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Original article

Intestinal Ultrasound as Non-Invasive Method in Assessment of Ulcerative Colitis Activity

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Abstract:

Background: Intestinal ultrasound (IUS) has become an essential, non-invasive tool for evaluating gastrointestinal involvement in inflammatory bowel disease (IBD), particularly ulcerative colitis (UC). With advancements in ultrasound technology, its diagnostic accuracy has significantly improved. This study aimed to evaluate UC activity by means of a new ultrasound-based activity index, with endoscopic results serving as the gold standard. **Methods:** Fifty patients with confirmed UC were enrolled from the Internal Medicine Department at Benha University Hospital in Egypt. They were categorized into two groups: 25 patients in remission (inactive UC) and 25 with active diseases. All participants underwent clinical evaluation, colonoscopy, laboratory investigations, and intestinal ultrasound examination. **Results:** Patients with active UC had significantly higher levels of bowel wall thickness (BWT) and the UC intestinal ultrasound severity index (UC-IUS) when contrasted with those in remission ($P < 0.001$). Active cases also showed more distortions in the stratification of the wall ($P = 0.015$) and aberrant haustrations ($P = 0.002$). The severity of the disease was significantly predicted by BWT. A BWT > 3 mm was associated with an AUC of 0.739 ($P = 0.001$), sensitivity of 83.33%, and negative predictive value (NPV) of 92% for severe UC. The AUC for moderate UC was 0.822 ($P < 0.001$), with a sensitivity of 90.91% and a 95.5 percent NPV, when the cutoff was >2.5 mm. **Conclusions:** For the evaluation of disease activity in UC, IUS is a dependable and non-invasive technique. BWT demonstrates strong potential as a marker for disease severity and could guide treatment decisions effectively.

Keywords: Intestinal Ultrasound; Non-Invasive Method; Ulcerative Colitis Activity; Endoscopy; Active Disease.

Introduction

Inflammatory bowel disease (IBD) consists of two chronic gastrointestinal disorders: Crohn's disease (CD) and ulcerative colitis (UC) [(1)]. Historically, documentation of IBD in Africa and the Middle East has been limited. While the prevalence rates of these diseases in certain regions are not well-defined or supported by extensive registry or cohort studies, the incidence of IBD in Egypt is increasing, with a UC-to-CD ratio of 6:1 [(2)].

Colonoscopy is still the most reliable way to detect disease activity in UC patients, which is why it is being used more and more in clinical trials to help with treatment decisions and evaluate results [(3, 4)]. A variety of endoscopic activity indicators have been developed and validated for evaluating mucosal disease activity [(5)]. However, the high costs and patient burden associated with frequent colonoscopies to monitor disease activity present significant challenges [(6)]. Additionally, complications such as intra-abdominal abscesses and colon perforation, although rare, may not always be detectable [(7)].

Repeated fecal calprotectin (FCP) measurement has been shown to accurately reflect disease activity in IBD patients [(8)]. However, this method does not provide a comprehensive assessment of the disease's severity, extent, and location. Blood tests, such as serum C-reactive protein (CRP), platelet counts, and serum albumin levels, have also been explored but lack the specificity and sensitivity necessary to reliably reflect disease activity [(9)]. As a result, there is a clear need for non-invasive, reliable alternatives to assess disease severity [(10)].

In the past two decades, the use of IUS to evaluate the gastrointestinal tract in IBD patients has grown significantly, thanks to advances in US technology and equipment. Patients typically report little to no discomfort when undergoing US, and the procedure is accessible, cheap, and non-invasive. Since its inception as a method for measuring CD-related transmural inflammation, IUS has expanded its utility to include the evaluation of disease progression, consequences, and response to therapy [(11, 12)]. However, its clinical application in UC is less well-documented than in CD[(13)].

The purpose of this study was to investigate the function of IUS in evaluating UC activity relative to endoscopy.

Patients and Methods

This cross-sectional study included 50 patients diagnosed with UC, recruited from the gastrointestinal unit of the Internal Medicine Department at Benha University Hospitals, Egypt. Before enrollment, all participants agreed to provide written informed consent, and the institutional ethics committee authorized the study. (Approval code: RC 28-11-2022). The study period extended from March 2023 to October 2024.

