

## Relationship between Psychological Factors and Quality of Life in Subtypes of Gastroesophageal Reflux Disease

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**Background/Aims:** Quality of life (QoL) is consistently decreased in gastroesophageal reflux disease (GERD), but the relationship between QoL and psychological factors in GERD has not yet been clearly defined. The present study investigated the relationship between the psychological factors of two subtypes of GERD and QoL. **Methods:** A cohort of 769 participants underwent upper endoscopic evaluation in the health-promotion center of St. Paul's Hospital. The severity of GERD symptoms, psychological factors, and QoL were analyzed using the Visual Analogue Scale, the Hospital Anxiety and Depression Scale, and the abbreviated version of the World Health Organization Quality of Life instrument, respectively. **Results:** Among the total of 769 participants, 153 participants were included in the exclusion criteria. Erosive reflux disease (ERD) and nonerosive reflux disease (NERD) were present in 106 (14%) and 61 (8%) of the participants, respectively, and 449 (58%) acted as controls. In each GERD group, the QoL had no correlation with the symptom severity. The scores for anxiety and depression were highest in the NERD group, and QoL scores were lower in both the ERD and NERD groups than in the control group. Anxiety and depression resulted in QoL scores being lower in both the ERD and NERD groups than in the nonanxiety and nondepressed groups, respectively. **Conclusions:** This study provides evidence that the QoL associated with the ERD and NERD subtypes may be more related to psychological factors than to symptom severity. (*Gut and Liver* 2009;3:259-265)

**Key Words:** Gastroesophageal reflux; Quality of life; Anxiety; Depression; Psychology

### INTRODUCTION

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders encountered by primary physicians in the clinical setting. In fact, GERD is so common that 20% of adults in western countries complain of typical symptoms including heartburn and acid regurgitation at least once a week.<sup>1,2</sup> In Asian countries, 3-7% of adults complain of GERD symptoms greater than once a week<sup>3,4</sup> and the disease prevalence has gradually increased.<sup>5</sup> GERD symptoms can be explained by a variety of pathophysiological mechanisms. GERD is thought to occur secondary to transient relaxation of the lower esophageal sphincter.<sup>6</sup> In cases of GERD in which there is a large drop in pH, the extent of proximal refluxate is high, or acid clearance is delayed, typical symptoms of reflux esophagitis present.<sup>7</sup> However, the correlation between reflux esophagitis and conscious perception of GERD symptoms is very complicated. In some patients, esophagitis causes symptoms to such an extent as to lower the patient's quality of life (QoL). In other patients, however, no symptoms are present despite the presence of reflux esophagitis.<sup>8</sup> The symptomatic presentation of GERD is associated with various psychological and psychosocial factors, including chronic stress,<sup>9</sup> anxiety or emotional instability, and the abnormal reflux of gastric acid.<sup>10</sup> Psychological factors affect how patients perceive

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Received on March 27, 2009. Accepted on July 29, 2009.

DOI: 10.5009/gnl.2009.3.4.259

the physiological symptoms. Anxiety and depression are generally two of the most common psychiatric symptoms and are associated with chronic diseases such as cardiovascular diseases and diabetes mellitus. It is widely acknowledged that medical diseases may be associated with a high incidence of anxiety and depression.<sup>11</sup> Recent studies have shown that patients with anxiety or depression are at an increased risk of developing reflux symptoms. This suggests that anxiety and depression are associated with these symptoms.<sup>12</sup> Previous studies have also reported a correlation between psychological factors, psychiatric disease, and GERD,<sup>13</sup> but further studies are warranted to elucidate this correlation in more detail.<sup>14</sup> The perception of QoL in patients with GERD can be as low as with diabetes mellitus or cancer as compared to healthy individuals.<sup>15</sup> Reflux symptoms that are present greater than once a week are sufficient to lower the patient's QoL.<sup>16</sup> In patients with significant reflux symptoms, pharmacologic therapies can help improve the QoL.<sup>17,18</sup> Until now, few studies have been performed to examine the relationship between poor QoL and psychological factors in patients with GERD. Additionally, there are a limited number of studies that examine the correlation differences between QoL and psychological factors among the subtypes of GERD: erosive reflux disease (ERD) and nonerosive reflux disease (NERD).

In this study, we decided to evaluate the QoL and severity of anxiety and depression in adults who were scheduled to undergo endoscopy for medical check-up. We compared these parameters between the GERD patient group, which consisted of patients with erosive reflux disease or non-erosive reflux disease, and the control group, which consisted of healthy individuals. In addition, we examined whether QoL is significantly correlated with degree of symptom severity and psychological factors. Furthermore, we also evaluated the above variables based on their correlation with different subtypes of GERD.

