

Original Article

Evaluation of Doppler-Derived Vascularity Indices as Non-Invasive Biomarkers for Monitoring Therapeutic Response and Mucosal Healing in Severe Inflammatory Bowel Disease

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ABSTRACT

Objectives: To evaluate Doppler-derived vascularity indices and bowel-wall measurements as markers of therapeutic response and mucosal healing in severe IBD.

Methodology: A prospective observational study included 96 patients aged 18–60 years at Jinnah Hospital, Lahore, recruited through non-probability purposive sampling following written informed consent. Intestinal ultrasound assessed bowel-wall thickness (BWT), peak systolic velocity (PSV), end-diastolic velocity (EDV), resistive index (RI), pulsatility index (PI), and vascularity grade at baseline and follow-up. We analyzed clinical, laboratory, and available endoscopic findings using SPSS version 25, with $p \leq 0.05$ considered significant.

Results: BWT decreased significantly from 5.63 ± 1.29 to 3.96 ± 1.15 mm ($p < 0.001$). PSV and EDV decreased, while RI and PI increased, indicating reduced bowel-wall hyperemia. ESR and fecal calprotectin decreased significantly. Follow-up BWT strongly correlated with fecal calprotectin ($r = 0.83$, $p < 0.001$). Mean BWT reductions were approximately 0.60, 1.48, and 2.56 mm among non-responders, partial responders, and complete responders, respectively.

Conclusion: BWT and Doppler parameters demonstrated promising associations with therapeutic response. Multiparametric intestinal ultrasound may complement clinical, laboratory, and endoscopic assessment for non-invasive monitoring; however, its ability to establish mucosal healing requires further validation against endoscopy.

Introduction

Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), is a chronic relapsing inflammatory disorder that can cause progressive bowel damage and substantially affect quality of life [1]. Its burden is increasing globally, including in developing regions, creating a growing need for effective long-term monitoring strategies [2]. Modern IBD management follows a treat-to-target approach in which objective control of inflammation and mucosal healing are important therapeutic goals [3]. Endoscopy remains the reference standard for assessing mucosal disease, but its invasiveness, cost, patient discomfort, and limited suitability for frequent repetition encourage the use of reliable non-invasive monitoring tools [4]. Intestinal ultrasound, particularly Doppler ultrasound, is a radiation-free, relatively inexpensive, repeatable technique that provides real-time assessment of bowel-wall thickness (BWT) and vascularity [5]. Inflammatory angiogenesis and vasodilation alter bowel-wall blood flow. Doppler parameters such as resistive index (RI), pulsatility index (PI), peak systolic velocity, end-diastolic velocity, and vascularity grade may reflect these changes [6]. Previous studies have reported associations between bowel-wall vascularity, clinical activity, inflammatory biomarkers, endoscopic findings, and treatment response [7]. Compared with laboratory biomarkers alone, Doppler ultrasound provides direct structural and hemodynamic information and may be especially useful where repeated endoscopy or advanced cross-sectional imaging is difficult to access [8,9]. However, operator dependence, variation in acquisition techniques, and the absence of universally accepted vascularity thresholds continue to limit standardization [10]. Therefore, further evaluation in local clinical settings is required.

The present study aimed to evaluate Doppler-derived vascularity indices as non-invasive markers of therapeutic response and mucosal healing in patients with severe IBD, and to correlate them with clinical, laboratory, and available endoscopic findings.

Material and Methods

This was a prospective observational study with non-interventional monitoring of patients over time from Jan 2025 to Dec 2025. Severe inflammatory bowel disease (IBD) patients were recruited at diagnosis and followed up in their regular clinical care. The design allowed data collection "on the spot" with no recall bias, and clinical and imaging findings were accurately documented. Standard treatment did not change, and all patients were treated according to institutional protocols. The study was designed to observe disease progression and to assess the changes in vascularity by Doppler as a measure of therapeutic response.

Clinical Settings

The study was conducted in the Department of Radiology and Gastroenterology at Jinnah Hospital, a tertiary care teaching hospital with advanced diagnostic facilities. The Radiology Department performed high-resolution ultrasound and Doppler imaging, and the Gastroenterology

Department carried out clinical evaluation, diagnosis, and treatment of patients with IBD. This multi-disciplinary arrangement allowed for a combined clinical & imaging assessment. Because the hospital had a high volume of IBD patients, there were enough patients to recruit, and they were representative of the overall patient population.

Study Population

This study involved patients who had severe inflammatory bowel disease (IBD) such as Crohn's and ulcerative colitis. The diagnosis was confirmed by clinical evaluation complemented by laboratory investigation, imaging findings, and/or endoscopy and/or histopathology. We included patients already being followed and diagnosed in the Gastroenterology Department. This allowed Doppler ultrasound to assess disease activity and therapeutic response. The population selected consisted of moderate to severe cases of IBD, and in these cases, assessing vascular changes was clinically significant as an indicator of treatment outcomes.

Sample Size

The required sample size is determined according to Cochran's formula

$$n = Z^2 \times p \times (1 - p) / e^2$$

Where:

n = Sample size required.

- Z = Z value at 95% confidence level (1.96)

The estimated prevalence (assumed 50% or 0.5 if unknown) is denoted as p.