Inclusion criteria: Aged over 18 years, patients of both genders, with a confirmed diagnosis of UC, were eligible for participation.

Exclusion criteria: Patients were excluded if they were pregnant, presented with complicated UC, or had notable changes in therapy or symptoms detected during endoscopic or IUS evaluations.

Patient grouping:

Participants were stratified into 2 groups:

• Group 1: 25 patients in remission (inactive UC).

• Group 2: 25 patients with active UC.

Comprehensive clinical data were collected from each participant, including age, gender, weight, height, body mass index (BMI), smoking status, disease localization, presence of abdominal pain, frequency of bowel movements, rectal bleeding, joint pain, drug history, and time of diagnosis. Risk factors such as diabetes, hypertension, dyslipidemia, and personal or family history of UC were also documented.

Laboratory investigations:

Blood samples were evaluated for hemoglobin levels, white blood cell (WBC) counts, platelet counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP).

Stool analysis and cultures were performed for all cases to exclude other causes and rule out infectious enterocolitis. Fecal calprotectin (FCP) levels were measured using an enzyme-linked immunosorbent assay (ELISA). To rule out Clostridium difficile infection, stool samples were also tested for C. difficile toxin using an enzyme immunoassay (EIA).

Colonoscopy:

Colonoscopy was performed within 72 hours of patient admission to assess disease severity while minimizing the risk of complications such as traumatic colonic dilatation or perforation. The procedure utilized minimal air insufflation. The Mayo Endoscopic Score (MES) was applied to evaluate disease activity and classifies it into four categories [(5)]:

- **3**: Severe condition characterized by ulceration and spontaneous bleeding.
- **2**: Moderate disease is characterized by pronounced erythema, lack of vascular patterns, friability, and erosions.
- **1**: Mild friability decreased vascular patterns, and kMild disease with erythema.
- **0**: inactive disease or Normal.

To further categorize the severity of the disease, the UC Endoscopic Severity Index (UCEIS) was implemented. This index is a simple sum determined by three descriptors). According to **Table 1**; erosions and ulceration (scored 0–3), hemorrhage (scored 0–3), vascular pattern (scored 0–2) the UCEIS score is between 0 and 8. We classified the UCEIS scores into four categories: severe (UCEIS 7–8), moderate (UCEIS 5–6), mild (UCEIS 2–4), (inactive UC) (UCEIS 0–1)[(5)].

Table 1: Ulcerative colitis endoscopic index of severity (UCEIS) scores and definitions [(5)]

Descriptor	Points	Definition
Vascular pattern	**Normal (0)**	Normal vascular pattern with arborization of capillaries clearly defined, or with blurring or patchy loss of capillary margins
	Patchy obliteration (1)	Patchy obliteration of vascular pattern
	Obliterated (2)	Complete obliteration of vascular pattern
Bleeding	**None (0)**	No visible blood
	Mucosal (1)	Some spots or streaks of coagulated blood on the surface of the mucosa ahead of the scope that can be washed away
	Luminal mild (2)	Some free liquid blood in the lumen
	Luminal moderate or severe (3)	Frank blood in the lumen ahead of endoscope or visible oozing from mucosa after washing intraluminal blood or visible oozing from a haemorrhagic mucosa
Erosions and ulcers	**None (0)**	Normal mucosa, no visible erosions, or ulcers
	Erosions (1)	Tiny (5 mm) defects in the mucosa, of a white or yellow colour with a flat edge
	Superficial ulcer (2)	Larger (>5 mm) defects in the mucosa, which are discrete fibrin-covered ulcers when compared with erosions, but remain superficial
	Deep ulcer (3)	Deeper excavated defects in the mucosa, with a slightly raised edge

Intestinal ultrasound (IUS) examinations:

IUS was conducted in the radiology department by a well experienced operator using a Philips Epiq 5 ultrasound machine equipped with C5-1 convex and L12-5 linear transducers. Patients underwent the examination following a minimum of six hours of fasting, in a supine position. The scanning process progressed from the terminal ileum to the rectum, identifying abnormalities such as thickened bowel walls, altered haustral patterns, and swollen lymph nodes. Color Doppler imaging was utilized to assess vascular activity in the bowel wall, employing standardized presets for optimal visualization of low-velocity flows. Cine loops of each bowel segment were recorded in longitudinal planes for subsequent analysis.

