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Authors:
Ana Zatarain Valles, Blanca Serrano Falcón, Ángel Álvarez Sánchez, Enrique Rey Díaz-Rubio

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Independent factors associated with the impact of gastroesophageal reflux disease on health-related quality of life

Ana Zatarain-Valles, Blanca Serrano-Falcón, Ángel Álvarez-Sánchez and Enrique Rey-Díaz-Rubio

Division of Digestive Disease. Hospital Clínico San Carlos. Madrid, Spain. Universidad Complutense. Instituto de Investigación Sanitaria San Carlos (IdISSC). Madrid, Spain

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Correspondence: Ana Zatarain Valles. Division of Digestive Disease. Hospital Clínico San Carlos. Planta Baja Norte. C/ Profesor Martín Lagos, s/n. 28040 Madrid, Spain

e-mail: ana.zatarain.valles@gmail.com

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ABSTRACT

Background: although a number of factors have been associated with a deterioration in quality of life in gastroesophageal reflux disease, it is not known which has an independent influence.

Objective: to evaluate factors independently associated with the impact of gastroesophageal reflux disease on health-related quality of life.

Methods: a post-hoc analysis of a prospective cohort of patients diagnosed with gastroesophageal reflux disease was performed. The patients completed validated questionnaires to evaluate health-related quality of life (SF 36), gastroesophageal reflux disease (GERQ) and psychological factors (STAI and SCL 90R)

Results: the study included 98 patients. The univariate analysis showed that a deterioration in the physical component of the SF36 was significantly associated with female gender, educational level, age, weight loss, severity of typical symptoms, supraesophageal symptoms and monthly income. The mental component was

significantly associated with alcohol consumption, epigastric pain and lower scores on the STAI and SCL90 questionnaires. The multivariate analysis showed an independent association between the physical component of the SF36 and educational level (β = 0.29; $p < 0.01$), severity of symptoms (β = -0.38; $p < 0.001$), body mass index (β = -0.30; $p < 0.005$), state anxiety (β = 0.28; $p < 0.01$), female gender (β = -0.23; $p < 0.05$) and dyspepsia (β = -0.21; $p<0.05$). Associated variables within the mental component included state anxiety (β = -0.39; $p < 0.01$) and depression (β = -0.32; $p < 0.05$).

Conclusions: the principal factors independently associated with a deterioration in health-related quality of life in patients with gastroesophageal reflux disease included the severity of typical symptoms and the presence of dyspepsia. There is also an additional impact of body mass index and the psychological component.

Key words: Gastroesophageal reflux. Health-Related quality of life. Dyspepsia. Multivariate analysis.

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is one of the most frequent digestive disorders in western societies. It has a variable prevalence ranging from 9% to 40% (1-3), obesity and somatization are the principal related factors (4). While heartburn and/or acid regurgitation are the typical symptoms of GERD (5), patients may also suffer from atypical symptoms (6) and it is frequently associated with dyspepsia (7). In addition, 25% of patients present with related anxiety (8).

A number of studies have reported an association between GERD and a deterioration in health-related quality of life (HRQoL) (9-11). Different studies have linked this deterioration to sociodemographic (age and sex) and anthropometric factors (Body Mass Index) (12), frequency and severity of typical symptoms (13), nocturnal pattern and atypical symptoms (5). Similarly, the presence of psychiatric disorders (14), functional dyspepsia and irritable bowel syndrome (15) may have a negative influence on their HRQoL in this group of patients.

The individual identification of the factors that affect quality of life (QoL) can be clinically useful for focusing therapeutic efforts on the final goal of improving quality of life. HRQoL is a concept that sees the patient as an indivisible whole with multiple

factors interacting to produce the final outcome of the individual (16). As there are many factors related with the deterioration of QoL of GERD patients, these may interact amongst themselves. Thus, it is of interest to identify those which are independently associated. This fact would enable therapeutic efforts in the clinical practice to be focused on the most relevant factors. Therefore, the aim of this study was to identify the clinical factors that were independently associated with deterioration of QoL in patients with GERD.

