Role of Intestinal Ultrasound in Monitoring the Response in Patients with Ulcerative Colitis under Biological Therapy

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Abstract:

Background:

Intestinal ultrasound (IUS) is a safe, fast, inexpensive method with high sensitivity and specificity, and is commonly used in many intestinal diseases, especially for diagnosing and monitoring inflammatory bowel diseases.

IUS is now reported to be accurate for ulcerative colitis (UC).

Aim: We aimed to evaluate the role of IUS in assessing the therapeutic response to biological therapy in patients with ulcerative colitis pre and post-treatment.

Patients and Methods: Participants were diagnosed with UC. History and physical examination, labs, severity scores, colonoscopy, and intestinal ultrasound were done before and after induction doses of infliximab.

Results: Fifty-two participants were initially evaluated. Among those patients, 6 underwent baseline investigations but were lost to follow-up. 63.5% males and 36.5% females. We found that IUS diagnosis of thickness of the Rectum at a threshold of mean thickness value of 4.8 mm was possible with sensitivity, specificity, and area under curve, PPV, NPV of 95%, 90%, 0.954, 94%, 78% respectively, while in sigmoid colon at mean thickness of 3.9 mm was 95%, 92%, and. 0.95, 93%, 82%, respectively. And in descending colon at a threshold of mean thickness value of 3.0 mm was 82%, 87%, 0.877, 91%, 75% respectively, and in transverse colon at thickness value of 3.1 mm was 84%, 82%, 0.69, 87%, 79% respectively, and in ascending colon at thickness value of 3.0 mm was 83%, 85%, and 0.685, 90%, 73% respectively.

Conclusion: The accuracy of IUS in monitoring wall thickness in UC pre and post-biological therapy. Compared with other parts of the colon, high-performance characteristics were found in the Rectum.

Trial registration: ClinicalTrials.gov ID: NCT05606939.

Keywords: Intestinal Ultrasound (IUS), Inflammatory Bowel Disease (IBD), Ulcerative Colitis (UC), Bowel Wall Thickness (BWT).

Introduction:

Intestinal ultrasound is a safe, rapid, and cost-effective imaging method with high sensitivity and specificity, widely used in diagnosing and monitoring many diseases, especially inflammatory bowel diseases **[1]**.

Intestinal ultrasound demonstrates high performance in detecting or excluding inflammatory activity in ulcerative colitis **[2]**. Its advantages include rapid bowel wall thickness and stratification assessment, reflecting histopathological changes in Crohn's disease (CD) and ulcerative colitis (UC). Additionally, color Doppler sonography allows visualization of bowel vascularization, while its third major advantage over other cross-sectional imaging

modalities is the direct observation of motility **[3]**.

Compared with ileocolonoscopy and other imaging modalities such as CT and MRI, intestinal ultrasound (IUS) accurately diagnoses UC, detects complications including fistulae, strictures, and abscesses, monitors disease activity, and identifies postoperative recurrence **[2]**. Biological therapy is currently recommended for moderate-to-severe ulcerative colitis (UC). Infliximab, adalimumab, and golimumab are anti-TNFα antibodies that block TNFα, a pro-inflammatory cytokine involved in acute-phase reactions and systemic inflammation, thereby mitigating tissue damage **[4]**.

A review of the published literature revealed a paucity of studies in Upper Egypt on using intestinal ultrasound to evaluate therapeutic responses in UC patients undergoing biological therapy.

Patients and Methods:

Study Design and Setting:

A prospective cohort study included 52 UC patients, 33 males and 19 females, with a mean age of 33.

Diagnosis of ulcerative colitis was based on clinical, endoscopic, and histopathological examination, and cases that were not responding or intolerant to conventional medical therapy and were eligible for biological therapy were recruited.

This study was conducted at Al-Rajhi University Hospital at the IBD outpatient clinic between October 2022 and December 2023.

Inclusion Criteria:

Any patient above the age of 18 years old and diagnosed with Ulcerative colitis was diagnosed by:

- Clinical features: rectal bleeding, frequent stools, and mucous discharge from the Rectum. Some patients also describe tenesmus. The onset is typically insidious.
- Endoscopic findings of ulcerative colitis include the following: loss of vascular pattern, granular and fragile mucosa, ulceration, erosions, and/or pseudo-polyposis
- Histological findings: most ulcerative colitis (UC) pathology is limited to the mucosa and submucosa. In fulminant cases, the muscularis propria can be affected. Pathologic features that are typically seen include intense infiltration of the mucosa and submucosa with neutrophils and crypt abscesses, lamina propria with lymphoid aggregates, plasma cells, and mast cells and eosinophils, as well as shortening and branching of the crypts. Goblet cell depletion is also notable.
- Severity of UC was assessed according to Mayo or partial Mayo scores **[5]**.

Indications of biological therapy are based on the current diagnostic and treatment recommendations of the Epidemiological Committee of European Crohn's and Colitis Organization (ECCO) as follows:

- Moderate to severe UC patients.
- Immunosuppressant or corticosteroid-refractory disease.
- Those with intolerance or contraindication to conventional therapies are eligible to be treated with biological therapy **[6]**.

