Systematic Review and Meta-Analysis

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Efficacy and safety of herbal medicine treatment on postsurgical recovery in gastric cancer patients

A systematic review and meta-analysis

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Abstract

Background: Gastric cancer (GC) is the second most prevalent cancer in Korea, and is associated with significant morbidity and mortality. Although advancements in early detection and treatment have improved survival rates, management of postsurgical recovery remains vital. Herbal medicine (HM) has emerged as a potential adjunct therapy for enhancing the recovery and quality of life (QoL) of patients post-GC surgery.

Methods: This systematic review and meta-analysis evaluated the efficacy and safety of HM in the postsurgical recovery of patients with GC. We searched both Korean and international databases and identified 16 randomized controlled trials that met our inclusion criteria. We assessed the study quality using the Cochrane Risk of Bias tool and analyzed the data using the Review Manager Software (RevMan).

Results: Our analysis included 1546 patients from selected studies, demonstrating that HM significantly improved gastrointestinal recovery times, including the time to first flatus, bowel movement, and return of bowel sounds. Significant improvements were also observed in nutritional markers, such as albumin and prealbumin, along with beneficial effects on immune markers, such as $CD3^+$ and $CD4^+$ levels. QoL assessments using the WHOQOL-BREF and QLQ-C30 indicated substantial improvements. HM had a favorable safety profile, showing a reduced incidence of adverse effects compared to the controls.

Conclusion: The findings suggest that HM can significantly enhance recovery and improve quality of life following GC surgery, with a favorable safety profile. However, due to the considerable heterogeneity in study results, extended clinical trials and rigorous follow-ups are recommended to comprehensively assess long-term effects and side effects.

Abbreviations: AEs = adverse events, ALB = albumin, CI = confidence interval, CRP = C-reactive protein, EORTC = European Organization for Research and Treatment of Cancer, ER = endoscopic resection, ERAS = enhanced recovery after surgery, GC = gastric cancer, GI = gastrointestinal, GSRS = gastrointestinal symptom rating scale, HM = herbal medicines, MCD = mosapride citrate dihydrate, MD = mean differences, PA = prealbumin, QLQ-C30 = quality of life questionnaire-core 30, QoL = quality of life, RCT = randomized controlled trials, RoB = risk of bias, RR = risk ratio, SF-36 = 36-item short form health survey, SMD = standardized mean difference, TP = total protein, TRF = transferrin.

Keywords: gastric cancer, herbal medicine, meta-analysis, postsurgical recovery, systematic review

SDK and SJP contributed to this article equally.

The authors have no conflicts of interest.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

This study did not involve new data collection with human participants or animals; it was a systematic review and meta-analysis of previously published studies. Therefore, approval by an ethics committee or an institutional review board was not necessary.

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1. Introduction

Gastric cancer (GC) comprises all cancers that arise in the stomach. Gastric adenocarcinoma, the predominant form of stomach cancer, originates from glandular cells of the gastric mucosa.[1,2] According to 2024 cancer prediction in Korea, GC is the fourth most prevalent cancer, with an estimated 24,769 new cases. It is responsible for 6291 estimated deaths and ranks fourth among all cancer deaths.[3]

Early diagnosis and intervention play pivotal roles in enhancing the survival and quality of life (QoL) of patients with GC.[4] In Korea, a national cancer screening initiative, initiated in 1999, subjects over 40 years of age undergo upper gastrointestinal endoscopy or upper gastrointestinal tract surgery every 2 years.[5,6] This effort has significantly reduced GC mortality, dropping from 29.0 per 100,000 persons in 2000 to 7.9 in 2020. The 5-year relative survival rate for GC has consistently increased, reaching 78.0% in 2016 to 2020. Patients with early stage GC undergoing surgery have a favorable prognosis, with a 5-year survival rate exceeding 90%.[6] Recent studies have highlighted the growing significance of post-surgery patient recovery and nutritional management.

With advancements in GC surgical technologies, patients with early GC and a low risk of lymph node metastasis undergo endoscopic resection (ER), and those who are ineligible for ER undergo gastrectomy.[7] Many patients experience postsurgical side effects, such as dumping syndrome, bile reflux, anastomotic leak, gastritis, and weight loss.[8,9] These complications often lead to a significant decline in QoL post-surgery, making it a priority in postoperative care to address these issues and support long-term recovery and quality of life improvements among GC patients. A previous study found that of 134 post-GC surgery patients, 55% experienced a decline in QoL compared to pre-surgery, and 1/3rd witnessed continuous deterioration even 6 months post-surgery.[10]

Recent studies have highlighted the role of herbal medicines (HM) in postsurgical GC treatment. As a complementary approach, HM shows potential for alleviating postsurgical complications and improving patient outcomes. In 2020, Shih et al in Taiwan explored the impact of HM on the survival of patients with GC undergoing chemotherapy post-surgery.[11] Similarly, Japanese research on Rikkunshito, a traditional HM, demonstrated notable enhancements in the quality of life and gastrointestinal function.[12] These studies underscore the potential of HM to significantly augment recovery and enhance outcomes in patients with postsurgical GC.

However, the landscape of HM in the context of postsurgical recovery in patients with GC remains unclear. While previous systematic reviews have examined HM in conjunction with chemotherapy or other HM treatments such as acupuncture and moxibustion after GC surgery, none have exclusively focused on HM post-surgery.[13–16] This knowledge gap necessitates a systematic review and meta-analysis to assess the effectiveness and safety of HM in fortifying postsurgical recovery among patients with GC. Therefore, our study aimed to comprehensively review the impact of HM alone on patients after GC surgery.

2. Methods

2.1. Objective and strategy

This study aimed to systematically review the research literature, assessing the impact of HM on the recovery of GC patients after surgery and suggesting directions for future clinical guidelines. The study protocol was registered on PROSPERO with registration number CRD42022354133.

A literature search was conducted for studies related to Korean Medicine GC treatment published until July 31, 2023, on search engines including the Korean web databases KMBASE, KISS, OASIS, RISS, and ScienceOn, and international web databases such as EMBASE, Medline, PubMed, CNKI, and CiNii. These databases were selected to ensure comprehensive coverage of both Korean and international studies relevant to GC treatments with HM. The PubMed database, which was searched in the corresponding database, yielded the search results provided in Table 1. This study focused solely on electronic search. Sixteen papers satisfied all inclusion and exclusion criteria.

2.2. Selection of studies

The collected research papers were organized using a literature management program (EndNote 20) and spreadsheet program (Excel). The selection and analysis of documents were independently performed by 2 researchers (SJP and KSD). In instances of disagreement, particularly during the full-text review stage of the final paper, the researchers resolved differences through thorough discussion and arrived at a consensus on the ultimate selection.

