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Different imaging techniques' diagnostic efficacy for Crohn's disease activity and external validation and comparison of MDCTAs, SES-CD and IBUSSAS

Xingyun Long[1], Chunyan Peng[2], Xiaoqi Zhang[2], Wentao Kong[1*] and Li Gong[1*]

Abstract

Background Crohn's disease (CD) is a chronic inflammatory disease of the digestive tract with unknown etiology. It follows a relapse-remission pattern, making disease activity assessment crucial for treatment. Our study aims to evaluate the diagnostic accuracy of various imaging modalities and to validate and compare the International Bowel Ultrasound Segmental Activity Score (IBUS-SAS), the multidetector computed tomography enterography score (MDCTEs), and the simplified endoscopic activity score for Crohn's disease (SES-CD).

Methods We assessed diagnostic performance using the CD Activity Index (CDAI). We first categorized patients into remission and active groups. For those in the active stage, we further categorized them into mild/moderate and severe activity groups. We used Spearman rank correlation to evaluate the relationships among IBUS-SAS, bowel wall thickness (BWT), Color Doppler imaging signal (CDS), inflammatory fat (i-fat), bowel wall stratification (BWS), and clinical inflammatory indicators.

Results A total of 103 CD patients were evaluated. The IBUS-SAS cut-off for remission and activity was 23.8, with an AUC of 0.923, sensitivity of 91.4%, and specificity of 84.8%. The SES-CD had an AUC of 0.801, sensitivity of 62.9%, and specificity of 84.4% at a cut-off of 4.5. The MDCTEs showed an AUC of 0.855, sensitivity of 77.1%, and specificity of 75.8% for a cut-off of 6.5. The Delong test revealed significant differences in diagnostic efficacy when comparing IBUS-SAS to SES-CD and IBUS-SAS to MDCTEs. In the group of mild or moderate-to-severe active, the IBUS-SAS had an AUC of 0.925, sensitivity of 83.7%, and specificity of 88.9% at a cut-off of 40. The SES-CD exhibited an AUC of 0.850, sensitivity of 90.7%, and specificity of 70.4% at a cut-off of 8.5. MDCTEs showed an AUC of 0.909, sensitivity of 83.7%, and specificity of 85.2% at a cut-off of 8.5. During Delong test, the IBUS-SAS, MDCTEs, and SES-CD showed no significant differences in assessing moderate-to-severe activity. Both IBUS-SAS and ultrasound parameters correlated with certain serum indicators ($p < 0.05$), although only weakly to moderately (all $r < 0.5$).

*Correspondence:
Wentao Kong
breezewen@163.com
Li Gong
gongli2010@163.com

Full list of author information is available at the end of the article

Conclusion The IBUS-SAS, MDCTEs and SES-CD can evaluate disease remission/active and mild/moderate-to-severe active in CD, and IBUS-SAS offers the potential to precisely define CD activity.

Highlights

- Evaluation of imaging techniques (IBUS-SAS, MDCTEs, and SES-CD) for accurate diagnosis of Crohn's disease (CD) activity.
- Diagnostic accuracy assessed using ROC curves, with Delong test and Spearman correlation analysis for efficacy and relationships.
- IBUS-SAS demonstrates high accuracy, while MDCTEs and SES-CD showed promising performance in assessing CD activity.
- First comparative analysis of IBUS-SAS, MDCTEs, and SES-CD in CD activity diagnosis, providing valuable clinical insights.
- Significance: Guiding selection of optimal imaging techniques for CD treatment decisions, improving early diagnosis and management strategies.

Keywords Crohn's Disease, Ultrasonography, Diagnostic imaging, Computed tomography, Endoscopy

Introduction

Crohn's disease (CD) is an inflammatory bowel disease characterized by chronic inflammation throughout the gastrointestinal tract and a rising global prevalence. CD primarily affects patients younger than 30 years of age, although the incidence among elderly individuals is increasing [1]. The age-standardized prevalence rate of inflammatory bowel disease (IBD) in China is 136.2 per 100,000 people [2], and CD is more prevalent in men within Asian populations [3]. This complex condition demands tailored care focusing on its pathogenic mechanisms. To reduce the severity of issues, future illness care can depend on severity scores that consider prognostic indicators, assessments of intestinal damage, and non-invasive monitoring of disease activity [4–6].

Clinicians must objectively assess disease activity to develop effective treatment strategies and monitor responses. Currently. endoscopy combined with a biopsy is the gold standard for diagnosing CD, and endoscopy can immediately show the degree of mucosal destruction [7–9]. Endoscopy is an invasive method that patients do not always agree to. CD is a transmural disease affecting the entire digestive tract, particularly the terminal ileum and colon. Research indicates that about 18% of CD patients show no findings via ileocolonoscopy alone [10]. Computed tomography enterography (CTE) serves as another important tool for assessing CD activity and complications. as it locates intestinal inflammation and evaluates complications like mesenteric venous occlusion [11, 12]. Yet, CTE poses radiation risks and should be used cautiously. Intestinal ultrasound (IUS) is a highly reliable and reproducible method for assessing the activity of CD lesions [13–15]. It is non-invasive and comfortable for the patient. In the recent European tissue diagnostic guidelines for CD and colitis, IUS was highlighted as a first-line imaging approach for monitoring CD activity [10].

