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Clinical Study

An Evil Backstage Manipulator: Psychological Factors Correlated with Health-Related Quality of Life in Chinese Patients with Crohn’s Disease

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Health-related quality of life (HRQoL) is recommended as one of essential parameters to evaluate treatment effect and clinical outcome in patients with Crohn’s disease (CD). Recent studies reported that psychological factors might play a role in HRQoL in Western and American CD patients. Sufficient evidences in Chinese CD patients are still unavailable. This study is dedicated to investigate the correlation of various psychological factors with HRQoL in Chinese CD patients. We prospectively collected 40 active and 40 quiescent CD patients in China and found that psychological factors, especially neuroticism and anxiety, significantly correlate with and affect HRQoL in both active and quiescent CD groups. This is the first report revealing correlation between psychological factors and HRQoL in Chinese CD patients. Therefore, we assume that our results can contribute to a better understanding of etiology and tailoring of management in Chinese patients with Crohn’s disease and are beneficial to our colleagues to compare the heterogeneous characteristics of Crohn’s disease in different ethnic groups.

1. Introduction

Crohn’s disease (CD) is characterized by chronic, transmural intestinal inflammation in which periods of remission with variable length are interrupted by relapse episodes [1]. Health-related quality of life (HRQoL) has been broadly defined as a concept that includes emotional, social, and physical dimensions of health functioning [2]. Improvement in quality of life in patients with CD has been increasingly attracting attention of clinical physicians. Inflammatory Bowel Disease Questionnaire (IBDQ) was therefore developed and being widely used to comprehensively assess healthy status and HRQoL in patients with inflammatory bowel disease (IBD) [3, 4]. On the basis of the assumption that IBDQ could effectively reflect patient’s symptom load, psychological fluctuation, and quality of life [4], IBDQ has also been recommended as one of essential instruments to evaluate treatment effect and clinical outcome [5]. In recent decades, a series of studies performed in Europe and North America reported several distinct psychological traits that relate to HRQoL and outcome of surgery in patients with CD [2, 4, 6, 7]. These findings intensively suggest that
some disease-unrelated variables may affect IBDQ score as well and, consequently, it is necessary to consider these variables into the evaluation of HRQoL and figure out to what extent that these variables would influence clinical outcome in patients with CD.

To our knowledge, there is no report investigating correlation between psychological factors and HRQoL in Chinese patients with CD. Considering the heterogeneous characteristics of Crohn's disease in different ethnic groups reported before, we assumed that there is a necessity to perform an investigation in Chinese population. Therefore, current study was dedicated to analyze the correlation between various psychological factors and HRQoL in patients with CD from China. All questionnaires adopted in current study have been validated for Chinese population.

2. Methods

2.1. Patients. Patients in current study were recruited from outpatient clinic of CD in Jinling Hospital between March 2012 and August 2012. Patients were first screened by a physician for eligibility assessment. Then, their blood sample would be collected for C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and whole blood analysis. Afterwards, they would be evaluated by another physician for disease activity using CDAI score. Subsequently, patients were required to accomplish all questionnaires (self-reporting) truthfully and independently, and then they were checked by a clinical nurse.

All enrolled patients were 18–65 years old and diagnosed as CD by clinical manifestations, radiologic, endoscopic, and histopathologic evidences. The exclusion criteria included current or previous mental disorders, receiving or used to receive psychotherapy, presence of major medical conditions or chronic disease history other than inflammatory bowel disease, and unwilling to participate in or cannot accomplish current study.

2.2. Health-Related Quality of Life and Psychological Evaluation. IBDQ is the most widely used and validated disease-specific instrument [3], which contains 32 items and assesses four aspects (subscales) of health-related quality of life: emotional function (12 items), social function (5 items), bowel function (10 items), and systemic symptom (5 items) [8]. Each item is scored with 7-level Likert scale; the higher score, the better health-related quality of life [4]. This questionnaire could provide a total score and four subscale scores of each aspect. The IBDQ used in current study has been translated and validated in Chinese population [9].

To assess neuroticism and social conformity and desirability, the Neuroticism and Lie subscales from the Eysenck Personality Inventory (EPI) were adopted in current study [10]. Twenty-three items are designed to evaluate neuroticism (Neuroticism subscale) and the other 21 items are assigned for social desirability (Lie subscale). The reliability and validity of this scale are well established in Chinese population [11].

The Hospital Anxiety and Depression Scale (HADS) was first developed in 1983 [12] and has been extensively used in subsequent studies to identify the potential anxiety and depression in nonpsychiatric hospitalized patients [13]. This questionnaire includes separated Anxiety and Depression subscales with seven items, respectively. Previous studies have confirmed the validity of this scale among Chinese patients [14, 15].

