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© 2024 Ou, Lin, Ni, Feng, Rong, Gao, Yu, Liu, Zhang, Xiao, Tang and Zhao. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms. Acupuncture and moxibustion as adjunctive therapy for postoperative gastrointestinal dysfunction in gastric cancer: a systematic review and network meta-analysis

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**Objectives:** This study aimed to evaluate and compare the efficacy and safety of different acupuncture and moxibustion techniques as adjunctive therapy in addressing Postoperative gastrointestinal dysfunction (PGD) associated with gastric cancer (GC).

**Methods:** Eight medical databases were comprehensively searched for relevant randomized controlled trials (RCTs) as of October 2024. A network meta-analysis (NMA) was performed using frequency models, combining all available direct and indirect evidence from RCTs. Time of first bowel sounds (TFBS) was set as the primary outcome, and time to first defecation (TFD) and time to first flatus (TFF) were set as the secondary outcomes. All outcomes were ranked using surface under the cumulative ranking curve (SUCRA) probabilities to determine a hierarchy of treatments, and the probability that the intervention will be in one of the top ranks increases with a higher SUCRA value.

**Results:** With 28 randomized controlled trials (RCTs) and 2,459 patients, 18 of which involved adjuvant acupuncture treatments. NMA based on SUCRA rankings showed that routine care (RC) with acupuncture (ACU), with acupressure (ACUP), with moxibustion (MOX) and acupoint injection (AI) were the top-ranked therapies for shortening TFBS and TFF in patients with GC compared with RC; additionally, RC + MOX + CUP and RC + MOX were the relatively best therapies for TFD. No serious adverse events were reported in the studies assessing the safety of adjunctive acupuncture therapy. Our study found that ST36, ST37, ST39, and PC6 were the most commonly used acupoints for adjuvant acupuncture treatments in treating PGD associated with GC.

**Conclusion:** Acupuncture and moxibustion, when used as supplementary therapies, demonstrated efficacy and relative safety in managing PGD associated with GC. The recommended order for adjunctive acupuncture- and moxibustion-related therapies for PGD in patients with GC, in terms of conservativeness, is as follows: RC + ACU, RC + MOX + AI, RC + ACUP, RC + MOX + CUP and RC + MOX. Despite their inclusion, the overall methodological quality of the

studies was poor, which need for further high-quality randomized controlled trials to support existing results.

Systematic review registration: https://www.crd.york.ac.uk/PROSPERO.

KEYWORDS

postoperative gastrointestinal dysfunction, network meta-analysis, systematic review, acupuncture, moxibustion, time of first bowel sounds

### **1** Introduction

Gastric cancer (GC), primarily adenocarcinoma, is a malignant tumor affecting the gastric sinus, body, and cardio (1), ranking as the fifth most prevalent cancer globally and the third leading cause of cancer-related deaths (2). Surgical removal stands as the primary treatment for GC, where postoperative gastrointestinal dysfunction (PGD) emerges as the most common complication (3), marked by perioperative drug stimulation, intraoperative straining injury, direct injury from gastrointestinal surgery, and an excessive postoperative inflammatory response. This function results in varying degrees of gastrointestinal dysfunction, including the loss of bowel sounds, absence of defecation, and flatus (4), posing considerable risks such as intestinal adhesion, intestinal obstruction, and psychological comorbidities including anxiety and depression, alongside reduced quality of life (5, 6). Consequently, effective treatment and management of PGD following GC surgery, as well as efforts to improve patients' quality of life and prognosis, have become pressing topics of research and clinical interest.

Conventional pharmacotherapy, featuring gastrin, erythromycin, domperidone, and cisapride (7). However, these Western medicine (WM) treatments exhibit limited efficacy and significant side effects, such as gastrointestinal inflammation, increased gastrointestinal burden, and cardiovascular complications from prolonged drug use (8–10). Current routine care (RC) for PGD in GC primarily involves fasting, gastrointestinal decompression, anti-infection, and nutritional support, aiming to maintain primary dietary status and prevent exacerbation; however, its impact on improving PGD in GC is limited. Consequently, complementary and alternative therapies, particularly RC-based adjuvant acupuncture-related treatments, have gained prominence in the management of PGD in GC.

Acupuncture, a traditional, non-pharmacological therapy, offers a green approach to addressing PGD in GC. Recent years have witnessed a surge in the use of various acupuncture- and moxibustionrelated adjunctive therapies for gastrointestinal disorders, including irritable bowel syndrome (11, 12), gastroparesis (13), and constipation (14). Adjunctive acupuncture therapies such as auricular acupuncture (AA) (15), electroacupuncture (EA) (16), moxibustion (MOX) (17), point application therapy (PAT) (18), transcutaneous electrical acupoint stimulation (TEAS) (19), acupoint injection (AI) (20), cupping (CUP) combined with RC might offer advantages in treating PGD compared to RC alone or sham acupuncture (SA). A 2021 systematic review (21) highlighted the positive impact of RC combined with auricular acupressure on gastrointestinal function post-GC surgery. Another systematic review in 2022 (22) found that acupuncture, including warm acupuncture (WA), MOX, AA, and standard acupuncture (ACU), significantly improved the time to first defecation (TFD) and time to first bowel sounds (TFBS) in those with PGD among patients with GC. While the current evidence supports the consideration of adjunctive acupuncture- and moxibustion-related therapies in PGD management, a comprehensive understanding of the efficacy of various adjunctive acupuncture treatments for PGD in GC is lacking, posing challenges for clinicians in selecting the most effective approach.

This study employed a frequency model-based network metaanalysis (NMA) to compare the effects of diverse adjuvant acupuncture-related treatments for PGD in GC. The results of this study provide a basis for optimal acupuncture-related adjuvant therapy for PGD of GC and guide clinical practice. Additionally, the results aim to serve as a reference for optimizing postoperative care for patients experiencing PGD following GC surgery.

# 2 Methods

#### 2.1 Registration

The study protocol was registered with the International Prospective Registry for Systematic Reviews (PROSPER) under CRD42022359145.

### 2.2 Search strategy

This study comprehensively searched eight databases from their inception to October 2024. Chinese databases included the Chinese Biomedical Literature Database, China National Knowledge Infrastructure, and the China Science and Technology Journal Database, Wan Fang database. English databases comprised PubMed, Embase, Web of Science, and The Cochrane Library. The inclusion criteria and search strategy were guided by the PRISMA protocol (23). Each database's search terms were tailored, combining subject and free words. The search focused on [stomach neoplasm OR gastric cancer OR Gastric neoplasm OR Tumor of stomach] AND [Surgical Procedures, Operative OR operation OR Surgery OR post-operation OR Postoperative OR Post operation] AND [gastrointestinal dysfunction OR dysfunctional gastro intestine OR gastrointestinal function disturbance] AND [acupuncture therapy OR acupuncture OR moxibustion]. All included studies were randomized controlled trials (RCTs) involving human participants. The search process was independently conducted and verified by both authors. Moreover, a manual search of original articles and reviews was performed to augment the list of relevant studies. The search strategy is shown in Supplementary Tables S1-S8.

