Effectiveness and Power of Abdominal Ultrasonography in the Assessment of Crohn's Disease Activity: Comparison with Clinical, Endoscopic, and CT Enterography Findings

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ABSTRACT

Background: *Non-invasive methods play an important role in clinical assessment of Crohn's disease. Recent studies have highlighted the effectiveness and reliability of intestinal ultrasonography. We aimed to examine the relationship between intestinal ultrasonography and the clinical, endoscopic, and computed tomography enterography findings, and to assess the activity of Crohn's disease.*

Methods: *This was a 1-year prospective study involving patients diagnosed with Crohn's Disease. Clinical and endoscopic activity indices, and intestinal ultrasonography and computed tomography enterography findings were evaluated. Intestinal wall thickness, mesenteric inflammation, lymphadenopathy, and complications were evaluated by intestinal ultrasonograpy and computed tomography enterography, while the superior mesenteric artery flow velocity, resistive index, and Limberg score were assessed by Doppler intestinal ultrasonography.*

Results: *Seventy-nine patients with Crohn's disease were included. A significant correlation was found between intestinal wall thickness, mesenteric inflammation, and complications in intestinal ultrasonography and computed tomography enterography ($P = .0001$). According to the receiver operating curve analysis, the intestinal wall thickness, and mesenteric inflammation were correlated with the Crohn's Disease Activity Index, Harvey–Bradshaw Index, and SES-CD scores ($P < .05$), and they were very effective in distinguishing active from inactive disease. According to the Crohn's Disease Activity Index and SES-CD scores, Doppler flow velocity of the superior mesenteric artery was significantly higher in the active group than in the inactive group ($P < .05$). The Limberg score was very consistent with the Crohn's Disease Activity Index, Harvey–Bradshaw Index , and the results of the Simple Endoscopic Score for Crohn's Disease ($P < .0001$).*

Conclusion: *Our study showed that intestinal ultrasonography is an effective and reliable method for assessment of Crohn's disease activity compared to clinical, endoscopic, and CTE findings.*

Keywords: *Computed tomography, Crohn's disease, enterography, intestinal ultrasonography*

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disease that can involve the whole gastrointestinal system (GIS), primarily the small intestine and the terminal ileum, and it progresses with stages of relapse and remission.[1] The diagnosis of CD and the assessment of its activity are confirmed by a combination of clinical, endoscopic, histological, radiological, and/or biochemical markers. Colonoscopy is the basic method in the diagnosis and follow-up of CD. However, since monitoring and recovery of transmural disease besides mucosal healing has been in question for a while due to the transmural and penetrant nature of CD, different imaging methods including computed tomography(CT)-based methods [multi-detector CT, CT enteroclysis, computed tomography enterography (CTE)], magnetic resonance enterography (MRE), and leukocyte scintigraphy are used to assess CD. The CTE or MRE techniques provide great convenience since they enable cross-sectional imaging and show both intraluminal and extraluminal pathologies.[2] Additionally, eccentric wall thickening, mural stratification, fibrofatty proliferation, increased mesenteric vascularity, a positive comb

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sign, and internal and perianal fistula can be identified by CTE.[2-4] However, a disadvantage of CTE is the x-ray, since the radiation dose is important in patients with CD, particularly in young adults. Intestinal ultrasonography (IUS) is a non-invasive, readily accessible, and cost-effective bedside imaging modality that does not involve ionizing radiation. It can be used for intestinal and extra-intestinal lesions, for assessment of intestinal wall thickening (IWT), evaluation of intestinal layers, imaging of mesenteric inflammation (MI), and detection of complications such as stenosis, dilatation, abscess, and fistula.[5-7] Even though numerous studies in the literature have extensively examined the role of CTE and IUS in the assessment of CD, no study comparing the findings of IUS and CTE is available. The aim of the present study was to evaluate the effectiveness and role of IUS in CD activity compared to CTE, and the severity of clinical and endoscopic findings.

MATERIALS AND METHODS

This prospective study included all consecutive patients who presented to our Gastroenterology Clinic between May 2018 and June 2019 with a definite diagnosis of CD for follow-up or recurrence. The eligible patients included those ≥18 years of age having examinations within the same 1-week period and a stable clinical presentation.

The study was approved by the Ethics Committee (22.06.2018/1313).

Exclusion Criteria

Patients who could not undergo concurrent colonoscopy, ultrasonography, and tomography tests were excluded. Patients with pregnancy, renal failure, malignancy, and a history abdominal operation other than Crohn's disease were also excluded.

