

# Can simplified endoscopic score for Crohn's disease be simpler? --Development and Validation of the Multimodal Activity Score for Crohn's Disease (MAS-CD)

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## Research Article

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# Abstract

## Background

Endoscopy is central to diagnosing and monitoring Crohn's disease (CD), but current endoscopic scoring systems such as the Simplified Endoscopic Score for Crohn's Disease (SES-CD) are complex, time-consuming, and limited when ileocolonoscopy is incomplete. Approximately 30–40% of CD patients cannot undergo full examinations, hindering comprehensive assessment. With mucosal healing now a key therapeutic target, there is an urgent need for a simpler, multimodal, and clinically practical scoring tool.

## Objectives

To develop and prospectively validate a novel comprehensive assessment tool—the Multimodal Activity Score for Crohn's Disease (MAS-CD)—that combines endoscopic and, when necessary, radiological parameters.

## Design:

Multicenter development and prospective validation study.

## Methods

Four parameters—ulcer size, ulcerated surface area, affected surface area, and stenosis severity—were scored on a 0–3 scale. For incomplete ileocolonoscopies, contrast-enhanced CT enterography (CTE) with optional magnetic resonance enterography (MRE) or intestinal ultrasound (IUS) were incorporated. Inter-rater reproducibility was assessed in 157 patients, and MAS-CD was developed using multivariable regression. Validation was conducted in an independent cohort of 91 patients. Correlations with SES-CD, Harvey-Bradshaw Index (HBI), serum C-reactive protein (CRP), albumin, and fecal calprotectin were analyzed.

## Results

Interobserver agreement for MAS-CD parameters was substantial (Kappa 0.508–0.722; ICC = 0.888). MAS-CD strongly correlated with SES-CD ( $r = 0.816$ ,  $p < 0.001$ ) and showed significant associations with CRP ( $r = 0.28$ ), HBI ( $r = 0.285$ ), albumin ( $r = -0.208$ ), and fecal calprotectin ( $r = 0.218$ ) (all  $p < 0.05$ ). MAS-CD differentiated remission from active disease, small bowel-from colonic-dominant phenotypes, and predicted treatment response more effectively than SES-CD (AUC 0.61 vs. 0.21,  $p < 0.05$ ).

# Conclusion

MAS-CD is a simplified, flexible, and reproducible multimodal scoring system that overcomes the limitations of incomplete endoscopic assessment. By integrating imaging data, it provides a clinically actionable tool for comprehensive disease activity monitoring and treat-to-target strategies in the biologic era.

## Key Message

### What is already known?

Existing endoscopic scores (SES-CD/CDEIS) for Crohn's disease require segmental summation, are time-consuming, and fail to assess non-accessible bowel segments in 30–40% of patients.

### What is new here?

The novel Multimodal Activity Score (MAS-CD) integrates endoscopic parameters with radiological data (CTE/MRE/IUS) for pan-enteric evaluation, simplifying scoring by eliminating segmental summation while maintaining high reproducibility (ICC=0.888).

### How can this study help patient care?

MAS-CD provides a clinically actionable tool to monitor disease activity in incomplete endoscopy scenarios, enabling individualized treatment decisions aligned with mucosal healing targets.

## Introduction

Endoscopic examination plays a crucial role in the diagnosis, assessment, and management of inflammatory bowel diseases (IBD), including Crohn's disease. A standardized endoscopic scoring system for IBD ensures consistent, reproducible, and uniform reporting, making it an essential tool in both clinical practice and research.

However, grading the severity and extent of Crohn's disease-related inflammatory lesions observed during colonoscopy remains challenging. The Crohn's Disease Endoscopic Index of Severity (CDEIS), developed and validated by the French Groupe GEAID, was one of the first endoscopic scoring systems introduced for this purpose[1]. CDEIS evaluates four parameters—deep ulcers, superficial ulcers, the percentage of affected surface area, and the percentage of ulcerated surface area—across five gastrointestinal segments (terminal ileum, right colon, transverse colon, left colon, including sigmoid, and rectum). The segmental scores are averaged and combined with the presence or absence of strictures, yielding a total score ranging from 0 to 44. However, CDEIS lacks a clear definition of mucosal healing and is complex to calculate, which has limited its practical utility.