Objective assessment of Crohn's disease activity enhances patient management. To assess disease activity, several scales have been established. The simplified endoscopic activity score for Crohn's disease (SES-CD) assessments of disease activity can be standardized [16]. However, the complexity of these systems hinders clinical application despite their reproducibility [17]. A straightforward, non-invasive alternative examination score is essential. The CD activity index (CDAI) widely assesses the clinical activity of CD in clinics [18, 19], but it requires patient cooperation and complicating implementation. According to the guidelines of the European Crohn's and Colitis Organization and the European Society of Gastrointestinal and Abdominal Radiology, CTE/MRE offers enhanced precision in the imaging modality for diagnosing intestinal lesions associated with CD [10]. However, there is no authoritative study to grade the activity of MDCTE score (MDCTEs) [20–22]. The Magnetic Resonance Index of Activity, while useful for assessing disease activity and therapeutic response. However, this index's calculation can be time-consuming [23]. In 2021, The International Bowel Ultrasound Segmental Activity Score (IBUS-SAS) was developed in order to evaluate disease activity through regression analysis [24]. Currently, IBUS-SAS is a relatively comprehensive IUS score, with a simple algorithm suitable for clinical use. This activity score has not undergone thorough external or clinical validation, and the exact cut-off number for active disease is unknown. No studies have yet directly compared the diagnostic value of IBUS-SAS, MDCTEs, and SES-CD in in assessing CD activity.

Our study aims to explore the application value of various imaging techniques in assessing the clinical active phase of CD and to compare the consistency of the clinically diagnostic efficacy among the three imaging scoring tools: IBUS-SAS, SES-CD, and MDCTEs.

Materials and methods

Patients

This retrospective study enrolled CD patients from the Nanjing Drum Tower Hospital from March 2021 to May 2023. Following were the criteria for inclusion: (1) Patients above the age of 18; (2) Diagnosed with CD; (3) All patients completed CTE, IUS, and either upper endoscopy, ileocolonoscopy, or both; and (4) All patients also underwent serological and fecal calprotectin (FC) tests; (4) No more than two weeks passed between the completion of each of these exams. The following were the exclusion criteria: (1) Previous colectomy; (2) Age < 18; (3) Pregnancy; (4) Digestive tract perforation or tumor; (5) Severe obesity hampering IUS evaluation; and (6) Other concurrent infections. It is excluded if any of these requirements were satisfied. We collected fecal calprotectin, and serum indicators such as white blood cells (WBC), platelets (PLT), hemoglobin (Hb), erythrocyte sedimentation rate (ESR), total bilirubin (TBIL), direct bilirubin (DBIL), creatinine (CR), and c-reactive protein (CRP). CDAI is the main index of clinical activity of disease, with 150 or more indicating active disease, 150 to 220 indicating mild activity, and 220 or more moderate-severe activity [25].

Endoscopy assessment

(1) Intestinal preparation: Check the previous night's low-residue diet. No food was taken on the day of examination, and 2000–2500 ml 2.5% low osmotic mannitol was taken orally. (2) Examination: All ileocolonoscopies were performed with the patient under heavy or light sedation, and the endoscopist had experience with IBD. (3) Image Analysis: Two senior gastroendoscopists diagnosed the endoscopic images, and the endoscopists were blinded to the imaging examination. The SES-CD evaluates four endoscopic variables (ulcer size, ulcerated surface, affected surface, and stenosis) in five segments of the bowel (rectum, left colon, transverse colon, right colon, and terminal ileum). The severity of each parameter yields a value between 0 and 3, and by summing the scores, segmental- and total endoscopic activity can be quantified [26, 27]. Each segment of the SES-CD ranges from 0 to 12, with a total range of 0 to 60. Remission is defined as a SES-CD of less than 2, mild activity as 3 to 6, and moderate to severe activity as over 7 [28].

CTE assessment

(1) Intestinal preparation: Do not consume food eight hours before the examination, before scanning, take 200 milliliters of a 2.5% mannitol solution at 30-minute intervals. (2) Examination: After the intravenous injection of contrast media (Visipaque), the dose was 1.5 mL/kg. The patient was scanned using a 64-slice spiral CT scanner (UNITED IMAGING, UCT 780). Multiplanar reformation and maximum intensity projection were performed. The slice thickness was 5 mm, and the layer spacing was 1.5 mm. (3) Image analysis: The images were independently diagnosed by two experienced imaging diagnosticians of digestive diseases, who were blinded to other imaging examinations. Image evaluation primarily included mucosal hyper-enhancement, which was graded from 0 to 2 (0: Normal; 1: Single-segment enhancement; 2: Multiple segmental bowel enhancement), wall thickening, which was graded from 1 to 4 (1:3–4 mm;2: 4–5 mm;3:5–6 mm;4:>6 mm), The degree of mesenteric vascular augmentation was graded from 0 to 2 (0: Normal; 1: Single intestinal segment comb sign; 2: Multiple segmental appears comb sign), and mesenteric fat density was graded from 0 to 2 (0: Normal; 1: Single intestinal segment turbidity; 2:Multiple segmental turbidity). The MDCTES total score is 13. Remission is defined as a MDCTEs of less than 3, mild activity as 4 to 6, and moderate to severe activity as over 7 [21].

