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ORIGINAL ARTICLE

Retrospective Study

Patients with irritable bowel syndrome-diarrhea have lower disease-specific quality of life than irritable bowel syndrome-constipation

Prashant Singh, Kyle Staller, Kenneth Barshop, Elaine Dai, Jennifer Newman, Sonia Yoon, Shahar Castel, Braden Kuo

Prashant Singh, Kyle Staller, Elaine Dai, Jennifer Newman, Shahar Castel, Braden Kuo, GI Unit, GRJ 719, Department of Medicine, Massachusetts General Hospital, Boston, MA 02114, United States

Kenneth Barshop, Pritzker School of Medicine, University of Chicago, Chicago, IL 60637, United States

Sonia Yoon, Division of Gastroenterology, Weill Cornell Medical College, New York, NY 10021, United States

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Correspondence to: Braden Kuo, MD, GI Unit, GRJ 719, Department of Medicine, Massachussets General Hospital, 55 Fruit Street, Boston, MA 02124, United States. bkuo@partners.org
Telephone: +1-617-7246038
Fax: +1-617-7262047

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Abstract

AIM: To determine effect of irritable bowel syndrome (IBS) subtype on IBS-specific quality of life (QOL) questionnaire and its subscales.

METHODS: We studied IBS patients visiting our functional gastroenterology disorder clinic at a tertiary care center of Unites States. IBS and IBS subtype were diagnosed using Rome-Ⅲ questionnaire. QOL was assessed using IBS-QOL questionnaire. IBS-QOL assesses quality of life along eight subscales: dysphoria, interference with activities, body image, health worry, food avoidance, social reactions, sexual health, and effect on relationships. IBS-QOL and its subscales were both scored on a range of 0-100 with higher scores suggestive of better QOL. Results of overall IBS-QOL scores and subscale scores are expressed as means with 95%CI. We compared mean IBS-QOL score and its subscales among various IBS-subtypes. Analysis of variance (ANOVA) was used to compare the mean difference between more than two groups after controlling for age and gender. A post-hoc analysis using Bonferroni correction was used only when *P* value for ANOVA was less than 0.05.

RESULTS: Of 542 patients screened, 243 had IBS as per Rome-Ⅲ criteria. IBS-mixed (IBS-M) was the most common IBS subtype (121 patients, 49.8%) followed by IBS- diarrhea (IBS-D) (56 patients, 23.1%), IBS-constipation (IBS-C) (54 patients, 22.2%) and IBS-unspecified (IBS-U) (12 patients, 4.9%). Overall IBS-QOL scores were significantly different among various IBS-subtypes (P = 0.01). IBS-QOL of patients with IBS-D (61.6, 95%CI: 54.0-69.1) and IBS-M (63.0, 95%CI: 58.1-68.0) was significantly lower than patients with IBS-C (74.5, 95%CI: 66.9-82.1) (P = 0.03 and 0.02 respectively). IBS-D patients scored significantly lower than IBS-C on food avoidance (45.0, 95%CI: 34.8-55.2 *vs* 61.1, 95%CI: 50.8-71.3, P = 0.04) and interference with activity (59.6, 95%CI: 51.4-67.7 *vs* 82.3, 95%CI: 74.1-90.6, P < 0.001). IBS-M patients had more interference in their activities (61.6, 95%CI: 56.3-66.9 *vs* 82.3, 95%CI: 74.1-90.6, P = 0.001) and greater impact on their relationships (73.3, 95%CI: 68.4-78.2 *vs* 84.7, 95%CI: 77.2-92.2, P = 0.02) than IBS-C patients. Patients with IBS-M also scored significantly lower than IBS-C on food avoidance (47.2, 95%CI: 40.7-53.7 *vs* 61.1, 95%CI: 50.8-71.3, P = 0.04) and social reaction (66.1, 95%CI: 61.1-71.1 *vs* 80.0, 95%CI: 72.1-87.7, P = 0.005).

CONCLUSION: IBS-D and IBS-M patients have lower IBS-QOL than IBS-C patients. Clinicians should recognize food avoidance, effects on daily activities and relationship problems in these patients.

