

Research article

Assessing health-related quality of life in patients with inflammatory bowel disease, in Crete, Greece

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Abstract

Background: Health Related Quality of Life (HRQoL) is an important outcome measure in Inflammatory Bowel Disease (IBD). The aim of our study was to assess HRQoL in a population of 135 Greek patients with IBD.

Methods: A cohort of 135 patients with IBD, 81 with ulcerative colitis (UC) and 54 with Crohn's disease (CD) were enrolled in our study. Demographic and disease-related data were recorded. HRQoL was assessed by a disease-specific and a generic questionnaire, IBDQ and SF-36, respectively. Disease activity was assessed by Harvey-Bradshaw Index and the Colitis Activity Index for CD and UC patients, respectively.

Results: Among all variables recorded in our study, only disease activity had a significant effect on HRQoL. Patients with active disease scored significantly lower on both IBDQ and SF-36 when compared to those in remission. Only two among the four IBDQ dimensions, bowel and systemic, had significant ability in distinguishing best patients in remission from those with active disease.

Conclusions: IBD has a negative impact on HRQoL. Patients with active disease are more impaired than patients in remission. In our population of patients bowel and systemic dimensions had a predominant value in patients' perception of quality of life. Patients in our study using the same instrument scored higher than previously reported.

Background

Inflammatory Bowel Diseases [Ulcerative Colitis (UC), Crohn's Disease (CD)] are chronic diseases of the alimentary tract, that can commence at any time during life but their highest incidence occurs between 15 and 35 years of age. They have a great impact during a very active period of life that often includes acquiring an education, developing a career and raising a family [1]. The prevalence of IBD in Europe is 160–320 patients per 100.000 inhabit-

ants and the incidence is around 16 new cases per 100.000 of population [2,3].

Traditionally treatment and follow-up of patients with Inflammatory Bowel Disease (IBD) is mainly based on clinical symptoms, laboratory tests, endoscopic and histologic findings. However these findings fail to reflect the patients' subjective experience of health [4,5].

Most patients need continuous medication and long term medical follow-up. The long term outcome of IBD today, with better treatment has improved considerably. The life expectancy is equal to those of people of the same age and sex [6,7]. The majority of patients are able to lead a normal social, family and professional life [1]. However IBD patients do have an impaired quality of life, with physical, social and emotional dysfunction, which is not necessarily examined using the traditional clinical approach [8-12].

A more comprehensive assessment may be provided by complementing the traditional measures of disease activity with measures of the patients' perceptions of their disease and received care. Such an approach may result into a better understanding of the patients' global situation and the many difficulties they experience due to their disease. This approach should contribute to better patient care.

The aim of our study was to assess the Health Related Quality of Life (HRQoL) in a population of unselected Greek patients with IBD, by using a validated disease-specific questionnaire the Inflammatory Bowel Disease Questionnaire.

Methods

Patients

One hundred and fifty-one IBD, consecutive, non-selected, patients fulfilling the Lennard-Jones criteria [13] were enrolled in the study. All patients gave prior informed consent. The great majority of our patients came from our outpatients' clinic. Some patients were hospitalized at the time of HRQoL assessment. Outpatients had the questionnaires administered to them at their follow-up visit and hospitalized patients within the first two days of their hospitalization. Patients with an ileostomy were excluded from the study.

Demographic data collected included age, gender, marital status and smoking habits. Data regarding the disease included disease duration, age at first diagnosis of disease, and disease activity.

From the original 151 patients 7 (4.6%) refused to participate in the study and 9 (6.0%) patients were excluded because of contradicting answers in the questionnaire. Thus the study comprised 135 IBD patients, 81 (60%) with UC and 54 (40%) with CD. Excluded patients were compared with those included and no significant differences were found regarding the demographic data. Patient characteristics are shown in table 1.