MATERIALS AND METHODS

Study population

Design

A post-hoc analysis of a prospective observational cohort of consecutive patients with a clinical diagnosis of GERD referred to the Department of Digestive Diseases at a tertiary referral hospital (Hospital Clínico San Carlos) was performed. The cohort included all patients over the age of 18 years with typical symptoms of GERD (heartburn and/or acid regurgitation) at least twice a week. The study was approved by the Institutional Ethics Committee of the Hospital Clínico San Carlos. All patients gave written informed consent before being included into the study.

Instruments

Sociodemographic data (age, sex, educational level, marital status, occupational status and monthly income), anthropometric data (BMI, plus data on weight change in the preceding year) and habits (tobacco and alcohol) were drawn from the relevant items within the Gastroesophageal Reflux Questionnaire (GERQ). A validated Spanish-version (17), which had been adequately applied in another population-based study, was used in this study (8). The GERQ is made up of 76 items which quantify GERD symptoms reliably and reproducibly. It lists the frequency, duration, severity and nocturnal presence of typical symptoms, as well as the existence of atypical and supraesophageal symptoms.

The instrument used to measure HRQoL was the SF36 questionnaire, which has been validated in Spanish and has reference values for the use in this population (18). The questionnaire is made up of 36 questions that rate positive and negative health states

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on the following eight scales: physical functioning; role-physical; bodily pain; general health; vitality; social functioning; role- emotional and mental health. The scale is scored from 0 (worst state of health for that dimension) to 100 (best state of health) for each dimension.

Two widely-used questionnaires validated in Spanish were used to measure the psychological factors, the State-Trait Anxiety Inventory (STAI) (19) and the Symptom Checklist-90-R (SCL-90R) (20). The STAI is made up of two components: trait anxiety (personality predisposition to experience or not experience anxiety) and state anxiety (environmental factors that protect against or generate anxiety). Both questionnaires comprise 20 items each, with a Likert-type response scale scored from 0 (not at all) to 3 (very much so).

The SCL-90R is made up of 90 questions, which are answered on a five-point scale scored from 0 (none at all) to 4 (very severe), in accordance with how the subject has been feeling during the preceding 7 days. It is interpreted by reference to nine primary dimensions and three global indices of psychological distress. Our study evaluated the somatization and depression scales along with the following three global indices, the Global Severity Index (GSI), the Positive Symptom Distress Index (PSDI) and the Positive Symptom Total (PST). The presence of dyspepsia and irritable bowel syndrome was evaluated by clinical diagnosis as per the Rome III criteria (21).

Variables and definitions

The main study variable was HRQoL, which was assessed on the basis of the SF 36 physical- and mental-component scores. The sociodemographic variables included as predictors in the models were age and BMI, the latter was calculated using the Quetelet formula [Weight (kg)/Height² (m^2)] and categorized into three groups (normal < 20; overweight 25 to 30 and obese > 30). Weight change was defined as a self-reported gain of more than 5 kg in the preceding year. Educational level was categorized as primary, secondary or university. Monthly income was measured in euros.

The following symptoms were evaluated and categorized as absence or presence: heartburn, acid regurgitation, nocturnal symptoms, thoracic pain (weekly), dysphagia (weekly), epigastric pain (weekly), supraesophageal symptoms (dysphonia, cough),

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indigestion (weekly) and postprandial distension (weekly). The self-reported severity of typical reflux symptoms was categorized as mild, moderate, severe or very severe. Irritable bowel syndrome was also categorized as a dichotomous variable (yes or no). The psychological variables included in the analysis were trait anxiety and state anxiety from the STAI questionnaire and the T score on the somatization and depression scales.

Statistical analysis

The descriptive statistical analysis included the mean and standard deviation for quantitative variables. A univariate analysis was performed to assess the relationship between the various study variables (independent variables) and the physical and mental components of the SF36 (dependent variable) using an analysis of variance (ANOVA). In line with the main aim of the study, all the above analyzed variables were included in two linear regression models as potential predictors of the physical and mental components of the SF36. The qualitative variables were transformed into dummy variables for inclusion into the models. The assumptions that justify the use of regression models (linearity, normality, homoscedasticity and independence) were fulfilled. A value of $p < 0.05$ was considered as significant. All statistical analyses were performed using the SPSS v22 software program.

