

Typical symptoms rather than extraesophageal symptoms affect the quality of life in gastroesophageal reflux disease

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Background/aims: Compared with the general population, the quality of life of patients with gastroesophageal reflux disease has been known to be impaired. The aim of this study was to assess and compare how typical esophageal symptoms and extraesophageal symptoms affect quality of life. **Materials and Methods:** This study was performed in patients who had visited the Health Promotion Center of St. Paul's Hospital and undergone an endoscopy. Two instruments were used to assess quality of life: a questionnaire on the symptoms of gastroesophageal reflux disease and the Korean version of the World Health Organization Quality of Life Scale, Abbreviated Version. For comparison purposes, data from an age-matched healthy control group were obtained. **Results:** In this study, 262 health check-up subjects were classified with gastroesophageal reflux disease. An additional 447 health check-up subjects, who had shown normal and asymptomatic results from endoscopy, were assigned to the control group. The quality of life in gastroesophageal reflux disease patients was lower than that of the control group (81.7 vs. 87.5, $p<0.05$). Compared to the group with asymptomatic erosive reflux disease and the control group, the quality of life was also lower in the group that manifested both typical symptoms and extraesophageal symptoms (79.9 vs. 84.5, $p<0.05$). Compared with the control group, the quality of life was lower in the group with typical symptoms than in the group with extraesophageal symptoms (79.6 vs. 87.5, $p<0.05$). **Conclusions:** Regardless of whether the esophagitis was erosive or non-erosive, the quality of life was deteriorated to a greater extent in symptomatic gastroesophageal reflux disease patients than in the control group, and the quality of life was even lower among patients who had typical symptoms than among patients with extraesophageal manifestations.

Key words: Gastroesophageal reflux disease, reflux esophagitis, quality of life

Gastroözofageal reflü hastalığında yaşam kalitesini ekstraözofageal semptomlardan çok tipik semptomlar etkilemektedir

Giriş ve Amaç: Gastroözofageal reflü hastalığı olan bireylerin yaşam kalitesinin genel popülasyona göre bozulduğu bilinmektedir. Bu çalışmanın amacı tipik özofageal ve ekstraözofageal semptomların yaşam kalitesini nasıl etkilediğinin tespit edilmesidir. **Gereç ve Yöntem:** Bu çalışma St. Paul Hastanesi "Health Promotion Center" merkezine başvuran ve endoskopi yapılan hastalar üzerinde yapılmıştır. Yaşam kalitesinin incelenmesi için reflü semptomları hakkında anket ve Dünya Sağlık Örgütü Yaşam Kalitesi Ölçeği'nin kısaltılmış Kore versiyonu kullanılmıştır. Karşılaştırma için yaşları eşleştirilmiş sağlıklı kontrollerden de veri toplanmıştır. **Bulgular:** Bu çalışmada 262 vaka gastroözofageal reflü hastalığı olarak sınıflanmıştır. Ayrıca normal olan ve asemptomatik reflü bulgusu olan 447 vaka kontrol grubu olarak ayrılmıştır. Gastroözofageal reflü hastalığı olanların yaşam kalitesi kontrol grubuna göre anlamlı olarak bozulmuş bulunmuştur (81.7 - 87.5; $p<0.05$). Asemptomatik eroziv reflü grubu ile ve kontrol grubu ile karşılaştırıldığında semptomatik grupta yaşam kalitesi hem tipik semptomları olanlarda hem de ekstraözofageal semptomları olanlarda bozulmuş bulunmuştur (79.9 - 84.5; $p<0.05$) Kontrol grubu ile karşılaştırıldığında, tipik semptomları olanların yaşam kalitesi ekstraözofageal semptomları olanlarından daha kötü bulunmuştur (79.6 - 87.5; $p<0.05$) **Sonuç:** Özofajit eroziv olsun veya olmasın, yaşam kalitesi semptomatik gastroözofageal reflü hastalığı olanlarda daha fazla bozulmaktadır ve tipik semptomları olanlarda bu bozulma ekstraözofageal semptomları olanlara göre daha belirgindir.

