Correlation of Rectal Bowel Wall Thickness Using Intestinal Ultrasound with Clinical and Laboratory Indices in Ulcerative Colitis Patients

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Abstract

Background: The inflammatory bowel disease ulcerative colitis (UC) is a chronic, idiopathic; debilitating disease that usually affects people in their 30s to 40s, characterized by intermittent recurring mucosal inflammation, originating in the rectum, and extending to the proximal areas of the colon. It has been noted that intestinal ultrasonography (IUS) is a reliable diagnostic tool for UC and can be used to assess the severity, activity, and extent of inflammation.

Objectives: The objective of the work was to evaluate the role of IUS BWT in the assessment of the severity of UC.

Patients and methods: Fifty patients diagnosed with UC were assessed clinically by the simple clinical colitis activity index (SCCAI), lab markers CRP and fecal calprotectin (FC), and an IUS assessment for the rectal bowel wall.

Results: BWT can assess the severity of UC. BWT can correlate with SCCAI ($r = 0.677$, $p<0.001$), CRP ($r = 0.412$, $p = 0.003$), and FC ($r = 0.474$, $p = 0.001$).

Conclusions: IUS is reliable, safe, and non-invasive radiology in the assessment of disease severity by measuring rectal BWT. BWT was consistent with different clinical and lab indices.

Keywords: Ulcerative colitis; Intestinal ultrasound; Bowel wall thickness.

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Introduction

The symptoms of UC include recurrent and intermittent mucosal inflammation that starts in the rectum and spreads to the colon's proximal regions. The goal of treatment is to achieve and maintain clinical and endoscopic remission **(Peyrin-Biroulet et al., 2015).**

Globally, the prevalence and frequency of UC have increased **(Molodecky et al., 2012).**

In Europe, UC incidence appears to vary by geography, with higher rates seen in western and northern nations than in eastern ones **(Burisch et al., 2013).**

The diagnosis of UC is made through a multifaceted process that includes the patient's medical history, physical examination, laboratory, endoscopic, histologic, and radiographic investigations. Accurate diagnosis is essential since it influences the course of treatment as well as the type and timing of any required surgery **(Wolf et al., 2012).**

The utilization of non-invasive research methods is essential. There is a necessity for diagnostic procedures with precision of diagnosis, standardization, ease of comprehension for medical professionals, and reproducibility. Unfortunately, none of the investigations had any of these characteristics. Acute-phase proteins and serologic markers are the primary biomarkers in UC. In clinical practice, the most often used laboratory tests to evaluate acute-phase reactions are the erythrocyte sedimentation rate (ESR) and the serum concentration of C-reactive protein (CRP). Leukocyte count, serum albumin (Alb), and platelets (PLT), are all indicators of acute phase response in UC **(Cioffi et al., 2015).**

A good-to-optimal association between intestinal ultrasonography (IUS) and colonic inflammation was found in research evaluating the accuracy of IUS measures in detecting disease activity, suggesting that IUS monitoring in UC and CD is equally possible. IUS is crucial for improving the diagnosis process as well as, as recent research has demonstrated, tracking treatment response to speed up therapeutic changes and decision-making due to its low cost, ease of use, and point-of-care availability **(Barchi et al., 2023).**

It has been reported that IUS can be used to evaluate the extent, location, and intensity of inflammation and is a valid diagnostic method for UC. This study sought to evaluate the effectiveness of intestinal US against colonoscopy in assessing UC's degree, severity, and activity **(Maaser et al., 2020).**

The assessment of IBD disease activity has undergone a paradigm shift as a result of therapeutic advancements in the management of the illness. As part of a "treat to target" approach, objective evaluation of inflammation is now crucial for directing treatment beyond clinical remission. There are several domains for evaluating disease activity in IBD, and while each has advantages, none is ideal **(Walsh et al., 2016).**

Rectal bowel wall thickness (BWT), an ultrasonography activity indicator that assesses the degree of disease activity in UC patients using endoscopy as the reference standard, can be used. BWT was measured from the central hyperechoic line of the lumen to the end of the outer hypoechoic wall edge, which represents the muscularis propria. All BWT measurements were performed twice on longitudinal portions since the thickest wall segment is most visible in a longitudinal position **(Bots et al., 2021).**

Patients and methods

Subjects

A cross-sectional study was conducted for 1 year from 2022 to 2023, and patients were recruited from the outpatient clinic after doing colonoscopy, scheduled

for IUS within 3 weeks before or after, or admitted in the inpatient ward of the gastroenterology unit at Alexandria Main University Hospital.

