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Association between disease activity and psychological change among Crohn's disease: a cross-sectional study

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Abstract

Objective: To assess the relative of social support and psychological distress in disease activity among Crohn's disease (CD) patients.

Design: Cross-sectional study.

Setting: A prospective study of adults recruited in China between March 2020 and March 2022.

Participants: A total of 184 patients with CD at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology were enrolled in this study; of these, 162 patients were included in the final analysis.

Results: A total of 162 CD patients (active 93, inactive 69) were enrolled. Compared with the inactive CD group, the active CD group had higher CRP (P=0.001), anemia (P<0.001) and relapse rates in the last year (P<0.001). Independent samples t tests indicated that the active CD group reported lower SSRS scores and higher SCL-90 scores than the inactive CD group. Moreover, men with CD had lower somatization (P=0.030) and anxiety (P=0.050) scores than women. In binary logistic regression models, the subjective support (Beta=0.903, P=0.013), the clinical factors of C-reactive protein (Beta=1.038, P=0.001) and psychological distress factors of anxiety (Beta=1.443, P=0.008) and other (Beta=1.235, P=0.042) were disease activity predictors.

Conclusion: The findings highlight the importance of the psychological distress and social support factors that may play a role in CD patients' health. Further exploration of these factors in longitudinal and intervention studies may help to develop effective CD management models.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

This was a prospective study of patients with CD recruited from a single medical centre in China over a 2-year period.

A cross-sectional study highlighted the importance of psychological change factors that may play a role in CD patients' health.

However, this cross-sectional study could not address the causality between disease activity and psychological change factors of patients with CD.

Keywords: Crohn's disease, social support, psychological distress, anxiety

Introduction

Crohn's disease (CD) is a chronic, nonspecific intestinal inflammatory disease characterized by recurrent abdominal pain and diarrhea that peaks in young adulthood(1). In addition to gastrointestinal manifestations, CD patients experience other systemic manifestations and complications. In recent years, the incidence of CD has increased rapidly in China(2, 3). Due to bowel damage and a long medical history, patients have a high prevalence of psychological impairment, such as anxiety and depression, compared to the general population(4, 5).

Although medical treatments are effective in controlling gastrointestinal inflammation, the relapsing behavior of CD can cause psychological disorders. Moreover, CD patients typically require lifelong medication, which seriously affects their quality of life and increases psychological distress. CD is associated with high medical costs, high rates of psychological disorders, and illness burdens associated with reduced productivity and activity. Studies have shown that approximately 20% of inflammatory bowel disease patients may have symptoms of anxiety, and approximately15% have symptoms of depression(6, 7). Healthcare services for CD are more demanding and costly for patients with symptoms of anxiety and depression. Xu et al. reported that poor sleep quality, anxiety and depression were related to having active IBD(8). In addition, disease activity was found to be associated with depression and anxiety, and psychological distress may increase the likelihood of disease relapse(9). However, most previous studies have focused on anxiety or depression, rarely focusing on other dimensions. Social support might be another dimension that plays a role in disease severity. Interestingly, there are few studies on the association between social support and disease activity in CD patients(10).

The aim of this study was to investigate the relative effects of social support and psychological distress on disease activity in patients with CD. In addition, we considered whether sex moderates the relationship between disease activity and social support and psychological distress in CD. Previous studies of IBD patients have found that older patients have higher symptoms of anxiety and depression. Therefore, in this study, age was used as a control variable. Thus, we proposed the following hypotheses: social support and psychological distress are correlated with disease activity, and there are differences in social support and psychological distress between men and women.

Methods

Ethical aspects

This study was approved by the institutional ethics committee of Tongji Medical College of Huazhong University of Science and Technology, and consent was acquired from all participants. All participants were informed of the purpose and methods of this study and provided written informed consent.

Participants

This study was a cross-sectional, single-center study. Participants were recruited between March 2020 and March 2022 at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology in China. The inclusion criteria were patients with a diagnosis of CD(11), adult patients (aged 18 years or more), patients with sufficient ability in spoken and written Chinese to complete all the questionnaires, patients without a diagnosis of concomitant mental disorders or dementia and patients not taking medication for CD. The exclusion criteria were as follows: (1) patients who could not complete the questionnaires; (2) patients who had tumors or other medical comorbidities; and (3) patients who were pregnant. The flow diagram of the enrolled patients and healthy controls is shown in Figure 1.

Data collection

Clinical and demographic data were collected, including age, sex, body mass index, employment status, living status, educational status, marital status and disease duration. The severity of CD was assessed using Crohn's disease activity index (CDAI) scores(12). A CDAI score of less than 150 was defined as disease inactivity. A CDAI score of 150 or more was defined as disease activity.

Social support was assessed using the Social Support Rating Scale (SSRS)(13, 14). The participants' social support was evaluated by the Chinese version of the SSRS, which was previously demonstrated to have reliability and validity. It can measure the characteristics of social support and its relationship with participants' mental health levels, mental illness and various physical diseases. The scale has 10 items, including items regarding objective support (3 items), subjective support (4 items) and the utilization of social support (3 items). The total score ranges from 11-59 and is acquired by adding the scores of each item. Lower scores on indices of the SSRS indicate less social support.

Psychological state was assessed using the Symptom Checklist-90 (SCL-90)(15, 16). The scale has a total of 90 items regarding a wide range of psychiatric symptoms, including feelings, emotions, thinking, consciousness, behaviors, habits, interpersonal relationships, diet and sleep. Ten factors are used to reflect 10 aspects of psychological symptoms, including psychoticism, paranoid ideation, phobic anxiety, hostility, anxiety, depression, interpersonal sensitivity, obsessive compulsive behaviors, and somatization. The statistical standard of the SCL-90 mainly consists of two items: the total score and the various factor scores. The total score is the sum of the scores of the 90 items, which reflects the severity of the disease. The factor score is the average score of all factors, which ranges from "0" ("no problem") to "4" ("very serious"). Each factor reflects a certain aspect of the participant's symptoms, so the symptom distribution characteristics of the participants can be understood through the factor score. According to the results of the Chinese norm, if the total score exceeds 160 points, the positive items exceed 43 points, or any factor scores exceeds 2 points, the participants is considered to have a positive screening, and further examination is needed. This version has excellent internal consistency for all items.

Statistical analysis

All statistical analyses were performed in SPSS 26.0, GraphPad Prism 8.0 and Origin 2021 software. The independent sample T test was used to determine the relationship between disease status and sex differences and scale factors. Correlation analysis was applied to evaluate the relationship among the clinical, psychological, and social support factors. Hierarchical multiple regression analysis (MRA) was used to examine the unique contribution of participant characteristics, psychological distress scores and SSRS factor scores on the composite factors of disease status. $P < 0.05$ was considered statistically significant.

Results

Sample characteristics

A total of 162 CD patients with complete survey responses were analyzed (active n=93, inactive n=69). Participants in the disease active group reported a disease course of 13 months, and those in the inactive group reported a disease course of 11 months. The Independent Sample T test and Chi Square Tests indicated no statistically significant difference in age, employment status, living status, marital status or years of education between the two groups. Compared with the inactive CD group, the active CD group had higher CRP (P=0.001) and ESR values(P<0.001). In addition, these patients tended to have higher anemia rate and relapse rates in the last year (P<0.001), which is shown in Table 1. Independent samples t tests indicated differences between the two groups,

with the active CD group reporting lower SSRS scores and higher SCL-90 scores than the inactive CD group, which is shown in Table 2. Moreover, women showed higher levels of somatization (P=0.030) and anxiety (P=0.050) than men, as shown in Table 2.

Preliminary analyses

Figure 2 shows the correlation between social support and the psychological distress scale. The results showed that objective support was negatively correlated with psychological distress (obsessive-compulsive, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid, psychoticism and other factors) (P<0.05). Subjective support was negatively correlated with psychological distress (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid, psychoticism and other) (P<0.05). Availability was negatively correlated with psychological distress (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, paranoid, psychoticism and other factors) (P<0.05).

Binary logistic regression models

Univariate analysis suggested that C-reactive protein levels(P=0.001), somatization (P=0.007), obsessive compulsiveness (P<0.001), interpersonal sensitivity (P<0.001), depression (P<0.001), anxiety (P=0.039), hostility (P=0.015), phobic anxiety (P=0.002), paranoid (P=0.001), psychoticism (P<0.001), other factors (P<0.001) and subjective support (P=0.003) were statistically significant and were included in the subsequent binary logistic regression analysis. Binary logistic regression analyses showed that the social support factors of subjective support (Beta=0.903, P=0.013), the clinical factors of C-reactive protein levels (Beta=1.038, P=0.001), the and psychological distress factors of anxiety (Beta=1.443, P=0.008) and other factors (Beta=1.235, P=0.042) were predictors of disease activity, as shown in Table 3.

Discussion

In this study, we described clinical, social support and psychological distress differences, and we also assessed the relationships between disease activity and dimensions of psychological distress and social support symptoms in a cohort of CD patients. As we previously hypothesized, our present results showed that active CD patients had higher SCL-90 and lower SSRS scores than inactive CD patients, and social support factors were related to psychological distress factors, both of which had an impact on disease activity. We also found that women showed higher levels of somatization and anxiety than men, but this was not observed for social support. Finally, we found that C-reactive protein, subjective support, anxiety and other factors were relevant determinants of disease activity in CD patients.

Psychological factors such as anxiety and depression have been studied in relation to CD (17), but the roles of other factors such as social support has been poorly investigated. The high correlations of social support factors with psychological distress symptoms in CD patients are consistent with a previous study about other illnesses (18) and indicate that the three factors of social support are likely a concept that reflects another dimension of psychological states. Social support is defined as behavioral or emotional support provided by family members, other people or other groups. Social support can be divided into three categories: objective support, subjective support and availability(19). However, in populations of patients with chronic disease, there are individual differences in the use of social support. Some people can receive support at any time but refuse the help of others. In addition, interpersonal support is a process of individual interaction. Past research has shown that social support has different effects on different diseases.

Consistent with previous research, the depressive, anxiety and somatization factors of patients with CD are different for different disease severities(20, 21). The three factors of social support are negatively correlated with psychological distress (somatization, anxiety, anxiety and other factors). Somatization mainly reflects the subjective body discomfort of patients, including discomfort due to cardiovascular, gastrointestinal, respiratory and other systems, as well as headaches, backaches and muscle soreness. Interestingly, the relationship between disease severity and most psychological distress and social support factors in addition to anxiety and subjective support factors was no longer significant after including social support factors in the model.

In binary logistic regression models, we also found that subjective support factors, anxiety, other psychological distress factors and C-reactive protein remained a significant predictors of disease severity, which may be related to the fluctuating course of progression and remission that characterizes this disease. Namely, patients with CD attach particular importance to their own subjective feelings and may be inclined to interpret any physical or subjective discomfort they experience as a sign of psychological distress, leading them to report lower levels of subjective support. However, these lower levels of subjective support result in worsening disease activity. This biopsychosocial explanation is consistent with what has been found in people with CD(22, 23).

In our study, the the psychological dimension data were obtained from the SCL-90. The results indicate that the psychological state of active CD patients is affected in some dimensions, compared with inactive CD patients. This is consistent with the results of Goodhand, J.R., et al. (24). Neither active nor inactive CD patients met the criteria for anxiety and depression in our study. In recent years, an increasing number of doctors have realized that psychological disorders are common in inflammatory bowel disease patients and may affect the disease condition and quality of life(13, 25). However, the etiology of psychological disorders appears to be multifactorial; for example, environmental factors may include stressful life events, disease activity, disease course, medications, income or marital status(26, 27). Regarding clinical factors, the inflammatory performance of CD may play a role in disease activity and quality of life. Active CD patients had higher anemia rates, CRP values, ESR values and relapse rates. It is possible to improve the psychological state and quality of life of patients with CD through early identification and intervention.

Consistent with previous research, women with CD tend to report greater depressive symptoms than men(21, 28). To our knowledge, this is the first study to compare the relationship between social support and disease activity across men and women with CD. The strengths of this study include the diversity of the sample in terms of social support and psychological distress scores, which allowed us to assess somatization in patients with different levels of disease activity.

Several limitations should be considered in this study. First, this was a single-center study in which all participants were of Han nationality and from Hubei Province, China. Second, the cross-sectional nature of the data precludes us from drawing conclusions about the causality of the relationships among social support, psychological distress and disease activity. In the future, longitudinal research should be conducted to establish a more robust connection between various clinical, psychological and social support factors and disease activity in CD patients.

Conclusions

In conclusion, this study indicates the importance of considering a broader range of psychological distress and social support factors that may play a role in the health of patients with CD. Further exploration of these factors in longitudinal and intervention studies may help to develop effective CD management models.

Contributors M.T.H and L.T substantial contributions to the conception, design, acquisition, analysis, and interpretation of data for the work. The also drafting the work or revising it critically for important intellectual content. L.X.W, Y.Z, X.L, X.F.Y and C.H substantial contributions to the acquire and interpretation of data for the work. P.L, Q.L and P.H substantial contributions to the revising it critically for important intellectual content. L.Y and L.R.Z substantial contributions to the conception, design and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Competing interests None declared.

Patient consent for publication All participants were informed of the purpose and methods of this study and provided written informed consent.

Ethics approval This study was approved by the institutional ethics committee of Tongji Medical College of Huazhong University of Science and Technology.

Conflict of Interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and Biometry:

No complex statistical methods were necessary for this paper.

Figure 1: Flow diagram of the enrolled patients.

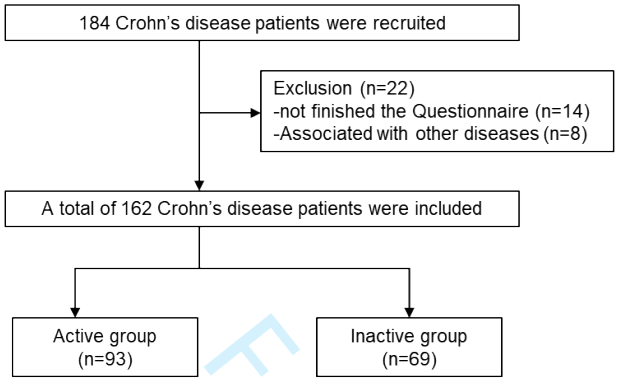
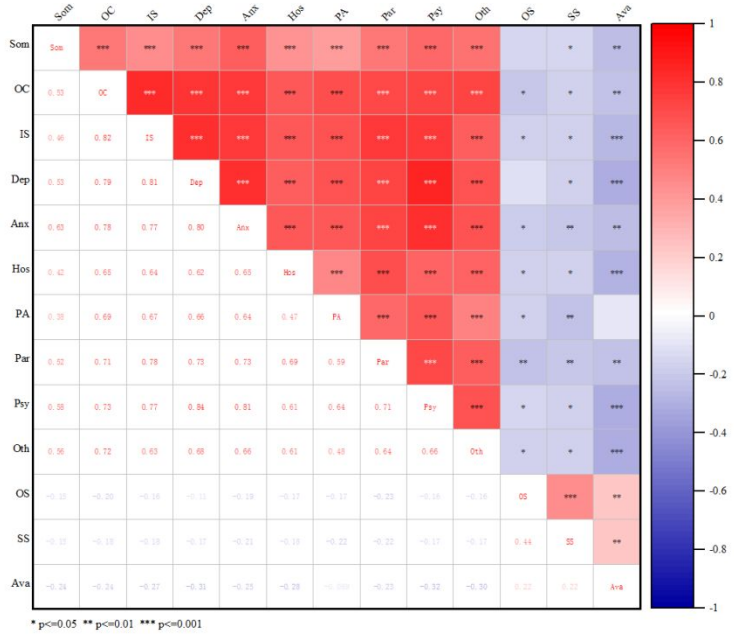


Figure 2. Analysis of the correlation of clinical data with social support and psychological factors



Note: Som=somatization, OC=obsessive-compulsive, IS=interpersonal sensitivity, Dep=depression, Anx=anxiety, Hos=hostility, PA=phobic anxiety, Par=paranoid, Psy=psychoticism, Oth=other, OS=objective support, SS=subjective support, Ava=availability.