#### 2.3 Eligibility criteria

(1) Patient(s): Those clinically diagnosed with GC (age > 18 years);

- (2) Intervention(s): All needle or moxibustion therapies or both (AA, EA, SA, TEAS, PAT [point application therapy], acupressure [ACUP], MOX) combined with RC (RC comprises fasting, gastrointestinal decompression, anti-infective nutritional support, and emotional care);
- (3) Control(s): RC, SA, sham moxibustion;
- (4) Outcomes: TFBS, TFD, time to first flatus (TFF);
- (5) Only RCTs were included.

### 2.4 Exclusion criteria

- (1) Duplicate articles;
- (2) Unavailable full-text studies;
- (3) Non-PGD studies;
- (4) Intervention group including oral herbal medicine;
- (5) Outcome indicators for which data are either unavailable or cannot be analyzed on a consolidated basis.

### 2.5 Study selection and data extraction

Two authors (JR and XG) independently conducted screening and cross-checked eligible literature based on study type, population, measures, and outcome indicators for both intervention and control groups. Screening involved duplicate checking, initial screening of titles and abstracts, and thorough full-text reading. Moreover, two authors (YY and JR) independently conducted and cross-checked data extraction, encompassing author details, age, title, publication year, country, sex ratio, disease duration, interventions, randomization method, blinding, concealment, sample size, treatment duration, outcome metrics, and follow-up. Any discrepancies were resolved through discussion with another author (YO) for a final consensus. In cases of unclear or missing data, we contacted the corresponding study's author via email.

### 2.6 Risk-of-bias assessment

Two authors (DL and YO) independently assessed the risk of bias assessment using the Cochrane Risk of Bias 2.0 (RoB 2.0) (24), and the five domains are: (1) bias arising from the randomization process; (2) bias due to deviations from the intended interventions; (3) bias due to missing outcome data; (4) bias in measurement of the outcome; and (5) bias in selection of the reported result (25). The results were categorized as "low risk of bias," "some concerns," or "high risk of bias." Controversial situations were resolved through discussion with another author (XW).

## 2.7 Data analysis

The study integrated evidence from RCTs, treating outcome indicators such as TFBS, TFD, and TFF as continuous variables reported through mean differences (MDs) with 95% confidence intervals (CIs). A random-effects model was chosen to accommodate potential differences in the studies (26).

Data analysis and graphing were performed using STATA 15.1 (StataCorp, College Station, TX), employing the nodal method for quantitative analysis. Consistency between direct and indirect comparisons was tested, with p > 0.05 indicating a passed consistency test (27).

STATA 15.1 was further utilized for characterizing network graphs of various adjunctive acupuncture-related therapies, where each node represents a different intervention method. The connecting lines between the nodes represent direct comparisons among various intervention methods. The size of each node and the width of the connecting lines are proportional to the number of studies (28).

Recommendations for intervention therapies were primarily based on the surface of the cumulative ranking curve (SUCRA) value, represented as a P-score. The P-score, ranging from 0 to 1, indicates treatment effect magnitude, with 1 indicating the best and 0 the worst effect. While SUCRA or P scores aid in interpreting the effective percentage of relevant adjuvant acupuncture treatments, cautious interpretation is advised unless clinically meaningful variations between treatments are observed.

# 2.8 Publication bias

Funnel plots in the NMA visually confirmed the detection of publication bias. The symmetry of funnel plots for outcome metrics was observed to determine the probability of publication bias.

# 2.9 Quality of evidence

The GRADE method was utilized to determine the level of the confidence in the NMA estimations for efficacy outcomes (29). This hierarchical approach involves both direct and indirect estimates. Direct estimation was performed by starting with a high confidence level derived from included RCTs and downgrading it to moderate, low, or very low based on indirectness, heterogeneity, imprecision, risk of bias, or publication bias. Ratings for indirect estimates started at the lowest rating for two pairs of estimates, first-order cycles of indirect estimates. They were further downgraded for non-transmissibility or imprecision (studies differing in statistical methods or clinical inclusion criteria). Higher ratings, whether from direct or indirect sources, contributed to the overall quality of evidence in the NMA and were categorized as high, medium, low, or very low.

# **3 Results**

### 3.1 Literature selection process

A total of 831 studies were retrieved from the database for review. Initially, 258 duplicate studies were excluded, followed by the exclusion of 359 studies after reading the titles and abstracts from the remaining 573. Subsequently, 214 studies were excluded after a full-text reading of the remaining 186 (exclusions based on non-RCT, secondary analyses, unavailable full text, study population, study type, outcome metrics, and intervention method). Ultimately, 28 studies were included in this review, as illustrated in Figure 1 PRISMA flow chart.



### 3.2 Study characteristics

Through literature screening, 28 RCTs were included with 2,459 independent participants. Interventions in the 28 studies' intervention groups mainly comprised RC combined with various acupressure-related treatments (RC + ACUP), point application therapy (RC + PAT), auricular acupuncture (RC + AA), acupuncture (RC + ACU), electroacupuncture (RC + EA), moxibustion (RC + MOX), electroacupuncture and point application therapy (RC + EA + PAT), and auricular acupuncture and acupressure (RC + AA+ACUP). The control group primarily involved RC, SA, RC + MOX, and RC combined with foot bath therapy (RC + FBT). Key acupoints included ST36 (Zusanli), ST37 (Shangjuxu), LI4 (Hegu),

ST39 (Xiajuxu), PC6 (Neiguan), ST25 (Tianshu), CV8 (Shenque), and auricular acupoints TF4 (Shenmen), AH6a (Jiaogan), CO4 (Wei), and AT4 (Pizhixia) (Table 1); The commonly used point combination is ST36-PC6. Network diagrams depicting primary and secondary outcome metrics are presented in Figure 2. The outcome network diagram for the primary outcome metric (TFBS) for this review is shown in Figure 2A, while the secondary outcome metrics (TFD, TFF) are shown in Figures 2B,C. The results of literature meeting study requirements were included in the systematic review, whereas some interventions were excluded from NMA analyses due to irrelevance or lack of available data.

In the included studies, gender characteristics were reported for 2,459 patients, with 1,223 (51.2%) being women. The mean sample

TABLE 1 Basic features of included RCTs.

