Effects of Neoadjuvant Chemotherapy on Early Postoperative Anxiety and Depression in Patients With Gastric Cancer: An Observational Study

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AIM: Neoadjuvant chemotherapy (NACT) improves surgical outcomes in gastric cancer, yet its effect on early postoperative mental health remains unclear. This study aims to investigate the association between NACT and postoperative anxiety and depression.
METHODS: A single-center, retrospective cohort study included 201 gastric cancer patients who underwent surgical resection from October 2023 to May 2024, categorized by NACT receipt. Psychological evaluation in the early postoperative phase was conducted using the Hospital Anxiety and Depression Scale (HADS), and associations with NACT were assessed through logistic regression.
RESULTS: Of the 201 patients, 57 (28.4%) received NACT. Postoperative assessments showed significantly higher rates of anxiety (78.95% vs. 61.11%, $p = 0.016$) and depression (56.14% vs. 38.89%, $p = 0.026$) in NACT recipients compared to non-NACT patients. After adjusting for confounders, NACT remained independently associated with an increased prevalence of anxiety (Odds Ratio [OR] = 2.25) and depression (OR = 2.00, both $p < 0.05$). Patients undergoing more than three NACT cycles exhibited increased anxiety (91.67% vs. 69.70%, $p = 0.045$) and depression (75.00% vs. 42.42%, $p = 0.014$), with higher mean HADS scores (both $p < 0.05$). These associations persisted in adjusted analyses for depression (OR, 4.07; 95% Confidence Interval [CI], 1.28–12.90; $p = 0.017$) and were marginal for anxiety (OR, 4.78; 95% CI, 0.94–24.33; $p = 0.059$). Patients with poor response (tumor regression grade [TRG] 2–3) also showed a trend toward increased anxiety risk (OR, 3.30; 95% CI, 0.83–13.12; $p = 0.089$).
CONCLUSIONS: NACT is independently associated with increased anxiety and depression in the early postoperative period, especially if chemotherapy cycles are prolonged.

Keywords: gastric cancer; neoadjuvant chemotherapy; anxiety; depression; chemotherapy cycles

Introduction

Gastric cancer (GC) remains a significant global health challenge, with the majority of patients diagnosed at a locally advanced stage [1,2]. For these patients, neoadjuvant therapy (NAT) has been widely adopted as an effective strategy to decrease tumor burden, facilitate pathological downstaging, and increase the probability of achieving complete (R0) resection [3]. The effectiveness of this approach was confirmed in clinical trials such as the Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC) and the Fédération Nationale des Centres de Lutte contre le Cancer (FNCLCC), which demonstrated that neoadjuvant chemotherapy (NACT) markedly improved R0 resection rates as well as long-term survival [4,5].

Patients diagnosed with cancer often encounter substantial psychological distress [6]. Among those with gastrointestinal malignancies, the reported prevalence rates of anxiety and depression are 19.1% and 31%, respectively [7]. Such symptoms can negatively affect quality of life, compromise adherence to treatment, and consequently worsen clinical outcomes including recovery, recurrence and overall survival [8–10].

In previous studies, several risk factors were identified for poor mental health in gastric cancer patients, including pain, divorce, a history of psychiatric disorders, stressful life events, and disease progression [8,9]. Postoperative complications and adverse effects from adjuvant chemotherapy are frequently associated with increased levels of anxiety and depression [9]. Nevertheless, the psychological effects of neoadjuvant chemotherapy have not been thoroughly studied. Specifically, how NACT influences emotional disturbances during the early postoperative phase, and whether these effects differ between treatment regimens, remains uncertain.

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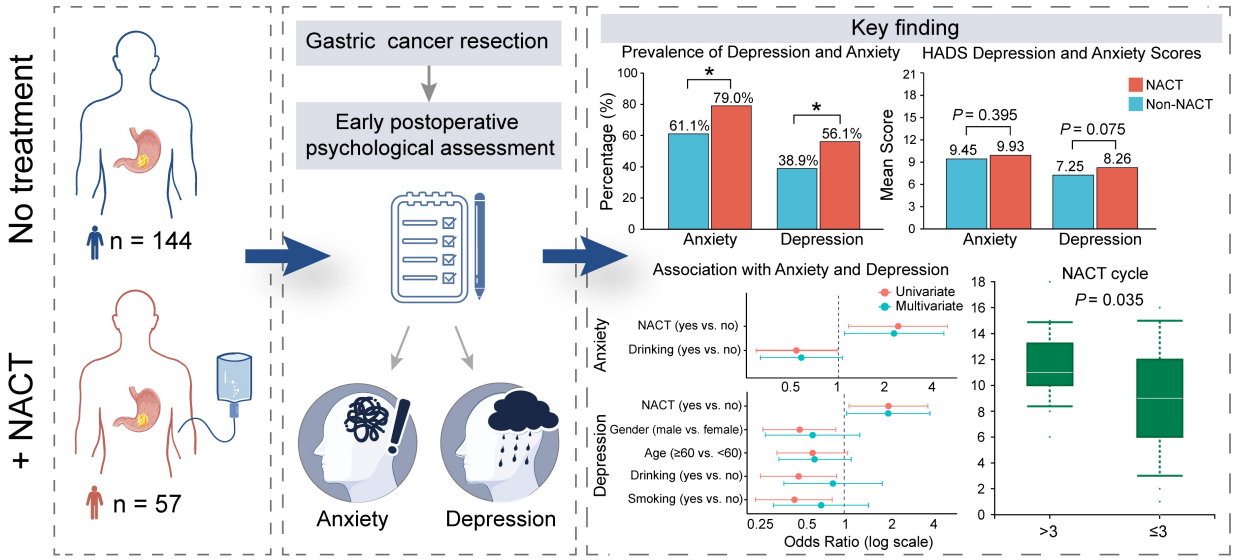