Table 1. Baseline characteristics of the study population

Characteristics	Active CD (n=93)	Inactive CD (n=69)	P value
Age	31±12	35±15	0.096
Sex(female)	36(38.7%)	31(44.9%)	0.427
Body Mass Index	19.5±3.9	20.8±4.3	0.049
Employment status	-	-	
no	27 (29.0%)	21 (30.5%)	0.961
retired	6 (6.5%)	3 (4.3%)	
yes	60 (64.5%)	45 (65.2%)	
Living status	-	-	
alone	3 (3.2%)	6 (8.7%)	0.248
with others	90 (96.8%)	63 (91.3%)	
Education	-	-	
up to 6 years	5 (5.4%)	4 (5.8%)	
up to 9 years	28 (30.1%)	18 (26.1%)	0.705
up to 12 years	44 (47.3%)	34 (49.3%)	
college	16 (17.2%)	13 (18.8%)	
Marital status	-	-	
married/cohabitating	53 (57.0%)	34 (49.3%)	0.579
widowed/divorced	7 (7.5%)	5 (7.2%)	
single	33 (35.5%)	30 (43.5%)	
Montreal location	-	-	
Ileal (L1)	35 (37.6%)	28 (40.7%)	
Colonic (L2)	15 (16.2%)	5 (7.2%)	0.808
Ileocolon (L3)	39 (41.9%)	33 (47.8%)	
upper gastrointestinal tract (L4)	1 (1.1%)	0 (0%)	
L4+L1/L2/L3	3 (3.2%)	3 (4.3%)	
Montreal behavior	-	-	
inflammatory	52 (55.9%)	45 (65.2%)	0.401
structuring	24 (25.8%)	16 (23.2%)	
penetrating	17 (18.3%)	8 (11.6%)	
Perianal disease	35 (37.6%)	28 (40.6%)	0.704
Current therapy	-	-	
no treatment	0 (0%)	2 (2.9%)	
corticosteroids	8 (8.6%)	7 (10.1%)	
5-aminosalicylates	21 (22.6%)	17 (24.6%)	0.169
immunomodulators	27 (29.0%)	22 (31.9%)	
antitumor necrosis factor	16 (17.2%)	9 (13.0%)	
combined therapy	21 (22.6%)	12 (17.5%)	
Anemia	-	-	
no	36 (38.7%)	55 (79.7%)	
mild	49 (52.7%)	10 (14.5%)	<0.001
moderate	6 (6.5%)	3 (4.3%)	
severe	2 (2.1%)	1 (1.5%)	
Relapses in the last year	-	-	
0	13 (14.0%)	35 (50.7%)	
1-2	57 (61.3%)	24 (34.8%)	<0.001
3	8 (8.6%)	8 (11.6%)	
≥4	15 (16.1%)	2 (2.9%)	
Disease duration (months)	13±25	11±19	0.594
C-reactive protein	24.3±34.4	8.8±18.8	0.001

Note: Data are presented as the number (%) or mean±standard deviation.

Table 2. Questionnaire survey in for Crohn's disease patients

Variable	Active CD	Inactive CD	P value	Men	Women	P value
SCL-90						
Somatization	18.8±5.9	16.3±4.7	0.004	17.2±5.0	19.5±6.4	0.030
Obsessive-compulsive	19.0±5.4	15.4±4.4	<0.0001	17.2±5.0	18.1±5.9	0.345
Interpersonal sensitivity	15.4±5.8	12.1±4.0	<0.0001	13.9±5.1	14.1±6.2	0.811
Depression	24.7±9.1	18.3±5.2	<0.0001	21.2±7.4	24.0±10.0	0.089
Anxiety	16.2±5.3	12.4±3.2	<0.0001	14.2±4.4	15.8±5.6	0.050
Hostility	10.3±3.8	8.8±3.6	0.012	9.6±3.6	9.5±4.3	0.932
Phobic anxiety	9.7±3.3	8.2±2.0	0.001	8.8±2.6	9.7±3.6	0.124
paranoid	8.9±3.2	7.3±2.3	<0.0001	8.1±2.8	8.5±3.4	0.515
psychoticism	14.9±4.3	12.3±3.6	<0.0001	13.7±4.1	13.9±4.3	0.734
Other	12.6±3.9	9.9±2.5	<0.0001	11.4±3.4	11.7±4.3	0.614
SSRS						
objective support	8.8±2.8	9.3±2.4	0.239	8.9±2.7	9.1±2.6	0.641
Subjective Support	15.1±5.6	18.0±6.2	0.003	16.4±5.7	16.1±6.6	0.757
availability	6.9±1.7	7.4±1.7	0.080	7.0±1.7	7.3±1.7	0.471

Note: Data are presented as the mean±standard deviation.

Table 3. Results of the analysis of binary logistic regression analysis on disease activity

The factors	Hosmer and Lemeshow Test	S.E.	Wald	Beta	95% CI	P value
Univariate		-		-	-	-
age	0.466	0.012	2.727	0.980	0.957-1.004	0.099
Body Mass Index	0.155	0.040	3.760	0.925	0.855-1.001	0.053
Disease duration	0.494	0.007	0.284	1.004	0.990-1.018	0.594
C-reactive protein	0.000	0.011	11.378	1.039	1.016-1.062	0.001
objective support	0.434	0.061	1.389	0.931	0.827-1.049	0.239
Subjective Support	0.339	0.028	8.551	0.921	0.872-0.973	0.003
availability	0.504	0.095	3.017	0.849	0.705-1.021	0.082
Somatization	0.090	0.034	7.296	1.096	1.025-1.171	0.007
Obsessive compulsive	0.163	0.037	16.349	1.161	1.080-1.248	<0.001
Interpersonal sensitivity	0.130	0.038	13.650	1.153	1.069-1.243	<0.001
Depression	0.785	0.032	19.579	1.154	1.083-1.230	<0.001
Anxiety	0.039	0.058	20.748	1.301	1.162-1.456	0.039
Hostility	0.056	0.049	5.876	1.126	1.023-1.240	0.015
Phobic anxiety	0.601	0.079	9.578	1.275	1.093-1.488	0.002
Paranoid	0.212	0.081	10.490	1.300	1.109-1.523	0.001
Psychoticism	0.029	0.055	13.645	1.224	1.099-1.362	<0.001
Other	0.382	0.061	18.473	1.301	1.154-1.467	<0.001
Multivariate		-	-	-	-	-
Subjective Support	0.519	0.041	6.216	0.903	0.834-0.979	0.013
C-reactive protein		0.012	10.486	1.038	1.105-1.062	0.001
Anxiety		0.138	7.009	1.443	1.100-1.893	0.008
Other		0.103	4.155	1.235	1.008-1.512	0.042

Note: SE: standardized error, Durbin-Watson:1.980.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
	Yes	(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2 Yes	Explain the scientific background and rationale for the investigation being reported
Objectives	3 Yes	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4 Yes	Present key elements of study design early in the paper
Setting	5 Yes	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6 Yes	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7 Yes	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8* Yes	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9 Yes	Describe any efforts to address potential sources of bias
Study size	10 Yes	Explain how the study size was arrived at
Quantitative variables	11 Yes	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12 Yes	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13* Yes	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14* Yes	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15* Yes	Report numbers of outcome events or summary measures
Main results	16 Yes	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17 Yes	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18 Yes	Summarise key results with reference to study objectives
Limitations	19 Yes	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20 Yes	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21 Yes	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22 Yes	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Association between disease activity and psychological change among Crohn's disease: a cross-sectional study

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Secondary Subject Heading:	Mental health

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Association between disease activity and psychological change among Crohn's disease: a cross-sectional study

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Abstract

Objective: To assess the relative of social support and psychological distress in disease activity among Crohn's disease (CD) patients.

Design: Cross-sectional study.

Setting: The study was conducted in Wuhan, China between March 2020 and March 2022.

Participants: A total of 184 patients with CD at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology were enrolled in this study; of these, 162 patients were included in the final analysis.

Results: A total of 162 CD patients (active 93, inactive 69) were enrolled. Compared with the inactive CD group, the active CD group had higher CRP (P=0.001), anemia (P<0.001), and relapse rates in the last year (P<0.001). Independent samples t-tests indicated that the active CD group reported lower SSRS scores and higher SCL-90 scores than the inactive CD group. Moreover, men with CD had lower somatization (P=0.030) and anxiety (P=0.050) scores than women. In binary logistic regression models, the subjective support (Beta=0.903, P=0.013), the clinical factors of C-reactive protein (Beta=1.038, P=0.001), and psychological distress factors of anxiety (Beta=1.443, P=0.008) and other (Beta=1.235, P=0.042) were disease activity predictors.

Conclusion: The findings highlight the importance of the psychological distress and social support factors that may play a role in CD patients' health. Interventions to address these issues should be part of management in CD.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

Our study improved the understanding of the differences in psychological distress and social support among CD patients at different active stages in developing countries, especially in central China to provide evidence for subsequent research attempts to establish an association between social support and psychological well-being and disease activity.

In this study, gender differences were considered in the analysis.

However, this cross-sectional study could not address the causality between disease activity and psychological change factors of patients with CD.

Keywords: Crohn's disease, social support, psychological distress, anxiety

Introduction

Crohn's disease (CD) is a chronic, nonspecific intestinal inflammatory disease characterized by recurrent abdominal pain and diarrhea that peaks in young adulthood(1). In addition to gastrointestinal manifestations, CD patients experience other systemic manifestations and complications. As of 2017, inflammatory bowel disease (IBD) affected 6.8 million people worldwide. The United States reported the highest incidence of IBD, followed by the United Kingdom(2). Epidemiological studies have shown that the incidence of IBD in China is 3.44 cases per one million people, which is the highest in Asia, and the incidence of IBD in mainland China is higher in the south and lower in the north(3). In recent years, the incidence of CD has increased rapidly in China(4, 5).

Due to bowel damage and a long medical history, patients have a high prevalence of psychological impairment, such as anxiety and depression, compared to the general population(6, 7). Although medical treatments are effective in controlling gastrointestinal inflammation, the relapsing behavior of CD can cause psychological disorders. Moreover, CD patients typically require lifelong medication, which seriously affects their quality of life and increases psychological distress. The CD is associated with high medical costs, high rates of psychological disorders, and illness burdens associated with reduced productivity and activity. Studies have shown that approximately 20% of inflammatory bowel disease patients may have symptoms of anxiety, and approximately 15% have symptoms of depression(8, 9). Large population studies showed that the prevalence of psychological distress and injury in IBD patients was significantly higher than that in non-IBD adults(10, 11). And regarding the relationship between the psychological state of IBD patients and gender differences, studies have pointed out that female IBD patients are more prone to anxiety, depression, and other psychological problems than male patients(9). For example, the prevalence of comorbidity anxiety and depression in female IBD patients was 33.8% and 21.2%, respectively, compared with 22.8% and 16.2% in male IBD patients(12).

The uncertainty of treatment results and psychological disorders may lead to disease recurrence, aggravate the course of the disease, and directly lead to the decline of patients' quality of life and the increase of treatment costs(13, 14). Patients with IBD and anxiety or depression have a higher risk of hospitalization, emergency room visits, readmissions, and use of outpatient services than patients without these symptoms(15). Thus, healthcare services for CD are more demanding and costly for patients with symptoms of anxiety and depression. Xu et al. reported that poor sleep quality, anxiety, and depression were related to having active IBD(16). In addition, disease activity was found to be associated with depression and anxiety, and psychological distress may increase the likelihood of disease relapse(17). However, most previous studies have focused on anxiety or depression, rarely focusing on other dimensions. Social support might be another dimension that plays a role in disease severity. Interestingly, there are few studies on the association between social support and disease activity in CD patients(18, 19).

This study aimed to improve the understanding of the differences in psychological distress and social support among CD patients at different active stages in China to provide evidence for subsequent research attempts to establish an association between social support and psychological well-being and disease activity. In addition, we considered whether sex moderates the relationship between disease activity and social support and psychological distress in CD. Previous studies of IBD patients have found that older patients have higher symptoms of anxiety and depression. Therefore, in this study, age was used as a control variable. Thus, we proposed the following hypotheses: there were significant differences in psychological disorders and social support between active and inactive CD patients, and there may be gender differences as well.

Methods

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Ethical aspects

This study was approved by the institutional ethics committee of Tongji Medical College of Huazhong University of Science and Technology, and consent was acquired from all participants. All participants were informed of the purpose and methods of this study and provided written informed consent.

Participants

This study was a cross-sectional, single-center study. Participants were recruited between March 2020 and March 2022 at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology in China. The inclusion criteria were patients with a diagnosis of CD(20), adult patients (aged 18 years or more), patients with sufficient ability in spoken and written Chinese to complete all the questionnaires, patients without a diagnosis of concomitant mental disorders or dementia and patients not taking psychotropic medication for CD. The exclusion criteria were as follows: (1) patients who could not complete the questionnaires; (2) patients who had tumors or other medical comorbidities; and (3) patients who were pregnant. The flow diagram of the enrolled patients and healthy controls is shown in Figure 1.

Data collection

Clinical and demographic data were collected, including age, sex, body mass index, employment status, living status, educational status, marital status, and disease duration. The severity of CD was assessed using Crohn's disease activity index (CDAI) scores(21). A CDAI score of less than 150 was defined as disease inactivity. A CDAI score of 150 or more was defined as disease activity.

Social support was assessed using the Social Support Rating Scale (SSRS)(22, 23). The participants' social support was evaluated by the Chinese version of the SSRS, which was previously demonstrated to have reliability and validity. It can measure the characteristics of social support and its relationship with participants' mental health levels, mental illness, and various physical diseases. The scale has 10 items, including items regarding objective support (3 items), subjective support (4 items), and the utilization of social support (3 items). The total score ranges from 11-59 and is acquired by adding the scores of each item. Lower scores on indices of the SSRS indicate less social support.

The psychological state was assessed using the Symptom Checklist-90 (SCL-90)(24, 25). The scale has a total of 90 items regarding a wide range of psychiatric symptoms, including feelings, emotions, thinking, consciousness, behaviors, habits, interpersonal relationships, diet, and sleep. Ten factors are used to reflect 10 aspects of psychological symptoms, including psychoticism, paranoid ideation, phobic anxiety, hostility, anxiety, depression, interpersonal sensitivity, obsessive-compulsive behaviors, and somatization. The statistical standard of the SCL-90 mainly consists of two items: the total score and the various factor scores. The total score is the sum of the scores of the 90 items, which reflects the severity of the disease. The factor score is the average score of all factors, which ranges from "0" ("no problem") to "4" ("very serious"). Each factor reflects a certain aspect of the participant's symptoms, so the symptom distribution characteristics of the participants can be understood through the factor score. According to the results of the Chinese norm, if the total score exceeds 160 points, the positive items exceed 43 points, or any factor score exceeds 2 points, the participants are considered to have a positive screening, and further examination is needed. This version has excellent internal consistency for all items.

