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# Clinical value analysis of routine ultrasound combined with endoscopic ultrasonography in judging ulcerative colitis

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ABSTRACT

**Objective:** To study the clinical value of routine ultrasound combined with endoscopic ultrasonography in judging ulcerative colitis. **Methods:** A total of 60 cases of patients with ulcerative colitis were collected as observation group of research and 60 cases of healthy volunteers were collected as control group of research. Intestinal wall thickness was detected by white light endoscopy, abdominal intestinal ultrasound and endoscopic ultrasonography; TNF- α , IL-1 β , IL-4 and IL-10 contents were detected by Elisa kit; Th1, Th2, Th17 and Treg ratios were detected by flow cytometry. **Results:** (1) intestinal wall thickness: intestinal wall thickness of both active UC patients and quiescent UC patients was significantly higher than that of control group, intestinal wall thickness of active UC patients was significantly higher than that of quiescent UC patients and the higher the degree of activity, the higher the intestinal wall thickness; (2) inflammatory mediators: TNF- α and IL-1 β contents in intestinal mucosa of active UC patients were higher than those of quiescent UC patients and positively correlated with intestinal wall thickness; IL-4 and IL-10 contents were lower than those of quiescent UC patients and negatively correlated with intestinal wall thickness; (3) T cell contents: Th1 and Th17 cell contents in intestinal mucosa of active UC patients were higher than those of quiescent UC patients and positively correlated with intestinal wall thickness; Th2 and Treg cell contents in intestinal mucosa of active UC patients were lower than those of quiescent UC patients and negatively correlated with intestinal wall thickness. **Conclusion:** Routine ultrasound combined with endoscopic ultrasonography can accurately determine the severity of ulcerative colitis; measured intestinal wall thickness is closely correlated with the degree of inflammation and abnormal immune response.

## 1. Introduction

Ulcerative colitis (UC) is a kind of etiology-unclear nonspecific inflammatory bowel disease and belongs to the category of inflammatory bowel disease. UC is progressive, and clinical symptoms are with protracted course of disease, recurrence and without obvious specificity. Clinical diagnosis and judgment of UC are difficult and currently rely mainly on clinical symptoms, signs, colonoscopy and biopsy, which have difficulty in accurately judging the severity. Endoscopic ultrasonography is an assistant examination method developed in recent years that can measure the ulcerative colitis lesion with the assistance of endoscopy. In the following research, the clinical value of routine ultrasound combined with endoscopic ultrasonography in judging ulcerative colitis was analyzed.

## 2. Materials and methods

### *2.1. Case origin*

A total of 60 cases of patients diagnosed with ulcerative colitis in outpatient and ward were collected as observation group of

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research, including 38 male cases and 22 female cases with age of (46.95±5.68) years; 60 cases of healthy volunteers were collected as control group of research, including 35 male cases and 25 female cases with age of (47.12±5.96) years. All subjects were informed of research matter and received white light endoscopy, abdominal intestinal ultrasound and endoscopic ultrasonography examination.

### 2.2. Staging criteria of UC patients under white light endoscopy

Stages were divided according to the mucosal morphology of UC under white light endoscopy: (1) quiescent stage: visible random arrangement of submucosal blood vessels or associated with inflammatory polyp; (2) active stage: decrease of submucosal vascular permeability as well as fine granular and local purulent secretion were considered as mild degree; obvious mucosal edema and hyperemia, multiple erosion or superficial geographic aphthae as well as purulent secretion attachment were considered as moderate degree; multiple ulcer with deep depth, integration of longitudinal and geographic ulcers as well as scattered island mucosal residue were considered as severe degree.

### 2.3. Detection of inflammatory mediator contents in intestinal mucosa biopsy tissue

Moderate amount of intestinal mucosa biopsy tissue was taken, added to PBS, then homogenized and centrifuged to get cell suspension, and human Elisa kits were used to detect TNF-α, IL-1β, IL-4 and IL-10 contents.

### 2.4. Detection of T cell contents in intestinal mucosa biopsy tissue

Moderate amount of intestinal mucosa biopsy tissue was taken, added to PBS, then homogenized and centrifuged to get cell suspension, which was added to red blood cell lysis buffer to break red blood cells, then centrifuged again and washed with PBS twice, then cells were separately put in flow cytometer reaction tubes to incubate different fluorescence-labeled monoclonal antibodies respectively and incubation time was 15 min; after incubation, PBS wash and centrifuge were carried out twice, finally PBS containing 5% FBS was added and ratios of Th1, Th2, Th17 and Treg cells were detected in flow cytometer.

