

Original Research Article

CONCORDANCE OF ENDOSCOPIC ULTRASONOGRAPHY WITH A HISTOPATHOLOGY-SUPPORTED REFERENCE DIAGNOSIS IN DIFFERENTIATING ULCERATIVE COLITIS AND CROHN'S DISEASE: A PROSPECTIVE DIAGNOSTIC-ACCURACY STUDY

Divya Prafulla¹, Sameeranandan Reddy², D Santhikiran³

¹Associate Professor, Department of Pathology, Kamineni Institute of Medical Sciences, Narketpally, Telangana, India.

²Associate Professor, Department of Pathology, Maheswara Medical College, Chitkul, Hyderabad, Telangana, India.

³Professor, Department of Pathology, Maheswara Medical College, Chitkul, Hyderabad, Telangana, India.

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Corresponding Author:

Dr. Divya Prafulla,
Associate Professor, Department of
Pathology, Kamineni Institute of
Medical Sciences, Narketpally, Telangan
a, India.
Email: mydina1989@gmail.com

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ABSTRACT

Background: Accurate differentiation of ulcerative colitis (UC) from Crohn's disease (CD) may be difficult when clinical, colonoscopic and histopathological findings overlap. Endoscopic ultrasonography (EUS) permits high-resolution assessment of individual bowel-wall layers and may complement conventional diagnostic methods. **Aim:** To evaluate the diagnostic accuracy and concordance of EUS in differentiating UC from CD against a histopathology-inclusive composite reference standard.

Materials and Methods: This prospective, single-centre, observer-blinded diagnostic-accuracy study included 70 participants: 60 patients with inflammatory bowel disease and 10 non-IBD controls. Before EUS-assisted reassessment, 26 patients were classified as UC and 34 as CD. Mucosal, submucosal and total bowel-wall thicknesses were measured at the mid-sigmoid colon. The final reference diagnosis incorporated histopathology, colonoscopy, clinical findings, inflammatory markers and cross-sectional imaging. Diagnostic accuracy, Cohen's kappa agreement, receiver operating characteristic analysis and correlations with disease-activity indices and inflammatory markers were assessed.

Results: Following reference-standard reassessment, 39 patients were classified as CD and 21 as UC. EUS yielded 39 true-positive, two false-positive, 19 true-negative and no false-negative results. Sensitivity was 100% (95% CI: 90.97–100%), specificity 90.5% (95% CI: 69.62–98.83%), positive predictive value 95.1%, negative predictive value 100% and overall accuracy 96.7%. Agreement with the final reference diagnosis was almost perfect ($\kappa=0.925$, $p<0.001$). Mean mucosal thickness was significantly greater in UC than in CD and controls (1.76 ± 0.56 vs 0.78 ± 0.45 and 0.60 ± 0.16 mm; $p<0.001$). Mean submucosal thickness was significantly greater in CD than in UC and controls (1.82 ± 0.65 vs 0.84 ± 0.50 and 0.70 ± 0.13 mm; $p<0.001$). Total wall thickness was greater in both IBD groups than in controls but did not significantly differentiate UC from CD. Mucosal thickness differentiated UC with an AUC of 0.93, while submucosal thickness differentiated CD with an AUC of 0.94. Total wall thickness correlated with Mayo score in UC ($r=0.56$, $p=0.003$), while submucosal thickness correlated with CDAI ($r=0.63$), ESR ($r=0.48$), CRP ($r=0.39$) and faecal calprotectin ($r=0.61$) in CD.

Conclusion: EUS demonstrated high diagnostic accuracy and almost-perfect concordance with a histopathology-inclusive composite reference diagnosis.

Predominant mucosal thickening favoured UC, whereas predominant submucosal thickening favoured CD. EUS may serve as a useful complementary modality in diagnostically uncertain IBD cases.

Keywords: Endoscopic ultrasonography; inflammatory bowel disease; ulcerative colitis; Crohn's disease; bowel-wall thickness; histopathology; diagnostic accuracy; concordance.

INTRODUCTION

Inflammatory bowel disease (IBD) comprises ulcerative colitis (UC) and Crohn's disease (CD), two chronic relapsing disorders that differ in distribution and depth of inflammation. UC typically causes continuous mucosal inflammation confined to the colon, whereas CD may affect any gastrointestinal segment with discontinuous and potentially transmural involvement.^[1]

The burden of IBD is increasing in Asia.^[2] In India, a colonoscopic study of 30,835 symptomatic individuals identified IBD in 5.4%, including CD in 3.2% and UC in 2.2%, with comparable rural and urban prevalence.^[3] Accurate subtype classification is important because it influences treatment, surgery and prognosis, yet no single clinical, endoscopic, histological or radiological feature is universally diagnostic.