Graphical Abstract.

Therefore, the present study was conducted to explore the relationship between NACT and early postoperative psychological status in patients with gastric cancer.

Materials and Methods

Research Design and Cohort

This was a single-center, retrospective study including patients with gastric cancer who received surgical resection from October 2023 to May 2024. Written informed consent was obtained from all participants before the administration of questionnaires and clinical data collection. Ethical approval was obtained from the Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine (No. I2025967). All procedures were conducted in compliance with the ethical principles of the Declaration of Helsinki and regulatory standards.

Inclusion criteria: (1) histopathological confirmation of gastric cancer; (2) age $\geq$18 years; (3) no evidence of distant metastasis; and (4) availability of complete clinical records. Exclusion criteria: (1) concurrent comorbidities or other malignancies that could significantly affect treatment outcomes; (2) pre-existing psychiatric disorders or cognitive impairments; (3) refusal to participate.

Measures

Patient Demographic and Clinical Variables

Demographic and clinical information was obtained from the hospital electronic health record system or through standardized online questionnaires completed 1–2 weeks postoperatively [8,11]. Two trained members of the research team independently collected and verified the data to ensure both accuracy and reliability.

Demographic variables included age, sex, body mass index (BMI), marital status, educational attainment, employment status, place of residence, monthly household income, and religious affiliation. Cancer-related variables included tumor pathology and Clinical Tumor-Node-Metastasis staging system (cTNM), NACT regimens, tumor response, surgical procedure and presence of postoperative complications. "Prolonged NACT" was prespecified as >3 cycles. Common neoadjuvant chemotherapy regimens include SOX (S-1 plus oxaliplatin), XELOX (capecitabine plus oxaliplatin), as well as FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel) and FOLFOX (fluorouracil, leucovorin, and oxaliplatin). In immunotherapy, PD-1 (programmed cell death protein 1) and PD-L1 (programmed cell death ligand 1) inhibitors are commonly used [3–5]. Tumor regression grade (TRG) is a pathological grading system for evaluating tumor response to NACT, as recommended by the National Comprehensive Cancer Network (NCCN) and the College of American Pathologists (CAP) (Version 2.2025) [12]. TRG 0–1 indicated complete or near-complete tumor regression, whereas TRG 2–3 represented moderate to poor response.

Mental Health Assessment

Pre-treatment psychological status was abstracted from medical records, which included clinical notes and prior psychological evaluations, rather than original HADS scale assessments. Early postoperative psychological status was assessed using the Hospital Anxiety and Depression Scale (HADS), a validated scale including anxiety (HADS-A) and depression (HADS-D) subdomains. Each subscale ranges from 0 to 21 points and a HADS-A or HADS-D score >7 was considered as anxiety or depression. Furthermore, the severity of symptoms was categorized as 0–7 (normal), 8–10 (mild), 11–14 (moderate), and 15–21 (severe) [13]. The HADS has demonstrated good reliability and validity in previous studies [14,15].

Statistical Method

All statistical analyses were conducted using R (version 4.5.1; R Foundation for Statistical Computing, Vienna, Austria). Continuous variables are presented as means with standard deviation (SD) or medians with interquartile ranges (IQR). Categorical variables are reported as frequencies and percentages. Normality of data distribution was assessed using the Shapiro-Wilk test, and homogeneity of variances was evaluated with Levene's test. Between-group comparisons, independent-sample *t*-tests or one-way analysis of variance (ANOVA) were employed for normally distributed continuous variables. In cases where data did not meet these parametric assumptions, the non-parametric Mann-Whitney U test or Kruskal-Wallis test was used as appropriate. Categorical variables were compared using Chi-square or Fisher's exact tests, as appropriate. The association between NACT and postoperative psychological outcomes was assessed through logistic regression analyses. To adjust for confounding, covariate selection for the multivariable models was based on statistical evidence from univariable analyses and clinical relevance. Subgroup and stratified analyses were subsequently conducted to explore heterogeneity and potential effect modification. First-adjusted logistic regression was applied when complete separation occurred. Statistical significance was set at a two-sided p value < 0.05.