Statistical analysis

All statistical analyses were performed in SPSS 26.0, GraphPad Prism 8.0, and Origin 2021 software. The independent sample T-test was used to determine the relationship between disease status and sex differences and scale factors. Correlation analysis was applied to evaluate the relationship among the clinical, psychological, and social support factors. Hierarchical multiple regression analysis (MRA) was used to examine the unique contribution of participant characteristics, psychological distress scores, and SSRS factor scores on the composite factors of disease status. $P < 0.05$ was considered statistically significant.

Results

Sample characteristics

A total of 162 CD patients with complete survey responses were analyzed (active n=93, inactive n=69). Participants in the disease-active group reported a disease course of 13 months, and those in the inactive group reported a disease course of 11 months. The Independent Sample T-test and Chi-Square Tests indicated no statistically significant difference in age, employment status, living status, marital status, or years of education between the two groups. Compared with the inactive CD group, the active CD group had higher CRP (P=0.001) and ESR values(P<0.001). In addition, these patients tended to have higher anemia rates and relapse rates in the last year (P<0.001), which is shown in Table 1. Independent samples t-tests indicated differences between the two groups, with the active CD group reporting lower SSRS scores and higher SCL-90 scores than the inactive CD group, which is shown in Table 2. Moreover, women showed higher levels of anemia rate (P=0.021), relapse rates in the last year (P=0.020) and somatization (P=0.030) and anxiety (P=0.050) than men, as shown in Table 3 and Supplementary materials Table 1.

Preliminary analyses

Figure 2 shows the correlation between social support and the psychological distress scale. The results showed that objective support was negatively correlated with psychological distress (obsessive-compulsive, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid, psychoticism, and other factors) (P<0.05). Subjective support was negatively correlated with psychological distress (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid, psychoticism, and other) (P<0.05). Availability was negatively correlated with psychological distress (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, paranoid, psychoticism, and other factors) (P<0.05).

Binary logistic regression models

Univariate analysis suggested that C-reactive protein levels(P=0.001), somatization (P=0.007), obsessive compulsiveness (P<0.001), interpersonal sensitivity (P<0.001), depression (P<0.001), anxiety (P=0.039), hostility (P=0.015), phobic anxiety (P=0.002), paranoid (P=0.001), psychoticism (P<0.001), other factors (P<0.001) and subjective support (P=0.003) were statistically significant and were included in the subsequent binary logistic regression analysis. Binary logistic regression analyses showed that the social support factors of subjective support (Beta=0.903, P=0.013), the clinical factors of C-reactive protein levels (Beta=1.038, P=0.001), the psychological distress factors of anxiety (Beta=1.443, P=0.008) and other factors (Beta=1.235, P=0.042) were predictors of disease activity, as shown in Table 4.

Discussion

In this study, we described clinical, social support, and psychological distress differences, and we also assessed the relationships between disease activity and dimensions of psychological distress and social support symptoms in a cohort of CD patients. As we previously hypothesized, our present results showed that active CD patients had higher SCL-90 and lower SSRS scores than inactive CD patients, and social support factors were related to psychological distress factors, both of which had an impact on disease activity. We also found that women showed higher levels of somatization and anxiety than men, but this was not observed for social support. Finally, we found that C-reactive protein, subjective support, anxiety, and other factors were relevant determinants of disease activity in CD patients.

Psychological factors such as anxiety and depression have been studied about CD (26), but the roles of other factors such as social support have been poorly investigated. The high correlations of social support factors with psychological distress symptoms in CD patients are consistent with a previous study about other illnesses (27) and indicate that the three factors of social support are likely a concept that reflects another dimension of psychological states. Social support is defined as behavioral or emotional support provided by family members, other people, or other groups.

Social support is a positive health resource that contributes to the well-being of people with chronic diseases. The ability of an actor to derive benefits from his or her membership in a social network or other social structure. This positive support helps individuals overcome difficulties and challenges in life, especially stress related to coping with chronic illness. This is consistent with a biobehavioral model in which patients' responses to illness and health are influenced by family and peer relationships. Social support can be divided into three categories: objective support, subjective support, and availability(3). However, in populations of patients with chronic disease, there are individual differences in the use of social support. Some people can receive support at any time but refuse the help of others. In addition, interpersonal support is a process of individual interaction. Past research has shown that social support has different effects on different diseases(28).

IBD is considered a bio-psychosocial disease characterized by psychological distress and psychological or psychiatric disorders such as depression or anxiety(29). Therefore, numerous previous studies have focused on anxiety or depression and quality of life. Recent studies have also looked at attachment and mentalizing dimensions. Based on evolutionary theory and behavioral science, attachment theory and research suggest that human infants are born with an evolutionarily pre-programmed psychobiological need to form social bonds with emotionally important caregivers to maximize protection and survival(30). As a result, they exhibit attachment behaviors characterized by seeking contact and comfort from one or more important caregivers when feelings of vulnerability arise. Thus, individuals with secure attachment styles may form positive relationships, experience confidence and a sense of self-worth, and have a realistic perception of others. Conversely, people with the anxious attachment type may have a sense of insecurity in their relationships, which they view as fragile and void.

Consistent with previous research, the depressive, anxiety, and somatization factors of patients with CD are different for different disease severities(31, 32). The three factors of social support are negatively correlated with psychological distress (somatization, anxiety, anxiety, and other factors). Somatization mainly reflects the subjective body discomfort of patients, including discomfort due to cardiovascular, gastrointestinal, respiratory, and other systems, as well as headaches, backaches, and muscle soreness. Interestingly, the relationship between disease severity and most psychological distress and social support factors in addition to anxiety and subjective support factors was no longer significant after including social support factors in the model.

In binary logistic regression models, we also found that subjective support factors, anxiety, other psychological distress factors, and C-reactive protein remained significant predictors of disease severity, which may be related to the fluctuating course of progression and remission that characterizes this disease. Namely, patients with CD attach

particular importance to their subjective feelings and may be inclined to interpret any physical or subjective discomfort they experience as a sign of psychological distress, leading them to report lower levels of subjective support. However, these lower levels of subjective support result in worsening disease activity. This biopsychosocial explanation is consistent with what has been found in people with CD(33, 34).

In our study, the psychological dimension data were obtained from the SCL-90. The results indicate that the psychological state of active CD patients is affected in some dimensions, compared with inactive CD patients. This is consistent with the results of Goodhand, J.R., et al. (35). Neither active nor inactive CD patients met the criteria for anxiety and depression in our study. In recent years, an increasing number of doctors have realized that psychological disorders are common in inflammatory bowel disease patients and may affect the disease condition and quality of life(22, 36). However, the etiology of psychological disorders appears to be multifactorial; for example, environmental factors may include stressful life events, disease activity, disease course, medications, income, or marital status(37, 38). Regarding clinical factors, the inflammatory performance of CD may play a role in disease activity and quality of life. Active CD patients had higher anemia rates, CRP values, ESR values, and relapse rates. It is possible to improve the psychological state and quality of life of patients with CD through early identification and intervention.

In recent years, some scholars have also studied the gender difference of IBD. At present, many studies have found that the differences in the psychological performance of IBD patients are related to gender, and females are predictors of IBD combined anxiety and depression(39, 40). However, the study of Nahon et al. pointed out that the incidence of anxiety and depression in female patients with IBD was not significantly increased, and gender was not correlated with the occurrence of anxiety and depression(41). In this study, we also found that women with CD tend to report greater depressive symptoms than men, which was consistent with previous research (32, 42). At the same time, epidemiological studies have confirmed that there are significant gender differences in the incidence of inflammatory bowel disease (IBD), and this difference shows significant regional differences. In the United States(43), Canada(44, 45), Israel(46), Spain(47), and Denmark(48), the incidence of women is higher than that of men. In Asian countries such as South Korea(49), India(50), and China(51), the incidence is higher in men than in women. The results indicate that female CD patients are more prone to anxiety and depression, which was mainly reflected in three aspects. First, women have a higher rate of anemia symptoms and disease recurrence than men, which may be more prone to psychological problems due to illness and reduced quality of life. Secondly, women are less likely than men to use immunosuppressives and biological agents. Although there were no statistically significant differences in these clinical characteristics between genders of patients with CD, which may be due to the insufficient sample size included in this study. Third, women's psychological activities are more delicate, more concerned about their symptoms, and pregnant with the next generation of problems. Therefore, in daily clinical diagnosis and treatment, more attention should be paid to whether women have mental and psychological abnormalities and their severity, and effective health education and psychological support should be provided according to the specific circumstances.

To our knowledge, this is the first study to compare the relationship between social support and disease activity across men and women with CD. The strengths of this study include the diversity of the sample in terms of social support and psychological distress scores, which allowed us to assess somatization in patients with different levels of disease activity.

Several limitations should be considered in this study. First, this was a single-center study in which all participants were of Han nationality and from Hubei Province, China. Second, the cross-sectional nature of the data precludes us from concluding the causality of the relationships among social support, psychological distress, and

disease activity. In the future, longitudinal research should be conducted to establish a more robust connection between various clinical, psychological, and social support factors and disease activity in CD patients.

Conclusions

In conclusion, this study indicates the importance of considering a broader range of psychological distress and social support factors that may play a role in the health of patients with CD. Further exploration of these factors in longitudinal and intervention studies may help to develop effective CD management models.

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Competing interests None declared.

Patient consent for publication All participants were informed of the purpose and methods of this study and provided written informed consent.

Ethics approval This study was approved by the institutional ethics committee of Tongji Medical College of Huazhong University of Science and Technology.

Conflict of Interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and Biometry:

No complex statistical methods were necessary for this paper.

Provide Data sharing No additional data available

Figure 1: Flow diagram of the enrolled patients.

Figure 2. Analysis of the correlation of clinical data with social support and psychological factors.

Note: Som=somatization, OC=obsessive-compulsive, IS=interpersonal sensitivity, Dep=depression, Anx=anxiety, Hos=hostility, PA=phobic anxiety, Par=paranoid, Psy=psychoticism, Oth=other, OS=objective support, SS=subjective support, Ava=availability. * P<=0.05; ** P<=0.01; *** P<=0.001.

Table 1. Baseline characteristics of the study population

Characteristics	Active CD (n=93)	Inactive CD (n=69)	P value
Age	31±12	35±15	0.096
Sex(female)	36(38.7%)	31(44.9%)	0.427
Body Mass Index	19.5±3.9	20.8±4.3	0.049
Employment status	-	-	
no	27 (29.0%)	21 (30.5%)	0.961
retired	6 (6.5%)	3 (4.3%)	
yes	60 (64.5%)	45 (65.2%)	
Living status	-	-	
alone	3 (3.2%)	6 (8.7%)	0.248
with others	90 (96.8%)	63 (91.3%)	
Education	-	-	
up to 6 years	5 (5.4%)	4 (5.8%)	
up to 9 years	28 (30.1%)	18 (26.1%)	0.705
up to 12 years	44 (47.3%)	34 (49.3%)	
college	16 (17.2%)	13 (18.8%)	
Marital status	-	-	
married/cohabitating	53 (57.0%)	34 (49.3%)	0.579
widowed/divorced	7 (7.5%)	5 (7.2%)	
single	33 (35.5%)	30 (43.5%)	
Montreal location	-	-	
Ileal (L1)	35 (37.6%)	28 (40.7%)	
Colonic (L2)	15 (16.2%)	5 (7.2%)	0.808
Ileocolon (L3)	39 (41.9%)	33 (47.8%)	
upper gastrointestinal tract (L4)	1 (1.1%)	0 (0%)	
L4+L1/L2/L3	3 (3.2%)	3 (4.3%)	
Montreal behavior	-	-	
inflammatory	52 (55.9%)	45 (65.2%)	0.401
structuring	24 (25.8%)	16 (23.2%)	
penetrating	17 (18.3%)	8 (11.6%)	
Perianal disease	35 (37.6%)	28 (40.6%)	0.704
Current therapy	-	-	
no treatment	0 (0%)	2 (2.9%)	
corticosteroids	8 (8.6%)	7 (10.1%)	
5-aminosalicylates	21 (22.6%)	17 (24.6%)	0.169
immunomodulators	27 (29.0%)	22 (31.9%)	
antitumor necrosis factor	16 (17.2%)	9 (13.0%)	
combined therapy	21 (22.6%)	12 (17.5%)	
Anemia	-	-	
no	36 (38.7%)	55 (79.7%)	
mild	49 (52.7%)	10 (14.5%)	<0.001
moderate	6 (6.5%)	3 (4.3%)	
severe	2 (2.1%)	1 (1.5%)	
Relapses in the last year	-	-	
0	13 (14.0%)	35 (50.7%)	
1-2	57 (61.3%)	24 (34.8%)	<0.001
3	8 (8.6%)	8 (11.6%)	
≥4	15 (16.1%)	2 (2.9%)	
Disease duration (months)	13±25	11±19	0.594
C-reactive protein	24.3±34.4	8.8±18.8	0.001

Note: Data are presented as the number (%) or mean±standard deviation. CD=Crohn's disease

Table 2. Questionnaire survey in for Crohn's disease patients

Variable	Active CD (n=93)	Inactive CD (n=69)	P value
SCL-90			
Somatization	18.8±5.9	16.3±4.7	0.004
Obsessive-compulsive	19.0±5.4	15.4±4.4	<0.0001
Interpersonal sensitivity	15.4±5.8	12.1±4.0	<0.0001
Depression	24.7±9.1	18.3±5.2	<0.0001
Anxiety	16.2±5.3	12.4±3.2	<0.0001
Hostility	10.3±3.8	8.8±3.6	0.012
Phobic anxiety	9.7±3.3	8.2±2.0	0.001
paranoid	8.9±3.2	7.3±2.3	<0.0001
psychoticism	14.9±4.3	12.3±3.6	<0.0001
Other	12.6±3.9	9.9±2.5	<0.0001
SSRS			
objective support	8.8±2.8	9.3±2.4	0.239
Subjective Support	15.1±5.6	18.0±6.2	0.003
availability	6.9±1.7	7.4±1.7	0.080

Note: Data are presented as the mean±standard deviation. CD=Crohn's disease; SCL-90=Check List-90; SSRS= Social Support Rating Scale.

Table 3. Differences in questionnaire survey results between men (n=95) and women (n=67).

Variable	Men	Women	P value
SCL-90			
Somatization	17.2±5.0	19.5±6.4	0.030
Obsessive-compulsive	17.2±5.0	18.1±5.9	0.345
Interpersonal sensitivity	13.9±5.1	14.1±6.2	0.811
Depression	21.2±7.4	24.0±10.0	0.089
Anxiety	14.2±4.4	15.8±5.6	0.050
Hostility	9.6±3.6	9.5±4.3	0.932
Phobic anxiety	8.8±2.6	9.7±3.6	0.124
paranoid	8.1±2.8	8.5±3.4	0.515
psychoticism	13.7±4.1	13.9±4.3	0.734
Other	11.4±3.4	11.7±4.3	0.614
SSRS			
objective support	8.9±2.7	9.1±2.6	0.641
Subjective Support	16.4±5.7	16.1±6.6	0.757
availability	7.0±1.7	7.3±1.7	0.471

Note: Data are presented as the mean±standard deviation. CD=Crohn's disease; SCL-90=Check List-90; SSRS= Social Support Rating Scale.