Histopathology remains central to diagnosis. Diffuse mucosal inflammation, crypt distortion and basal plasmacytosis support UC, whereas focal inflammation, fissuring ulcers, transmural lymphoid aggregates and non-caseating granulomas favour CD.^[4] However, granulomas are uncommon in mucosal biopsies, and diagnostic yield depends on specimen adequacy and distribution. Routine biopsies may also miss the deeper mural abnormalities of CD; therefore, findings must be integrated with clinical, endoscopic and imaging evidence.^[4,5]

Bowel ultrasonography is radiation-free, repeatable and capable of assessing wall thickness, mural stratification and extramural abnormalities.^[6] It is increasingly used to evaluate CD location, activity, complications and treatment response.^[7,8] Endoscopic ultrasonography (EUS) provides higher-resolution assessment of individual bowel-wall layers. Previous studies reported that predominant mucosal thickening favours UC, whereas submucosal and deeper mural involvement favour CD.^[9,11]

Ultrasound-histopathology studies further indicate that bowel-wall and mucosal thickness reflect acute inflammation, while mesenteric changes and mural abnormalities may correspond to chronic inflammation or fibrosis.^[10] However, overlap between inflammatory and fibrotic changes limits interpretation of individual sonographic findings.

Evidence regarding EUS-histopathology concordance in Indian patients remains limited. This study therefore evaluated the diagnostic performance of EUS in differentiating UC from CD using a composite reference diagnosis incorporating

histopathology, colonoscopy, imaging, clinical findings and inflammatory markers. It also assessed the discriminatory value of mucosal, submucosal and total bowel-wall thickness and their relationship with disease activity.

Aim

To evaluate the concordance and diagnostic performance of endoscopic ultrasonography in differentiating ulcerative colitis from Crohn's disease using a histopathology-supported composite reference diagnosis.

Objectives

1. To determine the concordance, sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy of EUS in differentiating CD from UC against a composite final diagnosis based on histopathology, colonoscopy, clinical findings, laboratory markers and cross-sectional imaging.
2. To compare mucosal, submucosal and total bowel-wall thickness among UC, CD and control groups and assess their discriminatory cut-offs and correlations with clinical disease-activity indices and inflammatory markers.

MATERIALS AND METHODS

Study Design and Setting

This prospective, single-centre, observer-blinded diagnostic-accuracy study was conducted in the Departments of Gastroenterology and Pathology at Kamineni Institute of Medical Sciences and Hospital from June 2025 to May 2026. Institutional Ethics Committee approval was obtained, and all participants provided written informed consent.

Study Population

Seventy participants were enrolled, comprising 60 adults with inflammatory bowel disease and 10 non-IBD controls. Before EUS, 26 patients were classified as having ulcerative colitis and 34 as having Crohn's disease based on clinical presentation, colonoscopy, histopathology, inflammatory markers and cross-sectional imaging. Participants were recruited consecutively from outpatient and inpatient gastroenterology services. Controls were adults without clinical, endoscopic or radiological evidence of IBD who underwent endoscopy for unrelated indications, such as evaluation of a submucosal lesion.

Eligibility Criteria

Adults aged above 18 years with an initial diagnosis of UC or CD, adequate biopsy material, suitability for EUS and written consent were included.

Exclusion criteria were acute intestinal obstruction, significant stenosis preventing echoendoscope passage, acute gastrointestinal infection, tumour, diverticulitis, unsafe enteric fistula, previous major colorectal surgery involving the sigmoid colon, inadequate bowel preparation, incomplete EUS, unavailable histopathology or refusal to participate. Controls with evidence of a personal or family history of IBD were excluded.

Clinical and Laboratory Assessment

All patients underwent history-taking, physical examination and measurement of erythrocyte sedimentation rate, C-reactive protein and faecal calprotectin.

UC activity was assessed using the Mayo score, ranging from 0 to 12, with a score above 3 indicating active disease. CD activity was assessed using the Crohn's Disease Activity Index, with a score above 150 indicating active disease.

Reference-Standard Diagnosis

The final diagnosis was established using a composite reference standard incorporating histopathology, colonoscopy, clinical findings, inflammatory markers and cross-sectional imaging. Cases showing disagreement between EUS and the initial diagnosis underwent reassessment of clinical, colonoscopic and histopathological findings, with magnetic resonance enterography or other imaging when indicated. The final diagnosis was assigned independently of EUS, which was not included in the reference standard.

Bowel-layer comparisons were based on the initial classification, whereas diagnostic-accuracy analyses used the final composite diagnosis.

Bowel Preparation

Participants followed a clear-liquid diet and received polyethylene glycol-based bowel preparation according to institutional protocol. Bisacodyl 5 mg was added when required, and preparation continued until clear rectal effluent was achieved. Adequacy was documented before EUS.

Endoscopic Ultrasonography

EUS was performed using a radial echoendoscope by a single experienced endosonographer blinded to the initial diagnosis, colonoscopy, histopathology,

imaging, laboratory findings and activity scores. Mucosal, submucosal and total wall thickness were measured three times at randomly selected sites in the mid-sigmoid colon, and the mean value was used for analysis.

Statistical Analysis

Data were analysed using SPSS version 23.0 or later, with ROC analysis performed using MedCalc. Categorical variables were reported as frequencies and percentages, and continuous variables as mean $\pm$ standard deviation. Normality was assessed before analysis. Two-group comparisons were performed using the independent-samples Student's t-test, with Welch's correction for unequal variances and appropriate non-parametric tests for non-normal data. Pearson or Spearman correlation was used as appropriate. Reproducibility was assessed using repeated EUS measurements, with a correlation coefficient above 0.70 and $p < 0.05$ considered acceptable. All tests were two-sided, and $p < 0.05$ indicated statistical significance.

RESULTS

Participant characteristics and initial diagnostic classification

Seventy participants were included: 60 patients with inflammatory bowel disease and 10 controls. Before EUS reassessment, 26 patients were classified as having ulcerative colitis and 34 as having Crohn's disease.