Exclusion Criteria

- Patients with UC who are under the age of 18 years old.
- Patients with UC who aren't eligible for biological therapy.
- Patients with complications of UC (fistula, intestinal obstruction, intestinal perforation, …).
- Patient refuses to participate in the study.

Methods

During this study, patients with UC underwent:

- **Thorough medical history** including history of abdominal pain, bloody Diarrhea and its frequency, tenesmus, and mucous with stool.
- **Physical examination (general and abdominal)** stressing on fever, tachycardia, abdominal tenderness, and significant weight loss…etc.
- **Laboratory investigations:** Complete blood count, liver function tests, C-

reactive protein, ESR, serum ferritin, and fecal calprotectin.

- **Colonoscopy** was done, and an assessment of severity was made according to the Mayo score.
- **Severity score assessment,** including Mayo score and Short Clinical Colitis Activity Index score (SSCAI).
- **Pre-biological** therapy: screening for infections such as (T.B., HCV, HBV, HIV) was done.

Intestinal Ultrasound Examination

I. Patient preparation: No specific preparation is needed, but fasting for 6-8 hours before examination decreases gaseous content and allows better visualization.

II. Machine

Examination was done using ultrasound machines (GE LOGIQ P7) and (GE LOGIQ S8).

Two different probes: low-frequency convex probe (3.0–3.5 MHz) and high-frequency linear probe (5–17 MHz). First, the abdomen is scanned by the convex low-frequency transducer to visualize deeper structures and detect grossly abnormal pathologies, such as significant thickening of the intestinal wall, bowel dilatation, and fistulae or abscesses. A linear high-frequency transducer for detailed evaluation of the intestinal wall follows this.

III. Items of examination:

- Bowel wall thickness.
- Vascularity according to the Limberg score.
- Stratification of bowel wall layers.
- Inflammatory fat wrapping.
- Haustration.
- Others, e.g, Lymph nodes, ascites,…
- **After the induction dose of infliximab was completed**, patients underwent the same previous evaluation sequelae (careful history taking and examination, lab investigation, colonoscopy, severity scores assessment, and intestinal ultrasound re-evaluation).
- -**Treatment response** to biological therapy determined as:

Clinical response: a decrease in Mayo score by 3 points or 30% of pre-treatment Mayo score.

Clinical remission: Mayo score became 0 or 1.

Otherwise, it is considered a **failure of treatment [7]**.

Ethical Consideration

The current study was applied in accordance with the Code of Good Practice and the guidelines of the Declaration of Helsinki, 7th revision, 2013, and after being approved by the Assiut University Faculty of Medicine, Institute Review Board (IRB no: 04-2023-200115). Also, written informed consent was obtained from all participants before being enrolled in the study.

Statistical Analysis

Data was collected in a pre-formed data collection form before being entered into the spreadsheet. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 20.0 for Windows. Continuous variables were expressed as mean and standard deviation, while categorical data were expressed as numbers and percentages. Level of confidence is kept at 95% hence, the p-value is significant if < 0.05.

Results:

In the studied population, 52 participants were initially evaluated. Among those patients, 6 underwent baseline investigations but were subsequently lost to follow-up. Their mean age was 32.87±7.85. Approximately 63.5% of the patients were males, while 36.5% were females, with 53.8% residing in urban areas. The majority of participants (92.3%) were non-smokers. Hypertension was present in 2% of participants, while none had diabetes.

Laboratory investigations before and after treatment showed that the hemoglobin level was significantly higher after treatment (P-value 0.008), ESR was significantly lower after treatment (P-value < 0.001), CRP was significantly lower after treatment (P-value < 0.001), Fecal calprotectin was significantly lower after treatment (P-value < 0.001),

serum ferritin was significantly lower after treatment (P-value 0.034). There was a statistically significant difference with a higher mean of MCV after follow-up, with a p-value of 0.003, as shown in **Table (1)**.

Regarding the endoscopic findings using colonoscopy at baseline and follow-up after the induction dose of biological therapy (6 weeks):

Before Treatment: At baseline, endoscopic findings using colonoscopy revealed that 50% of the study participants had left-sided colitis, while 36.5% exhibited extensive colitis. In 13.5% of cases, assessment was limited to a short sigmoidoscopy due to concerns about perforation. Among these cases, subsequent imaging studies (IUS examination) indicated various extents of inflammation: 2 cases involving the ascending colon, 2 involving the transverse colon, 2 extending to the splenic flexure, and 1 reaching the hepatic flexure.

After Treatment: Following the induction dose of biological therapy (6 weeks), the distribution of colitis among the patients changed. Specifically, 25.6% had pancolitis, 41% exhibited left-sided colitis, and 10% presented with proctosigmoiditis. However, no statistically significant difference was observed between these groups. Additionally, 7.69% of patients could not undergo a full colonoscopic assessment, with only a short sigmoidoscopy performed due to concerns about procedural risks. Among those categorized as "cannot be assessed," subsequent IUS examinations revealed further details: inflammation extending up to the splenic flexure in 2 cases, and one case of proctosigmoiditis.

Regarding the Colonoscopic Mayo Score, significant differences were observed between baseline findings and those after the induction dose of biological therapy (6 weeks). Initially, most (94.2%) patients had a Mayo Score of 3. However, after treatment, 41% achieved a Mayo Score of 0, 33.3% achieved a Mayo Score of 1, and 12.8% retained a score of 3. These changes were statistically significant.