## MATERIALS AND METHODS

### 1. Subjects

Of the subjects who underwent endoscopy in the health promotion center of Catholic University St. Paul's Hospital between August 2007 and February 2008, those who consented to the current questionnaire study were included for the analysis. The study was reviewed and approved by the institutional review board. The subjects were given an explanation regarding the aims of the study, and the included patients submitted a written informed consent form, filled out a questionnaire for reflux symptoms, and also submitted a questionnaire for anxiety

and depression or for QoL. Exclusion criteria for the study included a past history of gastrointestinal surgery, peptic ulcer, the concurrent presence of organic diseases including cancer, and the presence of abnormal laboratory findings (hemoglobin <10 g/dL, fasting blood sugar >200 mg/dL or AST or ALT >100). Patients with ulcer scarring were not excluded.

### 2. Measurements

In the current study, a questionnaire designed to examine the patient's symptoms of gastroesophageal reflux, psychological factors, QoL, and sociodemographic data was completed by each subject. The subjects were asked to respond to questions regarding the weekly frequency of symptoms such as (0) none, (1) less than once a month, (2) approximately once a month, (3) approximately once a week, (4) more than twice a week, and (5) everyday. This format is based on a questionnaire originally designed by the Mayo clinic for an epidemiological study, which was then adapted for our study.<sup>19,20</sup> To evaluate the severity of reflux symptoms, the visual analogue scale (VAS, ranging from 0 to 100 mm, 0=no pain, 100=very severe pain) was used. A questionnaire regarding anxiety and depression used the Korean version of the hospital anxiety and depression scale (HADS), which was developed by Zigmond *et al.*<sup>21</sup> and has been previously validated.<sup>22</sup> To assess perception of QoL, a questionnaire was administered using the The World Health Organization Quality of Life Assessment (WHOQOL)-BREF.<sup>23</sup> Following endoscopy, the findings were analyzed by two endoscopists.

ERD was defined based on the endoscopic findings according to the LA classification,

The minimal changes are not included in ERD subgroup. The subjects with symptomatic ERD have a heartburn or acid regurgitation at least once per week. NERD was defined as cases in which symptoms such as heartburn or acid regurgitation were present once a week in the absence of erosive esophagitis.

### 3. Statistical analyses

Group comparisons were performed using an unpaired t-test, Mann-Whitney U test, and an analysis of variance (ANOVA) test with Tukey's Honestly Significant Difference (HSD) post-hoc test where appropriate. Chi-square analyses were conducted to compare categorical variables. Pearson or Spearman correlation coefficients were calculated in order to assess the associations between the two continuous variables. Nonparametric methods were applied when the distribution was skewed or the number in a group was below 30. p-value less than 0.05 was defined statistically significant.

## RESULTS

### 1. Demographic and clinical characteristics of the subjects

The number of patients who completed the questionnaire was 769. Of these patients, the number of subjects who were found to have greater than LA classification A erosive esophagitis was 106. The number of subjects who presented with heartburn or acid regurgitation greater than once a week in the absence of erosive esophagitis was 61. On endoscopy, there was determined to be 90 patients with peptic ulcers, 14 patients who had undergone gastrointestinal surgery, 14 patients with gastrointestinal tumors, 12 patients with abnormal laboratory findings, and 23 other patients (including those who did not completely fill out a questionnaire) who were excluded from the study. The healthy control group consisted of 449 patients who had no erosive esophagitis or typical symptoms. All of the patients in the ERD group showed a mild level of esophagitis corresponding to A (86%) or B (14%) based on the LA classifications. Only one patient (1%) was classified as C based on the LA classifications. The demographic and clinical characteristics of the patients are shown in Table 1. There were significant differences in sex, body mass index (BMI, kg/m<sup>2</sup>), and personal histories of smoking and alcohol consumption between the three groups ( $\chi^2=22.5$ ,  $df=2$ ,  $p<0.0001$ ;  $F=10.6$ ,  $p<0.0001$ ;  $\chi^2=16.5$ ,  $df=4$ ,  $p=0.002$ ;  $\chi^2=12.9$ ,  $df=4$ ,  $p=0.012$ , respectively). The ERD group had higher BMI levels compared to the NERD and control groups ( $p<0.0001$ ;  $p=0.0001$ , respectively). Also, a higher proportion of male subjects and current

smokers and alcohol drinkers made up the ERD group as compared to the NERD and control groups. Though the differences in age between the three groups was not statistically significant ( $F=2.99$ ,  $p=0.051$ ), the NERD group was comprised of a lower mean age as compared to the ERD group ( $p=0.041$ ).

