

Original Article

Efficacy and safety of postoperative chemotherapy with capecitabine and oxaliplatin for advanced gastric cancer

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Received May 17, 2026; Accepted August 3, 2026; Epub September 15, 2026; Published September 30, 2026

Abstract: This retrospective study aimed to evaluate the efficacy and safety of postoperative chemotherapy with capecitabine (CAP) combined with oxaliplatin (OXA) in patients with advanced gastric cancer (AGC). A total of 90 AGC patients who received treatment at our center between January 2022 and January 2025 were enrolled. Among them, 47 patients who received CAP plus OXA (XELOX regimen) were assigned as the observation group, and the other 43 patients who received epirubicin, cisplatin, and fluorouracil (ECF regimen) were assigned as the control group. The evaluated criteria included therapeutic efficacy, safety profiles (hyperpigmentation, hepatic and renal dysfunction, alopecia, gastrointestinal reaction, and myelosuppression), serum tumor markers (carbohydrate antigen 199 [CA199], carcinoembryonic antigen [CEA], alpha-fetoprotein [AFP]), humoral immunity (immunoglobulin [Ig] A/M/G), gastric hormones (motilin [MTL], gastrin [GAS]), 1-year postoperative recurrence and survival rates, and quality of life (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 [EORTC QLQ-C30]). Compared to the control group, the observation group showed a significantly higher overall response rate ($P=0.022$), lower incidences of myelosuppression ($P=0.025$) and gastrointestinal reactions ($P=0.010$), and a higher incidence of peripheral neurotoxicity ($P=0.028$). Additionally, the post-treatment levels of serum tumor markers were significantly reduced in the observation group ($P<0.05$), whereas humoral immune indices and gastric hormones levels were significantly increased ($P<0.05$). The 1-year survival rate was also significantly higher in the observation group ($P=0.028$). After Bonferroni correction for multiple comparisons, the observation group demonstrated superior outcomes in CA199, MTL, GAS, physical functioning, nausea and vomiting, and pain compared to the control group (adjusted $P<0.00294$ for all). These findings suggest that the CAP-OXA combination may provide improved therapeutic efficacy and acceptable safety in postoperative chemotherapy for AGC patients.

Keywords: Capecitabine, oxaliplatin, advanced gastric cancer, postoperative chemotherapy, efficacy and safety

Introduction

Gastric cancer (GC), a major threat to human health, is characterized by complex pathologic mechanisms involving critical cancer-related cellular events, including oxidative stress, DNA damage, chronic inflammation, and apoptosis [1]. Many internal and external factors, including genetic predisposition, infection, eating habits, obesity, smoking, and environmental pollution, contribute to GC onset and progression [2, 3]. According to statistics, approximately 30,300 new GC cases and 10,780 GC-asso-

ciated deaths occurred in the United States in 2025 alone [4]. GC remains associated with high morbidity and mortality rates, particularly in East Asia, Eastern Europe, and South America. For patients with advanced gastric cancer (AGC), delayed diagnosis and tumor heterogeneity significantly increase the complexity of treatment [5]. AGC is defined as gastric cancer with tumor invasion reaching or exceeding the muscularis propria (i.e. T2 or higher), regardless of resectability or metastatic status [6]. For such patients, surgery alone is often insufficient to achieve satisfactory curative effects,

and postoperative chemotherapy (POCT) is required as a supplemental treatment strategy [7]. The XELOX regimen, consisting of capecitabine [CAP] and oxaliplatin [OXA], has been demonstrated as an effective postoperative adjuvant chemotherapy for GC patients, providing greater benefit in improving 5-year overall survival (OS) and prolonging disease-free survival (DFS) compared to surgery alone [8]. When applied for treating locally advanced GC, XELOX has shown advantages over conventional perioperative chemotherapy in tumor downstaging and local control, while maintaining an acceptable safety profile [9]. The ECF regimen, comprising epirubicin, cisplatin, and fluorouracil, is a classic perioperative chemotherapy protocol for GC. It has been used to improve survival outcomes in patients with unresectable locally advanced or metastatic gastric adenocarcinoma, with a complication risk comparable to that of surgical treatment [10]. However, it shows a limited prognosis-ameliorating effect, with a median OS of only 24 months, which is shorter than the 38 months reported for newer-generation chemotherapy regimens (e.g., the FLOT regimen) [11].

