

[ ORIGINAL ARTICLE ]

# The Colon Wall Thickness Measured Using Transabdominal Ultrasonography Is Useful for Detecting Mucosal Inflammation in Ulcerative Colitis

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## Abstract:

**Objective** Transabdominal ultrasonography (TUS) is a non-invasive procedure that is reportedly useful for managing ulcerative colitis (UC) and assessing bowel wall thickness (BWT), the most common measure of mucosal inflammation. However, the exact range of BWT that reflects disease activity remains undetermined. The present study clarified the BWT due to disease activity by comparing the use of TUS in each segment of the colon versus using colonoscopy (CS) and determined the usefulness of TUS in patients with UC.

**Methods** We divided the colon into five segments and measured the BWT using TUS. The results were then compared to the Mayo endoscopic subscore (MES) classification to determine the accuracy of BWT measurement.

**Patients** Eighty patients with UC who underwent TUS within 14 days of CS were retrospectively registered.

**Results** We evaluated a total of 268 images depicting each segment among 80 patients with UC. The BWT was positively correlated with endoscopic activity (0.69,  $p < 0.0001$ ). In each segment, the relationship between a BWT > 2 mm and an MES > 0 had the highest sensitivity, specificity, and accuracy (0.85-1.00, 0.67-0.92, and 0.81-0.97, respectively).

**Conclusion** This study concluded that TUS was a useful method of detecting an MES > 0, which indicates the presence of inflammation and its location among UC patients. MES > 0 was found to be highly accurate when a BWT > 2 mm was considered positive. This non-invasive method may help control disease activity in patients with UC.

**Key words:** bowel wall thickness, Mayo endoscopic subscore classification, transabdominal ultrasonography, ulcerative colitis

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## Introduction

Ulcerative colitis (UC) is characterized by chronic inflammation of the gastrointestinal tract that affects the colon and rectum, resulting in continuous inflammation and the need for lifelong treatment (1-4). An accurate assessment and

proper treatment are crucial for patients with UC. Endoscopy is the standard method for evaluating UC activity (5); however, as it is highly invasive, frequent examinations are difficult to conduct (6-8). In contrast, transabdominal ultrasonography (TUS) is a non-invasive method that can be performed frequently and is expected to be applicable in a wide range of clinical assessments, such as in the judgment of

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treatment effects and in the evaluation of disease conditions at the time of deterioration (9-11). Therefore, it is expected to be a useful tool for evaluating disease activity.

Recently, the treatment goal in UC has shifted from clinical remission to endoscopic remission, which is associated with sustained clinical remission and reduced rates of hospitalization and surgical resection (12, 13). Therefore, the recognition of disease severity and determination of the presence of mucosal inflammation are important factors to consider in the selection of therapeutic agents, including local therapy.

Active UC lesions appear on TUS as areas of increased wall thickness of the large intestine due to the infiltration of inflammatory cells into the mucosa and submucosa. These changes can be evaluated by measuring the bowel wall thickness (BWT) of the large intestine. However, while the BWT is a reliable parameter, the exact value that reflects the disease activity remains undetermined (14-16).

In this study, we compared the TUS and colonoscopy (CS) findings in each segment of the colon among UC patients and evaluated the relationship between the BWT, TUS, and MES to determine the usefulness of TUS in the treatment of UC.

## Materials and Methods

### Patients

Patients with UC visiting Okayama University Hospital between 2016 and December 2019 were included in this study. Specifically, we included patients who underwent TUS within 14 days of CS for an activity evaluation. We excluded those who exhibited aggravation or improvement of their clinical status due to changes in treatment between CS and TUS, those under 15 years old, and those with a proctitis phenotype. All patients had an established diagnosis of UC according to endoscopic and histological assessment findings and had received medical therapy.