Study	Age (E/C)	Male (E/C)	Female (E/C)	Intervent E	ions (E/C) C	Diagnostic criteria	Period of treatment (E/C)	Outcomes	Acupuncture points
Zhang 2014 (42)	53 ± 7.3/48 ± 9.6Y	12/28	10/30	RC + MOX	RC (① + ② + ③)	Clinical Diagnosis	Once daily (3D)/ Once daily (3D)	1. TFBS; 2. TFF	ST36 Zusanli 足三 里, ST37 Shangjuxu上巨虛, LI4 Hegu 合谷.
Ren 2016 (45)	63.27 ± 3.78/64.09 ± 3.74Y	18/14	19/13	RC + MOX	RC (0 + 0 + 0)	2013 Guidelines for the Standardized Treatment of Gastric Cancer	Once daily (1 W)/ NR	1. TFBS; 2. TFF	ST36 Zusanli 足三 里, CV8 Shenque 神 阙.
Ding, 2021 (31)	46.00 ± 13.67/45.81 ± 13.82Y	21/11	18/14	RC + EA	RC (0 + 2 + 3 + SA)	Clinical Diagnosis	Once daily (5D)/ Once daily (5D)	1. TFD; 2. TFF	GV20 Baihui 百会, ST36 Zusanli 足三 里, PC6 Neiguan 内 关, ST25 Tianshu 天 枢.
Que 2021 (16)	65.38 ± 6.28/65.36 ± 6.18Y	21/19	22/18	RC + TEAS	RC (① + ② + ③ + ④)	2017 Experts on Early Stomach Cancer Screening Process in China Consensus opinion	Twice daily (NR)/NR	1. TFD; 2. TFBS; 3. TFF	CV12 Zhongwan 中 脘, Hegu 合谷, ST25 Tianshu 天枢, ST37 Shangjuxu上巨虚
Sun, 2014 (46)	55.5 ± 5.7/54.5 ± 5.5Y	15/13	15/14	RC + AA	RC (① + ② + ③ + ④)	Clinical Diagnosis	Press 3–5 times a day, replacement once in two days (NR)/Press 3–5 times a day, replacement once in two days (NR)	1. TFD; 2. TFBS; 3. TFF	The following are auricular points: AT4 <i>Pizhixia</i> 皮质下, TF4 <i>Shenmen</i> 神门, AH6a Jiaogan 交感, CO7 Dachang 大肠, CO4 Wei 胃.
Nan, 2018 (51)	58.8 ± 4.7/59.3 ± 4.6Y	21/14	12/23	RC + AA	RC (0 + 9)	Clinical Diagnosis	Press 3–5 times a day, replacement once in two days (4D)/8 times (4 W)	1. TFD; 2. TFF	The following are auricular points: AT4 Pizhixia 皮质下, TF4 Shenmen 神门, AH6a Jiaogan 交感, CO7 Dachang 大肠, CO4 Wei 胃.

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#### TABLE 1 (Continued)

Study	Age (E/C)	Male (E/C)	Female (E/C)	Interventions (E/C)		Diagnostic	Period of	Outcomes	Acupuncture
				Е	С	criteria	(E/C)		points
Huang, 2014 (32)	63.02 ± 7.96/ 61.17 ± 7.47Y	52/48	60/40	RC + AA	RC (① + ② + ③)	Clinical Diagnosis	Press 3–5 times a day, replacement once in four days (1 W)/NR	1. TFD; 2. TFBS; 3. TFF	The following are auricular points: AT4 <i>Pizhixia</i> 皮质下, TF4 <i>Shenmen</i> 神门, AH6a <i>Jiaogan</i> 交感, CO7 <i>Dachang</i> 大肠, CO4 <i>Wei</i> 胃, CO13 <i>Pi</i> 脾.
Yuan, 2018 (50)	60.60 ± 11.00/58.60 ± 9.70Y	25/23	27/21	RC + AA+PAT	RC (① + ② + ③)	2011 Guidelines for the Standardized Treatment of Gastric Cancer	Press 3–4 times a day, replacement once in four days (NR)/NR	1. TFD; 2. TFF	ST36 Zusanli 足三 里, PC6 Neiguan 内 关, SP6 Sanyinjiao 三阴交.
Ye, 2018 (41)	52.86 ± 3.52/52.11 ± 3.26Y	50/37	49/39	RC + AA	RC (① + ② + ③)	Clinical Diagnosis	Press 3–4 times a day, replacement once in four days (1 W)/1 W	1. TFD; 2. TFBS; 3. TFF	The following are auricular points: TF4 Shenmen 神门, AT4 Pizhixia 皮质下, CO13 Pi 脾, AH6a Jiaogan 交感, CO7 Dachang 大肠, CO4 Wei 胃.
Tan, 2017 (38)	73.5 ± 7.5岁/74.6岁 ± 6.2Y	20/14	12/22	RC + AA	RC (① + ② + ③)	2011 Guidelines for the Standardized Treatment of Gastric Cancer	Press 3–4 times a day, replacement once in three days (1 W)/1 W	1. TFD; 2. TFBS; 3. TFF	The following are auricular points: CO7 Dachang 大肠, CO4 Wei 胃, CO10 Shen 肾, CO17 Sanjiao 三焦.
Zou, 2021 (15)	50. 35 ± 10. 98/49. 67 ± 11. 12Y	28/22	29/21	RC + AA	RC (① + ② + ③)	Gastric Cancer Surgery	Press 3–4 times a day, replacement once in one days (2 W)/Once daily (2 W)	1. TFD; 2. TFBS; 3. TFF	The following are auricular points: CO4 Wei 胃, CO7 Dachang 大肠, CO13 Pi 脾, CO18 Neifenmi 内分泌.
Xu, 2017 (40)	48 ± 4.11/53 ± 4.47Y	45/10	46/7	RC + MOX	RC (① + ② + ③) + FBT	Clinical Diagnosis	Once daily (6D)/ Once daily (6D)	1. TFD; 2. TFBS; 3. TFF	1

(Continued)

#### TABLE 1 (Continued)

Study	Age (E/C)	Male (E/C) Female (E/C) Interventions (E/C) Diagnostic criteria Period of treatment (E/C)	Period of	Outcomes	Acupuncture				
				E	С	criteria	(E/C)		points
Yang, 2022 (48)	51.79 ± 3.96/52.12 ± 4.27Y	28/12	26/14	RC + ACU	RC (① + ② + ③ + ④)	2013 Guidelines for the Standardized Treatment of Gastric Cancer	Once daily (10D)/ NR.	1. TFD; 2. TFF.	ST36 Zusanli 足三 里, SP9 Yinglingquan阴陵泉, SP6 Sanyinjiao 三阴 交, ST37 Shangjuxu上巨虚, ST39 Xiajuxu 下巨 虛
Liang, 2020 (34)	58.19 ± 8.92/57.47 ± 9.52Y	20/11	19/11	RC + MOX + CUP	RC (① + ② + ③) + MOX	2010 Diagnostic Criteria for Stomach Cancer	Once daily (5D)/ Once daily (5D)	1. TFD; 2. TFBS; 3. TFF	ST36 Zusanli 足三 里, ST36 Zusanli 足 三里, ST37 Shangjuxu上巨虚, ST39 Xiajuxu 下巨 虚.
Wu, 2020 (52)	62.40 ± 11.17/66.00 ± 2.12Y	13/2	11/4	RC + ACU	RC (① + ② + ③ + ④)	2010 Diagnostic Criteria for Stomach Cancer	NR/NR	1. TFD; 2.TFF.	ST37 Shangjuxu上巨 虚, ST39 Xiajuxu下 巨虚.
Xie, 2020 (47)	52.83 ± 7.08/51.52 ± 6.31	51/33	49/35	RC + AA	RC (① + ② + ③ + ④)	Diagnostic criteria for radical gastric cancer surgery with Chinese and Western medicine	Press 3–4 times a day, replacement once in one days (1 W)/NR (1 W)	1. TFD; 2. TFBS; 3.TFF	The following are auricular points: CO4 Wei 胃, CO7 Dachang 大肠, AT4 Pizhixia 皮质下, AH6a Jiaogan 交感, CO13 Pi 脾, CO6 Xiaochang 小肠.
Mei, 2013 (44)	56.2 ± 4.5/57.0 ± 4.8Y	38/12	33/9	RC + MOX + AI	RC (1 + 2 + 3 + 4)	Clinical Diagnosis	Once daily (1 W)/ Once daily (1 W)	1. TFD; 2. TFBS; 3. TFF	ST36 Zusanli 足三里
Wu, 2021 (39)	56. 43 ± 10. 01/57. 38 ± 9.79Y	28/21	27/22	RC + WA + ACUP	RC (① + ② + ③)	Guiding Principles for Clinical Research on New Chinese Medicines	Once daily (1 W)/ NR (1 W)	1. TFD; 2. TFBS; 3. TFF	PC6 Neiguan 内关, L14 Hegu 合谷, ST36 Zusanli 足三里, ST36 Zusanli 足三 里, PC6 Neiguan 内 关, SP6 Sanyinjiao 三阴交, LR3 Taichong 太冲.

