

Prevalence rate and influencing factors of preoperative anxiety and depression in gastric cancer patients in China: Preliminary study

Le Xu^{1,2}, Qiong Pan^{2*} and Renqin Lin^{2*}

Abstract

Objectives: To investigate the prevalence rate and influencing factors of preoperative anxiety and depression in patients with gastric cancer, in China.

Methods: Patients with gastric cancer who were diagnosed by gastroscopy and would accept laparoscopic surgery were eligible for the study. Each participant completed self-administered questionnaires, including the Hospital Anxiety and Depression Scale (HADS), Medical Coping Modes Questionnaire (MCMQ), Social Support Rating Scale, and Type D personality scale before surgery. Routine blood tests were undertaken within 7 days before surgery, to calculate the neutrophil-to-lymphocyte ratio (NLR). Based on HADS, patients were divided into an anxiety/depression group and a nonanxiety/depression group.

Results: Fifty-three patients with gastric cancer were included in the study. The prevalence of preoperative anxiety and/or depression was 20.75% (11/53). Factors influencing preoperative anxiety and depression were a resigned dimension of coping style, type D personality and NLR. Logistic regression analysis showed that a higher score for the resigned dimension of coping style on the MCMQ and a higher NLR were significantly associated with preoperative anxiety and depression.

Conclusions: The prevalence of preoperative anxiety and depression in Chinese patients with gastric cancer may be influenced by both the coping mode and NLR.

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*These authors are co-first authors.

Corresponding author:

Le Xu, Department of Nursing, Fujian Medical University Union Hospital, No. 29 Xin Quan Road, Gulou District, Fuzhou, Fujian Province, 350001, China.

Email: xl_8332@126.com

¹Department of Nursing, Fujian Medical University Union Hospital, Fuzhou, Fujian Province, China

²Fujian Medical University Union Clinical Medical Institute, Fuzhou, Fujian Province, China



Keywords

Gastric cancer, anxiety, depression, prevalence, influencing factors

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Introduction

Cancer poses a major threat to public health worldwide; cancer incidence rates have increased in most countries since 1990.¹ Cancer caused over 8.2 million deaths worldwide in 2013 and has moved from the third leading cause of death in 1990 to the second leading cause, behind cardiovascular disease, in 2013.¹ Cancer is currently recognized as a controllable chronic disease; its diagnosis and treatment conform to the biopsychosocial medical model proposed by the American scholar, George L. Engel.² In addition to providing treatment to achieve maximum control and reduce the physiological damage caused by cancer, patients should be closely monitored for the potential psychological consequences of cancer, to improve their disease resistance and maintain a high health-related quality-of-life (HRQoL).²

A good psychological state plays an important role in the diagnosis and treatment of cancer as a psychosomatic disease.³ Anxiety and depression have been reported to be the two most common psychological problems in cancer patients.⁴ Clinical research has shown that comorbid depression and anxiety are of major importance, resulting in more severe symptoms, impairment, subjective distress and a long-term course than either anxiety or depression alone.⁵ In 1997, British researchers considered all or at least some of the symptoms of anxiety to reflect depression.⁶ Thus, the combination of anxiety and depression has been deemed by some scholars to be critical to the diagnosis and treatment of cancer patients.⁷ To date, information about preoperative anxiety and depression in patients

with gastric cancer throughout the world has rarely been reported.⁸

This preliminary study aimed to investigate preoperative anxiety and depression in patients with gastric cancer, with a view to providing scientific evidence to support a theoretical basis for preventing preoperative anxiety and depression, improving postoperative rehabilitation, enhancing HRQoL, and increasing survival time.

Patients and methods

Patients

This preliminary cross-sectional study enrolled consecutive patients diagnosed with gastric cancer by gastroscopy and admitted to the Gastric Surgery Ward of Fujian Medical University Union Hospital, Fuzhou, Fujian Province, China between September 2014 and January 2015. Inclusion criteria were: (i) diagnosed with gastric cancer by gastroscopy and clinical pathology; (ii) aged ≥ 18 years; (iii) prepared to accept laparoscopic surgery; (iv) fully understood their medical conditions and agreed to participate in the survey. Exclusion criteria were: (i) concomitant mental or psychological disease, or communication disorders; (ii) took antianxiety drugs, antidepressants or β -blockers within 3 days prior to the start of the study; (iii) drug or alcohol dependence; (iv) concomitant inflammation.