Ultrasound parameters:

The following parameters were measured during IUS:

- Bowel wall thickness (BWT): measurement was taken from the central hyperechoic line of the lumen to the external hyperechoic layer, which corresponds to the serosa. For the terminal ileum, cecum, and colonic segments, normal values were established as less than 2 mm.
- Wall layer stratification (WLS): Classified as either normal or disrupted.
- Colonic haustrations: Defined as normal or abnormal based on structural appearance.
- Color Doppler signal (CDS): Categorized as absent, small spots, or large patches.
- Fat wrapping: Presence or absence of hyperechoic mesenteric fat surrounding the bowel.
- Reactive lymph nodes: Identified by a short axis >5 mm.

The UC-Intestinal Ultrasound Severity Index (UC-IUS) was calculated based on these parameters to provide a comprehensive assessment of disease activity. **Table 2**

Table 2: UC-IUS index [10]

Parameters		Points [0-7]
Bowel wall thickness	**>2mm**	1
	>3mm	2
	>4mm	3
Doppler signal spots		1
Stretches		2
Abnormal haustrations		1
Fat wrapping		1

Sample size calculation:

The required sample size was calculated using G*Power 3.1.9.2 software. Based on prior studies reporting 87.8% sensitivity for detecting BWT via IUS, with 100% discrimination between active and inactive UC cases, the study assumed a power of 90% and an alpha error of 0.05. To account for potential dropouts, 50 patients were recruited.

Statistical analysis:

The data was analyzed using SPSS version 28. The qualitative variables were shown using frequency and percentage breakdowns, while the quantitative data was shown using the mean ± standard deviation. For categorical data, statisticians compared the groups using t-tests, chi-square, and Fisher's exact tests. We used Pearson's correlation coefficient to look for trends in the numerical variables' associations to do this. The diagnostic performance was assessed by ROC curve analysis to find statistical significance, utilizing a significance level of $P < 0.05$.

Results

In baseline characteristics, including age, gender, weight, height, BMI, place of residence, smoking status, family history, medication use, disease location, or duration, the 2 groups demonstrated no significant differences. laboratory analyses revealed that fecal calprotectin (FCP), white blood cell counts (WBC), and C-reactive protein (CRP) levels were significantly elevated in the active UC group compared to the inactive group (P<0.05). No significant variations were observed in hemoglobin levels, platelet counts, or ESR between the groups. **Table 3**

Table 3: Baseline characteristics and clinical data of the studied groups

			Total (n=50)	Group 1 (Inactive cases) (n=25)	Group 2 (Active cases) (n=25)	P value
Baseline characteristics	**Age (years)**		46.88±9.29	44.96±10.76	48.8±7.51	0.150
	Gender	**Male**	34(68%)	16 (64%)	18 (72%)	0.544
		Female	16(32%)	9 (36%)	7 (28%)	
	Weight (Kg)		80.52±12.29	81.76±12.75	79.28±12.21	0.486
	Height (m)		1.69±0.05	1.68±0.05	1.69±0.04	0.718
	BMI (Kg/m^2)		28.31±4.32	28.84±4.58	27.77±4.15	0.389
Clinical data	**Residence**	**Urban**	26(52%)	12(48%)	14(56%)	0.571
		Rural	24(48%)	13(52%)	11(44%)	
	Smoking		8(16%)	5(20%)	3(12%)	0.440
	Family history		10(20%)	6(24%)	4(16%)	0.479
	Medication use		31(62%)	17(68%)	14(56%)	0.382
	Localization	**Left-sided**	21(42%)	13 (52%)	8 (32%)	0.152
		Pancolitis	29(58%)	12 (48%)	17 (68%)	
	Disease duration (years)		5.82±1.31	5.64±1.29	6.0±1.35	0.340
Laboratory investigations	**Hb (g/dL)**		11.53±0.53	11.43±0.49	11.62±0.57	0.198
	Platelets (*10^9/L)		326.92±37.99	323.8±39.46	330.04±37.81	0.571
	WBCs (*10^9/L)		8.52±1.59	7.46±1.14	9.57±1.3	**<0.001***
	ESR (mm/hr.)		17.62±1.8	17.84±1.8	17.4±1.85	0.397
	CRP (mg/L)		11.65±9.64	3.08±0.85	20.23±6.29	**<0.001***
	FCP (µg/g)		282 (96.75-572.5)	96 (89-253)	575 (308-827)	**<0.001***

Data presented as mean ± SD or frequency (%), BMI: body mass index, Hb: hemoglobin, FCP: Fecal calprotectin, WBCs: white blood cells, ESR: erythrocyte sedimentation rate, CRP: C- reactive protein*: statistically significant as p value <0.05.