The clinical disease activity was scored using the Mayo score classification (17), which is based on the following four criteria: stool frequency (0, normal number for this patient; 1, 1-2 stools more than normal; 2, 3-4 stools more than normal; and 3,  $\geq 5$  stools more than normal), rectal bleeding (0, no blood seen; 1, streaks of blood in stool less than half the time; 2, obvious blood in stool most of the time; and 3, blood alone passes), endoscopic findings (0, normal or inactive disease; 1, mild disease with erythema, decreased vascular pattern, mild friability; 2, moderate disease with marked erythema, absent vascular pattern, friability, erosions; and 3, severe disease with spontaneous bleeding and ulceration), and the physician global assessment (0, normal; 1, mild disease; 2, moderate disease; 3, severe disease). Clinical activity remission was defined as a Mayo stool frequency subscore of 0 or 1 and a Mayo rectal bleeding subscore of 0.

### TUS

Aplio XG and Aplio 500 TUS machines (Cannon Medical Systems, Otawara, Japan) were used in this study. Two doctors with three and six years of experience in performing TUS of the digestive tract performed the procedures. In some cases, previous endoscopic findings were used as references for disease activity and extent. TUS was performed after at least five hours of fasting. No preparations were used in this study. We first performed TUS using a 3.5-MHz convex transducer for whole abdominal screening. After screening, a 7.5-MHz high-frequency linear-array transducer was used to enable more detailed evaluations. Each part of the colon was sequentially assessed, except for the rectum, as it is located deep in the pelvis and is difficult to visualize by TUS (18-20). The colon was divided into five segments: ascending colon, right-sided and left-sided transverse colon, descending colon, and sigmoid colon. Using a 7.5-MHz high-frequency linear-array transducer, we measured the BWT, which is defined as the distance from the central hyperechoic line of the lumen (i.e. lumen of the digestive tract) to the outer hyperechoic margin of the wall (serosa of the digestive tract) (Fig. 1A, B).

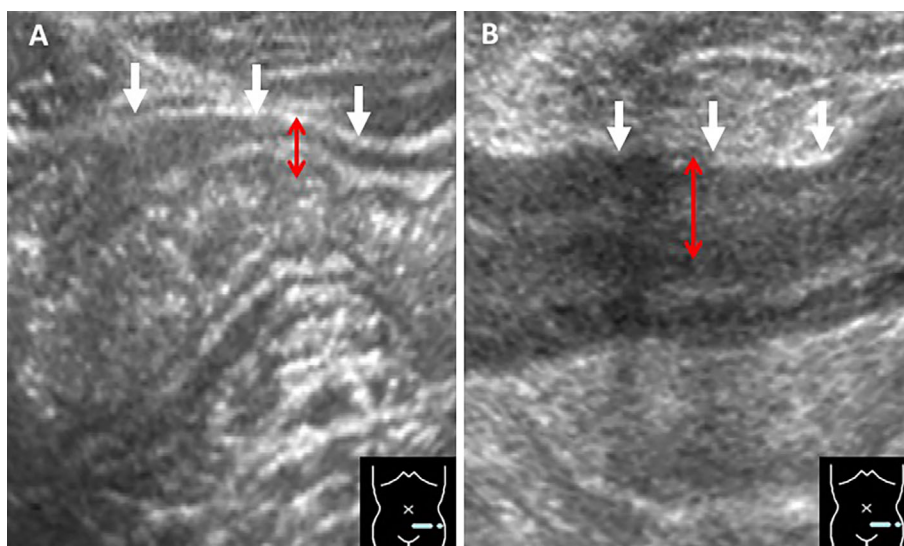
### CS

On the day of CS, patients performed polyethylene glycol-based bowel preparations in accordance with the manufacturer's instructions. After colonic lavage was completed, the patients underwent CS. For those with a severe disease status, to avoid the risk of disease deterioration, the possible range was observed using intestinal lavage by enteroclysis.