To determine the dynamics of aggression among individuals, the Buss-Perry Aggregation (BPA) questionnaire was employed in this study [16]. BPA has been one of the most popular self-report inventories for the measurement of four different dimensions (anger, hostility, physical aggression, and verbal aggression) during the past two decades since its publication in 1992 [17]. This 29-item questionnaire is scored with a 5-level scale for each question, contributing to a total score and four subscales of each dimension. A higher score suggests a higher level of aggression feelings [4]. BPA has been validated in Chinese version as well [17].

2.3. Statistical Consideration. All statistical tests were performed with SPSS software (SPSS for Windows, version 13.0, SPSS, Chicago, IL). All analyses were 2-tailed and differences were considered statistically significant when P values <0.05. Continuous variables were described as mean ± SD and compared with unpaired student's t-test. Categorical variables were presented as percentages and compared with Fisher's exact test or Chi-square test. Hierarchical multiple regression was performed to analyze the effect of different psychological factors on HRQoL independent of the influence of other parameters, such as disease activity (CDAI score). In this model, dependent parameters were IBDQ and its subscales; independent factors included demographic parameters (including age, gender, years of education, and duration of disease) entered in step 1, and CDAI score entered in step 2 as a control parameter, and then all psychological factors entered in step 3. Spearman correlation analysis was performed to investigate the correlation between psychological parameters and IBDQ and its subscales. Multiple linear regression analysis with forward stepwise methods was used to investigate to what extent that psychological factors could affect IBDQ and its subscales. Psychological variables that displayed a significant correlation with IBDQ or its subscales were entered in the regression analysis.

2.4. Ethical Statement. This study was approved by the Medical Ethics Committee of Jinling Hospital. A written informed consent was obtained from each enrolled patient.

3. Results

A total of 121 patients diagnosed with CD visited our clinics during the period of study. According to the exclusion criteria, 80 patients were eligible and finally enrolled (Figure 1).

To better investigate the correlation between psychological factors and HRQoL in these patients, we firstly performed a hierarchical multiple regression analysis to discover and then exclude potential confounding parameters. According to Table 1, demographics (step 1) did not contribute to IBDQ or any of its subscales. However, when CDAI score was entered into this model (step 2), R square elevated dramatically to a statistical significant degree, indicating that
CD patients from out-patient clinic
(n = 121)

Eligibility assessment
(n = 80)

Blood sample collection
(CRP, ESR, PLT)

Disease activity evaluation
(CDAI score)

Quiescent CD group
(n = 40)

Active CD group
(n = 40)

Questionnaires accomplishment

Health-related quality of life
- Inflammatory bowel disease questionnaire

Psychological factors:
- Neuroticism and lie subscales of eysenck personality inventory
- Hospital anxiety and depression scale
- Buss-Perry Aggregation (BPA) questionnaire

Figure 1: Study design of current prospective study. A total of 121 patients with Crohn’s disease from outpatient clinic were recruited in the current study. After eligibility assessment, 80 eligible patients were enrolled. Their blood samples were collected for CRP, ESR, and PLT analysis. Afterwards, they were evaluated for disease activity with Crohn’s disease activity index (CDAI score) and then divided into quiescent (CDAI ≤ 150 points) and active (CDAI > 150 points) CD groups. All enrolled patients were subsequently required to accomplish HRQoL-related questionnaire (Inflammatory Bowel Disease Questionnaire, IBDQ) and psychological factor-related questionnaires, including Neuroticism and Lie subscale from Eysenck Personality Inventory (EPI), Hospital Anxiety and Depression Scale (HADS), and Buss-Perry Aggregation (BPA) questionnaire. CD: Crohn’s disease.

disease activity was a significant covariant in the relationship between psychological factors and HRQoL. Notably, when psychological factors were entered into this model (step 3), the R square increased again, demonstrating that a predictive power was added to the model by the addition of psychological factors (Table 1).

Therefore, to reduce the confounding effect of disease activity in the relationship between psychological factors and HRQoL [18–20], we established two independent groups with different disease activity (active CD and quiescent CD), measured by Crohn’s disease activity index (CDAI), and analyzed them separately. Among them, 40 patients were assigned into active CD group (CDAI ≤ 150 points) and the other 40 participates were in quiescent CD group (CDAI > 150 points). Both of them displayed a male predominance, which was in accordance to our previous investigations [21]. The CDAI scores were 91.8 points and 247.8 points, respectively, suggesting a distinct variance of disease activity between the two groups (P < 0.001). Meanwhile, CRP (P < 0.001) and ESR (P = 0.022) levels increased significantly
in active group while platelet count was similar between these groups. Table 2 described demographics and clinical characteristics of all enrolled subjects.

