% of CINV- and retching-related symptoms are not controlled.[7] In addition, although the guidelines for CINV and retching were issued several years ago,[10] compliance in clinical practice in China and other countries remains unsatisfactory. Some of the drugs recommended in these guidelines have not been widely used because of their high cost or side effects, such as headaches, dizziness, constipation, and insomnia.[11] As CINV and retching cannot be well controlled using drugs, attempts are required to find alternative treatments.

According to current research, the incidence rate of CINV and retching in patients with gastrointestinal cancer after chemotherapy is approximately 60%–90%, which is a high percentage.[12] Fluorouracil (5-FU) is a chemotherapeutic drug widely used for treating gastrointestinal cancer; however, its efficacy as a single agent is limited. In recent years, with the introduction of irinotecan and oxaliplatin, significant progress has been made in the prognosis of gastrointestinal cancer. Oxaliplatin is a platinum-based drug, and irinotecan, a topo-1 inhibitor, prevents DNA replication and repair in cancer cells through different DNA structures and enzyme mechanisms. The combination of these drugs with 5-FU and its analogs can produce a synergistic effect, enhance the therapeutic effect, and reduce toxic side effects and drug resistance.[13] Patients with gastrointestinal cancer rarely experience acute or delayed nausea, vomiting, or retching during 5-FU-based chemotherapy. However, the addition of oxaliplatin increases the incidence of nausea, vomiting, and retching.[14] Furthermore, even with standard antiemetic prophylaxis, some patients with gastrointestinal cancer receiving fluorouracil, oxaliplatin, and leucovorin (FOLFOX) chemotherapy experience serious CINV and retching. For example, in the Multicenter International Study of Oxaliplatin/5-Fluorouracil/Leucovorin in the Adjuvant Treatment of Colon Cancer trial, the incidence of grade 3 and 4 vomiting in the FOLFOX group was 5.8%, which was significantly higher than that in the 5-FU and leucovorin groups (1.4%), indicating that some of the vomiting may have been caused by the addition of oxaliplatin.[15] Therefore, more active and reliable antiemetic treatments are needed to control CINV and retching in patients receiving FOLFOX.

Studies have shown that acupuncture is an effective intervention for relieving CINV and retching.[16] However, patient adherence to acupuncture treatment is frequently poor because of multiple long-term treatments and complex surgical methods.[17,18] The press needle, developed from the ancient Chinese nine needles, is a thumbtack-shaped needle with a flat needle handle and a slender needle body (diameter 0.2 mm, length 0.3–2 mm), which is fixed on the body surface with a self-adhesive tape, as shown in Fig. 1. Press needles can stimulate acupoints and regulate the nervous and endocrine systems of the human body, thereby reducing or eliminating the discomfort associated with nausea and vomiting. Compared to acupuncture, the press needle body is smaller and slender, which can reduce pain and prolong the therapeutic effect through longer needle retention.[19] Therefore, it is less traumatic, more acceptable to patients, and more convenient for clinical use.[20] Although the press needle has been increasingly used to prevent postoperative nausea and vomiting in patients undergoing craniotomy,[19] no trials have examined the effects of the press needle on CINV and retching. This randomized controlled trial aimed to assess the efficacy of press needle treatment in preventing CINV and retching in patients with gastrointestinal cancer after FOLFOX chemotherapy.

Methods

Study design

This study was a two-arm, parallel, randomized controlled trial. A total of 200 participants with gastrointestinal cancer who required FOLFOX chemotherapy were randomly assigned to the control or intervention group in a 1:1 ratio. A flowchart is shown in Fig. 2.

Study participants

All participants were recruited from the Integrated Hospital of Traditional Chinese Medicine (TCM) at Southern Medical University. For eligible participants who met all the required criteria, signed written informed consent was requested before randomization, and they were given sufficient time to decide whether they were willing to participate in this study. The inclusion criteria were as follows: (1) gastrointestinal malignant tumors confirmed by histopathology or cytology, no chemotherapy contraindications, and patients who volunteered to participate in the trial and signed an informed consent form; (2) expected survival $>$ 6 months; (3) a Zubrod–ECOG–WHO score between 1 and 2. The score classifies the patient's functional status into 0 to 5, with a total of 6 levels. Patients with functional status 3 and 4 are generally considered unsuitable for chemotherapy, and the Karnofsky score $\geq$ 70 (the Karnofsky scores, administered by the provider or support staff, assign scores to patients on a scale of 0%–100%, in increments of 10, where 100% is normal activity and 0% is dead); (4) there are no symptoms such as nausea, vomiting, retching, constipation, or diarrhea before chemotherapy; (5) at least two cycles of the FOLFOX chemotherapy regimen should be performed continuously in the future (a cycle of the FOLFOX chemotherapy regimen: Oxaliplatin 85 mg/m^2 and folinic acid 400 mg/m^2 intravenously injected for 2 h on the first day; 5-FU 400 mg/m^2 intravenous bolus on the first day, and 1200 mg/m^2 intravenous injection on the second and third days). The exclusion criteria were as follows: (1) patients with abnormalities in hematuria and liver, heart, brain, and kidney function before chemotherapy; (2) pregnant or lactating patients; (3) patients receiving radiotherapy simultaneously; (4) patients who received press needle treatment for 3 days for various reasons. Patients who needed to stop chemotherapy due to non-digestive tract problems after the first cycle were removed from the study.