2.3. Quality assessment

To evaluate the quality of the literature, the Risk of Bias in Randomized Controlled Trials (RCTs) was assessed using the Cochrane Risk of Bias (RoB) tool, which was chosen to ensure rigorous and standardized assessment of potential biases across studies. The Cochrane RoB tool was specifically selected because of its comprehensive framework for evaluating different types of bias (such as random allocation sequence generation, allocation sequence concealment, and blinding), which is essential for accurately assessing study reliability and internal validity in this systematic review. Two researchers (SJP and KSD) independently conducted the risk of bias assessment for the RCT literature. Discrepancies and agreements between evaluators were then analyzed through researcher meetings in which both researchers participated together. For 1 qualitative

Table 1

Search strategy.

No.	Search terms
1	gastric cancer [mesh]
2	gastric cancer [tiab]
3	#1 or #2
4	"Plants, medicinal" [mesh]
5	"Plant extracts" [mesh]
6	"Drugs, Chinese herbal" [mesh]
7	"Plant preparations" [mesh]
8	"Herbal medicine" [mesh]
9	"Medicine, East Asian traditional" [mesh]
10	"Medicine, Korean traditional" [mesh]
11	"Medicine, Chinese traditional" [mesh]
12	"Medicine, traditional" [mesh]
13	"Phytotherapy" [mesh]
14	"Plant extracts"[tiab] or "Herbal medicine"[tiab]
15	(Chinese adj3(medic*[tiab] or herb*[tiab] or drug*[tiab] or formul*[tiab] or plant*[tiab] or prescri*[tiab])) or (herb*[tiab] or plant*[tiab] or phytodrug*[tiab])
16	#4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15
17	randomized controlled trials [pt]
18	controlled clinical trial [pt]
19	randomized [tiab]
20	placebo [tiab]
21	RCT [tiab] or (random* [tiab] and allocat* [tiab]) or (random* [tiab] and assign * [tiab])
22	trial [tiab]
23	group [tiab]
24	#17 or #18 or #19 or #20 or #21 or #22 or #23
25	animals [mh] not humans [mh]
26	#24 not #25
27	#3 and #16 and #26

study, Cochrane RoB tool was designed to assess the risk of bias with 3 response options: low, high, and uncertain. The tool was translated into Korean to minimize variations in the evaluation criteria between evaluators. The quality assessment results provided a basis for determining the reliability of each study and were incorporated into the overall meta-analysis using Review Manager Software 5.4 (RevMan).

2.4. Data analysis

Among the studies subjected to analysis, 25 papers presented the mean and standard deviation of outcome variables for the intervention group, where patients with GC were treated with gastrectomy and HM, and a control group without HM treatment. These papers were thoroughly reviewed using RevMan. If the number of included studies was > 10, meta-analysis publication bias was assessed using funnel plots.

In this study, we used the risk ratio (RR) with a 95% confidence interval (CI) for dichotomous data and mean differences (MD) with a 95% CI for continuous data measured on the same scale. These measures were selected because they provide a robust way to compare relative and absolute differences in outcomes between intervention and control groups. For cases where measurement units varied across studies, we applied the standardized mean difference (SMD) with 95% CI to ensure consistency in effect size interpretation.

To gauge the heterogeneity within the studies, we calculated Higgins' I^2. A value of I^2 exceeding 50% was interpreted as a significant indicator of substantial heterogeneity. Higgins' I^2 was chosen as it allows quantification of the degree of variability across studies, helping to determine the robustness of combined results. The selected evaluation indicators included gastrointestinal recovery, nutritional markers, immune markers, inflammatory markers, QOL, and adverse effects.

3. Results

3.1. Study selection

In our study selection process, we initially screened 10 databases and identified 3712 articles. After excluding 483 duplicates, we evaluated the abstracts of 3226 papers. Among these, 3204 studies were subsequently excluded, resulting in 25 studies for full-text evaluation. Following our specific criteria, 9 of these 25 studies were further excluded for various reasons: 2 studies did not specifically target patients with EGC, 2 studies were RCTs, 4 studies did not incorporate HM treatments, and 1 study had an inappropriate outcome. Ultimately, our analysis was conducted based on the remaining 16 RCTs [17–32], which met our specific inclusion criteria (Fig. 1).

3.2. Study characteristics

This meta-analysis, finalized before 2023, collated data from 16 RCTs involving 1546 patients diagnosed with GC. These studies examined the efficacy and safety of HM interventions. While participants in the experimental group were treated with HM, those in the control group received standard care, placebos, or established usual care protocols. The treatments spanned a range of durations from 3 days to months. The study assessed gastrointestinal (GI) recovery; evaluated nutritional markers including Total Protein (TP), prealbumin (PA), albumin (ALB), and transferrin (TRF); measured specific immune markers such as CD4 + and $CD8^+$ cell counts; analyzed the inflammatory marker C-reactive protein (CRP) gauged participants' QoL using scales the 36-item short form health survey (SF-36) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (QLQ-C30); and recorded adverse effects as a measure of safety (Table 2).

3.3. Risk of bias in included trials

In our review, based on the Cochrane bias risk assessment, we identified a significant risk of bias due to insufficient methodological explanation (Fig. 2). Each study utilized random sequence generation.[17–32] However, 10 studies lacked clarity regarding allocation concealment, leading to an uncertain bias risk evaluation.[17–22,24,27,29,32] Aside from 1 study that implemented a placebo,[25] there was a high risk of performance and detection bias in 15 trials, as only the experimental group was treated with HM.[17–24,26–32] Except for 1 study with a confirmed protocol registration,[17] none of the other studies reported their pre-registered plans, leading to an unclear risk of reporting bias. These biases may impact the final research conclusions by potentially overestimating the efficacy of HM due to lack of blinding and incomplete reporting of study methods. Fortunately, we deemed all studies to have a minimal risk of attrition and other possible biases (Fig. 3).

3.4. Gastrointestinal recovery

3.4.1. Time to first flatus (h). In 9 RCTs, the effect of HM on the time to first flatus after GC surgery was assessed.[18,19,22,23,25,27–30] The pooled results from these trials showed that patients treated with HM experienced a noticeable enhancement in the time to the first flatus. This benefit was highlighted by an MD of −8.38 (95% CI [11.70, −5.06], I^2 = 84%, P < .00001, n = 838, Fig. 4).

3.4.2. Time to first bowel movement (h). Seven RCTs investigated the influence of HM on the first bowel movement as a parameter for GI recovery after GC surgery.[18,19,23,27–30] The consolidated data from these studies demonstrated a significant improvement for patients who received HM treatment with MD −10.10 (95% CI [−16.52, −3.68], I^2 = 94%, P = .002, n = 696, Fig. 5).