RESULTS

At the time of enrolment, the starting cohort included a total of 107 patients with GERD, 98 (91.6%) of whom agreed to participate and complete the questionnaires. 40 patients were male and 58 were female, the mean age was 41.06 ± 13.65 years [18-70]. With regard to BMI, 39 patients (40%) were overweight and 15 (15%) were obese. In addition, 11 (11%) patients reported having heartburn, 42 (43%) acid regurgitation and 45 (46%) reported both symptoms. These were regarded as mild intensity in 17 (17%) patients, moderate intensity in 71 (73%), severe intensity in 7 (7%) patients and a very severe intensity in 3 (3%) patients.

Univariate analysis

Female gender, primary educational level, age from 41 to 65 years, weight loss of at least 5 kg in the preceding year, severity of GERD symptoms and the presence of supraesophageal symptoms were significantly associated with worse SF36 physical-component scores. With regard to the mental dimension, secondary educational level, monthly income of 1,500-3,000 euros, weight loss of at least 5 kg in the preceding year, alcohol consumption, the presence of epigastric pain and lower STAI and SCL90 scores were significantly associated with worse SF36 scores (Table 1).

Multivariate analysis

Educational level, severity of GERD symptoms, BMI, state anxiety (STAI), female gender and the presence of symptoms of dyspepsia were factors independently associated with worse SF36 physical-component values according to the linear regression analysis. The model accounted for 38% of variance. State anxiety and depression were independent factors associated with the mental component, the model accounted for 42% of variance (Table 2).

DISCUSSION

Our study is the first of its kind to identify the clinically relevant variables which independently contribute to the deterioration in HRQoL among patients with GERD. The severity of typical symptoms and the association with dyspepsia and anxiety were the main factors that were objectively related with a worse QoL according to the SF-36 questionnaire. Other studies have shown that GERD has an adverse effect on HRQoL using general and disease-specific questionnaires (22). Indeed, the impact of GERD on QoL is similar to that of other chronic diseases, such as arthritis, depression, heart failure and diabetes (23,24). As a consequence, quality of life has become the principal therapeutic target in GERD (25). In order to achieve this therapeutic goal in the clinical practice, this would require from a practical standpoint, the ascertainment of factors with the greatest impact on QoL. Thus, treatment could be tailored to the individual patient. A number of studies have evaluated some of these factors, although not globally.

Typical symptoms of GERD

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Heartburn and acid regurgitation are the main symptoms of GERD and our study shows that only 11% of patients reported heartburn, whereas 43% of patients experienced acid regurgitation and 46% of cases experienced both. These differences can be explained by the poor understanding of the meaning of "heartburn" by patients and also the difficulty to recognize heartburn versus other gastro-esophageal symptoms, as previously reported Manabe N et al (26). In our study, the severity of typical GERD symptoms was associated with a deterioration in SF36 scores. This is in line with the results published by Tack *et al*. of a systematic review, which showed that the frequency and severity of typical symptoms and the presence of nocturnal symptoms results in a greater deterioration of HRQoL, in both SF36 components (22). Even so, our study failed to identify the presence of nocturnal symptoms as an independently associated factor. This may be due to the differences in the definitions used and also the use of GERD-specific quality-of-life questionnaires (Reflux-Qual® of QoLRAD) in previous studies that examined nocturnal symptoms more exhaustively.

Supraesophageal symptoms

Previous studies have associated supraesophageal symptoms with a greater deterioration in QoL of GERD patients (27) and the univariate analysis performed with our data confirmed this. Supraesophageal symptoms regarded as atypical manifestations, such as a cough, were significantly associated with worse SF36 physical-component scores. Nevertheless, this association was not statistically significant in the subsequent multivariate analysis. Accordingly, we are unable to rank atypical symptoms with a worse response to treatment as an independent risk factor of a poorer QoL. This fact highlights the complexity of the problem.