- e = margin of error (10% or 0.1)

$$n = (1.96)^2(0.5)(1-0.5) / (0.1)^2$$

$$n = 96.04 = 96$$

Sampling Technique

Patients included in this study were selected using the non-probability purposive sampling technique with pre-established inclusion and exclusion criteria. Patients were included only if they were on treatment and follow-up for severe inflammatory bowel disease (IBD). This technique enabled selection of clinically relevant cases appropriate for Doppler-derived vascularity indices within the study period.

Duration of Study

We recruited patients over 4 months. We obtained longitudinal follow-up assessments according to routine clinical scheduling at 3, 6, 9, or 12 months after baseline. Accordingly, the recruitment window and the maximum follow-up duration are reported separately and should not be interpreted as a total study duration of only 4 months.

Selection Criteria

Samples will be selected based on the inclusion and exclusion criteria.

Inclusion Criteria

Patients between the ages of 18 and 60 years

Male and female patients

Clinically diagnosed severe inflammatory bowel disease, based on laboratory, endoscopy, and/or histopathology.

Any patients who were on treatment for IBD

Patients who were willing to participate in the study

Exclusion Criteria

History of major abdominal surgery that affected the examination (such as resection, stoma).

Other gastrointestinal diseases (such as infectious colitis, ischemic bowel).

Pregnant females

Contraindications to ultrasound (extensive bowel gas, large weight of the patients that will make it difficult to visualize the bowel).

Ethical Consideration

The study will be carried out in accordance with the ethical guidelines approved by the Ethical Committee, Superior University, Lahore, which ensures that participants' rights and well-being are protected. All participants provided written informed consent before participating in the study.

All data and information collected were kept confidential and were not used for any purpose other than research. We kept participants' identities anonymous to protect their privacy.

Parents/legal guardians gave written informed consent after the purpose, procedures, potential risks, and potential benefits of the study were described understandably. Everyone is free to join or leave as they please, and withdrawing will not affect medical care.

Data Collection Procedure

After IHRC approval, eligible patients meeting the inclusion criteria were recruited from Jinnah Hospital. We obtained informed consent from all participants before inclusion. We used a structured proforma to record baseline demographic and clinical data, including age, gender, type of inflammatory bowel disease (IBD), disease duration, and current treatment status. We performed Doppler ultrasound examinations of affected bowel segments in all patients using a high-resolution ultrasound machine with Doppler capability. An experienced radiologist performed all examinations to ensure uniformity and reliability. We assessed bowel wall thickness, bowel wall vascularity, pulsatility index (PI), and resistive index (RI), as well as the presence of bowel wall hyperemia or increased blood flow. We obtained Doppler-derived vascularity indices at baseline and compared them with post-treatment indices. We associated imaging findings with clinical improvement, laboratory parameters (C-reactive protein [CRP] and fecal calprotectin [FCP], which were available for all 96 participants included in the reported analysis), and endoscopic parameters of mucosal healing.

Therapeutic efficacy was rated according to clinical response, laboratory parameters, and image changes. Mucosal healing was assessed by endoscopy (if available).

Disease-specific clinical and endoscopic assessment

The proforma specifies CDAI for CD and Mayo scoring for UC. CDAI_Baseline was used only in records coded

IBD_Type = 1 and Mayo_Baseline only in records coded IBD_Type = 2. CDAI_Mayo_FU was interpreted separately by subtype as follow-up CDAI or Mayo.

Study Variables

- Independent Variables:
- Age
- Gender
- Type of IBD
- Treatment status
- Dependent Variables

Doppler-derived vascularity indices (RI, PI, bowel wall vascularity)

Therapeutic response

Mucosal healing

Data Analysis

All the collected data were entered and analyzed using SPSS version 25. Quantitative variables, including age, bowel wall thickness, RI, and PI, were expressed as mean $\pm$ SD. Gender, therapeutic response, type of IBD, and mucosal healing were expressed as frequencies and percentages and were considered qualitative variables. We evaluated the relationship between Doppler-derived and clinical results using appropriate statistical tests. We used an independent t-test or Mann-Whitney U test to compare quantitative variables, and the Chi-square test for qualitative variables. We used Pearson or Spearman correlation to assess the relationship between Doppler indices and clinical or endoscopic findings. Disease-specific totals were summarised within subtypes using n, mean, SD, median, and range. We calculated paired baseline-to-follow-up change as follow-up minus baseline; we used paired t-tests descriptively. CDAI categories used were <150, 150–219, 220–450, and >450. UC totals were grouped into 0–2, 3–5, 6–10, and 11–12 under a provisional full-Mayo interpretation. Mayo categories are conditional on version confirmation; a total ≤ 2 alone does not establish remission. No between-subtype comparison of CDAI and Mayo was performed. We considered $p \leq 0.05$ statistically significant.