3.4.3. Time to bowel sounds return (h). Seven RCTs assessed the effect of HM on the time to return of bowel sound after GC surgery.[19,22,23,25,27,29,30] The results of these studies indicate a significant reduction in the time taken for bowel sounds to return in patients who received HM treatment. Consolidated data from these studies demonstrated that patients who received HM treatment showed a significant improvement in the time to bowel sound return, as evidenced by an MD of −7.84 (95% CI [−12.07, −3.62], I^2 = 94%, P = .0003, n = 674, Fig. 6).

3.5. Nutritional markers

Several RCTs have evaluated the influence of HM on various nutritional markers in patients post-GC surgery. The assessment encompassed markers, such as ALB, TRF, PA, and TP.

3.5.1. Albumin levels. Six RCTs assessed the effect of HM on nutritional markers, specifically ALB, in patients after GC surgery.[18,20,28,29,31,32] An analysis of the combined data indicated that patients treated with HM exhibited a notable increase in ALB levels compared with the control group. The compiled results from these investigations indicated that patients administered with HM treatment exhibited a notable enhancement in ALB levels, supported by an MD of 1.83 (95% CI [0.76, 2.90], I^2 = 80%, P = .0008, n = 532, Table 3).

3.5.2. Transferrin levels. The consolidated data from the selected studies indicated a variation in TRF levels in patients treated with HM.[29,31,32] This variation was emphasized by an SMD of 1.89 (95% CI [0.17, 3.96], I^2 = 98%, P = .07, n = 306, Table 3). However, there was substantial heterogeneity among the studies and the results were not significant.

3.5.3. Prealbumin levels. The compiled data from the studies showed a pronounced improvement in PA levels in patients

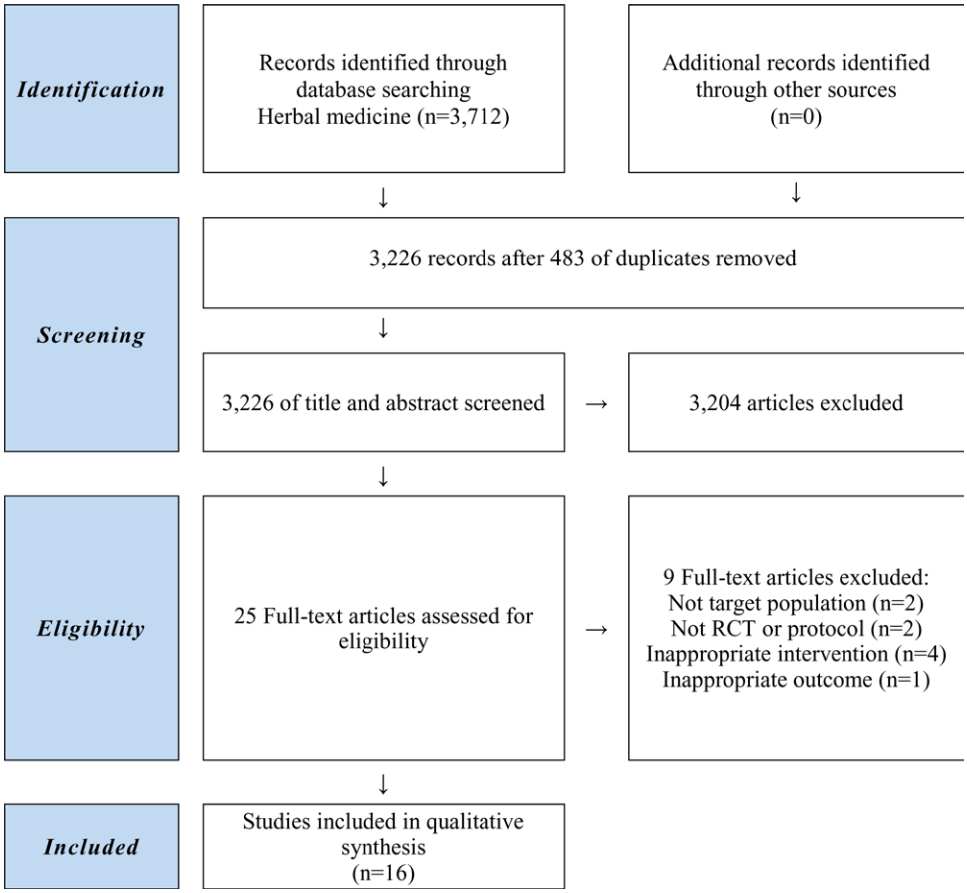

Figure 1. PRISMA flowchart. PRISMA = preferred reporting items for systematic reviews and meta-analyses.

treated with HM,[29,32] although there was considerable heterogeneity among the studies, with an MD of 36.70 (95% CI [18.53, 54.87], I^2 = 83%, P < .0001, n = 216, Table 3).

3.5.4. Total protein levels. The data gathered from the included studies highlight a clear elevation of TP levels in patients who were administered HM.[18,29] This was demonstrated by an MD of 2.18 (95% CI [0.49, 3.86], I^2 = 0%, P = .01, n = 176, Table 3). Notably, these studies showed no heterogeneity, suggesting a consistent positive effect of HM on TP levels.

3.6. Immune markers

3.6.1. CD3+ levels. From available studies on $CD3^+$ levels in post-GC surgery patients,[24,26,29] it was observed that HM had a notable effect on this immune marker. The consolidated data indicated that patients treated with HM exhibited a marked increase in $CD3^+$ levels compared to the control group. This observation was validated by an MD of 5.01 (95% CI [2.15, 7.87], I^2 = 88%, P = .0006, n = 311; Table 4).

3.6.2. $CD4^+$ levels. The aggregated results from the selected studies showed significant variation in $CD4^+$ levels in patients administered HM.[23,24,26,29,32] This variance was emphasized by an MD of 4.39 (95% CI [1.91, 6.87], I^2 = 94%, P = .0005, n = 487, Table 4). These findings suggest that HM has a beneficial effect on $CD4^+$ levels in the aforementioned patient groups.

3.6.3. $CD8^+$ levels. The compiled data from the studies indicated no significant difference in $CD8^+$ in patients treated with HM compared to controls.[23,26,32] The pooled findings showed an MD of –1.13 (95% CI [–4.28, 2.02], I^2 = 97%, P = .48, n = 293, Table 4), emphasizing the lack of significance and substantial heterogeneity among the studies.

3.6.4. $CD4^+/CD8^+$ ratio. The aggregated data from these studies suggest that there was no statistically significant improvement in the $CD4^+/CD8^+$ ratio in patients treated with HM.[23,26,29,32] The pooled results show a MD of 0.49 (95% CI [0.01, 0.91], I^2 = 99%, P = .06, n = 389, Table 4). Despite considerable heterogeneity among the studies, it is important to note that the results were not significant.