Intervention

There are two arms in this randomized controlled trial. Patients in the control group were treated with standard antiemetic drugs according to the clinical practice guidelines of National Comprehensive Cancer Network[21]: All patients were treated with 5-HT3 antagonists (such as dolasetron 100 mg PO or ondansetron 16–24 mg PO), dexamethasone 12 mg PO/IV 30 min before chemotherapy, and dexamethasone 8 mg PO/IV daily on days 2 and 3. Patients in the intervention group were treated additionally with a press needle (manufacturer: Suzhou Medical Appliance Factory, Lot number: 2011102, specification: 0.25 mm $\times$ 1.3 mm). The press needles were inserted into the bilateral Zusanli (ST36) and Neiguan (PC6) acupoints 30 min before the beginning of chemotherapy and then indwelled under the skin for the entire cycle of FOLFOX chemotherapy (days 1–3). During the chemotherapy cycle, the needles were pressed for 30 min before and after the daily injection of chemotherapy drugs (the duration of each needle press was 1 min). When the patient had symptoms such as nausea, vomiting, and retching, the supplementary press for 1 min was performed by experienced nurses, and the total number of presses was controlled at 5–10 times per day (the total number of daily presses depended on the severity of the patient's nausea, vomiting, and retching). The compression depth of the press needle was 0.5–1 cm, and the intensity was appropriate for slight pain at the acupoints. The needle insertion procedure and precautions adopted

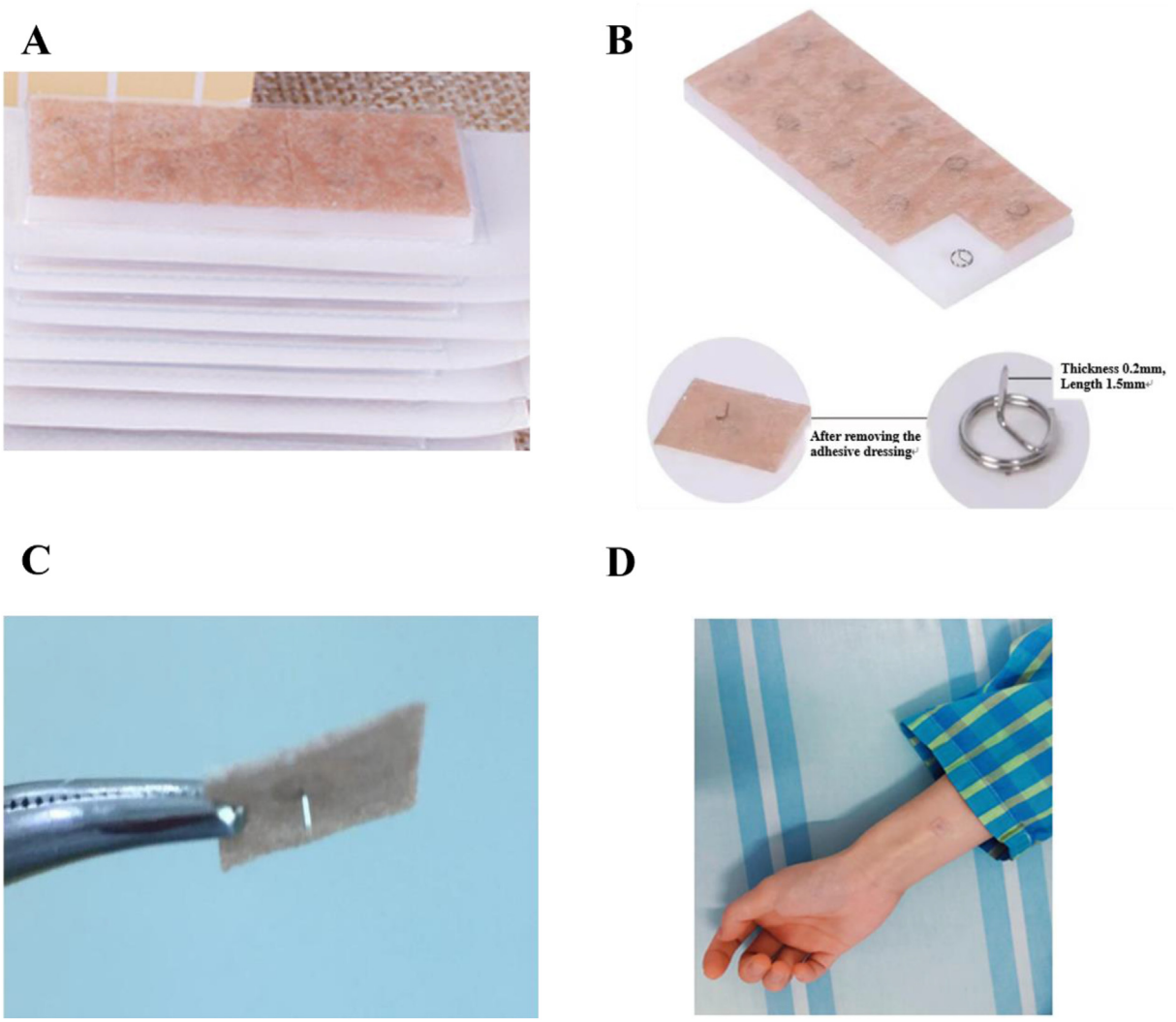

Fig. 1. Press needles. (**A**) The package of press needles; (**B**) The structure of the press needle; (**C**) The inserting status of the press needle; (**D**) The indwelling status of the press needle.

were as follows: the skin around the acupoints was disinfected with 75% alcohol; the diameter of the applied skin was greater than 5 cm; puncture was performed after the alcohol was volatilized. The needle was inserted 90° into the skin, and the action needed to be rapid and accurate to prevent damage to surrounding tissues. At the end of the puncture, a breathable dressing was used to prevent detachment, and local discomfort such as infection, pain, and allergy was recorded. During treatment, the patients were advised to avoid strenuous exercise and to wash the treatment area to prevent the dressing from falling off and becoming damp. If there was any fall-off, the acupoint was pressed for 5 min, and a replenishment needle was administered. If the patient fainted, had skin allergies, skin breaks, infections, hematomas, local pain, or other discomfort at the puncture site, or in cases of needle breakage, the treatment was stopped immediately. Needle operators included Guangdong TCM specialist nurses and national TCM nursing experts. Before implementation of the project, all needle operators underwent rigorous system training and passed an assessment.

Randomization and blinding

The participants were randomly assigned to two groups in a 1:1 ratio, according to the randomization table generated by a computer. This was an open-label trial because blinding could not be used due to the particularity of the press needle intervention, whereas all data collectors, research coordinators, and statisticians were blinded to the group assignments. A double data entry approach was adopted to minimize data entry errors.

