Impact of intestinal ultrasound for assessment of inflammatory bowel disease activity

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ORIGINAL RESEARCH

Impact of Intestinal Ultrasound for Assessment of Inflammatory Bowel Disease Activity

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Abstract

Background: Inflammatory bowel disease (IBD) is considered a chronic inflammatory disease that has two main forms: ulcerative colitis (UC) and Crohn's disease (CD). IBDU (unspecified) is used when a sure diagnosis of CD or UC cannot be made. Over time, most patients with IBDU (unspecified) will be assigned a definitive diagnosis of UC or CD (Ye Y et al., 2019). This study aimed to study the role of intestinal ultrasound in comparison to computed tomography enterography and colonoscopy in detecting bowel wall thickness (BWT) as an assessment tool for activity in IBD.

Patients and methods: We conducted a comparative study in Al-Azhar University Hospitals of previously diagnosed 70 IBD patients divided into two groups. Group A (30 patients with CD) and group B (40 patients with UC) in addition to positive clinical picture and laboratory data of activity. Group A underwent intestinal ultrasound (IUS), computed tomography enterography, and colonoscopy, while group B did IUS and colonoscopy. Statistical analysis and correlation were done.

Results: In group A (Crohn's cases), there was a positive correlation between BWT and the following: erythrocyte sedimentation rate (ESR), C-reactive protein, fecal calprotectin, and CD activity index as (r) correlation coefficient = 0.55, 0.57, 0.45, and 0.31, respectively, and P-value less than 0.05. In group B (UC cases), a positive relation was noticed between BWT, ESR, C-reactive protein, fecal calprotectin, and Mayo's score activity index as r = 0.55, 0.57, 0.45, and 0.31, respectively, and P-value below 0.05. In total, 24 cases with Crohn's activity were detected by IUS from 30 cases detected by colonoscopy with overall sensitivity of 80%, while in the UC group, 29 cases were detected by IUS from 40 cases by colonoscopy with sensitivity of 73%.

Conclusion: Using IUS by well-trained gastroenterologists is an add-on parameter for diagnosis of IBD activity.

Keywords: Bowel wall thickness, Crohn's disease and ulcerative colitis, Intestinal ultrasound

Introduction

Inflammatory bowel disease (IBD) is considered a chronic inflammatory disease that has two main forms: ulcerative colitis (UC) and Crohn's disease (CD). IBDU (unspecified) is used when a sure diagnosis of CD or UC cannot be made. Over time, most patients with IBDU (unspecified) will be assigned a definitive diagnosis of UC or CD. The etiology of IBD has been extensively studied in the past, but its pathogenesis is still not fully explained. Inflammatory bowel disease poses a significant physical problem and psychological stress on the patients due to the unpredictable course of the disease and the onset in many patients at a young age. A recent systematic review of the literature showed that the prevalence of IBD is increasing over time in different regions of the world, underscoring

the need for more, updated, and robust evidence on the disease.[1]

CD and UC are two inflammatory bowel problems with unknown etiology. The clinical course of both is unpredictable, characterized by alternating times of exacerbation and remission. UC is limited to the large intestine, but CD can affect the entire GIT system, from the mouth to the anus, and patients often present with abdominal pain, fever, and clinical signs of intestinal obstruction or pass diarrhea with blood or mucus or both. For most patients, CD has a great personal burden, with remitting and relapsing symptoms, no work time, the need for costly drugs, or operations and multidisciplinary concern, with an estimated prevalence of 0.1% (0.007–0.27% for CD and 0.008–0.35% for UC) in most of the developed countries. CD also puts a huge burden on public healthcare facilities. CD and UC are chronic diseases and have an important effect on quality of life and personal load through reduction in the ability to work, long-term and short-term interruptions in work, restrictions of comfort time, and out-of-pocket costs (e.g., travel, careers). For all the previous purposes, the indirect expenses of CD and UC are expected to have a significant role in the disease load.[2]

