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Analysis of the Correlation between Traditional Chinese Medicine Syndrome Types and Inflammatory Activity Factors in Ulcerative Colitis

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Abstract: *The purpose of this study is to explore the relationship between inflammatory active factors and traditional Chinese medicine (TCM) syndrome differentiation and classification of UC, and to provide a reference basis for the future treatment of this disease by combining traditional Chinese and Western medicine. We Collected 286 patients with Ulcerative colitis who were admitted to our hospital from January 2022 to April 2023 and met the diagnostic criteria. We classified the patients by disease stage, activity grade and lesion range, classified them according to their clinical data by TCM syndrome differentiation, and collected the measured values of peripheral blood erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and fecal calprotectin (FC), SPSS software was used to analyze the collected data, and 2-test, two independent sample t-test, one-way ANOVA and other methods were used to analyze, to explore the TCM syndrome types of Ulcerative colitis, and to analyze the correlation between the range of lesions, disease stages, activity grades and inflammatory activity factors of patients. The results showed that among 286 patients, there were 148 cases of dampness heat syndrome in the large intestine, with the highest proportion (51.75%), followed by 82 cases of spleen deficiency and dampness accumulation syndrome (28.67%), and 56 cases of liver depression and spleen deficiency syndrome (19.58%); The content of inflammatory activity factors (ESR, CRP, FC) in the large intestine dampness heat syndrome group was significantly higher than that in the other two syndrome types, while the content of inflammatory activity factors in the liver depression spleen deficiency syndrome group was slightly higher than that in the spleen deficiency dampness accumulation syndrome group (P<0.05). The content of inflammatory activity factors in the patients during the disease activity period was significantly higher than that in the clinical remission period (P<0.05); The content of inflammatory activity factors in the severe activity group was significantly higher than that in the mild and moderate activity groups, and there was no difference in the content between the moderate activity group and the mild activity group (P>0.05). In the range of lesion location, patients with extensive colon type have the highest expression of inflammatory activity factors, followed by the left colon type and the rectum type (P>0.05). The vast majority of patients in clinical remission stage have spleen deficiency and dampness accumulation syndrome, followed by liver depression and spleen deficiency syndrome, and a few patients have large intestine dampness heat syndrome; The main type of mild active phase patients is spleen deficiency and dampness accumulation syndrome, followed by large intestine dampness heat syndrome, and a few patients are spleen deficiency and liver stagnation syndrome; Both moderate and severe active stage patients are mainly characterized by large intestine dampness heat syndrome (P<0.05). Resultly, the levels of inflammatory activity factors in patients with ulcerative colitis can objectively reflect the clinical activity and severity of the disease. The vast majority of patients have dampness heat syndrome of the large intestine, which has higher predictive value.*

Keywords: *Ulcerative colitis; Traditional Chinese Medicine Syndrome Types; Inflammatory activity factor*

1. Introduction

Ulcerative colitis (UC) is a subtype of inflammatory bowel disease (IBD) and an autoimmune disease. Studies have shown that [1] environmental factors play an important role in the pathogenesis of IBD, including early events such as birth mode, breastfeeding, exposure to antibiotics, and other factors