The IUS findings were compared with the clinical, colonoscopic, and CTE findings. The Crohn's Disease Activity Index (CDAI) and the Harvey–Bradshaw Index (HBI) were used to evaluate the disease activity. For CDAI scoring, 0-149 points indicate disease in remission, 150-220 points indicate mild active CD, 221-450 points indicate moderately active CD, and 451-1100 points indicate severe-fulminant disease.[8] An HBI score of less than 5 was considered clinical remission.[9] The age at diagnosis, site of involvement, type of disease, and the presence of a perianal disease were determined according to the Montreal classification. The type of the disease was defined in 3 categories—inflammatory, stricturing, and penetrating disease—according to the presence of intestinal complications such as abscess, fistula, and stricture.[10]

Main Points

- *Transabdominal ultrasonography and computerized tomography enterography (CTE) parameters were correlated in evaluating the clinical and endoscopic activation of Crohn's disease (CD).*
- *Ultrasonographic intestinal wall thickening (IWT), mesenteric inflammation (MI), small bowel wall vascularity, and increased superior mesenteric artery (SMA) flow velocity can be used as parameters in the assessment of CD activities.*

Intestinal Ultrasonography Evaluation

All patients were examined by IUS after overnight fasting. The IUS examination was conducted using a Toshiba Applio HDI-300 ultrasound system (Toshiba Corporation, Tokyo, Japan). At first, patients underwent a conventional ultrasound examination in the supine position. A detailed transabdominal ultrasound scan was performed. After that, intestinal examination was started from the right inguinal region using a convex probe (3.5-5.5 MHz) while the patients were lying in the supine position, and the terminal ileum and cecum were determined and examined. Then, the right colon, the transverse colon, the left colon, and the rectal and peri-intestinal regions were examined in detail, in accordance with topographic anatomy. Wall thickness, wall echogenicity, mural stratification, involved segment, inflammation in mesenteric fat planes, lymphadenopathy, and intestinal complications such as stricture, abscess formation, and fistulas were examined using a linear probe (7-12 MHz). The intestinal wall thickness was obtained by measuring the distance between the mucosal and serosal surfaces in the segment where the intestinal wall was the thickest. A wall thickness greater than 3 mm was considered pathologic. Mesenteric inflammation was defined as increased echogenicity, thickness of peri-intestinal tissue, and vascularity as demonstrated by Doppler ultrasound. The short axis of mesenteric lymph nodes greater than 5 mm was considered pathologic. Linear tracts between 2 epithelial surfaces in the intestinal loops were defined as fistula and the fluid collections involving parietal contrast were defined as abscess. The SMA was examined by duplex color Doppler. After the SMA was scanned longitudinally, images were obtained using color Doppler US and then spectral Doppler US. In the spectral Doppler examination, the peak systolic velocity (PSV) and resistive index (RI) were assessed. The Limberg score was used to assess bowel wall vascularization.[11] According to Limberg, intestinal wall vascularity is classified in 5 grades:

- grade 0: normal bowel wall with no thickening, well-delineated mural stratification, no mural flow (no color Doppler signal);
- grade 1: wall thickening (hypoechoic wall thickening and partially obscured mural stratification) and absent mural flow;
- grade 2 ("hypo-flow"): wall thickening with intermittent (or "spot") increases in vascularity;
- grade 3 ("hyper-flow"): wall thickening with protracted stretches of increased vascularity; and
- grade 4 ("hyper-flow"): color flow Doppler signals in both the bowel wall and surrounding mesenteric fat show increased vascularization (Limberg score 2 or above), which is considered abnormal.

The measurements were recorded for each patient.

Computed Tomography Enterography Evaluation

Computerized tomography examinations were performed using a Siemens Somatom Definition AS 128-slice CT Scanner (Erlangen, Germany). Patients received the whole abdominal CTE scan protocol in the supine position by including the region as FOV = 350-420 in the image over the diaphragmatic cupolas till the end of the symphysis pubis, holding their hands and arms over the head. The slice thickness was selected as 1 mm for all patients and the pitch value was 1.

In the enterography protocol, a combination of lactulose solution was used as a neutral contrast agent in order to reduce absorption of drinking water and intraluminal fluid along the lumen of the small intestine for providing intestinal distention in the peroral route. After a fasting period of a minimum of 6 hours, patients were required to have a total of 1500 cc water intake, 250 cc every 10 minutes in the first hour, and then 2 hours before the imaging. Within the second hour, 100 cc lactulose solution (Osmolak 10 g/15 mL 250 mL, Biofarma) was added into 1400 cc water, and the patients had a total of 1500 cc water intake including 250 cc every 10 minutes. All patients also underwent scanning using an intravenous contrast agent (iopromide).

Any intestinal wall thickness of >3 mm in distant intestinal segments in the CTE findings was considered pathologic. Extension of the inflammatory process into mesentery and increased density in fat planes were considered inflammation. Any presence of abscess, fistula, narrowing and lymphadenopathy was monitored.

Endoscopic Examinations

All patients were scored according to the Simple Endoscopic Score for Crohn's Disease (SES-CD). In the SES-CD scoring system, the size of ulcers, the ulcerated surface area, affected surface, and the presence of narrowing are assessed in 5 regions: rectum, left colon, transverse colon, right colon, and ileum. Scores of 0 to 2 points are considered inactive disease.[12]

Statistical Method

The SPSS 24.0 program was used for analysis of data. Mean, standard deviation, median, frequency, and ratio values were the descriptive statistics used in the data analysis. Distribution of the variables was measured by the Kolmogorov–Smirnov test. The Mann–Whitney *U*-test was used for the analysis of quantitative independent data while the chi-square test and Fischer's test were used for the analysis of qualitative independent data. The Kappa statistic was used for the analysis of agreement. The effect level was measured using the ROC curve.