IUS assessment

(1) Intestinal preparation: Patients fasted for 8 h before the examination and required no special intestinal preparation. (2) Examination: The patient laid in a supine position, with full exposure of the abdomen. All abdominal IUS examinations used a GE LOGIQTM E20 machine (GE Healthcare, USA). Standard examinations included obtaining axial and longitudinal images of the entire bowel, and using a 1–5 MHz convex probe and a 5–12 MHz linear transducer, following its scanning sequence from the terminal ileum further distally to the rectum. Regular scanning covered the entire small intestine as well as the colon, while recording the relevant parameters. These parameters included the bowel wall thickness (BWT), the bowel wall stratification (BWS), the color Doppler imaging signal (CDS), and the inflammatory fat (i-fat). (3) Image analysis: All examinations were performed by two ultrasound doctors with CD diagnostic experience. Both ultrasound doctors were informed of the diagnosis of CD in advance, but were unaware of the endoscopic and CTE diagnoses. Four variables composed the IBUS-SAS: BWT, BWS, CDS, and i-fat. BWT was defined as the average thickness of the intestinal wall of the same segment measured three times at 1 cm intervals. The CDS was graded from 0 to 3 (0: no signal; 1: solitary small signals/pixels in the viscera; 2: the signal length in the intestinal wall is long without signals outside the intestinal wall; and 3: long signals inside and outside the intestinal wall). i-fat was graded from 0 to 2 (0 for absence, 1 for indeterminate, and 2 for presence). BWS was graded on a scale from 0 to 3 (0: absence; 1: indeterminant; 2: disruption of wall layers ≤ 3 cm; disruption of wall layers ≥ 3 cm). The following formula was used [24]: IBUS-SAS = 4* BWT + 15*i-fat + 7*CDS + 4*BWS.

Intestinal segment assessment

We focused our analysis on the most affected intestinal segment for each patient, as determined by the initial clinical assessment and imaging findings. This segment was consistently applied across IBUS-SAS, SES-CD, and MDCTEs evaluations to ensure a direct comparison of disease activity. The scoring for each patient was based on this specific segment, reflecting the peak inflammation and providing a clear measure of disease severity.

Statistical analysis

IBM SPSS Statistics 27.0.1 and RStudio 2023.03.0-386 were used for statistical analysis. Demographic data were analyzed using descriptive statistics. Quantitative data is displayed as the mean standard deviation or median values (interquartile ratio), whilst categorical data is shown as absolute (n) and relative (%) frequencies. The study utilized the chi-square test or Fisher's exact test to compare the population characteristic homogeneity across different groups. IBUS-SAS, MDCTEs, and SES-CD diagnostic accuracy was determined using sensitivity, specificity. Furthermore, receiver operating characteristic curve (ROC) analysis was performed to compare the diagnostic capabilities of various imaging examinations, and the area under the receiver operating characteristic curve (AUC) was computed. Using the Delong test, the diagnostic efficacy of the three scores ROC curves in pairs was compared. Spearman correlation analysis determined the correlation between IBUS-SAS-related parameters and clinical indexes. All tests for statistical significance were bilateral, with $p<0.05$.

Results

Study population

In total, 126 patients diagnosed with CD who had the potential to be eligible for the study participated. However, twelve patients were excluded because an admission CDAI assessment was not performed. Seven patients were excluded because they did not undergo endoscopy or CTE within 2 weeks of ultrasound. And four patients with a history of ileocolectomy were excluded. Eventually, 103 patients were enrolled in the study (Fig. 1). There were 64 males (62.2%) and 39 females (37.8%), with the median age of 32.0 (interquartile range [IQR] 26–42) years. The CD group's median disease duration was 24 (IQR: 12–55) months, and the median BMI was at 19.9 (IQR: 18.1–22.0) kg/m2. According to the Montreal classification determined by endoscopy, the terminal ileum disease (L1) affected 12 (11.6%) patients, the colonic disease (L2) affected 16 (15.5%), the ileocolonic disease (L3) affected 70 (67.9%), and the upper disease (L4) affected 5 (4.8%) patients. Classified by age at diagnosis (Montreal classification), we enrolled 76 (73.7%) patients aged 17–40 (A2) years and 27 (26.3%) patients ≥ 40 (A3) years. Based on the disease behavior (Montreal classification), 39 (37.8%) patients were non-stricuring and non-penetrating (B1), 50 (48.5%) were stricturing (B2), and only 14 (13.5%) were penetrating (B3). The analysis revealed no notable differences between the groups ($P>0.05$). In our study, the ileocecal was the most affected segment in 47 patients (45.6%). Additionally, 35 patients (34.0%) showed severe disease activity at the distal ileum. The ascending colon affected 10 patients (9.7%), the transverse colon 3 patients (2.9%), and the descending colon 8 patients (7.8%). Table 1 contains more detailed demographic and clinical data.

