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Functional Dyspepsia Affects Woman More Than Men in Daily Life: A Case-Control Study in Primary Care

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ABSTRACT

Background: Little is known about possible gender differences among patients with functional dyspepsia (FD). Few studies have measured health-related quality of life (HRQoL) in patients with FD using a population-based control group as a reference.

Objective: This study aimed to determine the degree of HRQoL impairment among patients with FD, assess the self-reported health impact resulting from the disease, and analyze any gender differences.

Methods: A questionnaire that included the HRQoL Short Form 36 (SF-36) Health Survey, the HAD Scale and other measurements was mailed to FD patients identified from medical records and control group randomly selected from the general population in the same geographical area. Responses to the SF-36 were transferred to a standard scale ranging from 0 (the worst possible score) to 100 (the best possible score).

Results: A total of 176 patients with FD and 688 controls responded to the questionnaire. Responders were assigned to 2 gender-specific subgroups of 88 patients with FD and 344 randomly matched controls, all aged 18 to 65 years. HRQoL of the patients with FD was impaired in all SF-36 dimensions except one—role limitations caused by emotional problems compared with the controls. Female patients with FD had a significantly lower SF-36 score in the physical functioning dimension than did male patients (82.4 vs 90.5, respectively; $P < 0.01$). Both groups of patients with FD had impaired HRQoL compared with their respective control group in the dimensions of bodily pain (women: 69.3 vs 80.6; $P < 0.001$; and men: 75.8 vs 84.8; $P < 0.001$) and general health (women: 62.0 vs 75.6; $P < 0.001$; and men: 70.6 vs 78.6; $P < 0.001$). Additionally, women with FD had significant

impairment compared with their respective control group in the dimensions of physical function (82.4 vs 89.3; $P < 0.01$) and physical role function (72.1 vs 85.9; $P < 0.001$). Depression was significantly more common among male patients with FD than among male controls (6.8% vs 2.0%, respectively; $P < 0.05$). More gastrointestinal comorbidity was reported among patients of both sexes compared with controls.

Conclusions: This population-based case-control study reported HRQoL impairment overall among patients with FD. This impairment was more apparent among female patients compared with female controls. Females with FD tend to be more negatively affected in their daily life compared with their male counterparts. These gender differences should be investigated further in future studies.

Key words: functional dyspepsia, HRQoL, gender, case-control study.

INTRODUCTION

Dyspepsia is a common gastrointestinal (GI) complaint among different populations worldwide.^{1,2} According the Rome II Definition (as developed by the Rome Committee a working group of gastroenterologists 1999) dyspepsia is regarded as "pain or discomfort centered in the upper abdomen."³ Symptoms that are associated with or described as discomfort are upper abdominal fullness, early satiety, bloating, belching, or nausea. Patients with predominant reflux symptoms, such as heartburn and acid regurgitation, are excluded from dyspepsia in this definition.

Many organic diseases are associated with the underlying etiology of dyspepsia. The most common are duodenal or gastric ulcers; others are gastric cancer, erythema, duodenal erosions, gastric polyps, and atrophy. In most dyspepsia cases, however, no visible pathology is identified by means of upper endoscopy and

no other tests indicate any organic abnormality, which therefore results in the diagnosis of functional dyspepsia (FD).^{1,2,4} The prevalence of FD has recently been estimated to be between 12% and 15% for populations in Scandinavia, Australia and USA.⁴⁻⁷

Mental and physical health have been reported to be reduced in individuals with FD, with anxiety being one of the key factors in diminished well-being.⁸ Moreover, several studies have reported statistically significant data regarding impairment in self-reported health-related quality of life (HRQoL) among patients with FD.⁸⁻¹¹ Several recent studies comparing gender differences in HRQoL among dyspeptic patients found greater impairment among women than among men.^{12,13} However, to our knowledge there are few reports focusing on gender differences among patients with FD.