(Continued)

Study	Age (E/C)	Male (E/C)	Female (E/C)	Interven	tions (E/C)	Diagnostic	Diagnostic Period of Outco criteria treatment (E/C)	Outcomes	Acupuncture points
				E	С	criteria			
Lin, 2015 (35)	55.82 ± 13.19/57.57 ± 10.87Y	24/15	11/29	RC + EA + PAT	RC (① + ② + ③)	Clinical Diagnosis	Twice daily (NR)/NR	1. TFD; 2. TFBS; 3. TFF	ST36 Zusanli 足三 里, CV8 Shenque 神 阙.
Cui, 2014 (20)	60.6 (40-72)/62 (42-75) 46.2 ± 6.50Y	7/5	6/5	RC + AI	RC (① + ② + ③)	Clinical Diagnosis	Once daily (7D)/NR (7D)	1. TFD; 2. TFBS; 3. TFF	ST36 Zusanli 足三里
Zhang, 2022 (21)	69. 48 ± 8. 35/68. 60 ± 9. 06Y	31/15	33/16	RC+ AA+ ACUP	RC (① + ② + ③)	Clinical Diagnosis	Press 3 times a day, replacement once in three days (NR)/NR	1. TFD; 2. TFBS; 3. TFF	ST36 Zusanli 足三 里, PC6 Neiguan 内 关. The following are auricular points: TF4 Shenmen 神门, CO12 Gan 肝, CO4 Wei 胃, AH6a Jiaogan 交感.
Song, 2019 (37)	55.8 ± 6.6/55.7 ± 6.6Y	30/20	28/22	RC + ACUP	RC (① + ② + ③)	Clinical Diagnosis	Twice daily (5D)/NR (5D)	TFF; 2.TFBS	ST36 Zusanli 足三 里, PC6 Neiguan 内 关, LI4 Hegu 合谷
Li, 2016 (33)	65.2 ± 2.8/63.9 ± 3.4Y	34/7	35/10	RC+ AA+AI	RC (① + ② + ③)	Clinical Diagnosis	Once daily (NR)/ Once daily (NR)	1. TFD; 2. TFBS; 3. TFF	ST36 Zusanli 足三里 The following are auricular points: TF4 Shenmen 神门, AT4 Pizhixia 皮质下, AH6a Jiaogan 交感, CO4 Wei 胃, CO7 Dachang 大肠, CO6 Xiaochang 小肠.
Qian, 2017 (36)	59 ± 10/60 ± 11Y	20/10	17/13	RC + ACU	RC (① + ② + ③)	Clinical Diagnosis	Once daily (1 W)/ NR (1 W)	TFF; 2.TFBS.	ST36 Zusanli 足三 里, ST37 Shangjuxu上巨虛, ST39 Xiajuxu 下巨 虛.

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Study	Age (E/C)	Male (E/C)	Female (E/C)	Interventions (E/C)		Diagnostic	Period of	Outcomes	Acupuncture
				E	С	criteria	(E/C)		points
Chen, 2017 (43)	44.9 ± 4.1/45.8 ± 3.9Y	28/19	24/18	RC + ACU + FT	RC (① + ④)	Clinical Diagnosis	Once daily (NR)/NR	1. TFD; 2.TFF	ST36 Zusanli 足三 里, ST44 Neiting内 庭 ST36 Zusanli 足 三里, PC6 Neiguan 内关, L14 Hegu 合 谷, ST44 Neiting内 庭.
Yuan, 2021 (49)	55.65 ± 7.49/55.69 ± 7.42Y	25/16	14/27	RC+ ACU+ PAT	RC (① + ② + ③)	Guidelines for the Treatment of Stomach Cancer	Twice daily (NR)/NR	1. TFD; 2. TFBS; 3. TFF	CV8 Shenque 神阙, LI4 Hegu 合谷, ST36 Zusanli 足三里, SP9 Yinglingquan阴陵泉.
Li, 2014 (18)	$60.63 \pm 7.81/58.91 \pm 10.29 Y$	30/26	20/24	RC + PAT	RC (① + ② + ③)	Clinical Diagnosis	Once daily (NR)/NR	1. TFD; 2.TFF	CV8 Shenque 神阙
Wan-Ting Hsiung, 2015 (30)	60.54 ± 10.89/64.11 ± 15.60Y	20/6	20/8	RC + ACUP	RC (① + ② + ③)	Clinical Diagnosis	Once daily (3D)/NR (3D)	1. TFD; 2. TFF	ST36 Zusanli 足三 里, PC6 Neiguan 内 关.

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E, experimental group; C, control group; D, day; W, week; M, month; Y, year; NR, not reported; N, none; WM, western medicine; Postoperative gastrointestinal dysfunction (PGD); RCTs, randomized controlled trials; AEs, adverse events; TFBS, Time of first bowel sounds; TFD, time to first defecation; TFF, Time to first flatus; RC, routine care; RCD, fasting; RCD, gastrointestinal decompression; RCD, anti-infective nutritional support; RCD, emotional care. RC + MOX, routine care; RCD, fasting; RCD, gastrointestinal decompression; RCD, anti-infective nutritional support; RCD, the second se care combined with electro-acupuncture; RC + TEAS, routine care combined with transcutaneous electrical acupoint stimulation; RC + SA, routine care combined with sham acupuncture; RC + AA, routine care combined with auricular acupuncture; RC + AA + PAT, routine care combined with auricular acupuncture and point application therapy; RC + ACU, routine care combined with acupuncture; RC + MOX + CUP, routine care combined with moxibustion and cupping; RC + MOX + AI, routine care combined with moxibustion and acupoint injection; RC + WA + ACUP, routine care combined with warming acupuncture and acupressure; RC + EA + PAT, routine care combined with electro-acupuncture and point application therapy; RC + AI, routine care combined with and acupoint injection; RC + AA + ACUP, routine care combined with auricular acupuncture and acupressure; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with auricular acupuncture and acupoint injection; RC + ACUP, routine care combined with acupaction; RC + ACUP, routine care combined w FT, routine care combined with acupuncture and functional training; RC + ACU + PAT, routine care combined with acupuncture and point application therapy; RC + FBT, routine care combined with point application therapy.



size was 90.3 (range, 60–200), and patient ages ranged from 28 to 80 years. All studies were conducted in China. Table 1 outlines the essential characteristics of the included literature.