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such as air pollution, smoking, mental state, exercise and diet. Both are potential environmental factors for the development or disease activity of IBD. UC is an idiopathic chronic inflammatory disease of the colon mucosa, characterized by a slow onset and a longer course of disease. The main clinical manifestations include abdominal pain, diarrhea, mucus and bloody stools, and the condition is persistent and difficult to cure. It is prone to recurrence and has a lifelong tendency to recur [2]. Patients with recurrent attacks and a longer course of disease have an increased probability of cancer transformation. The clinical course time is unpredictable, characterized by alternating periods of acute onset and remission, greatly reducing the quality of life of patients [3,4]. Moreover, in recent years, research has found that [5] UC patients with hypercoagulable blood and thromboembolic diseases pose a great threat to their lives. Therefore, it has increasingly attracted clinical attention. There is no word UC in Traditional Chinese medicine, but it can be classified into the categories of "diarrhea" and "enterophilia" according to the symptoms and signs [6]. The patients mostly show the symptoms of "retention of dampness toxin, qi injury and blood failure", which are caused by imbalance of yin and yang, emotional imbalance, stagnation of qi and blood, spleen and stomach weakness [7,8]. According to the correlation between UC activity index and its lesion range, disease stage, activity classification, and TCM syndrome types, Traditional Chinese medicine can divide it into four types: large intestine damp heat syndrome, spleen deficiency and damp accumulation syndrome, liver stagnation and spleen deficiency syndrome, and qi stagnation and blood stasis syndrome [9]. At present, western medicine mainly treats UC with oral and local aminosalicylic acid preparations, glucocorticoids, Immunosuppressive drug, biological agents, etc. Traditional Chinese medicine syndrome differentiation and treatment has become an indispensable treatment method for UC. In the treatment process, the staging of the disease is combined with traditional Chinese medicine syndrome differentiation. By observing the correlation with objective indicators, the focus of treatment is explored to improve the clinical treatment effect of the disease. Therefore, this article collects clinical data from 286 patients with UC, analyzes their lesion range, disease staging, and activity grading characteristics, explores the relationship between inflammatory activity factors and traditional Chinese medicine syndrome differentiation, and provides a reference basis for the future treatment of this disease with traditional Chinese and Western medicine.

2. Research methods and objects

2.1. Research subjects

Collect patients with ulcerative colitis who visited the anorectal department of our hospital from January 2022 to April 2023. (1) Diagnostic criteria: Refer to the Western medicine diagnostic criteria for ulcerative colitis [10] and the Disease Activity Index (UCAI) score based on the 2017 Consensus on the Integrated Diagnosis and Treatment of Chinese and Western Medicine for Ulcerative Colitis; The diagnostic criteria for traditional Chinese medicine syndromes [11] are based on the 2017 Consensus of Experts on the Diagnosis and Treatment of Ulcerative Colitis in Traditional Chinese Medicine. (2) Inclusion criteria: Those who meet the diagnostic criteria of Chinese and Western medicine and are over 18 years old. (3) Exclusion criteria: (a) Those with severe complications, such as local stenosis, intestinal obstruction, intestinal perforation, etc.; (b) Serious abnormalities of important organs or other life-threatening serious diseases; (c) Individuals with mental illness; (d) Women in special periods.

2.2. Research Methods

2.2.1. Staging and classification of UC

According to the improved Mayo scoring standard, evaluate the patient's bowel frequency, endoscopic mucosal lesions, bloody stools, and overall physician score. Relief period: 0-2 points; Activity period: ≥ 3 points, specifically: 3-5 points for mild activity period; Moderate activity period: 6-10 points; Severe activity period: 11-12 points. According to the Montreal classification, combined with the location and clinical manifestations of endoscopic lesions in patients, they are divided into rectal type, left colon type, and extensive colon type.

2.2.2. Traditional Chinese Medicine Syndrome Differentiation and Classification

We collected clinical data of patients, referred to the 2017 Consensus of Chinese Medicine Diagnosis and Treatment Experts on Ulcerative colitis, and classified patients according to TCM syndrome differentiation. The evaluation was jointly conducted by a chief physician and a deputy chief physician.

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2.2.3. Inflammatory activity factors

The peripheral blood erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and fecal calprotectin (FC) were recorded during the examination.

2.2.4. Statistical methods

SPSS 26.0 software was used for statistical analysis. Four chi square tests were used for counting data, while mean ± standard deviation was used for measurement data. Two independent sample t-tests or one-way analysis of variance were used for inter group comparison, with $P<0.05$ indicating statistically significant differences.

3. Results

3.1. General Information Results

The research results showed that among the 286 patients included, there were 152 males and 134 females, with an average age of (43.86 ± 6.51) years.