In studies investigating HRQoL in FD, questionnaire-specific reference values for the general population or other disease groups have been used as a reference. None of the studies compared findings from patients with FD with those from randomized population controls. Comparisons have only been made in studies reporting significant impact of HRQoL among patients with dyspepsia that included FD as a subgroup.^{14,15} In their review, El-Serag and Talley¹⁶ concluded that to optimally measure the outcomes in FD trials in terms of HRQoL, future studies should match an appropriate sample of control subjects without FD by age and sex with patients with FD. With this directive in mind, as well as the fact that there are few reports on FD from a gender perspective, we constructed a population-based case-control study and survey investigating HRQoL in men and woman with FD. The primary aim of this study was to determine the degree to which patients with the diagnosis of FD experience impairment of HRQoL. Secondary aims were to assess

the degree of self-reported health impact resulting from the disease and to analyze any gender differences in these aspects.

PATIENTS AND METHODS

This was a case-control study based on data collected both from medical records in primary care and from a questionnaire mailed to the general population focusing on people in their most active years (ie, aged 18–65 years). This study was approved in 2002 by the ethics committee of the Faculty of Health Sciences, Linköping University (Linköping, Sweden).

Data Collection

The study was conducted 1997-2001 in the city of Linköping, located in southeastern Sweden, which has a population of ~135,000 inhabitants. The 3 primary care centers randomly selected for the study covered a total population of >40,000 inhabitants and were responsible for all primary health care consultations for this population. The patients were identified on the basis of diagnoses (*International Classification of Diseases, 10th Revision (ICD-10)* P code K-30-p for FD) in the primary care medical records. According to the medical records, the general practitioners conducted tests to exclude organic diseases. Patients were included if they had a first-time diagnose of FD from a general practitioner during the 5-year study period. The retrospective analysis of medical records identified a total of 1986 cases. Of these, 500 patients with FD aged 18 to 65 years were randomly selected to participate in the study.

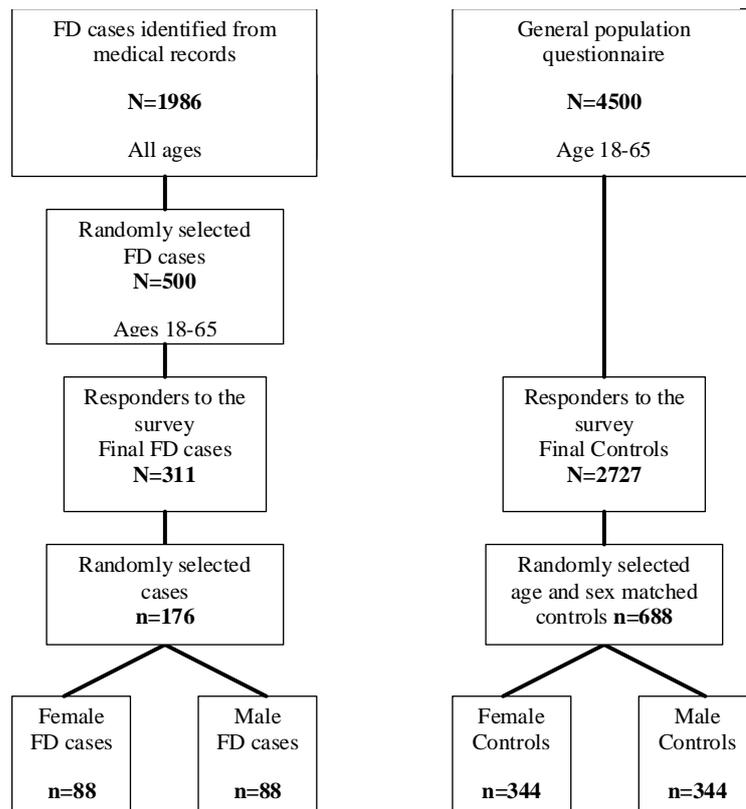
Using the local population census register, the control group was randomly selected from the same geographical area as the patients with FD. The total number

of individuals aged 18 to 65 years for the control group (N = 4500) was selected proportionally, based on the size of the actual population living in each of the 3 primary health care areas.^{17,18}

In 2003, a questionnaire was mailed to the 5000 individuals included in the study (500 patients with FD and 4500 controls). Of these, 25 patients with FD and 73 controls had an unknown address or had died, and the study then comprised 4902 individuals (475 patients with FD and 4427 controls). Two reminders were sent to those who did not initially respond to the questionnaire. The overall response rate was 63.1% (N=3038) (including 4 patients with FD and 59 controls who responded but refused to participate in the survey), resulting in a total of 311 patients with FD and 2727 controls participating in the study.