A statistically significant difference was observed regarding the SCCAI (Simple Clinical Colitis Activity Index). Before treatment, 63.5% of the study participants were classified as having severe disease based on SCCAI scores. However, following the induction dose of biological therapy (at 6 weeks), 76.9% of patients achieved remission, and none remained classified as having severe disease.

Regarding the Clinical Mayo Score, a statistically significant difference was observed. Before treatment, 69.2% of the patients were classified as having severe disease. After the induction dose of biological therapy (at 6 weeks), the distribution changed significantly: approximately 21.2% achieved remission, approximately 30.8% had mild disease, and approximately 11.5% continued to have severe disease, as illustrated in **Table (1)**.

Table (1): Laboratory investigations and Endoscopic diagnosis before and after the biological treatment:

Variable	At baseline	After follow-up	*P* value
Hemoglobin (mg/dl)	10.94± 2.39	12.08 ±1.60	0.008
leucocytes	7.59 ± 2.91	7.02 ± 2.56	0.491
MCV	78.19 ± 5.97	81.117 ± 4.50	0.003
Albumin (g/L)	38.38 ± 4.93	39.9 ± 4.65	0.135
ESR 2nd (mm/h)	82.15 ± 16.39	21.81 ± 10.22	< 0.001
ESR 1st Hour	55.95 ± 16.54	17.00 ± 15.82	< 0.001
C-reative protein mg /l	36.25 ± 41.36	13.16 ± 13.21	< 0.001
Ferretin ng/ml	26.08 ± 43.27	47.36 ± 122.84	0.034
Fecal calprotectin micro g /g	711.55 ± 203.90	121.97 ± 85.33	< 0.001

Table (1): Laboratory investigations and Endoscopic diagnosis before and after the biological treatment: ***(Cont.)***

Variable	At baseline	After follow-up	*P* value
Colonoscopy			**0.054**
Left sided	26 (50.0%)	16 (41%)	
Pancolitis	19 (36.5%)	10 (25.6%)	
Proctosigmoiditis	0(0%)	10 (25.6%)	
Cannot be assessed	7 (13.5%)	3 (7.69%)	
Colonoscopy Mayo score (endoscopic)			**≤ 0.001**
Score 0	2 (3.8%)	16(41%)	
Score 1	0 (0%)	13 (33.3%)	
Score 2	1 (1.9%)	5 (12..8%)	
Score 3	49 (94.2%)	5 (12.8%)	
SCCAI (Short Clinical Colitis Activity Index			**0.031**
Remission	5 (9.6%)	40(76.9%)	
Mild	8(15.4%)	4(7.7%)	
Moderate	6(11.5%)	2(3.8%)	
Severe	33(63.5%)	0(0%)	
Mayo Clinical			**0.027**
Remission	0(0%)	11(21.2%)	
Mild	1(1.9%)	16(30.8%)	
Moderate	14(26.9%)	6(11.5%)	
Severe	36(69.2%)	6(11.5%)	

Data expressed as mean ±SD, independent patients included in study, T-test was used to compare means between groups *P* P-value was significant if < 0.05. MCV(mean corpuscular volume).

Table (2) shows a statistically significant difference in colonic wall thickness observed in the Rectum, sigmoid colon, descending colon, and transverse colon before and after treatment (P-value = 0.001).

Table (2): Intestinal Ultrasound thickness before and after the biological treatment:

Variable	At baseline	At follow-up	*P* value
Rectum Thickness	4.55± 1.33	3.67 ±1.06	< **0.001**
Sigmoid Thickness	5.12 ± 1.18	3.23 ± 1.02	< **0.001**
Descending Thickness	4.65 ± 1.09	3.08±0.86	< **0.001**
Transverse Thickness	3.99±1.01	2.75± 0.63	< **0.001**
Ascending Thickness	3.67 ± 0.70	2.59± 0.62	0.064
Cecum Thickness	2.17± 0.44	2.40± 2.57	0.542

Data expressed as mean ±SD, independent patients included in the study; the T-test was used to compare means between groups. P-value was significant if < 0.05.

Table (3) presents the findings from intestinal ultrasound assessments at baseline and follow-up after completing the induction dose of Infliximab (6 weeks).

Regarding the Rectum before treatment, approximately 73.1% of the patients in the study were classified with a Limberg score of 4 vascularity. However, following the follow-up period, approximately 19.56% categorized as grade 0, approximately 34.8% as grade 1, approximately 32.6% as grade 2, and only 8.69% remained classified as grade 4.

Regarding sigmoid vascularity before treatment, most patients (69.2%) exhibited grade 4 vascularity. However, after follow-up, only 4.34% retained grade 4 vascularity, 34.78% showed grade 0 vascularity, and 28.26% exhibited grade 2 vascularity.

Regarding descending colon vascularity, the majority (67.3%) of the patients in the study exhibited grade 4 vascularity before treatment. After follow-up, approximately 43.47% showed grade 0 vascularity, while only 2.17% retained grade 4 vascularity.

