

# Study on the relationship of depression, anxiety, lifestyle and eating habits to the severity of reflux esophagitis

Rongxin Wang<sup>1\*</sup>, Jing Wang<sup>1</sup>, Shuiqing Hu<sup>2</sup>

1 Emergency Department, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

2 Department of Gastroenterology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

\*Correspondence to wangrongxin@sina.com

## Abstract

**Background:** The etiology of reflux esophagitis (RE) is multi-factorial. This study aims to analyze the risk factors of the RE, its severity and further explore the impact of anxiety and depression on the patients' symptoms and quality of life.

**Methods:** From September 2016 to February 2018, a total of 689 subjects at Xuanwu Hospital Capital Medical University participated in the survey. They were divided into RE group (patients diagnosed as RE on gastroscopy,  $n = 361$ ) and control group (healthy individuals without heartburn, regurgitation and other typical symptoms,  $n = 328$ ). The survey included general demographic data, lifestyle habits, eating habits, GERD questionnaire (GerdQ), PHQ-9 depression scale and GAD-7

anxiety scale.

**Results:** The mean age and sex ratio of the two groups were similar. Multivariate logistic regression analysis showed that low education level, drinking strong tea, preference for sweets and acidic foods, overeating, short interval between dinner and sleep, anxiety, depression, sleeping on low pillow and constipation were independent risk factors for RE ( $P < 0.05$ ). Ordinal logistic regression analysis showed positive correlation between sleeping on low pillow and the severity of RE ( $P=0.024$ ). Depression had positive correlation with the severity of symptoms ( $r_s=0.375$ ,  $P < 0.001$ ) and the quality of life ( $r_s=0.306$ ,  $P < 0.001$ ), whereas anxiety had no such association.

**Conclusions:** Many lifestyle and eating habits are independent risk factors for the development of RE. Sleeping on low pillow was positively correlated with the severity of RE. Depression was positively related to the severity of symptoms and the quality of life.

**Keywords:** Reflux esophagitis, Depression, Anxiety, Lifestyle, Eating habits, Severity of reflux esophagitis

## **1. Background**

Reflux esophagitis (RE) is a common type of gastroesophageal reflux disease (GERD). According to recent report, among

healthy adults undergoing endoscopy, the incidence rate of RE was 9.0% to 24.6% <sup>[1]</sup>. In some patients, RE can evolve into Barrett's esophagus (BE), and the risk of development of cancer in BE is about 0.5% per year. Moreover, 85% of esophageal adenocarcinomas occur in patients with BE<sup>[2]</sup>. In most patients, resolution of symptoms and RE can be achieved by inhibiting gastric acid secretions. However, in some RE patients, it becomes difficult to relieve the symptoms, even with the use of proton pump inhibitors (PPI). The etiology of RE is multi-factorial. Lifestyle and eating habits such as smoking, drinking, preference for high-fat and fried foods, overeating are closely associated with RE<sup>[3-6]</sup>. In addition, it has been reported in the literature in recent years that mental disorders, especially anxiety and depression are closely related to the onset and prognosis of RE<sup>[7]</sup>, which seriously affect the quality of life of patients. Till now, the studies on the relationship between these factors and RE have shown inconsistent results with very few studies on the factors related to the severity of RE. In China, there is a lack of large sample studies on the effects of anxiety and depression on the severity of symptoms and the quality of life of patients. This study aims to summarize and analyze the risk factors for the severity of RE, and further explore the role of

anxiety and depression on the symptoms and quality of life of these patients.

## **2. Methods**

### *2.1 Participants*

The experimental group included adult patients diagnosed with RE by gastroscopy at the Gastroenterology Department of Xuanwu Hospital of Capital Medical University from September 2016 to February 2018. The study was approved by the Ethics Committee of Xuanwu Hospital of Capital Medical University (reference number:2015–11), and was performed in accordance with the Declaration of Helsinki. All participants gave written informed consent for enrollment in this study.

RE was divided into 4 grades according to the Los Angeles (LA) classification as follows<sup>[8]</sup> : Grade A: One (or more) mucosal break < 5 mm, that does not extend between the top of two mucosal folds. Grade B: One (or more) mucosal break > 5 mm long that does not extend between the top of two mucosal folds. Grade C: One (or more) mucosal break that is continuous between the top of two or more mucosal folds but involves < 75% of the circumference. Grade D: One (or more) mucosal break which involves at least 75% of the esophageal circumference. The control group included healthy adults

without any symptoms of regurgitation or heartburn visiting the hospital for health check-up.