Two separate gender groups were identified from the 311 patients with FD and the 2727 controls. Because there were more female than male respondents to the questionnaire, the total of 88 responding male patients with FD was set as the standard when forming the groups. A random selection of 88 women was made from the 223 responding female patients with FD. To match patients with controls, 344 men and 344 women were randomly selected from the database for inclusion in the study, representing almost 4 controls per case. Thus, the two gender-specific groups included 176 patients with FD and 688 controls. A flowchart of the population followed in this study is shown in **Figure 1**.

Figure 1. Flow chart of the study population.



Questionnaire

Established and validated questionnaires and indexes—the HRQoL Short Form 36 (SF-36) Health Survey^{19,20} and the Hospital Anxiety and Depression (HAD) Scale²¹⁻²⁴—were used in the development of our survey. Also included were questions on self-perceived health, the experience of being in a stressful environment, and the experience of being depressed or anxious, as well as questions about sleep problems, comorbidities, and work-related complications due to GI problems. The questionnaire included sociodemographic data (eg, sex, marital status, education level, occupational status, and exercise habits and perceived stress level).

Before sending the survey to the entire study population, a pilot study was conducted by mailing the questionnaire to 17 randomly selected persons aged 30 to 75 years. The intention of this pilot study was to explore whether the questionnaire

had clear instructions, had too many questions, was difficult to answer or considered to be too personal/private. Valuable information was provided from the pilot that helped us to reformat the questionnaire.

The generic SF-36 is a well-established instrument that has been used extensively in epidemiology and public health studies as well as in clinical trials.^{19,20} The SF-36 includes 8 multi-item scales (35 items) that assess the extent to which an individual's health limits his or her physical, emotional, and social functioning. The items are distributed as follows: physical functioning (10 items), role limitations caused by physical health problems (4 items), bodily pain (2 items), general health (5 items), vitality (4 items), social functioning (2 items), role limitations caused by emotional problems (3 items), and mental health (5 items). All the questions concerned health status in the previous 4 weeks, with the exception of an additional item that assessed changes in the person's health over the preceding year. Responses to the SF-36 were transferred to a standard scale ranging from 0 (the worst possible score) to 100 (the best possible score).²¹

The HAD Scale was also included in our questionnaire. This instrument is self-administered and is designed to be a simple yet reliable tool for use in medical practice. The HAD Scale consists of 14 items (7 items each for anxiety and depression) and uses a 4-point Likert scale (0–3), in which 0 represents the most positive option and 3 the most negative option. After calculating a mean value for the items in each dimension, the score obtained indicates the respondent's anxiety or depression status. Of a maximum score of 21 on each subscale, a score of ≤ 7 denotes a noncase, 8 to 10 a doubtful case, and ≥ 11 a definite case.^{21–24}

Statistical Analysis

All the data in this study were stored in a common database and statistical analysis was performed using SPSS software, version 14.0 (SPSS Inc., Chicago, Illinois). The significance of differences between patients with FD and controls for the SF-36 and HAD scales was estimated using 2-sided analyses of variance. All SF-36 scores obtained in the analyses were adjusted using multivariate analysis with respect to chronic comorbidities (eg, heart disease, hypertension, rheumatic disease, diabetes, long-term pain, asthma, and allergy). Odds ratios and 95% CIs were also calculated. The χ^2 test was used for categorical variables. $P < 0.05$ was considered statistically significant.

RESULTS

All patients with FD and controls included in this study were compared with respect to sociodemographic characteristics (**Table I**). The only significant difference found between female patients with FD and female controls was that the patients were more likely to be pensioners or early-retirement pensioners, 14.9% (n=13) vs 6.7% (n=23), respectively; $P < 0.05$). Among the men, patients with FD were significantly more likely to have been on a long-term sick leave, 5.7% (n=5) vs 1.5% (n=5) respectively; $P < 0.05$). Female and male patients with FD were also compared, and no statistically significant differences were found.

Table II shows differences, separately for men and women, between FD patients and controls regarding self-reported complications and comorbidity.

Table 1. Sociodemographic characteristics among female and male patients with functional dyspepsia (FD) and age- and sex-matched controls.