Regarding transverse colon vascularity, 21.2% of patients exhibited grade 4 vascularity before treatment, and 30.8% had grade 2 vascularity. After treatment, 46.2% showed grade 0 vascularity, 38.5% had grade 1 vascularity, and none exhibited grade 4 vascularity.

Regarding ascending colon vascularity, approximately 30.8% of the patients had grade 0 vascularity before treatment, and 40.4% had grade 1 vascularity. After treatment, 56.5% of the patients showed grade 0 vascularity, and 41.3% exhibited grade 1 vascularity.

Regarding cecal vascularity, 94.2% of patients had grade 0 vascularity before treatment. After treatment, 88.5% continued to exhibit grade 0 vascularity.

Regarding rectal inflammatory fat wrapping, before treatment, approximately 65.4% of the patients in the study exhibited more than 50% fat wrapping of the circumference, while 34% had less than 50% fat wrapping. After 6 weeks of follow-up, only 23.1% of the patients showed more than 50% fat wrapping, 26.9% had no fat wrapping, and 36.9% had less than 50% fat wrapping of the circumference.

Regarding sigmoid inflammatory fat wrapping, before treatment, 40.4% of the patients in the study had less than 50% fat wrapping of the circumference, while 51.9% had more than 50% fat wrapping. At follow-up, approximately 43.4% showed absent fat wrapping of the circumference, 21.7% had less than 50% fat wrapping, and 34.8% had more than 50% fat wrapping.

Regarding descending colon inflammatory fat wrapping, before treatment, approximately 42.3% of the patients had less than 50% fat wrapping of the circumference, and 46.1% had more than 50% fat wrapping.

At follow-up after treatment, 56.5% of the patients exhibited absent fat wrapping of the circumference. Additionally, 21.7% had less than 50% fat wrapping, and another 21.7% had more than 50% fat wrapping of the circumference.

Regarding transverse colon inflammatory fat wrapping, before treatment, 34.6% of the patients had less than 50% fat wrapping of the circumference, and 28.6% had more than 50% fat wrapping. At follow-up, 61.5% showed absent inflammatory fat wrapping, and only 3.8% exhibited more than 50% inflammatory fat wrapping.

Regarding ascending colon inflammatory fat wrapping, 80.8% of the patients showed absent inflammatory fat wrapping of the circumference before treatment. After treatment, this percentage decreased to 76% exhibiting absent inflammatory fat wrapping of the circumference.

Regarding cecal inflammatory fat wrapping, both before and after treatment, there was no inflammatory fat wrapping of the circumference.

Table (3): Ultrasound findings at baseline and follow-up (6 weeks):

At baseline		After follow-up	P value
Rectal vascularity by	Limberg score		0.124
- Grade 0,1,2,3,4	1(1.9%),0(0%),6(11.5%), 7(13.5%),38(73.1%)	9(19.56%),16(34.8%), 15 (32.6%),2(4.34%),4(8.69%)	
Rectal inflammatory fat wrapping % of circumference			0.230
- Abscent	4(7.7%)	15(32.6%)	
- <50% of circumference	14 (26.9%)	19(36.5%)	
- >50% of circumference	34(65.4%)	12(23.1%)	
Sigmoid vascularity	Limberg score		0.561
- Grade 0,1,2,3,4	1(1.9%),2(3.8%),7(13.5%), 6(11.5%),36(69.2%)	16(34.78%),13(28.26%),15(32.6%),0(0%), 2(4.34%)	
Sigmoid inflammatory fat wrapping % of circumference			0.411
- Abscent	4(7.7%)	20(43.4%)	
- <50% of circumference	21(40.4%)	10(21.7%)	
- >50% of circumference	27(51.9%)	16(34.8%)	
Descending vascularity	Limberg score		0.330
- Grade 0,1,2,3,4	3(5.8%),6(11.5%),2(3.8%), 6(11.5%),35(67.3%)	20(43.47%),16(34.8%), 8(17.39%),1(2.17%), 1(2.17%)	
Descending inflammatory fat wrapping % of circumference			0.071
- Abscent	6(11.5%)	26(56.5%)	
- <50% of circumference	22(42.3%)	10(21.7%)	
- >50% of circumference	24(46.1%)	10(21.7%)	
Transverse vascularity	Limberg score		0.249
Grade 0,1,2,3,4	5(9.6%),15(28.8%),16(30.8%),16(30.8%),5(9.6%),11(21.2%)	24(46.2%),20(38.5%), 0(0%),1(1.9%),0(0 %)	
Transverse inflammatory fat wrapping %of circumference			0.071
- abscent	19(36.5%)	32(69.5%)	
- <50% of circumference	18(34.6%)	9(19.5%)	
- >50% of circumference	15(28.6%)	5(10.86%)	
Ascending vascularity	Limberg score		0.098
- Grade 0,1,2,3,4	16(30.8%),21(40.4%), 9(17.3%),1(1.9%),5(9.6%)	26(56.5%),19(41.3%), 1(2.1%),0(0%),0(0%)	
Ascending inflammatory fat wrapping %of circumference			0.154
- abscent	42(80.8%)	35(76%)	
- <50% of circumference	7(13.4%)	5 (10.8%)	
- >50% of circumference	3(4.7%)	6(13%)	
Cecum vascularity	Limberg score		0.781
- Grade 0,1	49(94.2%),3(5.8%)	46(88.5%),0(0%)	
Cecum inflammatory fat wrapping			--
- 0% of circumference	52(100.0%)	46(100.0%)	
Other findings			0.974
- Lymph nodes	7 (13.5%)	6 (11.6%)	
- Mild ascites	1(1.9%)	1(1.9%)	
Haustration			0.063
- Lost	30(57.7%)	17(32.7%)	
- Preserved	19(36.5%)	27(51.9%)	