Comparison of the diagnostic performance of IBUS-SAS, SES-CD and MDCTEs for disease activity

In evaluating CD activity, all three imaging scores demonstrated effectiveness. For the cut-off value of 23.8, the IBUS-SAS obtained an AUC of 0.923, with a sensitivity of 91.4% and a specificity of 84.8%, along with 95% CI of 0.860–0.986. At a cut-off value of 4.5, the SES-CD revealed an AUC of 0.801, with a sensitivity of 62.9% and a specificity of 84.8%, and 95% CI of 0.715–0.887. For the cut-off value of 6.5, the MDCTEs had an AUC of 0.855, with sensitivity at 77.1% and specificity at 75.8%, along with a 95% CI of 0.781–0.930 (Table 2). Figure 2 displays representative imaging. The Delong test revealed significant differences in diagnostic efficacy when comparing IBUS-SAS to SES-CD ($z=3.244$, $p=0.001$) and IBUS-SAS to MDCTEs ($z=2.180$, $P=0.029$), with IBUS-SAS had the highest diagnostic value (Table 3).

Comparison of the diagnostic performance of IBUS-SAS, SES-CD and MDCTEs for disease moderate-to-severe activity

To assess moderate-to-severe disease activity, three imaging scores performed effectively. For the cut-off value of 40, the IBUS-SAS obtained an AUC of 0.925, with a sensitivity of 83.7% and specificity of 88.9%, along with a 95% CI of 0.864–0.985. For the cut-off value of 8.5, the SES-CD revealed an AUC of 0.850, with a sensitivity of 90.7% and specificity of 70.4%, as well as a 95% CI of 0.746–0.954. At the same cut-off value of 8.5, the MDCTEs showed an AUC of 0.909, with a sensitivity of 83.7% and a specificity of 85.2%, and the 95% CI of 0.838–0.980 (Table 4). There was no significant difference among IBUS-SAS, SES-CD, and MDCTEs regarding the diagnostic accuracy of moderate-to-severe disease activity (Table 5).

Spearman correlation analysis of IBUS SAS, SES-CD, MDCTEs, and four ultrasound parameters with CDAI, FC, and serum indicators

IBUS-SAS, SES-CD, and MDCTEs had significant positive correlations with CDAI ($r=0.874$, $r=0.677$, and