	Women			Men			FD cases				
	FD cases (n=88)	Control group (n=344)	OR (95% CI)	FD cases (n=88)	Control group (n=344)	OR (95% CI)	Women (n=88)	Men (n=88)	OR (95% CI)		
	n	%		n	%		n	%	n	%	
Educational level:											
Low	63.2	52.9	1.48 (0.90-2.39)	67.0	57.7	1.49 (0.91-2.45)	63.2	67.0	67.0	67.0	0.84 (0.45-1.57)
Occupational situation:											
Full or part-time occupation	67.8	75.3	0.17 (0.40-1.10)	76.1	84.9	0.63 (0.34-1.12)	67.8	76.1	76.1	76.1	0.67 (0.34-1.30)
Pensioner/early retirement pension	14.9	6.7	2.45 (1.19-5.07)*	10.2	7.7	1.27 (0.58-2.80)	14.9	10.2	10.2	10.2	1.52 (0.61-3.76)
Unemployed	4.6	2.6	1.79 (0.54-5.97)	4.5	3.0	1.56 (0.48-5.10)	4.6	4.5	4.5	4.5	1.00 (0.24-4.13)
Long-term sick listed	6.9	3.8	1.88 (0.69-5.10)	5.7	1.5	3.98 (1.13-14.09)*	6.9	5.7	5.7	5.7	1.21 (0.35-4.13)
Exercising habits:											
None or little	16.3	12.4	1.38 (0.71-2.65)	19.5	21.7	0.88 (0.49-1.59)	16.3	19.5	19.5	19.5	0.79 (0.36-1.72)
Stressful environment:											
Often or very often experienced	48.2	38.8	1.47 (0.91-2.38)	37.6	28.0	1.51 (0.92-2.48)	48.2	37.6	37.6	37.6	1.52 (0.83-2.79)

*P < 0.05, determined by Pearson χ^2 test.

Table II. Comparison of co-morbidity and self-reported health impacts subsequent to functional dyspepsia (FD) between patients with FD and age- and sex-matched controls for women and men separately and between male and female patients with FD.

	Women			Men			FD cases		
	FD cases (n=88) n %	Control group (n=344) n %	OR (95% CI)	FD cases (n=88) n %	Control group (n=344) n %	OR (95% CI)	Women (n=88) n %	Men (n=88) n %	OR (95% CI)
Self-reported bad health	6.9	1.7	4.19 (1.32-13.31)**	5.7	0.6	10.27 (1.96-53.87)**	6.8	5.7	1.21 (0.35-4.13)
Self-reported depression or anxiety	42.4	21.3	2.71 (1.64-4.49)***	30.6	15.2	2.40 (1.39-4.15)**	42.4	30.6	1.15 (0.61-2.16)
Short-term sick leave (due to GI-problems)	27.3	9.5	3.58 (1.49-8.59)**	13.3	5.6	2.62 (0.83-8.25)	27.3	13.3	2.44 (0.82-7.23)
Daily affect of work (due to GI-problems)	37.2	17.5	2.79 (1.66-4.70)***	37.6	11.9	4.34 (2.51-7.49)***	37.2	37.6	1.00 (0.52-1.82)
Sleeping problems	50.6	39.0	1.60 (1.00-2.57)*	39.8	33.5	1.31 (0.81-2.12)	50.6	39.8	1.55 (0.85-2.82)
Anxiety (HAD score 11-21)	17.2	11.9	1.54 (0.81-2.93)	12.5	6.4	2.09 (0.97-4.49)	17.2	12.5	1.45 (0.63-3.38)
Depression (HAD score 11-21)	6.9	3.2	2.24 (0.81-6.24)	6.8	2.0	3.52 (1.15-10.76)*	6.9	6.8	1.00 (0.31-3.27)
Reflux	57.0	18.0	6.04 (3.63-10.04)***	54.5	18.0	5.56 (3.36-9.20)***	57.0	54.5	1.10 (0.61-2.00)
IBS	24.1	10.4	2.75 (1.50-5.02)**	15.7	7.1	2.31 (1.12-4.74)*	21.1	15.7	1.71 (0.80-3.70)
Gastroenteritis	24.1	18.0	1.44 (0.82-2.54)	29.8	14.5	2.38 (1.37-4.15)**	21.2	29.8	0.75 (0.38-1.48)

GI = gastrointestinal; HAD = Hospital and Anxiety Depression; IBS = irritable bowel syndrome. HAD Questionnaire scale: 14 items (7 items each for anxiety and depression), each rated from 0 = most positive option to 3 = most negative option.