Adult UC patients from both genders who were able to give consent either by themselves or by their guardians were included in the study.

Exclusion criteria include patients with gastrointestinal malignancy, indeterminate colitis, Crohn's disease**,** recent surgical intervention of the intestines, small or large, within the last 6 months, infectious diarrhea including bacterial, viral, parasitic diarrhea, colonic polyposis and diverticulosis, drugs abuse within the last month, allograft rejection, silicosis, tuberculosis, autoimmune diseases as rheumatoid arthritis, pregnancy, severe burn, sepsis, chronic renal and liver diseases, refusal to be involved in the study, inability to give consent as mentally challenged, non-steroidal anti-inflammatory, and corticosteroid use within the last year.

The study included fifty patients with UC. UC disease activity was assessed clinically by the simple clinical colitis activity index (SCCAI), lab CBC, CRP, and stool markers fecal calprotectin (FC), which were tested for correlation with rectal BWT by IUS **(Goodsall et al., 2023)**.

In our study, CRP, FC, and SCCAI were of statistical significance and were correlated with rectal BWT.

Ethical approval code: 0201655, where the study was conducted in a way that respects the rights and dignity of the included patients. All procedures performed in the study involving human participants followed the ethical standards of the institutional research committee (Medical Research Ethics Committee of Alexandria Faculty of Medicine, Egypt). An informed written consent was obtained from each patient before inclusion in the study.

Clinical Procedures

1. History-taking includes patient complaints and extra-intestinal manifestations (EIM) like arthritis, pyoderma gangrenosum, primary sclerosing cholangitis, and uveitis.
2. Simple clinical colitis activity index (SCCAI) for assessment of clinical activity; SCCAI evaluates disease severity during the previous week by measuring bowel frequency [day], urgency of defecation, blood in stool, bowel frequency [night], general well-being, and extra-colonic features, and the total SCCAI is calculated as the sum of these six measures [range: 0–19], with a higher score indicating greater symptom severity **(Goodsall et al., 2023)**.
3. Thorough systemic physical examination, including abdominal examination with stress on signs of disease such as tenderness, palpable organs or masses, or peri-anal fistula and EIM of UC.
4. UC was diagnosed by colonoscopy, and data was reported about the disease, including endoscopic appearance and UC endoscopic index of severity (UCEIS) **(Barchi et al., 2023)**.
5. Laboratory investigations: All UC patients were subjected to the following biochemical and hematological analyses. The investigations considered in our study were: complete blood picture (CBC), serum albumin, serum bilirubin, serum urea, serum creatinine, erythrocyte sedimentation rate (ESR), quantitative C reactive protein (CRP), prothrombin time (PT), partial thromboplastin time (PTT), fecal calprotectin, and stool analysis (to exclude parasitic infestations).
6. Imaging**:** All UC patients were subjected to IUS using the Mindray ultrasound system in China within 3 weeks before

or after the colonoscopic examination and after good patient preparation. The examination was performed after at least 12 hours of fasting with the patient in the supine position. The large intestine was scanned beginning at the terminal ileum and further following its course to the rectum by a single expert sonographer who was blinded to the results of colonoscopy using a greyscale ultrasound convex 7.5 megahertz (MHz) probe for a survey of the whole abdomen and pelvis, then a focused superficial linear probe (12–14 MHz) to assess the disease activity using certain parameters as an assessment of BWT. BWT was measured as the perpendicular distance from the echogenic luminal interface to the outer muscularis borderer on a cross-sectional image, as illustrated in **Fig. (1, 2) (Barchi et al., 2023)**.