3.2. Distribution of Traditional Chinese Medicine Syndrome Types, Disease Stages, and Range of Lesions

The results of traditional Chinese medicine syndrome differentiation and classification showed that among 286 UC patients, 148 cases (51.75%) had dampness and heat syndrome in the large intestine, 82 cases (28.67%) had spleen deficiency and dampness accumulation syndrome, and 56 cases (19.58%) had liver depression and spleen deficiency syndrome. The disease staging results showed that among 286 UC patients, 47 were in clinical remission stage (16.43%), 126 were mildly active (44.06%), 83 were moderately active (29.02%), and 30 were severely active (10.49%). The results of lesion distribution showed that among 286 UC patients, there were 137 cases of rectal type (47.90%), 101 cases of left hemicolon type (35.31%), and 48 cases of extensive colon type (16.78%). See Table 1.

Table 1: Distribution of Traditional Chinese Medicine Syndrome Types, Disease Stages, and Range of Lesions in UC

category	TCM syndrome	Number of cases	Percentage (%)
Pattern	Large intestinal dampness-heat pattern	148	51.75%
	Spleen deficiency with dampness accumulation	82	28.67%
	Liver depression and spleen deficiency pattern	56	19.58%
Stage	Remission stage	47	16.43%
	Mile active group	126	44.06%
	Moderate active group	83	29.02%
	Severe active group	30	10.49%
Type	Rectal UC	137	47.90%
	Left hemicolon UC	101	35.31%
	Extensive UC	48	16.78%

3.3. The relationship between UC Mayo activity grading and traditional Chinese medicine syndrome classification

The results of this study showed that in the distribution of traditional Chinese medicine syndrome types in 286 UC patients, the clinical remission period was mainly characterized by spleen deficiency and dampness accumulation syndrome, followed by liver depression and spleen deficiency syndrome, and again by large intestine dampness heat syndrome ($P<0.05$); Patients in mild active phase mainly have spleen deficiency and dampness accumulation syndrome, followed by large intestine dampness heat syndrome, and then spleen deficiency and liver stagnation syndrome ($P<0.05$); Both moderate and severe active stage patients are mainly characterized by large intestine dampness heat syndrome ($P<0.05$). See Table 2.

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Table 2: Relationship between UC Mayo activity grading and traditional Chinese medicine syndrome classification

Mayo Activity Rating	Number of cases	Large intestinal dampness-heat pattern		Liver depression and spleen deficiency pattern		Spleen deficiency with dampness accumulation	
		N	(%)	N	(%)	N	(%)
Remission stage	47	4	8.51	14	29.79	29	61.70
Mile active group	126	32	25.40	16	12.70	78	61.90
Moderate active group	83	55	66.27	17	20.48	11	13.25
Severe active group	30	21	70.00	6	20.00	3	10.00
$\chi 2$		26.77		18.02		21.96	
P		<0.001		<0.001		<0.001	

3.4. Comparison of inflammatory activity factors among different traditional Chinese medicine syndrome types in UC patients

The research results show that. The content of inflammatory activity factors (ESR, CRP, FC) in the large intestine dampness heat syndrome group was significantly higher than those in the other two groups, while the content of inflammatory activity factors in the liver depression spleen deficiency syndrome group was slightly higher than that in the spleen deficiency dampness accumulation syndrome group (P<0.05). See Table 3.

Table 3: Comparison of inflammatory activity factors among different traditional Chinese medicine syndrome types in UC patients (χ±s)

Pattern	Number of cases	ESR(mm/h)	CRP(mg/L)	FC(ug/g)
Large intestinal dampness-heat pattern	148	24.91±14.20*#	13.99±9.26*#	996.84±427.33*#
Spleen deficiency with dampness accumulation	82	8.14±3.88#	2.66±1.25	188.27±98.49#
Liver depression and spleen deficiency pattern	56	11.88±7.12	3.63±2.27#	326.86±213.02
F		14.873	28.531	300.019
P		<0.001	<0.001	<0.001

Note: Compared with liver depression and spleen deficiency syndrome* P<0.05; Compared with spleen deficiency and dampness accumulation syndrome, # P<0.05.