Exclusion criteria were age < 18 years, history of gastrointestinal tumors, gastrectomy, peptic ulcer, severe liver and kidney disorders, respiratory failure, heart failure, mental illness and pregnancy.

### *2.2 Study design*

Participants of both the groups were asked to complete the study questionnaires under the guidance of the physician. Questionnaire surveys included demographic information, GERD questionnaire (GerdQ)<sup>[9]</sup>, Patient Health Questionnaire (PHQ)-9 depression scale<sup>[10]</sup> and General Anxiety Disorder (GAD)-7 anxiety scale<sup>[10]</sup>.

### *2.3 Data collection*

Demographic information included name, gender, age, education, height, weight. Lifestyle habits included smoking, consumption of alcohol, strong tea, coffee, constipation, sleeping on low pillow. Eating habits included preference for sweets, spicy foods, acidic foods, fruits, noodles, fried and fatty foods, interval between dinner and sleep, and overeating.

### *2.4 Definitions*

A regular smoker was defined as a person who smoked  $\geq 1$

cigarette/day, for 6 months continuously or cumulatively, in accordance with World Health Organization (WHO) standards<sup>[3]</sup>. A drinker was defined as a person with a daily alcohol consumption level of >25 g for men or >15 g for women, for 6 months continuously or cumulatively, in accordance with the recommendations of the Chinese Ministry of Health<sup>[3]</sup>. Overeating was defined as continuing to eat beyond a sensation of fullness until unable to eat any more. The interval between dinner and sleep was said to be short if the duration was less than 2 h. Constipation was defined as the stool frequency of less than 3 times a week, dry and hard stools, and difficult to defecate.

Preference was defined as engaging in the habit >3 days/week, continuously or cumulatively for 6 months<sup>[3]</sup>. In this study, preference for strong tea (>3 g of tea), spicy foods. (e.g. onion, garlic, chili, pepper), fried foods and fatty foods (e.g. fatty, sesame, butter, animal offal), acidic foods (e.g. acid seasoning, yogurt, acidic drinks), sweets (e.g. cream, cake, chocolate) and fruits (e.g. hawthorn, lemon, orange) were recorded.

### *2.5 Questionnaires*

GerdQ questionnaire consisted of 6 items, mainly based on the common symptoms of GERD patients and the impact of the

disease on the daily life. This questionnaire has six parts: regurgitation, heartburn, upper abdominal pain, nausea, sleep disturbance and the need for additional medication to relieve symptoms. Patients were required to recall the past 7 days to fill the questionnaire, and the scores were added. The sum was the GerdQ score of the patient, and the total score was 0-18 points<sup>[9]</sup>. The higher the score, the more severe the symptoms.

The PHQ-9 depression scale was a depression screening scale based on the frequency of depression symptoms in the past 2 weeks. This scale has nine main parts: lack of interest in doing anything, low mood, difficulty in falling asleep or lethargy, feeling very tired, anorexia or overeating, dissatisfied with oneself, sluggish or slow to speech, difficulty in concentrating on work, and suicidal ideas. The sum of the points was the patient's scale score, the total score was 0-27 points. 0-4 points was normal, 5-9 points was mild depression, 10-14 points was moderate depression, 15-27 points was severe depression<sup>[10]</sup>.

The GAD-7 Anxiety Scale was an anxiety screening scale, which mainly reminded patients to recall the frequency of anxiety symptoms in their lives in the past 2 weeks. It mainly included 7 parts: feeling restless and irritable, uncontrollable worrying, worrying too much about things, nervousness and

difficulty in relaxing, anxious and unable to sit still, becoming easily upset or irritated, and feeling that terrible things will happen. The total sum of points was the patient's scale score, the total score was 0-21 points, 0-4 points was normal, 5-9 points was mild anxiety, 10-14 points was moderate anxiety, and 15-21 points was severe anxiety<sup>[10]</sup>.