Anahtar kelimeler: Gastroözofageal reflü hastalığı, reflü özofajit, yaşam editör kalitesi

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is a chronic and frequently occurring disease. Its prevalence had been found to be much higher in the Western world, where 20% of the adult population reports the typical symptoms of heartburn or acid regurgitation once or more per week as among the most common complaints (1,2). In the Eastern world, 3-7% of the adult population complains of the symptoms once or more per week (3,4). However, its prevalence has gradually increased (5), and domestic research reports have also indicated increasing trends (6).

Compared to healthy people, GERD-related quality of life (QoL) is known to be impaired to a similar extent as among patients with diabetes or cancer (7), which has been shown in Western and Eastern countries (7-9). Most studies on GERD-related QoL have been conducted among patients with typical symptoms and have not distinguished between esophageal and extraesophageal manifestations. However, a limited number of studies have compared QoL between patients with typical symptoms and patients with extraesophageal manifestations. This study was designed to compare adults who underwent endoscopies for early diagnosis of gastric cancer to compare the QoL between GERD patients and a healthy control group. The purpose was to determine which symptoms, between the typical and extraesophageal manifestations of GERD, had a greater impact on QoL.

MATERIALS AND METHODS

Subjects

The study was intended for subjects who underwent endoscopies for early diagnosis of gastric cancer between August 2007 and September 2008 at the Health Promotion Center of St. Paul's Hospital, which is affiliated with the Catholic University of Korea. All subjects provided informed consent before completing the questionnaire.

The study was approved by the Institutional Review Board. Subjects were provided with an explanation of the aims of the study before completing a questionnaire for reflux symptoms and QoL.

Subjects were excluded if they had a history of gastrointestinal surgery; organic diseases, such as digestive ulcer or gastric cancer; diabetes; any drug treatment for digestive diseases in the past three months; or abnormal laboratory findings (hemoglobin <10 g/dl, fasting glucose >200 mg/dl). Patients with an ulcer scar were not excluded from the study.

Questionnaires

Questionnaires were composed of questions about symptoms of GER, QoL and sociodemographic data. The questionnaires defined typical symptoms (heartburn and acid regurgitation) and extraesophageal reflux symptoms (dysphagia, sense of globus in throat, hoarseness in voice, coughing, and chest pain) and asked the subjects to indicate the frequency of their symptoms as 0) None, 1) less than once per month, 2) about once per month, 3) about once per week, and 5) daily. Their responses were classified and assessed. We adapted the Korean version of the questionnaire in our classroom; the original version was designed by the Mayo Clinic as an epidemiological tool to investigate GERD (10,11). Symptoms including heartburn or acid regurgitation were defined as typical symptoms, and symptoms including dysphagia, sense of globus in the throat, hoarseness, cough, and chest pain were defined as extraesophageal reflux symptoms.

To measure health-related QoL, the Korean version of the World Health Organization (WHO) Quality of Life Scale, Abbreviated Version (WHOQOL-BREF), was used. The WHOQOL-BREF has been tested for reliability and feasibility in comparison to the original WHOQOL scale (12,13). The questionnaire contained 26 items in the following four domains: total sum, physical health, social relationships, and environment. Each item score ranged from 1 to 5 points. The total was calculated as the sum of individual domain scores (0-120). After conducting endoscopies, two doctors who specialized in endoscopy analyzed the endoscopic images and classified the esophageal reflux based on the Los Angeles (LA) classifications. Patients who experienced only minimal changes to the classifications were not included in the GERD or control group.

Statistical Analyses

Chi-squared analyses were conducted to compare categorical variables. Group comparisons were performed using an unpaired t-test, analysis of variance (ANOVA) test and Tukey's Honestly Significant Difference (HSD) test. Differences were considered significant at $p < 0.05$.

RESULTS

Clinical Spectrum of the Study Subjects

The study included 262 subjects who were patients with GERD. Among those patients, 174 were classified as having erosive esophagitis, and 88

were classified as having non-erosive esophageal diseases. All of the subjects in the GERD group showed a mild level of esophagitis that corresponded to A (80%) or B (19%) in the LA classifications. Only one patient was classified as C in the LA classifications. The control group was comprised of 447 subjects with equal gender proportions; the control group patients showed normal endoscopic results without typical or extraesophageal reflux symptoms.