We compared the range of endoscopic observations with the ultrasound findings. Patients were excluded if the colonoscopic examination was limited to the rectum. The status of mucosal inflammation of each segment in UC was assessed using the Mayo endoscopic subscore (MES) classification (17) at each portion of the colon, as mentioned above. Mucosal inflammation at any segment was defined as an MES $>0$  (mucosal healing was defined as an MES=0). The MES was determined by experienced endoscopists with over 10 years of experience, blinded to the results of TUS. CS and TUS were performed by different doctors.

### Statistical analyses

All statistical analyses were conducted using the JMP software program, version 13 (SAS Institute, Cary, USA). To examine the relationship between the BWT and MES, the unaffected normal mucosa of left-side colitis (transverse-ascending colon) was also treated as MES 0. A Spearman's rank correlation analysis was performed to determine the association between the BWT and MES. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio, and negative likelihood ratio with 95% confidence intervals for MES by endoscopy were also determined using the TUS findings as the



**Figure 1.** US findings (sigmoid colon, 7.5 MHz). A: US findings of a BWT of 1.7 mm (mucosa without inflammation). B: US findings of a BWT of 3.7 mm (mucosa with inflammation). The sigmoid colon (white arrows) is indicated along with the representative measurement method of the BWT (red arrows). BWT: bowel wall thickness, US: ultrasonography

**Table 1.** Demographics and Clinical Characteristics of the Study Patients.

<b>Patients</b>	
Total	80
Median age (range)	44(16-85)
Median body mass index (range)	20.1(28.8-12.3)
<b>Gender</b>	
Male	56(70%)
Female	24(30%)
<b>Extent of disease</b>	
pancolitis	66(82.5%)
Left side colitis	14(17.5%)
<b>Evaluation site</b>	
ascending colon	37(46%)
right-sided transverse colon	41(51%)
left-sided transverse colon	50(63%)
descending colon	60(75%)
sigmoid colon	80(100%)
<b>Endoscopic activity</b>	
Remission states	3(4%)
Active states	77(96%)
<b>Concomitant medications</b>	
Aminosalicylate	59(74%)
Corticosteroids	39(49%)
Mercaptopurine/Azathioprine	20(25%)
Biologics/JAK inhibitor	11(14%)
Apheresis	14(18%)
Tacrolimus	11(14%)
<b>Median (range) interval between TUS and colonoscopy, days</b>	0(-14-14)

basis. All p values were two-sided and considered significant at  $p < 0.05$ . To estimate the appropriate cut-off values for the BWT and MES, a receiver operating characteristic curve analysis was performed.

### Ethical considerations

The study protocol was approved by the Institutional Review Board of Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences (IRB number: 1804-030). Informed consent was obtained from all patients. All methods were performed in accordance with the principles of the Declaration of Helsinki.