Outcome measures

The primary outcome was the nausea, vomiting, and retching scores, assessed using the Chinese version of the index of nausea, vomiting, and retching (INVR). The initial scale was introduced by Professor Rhodes in the United States in 1999[22] and has been widely used worldwide.[23] It was translated into Chinese in 2002, with a Cronbach's α coefficient of 0.95.[24] The scale is divided into three dimensions: nausea, vomiting, and retching, with three, three, and two items, respectively. There are five levels for each item: "none at all," "some," "moderate," "very obvious," and "very serious and unbearable," scored 0–4, respectively. The score was accumulated, with a minimum value of 0 points and maximum values of 12, 12, and 8 points for nausea, vomiting, and retching, respectively. The higher the score for each dimension, the more severe the degree of nausea, vomiting, and retching.

Considering that CINV and retching mainly occur 1–3 days after chemotherapy, the degree of CINV and retching was assessed at seven time points: before chemotherapy and 12, 24, 36, 48, 60, and 72 h after chemotherapy.

We also collected data on common adverse reactions occurring during acupuncture therapy (ie, local symptoms, including allergy, infection,

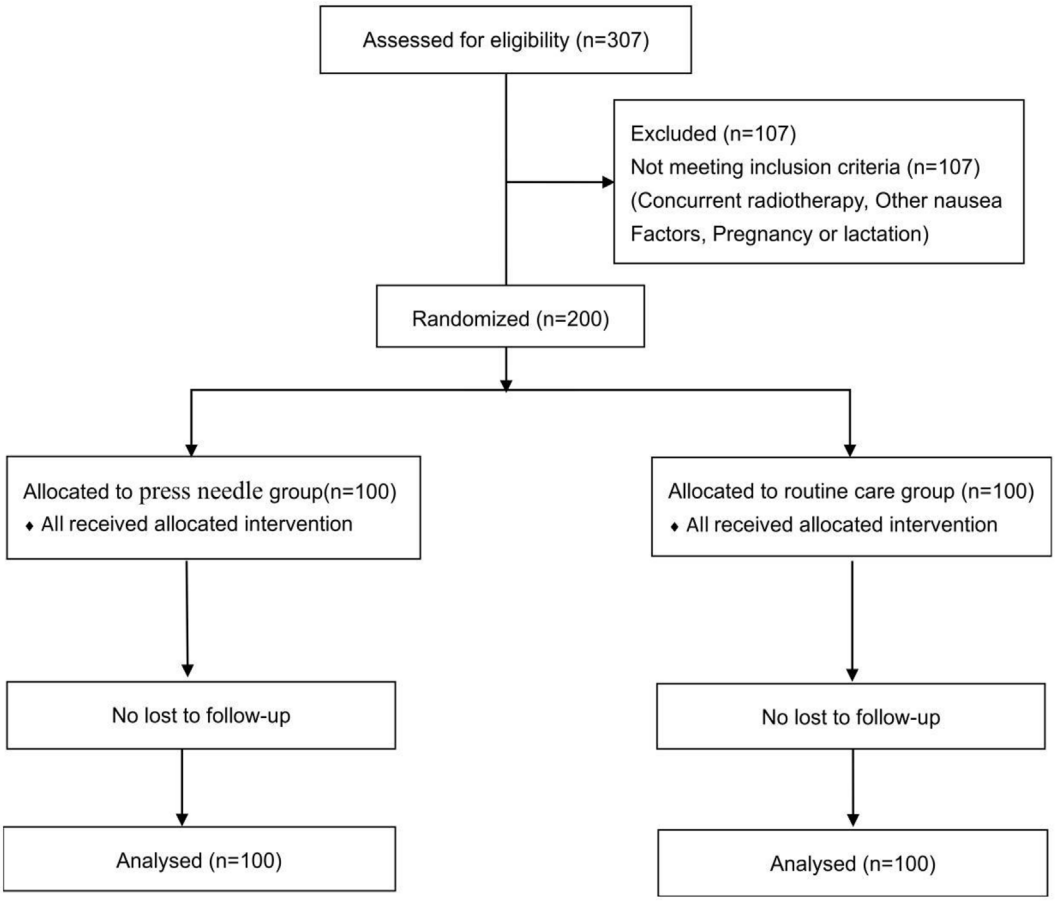

Fig. 2. Study design.

Table 1
Baseline characteristics of participants.

Item		Intervention group ($n = 100$), n (%)	Control group ($n = 100$), n (%)	x^2	P-value
Gender	Male	50 (50.0%)	52 (52.0%)	0.080	0.777
	Female	50 (50.0%)	48 (48.0%)		
Age (years)	≤ 39	12 (12.0%)	10 (10.0%)	0.623	0.891
	40–59	42 (42.0%)	39 (42.0%)		
	60–69	24 (24.0%)	28 (28.0%)		
	≥ 70	22 (22.0%)	23 (23.0%)		
Diagnosis	Bowel cancer	64 (64.0%)	64 (64.0%)	0.000	1.000
	Stomach cancer	36 (36.0%)	36 (36.0%)		
Chemotherapy cycle	1 time	2 (2.0%)	5 (50.0%)	3.323	0.345
	2–3 times	56 (56.0%)	51 (51.0%)		
	4–5 times	27 (27.0%)	34 (34.0%)		
	≥ 6 times	15 (15.0%)	10 (10.0%)		
Marital status	Not married	4 (4.0%)	4 (4.0%)	0.821	0.663
	Married	87 (87.0%)	83 (83.0%)		
	Divorced	9 (9.0%)	13.0 (1%)		

Case (percentage): Group comparison using the chi-square test. The chemotherapy cycle refers to the number of times patients received chemotherapy before the clinical trial.

Table 2
Comparison of nausea scores between the two groups.

Group	Before	After 12 h	After 24 h	After 36 h	After 48 h	After 60 h	After 72 h
Intervention group ($n = 100$), Mean ± SD	3.81 ± 0.24	5.29 ± 0.18	6.42 ± 0.16	5.62 ± 0.20	4.85 ± 0.21	4.91 ± 0.21	3.68 ± 0.20
Control group ($n = 100$), Mean ± SD	3.77 ± 0.21	5.95 ± 0.21	7.58 ± 0.26	6.38 ± 0.18	5.20 ± 0.17	5.23 ± 0.20	3.97 ± 0.19
Difference	0.04 ± 0.32	−0.66 ± 0.27	−1.16 ± 0.3	−0.76 ± 0.27	−0.35 ± 0.27	−0.32 ± 0.29	−0.29 ± 0.27
t	0.126	−2.428	−3.837	−2.852	−1.288	−1.122	−1.065
P	0.900	0.016	<0.001	0.005	0.199	0.263	0.288

Mauchly's spherical test $P < 0.001$ indicated that the hypothesis of sphericity was invalid, and the Greenhouse-Geisser correction was used. There were significant differences in the mean nausea scores between the two groups ($F = 6.757$, $P = 0.010$) and time ($F = 2.426$, $P < 0.001$), and a significant interaction between group and time was found ($F = 2.983$, $P = 0.041$).