Data expressed as frequency (percentage)

A statistically significant positive correlation was observed between the SCCAI score and the IUS thickness measurements in the ascending, transverse, descending, Rectum, and sigmoid colon. Similarly, there was a statistically significant positive correlation between the endoscopic Mayo score and the IUS thickness measurements in these same segments of the colon (ascending, transverse, descending, Rectum, and sigmoid). As shown in **Table (4).**

Table (4): Correlation between Short Clinical Colitis Activity Index and Bowel Wall thickness measured, and correlation between colonoscopy Mayo score (endoscopic) and Bowel Wall thickness measured by IUS:

Item	Cecum Thickness	Ascending Thickness	Transverse Thickness	Descending Thickness	Sigmoid Thickness	Rectum Thickness
SCCAI *r* correlation coefficient	0.12	0.92	0.188	0.275	0.292	0.278
P value	0.079	0.017	0.035	0.048	0.035	0.046
Colonoscopy Mayo score *r* correlation coefficient	0.158	0.052	0.32	0.39	0.325	0.234
P value	0.263	0.02	0.022	0.021	0.019	0.043

r value (Values between 0.2 and 0.39: mild correlation, Values between 0.4 and 0.59: Moderate correlation, Values between 0.6 and 1: strong correlation).

It was found that the IUS diagnosis of thickness of the sigmoid colon at a threshold of mean thickness value of 3.9 mm was possible with sensitivity, specificity, and area under the curve, PPV, and NPV of 95%, 92%, and 0.95, 93%, 82%, respectively. IUS diagnosis of thickness of the descending colon at a threshold of mean thickness value of 3.0 mm was possible with sensitivity, specificity, and area under the curve, PPV, and NPV of 82%, 87%, 0.877, 91%, 75% respectively. The IUS diagnosis of thickness of the transverse colon at a threshold of mean thickness value of 3.1 mm was possible with sensitivity, specificity, and area under the curve, PPV, and NPV of 84%, 82%, 0.69, and 87%, 79% respectively. The IUS diagnosis of thickness of the ascending colon at a threshold of mean thickness value of 3.0 mm was possible with sensitivity, specificity, and area under the curve, PPV, and NPV of 83%, 85%, 0.685, 90%, 73% respectively, as shown in **Table (5) and in figures from 1 to 6.**

Table (5): ROC Curve Bowel wall thickness, thickness sensitivity, Specificity, Area Under the Curve (AUC), Negative Predictive Value (NPV), and Positive Predictive Value (PPV)

Item	Rectum	Sigmoid	Descending	Transverse	Ascending	Cecum
Sensitivity	95%	95%,	82%	84%	83%	75%
Specificity	90%	92%,	87%	82%	85%	80%
AUC	0.954	0.95	0.877	0.69	0.685	0.710
NPV	94%	93%	91%,	87%	90%	88%
PPV	78%	82%	75%	79%	73%	68%

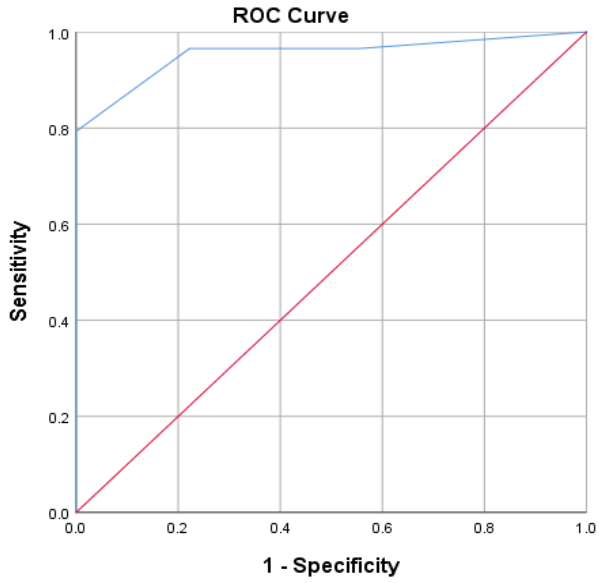


Figure. (1): The IUS diagnostic characteristics of the thickness of the Rectum, 4.8 mm, with sensitivity, specificity, and area under the curve, PPV, and NPV