RESULTS

Seventy-nine patients enrolled in the study. Of these patients, 72% were men and the average age was 37.5 years. The mean duration of disease was 48.6 months. The most common behavior of disease was inflammatory, and was localized in the ileum. Nine patients had perianal involvement. Complications included 8 fistulas (perianal 1, cutaneous 2, ileomesenteric 1, between ileum and psoas muscle 1, colocolic 1, ileocolic 2), 2 abscesses, and 1 stricture. The mean CDAI value was 192. According to CDAI, 45 patients had active disease and 34 patients were in remission. The mean HBI value was 5.9. The clinical, demographic, and laboratory data of the patients are shown in Table 1.

Increased IWT, MI, and complications detected by the IUS were highly consistent with CTE findings (P = .0001) (Table 2). However, there was no compatibility between CTE and IUS in terms of lymphadenopathy detection (P = .107).

Table 3 demonstrates the diagnostic accuracy of IUS. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the IUS in detecting IWT increase were 82%, 96.5%, 97.6%, and 75.6% respectively, with an accuracy rate of 87.6%. Its sensitivity, specificity, PPV, and NPV in detecting MI were 80%, 94.8%, 94.1%, and 82.2% respectively, with an accuracy rate of 87.3%. Its sensitivity, specificity, PPV, and NPV in

Table 1. Demographic and Clinical Characteristics of the Patients

	Min-Max	Mean ± SD
Age (years)	17-64	37.54 ± 11.49
Age at diagnosis (years)	13-62	33.70 ± 11.87
Diagnosis period (month)	0-240	46.85 ± 51.69
CDAI	23-528	192.4± 105.78
HBI	1-26	5.9 ± 4.15
SES-CD	0-27	6.4 ± 6.03
	n	%
Gender		
Male	57	72.10
Female	22	27.80
Smoking		
Yes	28	35.40
No	36	53
Quit	15	11.60
Alcohol		
Yes	6	7.59
No	73	92. 41
Operation for Crohn's Disease		
Yes	25	31.65
Reason for operation	Perforation (1) Abscesses (2) Fistulae (7) Fissurae (3) Abscess + Fistula (1) Fistula + Fissura (1) Stenoses Colonic CD (9) Unresponsive to medical treatment (1)	
Other operation		
Yes	27	34.18
Drugs used		
Azathioprine	17	21.50
Mesalazine	31	39.20
Steroid	6	7.50
Budesonide	10	12.60
Sulfasalazine	1	1.20
Biological agent	10	12.60
No drug used	22	27.80
Illness Behavior		
Inflammatory (B1)	62	78.48
Stricturing (B2)	14	17.72
Penetrating (B3)	3	3.80
Age (years)		
<16 years	3	3.80
17-40 years	53	67.09
≥40 years	23	29.11
Localization		
Ileal	38	48.10
Colonic	6	7.59
Ileocolonic	35	44.30
Perianal involvement	9	11.39

Min-Max, minimum-maximum; SD, standard deviation; CDAI, Crohn's Disease Activity Index; HBI, Harvey–Bradshaw Index; SES-CD, simple endoscopic score.

detecting complications were 66.6%, 100%, 100%, and 95.8% respectively, with an accuracy rate of 96.2%; its sensitivity, specificity, PPV, and NPV in detecting lymphadenopathy were 23.5%, 88.9%, 61.5%, and 60.6% respectively, with an accuracy rate of 60.8%.

In the ROC analysis, the IWT increase and the MI detection by IUS for predicting CDAI were 0.837 (P = .001) and 0.839 (P = .001), respectively (Figure 1). Predicted HBI values were 0.735 (P = .012) and 0.726 (P = .016) respectively, and the predicted SES-CD scores were 0.893 (P = .000), and 0.783 (P = .004) respectively. Predicted IWT and MI detected in CTE were 0.721 (P = .012) and 0.819 (P = .001) for CDAI (Figure 1), 0.744 (P = .009) and 0.818 (P = .001) for HBI, and 0.834 (P = .001) and 0.762 (P = .007) for SES-CD scores, respectively (Table 4).

In addition, the predictive effect of lymphadenopathy on disease activity was correlated only with HBI (0.689, P = .044) while complications, distinguishable wall layer, and decreased peristalsis detected on IUS and CTE had no significant correlation (P > .05) (Table 4).

Limberg scores determined by color Doppler US were highly compatible with the CDAI, HBI, and SES-CD scores (P = .0001) (Table 5).

While SMA Doppler flow velocity was significantly higher in the active group than in the inactive group in CDAI (P = .038), and SES-CD (P = .014), the RI value was significantly lower in CDAI (P < .037). In SES-CD scoring, there was no difference in the RI value between the active and inactive groups (O > .05). Similarly, in HBI, no significant difference was observed in both SMA flow velocity and RI value between the active and inactive groups (P > .05) (Table 6).