3.5. Comparison of inflammatory activity factors between remission and active stages of UC

The research results showed that the levels of inflammatory activity factors (ESR, CRP, FC) in the active phase group were significantly higher than those in the remission phase group, with statistical significance (P<0.05). See Table 4.

Table 4: Comparison of inflammatory activity factors between remission and active stages of UC (χ±s)

Stage	Number of cases	ESR(mm/h)	CRP(mg/L)	FC(ug/g)
Remission stage	47	5.76.91±2.20#	3.07±1.28#	83.54±107.03#
Activation	239	18.38±10.02#	8.27±10.60#	606.03±493.12#
t		7.805	12.72	131.04
P		<0.001	<0.001	<0.001

Note: Compared to the activity period, # P<0.05.

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3.6. UC comparison of inflammatory activity factors in patients with mild, moderate, and severe UC activity groups

The research results showed that the inflammatory activity factors in patients with severe activity were significantly higher than those in patients with moderate and mild activity (P<0.05); There was no difference in the content of inflammatory activity factors between the moderate and mild activity groups (P>0.05). See Table 5.

Table 5: Comparison of inflammatory activity factors in patients with mild, moderate, and severe UC activity groups (χ±s)

Group	Number of cases	ESR(mm/h)	CRP(mg/L)	FC(ug/g)
Mile active group	126	12.97±10.07*#	3.11±4.29*#	365.28±234.93*#
Moderate active group	83	18.28±11.72#	10.33±7.50#	629.82±508.35#
Severe active group	30	24.66±18.35	12.77±10.31	996.42±581.36
F		12.24	38.68	246.91
P		0.012	<0.001	<0.001

Note: Compared with the moderate activity group, * P<0.05; Compared with the severely active group, # P<0.05.

3.7. UC comparison of inflammatory activity factors in different lesion ranges

The research results showed that the content of inflammatory activity factors in the extensive colon type was the highest, and there was no statistically significant difference between the groups (P>0.05). See Table 6.

Table 6: Comparison of inflammatory activity factors in different lesion ranges of UC (χ±s)

Group	Number of cases	ESR(mm/h)	CRP(mg/L)	FC(ug/g)
Rectal UC	137	9.30±6.37*#	4.71±3.03*#	498.18±338.43*#
Left hemicolon UC	101	15.72±13.92#	7.22±7.30#	520.32±347.65#
Extensive UC	48	17.82±15.30	9.27±10.01	596.62±511.56
F		6.94	44.52	28641
P		0.16	0.57	0.82

3.8. The relationship between different lesion ranges and traditional Chinese medicine syndrome types

Table 7: Relationship between different lesion ranges and traditional Chinese medicine syndrome types (%)

Group	Number of cases	Large intestinal dampness-heat pattern		Liver depression and spleen deficiency pattern		Spleen deficiency with dampness accumulation	
		N	(%)	N	(%)	N	(%)
Rectal UC	137	73	53.28	30	21.90	34	24.82
Left hemicolon UC	101	41	40.59	12	11.88	48	47.52
Extensive UC	48	23	47.92	10	20.83	15	31.25
χ2		28.94		23.18		16.77	
P		<0.001		<0.001		<0.001	

The research results show that the traditional Chinese medicine syndrome types of patients with rectal UC are mainly large intestine dampness heat syndrome, while the traditional Chinese medicine syndrome types of patients with left half colon UC are mainly spleen deficiency dampness

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accumulation and large intestine dampness heat syndrome. The traditional Chinese medicine syndrome types of patients with extensive colon UC are mainly large intestine dampness heat syndrome. See Table 7.