*P < 0.01 (Pearson X² test).

†P < 0.001 (Pearson X² test).

‡P < 0.05 (Pearson X² test).

Compared with female controls, female patients with FD were significantly more likely to report self-perceived poor health, 6.9% (n=6) vs 1.7% (n=6), respectively; $P < 0.01$ and self-reported depression or anxiety, 42.4% (n=36) vs 21.3% (n=72), respectively; $P < 0.001$. Similarly, compared with male controls, male patients with FD were also significantly more likely to report self-perceived poor health, 5.7% (n=5) vs 0.6% (n=2), respectively; $P < 0.01$ and self-reported depression or anxiety 30.6% (n=26) vs 15.2% (n=51), respectively; $P < 0.01$. However, on assessing the occurrence of depression and anxiety using the HAD questionnaire, the only statistically significant difference found was in the male group, with depression being more common among male patients with FD than among male controls 6.8% (n=6) vs 2.0% (n=7), respectively; $P < 0.05$.

Self-reported health impact associated with GI problems was more common among patients with FD versus the control group. Compared with female controls, female patients with FD significantly more frequently reported being affected in their daily work 37.2% (n=32) vs 17.5% (n=59), respectively; $P < 0.001$; compared with male controls, male patients with FD also more frequently reported being affected in their daily work, 37.6% (n=32) vs 11.9% (n=40), respectively; $P < 0.001$. The female FD group was significantly more likely to report using short-term sick leave than were female controls, 27.3% (n=12) vs 9.5% (n=13), respectively; $P < 0.01$. Sleep problems were also more common among female patients with FD compared with women in the control group 50.6% (n=44) vs 39.0% (n=134), respectively; $P < 0.05$; these differences were not observed among the men.

There were statistically significant differences regarding comorbidities in both gender groups. Compared with male controls, male patients with FD were significantly more likely to report irritable bowel syndrome (IBS) 15.7% (n=13) vs

7.1% (n=24), respectively; $P < 0.05$, reflux 54.5% (n=48) vs 18.0% (n=61), respectively; $P < 0.001$, and gastroenteritis 29.8% (n=25) vs 14.5% (n=49), respectively; $P < 0.01$. Compared with female controls, female patients with FD were more likely to report IBS 24.1% (n=21) vs 10.4% (n=35), respectively; $P < 0.01$ and reflux 57.0% (n=49) vs 18.0% (n=61), respectively; $P < 0.001$.

The SF-36 scores of the patients with FD and the control groups are shown in **Table III**. Female patients with FD had significantly lower scores in the following dimensions compared with female controls: physical function 89.3 vs 82.4, respectively; $P < 0.01$, physical role function 85.9 vs 72.1, respectively; $P < 0.001$, bodily pain 80.6 vs 69.3, respectively; $P < 0.001$, and general health (GH) (62.0 vs 75.6, respectively; $P < 0.001$). In the vitality dimension, only the P value indicated a significant difference between female patients and female controls (55.7 vs 61.4, respectively; $P < 0.05$).

The SF-36 scores of male patients with FD were significantly lower compared with male controls in the dimensions of bodily pain (75.8 vs 84.8, respectively; $P < 0.001$) and general health (70.6 vs 78.6, respectively; $P < 0.001$) (**Table III**). Similar to the female groups, ambiguous statistical values were found for several dimensions. Only the P values were significant for the dimensions of physical function for male patients compared with male controls (90.5 vs 94.2, respectively; $P < 0.05$), vitality (61.7 vs 67.6, respectively; $P < 0.05$), social function (87.2 vs 91.7, respectively; $P < 0.05$), and mental health (75.7 vs 80.3, respectively; $P < 0.05$). A comparison (data not shown) of all patients with FD and all individuals in the control group, regardless of sex, found significantly lower scores among patients with FD in all SF-36 dimensions, except for the role limitations caused by emotional problems.

Table III. Differences in mean scores on health-related quality-of-life Short Form 36 (SF-36) Health Survey among female and male patients with functional dyspepsia (FD) compared with age- and sex-matched controls and between male and female patients with FD.