Results

Participant Characteristics

This study enrolled 201 patients with gastric cancer (Fig. 1), among whom 57 (28.4%) underwent neoadjuvant chemotherapy (NACT group) and 144 (71.6%) proceeded directly to surgery (non-NACT group). In general, the cohort was predominantly male (115 patients, 57.21%) and older, with 114 patients (56.72%) aged 60 years or above. Although the two groups were largely comparable, certain baseline sociodemographic differences were evident (Table 1). Patients in the NACT group were significantly more

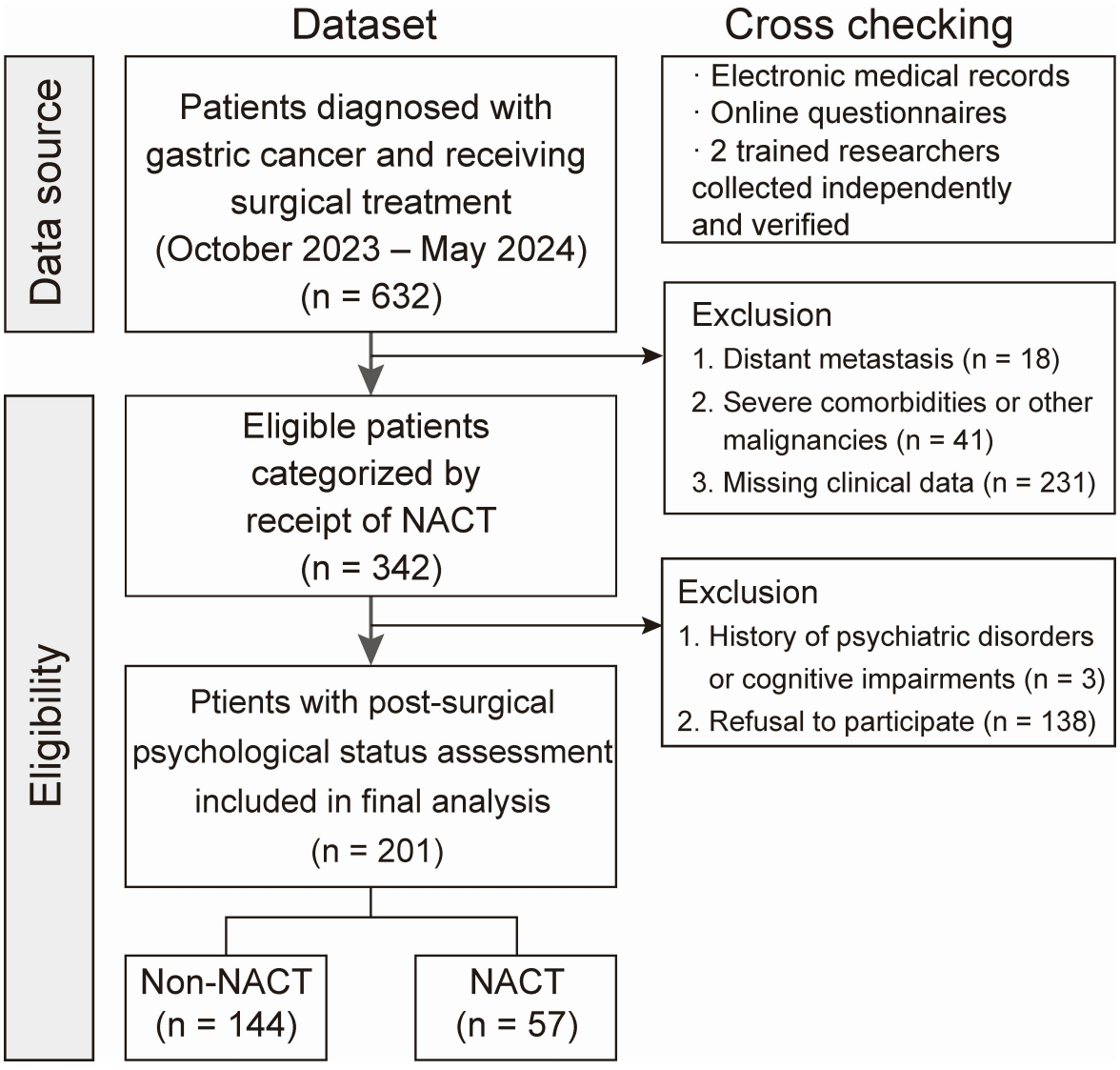

Fig. 1. Study design flowchart. NACT, neoadjuvant chemotherapy.

Table 1. Baseline demographics of the NACT and non-NACT groups.