Assessment of BWT alone has the potential to predict the activity of UC. The rectum is one of the limited colonic segments to be examined using IUS, where it is best visualized as an anterior wall of the upper third rectum using the convex probe **(Barchi et al., 2023)**.

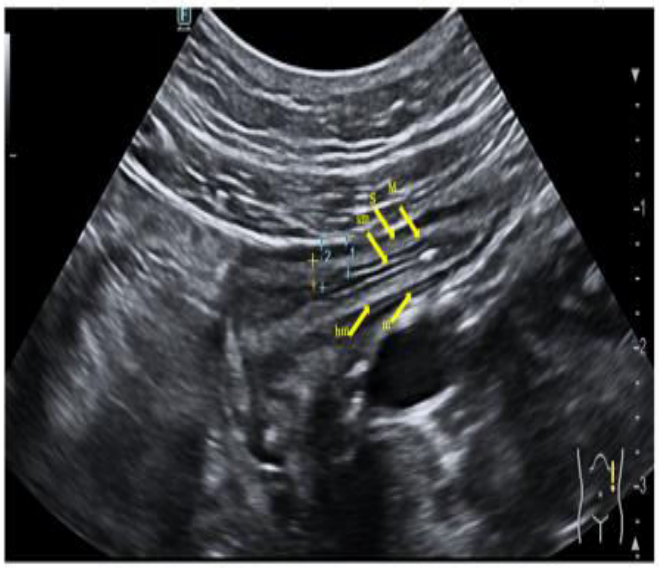

Fig.1. Bowel wall stratification at bowel ultrasound evaluation. hm: hyperechoic lumen interface of the mucosa; m: mucosa (hypoechoic); sm: submucosa (hyperechoic); M: muscularis propria(hypoechoic); S: serosa (hyperechoic) **(Barchi et al., 2023).**

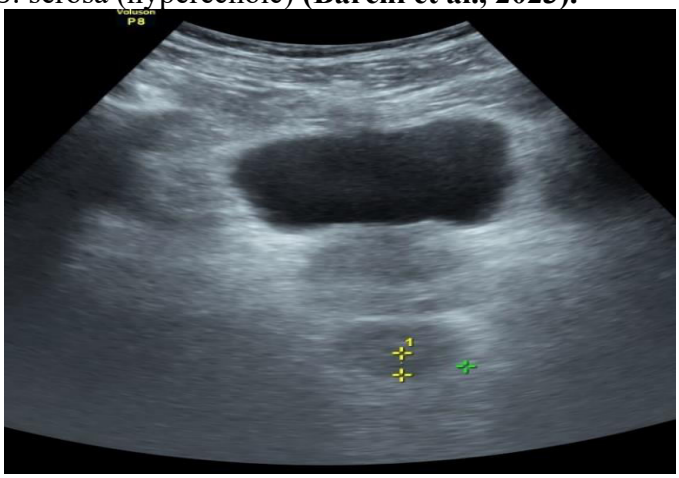

Fig.2. Active UC showing increased BWT in one of the studied cases

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. The Shapiro-Walk test was used to verify the normality of the data. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). Kruskal-Wallis, one-way analysis of variance (ANOVA), and post-hoc tests were applied when appropriate. To compare qualitative variables, the Chi-Square, Fisher's exact, and Monte Carlo tests were applied when appropriate. To evaluate correlations between various quantitative variables, the Pearson Correlation Coefficient was utilized. P 0.05 or less is considered significant.

Results

50 patients with UC were evaluated using the UC endoscopic index of severity (UCEIS), which categorizes patients into 3 groups: mild (n = 13), moderate (n = 16), and severe (n = 21).

No significant gender or mean age differences were found; the mean age of mild cases was 43.0 ± 13.25, moderate cases was 41.44 ± 8.85, and severe cases was 37.05 ± 9.70 years (**Table.1**).