Nevertheless, whether XELOX outperforms ECF as a POCT regimen for AGC remains unclear. Therefore, this study aimed to perform a comparative analysis of these two chemotherapy regimens to address evidence gap and identify a more favorable POCT regimen for AGC patients.

Patients and methods

General information

This retrospective study included 90 AGC patients who were treated at The Second Affiliated Hospital of Guangzhou University of Chinese Medicine between January 2022 and January 2025. Among them, 47 patients who received CAP+OXA (XELOX regimen) were assigned to the observation group, while 43 patients who received epirubicin, cisplatin, and fluorouracil (ECF regimen) were assigned to the control group. The study protocol was approved by the Ethics Committee of The Second Affiliated Hospital of Guangzhou University of Chinese Medicine. Clinical comparability of the study cohorts was supported by their balanced baseline data distributions ($P>0.05$).

Patient selection criteria

Inclusion criteria: (1) meeting the diagnostic criteria for AGC [12]; (2) age between 18 and 80 years; (3) postoperative pathologic stage III-IV; (4) an Eastern Cooperative Oncology Group (ECOG) performance status score of 0-1 [13]; (5) a Karnofsky Performance Status (KPS) score of ≥ 70 [14]; (6) an life expectancy of ≥ 3 months; (7) at least one measurable lesions; (8) no previous anti-tumor treatment; (9) tolerance to the assigned chemotherapy regimen; (10) normal communication and cognitive ability; and (11) complete clinical data.

Exclusion criteria: (1) the presence of other malignant tumors; (2) contraindications to chemotherapy; (3) pregnancy or lactation; (4) severe cardiac, pulmonary, or renal dysfunction; (5) a history of abdominal surgery; (6) coagulation disorders or infectious diseases; (7) severe hypoproteinemia; or (8) autoimmune diseases.

Treatment methods

Patients in the observation group received the CAP+OXA regimen (XELOX) as follows: OXA was administered by intravenous (IV) infusion at 130 mg/m^2 on day 1 of each chemotherapy cycle; and CAP was administered orally at $1,250 \text{ mg/m}^2$ twice daily from day 1 to day 14.

Patients in the control group received the ECF regimen, consisting of epirubicin, cisplatin, and fluorouracil. Epirubicin was administered by IV infusion at 60 mg/m^2 on day 1 of chemotherapy. Cisplatin was administered at 75 mg/m^2 via IV infusion, and fluorouracil was administered at 500 mg/m^2 by continuous IV infusion over 96 hours on days 1-3.

All patients received three chemotherapy cycles, each lasting for 3 weeks.

Outcome measures

Treatment responses. The therapeutic responses were evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST) [15], and classified as complete remission (CR), partial remission (PR), stable disease (SD), and progressive disease (PD). CR was defined as the complete disappearance of all lesions, with no recurrence within 4 weeks; PR was defined as a reduction of $\geq 30\%$ in the longest diameter of target lesions, with no recurrence within 4

weeks; SD was defined as a condition in which lesion size did not meet the criteria for PR; and PD was defined as an increase in lesion size or the appearance of new lesions. The overall response rate (ORR) was calculated as: (number of CR cases + number of PR cases)/total number of cases *100%.

Safety: Adverse reactions were graded from 0 to IV according to the Adverse Reaction Terminology developed by the World Health Organization, with grades I-II considered mild to moderate adverse reactions, whereas grades III-IV were deemed serious adverse reactions [16]. The occurrence of hyperpigmentation, hepatic and renal dysfunction, alopecia, gastrointestinal reactions, and myelosuppression was recorded, and the incidence of each adverse event was calculated.

Serum tumor markers (STMs): Enzyme-linked immunosorbent assays (ELISAs) were performed to measure serum levels of carbohydrate antigen 199 (CA199), carcinoembryonic antigen (CEA), and alpha-fetoprotein (AFP). Fasting peripheral venous blood (5 mL) were collected from each participant before treatment and 1 week after treatment. Serum samples were obtained by centrifugation for subsequent analysis.

Humoral immunity: Serum immunoglobulin (Ig) A, IgM, and IgG levels were measured using ELISA before treatment and 1 week following treatment.

Gastric hormones: Serum levels of motilin (MTL) and gastrin (GAS) contents were measured using ELISA before and after (at week 1) treatment.