HRQoL Assessment

The Inflammatory Bowel Disease Questionnaire is an interviewer administered, disease-specific questionnaire. It was developed and validated by Guyatt et al [14]. It contains 32 questions, which are divided into four health domains: bowel symptoms (10 questions), systemic symptoms (5 questions), emotional function (12 questions), and social function (5 questions). For each question there are graded responses on a 7-point Likert scale, ranging from 1 (representing the "worst" aspect) to 7 (representing the "best" aspect). Thus, the total IBDQ score ranges from 32 to 224, with higher scores reflecting better well-being. Subsequent validation of the IBDQ yielded a strong correlation with disease severity ($r = -0.5$; $p < 0.001$) and a test-retest reliability coefficient of 0.7 [14,15]. Mean score changes of 16 to 30 points have been linked to changes in therapy. Statistically significant differences also occur between active and inactive disease [14-17]. The IBDQ has been translated and validated in a cohort of 114 Greek IBD patients and proved to be a valid and reliable instrument [18]. The IBDQ has been translated and validated in Dutch, English, Spanish and Korean [19-24]. A self-administered version and a shortened version of the IBDQ have also been validated [25,26]. HRQoL was also assessed by a non-disease-specific questionnaire, the Short Form Health Survey (SF-36) [27-30]. The SF-36 is a widely used generic instrument, which has been used in Greek patients; results related to a study with IBD patients have been reported previously [18]. It consists of 36 questions grouped into eight dimensions: 'physical function' (10 items), 'role limitations due to physical health problems' (4 items), 'bodily pain' (2 items), 'general health perception' (6 items), 'energy and vitality' (4 items), 'social function' (2 items), 'role limitations due to emotional problems' (3 items), and 'mental health' (5 items) [27-30]. Each of the dimension scores is expressed as a value between 0 and 100, with higher scores representing better health. In order to have a valid comparison with IBDQ, the above eight dimensions were converted into four corresponding to the IBDQ dimensions. In this conversion 'bodily pain' represents bowel symptoms; 'health perception' and 'energy and vitality' represent systemic symptoms; 'physical function', 'role limitations due to physical health problems', and 'social function' represent social function; 'role limitations due to emotional problems' and 'mental health' represent emotional function [18,20,22]. Both questionnaires were administered during a patient interview, by a physician (AGP) who was not the treating doctor.

Disease Activity

Disease activity in CD patients was assessed by the Harvey Bradshaw Index (HBI) [31], which includes general well-being, abdominal pain, daily number of watery stools, complications and abdominal mass, while in UC patients

Table 1: Demographic characteristics of the study population.

	Crohn's disease	Ulcerative colitis	Total
Total number of patients	54	81	135
Age median, years (range)	39 (16–84)	41 (21–84)	
<60	42 (77.5%)	62 (76.6%)	104 (77.0%)
≥ 60	12(22.5%)	19 (23.4%)	31 (23.0%)
Smoking habits			
Never smoked	20 (37.1%)	51 (62.9%)	71 (52.6%)
Ex smoker	10 (18.5%)	17 (20.9%)	27 (20.0%)
Present smoker	24 (44.4%)	13 (16.2%)	37 (27.4%)
Civil status			
Married	38 (70.4%)	60 (74.1%)	98 (72.6%)
Single	12 (22.2%)	14 (17.3%)	26 (19.2%)
Divorced	1 (1.9%)	2 (2.5%)	3 (2.3%)
Widowed	3 (5.5%)	5 (6.1%)	8 (5.9%)
Duration of IBD, years (mean)	6.5	8.4	
Disease Activity			
Minor symptoms	42 (77.8%)	68 (84%)	110 (81.5%)
Severe symptoms	12 (22.2%)	13 (16%)	25 (18.5%)
Hospitalized	12 (22.2%)	12 (15%)	24 (17.8%)

was assessed by using the colitis activity index (CAI) [32]. The CAI includes 6 symptoms: general well-being, abdominal tenderness, pain or cramping, fecal incontinence, daily and nocturnal diarrhea, and visible blood in stool. This was chosen because it relies entirely on symptoms and does not require invasive procedures. Total scores range from 0 to 21, with scores less than 10 indicating remission. Patients were classified as having 'no or minor symptoms' (HBI score 1–5 for patients with CD and CAI score less than 10 for patients with UC) and 'severe symptoms' (HBI more than 5 for CD and CAI more than 10 for UC) [18].

Statistical Analysis

Descriptive statistics are reported as mean, standard deviation, median, and range. Statistical comparisons between the two groups were made either by Pearson χ^2 -test (for proportions) or by Student's t-test (for means). Comparisons involving two grouping factors were made by two-way analysis of variance. [33]. The independent influence of a number of demographic and clinical factors on HRQoL (total or dimensional IBDQ scores) was assessed by multiple linear regression; this was used stepwise (backward elimination of variables). The relative performance of the four IBDQ dimensions in distinguishing best patients with minor symptoms from those with severe, was studied by discriminant analysis. This method also was applied stepwise (backward elimination) [34]. Reclassification of observations was effected by cross-vali-

dation (leaving-one-out) method [35]; this method is known to provide unbiased re-classification results.