The mean ages of the UC, CD and control groups were 36.12 ± 10.24 , 35.41 ± 9.16 and 40.80 ± 10.72 years, respectively; males constituted 53.8%, 50.0% and 60.0% of these groups. Among patients with UC, 20 (76.9%) had extensive colitis or pancolitis, four (15.4%) had left-sided colitis and two (7.7%) had proctitis. Among those with CD, 16 (47.1%) had ileocolitis, 14 (41.2%) isolated colonic disease and four (11.8%) isolated ileal disease.

The demographic, clinical, laboratory and EUS measurements according to the initial diagnostic classification are presented in Table 1.

Table 1: Demographic, clinical and EUS characteristics according to the initial diagnostic classification

Variable	UC (n=26)	CD (n=34)	Controls (n=10)
Age, years, mean $\pm$ SD	36.12 ± 10.24	35.41 ± 9.16	40.80 ± 10.72
Male sex, n (%)	14 (53.8%)	17 (50.0%)	6 (60.0%)
CDAI, mean $\pm$ SD	—	91.40 ± 44.80	—
Mayo score, mean $\pm$ SD	7.42 ± 1.84	—	—
Proctitis, n (%)	2 (7.7%)	—	—
Left-sided colitis, n (%)	4 (15.4%)	—	—
Extensive colitis/pancolitis, n (%)	20 (76.9%)	—	—
Isolated Crohn's colitis, n (%)	—	14 (41.2%)	—
Ileocolitis, n (%)	—	16 (47.1%)	—
Isolated ileitis, n (%)	—	4 (11.8%)	—
ESR, mm/hour, mean $\pm$ SD	21.35 ± 11.62	20.12 ± 13.75	—
CRP, mg/L, mean $\pm$ SD	12.84 ± 29.70	12.10 ± 16.35	—
Faecal calprotectin, $\mu\text{g/g}$, mean $\pm$ SD	121.50 ± 110.20	133.70 ± 101.80	—
Mean mucosal thickness, mm	1.76 ± 0.56	0.78 ± 0.45	0.60 ± 0.16
Mean submucosal thickness, mm	0.84 ± 0.50	1.82 ± 0.65	0.70 ± 0.13
Mean total wall thickness, mm	3.55 ± 0.66	3.84 ± 0.74	2.32 ± 0.37

EUS classification and final reference-standard diagnosis

Of 26 patients initially diagnosed with UC, EUS classified 19 as UC and seven as CD. Reference-standard reassessment confirmed CD in five of these

seven cases, while two were retained as UC and considered false-positive EUS classifications.

All 34 patients initially diagnosed with CD were correctly classified and confirmed as CD. The final cohort therefore comprised 39 patients with CD and 21 with UC, as summarised in Table 2.

Table 2: Initial diagnostic classification, EUS classification and final reference-standard diagnosis

Initial diagnostic group	Number examined	Classified as UC by EUS	Classified as CD by EUS	Final CD diagnosis	False-positive EUS classification as CD
Initially classified UC	26	19	7	5	2
Initially classified CD	34	0	34	34	0
Total	60	19	41	39	2

The final cross-classification of EUS findings against the reference-standard diagnosis demonstrated 39 true-positive, two false-positive, 19 true-negative and no false-negative results.

Table 3: Cross-classification of EUS diagnosis against the final reference-standard diagnosis

Final reference-standard diagnosis	EUS classified as CD	EUS classified as UC	Total
Crohn's disease	39	0	39
Ulcerative colitis	2	19	21
Total	41	19	60

Diagnostic performance of EUS

For differentiating CD from UC, EUS demonstrated a sensitivity of 100% (95% CI: 90.97–100%) and a specificity of 90.5% (95% CI: 69.62–98.83%). The positive predictive value was 95.1%, the negative

predictive value was 100% and the overall diagnostic accuracy was 96.7%.

The observed agreement between EUS and the final reference-standard diagnosis was 96.7%. Cohen's kappa coefficient was 0.925, indicating almost-perfect agreement beyond chance ($p < 0.001$).

Table 4: Diagnostic performance of EUS for differentiating CD from UC

Diagnostic parameter	Result
Sensitivity	100%
95% CI for sensitivity	90.97–100%
Specificity	90.5%
95% CI for specificity	69.62–98.83%
Positive predictive value	95.1%
95% CI for positive predictive value	83.47–99.40%
Negative predictive value	100%
95% CI for negative predictive value	82.35–100%
Overall diagnostic accuracy	96.7%
95% CI for diagnostic accuracy	88.47–99.59%
False-positive rate	9.5%
False-negative rate	0%
Observed agreement	96.7%
Cohen's kappa	0.925
P-value for agreement	<0.001

Test–retest correlations of EUS measurements

Repeated EUS measurements demonstrated significant positive test–retest correlations for all

three bowel-wall layers. Submucosal thickness showed the highest correlation coefficient, followed by total wall thickness and mucosal thickness.