One-year postoperative recurrence and survival: Patients were followed up every 3 months through medical record review, telephone interviews, and outpatient re-examinations. 1-year OS and recurrence outcomes were assessed.

Quality of life (QoL): Quality of life was evaluated using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) [17] before and after the treatment. The questionnaire covers five functional domains (physical, role, emotional, cognitive, and social functioning), three symptom domains (fatigue, nausea and vomiting, and pain), and one global health status domain. Scores for each domain were

linearly transformed to a scale ranging from 0-100. For functional and global health status domains, the scores correlate positively with QoL, whereas higher scores in symptom domains indicate more severe symptoms.

Statistical methods

Statistical analyses were conducted using SPSS version 22.0, and graphical presentations were generated using GraphPad Prism version 7.0. Continuous variables were expressed as mean $\pm$ standard deviation (SD). Comparisons between groups were performed using the independent samples t-test, while intra-group comparisons (before and after treatment) were performed using paired t-test. Categorical variables were presented as frequencies and percentages and were analyzed using the χ^2 test for comparisons between groups. To control for the risk of Type I errors caused by multiple comparison, the Bonferroni correction was applied. In this study, 17 independent comparisons were performed to evaluate differences in various indicators between groups, and the adjusted significance threshold was set to $\alpha=0.05/17=0.00294$. A two-sided *P* value of <0.05 was considered significant.

Results

Comparison of baseline characteristics between groups

No significant differences were observed in baseline characteristics, including sex, age, body mass index [BMI], tumor diameter, and TNM stage between the observation and control groups (all $P>0.05$; **Table 1**).

Comparison of treatment responses between groups

In the observation group, 6 patients achieved CR and 26 achieved PR, achieving an ORR of 68.09%; In the control group, 3 patients achieved CR and 16 achieved PR, achieving an ORR of 44.19%. The ORR was significantly higher in the observation group than in the control group ($P=0.022$; risk difference: 23.9%, 95% CI: 3.5%-44.3%; **Table 2**).

Comparison of safety profiles between groups

The recorded adverse events included hyperpigmentation, hepatic and renal dysfunction, alopecia, gastrointestinal reactions, and myelo-

Table 1. Comparison of baseline characteristics between the two groups

Indicator	Observation group (n=47)	Control group (n=43)	χ^2/t	P
Sex			0.037	0.847
Male	25 (53.19)	22 (51.16)		
Female	22 (46.81)	21 (48.84)		
Age (years)	60.17±9.85	57.86±9.82	1.116	0.268
Body mass index (kg/m ²)	22.21±2.15	22.67±2.41	0.957	0.341
Tumor diameter (cm)	4.29±1.50	4.04±1.33	0.833	0.407
TNM staging			0.149	0.699
III	31 (65.96)	30 (69.77)		
IV	16 (34.04)	13 (30.23)		
Pathologic type			0.358	0.836
Poor differentiation adenocarcinoma	20 (42.55)	21 (48.84)		
Moderately differentiated adenocarcinoma	16 (34.04)	13 (30.23)		
Signet-ring cell carcinoma	11 (23.40)	9 (20.93)		
Lesion location			0.967	0.617
Gastric antrum	22 (46.81)	22 (51.16)		
Gastric body	16 (34.04)	16 (37.21)		
Fundus	9 (19.15)	5 (11.63)		
Surgical approach			0.721	0.697
Distal gastrectomy	26 (55.32)	21 (48.84)		
Total gastrectomy	16 (34.04)	15 (34.88)		
Proximal gastrectomy	5 (10.64)	7 (16.28)		
Lymphadenectomy extent			0.618	0.432
D1 lymphadenectomy	5 (10.64)	7 (16.28)		
D2 lymphadenectomy	42 (89.36)	36 (83.72)		

Table 2. Comparison of treatment responses between the two groups

Indicator	Observation group (n=47)	Control group (n=43)	χ^2	P
CR	6 (12.77)	3 (6.98)		
PR	26 (55.32)	16 (37.21)		
SD	8 (17.02)	15 (34.88)		
PD	7 (14.89)	9 (20.93)		
Overall response (CR + PR)	32 (68.09)	19 (44.19)	5.223	0.022

Note: CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease.

suppression. No significant differences were observed between the two groups in the incidence of hyperpigmentation, hepatic and renal dysfunction, or alopecia (all $P>0.05$). Compared to the control group, the observation group exhibited lower incidences of gastrointestinal reaction (42.55% vs. 69.77%) and myelosuppression (48.94% vs. 72.09%), but a higher incidence of peripheral neurotoxicity ($P<0.05$). The two groups were comparable regarding the

incidence of grade I-II or III-IV adverse events ($P>0.05$; **Table 3**).