Table 3
Comparison of vomiting scores between the two groups.

Group	Before	After 12 h	After 24 h	After 36 h	After 48 h	After 60 h	After 72 h
Intervention group ($n = 100$), Mean ± SD	2.24 ± 0.25	3.29 ± 0.25	5.35 ± 0.17	4.70 ± 0.11	4.24 ± 0.15	3.41 ± 0.22	2.86 ± 0.22
Control group ($n = 100$), Mean ± SD	2.22 ± 0.17	4.92 ± 0.16	6.14 ± 0.22	5.29 ± 0.19	4.40 ± 0.16	3.69 ± 0.21	3.05 ± 0.24
Difference	0.02 ± 0.30	−1.63 ± 0.30	−0.79 ± 0.28	−0.59 ± 0.22	−0.16 ± 0.22	−0.28 ± 0.30	−0.19 ± 0.33
t	0.066	−5.376	−2.835	−2.715	−0.733	−0.930	−0.580
P	0.947	<0.001	0.005	0.007	0.465	0.354	0.562

Mauchly's spherical test $P < 0.001$ indicated that the hypothesis of sphericity was invalid, and the Greenhouse-Geisser correction was used. There were significant differences in the mean vomiting scores between the two groups ($F = 7.798$, $P = 0.006$) and time ($F = 109.332$, $P < 0.001$), and a significant interaction between group and time was found ($F = 6.049$, $P = 0.001$).

Table 4
Comparison of retching scores between the two groups.

Group	Before	After 12 h	After 24 h	After 36 h	After 48 h	After 60 h	After 72 h
Intervention group ($n = 100$), Mean ± SD	2.17 ± 0.17	3.19 ± 0.09	3.82 ± 0.13	3.55 ± 0.10	3.16 ± 0.09	2.98 ± 0.12	2.55 ± 0.15
Control group ($n = 100$), Mean ± SD	2.30 ± 0.12	3.50 ± 0.13	4.55 ± 0.17	3.60 ± 0.09	3.18 ± 0.09	2.94 ± 0.12	2.60 ± 0.16
Difference	−0.13 ± 0.21	−0.31 ± 0.16	−0.73 ± 0.21	−0.05 ± 0.13	−0.02 ± 0.13	0.04 ± 0.17	−0.05 ± 0.22
t	−0.629	−1.989	−3.434	−0.376	−0.155	0.234	−0.228
P	0.530	0.048	0.001	0.707	0.877	0.815	0.820

Mauchly's spherical test $P < 0.001$ indicated that the hypothesis of sphericity was invalid, and the Greenhouse-Geisser correction was used. There were significant differences in the mean retching scores between the two groups ($F = 3.873$, $P = 0.050$) and time ($F = 60.092$, $P < 0.001$), and a significant interaction was observed between group and time ($F = 2.588$, $P = 0.045$).