Comparison of the QoL in GERD vs. Control Subjects (Table 1, Figure 1)

There was a significant difference in QoL between the GERD group and the control group (81.7 vs. 87.5, $p < 0.05$) (Figure 1). There was no difference by gender between the two groups ($p = 0.146$). The GERD group included more subjects who smoked (25.2 vs. 14.8, $p = 0.001$). Compared to non-smokers, smokers had a 1.47 times higher probabilistic susceptibility to GERD, which was statistically significant (relative risk: 1.47 (1.20-1.80)). Among patients with GERD, 47% (124/262) presented typical symptoms, and 39% (101/262) experienced extraesophageal symptoms.

Comparison of the QoL by Symptoms

Quality of life (QoL) was compared between the erosive esophagitis group, with both typical and extraesophageal symptoms, and the control group, which had shown neither of these symptoms. There were no differences according to age, gender or body mass index (BMI). Smoking was related to differences among the three groups (Table 2). Compared to the control group, groups with symptoms reported a lower QoL in every domain. However, compared to the group with no symptoms, these groups reported a lower QoL in two domains: physical health and social relationships. When the asymptomatic erosive esophagitis group

was compared to the control group, the erosive esophagitis group showed a lower QoL in the domain of physical health but not in the other domains.

When the GERD group was classified into four groups (typical and extraesophageal symptoms, typical symptoms only, extraesophageal symptoms only, and erosive esophagitis only), the group with typical symptoms was the only group with a lower QoL ($p < 0.05$) (Figure 2). The group with extraesophageal symptoms only and the group with erosive esophagitis only did not have significant differences in QoL compared to the control group. Among the sub-items, the group with symptoms had significant differences in the four domains in comparison to the control group. The group with symptoms also showed impairment in QoL for the sub-items physical health and social relationships compared with the asymptomatic GERD group. Meanwhile, compared to the control group, the asymptomatic GERD group had a lower QoL only for the sub-items of the physical health domain.

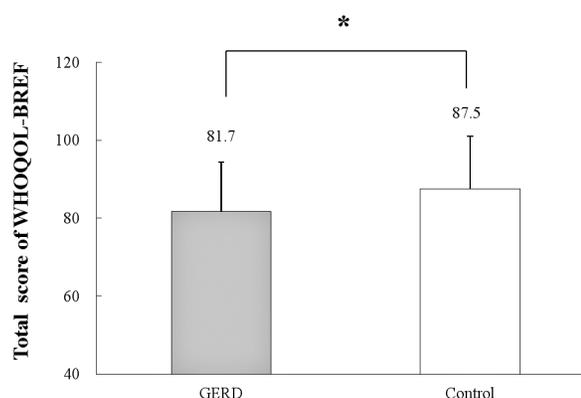


Figure 1. Comparisons of QoL between GERD and control subjects. QoL: Quality of life. GERD: Gastroesophageal reflux disease.

Table 1. Characteristics and quality of life between GERD and control subjects

	GERD N=262	Control N=447	P value
Demographics			
Age, mean (yrs)±SD	50.3±11.4	50.2±9.3	.847
Male (%)	54.2	48.5	.146
Clinical characteristics			
BMI, mean (kg/m ²)±SD	23.9±3.3	23.8±2.8	.581
Current smoker (%)	25.2	14.8	.001
Quality of Life			
Sum	81.7±12.8	87.5±13.5	.000

GERD: Gastroesophageal reflux disease. BMI: Body mass index.