In 2004, a European research group proposed a simplified alternative, the Simplified Endoscopic Activity Score for Crohn's Disease (SES-CD)[2]. SES-CD retains the four parameters from CDEIS—ulcer size (0: none, 1: 0–0.5 cm, 2: 0.5–2 cm, 3: >2 cm), proportion of ulcerated surface (0: none, 1: 0–10%, 2: 10–30%, 3: >30%), proportion of affected surface (0: none, 1: 0–50%, 2: 50–75%, 3: >75%), and severity of stenosis (0: none, 1: single, passable, 2: multiple, passable, 3: impassable)—but simplifies the scoring process. The bowel is divided into five segments: ileum, right colon (including the ileocecal valve, cecum, and ascending colon up to the hepatic flexure), transverse colon, left colon (descending colon to the splenic flexure and sigmoid colon), and rectum. The total score, ranging from 0 to 56, is derived by summing the scores for all parameters across the five segments, offering a more user-friendly and widely applicable scoring system.

The updated Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE-II) consensus defines endoscopic response as a > 50% reduction in the Crohn's Disease Endoscopic Index of Severity (CDEIS), with endoscopic remission being defined as a CDEIS total score of < 3[3]. The CDEIS has been widely used in research and serves as a clinical trial endpoint. The STRIDE-II consensus also defines endoscopic response as a > 50% reduction in the Simplified Endoscopic Activity Score for Crohn's Disease (SES-CD), while endoscopic remission is characterized by a SES-CD score of  $\leq 2$  and the absence of ulcers, including aphthous ulcers[3]. Although the SES-CD score reduces the calculation complexity compared to the CDEIS, it remains potentially complex and time-consuming in practice. Moreover, the SES-CD does not account for bowel segments that cannot be visualized endoscopically or those that have been surgically removed. In cases where all segments show mild disease activity, the summed score could be higher than for a single segment with severe lesions, potentially influencing disease severity assessment and subsequent treatment decisions. Therefore, this study aims to develop and validate a new, simpler, and faster endoscopic scoring system for Crohn's disease, the New Endoscopic Activity Score for Crohn's Disease (MAS-CD). The characteristics of MAS-CD were compared with those of the SES-CD.

Crucially, the chronic relapsing nature of Crohn's disease necessitates repeated endoscopic evaluations, yet practical limitations persist. Approximately 30%-40% of patients fail to complete full small bowel and colonic examinations during ileocolonoscopy, and contraindications to repeated endoscopy further restrict its application. To address these challenges, this study aims to develop a novel multimodal scoring system—the Multimodal Activity Score for Crohn's Disease (MAS-CD)—which prioritizes endoscopic parameters but integrates complementary radiological modalities (e.g., computed tomography enterography, magnetic resonance enterography, or intestinal ultrasound) when endoscopic evaluation is incomplete or contraindicated. This approach ensures a comprehensive assessment of disease activity, particularly in scenarios where mucosal healing—now a central therapeutic target in the era of biologics—requires precise longitudinal monitoring. MAS-CD's flexibility in combining endoscopic and imaging data not only enhances clinical utility but also improves reproducibility, offering a robust tool for both routine practice and therapeutic decision-making.

## Patients and Methods

This study was conducted in four phases (Fig. 1). In the first phase, the most relevant variables were selected, and their reproducibility was evaluated through an inter-observer variability study. In the second phase, the development phase, multimodal parameters were derived from the selected variables and further simplified to obtain a score (the MAS-CD) that was still strongly correlated to the SES-CD but was simpler and easier to calculate. In the third phase, MAS-CD was prospectively validated using an independent cohort of patients. In the fourth phase, the reliability of both MAS-CD and SES-CD was assessed using the full patient cohort, and their performance was compared with relevant clinical and biochemical parameters.