## *2.6 Statistical analysis*

Continuous normally distributed variables were expressed as mean  $\pm$  standard deviation (SD) and compared using Student's *t*-test. Non-normally distributed variables were expressed as median (upper and lower quartile) and compared by Mann-Whitney *U* test. Chi-square test was used to compare categorical data. Multivariate analysis used logistic regression analysis, Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by logistic regression. Rank correlation analysis used ordinal logistic regression analysis and Spearman rank correlation analysis. All analyses were two-tailed, and a *P* value  $<0.05$  was considered to be statistically significant. All statistical analyses were performed using SPSS version 22.0.

## **3. Results**

### *3.1 Comparison of demographic data*

A total of 361 patients with RE were included in this study.

There were 164 males and 197 females with the male: female ratio of 1:1.2. The mean age was  $49.5 \pm 12.9$  (20-82) years.

There were 328 healthy subjects in the control group with 141 males and 187 females and the male: female ratio of 1:1.3. The mean age was  $48.9 \pm 12.7$  (28-76) years.

There was no statistically significant difference in the sex ratio ( $P=0.519$ ) and the mean age ( $P=0.478$ ) between the two groups.

### 3.2 Univariate analysis of factors associated with RE

Univariate analysis showed that low education level, smoking, drinking strong tea, overeating, short interval between dinner and sleep, preference for sweets, acidic foods, fruits, noodles, fried and fatty foods, constipation, sleeping on low pillow and overweight/obesity were significantly different between the RE and the control group (Table 1).

Table 1 Univariate analysis of risk factors for RE

Risk factors	Number of cases (%)		P value
	RE group (n = 361)	Control group (n = 328)	
Education level			<0.001
Up to junior high school	95(26.3)	25(7.6)	
Higher than junior high school	266(73.7)	303(92.4)	
Smoking	84 (23.5)	50 (15.2)	0.008
Alcohol drinking	75(2.8)	64(19.5)	0.170
Drinking strong tea	87 (24.1)	35 (10.7)	<0.001
Drinking coffee	48(13.3)	60 (18.3)	0.072
Preference for sweets	172 (47.6)	86 (26.2)	<0.001
Overeating	200 (55.4)	55 (16.7)	<0.001
Short interval between dinner and sleep	192 (53.2)	72 (22.0)	<0.001

Preference for spicy foods	128 (35.5)	120 (36.6)	0.758
Preference for acidic foods	74 (20.5)	20 (6.1)	<0.001
Preference for noodles	193 (53.5)	88 (26.8)	<0.001
Preference for fried and fatty foods	93 (25.8)	59 (18.0)	0.014
Preference for fruits	93 (25.8)	59(18.0)	0.014
Constipation	76(21.1)	28 (8.5)	<0.001
Sleeping on low pillow	159(44.0)	49 (14.9)	<0.001
BMI			
(kg/m <sup>2</sup> ) <sup>a</sup> normal weight (18.5-23.9)	196(54.3)	231(70.4)	<0.001
overweight (24-27.9)	115(31.9)	76 (23.2)	0.011
obesity (>=28)	50 (13.9)	21 (6.4)	0.001

<sup>a</sup>BMI, body-mass index

### 3.3 Comparison of anxiety and depression between the two groups

The median GAD-7 anxiety score of the RE group [2.00 (0.00, 7.00)] was significantly higher than that of the control group [1.00 (0.00, 3.00)] ( $P < 0.01$ ). The median PHQ-9 depression score of the RE group [4.00 (1.00, 8.00)] was also significantly higher than that of the control group [1.00 (0.00, 4.00)] ( $P < 0.01$ ). 0-4 points was normal, in terms of composition ratio, the proportions of patients with anxiety and depression were significantly higher in the RE group than those in the control group (Table 2).

Table 2 Comparison of anxiety and depression in RE and control group [n (%)]

Groups	PHQ -9 depression score		GAD-7 anxiety score	
	0-4points	>4points	0-4points	>4 points
RE group (n = 361)	212 (58.7)	149 (41.3)	235 (65.1)	126 (34.9)
Control group (n = 328)	273 (83.2)	55 (16.8)	281 (85.7)	47 (14.3)
$\chi^2$ value	49.519		38.684	

### 3.4 Multivariate analysis for the risk factors of RE

Multivariate logistic regression analysis showed that low education level, drinking strong tea, preference for sweets and acidic foods, overeating, short interval between dinner and sleep, anxiety, depression, sleeping on low pillow and constipation were independent risk factors for RE (Table 3).

