



Effect of negative emotions on patients with advanced gastric cancer receiving systemic chemotherapy: a prospective study

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Background: Most patients with advanced gastric cancer (GC) are treated with systemic chemotherapy and many factors have remarkable impacts on their prognosis. However, the importance of psychological status in the prognosis of advanced GC patients is still unclear. This prospective study was performed to analyze the impact of negative emotions on GC patients treated with systemic chemotherapy.

Methods: Advanced GC patients admitted to our hospital between January 2017 and March 2019 were prospectively enrolled. Demographic and clinical data were collected, as were any adverse events (AEs) related to systemic chemotherapy. Self-rating anxiety scale (SAS) and self-rating depression scale (SDS) were used to assess negative emotions. The primary outcome was progression-free survival (PFS) and overall survival (OS), and the secondary outcome was the quality of life which was assessed by The European Organization for Research and Treatment of Quality of Life Questionnaire-Core 30. Cox proportional hazards models were used to analyze the effects of negative emotions on prognosis, and logistic regression models were used to analyze the risk factors related to negative emotions.

Results: A total of 178 advanced GC patients were enrolled in this study. A total of 83 patients were divided into a negative emotion group and 95 patients were divided into normal emotion group. 72 patients experienced AEs during treatment. Many more patients experienced AEs in the negative emotion group than in the normal emotion group (62.7% vs. 21.1%, $P < 0.001$). Enrolled patients were followed up for at least 3 years. It was found both PFS and OS were much lower in the negative emotion group than in the normal emotion group ($P = 0.0186$ and 0.0387 , respectively). Participants in negative emotion group had lower health status and more severe symptoms. Negative emotions, lower body mass index (BMI), and IV tumor stage were identified as risk factors. In addition, higher BMI and marital status were identified as protective factors of negative emotions.

Conclusions: Negative emotions have a significant adverse effect on the prognosis of GC patients. The main risk factor of negative emotions is AEs during treatment. It is necessary to closely monitor the treatment process and improve the psychological status of patients.

Keywords: Negative emotions; advanced gastric cancer (GC); systemic chemotherapy; prospective study

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Introduction

Gastric cancer (GC) is one of the most common gastrointestinal malignancies and one of the most common causes of cancer-related deaths (1,2). Early-stage GC can be treated by endoscopic submucosal dissection or surgical resection, which significantly prolongs the survival time of patients (3). However, more than half of GC patients have reached an advanced stage by the time of diagnosis, meaning that they have missed the opportunity for radical surgical treatment (4,5). At present, most patients with advanced GC are treated with systemic chemotherapy to prolong their survival time. The progression-free survival (PFS) and overall survival (OS) in advanced GC patients have been reported to be 4.9–6.0 months and 10.5–14.1 months, respectively (6,7). How to improve the treatment and nursing in patients with advanced GC receiving chemotherapy to further improve their prognosis is one of the current research hotspots.

There have been many studies on the factors related to the prognosis of GC patients treated with systemic chemotherapy (6,8-13). The most important factor is the sensitivity of GC cells to the treatment regimen (14). At present, there are a large number of randomized controlled trials (RCTs) on the efficacy of different therapeutic drugs and combinations on GC (15-17). In addition, the nutritional status, lymph node metastasis, and GC pathological type are also related to the prognosis of

patients (8,13,18). A study on other cancers pointed out that negative emotions were important for the quality of life in patients with thyroid cancer (19). Similarly, a recent study from South Korea pointed out that GC patients had a 1.28 times higher risk of depression than healthy people (20). Many studies have reported that the incidence of postoperative anxiety and depression in GC patients is more than 30%, and the occurrence of anxiety and depression will lead to the shortening of PFS and OS (20,21). Among patients with GC who relapsed after surgery, the incidence of negative emotions can be up to 52.4%, and the risk factors of negative emotions include old age, diabetes, and early recurrence (22). However, there have been few studies on the psychological status of advanced GC patients receiving systemic chemotherapy and it is still unclear whether negative emotions affect the prognosis of patients with advanced GC. Through decades of clinical work, our team found that the psychological state of patients with advanced GC often fluctuated significantly during the period of receiving systematic chemotherapy. We proposed a hypothesis that the occurrence of negative emotions may lead to patients' treatment failure and poor prognosis.