Table 4. Results of the analysis of binary logistic regression analysis on disease activity

The factors	Hosmer and Lemeshow Test	S.E.	Wald	Beta	95% CI	P value
Univariate		-		-	-	-
age	0.466	0.012	2.727	0.980	0.957-1.004	0.099
Body Mass Index	0.155	0.040	3.760	0.925	0.855-1.001	0.053
Disease duration	0.494	0.007	0.284	1.004	0.990-1.018	0.594
C-reactive protein	0.000	0.011	11.378	1.039	1.016-1.062	0.001
objective support	0.434	0.061	1.389	0.931	0.827-1.049	0.239
Subjective Support	0.339	0.028	8.551	0.921	0.872-0.973	0.003
availability	0.504	0.095	3.017	0.849	0.705-1.021	0.082
Somatization	0.090	0.034	7.296	1.096	1.025-1.171	0.007
Obsessive compulsive	0.163	0.037	16.349	1.161	1.080-1.248	<0.001
Interpersonal sensitivity	0.130	0.038	13.650	1.153	1.069-1.243	<0.001
Depression	0.785	0.032	19.579	1.154	1.083-1.230	<0.001
Anxiety	0.039	0.058	20.748	1.301	1.162-1.456	0.039
Hostility	0.056	0.049	5.876	1.126	1.023-1.240	0.015
Phobic anxiety	0.601	0.079	9.578	1.275	1.093-1.488	0.002
Paranoid	0.212	0.081	10.490	1.300	1.109-1.523	0.001
Psychoticism	0.029	0.055	13.645	1.224	1.099-1.362	<0.001
Other	0.382	0.061	18.473	1.301	1.154-1.467	<0.001
Multivariate		-	-	-	-	-
Subjective Support	0.519	0.041	6.216	0.903	0.834-0.979	0.013
C-reactive protein		0.012	10.486	1.038	1.105-1.062	0.001
Anxiety		0.138	7.009	1.443	1.100-1.893	0.008
Other		0.103	4.155	1.235	1.008-1.512	0.042

Note: SE: standardized error, Durbin-Watson:1.980.

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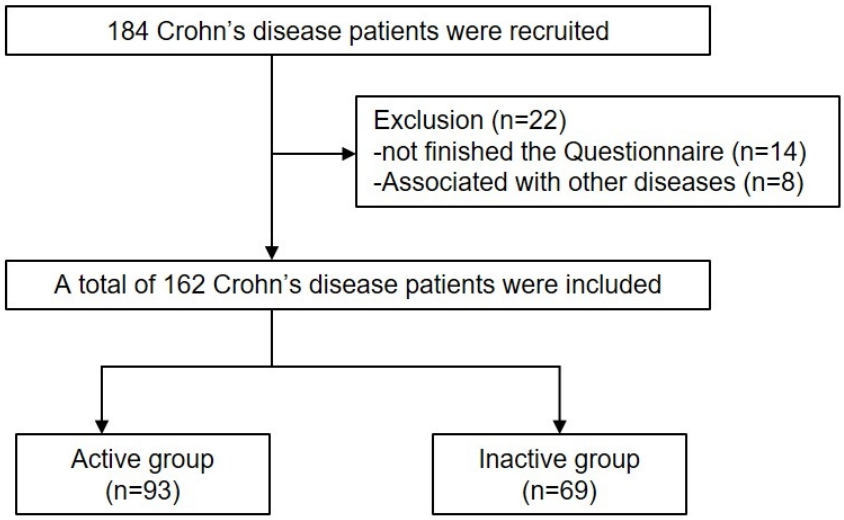

Figure 1: Flow diagram of the enrolled patients.

150x93mm (150 x 150 DPI)

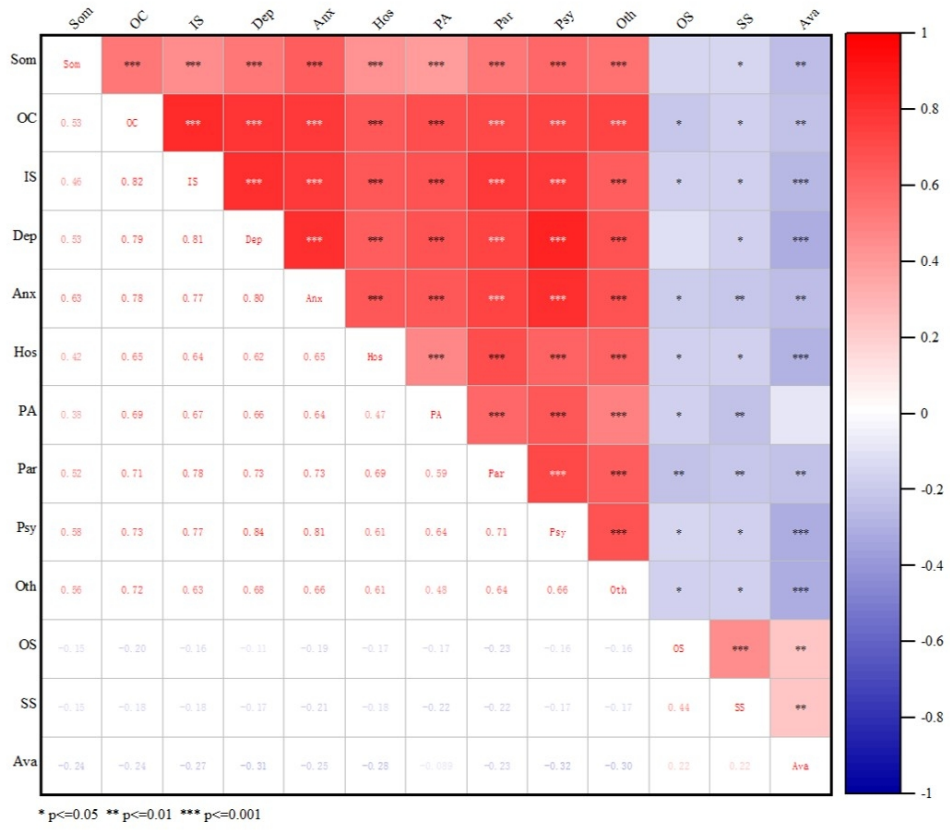

Figure 2. Analysis of the correlation of clinical data with social support and psychological factors.

192x165mm (143 x 143 DPI)

Supplementary materials

Table 1. Baseline characteristics of the study population of different genders

Characteristics	Male (n=95)	Female (n=67)	P value
Age	32±11	34±14	0.311
Disease activity (active)	57 (60.0%)	36 (53.7%)	0.427
Body Mass Index	20.0±4.3	19.7±3.6	0.641
Employment status	-	-	
no	26 (27.4%)	22 (32.8%)	0.448
retired	4 (4.2%)	5 (7.5%)	
yes	65 (68.4%)	40 (59.7%)	
Living status	-	-	
alone	5 (5.3%)	4 (6.0%)	0.847
with others	90 (94.7%)	63 (94.0%)	
Education	-	-	
up to 6 years	4 (4.2%)	5 (7.5%)	
up to 9 years	26 (27.4%)	20 (29.8%)	0.776
up to 12 years	48 (50.5%)	30 (44.8%)	
college	17 (17.9%)	12 (17.9%)	
Marital status	-	-	
married/cohabitating	52 (54.7%)	35 (52.2%)	0.736
widowed/divorced	8 (8.4%)	4 (6.0%)	
single	35 (36.9%)	28 (41.8%)	
Montreal location	-	-	
Ileal (L1)	33 (34.7%)	30 (44.8%)	
Colonic (L2)	12 (12.6%)	8 (11.9%)	0.674
Ileocolon (L3)	45 (47.4%)	27 (40.3%)	
upper gastrointestinal tract (L4)	1 (1.1%)	0 (0%)	
L4+L1/L2/L3	4 (4.2%)	2 (3.0%)	
Perianal disease	36 (37.9%)	27 (40.3%)	0.757
Current therapy	-	-	
no treatment	0 (0%)	2 (3.0%)	
corticosteroids	9 (9.5%)	6 (8.9%)	
5-aminosalicylates	20 (21.1%)	18 (26.9%)	0.497
immunomodulators	29 (30.5%)	20 (29.9%)	
antitumor necrosis factor	17 (17.8%)	8 (11.9%)	
combined therapy	20 (21.1%)	13 (19.4%)	
Anemia	-	-	
no	63 (66.3%)	28 (41.8%)	
mild	27 (28.4%)	32 (47.8%)	0.021
moderate	4 (4.2%)	5 (7.5%)	
severe	1 (1.1%)	2 (2.9%)	
Relapses in the last year	-	-	
0	26 (27.4%)	22 (32.8%)	
1-2	42 (44.2%)	39 (58.2%)	0.020
3	12 (12.6%)	4 (6.0%)	
≥4	15 (15.8%)	2 (3.0%)	
Disease duration (months)	13±25	11±19	0.582
C-reactive protein	13.2±24.7	11.5±18.5	0.634

Note: Data are presented as the number (%) or mean±standard deviation. CD, Crohn's disease.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
	Yes	(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2 Yes	Explain the scientific background and rationale for the investigation being reported
Objectives	3 Yes	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4 Yes	Present key elements of study design early in the paper
Setting	5 Yes	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6 Yes	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7 Yes	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8* Yes	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9 Yes	Describe any efforts to address potential sources of bias
Study size	10 Yes	Explain how the study size was arrived at
Quantitative variables	11 Yes	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12 Yes	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13* Yes	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14* Yes	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15* Yes	Report numbers of outcome events or summary measures
Main results	16 Yes	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17 Yes	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18 Yes	Summarise key results with reference to study objectives
Limitations	19 Yes	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20 Yes	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21 Yes	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22 Yes	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Association between disease activity and psychological change among Crohn's disease: a cross-sectional study

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Primary Subject Heading:	Gastroenterology and hepatology
Secondary Subject Heading:	Mental health

Keywords:	Coeliac disease < GASTROENTEROLOGY, Inflammatory bowel disease < GASTROENTEROLOGY, MENTAL HEALTH

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Association between disease activity and psychological change among Crohn's disease: a cross-sectional study

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Abstract

Objective: To assess the relative of social support and psychological distress in disease activity among Crohn's disease (CD) patients.

Design: Cross-sectional study.

Setting: The study was conducted in Wuhan, China between March 2020 and March 2022.

Participants: A total of 184 patients with CD at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology were enrolled in this study; of these, 162 patients were included in the final analysis.

Results: A total of 162 CD patients were enrolled. Compared with CD patients in remission (CD-R) , the CD patients in activity (CD-A) had higher CRP (P=0.001), anemia (P<0.001), and relapse rates in the last year (P<0.001). Independent samples t-tests indicated that the CD-A group reported lower SSRS scores and higher SCL-90 scores than the CD-R group. Moreover, men with CD had lower somatization (P=0.030) and anxiety (P=0.050) scores than women. In binary logistic regression models, the subjective support (Beta=0.903, P=0.013), the clinical factors of C-reactive protein (Beta=1.038, P=0.001), and psychological distress factors of anxiety (Beta=1.443, P=0.008) and other (Beta=1.235, P=0.042) were disease activity predictors.

Conclusion: The findings highlight the importance of the psychological distress and social support factors that may play a role in CD patients' health. Interventions to address these issues should be part of management in CD.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- ⇒ Our study improved the understanding of the differences in psychological distress and social support among CD patients at different active stages in developing countries, especially in central China.
- ⇒ Provide evidence for subsequent studies attempting to establish a relationship between social support and psychological well-being and disease activity.
- ⇒ In this study, gender differences were considered in the analysis.
- ⇒ However, this cross-sectional study could not address the causality between disease activity and psychological change factors of patients with CD.

Keywords: Crohn's disease, social support, psychological distress, anxiety

Introduction

Crohn's disease (CD) is a chronic, nonspecific intestinal inflammatory disease characterized by recurrent abdominal pain and diarrhea that peaks in young adulthood(1). In addition to gastrointestinal manifestations, CD patients experience other systemic manifestations and complications. As of 2017, inflammatory bowel disease (IBD) affected 6.8 million people worldwide. The United States reported the highest incidence of IBD, followed by the United Kingdom(2). Epidemiological studies have shown that the incidence of IBD in China is 3.44 cases per one million people, which is the highest in Asia, and the incidence of IBD in mainland China is higher in the south and lower in the north(3). In recent years, the incidence of CD has increased rapidly in China(4, 5).

Due to bowel damage and a long medical history, patients have a high prevalence of psychological impairment, such as anxiety and depression, compared to the general population(6, 7). Although medical treatments are effective in controlling gastrointestinal inflammation, the relapsing behavior of CD can cause psychological disorders. Moreover, CD patients typically require lifelong medication, which seriously affects their quality of life and increases psychological distress. The CD is associated with high medical costs, high rates of psychological disorders, and illness burdens associated with reduced productivity and activity. Studies have shown that approximately 20% of inflammatory bowel disease patients may have symptoms of anxiety, and approximately 15% have symptoms of depression(8, 9). Large population studies showed that the prevalence of psychological distress and injury in IBD patients was significantly higher than that in non-IBD adults(10, 11). And regarding the relationship between the psychological state of IBD patients and gender differences, studies have pointed out that female IBD patients are more prone to anxiety, depression, and other psychological problems than male patients(9). For example, the prevalence of comorbidity anxiety and depression in female IBD patients was 33.8% and 21.2%, respectively, compared with 22.8% and 16.2% in male IBD patients(12).

The uncertainty of treatment results and psychological disorders may lead to disease recurrence, aggravate the course of the disease, and directly lead to the decline of patients' quality of life and the increase of treatment costs(13, 14). Patients with IBD and anxiety or depression have a higher risk of hospitalization, emergency room visits, readmissions, and use of outpatient services than patients without these symptoms(15). Thus, healthcare services for CD are more demanding and costly for patients with symptoms of anxiety and depression. Xu et al. reported that poor sleep quality, anxiety, and depression were related to having inflammatory activity(16). In addition, disease activity was found to be associated with depression and anxiety, and psychological distress may increase the likelihood of disease relapse(17). However, most previous studies have focused on anxiety or depression, rarely focusing on other dimensions. Social support might be another dimension that plays a role in disease severity. Interestingly, there are few studies on the association between social support and disease activity in CD patients(18, 19).

This study aimed to improve the understanding of the differences in psychological distress and social support among CD patients at different active stages in China to provide evidence for subsequent research attempts to establish an association between social support and psychological well-being and disease activity. In addition, we considered whether sex moderates the relationship between disease activity and social support and psychological distress in CD. Previous studies of IBD patients have found that older patients have higher symptoms of anxiety and depression. Therefore, in this study, age was used as a control variable. Thus, we proposed the following hypotheses: there were significant differences in psychological disorders and social support between CD patients in activity (CD-A) and CD patients in remission (CD-R), and there may be gender differences as well.

Methods

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Ethical aspects

This study was approved by the institutional ethics committee of Tongji Medical College of Huazhong University of Science and Technology, and consent was acquired from all participants (Protocol Number ICH S016). All participants were informed of the purpose and methods of this study and provided written informed consent.

Participants

This study was a cross-sectional, single-center study. Participants were recruited between March 2020 and March 2022 at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology in China. The inclusion criteria were patients with a diagnosis of CD(20), adult patients (aged 18 years or more), patients with sufficient ability in spoken and written Chinese to complete all the questionnaires, patients without a diagnosis of concomitant mental disorders or dementia and patients not taking psychotropic medication for CD. The exclusion criteria were as follows: (1) patients who could not complete the questionnaires; (2) patients who had tumors or other medical comorbidities; and (3) patients who were pregnant. The flow diagram of the enrolled patients and healthy controls is shown in Figure 1.