Results

All continuous variables were assessed for normality first. We presented normally distributed variables as mean $\pm$ standard deviation (SD) and compared them using paired- or independent-samples t-tests; we reported non-normally distributed variables with their non-parametric equivalents: the Wilcoxon signed-rank test for paired data and the Mann-Whitney U test for independent groups. For categorical variables, we reported frequencies and percentages and used the chi-square (χ^2) test of independence to compare them. We used Pearson's and Spearman's correlation coefficients to assess associations between continuous sonographic and clinical/biochemical variables. We determined the diagnostic accuracy of sonographic bowel wall thickness using receiver operating characteristic (ROC) curve analysis. We identified the optimal cut-off point by calculating the

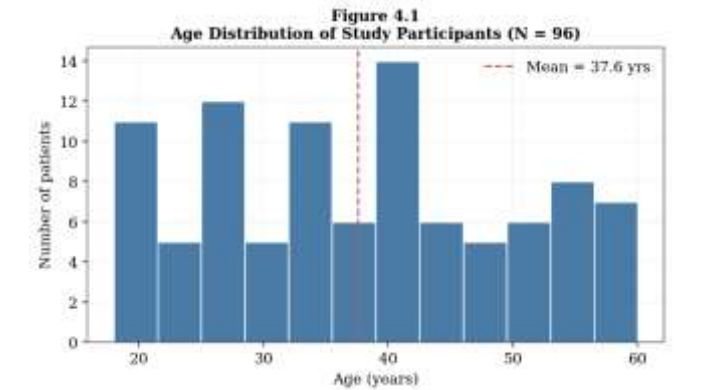
area under the curve (AUC) and the Youden index. In the case of a relatively small number of categorical fields in the source data set for which the coding of the data was not recorded separately, the field was coded with the most clinically conventional labels and is indicated in the notes to the tables; this does not influence the results of the numerical calculations, which are calculated directly from the recorded data.

Table 1 Descriptive Statistics for Continuous Demographic and Clinical History Variables

Variable	M	SD	Median	Min	Max	Skewness
Age (years)	37.59	12.07	38.00	18	60	0.13
Height (cm)	163.72	8.75	161.65	145.4	191.4	0.67
Weight (kg)	65.42	10.83	64.65	42.0	91.1	0.09
BMI (kg/m²)	24.49	4.24	24.38	15.9	35.9	0.46
Disease duration (months)	94.92	51.32	101.00	6	180	-0.04
Age at diagnosis (years)	29.60	12.31	29.50	12	58	0.23

Descriptive statistics are presented in Table 1 for the continuous variables of the demographic and disease-history variables. The mean age of the sample was 37.6 ± 12.1 years (range 18–60 years) and the mean body mass index (BMI) was 24.5 ± 4.2 kg/m², which is within the normal to overweight range. The mean disease duration was 94.9 ± 51.3 months (about 7.9 years) and the mean age of diagnosis was 29.6 ± 12.3 years.

Figure 1. Age distribution of study participants



By sex, the sample comprised 51 males (53.1%) and 45 females (46.9%). There was a simiThe proportion of IBD subtypes, with 50 patients (52.1%) diagnosed as having Crohn's disease and 46 patients (47.9%) as having ulcerative colitis (Table 2, Figure 2). An independent-samples t-test showed no significant difference in mean age between males and females ($p = .671$).

Table 2. Frequency Distribution of Sex and IBD Subtype

Variable	Category	n	%
Sex	Male	51	53.1
	Female	45	46.9
IBD subtype	Crohn's disease	50	52.1
	Ulcerative colitis	46	47.9

Figure 2 Frequency Distribution of Sex and IBD Subtype

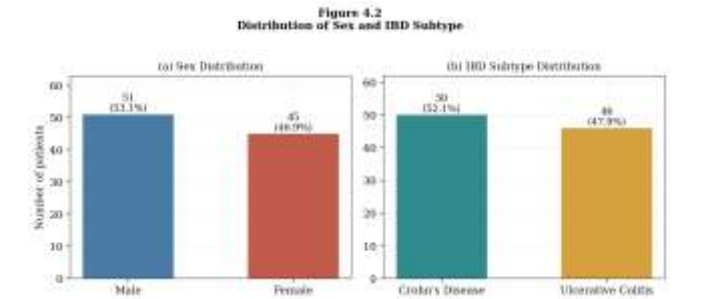
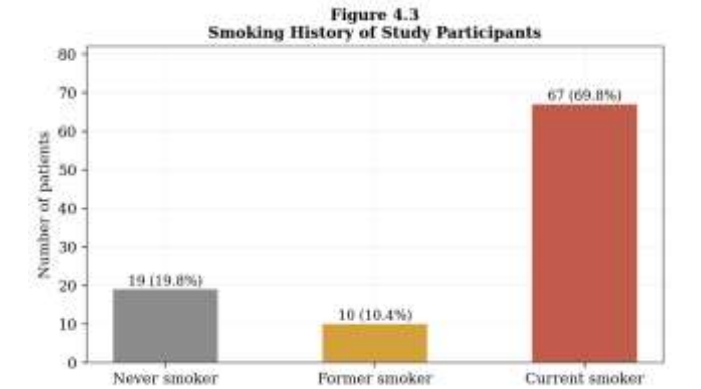


Table 3 Frequency Distribution of Family History, Smoking History, and Disease-Management History

Variable	Category	n	%
Family history of IBD	Yes	12	12.5
	No	84	87.5
Smoking history	Current smoker	67	69.8
	Never smoker	19	19.8
	Former smoker	10	10.4
History of corticosteroid use	Yes	54	56.3
	No	42	43.8
History of biologic use	Yes	60	62.5
	No	36	37.5
History of IBD-related surgery	Yes	13	13.5
	No	83	86.5

Figure 3 Smoking history of study participants.



The frequencies of family history of IBD, smoking history, and disease-management history (corticosteroid and biologic use, and surgery related to IBD) are reported in Table 3. 12.5% of participants had a positive family history of IBD. Most (69.8%) were current smokers, 19.8% had never smoked and 10.4% were former smokers (Figure 3). More than half of the sample (56.3%) had a history of corticosteroid use, 62.5% had a history of biologic use, and 13.5% had a history of surgery for IBD.