Based on this hypothesis, we performed this prospective study to enroll advanced GC patients receiving systemic chemotherapy in a single treatment center. The data of negative emotions, survival time, and quality of life of patients were collected to analyze the impact of negative emotions on patients with advanced GC. At the same time, the risk factors of negative emotions were also analyzed to provide a basis for clinical psychological nursing. We present the following article in accordance with the STROBE reporting checklist (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-23-248/rc>).

Methods

Study design

This was a prospective cohort study that was approved by the Ethics Committee of the Affiliated Hospital of Nantong University (No. 2017019). Written informed consents were provided by GC patients before they were enrolled in the study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Patient selection

Advanced GC patients who were admitted to the Affiliated

Highlight box

Key findings

- Negative emotions have a significant adverse effect on the prognosis of gastric cancer (GC) patients during systemic chemotherapy treatment. The main risk factor of negative emotions is adverse events during treatment.

What is known and what is new?

- The incidence of postoperative anxiety and depression in GC patients was more than 30%, and the occurrence of anxiety and depression will lead to the shortening of progression-free survival (PFS) and overall survival (OS).
- 46.6% of advanced GC patients experienced negative emotions during systemic chemotherapy treatment, which were related to shortened PFS and OS as well as diminished quality of life.

What is the implication, and what should change now?

- It is necessary to closely monitor and manage adverse events in patients during the process of GC treatment and improve the psychological status of patients.

Hospital of Nantong University between January 2017 and March 2019 were enrolled in this prospective study. The inclusion criteria were as follows: (I) adult patients with advanced GC, (II) patients receiving systemic chemotherapy without other treatments, (III) patients with an expected survival of more than 6 months. The exclusion criteria were as follows: (I) patients with secondary GC, (II) patients with serious organ dysfunctions, (III) patients with mental disease or family history of mental disease, (IV) patients who were lost to follow up, (V) patients with incomplete clinical data.

Data collection

The following data were prospectively collected: gender (male/female), age, body mass index (BMI), marital status (married/single or divorced or widowed), employment status (employed and unemployed), educational status (high school degree or above/below high school degree), hypertension, diabetes mellitus, chronic diseases (heart, liver, kidney and lung disease), smoking history, drinking history, tumor location (gastric fundus and cardia/gastric body/gastric antrum and pylorus), tumor-node-metastasis (TNM) staging, pathological type (tubular adenocarcinoma/mucinous adenocarcinoma/other), and tumor differentiation degree.

All enrolled patients were followed up for at least 3 years or until death via Internet or phone. Adverse events (AEs) which were related to systemic chemotherapy were recorded, including peripheral sensory neuropathy, nausea or vomiting, diarrhea, decreased neutrophil count, fatigue, constipation, pruritus, and anemia. The primary outcome in this study was the PFS and OS in enrolled patients. Besides, the quality of life of participants was assessed by The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) and Quality of Life Questionnaire-Stomach Cancer 22 (QLQ-STO22). A lower score in QLQ-C30 and a higher score in QLQ-STO22 indicated higher quality of life.

Negative emotion measurement

Negative emotions of enrolled GC patients in this study were assessed by self-rating anxiety scale (SAS) and self-rating depression scale (SDS). The total score of SAS and SDS was 100 points: <50 points indicated no anxiety

or depression, 50–70 points indicated mild anxiety or depression, 71–90 points indicated moderate anxiety or depression, and >90 points indicated severe anxiety or depression. A higher score indicated more severe anxiety or depression. Patients were assessed for anxiety and depression at admission and during follow-up, and the worst SAS score and SDS score of GC patients during the follow-up was recorded. If either the SAS or SDS score of the patient was greater than 50 points during the treatment, the patient was defined as having negative emotions. Participants were divided accordingly into a negative emotion group and a normal emotion group.

Statistical analysis

The software SPSS 22.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses in this study. Student's *t*-test was used to analyze the statistical difference of continuous variables between 2 groups, and chi-square test was used to analyze the statistical difference of category variables between 2 groups. A Kaplan–Meier curve was generated to analyze PFS and OS of enrolled patients. Univariate and forward stepwise multivariable Cox proportional hazards models were used to analyze the effects of negative emotions on prognosis in advanced GC patients. Then, univariate and multivariate logistic regression models were used to analyze the risk factors related to negative emotions in advanced GC patients. A two-sided *P* value less than 0.05 was considered a significant difference between 2 groups.