The mean duration of CD was 2.90 and 4.36 years for each group. The majority of enrolled patients in both groups had never received operation or less than 1 operation. 5-aminosalicylic acid (5-ASA), that mainly includes sulfasalazine and mesalazine, was prescribed to the majority of patients in both groups. TWP (Tripterygium wilfordii polyglycoside) is a traditional Chinese medicine which has been confirmed to be effective in the management of CD [22, 23] and therefore becomes a choice of medication prescriptions in our institute.

Table 3 demonstrated all psychological scores and IBDQ score and its subscales in both groups. Patients with active CD displayed a significant higher level of neuroticism, anxiety, depression, physical aggression, and hostility, paralleled to a significant decrease in HRQoL when compared to patients in quiescent CD group (Table 3). Meanwhile, there was not any statistical difference between groups in social desirability and anger (Table 3). Interestingly, verbal aggression seems to be more apparent in patients with quiescent CD (Table 3).

We further examined the correlation between various psychological factors and IBDQ together with its subscales in separate analyses of active CD (Table 4) and quiescent CD (Table 5) groups.

In the former group, neuroticism, anxiety, and depression were negatively correlated with IBDQ and its emotional function, bowel function, and systemic symptom subscales. Simultaneously, BPA was correlated with IBDQ and its emotional subscale, whilst physical aggression was correlated with IBDQ bowel function; anger and hostility were confirmed to correlate with IBDQ emotional subscale. However, social desirability did not correlate with any HRQoL parameters, while IBDQ social function did not correlate with any of the psychological variables (Table 4).

In the latter group, neuroticism, anxiety, and depression were significantly correlated with IBDQ and its all four subscales. Moreover, hostility was found to correlate with IBDQ and its emotional and social function subscales. There was not any other correlations in these patients (Table 5).

We subsequently employed multiple linear regression analysis to investigate to what extent that psychological factors could affect IBDQ and its each subscale. Psychological factors that displayed a statistical correlation with IBDQ or any subscale in previous correlation analysis were introduced as independent parameters into this regression model. Table 6 illustrated the results of regression analysis.

In quiescent CD group, a higher level of neuroticism leads to lower scores of IBDQ, IBDQ emotional function, and IBDQ bowel function. Meanwhile, a higher level of anxiety leads to a lower score of IBDQ systemic symptom (Table 6).

In active CD group, neuroticism was similarly confirmed as a remarkable factor to negatively affect IBDQ, IBDQ social function, IBDQ bowel function, and IBDQ systemic symptom. Moreover, IBDQ emotional function in this group was found to simultaneously interact with both neuroticism and anxiety. All interactions in this regression analysis were negative (Table 6).

4. Discussions

To the best of our knowledge, this is the first report investigating correlation between psychological factors and HRQoL in Chinese patients with Crohn’s disease. Similar studies have been performed in Europe and North America. Considering the heterogeneous characteristics of Crohn’s disease in different ethnic groups reported before, we believe that our description of psychological traits and their correlation with HRQoL in Chinese patients would be beneficial for our colleagues and would contribute to a better understanding of etiology and tailoring of management in Chinese patients with Crohn’s disease.

In current study, we discovered that disease activity could exert significant influence on HRQoL in the presence of psychological factors. This was in accordance with previous studies [24]. Vidal and his colleagues [25] confirmed disease activity as one of strongest predictors of HRQoL impairment. Haapamaki [26] discovered disease activity as a significant factor related to HRQoL impairment. Other studies also reported an adverse effect of disease activity on HRQoL in CD patients [27].

After dividing enrolled patients into two independent groups, we discovered that active CD patients were exposed to significant higher risks of neuroticism, anxiety, depression, physical aggression, and hostility, together with a significant

### Table 1: Analysis of potential confounding parameters in the relationship between psychological factors and HRQoL in patients with Crohn’s disease.

|                | Step 1 (demographics<sup>a</sup>) | Step 2 (CDAI score) | Step 3 (psychological factors<sup>b</sup>) |
|----------------|-----------------------------------|---------------------|------------------------------------------|
|                | R square  | P value | R square  | P value | R square  | P value |
| IBDQ           | 0.060     | 0.195   | 0.470     | <0.001  | 0.747     | <0.001  |
| IBDQ-E         | 0.081     | 0.090   | 0.376     | <0.001  | 0.780     | <0.001  |
| IBDQ-SF        | 0.018     | 0.709   | 0.196     | 0.002   | 0.345     | 0.002   |
| IBDQ-B         | 0.040     | 0.367   | 0.446     | <0.001  | 0.656     | <0.001  |
| IBDQ-SS        | 0.052     | 0.252   | 0.531     | <0.001  | 0.701     | <0.001  |