In the ERD group, asymptomatic and symptomatic subgroups contained 83 (78.3%) and 23 (21.7%) patients, respectively. The mean level of symptom severity in symptomatic ERD subjects was 41 (SD, 28). In the NERD group, the mean level of symptom severity was 40 (SD, 25).

ANOVA analyses revealed significant group differences between the scores of anxiety and the depression subscale of the HADS between the three groups ( $F=22.0$ ,  $p<0.0001$ ;  $F=15.4$ ,  $p<0.0001$ , respectively, Fig. 1A, B). The NERD group had higher anxiety scores compared to the ERD and control groups ( $p<0.0001$ ;  $p<0.0001$ , respectively), however, the higher anxiety scores in the ERD group versus the control group was not statistically significant ( $p=0.068$ ). Additionally, significant differences between the depression scores of the NERD and ERD groups ( $p=0.022$ ), the ERD and control groups ( $p=0.024$ ), and the NERD and control groups ( $p<0.0001$ ), respectively (NERD>ERD>control).

The overall QoL scores in the three groups showed significant inter-group differences ( $p<0.0001$ ; Fig. 1C). Post hoc analyses demonstrated that the NERD and ERD groups had a lower total QoL score as compared to the control group ( $p<0.0001$ ;  $p=0.002$ , respectively), but there was no significant difference observed in the total QoL scores between the NERD and ERD groups ( $p=$

Table 1. Demographic Characteristics of Subjects

Variables	ERD subjects (n=106)	NERD subjects (n=61)	Control subjects (n=449)	p-value
Age, mean (SD, years)	51.8 (10.0)	48.2 (9.6)	50.3 (9.1)	0.051
Sex, No. (%)				<0.0001
Male	66 (62.3)	21 (34.4)	170 (37.9)	
BMI, mean (SD, kg/m <sup>2</sup> )	24.9 (3.5)	22.8 (3.3)	23.7 (2.8)	<0.0001
Smoking, No. (%)				0.002
Never	51 (48.1)	41 (67.2)	310 (69.0)	
Past	24 (22.6)	8 (13.1)	65 (14.5)	
Current	30 (28.3)	12 (19.7)	73 (16.3)	
Missing	1 (0.9)	0 (0.0)	1 (0.2)	
Alcohol consumption, No. (%)				0.012
Never	32 (30.2)	23 (37.7)	204 (45.4)	
Past	6 (5.7)	5 (8.2)	12 (2.7)	
Current	66 (62.3)	32 (52.5)	228 (50.8)	
Missing	2 (1.9)	1 (1.6)	5 (1.1)	

ERD, erosive reflux disease; NERD, non-erosive gastroesophageal reflux disease; BMI, body mass index; SD, standard deviation.