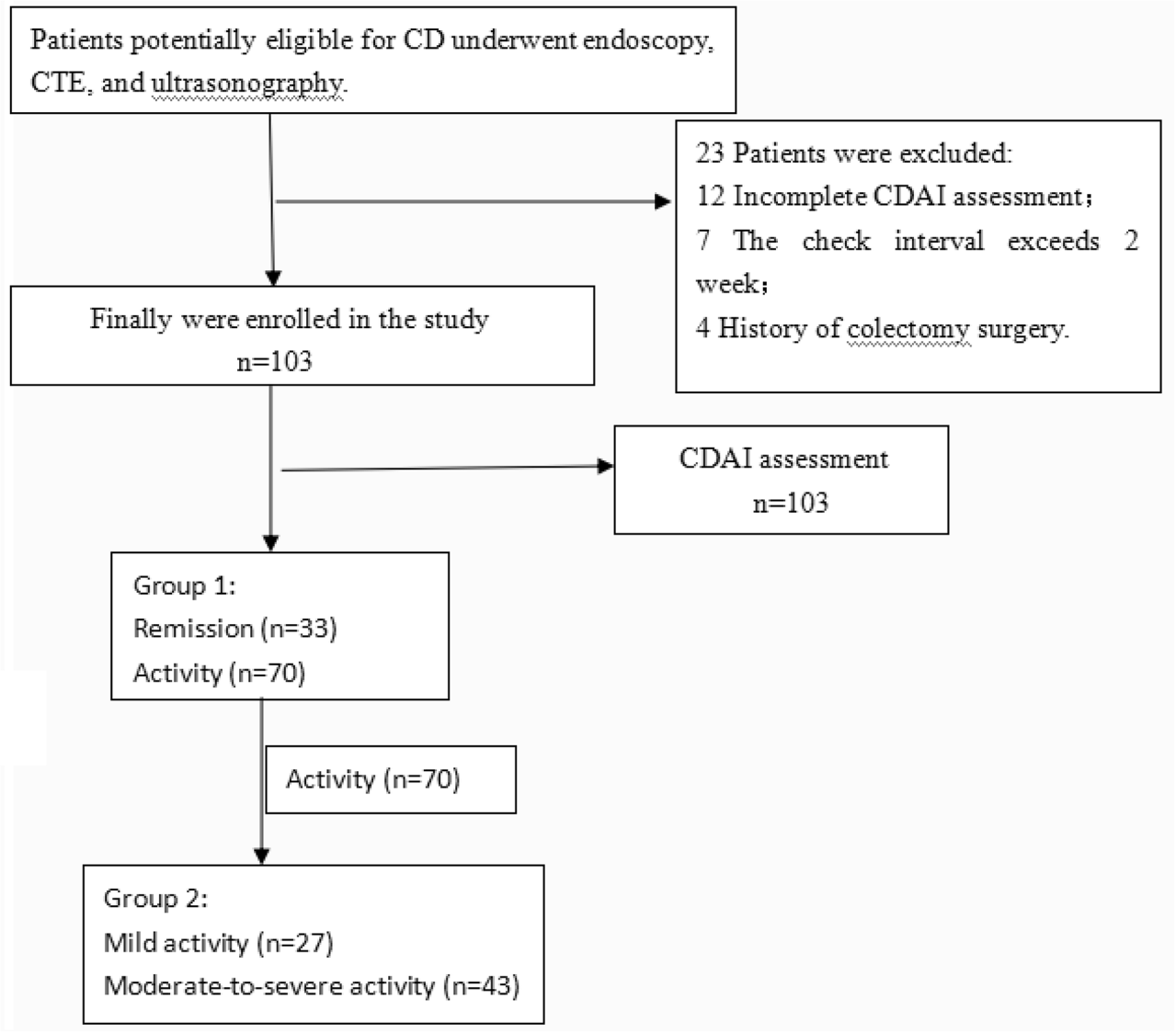

Fig. 1 Study analysis patient inclusion flowchart

r=0.762, respectively). IBUS-SAS, SES-CD, MDCTEs, and four ultrasound parameters showed a weak positive Spearman linear correlation with certain serum indicators, such as CRP, ESR, etc. while Hb exhibited a negative correlation. Additional data is available in Table 6.

Discussion

Crohn disease, a chronic gastrointestinal inflammatory disease. The disease's feature is its relapse-remission-relapse pattern. Long-term effects of uncontrolled inflammation include fibrotic strictures, enteric fistulae, and intestinal neoplasia. Consequently, it is crucial to assess disease activity and control inflammation quickly and efficiently [29]. CDAI is a common clinical activity index, but it requires patient cooperation and is difficult to evaluate continuously. SES-CD is the most reliable indicator of CD activity. Due to the invasive nature of endoscopy and related risks, such procedures may not be suitable for all patients, particularly those with coagulopathies or on anticoagulant therapy, and can be limited by patient tolerance and the presence of strictures or other anatomical challenges. IBUS-SAS is a recent inflammatory bowel disease score, which had a sufficient sample size, relied on competent expert opinion, and used quantitative and semi-quantitative criteria during its development phase [24]. IBUS-SAS aims to simplify the evaluation process. After gathering essential data, physicians can finalize the score rapidly. This system reduces the burden on doctors and improves the overall efficiency of diagnostics and treatment. However, IBUS-SAS lacked external validation for other valid and objective CD activities. There is considerable controversy between

Table 1 Patients' demographic characteristics

Study population	All (*N* = 103)
Sex	
Male, n (%)	64 (62.2)
Female, n (%)	39 (37.8)
Body mass index (kg/m^2), median (IQR)	19.9 (18.1–22.0)
Age (years), median (IQR)	32 (26–42)
Disease duration(months), median (IQR)	24 (12–55)
Age at diagnosis (years), (Montreal classification), n (%)	
≤ 16 (A1)	0 (0.0)
17–40 (A2)	76 (73.7)
≥ 40 (A3)	27 (26.3)
Disease location, (Montreal classification), n (%)	
Terminal ileum (L1)	12 (11.6)
Colonic (L2)	16 (15.5)
Ileo-colonic (L3)	70 (67.9)
Upper disease (L4)	5 (4.8)
Disease phenotype, (Montreal classification), n (%)	
Non-stricturing, non-penetrating (B1)	39 (37.8)
Stricturing (B2)	50 (48.5)
Penetrating (B3)	14 (13.5)
SES-CD, mean ± SD	11.9 ± 9.6
MDCTEs, mean ± SD	7.5 ± 3.1
IBUS-SAS, mean ± SD	37.5 ± 21,7
CDAI, mean ± SD	233.1 ± 128.3
Assessments, median (IQR)	
FC (ug/g)	426.8 (100.7–1000.0)
CRP (mg/L)	3.8 (2.0-13.7)
ESR (mm)	13.0 (4.0–21.0)
Hb (g/L)	121.0 (103.0-138.0)
PLT (10^9 /L)	254.0 (204.0-317.0)
WBC (10^9 /L)	5.4 (4.5-7.0)
TBIL (umol/L)	7.4 (6.0-10.9)
DBIL (umol/L)	1.7 (1.1–2.2)
CR (umol/L)	61.0 (48.0–69.0)
Intestinal segment assessment, n (%)	
Distal ileum	35 (34.0)
Ileocecum	47 (45.6)
Ascending colon	10 (9.7)
Transverse colon	3 (2.9)
Descending colon	8 (7.8)

IQR indicates interquartile range, SD standard deviation, SES-CD: the simplified endoscopic activity score for Crohn's disease; MDCTEs: multidetector computed tomography enterography score; IBUS-SAS: International Bowel Ultrasound Segmental Activity Score; CDAI: CD activity index; FC: fecal calprotectin; CRP: c-reactive protein; ESR: erythrocyte sedimentation rate; Hb: hemoglobin; PLT: platelets; WBC: white blood cells; TBIL: total bilirubin; DBIL: direct bilirubin; CR: creatinine

MDCTES and IBUS-SAS in assessing the accuracy of CD activity.