<sup>a</sup> Demographics included age, gender, years of education, and duration of disease; <sup>b</sup> psychological factors included Neuroticism and Lie scores, Hospital anxiety and depression scores, and Buss-Perry score and its subscales; IBDQ-E: IBDQ emotional function; IBDQ-SF: IBDQ social function; IBDQ-B: IBDQ bowel function; IBDQ-SS: IBDQ systemic symptom.
Table 2: Demographics and clinical characteristics in patients with Crohn’s disease.

|                                      | Quiescent CD (CDAI* ≤ 150 points) | Active CD (CDAI > 150 points) | P         |
|--------------------------------------|----------------------------------|-------------------------------|-----------|
| Number of patients                   | 40                               | 40                            | —         |
| Male (%)                             | 30 (75.0)                        | 31 (77.5)                     | ns        |
| Age (years)                          | 29.2 ± 10.1                      | 35.2 ± 11.4                   | 0.015     |
| Education (years)                    | 13.9 ± 2.92                      | 12.0 ± 3.55                   | ns        |
| Smoking history                      |                                  |                               | ns        |
| Never                                | 27                               | 24                            |           |
| Past smoker                          | 12                               | 11                            |           |
| Current smoker                       | 1                                | 5                             |           |
| Duration of disease (years)          | 2.90 ± 2.99                      | 4.36 ± 4.23                   | ns        |
| Times of previous gastrointestinal operations | 20                              | 17                            |           |
| 0                                    | 13                               | 14                            |           |
| 1                                    | 6                                | 3                             |           |
| ≥3                                   | 1                                | 6                             |           |
| Disease location                     |                                  |                               | ns        |
| L1 (ileal)                           | 18                               | 18                            |           |
| L2 (colonic)                         | 8                                | 10                            |           |
| L3 (ileocolonic)                     | 14                               | 12                            |           |
| +L4 (upper gastrointestinal)         | 2                                | 2                             |           |
| Disease behavior                     |                                  |                               | ns        |
| B1 (inflammatory)                   | 10                               | 10                            |           |
| B2 (stricturing)                     | 24                               | 23                            |           |
| B3 (penetrating)                     | 6                                | 7                             |           |
| +P (perianal)                        | 18                               | 17                            |           |
| Medications*                         |                                  |                               | ns        |
| None                                 | 5                                | 0                             |           |
| 5-ASA†                               | 22                               | 26                            |           |
| Azathioprine                         | 6                                | 6                             |           |
| TWP%                                 | 4                                | 6                             |           |
| Enteral nutrition                    | 18                               | 17                            |           |
| CDAI score                           | 91.8 ± 32.3                      | 247.8 ± 80.2                  | <0.001    |
| C-reactive protein (mg/L)            | 17.5 ± 5.32                      | 61.01 ± 12.99                 | <0.001    |
| Erythrocyte sedimentation rate (mm/hour) | 22.4 ± 4.40                     | 37.34 ± 5.29                  | 0.022     |
| Platelet count (×10⁹/L)              | 202 ± 9.88                       | 289 ± 17.5                    | ns        |

* Crohn’s disease activity score; † sum may be more than 100% as one patient may be prescribed with several medications; ‡-aminosalicylic acid mainly includes sulfasalazine and mesalazine; § Tripterygium wilfordii polyglycoside; ns: not significant.

decrease in HRQoL compared to patients in quiescent CD. In correlation analysis, we confirmed that psychological factors, particularly neuroticism, anxiety, and depression, are related to IBDQ and its subscales in both active and quiescent groups.

Neuroticism was demonstrated as a significant variable that leads to declined scores of IBDQ, IBDQ emotional function, and IBDQ bowel function in quiescent CD group and IBDQ, IBDQ social function, IBDQ bowel function, and IBDQ systemic symptom in active group. This is in line with the findings from previous studies of IBD [4, 6] and other disorders [28–30]. We believe that neuroticism should result from both genetic factor and somatic conditions and could contribute to vulnerable reaction with depressive symptoms to stressful life events in these patients [4, 31], which may be helpful to explain the correlation between neuroticism and IBDQ emotional function [32].