### 2.5. Statistical methods

Detected data was processed by SPSS 20.0 software, measurement data was by *t* test and correlation analysis was by *Pearson* test. Differences were considered to be statistically significant at a level of $P<0.05$.

## 3. Results

### 3.1. Image results of routine intestinal ultrasound and endoscopic ultrasonography

Image results of routine intestinal ultrasound were shown in Figure 1, left figure was the routine ultrasound image of normal intestine of healthy volunteer and right figure was the routine ultrasound image of intestinal lesion segment of UC patient; image results of endoscopic ultrasonography were shown in Figure 2, left figure was the endoscopic ultrasonography image of normal intestine of healthy volunteer and right figure was the endoscopic ultrasonography image of intestinal lesion segment of UC patient.

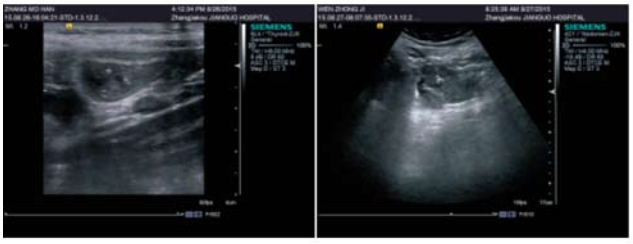

**Figure 1.** Image results of routine intestinal ultrasound. Left figure: for healthy volunteer; right figure: for UC patient.

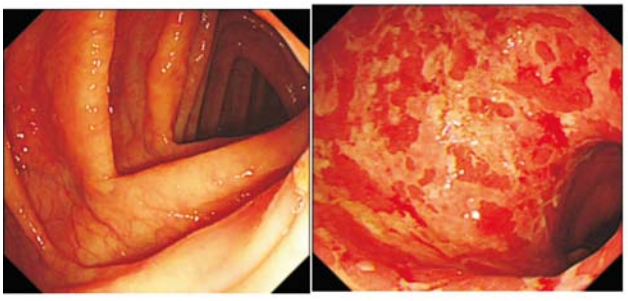

**Figure 2.** Image results of endoscopic ultrasonography. Left figure: for healthy volunteer; right figure: for UC patient.

### 3.2. Measurement results of intestinal wall thickness by endoscopic ultrasonography

Measurement results of intestinal wall thickness of healthy subjects and UC patients were shown in Figure 3 (Left), and detailed analysis was as follows: intestinal wall thickness of both active UC patients and quiescent UC patients was significantly higher than that of control group and intestinal wall thickness of active UC patients was significantly higher than that of quiescent UC patients; measurement results of intestinal wall thickness of active UC patients with different degrees of lesion were shown in Figure 3 (Right), and detailed analysis was as follows: and the higher the degree of activity, the higher the intestinal wall thickness.

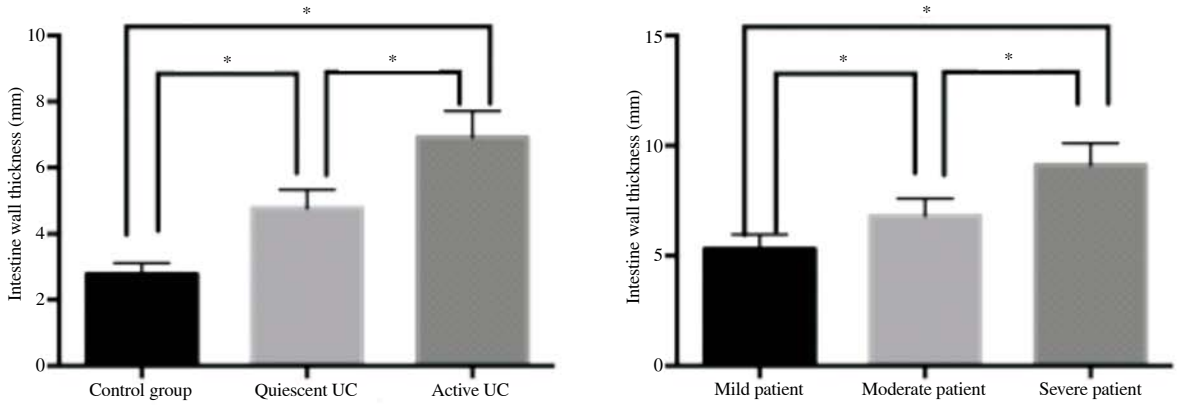


**Figure 3.** Measurement results of intestinal wall thickness by endoscopic ultrasonography. Left figure was the measurement results of intestinal wall thickness of healthy subjects and UC patients; right figure was the measurement results of intestinal wall thickness of active UC patients with different degrees of lesion.