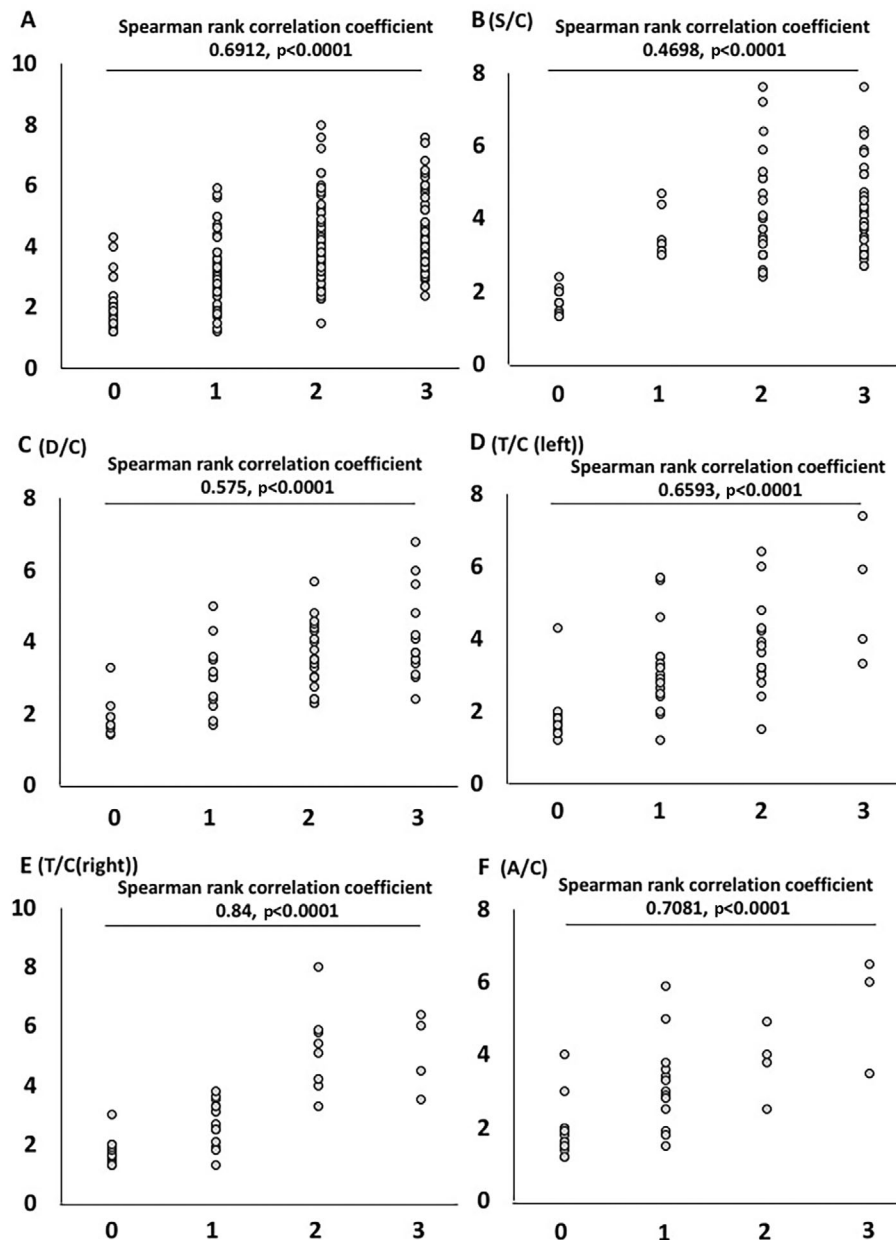
## Results

### Patient characteristics

A total of 80 patients with UC who underwent US and CS were enrolled in this study. The patients' demographic and clinical characteristics are presented in Table 1. Most of the patients were men [70.0% (n=56)] with a pancolitis phenotype. All patients underwent endoscopy to assess inflammation. Only three patients lacked inflammation in any part of the colorectum. To a greater or lesser degree, all other patients had inflammation along the colorectum. As some patients had severe disease, we refrained from examining the oral side of the colon in these patients, which decreased the number of these evaluations. Rectal lesions were not assessed because they are difficult to evaluate using TUS (18-20); therefore, we excluded patients with proctitis. Patients who underwent TUS within 14 days of CS were included in the study. Ten patients underwent changes in treatments during the examination, but none showed a clear change in disease activity.

### The correlation between the BWT and CS findings by colon section

The correlations between BWT and CS findings are



**Figure 2.** Correlation between the BWT and CS findings of each colon segment. The BWT was positively correlated with the endoscopic activity (Spearman rank correlation coefficient=0.47-0.84,  $p < 0.0001$ ). The vertical and horizontal axes show the BWT (mm) and Mayo endoscopic subscore, respectively. A/C: ascending colon, BWT: bowel wall thickness, CS: colonoscopy, D/C: descending colon, S/C: sigmoid colon, T/C left: left-sided transverse colon, T/C right: right-sided transverse colon

shown in Fig. 2A. The BWT was positively correlated with endoscopic activity (0.69,  $p < 0.0001$ ), and the correlations between the BWT and CS findings of each part of the colon are shown in Fig. 2B, C, D, E and F. Spearman's rank correlation coefficients and the corresponding p values for the correlation are shown in each figure. Although the correlation coefficient varied by segment (0.47-0.84,  $p < 0.0001$ ), a correlation was suggested between the BWT and MES.