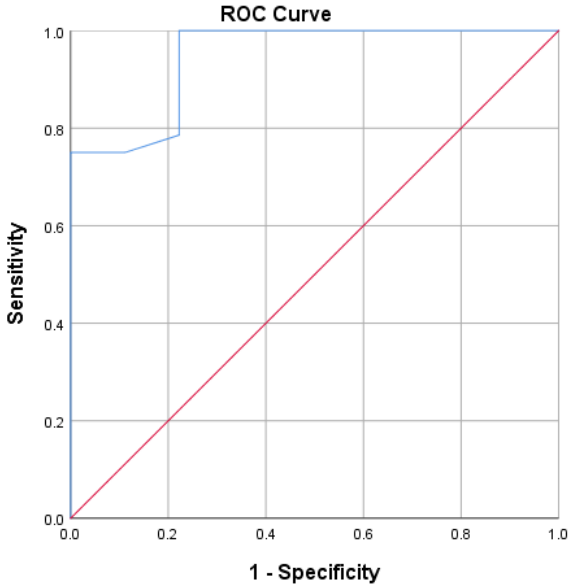
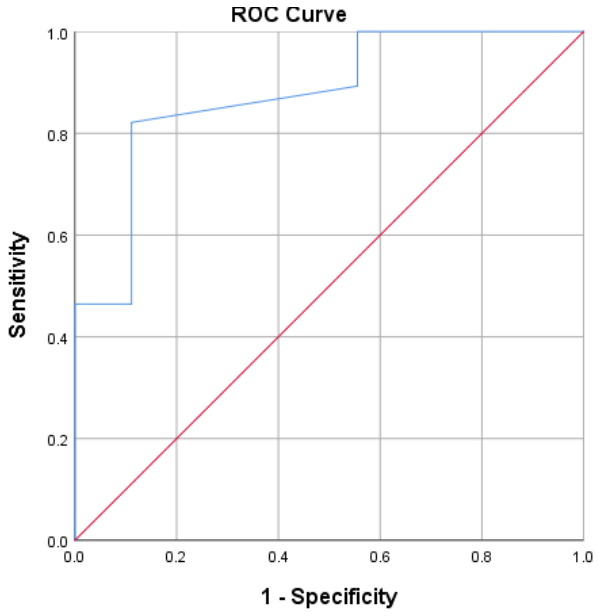


Figure. (2): The IUS diagnostic characteristics of the thickness of the segmoid 3.1 mm, with sensitivity, specificity, and area under the curve, PPV, and NPV



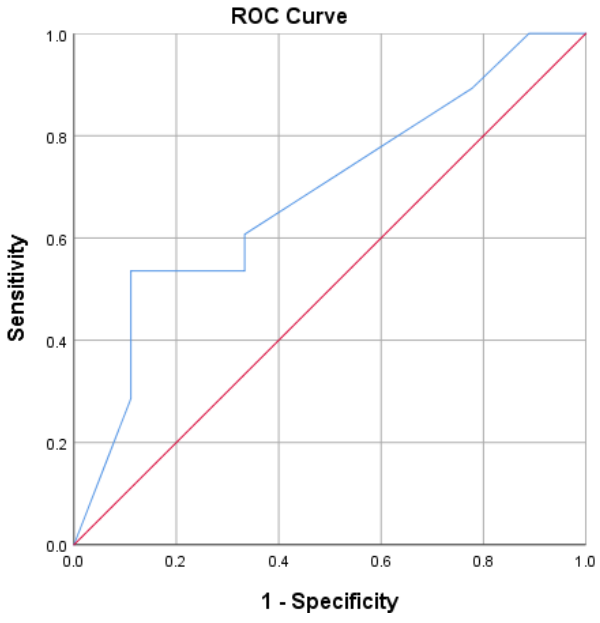


Figure. (3): The IUS diagnostic characteristics of the thickness of the descending colon, 3 mm, with sensitivity, specificity, area under the curve, PPV, and NPV

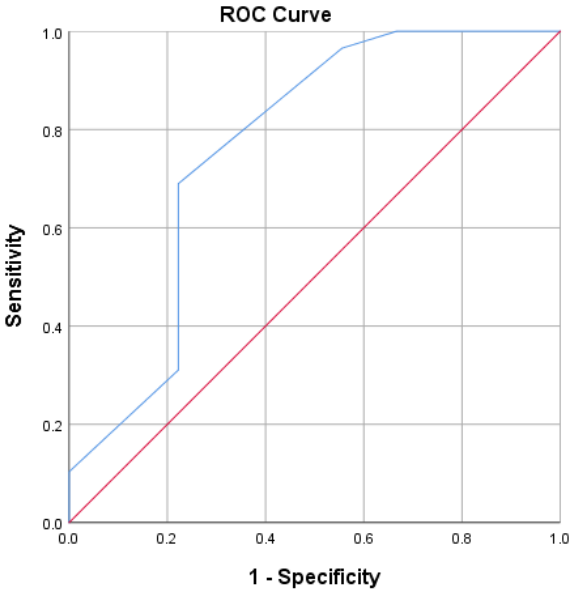


Figure.(4): The IUS diagnostic characteristics of the thickness of the transverse colon, 3.1 mm, with sensitivity, specificity, area under the curve, PPV, and NPV