### *3.3. Inflammatory mediator contents in intestinal mucosa biopsy tissue and their correlation with intestinal wall thickness*

Comparison of inflammatory mediator contents in intestinal mucosa biopsy tissue of active UC patients and quiescent UC patients showed that TNF-α and IL-1β contents in intestinal mucosa of active UC patients were higher than those of quiescent UC patients, IL-4 and IL-10 contents were lower than those of quiescent UC patients, and details were shown in Table 1; correlation analysis between inflammatory mediator contents and intestinal wall thickness showed that TNF-α and IL-1β contents in intestinal mucosa were positively correlated with intestinal wall thickness, IL-4 and IL-10 contents were negatively correlated with intestinal wall thickness, and details were shown in Table 2.

**Table 1.**
Inflammatory mediator contents in intestinal mucosa biopsy tissue.

| Group | TNF-α | IL-1β | IL-4 | IL-10 |
|---|---|---|---|---|
| Quiescent UC | 65.52±7.54 | 54.42±6.57 | 167.78±20.13 | 135.63±15.69 |
| Active UC | 129.79±14.18 | 89.25±10.34 | 104.52±12.12 | 80.39±9.49 |
| *T* | 9.492 | 8.182 | 7.384 | 6.974 |
| *P* | <0.05 | <0.05 | <0.05 | <0.05 |

**Table 2.**
Correlation between inflammatory mediator contents in intestinal mucosa biopsy tissue and intestinal wall thickness.

| Item | Regression coefficient b | Correlation coefficient r | Statistics | *P* |
|---|---|---|---|---|
| TNF-α | 1.184 | 0.772 | 12.032 | <0.05 |
| IL-1β | 1.304 | 0.714 | 9.485 | <0.05 |
| IL-4 | -0.981 | -0.810 | 18.784 | <0.05 |
| IL-10 | -1.157 | -0.753 | 14.689 | <0.05 |

### *3.4. T cell contents in intestinal mucosa biopsy tissue and their correlation with intestinal wall thickness*

Comparison of T cell contents in intestinal mucosa biopsy tissue of active UC patients and quiescent UC patients showed that Th1 and Th17 cell contents in intestinal mucosa of active UC patients were higher than those of quiescent UC patients and contents of Th2 and Treg cells were lower than those of quiescent UC patients. Correlation analysis between T cell contents and intestinal wall thickness showed that Th1 and Th17 cell contents were positively correlated with intestinal wall thickness and contents of Th2 and Treg cells were negatively correlated with intestinal wall thickness.

**Table 3.**
T cell contents in intestinal mucosa biopsy tissue (%).

| Group | Th1 | Th2 | Th17 | Treg |
|---|---|---|---|---|
| Quiescent UC | 8.34±0.92 | 9.23±1.03 | 2.01±0.23 | 5.54±0.60 |
| Active UC | 14.59±1.85 | 5.94±0.66 | 3.24±0.36 | 3.48±0.41 |
| *T* | 8.192 | 7.784 | 7.029 | 6.862 |
| *P* | <0.05 | <0.05 | <0.05 | <0.05 |

**Table 4.**
Correlation between T cell contents in intestinal mucosa biopsy tissue and intestinal wall thickness.

| Item | Regression coefficient b | Correlation coefficient r | Statistics | *P* |
|---|---|---|---|---|
| Th1 | 0.812 | 0.716 | 14.582 | <0.05 |
| Th2 | -1.039 | -0.774 | 12.964 | <0.05 |
| Th17 | 1.338 | 0.820 | 16.189 | <0.05 |
| Treg | -0.946 | -0.793 | 10.395 | <0.05 |

## 4. Discussion

Ulcerative colitis lesion is mainly confined to the mucosa and submucosa, manifested as diffuse infiltration of inflammatory cells, and severe cases may show extensive abnormality of mucosal structure, capillary dilation and hyperemia as well as formation of crypt abscess[1]. Conventional endoscopic examination and pathologic biopsy of tissue are able to observe the lesion on mucosal surface and evaluate the degree of inflammatory cell infiltration in the deep tissue, but they cannot accurately assess the edema and thickening condition in intestinal mucosa and submucosa or accurately judge the severity of illness[2]. Conventional abdominal intestinal ultrasound can observe the layers of intestinal wall through ultrasound, which are, in turn from outside to inside, high-echo serosal layer, low-echo muscular layer, high-echo submucosal layer, low-echo mucosal muscular layer and high-echo mucosal layer. Abdominal intestinal ultrasound can measure the intestinal wall

thickness of intestinal lesion segment of UC, but affected by patients' body position, anatomical structure occlusion and other factors, positioning of the involved intestinal segment is more difficult and measurement error is also greater[3].