### Sensitivity, specificity, PPV, and NPV of BWT for mucosal status

Next, we attempted to determine the highest BWT that can reflect disease activity. According to the receiver operat-

ing characteristic curve, the cut-off value of BWT for  $MES > 0$  was 2.2 mm, and the cut-off value of BWT for  $MES > 1$  in each segment was 2.0-2.4 mm (Table 2); it might therefore be ideal to check for  $BWT > 2$  mm to detect  $MES > 0$ . Table 3 shows the sensitivity, specificity, PPV, NPV, positive likelihood ratio, negative likelihood ratio, and accuracy for  $BWT > 2$  mm and  $MES > 0$ , including the results for each segment. The ratio of  $MES$  differed among segments, and the inspection accuracy varied slightly. However, we considered these results sufficient to detect mucosal inflammation.

We then examined whether or not an  $MES > 1$  could be determined using the BWT. Our results showed that the BWT cut-off value for an  $MES > 1$  was 3.0 mm, while that

**Table 2. The Cut off Value of BWT for MES>0 and AUC.**

	S/C	D/C	T/C left	T/C right	A/C
<b>Cut off value of BWT (mm)</b>	2.2	2.4	2.2	2.0	2.0
<b>AUC</b>	0.94	0.99	0.94	0.92	0.87

**Table 3. Sensitivity, specificity, and predictive values of TUS for mucosal inflammation (BWT>2 mm, MES>0).**

	S/C	D/C	T/C left	T/C right	A/C	
<b>Sensitivity</b>	0.94(0.92-0.96)	1.00(0.97-1.00)	0.96(0.91-0.98)	0.85(0.79-0.87)	0.86(0.79-0.92)	0.85(0.71-0.94)
<b>Specificity</b>	0.77(0.68-0.83)	0.67(0.45-0.67)	0.78(0.52-0.91)	0.90(0.64-0.98)	0.92(0.73-0.99)	0.77(0.60-0.87)
<b>PPV</b>	0.93(0.90-0.95)	0.96(0.93-0.96)	0.96(0.91-0.98)	0.97(0.90-0.99)	0.96(0.86-0.99)	0.96(0.68-0.89)
<b>NPV</b>	0.80(0.72-0.87)	1.00(0.67-1.00)	0.78(0.52-0.91)	0.60(0.43-0.65)	0.80(0.64-0.85)	0.80(0.67-0.89)
<b>Positive likelihood ratio</b>	4.02(2.88-5.59)	3.00(1.75-3.00)	4.33(1.90-11.1)	8.5(2.20-47.3)	11.5(2.95-62.7)	3.61(1.77-6.91)
<b>Negative likelihood ratio</b>	0.08(0.05-0.13)	0.00(0.00-0.06)	0.05(0.02-0.15)	0.17(0.13-0.33)	0.13(0.09-0.29)	0.20(0.08-0.48)
<b>Accuracy</b>	0.90(0.86-0.93)	0.97(0.91-0.96)	0.93(0.85-0.97)	0.86(0.76-0.89)	0.90(0.77-0.94)	0.81(0.66-0.90)

for an MES>1 in each segment was 2.3-4.0 mm (Supplementary material 1); the ideal cut-off value was therefore set at 3.0 mm. We also evaluated the sensitivity, specificity, PPV, NPV, positive likelihood ratio, negative likelihood ratio, and accuracy of BWT and MES>1 (Supplementary material 2). Overall, specificity dropped; as a result, accuracy was lower than that obtained from the analysis of BWT at MES>0. We also evaluated BWT at an MES>2. The ideal cut-off value was set at 3.5 mm (Supplementary material 3), and the sensitivity, specificity, PPV, NPV, positive likelihood ratio, negative likelihood ratio, and accuracy are shown in Supplementary material 4. The results also showed that the sensitivity, specificity, and accuracy were lower than those obtained from the analysis with an MES>0.