Patients and methods

Patients' selection:- we conducted an observational study in Al-Azhar University Hospitals of previously diagnosed 70 IBD patients divided into group A (30 patients with CD) and group B (40 patients with UC) in addition to positive clinical picture (CD activity index for Crohn's patients and Mayo's score activity index for UC) and laboratory data of activity [hemoglobin (Hb), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and fecal calprotectin]. Group A underwent intestinal ultrasound (IUS), computed tomography enterograpgy (CTE), and colonoscopy, while group B did IUS and colonoscopy during activity. The study protocol is approved by the Local Ethics Committee and written informed consents are obtained. Inclusion criteria: Previously confirmed diagnosis of IBD patients (by biopsy) with manifestations of activity achieving criteria of activity index for CD and UC. Exclusion criteria: Patients with age less than 16 years. Pregnant women, critically ill patients, and obese patients. Hb, ESR, CRP, and fecal calprotectin were withdrawn. Preparation of the patient: The Pt should fast for 8 h, only water was allowed during this period. Sonographic examination: A series of axial and longitudinal scans by using a low-frequency convex (2–5)-MHz probe and high-frequency (7–12)-MHz probe in Philips Clear Vue 350 model from the right flank to the left flank to detect bowel wall thickness (BWT) (Fig. 1) with a cutoff value (3 mm for the small intestine and 4 mm for the large intestine) and complications if present. Statistical analysis was done for laboratory data, BWT, and activity indices for Crohn's and UC patients, and correlations between BWT, previous laboratory data, and activity indices were done.

Ethical approval

An approval was obtained from the Ethical Research Board (ERB) of the Faculty of Medicine, Al-Azhar University, Cairo, Egypt. Before the study proceeding, all patients were assigned informed
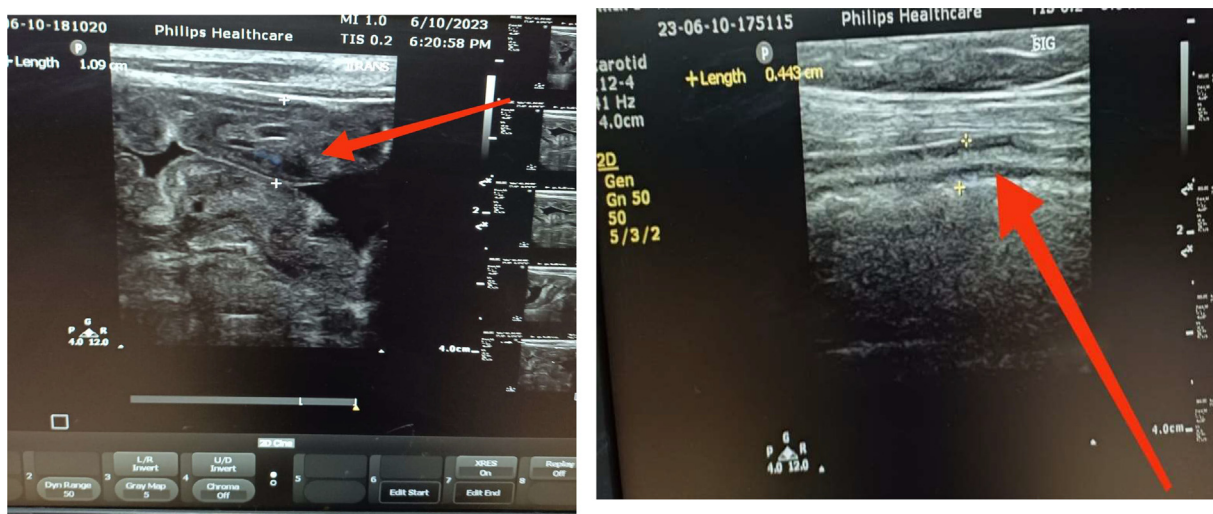

Fig. 1. Shows bowel wall thickness in different parts in the colon: the left picture shows thickness in the transverse colon measures 10.9 mm, while the right image shows thickness in the sigmoid colon measures 4.4 mm, which means the pt is in active disease.

consent after the obvious explanation of the possible adverse events.

Results

In our study, we divided IBD patients into two groups: group A: Crohn's group: 30 patients previously diagnosed as CD with biopsy, came to Al-Azhar University Hospitals from September 2021 to May 2023 with manifestations of activity (Crohn's disease activity index >150). B: Ulcerative group: 40 patients previously diagnosed as UC with biopsy, came to Al Azhar University Hospitals from September 2021 to May 2023 with manifestations of activity (Mayo score activity index for UC ≥ 3). Intestinal ultrasound had been done to all cases. Crohn's cases did CTE and colonoscopy. UC cases underwent colonoscopy. All cases fulfilled Hb, ESR, CRP, and fecal calprotectin. In group A, demographic data revealed that females represent

53% and males 47%. The mean age was 30 yrs (SD ± 11), mean Hb was 10.9 g/dl (SD ± 2.4), ESR ranges from 30 to 90 mm/h, CRP from 22 to 120 mg/L (see Table 1).