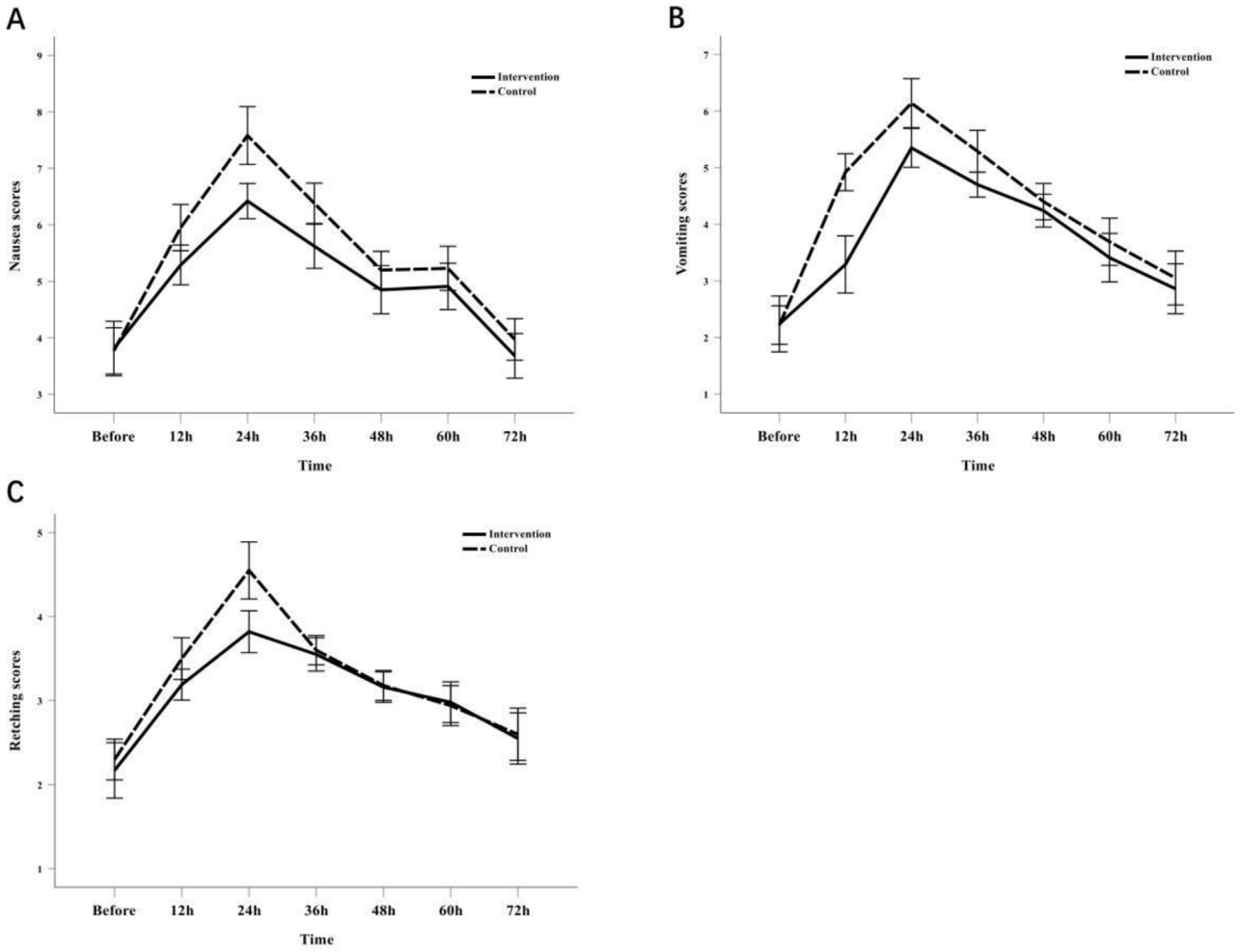

Fig. 3. Error line charts of the three symptoms over time. (**A**) The error line chart of nausea scores. There were significant differences between the two groups at 12 h ($P = 0.016$), 24 h ($P < 0.001$) and 36 h ($P = 0.005$) after chemotherapy; (**B**) The error line chart of vomiting scores. There were significant differences between the two groups at 12 h ($P < 0.001$), 24 h ($P = 0.005$) and 36 h ($P = 0.007$) after chemotherapy; (**C**) The error line chart of retching scores. There were significant differences between the two groups at 12 h ($P = 0.048$) and 24 h ($P = 0.001$) after chemotherapy.

pain, or numbness of the skin around the acupoints) and anti-CINV and retching drug therapy (ie, some systemic symptoms, including headaches, dizziness, constipation, and insomnia) at seven time points in the press needle treatment group. At each time point, after the patients completed the INVR scale, the nurse asked each patient whether one of the above adverse reactions had occurred in the previous 12 h and recorded the number of occurrences.

Sample size calculation

We performed a pilot randomized controlled study of 30 patients who were observed at seven time points from days 1–3. We found that INVR scores peaked 24 h after chemotherapy in both groups. Therefore, we calculated the sample size based on data obtained 24 h after chemotherapy. The mean INVR score was 15.59 in the intervention group and 18.27 in the control group, with an overall standard deviation (SD) of 5.4. The sample size was calculated to be 100 people per group, with a statistical power of 90%, a type I error of 5%, and a dropout rate of 15%.

Data analysis

The continuous data are expressed by mean ± SD, and the count data are expressed by percentage. For two independent samples, the chi-square test or *t*-test, if appropriate, was used to compare baseline characteristics between the two groups, including gender, age, diagnosis, chemotherapy cycle, and marital status. The difference in INVR scores between the two groups, the change in score over time, and the interactive effect between group and time were analyzed using a two-way analysis of variance (ANOVA) with repeated measures according to intention-to-treat. Mauchly's spherical test was performed before the ANOVA. If Mauchly's spherical assumption was invalid, the F-statistics of the ANOVA were corrected using the Greenhouse-Geisser method. Differences in INVR scores between the two groups at a specific time point were tested using two independent sample *t*-tests.

Ethical considerations

This study was approved by the Medical Ethics Committee of the Integrated Hospital of Traditional Chinese Medicine, Southern Medical University (IRB No. NFZXYEC-2019-001). All participants provided written informed consent and voluntarily participated in the study.

Results

Patients' characteristics

All 200 patients (102 males and 98 females) completed the assigned treatment, and no patients withdrew from the study after randomization. The mean patient age was 58 years, with a standard deviation of 14 years. A total of 128 patients had bowel cancer and 72 patients had stomach cancer. The baseline characteristics of the participants in each group are presented in Table 1. There were no statistically significant differences between the two groups in terms of sex, age, diagnosis, marital status, or chemotherapy cycles ($P > 0.05$).

Primary endpoint analyses

The two-way ANOVA with repeated measures revealed that the scores for nausea, vomiting, and retching changed significantly over time ($P < 0.05$). The scores peaked at 24 h after chemotherapy and