Table 4 Frequency Distribution of Presenting Symptoms at Baseline

Symptom	Category	n	%
Abdominal pain	None	7	7.3
	Mild	38	39.6
	Moderate	41	42.7
	Severe	10	10.4
Blood in stool	Present	52	54.2
	Absent	44	45.8

Weight loss	Present	38	39.6
	Absent	58	60.4
Fatigue	None	5	5.2
	Mild	41	42.7
	Moderate	32	33.3
	Severe	18	18.8

Figure 4. Severity distribution of key presenting symptoms (abdominal pain and fatigue

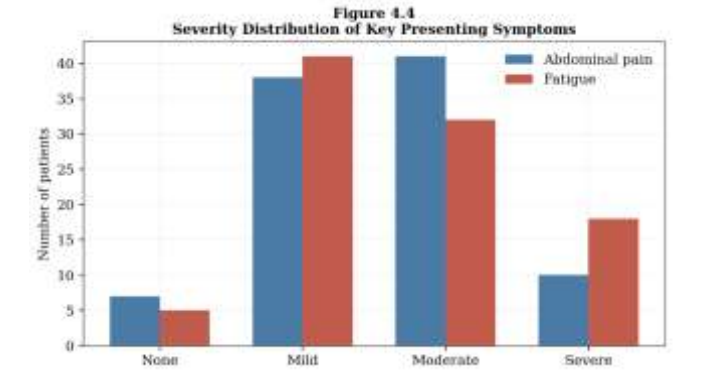


Table 4 shows the frequency and severity of the main presenting symptoms at baseline. The majority of patients reported abdominal pain, with moderate pain (42.7%) being the most common, followed by mild pain (39.6%), severe pain (10.4%), and no pain (7.3%). Blood in stool was present in 54.2% of patients, and 39.6% reported weight loss. Most participants (76.0%) reported mild-to-moderate fatigue, 18.8% reported severe fatigue, and 5.2% reported no fatigue. The mean self-reported diarrhea frequency was 6.01 ± 2.18 stools per day.

Table 5. Descriptive Statistics for Baseline Disease Activity Indices and Inflammatory Markers

Variable	n	M	SD	Median	Min	Max
CDAI (Crohn's disease only)	50	322.66	67.68	310.0	165	473
Mayo total (UC only; version not documented)	46	7.26	2.15	7.0	3	12
SESCD (Crohn's disease only)	50	16.08	4.94	16.0	7	27
ESR (mm/hr)	96	39.70	15.42	38.4	3.6	80.4
Fecal calprotectin (µg/g)	96	563.68	211.23	551.0	75.3	1180.8

We analyzed disease-specific activity scores within the appropriate IBD subtype: CDAI for Crohn's disease and Mayo total for ulcerative colitis. Disease-inappropriate score entries were excluded. The available dataset did not document the Mayo scoring version; therefore, Mayo totals are reported descriptively and are not interpreted as definitive remission categories.

Table 5a Baseline and Follow-up Disease-Specific Score Summaries

Score and time	n	Mean ± SD	Median	Range
CDAI baseline (CD)	50	322.66 ± 67.68	310	165–473
CDAI follow-up (CD)	50	184.22 ± 68.73	178	80–419
Mayo baseline (UC)	46	7.26 ± 2.15	7	3–12
Mayo follow-up (UC)	46	3.72 ± 2.33	4	0–10

All disease-specific totals were summarized within subtype. CDAI was analyzed only for Crohn's disease and Mayo total

only for ulcerative colitis. Because the Mayo version and component subscores were not fully documented, the Mayo total was not used to assign definitive clinical remission categories.

Table 5b CDAI Category Distribution in Crohn's Disease

Category	Baseline n (%)	Follow-up n (%)
<150: remission-range total	0 (0.0)	19 (38.0)
150–219: mild activity	3 (6.0)	18 (36.0)
220–450: moderate to severe	46 (92.0)	13 (26.0)
>450: severe activity	1 (2.0)	0 (0.0)
Total	50 (100.0)	50 (100.0)

CDAI categories are presented for Crohn's disease only. A reduction in the mean CDAI does not imply that every participant achieved remission [35].

Table 5c Paired Change in Disease-Specific Activity Scores

Index	Paired n	Mean change ± SD	(df)	p
CDAI (CD)	50	−138.44 ± 68.48	−14.29 (49)	<.001
Mayo (UC)	46	−3.54 ± 2.46	−9.75 (45)	<.001

Change was calculated as follow-up minus baseline; negative values indicate lower disease-activity totals. CDAI change was analyzed in Crohn's disease. Mayo change was analyzed descriptively in ulcerative colitis, without assigning remission categories because the scoring version was not fully documented. Within Crohn's disease, baseline BWT correlated with CDAI (Pearson $r = .838$; Spearman $\rho = .841$; both $p < .001$). Within ulcerative colitis, baseline BWT correlated with the recorded Mayo total (Pearson $r = .828$; Spearman $\rho = .775$; both $p < .001$). These subtype-specific associations support a relationship between bowel-wall thickness and disease-activity measures but do not, by themselves, validate imaging as a biomarker.