Comparison of STMs between groups

No significant inter-group differences were observed in baseline serum levels of CA199, CEA, or AFP between the two groups ($P>0.05$). After treatment, the levels of these tumor markers declined significantly

in both groups ($P<0.01$), with more pronounced decreases in these markers observed in the observation group compared with the control group ($P<0.05$). After Bonferroni correction, the reduction in CA199 remained significantly greater in the observation group than in control group (adjusted $P<0.001$), whereas no significant differences were found in the changes of CEA (adjusted $P=0.483$) and AFP (adjusted $P=0.256$; **Figure 1**).

Table 3. Comparison of safety profiles between the two groups

Indicator	Observation group (n=47)	Control group (n=43)	χ^2	P
Hyperpigmentation				
Grade I-II	4 (8.51)	5 (11.63)		0.732
Grade III-IV	0 (0.00)	0 (0.00)		>0.999
Total	4 (8.51)	5 (11.63)		0.732
Liver and kidney dysfunction				
Grade I-II	12 (25.53)	13 (30.23)	0.247	0.619
Grade III-IV	0 (0.00)	0 (0.00)		>0.999
Total	12 (25.53)	13 (30.23)	0.247	0.619
Alopecia				
Grade I-II	22 (46.81)	20 (46.51)	0.001	0.978
Grade III-IV	15 (31.91)	16 (37.21)	0.279	0.598
Total	37 (78.72)	36 (83.72)	0.366	0.545
Gastrointestinal reaction				
Grade I-II	16 (34.04)	23 (53.49)	3.458	0.063
Grade III-IV	4 (8.51)	7 (16.28)		0.340
Total	20 (42.55)	30 (69.77)	6.736	0.010
Myelosuppression				
Grade I-II	21 (44.68)	28 (65.12)	3.781	0.052
Grade III-IV	2 (4.26)	3 (6.98)		0.667
Total	23 (48.94)	31 (72.09)	5.017	0.025
Peripheral neurotoxicity				
Grade I-II	17 (36.17)	8 (18.60)	3.454	0.063
Grade III-IV	3 (6.38)	1 (2.33)		0.618
Total	20 (42.55)	9 (20.93)	4.807	0.028

Note: The hyperpigmentation incidence was analyzed using Fisher's exact test.

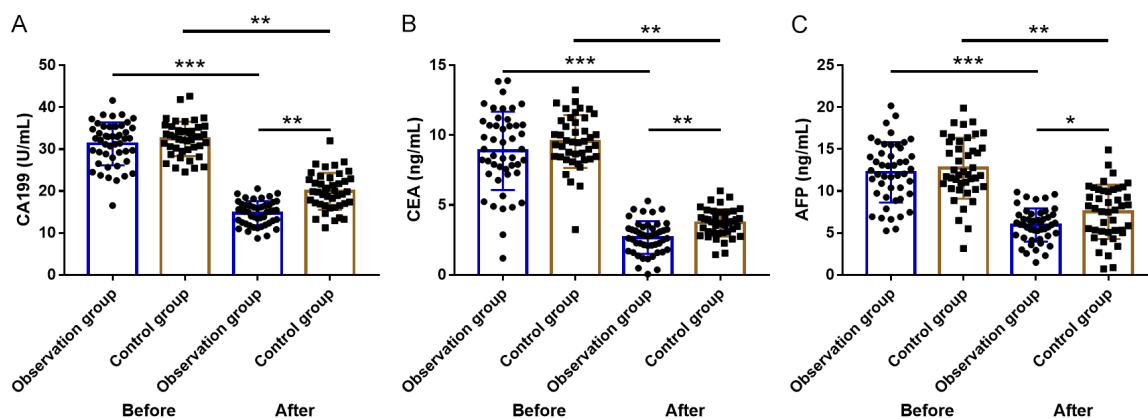


Figure 1. Comparison of serum tumor marker levels before and after treatment between the two groups. A. Carbohydrate antigen 199 (CA199). B. Carcinoembryonic antigen (CEA). C. Alpha-fetoprotein (AFP). Note: *P<0.05, **P<0.01, ***P<0.001.