Table 5: Test–retest correlations of EUS bowel-wall measurements

EUS measurement	Pearson correlation coefficient, r	P-value
Mucosal thickness	0.76	<0.001
Submucosal thickness	0.82	<0.001
Total wall thickness	0.78	<0.001

Comparison of bowel-wall thickness between UC and controls

Bowel-layer comparisons used the initial diagnostic classification. Compared with controls, patients with UC had significantly greater mucosal thickness (1.76 ± 0.56 vs 0.60 ± 0.16 mm; mean difference

1.16 ± 0.12 mm; $p < 0.001$) and total wall thickness (3.55 ± 0.66 vs 2.32 ± 0.37 mm; mean difference 1.23 ± 0.17 mm; $p < 0.001$). Submucosal thickness was not significantly different (0.84 ± 0.50 vs 0.70 ± 0.13 mm; $p = 0.197$).

Table 6: Comparison of EUS bowel-wall thickness between the initial UC group and controls

Measurement	Initial UC group, mean $\pm$ SD	Controls, mean $\pm$ SD	Mean difference $\pm$ SE	P-value
Mucosal thickness, mm	1.76 $\pm$ 0.56	0.60 $\pm$ 0.16	1.16 $\pm$ 0.12	<0.001
Submucosal thickness, mm	0.84 $\pm$ 0.50	0.70 $\pm$ 0.13	0.14 $\pm$ 0.11	0.197
Total wall thickness, mm	3.55 $\pm$ 0.66	2.32 $\pm$ 0.37	1.23 $\pm$ 0.17	<0.001

Comparison of bowel-wall thickness between CD and controls

Compared with controls, patients with CD had significantly greater submucosal thickness (1.82 $\pm$ 0.65 vs 0.70 $\pm$ 0.13 mm; mean difference 1.12 $\pm$

0.12 mm; $p < 0.001$) and total wall thickness (3.84 $\pm$ 0.74 vs 2.32 $\pm$ 0.37 mm; mean difference 1.52 $\pm$ 0.17 mm; $p < 0.001$). Mucosal thickness was higher in CD but not statistically significant (0.78 $\pm$ 0.45 vs 0.60 $\pm$ 0.16 mm; $p = 0.058$).

Table 7: Comparison of EUS bowel-wall thickness between the initial CD group and controls

Measurement	Initial CD group, mean $\pm$ SD	Controls, mean $\pm$ SD	Mean difference $\pm$ SE	P-value
Mucosal thickness, mm	0.78 $\pm$ 0.45	0.60 $\pm$ 0.16	0.18 $\pm$ 0.09	0.058
Submucosal thickness, mm	1.82 $\pm$ 0.65	0.70 $\pm$ 0.13	1.12 $\pm$ 0.12	<0.001
Total wall thickness, mm	3.84 $\pm$ 0.74	2.32 $\pm$ 0.37	1.52 $\pm$ 0.17	<0.001

Direct comparison of bowel-wall thickness between the initial UC and CD groups

Mucosal thickness was significantly greater in UC than CD (1.76 $\pm$ 0.56 vs 0.78 $\pm$ 0.45 mm; mean difference 0.98 $\pm$ 0.13 mm; $p < 0.001$), whereas submucosal thickness was significantly greater in

CD (1.82 $\pm$ 0.65 vs 0.84 $\pm$ 0.50 mm; mean difference 0.98 $\pm$ 0.15 mm; $p < 0.001$). Total wall thickness was slightly higher in CD, but the difference was not significant (3.84 $\pm$ 0.74 vs 3.55 $\pm$ 0.66 mm; $p = 0.115$).

Table 8: Direct comparison of EUS bowel-wall thickness between the initial UC and CD groups

Measurement	Initial UC group, mean $\pm$ SD	Initial CD group, mean $\pm$ SD	Absolute mean difference $\pm$ SE	P-value
Mucosal thickness, mm	1.76 $\pm$ 0.56	0.78 $\pm$ 0.45	0.98 $\pm$ 0.13	<0.001
Submucosal thickness, mm	0.84 $\pm$ 0.50	1.82 $\pm$ 0.65	0.98 $\pm$ 0.15	<0.001
Total wall thickness, mm	3.55 $\pm$ 0.66	3.84 $\pm$ 0.74	0.29 $\pm$ 0.18	0.115

ROC-curve analysis of bowel-wall measurements

Mucosal thickness identified UC at a 1.08-mm cut-off with 88.5% sensitivity, 90.9% specificity and an AUC of 0.93 (95% CI: 0.86–0.99; $p < 0.001$). Submucosal thickness identified CD at a 1.12-mm cut-off with 97.1% sensitivity, 88.9% specificity and an AUC of 0.94 (95% CI: 0.88–0.99; $p < 0.001$). Total wall thickness distinguished IBD from controls at a 2.80-mm cut-off with 96.7%

sensitivity, 100% specificity and an AUC of 0.97 (95% CI: 0.93–1.00; $p < 0.001$). For CD versus controls, a 2.96-mm cut-off yielded 94.1% sensitivity, 100% specificity and an AUC of 0.96 (95% CI: 0.90–1.00; $p < 0.001$). However, discrimination of CD from UC and controls was only fair at 3.43 mm, with 73.5% sensitivity, 61.1% specificity and an AUC of 0.70.

