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Observations and Research

Burden of Inflammatory Bowel Disease on Patient Mood, Fatigue, Work, and Health-Related Quality of Life in Thailand: A Case-Control Study

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Background: Inflammatory bowel disease (IBD) has become an emerging disease in Asia. The burden of disease affects health-related quality of life (HRQoL), economics, and society. We compared HRQoL of IBD patients with/without active disease to that of the general population.

Methods: Consecutive patients with active disease and patients in clinical remission were prospectively recruited. For each IBD patient, an age- and sex-matched healthy control was invited. Active disease was defined as patient-reported clinical symptoms (ClinPRO) with endoscopic inflammation. All participants completed five questionnaires: (1) Short IBD Questionnaire (SIBDQ); (2) Hospital Anxiety and Depression Scale (HADS); (3) Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue); (4) Work Productivity and Activity Impairment questionnaire (WPAI); and (5) EuroQol 5-Dimension 5-Level scale (EQ5D5L). Multiple regression analyses were used to assess differences in HRQoL scores between IBD patients and controls.

Results: A total of 418 participants (209 IBD, 209 controls) were included. There were 101 patients with active disease and 108 patients in clinical remission. Regarding patients with active disease compared with controls, there was a significant mean difference in scores (95% CI) of 12.3 (9.5–15.2) on the SIBDQ; 6.7 (4.7–8.8), FACIT-fatigue; 1.6 (0.6–2.7), HADS-anxiety; 1.6 (0.8–2.4), HADS-depression; 20.3% (13.0%–27.7%), work productivity impairment; and 0.089 (0.045–0.134), EQ5Q5L ($P < .05$, all comparisons). Regarding patients in clinical remission compared with controls, none of these mean differences achieved a minimal clinically important difference.

Conclusions: Active IBD has a negative impact on HRQoL, whereas patients in clinical remission showed no clinically significant difference from the general population on HRQoL.

Lay Summary

The presence of active IBD significantly decreased patient's quality of life in all dimensions whereas patients in clinical remission showed no clinically significant difference from the general population on quality of life.

Key Words: Crohn's disease, ulcerative colitis, inflammatory bowel disease, health-related quality of life, clinical outcome

Introduction

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is characterized by chronic progressive gastrointestinal inflammation. Over the past few decades, the incidence of CD has been increasing in Asia from 0.05 to 1.34 per 100 000 individuals, while the incidence of UC is 0.4–2.1 per 100 000 individuals.[1–4] The clinical manifestations of IBD, consisting of abdominal pain, chronic diarrhea, weight loss and malaise, could disrupt normal daily life.[5] Uncontrolled inflammation can lead to an increased risk of intestinal complications and surgery, which impact patient quality of life.[6–8]

From physician and patient perspectives, the resolution of patient-reported clinical outcomes (ClinPRO) and achieving mucosal healing are treatment targets.[9] The restoration of patient quality of life is an ultimate goal of value-based healthcare policy.[10] Quality of life (QoL) was defined by the World Health Organization (WHO) as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.[11] In addition, the US Food and Drug Administration (FDA) suggested that outcomes reported by patients should focus on patient-reported outcomes (PROs) of health-related quality of life (HRQoL), including the general psychosocial domain.[12] Various instruments, in relation to both specific and generic disease, have been used to measure HRQoL. The Short Inflammatory Bowel Disease Questionnaire (SIBDQ) has been used as a disease-specific questionnaire. For generalizability, the EuroQoL five-dimensional questionnaire (EQ-5D), a standardized generic

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questionnaire, has been widely used to assess quality of life in various disease states.

However, previous studies of HRQoL in patients with IBD were conducted in Western countries, which may not be representative of the Asian population due to differences in cultures, living environment and life values.[13] Currently, the data on the impact of IBD on HRQoL in Asian populations are limited. Therefore, we aimed to compare HRQoL, including aspects of emotion, work and fatigability, between IBD patients in active disease, clinical remission and steroid-free clinical remission with the general population.