Data collection

Clinical and demographic data were collected, including age, sex, body mass index, employment status, living status, educational status, marital status, and disease duration. The severity of CD was assessed using Crohn's disease activity index (CDAI) scores(21). A CDAI score of less than 150 was defined as disease in remission. A CDAI score of 150 or more was defined as disease in activity.

Social support was assessed using the Social Support Rating Scale (SSRS)(22, 23). The participants' social support was evaluated by the Chinese version of the SSRS, which was previously demonstrated to have reliability and validity. It can measure the characteristics of social support and its relationship with participants' mental health levels, mental illness, and various physical diseases. The scale has 10 items, including items regarding objective support (3 items), subjective support (4 items), and the utilization of social support (3 items). The total score ranges from 11-59 and is acquired by adding the scores of each item. Lower scores on indices of the SSRS indicate less social support.

The psychological state was assessed using the Symptom Checklist-90 (SCL-90)(24, 25). The scale has a total of 90 items regarding a wide range of psychiatric symptoms, including feelings, emotions, thinking, consciousness, behaviors, habits, interpersonal relationships, diet, and sleep. Ten factors are used to reflect 10 aspects of psychological symptoms, including psychoticism, paranoid ideation, phobic anxiety, hostility, anxiety, depression, interpersonal sensitivity, obsessive-compulsive behaviors, and somatization. The statistical standard of the SCL-90 mainly consists of two items: the total score and the various factor scores. The total score is the sum of the scores of the 90 items, which reflects the severity of the disease. The factor score is the average score of all factors, which ranges from "0" ("no problem") to "4" ("very serious"). Each factor reflects a certain aspect of the participant's symptoms, so the symptom distribution characteristics of the participants can be understood through the factor score. According to the results of the Chinese norm, if the total score exceeds 160 points, the positive items exceed 43 points, or any factor score exceeds 2 points, the participants are considered to have a positive screening, and further examination is needed. This version has excellent internal consistency for all items.

Statistical analysis

All statistical analyses were performed in SPSS 26.0, GraphPad Prism 8.0, and Origin 2021 software. The independent sample T-test was used to determine the relationship between disease status and sex differences and scale factors. Correlation analysis was applied to evaluate the relationship among the clinical, psychological, and social support factors. Hierarchical multiple regression analysis (MRA) was used to examine the unique contribution of participant characteristics, psychological distress scores, and SSRS factor scores on the composite factors of disease status. $P < 0.05$ was considered statistically significant.

Results

Sample characteristics

A total of 162 CD patients with complete survey responses were analyzed (CD-A n=93, CD-R n=69). Participants in the CD-A group reported a disease course of 13 months, and those in the CD-R group reported a disease course of 11 months. The Independent Sample T-test and Chi-Square Tests indicated no statistically significant difference in age, employment status, living status, marital status, or years of education between the two groups. Compared with the CD-R group, the CD-A group had higher CRP (P=0.001) and ESR values(P<0.001). In addition, these patients tended to have higher anemia rates and relapse rates in the last year (P<0.001), which is shown in Table 1. Independent samples t-tests indicated differences between the two groups, with the CD-A group reporting lower SSRS scores and higher SCL-90 scores than the CD-R group, which is shown in Table 2. Moreover, women showed higher levels of anemia rate (P=0.021), relapse rates in the last year (P=0.020) and somatization (P=0.030) and anxiety (P=0.050) than men, as shown in Table 3 and Supplementary materials Table 1.

Preliminary analyses

Figure 2 shows the correlation between social support and the psychological distress scale. The results showed that objective support was negatively correlated with psychological distress (obsessive-compulsive, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid, psychoticism, and other factors) (P<0.05). Subjective support was negatively correlated with psychological distress (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid, psychoticism, and other) (P<0.05). Availability was negatively correlated with psychological distress (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, paranoid, psychoticism, and other factors) (P<0.05).

Binary logistic regression models

Univariate analysis suggested that C-reactive protein levels(P=0.001), somatization (P=0.007), obsessive compulsiveness (P<0.001), interpersonal sensitivity (P<0.001), depression (P<0.001), anxiety (P=0.039), hostility (P=0.015), phobic anxiety (P=0.002), paranoid (P=0.001), psychoticism (P<0.001), other factors (P<0.001) and subjective support (P=0.003) were statistically significant and were included in the subsequent binary logistic regression analysis. Binary logistic regression analyses showed that the social support factors of subjective support (Beta=0.903, P=0.013), the clinical factors of C-reactive protein levels (Beta=1.038, P=0.001), the psychological distress factors of anxiety (Beta=1.443, P=0.008) and other factors (Beta=1.235, P=0.042) were predictors of disease activity, as shown in Table 4.

Discussion

In this study, we described clinical, social support, and psychological distress differences, and we also assessed the relationships between disease activity and dimensions of psychological distress and social support symptoms in a

cohort of CD patients. As we previously hypothesized, our present results showed that CD-A patients had higher SCL-90 and lower SSRS scores than CD-R patients, and social support factors were related to psychological distress factors, both of which had an impact on disease activity. We also found that women showed higher levels of somatization and anxiety than men, but this was not observed for social support. Finally, we found that C-reactive protein, subjective support, anxiety, and other factors were relevant determinants of disease activity in CD patients.

Psychological factors such as anxiety and depression have been studied about CD (26), but the roles of other factors such as social support have been poorly investigated. The high correlations of social support factors with psychological distress symptoms in CD patients are consistent with a previous study about other illnesses (27) and indicate that the three factors of social support are likely a concept that reflects another dimension of psychological states. Social support is defined as behavioral or emotional support provided by family members, other people, or other groups.

Social support is a positive health resource that contributes to the well-being of people with chronic diseases. The ability of an actor to derive benefits from his or her membership in a social network or other social structure. This positive support helps individuals overcome difficulties and challenges in life, especially stress related to coping with chronic illness. This is consistent with a biobehavioral model in which patients' responses to illness and health are influenced by family and peer relationships. Social support can be divided into three categories: objective support, subjective support, and availability(3). However, in populations of patients with chronic disease, there are individual differences in the use of social support. Some people can receive support at any time but refuse the help of others. In addition, interpersonal support is a process of individual interaction. Past research has shown that social support has different effects on different diseases(28).

IBD is considered a bio-psychosocial disease characterized by psychological distress and psychological or psychiatric disorders, which is associated with stress, social interactions and attachment insecurity(29, 30). Chronic diseases are thought to affect a patient's mental capacity and determine the patient's transition to attachment insecurity. Recently, several studies have begun investigating attachment dimensionality in people with IBD. According to attachment theory and research and social interaction are regulated by individual's attachment system, which begins to develop in infancy. Individuals with secure attachment styles may form positive relationships, experience a sense of self-confidence and have realistic perceptions of others. Conversely, people with anxious attachment types may have a sense of insecurity in relationships. Sound social support may provide individuals with positive emotional experiences and secure attachment styles(31, 32). Social support for family members and friends includes the ability to communicate stress problems, discuss fears and worries, make decisions together, plan social activities together, and get along together in difficult situations. This positive support helps individuals overcome difficulties and challenges in life, especially the stress associated with coping with chronic diseases. On the contrary, patients with insecure attachment may be less able to form positive relationships with doctors and less able to receive help and support from close people, which can lead to worsening disease management.

Consistent with previous research, the depressive, anxiety, and somatization factors of patients with CD are different for different disease severities(33, 34). The three factors of social support are negatively correlated with psychological distress (somatization, anxiety, anxiety, and other factors). Somatization mainly reflects the subjective body discomfort of patients, including discomfort due to cardiovascular, gastrointestinal, respiratory, and other systems, as well as headaches, backaches, and muscle soreness. Interestingly, the relationship between disease severity and most psychological distress and social support factors in addition to anxiety and subjective support factors was no longer significant after including social support factors in the model.

In binary logistic regression models, we also found that subjective support factors, anxiety, other psychological distress factors, and C-reactive protein remained significant predictors of disease severity, which may be related to the fluctuating course of progression and remission that characterizes this disease. Namely, patients with CD attach particular importance to their subjective feelings and may be inclined to interpret any physical or subjective discomfort they experience as a sign of psychological distress, leading them to report lower levels of subjective support. However, these lower levels of subjective support result in worsening disease activity. This biopsychosocial explanation is consistent with what has been found in people with CD(35, 36).

In our study, the psychological dimension data were obtained from the SCL-90. The results indicate that the psychological state of CD-A is affected in some dimensions, compared with CD-R. This is consistent with the results of Goodhand, J.R., et al. (37). Neither CD-A nor CD-R met the criteria for anxiety and depression in our study. In recent years, an increasing number of doctors have realized that psychological disorders are common in inflammatory bowel disease patients and may affect the disease condition and quality of life(22, 38). However, the etiology of psychological disorders appears to be multifactorial; for example, environmental factors may include stressful life events, disease activity, disease course, medications, income, or marital status(39, 40). Regarding clinical factors, the inflammatory performance of CD may play a role in disease activity and quality of life. CD-A had higher anemia rates, CRP values, ESR values, and relapse rates. It is possible to improve the psychological state and quality of life of patients with CD through early identification and intervention.

In recent years, some scholars have also studied the gender difference of IBD. At present, many studies have found that the differences in the psychological performance of IBD patients are related to gender, and females are predictors of IBD combined anxiety and depression(41, 42). However, the study of Nahon et al. pointed out that the incidence of anxiety and depression in female patients with IBD was not significantly increased, and gender was not correlated with the occurrence of anxiety and depression(43). In this study, we also found that women with CD tend to report greater depressive symptoms than men, which was consistent with previous research (34, 44). At the same time, epidemiological studies have confirmed that there are significant gender differences in the incidence of inflammatory bowel disease (IBD), and this difference shows significant regional differences. In the United States(45), Canada(46, 47), Israel(48), Spain(49), and Denmark(50), the incidence of women is higher than that of men. In Asian countries such as South Korea(51), India(52), and China(53), the incidence is higher in men than in women. The results indicate that female CD patients are more prone to anxiety and depression, which was mainly reflected in three aspects. First, women have a higher rate of anemia symptoms and disease recurrence than men, which may be more prone to psychological problems due to illness and reduced quality of life. Secondly, women are less likely than men to use immunosuppressives and biological agents. Although there were no statistically significant differences in these clinical characteristics between genders of patients with CD, which may be due to the insufficient sample size included in this study. Third, women's psychological activities are more delicate, more concerned about their symptoms, and pregnant with the next generation of problems. Therefore, in daily clinical diagnosis and treatment, more attention should be paid to whether women have mental and psychological abnormalities and their severity, and effective health education and psychological support should be provided according to the specific circumstances.

To our knowledge, this is the first study to compare the relationship between social support and disease activity across men and women with CD. The strengths of this study include the diversity of the sample in terms of social support and psychological distress scores, which allowed us to assess somatization in patients with different levels of disease activity.

Several limitations should be considered in this study. First, this was a single-center study in which all participants were of Han nationality and from Hubei Province, China. Second, the cross-sectional nature of the data

precludes us from concluding the causality of the relationships among social support, psychological distress, and disease activity. In the future, longitudinal research should be conducted to establish a more robust connection between various clinical, psychological, and social support factors and disease activity in CD patients.

Conclusions

In conclusion, this study indicates the importance of considering a broader range of psychological distress and social support factors that may play a role in the health of patients with CD. Further exploration of these factors in longitudinal and intervention studies may help to develop effective CD management models.

Contributors M.T.H and L.T substantial contributions to the conception, design, acquisition, analysis, and interpretation of data for the work. They also draft the work or revise it critically for important intellectual content. L.X.W, Y.Z, X.L, X.F.Y, and C.H substantial contributions to the acquisition and interpretation of data for the work. P.L, Q.L, and P.H substantial contributions to revising it critically for important intellectual content. L.Y and L.R.Z substantial contributions to the conception, design, and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Disclaimer The funding sources had no role in the study conduct, data collection, analyses, data interpretation, and the decision to submit the manuscript.

Competing interests None declared.

Patient consent for publication All participants were informed of the purpose and methods of this study and provided written informed consent.

Ethics approval This study was approved by the institutional ethics committee of Tongji Medical College of Huazhong University of Science and Technology (Protocol Number ICH S016).

Conflict of Interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and Biometry:

No complex statistical methods were necessary for this paper.

Provide Data sharing No additional data available

Figure 1: Flow diagram of the enrolled patients.

Figure 2. Analysis of the correlation of clinical data with social support and psychological factors.

Note: Som=somatization, OC=obsessive-compulsive, IS=interpersonal sensitivity, Dep=depression, Anx=anxiety, Hos=hostility, PA=phobic anxiety, Par=paranoid, Psy=psychoticism, Oth=other, OS=objective support, SS=subjective support, Ava=availability. * P<=0.05; ** P<=0.01; *** P<=0.001.

Table 1. Baseline characteristics of the study population

Characteristics	CD-A (n=93)	CD-R (n=69)	P value
Age	31±12	35±15	0.096
Sex(female)	36(38.7%)	31(44.9%)	0.427
Body Mass Index	19.5±3.9	20.8±4.3	0.049
Employment status	-	-	
no	27 (29.0%)	21 (30.5%)	0.961
retired	6 (6.5%)	3 (4.3%)	
yes	60 (64.5%)	45 (65.2%)	
Living status	-	-	
alone	3 (3.2%)	6 (8.7%)	0.248
with others	90 (96.8%)	63 (91.3%)	
Education	-	-	
up to 6 years	5 (5.4%)	4 (5.8%)	
up to 9 years	28 (30.1%)	18 (26.1%)	0.705
up to 12 years	44 (47.3%)	34 (49.3%)	
college	16 (17.2%)	13 (18.8%)	
Marital status	-	-	
married/cohabitating	53 (57.0%)	34 (49.3%)	0.579
widowed/divorced	7 (7.5%)	5 (7.2%)	
single	33 (35.5%)	30 (43.5%)	
Montreal location	-	-	
Ileal (L1)	35 (37.6%)	28 (40.7%)	
Colonic (L2)	15 (16.2%)	5 (7.2%)	0.808
Ileocolon (L3)	39 (41.9%)	33 (47.8%)	
upper gastrointestinal tract (L4)	1 (1.1%)	0 (0%)	
L4+L1/L2/L3	3 (3.2%)	3 (4.3%)	
Montreal behavior	-	-	
inflammatory	52 (55.9%)	45 (65.2%)	0.401
structuring	24 (25.8%)	16 (23.2%)	
penetrating	17 (18.3%)	8 (11.6%)	
Perianal disease	35 (37.6%)	28 (40.6%)	0.704
Current therapy	-	-	
no treatment	0 (0%)	2 (2.9%)	
corticosteroids	8 (8.6%)	7 (10.1%)	
5-aminosalicylates	21 (22.6%)	17 (24.6%)	0.169
immunomodulators	27 (29.0%)	22 (31.9%)	
antitumor necrosis factor	16 (17.2%)	9 (13.0%)	
combined therapy	21 (22.6%)	12 (17.5%)	
Anemia	-	-	
no	36 (38.7%)	55 (79.7%)	
mild	49 (52.7%)	10 (14.5%)	<0.001
moderate	6 (6.5%)	3 (4.3%)	
severe	2 (2.1%)	1 (1.5%)	
Relapses in the last year	-	-	
0	13 (14.0%)	35 (50.7%)	
1-2	57 (61.3%)	24 (34.8%)	<0.001
3	8 (8.6%)	8 (11.6%)	
≥4	15 (16.1%)	2 (2.9%)	
Disease duration (months)	13±25	11±19	0.594
C-reactive protein	24.3±34.4	8.8±18.8	0.001

Note: Data are presented as the number (%) or mean±standard deviation. CD-A refers to Crohn's disease patients in activity. CD-R refers to Crohn's disease patients in remission. CD=Crohn's disease

Table 2. Questionnaire survey in for Crohn's disease patients

Variable	CD-A (n=93)	CD-R (n=69)	P value
SCL-90			
Somatization	18.8±5.9	16.3±4.7	0.004
Obsessive-compulsive	19.0±5.4	15.4±4.4	<0.0001
Interpersonal sensitivity	15.4±5.8	12.1±4.0	<0.0001
Depression	24.7±9.1	18.3±5.2	<0.0001
Anxiety	16.2±5.3	12.4±3.2	<0.0001
Hostility	10.3±3.8	8.8±3.6	0.012
Phobic anxiety	9.7±3.3	8.2±2.0	0.001
paranoid	8.9±3.2	7.3±2.3	<0.0001
psychoticism	14.9±4.3	12.3±3.6	<0.0001
Other	12.6±3.9	9.9±2.5	<0.0001
SSRS			
objective support	8.8±2.8	9.3±2.4	0.239
Subjective Support	15.1±5.6	18.0±6.2	0.003
availability	6.9±1.7	7.4±1.7	0.080

Note: Data are presented as the mean±standard deviation. CD-A refers to Crohn's disease patients in activity. CD-R refers to Crohn's disease patients in remission. CD=Crohn's disease; SCL-90=Check List-90; SSRS= Social Support Rating Scale.