Findings from IUS

IUS revealed significant differences in BWT and UC-IUS between the groups, with both measures being markedly higher in the active UC group (P<0.001 for both). Wall layer stratification was significantly disrupted in the active group compared to inactive group (P=0.015). Abnormal haustrations were more frequently observed in the active group (P=0.002), and the color Doppler signal showed significant differences, with larger patches identified in the active group (P=0.001). No significant differences were observed between the groups regarding fat wrapping or reactive lymph nodes. Endoscopic examination findings and UC endoscopic index scores were significantly different between the groups (P<0.001 and P=0.001, respectively), with higher scores noted in the active UC group. **Table 4, Figure 1**

Table 4: Intestinal ultrasound examination and endoscopic findings of the studied groups

			Total (n=50)	Group 1 (inactive cases) (n=25)	Group 2 (Active cases) (n=25)	P value
Intestinal ultrasound examination	**BWT (mm)**		2.92±1.16	2.27±1.27	3.57±0.55	**<0.001***
	Colour Doppler signal	**Absent**	22(44%)	17 (68%)	5 (20%)	**0.001***
		Small spots	14(28%)	6 (24%)	8 (32%)	
		Large spots	14(28%)	2 (8%)	12 (48%)	
	Wall layer stratification	**Normal**	34(68%)	21 (84%)	13 (52%)	**0.015***
		Disturbed	16(32%)	4 (16%)	12 (48%)	
	Fat creeping	**Present**	2(4%)	0 (0%)	2 (8%)	0.148
		Absent	48(96%)	25 (100%)	23 (92%)	
	Reactive lymph nodes	**Present**	1(2%)	0 (0%)	1 (4%)	0.312
		Absent	49(98%)	25 (100%)	24 (96%)	
	Haustrations	**Normal**	29 (58%)	20 (80%)	9 (36%)	**0.002***
		Abnormal	21 (42%)	5 (20%)	16 (64%)	
Endoscopic findings	**UC-IUS index**		3.12±2.54	1.32±1.86	4.92±1.73	**<0.001***
			3 (0 -5.75)	0 (0-2)	5 (4-6)	
	Mayo 0		٢٥ (٥٠%)	٢٥ (١٠٠%)	0 (0%)	**<0.001***
	Mayo 1		٥ (١٠%)	٠ (٠%)	5 (20%)	
	Mayo 2		٨ (١٦%)	٠ (٠%)	8 (32%)	
	Mayo 3		12 (24%)	0 (0%)	12 (48%)	
	Ulcerative colitis endoscopic index score		2.68±2.59	0.44±0.51	4.92±1.73	**0.001***
			١.٥ (٠-٥)	٠ (٠-١)	6 (5-7)	

Data presented as mean ± SD or median (IQR), BWT: bowel wall thickness, UC-IUS: ulcerative colitis- intestinal ultrasound*: statistically significant as p value <0.05.