Results

There was a predominance of men in the whole study population (male to female ratio = 1:0.63) and similarly in each of the two disease groups (male to female ratio = 1:0.76 for UC and 1:0.46 for CD). The proportion of females in the UC group (43.2%) was higher than in the CD group (31.5%), but not significantly different ($p = 0.17$). The median age of patients with UC did not differ significantly ($p = 0.424$) from that of patients with CD (median age 41 vs 39). As expected [36–43] the pattern of smoking habits was different in UC group compared to CD group. There was a predominance of non-smokers (62.3%) and ex-smokers (21.3%) among the UC patients compared to those among CD patients (37.8% and 17.8%, respectively) ($p = 0.006$). The mean duration of disease was 8.4 years for UC (range 0.1–38.0) and 6.5 years for CD (range 0.2–30.0); the difference was not significant ($p = 0.187$). Disease activity as measured by CAI for UC and HBI for CD, was generally low, with the great majority of patients having no or minor symptoms. The distribution between mild and severe cases was similar in UC and CD patients ($p = 0.386$).

The mean IBDQ score of the UC patients was 178.5 (Standard deviation, SD = 35.3), while for CD patients was 177.6 (SD = 39.6); the difference was not statistically significant ($p = 0.892$). Similarly, no statistical differences

Table 2: Total and dimensional IBDQ scores (standard deviations in brackets) in the UC and CD group.

	Crohn's disease (mean ± SD)	Ulcerative Colitis (mean ± SD)	p value (t-test)	Total (mean ± SD)
Bowel	58.6 (11.2)	59.1 (10.4)	0.799	58.9 (10.7)
Systemic	27.3 (7.4)	27.9 (6.5)	0.592	27.7 (6.9)
Emotional	63.2 (15.9)	61.9 (15.4)	0.659	62.4 (15.6)
Social	28.5 (8.1)	29.4 (7.1)	0.468	29.1 (7.5)
Total	177.6 (39.6)	178.4 (35.3)	0.892	178.1 (36.9)

Table 3: Comparison of the total and dimensional IBDQ scores between the young (<60) and old (>60) population group.

		CD (mean ± SD)	UC (mean ± SD)	Disease*	Age Group*	Interaction*
Bowel	<60	57.73 ± 11.7	60.06 ± 10.4	0.406	0.741	NS
	>60	61.27 ± 9.1	54.92 ± 9.9			
Systemic	<60	26.90 ± 7.8	28.30 ± 6.4	0.815	0.801	NS
	>60	28.27 ± 5.9	26.14 ± 7.1			
Emotional	<60	61.00 ± 16.6	62.14 ± 15.4	0.205	0.391	NS
	>60	69.54 ± 9.7	59.57 ± 14.6			
Social	<60	28.21 ± 8.4	30.66 ± 6.4	0.346	0.060	0.017
	>60	29.09 ± 7.2	23.50 ± 8.1			
Total	<60	173.76 ± 41.5	181.04 ± 35.3	0.318	0.888	NS
	>60	188.18 ± 29.4	164.28 ± 32.8			

* P-values for differences between disease, age group and 'disease by age group' interaction derived by two-way analysis of variance; NS: non significant

were observed in any of the four dimensional IBDQ scores. Total and dimensional IBDQ scores are presented in table 2. Very few of the patients scored the worst or best possible scores, except for the social subscore, in which 44% of the patients scored 34 or 35 (the best possible score is 35). With respect to SF-36 the mean score of the UC patients was 73.7 (SD = 14.1), while for CD patients was 72.7 (SD = 13.7); the difference was not statistically significant ($p = 0.808$) and similarly no statistical differences were observed in all "four dimensional" SF-36 scores.

Patients were classified according age at the time of diagnosis into two groups; those who were less than 60 years old and those who were equal or older than 60 years. The mean IBDQ score was 178.13 (SD = 37.9) for the young

group and 174.80 (SD = 33.0) for the elderly group. The results of the two-way analysis with disease and age group as independent factors, showed in table 3, indicated no significant difference in IBDQ dimensional scores between the two disease groups or between the two age groups. The only exception was the social dimension where the younger group had significantly higher scores than the older group (29.7 and 26.0, respectively) and this difference was more pronounced within the UC group of patients than the CD (disease by age interaction was significant; $p = 0.017$). Similarly, with respect to SF-36, no statistical significant differences were observed among the four dimensional scores between the two age groups, with the only exception of the social dimension where the younger group scored better than the older one ($p = 0.008$).