Table 9: ROC performance of EUS bowel-wall measurements

EUS parameter and diagnostic comparison	Sensitivity	Specificity	Cut-off	AUC	95% CI	P-value
Mucosal thickness: initial UC versus initial CD and controls	88.5%	90.9%	1.08 mm	0.93	0.86–0.99	<0.001
Submucosal thickness: initial CD versus initial UC and controls	97.1%	88.9%	1.12 mm	0.94	0.88–0.99	<0.001
Total wall thickness: IBD versus controls	96.7%	100%	2.80 mm	0.97	0.93–1.00	<0.001
Total wall thickness: initial CD versus controls	94.1%	100%	2.96 mm	0.96	0.90–1.00	<0.001
Total wall thickness: initial CD versus initial UC and controls	73.5%	61.1%	3.43 mm	0.70	0.57–0.83	0.004

Correlation Between EUS Measurements and Disease Activity

In UC, total wall thickness showed a moderate positive correlation with Mayo score ($r = 0.56$, $p = 0.003$). In CD, submucosal thickness correlated significantly with CDAI ($r = 0.63$, $p < 0.001$), ESR

($r = 0.48$, $p = 0.004$), CRP ($r = 0.39$, $p = 0.023$) and faecal calprotectin ($r = 0.61$, $p < 0.001$). The strongest correlations were with CDAI and faecal calprotectin.

Table 10: Correlation of EUS measurements with disease-activity indices and inflammatory markers

Initial diagnostic group	EUS measurement	Clinical or laboratory parameter	Correlation coefficient, r	P-value
UC	Total wall thickness	Mayo score	0.56	0.003
CD	Submucosal thickness	CDAI	0.63	<0.001
CD	Submucosal thickness	ESR	0.48	0.004
CD	Submucosal thickness	CRP	0.39	0.023
CD	Submucosal thickness	Faecal calprotectin	0.61	<0.001

Overall, EUS demonstrated excellent diagnostic performance and almost-perfect agreement with the final reference-standard diagnosis. Predominant mucosal thickening was associated with UC, whereas predominant submucosal thickening was associated with CD. Total wall thickness effectively differentiated patients with IBD from healthy controls but showed limited discriminatory ability for differentiating UC from CD.

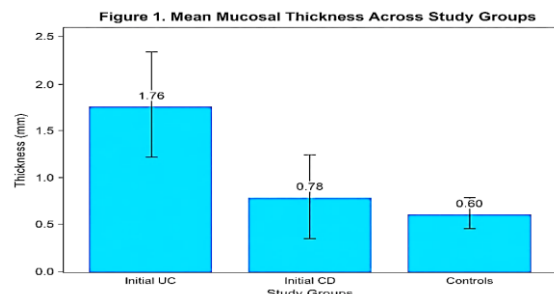


Figure 1. Mean Mucosal Thickness Across the Ulcerative Colitis, Crohn's Disease and Control Groups

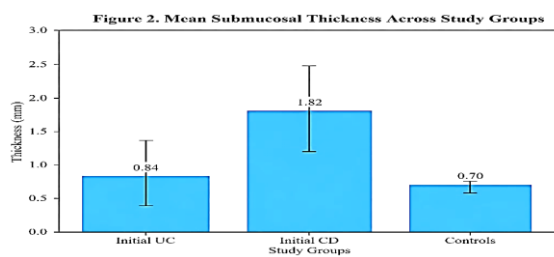


Figure 2. Mean Submucosal Thickness Across the Ulcerative Colitis, Crohn's Disease and Control Groups

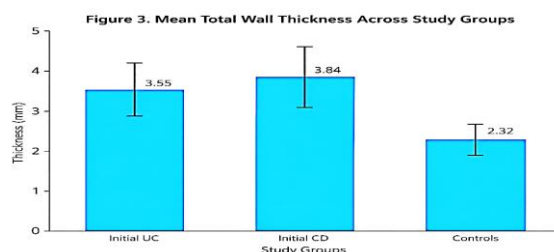


Figure 3. Mean Total Bowel-Wall Thickness Across the Ulcerative Colitis, Crohn's Disease and Control Groups

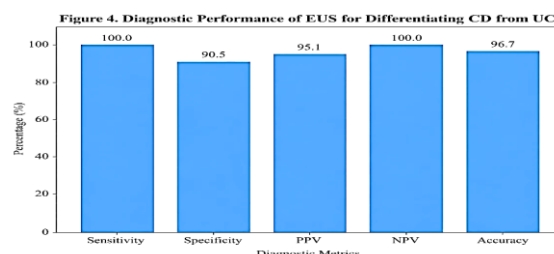


Figure 4. Diagnostic Performance of Endoscopic Ultrasonography for Differentiating Crohn's Disease from Ulcerative Colitis

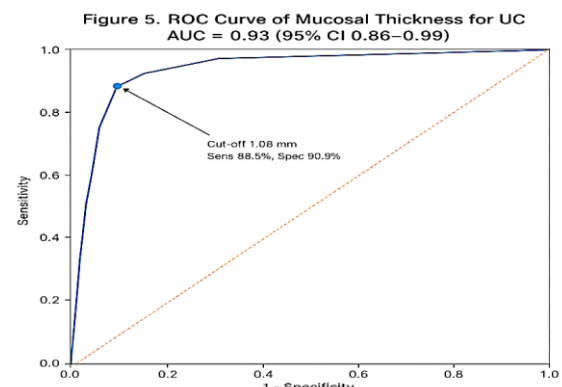


Figure 5. Receiver Operating Characteristic Curve of Mucosal Thickness for Differentiating Ulcerative Colitis from Crohn's Disease and Controls