### 3.3 Assessment of risk of bias

The assessment of the risk of bias is illustrated in Figure 3. Across the five domains, 12 studies had "some concerns" as an overall rating, 14 had a "high risk of bias" and two was rated as of "low risk of bias." Regarding randomization process, numerous studies employed random sequence generation methods with a low risk of bias (15–18, 30–42). Fifteen of these studies utilized random number tables (15–18, 32–42), one opted for random sampling (31), and another employed computer randomization (30). Studies that did not describe

the randomization method were assigned an unclear risk of bias (20, 43–50). Concerning allocation concealment, one study utilized sealed opaque envelopes (30), and another employed central randomization (31). However, the remaining studies did not provide details about allocation concealment. Only the Wan-Ting Hsiung et al. study implemented blinding for researchers, outcome assessors, and participants (30). The other 11 studies did not specify their blinding methods and were assessed as having unclear risks (15, 32, 37, 38, 41, 42, 45–47, 50, 51). Furthermore, regarding bias due to deviations from the intended interventions, several studies were deemed high risk due to considerations related to the intervention's nature (16, 18, 20, 33–36, 39, 40, 43, 44, 47–49, 52).

Concerning the blinding of outcome assessment, Ding et al. (31) and Wan-Ting Hsiung (30) et al. described blinding of outcome assessors and were rated as low risk. At the same time, the remaining



studies did not mention blinding and were considered unclear. Regarding outcome data, 25 studies with complete data were regarded as low risk. For selective reporting, 16 studies had a low risk of bias, of which 8 (15, 30, 31, 38, 39, 41, 49, 52) received ethical approval; the remaining 20 were assessed as unclear. According to our study protocol, 21 studies that included specific statistical methods, baseline data, and exclusion criteria were considered low risk. The remaining studies (20, 38, 44, 46, 50, 51) were rated as unclear risk (20, 38, 44, 46, 50, 51). No dropouts were reported in the 28 studies.

#### 3.4 Network meta-analysis

#### 3.4.1 Ranking of interventions

Ranking of interventions Using ranking probabilities and the surface under the cumulative ranking curves, the relative ranking of the various adjunctive acupuncture- and moxibustion-related interventions for each outcome was calculated. The cumulative probabilities of each treatment were expressed by a single value between 0 and 100%. The probability that the intervention will be in the top rank or in one of the top ranks increases with a higher percentage or SUCRA value (53).

#### 3.4.2 Results of NMA of TFBS

The review tested the consistency and inconsistency of all *p*-values for direct and indirect comparisons related to the TFBS. The results showed that the consistency model was acceptable (p = 0.62).

The comparison of efficacy based on adjuvant acupuncturerelated therapies (marked in bold) is presented in Supplementary Table S9. RC + ACU (MD -23.9, 95%CI -35.39 to -12.41), RC + MOX + AI (MD -19.70, 95%CI -30.97 to -8.43), RC + ACUP (MD -19.20, 95%CI -30.22 to -8.18), RC + AA +AI (MD -18.70, 95%CI -29.90 to -7.50), RC + AI (MD -17.20, 95%CI -28.86 to -5.54), RC + WA + ACU (MD -13.37, 95%CI -24.40 to -2.34), and RC + ACU + PAT (MD -12.90, 95%CI -23.72 to -2.08) were all significantly different from RC. RC + ACU (MD -16.51, 95%CI -28.92 to -4.09) and RC + AI+MOX (MD -12.31, 95%CI -24.52 to -0.10) was all significantly different from RC + AA. RC + ACU (MD -20.57, 95%CI -36.37 to -4.77), RC + MOX + AI (MD -16.37, 95%CI -32.01 to -0.73), and RC + ACUP (MD -15.87, 95%CI -31.34 to -0.40) was significantly different from RC + AA+ACUP.

The relative efficacy of the 14 interventions, including 21 trials, was estimated by NMA of the total TFBS score. The efficacy prioritization, based on SUCRA and mean rankings, is detailed in Figure 4A: RC + ACU (SUCRA 89.9%), RC + MOX + AI (79.4%),



SUCRA for total score. (A) SUCRA for TFBS score of gastric cancer. (b) SUCRA for TFD score of gastric cancer. (C) SUCRA for TFF score of gastric cancer. TFBS, Time of first bowel sounds; TFD, time to first defecation; TFF, Time to first flatus; RC, routine care; RC + MOX, routine care combined with moxibustion; RC + AA, routine care combined with auricular acupuncture; RC + ACUP, routine care combined with acupuncture; RC + AACUP, routine care combined with acupuncture; RC + MOX + CUP, routine care combined with auricular acupuncture and acupressure; RC + ACU, routine care combined with acupont; RC + MOX + CUP, routine care combined with moxibustion and cupping; RC + MOX + AI, routine care combined with moxibustion and cupping; RC + MOX + AI, routine care combined with moxibustion and cuppint; RC + MOX + AI, routine care combined with moxibustion and acupoint injection; RC + WA + ACUP, routine care combined with warming acupuncture and acupressure; RC + EA + PAT, routine care combined with electro-acupuncture and point application therapy; RC + AI, routine care combined with acupuncture and functional training; RC + ACU + PAT, routine care combined with acupuncture and acupoint injection; RC + ACU + FT, routine care combined with Foot bath therapy; RC + TEAS, routine care combined with transcutaneous electrical acupoint simulation; RC + ACU + FT, routine care combined with foot bath therapy; RC + TEAS, routine care combined with therapy. routine care combined with acupuncture and functional training; RC + AA+PAT, routine care combined with auricular acupoint application therapy.

RC + ACUP (78.5%), RC + AA+AI (76.7%), RC + AI (71.8%), RC + WA + ACUP (59.1%), RC + ACU + PAT (57.5%), RC + MOX + CUP (42.7%), RC + TEAS (40.2%), RC + AA (36.7%), RC + MOX (23.8%), RC + AA+ACUP (22.8%), RC + EA + PAT (14.4%), and RC (7.3%).

#### 3.4.3 Results of NMA of TFD

The comparison of efficacy based on adjuvant acupuncturerelated therapies (marked in bold) is presented in Supplementary Table S10. RC + MOX + CUP (MD -61.01, 95%CI -88.82, -33.21), RC + ACU (MD -16.80, 95%CI -30.86, -2.75), RC + MOX + AI (MD –20.80, 95%CI –39.83, –1.77), RC + AI (MD –24.60, 95%CI –44.43, –4.77), and RC + FBT (MD –33.46, 95%CI –62.22, –4.70) were all significantly different from RC. RC + ACU (MD –44.21, 95%CI –75.37, –13.06) and RC + AA (MD –56.60, 95%CI –85.34, –27.86) were all significantly different from RC + MOX + CUP.