Table 4: Comparison of HRQoL between patients with minor or severe disease symptoms

		CD (mean ± SD)	UC (mean ± SD)	Disease*	Disease Activity*	Interaction*
Bowel	minor	62.92 ± 8.1	62.51 ± 6.1	0.410	0.001	NS
	severe	43.58 ± 6.9	41.30 ± 10.4			
Systemic	minor	30.71 ± 3.3	30.00 ± 4.3	0.524	0.001	NS
	severe	15.50 ± 5.6	17.46 ± 6.3			
Emotional	minor	69.66 ± 10.6	69.66 ± 12.6	0.458	0.001	NS
	severe	40.41 ± 8.5	40.41 ± 9.9			
Social	minor	31.92 ± 4.6	31.54 ± 4.9	0.459	0.001	NS
	severe	16.58 ± 6.2	18.69 ± 7.1			
Total	minor	195.21 ± 21.6	190.05 ± 22.7	0.750	0.001	NS
	severe	115.83 ± 21.8	117.76 ± 25.7			

* P-values for differences between disease group, disease activity and 'disease group by disease activity' interaction derived by two-way analysis of variance; NS: non significant

No significant difference regarding HRQoL was observed between smokers and non-smokers/ex-smokers and this result was consistent in both disease groups.

Patients were classified into three groups according to disease duration: a) those who had the disease less than 1 year, b) between 1 and 5 years and c) more than five years [44]. No significant difference regarding HRQoL was observed between the three duration groups and this result was consistent in both disease groups.

Of the 135 patients participated in the study according to the disease activity indexes (HBI for CD, CAI for UC) 110 patients were thought to have minor symptoms and 25 patients as having severe symptoms. The results of the two-way analysis with disease and disease activity as independent factors, showed in table 4, indicated highly significant differences in all IBDQ scores between the two disease activity groups (those with minor symptoms scored significantly higher than those with severe symptoms) and these differences were consistent in both diseases (non-significant interactions). The mean total IBDQ score was 192 for the 'minor or no' symptoms group and 116 for the 'severe' symptoms group. Analogous results were observed with the use of the generic SF-36 questionnaire. The mean total SF-36 score was 82.2 for the "minor

or no" symptoms group, while for the "severe" symptoms group were 70.6 (p = 0.001).

The independent influence of age, gender, disease activity, duration of disease and smoking on quality of life (as measured by the IBDQ total score) was studied by multiple linear regression analysis. Three of the independent variables, gender, disease activity and smoking were categorical. These variables were transformed appropriately to dummy variables. The analysis revealed that only disease activity had a significant effect on quality of life; the deletion of the other variables was not significant (p = 0.954). It appears that, all other factors staying stable, a patient changing from "minor symptoms" to "severe symptoms" level is expected to have an average decrease of about 87 units in his/her quality of life score.

The application of discriminant analysis, for distinguishing patients with minor symptoms from those with severe, revealed that only two IBDQ dimensional sub-scores had significant discriminating ability (p < 0.001). These were the bowel and systemic dimensions. The estimate of Fisher's linear discriminant function (LDF) was:

$$\text{LDF} = - 25.637 + 0.241 * \text{Bowel} + 0.544 * \text{Systemic}$$

Table 5: Cross-Validated Count Re-classification results according to discriminant analysis

	Predicted Group Membership (according to discriminant analysis)		Total
	Minor	Severe	
Group Membership (according to disease activity indexes)			
Minor	105	5	110
Severe	2	23	25
Minor	95.5%	4.5%	100.0%
Severe	8.0%	92.0%	100.0%

c. 94.8% of cross-validated grouped cases correctly classified

Using this index and boring in mind that higher scores correspond to higher quality of life, one can classify patients with LDF > 0 into the "minor symptoms" group, and patients with LDF < 0 in the "severe symptoms" group. On this basis, the whole sample was reclassified by the leaving-one-out method. Table 5 shows the results; note that the correct re-classification rate was very high at 94.8%.

Discussion

In this study the IBDQ dimensional scores were high; the mean total score was greater than 178, showing that our sample of IBD patients had a relatively good quality of life [16,17,45,46]. It would be interesting if we could compare these results, with the results coming from another group of patients with chronic disease, such as rheumatoid arthritis. Unfortunately there are no published data, regarding the Greek population. This study also examined the relative ability of the four IBDQ dimensional scores in distinguishing patients with minor or severe symptoms. Discriminant analysis showed that emotional and social scores had no significant discriminatory power once the bowel and systemic symptoms were taken into account. This is an important observation, which leads to the conclusion that in our population of patients the disease severity is associated with HRQoL only in as much as bowel and systemic dimensions are concerned. The emotional and social dimensions offer no extra gain in this association and should be regarded as indicators of other aspects.