In terms of selecting the correct sample size, according to the multivariate statistical method, the sample size should be 5 to 20 times as large as the independent variables that are being measured. Nine independent variables were measured in the present study: patients' age; sex; residence;

insurance status; clinical staging; social support; coping styles; type D personality; neutrophil-to-lymphocyte ratio (NLR).

Ethical approval for the study was provided by the Ethics Committee of The Union Hospital of Fujian Medical University (reference no. 2015KY017). All patients provided verbal informed consent.

Investigational methods

On obtaining verbal informed consent, patients were asked to complete self-administered questionnaires independently on the day before surgery. If patients had difficulties completing the questionnaire, healthcare personnel were there to help them, which guaranteed the consistency of explanations regarding the questions being asked.

Routine blood samples were collected from all patients within 7 days prior to surgery and the NLR was calculated. A blood sample (3–5 ml) was taken from the cubital vein using standard methods, and added to 3.7–5.4 $\mu\text{mol/ml}$ of ethylenediaminetetra-acetic acid-K2. Blood samples were stored at 18–22°C and tested within 2 h of being drawn.

Anxiety and depression instruments

Patients completed a general information form that included age, sex, place of residence and source of medical payments; they also completed several mental health questionnaires. The Hospital Anxiety and Depression Scale (HADS), which contains 14 items, was used to assess anxiety and depression (seven anxiety items and seven depression items); the cut-off score for screening anxiety and depression is 11 and the effectiveness of the Chinese version of the HADS has been validated.⁹ Patient coping was measured using the Medical Coping Modes Questionnaire (MCMQ).¹⁰ The MCMQ contains 20 items and three

dimensions that correspond to three disease-related cognitive and behavioural coping modes: confrontive, avoidant and resigned. Each item is scored on a four-point Likert scale (from 1 to 4, with each score indicating a different frequency of each coping mode's use (e.g. never, sometimes, often, always); this scale has good reliability and validity.¹¹ Social support was measured using the Social Support Rating Scale (SSRS),¹² which also has good reliability and validity.¹³ The SSRS contains 10 items, each of which is also scored on a four-point Likert scale (from 1 to 4, with a higher total score indicating a higher level of total support). The SSRS evaluates social support on three dimensions: objective support, subjective support and support utilization. The type D scale-14 (DS-14) was used for psychological assessment;¹⁴ the Chinese version of the DS-14 has demonstrated good reliability and validity.¹⁵ The DS-14 includes two subscales: negative affectivity (NA) and social inhibition (SI); each subscale contains seven items and each item is rated on a five-point scale (ranging from 0, false to 4, true). A type D personality is defined as $NA \geq 10$ and $SI \geq 10$.

Based on the findings from HADS,⁹ patients were stratified into two groups: those with anxiety and/or depression were included in the anxiety/depression group; those with no symptoms of anxiety and/or depression were included in the nonanxiety/depression group.

Statistical analyses

All statistical analyses were performed using the SPSS[®] statistical package, version 19.0 (SPSS Inc., Chicago, IL, USA) for Windows[®]. The level of anxiety and depression among patients with gastric cancer was represented as n (%) of patients. Student's t -test was used to compare the means of the two groups for continuous data; χ^2 -test and Fisher's exact test were used to compare

categorical data. Logistic regression analysis was used to examine the independent effects of a resigned coping style, type D personality and NLR. A P -value < 0.05 was considered statistically significant.

Results

Fifty-three participants diagnosed with gastric cancer were included in the study; prior to surgery, each participant's levels of anxiety and depression were measured using HADS. According to the results, two patients had preoperative anxiety symptoms, four had preoperative depression symptoms, and five had both anxiety and depression symptoms. Consequently, these 11 patients formed the anxiety/depression group and the remaining 42 patients without symptoms of anxiety and/or depression formed the nonanxiety/depression group.