Table 2. Comparison of the Findings for Wall Thickness Increase, Inflammation in Mesenteric Fat Planes, Lymphadenopathy, and Complications, Between CTE and IUS

		Wall Thickness Increase in CTE						
		Total		Pathologic		Normal		
Wall thickness increase in IUS	Pathologic	42	53.16%	41	82.00%	1	3.45%	κ_w:0.743
	Normal	37	46.84%	9	18.00%	28	96.55%	*P* = .0001
		Inflammation in Mesenteric Fat Planes in CTE						
		Total		Pathologic		Normal		
Inflammation in mesenteric fat planes in IUS	Pathologic	34	43.04%	32	80%	2	5.13%	κ_w:0.747
	Normal	45	56.96%	8	20%	37	94.87%	*P* = .0001
		Lymphadenopathy in CTE						
		Total		Pathologic		Normal		
Lymphadenopathy in IUS	Pathologic	13	16.46%	8	23.53%	5	11.11%	κ_w:0.134
	Normal	66	83.54%	26	76.47%	40	88.89%	*P* = .140
		Complication in CTE						
		Total		Pathologic		Normal		
Complication in IUS	Pathologic	6	7.59%	6	66.67%	0	0.00%	κ_w:0.780
	Normal	73	92.41%	3	33.33%	70	100%	*P*= .0001

DISCUSSION

Crohn's disease may often become active during its natural course, where early diagnosis and detection of complications are vital. For this purpose, clinical indices, laboratory parameters, and colonoscopy have been used for a long time. At present, imaging methods such as IUS, CT, and MRI are increasingly employed to provide extensive information about the bowel and the surrounding tissues. However, the superiority of any method over others or the question on which one should take the first place is still controversial.

Our study revealed that clinical and endoscopic parameters were correlated with IUS and CTE findings in the detection of intestinal inflammation in patients suffering from Crohn's disease. Tarjan et al[13] reported that CT was more sensitive, but less specific than IUS in Crohn's disease.[13] However, the sensitivity, specificity, and accuracy of ultrasound were 88.4%, 93.3%, and 90.4%, respectively. The accuracy of IUS and CT were similar. Intra- and perimural abscesses, sinus tracts, and stenoses were also more frequently visualized by IUS. They concluded that IUS was an excellent tool in known Crohn's disease for following the course of disease and for evaluating relapses and extramural manifestations. Astegiano et al[14] found a sensitivity of 74%, specificity of 98%, PPV of 92%, and NPV of 92% by IUS for diagnosis of IBD.[14] Sakurai et al[15] found that the inflammation in the mesenteric fat planes detected in CTE in patients with CD was highly correlated with the SES-CD scores.

Table 3. Diagnostic Accuracy of Findings for Wall Thickness Increase, Inflammation in Mesenteric Fat Planes, Lymphadenopathy, and Complications in CD, in IUS

CTE	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Accuracy (%)
IUS wall thickness increase	82 (68.5-91.4)	96.55 (82.2-99.9)	97.62 (85.6-99.6)	75.68 (63.1-84.9)	87.68 (63.1-84.9)
Inflammation in mesenteric fat planes	80 (64.3-90.9)	94.87 (82.6-99.3)	94.12 (80.4-98.4)	82.22 (71.2-89.6)	87.34 (77.9-93.7)
Lymphadenopathy	23.53 (10.75-41.17)	88.89 (75.95-96.29)	61.54 (36.48-81.68)	60.61 (55.42-65.56)	60.76 (49.13-71.56)
Complication	66.67 (29.9-92.5)	100 (94.8-100)	100 (100-100)	95.89 (90.2-98.3)	96.2 (89.3-99.2)

IUS, intestinal ultrasonography; CTE, computed tomography enterography; CD, Crohn's disease.

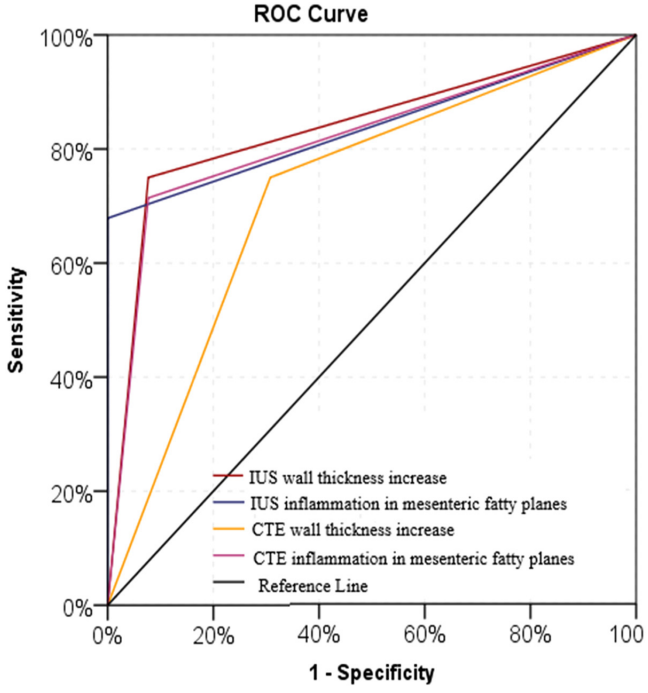

Figure 1. Receiver operating characteristic curve analyses of the wall thickness increase and inflammation in mesenteric fat planes in inactive and active patients for predicting CDAI. The area under the curve of wall thickness increase, and inflammation in mesenteric fat planes were 0.837 and 0.839, respectively ($P < .001$).