In table 6 the IBDQ dimensional scores are compared with those from previous HRQoL assessing studies on IBD patients in the Netherlands and England [19,22]. Our study shares similar results with the study by Han et al [22], while DeBoer et al found significantly lower scores [19]. Several reasons could account for this discrepancy: First, methodological reasons such as different patients populations or different conditions under which patients completed the questionnaire. Cultural reasons concerning

different attitudes and priorities may be a further reason. Finally, these differences might be due to inclusion of patients with more severe symptoms.

It is well known and proved in several studies that disease activity has a great impact on quality of life [8,18–24,47]. Patients with 'severe' symptoms, as expected, scored much lower than those with 'minor or no' symptoms and there was a significant difference in every dimensional score of the questionnaire in the UC and CD patients group, as well as in the whole population. In patients with relapse emotional and systemic dimensions were more disturbed. This demonstrates that patients with IBD suffer from significant psychological distress due to their chronic disease. Such an issue cannot be evaluated by using the clinical activity indexes only. Drossman et al [47] also showed using an instrument focused on patients' worries and concerns that CD patients had a worse quality of life compared to UC patients. He attributed this finding to more severe disease, troublesome complications of steroid therapy and to a higher incidence of surgical interventions in CD patients. We however found no differences in HRQoL between UC and CD patients either with severe or with minor or no symptoms. The reason for this discrepancy could be ascribed to different instruments used.

It has been reported and disputed that IBD runs a more serious clinical course in older patients [48,49]. A different clinical course of the disease could have a different impact on HRQoL. In a large cohort of UC and CD patients from 20 European centres (EC-IBD Study) a similar clinical course during the first year after manifestation of the disease was found in young and older patients [50,51]. In this study, the only difference observed regarding HRQoL between younger and older patients concerned the social impairment that was higher in the elderly group. This difference however could be connected to specific health and community problems that are related to the elderly per se and not to IBD.

Table 6: IBDQ scores reported in several HRQoL studies

	Bowel (mean \pm SD)	Systemic (mean \pm SD)	Emotional (mean \pm SD)	Social (mean \pm SD)	Total (mean \pm SD)
De Boer et al (n = 271)	37.3 \pm 7.7	17.0 \pm 4.4	44.9 \pm 9.1	20.0 \pm 4.7	119.1 \pm 22.0
Han et al (n = 30)	54.9 \pm 10.4	25.3 \pm 5.9	64.1 \pm 13.7	29.4 \pm 8.1	173.7 \pm 33.1
Present study (n = 135)	58.9 \pm 10.7	27.7 \pm 6.9	62.4 \pm 15.6	29.1 \pm 7.5	178.1 \pm 36.9

It is well known that there is a different pattern of smoking between patients with UC and CD. Smoking is associated with an increased risk for developing CD and a decreased risk for developing UC [42], and has a significant impact on the course of the disease [36–43]. Although smoking has been reported to have a different impact on patients with high compared to those with low disease activity [52] we found no significant difference in our patients. Although further studies are necessary to analyse fully the correlation between HRQoL and smoking.

Differences in HRQoL observed between patients with short and long disease duration may be due to more worries and concerns that patients with a recent diagnosis of IBD have compared to patients with a long history of IBD. Patients with a long history of IBD may acquire with time a better way to cope with their disease, especially when they experience no frequent relapses [44]. We found no report on differences in HRQoL in patients with either short or long history of IBD. In this study no difference in HRQoL was found among the three groups of patients concerning disease duration: less than one year, between one and five years and more than five years.

Multiple regression analysis revealed that only severity of disease has an independent influence on quality of life. All other variables recorded in our study were found no significant. This is an important observation leading to the conclusion that, at least in Greek IBD patients, disease activity plays a major role in their perception of quality of life. Several other variables with a significant impact on the clinical course of IBD have no important influence on quality of life.

Table 6 shows the average scores (and standard deviations in brackets) for all four dimensions and total IBDQ reported by the present study and by two other similar studies (De Boer et al and Han et al) [19,22]. First, the comparison between the present study and the one by Han et al yielded no significant differences in any of the four dimensions or total score; note however that two dimensions, bowel and systemic had marked differences, failing however to reach statistical significance. In con-

trast, the comparison between this study and the one by De Boer et al yielded highly significant differences in all four dimensions and total score.

In conclusion, IBD has a negative impact on HRQoL of Greek patients although to a lesser degree than has been previously reported from other countries using IBDQ as an assessing tool. Patients with higher disease activity had a more pronounced negative impact on HRQoL. Bowel and systemic dimensions of the IBDQ were the main determinants of the patients' perception of quality of life.

Competing Interests

None declared

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