Table 3 Multivariate logistic regression analysis for the risk factors of RE

Factors	P value	OR value	95%CI	
			Lower limit	Upper limit
Smoking	0.992	1.003	0.546	1.845
Drinking strong tea	0.005	2.517	1.322	4.891
Preference for sweets	0.009	1.879	1.171	3.015
Overeating	<0.001	3.387	2.039	5.629
Short interval between dinner and sleep	0.008	1.934	1.186	3.153
Preference for acidic foods	0.002	3.328	1.549	7.152
Preference for noodles	0.051	1.687	1.104	2.782
Preference for fried and fatty foods	0.609	0.856	0.472	1.553
Preference for fruits	0.581	1.176	0.991	2.090
Sleeping on low pillow	<0.001	4.342	2.483	7.593
Constipation	0.001	3.011	1.547	5.860
Overweight /obesity	0.053	1.672	0.993	2.815
Depression	0.023	2.007	1.115	3.994
Anxiety	0.044	1.776	1.001	3.006
Low Education level	<0.001	23.084	13.576	39.252

### 3.5 Analysis of risk factors related to the severity of RE

In order to further explore the relationship between the

above-mentioned risk factors and the severity of RE based on the LA classification, ordinal logistic regression analysis was performed. The results showed that patients sleeping on low pillow had higher severity of RE ( $P=0.024$ ). On the other hand, drinking strong tea ( $P=0.248$ ) and preference for sweets ( $P=0.562$ ), overeating ( $P=0.865$ ), short interval between dinner and sleep ( $P=0.107$ ), preference for acidic foods ( $P=0.656$ ), anxiety ( $P=0.926$ ), depression ( $P=0.956$ ), low education level ( $P = 0.052$ ) and constipation ( $P = 0.673$ ) were not related to the severity of the disease.

### *3.6 Influence of anxiety and depression on patients' regurgitation and heartburn symptoms*

Among the 361 RE patients, 303 patients had regurgitation and/or heartburn, while 58 patients were asymptomatic. The median depression and anxiety score of the symptomatic group were 4.00 (2.00, 8.00) and 4.00 (1.00,7.00) respectively, while these scores in the asymptomatic group were 3.00 (0.75, 4.25)points and 2.00 (0.00, 6.25)points respectively, and the differences were statistically significant ( $P<0.05$ ).

According to the GerdQ A score (frequency of reflux and heartburn within 1 week), the numbers of patients from 1 to 6 points were 55, 85, 50, 61, 17 and 35, respectively. Spearman

rank correlation analysis showed that depression scores positively correlated with the severity of symptoms ( $r_s=0.375$ ,  $P<0.001$ ), while there was no obvious correlation between the anxiety score and the severity of the symptoms ( $r_s=0.073$ ,  $P=0.205$ )(Figure 1 and 2).

Figure 1 Spearman rank correlation analysis for influence of depression on patients' symptoms