Comparison of humoral immunity markers between the two groups

Baseline serum Ig A/M/G levels were comparable between the two groups (P>0.05). Following treatment, all immune markers

increased to varying degrees in both groups, with significantly higher levels observed in the observation group than in the control group (P<0.05). Following Bonferroni correction, no significant differences were observed between groups in the changes of Ig A/M/G levels

Table 4. Comparison of humoral immunity marker levels before and after treatment between the two groups

Indicator	Observation group (n=47)	Control group (n=43)	t	P
Ig A (g/L)				
Pre-treatment	1.58±0.56	1.49±0.41	0.863	0.390
Post-treatment	2.18±0.60	1.88±0.55	2.465	0.016
Ig M (g/L)				
Pre-treatment	0.79±0.18	0.77±0.23	0.461	0.646
Post-treatment	1.24±0.22	1.01±0.31	4.086	<0.001
Ig G (g/L)				
Pre-treatment	6.44±1.96	6.26±1.90	0.442	0.660
Post-treatment	9.35±1.98	8.16±2.42	2.562	0.012

Note: Ig, immunoglobulin.

Table 5. Comparison of gastric hormone levels before and after treatment between the two groups

Indicator	Observation group (n=47)	Control group (n=43)	t	P
MTL (ng/L)				
Pre-treatment	25.28±4.55	23.76±7.65	1.157	0.250
Post-treatment	42.34±6.71	32.00±4.73	8.377	<0.001
GAS (ng/L)				
Pre-treatment	126.43±15.68	124.23±12.29	0.736	0.464
Post-treatment	160.57±17.74	141.09±17.96	5.173	<0.001

Note: MTL, motilin; GAS, gastrin.

(adjusted $P=0.198$, 0.007 , and 0.088 , respectively; **Table 4**).

Comparison of gastric hormone levels between the two groups

The baseline levels of MTL and GAS were comparable between the two groups ($P>0.05$). After treatment, both groups exhibited increased levels of MTL and GAS, with a greater increase observed in the observation group ($P<0.05$). After Bonferroni correction, the increases in MTL and GAS remained significantly greater in the observation group compared to the control group (adjusted $P<0.001$; **Table 5**).

Comparison of 1-year recurrence and survival rate between the two groups

All participants completed the 1-year follow-up. The 1-year recurrence rates were 40.43% in the observation group and 46.51% in the control group ($P>0.05$). The 1-year OS rate was 82.98% in the observation group, significantly higher than the 62.79% in the control group ($P<0.05$).

Moreover, because the 1-year recurrence rates were below 50% and the 1-year OS rates exceeded 50% in both groups, the median recurrence-free survival and median OS were not reached (undefined; **Figure 2**; **Table 6**).

Comparison of QoL scores between the two groups

This EORTC QLQ-C30 questionnaire was used to evaluate patients' QoL. Baseline scores for all dimensions were comparable between the two groups ($P>0.05$). Following the treatment, functional domain scores increased significantly in both cohorts, with greater improvements observed in the observation group ($P<0.05$). Fatigue and pain scores decreased notably after treatment in both groups, whereas nausea and vomiting scores increased markedly ($P<0.05$). Further between-group comparisons revealed lower scores in all symptom domains in the

observation group compared to the control group ($P<0.05$).

After Bonferroni correction, the improvement in physical functioning remained greater in the observation group than in the control group (adjusted $P<0.001$). In addition, the increase in nausea and vomiting scores was less pronounced, and the reduction in pain scores was greater in the observation group (both adjusted $P<0.001$). However, the between-group differences in changes in global health status (adjusted $P=0.029$), role functioning (adjusted $P=0.031$), emotional functioning (adjusted $P=0.236$), cognitive functioning (adjusted $P=0.522$), social functioning (adjusted $P=0.050$), and fatigue (adjusted $P=0.061$) did not remain statistically significant after correction (**Figure 3**).