Results

The flow chart of GC patients admitted to our hospital is shown in *Figure 1*, and a total of 178 advanced GC patients were enrolled in this study. The demographic and clinical data of enrolled patients are exhibited in *Table 1*. A total of 129 (72.5%) patients were male and 49 (27.5%) patients were female. Their mean age was 60.1 ± 5.7 years and mean BMI was 23.0 ± 4.2 . A total of 136 (76.4%) participants were married and 135 (75.8%) were employed. There were 58 (32.6%), 32 (18.0%), and 26 (14.6%) patients with hypertension, diabetes mellitus, and chronic diseases, respectively. About one-third of participants had a history of smoking and drinking. All participants had advanced GC, who were diagnosed as stage III and IV. The most common pathological type was tubular adenocarcinoma and mucinous

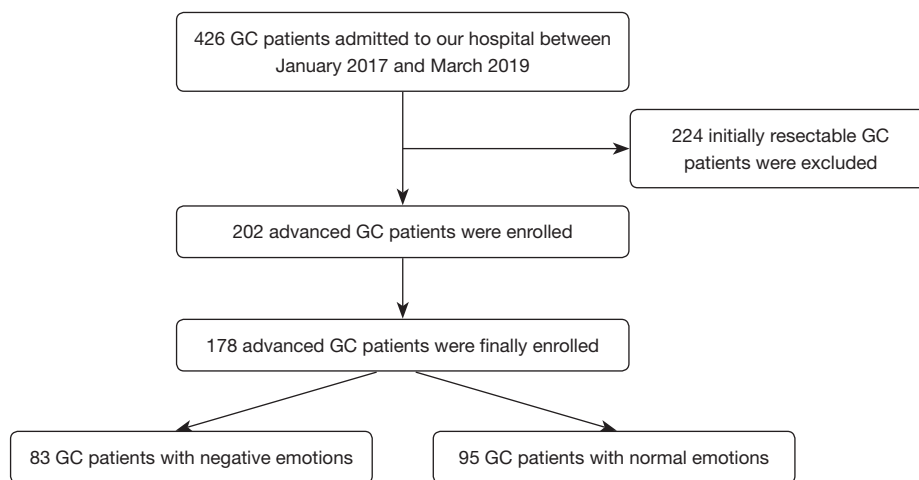


Figure 1 Flow chart. GC, gastric cancer.

Table 1 Demographic and clinical data of patients

Variables	Number (n=178)
Gender, n (%)	
Male	129 (72.5)
Female	49 (27.5)
Age (year), mean \pm SD	60.1 \pm 5.7
BMI, mean \pm SD	23.0 \pm 4.2
Marital status, n (%)	
Married	136 (76.4)
Single or divorced or widowed	42 (23.6)
Employed status, n (%)	
Employed	135 (75.8)
Unemployed	43 (24.2)
Educational status, n (%)	
High school degree or above	48 (27.0)
Below high school degree	130 (73.0)
Hypertension, n (%)	58 (32.6)
Diabetes mellitus, n (%)	32 (18.0)
Chronic diseases, n (%)	26 (14.6)
Smoking history, n (%)	58 (32.6)
Drinking history, n (%)	66 (37.1)

Table 1 (continued)

Table 1 (continued)

Variables	Number (n=178)
Tumor location, n (%)	
Gastric fundus and cardia	43 (24.2)
Gastric body	37 (20.8)
Gastric antrum and pylorus	98 (55.1)
TNM staging, n (%)	
III	84 (47.2)
IV	94 (52.8)
Pathological type, n (%)	
Tubular adenocarcinoma	84 (47.2)
Mucinous adenocarcinoma	61 (34.3)
Other	33 (18.5)
Differentiation degree, n (%)	
Well differentiation	84 (47.2)
Moderate or poor differentiation	94 (52.8)
SAS score at admission, mean \pm SD	50.4 \pm 11.9
Worst SAS score during treatment, mean \pm SD	53.5 \pm 12.4
SDS score at admission, mean \pm SD	48.7 \pm 9.4
Worst SDS score during treatment, mean \pm SD	51.7 \pm 11.8

SD, standard deviation; BMI, body mass index; TNM, tumor-node-metastasis; SAS, self-rating anxiety scale; SDS, self-rating depression scale.

adenocarcinoma. About half of GC cases were well differentiated. The mean SAS and SDS score at admission of participants was 50.4 ± 11.9 points and 48.7 ± 9.4 points, respectively. Besides, mean worst SAS and SDS score during treatment of participants were 53.5 ± 12.4 points and 51.7 ± 11.8 points, respectively.