Our research investigates the practical utility of different imaging modalities in evaluating the clinically active phase of CD. We also compare the diagnostic consistency among three imaging scoring systems: IBUS-SAS, SES-CD, and MDCTEs. In this study, we examined whether the IBUS-SAS, SES-CD, and MDCTEs can be regarded as accurate and dependable scoring systems for the diagnosis of active or moderate-to-severe active disease. Our studies conclusively showed that the IBUS-SAS, SES-CD, and MDCTEs could quantify the CD disease activity or moderate-to-severe activity. For assessing disease activity, one study [30] reported IBUS-SAS ROC curves demonstrating the highest accuracy (89.0%), with an AUC of 0.95 (95% CI 0.87–0.99), 82.2% sensitivity, and 100% specificity at a cut-off of 25.2. An IBUS-SAS threshold of 34.0 accurately identified mild-severe endoscopic activity, achieving 100% sensitivity and 84.3% specificity (AUC of 0.96, 95% CI 0.89–0.99). Our study found an AUC of 0.923, with an optimal cut-off value of 23.8 for predicting active disease in proving the IBUS-SAS, and revealed an AUC of 0.925, with an optimal cut-off value of 40.0 for predicting moderate-to-severe endoscopic activity disease. These results suggest similar results to previous studies. Another study [28] showed a cut-off of 2 for endoscopic activity and 7 for moderate-to-severe activity. In contrast, our study showed that the SES-CD's disease activity AUC is 0.801, with a cut-off value of 4.5, and revealed that the SES-CD's AUC for assessing disease moderate-to-severe activity is 0.850, with a cut-off value of 8.5, both of which are higher than the previous study. In the study by Hu J et al. [21], the cutoff for detecting CTE activity was defined as 3, and the cut-off for detecting moderate-to-severe CTE activity was defined as 7. In our study, the MDCTE's AUC for disease activity is 0.855, with a cut-off value of 6.5, and that the SES-CD's AUC for assessing moderate-to-severe disease activity is 0.909, with a cut-off value of 8.5, both of which are more than the previous study. In our study, the patient cohort was comprised exclusively of individuals who had been hospitalized, a factor that could account for the observed discrepancies in disease activity when compared to the existing literature. Specifically, within our sample of 103 patients, 33 were identified as being in remission, while 43 out of the remaining 70 exhibited moderate-to-severe disease activity. This skewed distribution, with a lower proportion of patients in remission and a higher proportion presenting with significant disease activity, may have introduced a selection bias that influenced the assessment of diagnostic accuracy. The impact of this selection bias is further compounded by the methodological approach to determining the predictive cut-off values for SES-CD and MDCTEs, which were predicated on the CDAI. Given that CDAI is known to have certain limitations, particularly in its sensitivity to changes in patients with stricturing or penetrating disease behaviors, our reliance on this index may have skewed the cut-off values upwards. This could have led to an overestimation of

Table 2 Diagnostic performance of IBUS-SAS, SES-CD and MDCTEs in disease activity detection against the CDAI (gold standard)

	AUC	95%CI	Sensitivity (%)	Specificity (%)	Cut-off	*P*
IBUS-SAS	0.923	0.860–0.986	91.4	84.8	23.8	0.000
SES-CD	0.801	0.715–0.887	62.9	84.8	4.5	0.000
MDCTEs	0.855	0.781–0.930	77.1	75.8	6.5	0.000

AUCs: area under receiver operating characteristic curves; CI indicates confidence interval; SES-CD: the simplified endoscopic activity score for Crohn's disease; MDCTEs: multidetector computed tomography enterography score; IBUS-SAS: International Bowel Ultrasound Segmental Activity Score; CDAI: CD activity index

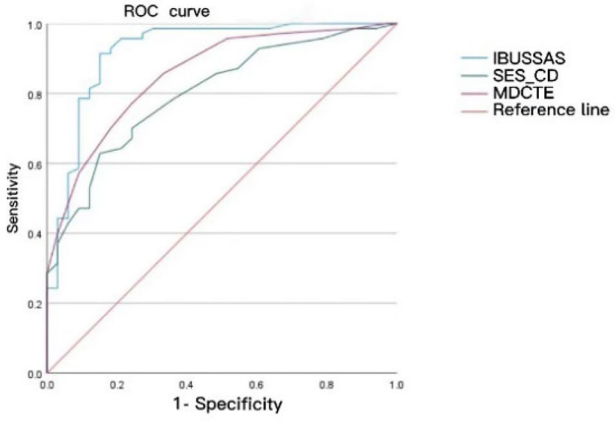

Fig. 2 The ROC curves of the IBUS-SAS, SES-CD and MDCTEs for the diagnosis of active disease in CD patients. SES-CD: the simplified endoscopic activity score for Crohn's disease; MDCTEs: multidetector computed tomography enterography score; IBUS-SAS: International Bowel Ultrasound Segmental Activity Score

Table 3 Comparing the diagnostic disease activity efficacy of the DeLong test for three scoring systems ROC curves in pairings

	z	*P*
IBUS-SAS vs. SES-CD	3.244	0.001
IBUS-SAS vs. MDCTEs	2.180	0.029
SES-CDvs MDCTEs	1.382	0.167

SES-CD: the simplified endoscopic activity score for Crohn's disease; MDCTEs: multidetector computed tomography enterography score; IBUS-SAS: International Bowel Ultrasound Segmental Activity Score

disease severity in our cohort, thereby affecting the overall diagnostic performance metrics.