Obesity

Both obesity (28) and simple weight gain (29) are associated with a higher probability of suffering from and developing GERD (4). Although the exact mechanism remains unknown. Furthermore, obesity has previously been associated with a greater deterioration in QoL in GERD patients (30). Our results are in line with these previous studies, as obesity was shown to be independently associated with a deterioration in QoL in GERD patients.

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Associated functional digestive disorders

Dyspepsia and irritable bowel syndrome are associated with GERD (31–34) more frequently than would be expected randomly. Bearing in mind that both of these disorders have been linked to a deterioration in QoL (15)(35), it is reasonable to surmise that they would be associated with a greater deterioration in the QoL of GERD patients. In fact, dyspepsia has been shown to be associated with such a deterioration (27). According to our results, dyspeptic symptoms are independently associated with deterioration in GERD QoL, thus implying the need for special clinical care in this respect. In contrast, we were unable to find evidence of a deterioration in the HRQoL of GERD patients who presented with irritable bowel syndrome.

Anxiety

It is known that GERD patients have a higher prevalence of psychological disorders (36) and that their QoL is reduced in the presence of anxiety, depression (37) and other nonpsychotic psychiatric disorders (14). Similarly, some reflux symptoms such as pyrosis have been shown to be associated with psychiatric diseases (38). Our results identified anxiety as an independent risk factor for the deterioration in GERD QoL.

Sociodemographic aspects

The non-modifiable variables shown by our study to be independently associated with lower SF 36 scores were female gender and primary educational level. The presence of GERD in females has been linked to a worse HRQoL in many studies (12,30,39). Even though a low educational level is known to act as a risk factor for GERD (40), it had not been associated with a reduction in QoL. In other diseases, individuals with a higher educational level have registered better scores on their HRQoL-specific questionnaires, by virtue of being better equipped to tackle their respective ailments (41).

Independently associated factors

The results of our analysis show that the following modifiable variables were independently associated with a deterioration in QoL: severity of GERD symptoms, BMI, the presence of symptoms of dyspepsia, a state anxiety (STAI) and depression.

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From a practical point of view, if improvement in QoL is identified as a therapeutic goal, then our attention should not solely focus on the typical symptoms of the disease.

In conclusion, this is the first study to use a multivariate analysis to analyze the factors associated with the impact of GERD on the QoL of patients. Once the independent variables that cause this effect are known, it is essential to optimize the hygienic-dietary and therapeutic measures that target severe gastroesophageal reflux, which is associated with being overweight, dyspeptic symptoms, anxiety and depression. The improvement in QoL of GERD patients reflects the success of our intervention.

LIMITATIONS

This was a post-hoc evaluation of a prospective study that was not initially designed with this aim in mind. Thus, information pertaining to comorbidities and other variables associated with a deterioration in GERD QoL of potential interest could not be assessed. However, this did not prevent the main objective of this study from being achieved. Therefore, new studies are required to test our results and these variables should be included in the study design.

REFERENCES

1. Dent J. Epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut 2005;54(5):710-7. DOI: 10.1136/gut.2004.051821

2. Díaz-Rubio M, Moreno-Elola-Olaso C, Rey E, et al. Symptoms of gastro-oesophageal reflux: prevalence, severity, duration and associated factors in a Spanish population. Aliment Pharmacol Ther 2004;19(1):95-105. DOI: 10.1046/j.1365-2036.2003.01769.x

3. Rey E, Álvarez-Sánchez A, Rodríguez-Artalejo F, et al. Onset and disappearance rates of gastroesophageal reflux symptoms in the Spanish population, and their impact on quality of life. Rev Esp Enferm Dig 2009;101(7):477. DOI: 10.4321/S1130-01082009000700005

4. Barceló M, Sánchez AA, Sánchez RG, et al. Weight gain and somatization are associated with the onset of gastroesophageal reflux diseases: results of two 5-year follow-up studies. J Clin Gastroenterol 2016;50(3):202-7. DOI: 10.1097/MCG.0000000000000364