According to the worst SAS and SDS score during treatment, participants were divided into a negative emotion group and a normal emotion group. Comparing the demographic and clinical data of 2 groups, it was found that patients in the negative emotion group were much older than those in the normal emotion group (61.2 ± 6.1 vs. 59.2 ± 5.1 , $P=0.017$) as shown in *Table 2*. Mean BMI was lower in the negative emotion group than in the normal emotion group (22.2 ± 4.5 vs. 23.7 ± 3.8 , $P=0.015$). Besides, more patients were single or divorced or widowed in the negative emotion group than in the normal emotion group (31.3% vs. 16.8% , $P=0.023$). There was no significant difference found between the 2 groups in other data.

The AEs are recorded in *Table 3*. Totally, 72 patients experienced AEs during treatment, 49 events led to dose reduction, and 12 events led to treatment discontinuation. The most common AE was nausea or vomiting, following by diarrhea, decreased neutrophil count, fatigue, peripheral sensory neuropathy, constipation, pruritus, and anemia. Comparison of the incidence of AEs in 2 groups revealed that many more patients experienced AEs in the negative emotion group than in the normal emotion group (62.7% vs. 21.1% , $P<0.001$).

Participants were followed up for at least 3 years, and PFS and OS were analyzed using Kaplan–Meier curves, as shown in *Figure 2*. It was found that both PFS and OS were much lower in the negative emotion group than in the normal emotion group ($P=0.0186$ and 0.0387 , respectively). Then EORTC QLQ-C30 and QLQ-STO22 scores are summarized in *Figure 3* and were compared between the 2 groups. The results indicated that negative emotion group participants had a much lower global health status score, physical function score, and emotional function score than those in the normal emotion group ($P<0.001$). Besides, patients in the negative emotion group had a much higher fatigue score, dyspnea score, appetite loss score, nausea/vomiting score, and diarrhea score ($P<0.001$). Some 9 items of QLQ-STO22 were also compared between the 2 groups, which indicated that patients in the negative emotion group had much higher dysphasia score, reflux symptoms score, abnormal taste score, and anxiety score ($P<0.001$).

The risk factors of OS were calculated according to the Cox proportional hazards model as shown in *Table 4*. It was indicated that negative emotions, older age, lower BMI, diabetes mellitus, IV tumor stage, and moderate or poor differentiation degree may be related to OS in the univariable model. Then, negative emotions, lower BMI, and IV tumor stage were identified as risk factors in multivariable model. In addition, higher BMI and marital status were identified as protective factors of negative emotions according to multivariable logistic regression model as shown in *Table 5*. The occurrence of AEs acted as the most important factor of negative emotions in advanced GC patients.

Discussion

To our knowledge, this is the first study to investigate the effects of negative emotions on the prognosis of advanced GC patients. This prospective study enrolled 178 patients between January 2017 and March 2019 collected their demographic and clinical data and followed up the participants for at least 3 years. The results indicated that 46.6% of advanced GC patients had negative emotions during treatment of systemic chemotherapy. Negative emotions were related to shortened PFS and OS as well as worse quality of life. Negative emotions, lower BMI, and IV tumor stage were identified as risk factors of OS. The occurrence of AEs acted as the most important factor of negative emotions in advanced GC patients.

Our study recorded the negative emotions of advanced GC patients at admission and during treatment. The results showed that 44.4% of the patients had negative emotions at admission, and there was a trend of deterioration during the treatment. This is similar to the results of previous studies. The probability of negative emotions in patients with postoperative recurrence of GC can reach 52.4% (22). A meta-analysis including 18 studies reported that the pooled prevalence of negative emotions among GC patients was 37% (21). This also suggests that negative emotions are widespread in GC patients and need to be paid attention to.