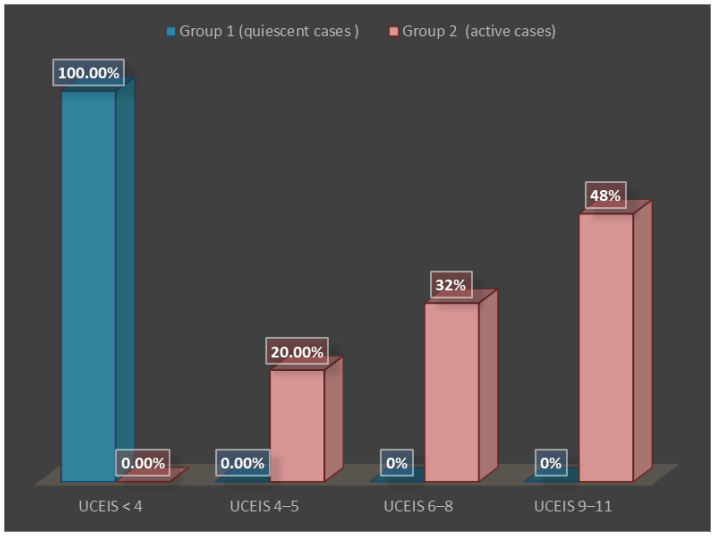

Figure 1: Ulcerative colitis endoscopic index of the studied groups.

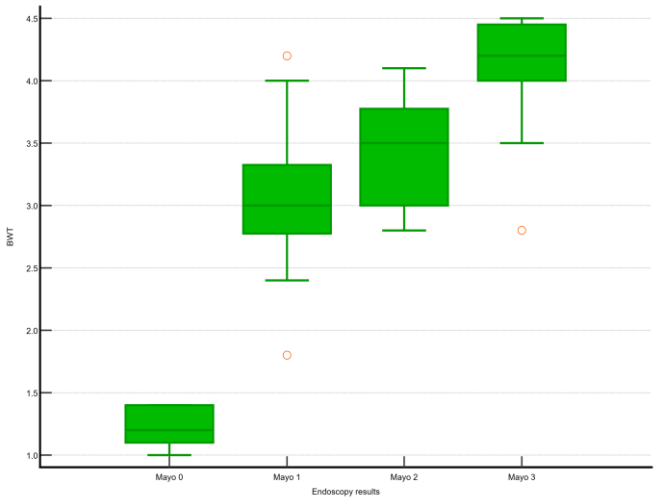

Figure 2: Relation between endoscopy results and BWT

Figure 2 demonstrates a strong correlation between the Mayo score and the endoscopic severity indicator for ulcerative colitis, as well as the association between the Mayo score and BWT.

Correlation analysis:

A significant positive correlation was found between the UC-IUS index and endoscopic findings (r=0.895, P<0.001). Likewise, BWT showed strong positive correlations with endoscopy results, FCP levels, and the UC-IUS index, with P-values of less than 0.001 for all. **Table 5**, **Figure 2**

Table 5: Correlation between BWT and different parameters and between UC-IUS index and Endoscopy results

	BWT (mm)	
	R	**P**
Endoscopy results	0.821	**<0.001***
Ulcerative colitis endoscopic index score	0.656	**<0.001***
FCP(µg/g)	0.666	**<0.001***
UC-IUS index	0.789	**<0.001***
	UC-IUS index	
Endoscopy results	**R**	**P**
	0.895	**<0.001***

Data was presented as r: correlation coefficient, FCP: Fecal calprotectin, BWT: bowel wall thickness, UC-IUS: ulcerative colitis- intestinal ultrasound, *: statistically significant as p value <0.05.

Diagnostic performance

FCP demonstrated excellent diagnostic accuracy for predicting severe UC, with an AUC of 0.995 (P<0.001) at a cutoff value of >575 µg/g. This threshold provided 83.33% sensitivity, 100% specificity, 100% positive predictive value (PPV), and 94.9% negative predictive value (NPV). For moderate UC, FCP had an AUC of 0.683 (P=0.012) at a cutoff of >288 µg/g, yielding 90.91% sensitivity, 69.23% specificity, 45.5% PPV, and 96.4% NPV. BWT also demonstrated notable diagnostic potential. For severe UC, an AUC of 0.739 (P=0.001) was achieved at a cutoff of >3 mm, with 83.33% sensitivity, 62.16% specificity, 41.7% PPV, and 92%NPV. For moderate UC, the AUC was 0.822 (P<0.001) at a cutoff of >2.5 mm, providing 90.91% sensitivity, 53.85% specificity, 35.7% PPV, and 95.5% NPV. **Table 6 and Figure 3**.