Methods

Study Population

We conducted a cross-sectional study between March 2019 and February 2021 in the King Chulalongkorn Memorial Hospital (KCMH) and Siriraj Hospital, Bangkok, Thailand, which are university hospitals. Consecutive IBD patients aged ≥18 years who visited the IBD clinic in these two hospitals were eligible. All patients were required to meet IBD diagnostic criteria based on clinical symptoms, endoscopy, histology, and radiology according to European Crohn's and Colitis Organization (ECCO) and the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) guidelines.[14] The exclusion criteria were patients who had comorbid conditions such as stroke, chronic kidney disease, cirrhosis, chronic heart failure, rheumatoid arthritis, primary sclerosing cholangitis, psoriasis, and cancer. For each IBD patient, one healthy control matched by age and sex was invited to complete QoL questionnaires. Healthy controls were randomly selected and invited from the national blood donation center, Thai Red Cross Society or the Lumphini Central Public Park in Bangkok. We excluded potential control participants if underlying disease was reported or family members had an IBD diagnosis.

Data Collection

Baseline characteristics such as age, sex, smoking status, and comorbid conditions were collected. At the time of inclusion, data on IBD subtypes, disease phenotypes, disease location, disease activity, extraintestinal manifestations, current medical treatment, and comorbid conditions were recorded. All patients completed the self-reported clinical outcomes (ClinPRO2). For UC patients, ClinPRO2 comprised (1) rectal bleeding and (2) stool frequency using a 6-point Mayo score. For CD patients, ClinPRO2 comprised (1) abdominal pain (rated as no pain (score = 0), mild (score = 1), moderate (score = 2) and severe (score = 3)) and (2) diarrhea (rated as no diarrhea (score = 0), 1–2 bowel movements per day (score = 1), 3–4 bowel movements per day (score = 2), and ≥5 bowel movements per day (score = 3)). Endoscopy or radiology within 3 months before or after the index date of enrollment was collected.

We classified patients into (1) active disease and (2) clinical remission groups. Among clinical remission group, we also sub-classified for steroid-free clinical remission. For UC patients, active disease was defined as a ClinPRO2 score ≥1 with a Mayo endoscopic subscore ≥2, whereas clinical remission was defined as no symptom (ClinPRO2 score = 0). For CD patients, active disease was defined as a ClinPRO2 score ≥1 with evidence of active inflammation by endoscopy or radiology, whereas clinical remission was defined as no symptom (ClinPRO2 score = 0). Steroid-free clinical remission was defined as clinical remission without corticosteroid.

Outcomes

Primary outcomes assessed HRQoL. All patients and healthy controls answered the following 5 validated HRQoL questionnaires:

1) The *Short IBD Questionnaire* consists of 10 items measuring the 4 domains of bowel function, general well-being, emotion, and social performance. Each item was rated on a 7-point scale from 1 to 7, resulting in a total score ranging from 10 to 70. Lower scores indicate poorer QoL.[15] The difference in the SIBDQ score of 10 points was defined as the minimal clinically important difference[16]
2) The *Hospital Anxiety and Depression Scale (HADS)* consists of 7 items measuring anxiety and 7 items measuring depression. Each item was rated on a scale ranging from 0 to 3. Each subscore for anxiety and depression ranges from 0 to 21. Higher scores indicate higher levels of anxiety and depression. A cutoff score ≥8 for each mood indicates significant symptoms of depression and/or anxiety.[17]
3) The *Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F)* scale consists of 13 items measuring fatigue associated with chronic disease. Each item was rated on a scale ranging from 0 to 4. Total scores range from 0 to 52. Higher scores indicate a lower degree of fatigue.[18] A difference in FACIT-F score of 4 points was considered a minimal clinically important difference.[18]
4) The *Work Productivity and Activity Impairment questionnaire (WPAI)* consists of 6 items measuring work impairment in 4 domains—work time absence, impairment while working, overall work impairment and activity impairment. The result is reported as the overall percentage of work impairment ranging from 0% to 100%, with higher scores representing poor work productivity.[19]
5) The *EuroQol 5-Dimensions* Time-Trade-Off and visual analog scale (EQ5D5L–TTO, VAS) is a generic health utility instrument that consists of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension scale ranges 1 to 5. Scores are converted into a Thai TTO score ranging from –0.283 to 1. The EQ VAS is quantitatively measured by self-rating on their own judgment, ranging from 0 to 100, with 0 meaning "the worst health you can imagine" and 100 meaning "the best health you can imagine". Higher EQ5D scores indicate better QoL.[15] A difference of 0.08 points in EQ5D5L–TTO scores and 10 points on the VAS were considered minimal clinically important differences.[20, 21]