After grouping patients according to whether they had negative emotions, we focused on the impact of negative emotions on the prognosis of advanced GC patients. Overall, the PFS rate and OS rate of GC patients in our study are relatively low, similar to previous studies (23,24). Moreover, our results indicated that the occurrence of negative emotions would significantly affect both PFS and

Table 2 Comparisons between patients in 2 groups

Variables	Negative emotion group (n=83)	Normal emotion group (n=95)	P value
Gender, n (%)			
Male	61 (73.5)	68 (71.6)	0.775
Female	22 (26.5)	27 (28.4)	
Age (year), mean \pm SD	61.2 \pm 6.1	59.2 \pm 5.1	0.017
BMI, mean \pm SD	22.2 \pm 4.5	23.7 \pm 3.8	0.015
Marital status, n (%)			
Married	57 (68.7)	79 (83.2)	0.023
Single or divorced or widowed	26 (31.3)	16 (16.8)	
Employed status, n (%)			
Employed	60 (72.3)	75 (78.9)	0.301
Unemployed	23 (27.7)	20 (21.1)	
Educational status, n (%)			
High school degree or above	20 (24.1)	28 (29.5)	0.420
Below high school degree	63 (75.9)	67 (70.5)	
Hypertension, n (%)	30 (36.1)	28 (29.5)	0.343
Diabetes mellitus, n (%)	16 (19.3)	16 (16.8)	0.673
Chronic diseases, n (%)	11 (13.3)	15 (15.8)	0.633
Smoking history, n (%)	28 (33.7)	30 (31.6)	0.759
Drinking history, n (%)	33 (39.8)	33 (34.7)	0.489
Tumor location, n (%)			
Gastric fundus and cardia	22 (26.5)	21 (22.1)	0.787
Gastric body	17 (20.5)	20 (21.1)	
Gastric antrum and pylorus	44 (53.0)	54 (56.8)	
TNM staging, n (%)			
III	38 (45.8)	46 (48.4)	0.725
IV	45 (54.2)	49 (51.6)	
Pathological type, n (%)			
Tubular adenocarcinoma	37 (44.6)	47 (49.5)	0.714
Mucinous adenocarcinoma	31 (37.3)	30 (31.6)	
Other	15 (18.1)	18 (18.9)	
Differentiation degree, n (%)			
Well differentiation	35 (42.2)	49 (51.6)	0.210
Moderate or poor differentiation	48 (57.8)	46 (48.4)	

Table 2 (continued)

Table 2 (continued)

Variables	Negative emotion group (n=83)	Normal emotion group (n=95)	P value
SAS score at admission, mean \pm SD	51.3 \pm 10.6	49.6 \pm 12.9	0.336
Worst SAS score during treatment, mean \pm SD	65.3 \pm 6.7	43.2 \pm 4.1	<0.001
SDS score at admission, mean \pm SD	48.9 \pm 8.0	48.6 \pm 10.5	0.833
Worst SDS score during treatment, mean \pm SD	62.5 \pm 6.7	42.3 \pm 5.6	<0.001

SD, standard deviation; BMI, body mass index; TNM, tumor-node-metastasis; SAS, self-rating anxiety scale; SDS, self-rating depression scale.

Table 3 Adverse events in 2 groups

Variables	Total (n=178)	Negative emotion group (n=83)	Normal emotion group (n=95)	P value
Patients with adverse events, n (%)	72 (40.4)	52 (62.7)	20 (21.1)	<0.001
Events leading to dose reduction, n (%)	49 (27.5)	37 (44.6)	12 (12.6)	<0.001
Events leading to discontinuation, n (%)	12 (6.7)	9 (10.8)	3 (3.2)	0.041
Nausea or vomiting, n (%)	42 (23.6)	31 (37.3)	11 (11.6)	<0.001
Diarrhea, n (%)	29 (16.3)	18 (21.7)	11 (11.6)	0.069
Decreased neutrophil count, n (%)	25 (14.0)	18 (21.7)	7 (7.4)	0.006
Fatigue, n (%)	19 (10.7)	14 (16.9)	5 (5.3)	0.012
Peripheral sensory neuropathy, n (%)	17 (9.6)	9 (10.8)	8 (8.4)	0.583
Constipation, n (%)	13 (7.3)	9 (10.8)	4 (4.2)	0.090
Pruritus, n (%)	12 (6.7)	6 (7.2)	6 (6.3)	0.808
Anemia, n (%)	8 (4.5)	4 (4.8)	4 (4.2)	0.845