Discussion

In this study, we first demonstrated that XELOX achieved superior tumor control compared to ECF as postoperative chemotherapy (POCT) for

Postoperative chemotherapy for advanced gastric cancer

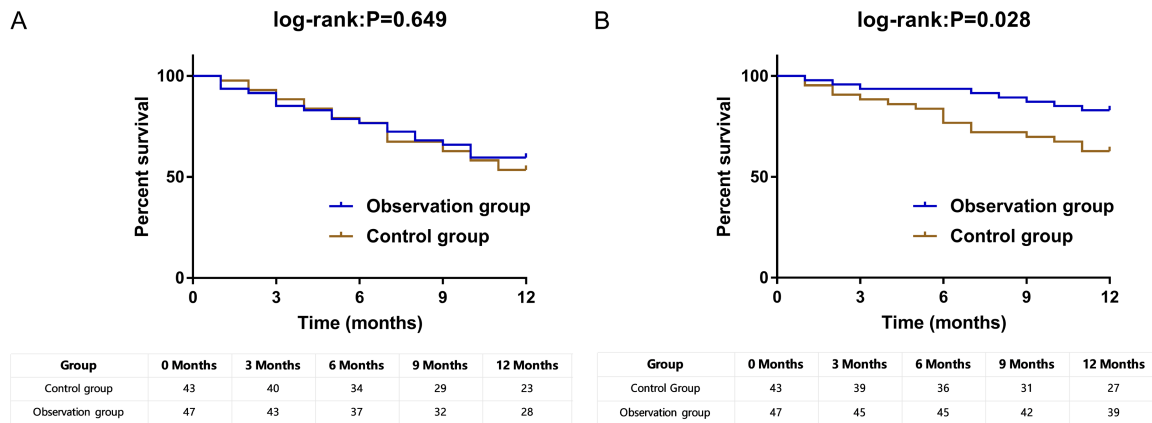


Figure 2. Comparison of survival outcomes between the two groups. A. One-year recurrence-free survival curves of the two groups. B. One-year overall survival curves of two groups.

Table 6. Comparison of 1-year recurrence and survival between the two groups

Indicator	Observation group (n=47)	Control group (n=43)	χ^2	P
1-year recurrence	19 (40.43)	20 (46.51)	0.339	0.561
1-year overall survival	39 (82.98)	27 (62.79)	4.680	0.031

patients with advanced gastric cancer (AGC) (ORR: 68.09% vs. 44.19%). In a GC xenograft model, XELOX was shown to enhance the anti-tumor activity of CAP by up-regulating thymidine phosphorylase, thereby synergistically enhancing therapeutic effects in GC treatment [18]. He et al. [19] reported that perioperative treatment with Camrelizumab combined with XELOX for locally advanced gastric or gastro-esophageal junction adenocarcinoma achieved favorable pathologic responses with acceptable safety profiles. These findings further support the clinical efficacy of XELOX observed in this study and suggest that combination strategies involving Camrelizumab may enable improvement of therapeutic outcomes. Similarly, Zhang et al. [20] reported that the combination of XELOX with Fuzi Lizhong decoction and Sintilimab enhanced therapeutic efficacy and reduced tumor marker levels in AGC patients, further supporting our findings.

It is important to distinguish the treatment setting of this study from the contemporary first-line immunotherapy strategies. Although PD-1 inhibitor-based immunochemotherapy has become an established treatment option for advanced or metastatic gastric cancer, its role in the postoperative adjuvant setting remains

insufficiently established and it is not currently recommended as routine clinical practice. Therefore, evaluation of appropriate adjuvant chemotherapy regimens remains clinically meaningful. Despite the emergence of regimens such as

FLOT and SOX, XELOX remains recommended as one of the adjuvant chemotherapy options in domestic guidelines, including those issued by the Chinese Anti-Cancer Association (CACA). Thus, our comparison between XELOX and ECF in the adjuvant setting addresses an important clinical question that remains relevant despite advances in immunotherapy.

In terms of safety, XELOX exhibited significant clinical advantages over ECF in reducing the incidences of gastrointestinal reactions and myelosuppression in AGC patients undergoing POCT, although it was associated with an increased risk of peripheral neurotoxicity. Overall, the two regimens showed comparable incidences of grade III-IV adverse events. These findings may be related to the distinct toxicity profiles of CAP and OXA. CAP was orally administered and converted into 5-fluorouracil through a multistep metabolic pathway, with preferential activation in tumor tissues through thymidine phosphorylase, thereby potentially reducing systemic toxicity. Although OXA-associated neurotoxicity remains a major concern, it is generally reversible to some extent after treatment discontinuation [21, 22]. Zhao et al. [23] reported that XELOX was associated with a lower incidence of grade 3-4 treatment-