Accepted Article

5. Dean BB, Aguilar D, Johnson LF, et al. Night-time and daytime atypical manifestations of gastro-oesophageal reflux disease: frequency, severity and impact on health-related quality of life: atypical manifestations of gerd. Aliment Pharmacol Ther 2007;27(4):327-37. DOI: 10.1111/j.1365-2036.2007.03574.x

6. Rey E, Elola-Olaso CM, Rodríguez-Artalejo F, et al. Prevalence of atypical symptoms and their association with typical symptoms of gastroesophageal reflux in Spain. Eur J Gastroenterol Hepatol 2006;18(9):969-75. DOI: 10.1097/01.meg.0000230081.53298.03

7. Rasmussen S, Jensen TH, Henriksen SL, et al. Overlap of symptoms of gastroesophageal reflux disease, dyspepsia and irritable bowel syndrome in the general population. Scand J Gastroenterol 2015;50(2):162-9. DOI: 10.3109/00365521.2014.983157

8. Rey E, García-Alonso M, Moreno-Ortega M, et al. Influence of Psychological Distress on Characteristics of Symptoms in Patients with GERD: The Role of IBS Comorbidity. Dig Dis Sci 2009;54(2):321-7. DOI: 10.1007/s10620-008-0352-5

9. Hansen JM, Wildner-Christensen M, Schaffalitzky de Muckadell OB. Gastroesophageal Reflux Symptoms in a Danish Population: A Prospective Follow-Up Analysis of Symptoms, Quality of Life, and Health-Care Use. Am J Gastroenterol 2009;104(10):2394-403. DOI: 10.1038/ajg.2009.391

10. Gisbert JP, Cooper A, Karagiannis D, et al. Impact of gastroesophageal reflux disease on patients' daily lives: a European observational study in the primary care setting. Health Qual Life Outcomes 2009;7(1):60. DOI: 10.1186/1477-7525-7-60

11. Ronkainen J, Aro P, Storskrubb T, et al. Gastro-oesophageal reflux symptoms and health-related quality of life in the adult general population - the Kalixanda study. Aliment Pharmacol Ther 2006;23(12):1725-33. DOI: 10.1111/j.1365-2036.2006.02952.x

12. Ponce J, Beltrán 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(6):620-9. DOI: 10.1097/MEG.0b013e328310abe9

13. Des Varannes SB, Marek L, Humeau B, et al. Gastroesophageal reflux disease in primary care. Gastroentérologie Clin Biol 2006;1224(3):351-501. DOI: 10.1016/S0399-8320(06)73189-X

Accepted Article

14. Díaz de Liaño Á, Yárnoz C, Artieda C, et al. Gastroesophageal reflux: prevalence of psychopathological disorders and quality of life implications. Dis Esophagus 2006;19(5):373-6. DOI: 10.1111/j.1442-2050.2006.00597.x

15. De Vries DR, Van Herwaarden MA, Baron A, et al. Concomitant functional dyspepsia and irritable bowel syndrome decrease health-related quality of life in gastroesophageal reflux disease. Scand J Gastroenterol 2007;42(8):951-6. DOI: 10.1080/00365520701204204

16. Testa MA, Simonson DC. Assessment of quality-of-life outcomes. N Engl J Med 1996;334(13):835-40. DOI: 10.1056/NEJM199603283341306

17. Moreno Elola-Olaso C, Rey E, Rodríguez-Artalejo, et al. Adaptation and validation of a gastroesophageal reflux questionnaire for use on a Spanish population. Rev Esp Enferm Dig 2002;94(12):745-58.

18. Alonso J, Prieto L, Antó JM. La versión española del SF-36 Health Survey (Cuestionario de Salud SF-36): un instrumento para la medida de los resultados clínicos. Med Clin Barc 1995;104(20):771-6.

19. Spielberger C, Gorsuch R, Lushene R. STAI Cuestionario de ansiedad estado rasgo. (Adaptación española: Nicolás Seisdedos Cubero); 1994.

20. González de Rivera JL, de las Cuevas C, Rodríguez M, et al. Cuestionario de 90 síntomas SCL-90-R de L. Derogatis. Adapt Esp Madr. Madrid: TEA Ediciones; 2002.