Fecal calprotectin from 120 to 618 μg/g with mean 258.9, SD ± 108.8, BWT minimum length was 1.2 mm and maximum was 12 mm (Fig. 2) (mean 5.4, SD ± 1.98), and activity index greater than 153 (mean 243, SD ± 82.9). There was a positive correlation between BWT, ESR, CRP, fecal calprotectin, and activity index as (r (correlation coefficient) = 0.630, 0.12, 0.135, and 0.005, respectively) (Table 2) and P-value less than 0.05 (means these results were statistically significant). But a negative correlation between BWT and Hb was not statistically significant as P-value greater than 0.05.

Colonoscopy detected 28 cases with Crohn's activity in the terminal ileum, 5 of them associated with diffuse scattered colitis, 1 case with transverse colitis, and another in the ascending colon. CTE detected 25 cases with Crohn's activity in the terminal ileum, 4 of them associated with cecal involvement. IUS detected 23 cases with Crohn's activity in the terminal ileum, 3 of them with cercal involvement and diffuse scattered colitis, except the rectum, only 1 case detected by IUS, and one case with transverse colitis as shown in Fig. 3.

On the other hand, group B had the following demographic data as females possessed 45% and males 55%, mean age was 30 yrs. (SD ± 7.5), mean Hb (11.5 g/dl, SD ± 2.1), ESR range (32–90 mm/h), CRP (24–116 mg/L), fecal calprotectin (118–1770 μg/

Table 1. Crohn's cases' statistical data.

Frequency	Minimum	Maximum	Mean ± SD
Age (y)	16	67	30 ± 11.6
Hb (g/dl)	6	15	10.9 ± 2.4
ESR (mm/hr.)	30	90	53.07 ± 18.3
CRP (mg/L)	22	120	47.6 ± 25.6
Calprotectin (μg/g)	120	618	258.9 ± 108.8
Crohn's activity index	153	444	243.6 ± 82.9
Bowel wall thickness (mm)	1.2	12	5.4 ± 1.98

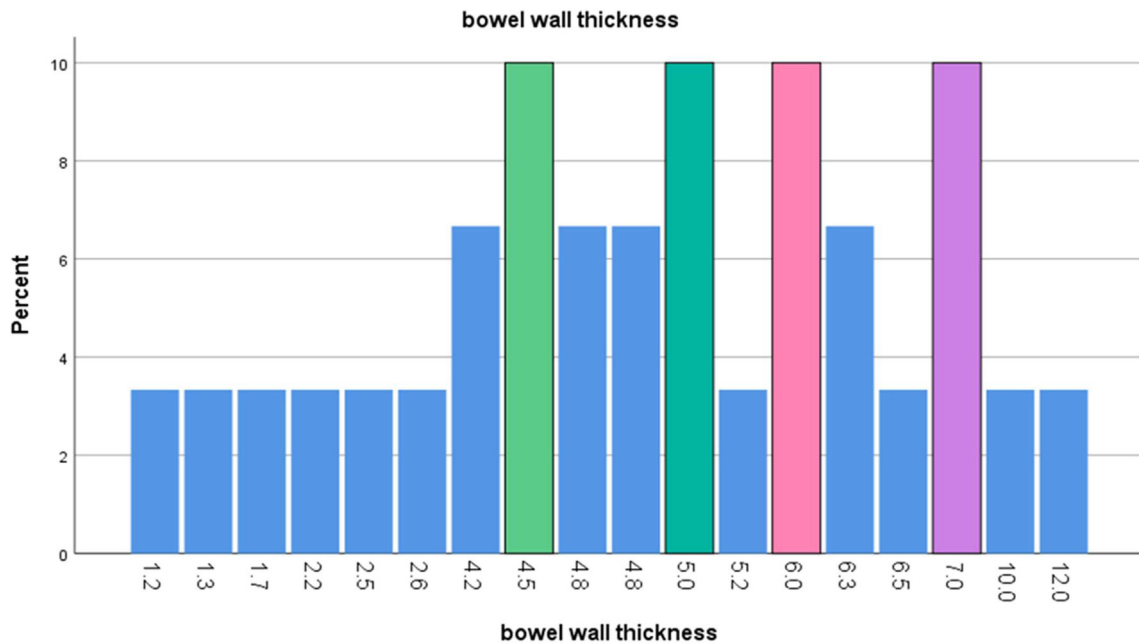ESR, erythrocyte sedimentation rate.