The prevalence of preoperative anxiety and depression in gastric cancer patients was therefore 20.75% (11/53). The demographic and clinical characteristics of the two groups are presented in Table 1; there were no significant differences between the two groups.

The results of the MCMQ showed no significant differences between the two groups on the confrontive and avoidant dimensions, but the anxiety/depression group had a significantly higher score on the resigned dimension ($P < 0.05$) (Table 2). Furthermore, confrontive dimension scores in the two groups were significantly lower than the Chinese population norm (19.48 ± 3.81 ; $P < 0.05$), whereas avoidant dimension scores in the two groups were similar to the Chinese population norm (14.44 ± 2.97).¹⁶

The results of the SSRS showed no significant differences between the two groups for objective support, subjective support and support utilization (Table 3). Furthermore, total scores for social support in the two groups were significantly higher

Table 1. Demographic and clinical characteristics of patients with gastric cancer ($n = 53$), included in a study to investigate the extent of preoperative anxiety and depression.

Characteristic	Anxiety/ depression group $n = 11$	Nonanxiety/ depression group $n = 42$
Age, years	59.0 ± 10.4	58.1 ± 10.9
Age range, years	42–78	29–77
Age categories, years		
<60	6 (54.5)	22 (52.4)
≥ 60	5 (45.5)	20 (47.6)
Sex		
Male	6 (54.5)	29 (69.0)
Female	5 (45.5)	13 (31.0)
Residence		
Rural	7 (63.6)	22 (52.4)
Urban	4 (36.4)	20 (47.6)
Medical insurance		
No	1 (9.1)	7 (16.7)
Yes	10 (90.9)	35 (83.3)
Cancer staging		
I	4 (36.4)	9 (21.4)
II	3 (27.3)	8 (19.0)
III	3 (27.3)	21 (50.0)
IV	1 (9.1)	4 (9.5)

Data presented as mean \pm SD or n (%) of patients. Cancer staging was undertaken in accordance with the tumour, node, metastasis staging system of the American Joint Committee on Cancer.⁵⁸

than the Chinese population norm (34.56 ± 3.73 ; $P < 0.05$).¹⁷

The results of the DS-14 instrument showed that the proportion of type D personality in the anxiety/depression group was significantly higher than in the nonanxiety/depression group ($P = 0.0497$) (Table 4).

Blood studies showed that the NLR was significantly higher in the anxiety/depression group compared with the nonanxiety/depression group ($P < 0.05$) (Table 5).

Logistic regression analysis showed that, at $\alpha = 0.05$ significance level, influencing factors of preoperative anxiety and

Table 2. Comparison of coping modes between patients with gastric cancer ($n = 53$), categorized according to presence or absence of preoperative anxiety and depression.

Coping mode	Anxiety/ depression group $n = 11$	Nonanxiety/ depression group $n = 42$
	Confrontive	15.27 ± 5.39
Avoidant	14.45 ± 1.51	14.57 ± 2.63
Resigned	12.18 ± 3.55	8.86 ± 2.01*

Data presented as mean ± SD.

* $P < 0.05$ compared with anxiety/depression group; Student's *t*-test.

Table 3. Comparison of the levels of the different types of social support experienced by patients with gastric cancer ($n = 53$) categorized according to presence or absence of preoperative anxiety and depression.

Type of support	Anxiety/ depression group $n = 11$	Nonanxiety/ depression group $n = 42$
	Objective	9.18 ± 2.48
Subjective	24.36 ± 3.61	24.00 ± 3.85
Utilization	7.64 ± 2.36	7.02 ± 2.17
Total score	41.18 ± 5.89	40.00 ± 5.71

Data presented as mean ± SD.

depression were a resigned dimension of coping style ($P < 0.05$) and NLR ($P < 0.05$).

Discussion

In people with cancer, psychological factors play vital roles in not only tumorigenesis, but also in tumour therapy, subsequent rehabilitation and improvements in HRQoL.^{18,19} Therefore, exploring the psychological state of patients and its influence on cancer patients has become the focus of considerable research.²⁰ Gastric cancer is

Table 4. Comparison of the prevalence of type D personality in patients with gastric cancer ($n = 53$) categorized according to presence or absence of preoperative anxiety and depression.