21. Longstreth GF, Thompson WG, Chey WD, et al. Functional Bowel Disorders. Gastroenterology 2006;130(5):1480-91. DOI: 10.1053/j.gastro.2005.11.061

22. Tack J, Becher A, Mulligan C, et al. Systematic review: the burden of disruptive gastro-oesophageal reflux disease on health-related quality of life. Aliment Pharmacol Ther 2012;35(11):1257-66. DOI: 10.1111/j.1365-2036.2012.05086.x

23. Wiklund I. Review of the Quality of Life and Burden of Illness in Gastroesophageal Reflux Disease. Dig Dis 2004;22(2):108-14. DOI: 10.1159/000080308

24. Wahlqvist P. Symptoms of gastroesophageal reflux disease, perceived productivity, and health-related quality of life. Am J Gastroenterol 2001;96(8):S57-S61. DOI: 10.1016/S0002-9270(01)02590-4

25. Irvine EJ. Quality of life assessment in gastro-oesophageal reflux disease. Gut 2004;53(Suppl. 4):iv35-9. DOI: 10.1136/gut.2003.034314

Accepted Article

26. Manabe N, Haruma K, Hata J, et al. Differences in recognition of heartburn symptoms between Japanese patients with gastroesophageal reflux, physicians, nurses, and healthy lay subjects. Scand J Gastroenterol 2008;43(4):398-402. DOI: 10.1080/00365520701815074

27. Mearin F, Ponce J, Ponce M, et al. Frequency and clinical implications of supraesophageal and dyspeptic symptoms in gastroesophageal reflux disease: Eur J Gastroenterol Hepatol 2012;24(6):665-74. DOI: 10.1097/MEG.0b013e3283512139

28. Friedenberg FK, Xanthopoulos M, Foster GD, et al. The Association Between Gastroesophageal Reflux Disease and Obesity. Am J Gastroenterol 2008;103(8):2111-22. DOI: 10.1111/j.1572-0241.2008.01946.x

29. Rey E, Moreno-Elola-Olaso C, Artalejo FR, et al. Association between Weight Gain and Symptoms of Gastroesophageal Reflux in the General Population. Am J Gastroenterol 2006;101(2):229-33. DOI: 10.1111/j.1572-0241.2006.00412.x

30. Lee S-W. Impact of body mass index and gender on quality of life in patients with gastroesophageal reflux disease. World J Gastroenterol 2012;18(36):5090. DOI: 10.3748/wjg.v18.i36.5090

31. Lee SY, Lee KJ, Kim SJ, et al. Prevalence and Risk Factors for Overlaps between Gastroesophageal Reflux Disease, Dyspepsia, and Irritable Bowel Syndrome: A Population-Based Study. Digestion 2009;79(3):196-201. DOI: 10.1159/000211715

32. Jung H-K, Halder S, Mcnally M, et al. Overlap of gastro-oesophageal reflux disease and irritable bowel syndrome: prevalence and risk factors in the general population: OVERLAP OF GERD AND IBS. Aliment Pharmacol Ther 2007;26(3):453-61. DOI: 10.1111/j.1365-2036.2007.03366.x

33. Bortoli N. Overlap of functional heartburn and gastroesophageal reflux disease with irritable bowel syndrome. World J Gastroenterol 2013;19(35):5787. DOI: 10.3748/wjg.v19.i35.5787

34. Rey E, García-Arredondo M. Enfermedad por reflujo gastroesofágico y síndrome de intestino irritable: ¿por qué se asocian? Rev Esp Enfermedades Dig 2010;102(4):225-8.