Fig. 2. Bar chart shows bowel wall thickness in Crohn's cases.

Table 2. Correlation in Crohn's cases.

Bowel wall thickness	Hemoglobin	ESR	C-reactive protein	Calprotectin	Activity index	
	−0.350	0.43	0.29	0.35	0.45	Correlation coefficient (r)
	0.058	0.04	0.006	0.004	0.009	P-value

Spearman's Rho correlation, P-value considered statistically significant if below 0.05, (r) value means direct relation if positive and inverse relation if negative.
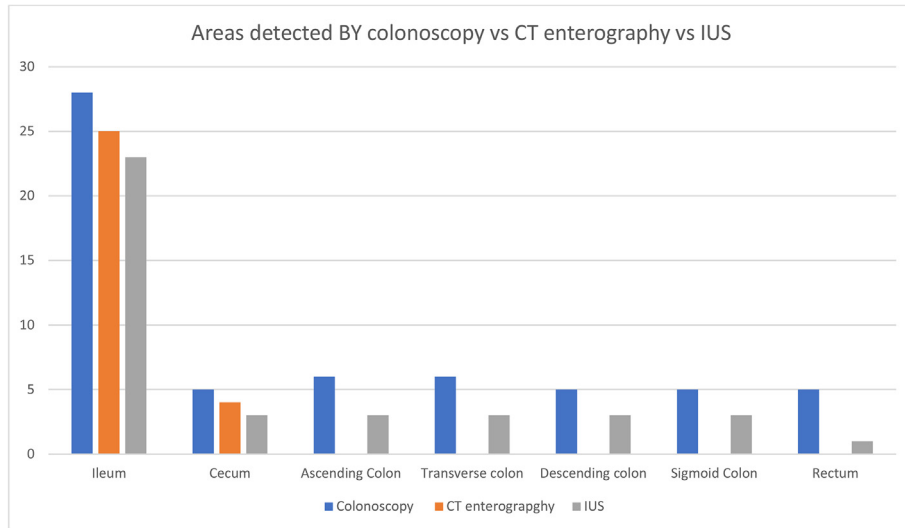ESR, erythrocyte sedimentation rate.

Fig. 3. Bar chart shows areas detected by colonoscopy versus computed tomography enterography versus intestinal ultrasound.

Table 3. Ulcerative colitis group (statistical data).

	Minimum	Maximum	Mean ± SD
Age (y)	18	42	30 ± 7.5
HB (g/dl)	7	14.8	11.5 ± 2.1
ESR (mm/hr.)	32	90	52.6 ± 12.7
CRP (mg/L)	24	116	52.2 ± 21.9
Calprotectin (μg/g)	118	1770	555.55 ± 423.9
Mayo's score for activity	3	9	5.58 ± 1.92
Bowel wall thickness (mm)	1.5	10.2	5.7 ± 1.62

ESR, erythrocyte sedimentation rate.

g) (see Table 3), BWT ranged from 1.5 to 10.2 mm (mean 5.7, SD ± 1.6), and Mayo score for UC (mean 5.58, SD ± 1.92). Positive relation was noticed between BWT, ESR, CRP, fecal calprotectin, and Mayo score activity index as r values = 0.55, 0.57, 0.45, and 0.31, respectively, and P-value below 0.05 (see Table 4), but the relation between BWT and Hb was not statistically significant as P-value was more than 0.05.