Endoscopic ultrasonography (EUS) is a newly developed assistant examination method, combines the characteristics of digestive endoscopy and ultrasound examination, and can clearly show the internal structure of digestive tract wall as well as accurately orientate and measure the edema and thickening area in submucosa[4,5]. EUS measurement can directly orientate the intestinal lesion segment and the influence factors of measurement results are few[6]. Therefore, measurement results of EUS are more accurate and credible. According to research of related scholars, normal intestinal wall thickness is <3.2 mm, that of quiescent UC patients is 3.2-5.4 mm and that of active UC patients is >5.5 mm[7]. In the research, analysis results of intestinal wall thickness of UC patients by EUS showed that intestinal wall thickness of active UC patients was (6.92±0.79) mm, that of quiescent UC patients was (4.78±0.55) mm, and both were significantly higher than that of healthy volunteers, which was (2.78±0.33) mm; that intestinal wall thickness of active UC patients was higher than that of quiescent UC patients. EUS detection of intestinal wall thickness of UC patients was consistent with research of Dagli. Further analysis of intestinal wall thickness of active UC patients with different degrees of lesion showed that the higher the degree of activity, the higher the intestinal wall thickness.

Ulcerative colitis is a nonspecific inflammatory disease and the most prominent characteristics are extensive inflammatory cell infiltration in intestinal mucosa and submucosa as well as large synthesis of inflammatory mediators. TNF-α is an inflammatory factor produced by mononuclear macrophages and T lymphocytes, and it can not only promote and amplify inflammation and regulate immune response, but also cause intestinal mucosal epithelial cell damage and intravascular microthrombosis by promoting the release of platelet activating factors, inducing the generation of oxygen free radicals and so on[8,9]. IL-1β is a class of pleiotropic cytokine with multiple biological effects, and can cause intestinal mucosal damage and chemotaxis of multiple inflammatory factors into intestinal mucosa as well as induce and amplify inflammation[10]. IL-4 and IL-10 are two important types of anti-inflammatory factors in the body, and can inhibit the activation of inflammatory cells and immune cells as well as reduce the synthesis of pro-inflammatory factors TNF-α and IL-1β[11]. In the research, analysis results of inflammatory mediator contents in intestinal mucosa of UC patients showed that TNF-α and IL-1β contents in intestinal mucosa of active UC patients were higher than those of quiescent UC patients and positively correlated with intestinal wall thickness, and contents of IL-4 and IL-10 were lower than those of quiescent UC patients and negatively correlated with intestinal wall thickness.

Studies in recent years suggest that abnormal immune response is involved in the occurrence of UC and its development. Unbalanced helper T cell 1 (Th1)/Th2 ratio and regulatory T cell (Treg)/Th17 ratio are closely related to the pathogenesis of UC[12]. When induced by IFN-γ, etc, $CD4^+$ T lymphocytes can differentiate into Th1, which enhances inflammatory response through secreting IL-2, TNF-α and other pro-inflammatory mediators[13]; and when induced by IL-4, they can differentiate into Th2, which inhibits Th1 cell differentiation and maturation through secreting IL-4, IL-5, IL-10 and other suppressive factors[14]. Treg is another type of T cell subset with immune regulation function, and its function includes inhibiting Th17 cell differentiation and maturation as well as reducing autoimmune reaction and intestinal inflammation; Th17 cell is a type of helper T cell that can produce IL-17, and can enhance inflammation[15]. Th1 and Th17 cell contents in intestinal mucosa of active UC patients were higher than those of quiescent UC patients and positively correlated with intestinal wall thickness, and contents of Th2 and Treg cells in intestinal mucosa of active UC patients were lower than those of quiescent UC patients and negatively correlated with intestinal wall thickness.

Based on above discussion, it can be concluded that routine ultrasound combined with endoscopic ultrasonography can accurately determine the severity of ulcerative colitis, and measured intestinal wall thickness is closely correlated with the degree of inflammation and abnormal immune response.

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