Several previous studies have investigated the association between neuroticism and IBDQ and its subscales [4, 33]. They consistently confirmed the remarkable role of neuroticism in the influence of HRQoL on IBD patients. However, they perform analyses in mixed IBD samples and not effectively excluded the potential effect that disease activity exerted on HRQoL. In our study, we divided patients into quiescent and active CD groups and analyzed them separately to reduce the interactions among disease activity, psychological factors, and HRQoL in these patients. In fact, our results confirmed the distinct variance of psychological scores between active...
Table 3: Psychological variables and HRQoL in patients with Crohn’s disease.

|                          | Quiescent CD (CDAI ≤ 150 points) | Active CD (CDAI > 150 points) | P   |
|--------------------------|----------------------------------|--------------------------------|-----|
| Neuroticism score        | 8.08 ± 5.02                      | 11.0 ± 5.83                    | 0.019 |
| Lie (social conformity/desirability) score | 13.5 ± 2.73                      | 12.7 ± 3.06                    | ns   |
| Hospital anxiety score   | 5.20 ± 2.91                      | 7.30 ± 3.14                    | 0.003 |
| Hospital depression score| 5.03 ± 3.17                      | 6.98 ± 3.08                    | 0.007 |
| Buss-Perry score         | 69.7 ± 14.0                      | 79.1 ± 16.9                    | 0.008 |
| PA (physical aggression) score | 19.5 ± 4.79                      | 21.9 ± 5.79                    | 0.049 |
| VA (verbal aggression) score | 19.5 ± 5.25                      | 15.6 ± 3.93                    | 0.011 |
| A (anger) score          | 13.4 ± 3.64                      | 18.7 ± 5.21                    | ns   |
| H (hostility) score      | 17.3 ± 6.54                      | 22.9 ± 5.78                    | 0.007 |
| IBDQ                      | 181.4 ± 22.3                     | 146.0 ± 31.9                   | <0.001 |
| Emotional function score | 69.7 ± 9.79                      | 57.5 ± 12.8                    | <0.001 |
| Social function score    | 23.0 ± 7.01                      | 18.6 ± 7.05                    | 0.006 |
| Bowel function score     | 60.5 ± 6.68                      | 49.9 ± 9.53                    | <0.001 |
| Systemic symptom score   | 28.2 ± 4.68                      | 20.0 ± 5.73                    | <0.001 |

* Crohn’s disease activity score; & Inflammatory Bowel Disease Questionnaire; ns: Not significant.

Table 4: Spearman correlation analysis (P value) between different psychological variables and Inflammatory Bowel Disease Questionnaire and its subscales in patients with quiescent Crohn’s disease (CDAI ≤ 150 points).

|                          | Quiescent CD (CDAI ≤ 150 points)                |
|--------------------------|-----------------------------------------------|
|                          | IBDQ  | IBDQ-E | IBDQ-SF | IBDQ-B | IBDQ-SS                      |
| Neuroticism              | -0.617*** | -0.768*** | -0.116  | -0.389* | -0.476**                     |
| Lie (social conformity/desirability) | 0.134  | 0.149  | 0.038  | 0.063  | 0.128                        |
| Hospital anxiety         | -0.421** | -0.562*** | 0.157   | -0.392* | -0.522***                    |
| Hospital depression      | -0.469** | -0.537*** | 0.012   | -0.428** | -0.464**                     |
| Buss-Perry score         | -0.330*  | -0.481** | 0.056   | -0.309  | -0.261                       |
| PA (physical aggression) | -0.196  | -0.208  | 0.077   | -0.362* | -0.137                       |
| VA (verbal aggression)   | -0.142  | -0.135  | -0.051  | -0.124  | -0.215                       |
| A (anger)                | -0.249  | -0.405** | 0.078   | -0.231  | -0.168                       |
| H (hostility)            | -0.266  | -0.465** | 0.059   | -0.166  | -0.208                       |

IBDQ-E: IBDQ emotional function; IBDQ-SF: IBDQ social function; IBDQ-B: IBDQ bowel function; IBDQ-SS: IBDQ systemic symptom. *P < 0.05; **P < 0.01; ***P < 0.001. The bold data indicates a statistical significance in the Spearman correlation analysis.

Table 5: Spearman correlation analysis (P value) between different psychological variables and Inflammatory Bowel Disease Questionnaire and its subscales in patients with active Crohn’s disease (CDAI > 150 points).