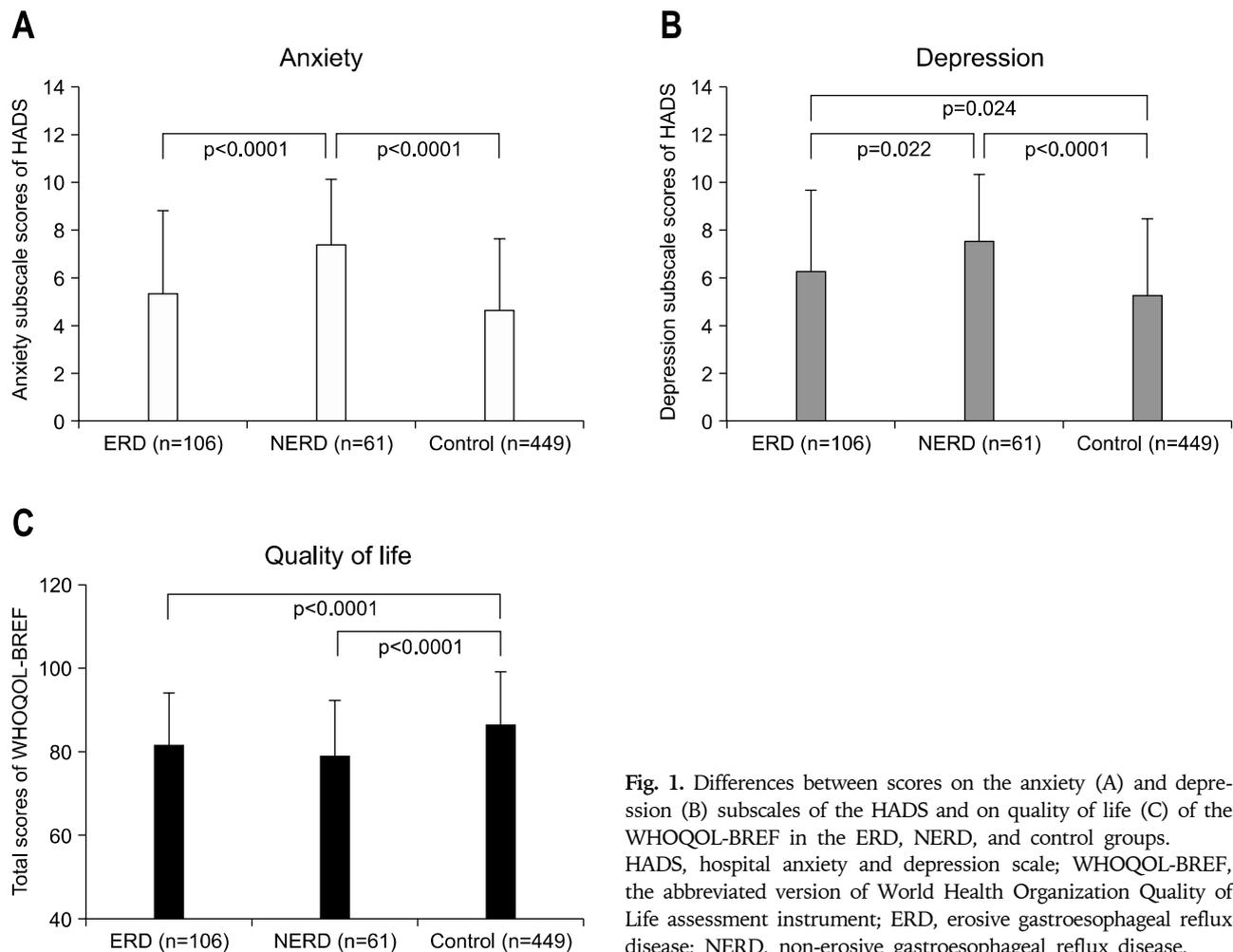


Fig. 1. Differences between scores on the anxiety (A) and depression (B) subscales of the HADS and on quality of life (C) of the WHOQOL-BREF in the ERD, NERD, and control groups. HADS, hospital anxiety and depression scale; WHOQOL-BREF, the abbreviated version of World Health Organization Quality of Life assessment instrument; ERD, erosive gastroesophageal reflux disease; NERD, non-erosive gastroesophageal reflux disease.

0.427).