Key words: Irritable bowel syndrome; Irritable bowel syndrome subtype; Quality of life; Irritable bowel syndrome-quality of life; Constipation; Diarrhea

Core tip: There is paucity of data on effect of irritable bowel syndrome (IBS)-subtype on disease specific quality of life as most of the earlier studies have utilized general questionnaires like SF-36 *etc*. We studied the effect of IBS subtype on IBS-specific quality of life (QOL), the most validated disease specific questionnaire for IBS. We found that IBS-diarrhea (IBS-D) and IBS-mixed (IBS-M) have lower disease specific QOL than IBS-constipation patients. Our study also points out that clinicians should pay special attention to certain domains of QOL such as food avoidance, relationship problems, effect on daily activities and social reaction in patients with IBS-D and IBS-M as these domains significantly affect QOL in these patients.

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INTRODUCTION

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain or discomfort and alteration of bowel habits in the absence of an organic disorder[1-4]. It is the most common gastrointestinal disorder, affecting between 4%-22% of general population[1-4]. IBS is a generally non life-threatening disorder that is not associated with decreased life expectancy, which may potentially lead clinicians to underestimate its impact on patients' lives and the healthcare system as a whole[5]. Nevertheless, studies have shown that patients with IBS make two to three times the number of health care visits per year compared to age-matched controls[6-8]. Additionally, many studies have also shown that patients with IBS have poorer quality of life (QOL) when compared to the general population as well as patients with other chronic diseases such as diabetes and end stage renal disease[8,9]. QOL has also been shown to correlate with disability, healthcare resource utilization, and clinical response to treatment. Thus, it is important to understand the variables affecting the QOL in patients with IBS[10].

While QOL in IBS has been shown to be affected by extraintestinal symptoms, psychiatric symptoms, disease severity, and gender, the effect of IBS-subtype is unclear[10,11]. Previous studies studying the effect of IBS subtype on QOL have failed to show any difference[11-15]. Most of these studies used general health-related QOL questionnaires like the SF-36 and WHO-QOL, which do not capture the specific issues pertinent to IBS[11-14]; thus, these general questionnaires could have minimized the impact of gastrointestinal symptoms on overall QOL. Disease-specific instruments have been developed and validated for IBS, such as the QOL measure specific to IBS (IBS-QOL), the IBS QOL questionnaire, and the functional digestive disorder QOL questionnaire[15-18]. These questionnaires aim to address the specific QOL domains that are most heavily affected by IBS, yet there is a paucity of data on effect of IBS subtype on IBS-QOL.

In order to better understand the interactions between IBS subtype and IBS-QOL, we studied the impact of IBS subtype on disease-specific QOL using the IBS-QOL questionnaire in our cohort of IBS patients.

MATERIALS AND METHODS

Study population

The data was collected between June 2011 and August 2014 at the gastrointestinal motility clinic of Massachusetts General Hospital, Boston. Only adult patients greater than 18 years of age were enrolled in the study. All patients coming to the clinic completed Rome-Ⅲ questionnaires[19]. Patients who were diagnosed with IBS *via* the Rome Ⅲ questionnaires were further classified into four subtypes: IBS-C,

Table 1 Baseline characteristics of three irritable bowel syndrome-subtypes *n* (%)

Baseline characteristics	IBS-C (*n* = 54)	IBS-D (*n* = 56)	IBS-M (*n* = 121)	*P* value
Age (yr) (mean ± SD)	45.4 (16.0)	42.8 (15.3)	41.3 (14.9)	0.250
Gender				
Male	7 (13.0)	5 (9.8)	36 (29.8)	0.002[1]
Female	47 (87.0)	51 (90.2)	85 (70.2)	

[1]There was significant difference between gender distribution of irritable bowel syndrome (IBS)-mixed (IBS-M) *vs* IBS-constipation (IBS-C) ($P = 0.02$) and IBS-M *vs* IBS- diarrhea (IBS-D) ($P = 0.002$).

IBS-D, IBS-mixed type (IBS-M) and IBS-unclassified (IBS-U)[19]. Patients diagnosed with IBS were further assessed for upper gastrointestinal symptom severity and IBS-QOL on their first visit.