Lopes et al[16] showed that CTE findings significantly correlated with endoscopic findings in evaluating activity.

Horsthuis et al[17] assessed 33 prospective studies in order to assess the accuracy of the imaging methods and published a meta-analysis. They reported that patient-based sensitivity was 89.7%, 93.0%, 87.8%, and 84.3% for IUS, MRE, scintigraphy, and CTE in the diagnosis of CD, respectively, while specificity was 74.5%, 70.3%, 77.3%, and 67.4% for IUS, MRE, scintigraphy, and CTE, respectively.[17] One advantage of our study over similar studies was that the parameters (IWT, MI, lymphadenopathy, presence of complication) were assessed individually in comparison with CTE and IUS. The measurements of IWT and MI, and the complications detected in CTE and IUS were compatible with each other. However, no significant correlation was found between the 2 examinations in terms of lymphadenopathy. The sensitivity of IUS was 82%, 80%, 23.5%, and 66.7% for IWT, MI, lymphadenopathy, and complication detected in CTE, respectively, while the specificity was 96.5%, 94.8%, 88.9%, and 100%, respectively (Table 3). We were able to to detect 3 fistulas, 2 abscesses and 1 stricture on IUS and CTE. Three fistula lines (anal, ileo-mesenteric, and cutaneous) that were evident in CTE could not be detected on IUS. The low sensitivity of IUS in detecting complications compared to CTE maybe associated with easy monitoring of bowel loops in cross-sectional examination (in terms of detecting fistula etc), use of a contrast agent, lack of patient-related factors (IUS's examination performance difficulty in painful areas with probe pressure, conditions associated with meteorism, etc.,), which make CTE more favorable compared to IUS.

Clinical indices are very important in determining the clinical status of CD at the time of diagnosis and the response to treatment, and in monitoring activation. Haber and Martinez showed that CDAI was significantly correlated with IWT detected on IUS.[18,19] In the literature, there is no study investigating the correlation between the CDAI and the inflammation in mesenteric fat planes detected on IUS. In our study, the increase in wall thickness and the presence of inflammation in mesenteric fat planes detected on both IUS and CTE were similarly effective in differentiating active and inactive disease according to the CDAI, HBI, and SES-CD scores. In addition, lymphadenopathy detected in CTE was associated with HBI in distinguishing activity (Table 4). However, no correlation was detected between mural stratification and reduced peristaltis with CDAI, HBI, and SES-CD scores.

Park et al[20] and Lo et al[21] reported that CDAI was significantly correlated with the IWT, MI, and the presence of lymphadenopathy detected in CTE.[20,21]

In a prospective study conducted by Kucharzik et al[22] including 234 patients with CD, the patients were assessed at months 3, 6, and 12. The number of the findings detected on IUS following treatment decreased significantly and the HBI scores also showed a significant reduction.[22]

In the literature, there is no study examining the correlation between HBI and CTE. However, our study showed that IWT, MI, and presence of lymphadenopathy examined in CTE were significantly effective in predicting the patients in whom CD was active or inactive, based on the HBI.

Of course, due to the nature of CD, endoscopic evaluation is very valuable, both during diagnosis and follow-up. However, colonoscopy is compared to cross-sectional imaging methods because it is invasive and sometimes limited in assessing the entire intestine and its segments. Calabrese et al[7] found that endoscopic scoring and IWT on

Table 4. CDAI, HBI, and SES-CD Prediction Level of IUS Versus CTE in CD

	CDAI (–/+) Prediction		
	Area Under Curve	95% CI	*P*
IUS Wall thickness increase	*0.837*	*0.706-0.967*	*.001*
IUS Inflammation in mesenteric fat planes	*0.839*	*0.720-0.958*	*.001*
IUS Lymphadenopathy	0.661	0.495-0.826	.101
IUS Complication	0.589	0.411-0.768	.363
IUS Mural stratification	0.554	0.369-0.738	.585
IUS Peristalsis	0.607	0.432-0.783	.275
CTE Wall thickness increase	*0.721*	*0.547-0.895*	*.024*
CTE Inflammation in mesenteric fat planes	*0.819*	*0.683-0.954*	*.001*
CTE Lymphadenopathy	0.658	0.488-0.828	.107
CTE Complication	0.607	0.432-0.783	.275
	HBI (–/+)Prediction		*P*
	Area Under Curve	95% CI	
IUS Wall thickness increase	*0.735*	*0.574-0.896*	*.012*
IUS Inflammation in mesenteric fat planes	*0.726*	*0.566-0.886*	*.016*
IUS Lymphadenopathy	0.578	0.400-0.755	.407
IUS Complication	0.600	0.427-0.773	.285
IUS Mural stratification	0.509	0.326-0.691	.925
IUS Peristalsis	0.569	0.391-0.746	.462
CTE Wall thickness increase	*0.744*	*0.581-0.906*	*.009*
CTE Inflammation in mesenteric fat planes	*0.818*	*0.680-0.955*	*.001*
CTE Lymphadenopathy	*0.689*	*0.527-0.850*	*.044*
CTE Complication	0.620	0.450-0.790	.200
	SES-CD (–/+)Prediction		
	Area Under Curve	Confidence Interval of 95%	
IUS Wall thickness increase	*0.893*	*0.794-0.991*	*.000*
IUS Inflammation in mesenteric fat planes	*0.783*	*0.638-0.928*	*.004*
IUS Lymphadenopathy	0.604	0.426-0.783	.287
IUS Complication	0.533	0.345-0.721	.737
IUS Mural stratification	0.554	0.369-0.738	.585
IUS Peristalsis	0.607	0.432-0.783	.275
CTE Wall thickness increase	*0.834*	*0.692-0.975*	*.001*
CTE Inflammation in mesenteric fat planes	*0.762*	*0.606-0.919*	*.007*
CTE Lymphadenopathy	0.602	0.602-0.783	.300
CTE Complication	0.551	0.551-0.737	.604