Table 3. Differences in questionnaire survey results between men (n=95) and women (n=67).

Variable	Men	Women	P value
SCL-90			
Somatization	17.2±5.0	19.5±6.4	0.030
Obsessive-compulsive	17.2±5.0	18.1±5.9	0.345
Interpersonal sensitivity	13.9±5.1	14.1±6.2	0.811
Depression	21.2±7.4	24.0±10.0	0.089
Anxiety	14.2±4.4	15.8±5.6	0.050
Hostility	9.6±3.6	9.5±4.3	0.932
Phobic anxiety	8.8±2.6	9.7±3.6	0.124
paranoid	8.1±2.8	8.5±3.4	0.515
psychoticism	13.7±4.1	13.9±4.3	0.734
Other	11.4±3.4	11.7±4.3	0.614
SSRS			
objective support	8.9±2.7	9.1±2.6	0.641
Subjective Support	16.4±5.7	16.1±6.6	0.757
availability	7.0±1.7	7.3±1.7	0.471

Note: Data are presented as the mean±standard deviation. CD=Crohn's disease; SCL-90=Check List-90; SSRS= Social Support Rating Scale.

Table 4. Results of the analysis of binary logistic regression analysis on disease activity

The factors	Hosmer and Lemeshow Test	S.E.	Wald	Beta	95% CI	P value
Univariate		-		-	-	-
age	0.466	0.012	2.727	0.980	0.957-1.004	0.099
Body Mass Index	0.155	0.040	3.760	0.925	0.855-1.001	0.053
Disease duration	0.494	0.007	0.284	1.004	0.990-1.018	0.594
C-reactive protein	0.000	0.011	11.378	1.039	1.016-1.062	0.001
objective support	0.434	0.061	1.389	0.931	0.827-1.049	0.239
Subjective Support	0.339	0.028	8.551	0.921	0.872-0.973	0.003
availability	0.504	0.095	3.017	0.849	0.705-1.021	0.082
Somatization	0.090	0.034	7.296	1.096	1.025-1.171	0.007
Obsessive compulsive	0.163	0.037	16.349	1.161	1.080-1.248	<0.001
Interpersonal sensitivity	0.130	0.038	13.650	1.153	1.069-1.243	<0.001
Depression	0.785	0.032	19.579	1.154	1.083-1.230	<0.001
Anxiety	0.039	0.058	20.748	1.301	1.162-1.456	0.039
Hostility	0.056	0.049	5.876	1.126	1.023-1.240	0.015
Phobic anxiety	0.601	0.079	9.578	1.275	1.093-1.488	0.002
Paranoid	0.212	0.081	10.490	1.300	1.109-1.523	0.001
Psychoticism	0.029	0.055	13.645	1.224	1.099-1.362	<0.001
Other	0.382	0.061	18.473	1.301	1.154-1.467	<0.001
Multivariate		-	-	-	-	-
Subjective Support	0.519	0.041	6.216	0.903	0.834-0.979	0.013
C-reactive protein		0.012	10.486	1.038	1.105-1.062	0.001
Anxiety		0.138	7.009	1.443	1.100-1.893	0.008
Other		0.103	4.155	1.235	1.008-1.512	0.042

Note: SE: standardized error, Durbin-Watson:1.980.

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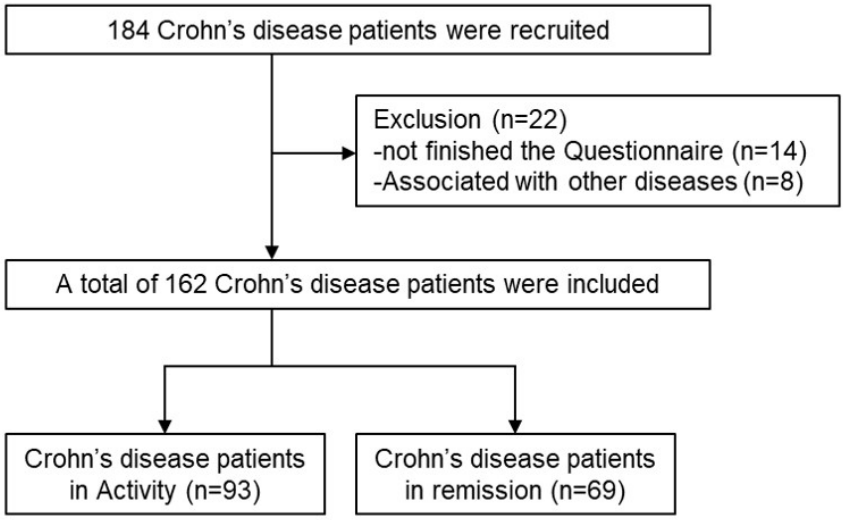

Figure 1: Flow diagram of the enrolled patients.

150x94mm (149 x 149 DPI)

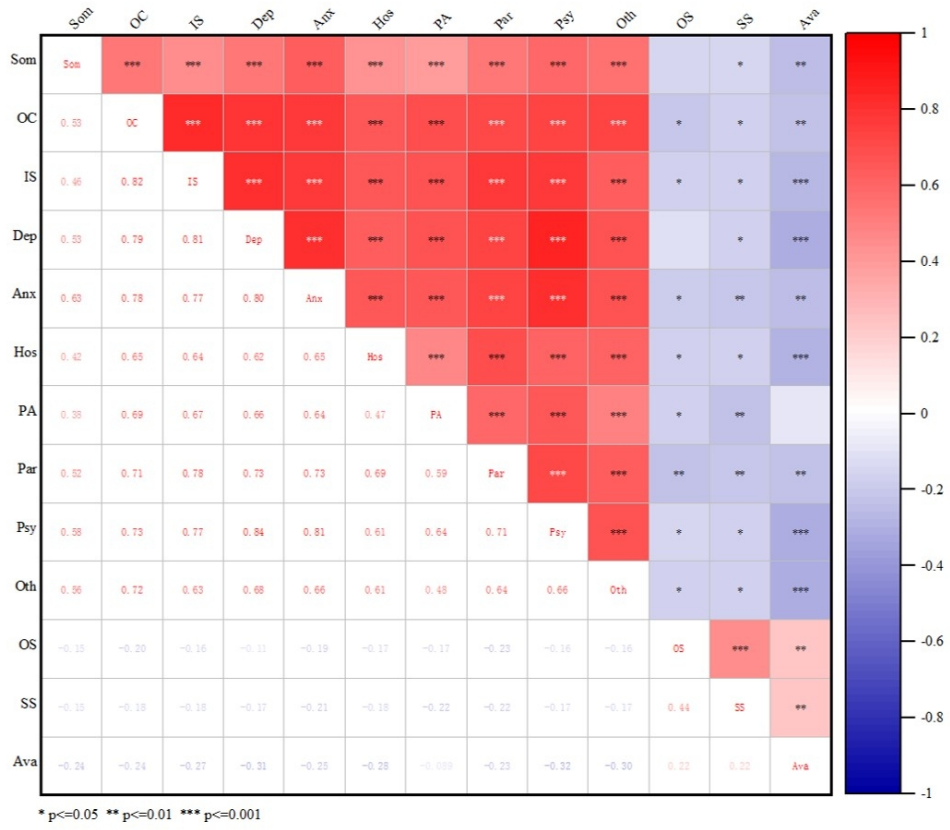

Figure 2. Analysis of the correlation of clinical data with social support and psychological factors.

192x165mm (143 x 143 DPI)

Supplementary materials

Table 1. Baseline characteristics of the study population of different genders

Characteristics	Male (n=95)	Female (n=67)	P value
Age	32±11	34±14	0.311
Disease activity (active)	57 (60.0%)	36 (53.7%)	0.427
Body Mass Index	20.0±4.3	19.7±3.6	0.641
Employment status	-	-	
no	26 (27.4%)	22 (32.8%)	0.448
retired	4 (4.2%)	5 (7.5%)	
yes	65 (68.4%)	40 (59.7%)	
Living status	-	-	
alone	5 (5.3%)	4 (6.0%)	0.847
with others	90 (94.7%)	63 (94.0%)	
Education	-	-	
up to 6 years	4 (4.2%)	5 (7.5%)	
up to 9 years	26 (27.4%)	20 (29.8%)	0.776
up to 12 years	48 (50.5%)	30 (44.8%)	
college	17 (17.9%)	12 (17.9%)	
Marital status	-	-	
married/cohabitating	52 (54.7%)	35 (52.2%)	0.736
widowed/divorced	8 (8.4%)	4 (6.0%)	
single	35 (36.9%)	28 (41.8%)	
Montreal location	-	-	
Ileal (L1)	33 (34.7%)	30 (44.8%)	
Colonic (L2)	12 (12.6%)	8 (11.9%)	0.674
Ileocolon (L3)	45 (47.4%)	27 (40.3%)	
upper gastrointestinal tract (L4)	1 (1.1%)	0 (0%)	
L4+L1/L2/L3	4 (4.2%)	2 (3.0%)	
Perianal disease	36 (37.9%)	27 (40.3%)	0.757
Current therapy	-	-	
no treatment	0 (0%)	2 (3.0%)	
corticosteroids	9 (9.5%)	6 (8.9%)	
5-aminosalicylates	20 (21.1%)	18 (26.9%)	0.497
immunomodulators	29 (30.5%)	20 (29.9%)	
antitumor necrosis factor	17 (17.8%)	8 (11.9%)	
combined therapy	20 (21.1%)	13 (19.4%)	
Anemia	-	-	
no	63 (66.3%)	28 (41.8%)	
mild	27 (28.4%)	32 (47.8%)	0.021
moderate	4 (4.2%)	5 (7.5%)	
severe	1 (1.1%)	2 (2.9%)	
Relapses in the last year	-	-	
0	26 (27.4%)	22 (32.8%)	
1-2	42 (44.2%)	39 (58.2%)	0.020
3	12 (12.6%)	4 (6.0%)	
≥4	15 (15.8%)	2 (3.0%)	
Disease duration (months)	13±25	11±19	0.582
C-reactive protein	13.2±24.7	11.5±18.5	0.634

Note: Data are presented as the number (%) or mean±standard deviation. CD, Crohn's disease.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
	Yes	(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2 Yes	Explain the scientific background and rationale for the investigation being reported
Objectives	3 Yes	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4 Yes	Present key elements of study design early in the paper
Setting	5 Yes	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6 Yes	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7 Yes	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8* Yes	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9 Yes	Describe any efforts to address potential sources of bias
Study size	10 Yes	Explain how the study size was arrived at
Quantitative variables	11 Yes	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12 Yes	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13* Yes	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14* Yes	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15* Yes	Report numbers of outcome events or summary measures
Main results	16 Yes	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17 Yes	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18 Yes	Summarise key results with reference to study objectives
Limitations	19 Yes	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20 Yes	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21 Yes	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22 Yes	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Is disease activity associated with social support and psychological distress in Crohn's disease patients? Results of a cross-sectional study in a Chinese hospital population

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Is disease activity associated with social support and psychological distress in Crohn's disease patients? Results of a cross-sectional study in a Chinese hospital population

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Abstract

Objectives: This study aims to assess the relative of social support and psychological distress in disease activity among Crohn's disease (CD) patients in China, and explore whether sex moderates the relationship between disease activity and social support and psychological distress in CD.

Design: Our study has a cross-sectional design.

Setting: This was a single-center study, which was conducted in Wuhan, China.

Participants: A total of 184 patients with CD at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology were enrolled in this study; of these,162 patients were included in the final analysis.

Primary and secondary outcome measures: The main study outcome was the CD patients' clinical and questionnaire data. The association of disease activity, social support, and psychological distress with CD patients was also evaluated based on the collected data.

Results: A total of 162 CD patients were enrolled. Compared with CD patients in remission (CD-R), the CD patients in activity (CD-A) had higher CRP (P=0.001), anemia (P<0.001), and relapse rates in the last year (P<0.001). Independent samples t-tests indicated that the CD-A group reported lower SSRS scores and higher SCL-90 scores than the CD-R group. Moreover, men with CD had lower somatization (P=0.030) and anxiety (P=0.050) scores than women. In binary logistic regression models, the subjective support (Beta=0.903, P=0.013), the clinical factors of C-

reactive protein (Beta=1.038, P=0.001), and psychological distress factors of anxiety (Beta=1.443, P=0.008) and other (Beta=1.235, P=0.042) were disease activity predictors.

Conclusion: The findings highlight the importance of the psychological distress and social support factors that may play a role in CD patients' health. Interventions to address these issues should be part of management in CD.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

- ⇒ Our study improved the understanding of the differences in psychological distress and social support among CD patients at different active stages in developing countries, especially in central China.
- ⇒ Provide evidence for subsequent studies attempting to establish a relationship between social support and psychological well-being and disease activity.
- ⇒ In this study, gender differences were considered in the analysis.
- ⇒ However, this cross-sectional study could not address the causality between disease activity and psychological change factors of patients with CD.

Keywords: Crohn's disease, social support, psychological distress, anxiety

Introduction

Crohn's disease (CD) is a chronic, nonspecific intestinal inflammatory disease characterized by recurrent abdominal pain and diarrhea that peaks in young adulthood(1). In addition to gastrointestinal manifestations, CD patients experience other systemic manifestations and complications. As of 2017, inflammatory bowel disease (IBD) affected 6.8 million people worldwide. The United States reported the highest incidence of IBD, followed by the United Kingdom(2). Epidemiological studies have shown that the incidence of IBD in China is 3.44 cases per one million people, which is the highest in Asia, and the incidence of IBD in mainland China is higher in the south and lower in the north(3). In recent years, the incidence of CD has increased rapidly in China(4, 5).