35. Kaji M, Fujiwara Y, Shiba M, et al. Prevalence of overlaps between GERD, FD and IBS and impact on health-related quality of life: Overlap of FGIDs and HR-QOL. J Gastroenterol Hepatol 2010;25(6):1151-6. DOI: 10.1111/j.1440-1746.2010.06249.x

Accepted Article

36. Hartono JL, Mahadeva S, Goh K-L. Anxiety and depression in various functional gastrointestinal disorders: Do differences exist?: Anxiety and depression in FGIDs. J Dig Dis 2012;13(5):252-7. DOI: 10.1111/j.1751-2980.2012.00581.x

37. Yang X-J. Anxiety and depression in patients with gastroesophageal reflux disease and their effect on quality of life. World J Gastroenterol 2015;21(14):4302. DOI: 10.3748/wjg.v21.i14.4302

38. Avidan B, Sonnenberg A, Giblovich H, et al. Reflux symptoms are associated with psychiatric disease. Aliment Pharmacol Ther 2001;15(12):1907-12. DOI: 10.1046/j.1365-2036.2001.01131.x

39. Lippmann QK, Crockett SD, Dellon ES, et al. Quality of Life in GERD and Barrett's Esophagus Is Related to Gender and Manifestation of Disease. Am J Gastroenterol 2009;104(11):2695-703. DOI: 10.1016/j.cgh.2009.02.024

40. Dore MP, Maragkoudakis E, Fraley K, et al. Diet, Lifestyle and Gender in Gastro-Esophageal Reflux Disease. Dig Dis Sci 2008;53(8):2027-32. DOI: 10.1007/s10620-007-0108-7

41. Verma AK, Schulte PJ, Bittner V, et al. Socioeconomic and partner status in chronic heart failure: Relationship to exercise capacity, quality of life, and clinical outcomes. Am Heart J 2017;183:54-61. DOI: 10.1016/j.ahj.2016.10.007

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Table 1. Univariate analysis of the association between patients' baseline characteristics and the results of the SF36 questionnaire

Variable	**Category**	**SF36 Physical component**	**SF36 Mental component**	***p* value**	
				SF36 Physical	**SF36 Mental**
Age	< 40 years	50.4 ± 6.6	41.2 ± 12.6	0.002	0.279
	41-65 years	44.2 ± 9.7	45.2 ± 12.7		
	> 65 years	45.2 ± 8.8	46.1 ± 11.2		
Sex	Male	50.3 ± 6.4	45.9 ± 11.3	0.006	0.076
	Female	45.5 ± 9.4	41.3 ± 13.3		

Educational level	Primary	42.2 ± 9.9	44.6 ± 13	0.0001	0.003
	Secondary	48.8 ± 8.9	36.6 ± 13.1		
	University	50.1 ± 5.6	46.8 ± 10.5		
Marital status	Single	49.7 ± 7.6	41.3 ± 11.3	0.071	0.419
	Married/Partner	46.8 ± 8.0	43.6 ± 12.9		
	Divorced/Widowed	43.0 ± 12.9	47.0 ± 15.8		
Occupational status	Student	49.4 ± 8.6	43.0 ± 13.1	0.680	0.579
	Gainfully employed	47.6 ± 8.4	42.9 ± 12.9		
	Unemployed	44.8 ± 11.1	51.7 ± 5.1		
	Retired	43.6 ± 12.7	40.9 ± 13.7		
Monthly income	< €1,500	46.2 ± 10.7	44.1 ± 12.7	0.596	0.025
	€ 1,500 - €3,000	47.8 ± 8.2	40.1 ± 13.2		
	> €3,000	48.6 ± 5.6	49.3 ± 8.1		
BMI	Normal	47.7 ± 8.7	42.3 ± 12.1	0.259	0.821
	Overweight	48.3 ± 6.5	43.5 ± 12.7		
	Obese	43.9 ± 13.1	44.6 ± 15.5		
Weight change in the preceding year	Loss of ≥ 5 kg	42.9 ± 9.3	33.0 ± 16.8	0.028	0.044
	Stable	49.0 ± 7.2	44.6 ± 11. 1		
	Gain of ≥ 5 kg	44.0 ± 12.4	41.8 ± 15.1		
Smoking	Nonsmoker	46.7 ± 7.2	43.4 ± 10.1	0.825	0,217
	Smoker	47.9 ± 9.1	41.1 ± 13.5		
	Ex-smoker	47.8 ± 10.4	47.2 ± 14.6		
	None	46.4 ± 8.1	38.8 ± 13.8		
	< 75 g / week	47.0 ± 9.7	44.2 ± 12.3		
	75-175 g / week	49.4 ± 7.8	44.6 ± 10.6		