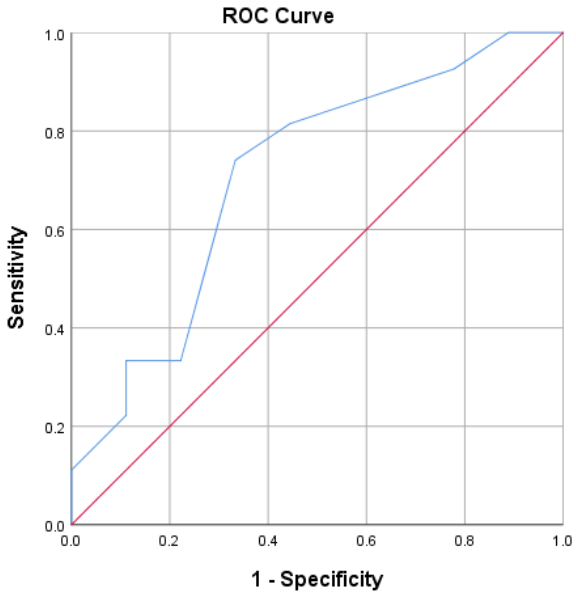


Figure. (5): The IUS diagnostic characteristics of the thickness of the ascending colon, 3 mm, with sensitivity, specificity, area under the curve, PPV, and NPV

Figure. (6): The IUS diagnostic characteristics of the thickness of the cecum, 2.9 mm, with sensitivity, specificity, and area under the curve, PPV, and NPV

Discussion

Ulcerative colitis (UC) is a chronic inflammatory condition affecting the colon and Rectum, characterized by inflammation and ulceration. It is one of the two major forms of inflammatory bowel disease (IBD), alongside Crohn's disease (CD). Unlike CD, which can affect any part of the gastrointestinal tract, UC is confined to the large intestine **[8]**.

Biological therapy has proven effective in managing UC; however, response monitoring has traditionally depended on endoscopy, an invasive procedure. Intestinal ultrasound (IUS) is a non-invasive alternative with an expanding body of evidence supporting its efficacy in assessing therapeutic response in UC patients undergoing biological therapy **[9]**.

The primary strength of IUS lies in its ability to assess bowel wall thickness (BWT), a critical marker of inflammation. Increased BWT indicates active disease, especially in the mucosal and submucosal layers. Recent studies highlight IUS's capability to detect these changes, providing valuable insights into disease activity and response to biological therapy **[3]**.

Moreover, IUS offers several advantages over other imaging modalities. Unlike magnetic resonance imaging (MRI) or computed tomography (CT), IUS is more accessible, cost-effective, and avoids ionizing radiation, making it a patient-friendly option for regular monitoring, particularly in the long-term management of UC **[10]**.

Serum ferritin, fecal calprotectin, hemoglobin, and acute-phase reactants (ESR, CRP) showed statistically significant improvement post-treatment compared to pre-treatment ($p < 0.05$). These findings align with a study by **Loftus Jr et al. [11]**, which reported a significant increase in hemoglobin levels following biological therapy (13.7 g/dL vs. 12.3 g/dL; $p < 0.001$).

A meta-analysis by **Hindryckx et al. [12]** reported significant reductions in ESR and CRP levels compared to placebo. This finding is consistent with our observation of statistically significant decreases in ESR and CRP after treatment. Additionally, a study by **Frühauf [13]** investigating the use of fecal calprotectin to monitor response to biological therapy in IBD demonstrated a significant decrease in fecal calprotectin levels following induction of biological therapy.

Endoscopic findings from colonoscopy at baseline and follow-up (6 weeks post-induction dose of biological therapy) revealed that 50% of the study participants had left-sided colitis, while 36.5% had pancolitis. In 13.5% of cases, assessment was limited to a short sigmoidoscopy due to concerns about perforation. Follow-up imaging with IUS indicated varying degrees of inflammation in these cases: two involved the ascending colon, two the transverse colon, two extended to the splenic flexure, and one reached the hepatic flexure.

This is consistent with the findings of **Esmat et al. [14],** who reported that 65% of patients had left-sided UC, 18.5% had proctitis, and 16.2% had pancolitis. Similarly, a study by **de Voogd et al. [7]** involving 51 patients found that, at baseline endoscopy, 33 (65%) patients had proximal disease extension, with 51% having left-sided colitis and 49% exhibiting extensive colitis. In the subgroup of patients with no proximal disease extension on endoscopy, IUS identified additional affected segments in 10 (20%) patients.

Regarding the Mayo Endoscopic Score (MES), significant differences were observed between baseline and post-treatment (6 weeks after induction dose) findings. Initially, most patients (94.2%) had a MES of 3. After treatment, 30.8% achieved a MES of 0, 25% achieved a MES of 1, and 9.6% retained a MES of 3. These changes were statistically significant ($p < 0.001$).

Consistent with our findings, an Egyptian study by **Kamal et al. [15]** involving 22 ulcerative colitis patients treated with infliximab observed a significant decrease in MES after treatment ($P = 0.026$). Regarding treatment response, we found that most patients exhibited a clinical response to biological therapy, with 24% achieving clinical remission, 56.5% showing clinical improvement, and 19.5% experiencing treatment failure. Similarly, a study by **Hassan et al. [16]** reported that clinical remission was achieved in 54.5% of patients following an infliximab induction course.

Bowel wall thickness (BWT) is a key parameter in intestinal ultrasound (IUS) assessment and is crucial for detecting intestinal disease. BWT is measured by evaluating all wall layers from the lumen interface to the serosa. Typically, a wall thickness between 3 and 4 mm is considered normal, except for the gastric wall, where thickness can range up to 5 or 6 mm **[17]**.