These results indicated a good relationship between a BWT>2 mm and an MES>0, suggesting that this 2-mm assessment criterion using the BWT was a useful indicator of the presence of mucosal inflammation by TUS.

## Discussion

UC is characterized by chronic inflammation of the gastrointestinal tract. Currently, there are no radical treatments for UC, and patients require lifelong management (4). To select UC treatments and determine the efficacy of those treatments, it is important to understand the pathophysiology, such as the disease severity and extent. However, CS, as the disease assessment standard for UC, is invasive and may place mental and physical burdens on patients and worsen their condition. In contrast, TUS is a non-invasive procedure that enables the observation of almost all of the colon and is expected to be a viable method for evaluating UC activity. The presence of inflammation on TUS is reflected by an increased BWT; however, the BWT value that reflects disease activity remains undetermined (14-16). Therefore, in this study, we compared the BWT determined using TUS with the MES in each colon segment to clarify the appropriate BWT that reflects the disease severity.

Based on our results, a positive BWT (BWT>2 mm) of the colon accurately identified the presence of mucosal inflammation (MES>0) in UC patients. In previous reports, a BWT of >3 or 4 mm was commonly considered a positive finding indicative of the presence of mucosal inflammation (19-22), with the presence of mucosal inflammation defined as MES>1 (mucosal healing was defined as an MES of 0 or 1). There has been a recent trend in using an MES of 0 as an indicator of mucosal healing; however, our results suggest that a BWT>2 mm and an MES>0 might be new indicators. Bots et al. recently reported the relationship between BWT and MES in UC patients in a single-center retrospective study (23) and found that a BWT>2.1 mm was the most useful value for detecting an MES>0 in UC patients. Since similar results to ours were reported in other countries, we considered this a significant report that supports our results.

We also examined the relationship between BWT and MES>1 or MES>2. Based on the results (Supplementary material 2, 4), the sensitivity, specificity, and accuracy were found to be lower than when the value of MES was MES>0; however, our results suggested that it was possible to assess the disease severity to some extent. Recent reports (14, 20, 22, 24, 25) have shown that other methods, such as blood flow, have been incorporated to assess the disease severity by TUS. Our results suggest that the BWT alone may reflect the disease severity of UC; however, since inflammation increases the blood flow and changes the mucosal structure, it is necessary to add evaluation methods that reflect the pathology, such as blood flow measurement, to further improve accuracy. Such examinations require further consideration.

A low accuracy rate has been reported for rectal assessments by TUS (18-20), and some reports have excluded this site from evaluations (22, 26). The rectum is difficult to visualize by TUS because of its location in the deep pelvic cavity and the effect of small bowel gas on its evaluation. Recently, Sagami et al. reported the usefulness of US with a

transanal approach for evaluating the activity of the rectum in patients with UC (20). However, TUS is not suitable for evaluating the rectum, and a different evaluation method is needed, which should be explored in future research.

Several limitations associated with the present study warrant mention. First, the number of cases at each site varied, and the right-sided tracts, such as the ascending and transverse colon, have numerous normal mucosa, while the amount of inflammatory mucosa increases toward the anal side. This imbalance may be due to the difficulty for patients with severe conditions to undergo a complete CS examination because of concerns about pain and disease exacerbation, which may have led to an overestimation and differences in sensitivity, specificity, accuracy, as well as the correlation coefficient among segments. To avoid this bias, one possible solution may be to evaluate patients in whom the entire colon can be observed by CS. Another limitation is that this was a retrospective analysis. Therefore, there were some biases due to the possibility of additional treatment modifications being included, the examination period being incorrect, tests not being completely blind, BWT measurement methods, and cases not being evaluated by multiple individuals. Therefore, to obtain more reliable results, multicenter prospective studies are necessary.