Statistical Analysis

Descriptive statistics were used to report patient characteristics and demographic data. Categorical data such as sex, smoking status, IBD subtype, IBD location, and current IBD medication are presented as numbers and percentages. Continuous data are reported as the mean and standard deviation or median and interquartile range (IQR). Differences in

HRQoL scores between patients and controls were compared using Student's *t* test. Multiple regression models including marriage status and educational level were analyzed to derive the adjusted mean differences in HRQoL scores and 95% confidence interval (95% CI) for comparisons of IBD patients against the control group. A *P*-value <.05 was considered statistically significant. Statistical analyses were performed using the Statistical Package for the Social Science (SPSS).

Ethical Considerations

All participants provided written informed consent. The study was approved by the local ethics committees of each center (IRB approval numbers 886/2561 and 680/62).

Results

Characteristics of Overall IBD Patients

A total of 209 IBD patients (106 UC, 103 CD) were included in the study. The mean age (± SD) was 47.3 ± 15.6 years, and 49.3% were male. Table 1 shows demographic characteristics of the patients. The mean ± SD scores in the IBD patients was 55.0 ± 13.6 on the SIBDQ; 40.9 ± 8.5, FACIT fatigue; 4.0 ± 4.0, HADS-anxiety; 3.4 ± 3.1, HADS-depression; 17.8% ± 25.3%, work productivity impairment; 0.913 ± 0.167, EQ5D5L-TTO; and 77.9 ± 16.2, EQ5Q5L-VAS (Table 2). Anxiety and depression were identified in 39 patients (18.7%) and 23 patients (11%), respectively.

Table 1. Characteristics of 209 patients with inflammatory bowel disease and 209 healthy controls.

Characteristics	IBD patients (*n* = 209)	Controls (*n* = 209)
Male (%)	103 (49.3%)	103 (49.3%)
Age (mean ± SD, years)	47.3 ± 15.7	45.1 ± 15
Current smoking (*n*, %)	6 (2.8%)	10 (4.8%)
Current NSAID use (*n*, %)	3 (1.5%)	2 (1%)
Married (*n*, %)	125 (59.8%)	87 (41.6%)
Postgraduate Certificate Diploma (*n*, %)	145 (69.4%)	136 (65.1%)
Crohn's disease (*n*, %)	103 (49.3%)	—
Location		
L1: ileum	27/103 (26.2%)	
L2: colon	21/103 (20.4%)	
L3: ileocolon	51/103 (49.5%)	
L4: upper GI	4/103 (3.9%)	
Behavior		
B1: inflammatory	65/103 (63.1%)	
B2: stricturing	13/103 (12.6%)	
B3: penetrating	25/103 (24.3%)	
Perianal disease	11/103 (10.7%)	
Ulcerative colitis	106 (50.7%)	—
E1: proctitis	13/106 (12.2%)	
E2: left-sided colitis	42/106 (39.6%)	
E3: extensive colitis	51/106 (48.2%)	
Current IBD medication		—
Corticosteroids	75 (35.9%)	
5-Aminosalicylic acid	145 (69.4%)	
Immunomodulators	139 (66.5%)	
Biologic agents	24 (11.9%)	

Table 2. Health-related quality of life between patients with inflammatory bowel diseases and healthy controls.