3.7. Inflammatory markers

Two RCTs explored the potential effects of HM on inflammatory markers,[28,29] specifically focusing on CRP levels in the context of medical interventions. Comprehensive data analysis indicated that there was no statistically significant difference in CRP levels for patients in the HM group compared to the control group, with an MD of –7.55 (95% CI [–21.78, 6.67]; I^2 = 98%, P = .30, n = 180, Fig. 7).

3.8. Quality of life assessments

3.8.1. SF-36 score. Based on studies assessing the SF-36 score, which evaluates general health status and QoL, there was no statistically significant enhancement in scores for patients treated with HM compared to the control group.[22,31] Although the data showed a mean difference of 11.33 favoring HM, the wide CI (95% CI [3.50, 26.17]) and high heterogeneity (I^2 = 96%) suggest variability among the studies. A P-value of 13 indicated that the results were not statistically significant (Table 5).

Table 2

Characteristics of included trials.

Study	Sample size	Intervention	Control	Duration	Outcome measures
Sang 2020[17]	120	Ba Zhen decoction + usual care	Usual care	2 wk	TRF, PA, ALB, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$, QoL
Gao2020[18]	96	Bu Qi formula + usual care	Usual care	1 wk	GI functions, $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, CRP, TP, PA, ALB, TRF
Ji 2020[19]	200	Da Cheng Qi decoction + MCD	MCD	3 d	GI functions,
Liu 2020[20]	90	Qixue Shuangbu formula + usual care	Usual care	15 d	SF-36, ALB, TRF, AEs
Chen 2020[21]	84	Zishao Liujunzi decoction + ERAS	ERAS + usual care	1 wk	GI functions, ALB, CRP
Lü 2018[22]	60	Jianpi Liqi formula + usual care	Placebo + usual care	4 d	GI functions
Ma 2018[23]	117	Fuyuan formula	Usual care	1 wk	$CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$, AEs
Guo 2018[24]	56	Shenqi Yizhu decoction + usual care	Usual care	10 d	GI functions, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$, AEs
Ge 2018[25]	82	Renshen Dahuang decoction + usual care	Usual care	1 wk	GI functions, SF-36
Ye 2018[26]	80	Tongfu Huoxue decoction + usual care + glutamine	Usual care + glutamine	1 wk	GI functions, AEs
He 2017[27]	120	Dialectical treatment + usual care	Usual care	2 wk	QLQ-C30, AEs
Pan 2016[28]	100	Sini Tongli decoction + usual care	Usual care	1 wk	GI functions, AEs
Zou 2016[29]	68	Jianpi Tongfu formula + usual care	Usual care	1 wk	GI functions, ALB, AEs
Liu 2016[30]	80	Shengyang Yiwei decoction + ERAS	ERAS	1 wk	GI functions, ALB, TP
Akamaru 2015[31]	100	Daikenchuto extract powder	Usual care	3 mo	GI functions, GSRS
Liu 2018[32]	93	Xiaoai decoction	Usual care	3 mo	$CD3^+$, $CD4^+$

Abbreviations: AEs = adverse events, ALB = albumin, CRP = C-reactive Protein, ERAS = enhanced recovery after surgery, GI = gastrointestinal, GSRS = gastrointestinal symptom rating scale, MCD = mosapride citrate dihydrate, PA = prealbumin (transthyretin), QoL = quality of life, TP = total protein, TRF = transferrin.

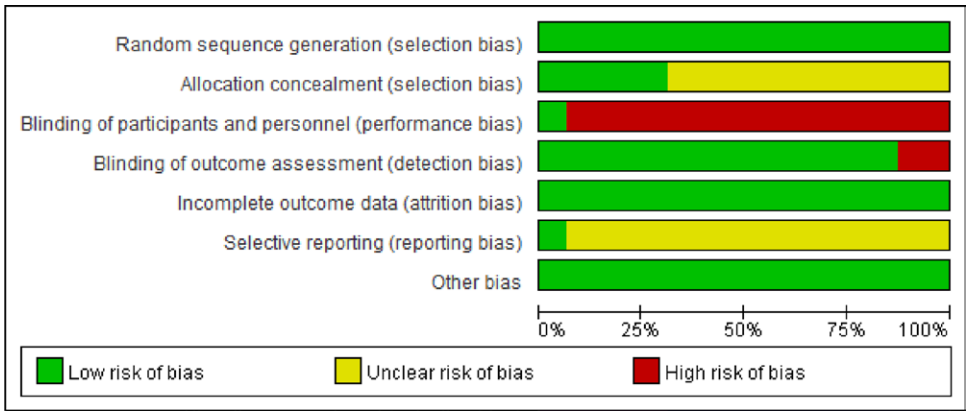

Figure 2. Risk of bias graph with included trials.

3.8.2. WHOQOL-BREF score. The aggregated results from the studies regarding the WHOQOL-BREF score, an essential tool to measure QoL across various dimensions, revealed significant enhancements in scores for patients administered HM.[32] This was substantiated by an MD of 6.54 (95% CI [5.42, 7.66], $P < .00001$, n = 60, Table 5). This confirms the positive effects of HM on patients' QoL as measured by the WHOQOL-BREF.

3.8.3. QLQ-C30 score. With regard to the QLQ-C30 score, which is specifically designed to assess QoL in cancer patients, the combined results from the included studies indicated a remarkable difference in scores between the HM and control.[21] The pooled findings revealed an MD of 18.04 (95% CI [15.87, 20.21], $P < .00001$, n = 60, Table 5). These results unequivocally favored the HM group, suggesting its efficacy in enhancing QoL in patients after GC surgery.

3.9. Safety

3.9.1. Incidence of adverse effects. The safety profile of HM was evaluated based on the incidence of adverse effects, and the pooled data from various studies suggest that HM is associated with a reduced risk of adverse effects compared to the control.[19–21,23,26,27,31] The cumulative findings yielded an RR of 0.48 with a 95% CI ranging from 0.31 to 0.74. This indicates that patients undergoing HM treatment are approximately half as likely to experience adverse effects as those in the control group (Fig. 8).

Notably, the analysis revealed a consistently low heterogeneity among the studies, with an I^2 value of 0%, signifying minimal variability in the results across different studies. The statistical significance of these findings was further emphasized by a P-value of .0009, suggesting a strong association between HM and a reduced risk of adverse effects.