Table 2. Characteristics and quality of life according to the presence of GERD symptoms

	Symptomatic GERD N=159	Asymptomatic EE N=103	Control N=447	P value
Demographics				
Age, mean (yrs)±SD	49.6±11.4	51.5±11.5	50.2±9.3	0.357
Male (%)	52.2	57.3	48.5	0.252
Clinical characteristics				
BMI, mean (kg/m ²)±SD	23.9±3.5	24.0±2.8	23.8±3.0	0.855
Current smoker (%)	28.3	20.4	14.8	0.001
Quality of Life				
Sum, mean±SD	79.9±12.4*+	84.5±12.9	87.5±13.5	0.000
Physical health	22.6±4.3*+	24.7±4.3*	24.9±4.3	
Psychological	18.4±3.7*	19.4±3.7	19.9±3.8	
Social relationships	9.1±1.9*+	9.9±1.8	9.9±1.9	
Environment	23.8±4.5*	24.0±4.5	25.1±4.9	

BMI: Body mass index. GERD: Gastroesophageal reflux disease. EE: Erosive esophagitis. *p<0.05 vs. control, +p<0.05 vs. asymptomatic EE.

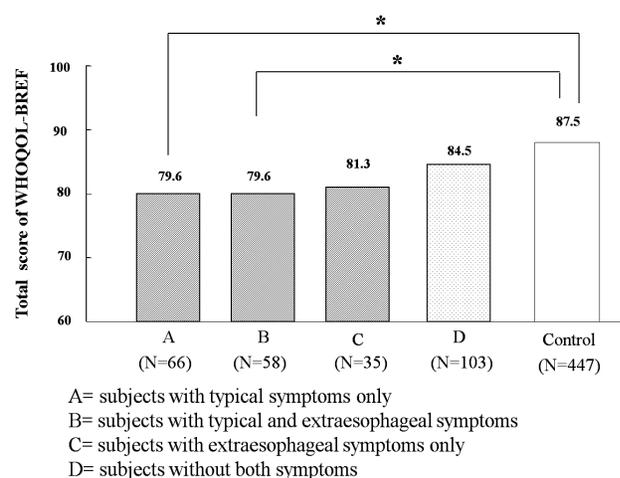


Figure 2. Differences of the total score (±SD) of WHOQOL-BREF according to GERD symptoms. QoL: Quality of life. GERD: Gastroesophageal reflux disease.

DISCUSSION

The study results showed that the GERD group had a lower QoL than the healthy control group. In the classification by symptoms, the group with typical symptoms had a significantly impaired QoL compared to the group with extraesophageal symptoms. The Genval Workshop Report (J Dent) had considered the frequency of symptoms and all aspects of QoL by defining GERD as involving symptoms that occurred twice a week or more (14). On the contrary, the Montreal Consensus and the Asia-Pacific Consensus emphasized symptom-related QoL by defining GERD as involving patient discomfort from reflux symptoms, which does not rely on symptom frequency (15,16).

This study demonstrated that the severity and frequency of symptoms lowered the QoL and productivity of GERD patients (17), and the severity of symptoms was related more to QoL than was the frequency of symptoms (18). Existing studies of QoL focused mostly on classical symptoms, but there have also been studies related to atypical symptoms and the QoL. When assessing QoL with the Short Form (SF)-36 in a group with laryngopharyngeal reflux (LPR) symptoms, the LPR group had a lower QoL than that of a control group. When the study subjects with LPR symptoms were separated into a GERD-related and a non-related group, the subjects in the GERD-related group had a lower QoL (as diagnosed by the validated Chinese GERDQ and/or the presence of erosive esophagitis). The GERD symptoms, rather than the laryngopharyngeal symptoms, were the main contributors to the decrease in QoL in the LPR patients (19). In other words, GERD was the main cause of impaired QoL in patients with LPR. The present study also demonstrated that the group with typical symptoms had a lower QoL than the group with extraesophageal symptoms, which means that typical symptoms are related to a lower QoL. In another study, QoL was poorer in women and in obese individuals (20), but the present study found no differences by sex or body weight.