Table 6. Frequency of Current Medication Use at Baseline

Medication class	n	%
Aminosalicylates	57	59.4
Corticosteroids	37	38.5
Immunomodulators	43	44.8
Biologics	39	40.6
Other	17	17.7

The table shows current medication use at baseline. The most common class was Aminosalicylates (59.4%), followed by immunomodulators (44.8%), biologic agents (40.6%), and corticosteroids (38.5%), with 17.7% using another unspecified class. As is common in moderate to severe IBD, the majority of patients were taking multiple classes of medications at the same time.

Table 7 Descriptive Statistics for Baseline Sonographic Parameters

Parameter	M	SD	Median	Min	Max
Bowel wall thickness (mm)	5.63	1.29	5.60	2.8	8.7
Peak systolic velocity, PSV (cm/s)	32.61	6.64	32.4	15.6	48.9
End-diastolic velocity, EDV (cm/s)	9.28	2.77	9.2	3.2	16.6
Resistive index, RI	0.66	0.09	0.66	0.44	0.87
Pulsatility index, PI	1.31	0.20	1.30	0.83	1.82

Descriptive data for baseline sonographic parameters are shown in Table 7. Mean bowel-wall thickness (BWT) was 5.63 ± 1.29 mm, suggesting bowel-wall thickening consistent with active intestinal inflammation. Doppler parameters showed a pattern compatible with inflammatory hyperemia at the group level; however, Table 8 shows that 7.3% of participants had Grade 0 vascularity, indicating that increased Doppler vascularity was not present in every participant despite the moderate-to-severe clinical cohort. Mean PSV was 32.61 ± 6.64 cm/s, mean EDV was 9.28 ± 2.77 cm/s, mean RI was 0.66 ± 0.09 , and mean PI was 1.31 ± 0.20 . Mean BWT was 5.97 ± 1.24 mm in Crohn’s disease and 5.26 ± 1.24 mm in ulcerative colitis; the difference was statistically significant (independent-samples t-test, $t \approx 2.80$, $p = .006$). Interpret this between-subtype difference as an association, not evidence of causality or transmural inflammation in individual patients.

Table 8 Frequency Distribution of Baseline Vascularity Grade, Endoscopy Completion, Complications, and Prior Colonoscopy

Variable	Category	n	%
Vascularity grade (baseline)	Grade 0 (Absent)	7	7.3
	Grade 1 (Mild)	40	41.7
	Grade 2 (Moderate)	35	36.5
	Grade 3 (Marked)	14	14.6
Endoscopy completed at baseline	Yes	84	87.5
	No	12	12.5
Complications present at baseline	Yes	12	12.5
	No	84	87.5
Prior colonoscopies	One	17	17.7
	Two	52	54.2
	Three or more	27	28.1

We used the Limberg classification (Grade 0 = absent to 3 = marked) to assess sonographic vascularity. Overall, most patients had Grade 1 (mild) or Grade 2 (moderate) vascularity, with 14.6% having Grade 3 (marked) vascularity and 7.3% having no increased vascularity (Grade 0). Additionally, the baseline procedural characteristics are summarized in Table 8: 87.5% of patients completed endoscopy, 12.5% had a disease-related complication (e.g., stricture, abscess, or fistula), and over half of the sample (54.2%) had had two previous colonoscopies.

Table 9 Paired Comparison of Sonographic and Laboratory Parameters at Baseline and Follow-up

Parameter	Baseline M (SD)	Follow-up M (SD)	Mean Δ (SD)	t (df=95)	p-value
BWT (mm)	5.63 (1.29)	3.96 (1.15)	-1.67 (1.24)	-13.20	< .001
PSV (cm/s)	32.61 (6.64)	27.32 (6.25)	-5.29 (4.82)	-10.75	< .001
EDV (cm/s)	9.28 (2.77)	7.16 (2.23)	-2.12 (1.69)	-12.29	< .001
RI	0.66 (0.09)	0.73 (0.08)	0.07 (0.07)	9.80	< .001
PI	1.31 (0.20)	1.44 (0.16)	0.13 (0.14)	9.10	< .001
ESR (mm/hr)	39.70 (15.42)	23.25 (10.92)	-16.45 (13.90)	-11.60	< .001

Fecal calprotectin (μg/g)	563.68 (211.23)	286.59 (173.48)	-277.09 (187.14)	-14.51	< .001
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Figure 5 Bowel wall thickness at baseline versus follow-up

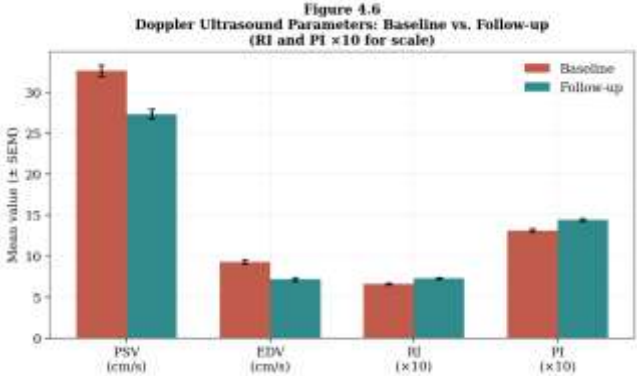
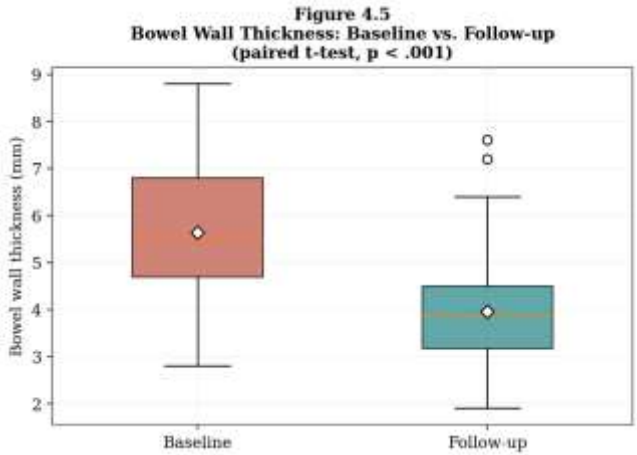


Figure 6 Doppler ultrasound parameters at baseline versus follow-up (RI and PI multiplied by 10 for scale).