Regarding the change in the BWT related to additional treatments and an insufficient examination period, in cases where drugs with relatively immediate effects, such as infliximab or tacrolimus, were used for treatment, the drugs might have affected the TUS findings if the examination period had been longer. A recent report showed that the BWT decreased within two to six weeks after successful treatment (27). Therefore, the interval between the endoscopy examination and TUS was set to two weeks or less. In our study, a few patients had an examination period of 14 days. However, the treatment was not found to be very effective in these patients, and the clinical findings, such as the stool frequency and blood data, did not change significantly. Therefore, although additional treatments might have had some effect on the severity assessment, there were no significant effects on the detection of mucosal inflammation in the interval between the two examination methods.

In conclusion, our results show that the detectability of endoscopic activity at an  $MES > 0$  is adequate when the criterion for positive cases is set at a  $BWT > 2$  mm. This is the first report to describe the relationship between a  $BWT > 2$  mm determined using TUS and an  $MES > 0$  in UC patients. Our study showed that mucosal inflammation was able to be detected by measuring the BWT with high accuracy. Using these new assessment criteria, this minimally invasive and repeatable examination is expected to be useful for evaluating mucosal inflammation. Furthermore, this examination can quickly provide results, making it possible to increase the speed of developing treatment strategies and controlling UC disease activity. Even if only mild inflammatory findings are detected using TUS, it may be possible to control the inflammation by increasing the dose of oral 5-

aminosalicylic acid (5-ASA) or administering local therapy, such as 5-ASA or steroid enema. Our findings also suggest that BWT reflects the disease severity at  $MES > 1$  and  $MES > 2$ . To increase the accuracy and reliability of these data, multicenter prospective studies that including various parameters, such as the blood flow measurement, are necessary to evaluate the disease severity.

**The authors state that they have no Conflict of Interest (COI).**

## References

- Head KA, Jurenka JS. Inflammatory bowel disease. Part 1: ulcerative colitis pathophysiology and conventional and alternative treatment options. *Altern Med Rev* **8**: 247-283, 2003.
- Ungaro R, Mehandru S, Allen PB, et al. Ulcerative colitis. *Lancet* **389**: 1756-1770, 2017.
- Danese S, Fiocchi C. Ulcerative colitis. *N Engl J Med* **365**: 1713-1725, 2011.
- Abraham C, Cho JH. Inflammatory bowel disease. *N Engl J Med* **361**: 2066-2078, 2009.
- Dignass A, Lindsay JO, Sturm A, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis. Part 2: current management. *J Crohns Colitis* **6**: 991-1030, 2012.
- Damore LJ 2nd, Rantis PC, Vernava AM 3rd, Longo WE. Colonoscopic perforations. Etiology, diagnosis, and management. *Dis Colon Rectum* **39**: 1308-1314, 1996.
- Levin TR, Conell C, Shapiro JA, Chazan SG, Nadel MR, Selby JV. Complications of screening flexible sigmoidoscopy. *Gastroenterology* **123**: 1786-1792, 2002.
- Menees S, Higgins P, Korsnes S, Elta G. Does colonoscopy cause increased ulcerative colitis symptoms? *Inflamm Bowel Dis* **13**: 12-18, 2007.
- Hata J, Haruma K, Suenaga K, et al. Ultrasonographic assessment of inflammatory bowel disease. *Am J Gastroenterol* **87**: 443-447, 1992.
- Parente F, Greco S, Molteni M, Anderloni A, Bianchi Porro G. Imaging inflammatory bowel disease using bowel ultrasound. *Eur J Gastroenterol Hepatol* **17**: 283-291, 2005.
- Novak KL, Jacob D, Kaplan GG, et al. Point of care ultrasound accurately distinguishes inflammatory from noninflammatory disease in patients presenting with abdominal pain and diarrhea. *Can J Gastroenterol Hepatol* **2016**: 4023065, 2016.
- Ardizzone S, Cassinotti A, Duca P, et al. Mucosal healing predicts late outcomes after the first course of corticosteroids for newly diagnosed ulcerative colitis. *Clin Gastroenterol Hepatol* **9**: 483.e3-489.e3, 2011.
- Pineton de Chambrun G, Peyrin-Biroulet L, Lémann M, Colombel JF. Clinical implications of mucosal healing for the management of IBD. *Nat Rev Gastroenterol Hepatol* **7**: 15-29, 2010.
- De Voogd F, Wilkens R, Gecse K, et al. A reliability study - strong inter-observer agreement of an expert panel for intestinal ultrasound in ulcerative colitis. *J Crohns Colitis* **15**: 1284-1290, 2021.
- Smith RL, Taylor KM, Friedman AB, Gibson RN, Gibson PR. Systematic review: clinical utility of gastrointestinal ultrasound in the diagnosis, assessment and management of patients with ulcerative colitis. *J Crohns Colitis* **14**: 465-479, 2020.
- Bots S, Nylund K, Löwenberg M, Gecse K, Gilja OH, D'Haens G. Ultrasound for assessing disease activity in IBD patients: a systematic review of activity scores. *J Crohns Colitis* **12**: 920-929, 2018.
- Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-

- aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. *N Engl J Med* **317**: 1625-1629, 1987.
18. Parente F, Greco S, Molteni M, et al. Role of early ultrasound in detecting inflammatory intestinal disorders and identifying their anatomical location within the bowel. *Aliment Pharmacol Ther* **18**: 1009-1016, 2003.
  19. Kinoshita K, Katsurada T, Nishida M, et al. Usefulness of transabdominal ultrasonography for assessing ulcerative colitis: a prospective, multicenter study. *J Gastroenterol* **54**: 521-529, 2019.
  20. Sagami S, Kobayashi T, Aihara K, et al. Transperineal ultrasound predicts endoscopic and histological healing in ulcerative colitis. *Aliment Pharmacol Ther* **51**: 1373-1383, 2020.
  21. Baval AS, Somi MH, Nemat M, et al. Ultrasonographic evaluation of bowel wall thickness and intramural blood flow in ulcerative colitis. *ISRN Gastroenterol* **2012**: 370495, 2012.
  22. Allocca M, Fiorino G, Bonovas S, et al. Accuracy of humanitas ultrasound criteria in assessing disease activity and severity in ulcerative colitis: a prospective study. *J Crohns Colitis* **12**: 1385-1391, 2018.
  23. Bots S, Nylund K, Löwenberg M, Gecse K, D'Haens G. Intestinal ultrasound to assess disease activity in ulcerative colitis: development of a novel UC-ultrasound index. *J Crohns Colitis* **15**: 1264-1271, 2021.
  24. Parente F, Molteni M, Marino B, et al. Bowel ultrasound and mucosal healing in ulcerative colitis. *Dig Dis* **27**: 285-290, 2009.
  25. Parente F, Molteni M, Marino B, et al. Are colonoscopy and bowel ultrasound useful for assessing response to short-term therapy and predicting disease outcome of moderate-to-severe forms of ulcerative colitis? A prospective study. *Am J Gastroenterol* **105**: 1150-1157, 2010.
  26. Pascu M, Roznowski AB, Müller HP, Adler A, Wiedenmann B, Dignass AU. Clinical relevance of transabdominal ultrasonography and magnetic resonance imaging in patients with inflammatory bowel disease of the terminal ileum and large bowel. *Inflamm Bowel Dis* **10**: 373-382, 2004.
  27. Maaser C, Petersen F, Helwig U, et al.; German IBD Study Group and the TRUST&UC study group. Intestinal ultrasound for monitoring therapeutic response in patients with ulcerative colitis: results from the TRUST&UC study. *Gut* **69**: 1629-1636, 2020.

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