Table 6: Diagnostic accuracy for prediction of the severity of the disease

		Cutoff	Sensitivity	Specificity	PPV	NPV	AUC	P value
FCP	**Severe**	>575	83.33	100	100	94.9	0.995	**<0.001***
(µg/g)	**Moderate**	>288	90.91	69.23	45.5	96.4	0.683	**0.012***
BWT	**Severe**	>3	83.33	62.16	41.7	92	0.739	0.001*
(mm)	**Moderate**	>2.5	90.91	53.85	35.7	95.5	0.822	**<0.001***

Data was presented as frequency (%). FCP: Fecal calprotectin, BWT: bowel wall thickness, PPV: positive predictive value, NPV: negative predictive value, AUC: area under the curve, *: statistically significant as p value <0.05.

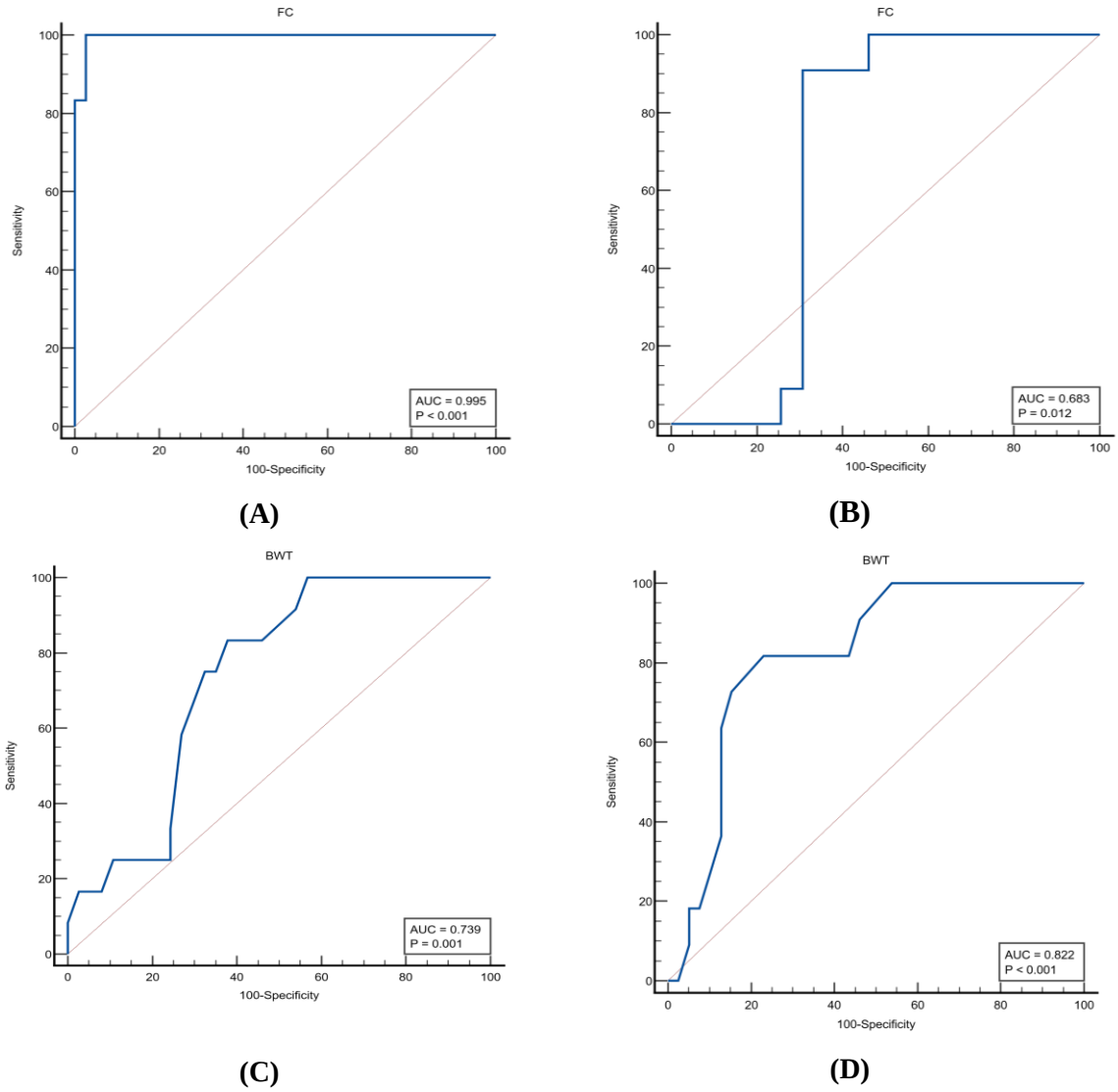

Figure 3: Illustrates the diagnostic accuracy of certain parameters (FCP and BWT) in predicting the severity of UC. (A) ROC curve analysis for FCP in severe cases, (B) ROC curve analysis for FCP in moderate cases, (C) ROC Curve for BWT in severe cases, (D)ROC curve for BWT in moderate cases