In addition, in group 1, the diagnostic potential of the IBUS-SAS was significantly superior to that of the SES-CD and MDCTEs (AUC 0.923, 0.801, 0.855, respectively), with IBUS-SAS had the highest diagnostic value for assessing disease activity. The Delong test revealed

Table 5 Comparing the diagnostic disease moderate-to-severe activity efficacy of the Delong test for three scoring systems ROC curves in pairings

	z	*P*
IBUS-SAS vs. SES-CD	1.334	0.182
IBUS-SAS vs. MDCTEs	0.540	0.589
SES-CD vs. MDCTEs	1.125	0.260

SES-CD: the simplified endoscopic activity score for Crohn's disease; MDCTEs: multidetector computed tomography enterography score; IBUS-SAS: International Bowel Ultrasound Segmental Activity Score

significant differences in diagnostic efficacy when comparing IBUS-SAS to SES-CD and IBUS-SAS to MDCTEs. In group 2, the diagnostic potential of the IBUS-SAS was significantly superior to that of the SES-CD and MDCTEs (AUC 0.925, 0.850, 0.909, respectively), with IBUS-SAS had the highest diagnostic value for assessing disease moderate-to-severe activity, but without a significant difference. In both groups of studies, the diagnostic potential of the SES-CD, which is often used as a standard, was inferior to that of IBUS-SAS or MDCTES. Due to the fact that CD is a transmural disease. Endoscopy is able to assess the degree of mucosal remission in the intestinal cavity, it cannot accurately evaluate the improvement of the entire intestinal wall. Conversely, IBUS-SAS, with its capacity to probe deeper intestinal layers, offers a distinct advantage in detecting submucosal and transmural inflammation. This capability is instrumental in elucidating the discrepancies observed in the diagnostic performance of SES-CD versus IBUS-SAS. The ultrasound's penetration beyond the mucosal surface allows for a more comprehensive assessment of the disease's impact on the intestinal wall, thereby providing a more accurate representation of the inflammatory burden. Furthermore, complications such as luminal fibrous stenosis in CD patients can impede endoscopic detection

Table 4 Diagnostic performance of IBUS-SAS, SES-CD and MDCTEs in disease moderate-to-severe activity detection against the CDAI (gold standard)

	AUC	95%CI	Sensitivity (%)	Specificity (%)	Cut-off	*P*
IBUS-SAS	0.925	0.864–0.985	83.7	88.9	40.0	0.000
SES-CD	0.850	0.746–0.954	90.7	70.4	8.5	0.000
MDCTEs	0.909	0.838–0.980	83.7	85.2	8.5	0.000

AUCs: area under receiver operating characteristic curves; CI indicates confidence interval; SES-CD: the simplified endoscopic activity score for Crohn's disease; MDCTEs: multidetector computed tomography enterography score; IBUS-SAS: International Bowel Ultrasound Segmental Activity Score; CDAI: CD activity index

Table 6 Spearman correlation analysis of IBUS SAS, SES-CD, MDCTEs, and four ultrasound parameters with CDAI, FC, and serum indicators

	BWT		CDS		i-fat		BWS		IBUS_SAS		SES-CD		MECTEs	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
WBC	0.038	0.701	0.105	0.289	-0.082	0.413	0.027	0.784	0.020	0.845	0.036	0.722	-0.010	0.920
PLT	0.167	0.091	0.228	0.021	0.172	0.082	0.158	0.111	0.220	0.026	0.211	0.032	0.150	0.129
Hb	-0.142	0.153	-0.231	0.019	-0.315	0.001	-0.142	0.154	-0.258	0.009	-0.218	0.027	-0.293	0.003
ESR	0.324	<0.001	0.451	<0.001	0.318	0.001	0.253	0.010	0.409	<0.001	0.376	<0.001	0.337	<0.001
TBIL	-0.188	0.057	-0.151	0.129	-0.208	0.035	-0.140	0.159	-0.206	0.036	-0.179	0.070	-0.212	0.031
DBIL	-0.145	0.143	-0.241	0.014	-0.191	0.054	-0.142	0.153	-0.225	0.022	-0.284	0.004	-0.313	0.001
CR	-0.094	0.346	-0.065	0.517	-0.098	0.324	-0.085	0.392	-0.098	0.325	-0.022	0.822	-0.083	0.403
CRP	0.333	<0.001	0.396	<0.001	0.325	<0.001	0.179	0.071	0.393	<0.001	0.385	<0.001	0.356	<0.001
FC	0.318	0.001	0.350	<0.001	0.252	0.011	0.196	0.049	0.331	<0.001	0.259	0.009	0.389	<0.001
CDAI	0.840	<0.001	0.750	<0.001	0.637	<0.001	0.460	<0.001	0.874	<0.001	0.677	<0.001	0.762	<0.001