|                          | Active CD (CDAI > 150 points)                |
|--------------------------|---------------------------------------------|
|                          | IBDQ  | IBDQ-E | IBDQ-SF | IBDQ-B | IBDQ-SS                      |
| Neuroticism              | -0.690*** | -0.745*** | -0.651*** | -0.378*** | -0.452**                     |
| Lie (social conformity/desirability) | 0.198  | 0.240  | 0.144  | 0.193  | 0.222                        |
| Hospital anxiety         | -0.572*** | -0.669*** | -0.543*** | -0.370*  | -0.394*                      |
| Hospital depression      | -0.463** | -0.560*** | -0.399*  | -0.363*  | -0.330*                      |
| Buss-Perry score         | -0.251  | -0.238  | -0.208  | -0.163  | -0.125                       |
| PA (physical aggression) | 0.002  | -0.034  | -0.025  | 0.002  | -0.024                       |
| VA (verbal aggression)   | -0.080  | -0.034  | -0.076  | -0.111  | 0.087                        |
| A (anger)                | -0.289  | -0.272  | -0.162  | -0.281  | -0.234                       |
| H (hostility)            | -0.434** | -0.467** | -0.388*  | -0.226  | -0.292                       |

IBDQ-E: IBDQ emotional function; IBDQ-SF: IBDQ social function; IBDQ-B: IBDQ bowel function; IBDQ-SS: IBDQ systemic symptom. *P < 0.05; **P < 0.01; ***P < 0.001. The bold data indicates a statistical significance in the Spearman correlation analysis.
and quiescent CD groups (Table 2), making it reasonable to perform separate analyses which could decrease the bias brought by mixed samples of patients with various disease activities.

Our study found anxiety to be a significant factor that leads to declined scores of IBDQ systemic symptom in quiescent CD and IBDQ emotional function (together with neuroticism) in active CD patients. Prior studies demonstrated some controversies regarding the role that anxiety plays in IBD patients. While some studies reported a prevalence of anxiety as high as 29–35% in remission and 80% in relapse [34], others found no evidence of any correlation between anxiety and CD [35]. A recent study in Korea reported an incidence of 27.4% in IBD patients, accompanied with a significant lower quality of life in these patients compared with healthy controls [36]. We agree with the authors that anxiety could originate from various concerns and worries about incurability and uncertain course and prognosis in Crohn's disease, as well as fear of surgery or development of cancer [24, 37].

Our results suggested that in both quiescent and active CD patients, an increased level of neuroticism and anxiety might reduce the total IBDQ and some other subscales at a magnitude that might be of clinical significance. Therefore, psychological factors, especially neuroticism and anxiety, should be taken in account when using IBDQ to measure clinical outcome of interventions in patients with CD.

We confirmed in current study that psychological distress, concerns, and illnesses could lead to decreased HRQoL and should draw attention of professional staff. However, the majority of current strategies for CD did not pay attention to psychological conditions or concerns in CD patients [24]. Instead, some of their side effects were associated with mental or mood changes, depressions, and other psychological distresses. Therefore, it could be beneficial if integrating conventional medical therapy with psychological interventions improves HRQoL in patients with CD.

We are aware of the limitations in this study. First, a potential risk of selection bias might exist because of the limited sample size from a single center, which may not completely reflect the comprehensive relationship between psychological factors and HRQoL.

Second, this study lacks follow-up prospective data after receiving psychological interventions in all enrolled patients, and thus we were deprived of the ability of evaluating efficacy of psychological treatments in CD patients. However, Boye and his colleagues [38] in their INSPIRE study declared that psychotherapy could improve quality of life in UC but not in CD. Therefore, role of psychotherapy needs to be determined by further studies.

Third, a disease-specific HRQoL questionnaire (IBDQ) was adopted in current study, but not a generic questionnaire, such as SF-36. McColl [39] recommended that generic and disease-specific measures of quality of life are complementary and thus should be used in parallel in IBD. We agree with McColl's suggestion, but we tried to reduce the total time that all questionnaires take in each participant, therefore assisting them to answer all questions truthfully and accurately in this self-reporting investigation.

In conclusion, psychological factors, especially neuroticism and anxiety, can significantly affect HRQoL in patients with both active and quiescent CD. Therefore, more attention toward psychological status in Crohn's patients is required in current and future management. Furthermore, continued large studies are expected to enhance our capacity to design interventions to improve HRQoL and maximize health outcomes in the management of Crohn's disease in the future.

Disclosure

This paper has been orally presented in 99th Clinical Congress of the American College of Surgeons, October 2013, Washington DC.

Conflict of Interest

The authors declare that there is no conflict of interests.

Authors’ Contribution

Song Liu and Zhiwu Hong contributed equally to this work.

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References

[1] S. Liu, J. Ren, G. Han et al., “Mean platelet volume: a controversial marker of disease activity in Crohn’s disease,” European Journal of Medical Research, vol. 17, article 27, 2012.

[2] C. A. Karwowski, D. Keljo, and E. Szegedy, “Strategies to improve quality of life in adolescents with inflammatory bowel disease,” Inflammatory Bowel Diseases, vol. 15, no. 11, pp. 1755–1864, 2009.