4. Discussion

In the realm of postsurgical care for patients with GC, the management of GI recovery and nutrition plays a pivotal role in improving survival rates and QoL.[33,34] The postoperative hurdles faced by these patients, such as impaired GI function and nutritional deficiencies, profoundly affect their recovery and overall prognosis. This underscores the need for innovative and effective treatment approaches.[35,36] Therefore, the exploration of alternative treatments, particularly HM, has emerged as a promising solution. Previous studies have indicated that herbal treatments have the potential to significantly enhance GI function, nutritional status, and immune function while potentially mitigating complications associated with GC surgery.[37,38] This study was undertaken to systematically investigate the efficacy of HM in addressing these challenges and to assess its impact

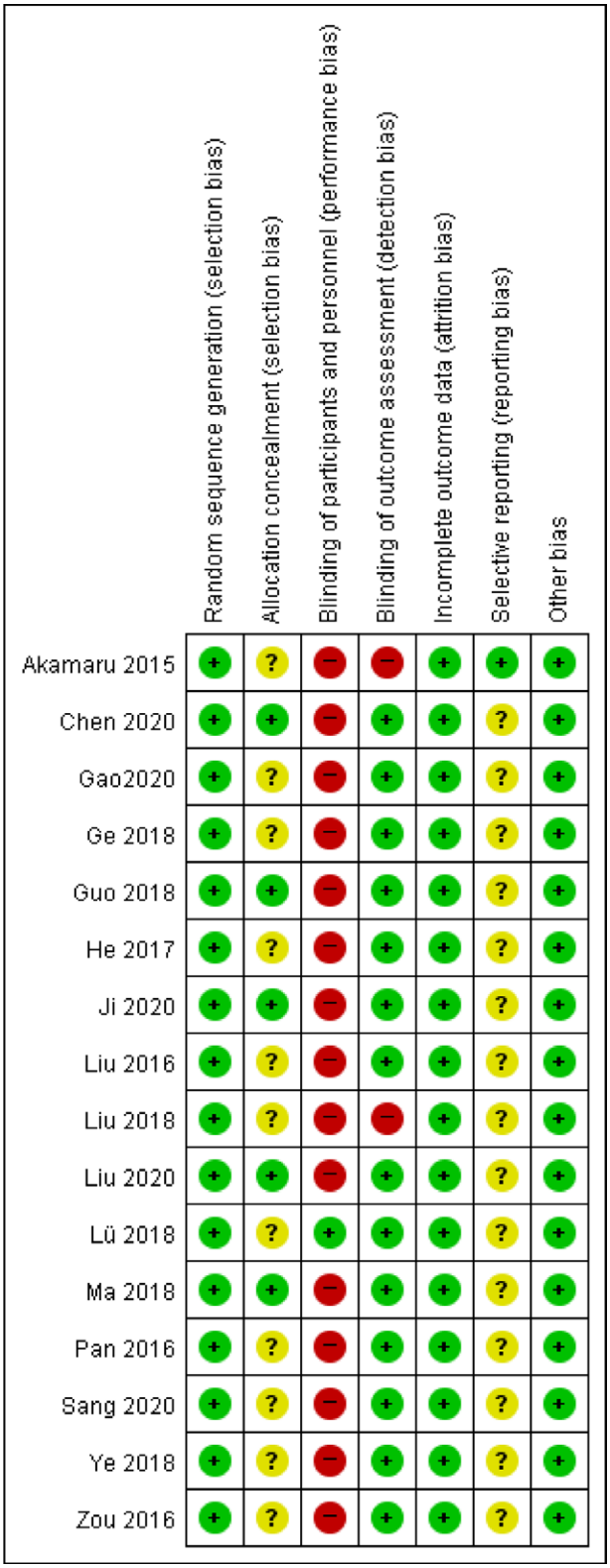

Figure 3. Risk of bias summary with included trials.

on the recovery of patients with early GC. The focus areas were GI recovery, nutrition, immune responses, and overall QoL. Through the exploration of these critical aspects, this study aimed to provide valuable insights into postoperative care for GC, contributing to the existing body of knowledge and investigating alternative therapies that could markedly improve patient outcomes.

Our study evaluated HM effects of HM in patients with early GC in detail, focusing on GI recovery, nutrition, immune response, and overall QoL. In the GI recovery assessment, we observed significant improvements in patients treated with HM, particularly in the time to first flatus ($P < .00001$), time to first bowel movement ($P = .002$), and time to bowel sound return ($P = .0003$), compared with the control group. This improvement is crucial, as it directly impacts the overall health and recovery speed post-surgery.[39]

Our study found significant improvements in ALB, PA, and TP levels among patients with early GC treated with HM, with ALB ($P = .0008$) and PA ($P < .0001$) improving markedly, and TP levels also showing significant enhancements ($P = .01$). Although the TRF results were not statistically significant, these overall findings underscore the potential of HM in enhancing the postoperative nutritional status of patients with GC. Proper nutrition is essential for the healing and well-being of postsurgical patients.[40]

In terms of immune response, patients with early GC treated with HM showed significant improvements in immune markers, including $CD3^+$ ($P = .0006$) and $CD4^+$ levels ($P = .0005$) improving significantly. However, $CD8^+$ levels and CD4+/$CD8^+$ ratio did not show any significant changes. This indicates a complex and varied impact of HM on the immune system post-surgery. CD4, another T-cell surface protein, is mainly used to identify helper T cells. Helper T cells play a role in regulate the immune response by providing instructions to other immune cells. CD8, a surface protein predominantly expressed on cytotoxic T cells, is involved in direct destruction of infected or abnormal cells. $CD8^+$ T cells contribute to immune defense by exerting cytotoxic effects. The CD4/CD8 ratio indicates the relative numbers of helper and cytotoxic T cells. This ratio is balanced in a healthy immune state. An abnormal ratio may indicate an immune dysfunction.[41] These findings suggest that, while HM may enhance certain immune functions in patients with early GC, its effects on different immune markers can vary.

Our study showed mixed results in assessing the QoL of patients with early GC treated with HM. The SF-36 assessment, involving 172 participants, indicated a non-significant improvement in QoL ($P = .13$), whereas the WHOQOL-BREF and QLQ-C30 assessments, each with 120 participants, demonstrated significant enhancements in QoL (both with $P < .00001$). This finding suggests that HM may have a substantial positive impact on certain QoL aspects in patients with early GC, although the effects vary based on the measurement tool.

In the safety evaluation, the pooled data from 8 studies, encompassing a total of 631 participants, revealed an RR of 0.48 with a 95% CI [0.31, 0.74]. This significant result ($P = .0009$) indicates that patients in the HM group were less likely to experience adverse events than those in the control group. The analysis showed no heterogeneity ($I^2 = 0\%$), suggesting consistent findings across the included studies. This evidence underscores the potential of HM as a safer alternative for the postoperative management of patients with GC, with a reduced risk of adverse effects.

Given that most studies involved a usual care control group compared with the HM treatment group, there are inherent limitations. Furthermore, the unknown efficacy and safety profiles of HM in combination with other drugs highlight the need for additional research. To address these challenges, future investigations should focus on reducing heterogeneity through the development of standardized preparations. In addition, the establishment of a core outcome set is imperative to ensure consistent outcome indicators.