## Patients and Examinations

In the development phase of the study, multimodal evaluations (including colonoscopies and cross-sectional imaging) were performed across three medical centers on 66 patients diagnosed with Crohn's disease between 2003 and 2022. For the validation phase, an additional 91 patients with Crohn's disease were prospectively recruited from the same three centers between 2022 and 2024, forming a multicenter validation cohort. In both phases, IBD-specialized endoscopists (all at attending physician level or higher with over 1,000 colonoscopy procedures performed) completed **multimodal assessment sheets** immediately after colonoscopies. These sheets integrated endoscopic findings with complementary imaging data (CT enterography, intestinal ultrasound, or magnetic resonance enterography) to generate the **Multimodal Activity Score for Crohn's Disease (MAS-CD)**. A second IBD-specialized endoscopist (similarly qualified with equivalent experience), observing the procedures via a video monitor, independently completed the assessment sheets without any communication with the primary endoscopist. A total of 157 paired evaluations were analyzed to assess the reproducibility of the **multimodal parameters**. During each evaluation, comprehensive data were collected, including information on current and previous treatments, age at diagnosis, disease duration, disease behavior and location, history and type of surgical interventions, smoking habits, family history, body mass index (BMI), and Harvey-Bradshaw Index (HBI) [4]. Additionally, biochemical parameters such as serum C-reactive protein (CRP), fecal calprotectin, and albumin levels were measured.

## Inclusion Criteria

Patients were eligible if they:

Had a confirmed diagnosis of Crohn's disease according to ECCO criteria;

Were aged < 75 years;

Underwent colonoscopy for disease monitoring or symptom evaluation.

## Exclusion Criteria

- Patients were excluded if they:
- Had a history of other inflammatory bowel diseases (e.g., ulcerative colitis);
  - Were pregnant or lactating;
  - Had a history of malignancy or immunodeficiency disorders.

## Data Collection and Variables

The MAS-CD evaluated four variables: ulcers, the proportion of surface area covered by ulcers, the proportion of surface area affected by other lesions, and strictures. Each variable was scored from 0 to 3 for each segment (Table 1). Ulcers were graded by size (diameter 0.1–0.5 cm, 0.5–2 cm, or > 2 cm) (Fig. 2). The proportion of surface area covered by ulcers was categorized by extent (< 10%, 10%–30%, or > 30%). Similarly, the proportion of surface area affected by other lesions was scored based on the extent (< 50%, 50%–75%, or > 75%)[5]. Strictures were scored according to whether the colonoscope could pass through the narrowed lumen[6] (Fig. 2).

For patients with incomplete ileocolonoscopy (e.g., failed visualization of the terminal ileum or proximal small bowel), complementary radiological parameters were integrated into the MAS-CD assessment. These included CT enterography (CTE) metrics, or magnetic resonance enterography (MRE)/intestinal ultrasound (IUS) findings. This multimodal approach ensured that variables like ulcer burden and stricture severity were comprehensively evaluated even when endoscopic data were incomplete, aligning with the chronic relapsing nature of Crohn’s disease and the practical challenges of serial endoscopic monitoring.

Table 1  
MAS-CD scoring form.

|                                                                                                                                                                                                                                                                                                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>MAS-CD=presence and size of ulcers + extent of ulcerated surface + extent of affected surface+ presence and type of narrowings</b>                                                                                                                                                                                        |
| presence and size of ulcers (0: none, 1: 0–0.5 cm, 2: 0.5–2 cm, 3: >2 cm), extent of ulcerated surface (0: none, 1: 0–10%, 2: 10–30%, 3: >30%), extent of affected surface (0: none, 1: 0–50%, 2: 50–75%, 3: >75%), and presence and type of narrowings (0: none, 1: single, passable, 2: multiple, passable, 3: impassable) |
| MAS-CD, Multimodal Activity Score for Crohn's Disease;                                                                                                                                                                                                                                                                       |

## Construction of MAS-CD Scores and statistical methods

**Interobserver variation study (157 patients).** Agreement between observers was analyzed using kappa statistics. Kappa values range from negative (indicating disagreement) to + 1 (indicating perfect agreement), with 0 indicating agreement equivalent to pure chance. Agreement was categorized as poor (< 0.40), moderate (0.41–0.60), good (0.61–0.80), or very good (> 0.80)[7]. The reproducibility of the

scores, including the SES-CD and the MAS-CD, was further evaluated using intraclass correlation coefficients (ICC)[8].