## 2. Relationships between psychological factors and QoL in the ERD and NERD groups

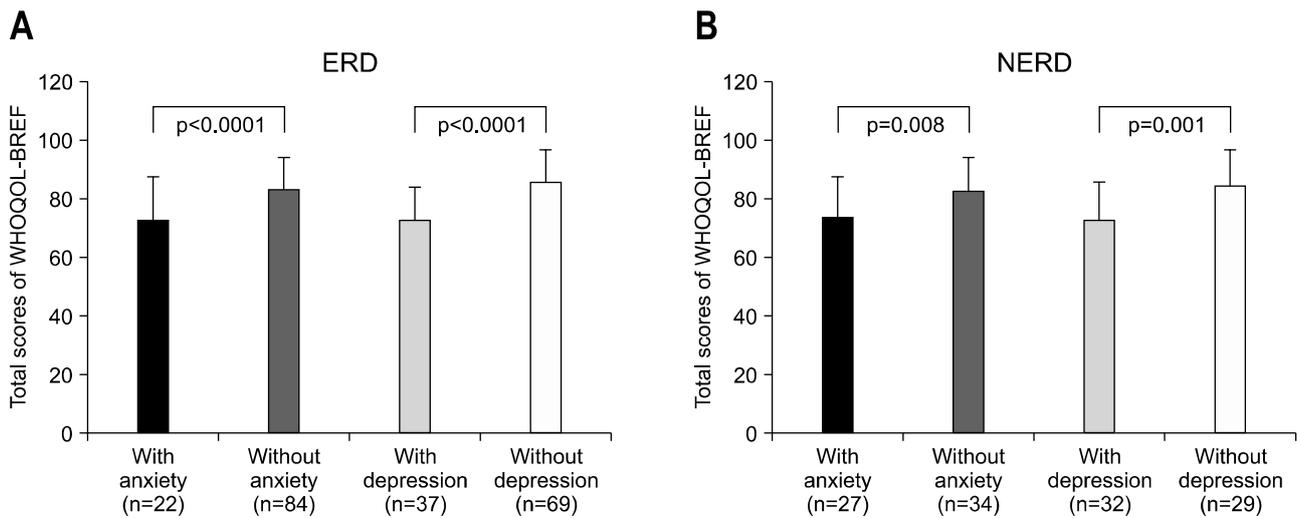
The diagnosis of anxiety and depression is defined by a total score of eight or above on each subscale of HADS. Within the ERD group, anxious ERD patients ( $n=22$ ,  $72.6 \pm 14.9$ ) had lower total QoL scores compared to non-anxious ERD subjects ( $n=84$ ,  $84.0 \pm 10.7$ ) ( $Z=-3.62$ ,  $p<0.0001$ ; Fig. 2A). Also, depressed ERD subjects ( $n=37$ ,  $73.3 \pm 11.2$ ) demonstrated lower overall QoL scores compared to non-depressed ERD patients ( $n=69$ ,  $86.1 \pm 10.8$ ) ( $Z=-5.18$ ,  $p<0.0001$ ; Fig. 2A). However, the lower overall QoL scores of symptomatic ERD subjects ( $n=23$ ,  $76.6 \pm 12.4$ ) compared to asymptomatic ERD subjects ( $n=83$ ,  $83.0 \pm 12.2$ ) were not statistically significant ( $Z=-1.91$ ,  $p=0.056$ ). In symptomatic ERD subjects, the total QoL scores negatively correlate with anxiety and depression subscale scores ( $\rho=-0.507$ ,  $p=0.014$ ;  $\rho=-0.616$ ,  $p=0.002$ , respectively), but no corre-

lation was seen with the level of symptom severity ( $p=0.926$ ).

Within the NERD group, anxious NERD subjects ( $n=27$ ,  $74.0 \pm 14.1$ ) had lower total QoL scores as compared to non-anxious NERD subjects ( $n=34$ ,  $83.0 \pm 11.1$ ) ( $Z=-2.67$ ,  $p=0.008$ ; Fig. 2B). Depressed ERD subjects ( $n=32$ ,  $73.6 \pm 12.4$ ) also had lower total QoL scores as compared to non-depressed ERD patients ( $n=29$ ,  $85.0 \pm 11.6$ ) ( $Z=-3.23$ ,  $p=0.001$ ; Fig. 2B). In all NERD subjects, the total QoL score negatively correlated with anxiety and depression subscale scores ( $r=-0.276$ ,  $p=0.031$ ;  $r=-0.541$ ,  $p<0.0001$ , respectively), but no correlation was evident with the level of symptom severity ( $p=0.504$ ).

## DISCUSSION

In the present study, the degree of anxiety and depression was higher and perception of QoL was poorer in the GERD patient group compared to the control group.



**Fig. 2.** Differences in the total score of WHOQOL-BREF according to the presence of anxiety or depression in the ERD (A) and NERD (B) groups.

WHOQOL-BREF, the abbreviated version of World Health Organization Quality of Life assessment instrument; ERD, erosive gastroesophageal reflux disease; NERD, non-erosive gastroesophageal reflux disease.

Some patients with GERD do not complain of the typical symptoms. In a community-based study, one-third of patients with erosive esophagitis presented with no symptoms. Only one-fourth of patients who presented with typical symptoms were found to have erosive esophagitis.<sup>24</sup> On a routine medical check-up, only 8% of patients with reflux esophagitis complained of symptoms more than once a week. Only 14% of patients with typical symptoms were found to have erosive esophagitis.<sup>25</sup> Also, in the current study, only 22% of patients with erosive esophagitis presented with symptoms greater than once per week. As described in this study, only a small number of subjects actually had erosive esophagitis. There was found to be a discord between the patients' perception of symptom severity and the level of esophageal mucosal injury seen on endoscopy. This disconnect indicates that other factors in addition to the actual disease pathology affect the subject's symptoms. This suggests that GERD is associated with the psychological factors as well. There is a broad spectrum of GERD clinical presentations, and these presentations are caused by subjective reflux symptoms as well as a variety of pathophysiological states. It has been reported that psychological aspects of disease including stress, emotion, and personality may affect the severity of GERD symptoms.<sup>13</sup> Several explanations have been proposed regarding the correlation between psychological factors and GERD. The first theory is that anxiety and depression are developed secondary to the reflux and then they make the reflux symptoms more sensitive. The second explanation is that reflux severity is