Group	Type D personality	
	Yes	No
Anxiety/ depression $n = 11$	8 (72.7)*	3 (27.3)
Nonanxiety/ depression $n = 42$	16 (38.1)	26 (61.9)

Data presented as n (%) of patients.

* $P < 0.05$ compared with the nonanxiety/depression group; Fisher's exact test.

Table 5. Comparison of the neutrophil-to-lymphocyte ratio (NLR) in patients with gastric cancer ($n = 53$) categorized according to the presence or absence of preoperative anxiety and depression.

Parameter	Anxiety/ depression group $n = 11$	Nonanxiety/ depression group $n = 42$
	NLR	2.65 ± 8.57

Data presented as mean ± SD.

* $P < 0.05$ compared with anxiety/depression group; Student's *t*-test.

one of the most frequent cancers in the world, with almost two-thirds of gastric cancer cases and deaths occurring in less-developed global regions.^{1,21}

Comprehensive therapy encompassing surgery, chemotherapy and radiotherapy has become the major treatment modality for gastric cancer.²² Studies on anxiety and depression in patients with gastric cancer have mainly examined the diagnosis and treatment of anxiety and depression following chemotherapy or surgery.^{20,23,24} A study in the Republic of Korea reported that, before chemotherapy, the proportion of anxiety-depressive disorders was as high as

63% in 43 patients with advanced gastric cancer.²³ Another study undertaken in the Republic of Korea reported that the prevalence of postoperative depression was 44% in 391 patients with gastric cancer.²⁴ In China, the prevalence rates for anxiety and depression were 30.24% and 63.42%, respectively, in 205 patients with gastric cancer among a total of 1217 cancer patients surveyed.²⁰ Although prevalence rates for preoperative anxiety and depression in patients with gastric cancer have rarely been reported, such rates were 44.7% and 17.1%, respectively, for patients with lung cancer.²⁵ In patients with breast cancer, the prevalence rates of preoperative anxiety and depression reached 70% and 37%, respectively.²⁶ This present study demonstrated a prevalence rate of preoperative anxiety and/or depression of 20.75% in 53 patients with gastric cancer, which was lower than that found in the aforementioned studies.

These current, preliminary, results demonstrate a low prevalence rate of preoperative anxiety and depression in patients with gastric cancer in China, probably owing to the following reasons. First, China's economic development has brought an enormous government investment in all fields of medical insurance, which ensures the medical reimbursement of patients with gastric cancer. Secondly, the continuous rise in the level of medical care in China has made comprehensive therapy accessible to most patients with gastric cancer. Finally, when healthcare personnel actively provide education on the prevention and treatment of tumours (such as gastric cancer), patients affected by the disease (and their family members) can fully understand gastric cancer; thus we believe that they develop a more positive attitude to the disease.

In this present study, 11 patients with gastric cancer presented obvious preoperative symptoms of anxiety and depression. As the major purveyors of cancer prevention and treatment, healthcare personnel should

identify such patients in a timely manner and perform effective interventions, to control their psychological symptoms and improve outcomes.

When Japanese researchers investigated the factors related to depression in 1334 patients with lung cancer, depression was not only correlated with biological factors such as cancer classification, stage and patient sex and age, but was also significantly correlated with psychological factors (such as coping mode and neurotic personality).²⁷ Coping refers to one's ability to change cognitive and behavioural efforts constantly, to manage specific external or internal demands that are appraised as taxing or exceeding the resources of the person; this concept originated from theories of self-defence.²⁸ Anna Freud proposed the idea of the self-defence mechanism, based on Sigmund Freud's theory of defence mechanisms.²⁹ Self-defence is a method in which, to adjust the relationship between internal conflict and external reality, the individual gets rid of anxiety and controls the emotional and instinct desires that would cause excessive impulse behaviours.²⁹ In different periods, the term ego has taken on specific meanings, depending on the characteristics of the actual context and how the context correlates with the subjective structure.³⁰