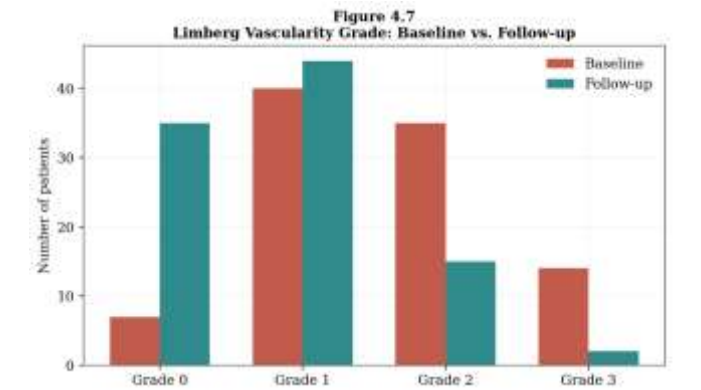


Paired baseline-to-follow-up comparisons are presented in Table 9 with mean differences, t statistics, and p-values. BWT, PSV, EDV, ESR, and fecal calprotectin decreased, whereas RI and PI increased. Each paired comparison was statistically significant (all $p < .001$), with the direction of change consistent with reduced inflammatory activity. Wilcoxon signed-rank analyses were used as non-parametric sensitivity analyses where appropriate.

Table 10 Cross-tabulation of Sonographic Vascularity Grade at Baseline and Follow-up

Baseline Grade	FU: Grade 0	FU: Grade 1	FU: Grade 2	FU: Grade 3	Total
Grade 0 (Absent)	7	0	0	0	7
Grade 1 (Mild)	20	18	2	0	40
Grade 2 (Moderate)	6	21	7	1	35
Grade 3 (Marked)	2	5	6	1	14
Total	35	44	15	2	96

Figure 7 Distribution of Limberg vascularity grade at baseline and follow-up



Sonographic vascularity grade was assessed using the Wilcoxon signed-rank test for paired ordinal data and decreased significantly from baseline to follow-up ($Z = -6.83$, $p < .001$). Because Limberg grades are ordered from Grade 0 (absent) to Grade 3 (marked), movement to a lower numerical grade represents reduced vascularity. Among 40 participants with Grade 1 at baseline, 20 (50.0%) were Grade 0 at follow-up; among 35 with Grade 2 at baseline, 27 (77.1%) were Grade 0 or Grade 1 at follow-up. Few moved to a higher grade. Table note: Wilcoxon signed-rank test, $Z = -6.83$, $p < .001$.

Table 11 Correlation Between Baseline Bowel Wall Thickness and Baseline Clinical, Endoscopic, and Biochemical Measures

Variable	Pearson r	Spearman ρ	p (Pearson)
CDAI (Crohn's disease only)	.838	.841	<.001
ESR (mm/hr)	.765	.780	<.001
Fecal calprotectin ($\mu\text{g/g}$)	.847	.845	<.001
PSV (cm/s)	.724	.730	<.001
EDV (cm/s)	.694	.702	<.001
Resistive index (RI)	-.791	-.811	<.001
Pulsatility index (PI)	-.695	-.705	<.001
Mayo total (UC only; version not documented)	.828	.775	<.001

Table 11 presents disease-appropriate correlations between baseline BWT and baseline clinical, biochemical, and Doppler measures. Baseline BWT showed strong positive correlations with fecal calprotectin ($r = .847$, $p < .001$) and ESR ($r = .765$, $p < .001$), positive correlations with PSV ($r = .724$, $p < .001$) and EDV ($r = .694$, $p < .001$), and negative correlations with RI and PI. We interpreted disease-specific activity scores only within their appropriate subtype. These correlations indicate association and do not establish causality or validity on their own.

Table 12 Correlation Between Change (Baseline to Follow-up) in Bowel Wall Thickness and Change in Inflammatory Markers

Variable (Δ baseline to follow-up)	Pearson r	p
Δ Fecal calprotectin	.872	<.001
Δ ESR	.807	<.001

The magnitude of change in BWT was strongly associated with change in inflammatory markers. A decrease in BWT correlated with decreases in fecal calprotectin ($r = .872$, $p < .001$) and ESR ($r = .807$, $p < .001$). These findings provide supportive evidence of an association between changes in BWT and changes in inflammatory markers; correlation alone does not confirm construct validity.