Characteristics	IBD patients (*n* = 209)	Controls (*n* = 209)	P
SIBDQ (mean ± SD)[a]	55.0 ± 13.6	63.0 ± 5.0	<.01
HADS-anxiety (mean ± SD)[b]	4.0 ± 4.0	3.4 ± 2.5	.04
HADS-depression (mean ± SD)[b]	3.4 ± 3.1	2.3 ± 2.3	<.01
FACIT-Fatigue (mean± SD)[a]	40.9 ± 8.5	45.6 ± 4.3	<.01
Work productivity impairment %(mean± SD)[b]	17.8 ± 25.3	6.8 ± 10.9	<.01
EQ5D5L-TTO (mean± SD)[a]	0.913 ± 0.167	0.963 ± 0.056	<.01
EQ5D5L-VAS (mean± SD)[a]	77.9 ± 16.2	88.0 ± 8.8	<.01

Abbreviations: SIBDQ: Short Inflammatory Bowel Disease Questionnaire; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; Percentage of Work Productivity Impairment questionnaire; EQ5D5L-TTO and VAS: European Quality of Life 5-Dimensions 3-Level; time-trade-off and visual analog scale; HADS: Hospital Anxiety and Depression Scale.
[a]Higher values for SIBDQ, FACIT-F, EQ5D5L scores indicate good quality of life.
[b]Higher values for WPAI, HADS scores indicate poor quality of life.

The mean difference (95% CI) in scores between overall group of IBD patients and the control group was 8 (6–10) on the SIBDQ; 4.7 (3.4–6), FACIT-fatigue; 0.6 (0.1–1.2), HADS-anxiety; 1.0 (0.5–1.6), HADS-depression; 10.9% (6.2–15.6%), work productivity impairment; 0.049 (0.026–0.074), EQ5Q5L-TTO; and 10.1 (7.5–12.8), EQ5Q5L-VAS. These were significant differences between the two groups (*P* < .05, all comparisons).

Active Disease and Health-Related Quality of Life

One hundred and one patients (48%) were classified as having active disease, and 108 patients (52%) were in clinical remission. Seventy-eight patients were in steroid-free clinical remission. Clinical information for the patients in active disease, those in clinical remission and those in steroid-free clinical remission is shown in Table 3. No differences in age, sex, and phenotypic diseases between active disease, clinical remission, and steroid-free clinical remission groups were observed (Supplementary Tables S1 and S2).

The patients with active disease reported poor HRQoL in all dimensions. Among those patients, the mean ± SD was 50.8 ± 13.7 on the SIBDQ; 39.2 ± 9.4, FACIT fatigue; 4.9 ± 4.5, HADS-anxiety; 3.8 ± 3.2, HADS-depression; 25% ± 27.9%, work productivity impairment; 0.871 ± 0.218, EQ5D5L-TTO; and 84 ± 16.5, EQ5Q5L-VAS. The number of patients with anxiety and depression was 28 patients (27.7%) and 11 patients (10.9%), respectively.

HRQoL scores indicated significantly impaired HRQoL for the IBD patients with active disease relative to the controls. The mean difference for each HRQoL score was significantly different between the two groups (*P* < .01, all comparisons). The mean score differences (95% CI) were 12.3 (9.5–15.2)

Table 3. Clinical information of IBD patients with active disease, clinical remission and steroid-free clinical remission.