Gastroesophageal reflux disease (GERD) has impacts on the QoL in terms of one's physical state, emotional state, social function, and productivity (21). In this study, the QoL was assessed with the questionnaires of the WHOQOL-BREF, which enabled assessments of physical health, psycholo-

gical health, social health, and spiritual health. In a study that used the WHOQOL-BREF to assess QoL in patients with diabetes, the QoL in GERD patients was better than in the diabetes patients who controlled their symptoms 1-2 times daily and in diabetes patients who controlled their symptoms 4 times or more in a day (22) (GERD: 81.7; DM 1-2 times: 75.3; DM >4 times: 74.3). The QoL score in the GERD group was 81.7, but it was reduced to 79.9 when patients with asymptomatic erosive esophagitis were excluded. As this study was performed in health check-up patients and not in patients who visited the hospital for their symptoms, only minor degrees of GERD were included; if the study had been performed in actual patients, the QoL scores would have likely been much lower.

In this study, 80% of patients with erosive esophagitis had no symptoms, while 29% of patients with extraesophageal symptoms had esophagitis. These results were similar to the health check-up study subjects, in which 70-80% of patients with erosive esophagitis did not have classical symptoms (23,24). In a Swedish study, Ronkainen et al. (25) reported that one-third of patients with erosive esophagitis had no symptoms, and only one-fourth of patients with typical symptoms had esophagitis. The reason that there was more asymptomatic esophagitis was because the study was performed in health check-up subjects who were likely to have minor symptoms. In fact, 80% of subjects were Class A in the LA classifications, which represents the mild form. Our hospital is not a tertiary center, and the study subjects were health check-up subjects who were not representative of the population. However, by excluding those who had taken any drug for gastrointestinal treatment in the past three months, we minimized the occlusion of symptoms because of medication. Furthermore, no appropriate terminology was available for the interpretation of classical symptoms. Nevertheless, even when the interpretation of typical symptoms was expanded to include upper abdominal heartburn and upper abdominal pain, 72% of patients

with erosive esophagitis were asymptomatic. The QoL in asymptomatic esophagitis was comparatively lower than that of the control group in terms of physical health, and there was no difference in total scores.

As the prevalence of GERD increases, asymptomatic esophagitis will also increase. Patients will not visit medical institutions because there have been no studies of the risk factors and the clinical profile of asymptomatic esophagitis; furthermore, because the disease has no symptoms, studies are needed on its natural progression when it is left untreated.

This study has its limitations. First, because this study was cross-sectional, it was unable to demonstrate any improvement in QoL that could have resulted from anti-gastric acid secretory treatment. Therefore, this study was unable to identify direct connections between QoL and symptoms. Second, this study has a sampling limitation. Because the study was conducted in health check-up subjects, most subjects in the group with erosive esophagitis had minor esophagitis and belonged to classes A and B of the LA Classifications. Our study did increase its reliability by excluding patients who took digestive medication in the previous three months. In the selection of the control group, the gender proportions were adjusted so that there were equal numbers of males and females. Additionally, subjects who had no classical and/or atypical symptoms were included in the control group. Third, there is a possibility that the GERD group includes patients with functional heartburn. In this study, 24-hour ambulatory pH tests and proton pump inhibitor (PPI) tests were not carried out.

In conclusion, the subjects with GERD had a deteriorated QoL compared to the healthy control group. When classic symptoms were present, the QoL was lowered further. Therefore, medication treatments should be required in patients with these symptoms to improve their QoL.

REFERENCES

1. Agreus L, Svardsudd K, Talley NJ, et al. Natural history of gastroesophageal reflux disease and functional abdominal disorders: a population-based study. *Am J Gastroenterol* 2001; 96: 2905-14.
2. Locke GR 3rd, Talley NJ, Fett SL, et al. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. *Gastroenterology* 1997; 112: 1448-56.
3. Wong WM, Lai KC, Lam KF, et al. Prevalence, clinical spectrum and health care utilization of gastro-oesophageal reflux disease in a Chinese population: a population-based study. *Aliment Pharmacol Ther* 2003; 18: 595-604.
4. Yang SY, Lee OY, Bak YT, et al. Prevalence of gastroesophageal reflux disease symptoms and uninvestigated dyspepsia in Korea: a population-based study. *Dig Dis Sci* 2008; 53: 188-93.