In this study, we confirmed the effectiveness of HM in enhancing postoperative recovery after early GC surgery, notably in GI function and QoL. Although our findings support the role of HM in clinical practice, it is essential to

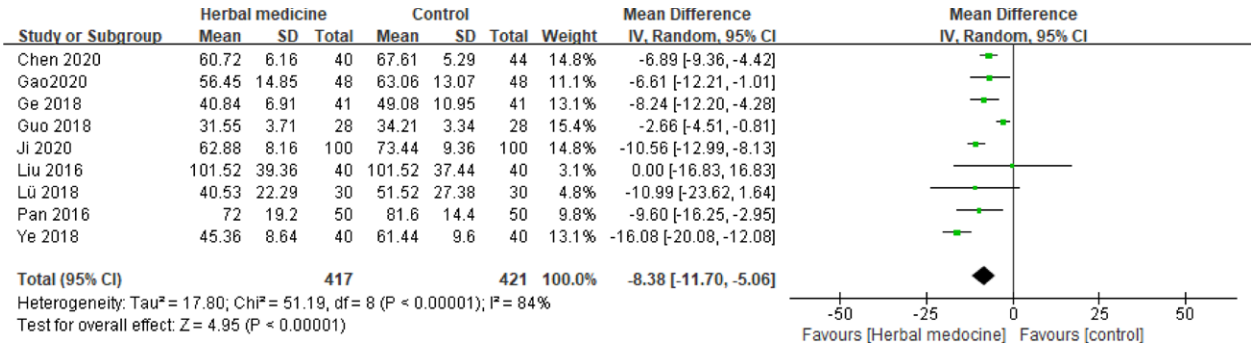

Figure 4. Effect of herbal medicine on time to first flatus post-gastric cancer (GC) surgery.

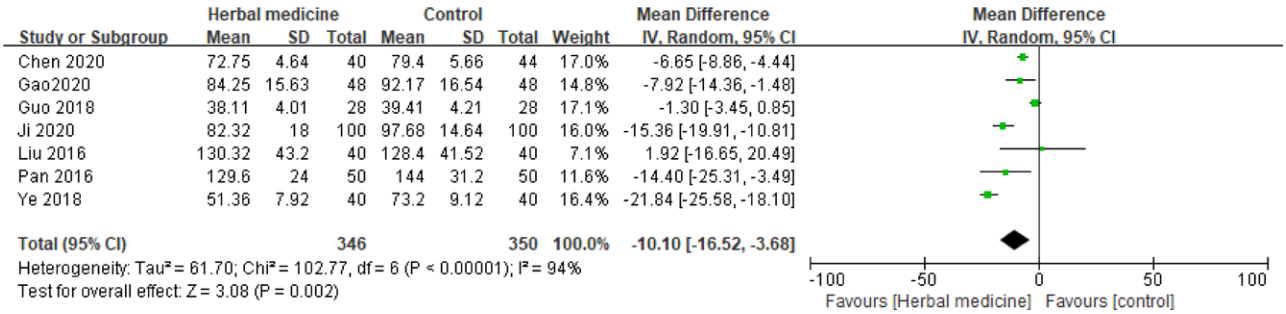

Figure 5. Time to first bowel movement.

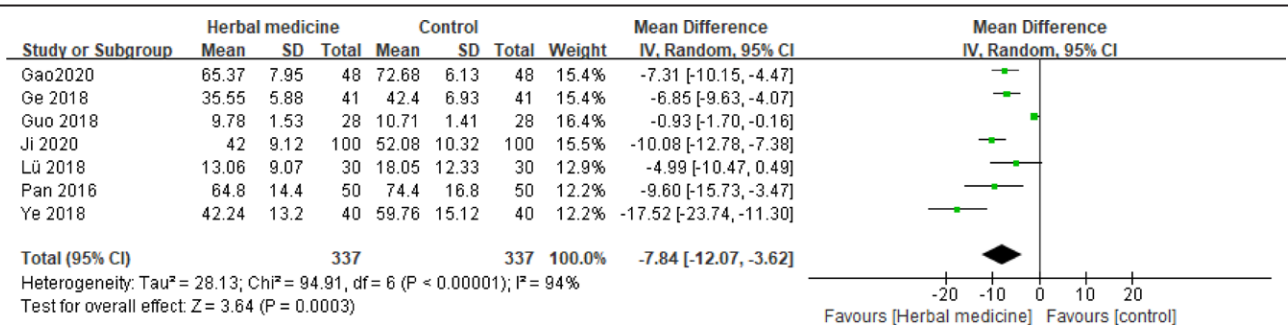

Figure 6. Time to bowel sounds.

Table 3

Nutritional markers of HM in post-gastric cancer surgery patients.

Nutritional markers	Studies	Participants	Effect size (95% CI)	*P*-value	Study ID references
ALB	6	532	MD 1.83, 95% CI (0.76, 2.90), I^2 = 80%	*P* = .0008***	Chen 2020, Gao2020, Liu 2016, Liu 2020, Sang 2020, Zou 2016
TRF	3	306	SMD 1.89, 95%CI (0.17, 3.96), I^2 = 98%	*P* = .07	Gao2020, Liu 2020, Sang 2020
PA	2	216	MD 36.70, 95%CI (18.53, 54.87), I^2 = 83%	*P* < .0001***	Gao2020, Sang 2020
TP	2	176	MD 2.18, 95% CI (0.49, 3.86), I^2 = 0%	*P* = .01**	Gao2020, Liu 2016

Abbreviations: CI = confidence interval, HM = herbal medicine, MD = mean differences, SMD = standardized mean difference.
***P*<.01.
****P*<.001.

explore the mechanisms through which HM contributes to recovery, potentially by modulating immune response and improving nutritional status. Further research should investigate these underlying mechanisms to optimize HM interventions and fully understand their therapeutic potential in GC patient rehabilitation. Additionally, addressing the observed heterogeneity in RCTs, likely due to diverse patient groups and varied HM prescriptions, will be essential to strengthen future evidence.

5. Conclusion

This study substantiated the effectiveness of HMs in enhancing recovery after GC surgery. HM exhibits significant positive effects in improving patients' bowel function and overall quality of life. Our findings indicate that incorporating postoperative HM treatment in patients with GC could be a practical consideration in clinical practice.

Nevertheless, as highlighted earlier, it is crucial to recognize that variations in subjects and prescriptions contribute to considerable

Table 4

Immune markers of HM in post-gastric cancer surgery patients.