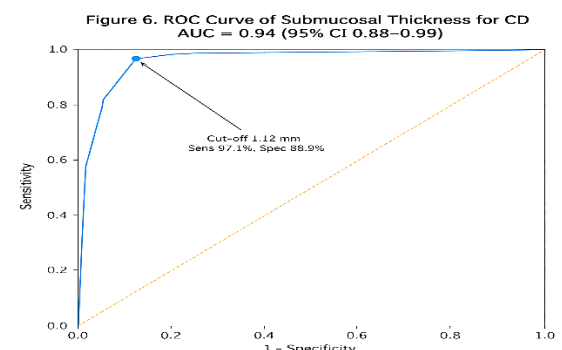


Figure 6. Receiver Operating Characteristic Curve of Submucosal Thickness for Differentiating Crohn's Disease from Ulcerative Colitis and Controls

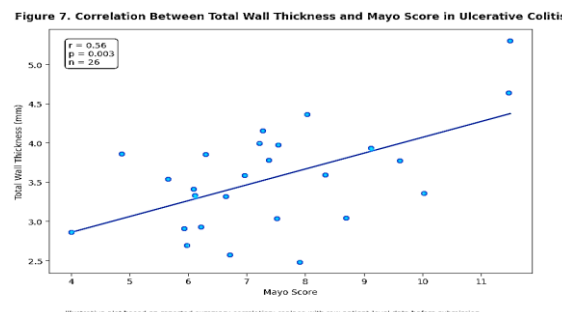


Figure 7. Correlation Between Total Bowel-Wall Thickness and Mayo Disease Activity Score in Patients with Ulcerative Colitis

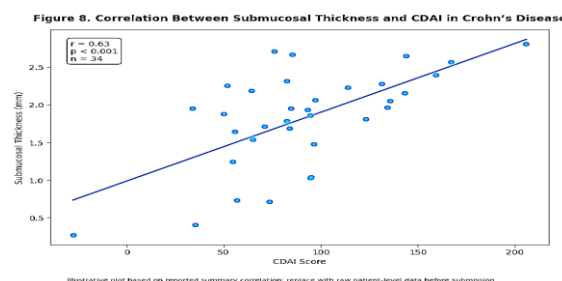


Figure 8. Correlation Between Submucosal Thickness and Crohn's Disease Activity Index in Patients with Crohn's Disease

Figure 9. Correlation Between Submucosal Thickness and Faecal Calprotectin in Crohn's Disease

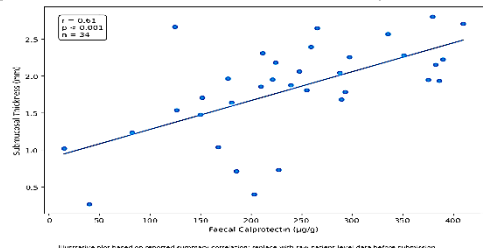


Figure 9: Correlation Between Submucosal Thickness and Faecal Calprotectin Levels in Patients with Crohn's Disease

DISCUSSION

The present prospective diagnostic-accuracy study evaluated EUS as an adjunct to histopathology and conventional assessment for differentiating UC from CD. Against the final histopathology-supported composite diagnosis, EUS produced 39 true-positive, two false-positive, 19 true-negative and no false-negative classifications. Sensitivity was 100%, specificity 90.5%, positive predictive value 95.1%, negative predictive value 100% and overall accuracy 96.7%. Cohen's kappa was 0.925, indicating almost-perfect agreement.

These findings suggest that layer-specific bowel-wall assessment provides clinically useful information when clinical, colonoscopic and histopathological features overlap. The high sensitivity and negative predictive value indicate that an EUS pattern not supporting CD effectively excluded CD in this cohort. However, the two false-positive classifications confirm that EUS should complement, rather than replace, histopathology, colonoscopy and cross-sectional imaging.

The results closely resemble those of Roushan et al., who reported 100% sensitivity and 90.9% specificity for sigmoid EUS in differentiating CD from UC.^[9] Ellrichmann et al. similarly found that total wall thickness, layer-specific thickening and pericolic findings assisted IBD classification.^[11] Both studies support the distinction between predominantly mucosal involvement in UC and deeper submucosal or transmural involvement in CD.

The diagnostic performance also compares favourably with conventional bowel ultrasonography. Fraquelli et al. reported sensitivities of 75–94% and specificities of 67–100% for ultrasound detection of CD, with pooled sensitivity and specificity of approximately 88.8% and 93% at a 3-mm bowel-wall threshold.^[12] Panés et al. reported approximately 85% sensitivity and 98% specificity.^[13] The higher sensitivity observed here may reflect the close proximity and spatial resolution of EUS, standardised sigmoid measurements and assessment of individual bowel-wall layers.

Pascu et al. reported an accuracy of 89% for transabdominal ultrasound and 73% for MRI in identifying active IBD.^[14] Although direct

comparison is limited by differences in technique and diagnostic targets, these findings support ultrasonography as a useful radiation-free modality for objective bowel assessment.