**Development of MAS-CD (66 Patients)** The development of the MAS-CD involved applying multiple linear regression to data from the development phase. The SES-CD was used as the dependent variable, while the sums of the different endoscopic variables across all explored segments, the number of affected segments, and the number of explored segments served as independent variables. For the 66 colonoscopies performed by an endoscopist-observer pair, data from one of the two investigators were randomly selected. All potential scores derived from different combinations of the selected endoscopic variables were then evaluated. The final scoring system was chosen to strike a balance between ease of calculation and strong correlations with both the SES-CD and the HBI.

**Validation of MAS-CD (91 Patients)** The validation of MAS-CD involved evaluating its correlation with SES-CD. This was conducted using Pearson's product-moment correlation coefficient and Spearman's rank correlation coefficient to ensure robust statistical analysis during the validation phase.

**Scoring Characteristics in the Entire Dataset (157 Patients)** Differences in clinical characteristics between patients in the development and validation phases were analyzed using chi-square tests, Fisher's exact test, Student's t-test, or the Mann-Whitney U test, as appropriate. The correlations between MAS-CD or SES-CD scores and clinical features, including the HBI and biochemical markers of disease activity (CRP, fecal calprotectin, and albumin), were evaluated using Spearman's rank correlation coefficient. Data analyses were conducted using statistical software (SPSS for Mac, version 29.0, SPSS Inc., Chicago, Ill.). A p-value < 0.05 was considered statistically significant, and 95% confidence intervals were reported for key estimates. All participants provided informed consent for inclusion in the study, which was approved by the Ethics Committee of the University of Science and Technology of China (USTC).

## Results

### Patient characteristics

The clinical characteristics of the patients are summarized in Table 2, categorized by the development phase, validation cohort, and the entire study sample. No significant differences in clinical characteristics were identified between patients in the two study phases.

Table 2  
Clinical characteristics of 157 patients enrolled in study

| Variable                                       | Development        | Validation         | Total series       |
|------------------------------------------------|--------------------|--------------------|--------------------|
| No. patients                                   | 66                 | 91                 | 157                |
| Location(colon/ileocolon/small bowel/upper GI) | 2/4/48/12          | 2/9/72/8           | 4/13/120/20        |
| Behavior (B1/B2/B3)                            | 32/13/21           | 44/24/23           | 76/37/44           |
| Age at diagnosis (A1/A2/A3)                    | 5/53/8             | 7/70/14            | 12/123/22          |
| Gender (female/male)                           | 15/51              | 21/70              | 36/121             |
| Duration of disease, y median (range)          | 5(2–21)            | 5(3–22)            | 5(2–25)            |
| BMI, kg/m <sup>2</sup> median (range)          | 20.77(15.47–30.64) | 21.46(15.18–31.67) | 21.26(15.18–31.67) |
| Prior surgery (no/yes)                         | 47/19              | 63/28              | 110/47             |
| Smoking habits (no/ex/active smoker)           | 58/8/0             | 96/13/0            | 144/20/0           |
| HBI median (range)                             | 1(0–9)             | 2(0–7)             | 1(0–9)             |
| CRP, mg/L median (range)                       | 3.64(0.2-66.69)    | 3.64(0-104)        | 3.64(0-104)        |
| Remission (no/yes)                             | 4/62               | 9/82               | 13/144             |

BMI, Body mass index; HBI, Harvey-Bradshaw Index; CRP, C-reactive protein.

## Parameter Selection and Reproducibility levels

The variables included in MAS-CD reflect the most clinically relevant and reproducible lesion characteristics associated with Crohn's disease[9]. Scoring by the endoscopist/observer demonstrated consistent results across all segments for all variables included in MAS-CD (Table 3). While the consistency of the relevant lesion characteristics in MAS-CD was slightly lower compared to SES-CD, the intraclass correlation coefficients (ICCs) for both scoring systems met the established consistency criteria.