[3] G. Guyatt, A. Mitchell, E. J. Irvine et al., “A new measure of health status for clinical trials in inflammatory bowel disease,” Gastroenterology, vol. 96, no. 3, pp. 804–810, 1989.

[4] B. Boye, J. Johnsen, K. Mokleby et al., “The INSPIRE study: do personality traits predict general quality of life (short form–36) in distressed patients with ulcerative colitis and Crohn’s disease?” Inflammatory Bowel Diseases, vol. 14, no. 5, pp. 680–686, 2008.

[5] W. J. Sandborn, B. G. Feagan, S. B. Hanauer et al., “A review of activity indices and efficacy endpoints for clinical trials of medical therapy in adults with Crohn’s disease,” Gastroenterology, vol. 122, no. 2, pp. 512–530, 2002.

[6] B. Boye, K. E. A. Lundin, S. Leganger et al., “The INSPIRE study: do personality traits predict general quality of life (short form–36) in distressed patients with ulcerative colitis and Crohn’s disease?” Scandinavian Journal of Gastroenterology, vol. 43, no. 12, pp. 1505–1513, 2008.

[7] S. Nahon, P. Lahmek, C. Saas et al., “Socioeconomic and psychological factors associated with nonadherence to treatment in inflammatory bowel disease patients: results of the ISSEO survey,” Inflammatory Bowel Diseases, vol. 17, no. 6, pp. 1270–1276, 2011.

[8] A. Sainsbury and R. V. Heatley, “Review article: psychosocial factors in the quality of life of patients with inflammatory bowel disease,” Alimentary Pharmacology and Therapeutics, vol. 21, no. 5, pp. 499–508, 2005.

[9] W. H. Ren, M. Lai, Y. Chen, E. J. Irvine, and Y. X. Zhou, “Validation of the mainland Chinese version of the Inflammatory Bowel Disease Questionnaire (IBDQ) for ulcerative colitis and Crohn’s disease,” Inflammatory Bowel Diseases, vol. 13, no. 7, pp. 903–910, 2007.

[10] H. J. Eysenck and S. G. B. Eysenck, The Manual of the Eysenck Personality Questionnaire, Hodder & Stoughton, London, UK, 1975.

[11] Y. X. Gong, “Eysenck Personality Questionnaire revised in China,” Personality and Individual Differences, vol. 4, pp. 11–18, 1984.

[12] A. S. Zigmond and R. P. Snaith, “The hospital anxiety and depression scale,” Acta Psychiatrica Scandinavica, vol. 67, no. 6, pp. 361–370, 1983.

[13] I. Bjelland, A. A. Dahl, T. T. Haug, and D. Neckelmann, “The validity of the Hospital Anxiety and Depression Scale: an updated literature review,” Journal of Psychosomatic Research, vol. 52, no. 2, pp. 69–77, 2002.

[14] C. M. Leung, S. Ho, C. S. Kan, C. H. Hung, and C. N. Chen, “Evaluation of the Chinese version of the Hospital anxiety and depression scale,” International Journal of Psychosomatics, vol. 40, no. 1–4, pp. 29–34, 1993.

[15] C. L. K. Lam, P.-C. Pan, A. W. T. Chan, S.-Y. Chan, and C. Munro, “Can the Hospital Anxiety and Depression (HAD) Scale be used on Chinese elderly in general practice?” Family Practice, vol. 12, no. 2, pp. 149–154, 1995.

[16] A. H. Buss and M. Perry, “The aggression questionnaire,” Journal of Personality and Social Psychology, vol. 63, no. 3, pp. 452–459, 1992.

[17] J. P. Maxwell, “Development and preliminary validation of a Chinese version of the Buss-Perry Aggression Questionnaire in a population of Hong Kong Chinese,” Journal of Personality Assessment, vol. 88, no. 3, pp. 284–294, 2007.

[18] L. A. Graff, J. R. Walker, L. Lix et al., “The relationship of inflammatory bowel disease type and activity to psychological functioning and quality of life,” Clinical Gastroenterology and Hepatology, vol. 4, pp. 1491–1501, 2006.

[19] G. F. Wang, J. A. Ren, S. Liu et al., “Clinical characteristics of non-perianal fistulating Crohn’s disease in China: a single-center experience of 184 cases,” Chinese Medical Journal, vol. 125, pp. 2405–2410, 2012.

[20] J. Ren, Q. Tao, X. Wang, Z. Wang, and J. Li, “Efficacy of T2 in active Crohn’s disease: a prospective study report,” Digestive Diseases and Sciences, vol. 52, no. 8, pp. 1790–1797, 2007.