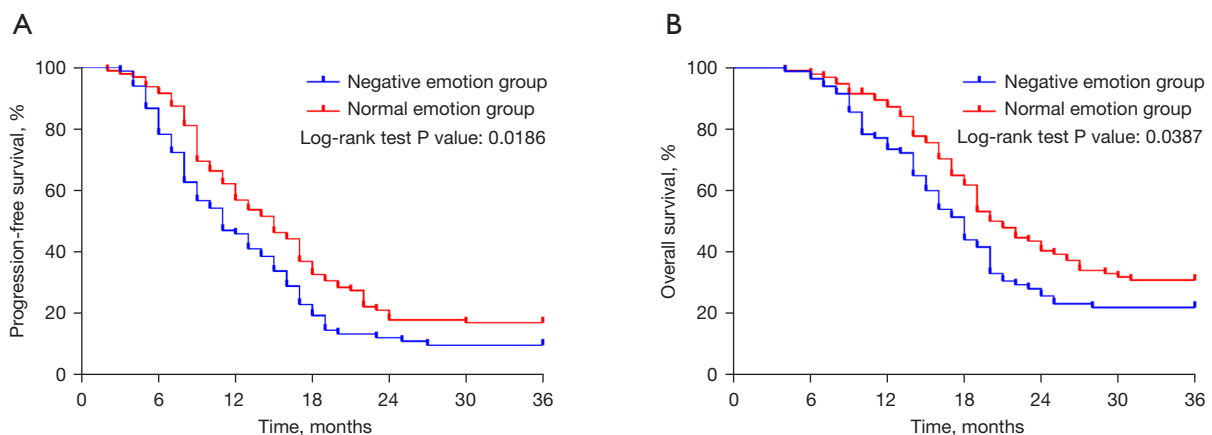


Figure 2 PFS (A) and OS (B) of GC patients in negative emotion group and normal emotion group. PFS, progression-free survival; OS, overall survival; GC, gastric cancer.