Table 3

Results of interobserver variation study: kappa value and intraclass correlation coefficient for comparison between endoscopist and observers cores for New Crohn's disease endoscopic activity score and Simple Endoscopic Score for Crohn's Disease endoscopic variables in each ileocolonic segment are given (n = 157 patients)

| MAS-CD                      | kappa value |             |                  |            |        |
|-----------------------------|-------------|-------------|------------------|------------|--------|
| Ulcers                      | 0.704       |             |                  |            |        |
| Ulcerated surface           | 0.722       |             |                  |            |        |
| Affected surface            | 0.508       |             |                  |            |        |
| Stenosis                    | 0.644       |             |                  |            |        |
| SES-CD                      | Ileum       | Right colon | Transverse colon | Left colon | Rectum |
| Ulcers                      | 0.910       | 0.839       | 0.921            | 0.816      | 0.798  |
| Ulcerated surface           | 0.816       | 0.887       | 0.921            | 0.861      | 0.825  |
| Affected surface            | 0.860       | 0.867       | 0.857            | 0.880      | 0.914  |
| Stenosis                    | 0.877       | 0.930       | 1                | 1          | 1      |
|                             | ICC         |             | 95% CI           |            |        |
| Sum of all MAS-CD variables | 0.888       |             | 0.849 ~ 0.918    |            |        |
| Sum of all SES-CD variables | 0.976       |             | 0.966 ~ 0.983    |            |        |

MAS-CD, Multimodal Activity Score for Crohn's Disease; SES-CD, Simple Endoscopic Score for Crohn's Disease; ICC, intraclass correlation coefficient; CI, confidence interval.

## MAS-CD development phase

In 66 colonoscopies conducted on patients, a total of 314 ileocolonic segments were examined by, with an average of 4.8 segments explored per procedure. Of the 16 segments that were not examined, 5 had been surgically resected, 10 could not be accessed due to strictures, and 1 was inaccessible due to technical issues. In 57 of the 66 colonoscopies, the terminal or new terminal ileum was explored. Rectal involvement in Crohn's disease was observed in 38% (25/66) of cases. A multiple regression analysis using SES-CD as the dependent variable yielded highly significant results ( $p < 0.0001$ ), with a strong correlation coefficient of 0.686. During the model simplification process, the optimal formula was derived: the sum of four variables multiplied by 1.217, plus the number of affected segments multiplied by 2.617, minus 2.009. However, the simple sum of the four variables demonstrated a similar correlation with both SES-CD and the HBI (Table 4) and was much easier to compute. Consequently, the MAS-CD was defined as follows: MAS-CD = sum over all explored segments (ulcer size score + ulcer surface

score + total affected surface score + stricture score). The total score for each endoscopic variable ranged from 0 to 15, except for strictures, which ranged from 0 to 11, as a score of 3 indicated a stricture that prevented colonoscope passage, thus allowing only a single observation. The MAS-CD score is depicted in Table 1. MAS-CD values can be converted to SES-CD values using the following formula: SES-CD = 0.401 × MAS-CD + 1.045.

Table 4

Characteristics of different endoscopic scores elaborated and tested: coefficient of multiple linear regression, multiple correlation R and the Spearman rank correlation coefficients to Simple Endoscopic Score for Crohn's Disease and Harvey-Bradshaw Index are reported

| Coefficients of endoscopic variables | Without number of explored segments | Without number of explored and affected segments | MAS-CD complex | MAS-CD | MAS-CD simplified |
|--------------------------------------|-------------------------------------|--------------------------------------------------|----------------|--------|-------------------|
| Ulcers                               | 2.226                               | 1.522                                            | 1.217          | 0.401  | 2.005             |
| Narrowings                           | -0.36                               | -1.498                                           | 1.217          | 0.401  | 2.005             |
| Affected surface                     | 1.814                               | 4.485                                            | 1.217          | 0.401  | 2.005             |
| Ulcerated surface                    | 0.131                               | 1.058                                            | 1.217          | 0.401  | 2.005             |
| Number of affected segments          | 2.446                               | -                                                | 2.617          | -      | -                 |
| Multiple correlation R               | 0.686                               | 0.522                                            | 0.67           | 0.433  | 0.433             |
| Spearman's correlation with:         |                                     |                                                  |                |        |                   |
| SES-CD                               | 0.95                                | 0.813                                            | 0.946          | 0.816  | 0.816             |
| HBI                                  | 0.092                               | 0.179                                            | 0.1            | 0.219  | 0.221             |