Assessment of gastrointestinal symptom severity

Severity of upper gastrointestinal symptoms was assessed using the patient assessment of upper gastrointestinal symptom severity index (PAGI-SYM)[20]. It assesses the severity of upper gastrointestinal symptoms along six subscales: heartburn/regurgitation, fullness/early satiety, nausea/vomiting, bloating, upper abdominal pain, and lower abdominal pain[20]. For each patient, we calculated a PAGI-SYM subscale score by taking the mean of the items in each subscale; the subscale scores varied from 0 (absent) to 5 (very severe)[20]. The total scores were calculated by taking the mean of subscales. If any subscale score was missing, the PAGI-SYM score was also considered to be missing[20]. Although PAGI-SYM is not validated in IBS-patients, it was used in our study as it is routinely administered to every patient coming to our functional gastrointestinal disorder clinic and has many overlapping questions with other IBS-severity scores.

Disease-related QOL

Disease-specific QOL was assessed using the IBS-QOL questionnaire[18]. It is a 34-item questionnaire assessing QOL along eight domains: dysphoria, interference with activities, body image, health worry, food avoidance, social reactions, sexual health, and effect on relationships[18]. All items are negatively-framed with the greatest response scale indicating poorer QOL. As per the IBS-QOL scoring manual, all items were reversed when scored so that as the IBS scores increases, QOL increases as well. All the final raw scores were transformed into a 0 to 100 scale. Using this scale, lowest possible score (worst QOL) and highest possible score (best QOL) were transformed to 0 and 100, respectively. Scores between these values indicate the percentage of the total possible score achieved[18]. Similarly, for each subscale, the raw scores were transformed into a scale of 0 to 100 and results were presented as a percentage of the total possible score achieved[18].

Ethical clearance

Ethics approval for the study was obtained prior to the initiation of the study by Massachusetts General Hospital Institutional Review Board (Protocol number-2012P002255/MGH).

Statistical analysis

Statistical analysis was performed using Stata 11.0 (StataCorp.2009, College station, Texas). Proportion of males and females among various IBS subgroups were compared using χ^2 test (Table 1). Mean age among various subgroups was compared using analysis of variance (ANOVA) (Table 1). Results of overall IBS-QOL scores and subscale scores were expressed as means with 95%CI. These were calculated using model based estimates from ANOVA. Mean differences in overall IBS-QOL scores and their subscales were compared among various IBS subgroups using ANOVA controlling for age and gender. A post-hoc analysis using Bonferroni correction was used only when *P* value for ANOVA was less than 0.05. For both ANOVA and Bonferroni tests, *P* values less than 0.05 were considered statistically significant.

The statistical methods of this study were reviewed by Douglas Hayden of Biostatistics center, Massachusetts General Hospital. This was done with support from Harvard Catalyst, the Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award UL1 TR001102).

RESULTS

Two hundred fifty one of 572 patients screened during the study period were diagnosed with IBS. The mean age of the study population was 44.3 years. More than three-fourths of the patients (79.7%) were females (200 females, 51 males). Eight patients who were diagnosed with IBS did not have sufficient information to classify them into subtypes. Of the remaining 243 patients, IBS-mixed type (IBS-M) was the most common subtype (121 patients, 49.8%), followed by IBS-diarrhea (IBS-D) (56 patients, 23.1%), IBS-constipation (IBS-C) (54 patients, 22.2%), and IBS-unspecified (IBS-U) (12 patients, 4.9%). For the purpose of statistical analysis, patients with IBS-U were excluded given their small sample size in addition to the uncertainty of what IBS-U category means clinically.