In 1985, Folkman and Lazarus^{31,32} proposed that a coping mode was a crucial intermediate factor that affected the outcome of a stressful event, and that different coping modes resulted in different emotional states that influenced psychosomatic health. A positive coping mode in cancer patients is correlated with good psychological adjustment, whereas a negative coping mode is correlated with psychological disorder.³³ Moreover, a negative coping mode can, to some extent, result in anxiety and depression in cancer patients.³⁴ In this current study, there were no significant differences between the anxiety/depression group and

the nonanxiety/depression group in confrontive or avoidant dimensions of the MCMQ, but the groups' results were significantly different in the resigned dimension. However, both groups had scores on the confrontive dimension of the MCMQ that were lower than the Chinese population norm, indicating that patients with gastric cancer failed to adopt a positive and mature 'confrontive' coping mode after being told of the diagnosis, no matter whether they presented with anxious or depressive emotions. In both groups, avoidant mode scores for the MCMQ were similar to the Chinese population norm, probably due to the relatively insignificant effects of avoidance on patients' psychological and emotional states: most patients felt that they had a 'deadly disease'. However, the anxiety/depression group tended to choose 'resigned' as a negative coping mode, which may be related to personality. This type of negative coping is likely to induce or worsen the anxious and depressive psychological symptoms of anxious/depressed patients, leading to a vicious cycle of symptoms. Thus, healthcare personnel should provide relevant psychological counselling for patients with gastric cancer who have preoperative anxiety and depression, to help them develop more optimistic attitudes towards cancer.

In 1960, psychologists began to investigate the effects of social support as part of research on the role of life stress in physical and psychological health. Social support was proposed as a scientific concept in the 1970s,^{35,36} after which many scholars started to study social support. Social support is described as the psychological and material help offered to an individual by all types of social sources, including family members, friends, colleagues and medical personnel, which reflect how closely an individual is integrated into society.³⁷

Social support can be divided into objective support and subjective (perceived)

support, as well as support utilization. In this present study, there were no significant differences in any dimension of social support between the anxiety/depression group and the nonanxiety/depression group; total scores in both groups were higher than the norm for the Chinese population. This indicates that material, psychological, diagnostic and therapeutic support (provided by the government, patient's relatives and friends, and healthcare personnel) were basically satisfying the demands of patients with gastric cancer in medical settings in China. The findings of this current study are relatively consistent with other research from China, possibly because of the powerful traditional role that the family plays in facilitating the acquisition of a great many types of social support for patients.³⁸

However, another point of view should be considered: the suggestion that the social network formed in an organization may not always be positive; it can have a negative effect on individual support, which can be a stressor that affects other kinds of support.³⁹ In addition, social support should be perceived and accepted by an individual rather than only being offered by some person or entity.³⁹ Therefore, utilization or acceptance of support by patients should also be considered when social support is provided to patients with gastric cancer.

In 1996, Denollet et al.⁴⁰ proposed a more integral personality trait called the type D personality. This unique personality subtype includes NA and SI; it is characterized by introversion, pessimism, becoming anxious easily and, invariably, nervous behaviours. International studies have demonstrated a link between type D personality and cardiovascular disease, and found correlations between type D personality and anxiety and depression.^{41,42} A study that investigated the relationship between type D personality and psychological health in 3080 cancer survivors demonstrated that the 572 survivors (19%) who had type D personality

were more likely to feel anxious (51% versus 14% in nontype D personality, $P < 0.0001$) and depressed (44% versus 13% in nontype D personality, $P < 0.0001$).¹⁴ In the present study, significantly more patients with gastric cancer had type D personality in the anxiety/depression group (eight of 11; 72.7%) than in the nonanxiety/depression group (16/42; 38.1%). This suggests that that type D personality is predictive of anxiety and depression in patients with gastric cancer, and that those with type D personality are more likely to present with anxiety and depression prior to surgery, compared with other personality subtypes. Since type D personality is stable and it is a long and difficult process to change personality, healthcare personnel should intensify preoperative psychological interventions for patients with type D personality to counteract the adverse emotional effects (which are relatively transient), in order to prevent anxiety and depression effectively.