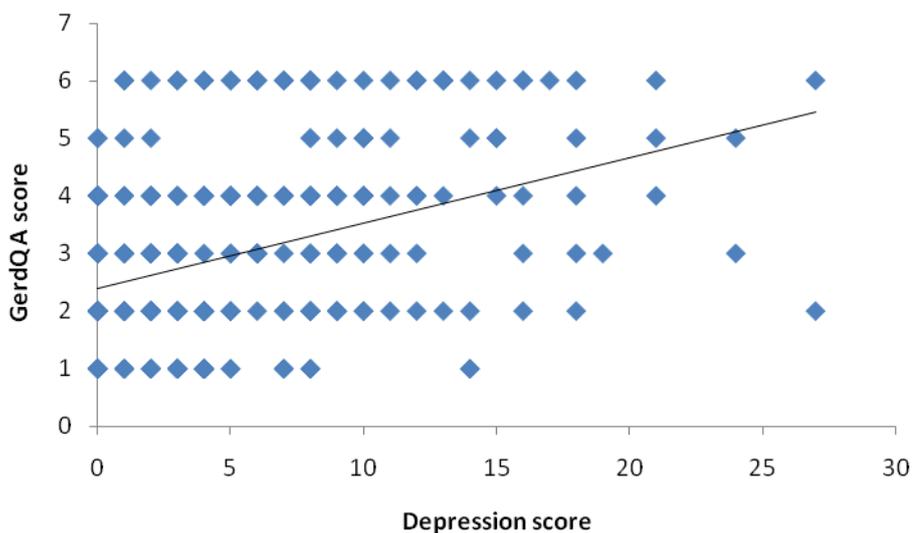
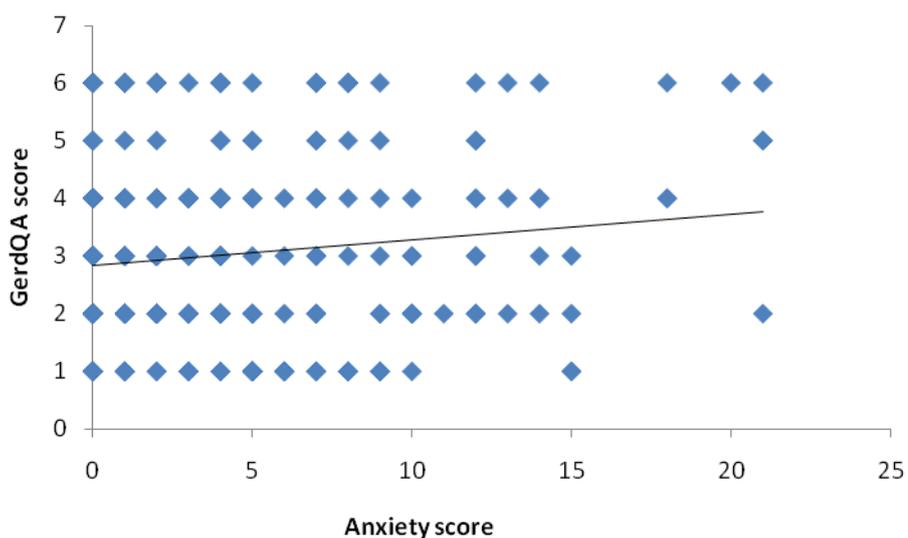


Figure 2 Spearman rank correlation analysis for influence of anxiety on patients' symptoms



### *3.7 The relationship between anxiety, depression and RE's impact on the quality of life*

The GerdQ C item mainly estimates the impact of GERD on the quality of life and has two parts, namely, nocturnal reflux affecting sleep and need for additional medication to relieve symptoms to maintain a normal life in addition to regular treatment. A total of 180 patients were affected in their daily life by GERD (affected group) while 181 patients had no effect (unaffected group). The median depression score [3.00 (1.00, 6.50) vs. 4.00 (2.00, 9.00),  $P= 0.012$ ] and the median anxiety score [2.00 (0.00, 6.00) vs.3.00 (2.00, 7.00) ,  $P =0.043$ ] of the unaffected group were significantly lower than those of the affected group.

According to the GerdQ C score, the numbers of patients from 1 to 6 points were 56, 51, 34, 19, 13 and 7, respectively. According to Spearman rank correlation analysis, the severity of depression positively correlated with severity of the impact of the disease on daily life ( $r_s=0.306$ ,  $P<0.001$ ) while the severity of anxiety had no obvious correlation with it ( $r_s =0.049$ ,  $P=0.515$ )(Figure 3 and 4).

Figure 3 Analysis for the relationship between depression and RE's impact on the quality of life