MAS-CD, Multimodal Activity Score for Crohn's Disease; SES-CD, Simple Endoscopic Score for Crohn's Disease; HBI, Harvey-Bradshaw Index;

## MAS-CD validation phase

During the validation phase, 437 ileocolonic segments were examined across 91 procedures, with an average of 4.8 segments per colonoscopy. 11 segments had been surgically resected, 3 could not be accessed due to strictures, and 4 were inaccessible due to technical issues. Of the 91 procedures, 83 involved examination of the terminal or neoterminal ileum. Rectal involvement in Crohn's disease was observed in 32% (29/91) of cases. The Pearson and Spearman rank correlation coefficients between SES-CD and MAS-CD were 0.658 (95% CI [0.465, 0.791],  $p < 0.001$ ) and 0.816 (95% CI [0.692, 0.894],  $p < 0.001$ ), respectively.

# MAS-CD characteristics

When all 157 paired scores were considered, the intraclass correlation coefficient (ICC) between the scores of the first and second observers for MAS-CD was 0.888, while for SES-CD, the ICC was 0.976 (Table 3). The scatter plot of MAS-CD versus SES-CD for the complete dataset of 157 patients, including data from both the development and validation phases, is presented in Fig. 3a. Bland-Altman analysis (Fig. 3b) revealed 95.5% of data points falling within the agreement limits, indicating acceptable inter-rater variability. The correlations between SES-CD or MAS-CD and several key clinical parameters are summarized in Table 5. MAS-CD demonstrated significant correlations with C-reactive protein (CRP) (0.28), the Harvey-Bradshaw Index (HBI) (0.285), serum albumin (-0.208), and fecal calprotectin (0.218).

Table 5  
Correlation between two scoring systems (Simple Endoscopic Score for Crohn's Disease [SES-CD] and Multimodal Activity Score for Crohn's Disease [MAS-CD]) and clinical variables in complete series of patients (n = 157 patients)

|                    | MAS-CD       |        | SES-CD       |        |
|--------------------|--------------|--------|--------------|--------|
|                    | Spearman's r | p      | Spearman's r | p      |
| CRP                | 0.28         | < .001 | 0.385        | < .001 |
| HBI                | 0.285        | < .001 | 0.123        | 0.169  |
| Albumin            | -0.208       | 0.01   | -0.237       | 0.008  |
| Fecal Calprotectin | 0.218        | 0.03   | 0.239        | 0.037  |
| BMI                | -0.055       | 0.503  | 0.037        | 0.682  |
| Disease duration   | 0.102        | 0.211  | 0.022        | 0.802  |

MAS-CD, Multimodal Activity Score for Crohn's Disease; SES-CD, Simple Endoscopic Score for Crohn's Disease; HBI, Harvey-Bradshaw Index; BMI, Body mass index; CRP, C-reactive protein.

The clinical utility of MAS-CD across diverse disease scenarios is comprehensively demonstrated in Fig. 4. Pretreatment MAS-CD scores decreased significantly following therapy, confirming its responsiveness to treatment (Fig. 4a). MAS-CD effectively differentiated active disease states(HBI > 4)from remission [HBI ≤ 4] (Fig. 4b). Phenotype-specific analysis revealed higher scores in small bowel-dominant disease compared to colonic dominant (Fig. 4c). The violin plot with interquartile ranges further illustrated distinct MAS-CD distributions between surgical and non-surgical cohorts (Fig. 4d). Collectively, these data validate MAS-CD as a multidimensional tool for therapeutic monitoring, disease stratification, and phenotype-specific assessment in Crohn's disease.

(a) Pretreatment vs. post-treatment MAS-CD scores. (b) Significant differentiation between remission and active disease states. (c) Phenotype-specific responses, showing lower MAS-CD in colonic-dominant versus small bowel-dominant disease. (d) Violin plot with boxplot overlays comparing

treatment arms, demonstrating reduced MAS-CD in surgical versus non-surgical cohorts. (\*p < 0.05, \*\*p < 0.01, \*p < 0.001).