	Women			Men			FD cases		
	FD cases (n=88) Mean score (95%CI)	Controls (n=344) Mean score (95%CI)		FD cases (n=88) Mean score (95%CI)	Controls (n=344) Mean score (95%CI)		Women (n=88) Mean score (95%CI)	Men (n=88) Mean score (95%CI)	
Physical functioning	82.4 (77.7-87.1)	89.3 (87.5-91.1)	**	90.5 (87.3-93.6)	94.2 (92.9-95.4)	*	82.4 (77.7-87.1)	90.5 (87.3-93.6)	
Physical role	72.1 (63.9-80.3)	85.9 (82.8-89.0)	***	83.6 (77.1-90.2)	89.0 (86.4-91.6)		72.1 (63.9-80.3)	83.6 (77.1-90.2)	
Bodily pain	69.3 (64.2-74.3)	80.6 (78.3-82.9)	***	75.8 (70.9-80.6)	84.8 (82.6-86.9)	***	69.3 (64.2-74.3)	75.8 (70.9-80.6)	
General health	62.0 (57.1-67.0)	75.6 (73.4-77.8)	***	70.6 (66.0-75.1)	78.6 (76.7-80.5)	***	62.0 (57.1-67.0)	70.6 (66.0-75.1)	
Vitality	55.7 (50.9-60.4)	61.4 (59.1-63.7)	*	61.7 (57.0-66.5)	67.6 (65.5-69.8)	*	55.7 (50.9-60.4)	61.7 (57.0-66.5)	
Social functioning	82.8 (77.8-87.8)	87.5 (85.2-89.7)		87.2 (82.8-91.7)	91.7 (90.1-93.4)	*	82.8 (77.8-87.8)	87.2 (82.8-91.7)	
Emotional role	81.0 (73.8-88.2)	84.6 (81.4-87.9)		87.4 (81.1-93.6)	87.5 (84.7-90.3)		81.0 (73.8-88.2)	87.4 (81.1-93.6)	
Mental health	74.5 (71.1-77.9)	76.3 (74.4-78.3)		75.7 (71.8-79.6)	80.3 (78.6-81.9)	*	74.5 (71.1-77.9)	75.7 (71.8-79.6)	

SF-36 scale: 0 = worst possible score to 100 = best possible score.

*All differences in SF-36 scores were adjusted in multivariate analysis with respect to chronic co-morbidities (e.g., heart disease, hypertension, rheumatic disease, long-term pain, asthma, and allergy).

†P < 0.01, determined by Pearson χ^2 test.

‡P < 0.05, determined by Pearson χ^2 test.

§P < 0.001, determined by Pearson χ^2 test.