Table 1. Demographic data in the studied groups

Demographic data	Total (n = 50)		UC endoscopic index of severity (UCEIS)						Test of sig.	P value
			Mild (n = 13)		Moderate (n = 16)		Severe (n = 21)			
	No.	%	No.	%	No.	%	No.	%		
Sex										
Male	19	38.0	4	30.8	8	50.0	7	33.3	χ^2= 1.461	0.482
Female	31	62.0	9	69.2	8	50.0	14	66.7		
Age (years)										
Median (IQR)	39 (32.0 – 48.0)		43 (35.0 – 52.0)		39 (36.0 – 46.0)		36 (31.0 – 45.0)		F= 1.516	0.230
Mean ± SD.	40.0 ± 10.59		43.0 ± 13.25		41.44 ± 8.85		37.05 ± 9.70			
Min. – Max.	18.0 – 61.0		22.0 – 61.0		28.0 – 57.0		18.0 – 51.0			

IQR: Inter quartile range; SD: Standard deviation; χ2: Chi square test; F: F for One way ANOVA test.

CRP mean level showed a significant increase with increasing severity of UCEIS (9.31 ± 6.05) in mild cases (43.12 ± 39.34), in moderate cases and (52.48 ± 37.44) in severe cases (p<0.001), (**Table.2**).

Table 2. CRP in the studied groups

CRP (mg/dl)	Total (n = 50)	UC endoscopic index of severity (UCEIS)			Test of sig.	P value
		Mild (n = 13)	Moderate (n = 16)	Severe (n = 21)		
Median (IQR)	31 (9 – 50)	8 (4 – 11)	31 (11 –59.5)	45 (40 – 60)	H= 17.027*	<0.001*
Mean ± SD.	38.26 ± 37.03	9.31 ± 6.05	43.12 ± 39.34	52.48 ± 37.44		
Min. – Max.	3.0 – 170	3.0 – 20	5.0 – 122	3.0 – 170		
Comparison between Groups	$P_1 = 0.004^*$, $P_2 < 0.001^*$, $P_3 = 0.286$					

IQR: Inter quartile range; SD: Standard deviation; F: F for One way ANOVA test; H for Kruskal Wallis test; P_1: comparing between mild and moderate; P2: comparing between mild and severe; P3: comparing between moderate and severe.

The mean faecal calprotectin (FC) level was increasing with increasing severity of UCEIS in mild cases (56.85 ± 24.22 mg/kg), in moderate cases (264.5 ± 242.9

mg/kg), in severe cases (561.6 ± 469.6 mg/kg) (P<0.001), (**Table.3**).There was no statistically significant difference in CBC findings (**Table.4**).

Table 3.Faecal calprotectin in the studied groups

Faecal calprotectin (µg/g)	Total (n = 50)	UC endoscopic index of severity (UCEIS)			H	P value
		Mild (n = 13)	Moderate (n = 16)	Severe (n = 21)		
Median (IQR)	200 (60-543)	50 (40 – 70)	190 (105.5 –342.5)	535 (233– 659)	24.305*	<0.001*
Min. – Max.	23 – 2200	23 – 100	28 – 789	60– 2200		
Comparison between Groups	$P_1 = 0.005^*$, $P_2 < 0.001^*$, $P_3 = 0.37^*$					

IQR: Inter quartile range; SD: Standard deviation; H for Kruskal Wallis test; Pairwise comparison was done using Post Hoc Test (Duns for multiple comparison tests); p comparing between the three studied groups; p_1: p comparing between Mild and Moderate; p_2: p comparing between Mild and Severe; p_3: p comparing between Moderate and Severe