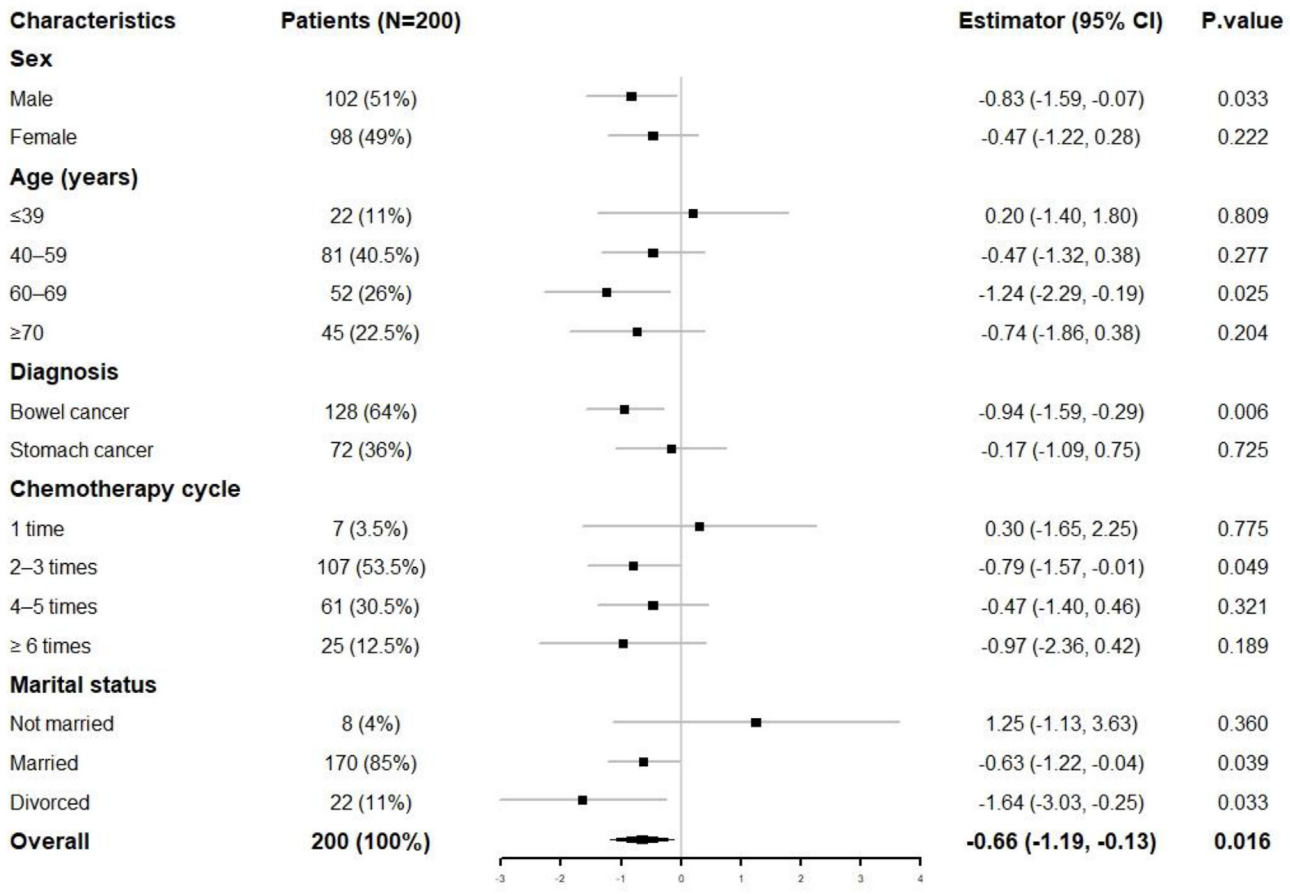

Fig. 4. Forest plot of nausea scores for subgroup analysis.

decreased thereafter in both groups. The scores for all three symptoms were significantly lower in the press needle group than in the control group ($P < 0.05$). We also found a significant interaction between the group and time ($P < 0.05$). Furthermore, analyses were performed for each specific time point, and the two independent sample *t*-tests showed that before the beginning of chemotherapy, the baseline scores were very similar in the two groups and did not show a statistical difference ($P > 0.05$). At 12 h after chemotherapy, a significantly lower score of nausea was observed in the press needle group than the control group (0.66 [95% confidence interval [CI]: 0.12–1.19], $P = 0.016$), and such an immediate effect was also found for vomiting and retching with a reduction of 1.63 (95% CI: 1.03–2.22, $P < 0.001$) and 0.31 (95% CI: 0.01–0.61, $P = 0.048$), respectively. At 24 h after chemotherapy, the differences became greater for nausea (1.16 [95% CI: 0.56–1.75], $P < 0.001$), vomiting (0.79 [95% CI: 0.24–1.34], $P = 0.005$), and retching (0.73 [95% CI: 0.31–1.15], $P = 0.001$). At 36 h after chemotherapy, the differences between the two groups remained statistically significant for nausea (0.76 [95% CI: 0.23–1.28], $P = 0.005$) and vomiting (0.59 [95% CI: 0.16–1.01], $P = 0.007$) but not for retching. At 48 h and thereafter, the scores tended to be lower in the press needle group than in the control group, but the differences were not statistically significant (Tables 2–4 and Fig. 3).

Subgroup analysis

We conducted a subgroup analysis of the scores of the three symptoms (nausea, vomiting, and retching) at 12 h based on sex, age, diagnosis, chemotherapy cycle, and marital status. The forest plots of the subgroup analyses are shown in Figs. 4–6. The variable "Estimator (95% CI)" in Figs. 4–6 represents the difference of means between the two groups (the mean of the press needle group subtracts that of the control group) and its corresponding 95% CI. We found that the press needle group had a lower score for all three symptoms than the control group in most subgroups, except for some subgroups with small sample sizes (patients aged < 39 years, patients with a 1-time chemotherapy cycle, and unmarried patients). In general, the estimators of males were lower than those of females; those of the 60–69 age group were lower than those of other age groups; those of bowel cancer were lower than those of stomach cancer; and those of divorced patients were lower than those of married patients. As for the chemotherapy cycle, the group with over six cycles had the lowest estimator for nausea, the group with a 1-time cycle had the lowest estimator for vomiting, and the group with 2–3 cycles had the lowest estimator for retching.

Safety analysis

No patients in the press needle treatment group experienced any adverse reactions (including allergy, infection, pain, or numbness of the skin around the acupoints, headaches, dizziness, constipation, and insomnia) at any time point, highlighting the safety of the press needle therapy.

Discussion

Summary of key findings

In this randomized controlled trial, we found that press needle treatment combined with a 5-HT3 antagonist significantly reduced INVR