Variables	Total (n = 201)	Non-NACT (n = 144)	NACT (n = 57)	*p*
BMI (kg/m^2), Mean ± SD	22.79 ± 3.31	22.93 ± 3.42	22.44 ± 3.02	0.343
Gender, n (%)				0.284
Female	86 (42.79)	65 (45.14)	21 (36.84)	
Male	115 (57.21)	79 (54.86)	36 (63.16)	
Age (years), n (%)				0.172
<60	87 (43.28)	58 (40.28)	29 (50.88)	
≥60	114 (56.72)	86 (59.72)	28 (49.12)	
Drinking, n (%)				0.100
No	123 (61.19)	83 (57.64)	40 (70.18)	
Yes	78 (38.81)	61 (42.36)	17 (29.82)	
Smoking, n (%)				0.043
No	126 (62.69)	84 (58.33)	42 (73.68)	
Yes	75 (37.31)	60 (41.67)	15 (26.32)	
Marital status, n (%)				0.028
Married	178 (88.56)	132 (91.67)	46 (80.70)	
No partner	23 (11.44)	12 (8.33)	11 (19.30)	
Residence, n (%)				0.763
Rural	88 (43.78)	64 (44.44)	24 (42.11)	
Urban	113 (56.22)	80 (55.56)	33 (57.89)	
Education background, n (%)				0.086
Junior high and below	112 (55.72)	86 (59.72)	26 (45.61)	
Senior high	59 (29.35)	41 (28.47)	18 (31.58)	
College and above	30 (14.93)	17 (11.81)	13 (22.81)	
Religious affiliation, n (%)				0.605
No	188 (93.53)	136 (94.44)	52 (91.23)	
Yes	13 (6.47)	8 (5.56)	5 (8.77)	
Monthly incoming (CNY), n (%)				0.763
<5000	128 (63.68)	94 (65.28)	34 (59.65)	
>20,000	10 (4.98)	7 (4.86)	3 (5.26)	
10,000–20,000	10 (4.98)	6 (4.17)	4 (7.02)	
5000–10,000	53 (26.37)	37 (25.69)	16 (28.07)	
Surgical history, n (%)				0.775
No	109 (54.23)	79 (54.86)	30 (52.63)	
Yes	92 (45.77)	65 (45.14)	27 (47.37)	

BMI, body mass index; SD, standard deviation. Exchange rate: 1 USD ≈ 7.12 CNY.

likely to be non-smokers (73.68% vs. 58.33%, $p = 0.043$) and unmarried (19.30% vs. 8.33%, $p = 0.028$) compared with the non-NACT group. Moreover, individuals in the NACT group tended to have attained higher educational levels, though this difference was only marginally significant ($p = 0.086$).

Regarding clinical and psychological characteristics (Table 2), patients in the NACT group were more likely to present with advanced tumor stages (cTNM stage III 54.39% vs. 38.89%, $p = 0.073$). Nevertheless, the NACT group exhibited a lower incidence of postoperative complications (3.51% vs. 16.67%, $p = 0.012$). At the initiation of treatment, review of medical records confirmed that no patients had documented anxiety or depression. Early postoperative psychological evaluation demonstrated significantly higher proportions of anxiety (78.95% vs. 61.11%, $p = 0.016$) and depression (56.14% vs. 38.89%, $p = 0.026$) in the NACT group. However, this difference was not clearly reflected in the mean severity scores; HADS-anxiety values were similar between groups ($p = 0.395$), whereas the mean HADS-depression score showed a borderline elevation in the NACT cohort ($p = 0.075$).

Stratification of patients according to HADS severity categories indicated that NACT recipients had higher scores in the moderate-to-severe anxiety and depression categories compared with the non-NACT cohort, although these differences did not reach statistical significance (Fig. 2, both $p > 0.05$). Within the highest-severity group, the NACT cohort included a greater proportion of males and individuals who were divorced, widowed, or unmarried. In addition, patients with less than a junior-high education were less frequent in the NACT group across all HADS severity levels.

Table 2. Treatment characteristics and early postoperative psychological status of patients.

Variables	Total (n = 201)	Non-NACT (n = 144)	NACT (n = 57)	*p*
Disease awareness, n (%)				0.210
No	19 (9.45)	15 (10.42)	4 (7.02)	
Yes	161 (80.10)	111 (77.08)	50 (87.72)	
Uncertain	21 (10.45)	18 (12.50)	3 (5.26)	
Operation, n (%)				0.103
Partial	150 (74.63)	112 (77.78)	38 (66.67)	
Total	51 (25.37)	32 (22.22)	19 (33.33)	
Surgical complications, n (%)				0.012
No	175 (87.06)	120 (83.33)	55 (96.49)	
Yes	26 (12.94)	24 (16.67)	2 (3.51)	
cTNM stage, n (%)				0.073
I	42 (20.90)	35 (24.31)	7 (12.28)	
II	72 (35.82)	53 (36.81)	19 (33.33)	
III	87 (43.28)	56 (38.89)	31 (54.39)	
Anxiety, n (%)				0.016
No	68 (33.83)	56 (38.89)	12 (21.05)	
Yes	133 (66.17)	88 (61.11)	45 (78.95)	
Depression, n (%)				0.026
No	113 (56.22)	88 (61.11)	25 (43.86)	
Yes	88 (43.78)	56 (38.89)	32 (56.14)	
HADS-anxiety score, Mean ± SD	9.59 ± 3.58	9.45 ± 3.50	9.93 ± 3.81	0.395
HADS-depression score, Mean ± SD	7.54 ± 3.30	7.25 ± 3.06	8.26 ± 3.79	0.075

cTNM, Clinical Tumor-Node-Metastasis staging system; HADS, Hospital Anxiety and Depression Scale.