Overall IBS-QOL

Patients with IBS-D had the lowest IBS-specific QOL (61.6; 95%CI: 54.0-69.1) followed by IBS-M (63.0; 95%CI: 58.1-68.0) and IBS-C (74.5; 95%CI: 66.9-82.1) ($P = 0.01$ overall by ANOVA) after controlling for age and gender (Table 2). In post hoc analysis, overall IBS-QOL was significantly-lower in patients with

Table 2 Irritable bowel syndrome specific quality of life subscale scores among three irritable bowel syndrome subtypes

IBS-QOL subscale	IBS-C (*n* = 54)	IBS-D (*n* = 56)	IBS-M (*n* = 121)	ANOVA *F*-test *P* value
Interference with activity	82.3 (74.1-90.6)	59.6 (51.4-67.7)	61.6 (56.3-66.9)	< 0.001[1]
Social reaction	80.0 (72.1-87.7)	70.7 (63.0-78.4)	66.1 (61.1-71.1)	0.008[2]
Food Avoidance	61.1 (50.8-71.3)	45.0 (34.8-55.2)	47.2 (40.7-53.7)	0.020[3]
Relationships	84.7 (77.2-92.2)	75.4 (67.9-83.0)	73.3 (68.4-78.2)	0.030[4]
Dysphoria	69.2 (60.0-78.4)	57.1 (47.9-66.4)	58.0 (51.9-64.0)	0.060
Health worry	64.3 (56.3-72.3)	60.9 (53.0-68.9)	57.3 (52.1-62.4)	0.280
Sexual	73.9 (63.7-84.1)	74.6 (64.6-84.7)	68.8 (62.3-75.3)	0.500
Body Image	69.2 (61.2-77.2)	66.0 (58.1-73.9)	64.9 (59.7-70.1)	0.631
Total	74.5 (66.9-82.1)	61.6 (54.0-69.1)	63.0 (58.1-68.0)	0.010[5]

All the results of mean irritable bowel syndrome (IBS) - quality of life scores and its subscales are compared after controlling for age and gender. [1]IBS-constipation (IBS-C) *vs* diarrhea (IBS-D) ($P < 0.001$) and IBS-C *vs* IBS-mixed (IBS-M) ($P < 0.001$) by Bonferroni test; [2]IBS-C *vs* IBS-M ($P = 0.005$) by Bonferroni test; IBS-C *vs* IBS-D ($P = 0.04$) and IBS-C *vs* IBS-M ($P = 0.04$) by Bonferroni test; IBS-C *vs* IBS-M ($P = 0.02$) by Bonferroni test; [5]IBS-C *vs* IBS-D ($P = 0.03$) and IBS-C *vs* IBS-M ($P = 0.02$) by Bonferroni test. IBS-QOL: Irritable bowel syndrome specific quality of life.

IBS-D than in patients with IBS-C ($P = 0.03$). Also, IBS-M had significantly lower IBS-QOL scores when compared with IBS-C patients ($P = 0.02$). There were no significant differences among IBS-QOL scores of IBS-D and IBS-M.

Individual subscales

Food avoidance: Food avoidance score was significantly different amongst IBS-subtypes ($P = 0.02$). Patients with IBS-D (45.0; 95%CI: 34.8-55.2) and IBS-M (47.2; 95%CI: 40.7-53.7) had a significantly lower food avoidance score than IBS-C (61.1; 95%CI: 50.8-71.3, $P = 0.04$ for both). IBS-D and IBS-M had comparable food avoidance subscale scores.

Interference with activity: There was significant difference in interference with activity subscale score amongst IBS-subtypes ($P < 0.001$). IBS-D patients (59.6; 95%CI: 51.4-67.7) and IBS-M patients (82.3; 95%CI: 74.1-90.6) both had significantly more interference with their activities than patients with IBS-C (81.0; 95%CI: 74.6-87.4, $P < 0.001$ for both).

Relationship: Relationship subscale was also significantly different amongst IBS-subtypes ($P = 0.03$). Relationships were significantly more affected in patients with IBS-M (73.3; 95%CI: 68.4-78.2) when compared with patients with IBS-C (84.7; 95%CI: 77.2-92.2, $P = 0.02$).

Social reaction: There was significant difference in social reaction subscale score amongst IBS-subtypes ($P = 0.008$). IBS-M patients had significantly lower social reaction score (66.1; 95%CI: 61.1-71.1) than IBS-C patients (80.0; 95%CI: 72.1-87.7, $P = 0.005$).

Other subscales: There was no statistical difference among the dysphoria, sexual health, health worries and body image subscale score of the various IBS subtypes (Table 2).