5. Goh KL. Changing epidemiology of gastroesophageal reflux disease in the Asian-Pacific region: an overview. *J Gastroenterol Hepatol* 2004; 19 (Suppl): S22-5.
6. Kim JI, Kim SG, Kim N, et al. Changing prevalence of upper gastrointestinal disease in 28 893 Koreans from 1995 to 2005. *Eur J Gastroenterol* 2009; 21: 787-93.
7. Kulig M, Leodolter A, Vieth M, et al. Quality of life in relation to symptoms in patients with gastro-oesophageal reflux disease-- an analysis based on the ProGERD initiative. *Aliment Pharmacol Ther* 2003; 18: 767-76.
8. Bruley Des Varannes S, Marek L, Humeau B, et al. Gastroesophageal reflux disease in primary care. Prevalence, epidemiology and quality of life of patients. *Gastroenterol Clin Biol* 2006; 30: 364-70.
9. Hongo M, Kinoshita Y, Shimozuma K, et al. Psychometric validation of the Japanese translation of the Quality of Life in Reflux and Dyspepsia questionnaire in patients with heartburn. *J Gastroenterol* 2007; 42: 807-15.
10. Locke GR, Talley NJ, Weaver AL, et al. A new questionnaire for gastroesophageal reflux disease. *Mayo Clin Proc* 1994; 69: 539-47.
11. Cho YS, Choi MG, Jeong JJ, et al. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Asan-si, Korea. *Am J Gastroenterol* 2005; 100: 747-53.
12. The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. *Psychol Med* 1998; 28: 551-8.
13. Min SK, Lee CI, Kim KI, et al. Development of Korean version of WHO quality of life scale abbreviated version (WHOQOL-BREF). *J Korean Neuropsychiatr Assoc* 2000; 39: 571-9.
14. Dent J, Armstrong D, Delaney B, et al. Symptom evaluation in reflux disease: workshop background, processes, terminology, recommendations, and discussion outputs. *Gut* 2004; 53 (Suppl): iv1-24.
15. Vakil N, van Zanten SV, Kahrilas P, et al. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2006; 101: 1900-20; quiz 1943.
16. Fock KM, Talley NJ, Fass R, et al. Asia-Pacific consensus on the management of gastroesophageal reflux disease: update. *J Gastroenterol Hepatol* 2008; 23: 8-22.
17. Wahlqvist P, Karlsson M, Johnson D, et al. Relationship between symptom load of gastro-oesophageal reflux disease and health-related quality of life, work productivity, resource utilization and concomitant diseases: survey of a US cohort. *Aliment Pharmacol Ther* 2008; 27: 960-70.
18. Eslick GD, Talley NJ. Gastroesophageal reflux disease (GERD): risk factors, and impact on quality of life-a population-based study. *J Clin Gastroenterol* 2009; 43: 111-7.
19. Cheung TK, Lam PK, Wei WI, et al. Quality of life in patients with laryngopharyngeal reflux. *Digestion* 2009; 79: 52-7.
20. Ponce J, Beltran B, Ponce M, et al. Impact of gastroesophageal reflux disease on the quality of life of Spanish patients: the relevance of the biometric factors and the severity of symptoms. *Eur J Gastroenterol Hepatol* 2009; 21: 620-9.
21. Quigley EM, Hungin AP. Review article: quality-of-life issues in gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2005; 22 (Suppl): 41-7.
22. Park YR, Kim TS, Park YG, et al. Influence of multiple insulin injections on quality of life, anxiety levels, and depression in type 2 diabetics. *Korean J Med* 2009; 77: 60-7.
23. Oh JH, Choi MG, Kim HR, et al. Clinical spectrum of endoscopic reflux esophagitis in routine check-up subjects in Korea. *Kor J Neurogastroenterol* 2006; 12: 12-8.
24. Kim HY, Kim N, Kim SN, et al. Clinical spectrum and risk factors of erosive and non-erosive GERD in health check-up subjects. *Korean J Med* 2006; 71: 491-500.
25. Ronkainen J, Aro P, Storskrubb T, et al. High prevalence of gastroesophageal reflux symptoms and esophagitis with or without symptoms in the general adult Swedish population: a Kalixanda study report. *Scand J Gastroenterol* 2005; 40: 275-85.