Characteristics	IBD patients (n = 209)		
	Active disease (n = 101)	Clinical remission (n = 108)	Steroid-free clinical remission (n = 78)
Male (%)	53 (52.5%)	50 (46.3%)	37 (47.4%)
Age (mean ± SD, years)	45.2 ± 15.2	49.2 ± 16.1	50.1 ± 16.3
Current smoking (n, %)	0 (0%)	6 (2.8%)	5 (6.4%)
Current NSAID use (n, %)	1 (0.5%)	2 (1%)	2 (2.6%)
Married (n, %)	55 (54.5%)	70 (64.8%)	27 (34.6%)
Postgraduate Certificate Diploma (n, %)	68 (67.3%)	77 (71.3%)	55 (70.5%)
Ulcerative colitis	50 (49.5%)	56 (51.9%)	43 (55.1%)
E1: proctitis	8 (16%)	5 (8.9%)	5(11.6%)
E2: left-sided colitis	18 (36%)	24 (42.9%)	17 (39.5%)
E3: extensive colitis	24 (48%)	27 (48.2%)	20(46.5%)
Crohn's disease	51(50.5%)	52 (48.1%)	35 (44.8%)
Location			
L1: ileum	14 (27.5%)	13 (25%)	9(25.7%)
L2: colon	9 (17.5%)	12 (23.1%)	10 (48.6%)
L3: ileocolon	27 (53%)	24 (46.2%)	16 (45.7%)
L4: upper GI	1 (2%)	3 (5.7%)	0 (0%)
Behavior			
B1: inflammatory	29 (56.9%)	36 (69.2%)	25(71.4%)
B2: stricturing	9 (17.6%)	4 (7.7%)	1 (2.9%)
B3: penetrating	13 (25.5%)	12 (23.1%)	9 (25.7%)
Perianal disease	6 (5.9%)	5 (4.6%)	3 (3.8%)
Current IBD medication			
Corticosteroids	45 (44.6%)	30 (27.8%)	0 (0%)
5-Aminosalicylate	72 (71.3%)	73 (67.6%)	52 (66.7%)
Immunomodulators	65 (64.3%)	74 (68.5%)	53 (67.9%)
Biologic agents	13 (12.9%)	11 (10.2%)	7 (9%)

on the SIBDQ; 6.7 (4.7–8.8), FACIT-fatigue; 1.6 (0.6–2.7), HADS-anxiety; 1.6 (0.8–2.4), HADS-depression; 20.3% (13.0%–27.7%), work productivity impairment; 0.089 (0.045–0.134); EQ5Q5L-TTO; and 15.6 (11.7–19.6), for EQ5Q5L-VAS. After adjusting for marital status and educational level, there were minimal changes in the absolute mean differences for each HRQoL score (Table 4).

Clinical Remission and Health-Related Quality of Life

Of 108 IBD patients in clinical remission, the mean ± SD score was 58.8 ± 12.3 on the SIBDQ; 42.5 ± 7.2, FACIT-fatigue; 3.1 ± 3.3, HADS-anxiety; 3.0 ± 2.9, HADS-depression; 10.0 ± 19.7%, work productivity impairment; 0.955 ± 0.074, EQ5D5L-TTO; and 83.1 ± 14.2, EQ5Q5L-VAS. The prevalence of anxiety and depression was 10.2% and 11.1%, respectively.

After adjustment for marital status and educational level, HADS-anxiety, HADS-depression, work productivity impairment and EQ5D5L-TTO scores for the IBD patients in clinical remission were similar to those in the controls. Consistent with the trends seen with the patients in active disease, the SIBDQ, FACIT-fatigue and EQ5D5L-VAS scores for patients in clinical remission were significantly different relative to the controls (Table 4). None of these mean differences achieved a minimal clinically important difference.

Steroid-Free Clinical Remission and Health-Related Quality of Life

Of 108 patients in clinical remission, 78 patients were considered steroid-free clinical remission. In steroid-free clinical remission group, the mean ± SD score was 59.8 ± 11.3 on the SIBDQ; 42.8 ± 6.5, FACIT-fatigue; 2.7 ± 2.6, HADS-anxiety; 2.8 ± 2.7, HADS-depression; 12.0 ± 21.7%, work productivity impairment; 0.957 ± 0.065, EQ5D5L-TTO; and 83.9 ± 13.6, EQ5Q5L-VAS. The prevalence of anxiety and depression was 6.4% and 9.0%, respectively.