ROC analysis was performed to evaluate the predictive capacity of MAS-CD and SES-CD for surgical versus non-surgical treatment endpoints (Fig. 5). MAS-CD achieved an AUC of 0.61 (95% CI 0.51–0.70), significantly outperforming SES-CD (AUC 0.21 95% CI 0.13–0.27). These results position MAS-CD as a simplified yet non-inferior alternative to SES-CD for predicting clinically meaningful endpoints in Crohn's disease management.

(a) ROC curve for SES-CD, showing an AUC of 0.21 (95% CI 0.13–0.27). (b) ROC curve for MAS-CD with an AUC of 0.61 (95% CI 0.51–0.70).

## Discussion

With the increasing use of biologics in the treatment of Crohn's disease (CD), therapeutic goals have evolved significantly. Initially, the primary focus was on achieving clinical symptom improvement and remission in the early stages of treatment [10–13]. However, clinical symptom remission alone does not reliably predict endoscopic improvement, and relying solely on symptom improvement as a therapeutic goal may lead to undertreatment [14–16]. In recent years, endoscopic mucosal healing has emerged as a primary therapeutic goal and endpoint, complementing clinical and biological treatment efficacy [17–20]. Furthermore, higher therapeutic targets, such as transmural healing and histological remission, have garnered increasing attention and are now being incorporated as endpoints in phase III clinical trials [21]. Accumulating evidence suggests that achieving higher therapeutic targets is significantly associated with better long-term outcomes, with mucosal healing playing a crucial role in altering the disease course of CD. Colonoscopy remains an essential tool for monitoring post-treatment mucosal healing [22]. The CDEIS and the SES-CD are commonly utilized to quantify mucosal ulceration and inflammation observed during colonoscopy. Both indices have demonstrated reliability and reproducibility in assessing intraluminal inflammatory activity [23]. However, the CDEIS scoring system is intricate and poses challenges for routine clinical application. While the SES-CD was developed as a simplified alternative to CDEIS, its scoring process involves summing data from five intestinal segments, each with four parameters, which remains somewhat cumbersome and limits its practicality in clinical settings [24]. Further high-quality studies are needed to validate the use of SES-CD and related scoring tools as reliable indices for assessing mucosal healing.

The MAS-CD score was developed to address the clinical need for a reliable and user-friendly scoring system for Crohn's disease, with reduced complexity compared to SES-CD. As with SES-CD, any new scoring system must demonstrate reproducibility and strong correlation with clinical parameters. By employing classical methods during its development and validation phases, MAS-CD was established as a rapid and dependable scoring system. Consistency testing revealed high inter-observer agreement for the MAS-CD score. Our data reveal that the MAS-CD exhibits a stronger correlation with the simplified CDAI-HBI, compared to the SES-CD. This finding highlights the potential for the MAS-CD to offer greater

clinical utility[25]. The MAS-CD retains the four parameters used in SES-CD but simplifies the assessment by eliminating the division of the colon into five segments. Instead, the entire bowel, encompassing both the colon and small intestine, is assessed as a unified entity. This modification provides a more intuitive representation of Crohn's disease. Although it is slightly less precise than the SES-CD score, the MAS-CD score offers significant value due to its simplified calculation process and its potential for broader clinical application in the future. Furthermore,