Colonoscopy detected 40 cases with rectal affection, 35 of them associated with sigmoid colon affection, 25 cases of them extend to descending colon, 15 cases extend to transverse colon, 6 cases to ascending colon, 5 cases to the cecum, and 2 cases extend to the terminal ileum (5 cases had pancolitis and 2 cases had backwash ileitis), while by IUS, it can detect only 5 cases in the rectum (from 29 cases extending to the sigmoid), 29 cases in the sigmoid colon, 22 cases in descending colon, 15 cases in transverse colon, 5 cases in ascending colon, 5 in the cecum, and only 1 case in the terminal ileum with overall sensitivity 73% as shown in Fig. 4. The

Table 4. Correlations between different parameters in Ulcerative colitis patients.

Bowel wall thickness	Hemoglobin	ESR	C-reactive protein	Calprotectin	Activity index	
	−0.135	0.55	0.57	0.45	0.31	Correlation coefficient
	0.407	0.011	0.002	0.020	0.006	P-value

Spearman's rho correlation P-value was considered significant below 0.05.
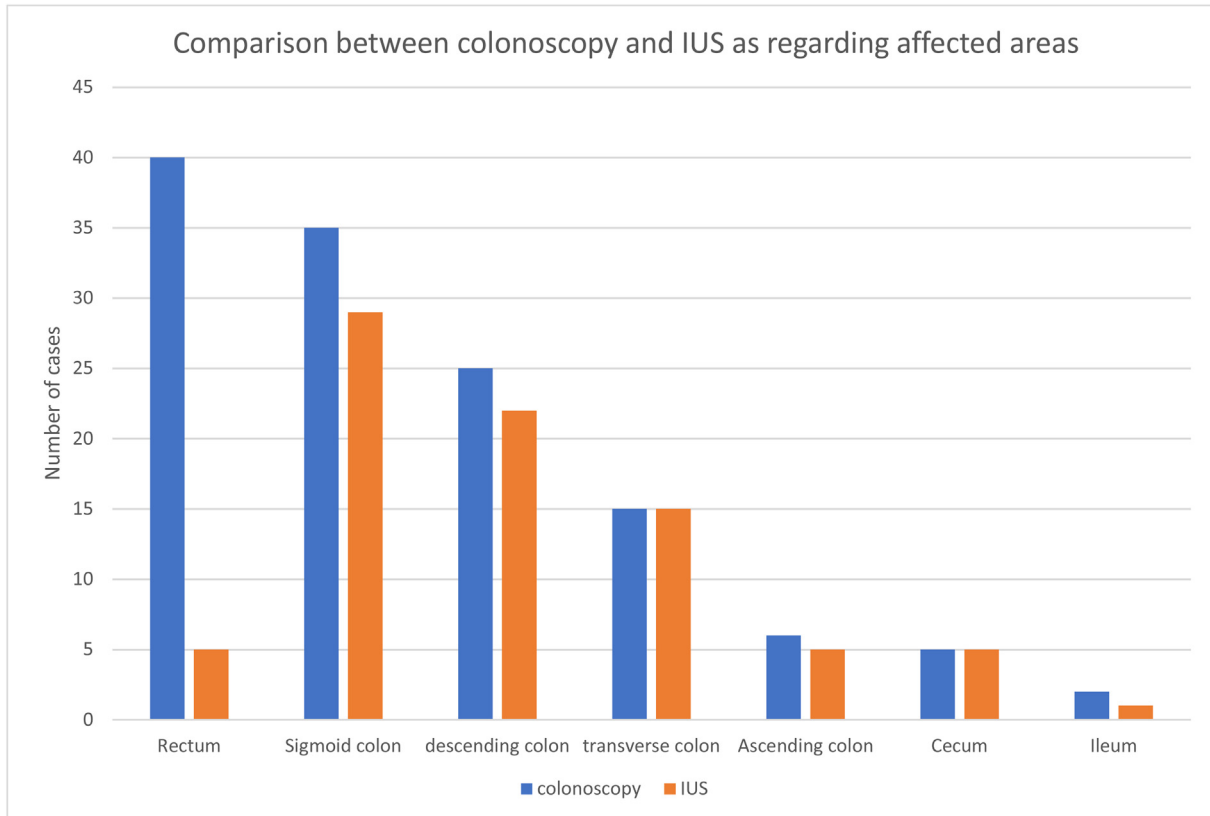ESR, erythrocyte sedimentation rate.