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Alcohol	> 175 g / week	49.8 ± 7.2	52.9 ± 7.9	0.557	0.036
Type of symptoms	Pyrosis	49.8 ± 6.9	41.5 ± 12.1		
	Regurgitation	47.4 ± 9.0	43.4 ± 11.4		
	Both	46.5 ± 8.7	42.7 ± 14.1	0.534	0.901
Severity of symptoms	Mild	50.3 ± 6.1	44.5 ± 10.8		
	Moderate	47.5 ± 8.7	43.6 ± 12.9		
	Severe	43.1 ± 8.9	34.0 ± 10.0		
	Very severe	33.9 ± 4.9	39.6 ± 20.9	0.011	0.255
Disease progression	1 year or less	47.9 ± 8.4	42.5 ± 13.4		
	1-5 years	48.5 ± 8.0	41.2 ± 11.1		
	More than 5 years	46.6 ± 9.2	44.7 ± 13.4	0.629	0.489
Nocturnal symptoms	No	49.1 ± 8.0	43.8 ± 12.7		
	Yes	46.6 ± 8.9	42.8 ± 12.7	0.184	0.707
Thoracic pain	No	48.6 ± 7.9	44.5 ± 11.9		
	Yes	45.3 ± 9.7	40.6 ± 13.9	0.078	0.148
Dysphagia	No	48.2 ± 8.4	43.8 ± 12.3		
	Yes	44.8 ± 9.2	40.7 ± 14.6	0.339	0.034
Extraesophageal symptoms	No	49.7 ± 7.0	46.1 ± 10.5		
	Yes	45.9 ± 9.3	41.1 ± 13.7	0.034	0.056
Epigastric pain	No	49.2 ± 7.9	47.2 ± 9.2		
	Yes	46.6 ± 9.0	40.8 ± 13.9	0.150	0.017
Dyspepsia	No	50.1 ± 8.9	44.5 ± 12.1		
	Yes	46.9 ± 8.5	42.8 ± 12.9	0.143	0.594
Irritable bowel syndrome	No	48.2 ± 8.2	45.4 ± 11.5		
	Yes	47.1 ± 8.9	42.2 ± 13.1	0.582	0.249
State anxiety (STAI)	< P25	48.3 ± 9.2	49.5 ± 11.3		
	P25-P75	46.2 ± 8.3	41.8 ± 11.5		
	> P75	49.4 ± 8.4	35.8 ± 13.5	0.328	0.0001
	< P25	48.3 ± 9.2	49.5 ± 11.3		

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Trait anxiety (STAI)	P25-P75	45.9 ± 8.2	42.2 ± 11.3		
	> P75	49.4 ± 8.4	35.8 ± 13.5	0.265	0.001
Somatization (SCL90)	T score < 40	57.5 ± 9.2	55.6 ± 11.7		
	T score 40-60	48.3 ± 8.3	48.0 ± 10.6		
	T score > 60	46.8 ± 9.5	39.5 ± 13.5	0.416	0.009
Depression (SL90)	T score < 40	51.0 ± 5.9	53.8 ± 8.2		
	T score 40-60	47.3 ± 9.2	44.7 ± 11.4		
	T score > 60	46.3 ± 10.0	32.3 ± 13.3	0.441	0.0001

Table 2**.** Multivariate analysis of factors associated with a reduction in HRQoL in patients with GERD

	Standardized coefficient (β)	***P*-value**	**Model (r^2)**
Physical component of the SF36 questionnaire			0.38
Educational level	0.29	< 0.01	
Severity of symptoms	-0.38	< 0.001	
Body mass index	-0.30	< 0.005	
State anxiety	0.28	< 0.01	
Female gender	-0.23	< 0.05	
Presence of dyspepsia	-0.21	< 0.05	
Mental component of the SF-36 questionnaire			0.42
State anxiety	-0.39	< 0.01	
Depression	-0.32	< 0.05	

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