Concordance with Histopathology-Supported Diagnosis

Bhatnagar et al. demonstrated that bowel-wall and mucosal thickness were independently associated with acute histological inflammation, mesenteric fat echogenicity with chronic inflammation and mucosal thickness with fibrosis.^[10] Other ultrasound–histology studies have linked mural thickening, altered stratification and submucosal echogenicity with inflammation, fibrosis and bowel-wall remodelling.^[15–17]

However, inflammation and fibrosis may produce overlapping sonographic appearances. Wilkens et al. found that increased wall thickness could reflect both processes.^[18] EUS should therefore strengthen multidisciplinary diagnostic confidence rather than independently determine histological composition.

Layer-Specific Bowel-Wall Thickness

The principal morphological finding was the reciprocal distribution of mucosal and submucosal thickening. Mucosal thickness was significantly greater in UC than in CD and controls: 1.76 ± 0.56 mm compared with 0.78 ± 0.45 mm and 0.60 ± 0.16 mm, respectively. Mucosal thickness in CD did not differ significantly from controls.

Conversely, submucosal thickness was significantly greater in CD than in UC and controls: 1.82 ± 0.65 mm compared with 0.84 ± 0.50 mm and 0.70 ± 0.13 mm, respectively. Submucosal thickness in UC was comparable to that in controls. This pattern corresponds to predominantly mucosal inflammation in UC and deeper mural involvement in CD.

These findings agree with Roushan et al., who observed greater mucosal thickness in UC and greater submucosal thickness in CD.^[9] Transrectal and endoscopic ultrasound studies have likewise shown predominantly mucosal changes in UC and deeper or transmural abnormalities in CD.^[20,22]

Total wall thickness was significantly greater in both IBD groups than in controls: 3.55 ± 0.66 mm in UC, 3.84 ± 0.74 mm in CD and 2.32 ± 0.37 mm in controls. However, it did not differ significantly between UC and CD, indicating that total wall thickness identifies bowel inflammation more effectively than IBD subtype.

At a cut-off of 2.80 mm, total wall thickness differentiated IBD from controls with 96.7% sensitivity, 100% specificity and an AUC of 0.97. In contrast, its performance for differentiating CD from UC and controls was limited, with 73.5% sensitivity, 61.1% specificity and an AUC of 0.70. Thus, overall thickening reflects inflammatory burden, whereas the predominant affected layer provides greater phenotypic discrimination.

ROC Performance of Individual Layers

Mucosal thickness identified UC at a cut-off of 1.08 mm with 88.5% sensitivity, 90.9% specificity and

an AUC of 0.93. Submucosal thickness identified CD at a cut-off of 1.12 mm with 97.1% sensitivity, 88.9% specificity and an AUC of 0.94.

Roushan et al. reported comparable cut-offs of 1.10 mm for mucosal thickness in UC and 1.08 mm for submucosal thickness in CD.^[9] This similarity supports the plausibility of layer-specific thresholds. Nevertheless, cut-offs from a single-centre study may be affected by equipment, probe compression, measurement technique, disease activity and operator experience. External validation is therefore required before universal application.

Relationship with Disease Activity

In UC, total wall thickness showed a moderate positive correlation with Mayo score ($r=0.56$, $p=0.003$), suggesting increasing mural thickening with greater clinical and endoscopic activity. Previous studies have similarly associated bowel-wall thickening with active disease and subsequent relapse.^[20,21]

In CD, submucosal thickness correlated with CDAI ($r=0.63$), ESR ($r=0.48$), CRP ($r=0.39$) and faecal calprotectin ($r=0.61$). The strongest correlations were with CDAI and faecal calprotectin, supporting the association between deeper mural thickening and active intestinal inflammation.

These findings are consistent with EUS and conventional ultrasound studies demonstrating associations between bowel-wall measurements, disease-activity indices, inflammatory markers, Doppler vascularity and treatment response.^[9,14,19] EUS may therefore have potential roles in both initial classification and longitudinal disease assessment, although prospective multicentre validation is required.

Strengths and Limitations

Strengths included the prospective design, blinded EUS assessment, standardised mid-sigmoid measurements, repeated measurements, healthy controls, ROC analysis and calculation of Cohen's kappa. The composite reference diagnosis reflected real-world multidisciplinary practice.

Limitations included the single-centre design, modest sample size and wide confidence interval for specificity. All examinations were performed by one experienced endosonographer; therefore, interobserver reproducibility and applicability to less-experienced operators remain uncertain.

Bowel-layer comparisons used the initial classification, whereas diagnostic-accuracy analyses used the final reference diagnosis. Additionally, assessment was limited to the mid-sigmoid colon and may not reflect the most affected segment, particularly in isolated ileal or proximal CD.

The composite reference standard included histopathology but did not provide location-matched full-thickness histological validation. Thus, EUS–histopathology concordance refers to agreement with a histopathology-supported final diagnosis rather than direct correlation of individual mural layers.

Future multicentre studies should include multiple sonographers, specialist gastrointestinal pathologists, predefined histological activity scores, segment-matched specimens and external validation of ROC thresholds.

CONCLUSION

EUS demonstrated almost-perfect agreement with the histopathology-supported final diagnosis and high accuracy in differentiating CD from UC. Predominant mucosal thickening favoured UC, whereas predominant submucosal thickening favoured CD. Total wall thickness effectively distinguished IBD from normal bowel but had limited value for subtype differentiation.

Correlations with disease-activity indices and inflammatory markers supported the biological relevance of EUS findings. EUS should therefore be used alongside histopathology, colonoscopy and cross-sectional imaging, particularly in indeterminate or diagnostically discordant cases.