Our study observed a statistically significant reduction in bowel wall thickness in the Rectum, sigmoid, descending colon, and transverse colon following treatment compared to pre-treatment measurements. These findings align with those of **Ilvemark et al. [18],** who also reported a significant decrease in bowel wall thickness in these regions after treatment ($p < 0.05$). Similarly, a study by **Maaser et al. [10]** involving 244 ulcerative colitis patients undergoing biological therapy across 12 centers in Germany found a significant decrease in bowel wall thickness. This study, which assessed patients at baseline and after 12 weeks, follows a similar methodology with different time points.

Also, in a study by de Voogd et al. [7], 57% of patients demonstrated a significant decrease in BWT after 18 weeks of treatment for the sigmoid and descending colon, respectively, p-value < 0.05.

Our study examined several regions, including the Rectum, sigmoid colon, descending colon, transverse colon, and ascending colon. Vascularity, assessed according to the Limberg score, showed significant improvement after treatment in all these areas. For instance, in the Rectum, most patients had the worst grade (grade 4)

before treatment, but only a small percentage retained this grade post-treatment. Similarly, inflammatory fat wrapping (fatty tissue surrounding the colon) also showed improvement. Before treatment, many patients had significant wrapping, but after treatment, many exhibited either no or minimal wrapping. These findings suggest that the treatment improved blood flow and reduced inflammatory fat wrapping in the examined regions.

A study by **de Voogd et al. [7]** similarly reported that 57% of patients showed the presence of inflammatory fat wrapping, which decreased after infliximab therapy (6 weeks, $p < 0.05$). The study also found significant improvement in the color Doppler signal after treatment.

Furthermore, our study identified a significant positive correlation between the Simple Clinical Colitis Activity Index (SCCAI) score and intestinal ultrasound (IUS) measurements of bowel wall thickness (BWT) in the ascending, transverse, descending, Rectum, and sigmoid colon. These findings are consistent with those of **de Voogd et al. [7]**, who investigated using IUS to monitor treatment response in UC. Their study demonstrated a significant correlation between the SCCAI score and BWT across all colonic segments at baseline ($\rho = 0.54$ to 0.64, $P < 0.001$), supporting our findings of a positive correlation between SCCAI scores and IUS measurements of bowel wall thickness.

Sharara et al. [19] explored the role of intestinal ultrasound (IUS) in assessing disease activity in ulcerative colitis, comparing it with the Mayo endoscopic score (MES). The study found a significant correlation between the Simple Clinical Colitis Activity Index (SCCAI) and maximal bowel wall thickness (BWT) ($\rho = 0.62$, $P < 0.001$), aligning with our observation of a positive correlation between these measures. Additionally, we found a significant positive correlation between the Mayo endoscopic score and IUS measurements of BWT in the ascending, transverse, descending, Rectum, and sigmoid colon.

These findings are consistent with **Takahara et al. [20]**, who also reported a positive correlation between BWT and endoscopic activity ($\rho = 0.69$, $p < 0.0001$) in UC patients. Their study demonstrated that BWT increased with rising Mayo endoscopic scores ($p < 0.0001$), further supporting the positive correlation between higher Mayo scores and increased ultrasonographic thickness.

In our study, we assessed the effectiveness of IUS in measuring colon wall thickness across various segments. IUS proved a reliable diagnostic tool for detecting abnormal colon wall thickness, particularly in the Rectum and sigmoid colon. For the Rectum, IUS had a cut-off value of 4.8 mm for abnormal thickness, yielding a sensitivity of 95%, specificity of 90%, and an Area Under the Curve (AUC) of 0.954. In the sigmoid colon, the cut-off value was 3.9 mm, with a sensitivity of 95%, specificity of 92%, and an AUC of 0.95.

However, the diagnostic accuracy of IUS decreased when assessing the transverse and ascending colon. For the transverse colon, with a cut-off value of 3.1 mm, sensitivity was 84%, specificity 82%, and AUC 0.87. In the ascending colon, the cut-off value was 3.0 mm, but the sensitivity (83%), specificity (85%), and AUC (0.685) were the lowest among the segments evaluated. These results suggest that IUS is less effective in diagnosing transverse and ascending colon abnormalities than other regions.

These findings are consistent with a study by **Frias-Gomes et al. [21]**, which compared ultrasound (US) with colonoscopy for assessing colonic wall thickness in patients with inflammatory bowel disease (IBD). Their results supported our observations, demonstrating high accuracy in the Rectum, with a sensitivity of 94% and specificity of 93%, and in the sigmoid colon, with a sensitivity of 90% and specificity of 89%. However, in the right colon (including the transverse and ascending segments),

sensitivity and specificity decreased to 78% and 79%, respectively. These results further reinforce our observation of reduced diagnostic efficacy of US in the ascending and transverse colon.

Conclusion:

The accuracy of IUS in monitoring wall thickness in UC pre and post-biological therapy. High performance characteristics was found in the Rectum (sensitivity, specificity, AUC, PPV and NPV of 95%, 90%, 0.954, 94%, 78% respectively), and sigmoid colon (with (sensitivity, specificity, AUC, PPV and NPV of 95%, 92%, 0.95, 93%, and 82%, respectively) (compared with other parts of the colon.

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