Correlation Between NACT and Psychological Outcomes

Univariate logistic regression showed that receipt of NACT was significantly associated with a higher risk of both postoperative anxiety and depression ($p < 0.05$ for both, Table 3 and **Supplementary Tables 1,2**). In the multivariate models, NACT remained an independent risk factor for anxiety (Odds Ratio [OR] = 2.25) and depression (OR = 2.00), with both associations retaining statistical significance ($p < 0.05$).

In addition, current alcohol consumption was inversely associated with anxiety (OR = 0.54) and depression (OR = 0.49) in univariate analyses ($p < 0.05$), but these protective associations disappeared after multivariable adjustment. Similarly, male sex, age ≥60 years, and smoking status were linked to a lower risk of depression in unadjusted models (all $p < 0.05$), yet none retained significance in the multivariate analyses.

Subgroup analyses provided further observations. Smoking and alcohol use appeared to mitigate anxious symptoms among patients receiving NACT (**Supplementary Table 3**). However, these same subgroups displayed an overall higher likelihood of depressive symptoms (**Supplementary Table 4**). Moreover, the risk of depression was elevated among males, patients younger than 60 years, individuals with higher educational attainment, and those earning between ¥5000 and ¥10,000 per month (1 USD ≈ 7.12 CNY). Additionally, religious affiliation seemed to lower the risk of postoperative emotional disorders in this population (**Supplementary Table 4**). A greater understanding of one's disease course also appeared to buffer the negative emotional effects of NACT, although this association did not reach statistical significance.

Influence of NACT Characteristics on Psychological Outcomes

A stratified analysis within the NACT cohort was further conducted based on treatment-related variables. Neither the chemotherapy regimen (e.g., SOX/XELOX vs. FLOT/FOLFOX) nor the use of PD-1/PD-L1 inhibitors showed significant differences in anxiety or depression rates (both $p > 0.05$, Table 4). These regimens were also not associated with postoperative anxiety or depression (all $p > 0.05$, Table 5). Group comparisons indicated that patients receiving a prolonged course (>3 cycles) experienced a significantly higher incidence of both anxiety and depression ($p = 0.045$ and $p = 0.014$, respectively; Table 4) along with higher mean HADS scores (both $p < 0.05$; Fig. 3). This relationship was confirmed after multivariable adjustment, where prolonged NACT was linked to a four-fold increase in depression risk (OR = 4.07; 95% CI, 1.28–12.90; $p = 0.017$) and showed a strong trend toward higher anxiety risk (OR = 4.78; 95% CI, 0.94–24.33; $p = 0.059$) (Table 5). Although not statistically significant, patients with favorable pathological responses (TRG 0–1) reported lower rates of anxiety (61.5% vs. 84.1%, $p = 0.172$) and depression (38.5% vs. 61.4%, $p = 0.144$; Table 4) compared with those with poor responses (TRG 2–3). After adjustment, regression analysis revealed a borderline association between