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REFERENCES

1. Baumgart DC, Sandborn WJ. Inflammatory bowel disease: clinical aspects and established and evolving therapies. *Lancet*. 2007;369(9573):1641-1657.
2. Ng SC, Shi HY, Hamidi N, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet*. 2017;390(10114):2769-2778.
3. Banerjee R, Pal P, Patel R, et al. Inflammatory bowel disease in rural and urban India: results from community colonoscopic evaluation of more than 30,000 symptomatic patients. *Lancet Reg Health Southeast Asia*. 2023;19:100259.
4. Magro F, Langner C, Driessen A, et al. European consensus on the histopathology of inflammatory bowel disease. *J Crohns Colitis*. 2013;7(10):827-851.
5. Feakins RM. Inflammatory bowel disease biopsies: updated British Society of Gastroenterology reporting guidelines. *J Clin Pathol*. 2013;66(12):1005-1026.
6. Strobel D, Goertz RS, Bernatik T. Diagnostics in inflammatory bowel disease: ultrasound. *World J Gastroenterol*. 2011;17(27):3192-3197.
7. Calabrese E, Maaser C, Zorzi F, et al. Bowel ultrasonography in the management of Crohn's disease: a review with recommendations of an international panel of experts. *Inflamm Bowel Dis*. 2016;22(5):1168-1183.
8. Taylor SA, Mallett S, Bhatnagar G, et al. Diagnostic accuracy of magnetic resonance enterography and small bowel ultrasound for the extent and activity of newly diagnosed and relapsed Crohn's disease: the METRIC multicentre trial. *Lancet Gastroenterol Hepatol*. 2018;3(8):548-558.
9. Roushan N, Ebrahimi Daryani N, Azizi Z, Pournaghshband H, Niksirat A. Differentiation of Crohn's disease and ulcerative colitis using intestinal wall thickness of the colon: a diagnostic accuracy study of endoscopic ultrasonography. *Med J Islam Repub Iran*. 2019;33:57.
10. Bhatnagar G, Rodriguez-Justo M, Higginson A, et al. Inflammation and fibrosis in Crohn's disease: location-matched histological correlation of small bowel ultrasound features. *Abdom Radiol (NY)*. 2021;46(1):144-155.
11. Ellrichmann M, Wietzke-Braun P, Dhar S, et al. Endoscopic ultrasound of the colon for the differentiation of Crohn's

- disease and ulcerative colitis in comparison with healthy controls. *Aliment Pharmacol Ther.* 2014;39(8):823-833.
12. Fraquelli M, Colli A, Casazza G, et al. Role of US in detection of Crohn disease: meta-analysis. *Radiology.* 2005;236(1):95-101.
 13. Panés J, Bouzas R, Chaparro M, et al. Systematic review: the use of ultrasonography, computed tomography and magnetic resonance imaging for the diagnosis, assessment of activity and abdominal complications of Crohn's disease. *Aliment Pharmacol Ther.* 2011;34(2):125-145.
 14. Pascu M, Roznowski AB, Müller HP, Adler A, Wiedenmann B, Dignass AU. Clinical relevance of transabdominal ultrasonography and magnetic resonance imaging in patients with inflammatory bowel disease of the terminal ileum and large bowel. *Inflamm Bowel Dis.* 2004;10(4):373-382.
 15. Hata J, Haruma K, Yamanaka H, et al. Ultrasonographic evaluation of the bowel wall in inflammatory bowel disease: comparison of in vivo and in vitro studies. *Abdom Imaging.* 1994;19(5):395-399.
 16. Nylund K, Leh S, Immervoll H, et al. Crohn's disease: comparison of in vitro ultrasonographic images and histology. *Scand J Gastroenterol.* 2008;43(6):719-726.
 17. Maconi G, Carsana L, Fociani P, et al. Small bowel stenosis in Crohn's disease: clinical, biochemical and ultrasonographic evaluation of histological features. *Aliment Pharmacol Ther.* 2003;18(7):749-756.
 18. Wilkens R, Hagemann-Madsen RH, Peters DA, et al. Validity of contrast-enhanced ultrasonography and dynamic contrast-enhanced MR enterography in the assessment of transmural activity and fibrosis in Crohn's disease. *J Crohns Colitis.* 2018;12(1):48-56.
 19. Moreno N, Ripollés T, Paredes JM, et al. Usefulness of abdominal ultrasonography in the analysis of endoscopic activity in patients with Crohn's disease: changes following treatment with immunomodulators and/or anti-TNF antibodies. *J Crohns Colitis.* 2014;8(9):1079-1087.
 20. Dağlı U, Över H, Tezel A, Ülker A, Temuçin G. Transrectal ultrasound in the diagnosis and management of inflammatory bowel disease. *Endoscopy.* 1999;31(2):152-157.
 21. Higaki S, Nohara H, Saitoh Y, et al. Increased rectal wall thickness may predict relapse in ulcerative colitis: a pilot follow-up study by ultrasonographic colonoscopy. *Endoscopy.* 2002;34(3):212-219.
 22. Shimizu S, Tada M, Kawai K. Endoscopic ultrasonography in inflammatory bowel diseases. *Gastrointest Endosc Clin N Am.* 1995;5(4):851-859.