Contemporary oncobiology research has found that tumour genesis and development are related to multiple factors.⁴³ Other evidence indicates a close link between the inflammatory immune response and tumourigenesis and development.⁴⁴ Research in psychosocial oncology and psychoneuroimmunology has found an interaction between inflammatory immune response and psychosocial factors.⁴⁵ Inflammation is an important component of tumour progression, and inflammatory cells in tumour microenvironments are critical precursors for the genesis and development of tumours; a series of inflammatory mediators released by tumour cells change the tumour microenvironment and facilitate proliferation and metastasis.⁴⁶ The peripheral neutrophil level can reflect the systemic inflammatory state in humans.⁴⁷ The lymphocyte, which is an immune-effector cell, is a major component of the tumour-specific immune response.⁴⁸ After being stimulated by a tumour, systemic inflammatory cells provide a favourable

tumour environment for cancer progression by secreting cytokines: this leads to a decrease in the lymphocyte count as well as lymphocyte dysfunction.⁴⁹ An elevation of the NLR indicates a relative increase in neutrophils and a relative decrease in lymphocytes. The occurrence of such an imbalance (that is, the development of the inflammatory response for tumour promotion and the relative reduction of lymphocytes) predicts a poor prognosis.⁵⁰ Research has revealed that the elevation of proinflammatory cytokines in the peripheral blood of cancer patients is closely correlated with the development of anxiety and depression.⁵¹ Anxiety and depression can impair human immunity through the excessive release of hormones, such as catecholamines, by the hypothalamic–pituitary–adrenal axis.⁵² Meanwhile, this would decrease the number and the percentage of lymphocytes, and increase the number and the percentage of neutrophils significantly.⁵² Furthermore, psychological stress has been linked with immune function, and good psychological care can, to some extent, alleviate immune injury and improve HRQoL in cancer patients.⁵³ A controlled study of 22 patients with ovarian cancer on chemotherapy demonstrated a significantly higher peripheral lymphocyte count in the ‘clinical psychological relaxation training group’ compared with the control group.⁵⁴ In addition to being an inflammatory immune index, NLR can be used as a prognostic biological index for factors such as tumour therapy,⁵⁵ cardiovascular intervention⁵⁶ and Alzheimer’s disease.⁵⁷ Nevertheless, no reports have answered whether preoperative NLR has specific effects on anxiety and depression in patients with gastric cancer. This present study found a significantly higher preoperative NLR in the anxiety/depression group than in the nonanxiety/depression group, suggesting that NLR was not only related to the prognosis of gastric cancer as shown

previously,⁵⁰ but was also closely correlated with the occurrence of preoperative anxiety and depression in patients with gastric cancer. Besides being a biological index that reflects preoperative inflammation, NLR can, relatively accurately, indicate the inflammatory response and immune function of patients with gastric cancer, and is simple and economic to measure. As the NLR might play an important role in the diagnosis and treatment of preoperative anxiety and depression in patients with gastric cancer it is worthy of further study. In addition to providing humanistic and psychological care, healthcare personnel should study the psychological states of patients with gastric cancer at the biomolecular level, provide appropriate preoperative psychological care for those at high risk, actively control the inflammatory response and decreased immunity induced by tumours, and reduce the prevalence of anxiety and depression.

This study had a number of limitations. First, the study methodology was relatively simple. It would be more valuable for clinical prevention and treatment if gene expression and polymorphisms were considered in the exploration of the pathogenesis of preoperative anxiety and depression in patients with gastric cancer. Secondly, this was a single-centre study with a relatively small sample size and potential bias may exist. The present results suggest the need for a high-quality, multicentre trial with a large sample size to be conducted in the future.

In conclusion, this study demonstrated that the prevalence of preoperative anxiety and depression in patients with gastric cancer in China appears to be relatively low compared with other studies of patients with gastric cancer; the rate was affected by the coping mode and NLR. These preliminary findings suggest that healthcare personnel should provide appropriate psychological and medical therapy, and provide cognitive guidance, to patients with gastric

cancer prior to surgery; this is in keeping with their personality and coping mode. In addition, NLR should be actively monitored so that the inflammatory response can be controlled, and the immune function boosted, in order to help prevent and treat preoperative anxiety and depression in patients with gastric cancer. A variety of psychological care activities could be offered in order to prevent and treat preoperative anxiety and depression in patients with gastric cancer.

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Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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