The relative efficacy of the 18 interventions, including 21 trials, was estimated by NMA of the total TFD score. The efficacy prioritization, based on SUCRA and mean rankings in Figure 4B: RC + MOX + CUP (SUCRA 97.9%), RC + MOX (94%), RC + FBT (76.9%), RC + AI (68.5%), RC + EA + PAT (64.4%), RC + MOX + AI (62.2%), RC + ACU (54.7%), RC + WA + ACUP (51.2%), RC + AA+PAT (49.7%), RC + TEAS (46.9%), RC + AA+AI (45.3%), RC + ACU + PAT (44.0%), RC + ACUP (30.6%), RC + AA+ACUP (22.2%), RC + PAT (27.4%), RC + AA (23.7%), RC + AA+ACUP (22.2%), and RC (11.0%).

#### 3.4.4 Results of NMA of TFF

The comparison of efficacy based on adjuvant acupuncturerelated therapies, as highlighted in Supplementary Table S11, revealed that RC + AI (MD -28.00, 95%CI -43.22, -12.78), RC + ACU (MD -20.45, 95%CI -29.76, -11.13), RC + MOX + AI (MD -20.50, 95%CI -35.67, -5.33), RC + ACUP (MD -18.85, 95%CI -31.01, -6.69), RC + MOX (MD -14.30, -21.83, -6.76), and RC + AA (MD -8.34, 95%CI -14.21, -2.46) were all significantly different from RC. Moreover, RC + AI (MD -19.66, 95%CI -35.98, -3.35) substantially differed from RC + AA.

The relative efficacy of the 17 interventions, encompassing 21 trials, was assessed through NMA of the total TFF score. The prioritization of efficacy, based on SUCRA and mean rankings Figure 4C, is as follows: RC + AI (SUCRA 90.3%), RC + ACU (76.7%), RC + MOX + AI (74.4%), RC + ACUP (70.9%), RC + EA + PAT (70.8%), RC + WA + ACUP (66.8%), RC + MOX (56.5%), RC + AA+AI (52.0%), RC + MOX + CUP (50.6%), RC + TEAS (49.0%); RC + ACU + PAT (40.7%), RC + AA+PAT (37.1%), RC + AA (34.4%), RC + PAT (34.0%), RC + ACU + FT (22.9%), RC + AA+ACUP (19.2%), and RC (8.6%).

#### 3.4.5 Publication bias

The funnel plots examining publication bias for primary and secondary outcomes are presented in Figure 5. Visual inspection of the plots did not reveal any significant publication bias.

## 3.5 Safety

#### 3.5.1 Adverse events

Among the six RCTs assessing AEs (30, 32, 34, 36, 41, 46), four studies on the RC + AA group reported AEs, such as nausea and vomiting, primarily attributed to postoperative reactions rather than acupuncture. The incidence remained lower than in the RC-only group (32, 36, 41, 46). One study on ACUP reported AEs (30), including one case of fatigue. Another study mentioned two patients transferred to the ICU due to infection exacerbation, likely associated with non-compliance with postoperative fasting (34). Therefore, these events are more likely related to surgery or patient compliance than acupuncture. Overall, acupuncture exhibited a low incidence of adverse events (AEs).

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### 3.6 Quality of evidence

The overall quality of this review was assessed as follows: the NMA grading levels of the primary outcome indicator (TFBS) were mainly rated as three types: moderate, low, and very low (Supplementary Table S12). Moreover, the NMA grading levels of secondary outcome indicators (TFD, TFF) were predominantly rated as low and very low (Supplementary Tables S13, S14). The primary reasons for downgrading included imprecision in NMA results and the potential risk of bias.

# 4 Discussion

### 4.1 Summary of the main results

This study represents the initial attempt to assess the efficacy and safety of different acupuncture-assisted therapies in managing PGD in GC. It encompasses 28 studies with 2,459 patients.

Compared to RC, adjunctive acupuncture- and moxibustionrelated therapies, such as RC + ACU, RC+ MOX + AI, RC + ACUP, RC+ AI, RC + MOX + CUP, and RC + MOX—demonstrated superior efficacy in alleviating PGD in GC. Specifically, NMA based on SUCRA rankings indicated that RC + ACU, RC + AI+MOX, RC + ACUP, and RC + AI were the top-ranked therapies for reducing the TFBS and TFF in patients with GC compared to RC. Additionally, we found that RC + MOX + CUP and RC + MOX had the highest probabilities of ranking first and second in treating TFD. There is a certain level of consistency among the various adjunctive acupuncture and moxibustion therapies for PGD in GC. However, it is essential to interpret these findings with caution due to the limited scope of interventions in this study. While few AEs were reported, apart from instances of nausea, vomiting, and fatigue associated with adjunctive acupuncture-related treatments, no severe AEs were documented.

# 4.2 Possible explanations for the present findings

The primary pathogenesis of postoperative PGD in patients with GC involves the inflammatory response and dysregulation of gastrointestinal hormonal activity triggered by surgical trauma, inhibiting gastrointestinal hormone secretion and the subsequent onset of PGD (4). Additionally, TFBS, TFF, and TFD may recover at various times following GC surgery, depending on the individual patient's gastrointestinal health status.

# 4.2.1 The role of acupuncture-related therapies in TFBS and TFF

In our review, acupuncture and moxibustion therapies, such as RC + ACU, RC + MOX + AI, and RC + ACUP, have emerged as more effective and relatively safe approaches for managing PGD, including TFBS and TFF in patients with GC. Previous studies have indicated that RC + ACU and RC + ACUP can significantly improve PGD in these patients, aligning with our findings (54, 55). TFBS indicates the onset of gastrointestinal activity, while TFF serves as a crucial marker for the recovery of intestinal function, both of which are important indicators of early gastrointestinal recovery after GC



routine care, western medicine, b. RC + MOX, routine care combined with moxibustion, C. RC + AA, routine care combined with adricular acupuncture; D: RC + ACUP, routine care combined with acupressure; E: RC + TEAS, routine care combined with transcutaneous electrical acupoint stimulation; F: RC + AA+ACUP, routine care combined with auricular acupuncture and acupressure; G: RC + AA+PAT, routine care combined with auricular acupuncture and acupressure; H: RC + ACU, routine care combined with auricular acupuncture; I: RC + MOX + CUP, routine care combined with moxibustion and cupping; J: RC + PAT, routine care combined with point application therapy; K: RC + MOX + AI, routine care combined with moxibustion and acupoint injection; L: RC + WA + ACUP, routine care combined with warming acupuncture and acupressure; M: RC + EA + PAT, routine care combined with electro-acupuncture and point application therapy; N: RC + AI, routine care combined with acupuncture and functional training; Q: RC + ACU+ PAT, routine care combined with acupuncture and point application therapy; R: RC + AA+AI, routine care combined with acupuncture and functional training; Q: RC + ACU+ PAT, routine care combined with acupuncture and point application therapy; R: RC + AA+AI, routine care combined with acupuncture combined with auricular acupuncture and acupoint injection; P: RC + ACU+ FT, routine care combined with acupuncture and functional training; Q: RC + ACU+ PAT, routine care combined with acupuncture and point application therapy; R: RC + AA+AI, routine care combined with auricular acupuncture and acupoint injection.

surgery. ACU involves mechanical stimulation of acupoints on the body's surface, which promotes bowel sound production and facilitates the expulsion of intestinal gas by enhancing gastrointestinal peristalsis, stimulating hormone secretion, and reducing inflammation levels (56-58). Clinical studies have shown that applying ACU at ST37 and ST39 within 24 h post-GC surgery can restore abdominal bowel sound fluctuations to normal peristalsis, suggesting that ACU accelerates gastrointestinal recovery (51). Animal studies further indicate that ACU can elevate gastric motilin (MTL) levels, enhancing gastric motility and blood flow to the gastric mucosa, thereby promoting gastrointestinal function recovery (59). Additionally, ACU stimulation may activate 7nAchR, leading to changes in NF-KB activity and affecting inflammatory factor expression, which helps reduce intestinal inflammation and accelerates the production of bowel sounds and gas expulsion (60). However, the optimal frequency and timing of acupuncture for

PGD in GC patients remain unclear and warrant further investigation.