IUS, intestinal ultrasonography; CTE, Computed tomography enterography; CD, Crohn's Disease; CDAI, Crohn's Disease Activity Index; HBI, Harvey–Bradshaw Index; SES-CD, Simple Endoscopic Score for Crohn's Disease.

IUS were correlated. A literature review showed that there was no study investigating the correlation between the finding of MI on IUS and SES-CD. However, we observed that IWT and MI on IUS were significantly effective in predicting the active and inactive CD in patients based on the SES-CD scoring (Table 4).

Table 5. Correlation between the Limberg score and the CDAI, HBI, and SES-CD scorings

		Limberg Scoring						
		Total		Pathologic		Normal		
CDAI	Pathologic	44	56.41%	33	78.57%	11	30.56%	κ:*0.482 w*
	Normal	34	43.59%	9	21.43%	25	69.44%	*p=0.0001*
SES-CD	Pathologic	50	64.10%	40	95.24%	10	27.78%	κ:*0.685 w*
	Normal	28	35.90%	2	4.76%	26	72.22%	*p=0.0001*
HBI	Pathologic	41	52.56%	30	71.43%	11	30.56%	κ:*0.408 w*
	Normal	37	47.44%	12	28.57%	25	69.44%	*p=0.0001*

CDAI, Crohn's Disease Activity Index; HBI, Harvey–Bradshaw Index; SES-CD, Simple Endoscopic Score for Crohn's Disease.

In a study conducted by Cheng et al[23] including 49 patients with CD, they found a significant correlation between the SES-CD and the IWT observed in CTE. Colombel et al[24] reported a significant correlation between IWT and fat density in CTE and SES-CD.[24] We also found a significant correlation between the SES-CD scores and IWT and MI in CTE and IUS.

Doppler ultrasound helps show increased splanchnic blood flow due to inflammatory changes in the region affected in patients with CD. In the literature, there are some studies investigating the diagnostic and activity-discriminant accuracy of the examination of the SMA via Doppler USG in patients with CD. These studies have shown that the flow velocity of SMA increases and RI decreases in active CD patients vs. inactive CD patients in correlation with CDAI.[25-27] Likewise, in our study, the flow velocity of SMA was significantly higher in the active patients than in the inactive patients based on CDAI, and the RI value was significantly lower. We found no correlation between SMA flow velocity and RI and HBI (Table 6). Esteban et al[28] found that RI significantly decreased in active patients based on CDAI and HBI. There was no study investigating the correlation between SES-CD and Doppler US in the literature. However; we found a significant correlation between the SES-CD and the Doppler USG flow velocity of SMA, but there was no correlation between the SES-CD score and the RI.

The Limberg score is a semi-quantitative method used to assess the vascularity of the small intestinal wall in CD via color Doppler US (CD-US). The grading is done according to the intestinal wall thickness and density of the capillary

Table 6. Correlation Between the SMA Doppler Measurements and the CDAI, HBI, and SES-CD Scorings

	CDAI (0-149)		CDAI (≥150)		
	Mean ± SD	Median	Mean ± SD	Median	*P*
IUS flow velocity (ml/min)	501.1 ± 71.4	486.0	652.4 ± 255.6	585.0	*.038*[m]
IUS RI	0.8 ± 0.1	0.8	0.7 ± 0.1	0.7	*.037*[m]
	SES-CD (0-2)		SES-CD (≥3)		*P*
	Mean ± SD	Median	Mean ± SD	Median	
IUS flow velocity (mL/Dk**)**	488.3 ± 75.9	450.0	652.9 ± 249.1	580.0	*.014*[m]
IUS RI	0.8 ± 0.1	0.8	0.7 ± 0.1	0.8	.871[m]
	HBI (0-4)		HBI (≥5)		*P*
	Mean ± SD	Median	Mean ± SD	Median	
IUS flow velocity (mL/Dk)	542.0 ± 120.9	534.0	643.5 ± 265.9	560.0	.305[m]
IUS RI	0.8 ± 0.1	0.8	0.7 ± 0.1	0.8	.075[m]

[m]Mann–Whitney U-test.
SMA, Superior mesenteric artery; CDAI, Crohn's Disease Activity Index; HBI, Harvey–Bradshaw Index; SES-CD, Simple Endoscopic Score for Crohn's Disease; CD, Crohn's disease.

flow around the bowel loop.[11] Drews et al[29] found a significant correlation between the CDAI and the Limberg score,[29] while Sasaki T et al[30] observed a significant correlation between the SES-CD and the Limberg score. However, we showed that Limberg scores were highly compatible with the CDAI, HBI, and SES-CD results (Table 5).