Immune markers	Studies	Participants	Effect size (95% CI)	*P*-value	Study ID references
CD3+	3	311	MD 5.01, 95% CI (2.15, 7.87), I^2 = 88%	*P* = .0006***	Gao2020, Liu 2018, Ma 2018
CD4+	4	487	MD 4.39, 95%CI (1.91, 6.87), I^2 = 94%	*P* = .0005***	Gao2020, Guo 2018, Liu 2018, Sang 2020
CD8+	3	293	MD −1.13, 95%CI (−4.28, 2.02), I^2 = 97%	*P* = .48	Guo 2018, Ma 2018, Sang 2020
CD4+/CD8+	3	389	MD 0.49, 95%CI (0.01, 0.91), I^2 = 99%	*P* = .06	Gao2020, Guo 2018, Sang 2020

Abbreviations: CI = confidence interval, HM = herbal medicine, MD = mean differences.
***P<.001.

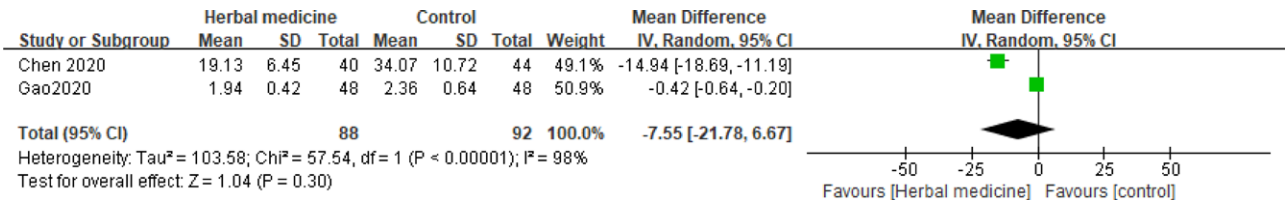

Figure 7. C-reactive protein levels.

Table 5

Quality of life assessments of HM in post-gastric cancer surgery patients.

Quality of life assessment	Studies	Participants	Effect size (95% CI)	*P*-value	Study ID references
SF-36	2	172	MD 11.33, 95% CI (3.50, 26.17), I^2 = 96%	*P* = .13	Ge 2018, Liu 2020
WHOQOL-BREF	1	120	MD 6.54, 95% CI (5.42, 7.66)	*P* < .00001***	Sang 2020
QLQ-C30	1	120	MD 18.04, 95% CI (15.87, 20.21)	*P* < .00001***	He 2017

Abbreviations: CI = confidence interval, HM = herbal medicine, MD = mean differences, QLQ-C30 = quality of life questionnaire-core 30, SF-36 = 36-item short form health survey.
***P<.001.

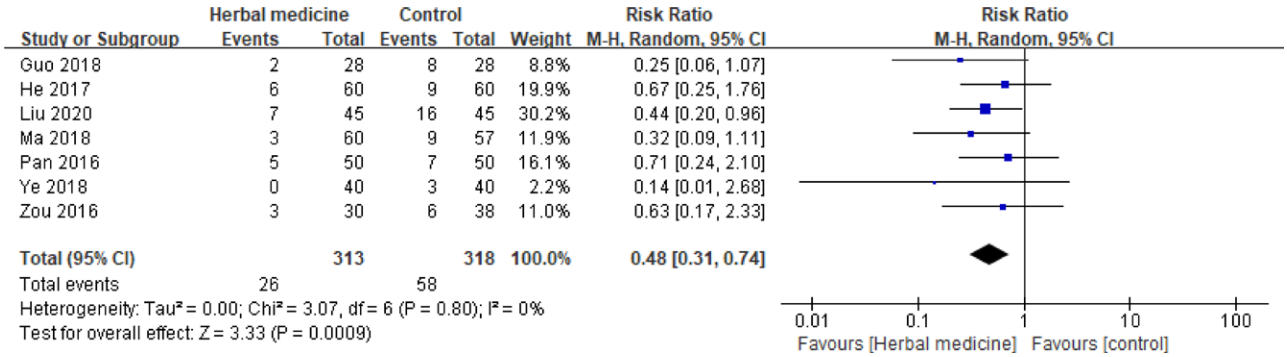

Figure 8. Comparative risk of adverse effects.

heterogeneity. Therefore, we recommend the implementation of long-term clinical trials or follow-ups with rigorous criteria. This study aimed to observe lasting effects and evaluate potential side effects, providing a comprehensive understanding of the enduring impact of HM treatment in the context of patient recovery after GC surgery. Therefore, further research is essential.

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References

[1] Jung KW, Kang MJ, Park EH, et al. Prediction of cancer incidence and mortality in Korea, 2023. Cancer Res Treat. 2023;55:400–7.
[2] Machlowska J, Baj J, Sitarz M, Maciejewski R, Sitarz R. Gastric cancer: epidemiology, risk factors, classification, genomic characteristics and treatment strategies. Int J Mol Sci. 2020;21:4012.
[3] Jung KW, Kang MJ, Park EH, et al. Prediction of cancer incidence and mortality in Korea, 2024. Cancer Res Treat. 2024;56:372–9.