PAGI-SYM scores

PAGI-SYM scores were comparable among patients with IBS-C (2.6; 95%CI: 2.2-2.9), IBS-D (2.7; 95%CI: 2.4-3.1) and IBS-M (2.9; 95%CI: 2.7-3.1). There was no significant difference among IBS-subtypes for mean upper abdominal pain scores ($P = 0.30$), mean lower abdominal pain score ($P = 0.6$), mean bloating scores ($P = 0.52$) and early satiety scores ($P = 0.49$) using ANOVA.

DISCUSSION

In this analysis of IBS patients presenting for evaluation at a tertiary care clinic, we found that IBS-D and IBS-M patients have a significantly-worse disease-specific QOL than IBS-C subtype. IBS-D patients also have more interference with their daily activities and avoided food more commonly when compared to patients with IBS-C. Similarly, patients with IBS-M also had more interference in their activities, greater impact on their relationships and lower social reaction score than IBS-C patients. To our knowledge, this data is unique in demonstrating subtype-specific QOL differences in this population.

Most of the previous studies studying the effect of IBS subtype on QOL failed to show any difference in QOL between the subtypes[12-15,18,21-23]. Like our study, most of these studies are from tertiary healthcare settings and have comparable sample sizes. However, most of these studies used general health-related QOL questionnaires like the SF-36 and WHO-QOL[11,12,14,22,24]. The use of such general QOL questionnaires could have minimized the impact of gastrointestinal symptoms on overall QOL. Our study used IBS-QOL, which captures the specific concerns of patients with IBS.

Notably, other studies using IBS-QOL have failed to show similar differences when IBS-QOL is compared by IBS subtype[15,21,25]. All three of these studies analyzed patients from outside the United States and therefore may be examining a slightly-different IBS population than our own. In line with our results, Patrick *et al*[18] and Schmulson *et al*[23] also found lower IBS-QOL scores in United States patients with IBS-D and IBS-M compared to those with IBS-C, but these differences failed to reach statistical significance. Both these studies enrolled fewer IBS patients than ours.

By overall IBS-QOL and all eight individual subscale scores, IBS-D and IBS-M were very similar to each other and distinct from IBS-C patients. Mearin *et al*[26] previously reported that many patients with IBS-D

or IBS-C may qualify for the diagnosis of IBS-M over time. It is possible that these mixed patients were more similar to IBS-D patients than those with IBS-C in our population. Others have reported similarities between IBS-M patients and IBS-D in terms of defecation urgency, which at least partly explains low subscale scoring in the food avoidance and interference with activity domains in patients with IBS-M[14].

We found that patients with IBS-D and IBS-M had significantly more food avoidance when compared with IBS-C patients. Many patients with IBS attribute their gastrointestinal symptoms to diet and - as a result - a majority of patients restrict the consumption of perceived culprit foods[27]. Self-reported food avoidance has also been associated with high symptom burden and a reduced QOL[28]. Studies have shown that fermentable carbohydrates could increase colonic gas production, small intestinal water volume, and small intestinal motility and thus exacerbate IBS symptoms like pain, bloating, and diarrhea. In fact, fasting and diets restricted in fermentable carbohydrates were demonstrated to improve gastrointestinal symptoms including pain, bloating, and diarrhea in patients with IBS[29-31]. Thus, significantly higher food avoidance in IBS-D patients could be result of self- or physician-advised restriction to minimize these gastrointestinal symptoms.

IBS is known to interfere with the physical aspects of health-related QOL including daily activities and work productivity[11,32,33], yet limited data is available on the effect of IBS subtype on daily activities. In our study, patients with IBS-D and IBS-M had significantly more interference with their activities because of their disease than other IBS subtypes. Schmulson *et al*[23] also reported similar findings in female patients with IBS. Increased bowel frequency could understandably limit the ability of individual to go out and thus engage in daily activities like work, travel, and other social/leisure activities.

Thus, bowel frequency appears to be an important determinant of physical activity domain of QOL. This is further confirmed by the observation that the 5HT3-receptor antagonist alosetron, which improves stool consistency and frequency in these patients, also improved physical activity and work productivity[34]. This data argues that clinicians should focus on adequately controlling diarrheal symptoms in IBS-D patients in addition to addressing the pain and abdominal discomfort that are the hallmarks of IBS.