Table 4. CBC in the studied groups

CBC	Total (n = 50)	UC endoscopic index of severity (UCEIS)			Test of sig.	P value
		Mild (n = 13)	Moderate (n = 16)	Severe (n = 21)		
Hb (gm/dl)					F = 0.055	0.947
Median (IQR)	12 (11 – 14)	12 (11.6 –13)	11.9(10.8–13.5	13 (12 – 14)		
Mean ± SD.	12.39 ± 2.05	12.25 ± 1.47	12.38 ± 2.22	12.49 ± 2.31		
Min. – Max.	5.0 – 17.0	9.50 – 15.10	9.0 – 17.0	5.0 – 16.0		
PLTs (×10⁹/L)					H= 4.167	0.124
Median (IQR)	341 (255– 400)	321 (233– 387)	312 (256 – 377)	370 (309 – 470)		
Mean ± SD.	350.2 ± 138.0	305.08 ± 88.47	332.0 ±128.55	392.0 ± 161.6		
Min. – Max.	9.0 – 800.0	167.0 – 410.0	189.0 – 743.0	9.0 – 800.0		
WBCs (×10⁹/L)					F= 1.238	0.299
Median (IQR)	8.55 (7– 10.50)	7.50 (7 – 8.60)	9.1(8.4 – 10.8)	9 (7 – 11)		
Mean ± SD.	8.77 ± 2.29	7.94 ± 1.64	9.23 ± 2.07	8.93 ± 2.71		
Min. – Max.	4.70 – 14.0	5.60 – 11.0	5.0 – 12.10	4.70 – 14.0		

IQR: Inter quartile range; SD: Standard deviation; F: F for One way ANOVA test; H for Kruskal Wallis test

The mean level of SCCAI showed a significant increase with increasing UCEIS severity in the mild group (4.15 ± 1.95), in moderate cases (10.81 ± 1.52), and in the severe group (12.67 ± 2.69) (P < 0.001), (**Table.5**).

Table 5. Comparison between the three studied groups according to SCCAI

SCCAI	Total (n = 50)		UC endoscopic index of severity (UCEIS)						Test of sig.	P value
			Mild (n = 13)		Moderate (n = 16)		Severe (n = 21)			
	No.	%	No.	%	No.	%	No.	%		
Inactive (0 – 4)	11	22.0	11	84.6	0	0.0	0	0.0	χ^2= 35.353*	^{MC}p <0.001*
Active (5+)	39	78.0	2	15.4	16	100.0	21	100.0		
Median (IQR)	11 (7 – 13)		4 (3 – 4)		11 (10 – 12)		13 (11 – 15)		F=	<0.001*

Mean ± SD.	**9.86 ± 4.11**	**4.15 ± 1.95**	**10.81 ± 1.52**	**12.67 ± 2.69**	**63.060***	
Min. – Max.	**3 – 19**	**3 – 10**	**8 – 13**	**7 – 19**		
Comparison between Groups	**$P_1 < 0.001^*$, $P_2 < 0.001^*$, $P_3 = 0.036^*$**					

IQR: Inter quartile range; SD: Standard deviation; $\chi 2$: Chi square test; MC: Monte Carlo; F: One way ANOVA test Pairwise comparison was done using Post Hoc Test (Tukey); p1: comparing between mild and moderate; P2: comparing between mild and severe; P3: comparing between moderate and severe.

The correlation study revealed that rectal BWT showed a significant positive correlation with CRP (r = 0.412, p = 0.003), fecal Calprotectin (r = 0.474, p = 0.001), and SCCAI (r = 0.677, p < 0.001) (**Fig. 3–5, Table. 6**).