Due to bowel damage and a long medical history, patients have a high prevalence of psychological impairment, such as anxiety and depression, compared to the general population(6, 7). Although medical treatments are effective in controlling gastrointestinal inflammation, the relapsing behavior of CD can cause psychological disorders. Moreover, CD patients typically require lifelong medication, which seriously affects their quality of life and increases psychological distress. The CD is associated with high medical costs, high rates of psychological disorders, and illness burdens associated with reduced productivity and activity. Studies have shown that approximately 20% of inflammatory bowel disease patients may have symptoms of anxiety, and approximately 15% have symptoms of depression(8, 9). Large population studies showed that the prevalence of psychological distress and injury in IBD patients was significantly higher than that in non-IBD adults(10, 11). Regarding the relationship between the psychological state of IBD patients and gender differences, studies have pointed out that female IBD patients are more prone to anxiety, depression, and other psychological problems than male patients(9). For example, the prevalence of comorbidity anxiety and depression in female IBD patients was 33.8% and 21.2%, respectively, compared with 22.8% and 16.2% in male IBD patients(12).

The uncertainty of treatment results and psychological disorders may lead to disease recurrence, aggravate the course of the disease, and directly lead to the decline of patients' quality of life and the increase of treatment costs(13, 14). Patients with IBD and anxiety or depression have a higher risk of hospitalization, emergency room visits, readmissions, and use of outpatient services than patients without these symptoms(15). Thus, healthcare services for CD are more demanding and costly for patients with symptoms of anxiety and depression. Xu et al. reported that poor sleep quality, anxiety, and depression were related to inflammatory activity(16). In addition, disease activity was found to be associated with depression and anxiety, and psychological distress may increase the likelihood of disease relapse(17). However, most previous studies have focused on anxiety or depression, rarely focusing on other dimensions. Social support might be another dimension that plays a role in disease severity. Interestingly, there are few studies on the association between social support and disease activity in CD patients(18, 19).

This study aimed to improve the understanding of the differences in psychological distress and social support among CD patients at different active stages in China to provide evidence for subsequent research attempts to establish an association between social support and psychological well-being and disease activity. In addition, we considered whether sex moderates the relationship between disease activity and social support and psychological distress in CD. Previous studies of IBD patients have found that older patients have higher symptoms of anxiety and depression. Therefore, in this study, age was used as a control variable. Thus, we proposed the following hypotheses: there were significant differences in psychological disorders and social support between CD patients in activity (CD-A) and CD patients in remission (CD-R), and there may be gender differences as well.

Methods

Patient and Public Involvement

Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Ethical aspects

This study was approved by the institutional ethics committee of Tongji Medical College of Huazhong University of Science and Technology, and consent was acquired from all participants (Protocol Number ICH S016). All participants were informed of the purpose and methods of this study and provided written informed consent.

Participants

This study was a cross-sectional, single-center study. Participants were recruited between March 2020 and March 2022 at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology in China. The inclusion criteria were patients with a diagnosis of CD(20), adult patients (aged 18 years or more), patients with sufficient ability in spoken and written Chinese to complete all the questionnaires, patients without a diagnosis of concomitant mental disorders or dementia and patients not taking psychotropic medication for CD. The exclusion criteria were as follows: (1) patients who could not complete the questionnaires; (2) patients who had tumors or other medical comorbidities; and (3) patients who were pregnant. The flow diagram of the enrolled patients and healthy controls is shown in Figure 1.

Data collection

Clinical and demographic data were collected, including age, sex, body mass index, employment status, living status, educational status, marital status, and disease duration. The severity of CD was assessed using Crohn's disease activity index (CDAI) scores(21). A CDAI score of less than 150 was defined as disease in remission. A CDAI score of 150 or more was defined as disease in activity.

Social support was assessed using the Social Support Rating Scale (SSRS)(22, 23). The participants' social support was evaluated by the Chinese version of the SSRS, which was previously demonstrated to have reliability and validity. It can measure the characteristics of social support and its relationship with participants' mental health levels, mental illness, and various physical diseases. The scale has 10 items, including items regarding objective support (3 items), subjective support (4 items), and the utilization of social support (3 items). The total score ranges from 11-59 and is acquired by adding the scores of each item. Lower scores on indices of the SSRS indicate less social support.

The psychological state was assessed using the Symptom Checklist-90 (SCL-90)(24, 25). The scale has a total of 90 items regarding a wide range of psychiatric symptoms, including feelings, emotions, thinking, consciousness, behaviors, habits, interpersonal relationships, diet, and sleep. Ten factors are used to reflect 10 aspects of psychological symptoms, including psychoticism, paranoid ideation, phobic anxiety, hostility, anxiety, depression, interpersonal sensitivity, obsessive-compulsive behaviors, and somatization. The statistical standard of the SCL-90 mainly consists of two items: the total score and the various factor scores. The total score is the sum of the scores of the 90 items, which reflects the severity of the disease. The factor score is the average score of all factors, which ranges from "0" ("no problem") to "4" ("very serious"). Each factor reflects a certain aspect of the participant's symptoms, so the symptom distribution characteristics of the participants can be understood through the factor score. According to the results of the Chinese norm, if the total score exceeds 160 points, the positive items exceed 43 points, or any factor score exceeds 2 points, the participants are considered to have a positive screening, and further examination is needed. This version has excellent internal consistency for all items.

Statistical analysis

All statistical analyses were performed in SPSS 26.0, GraphPad Prism 8.0, and Origin 2021 software. The independent sample T-test was used to determine the relationship between disease status and sex differences and scale factors. Correlation analysis was applied to evaluate the relationship among the clinical, psychological, and social support factors. Hierarchical multiple regression analysis (MRA) was used to examine the unique contribution of participant characteristics, psychological distress scores, and SSRS factor scores on the composite factors of disease status. $P < 0.05$ was considered statistically significant.

Results

Sample characteristics

A total of 162 CD patients with complete survey responses were analyzed (CD-A n=93, CD-R n=69). Participants in the CD-A group reported a disease course of 13 months, and those in the CD-R group reported a disease course of 11 months. The Independent Sample T-test and Chi-Square Tests indicated no statistically significant difference in age, employment status, living status, marital status, or years of education between the two groups. Compared with the CD-R group, the CD-A group had higher CRP (P=0.001) and ESR values(P<0.001). In addition, these patients tended to have higher anemia rates and relapse rates in the last year (P<0.001), which is shown in Table 1. Independent samples t-tests indicated differences between the two groups, with the CD-A group reporting lower SSRS scores and higher SCL-90 scores than the CD-R group, which is shown in Table 2. Moreover, women showed higher levels of anemia rate (P=0.021), relapse rates in the last year (P=0.020) and somatization (P=0.030) and anxiety (P=0.050) than men, as shown in Table 3 and Supplementary materials Table 1.

Preliminary analyses

Figure 2 shows the correlation between social support and the psychological distress scale. The results showed that objective support was negatively correlated with psychological distress (obsessive-compulsive, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid, psychoticism, and other factors) (P<0.05). Subjective support was negatively correlated with psychological distress (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid, psychoticism, and other) (P<0.05). Availability was negatively correlated with psychological distress (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, paranoid, psychoticism, and other factors) (P<0.05).

Binary logistic regression models

Univariate analysis suggested that C-reactive protein levels(P=0.001), somatization (P=0.007), obsessive compulsiveness (P<0.001), interpersonal sensitivity (P<0.001), depression (P<0.001), anxiety (P=0.039), hostility (P=0.015), phobic anxiety (P=0.002), paranoid (P=0.001), psychoticism (P<0.001), other factors (P<0.001) and subjective support (P=0.003) were statistically significant and were included in the subsequent binary logistic regression analysis. Binary logistic regression analyses showed that the social support factors of subjective support (Beta=0.903, P=0.013), the clinical factors of C-reactive protein levels (Beta=1.038, P=0.001), the psychological distress factors of anxiety (Beta=1.443, P=0.008) and other factors (Beta=1.235, P=0.042) were predictors of disease activity, as shown in Table 4.

Discussion

In this study, we described clinical, social support, and psychological distress differences, and we also assessed the relationships between disease activity and dimensions of psychological distress and social support symptoms in a

cohort of CD patients. As we previously hypothesized, our present results showed that CD-A patients had higher SCL-90 and lower SSRS scores than CD-R patients, and social support factors were related to psychological distress factors, both of which had an impact on disease activity. We also found that women showed higher levels of somatization and anxiety than men, but this was not observed for social support. Finally, we found that C-reactive protein, subjective support, anxiety, and other factors were relevant determinants of disease activity in CD patients.

Psychological factors such as anxiety and depression have been studied about CD (26), but the roles of other factors such as social support have been poorly investigated. The high correlations of social support factors with psychological distress symptoms in CD patients are consistent with a previous study about other illnesses (27) and indicate that the three factors of social support are likely a concept that reflects another dimension of psychological states. Social support is defined as behavioral or emotional support provided by family members, other people, or other groups.

Social support is a positive health resource that contributes to the well-being of people with chronic diseases. The ability of an actor to derive benefits from his or her membership in a social network or other social structure. This positive support helps individuals overcome difficulties and challenges in life, especially stress related to coping with chronic illness. This is consistent with a biobehavioral model in which patients' responses to illness and health are influenced by family and peer relationships. Social support can be divided into three categories: objective support, subjective support, and availability(3). However, in populations of patients with chronic disease, there are individual differences in the use of social support. Some people can receive support at any time but refuse the help of others. In addition, interpersonal support is a process of individual interaction. Past research has shown that social support has different effects on different diseases(28).

IBD is considered a bio-psychosocial disease characterized by psychological distress and psychological or psychiatric disorders, which is associated with stress, social interactions and attachment insecurity(29, 30). Chronic diseases are thought to affect a patient's mental capacity and determine the patient's transition to attachment insecurity. Recently, several studies have begun investigating attachment dimensionality in people with IBD. According to attachment theory and research and social interaction are regulated by individual's attachment system, which begins to develop in infancy. Individuals with secure attachment styles may form positive relationships, experience a sense of self-confidence and have realistic perceptions of others. Conversely, people with anxious attachment types may have a sense of insecurity in relationships. Sound social support may provide individuals with positive emotional experiences and secure attachment styles(31, 32). Social support for family members and friends includes the ability to communicate stress problems, discuss fears and worries, make decisions together, plan social activities together, and get along together in difficult situations. This positive support helps individuals overcome difficulties and challenges in life, especially the stress associated with coping with chronic diseases. On the contrary, patients with insecure attachment may be less able to form positive relationships with doctors and less able to receive help and support from close people, which can lead to worsening disease management.

Consistent with previous research, the depressive, anxiety, and somatization factors of patients with CD are different for different disease severities(33, 34). The three factors of social support are negatively correlated with psychological distress (somatization, anxiety, anxiety, and other factors). Somatization mainly reflects the subjective body discomfort of patients, including discomfort due to cardiovascular, gastrointestinal, respiratory, and other systems, as well as headaches, backaches, and muscle soreness. Interestingly, the relationship between disease severity and most psychological distress and social support factors in addition to anxiety and subjective support factors was no longer significant after including social support factors in the model.

In binary logistic regression models, we also found that subjective support factors, anxiety, other psychological distress factors, and C-reactive protein remained significant predictors of disease severity, which may be related to the fluctuating course of progression and remission that characterizes this disease. Namely, patients with CD attach particular importance to their subjective feelings and may be inclined to interpret any physical or subjective discomfort they experience as a sign of psychological distress, leading them to report lower levels of subjective support. However, these lower levels of subjective support result in worsening disease activity. This biopsychosocial explanation is consistent with what has been found in people with CD(35, 36).

In our study, the psychological dimension data were obtained from the SCL-90. The results indicate that the psychological state of CD-A is affected in some dimensions, compared with CD-R. This is consistent with the results of Goodhand, J.R., et al. (37). Neither CD-A nor CD-R met the criteria for anxiety and depression in our study. In recent years, an increasing number of doctors have realized that psychological disorders are common in inflammatory bowel disease patients and may affect the disease condition and quality of life(22, 38). However, the etiology of psychological disorders appears to be multifactorial; for example, environmental factors may include stressful life events, disease activity, disease course, medications, income, or marital status(39, 40). Regarding clinical factors, the inflammatory performance of CD may play a role in disease activity and quality of life. CD-A had higher anemia rates, CRP values, ESR values, and relapse rates. It is possible to improve the psychological state and quality of life of patients with CD through early identification and intervention.

In recent years, some scholars have also studied the gender difference of IBD. At present, many studies have found that the differences in the psychological performance of IBD patients are related to gender, and females are predictors of IBD combined anxiety and depression(41, 42). However, the study of Nahon et al. pointed out that the incidence of anxiety and depression in female patients with IBD was not significantly increased, and gender was not correlated with the occurrence of anxiety and depression(43). In this study, we also found that women with CD tend to report greater depressive symptoms than men, which was consistent with previous research (34, 44). At the same time, epidemiological studies have confirmed that there are significant gender differences in the incidence of inflammatory bowel disease (IBD), and this difference shows significant regional differences. In the United States(45), Canada(46, 47), Israel(48), Spain(49), and Denmark(50), the incidence of women is higher than that of men. In Asian countries such as South Korea(51), India(52), and China(53), the incidence is higher in men than in women. The results indicate that female CD patients are more prone to anxiety and depression, which was mainly reflected in three aspects. First, women have a higher rate of anemia symptoms and disease recurrence than men, which may be more prone to psychological problems due to illness and reduced quality of life. Secondly, women are less likely than men to use immunosuppressives and biological agents. Although there were no statistically significant differences in these clinical characteristics between genders of patients with CD, which may be due to the insufficient sample size included in this study. Third, women's psychological activities are more delicate, more concerned about their symptoms, and pregnant with the next generation of problems. Therefore, in daily clinical diagnosis and treatment, more attention should be paid to whether women have mental and psychological abnormalities and their severity, and effective health education and psychological support should be provided according to the specific circumstances.

To our knowledge, this is the first study to compare the relationship between social support and disease activity across men and women with CD. The strengths of this study include the diversity of the sample in terms of social support and psychological distress scores, which allowed us to assess somatization in patients with different levels of disease activity.

Several limitations should be considered in this study. First, this was a single-center study in which all participants were of Han nationality and from Hubei Province, China. Second, the cross-sectional nature of the data

precludes us from concluding the causality of the relationships among social support, psychological distress, and disease activity. In the future, longitudinal research should be conducted to establish a more robust connection between various clinical, psychological, and social support factors and disease activity in CD patients.

Conclusions

In conclusion, this study indicates the importance of considering a broader range of psychological distress and social support factors that may play a role in the health of patients with CD. Further exploration of these factors in longitudinal and intervention studies may help to develop effective CD management models.

Contributors M.T.H and L.T substantial contributions to the conception, design, acquisition, analysis, and interpretation of data for the work. They also draft the work or revise it critically for important intellectual content. L.X.W, Y.Z, X.L, X.F.Y, and C.H substantial contributions to the acquisition and interpretation of data for the work. P.L, Q.L, and P.H substantial contributions to revising it critically for important intellectual content. L.Y and L.R.Z substantial contributions to the conception, design, and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Competing interests None declared.

Patient consent for publication All participants were informed of the purpose and methods of this study and provided written informed consent.

Ethics approval This study was approved by the institutional ethics committee of Tongji Medical College of Huazhong University of Science and Technology (Protocol Number ICH S016).

Conflict of Interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and Biometry:

No complex statistical methods were necessary for this paper.

Provide Data sharing No additional data available

Figure 1: Flow diagram of the enrolled patients.