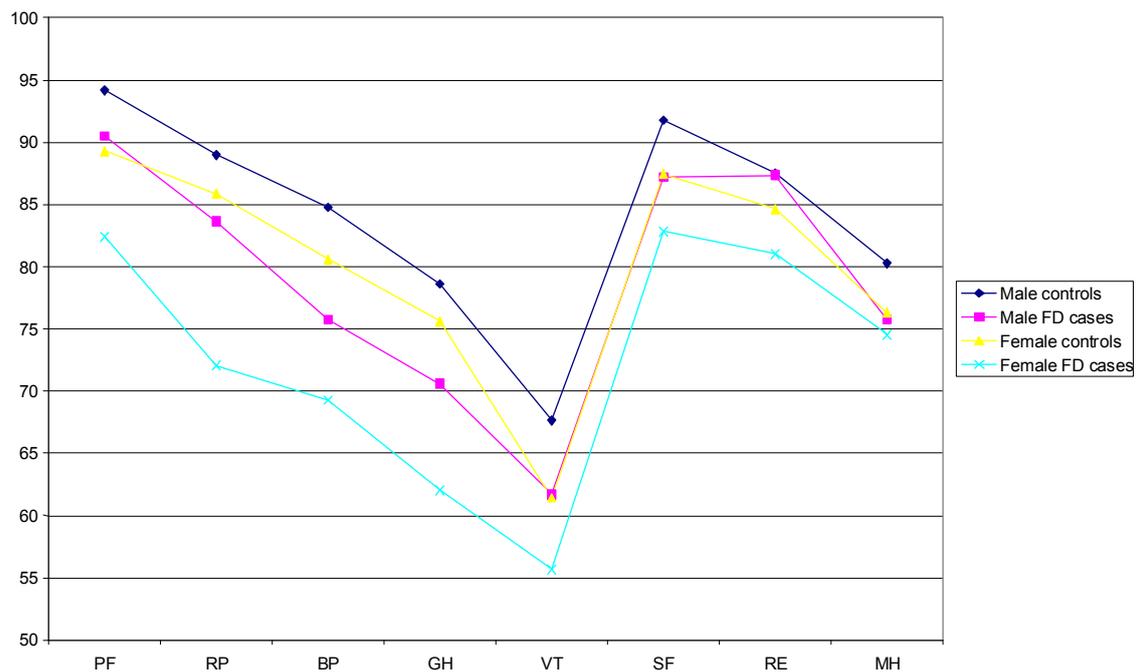


Figure 2. SF-36 score among women and men

Figure 2 shows the SF-36 scores of the 4 groups separately, indicating the lowest scores among female patients with FD, followed by male patients with FD. The highest scores were found among male controls in all dimensions. The data comparing the SF-36 scores of the female FD group with the male FD group are also shown in **Table III**. The SF-36 scores of the female FD group were significantly lower than those of the male FD group only in the physical function dimension (82.4 vs 90.5, respectively; $P < 0.01$). Only the P value was statistically significant between the female and male FD groups for the dimensions of physical role function (72.1 vs 83.6, respectively; $P < 0.05$) and general health (62.0 vs 70.6, respectively; $P < 0.05$). All SF-36 scores obtained in the analyses were adjusted with respect to chronic comorbidities (eg, heart disease, hypertension, rheumatic disease, diabetes, long-term pain, asthma, and allergy); however, this did not affect the outcome of the analyses.

DISCUSSION

In this population-based case-control study, the HRQoL impairments among patients with FD were obvious, with lower SF-36 scores in all dimensions except role limitations caused by emotional problems. These scores indicated that both the mental and physical health of a patient with the diagnosis of FD were reduced. The fact that there were few significant differences in sociodemographic variables (only more pensioners among female cases than their controls and more men with long-term sick leave among male cases than male controls) between the patients with FD and the control groups strengthens the reliability of this finding.

HRQoL has been reported to be impaired among patients with FD in several previous studies.⁸⁻¹¹ However; we employed a case-control design with age- and sex-matched control groups from the general population, which is an unusual study design. In our study, controls were required to have no diagnosis of dyspepsia documented in their medical records. Before the survey, we ascertained that individuals in the control group did not have a registered dyspepsia diagnosis during the five year study period. However, this did not exclude the possibility that some individuals with untreated and unknown dyspeptic disease or dyspeptic symptoms might have been included among the controls.

Because few studies have investigated possible gender differences in HRQoL among patients with FD, we decided to focus on this area. Accordingly, the patients with FD and the controls were divided into 2 gender-specific groups, which were analyzed separately. That female patients with FD were more likely to be pensioners or early-retirement pensioners, and that male patients with FD were more likely to be long-term sick-listed, could be considered as consequences of their disease rather than factors contributing to their FD diagnosis. This is supported by the fact that the

variable—the experience of being in a stressful environment—was not more common among patients with FD than among controls in either of the groups. Accordingly, we considered the work-related differences to have had little impact on the outcomes of our analyses.

In our questionnaire, we asked about self-perceived health, self-perceived depression or anxiety, sleep problems, and work-related issues connected to GI problems. The analyses of these questions clearly indicated that there were health impacts in these areas associated with the diagnosis of FD. Female patients with FD were significantly more likely to report being affected in the previously mentioned areas than were the female controls, although their self-perceived depression and anxiety were not verified with the HAD questions included in our questionnaire. Male patients with FD, on the other hand, did not report the same number of complications associated with the diagnosis of FD. In this instance, the difference in self-reported depression was verified by the HAD questions, whereas the difference in self-reported anxiety was not. It is difficult to assess whether the higher prevalence of depression was actually correlated to the diagnosis of FD or whether it was a consequence of the male patients with FD having a greater likelihood of being long-term sick-listed. The discrepancy between the self-reported variables and the HAD variables might have been due to the fact that the HAD questions were intended to define definite clinical cases of anxiety or depression whereas the self-reported variable focused on present or previous health care contacts and treatments for depression or anxiety.