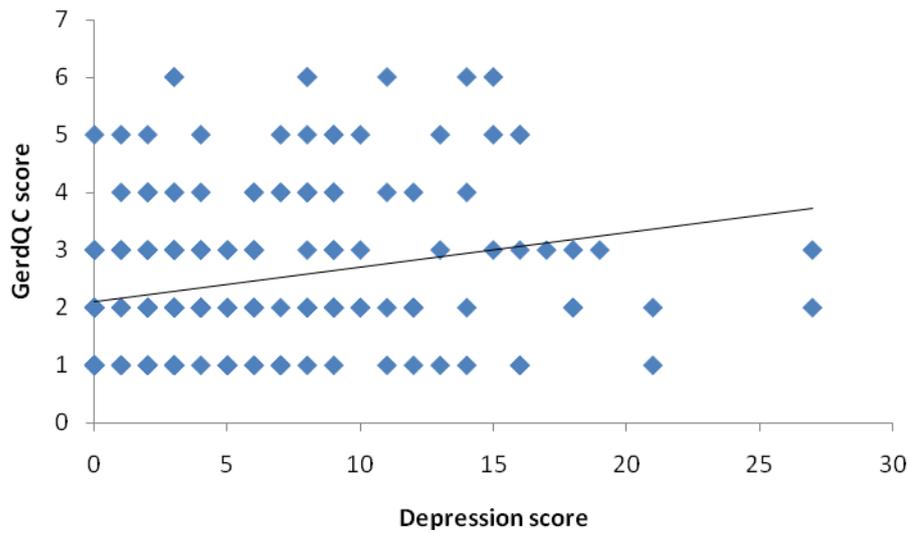
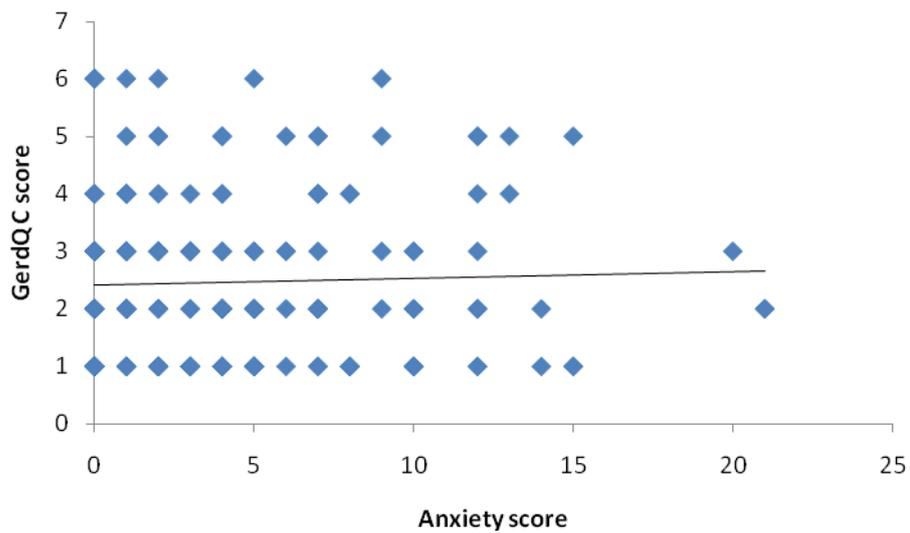


Figure 4 Analysis for the relationship between anxiety and RE's impact on the quality of life



#### 4. Discussion

This study showed that low education level, drinking strong tea, overeating, short interval between dinner and sleep, preference for sweets and/or acidic foods, anxiety, depression, sleeping on low pillow and constipation were risk factors for the onset of RE.

From the perspective of education level, previous studies have reported that lower education level was a high risk factor for RE as found in this study<sup>[4,5]</sup>. It is believed that lower education level may lead to RE by affecting patients' eating habits, psychological pressure and hygiene habits<sup>[6]</sup>.

Tea is considered a healthy drink by two thirds of people in the world<sup>[11]</sup>. Studies had shown that drinking green tea was one of the factors related to RE<sup>[12]</sup>. Theophylline, the main ingredient in tea, is currently believed to promote gastric acid secretion, relax the lower esophageal sphincter (LES) and reduces LES pressure, thereby increasing the reflux of stomach acid into the esophagus<sup>[12]</sup>. In a Chinese study, drinking strong tea was closely related to RE<sup>[13]</sup>. In this study also, we found that habit of drinking strong tea was a risk factor of RE but was not associated with its severity. In view of the popularity of drinking tea around the world, tea may be playing an important in the increasing number of new RE cases. However, further studies are required to determine the quantity, type and quality of tea contributing in the occurrence of RE.

Some reports have showed that fatty foods, spicy foods, sweets, noodles were closely related to the occurrence of RE<sup>[3, 14-18]</sup>. Our study found that preference for sweets and acidic

foods were risk factors for RE, while fried foods, noodles, fruits were not independent risk factors for RE. The differences in the results may be related to the race, geographic location, eating habits, etc.