[4] Yang K, Lu L, Liu H, et al. A comprehensive update on early gastric cancer: defining terms, etiology, and alarming risk factors. Expert Rev Gastroenterol Hepatol. 2021;15:255–73.
[5] Jun JK, Choi KS, Lee HY, et al. Effectiveness of the Korean national cancer screening program in reducing gastric cancer mortality. Gastroenterology. 2017;152:1319–28.e7.
[6] Hoang T, Woo H, Cho S, Lee J, Kazmi SZ, Shin A. Descriptive analysis of gastric cancer mortality in Korea, 2000-2020. Cancer Res Treat. 2023;55:603–17.
[7] Conti CB, Agnesi S, Scaravaglio M, et al. Early gastric cancer: update on prevention, diagnosis and treatment. Int J Environ Res Public Health. 2023;20:2149.
[8] Schütte K, Schulz C, Middelberg-Bisping K. Impact of gastric cancer treatment on quality of life of patients. Best Pract Res Clin Gastroenterol. 2021;50-51:101727.
[9] McCall MD, Graham PJ, Bathe OF. Quality of life: a critical outcome for all surgical treatments of gastric cancer. World J Gastroenterol. 2016;22:1101–13.
[10] Karanicolas PJ, Graham D, Gönen M, Strong VE, Brennan MF, Coit DG. Quality of life after gastrectomy for adenocarcinoma: a prospective cohort study. Ann Surg. 2013;257:1039–46.
[11] Shih WT, Yang PR, Shen YC, Yang YH, Wu CY. Traditional Chinese medicine enhances survival in patients with gastric cancer after surgery and adjuvant chemotherapy in Taiwan: a nationwide matched cohort study. Evid Based Complement Alternat Med. 2021;2021:7584631.
[12] Gunji S, Ueda S, Yoshida M, Kanai M, Terajima H, Takabayashi A. Effects of rikkunshito, a kampo medicine, on quality of life after proximal gastrectomy. J Surg Res. 2013;185:575–80.
[13] Fan L, He Y, Li Y, Li X, Liu D, Wang R. Efficacy and safety of traditional Chinese medicine nursing intervention in postoperative patients after gastrectomy. Oncol Lett. 2023;26:537.
[14] Zhang Y, Wang X, Yang H. Effect of traditional Chinese medicine nursing on postoperative patients with gastric cancer and its impact on quality of life. Am J Transl Res. 2021;13:5589–95.
[15] Wang Y, Wang L, Ni X, Jiang M, Zhao L. Effect of acupuncture therapy for postoperative gastrointestinal dysfunction in gastric and colorectal cancers: an umbrella review. Front Oncol. 2024;14:1291524.
[16] Bae H-R, Kim E-J, Seo H-S, Lee N-H. The effectiveness of traditional Korean medicine for treating postoperative ileus in gastric cancer patients: a systematic review and meta-analysis. J Int Korean Med. 2022;43:625–42.
[17] Akamaru Y, Takahashi T, Nishida T, et al. Effects of daikenchuto, a Japanese herb, on intestinal motility after total gastrectomy: a prospective randomized trial. J Gastrointest Surg. 2015;19:467–72.
[18] Liu Z. The observation of the fast track with shengyangyiwei decoction after laparoscopic distal gastrectomy. MA Thesis. Guangzhou University of Traditional Chinese Medicine; 2016.
[19] Pan A, Shi P, Ye G, et al. Research on the efficacy of Sini Tongli decoction instilled in the small intestine to promote postoperative intestinal function recovery in patients with gastric cancer. Nurs Rehabil. 2016;15:783–4.
[20] Zou L, Mo D, Yang S, et al. Clinical observation on early enteral nutrition combined with traditional Chinese medicine for strengthening the spleen and tonifying the bowels after laparoscopic radical gastrectomy for gastric cancer to promote postoperative gastrointestinal function recovery. New Tradit Chin Med. 2016;48:192–4.
[21] He Y, Liu S, Wang L, et al. Research on TCM syndrome differentiation and treatment of early gastric cancer after radical surgery with combined anesthesia. J Mod Integr Tradit Chin West Med. 2017;26:955–7.
[22] Ge S, Sun B, Du H, et al. Observation on the efficacy of ginseng and dahuang decoction in improving gastrointestinal motility disorder caused by qi stagnation and blood stasis in patients after gastric cancer surgery. Chin J Chronic Dis Prev Control. 2018;26:617–9.
[23] Guo W. Clinical observation of 28 cases of enteral nutritional support and traditional Chinese medicine combined after gastric cancer surgery. Chin Ethn Folk Med. 2018;27:71–3.
[24] Liu W. Effects of Xiaoaitang based on the pathogenesis theory of cancerous toxin combined with laparoscopic assisted distal gastrectomy in the treatment of elderly patients with gastric cancer. J Pract Oncol. 2018;33:222–7.
[25] Lü S. Clinical study on Jianpiliqi prescription in promoting the recovery of intestinal motility after radical resection of gastric cancer. Electron J Integr Tradit Chin West Med Cardiovasc Dis. 2018;6:162+164.
[26] Ma X. Influences of Fuyuan Tang small intestine instillation on fatigue, T-lymphocyte subset complication of patients with radical operation for stomach carcinoma. China Tradit Chin Med Sci Technol. 2018;25:834–5.
[27] Ye Z, Gu H, Yang J, et al. Effects of Tongfu Huoxue decoction combined with Glutamine on the recovery of oxidative stress, vintestinal mucosal barrier function and gastrointestinal function after radical operation of gastric cancer. Hebei Tradit Chin Med. 2018;40:68–72.
[28] Chen N, Liu H, Ni Z, et al. Effects of modified Chaishao Liujunzi decoction combined with enhanced recovery after surgery on rehabilitation of laparoscopic gastric cancer surgery. J Hunan Univ Tradit Chin Med. 2020;40:626–9.
[29] Gao X, Li Y, Wang N. Effect of Buqi recipe combined with enteral nutrition on postoperative immune function and intestinal function of patients with gastric cancer. J Guangzhou Univ Tradit Chin Med. 2020;37:2103–8.
[30] Ji S, Kang J. Effects of Dachengqi decoction combined with Mosapride citrate tablets on gastrointestinal motility function and gastrointestinal hormone levels in patients after radical resection of gastric cancer. Chin Folk Ther. 2020;28:83–4.
[31] Liu B, Wang Y, Zhou S. Efficacy of Qixue Shuangbu formula combined with enteral nutrition in the treatment of deficiency of both qi and blood after laparoscopic surgery for gastric cancer. World Tradit Chin Med. 2020;15:2941–4.
[32] Xl S. Effect of modified Bazhen decoction treatment on the quality of life of patients with gastric cancer after surgery. J Guangzhou Univ Tradit Chin Med. 2020;28:134–6.
[33] Wobith M, Weimann A. Postoperative nutrition management: who needs what? Visc Med. 2022;38:354–62.
[34] Martínez-Ortega AJ, Piñar-Gutiérrez A, Serrano-Aguayo P, et al. Perioperative nutritional support: a review of current literature. Nutrients. 2022;14:1601.
[35] Baji DB, Patel JP, Konanur Srinivasa NK, Gande A, Anusha M, Dar H. Nutrition care in cancer surgery patients: a narrative review of nutritional screening and assessment methods and nutritional considerations. Cureus. 2022;14:e33094.
[36] Lee I, Oh Y, Park SH, Kwon Y, Park S. Postoperative nutritional outcomes and quality of life-related complications of proximal versus total gastrectomy for upper-third early gastric cancer: a meta-analysis. Sci Rep. 2020;10:21460.
[37] Yu Q, Chen Z, Tang X. Study on early application of Chinese medicinal herbs after total gastrectomy. Zhongguo Zhong Xi Yi Jie He Za Zhi. 1999;19:592–4.
[38] Hong S, Park B, Noh H, Choi DJ. Herbal medicine for dumping syndrome: a systematic review and meta-analysis. Integr Cancer Ther. 2019;18:1534735419873404.
[39] Chapman SJ, Thorpe G, Vallance AE, Harji DP, Lee MJ, Fearnhead NS; Association of Coloproctology of Great Britain and Ireland Gastrointestinal Recovery Group. Systematic review of definitions and outcome measures for return of bowel function after gastrointestinal surgery. BJS Open. 2019;3:1–10.
[40] Serra F, Pedrazzoli P, Brugnatelli S, et al. Nutritional support management in resectable gastric cancer. Drugs Context. 2022;11:2022-5-1.
[41] McBride JA, Striker R. Imbalance in the game of T cells: what can the CD4/CD8 T-cell ratio tell us about HIV and health? PLoS Pathog. 2017;13:e1006624.