We found that IUS is highly effective and reliable in evaluating CD activity. The IUS approach has been increasingly used for diagnosis of CD, determination of its localization and activity, and treatment follow-up.[31,32] Although it is an operator-dependent technique, its reproducibility has also been demonstrated.[33] To a lesser extent than IUS, the interpretation and assessment of the CTE images are also person-dependent and radiologists may have different interpretations depending on their experience. Today, ultrasound technology is constantly developing, as it is directly reflected in the assessment of CD. Furthermore, studies on the use of elastography are gradually increasing.[34-37]

We determined the accuracy rate of the IUS according to the IWT value, but no cut-off value was defined for the IWT.

In conclusion, in our study has revealed that IUS, which is a non-invasive, cost-effective, bedside modality which requires no preparation, is as effective as CTE in correlation with clinical and endoscopic scores to evaluate the activity of the CD.

Ethics Committee Approval: The approval was obtained from the ethics committee of the Ministry of Health Bağcılar Training and Research Hospital to conduct the study (22.06.2018/1313).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

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REFERENCES

1. M'koma AE. Inflammatory bowel disease: an expanding global health problem. Clin Med Insights Gastroenterol. 2013;6:33-47. [CrossRef]
2. Gatta G, Di Grezia G, Di Mizio V, et al. Crohn's disease imaging: a review. Gastroenterol Res Pract. 2012;2012:816920. [CrossRef]
3. Park MJ, Lim JS. Computed tomography enterography for evaluation of inflammatory bowel disease. Clin Endosc. 2013;46(4):327-366. [CrossRef]
4. Elsayes KM, Al-Hawary MM, Jagdish J, Ganesh HS, Platt JF. CT enterography: principles, trends, and interpretation of findings. RadioGraphics. 2010;30(7):1955-1970. [CrossRef]
5. Calabrese E. Bowel ultrasound for the assessment of Crohn's disease. Gastroenterol Hepatol. 2011;7(2):107-109.
6. Kucharzik T, Kannengiesser K, Petersen F. The use of ultrasound in inflammatory bowel disease. Ann Gastroenterol. 2017;30(2):135-144. [CrossRef].
7. Calabrese E, Petruzziello C, Onali S, et al. Severity of postoperative recurrence in Crohn's disease: correlation between endoscopic and sonographic findings. Inflamm Bowel Dis. 2009;15(11):1635-1642. [CrossRef]
8. Yoshida EM. The Crohn's Disease Activity Index, its derivatives and the Inflammatory Bowel Disease Questionnaire: a review of instruments to assess Crohn's disease Can J Gastroenterol. 1999;13(1):65-73.
9. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet. 1980;1(8167):514. [CrossRef]
10. Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut. 2006;55(6):749-753. [CrossRef]
11. Limberg B. Diagnosis of chronic inflammatory bowel disease by ultrasonography. Z Gastroenterol. 1999;37(6):495-508.
12. Daperno M, D'Haens G, Van Assche G, et al. Development and validation of a new, simplified endoscopic activity score for Crohn's disease: the SES-CD. Gastrointest Endosc. 2004;60(4):505-512. [CrossRef]
13. Tarján Z, Tóth G, Györke T, Mester A, Karlinger K, Makó EK. Ultrasound in Crohn's disease of the small bowel. Eur J Radiol. 2000;35(3):176-182. [CrossRef]
14. Astegiano M, Bresso F, Cammarota T, et al. Abdominal pain and bowel dysfunction: diagnostic role of intestinal ultrasound. Eur J Gastroenterol Hepatol. 2001;13(8):927-931. [CrossRef]
15. Sakurai T, Katsuno T, Saito K, et al. Mesenteric findings of CT enterography are well correlated with the endoscopic severity of Crohn's disease. Eur J Radiol. 2017;89:242-248. [CrossRef]
16. Lopes S, Andrade P, Afonso J, et al. Monitoring Crohn's disease activity: endoscopy, fecal markers and computed tomography enterography. Therap Adv Gastroenterol. 2018;11:1756284818769075. [CrossRef]
17. Horsthuis K, Bipat S, Bennink RJ, Stoker J. Inflammatory bowel disease diagnosed with US, MR, scintigraphy, and CT: meta-analysis of prospective studies. Radiology. 2008;247(1):64-79. [CrossRef]
18. Haber HP, Busch A, Ziebach R, Stern M. Bowel wall thickness measured by ultrasound as a marker of Crohn's disease activity in children. Lancet. 2000;355(9211):1239-1240. [CrossRef]
19. Martínez MJ, Ripollés T, Paredes JM, Blanc E, Martí-Bonmatí L. Assessment of the extension and the inflammatory activity in Crohn's disease: comparison of ultrasound and MRI. Abdom Imaging. 2009;34(2):141-148. [CrossRef]
20. Park EK, Han NY, Park BJ, et al. Value of computerized tomography enterography in predicting Crohn's disease activity: correlation