Consistent with the trends seen with the patients in clinical remission, HADS-anxiety, HADS-depression, work productivity impairment and EQ5D5L-TTO scores for patients in steroid-free clinical remission were similar to those in the controls. The SIBDQ, and FACIT-fatigue for patients in steroid-free clinical remission were significantly different relative to the controls. However these mean differences did not achieve a minimal clinically important difference (Table 4).

HRQoL Between Active Disease, Clinical Remission, and Steroid-Free Clinical Remission

When compared with patients in active disease, all HRQoL scores indicated significantly better HRQoL for both patients in clinical remission and patients in steroid-free clinical remission (Supplementary Table S3).

Table 4. Health-related quality of life compared between patients with inflammatory bowel diseases and healthy controls.

HRQoL measurement (mean ± SD)	IBD patients	Healthy control	Unadjusted		Adjusted[a]	
			Mean differences (95% CI)	P	Mean differences (95% CI)	P
Active disease (*n*; IBD = 101, control = 101)						
SIBDQ[b]	50.8 ± 13.7	63.2 ± 5.1	12.3 (9.5–15.2)	<.01	12.4(9.5–15.2)	<.01
HADS-anxiety[c]	4.9 ± 4.5	3.3 ± 2.5	1.6 (0.6–2.7)	<.01	1.7 (0.7–2.8)	<.01
HADS-depression[c]	3.8 ± 3.2	2.2 ± 2.2	1.6 (0.8–2.4)	<.01	1.7 (0.9–2.5)	<.01
FACIT-Fatigue[b]	39.2 ± 9.4	45.9 ± 4.1	6.7 (4.7–8.8)	<.01	6.8 (4.8–8.8)	<.01
Work productivity impairment %[c]	25.0 ± 27.9	4.7 ± 7.7	20.3 (13.0–27.7)	<.01	21.1 (13.9–28.3)	<.01
EQ5D5L-TTO[b]	0.871 ± 0.218	0.960 ± 0.064	0.089 (0.045–0.134)	<.01	0.096 (0.052–0.140)	<.01
EQ5D5L-VAS[b]	84.0 ± 16.5	88.1 ± 9.5	15.6 (11.7–19.6)	<.01	16.3 (12.4–20.1)	<.01
Clinical remission (*n*; IBD = 108, control = 108)						
SIBDQ[b]	58.8 ± 12.3	62.8 ± 4.9	3.9 (1.4–6.5)	<.01	3.7 (1.1–6.2)	<.01
HADS-anxiety[c]	3.1 ± 3.3	3.5 ± 2.4	0.4 (–0.4 to 1.1)	.35	0.4 (–0.4 to 1.1)	.34
HADS-depression[c]	3.0 ± 2.9	2.5 ± 2.5	0.5 (–1.2 to 0.2)	.16	0.5 (–1.2 to 0.2)	.16
FACIT-Fatigue[b]	42.5 ± 7.2	45.3 ± 4.4	2.8 (1.2–4.4)	<.01	2.7 (1.0–4.3)	<.01
Work productivity impairment %[c]	10.0 ± 19.7	8.5 ± 12.8	1.5 (–7.2 to 4.3)	.61	1.5 (–7.2 to 4.2)	.61
EQ5D5L-TTO[b]	0.955 ± 0.074	0.967 ± 0.048	0.012 (–0.004 to 0.029)	.16	0.012 (–0.005 to 0.029)	.16
EQ5D5L-VAS[b]	83.1 ± 14.2	87.9 ± 8.2	4.8 (1.5–8.1)	<.01	3.9 (0.5–7.2)	.02
Steroid-free clinical remission (*n*; IBD = 78, control = 78)						
SIBDQ[b]	59.8 ± 11.3	63.3 ± 4.5	3.4 (0.7–6.1)	<.01	3.1 (0.4–5.8)	.03
HADS-anxiety[c]	2.7 ± 2.6	3.4 ± 2.5	0.7 (–1.4 to 0.1)	.11	0.6 (–1.5 to 0.2)	.12
HADS-depression[c]	2.8 ± 2.7	2.6 ± 2.5	0.5 (–0.6 to 1.1)	.58	0.4 (–0.5 to 1.1)	.47
FACIT-Fatigue[b]	42.8 ± 6.5	45.3 ± 4.3	2.5 (0.8–4.3)	<.01	2.3 (0.5–4.0)	.01
Work productivity impairment %[c]	12.0 ± 21.6	6.9 ± 11.0	5.1 (–1.7 to 11.8)	.14	4.8 (–1.8 to 11.3)	.15
EQ5D5L-TTO[b]	0.957 ± 0.065	0.971 ± 0.037	0.014 (–0.031 to 0.003)	.12	0.015 (–0.032 to 0.002)	.08
EQ5D5L-VAS[b]	83.9 ± 13.6	87.9 ± 8.2	3.9 (0.1–7.8)	.48	3.0 (0.9–6.9)	.13