4. Discussions

Ulcerative colitis (UC) is a subtype of inflammatory bowel disease, an autoimmune disease, and an idiopathic chronic inflammatory disease of the colonic mucosa. Bloody diarrhea is the characteristic symptom of the disease, and the determination of its disease activity is crucial for guiding treatment, therapeutic efficacy evaluation, and prognosis judgment [12]. Therefore, the treatment process of UC patients requires long-term and frequent monitoring of the degree of intestinal mucosal healing or inflammation. Repeated endoscopic examinations and mucosal biopsies increase the patient's pain and economic burden, thereby reducing their compliance. Related studies have shown [13] that CRP and ESR, as sensitive indicators of inflammatory activity, have significant value in evaluating the severity and prognosis of UC, and are significantly correlated with the disease activity stage and endoscopic mucosal tissue manifestations of patients. Scholars have evaluated the Baron score of UC patients under endoscopy [14] and found that FC has the best correlation with endoscopic disease activity, which is suitable for non-invasive monitoring of disease activity in UC patients. Therefore, FC combined with ESR and CRP can help determine the activity of UC, evaluate treatment effectiveness, and predict disease recurrence. This study compared the content of inflammatory activity factors in different disease stages and activity grades of UC, confirming that the content of inflammatory activity factors in patients is closely related to disease stages and activity grades. The content of ESR, CRP, and FC objectively reflects the clinical disease activity and severity of UC. Alternatively, it can be used to predict disease recurrence, evaluate treatment effectiveness, and apply it to clinical disease activity monitoring in UC.

The results of this study showed that among 286 patients with UC, patients in clinical remission were mainly characterized by spleen deficiency and dampness accumulation syndrome (61.7%), followed by liver depression and spleen deficiency syndrome (29.79%), and large intestine dampness heat syndrome (8.51%), with a statistically significant difference ($P<0.05$); Patients in mild active phase mainly have spleen deficiency and dampness accumulation syndrome, followed by large intestine dampness heat syndrome, and then spleen deficiency and liver stagnation syndrome ($P<0.05$); Both moderate and severe active stage patients are mainly characterized by large intestine dampness heat syndrome, which is consistent with the research results of Zhang Tianhan and Hu Jiangtao [7,15]. Scholars such as Wang Volunteer [16] identified three main syndrome types from 120 UC patients through factor analysis and cluster analysis, namely the large intestine dampness heat syndrome with spleen deficiency dampness obstruction syndrome (45%), the mixed cold and heat syndrome with liver depression and spleen deficiency syndrome (28%), and the liver depression and spleen deficiency syndrome with spleen yang deficiency syndrome (27%); Zhou Yuqian et al. [17] analyzed the proportion of traditional Chinese medicine differentiation in 80 UC patients, and found that the proportion of syndrome types was in descending order: large intestine dampness heat syndrome, liver depression spleen deficiency syndrome, spleen qi weakness syndrome, spleen kidney yang deficiency syndrome, blood stasis intestinal collateral syndrome, yin blood deficiency syndrome. Compared with patients in the active phase and in the remission phase, liver depression spleen deficiency syndrome and large intestine dampness heat syndrome appeared more frequently ($P<0.05$), which is basically consistent with the results of this study. The possible reason for this may be that during the active period of UC, the body is mainly pathogenic, with damp heat accumulating in the intestines, intersecting with qi and blood, transforming into pus, internal ulceration into ulcers, collateral damage and blood overflow, leading to the onset of red and white dysentery. Damp heat is an important trigger factor for disease activity and also an important reason for the recurrence and persistence of UC. The remission period is usually characterized by a combination of deficiency and excess. Diarrhea originates from the spleen and stomach, based on the deficiency and cold of the spleen and stomach. The spleen and stomach are weak, and the liver qi is reversed, damaging the spleen soil and making the spleen more deficient. There is also dampness and heat, which can linger on the intestines, damage the intestinal collaterals, and lead to persistent diarrhea.