Table 13 Frequency Distribution of Follow-up Outcome Variables

Variable	Category	n	%
Clinical response	Complete response	36	37.5
	Partial response	37	38.5
	No response	23	24.0
Mucosal healing	Yes	36	37.5
	No	60	62.5
Endoscopic response	Yes	32	33.3
	No	64	66.7
Vascularity change	Decreased	60	62.5
	Unchanged	33	34.4
	Increased	3	3.1
Follow-up interval	3 months	19	19.8
	6 months	34	35.4
	9 months	36	37.5
	12 months	7	7.3

The distribution of follow-up outcomes is summarized in Table 13. Complete clinical response was recorded in 36 participants (37.5%), partial response in 37 (38.5%), and no response in 23 (24.0%). Mucosal healing was recorded in 36 participants (37.5%) and endoscopic response in 32 (33.3%). Sonographic vascularity decreased in 60 (62.5%), was unchanged in 33 (34.4%), and increased in 3 (3.1%). Follow-up intervals were 3 months in 19 (19.8%), 6 months in 34 (35.4%), 9 months in 36 (37.5%), and 12 months in 7 (7.3%). Because follow-up timing was non-uniform, interpret outcome comparisons with this limitation in mind.

Figure 8 Overall clinical response at follow-up

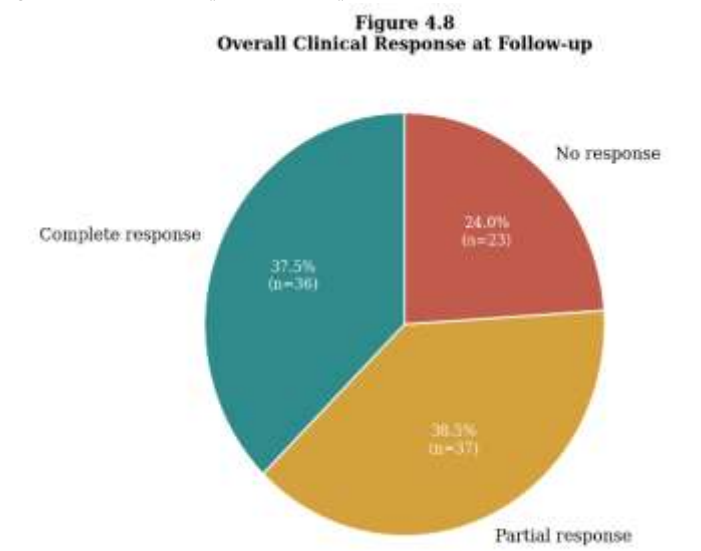


Table 14 Cross-tabulation of IBD Subtype by Clinical Response

IBD subtype	Complete response	Partial response	No response	Total
Crohn's disease	22	20	8	50
Ulcerative colitis	14	17	15	46
Total	36	37	23	96

Clinical response and mucosal healing were both recorded as categorical follow-up outcomes. The previous narrative cross-tabulation was internally inconsistent with Table 13 (36 participants with mucosal healing versus a statement

referring to 32 participants) and was therefore removed. Report a complete 3 × 2 cross-tabulation of clinical response (complete/partial/no response) by mucosal healing (yes/no), along with χ^2 , degrees of freedom, p-value, and an effect-size measure such as Cramér’s V, only after verifying it against the participant-level dataset. No association is claimed here without that verified cross-tabulation. The IBD subtype-by-clinical-response distribution is shown separately in Table 14.

Table 15 Follow-up Bowel Wall Thickness and Change in Bowel Wall Thickness by Mucosal Healing Status

Variable	Healed M (SD), n = 36	Not healed M (SD), n = 60	t	p
Follow-up BWT (mm)	3.19 (0.75)	4.42 (1.11)	−5.87	< .001
Δ BWT, baseline to follow-up (mm)	−2.47 (1.22)	−1.20 (1.00)	−5.58	< .001

Follow-up BWT was lower among participants with mucosal healing (3.19 ± 0.75 mm) than among those without mucosal healing (4.42 ± 1.11 mm), $t(94) = -5.87$, $p < .001$. The reduction in BWT was also greater in the mucosal-healing group (−2.47 ± 1.22 mm) than in the group without healing (−1.20 ± 1.00 mm), $t(94) = -5.58$, $p < .001$. These results are reported using independent-samples t-tests; the Mann-Whitney U test is not included in the primary results because its U statistic was not documented.

Discussion

This study evaluated multiparametric intestinal ultrasound, particularly BWT and Doppler-derived vascular parameters, to monitor therapeutic response and mucosal healing in severe IBD. Overall, sonographic findings improved from baseline to follow-up: BWT decreased significantly, Doppler flow velocities declined, RI and PI increased, and vascularity grades shifted toward lower activity. These changes occurred alongside improvement in inflammatory markers and clinical outcomes, supporting the value of ultrasound as a complementary objective monitoring tool. BWT showed one of the clearest treatment-related changes and was strongly associated with follow-up fecal calprotectin. Patients with better clinical response also had greater reductions in BWT, while lower follow-up BWT was associated with mucosal healing. These findings are consistent with previous work showing that reductions in bowel-wall thickness and Doppler vascularity can reflect therapeutic response and may be associated with later endoscopic improvement [11-15]. The Doppler findings provide additional functional information. Decreases in PSV and EDV together with increases in RI and PI are compatible with reduced inflammatory hyperemia after treatment. The shift toward lower Limberg vascularity grades further supports improvement in bowel-wall perfusion. Previous studies have similarly emphasized Doppler vascularity as a marker of inflammatory activity and response, including newer microvascular imaging approaches [17-22]. However, Doppler indices remain sensitive to acquisition technique and operator factors, so they are best interpreted together with BWT, clinical findings, and laboratory markers rather than as isolated measures. Disease-specific activity scores also