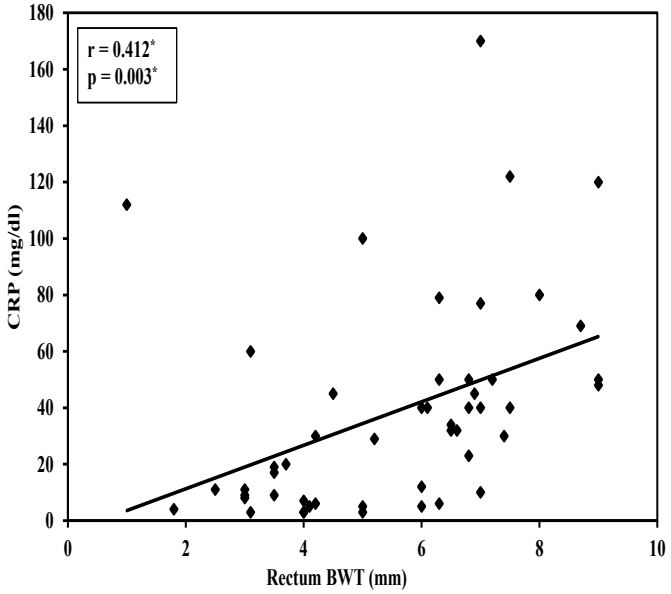

Fig.3. Correlation between rectal BWT and CRP

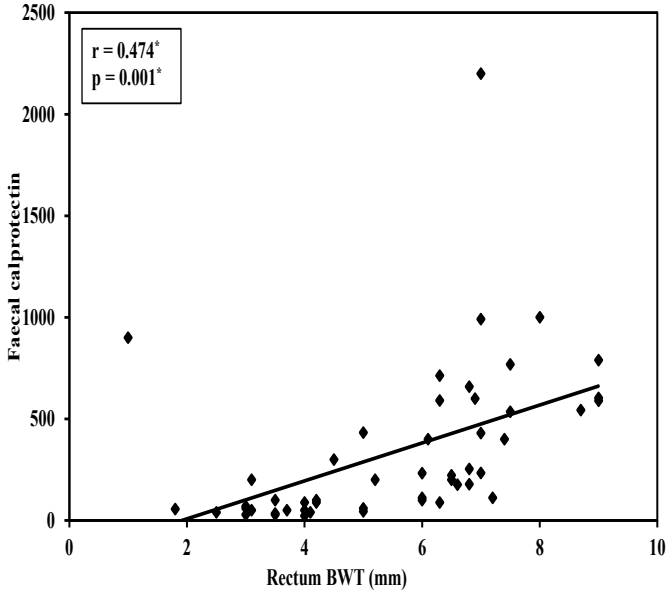

Fig.4. Correlation between rectal BWT and faecal calprotectin

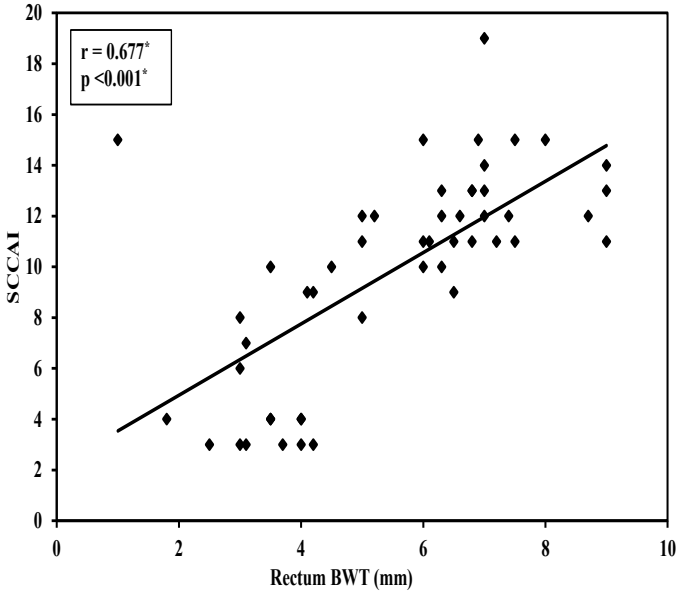

Fig.5. Correlation between rectal BWT and SCCAI

Table 6.Correlation between rectal BWT and CRP, Fecal calprotectin, and SCCAI

Variables	r value	p value
CRP (mg/dl)	0.412	0.003*
Faecal calprotectin (µg/g)	0.474	0.001*
SCCAI	0.677	<0.001*