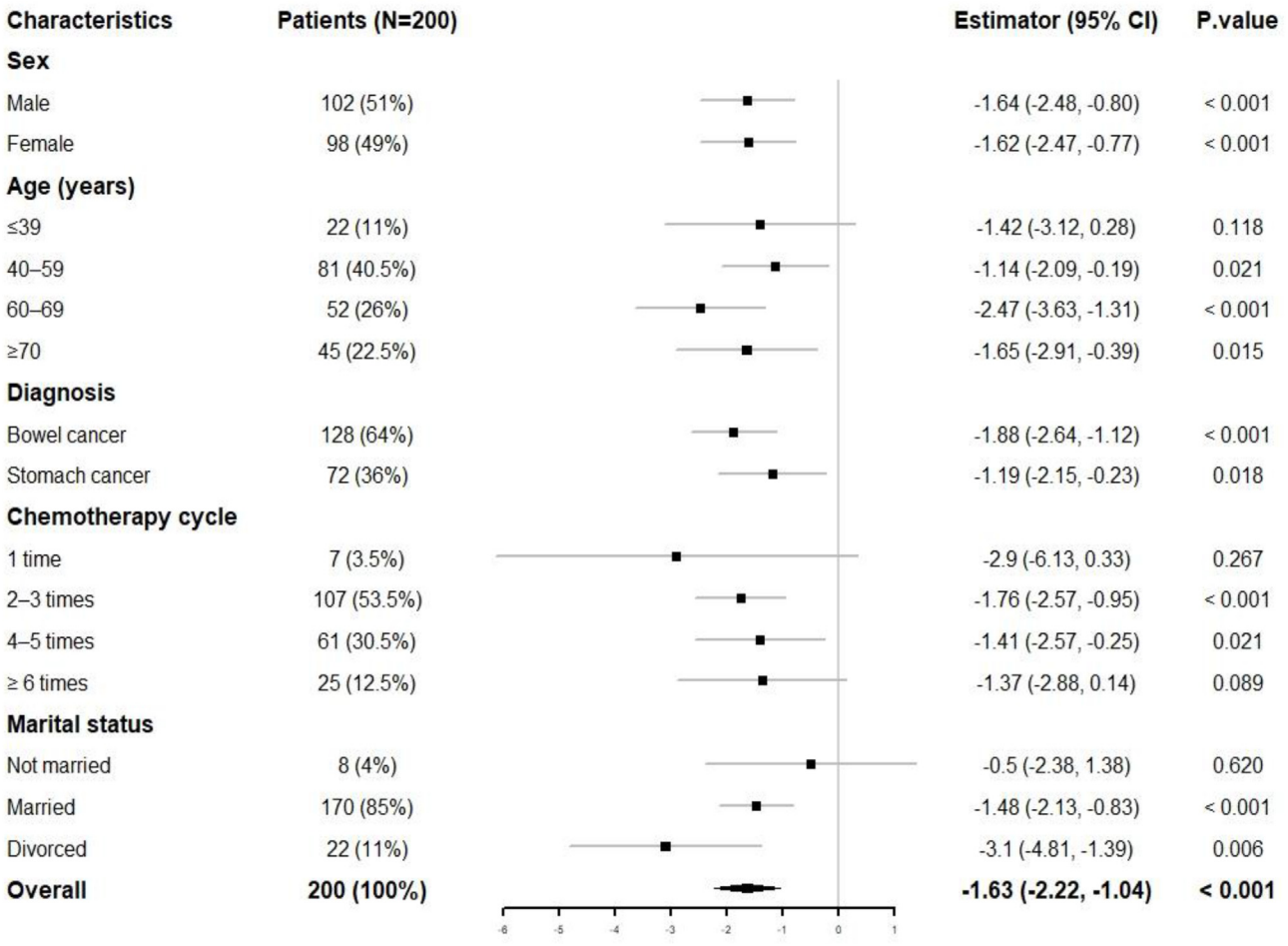

Fig. 5. Forest plot of vomiting scores for subgroup analysis.

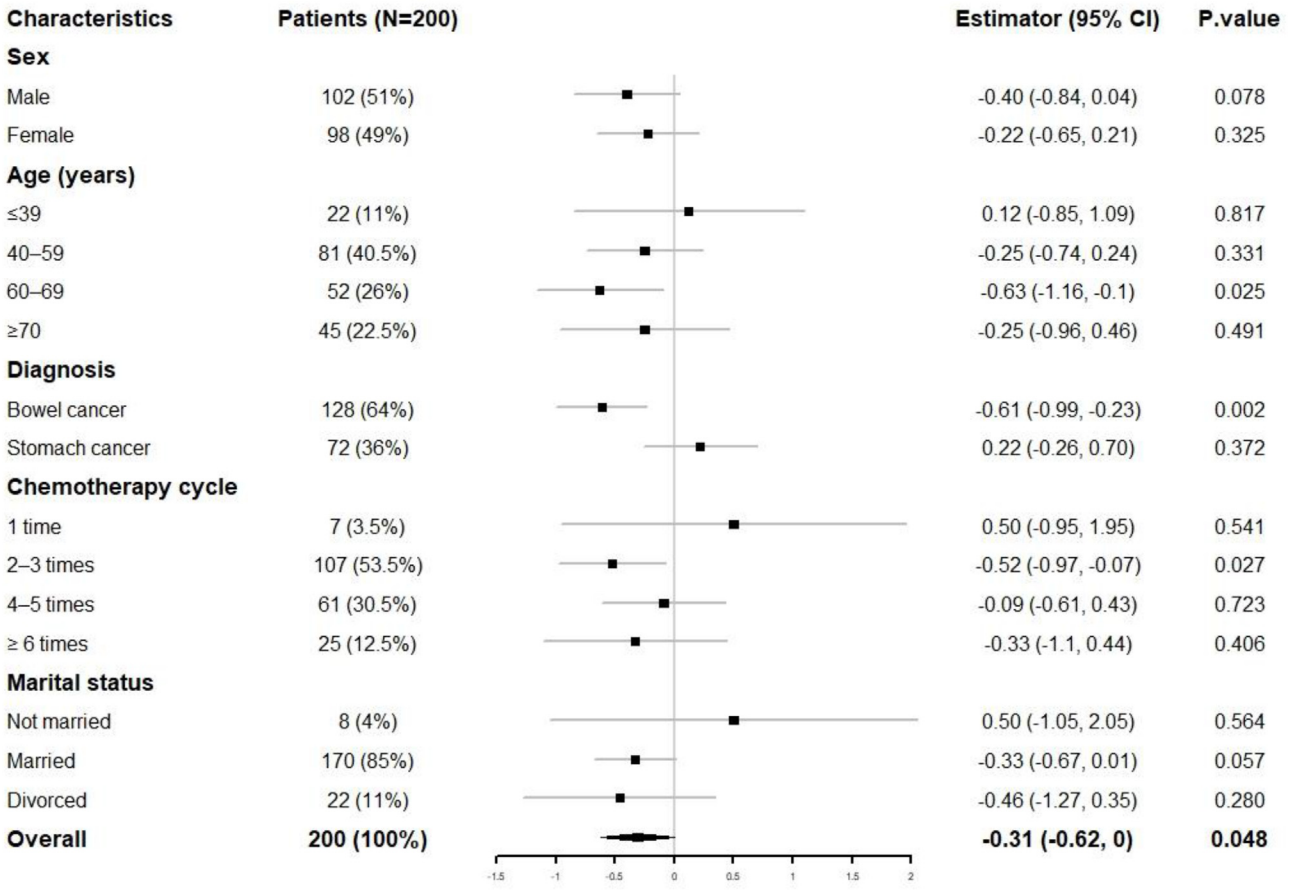

Fig. 6. Forest plot of retching scores for subgroup analysis.

at 12, 24, and 36 h of chemotherapy compared to the control group administered only the 5-HT3 antagonist.