with Crohn's disease activity index and C-reactive protein. Iran J Radiol. 2016;13(4):e34301. [CrossRef]
21. Lo Re GR, Cappello M, Tudisca C, et al. CT enterography as a powerful tool for the evaluation of inflammatory activity in Crohn's disease: relationship of CT findings with CDAI and acute-phase reactants. Radiol Med. 2014;119(9):658-666. [CrossRef]
22. Kucharzik T, Wittig BM, Helwig U, et al. Use of intestinal ultrasound to monitor Crohn's disease activity. Clin Gastroenterol Hepatol. 2017;15(4):535-542.e2. [CrossRef]
23. Cheng J, Xie H, Yang H, Wang K, Xu G, Wu G. Computed tomography enterography: quantitative evaluation on Crohn's disease activity. Gastroenterol Res Pract. 2018;2018:7351936. [CrossRef]
24. Colombel JF, Solem CA, Sandborn WJ, et al. Quantitative measurement and visual assessment of ileal Crohn's disease activity by computed tomography enterography: correlation with endoscopic severity and C reactive protein. Gut. 2006;55(11):1561-1567. [CrossRef]
25. Yekeler E, Danalioglu A, Movasseghi B, et al. Crohn disease activity evaluated by Doppler ultrasonography of the superior mesenteric artery and the affected small-bowel segments. J Ultrasound Med. 2005;24(1):59-65. [CrossRef]
26. Na Y, Zhou J, Xiao XM, et al. Assessment of Crohn's disease activity by Doppler sonography. Saudi Med J. 2017;38(4):391-395. [CrossRef]
27. Sjekavica I, Barbarić-Babić V, Krznarić Z, Molnar M, Čuković-Čavka S, Štern-Padovan R. Assessment of Crohn's disease activity by Doppler ultrasound of superior mesenteric artery and mural arteries in thickened bowel wall: cross-sectional study. Croat Med J. 2007;48(6):822-830. [CrossRef]
28. Esteban JM, Maldonado L, Sanchiz V, Minguez M, Benages A. Activity of Crohn's disease assessed by colour Doppler ultrasound analysis of the affected loops. Eur Radiol. 2001;11(8):1423-1428. [CrossRef]
29. Drews BH, Barth TF, Hänle MM, et al. Comparison of sonographically measured bowel wall vascularity, histology, and disease activity in Crohn's disease. Eur Radiol. 2009;19(6):1379-1386. [CrossRef]
30. Sasaki T, Kunisaki R, Kinoshita H, et al. Use of color Doppler ultrasonography for evaluating vascularity of small intestinal lesions in Crohn's disease: correlation with endoscopic and surgical macroscopic findings. Scand J Gastroenterol. 2014;49(3):295-301. [CrossRef]
31. Conti CB, Giunta M, Gridavilla D, Conte D, Fraquelli M. Role of bowel ultrasound in the diagnosis and follow-up of patients with Crohn's disease. Ultrasound Med Biol. 2017;43(4):725-734. [CrossRef]
32. Liu C, Ding SS, Zhang K, et al. Correlation between ultrasound consolidated score and simple endoscopic score for determining the activity of Crohn's disease. Br J Radiol. 2020;93(1109):20190614. [CrossRef]
33. Fraquelli M, Sarno A, Girelli C, et al. Reproducibility of bowel ultrasonography in the evaluation of Crohn's disease. Dig Liver Dis. 2008;40(11):860-866. [CrossRef]
34.Goertz RS, Lueke C, Wildner D, Vitali F, Neurath MF, Strobel D. Acoustic radiation force impulse (ARFI) elastography of the bowel wall as a possible marker of inflammatory activity in patients with Crohn's disease. Clin Radiol. 2018;73(7):678.e1-678.e5. [CrossRef]
35.Lu C, Merrill C, Medellin A, Novak K, Wilson SR. Bowel ultrasound state of the art: grayscale and Doppler ultrasound, contrast enhancement, and elastography in Crohn disease. J Ultrasound Med. 2019;38(2):271-288. [CrossRef]
36. Pescatori LC, Mauri G, Savarino E, Pastorelli L, Vecchi M, Sconfienza LM. Bowel sonoelastography in patients with Crohn's disease: a systematic review. Ultrasound Med Biol. 2018;44(2):297-302. [CrossRef]
37. Marin AM, Calapod OP, Moldoveanu AC, Tribus LC, Fierbințeanu-Braticevici C. Non-invasive ultrasonographic score for assessment of the severity of inflammatory bowel disease. Ultrasound Med Biol. 2021;47(4):932-940. [CrossRef]