Abbreviations: SIBDQ: Short Inflammatory Bowel Disease Questionnaire; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue, Percentage of Work oductivity Impairment questionnaire; EQ5D5L-TTO and VAS: European Quality of Life 5-Dimensions 3-Level, time-trade-off and visual analog scale; HADS: Hospital Anxiety and Depression Scale.
[a]Adjusted for marriage status and educational level.
[b]Higher values for SIBDQ, FACIT-F, EQ5D5L scores indicate good quality of life.
[c]Higher values for WPAI, HADS scores indicate poor quality of life.

Discussion

The results of this study demonstrated a significant impact of active IBD on HRQoL impairments in all dimensions, including disease-specific and general HRQoL, fatigability, anxiety, depression, and work productivity. The patients in remission from disease showed no clinically significant difference in HRQoL when compared with the general population.

A previous study, which included American and European populations, demonstrated the association between general HRQoL and disease activity in UC patients with moderate-to-severe activity by using the Simple Clinical Colitis Activity Index or the partial Mayo score.[22] The authors reported that the EQ5D3L-TTO and EQ5D-VAS scores among patients with active UC were lower than those in remission (mean difference: 0.05 for TTO and 11.6 for EQ5D-VAS). Active UC negatively affected patients' work productivity (WPAI; 34.5% in active disease vs 13.1% in remission).[22] Another study by Min Ho et al. from Singapore showed that IBD patients with active disease based on a partial Mayo score ≥2 for UC and a Harvey-Bradshaw Index (HBI) score ≥5 for CD were significantly associated with decreased HRQoL measured by the SIBDQ (mean difference: 6.41) and EQ5D5L-VAS (mean difference: 5.55) when compared with patients in remission.[23] A cross-sectional study by Fu and colleagues demonstrated a modest correlation between disease activity using the SSCAI for UC or the HBI for CD and emotional symptoms using HADS-anxiety and HADS-depression in Chinese IBD patients (r = 0.544 and r = 0.595, respectively).[24]

Our findings are consistent with previous studies.[25–29] However, the definitions of active disease differed between previous studies and our present study. Instead of determining disease activity by disease active indexes or symptoms alone, we combined the ClinPRO2 with evidence of endoscopic inflammation to determine the disease activity of patients. Aniwan et al.[28] showed that the combination of the ClinPRO2 (i.e., rectal bleeding and stool frequency) and Mayo endoscopic subscore in patients with UC correlated well with both disease-specific and generic HRQoL (i.e., SIBDQ, EQ5D3L), WPAI, FACIT-fatigue, HADS-depression and HADS-anxiety. In addition, we assessed the difference between patients' health status valuations and those of the general population. We found that patient-reported clinical outcomes and endoscopic inflammation were associated with worse HRQoL scores, and all individual scores reached clinically important differences compared to the general population, indicating that patients with active disease perceived their health status to be lower than the general population did.