Mechanisms of press needles treating CINV and retching

The press needle can be inserted and fixed under the skin of the acupoint, and through gentle and long-term stimulation of the acupoint, it can achieve the effect of clearing the meridians, regulating Qi and blood, and nourishing internal organs in the human body.[25] The Zusanli (ST36) acupoint is located where the Qi of Yangming and Sanjiao is produced. Stimulating the Zusanli (ST36) acupoint can promote the production of these two types of Qi, which strengthen the spleen and stomach and activate channels and blood.[26] The Neiguan (PC6) acupoint is from the TCM book "Lingshu Meridians" and is located on the palm of the forearm, 2 inches above the wrist stripe, between the tendon of the palm and the flexor tendon of the wrist. Stimulating the Neiguan acupoint can produce the Qi of Zhongjiao, which calms the Qi in the upper reverse of the stomach and stops nausea and vomiting in the stomach.[27] Therefore, we selected the Neiguan (PC6) and Zusanli (ST36) acupoints for the press needle treatment in this study.

Differences between the two groups at each time point

Our findings showed that, before initiating chemotherapy, there were no significant differences in nausea, vomiting, and retching scores between the intervention and control groups. However, with the extension of chemotherapy time, all three scores increased, peaked at 24 h, and then decreased. The peak time point coincided with acute nausea and vomiting periods caused by the peripheral pathway.[7] The values of symptoms decreased after 24 h, while the scores of the intervention group were consistently lower than those of the control group at all six time points after chemotherapy. Two-way repeated measures ANOVA showed a significant difference in all three scores between the two groups, suggesting that the press needle had a positive therapeutic effect against CINV and retching. In addition, there was a significant interaction between group and time, suggesting that the therapeutic effect of the press needle changed over time. It is necessary to further examine the differences between the two groups separately at each time point.

The differences between the two groups for the three symptoms were statistically significant at 12, 24, and 36 h after chemotherapy, indicating that press needle treatment had both immediate and delayed acute effects on alleviating CINV and retching. The scores of the three symptoms peaked at 24 h after chemotherapy, and the most significant difference for nausea and retching also occurred at 24 h, suggesting that the press needle can significantly reduce the peak of nausea and retching. As for vomiting, the score increased rapidly before 12 h but decreased within 12 and 24 h, with the most significant difference between the two groups occurring 12 h after chemotherapy. This may be because food was vomited during the first 12 h; thus, a part of the vomiting has been converted to retching after 12 h. After 48 h, the scores for all three symptoms in the press needle group were still lower than those in the control group; however, the differences were not statistically significant. This can be explained by the decrease in the concentration of chemotherapy drugs in the human body after 48 h. Note that the scores of all three symptoms within 48 h and 72 h were still higher than those before chemotherapy. Therefore, we recommend increasing the stimulation frequency of the press needle after 48 h (eg, stimulating each acupoint 10–15 times per day) or reinserting the needle after 48 h in the future, which may be effective in reducing CINV and retching within 48 h and 72 h after chemotherapy.

The results of the subgroup analysis showed that the press needle group generally had lower scores than the control group for most subgroups. The effect of press needles on alleviating CINV and retching was significantly better in patients aged 60–69 years with bowel cancer than in other subgroups, which suggests that further research should be carried out in patients aged 60–69 years with bowel cancer. Safety analysis showed that none of the patients in the press needle group had an allergy, infection, pain, or numbness within 3 days, indicating that the press needle treatment is safe.

Limitations

In this study, there was no placebo press needle intervention for the control group because the blind design of non-drug treatments such as acupuncture has always been a challenge in clinical trials. The setting of placebo acupuncture interventions remains controversial. Some authors have suggested that placebo acupuncture interventions are not completely inert and are often associated with moderately non-specific effects.[28–30] However, the data collectors and statistical analysts were blinded to minimize bias. Second, all the patients were recruited from a single hospital. Third, because the severity of nausea and vomiting is difficult to measure using objective indicators (eg, fasting blood glucose level for diabetes), we used the INVR scale to measure the severity of patients' CINV and retching. The results of the scale may be slightly influenced by the subjective perceptions of patients, which may present potential bias in accurately interpreting the study's results. Finally, we only observed the acute effects of press needle treatment on CINV and retching because CINV and retching commonly occur three days after chemotherapy. The long-term efficacy and safety of other outcomes should be determined based on a longer follow-up period.

Implications in nursing

The press needle is small and safe, and the needle body is inserted only into the superficial skin of the human body. Therefore, the operation is simple for nurses, painless, or slightly painful for patients. In addition, the effect of the press needle is immediate and long-lasting, which is conducive to reducing or eliminating the patients' anxiety and fear of acupuncture pain. The widespread use of press needles contributes to the enhancement of nurses' values by improving professional pride, stimulating work enthusiasm, and facilitating the development of nursing careers.

Conclusions

Press needle treatment effectively alleviates nausea, vomiting, and retching in patients with gastrointestinal cancer receiving FOLFOX chemotherapy. It provides a safe, effective, and convenient supplement to preventive treatment with 5-HT3 antagonists. To ensure a therapeutic effect, acupuncture should last for at least two days after chemotherapy.

CRediT author statement

Jin Zhou: Conceptualization, Supervision, Writing – Review and Editing. **Fenyu Liu:** Methodology, Formal analysis, Writing – Original draft preparation. **Rongrong Liao:** Software, Visualization. **Jianhong Cai**: Investigation, Validation. **Mengru Bu:** Investigation, Writing – Review and Editing. **Ningjun Xu:** Data curation. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of competing interest

The authors declare no conflict of interest.

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Data availability statement

The data supporting the findings of this study are available in ["Clinical Trail Management Public Platform"] at http://www.medresman.org.cn/login.aspx, reference number [ChiCTR 1900024554].

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