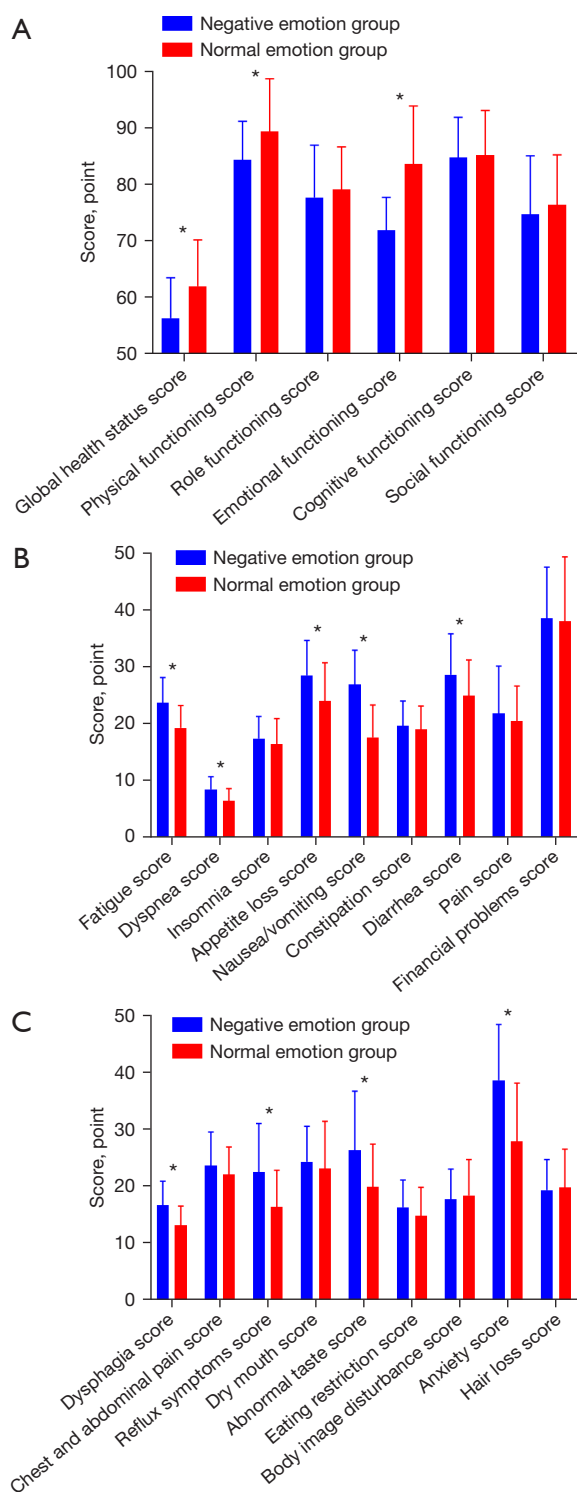


Figure 3 QLQ-C30 healthy status scores (A), symptom scores (B) and QLQ-STO22 scores (C) of GC patients in negative emotion group and normal emotion group. *, $P < 0.001$. QLQ-C30, Quality of Life Questionnaire-Core 30; QLQ-STO22, Quality of Life Questionnaire-Stomach Cancer 22; GC, gastric cancer.

OS. Negative emotions were identified as an important risk factor of OS according to Cox proportional hazards models. Previous studies have shown that the occurrence of negative emotions was associated with postoperative recurrence and postoperative complications in GC patients (25-27). In general, in view of the adverse effects of negative emotions on the prognosis of GC patients, it is necessary to prevent and intervene them at an early stage.

In order to provide guidance for clinical nursing and intervention of negative emotions, we analyzed the potential risk factors of negative emotions through multi factor logistic regression models. Our study pointed out that BMI, marital status, and AEs of systemic chemotherapy were related to the occurrence of negative emotions. Previous studies have found that older age was also a risk factor for negative emotions (22,28). However, after adjustment of multivariate analysis, age may not have been related to negative emotions in our study. Other studies have pointed out that women are more likely to experience negative emotions (29). Some studies have improved a series of nursing measures to improve the psychological status of GC patients, so as to improve the prognosis of patients (4,5). Our research also suggested that the prevention and active management of AEs of systemic chemotherapy can effectively reduce the occurrence of negative emotions, further improve the prognosis of patients, and prolong the survival time of patients.

Some limitations should be noted in this study. First, this study was a single center, small sample study, which may limit the accuracy of the results. Second, there may be some differences in the systemic chemotherapy regimen of patients in this study, and the change of treatment regimen during the treatment process may affect the OS. Third, the evaluation of negative emotions depends on SAS and SDS. These 2 scales are highly subjective, which may lead to the bias of study results.

Conclusions

Our study revealed that negative emotions are one of the common adverse status in advanced GC patients, and they may exhibit a worsening trend during treatment of systemic chemotherapy. The occurrence of negative emotions will have a significant adverse impact on the prognosis of GC patients, and shorten the PFS time and OS time of GC patients. The main risk factor of negative emotions is AEs during treatment. Thus, it is necessary to closely monitor and manage AEs in patients during the

Table 4 Risk factors of overall survival according to Cox proportional hazards model

Variables	Multivariable	
	HR (95% CI)	P value
Negative emotions	0.702 (0.497, 0.997)	0.045
Older age	0.974 (0.944, 1.005)	0.092
Lower BMI	0.950 (0.910, 0.992)	0.020
Diabetes mellitus	0.544 (0.275, 1.078)	0.081
TNM stage (IV vs. III)	0.634 (0.438, 0.918)	0.016
Differentiation degree (moderate or poor vs. well)	0.769 (0.528, 1.121)	0.173

HR, hazard ratio; CI, confidence interval; BMI, body mass index; TNM, tumor-node-metastasis

Table 5 Risk factors of negative emotions according to logistic regression model

Variables	Multivariable	
	OR (95% CI)	P value
Older age	1.049 (0.987, 1.115)	0.127
Higher BMI	0.917 (0.843, 0.997)	0.042
Marital status (married vs. others)	0.448 (0.204, 0.987)	0.046
Adverse events	6.058 (3.045, 12.052)	<0.001

OR, odds ratio; CI, confidence interval; BMI, body mass index.

process of GC treatment and improve the psychological status of patients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://jgo.amegroups.com/article/view/10.21037/jgo-23-248/rc>

Data Sharing Statement: Available at <https://jgo.amegroups.com/article/view/10.21037/jgo-23-248/dss>

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Conflicts of Interest: All authors have completed the ICMJE

uniform disclosure form (available at <https://jgo.amegroups.com/article/view/10.21037/jgo-23-248/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This was a prospective cohort study that was approved by the Ethics Committee of the Affiliated Hospital of Nantong University (No. 2017019). Written informed consents were provided by GC patients before they were enrolled in the study.

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