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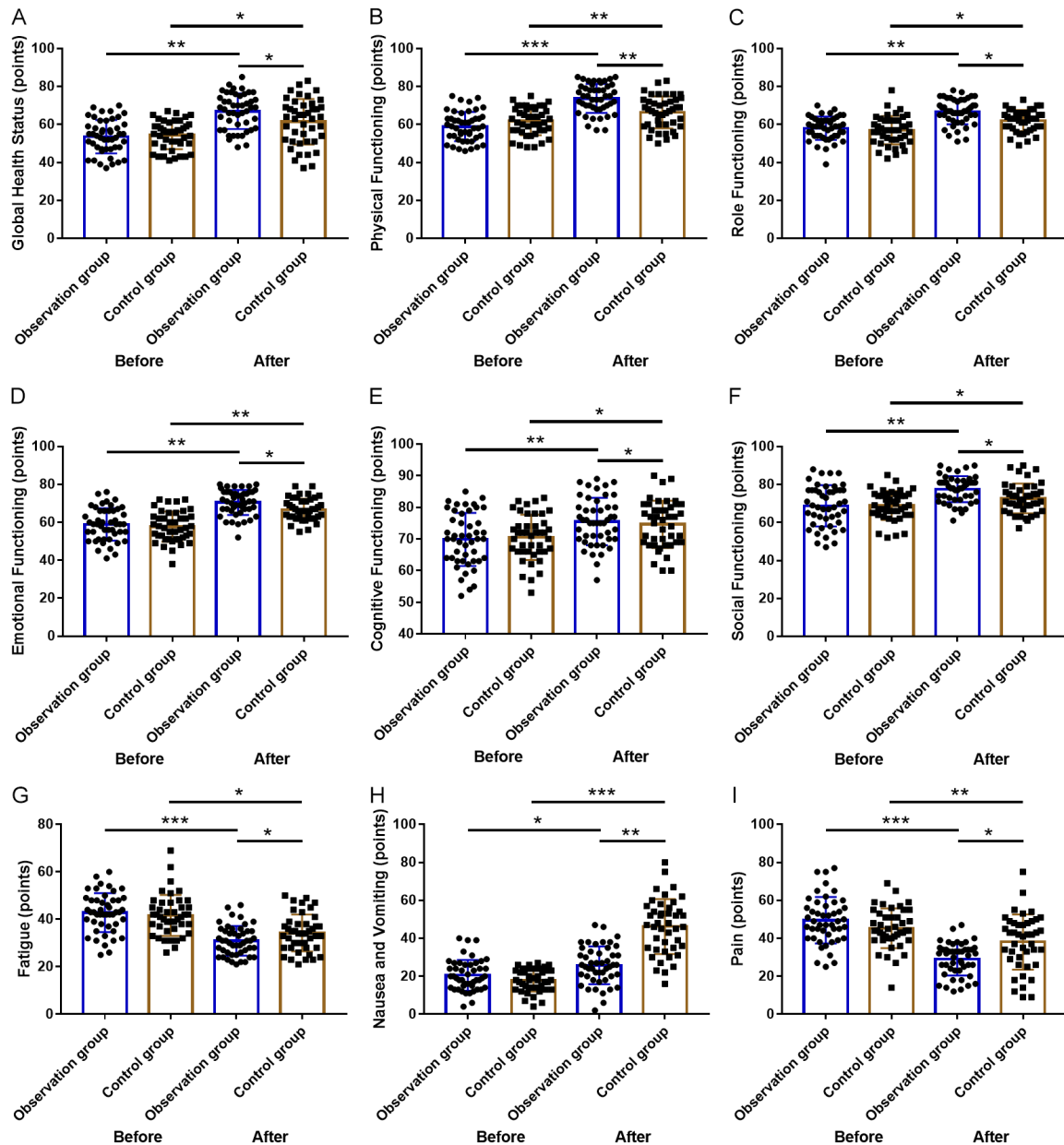


Figure 3. Comparison of quality-of-life scores before and after treatment between the two groups. A. Global health status scores. B. Physical functioning scores. C. Role functioning scores. D. Emotional functioning scores. E. Cognitive functioning scores. F. Social functioning scores. G. Fatigue scores. H. Nausea and vomiting scores. I. Pain scores. Note: *P<0.05, **P<0.01, ***P<0.001.

related adverse events compared to the TX regimen (docetaxel + CAP) in patients with metastatic GC, further supporting the favorable safety profile of XELOX.