greater in patients with psychiatric diseases. This can be interpreted as a low threshold for bodily sensation or a distorted perception of pain.<sup>14</sup> Therefore, the correlation between anxiety, depression, and reflux symptoms cannot be explained using a single model because various interactions are involved in this relationship.<sup>12</sup> Despite the observation that reflux occurs with the same incidence, it remains unclear why the symptoms were present in some cases but not in others.<sup>8</sup> Therefore, it can be inferred that the typical presentation of GERD can be interpreted as partially associated with psychological factors in some cases (the somatization can be omitted) even when esophagitis has been confirmed on endoscopy.

It has been reported that the likelihood of complaining of reflux symptoms increased by 2.8 times in a patient group in which anxiety and depression were present. This study illustrates the correlation between the anxiety, depression, and reflux symptoms.<sup>12</sup> This study was conducted using a questionnaire in the absence of endoscopy in GERD patients, which demonstrated a positive correlation between reflux symptoms and psychological factors. In the current study, QoL, anxiety, and depression were compared between the GERD group and control group using a questionnaire. For subgroup analyses, the GERD group was further divided into the ERD subgroup and the NERD subgroup. This study demonstrated that the severity of anxiety was higher in the ERD subgroup compared to normal controls, but this difference was not statistically significant. The severity of anxiety and depression was also observed to be significantly higher in the ERD

subgroup and NERD subgroup as compared to normal controls. Additionally, the severity of anxiety and depression was higher in the NERD subgroup than in the ERD subgroup or the control group. Since there were differences between the degrees of heartburn improvement secondary to PPI between the NERD and ERD subgroups, GERD pathophysiology might also be different between the two subgroups.<sup>26</sup> It can therefore be inferred that anxiolytics or anti-depressants may be effective for patients with NERD who are refractory to PPI. In the current study, using a questionnaire from the WHOQOL-BREF, QoL was compared between the GERD and control groups. As seen in previous studies, QoL was decreased in the GERD group compared to controls. A tool for evaluating QoL, the WHOQOL consists of six domains including the physical domain, psychological domain, levels of independence, social relationships, environment domain, and spiritual domain. It is therefore a useful tool in evaluating the status of the patient's psychological, social, and spiritual health as well as their physical health.<sup>27</sup> The WHOQOL contains a lot of useful material but consists of a large number of questions (100 questions) and cannot be conveniently used. An abbreviated form of the WHOQOL, WHOQOL-BREF, was developed. WHOQOL-BREF is composed of 24 questions regarding QoL and is a tool for evaluating QoL. This tool has a small number of questions and a high level of validity and reliability. Since it has a small number of questions and high validity and reliability, this tool can be used as an alternative to the longer version.<sup>23</sup> To date, no studies have evaluated QoL using WHOQOL-BREF in patients with GERD.

In addition to anxiety and depression, QoL was also negatively correlated with depression irrespective of the degree of symptoms or endoscopic findings in patients suffering from GERD. This suggests that the anxiety and depression affect QoL.

The limitations of the current study are as follows: first, this is a cross-sectional study, and it is insufficient for clarifying the correlations between anxiety, depression and the QoL. Further studies are warranted to elucidate the correlation between psychological factors and GERD. However, this study also looked at patients with GERD who were subdivided into two groups (the ERD group and the NERD group) and the QoL, anxiety and depression in both groups were compared to those factors in the control group. Secondly, the samples disclose the limitations of the study. The current study was conducted using patients who received medical check-ups. The ERD group showed a male predominance, but the NERD group and the control group contained more Females. This

study should be performed in outpatient settings if these results would be correlated with those of outpatient. Thirdly, there might be functional heartburn patients who cannot be anymore included in the realm of GERD by Rome III criteria among NERD patients in our study.

In conclusion, the severity of anxiety and depression was higher and the QoL poorer in patients with GERD as compared to normal, healthy people. Particularly in patients with NERD, the severity of anxiety and depression was higher. This may affect the patient's QoL. The QoL in patients with GERD is not proportional to the subjective symptoms but affects the psychological factors including anxiety and depression.

## ACKNOWLEDGEMENTS

This study was supported by a grant from the Korean Health 21 R&D Project, Ministry of Health and Welfare, Republic of Korea (A050047).

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