Early studies have pointed out that [18] dampness heat syndrome is associated with high levels of inflammatory cytokines (CRP, TNF)- α, IL-6, IL-8), Humoral immunity hyperfunction (IgG, IgM), and low cellular immune status (CD4, CD4/CD8). Scholar Yang Lichun [19] and other experiments analyzed the syndrome types of 180 patients with UC, detected the levels of IL-6 and IL-8 in the serum of UC patients and healthy volunteers, and found that the syndrome of damp heat accumulation was the

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highest proportion of UC patients. Subsequently, domestic scholars Zhang Tianhan et al. [9] also found in their research that ESR, CRP, and FC were expressed the highest in patients with large intestine dampness heat syndrome, which is consistent with the results of this study and increases the credibility of this study. According to a study by domestic scholar Jia Zijun [20], TNF levels in the serum of patients with dampness heat syndrome and excessive heat toxin syndrome in the large intestine- α, IL-1 β, the levels of IL-6 and IL-8 significantly increased, indicating a correlation between dampness heat syndrome and inflammation. Analysis of its mechanism may be that the local inflammatory factors in the mucosa of damp heat syndrome increase, and induce neutrophils and Monocyte to secrete and release Prostaglandin, Leukotriene and other inflammatory substances, which promote the congestion, edema, degeneration and necrosis of the intestinal mucosa, and eventually erosion, forming ulcers, while the intestinal epithelial barrier dysfunction causes the abnormal displacement of intestinal bacteria, which aggravates the inflammatory reaction again, not only that, the weakening of intestinal mucosal protective factors stimulated by inflammatory substances leads to a decrease in protective function, resulting in an imbalance between inflammatory and anti-inflammatory cytokines, leading to the chronic inflammatory process of the disease. In addition, from the results of this study, it can be seen that the content of inflammatory activity factors in patients during the active phase of the disease is significantly higher than that in the remission phase, especially in patients during the severe active phase. The levels of ES, RCR, and PFC are (24.66±18.35) mm/h, (12.77±10.31) mg/L, and (996.42±581.36) ug/g, respectively, which are significantly higher than those in other active periods, and the difference is statistically significant ($P<0.05$).

In addition, the results of this study also showed that patients with extensive colon type UC had the highest content of inflammatory activity factors, with a statistically significant difference compared to other types ($P<0.05$). In patients with rectal type UC, the traditional Chinese medicine syndrome was mainly characterized by large intestine dampness heat syndrome. In patients with left hemicolon type UC, the traditional Chinese medicine syndrome was mainly characterized by spleen deficiency dampness accumulation and large intestine dampness heat syndrome. In patients with extensive colon type UC, the traditional Chinese medicine syndrome was mainly characterized by large intestine dampness heat syndrome, Consistent with other domestic research results [15]. The reason may be that UC belongs to Inflammatory bowel disease, and most of the inflammatory diseases are caused by heat. According to "Lingshu Carbuncle and Gangrene", "excessive heat leads to meat rot, and meat rot leads to pus". The accumulation of heat in the local area often leads to ulceration and erosion, while improper diet, emotional imbalance, and excessive phlegm and dampness can all accumulate heat and cause stagnation, leading to the transformation of fire; However, when the pathogenic gas of pestilence damages the air component, the patchy or complete disappearance of mucosal blood vessels occurs. When the pathogenic gas of pestilence damages the blood component, the bleeding mucosa oozes blood, and bleeding occurs to different degrees. When the pathogenic gas of dampness and heat continues to be unsolved, the blood flows inside, and knots in the lipid membrane of the intestines, widespread erosion and ulcers appear. Among them, granulocytes and Monocyte release more inflammatory substances, which aggravate the congestion, edema, degeneration, and necrosis of intestinal mucosa, causing tissue erosion, Eventually, ulcers form.

In summary, measuring the levels of inflammatory activity factors (ESR, CRP, and FC) in UC patients through the Mayo disease activity score is helpful for traditional Chinese medicine syndrome differentiation and classification, reflecting the degree and prognosis of UC lesions, determining treatment plans, and providing reference basis for precise TCM syndrome differentiation in clinical practice, improving the clinical diagnosis and treatment effectiveness of this disease.

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