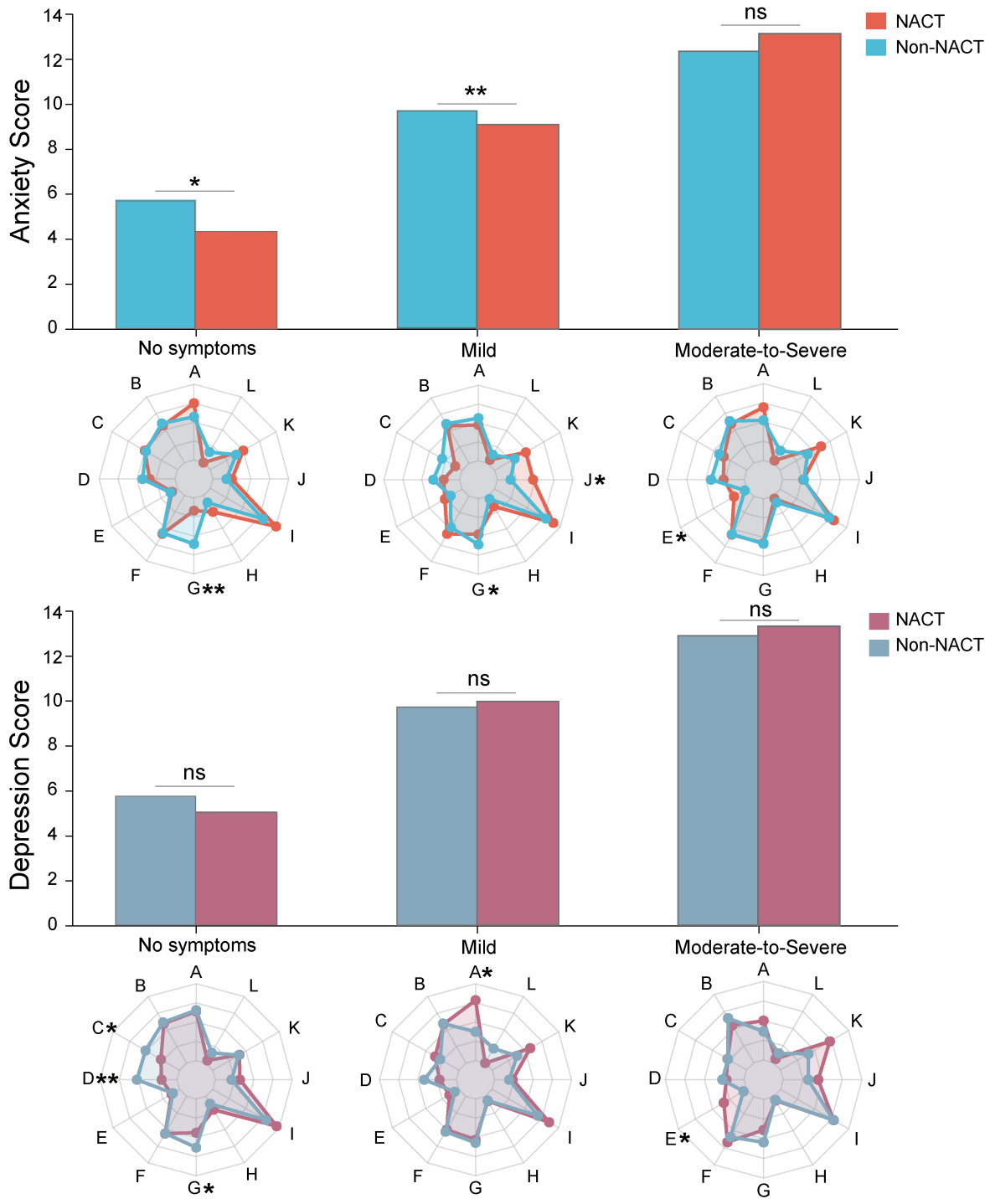

Fig. 2. Severity-stratified anxiety, depression scores and demographics in NACT vs. non-NACT groups. A, Male; B, Age ≥60 years; C, Current drinking; D, Current smoking; E, No partner; F, Urban living; G, Junior-high and below; H, Monthly income >¥10,000 (1 USD ≈ 7.12 CNY); I, awareness of disease; J, Total resection; K, cTNM III stage; L, Postoperative complications. Statistical significance: ns, not significant; *$p < 0.05$; **$p < 0.01$.

poor pathological response and increased anxiety risk (OR = 3.30; 95% CI, 0.83–13.12; $p = 0.089$).

Discussion

Psychological distress following surgery is a multifactorial phenomenon among individuals with gastric cancer. This study focused on the early postoperative period, during which receipt of NACT was identified as a significant risk factor for both anxiety and depression.

Previous reports have documented variability in the prevalence of psychiatric disorders among gastric cancer patients, with estimates ranging from 18% to 49% for anxi-

Table 3. Association between NACT and postoperative anxiety and depression.

Variables	Univariate		Multivariate	
	p	OR (95% CI)	*p*	OR (95% CI)
Anxiety				
NACT, yes vs. no	0.018	2.39 (1.16–4.90)	0.028	2.25 (1.09–4.65)
Drinking, yes vs. no	0.044	0.54 (0.30–0.98)	0.078	0.58 (0.32–1.06)
Depression				
NACT, yes vs. no	0.027	2.01 (1.08–3.74)	0.038	2.00 (1.04–3.85)
Gender, male vs. female	0.017	0.50 (0.28–0.88)	0.194	0.61 (0.29–1.28)
Age, ≥60 years vs. <60 years	0.091	0.61 (0.35–1.08)	0.086	0.63 (0.36–1.12)
Drinking, yes vs. no	0.018	0.49 (0.27–0.89)	0.651	0.84 (0.39–1.82)
Smoking, yes vs. no	0.010	0.46 (0.25–0.83)	0.342	0.70 (0.33–1.47)

OR, Odds Ratio; CI, Confidence Interval.