Fig. 4. Areas detected by colonoscopy versus intestinal ultrasound in the Ulcerative colitis group.
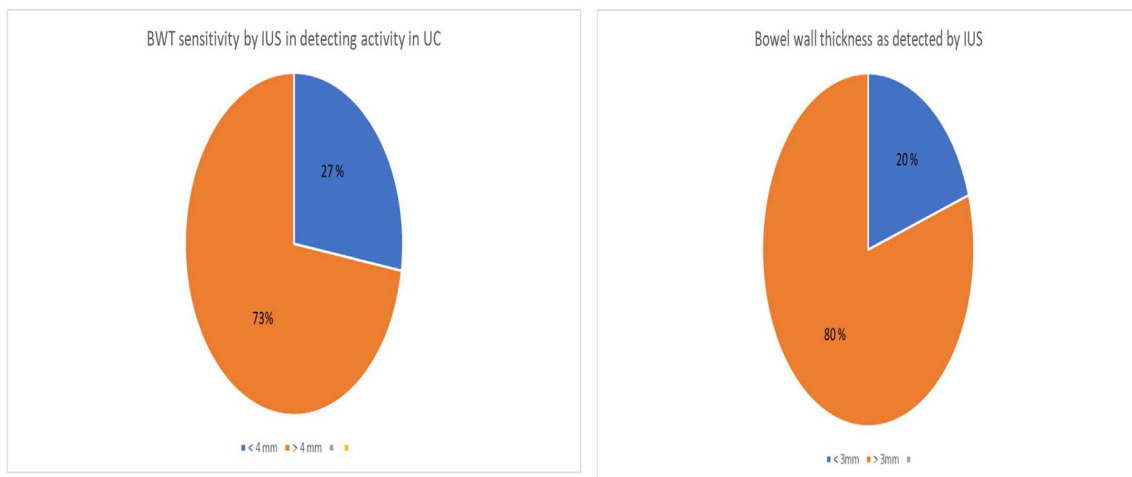

Fig. 5. Shows sensitivity of intestinal ultrasound in Crohn's (left) and Ulcerative colitis (right).

overall sensitivity of IUS in detecting activity of CD and UC is 80% and 73%, respectively, as shown in Fig. 5.

Discussion

There was a positive correlation between BWT and fecal calprotectin and the results are consistent with Dilillo et al.,[3] Iordache et al.,[4] Montero Moretón et al.,[5] Morão, Revés et al.,[6] and Flanagan et al.,[7] as P-values less than 0.05 as the following: Dilillo et al.[3] said that 'the combination of Fecal calprotectin and IUS showed excellent precision in detecting IBD with a positive predictive value: 100%, negative predictive value: 88.5%', Iordache et al.[4] said that 'we observed the existence of correlations between

sonographic parameters, biological markers including fecal calprotectin and scores used to assess disease severity', and Montero Moretón et al.[5] said that 'IUS parameters were significantly associated with fecal calprotectin and CRP levels, particularly with the BWT and fecal calprotectin ($r = 0.35$, $P < 0.05$)', while Morão, Revés et al.[6] and Flanagan et al.[7] said that 'there is correlation BWT and fecal calprotectin as ($r = 0.47, 0.26$, $P = 0.006$, 0.03, respectively)'. A positive correlation between BWT and CD activity index is consistent with Martínez et al.,[8] Kucharzik et al.,[9] and Hoffmann et al.,[10] as P-value less than 0.05, but Morão, Revés et al.[6] considered correlation not significant as the following: Martínez et al.[8] said that 'the wall thickness measured by ultrasound was significantly higher in the group of patients with clinical activity ($P = 0.023$)', Kucharzik et al.[9] said that 'Several studies have shown a good correlation between clinical activity and ultrasound parameters such as BWT, while other studies have not shown this. Although we observed a concomitant reduction in BWT with a decrease in activity score in our study', and Hoffmann et al.[10] said that 'with a decrease in BWT greater than or equal to 1 mm, we observed a significant reduction in CDAI greater than or equal to 70 points in 9/10 patients and a significant reduction in CRP greater than or equal to 0.5 mg/dl in 8/10 patients' but Morão, Revés et al.[6] considered this correlation is not statistically significant, which may be interpreted by children's group in the study and not adults like our study.