improved during follow-up. Mean CDAI decreased in Crohn's disease, and the mean Mayo total decreased in ulcerative colitis. These scores must be interpreted within their respective disease subtypes, and the available UC totals cannot by themselves confirm remission because the Mayo version and individual subscores were not uniformly available [35,36]. Similarly, ultrasound cannot directly demonstrate mucosal healing as endoscopy can or provide histologic confirmation. Its role is therefore complementary rather than a replacement for endoscopic assessment. The study has practical relevance because IUS is repeatable, radiation-free, and potentially useful in resource-constrained settings where frequent endoscopy may be difficult. Combining BWT, Doppler vascularity, and fecal calprotectin may provide a useful non-invasive follow-up pathway and help identify patients who require further endoscopic or cross-sectional assessment. This interpretation is consistent with recommendations favoring standardized, multiparametric IUS monitoring [11,19]. Several limitations include the single-center design, non-probability purposive sampling, non-uniform follow-up intervals, heterogeneous treatment exposure, operator dependence, the absence of formal inter- and intra-observer reliability testing, and incomplete quantitative endoscopic correlation. Despite these limitations, the concordant improvement across structural, vascular, biochemical, and clinical measures supports further investigation of multiparametric IUS. Larger prospective studies with standardized acquisition, fixed follow-up intervals, and complete endoscopic validation are required before specific ultrasound thresholds can be adopted as independent treatment targets.

Limitations

Single-center sample size and setting: the cohort included 96 participants from one tertiary-care center, limiting precision in subgroup analyses and potentially reducing generalizability to other populations and practice settings. Non-uniform follow-up: the interval between baseline and follow-up ultrasound was not identical across participants (3, 6, 9, or 12 months), which may influence the magnitude of observed sonographic change independently of treatment response. Operator dependence and reliability: intestinal ultrasound is operator-dependent, and we did not formally evaluate inter-observer and intra-observer reliability for BWT, Doppler indices, and vascularity grading. Incomplete endoscopic correlation: we recorded follow-up endoscopic response and mucosal healing categorically. In contrast, repeat quantitative endoscopic scores (SES-CD for Crohn's disease or Mayo endoscopic subscore for ulcerative colitis) were not available for all participants. This limited direct continuous endoscopic-sonographic correlation. Treatment heterogeneity: participants received different combinations of aminosalicylates, corticosteroids, immunomodulators, and biologic therapies. Analyses were not stratified by treatment class, so treatment-specific response kinetics could not be determined. Non-probability purposive sampling: participants were selected according to predefined clinical

criteria rather than probability sampling, which may introduce selection bias and limit generalizability beyond similar clinical populations.

CONCLUSION

This study evaluated multiparametric intestinal ultrasound as a non-invasive approach to assessing treatment response in inflammatory bowel disease. Bowel-wall thickness, Doppler flow velocities, resistive index, pulsatility index, and vascularity grade changed significantly and coherently between baseline and follow-up, consistent with reduced inflammatory activity. These sonographic changes occurred alongside reductions in erythrocyte sedimentation rate and fecal calprotectin, and follow-up BWT was associated with follow-up fecal calprotectin. Together, these findings support using IUS as a complementary objective monitoring tool. The magnitude of BWT reduction differed across clinical response categories, and participants with mucosal healing had lower follow-up BWT. These findings are consistent with the principles of a treat-to-target approach, in which objective measures of disease activity complement clinical assessment. The study did not directly test a treat-to-target strategy, and the observed associations should not be interpreted as proof that IUS can replace endoscopic targets.

Overall, multiparametric IUS showed changes in a coherent direction during follow-up in both Crohn's disease and ulcerative colitis. BWT provided graded information across clinical response categories, while Doppler parameters contributed functional information about bowel-wall perfusion. IUS may serve as a complementary bedside marker when repeat endoscopy is not immediately available, although endoscopic confirmation remains necessary to assess mucosal healing. Larger prospective multicenter studies with standardized timing, disease-specific scoring, complete endoscopic correlation, and formal reliability testing are required before IUS measures can be adopted as independent treatment targets or validated biomarkers.

Recommendations

Perform larger prospective multicenter studies using standardized, prespecified follow-up intervals. Time points such as 8 and 26 weeks should be used only when justified by established IUS consensus recommendations and the expected response kinetics of the treatment being studied [11]. Use ultrasound follow-up paired with a quantitative endoscopic score (SES-CD for Crohn's disease or Mayo endoscopic subscore for UC) instead of a healed/not-healed endpoint, which will allow direct correlation between continuous change in ultrasound and continuous change in endoscopic score. Prospectively define and validate disease-specific cut-off values for BWT reduction and RI/PI change for sonographic response. If "transmural remission" is used as an outcome, its definition should be prespecified using validated consensus criteria rather than inferred from BWT alone [11]. Before recommending intestinal ultrasound as a stand-alone monitoring tool in general clinical practice, formally evaluate inter-observer and intra-observer reliability

of BWT measurement and Doppler-based intestinal ultrasound indices. Stratify future analyses by treatment class (aminosalicylates, corticosteroids, immunomodulators, and biologics) to assess whether sonographic improvement occurs differently by treatment class (mechanism of action) and to determine the cost-effectiveness of monitoring with IUS versus conventional endoscopy and MRE.

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