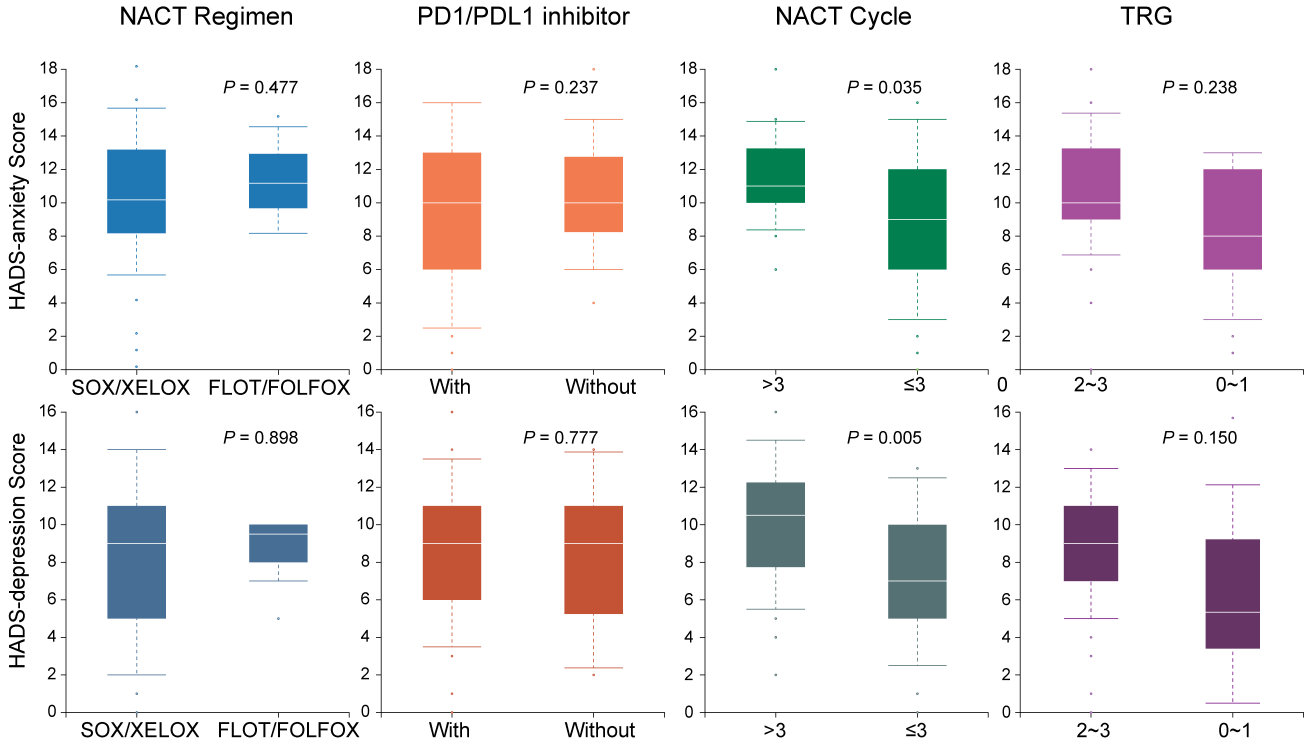

Fig. 3. Anxiety and depression scores by NACT-related characteristics. TRG, tumor regression grade; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; SOX, S-1 plus oxaliplatin; XELOX, capecitabine plus oxaliplatin; FLOT, fluorouracil, leucovorin, oxaliplatin, and docetaxel; FOLFOX, fluorouracil, leucovorin, and oxaliplatin.

ety and 12% to 42% for depression [7,8,16]. In contrast, our study revealed even higher rates, with more than half of the patients who received NACT exhibiting symptoms of anxiety or depression in the early postoperative period. These findings were reflected in elevated mean scores on both the HADS-anxiety and HADS-depression subscales, particularly within the moderate-to-severe category.

Multivariate analyses confirmed the strong association between NACT and early postoperative psychological disorders, in line with emerging evidence from gastrointestinal oncology [9]. This relationship is likely multifactorial, reflecting the combined effects of cumulative physiological toxicity and sustained emotional strain during neoadjuvant treatment. Physiologically, patients undergoing NACT often experience debilitating side effects such as fatigue, nausea, pain, and nutritional deficiencies, which directly compromise physical well-being and exacerbate emotional distress [17,18].

Concurrently, the prolonged treatment period introduces profound psychological stressors, including uncertainty regarding treatment efficacy, fear of adverse effects, and disruption of social and occupational roles [19,20]. Consistent with these mechanisms, we observed a dose–response trend: patients who underwent prolonged NACT (>3 cycles) reported worse psychological outcomes. This supports the cumulative-burden hypothesis, suggesting that extended exposure to cytotoxic agents and related stressors progressively erodes psychological resilience, leaving pa-

Table 4. Variation in psychological outcomes within the NACT cohort.

Variables	Total (n = 57)	NACT regimen			PD-1/PD-L1 inhibitor			NACT cycle			TRG		
		FLOT/FOLFOX (n = 4)	SOX/XELOX (n = 53)	*p*	With (n = 27)	Without (n = 30)	*p*	>3 (n = 24)	≤3 (n = 33)	*p*	0–1 (n = 13)	2–3 (n = 44)	*p*
Anxiety, n (%)				0.569			0.132			0.045			0.172
No	12 (21.05)	0 (0.00)	12 (22.64)		8 (29.63)	4 (13.33)		2 (8.33)	10 (30.30)		5 (38.46)	7 (15.91)	
Yes	45 (78.95)	4 (100.00)	41 (77.36)		19 (70.37)	26 (86.67)		22 (91.67)	23 (69.70)		8 (61.54)	37 (84.09)	
Depression, n (%)				0.790			0.653			0.014			0.144
No	25 (43.86)	1 (25.00)	24 (45.28)		11 (40.74)	14 (46.67)		6 (25.00)	19 (57.58)		8 (61.54)	17 (38.64)	
Yes	32 (56.14)	3 (75.00)	29 (54.72)		16 (59.26)	16 (53.33)		18 (75.00)	14 (42.42)		5 (38.46)	27 (61.36)	

TRG, tumor regression grade; FLOT, fluorouracil, leucovorin, oxaliplatin, and docetaxel; FOLFOX, fluorouracil, leucovorin, and oxaliplatin; SOX, S-1 plus oxaliplatin; XELOX, capecitabine plus oxaliplatin; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1.