Discussion

Subtle and unusual symptoms can cause a delay in diagnosing UC, which could harm the course of treatment. Traditionally, endoscopic, histological, and radiological findings have been used to diagnose UC. Repeated endoscopy is time-consuming and intrusive, making it neither viable nor practical. Clinically, non-invasive UC assessment is still a difficulty. For a screening test to measure gastrointestinal inflammation objectively, it should be non-invasive, affordable, simple to use, quick, and accurate **(Bots et al., 2021; El-Feky et al., 2023; Dolinger and Kayal, 2023).**

Out of fifty patients, nineteen were males and thirty-one were females. In the three studied groups, there was no statistically significant difference (p = 0.482) as there was no certain sex predilection in UC, which was comparable to other studies **(Bots et al., 2021).**

There are no statistically significant results regarding CBC findings; abnormal CBC findings are not needed either for diagnosis or follow-up, as CBC can be affected by variable diseases other than UC activity **(Antunes et al., 2015).**

In our study, the rectal BWT showed a significant positive correlation with CRP (r = 0.412, p = 0.003), fecal Calprotectin (r = 0.474, p = 0.001), and SCCAI (r = 0.677, p < 0.001).

UC mostly affects the colon's mucosal and submucosal layers, excluding the peri-intestinal structures. Especially as compared to CD, the application of transmural examination by cross-sectional imaging techniques, primarily IUS, has long been neglected, given the predominant mucosal site of UC inflammation **(Bots et al., 2021).**

Many parameters are used to assess disease, and non-invasive parameters are valuable as CRP, FC, and clinical score as

SCCAI. Numerous studies assess FC in UC and its usefulness in relapse prevention, disease activity assessment, and diagnosis. The guidelines for FC diagnostic tests for inflammatory bowel disease (IBD) published by the National Institute for Health and Care Excellence (NICE) guide for the differential diagnosis of IBD or IBS in adults and children **(Brookes et al., 2018; Freeman et al., 2019).**

Although stool sample collection is less practical than peripheral blood tests, fecal biomarkers have been discovered to closely represent intestinal inflammatory status and have emerged as important markers in monitoring disease activity in UC patients **(Darr and Khan, 2017).**

In a similar study, they studied 60 UC patients. Using Truelove and Witt's criteria for grading UC severity (based on 6 or more blood-stained stools daily, with 1 or more of the 4 additional criteria: hemoglobin <105 g/L, ESR >30 mm/h, fever >37.8 °C, and tachycardia >90/min), participants were split into two patient groups **(Jain et al., 2018).**

Thirty patients with active UC made up Group I, and thirty patients with inactive UC (in remission) made up Group II. The laboratory tests, colonoscopy, and IUS were performed. They reported that at a cutoff level of > 3.5 (P = 0.002), BWT can be utilized to distinguish between patients with active and inactive UC **(El-Feky et al., 2023).**

In our study, there is **a correlation** between rectal BWT and SCCAI, while in previous studies, intestinal ultrasound activity demonstrated a significant linear association with the total Mayo score (coefficient 0.307; 95% CI, 0.020–0.595; P =.036) and UCEIS (coefficient 0.32; 95% CI, 0.14-0.49; P < 0.001) **(Goodsall et al., 2023).**

Our study was limited by the number of patients (only 50 subjects) and lacked the use of a contrast-enhanced modality. To study the role of IUS in pediatrics and follow-up using IUS, further studies are needed to complete our work.

Conclusion

Rectal BWT as an IUS radiological parameter correlates successfully with the studied laboratory (FC, CRP) and clinical UC activity parameters (SCCAI) due to the accurate assessment of inflammation by measuring BWT (numerical value), so IUS may be a promising independent assessment tool to assess disease activity and follow-up disease course.

List of abbreviations:

IUS: Intestinal Ultrasound
BWT: Bowel Wall Thickness
UC: Ulcerative Colitis
FC: Fecal Calprotectin
CRP: C Reactive protein
SCCAI: Simple Clinical Colitis Activity Index

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Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

Consent to publication: Not applicable

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