Moreover, RC + MOX + AI is recommended for enhancing the recovery of TFBS and TFF following GC surgery. MOX provides warm stimulation to specific acupuncture points. Several clinical studies have demonstrated that MOX applied at the ST36, ST37, and LI4 acupoints based on RC can significantly shorten the recovery time for TFBS and TFF in patients with PGD related to GC, which is associated with improvements in local and systemic blood circulation, regulation of parasympathetic activity, and restoration of gastrointestinal rhythms (17, 45). Research indicates that gentle MOX at ST36 and ST39 in rats can downregulate the expression levels of substance P (SP) and vasoactive intestinal peptide (VIP) in the hypothalamus and colon tissues, highlighting the brain-gut interaction as a key neurological mechanism for enhancing gastrointestinal function through MOX (61). Neurotransmitters secreted by the

autonomic nervous system can directly influence the enteric nervous system, facilitating rhythmic movements of the stomach and intestines. Studies have also shown that MOX at ST36 can increase the expression levels of gastric mucosa-associated factors nitric oxide (NO) and Bcl-2, emphasizing the nucleus tractus solitarius as the primary regulator of gastrointestinal reflexes (62). However, further clarification is needed regarding the temperature of MOX, the selection of MOX methods, and the timing of the procedure.

AI, which involves the injection of specific Chinese medicines such as Astragalus membranaceus and Western drugs like neostigmine into relevant acupoints, is used to prevent and treat diseases. A review study emphasized that AI can shorten the recovery time for PGD, aligning with our findings (63). Research indicates a close relationship between gastrin levels and gastrointestinal function, with neostigmine- a cholinesterase inhibitor- increasing gastrin content in the central nervous system, bloodstream, and local gastrointestinal tissues, thereby accelerating the recovery of TFBS and TFF (64). Astragalus membranaceus is renowned for its immune-enhancing properties, promoting tumor cell apoptosis and inhibiting tumor growth (65). AI therapy significantly prolongs the duration of drug action, enhances the therapeutic effects at acupoints, and combines the benefits of both drugs and acupuncture (20). It is believed to have longer-lasting effects compared to traditional acupuncture or simple intramuscular injections (66). Notably, studies have shown that the combination of RC + MOX + AI can promote the recovery of gastrointestinal function, improve tissue metabolism, and enhance immune function, proving to be more effective than RC or RC + MOX alone (44). However, further clarification is needed regarding the specific types and doses of drugs used in AI, as well as the mechanisms underlying the efficacy of RC + MOX + AI in treating PGD in GC patients.

Furthermore, RC + ACUP is recommended as a therapeutic option for PGD. ACUP involves stimulating acupoints on the body surface using fingers and palms, guided by the principles of meridian theory in traditional Chinese medicine. In Western medicine, ACUP is thought to engage vagal and parasympathetic efferent pathways, which release acetylcholine and adrenocorticotropic hormone, thereby inhibiting gastrointestinal inflammation and promoting recovery in PGD patients (67-69). ACUP enhances local blood circulation, nutrient and metabolite transport, and overall blood supply, reducing postoperative abdominal distension and effectively improving PGD indicators such as TFBS and TFF (70, 71). For patients with GC, ACUP can rapidly activate neural functions, enhance intestinal peristalsis, and ensure smooth intestinal transit (39, 42). The mechanical stimulation from abdominal acupressure accelerates peristalsis and promotes gastrointestinal flatus and defecation. Combining acupressure with acupuncture minimizes intestinal stimulation and reduces the burden on the liver and kidneys, improving patients' tolerance to enteral nutrition (72, 73). However, further investigation is needed to clarify the specifics of acupressure, including its frequency, force, and duration.

# 4.2.2 The role of acupuncture-related therapies in TFD

In our review, acupuncture and moxibustion-related therapies, such as RC + MOX + CUP and RC + MOX, demonstrated notable efficacy in treating PGD, particularly in relation to TFD in GC patients. TFD typically emerges last, often occurring several days post-surgery, and reflects further recovery of the intestinal tract. This process involves complex physiological functions, including the digestion and absorption of food as well as the formation and elimination of feces, making TFD an important marker of the patient's return to a normal diet and gastrointestinal activity (74). As previously mentioned, RC + MOX plays a critical role in promoting peristalsis, enhancing the secretion of digestive juices, and regulating autonomic functions in the postoperative gastrointestinal tract. Interestingly, our findings indicate that the efficacy of RC + MOX + CUP surpasses that of both RC + MOX and RC alone. Cupping therapy employs specialized tools to create negative pressure on the skin's surface, which promotes blood circulation, enhances tissue metabolism, and boosts immune function (75). Several studies have noted that combining moxibustion with cupping at acupoints ST36, ST37, and ST38 can significantly reduce the postoperative TFD and the time to resume eating compared to RC and RC + MOX (34, 76), aligning with the results of our study. Furthermore, RC + MOX + CUP was found to facilitate gastrointestinal motility and expedite the TFD process by modulating levels of gastrin (GAS), MTL, and cholecystokinin (CCK) (77). However, further investigation is needed to elucidate the operational details of cupping therapy, such as treatment frequency and retention time, as well as the mechanisms underlying the efficacy of RC + MOX + CUP.

In summary, we cautiously propose that adjunct therapies such as RC + ACU, RC + MOX + AI, and RC + ACUP may be beneficial in the early stages of PGD in patients with GC, potentially contributing to a reduction in TFBS and TFF. In the middle and late stages of recovery, RC + MOX + CUP and RC + MOX may prove more effective in accelerating TFD. In future clinical practice, the selection of postoperative care and complementary acupuncture therapies should be tailored to the patient's postoperative timeline and gastrointestinal function status, as this may enhance overall recovery. We hope that higher-quality studies will be conducted in the future to further validate our findings and to elucidate the mechanisms underlying the efficacy of acupuncture in treating PGD in patients with GC.