Discussion

Effective management of UC and activity. Although colonoscopy remains gold standard for assessing disease status in UC patients, there is an ongoing need for a non-invasive, safe, and reliable method to evaluate disease extent and activity [(14)].

This study highlights the utility of IUS parameters, particularly BWT, in assessing UC activity. The findings corroborate

previous studies that underscore the diagnostic value of IUS in distinguishing between active and quiescent disease. For instance, a prospective study by Kinoshita et al.[15] reported that BWT and other ultrasound parameters effectively gauge disease activity in UC. Similarly, Smith et al. [16] suggested that a BWT greater than 4 mm strongly indicates UC activity, consistent with our findings.

Consistent with previous research, this study found that the active UC group had considerably greater BWT than the inactive group. TRUST&UC trial [17], which identified BWT as a crucial parameter for evaluating disease activity. Comparable results were reported by El-Feky et al. [18], who observed a mean BWT of 5.2±0.7 mm in active patients, significantly higher than the 2.6±0.2 mm seen in inactive patients. Other studies, such as Nassef et al. [19], and Gao et al. [20], have similarly demonstrated that ultrasound abnormalities, particularly BWT, can effectively differentiate between patients with non-IBD controls and IBD.

In contrast to the resting group, the active group had a UC-IUS index that was much higher, as well as a greater frequency of aberrant haustrations, wall layer stratification disruption, and noticeable color Doppler signals. Results from research conducted by Ruess et al. [21] and Shirahama et al. [22], which highlighted the role of Doppler signal as a marker of disease activity.

FCP levels in study were markedly greater in the active UC group, with FCP demonstrating excellent diagnostic accuracy for severe UC (AUC = 0.995, $P<0.001$) at a threshold of >575 μg/g. These findings are consistent with those of Dulai et al. [23], who revealed that FCP levels ≤250 μg/g strongly predict disease remission.

BWT also showed robust diagnostic performance, with significant predictive accuracy for both severe and moderate UC. A threshold of >3 mm for severe UC achieved an AUC of 0.739, while >2.5 mm for moderate UC yielded an AUC of 0.822. These results align with those of Bots et al. [10] ,who reported similar cutoff values for distinguishing disease severity using BWT. However, variations in thresholds across studies may reflect methodological differences, such as segment-specific measurements, as noted by Stojkovic et al. [14], who reported a higher cutoff of 4.75 mm in the sigmoid colon.

Correlations between IUS parameters and inflammatory markers, including FCP and CRP, were consistent with previous studies. Pascu et al.[24] demonstrated strong associations between BWT, vascular signals, wall layer stratification, and ileocolonoscopic activity indices. Similarly, Rowan et al. [25] highlighted positive correlations between FCP and CRP with BWT, further supporting the validity of IUS as a non-invasive assessment tool.

Overall, this study underscores the clinical value of IUS, particularly BWT and the UC-IUS index, in monitoring UC activity. These parameters not only correlate strongly with endoscopic findings but also offer a non-invasive alternative for assessing disease severity, potentially reducing the need for frequent colonoscopies.

In conclusion, our study reaffirms the value of intestinal ultrasound as a non-invasive, patient-friendly tool for assessing UC activity. BWT, in conjunction with complementary ultrasound parameters and biomarkers such as FCP, provides clinicians with a reliable alternative to invasive endoscopic procedures. This approach not only facilitates effective monitoring of disease progression but also aids in informing treatment decisions, ultimately enhancing patient care and outcomes. By incorporating these non-invasive techniques into clinical practice, we can improve the management of UC while minimizing patient discomfort and risk associated with traditional methods.

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Conflict of Interest: Nil

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