Furthermore, XELOX demonstrated greater reductions in serum tumor markers, particularly CA199, compared to ECF. Zhou et al. [24] reported that the addition of bevacizumab and CAP to XELOX further reduced tumor marker

levels in patients with metastatic colorectal cancer, which is consistent with and provides additional support for our findings. Compared to ECF, POCT with XELOX also contributed to greater improvements in humoral immune function in AGC patients. A preliminary study showed that XELOX chemotherapy combined with intraperitoneal infusion of cytokine-induced killer cells in AGC patients with ascites not only improved therapeutic efficacy but also

enhanced immune function without causing serious adverse reactions, which is consistent with the immune-related findings of this study [25]. Moreover, XELOX showed a greater ability than ECF to regulate gastric hormone levels (MTL, GAS) in AGC patients, which may contribute to the improvement of gastrointestinal function. However, the underlying mechanisms require further investigation.

From the perspective of survival outcomes, although the two chemotherapy regimens showed comparable effects on the 1-year recurrence rate in AGC patients, the XELOX regimen demonstrated significant advantages in improving 1-year OS. In patients with unresectable AGC or those who were resistant or intolerant to cisplatin, Sugimoto et al. [26] reported that salvage chemotherapy with XELOX provided certain clinical benefits, with a median PFS and OS of 4.2 months and 7.1 months, respectively, which further supports and complements our findings. Finally, QoL assessment found that XELOX treatment resulted in more comprehensive improvements across multiple QoL domains and reduced disease-related symptom burden in patients with AGC. This may be attributed to the enhanced antitumor efficacy, better disease control, reduced disease-related symptom burden, and potential improvements in immune and gastrointestinal functions, associated with XELOX treatment, thereby contributing to overall QoL improvement.

In addition, this study applied the Bonferroni correction for 17 indicators analyzed to strictly control the risk of type I errors caused by multiple comparisons. After correction, several indicators, including CEA, AFP, Ig A/M/G, global health status, role/emotional/cognitive/social functioning, and fatigue, no longer showed statistically significant differences between groups. These findings may be explained by the relatively small sample size, potential confounding factors inherent to the retrospective design, and the possibility that these indicators mainly reflect supplementary aspects of disease status. Further prospective studies with larger cohorts are needed to further verify these findings.

Several limitations of this study should be addressed. First, as a retrospective non-randomized study, selection bias could not be completely avoided. Future prospective ran-

domized controlled trials are needed to minimize potential bias. Second, the relatively small sample size and single-center design, involving only 90 patients treated during a specific period (January 2022-January 2025), may have limited the representativeness of the findings. Hence, multi-center studies with larger sample sizes are required to confirm the results. Third, longer follow-up time (e.g., extending to 5 years), are needed to further verify the long-term survival outcomes associated with the two schemes. Fourth, this study focused on postoperative adjuvant chemotherapy after radical surgery and was not designed to challenge the established benefits of ECF-based perioperative treatment. Therefore, the conclusions of this study are limited to the postoperative adjuvant chemotherapy scenarios. This limitation is inherent to the retrospective design and should be addressed in future prospective studies to improve the generalizability of the findings. Finally, this study compared XELOX and ECF as POCT regimens. Although FLOT regimen has become a widely adopted regimen in western countries and SOX is commonly used in Asia, these regimens were not the first choice in clinical practice. Nevertheless, this study provides real-world data supporting the clinical application of XELOX by demonstrating its advantages over ECF, thereby maintaining certain clinical value.

Conclusion

Based on the findings of this study, the XELOX regimen may represent a preferable option to the ECF regimen for POCT in AGC patients. XELOX was associated with improved tumor response, lower incidences of gastrointestinal reactions and myelosuppression, although with an increased risk of peripheral neurotoxicity. In addition, XELOX more effectively reduced STM levels and improved certain clinical outcomes. However, although XELOX demonstrated superior performance in several indicators, including CA199, MTL, GAS, physical functioning, nausea and vomiting, and pain, some of these differences did not remain statistically significant after adjustment. Therefore, the findings of this study should be interpreted with caution. Further prospective studies with larger sample sizes are required to validate the clinical benefits of XELOX for the postoperative treatment of AGC.

Disclosure of conflict of interest

None.

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