Table 5. Anxiety and Depression related factors within the NACT cohort.

Variables	Anxiety		Depression	
	p	OR (95% CI)	*p*	OR (95% CI)
NACT regimen, SOX/XELOX vs. FLOT/FOLFOX	0.993	NE	0.444	0.40 (0.04–4.13)
PD-1/PD-L1 inhibitor, with vs. without	0.140	0.37 (0.10–1.39)	0.653	1.27 (0.45–3.64)
Chemotherapy cycle, >3 vs. ≤3	0.059	4.78 (0.94–24.33)	0.017	4.07 (1.28–12.90)
TRG, 2–3 vs. 0–1	0.089	3.30 (0.83–13.12)	0.151	2.54 (0.71–9.06)

OR, Odds Ratio; CI, Confidence Interval; NE, not estimable after Firth-adjusted logistic regression. Models were adjusted for age, sex, clinical TNM stage, planned surgical procedure, education and income.

tients more vulnerable at the time of surgery [21]. Moreover, previous studies have demonstrated that poor psychological status correlates with unfavorable overall survival in gastrointestinal malignancies [8,22]. Collectively, these findings highlight the importance of integrating routine psychological screening and targeted mental health interventions into perioperative care, especially for patients receiving extended NACT.

No significant psychological differences were found between patients treated with SOX/XELOX and those receiving FLOT/FOLFOX, consistent with prior research demonstrating comparable efficacy and recovery outcomes across these regimens [23,24]. Although psychiatric side effects of immune checkpoint inhibitors have been reported in other malignancies, evidence in [25–27] gastric cancer remains scarce [25–27]. In our analysis, no statistically significant association was observed between PD-1/PD-L1 inhibitor use and psychological outcomes. Taken together, these results indicate that the psychological burden among NACT recipients is more likely attributable to the cumulative effects of multidrug chemotherapy and associated physiological and emotional stress, rather than to any specific regimen.

In addition, a favorable response to NACT appeared to alleviate psychological burden. Patients who achieved major tumor regression reported lower levels of anxiety and depression, suggesting that clear evidence of treatment efficacy may confer psychological benefits by reducing illness-related uncertainty and fostering hope. This observation aligns with established findings in psycho-oncology [28].

Beyond treatment-related factors, sociodemographic characteristics also influenced psychological well-being. Unmarried individuals and those with lower income levels were more likely to experience anxiety and depression, likely due to reduced social support, financial strain, and social isolation [8,9].

Although smoking and alcohol use initially appeared protective in univariate models, these associations diminished after adjustment, possibly reflecting short-term coping mechanisms rather than genuine protective effects [29]. Furthermore, patients with religious affiliation or greater awareness of their disease tended to demonstrate better psychological status. While these trends did not achieve statistical significance, they suggest that interventions designed to strengthen emotional support and manage patient expectations may serve as effective strategies to mitigate distress.

This study has several limitations. First, its single-center, observational design and modest sample size may reduce generalizability. Second, the unequal distribution between the NACT and surgery-only groups, together with differential participation, resulted in small subgroups and potential bias, lowering statistical power. Third, pre-treatment psychological status was sourced from medical documentation rather than HADS assessment; direct comparison with postoperative scores may be limited, and raising the possibility of underreporting baseline psychological distress. Psychological outcomes were measured only during the early postoperative period, when most patients had not yet received final pathology or adjuvant-therapy recommendations; thus, the findings primarily reflect the immediate psychological burden of NACT and surgery rather than long-term trajectories. Finally, as patients receiving NACT often present with more advanced disease, residual confounding may remain despite multivariable adjustment.

Conclusions

This study demonstrated that NACT, particularly when prolonged, imposes a significant psychological burden on patients undergoing surgery for gastric cancer. Comprehensive cancer care should therefore include early screening, psychosocial support, and individualized interventions to address mental health needs, thereby improving both emotional well-being and clinical outcomes.

Availability of Data and Materials

The data used and analyzed during the current study are available from the corresponding authors upon reasonable request.

Author Contributions

HL, RY and DC designed the study. YL and WG reviewed and revised the research protocol, refined the methodology and supervised the project. HL, RY, DC, WX, FL and CT were responsible for data collection and analysis. CT, JH, BL and CH performed data interpretation and statistical analysis. WX, BL, and JH contributed to the visualization. HL and RY wrote the original manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine (No. I2025967). All procedures were conducted in compliance with the ethical principles of the Declaration of Helsinki and regulatory standards. Written informed consent was obtained from all participants prior to the administration of questionnaires and clinical data collection.

Acknowledgment

Not applicable.

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Conflict of Interest

Weihua Gong is serving as one of the Editorial Board Members of this journal. We declare that Weihua Gong had no involvement in the peer review of this article and has no access to information regarding its peer review. Other authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.62713/aic.4344.

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