SES-CD: the simplified endoscopic activity score for Crohn's disease; MDCTEs: multidetector computed tomography enterography score; IBUS-SAS: International Bowel Ultrasound Segmental Activity Score; CDAI: CD activity index. FC: fecal calprotectin; CRP: c-reactive protein; ESR: erythrocyte sedimentation rate; Hb: hemoglobin; PLT: platelets; WBC: white blood cells; TBIL: total bilirubin; DBIL: direct bilirubin; CR: creatinine

Fig. 3 IUS, CTE, and endoscopic results in a representative Crohn's disease patient. A 22-year-old male was diagnosed as A2L3B2 according to the Montreal classification. **a**: IUS shows thickening and loss of stratifcation of the terminal ileal wall; **b**: Color Doppler imaging reveals that the terminal ileum has full blood flow signals with a score of 3; **c**: CTE reveals multiple diffuse intestinal wall thickening with comb-like features; **d**: Colonoscopy finds extensive ileocecal mucosal ulceration and typical lithoid hyperplasia

of lesions. The stenosis may obstruct the passage of the endoscope, precluding a thorough examination of the affected areas. IBUS-SAS will play an essential role in the continuous detection of CD disease activity in the future. In addition, similar to the previous report [28, 31–33], the IUS scores revealed a strong correlation with the CDAI. In this study, IBUS-SAS, SES-CD, and MDCTEs showed significant positive correlations with CDAI (r=0.874, r=0.677, and r=0.762, respectively). This suggests that IBUS-SAS has a greater ability to predict treatment efficacy before a patient's clinical symptoms resolve. Specifically, the high correlation between IBUS-SAS and CDAI scores indicates a close relationship between the ultrasound assessment of intestinal wall inflammation and the clinical manifestations of CD as measured by CDAI. This strong association implies that changes in IBUS-SAS scores may reflect changes in disease activity, thereby providing a sensitive indicator of the patient's response to treatment. Figure 3 was a representative case of Crohn's disease in which IUS, CTE, and endoscopic findings are well consistent with the clinical.

At the present, we are the first study to compare the accuracy of three scores (IBUS-SAS, SES-CD and MDCTES) for the diagnosis of CD activity and moderate-to-severe activity. Meanwhile, our study is an independent external validation of the IBUS-SAS to predict Chinese CD patients. As understanding of its evaluative value grows, it may become a key indicator for assessing "transmural healing." Thus, it aims to improve disease activity assessment and treatment monitoring in

clinical settings. However, our study had some limitations. First, the populations mainly enrolled in hospitalized patients with obvious clinical symptoms. Thus, there were few samples in clinical remission. To reduce selection bias, it is essential to expand the number and resource of samples. Second, the primary objective of this study was to investigate the utility of various imaging techniques in assessing the clinical activity of CD and to compare the consistency of clinical diagnostic efficacy among three imaging scoring tools. In this study, the CDAI was employed as the basis for patient stratification. However, the complexity of the CDAI scoring system, its reliance on patient cooperation, and the significant individual variability among patients may all compromise the objectivity of CDAI. Therefore, we plan to adopt more objective scoring criteria in future research. For instance, endoscopic scoring systems will be considered, which are expected to minimize the interference of subjective patient factors and enhance the accuracy and reproducibility of the assessments. Finally, we deeply recognize the shortcomings of this study in exploring complications associated with CD, such as intestinal fistulas and stenosis. In future research, we will employ a variety of imaging methods to more comprehensively assess these complications, with the aim of providing more precise diagnostic and therapeutic bases for clinical practice.

Conclusion

In conclusion, our analysis confirms that the IBUS-SAS, MDCTEs and SUS-CD can evaluate disease active and moderate-to-severe active in CD, and IBUS-SAS has the most potential to precisely define CD activity. Meanwhile, our research indicates that the optimal cut-off value for diagnosing activity with IBUS-SAS is 23.8, while the optimal cut-off value for diagnosing moderate-to-severe activity is 40.0. CRP and ESR are positively correlated with IUS parameters and three score systems, and the correlation between IBUS-SAS and CRP or ESR was also slightly higher than the other two scores. IBUS-SAS presents significant potential for use in assessing disease activity. It merits additional investigation and implementation in upcoming clinical practices and research endeavors.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Conceptualization, X.Y.L., X.Q.Z., and C.Y.P.; Methodology and Data curation, X.Y.L., L.G.; Investigation. X.Q.Z. and C.Y.P.; Writing- Original draft preparation, X.Y.L.; Writing- Reviewing and Editing, W.T.K.; All authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Drum Tower Hospital affiliated to Nanjing University School of Medicine (approval number: 2023-342-01). Patients were consented by an informed consent process that was reviewed by the Ethics Committee of Nanjing Drum Tower Hospital and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinkl. Written informed consent has been obtained from the patients, and their anonymous information will be published in this article.

Consent for publication
All authors and hospitals agreed to publish this article. Informed consent for publication of images were obtained from all participants.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Ultrasonography, Nanjing Drum Tower Hospital, Drum Tower Clinical Medical College, Nanjing Medical University, Nanjing 21009, China
[2]Department of Gastroenterology, Nanjing Drum Tower Hospital, Nanjing 21009, China

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