With regard to psychological aspects, a meta-analysis estimated the prevalence of anxiety and depression in more than 150 000 IBD patients.[30] With a HADS score ≥8 for anxiety and depression, the prevalence of anxiety symptoms in all IBD patients was 39.4% (95% CI, 34.3%–44.4%), and the prevalence of depressive symptoms was 18.7% (95% CI, 15.6%–22.0%). IBD patients with active disease were two times as likely as patients with inactive disease to perceive anxiety and depressive symptoms.[30] Of note, there was high heterogeneity in this study. In our study, the proportion of patients with active disease who had anxiety symptoms was 2-fold higher than that of the patients in remission and 9-fold higher than that in the general population. The IBD patients with either active disease or disease remission had depressive symptoms approximately 2-fold higher than the general population.

Regardless of disease activity, the IBD patients reported higher fatigability than the general population, and no clinical differences between patients with active disease and those in remission were observed, which is in accordance with previous studies.[31, 32] A study from The Netherlands reported that 41% of quiescent IBD patients reported fatigue. IBD patients had significantly higher levels of fatigue than the Dutch population.[32] Interestingly, none of the laboratory results (i.e., anemia, albumin and cortisol levels) in quiescent IBD patients were associated with fatigue.[31, 32] As fatigue is common in those with chronic medical illness, the reason is possibly multifactorial, and psychosocial factors may contribute to these issues. Even though the mean difference in FACIT-fatigue scores in our results was statistically significant, the absolute difference (2.7) did not reach the minimal clinically important difference.

The disease onset of IBD usually develops in the 3rd to 4th decades of life and can affect life productivity. Not surprisingly, the patients reported that having active disease reduced their work productivity by 20.3%, which was consistent with earlier reports, ranging from 18.8–28%.[33–35] In addition, the patients perceived that having active IBD impaired their general health status, as determined by a significantly lower utility score, relative to the Thai population. On the other hand, the work productivity and utility scores (EQ5D5L-TTO: 0.913) of the patients in disease remission did not differ from the Thai population. Additionally, their utility scores seemed to be higher than data from Europe (0.77)[36] and the United States (0.87).[22] These differences across different geographic regions may be explained by differences in patient perceptions, disease characteristics, health care policies, cultures or social structures.

The major strength of this study is that all participants provided self-administered symptoms and various self-reported HRQoL questionnaires. Disease activity was assessed by pure patient-reported symptoms and endoscopic inflammation instead of only clinical disease activity indexes. Therefore, we were able to compare different patients' symptom-reported disease activity to the healthy controls. However, there were some limitations of this study. Due to the case-control cross-sectional study design, the results could have reflected the difference in HRQoL between IBD patients with/without active disease and controls. Further longitudinal studies are needed to explore whether improving disease activity can restore quality of life of IBD patients to levels comparable to the general population. Another limitation is that our participants were all Thai. The generalization of these data to different racial and ethnic populations may not be possible.

In conclusion, the presence of active IBD significantly decreased patient quality of life, anxiety, depression, fatigability, and work productivity impairment compared to these measures in the general population. Patients experiencing a resolution of active IBD symptoms showed no clinically significant difference from the general population on quality of life.

Supplementary Data

Supplementary data is available at *Crohn's and Colitis 360* online.

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Author Contributions

Conceptualization: SA. Methodology: SA. Formal analysis: KT. Data acquisition: NP, JL, PP, NS, NK, and SA. Writing—original draft: KT and SA. Writing—review and editing: KT, JL, and SA. Approval of final manuscript: all authors.

Conflict of Interest

None of the authors have any relevant conflicts of interests.

Data Availability

Data for this manuscript are not publically available.

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