We found that IBS had a significantly greater impact on relationships in IBS-M patients when compared to IBS-C patients. Silk[33] reported that about one-fifth of married or cohabitating IBS patients reported difficulties in personal relationships due to their illness. More than half also reported embarrassment at the workplace. Interpersonal problems are reported to be more pronounced IBS-D patients[35]. Psychodynamic interpersonal therapy and improvement in interpersonal difficulties have not only been shown to improve psychological distress but also overall health status in patients with IBS[36]. Thus, patients with IBS-M might be benefit from counseling and interpersonal therapy.

Our study has some limitations. We did not study other factors known to affect the QOL in IBS such as somatic comorbidities, psychiatric comorbidities, and disease severity - which could have confounded our results. As a surrogate of gastrointestinal symptom severity, PAGI-SYM was used in our study as it is routinely administered to every patient coming to our functional gastrointestinal disorder clinic. Although PAGI-SYM has not been validated as a measure of symptoms severity in IBS patients, the components of the PAGI-SYM score, including bloating, lower abdominal pain, upper abdominal pain, and early satiety are all domains used to assess IBS symptom severity in IBS severity scales[37].

We found that overall PAGI-SYM score as well as individual subcomponent scores did not differ significantly among IBS subtype, suggesting similar disease severity amongst patients in our study population. The sample size of our study was also small, and similar studies should be repeated on larger number of IBS patients. Because these findings are derived from patients attending a tertiary care center, our study may not be easily generalized to IBS patients seen in community gastrointestinal practices or in the primary care setting. However, clinicians in these settings should also pay attention to these QOL domains.

We demonstrated that IBS-D and IBS-M patients have an overall lower IBS-QOL than IBS-C patients. Clinicians should pay special attention to patient-reported food avoidance, interference with daily activities, social reactions and problems with relationships, which are more prominent in IBS-D and IBS-M than other subtypes patients and drive a lower disease-specific QOL.

COMMENTS

Background

Patients with irritable bowel syndrome (IBS) have been shown to have poorer specific quality of life (QOL) than normal population and those with chronic diseases. QOL has been shown to correlate with health-care utilization, economic burden, disability and response to treatment.

Research frontiers

As general QOL questionnaires could minimize the impact of gastrointestinal symptoms on QOL in patients with IBS, researchers have developed several disease specific QOL. IBS-QOL is the most validated disease specific QOL measuring instrument. The current research hotspot is to understand the determinants of IBS-QOL.

Innovations and breakthroughs

The effect of IBS-subtypes on IBS-QOL is not very clear as most of the previous studies have used generalized QOL questionnaires like SF-36. To overcome this problem, the authors studied the effect of IBS-subtype on IBS-QOL and its eight subscales in patients with IBS at a tertiary healthcare center in the United States. The authors showed that IBS- diarrhea (IBS-D) and IBS-mixed (IBS-M)

patients have an overall lower IBS-QOL than IBS-constipation patients.

Applications

The study results suggest that clinicians should pay special attention to patient-reported food avoidance, interference with daily activities, and problems with relationships, which are more prominent in IBS-D and IBS-M than other subtypes patients and drive a lower disease-specific QOL in these patients.

Terminology

IBS is the most common functional gastrointestinal disorder characterized by abdominal pain or discomfort along with alteration of bowel habits (frequency and/or or consistency) in absence of an organic cause. Based on predominant bowel habit, it is further divided into IBS-diarrhea, IBS-constipation, IBS-mixed and IBS-unspecified. IBS-QOL is a disease specific QOL questionnaire that assesses QOL in IBS patients along eight domains: dysphoria, interference with activities, body image, health worry, food avoidance, social reactions, sexual health, and effect on relationships.

Peer-review

This is an interesting study where authors have shown that IBS-subtype could affect the IBS-QOL. This suggests that clinicians (gastroenterologists and primary care doctors) should pay attention to patients' specific complaints like food avoidance, interference with activity, social reactions and relationship problems which lower the QOL in IBS-D and IBS-M patients.

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