Figure 2. Analysis of the correlation of clinical data with social support and psychological factors.

Note: Som=somatization, OC=obsessive-compulsive, IS=interpersonal sensitivity, Dep=depression, Anx=anxiety, Hos=hostility, PA=phobic anxiety, Par=paranoid, Psy=psychoticism, Oth=other, OS=objective support, SS=subjective support, Ava=availability. * P<=0.05; ** P<=0.01; *** P<=0.001.

Table 1. Baseline characteristics of the study population

Characteristics	CD-A (n=93)	CD-R (n=69)	P value
Age	31±12	35±15	0.096
Sex(female)	36(38.7%)	31(44.9%)	0.427
Body Mass Index	19.5±3.9	20.8±4.3	0.049
Employment status	-	-	
no	27 (29.0%)	21 (30.5%)	0.961
retired	6 (6.5%)	3 (4.3%)	
yes	60 (64.5%)	45 (65.2%)	
Living status	-	-	
alone	3 (3.2%)	6 (8.7%)	0.248
with others	90 (96.8%)	63 (91.3%)	
Education	-	-	
up to 6 years	5 (5.4%)	4 (5.8%)	
up to 9 years	28 (30.1%)	18 (26.1%)	0.705
up to 12 years	44 (47.3%)	34 (49.3%)	
college	16 (17.2%)	13 (18.8%)	
Marital status	-	-	
married/cohabitating	53 (57.0%)	34 (49.3%)	0.579
widowed/divorced	7 (7.5%)	5 (7.2%)	
single	33 (35.5%)	30 (43.5%)	
Montreal location	-	-	
Ileal (L1)	35 (37.6%)	28 (40.7%)	
Colonic (L2)	15 (16.2%)	5 (7.2%)	0.808
Ileocolon (L3)	39 (41.9%)	33 (47.8%)	
upper gastrointestinal tract (L4)	1 (1.1%)	0 (0%)	
L4+L1/L2/L3	3 (3.2%)	3 (4.3%)	
Montreal behavior	-	-	
inflammatory	52 (55.9%)	45 (65.2%)	0.401
structuring	24 (25.8%)	16 (23.2%)	
penetrating	17 (18.3%)	8 (11.6%)	
Perianal disease	35 (37.6%)	28 (40.6%)	0.704
Current therapy	-	-	
no treatment	0 (0%)	2 (2.9%)	
corticosteroids	8 (8.6%)	7 (10.1%)	
5-aminosalicylates	21 (22.6%)	17 (24.6%)	0.169
immunomodulators	27 (29.0%)	22 (31.9%)	
antitumor necrosis factor	16 (17.2%)	9 (13.0%)	
combined therapy	21 (22.6%)	12 (17.5%)	
Anemia	-	-	
no	36 (38.7%)	55 (79.7%)	
mild	49 (52.7%)	10 (14.5%)	<0.001
moderate	6 (6.5%)	3 (4.3%)	
severe	2 (2.1%)	1 (1.5%)	
Relapses in the last year	-	-	
0	13 (14.0%)	35 (50.7%)	
1-2	57 (61.3%)	24 (34.8%)	<0.001
3	8 (8.6%)	8 (11.6%)	
≥4	15 (16.1%)	2 (2.9%)	
Disease duration (months)	13±25	11±19	0.594
C-reactive protein	24.3±34.4	8.8±18.8	0.001

Note: Data are presented as the number (%) or mean±standard deviation. CD-A refers to Crohn's disease patients in activity. CD-R refers to Crohn's disease patients in remission. CD=Crohn's disease

Table 2. Questionnaire survey in for Crohn's disease patients

Variable	CD-A (n=93)	CD-R (n=69)	P value
SCL-90			
Somatization	18.8±5.9	16.3±4.7	0.004
Obsessive-compulsive	19.0±5.4	15.4±4.4	<0.0001
Interpersonal sensitivity	15.4±5.8	12.1±4.0	<0.0001
Depression	24.7±9.1	18.3±5.2	<0.0001
Anxiety	16.2±5.3	12.4±3.2	<0.0001
Hostility	10.3±3.8	8.8±3.6	0.012
Phobic anxiety	9.7±3.3	8.2±2.0	0.001
paranoid	8.9±3.2	7.3±2.3	<0.0001
psychoticism	14.9±4.3	12.3±3.6	<0.0001
Other	12.6±3.9	9.9±2.5	<0.0001
SSRS			
objective support	8.8±2.8	9.3±2.4	0.239
Subjective Support	15.1±5.6	18.0±6.2	0.003
availability	6.9±1.7	7.4±1.7	0.080

Note: Data are presented as the mean±standard deviation. CD-A refers to Crohn's disease patients in activity. CD-R refers to Crohn's disease patients in remission. CD=Crohn's disease; SCL-90=Check List-90; SSRS= Social Support Rating Scale.

Table 3. Differences in questionnaire survey results between men (n=95) and women (n=67).

Variable	Men	Women	P value
SCL-90			
Somatization	17.2±5.0	19.5±6.4	0.030
Obsessive-compulsive	17.2±5.0	18.1±5.9	0.345
Interpersonal sensitivity	13.9±5.1	14.1±6.2	0.811
Depression	21.2±7.4	24.0±10.0	0.089
Anxiety	14.2±4.4	15.8±5.6	0.050
Hostility	9.6±3.6	9.5±4.3	0.932
Phobic anxiety	8.8±2.6	9.7±3.6	0.124
paranoid	8.1±2.8	8.5±3.4	0.515
psychoticism	13.7±4.1	13.9±4.3	0.734
Other	11.4±3.4	11.7±4.3	0.614
SSRS			
objective support	8.9±2.7	9.1±2.6	0.641
Subjective Support	16.4±5.7	16.1±6.6	0.757
availability	7.0±1.7	7.3±1.7	0.471

Note: Data are presented as the mean±standard deviation. CD=Crohn's disease; SCL-90=Check List-90; SSRS= Social Support Rating Scale.

Table 4. Results of the analysis of binary logistic regression analysis on disease activity

The factors	Hosmer and Lemeshow Test	S.E.	Wald	Beta	95% CI	P value
Univariate		-		-	-	-
age	0.466	0.012	2.727	0.980	0.957-1.004	0.099
Body Mass Index	0.155	0.040	3.760	0.925	0.855-1.001	0.053
Disease duration	0.494	0.007	0.284	1.004	0.990-1.018	0.594
C-reactive protein	0.000	0.011	11.378	1.039	1.016-1.062	0.001
objective support	0.434	0.061	1.389	0.931	0.827-1.049	0.239
Subjective Support	0.339	0.028	8.551	0.921	0.872-0.973	0.003
availability	0.504	0.095	3.017	0.849	0.705-1.021	0.082
Somatization	0.090	0.034	7.296	1.096	1.025-1.171	0.007
Obsessive compulsive	0.163	0.037	16.349	1.161	1.080-1.248	<0.001
Interpersonal sensitivity	0.130	0.038	13.650	1.153	1.069-1.243	<0.001
Depression	0.785	0.032	19.579	1.154	1.083-1.230	<0.001
Anxiety	0.039	0.058	20.748	1.301	1.162-1.456	0.039
Hostility	0.056	0.049	5.876	1.126	1.023-1.240	0.015
Phobic anxiety	0.601	0.079	9.578	1.275	1.093-1.488	0.002
Paranoid	0.212	0.081	10.490	1.300	1.109-1.523	0.001
Psychoticism	0.029	0.055	13.645	1.224	1.099-1.362	<0.001
Other	0.382	0.061	18.473	1.301	1.154-1.467	<0.001
Multivariate		-	-	-	-	-
Subjective Support	0.519	0.041	6.216	0.903	0.834-0.979	0.013
C-reactive protein		0.012	10.486	1.038	1.105-1.062	0.001
Anxiety		0.138	7.009	1.443	1.100-1.893	0.008
Other		0.103	4.155	1.235	1.008-1.512	0.042

Note: SE: standardized error, Durbin-Watson:1.980.

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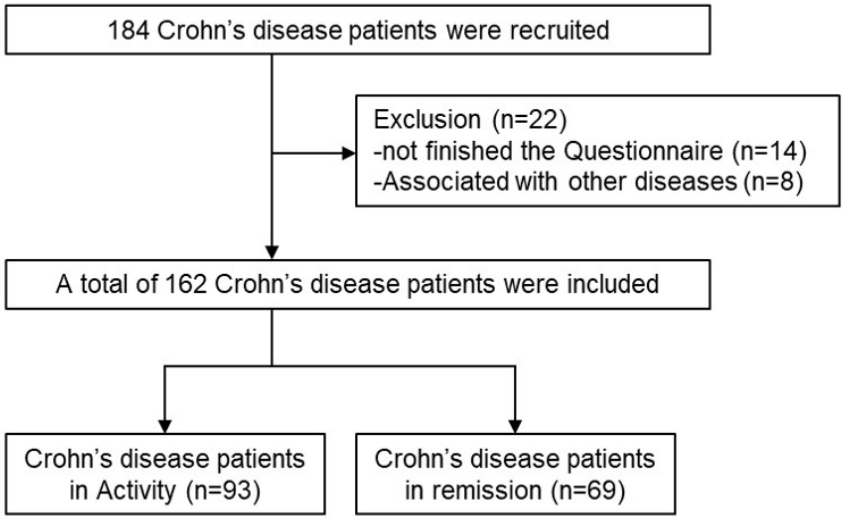

Figure 1: Flow diagram of the enrolled patients.

150x94mm (149 x 149 DPI)

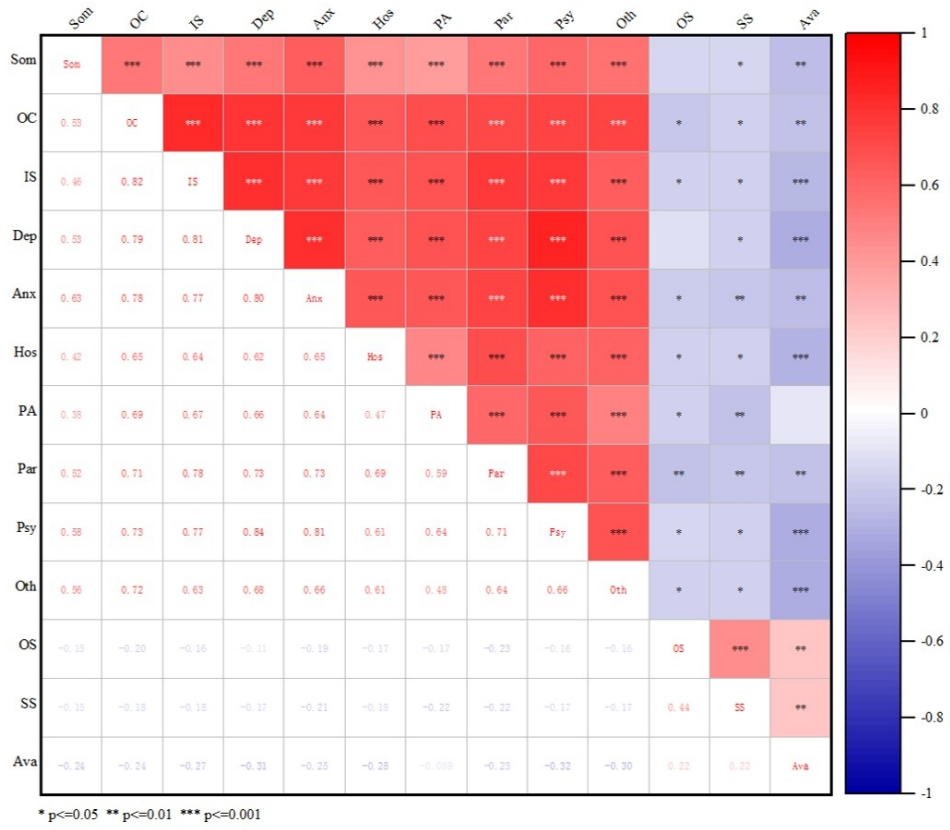

Figure 2. Analysis of the correlation of clinical data with social support and psychological factors.

192x165mm (143 x 143 DPI)

Supplementary materials

Table 1. Baseline characteristics of the study population of different genders

Characteristics	Male (n=95)	Female (n=67)	P value
Age	32±11	34±14	0.311
Disease activity (active)	57 (60.0%)	36 (53.7%)	0.427
Body Mass Index	20.0±4.3	19.7±3.6	0.641
Employment status	-	-	
no	26 (27.4%)	22 (32.8%)	0.448
retired	4 (4.2%)	5 (7.5%)	
yes	65 (68.4%)	40 (59.7%)	
Living status	-	-	
alone	5 (5.3%)	4 (6.0%)	0.847
with others	90 (94.7%)	63 (94.0%)	
Education	-	-	
up to 6 years	4 (4.2%)	5 (7.5%)	
up to 9 years	26 (27.4%)	20 (29.8%)	0.776
up to 12 years	48 (50.5%)	30 (44.8%)	
college	17 (17.9%)	12 (17.9%)	
Marital status	-	-	
married/cohabitating	52 (54.7%)	35 (52.2%)	0.736
widowed/divorced	8 (8.4%)	4 (6.0%)	
single	35 (36.9%)	28 (41.8%)	
Montreal location	-	-	
Ileal (L1)	33 (34.7%)	30 (44.8%)	
Colonic (L2)	12 (12.6%)	8 (11.9%)	0.674
Ileocolon (L3)	45 (47.4%)	27 (40.3%)	
upper gastrointestinal tract (L4)	1 (1.1%)	0 (0%)	
L4+L1/L2/L3	4 (4.2%)	2 (3.0%)	
Perianal disease	36 (37.9%)	27 (40.3%)	0.757
Current therapy	-	-	
no treatment	0 (0%)	2 (3.0%)	
corticosteroids	9 (9.5%)	6 (8.9%)	
5-aminosalicylates	20 (21.1%)	18 (26.9%)	0.497
immunomodulators	29 (30.5%)	20 (29.9%)	
antitumor necrosis factor	17 (17.8%)	8 (11.9%)	
combined therapy	20 (21.1%)	13 (19.4%)	
Anemia	-	-	
no	63 (66.3%)	28 (41.8%)	
mild	27 (28.4%)	32 (47.8%)	0.021
moderate	4 (4.2%)	5 (7.5%)	
severe	1 (1.1%)	2 (2.9%)	
Relapses in the last year	-	-	
0	26 (27.4%)	22 (32.8%)	
1-2	42 (44.2%)	39 (58.2%)	0.020
3	12 (12.6%)	4 (6.0%)	
≥4	15 (15.8%)	2 (3.0%)	
Disease duration (months)	13±25	11±19	0.582
C-reactive protein	13.2±24.7	11.5±18.5	0.634

Note: Data are presented as the number (%) or mean±standard deviation. CD, Crohn's disease.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
	Yes	(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2 Yes	Explain the scientific background and rationale for the investigation being reported
Objectives	3 Yes	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4 Yes	Present key elements of study design early in the paper
Setting	5 Yes	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6 Yes	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7 Yes	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8* Yes	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9 Yes	Describe any efforts to address potential sources of bias
Study size	10 Yes	Explain how the study size was arrived at
Quantitative variables	11 Yes	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12 Yes	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13* Yes	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14* Yes	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15* Yes	Report numbers of outcome events or summary measures
Main results	16 Yes	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17 Yes	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18 Yes	Summarise key results with reference to study objectives
Limitations	19 Yes	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20 Yes	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21 Yes	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22 Yes	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.