From lifestyle perspective, our study showed that overeating, short interval between dinner and sleep, and constipation were independent risk factors for RE. These lifestyle habits can increase abdominal pressure, promote gastric dilatation and increase transient lower esophageal sphincter relaxation, thereby increasing the probability of gastroesophageal reflux. Previous studies have also reported similar findings<sup>[3, 17-20]</sup>.

Till now, there were few studies on the factors related to the severity of RE. This study found that sleeping on low pillow was not only a high-risk factor for the development of RE, but also closely related to the severity of the disease. In patients with lax lower esophageal sphincter, sleeping on low pillow increases the risk of reflux. Moreover, salivary secretion is very less during night sleep, secondary esophageal peristalsis is rare, and esophageal acid clearance at night is significantly delayed. All these factors make the night reflux more harmful. Hence, all these reports should be taken seriously<sup>[21]</sup>.

The relationship between body-mass index(BMI) and RE had

always been controversial <sup>[5,22,23]</sup>. In this study, univariate analysis showed that high BMI was associated with RE, but this correlation was not found to be significant on multivariate analysis. There were also significant differences in the relationship between smoking, drinking alcohol, coffee and other lifestyles and RE similar to previous some of the previous studies <sup>[1,12]</sup>. But other studies showed no relation <sup>[5,6]</sup>. This study showed that smoking, drinking alcohol and coffee were not independent risk factors for RE, which may be related to race, geographic location, sample size, data collection and evaluation methods.

In recent years, it had been reported that anxiety and depression were closely related to RE <sup>[7,22-24]</sup>, but there were few reports on the relationship between them and the severity of RE. In this study, multivariate analysis confirmed that these mental disorders were associated with RE, but there was no correlation between the severity of anxiety/depression and the severity of RE. Similarly, these disorders were found to be closely related to the symptoms of RE <sup>[7,24-28]</sup>, but there were few studies on their influence on the severity of symptoms. In this study, we found that depression positively correlated with the severity of RE symptoms determined by GerdQ questionnaire, while

anxiety had no obvious correlation with the severity of RE symptoms. The pathophysiological mechanisms behind the relationship between psychological factors and RE symptoms are not very clear. One possibility is that depression is secondary to reflux, which in turn increases the sensitivity of patients to reflux symptoms. The second possibility is that delayed gastric emptying in patients with depression would increase transient lower esophageal sphincter relaxation due to the influence of the central nervous system, which in turn can aggravate gastroesophageal reflux <sup>[29,30]</sup>.

RE can lead to serious impact on the daily life of patients. In this study, Spearman rank analysis showed that depression positively correlated with severity of RE on the patients' quality of life while anxiety had no obvious correlation with it. Recent studies had shown that after the addition of antidepressants, the symptoms, nocturnal reflux and the number of additional medications in RE patients were significantly improved, which further confirmed this finding <sup>[24,31,32]</sup>.

This study has some limitations. First, this was a single-center study and could not be generalized to the other population. Second, this study only included patients with RE and did not consider patients with non-erosive reflux disease. Future

prospective multicenter studies are required to validate the findings of this study and develop better preventive and treatment strategy for RE.

### **Conclusions**

We found that lifestyle, eating habits and mental factors were closely related to the incidence of RE. Low education level, drinking strong tea, preference for sweets and acidic foods, overeating, short interval between dinner and sleep, anxiety, depression, sleeping on low pillow and constipation were closely related to the onset of RE. Sleeping on low pillow positively correlated with the severity of RE. Depression positively co-related with the severity of symptoms and the impact of the disease on daily life, while anxiety had no such association.

### **Declarations:**

#### **Availability of data and material**

On a reasonable request, data from this study are available from the corresponding author.

#### **Author contributions**

Rongxin Wang: Study design, methodology, software, writing-original draft preparation.

Jing Wang: Revising the manuscript.

Shuiqing Hu: Data collecting.

All authors reviewed the manuscript.

### **Competing Interests**

The authors have declared that no competing interest exists.

### **Author details**

1 Emergency Department, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

2 Department of Gastroenterology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

### **Ethics approval and consent to participate**

The study was approved by the Ethics Committee of Xuanwu Hospital of Capital Medical University (reference number:2015–11), and was performed in accordance with the Declaration of Helsinki. All participants gave written informed consent for enrollment in this study.

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Not applicable

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### **Supplementary information**

Additional file 1: Table S1-Questionnaire on demographic information, lifestyle and eating habits

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