The sensitivity of IUS, which was 80%, is nearly consistent with Flanagan et al.,[7] Kucharzik et al.,[9] Bots et al.,[11] Conti et al.,[12] and Martínez et al.,[8] with sensitivities of 74, 79.7, 86, 89, and 91%, respectively. While sensitivity of CTE is consistent with Gale et al.[13] and Bruining et al.,[14] as sensitivity is 84% and 90%, respectively. But the sensitivity of IUS in the rectum (20%) is consistent with Parente et al.,[15] with a sensitivity of 14.2%. IUS detected 4 cases with transmural complications (3 strictures and 1 intestino-intestinal fistula) from 6 cases detected by CTE (4 strictures and 2 intestino-intestinal fistula) with IUS' sensitivity of 67%, which is consistent with Conti et al.,[12] Kucharzik and Maaser[16] Martínez et al.,[8] and Neye et al.,[17] with sensitivities of 80, 74, 80, and 78%, respectively. This difference between IUS and CTE in detecting BWT and complications may be explained by that US is real-time examination and operator-dependent, and the difference between both IUS and CTE and colonoscopy explained by that activity was detected by BWT that depends on transmural affection that may not appear in early activity. In group B, there was positive correlation of BWT, fecal calprotectin, and clinical activity index, which is consistent with Morão et al.,[18] Bots et al.,[19] and Goodsall et al.,[20] as the following: Morão et al.[18] said 'there is positive correlation between BWT, fecal calprotectin and Mayo's score activity index as r values = 0.4 and 0.73 respectively and P values (<0.006 and 0.001 respectively)', Bots et al.[19] said that 'there is strong correlation between IUS, fecal calprotectin and activity index as $r = 0.37$, 0.83 and P value less than 0.001'. Goodsall et al.[20] said that 'there is greatest association between BWT and fecal calprotectin as $r = 0.43$, P value = 0.003 and also with mayo score as $r = 0.31$ and P value = 0.036'. In total, 29 cases have BWT greater than or equal to 4 mm and 11 cases with BWT less than 4 mm with overall sensitivity 73%, which is nearly consistent with Maaser et al.[21] 'as sensitivity is 89.3% in sigmoid colon and 83% in descending colon with overall sensitivity is 86% ', Ilvemark et al.[22] as sensitivity is 84%, Van Wassenaer et al.,[23] 'as sensitivity: 88%, 100%, and 90% in the ascending, transverse, and descending colon, respectively,' and Hudson et al.[24] said 'that sensitivity of IUD in detecting activity is 80%'. IUS' sensitivity in the rectum (12.5%) is consistent with Bor, Fábián, and Szepes[25] who said 'that the sensitivity of IUS is only 15% in rectum'.

From previous data, we can extract the following: first, the sensitivity of IUS versus colonoscopy is 73%, which is explained by that UC is mucosal disease and not transmural, which means BWT that IUS depends on, may be normal in early activity, making it difficult to be detected by IUS, adding to this, UC is mainly rectal disease and trans-abdominal US has lower sensitivity in detecting rectal thickness because the rectum is a deep organ, needs a curved deep low-frequency probe (2–5 HZ) and not a superficial high-frequency probe (7–12 HZ), which makes measuring the delicate, thin wall thickness difficult to be detected. On the other hand, in Crohn's cases, IUS had a higher sensitivity (80%) in detecting cases during activity than UC cases (73%), which may be demonstrated by CD that is transmural, mainly ileal disease, making IUS easier to detect thickness and activity rather than UC that is a mucosal and rectal disease that carries lower sensitivity (12.5%) in detection. Also, the sensitivity of IUS in detecting complications in Crohn's cases is 67% explained by that IUS is operator-dependent, real-time exam extraluminal, and field of imaging during examination is chaotic with the inflammatory environment outside rather than CTE that takes fixed images intraluminal away

from chaotic area extraluminal. In contrast, colonoscopy's potency in detecting Crohn's cases' complications versus IUS and CTE is limited, colonoscopy cannot pass beyond stricture, so no information proximal to stricture can be obtained, making IUS and CTE superior to colonoscopy in Crohn's cases with strictures. Also during fistulization in Crohn's cases, colonoscopy is not allowed to be introduced to the colon for fear of more complications such as perforation, while IUS and CTE can be introduced instead.

Conclusion

Using IUS by well-trained gastroenterologists is an add-on parameter for the diagnosis of IBD activity.

Conflicts of interest

There are no conflicts of interest.

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