[21] J. Ren, X. Wu, N.S. Liao et al., “Prevention of postoperative recurrence of Crohn’s disease: Tripterium wilfordii polyglycoside versus mesalazine,” Journal of International Medical Research, vol. 41, pp. 176–187, 2013.

[22] M. S. Sajadinejad, K. Asgari, H. Molavi et al., “Psychological issues in inflammatory bowel disease: an overview,” Gastroenterology Research and Practice, vol. 2012, Article ID 106502, 11 pages, 2012.

[23] A. Vidal, E. Gomez-Gil, M. Sans et al., “Health-related quality of life in inflammatory bowel disease patients: the role of psychopathology and personality,” Inflammatory Bowel Diseases, vol. 14, no. 7, pp. 977–983, 2008.

[24] J. Haapamaki, Health-related quality of life, symptoms and comorbidity in inflammatory bowel disease [Ph.D. dissertation], The Medical Faculty of the University of Helsinki, 2011.

[25] L. A. Graff, J. R. Walker, L. Lix et al., “The relationship of inflammatory bowel disease type and activity to psychological functioning and quality of life,” Clinical Gastroenterology and Hepatology, vol. 4, pp. 1491–1501, 2006.

[26] I. Schou, Ø. Ekeberg, L. Sandvik, M. J. Hjemstad, and C. M. Ruland, “Multiple predictors of health-related quality of life in early stage breast cancer. Data from a year follow-up study compared with the general population,” Quality of Life Research, vol. 14, no. 8, pp. 1813–1823, 2005.
[29] R. E. O’Carroll, M. Couston, J. Cossar, G. Masterton, and P. C. Hayes, “Psychological outcome and quality of life following liver transplantation: a prospective, national, single-center study,” Liver Transplantation, vol. 9, no. 7, pp. 712–720, 2003.

[30] C. Westlake, K. Dracup, J. Creaser et al., “Correlates of health-related quality of life in patients with heart failure,” Heart and Lung, vol. 31, no. 2, pp. 85–93, 2002.

[31] I. Wilhelmsen and A. Berstad, “Reduced relapse rate in duodenal ulcer disease leads to normalization of psychological distress: twelve-year follow-up,” Scandinavian Journal of Gastroenterology, vol. 39, no. 8, pp. 717–721, 2004.

[32] N. Jacobs, G. Kenis, F. Peeters, C. Derom, R. Vlietinck, and J. Van Os, “Stress-related negative affectivity and genetically altered serotonin transporter function: evidence of synergism in shaping risk of depression,” Archives of General Psychiatry, vol. 63, no. 9, pp. 989–996, 2006.

[33] K. Scheeres, M. Wensing, H. Severens, E. Adang, and G. Bleijenberg, “Determinants of health care use in chronic fatigue syndrome patients: a cross-sectional study,” Journal of Psychosomatic Research, vol. 65, no. 1, pp. 39–46, 2008.

[34] E. Guthrie, J. Jackson, J. Shaffer, D. Thompson, B. Tomenson, and F. Creed, “Psychological disorder and severity of inflammatory bowel disease predict health-related quality of life in ulcerative colitis and Crohn’s disease,” American Journal of Gastroenterology, vol. 97, no. 8, pp. 1994–1999, 2002.

[35] C. Mittermaier, C. Dejaco, T. Waldhoer et al., “Impact of depressive mood on relapse in patients with inflammatory bowel disease: a prospective 18-month follow-up study,” Psychosomatic Medicine, vol. 66, no. 1, pp. 79–84, 2004.

[36] E. S. Kim, K. B. Cho, K. S. Park et al., “Predictive factors of impaired quality of life in Korean patients with inactive inflammatory bowel disease: association with functional gastrointestinal disorders and mood disorders,” Journal of Clinical Gastroenterology, vol. 47, pp. e38–e44, 2013.

[37] L. A. Graff, J. R. Walker, and C. N. Bernstein, “Depression and anxiety in inflammatory bowel disease: a review of comorbidity and management,” Inflammatory Bowel Diseases, vol. 15, no. 7, pp. 1105–1118, 2009.

[38] B. Boye, K. E. A. Lundin, G. Jantschek et al., “INSPIRE study: does stress management improve the course of inflammatory bowel disease and disease-specific quality of life in distressed patients with ulcerative colitis or Crohn’s disease? A randomized controlled trial,” Inflammatory Bowel Diseases, vol. 17, no. 9, pp. 1863–1873, 2011.

[39] E. McColl, S. W. Han, J. R. Barton, and M. R. Welfare, “A comparison of the discriminatory power of the Inflammatory Bowel Disease Questionnaire and the SF-36 in people with ulcerative colitis,” Quality of Life Research, vol. 13, no. 4, pp. 805–811, 2004.