In both gender groups, GI comorbidity was more common among patients with FD than among controls. In addition to reflux and IBS, which were reported significantly more frequently by female patients with FD, male patients with FD also

significantly more frequently reported having gastroenteritis. These findings were not surprising, because functional disorders often manifest themselves together and exhibit a high degree of symptom overlap.³ It is thus reasonable to believe that GI comorbidity indicates some reduction in HRQoL. However it is difficult, even with multivariate analysis, to distinguish between the effects of the different comorbidities and their impact on HRQoL.

The prevalence of possible health impacts associated with FD and comorbidity were compared in the female and male FD groups. Although no statistically significant differences were found, female patients with FD tended to report greater impact in almost all areas.

When measuring HRQoL using the SF-36, obvious impairments in 2 dimensions were found among male patients with FD compared with male controls, whereas among women, there were significant impairments in 4 dimensions in female patients with FD compared with female controls. We also compared female and male patients with FD to each other. In this analysis, we found that female patients with FD had a statistically significant impairment in their SF-36 score in the physical function dimension. There was a tendency for women to have lower SF-36 scores in all other dimensions. However, this tendency was nonsignificant, which can probably be explained by the relatively small number of patients in the 2 groups.

The findings from the SF-36 analysis, together with the previously mentioned fact that female patients with FD reported more complications, imply that women are more affected by FD than are men with the same diagnosis. It is difficult to explain this finding, because gender differences in relation to social conditions and psychological symptoms among patients with functional GI disorders have not been adequately studied.²⁵ One possibly contributory factor might be that cultural

expectations of female behavior make women feel uncomfortable when experiencing symptoms such as flatulence and abdominal pain.²⁶ The overall low scores of women on the SF-36 compared with men might also reflect that having this disease caused women to have a feeling of being out of the ordinary abnormal when affected. This disease is a sensitive subject and embarrassing condition that might be more difficult for women to cope with than for men because of issues of femininity. Women might also be more aware of their body and symptoms. Moreover, women are known to run a higher risk of functional GI disorders, such as FD and IBS; this is probably due to biological, gender, and social differences between the sexes.²⁷ Consequently, the findings of the current study, together with the dearth of research in this area, clearly point to the need for future studies to investigate this topic more thoroughly.

In a review in 2003, El-Serag and Talley¹⁶ recommended that future research investigating HRQoL in patients with FD take the form of case-control studies in primary care using an age- and gender-matched population control group. The fact that ours was a case-control study strengthens the validity of our findings. Strength of our study is that there were few differences between the patients with FD and the control group in demographic variables, which implies that the groups were well matched. A larger sample might have decreased the ambiguity of the values in the statistical analysis of the SF-36 measurements, which could be considered a limitation of our study. El-Serag and Talley¹⁶ recommended that future studies be designed prospectively to reduce the risk of bias. Although our study was retrospective and cross-sectional, and the data were based on self-estimated values, we consider the resulting bias to be low. The SF-36 provides a generic, not a disease-specific, measurement. Generic HRQoL measures are designed to assess aspects that are applicable across diseases, treatments, and populations, and can

therefore provide a basis for comparisons with data from the general population. Because the comparisons of HRQoL in our study were made between dyspepsia patients and healthy controls from the general population, a generic measurement seems reasonable.

Possible sources of bias in our study were the phenomenon of recall bias concerning estimation of symptoms and their characteristics and severity. Another possible bias may have been the likelihood that the more seriously affected individuals overestimated their symptoms and that the healthier individuals underestimated theirs. In general, however, self-reports are reliable and well established.²⁸ Even though these issues may modify the findings to some extent, it can be assumed that they affected both groups equally and thus did not alter the eventual outcomes.

By using well-established self-administrated generic instruments, such as the SF-36 and HAD Scale, we believe that we obtained reliable data and results. The questionnaires have been used extensively in epidemiologic and public health studies, as well as in clinical trials, and are well documented in terms of validity and reliability.^{19,20}

CONCLUSIONS

In this population-based case-control study, it can be concluded that the diagnosis of FD denoted manifest impairment of HRQoL. This impairment was more apparent among female patients compared with female controls. Females with FD tend to be more negatively affected in their daily life compared with their male counterparts. These gender differences should be investigated further in future studies. To

elucidate these gender-specific differences, future studies could include larger samples and have a prospective design.

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