# 4.2.3 Explanations related to the selection of acupuncture points

This study identified ST36, ST37, ST39, and PC6 as the most frequently used acupoints for treating PGD in GC. The emerging "gastrointestinal-neuro-endocrine-immune network regulation" theory has spotlighted acupuncture as a mechanism for gastrointestinal function regulation. Clinical and experimental evidence supports postoperative acupuncture's role in modulating brain-gut peptide (BGP) expression, promoting gastrin secretion, enhancing gastrointestinal motility, and expediting postoperative recovery, reducing complications (72, 78). Abdominal acupoint stimulation inhibits motility in specific gastrointestinal segments by increasing the activity of sympathetic efferent fibers. In contrast, extremity acupoint stimulation promotes gastrointestinal motility by stimulating the activity of vagal efferent fibers (79, 80). Huang et al. found that EA on ST37 modulates gastrointestinal motility by activating the solitary tract's nucleus and the vagus nerve's dorsal motor nucleus, indicating a neural pathway-based modulatory effect (81). The auricular region represents the only area on the body surface where vagus nerve distributions are concentrated. The frequently used auricular acupoints in this study included CO4 (Wei), AH6a (Jiaogan), AT4 (Pizhixia), and TF4 (Shenmen). Stimulation of AT4 (Pizhixia) and TF4 (Shenmen) primarily affects the regulation of the cerebral cortex, while stimulation of CO4 (Wei) and AH6a (Jiaogan) can influence the vagus nerve, thereby promoting gastrointestinal peristalsis and the secretion of digestive juices, ultimately facilitating the recovery of gastrointestinal function (51, 82).

Among acupuncture point combinations, the pairing of ST36-PC6 is deemed the most stable in acupuncture prescriptions for PGD in GC. ST36 stimulation reduces gastrointestinal tract inflammation, improves blood flow, and regulates gastric motility production (83, 84). Simultaneously, PC6 regulates endocrine function, primarily adrenaline and antidiuretic hormone, reducing gastric acid secretion and regulating gastrointestinal function (85). Acupuncture at PC6-ST36 addresses the inflammatory state of the gastrointestinal tract, regulates gastrointestinal hormone levels, and facilitates the recovery of gastrointestinal function in patients with GC (86, 87). In summary, acupuncture primarily modulates PGD by regulating the gastrointestinal "neural-endocrine-immune" pathway.

#### 4.3 Limitations

#### 4.3.1 Quality evidence of included studies

For several reasons, all outcome indicators (TFBS, TFD, TFF) in this review exhibited low-quality evidence for most studies, as per GRADE scores. Firstly, the randomization methods in the enrolled studies were vaguely described: among the 28 included RCTs, nine did not describe the randomization process (20, 43–50). Secondly, allocation concealment was mainly absent in the included studies, with only one RCT providing information on allocation concealment (30). Thirdly, there was a lack of standardization in the statistical methods, baseline data, and diagnostic criteria used across the included studies, introducing heterogeneity that needs consideration when interpreting the review results for potential bias. In summary, the quality of evidence for the results of the included studies was generally low. The biases mentioned above could contribute to falsepositive results, and we should approach the findings cautiously.

#### 4.3.2 Inconsistent interventions

Due to the limited literature included in this review, it was impossible to encompass all interventions. Some interventions were represented by only one or two studies, introducing limitations to the results. Furthermore, the potential bias of the included studies should be noted concerning the duration, frequency, acupuncture point selection, number of points, needle retention duration, and needle depth, which may have varied. Therefore, a cautious interpretation of the final ranking results of this review is warranted.

#### 4.3.3 Limited outcomes

This review had limited coverage of outcome indicators, hindering a comprehensive evaluation of the differences in the efficacy of adjuvant acupuncture for treating patients with PGD in GC. Only six studies reported AEs, and none addressed follow-up. Consequently, the safety and long-term effects of adjuvant acupuncture-related treatments for PGD in GC warrant more in-depth and comprehensive investigations.

# 4.4 Comparison with other reviews and strengths and limitations of this review

Two previous meta-analyses have assessed the efficacy of acupuncture for treating PGD in patients with GC. The findings indicated that acupuncture may facilitate the recovery of PGD; however, the comparisons between various acupuncture interventions remain unclear (22, 88). Another meta-analysis demonstrated that, compared to RC, acupuncture can reduce TFF and TFBS following cancer surgery. Nonetheless, the safety evaluation of different interventions for PGD in the context of cancer surgery remains contentious (54). A recently published review examining various acupuncture therapies for gastrointestinal dysfunction post-gastric and colorectal cancer indicated that MOX, WA, ACUP, and ACUP were superior to RC. However, a systematic network meta-analysis comparing the efficacy of these different interventions is currently lacking (55). In summary, prior reviews and meta-analyses have preliminarily suggested that acupuncture can aid in the recovery of PGD in patients with GC. However, there is a notable absence of systematic and comprehensive evaluations of the efficacy and safety of different therapies, which represents a significant strength of the present study.

NMA is as an excellent tool for selecting the best therapy among multiple options. Given the limitations of available treatments for PGD in patients with GC, complementary alternative therapies offer additional options; however, few studies have comprehensively evaluated the efficacy of different adjuvant acupuncture therapies. The strength of this review lies in comparing the efficacy and safety of various adjuvant acupuncture therapies for PGD in GC using the NMA method, providing a valuable reference for patients and clinicians in selecting optimal adjuvant acupuncture.

This study has several limitations, including the following points. Firstly, the search language of this study included only Chinese and English, which could introduce potential bias due to language restrictions. Second, the effect of adjuvant acupuncture on PGD in patients with GC remains unclear as none of the included literature reported on follow-up. Third, the quality of the included literature was generally rated as low, possibly due to poor study design and the limited number of included studies. Fourth, the severity of PGD after GC was missing from the included studies, so the results of the efficacy of acupuncture of different severity of PGD are unclear.

Upon analysis and summary of this review, it becomes apparent that few studies have focused on observing the course and follow-up of PGD in GC. Therefore, more high-quality studies are encouraged to investigate the effects of adjuvant acupuncture on the treatment of PGD in GC further, covering aspects such as durability, safety, and efficacy.

## 5 Conclusion

Acupuncture and moxibustion emerged as effective and welltolerated adjuvant therapies for managing PGD in GC. In a relatively conservative hierarchy, the recommended order of adjunctive acupuncture- and moxibustion-related treatments for PGD in GC includes RC + ACU, RC + MOX + AI, RC + ACUP, RC + MOX + CUP and RC + MOX. Nevertheless, the methodological quality of the included studies was generally poor, which need further well-designed, high-quality, large-scale, multicenter RCTs studies to substantiate our results.

## Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

## Author contributions

YO: Writing – original draft, Data curation. DL: Writing – original draft, Data curation. XN: Writing – original draft, Investigation. CF: Writing – original draft, Investigation, Formal analysis. JR: Writing – original draft, Methodology, Investigation. XG: Writing – original draft, Methodology, Investigation. YY: Writing – original draft, Project administration, Formal analysis. XL: Writing – original draft, Project administration, Data curation. ZZ: Writing – original draft, Methodology, Investigation. WX: Writing – original draft, Methodology, Investigation. WX: Writing – original draft, Methodology, Investigation. ZT: Writing – original draft, Methodology, Investigation. ZT: Writing – original draft, Methodology, Investigation. LZ: Writing – review & editing, Project administration, Methodology, Funding acquisition.

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# **Conflict of interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2024.1464749/ full#supplementary-material

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