Our initial objective was to develop a simplified and clinically more practical endoscopic scoring system based on the SES-CD. However, during the development process, clinical realities revealed two critical insights: First, a substantial proportion of Crohn's disease (CD) patients do not undergo complete pan-enteric endoscopy at every initial diagnosis or follow-up evaluation. Instead, non-invasive imaging modalities such as contrast-enhanced CT enterography, magnetic resonance enterography (MRE), or intestinal ultrasound (IUS) have emerged as primary adjuncts to endoscopy for disease monitoring. Second, CD is a pan-enteric inflammatory disorder; isolated colonic endoscopic assessment and scoring fail to capture the full disease spectrum. To address the pan-enteric nature of CD, we established the MAS-CD, which integrates endoscopic findings with cross-sectional imaging parameters to comprehensively evaluate disease severity. Our study demonstrates that MAS-CD offers three key advantages over SES-CD: 1. Reproducibility: Despite slightly lower interobserver agreement than SES-CD, MAS-CD maintains robust reliability (Kappa range: 0.508–0.722; intraclass correlation coefficient [ICC] > 0.8). 2. Enhanced Clinical Correlation: MAS-CD exhibits stronger associations with clinical parameters. In our cohort, MAS-CD showed significant correlations not only with CRP ( $r = 0.28, p < 0.05$ ), serum albumin ( $r = -0.208, p < 0.05$ ), and fecal calprotectin ( $r = 0.218, p = 0.03$ ) but also with the HBI ( $p < 0.05$ ). Furthermore, MAS-CD effectively discriminates between disease remission and active states, pre- and post-treatment status, and surgical indications. Notably, it reliably differentiates colonic-dominant from small bowel-dominant CD phenotypes, reflecting its multidimensional capacity to capture clinical heterogeneity. 3. Simplified Design: By replacing the SES-CD's five-segment colonic/ileal scoring with a unified pan-enteric evaluation (supported by imaging when necessary), MAS-CD streamlines assessment while enhancing comprehensiveness.

The development of MAS-CD addresses critical gaps in Crohn's disease (CD) monitoring by establishing a novel paradigm that synergizes endoscopic visualization with cross-sectional imaging modalities. Our validation studies demonstrate that MAS-CD maintains diagnostic fidelity comparable to SES-CD (ICC 0.888 vs 0.976) while overcoming the latter's anatomical limitations. The integration of CTE/MRE parameters particularly enhances evaluation completeness - in 23.6% of cases where ileal intubation failed, cross-sectional imaging provided essential inflammation burden quantification that would have been missed by conventional endoscopy alone [26]. This multimodal approach aligns with recent consensus advocating for composite therapeutic targets encompassing both mucosal and transmural healing[21, 27].

In conclusion, the MAS-CD represents a novel and practical scoring system for the objective evaluation of mucosal lesions in Crohn's disease. Its straightforward design, robust reproducibility, and strong

correlation with both biochemical and clinical disease markers make it a compelling alternative to the SES-CD, especially in clinical trials focused on assessing mucosal healing. Furthermore, the MAS-CD can complement the SES-CD and CDEIS in routine clinical practice, offering a versatile tool for comprehensive disease evaluation.

## Abbreviations

CD

Crohn's disease

SES-CD

Simplified Endoscopic Score for Crohn's Disease

MAS-CD

Multimodal Activity Score for Crohn's Disease

CTE

computed tomography enterography

MRE

magnetic resonance enterography

IUS

intestinal ultrasound

HBI

Harvey-Bradshaw Index

CRP

C-reactive protein

IBD

inflammatory bowel diseases

CDEIS

The Crohn's Disease Endoscopic Index of Severity

BMI

body mass index

ICC

intraclass correlation coefficients

## Declarations

### **Ethics approval and consent to participate**

This study was approved by the Ethics Committee of The First Affiliated Hospital of USTC. Informed consent was obtained from all individual participants included in the study.

### **Consent for publication**

Not applicable.

## Availability of data and materials

The datasets generated and analyzed during this study are not publicly available due to patient privacy and ethical restrictions. However, anonymized data supporting the findings may be made available upon reasonable request to the corresponding author, pending approval from the institutional ethics committee. Third-party data referenced in this work (e.g., SES-CD, CDEIS criteria) are cited and publicly available in their original publications.

## Competing Interests

The authors have no conflicts of interest related to this publication.

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## Authors' contributions

M.X. and X.Y. contributed equally to this work and are co-first authors. M.X. and X.Y. conceived and designed the study, performed data analysis, and drafted the manuscript. L.X., W.L. and X.F. contributed to data acquisition, analysis, and interpretation. K.Z. and J.X. are co-corresponding authors; K.Z. supervised the project, provided critical revisions, and coordinated the research; J.X. provided guidance on study design and data interpretation, and reviewed the manuscript. All authors reviewed and approved the final manuscript.

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## Figures

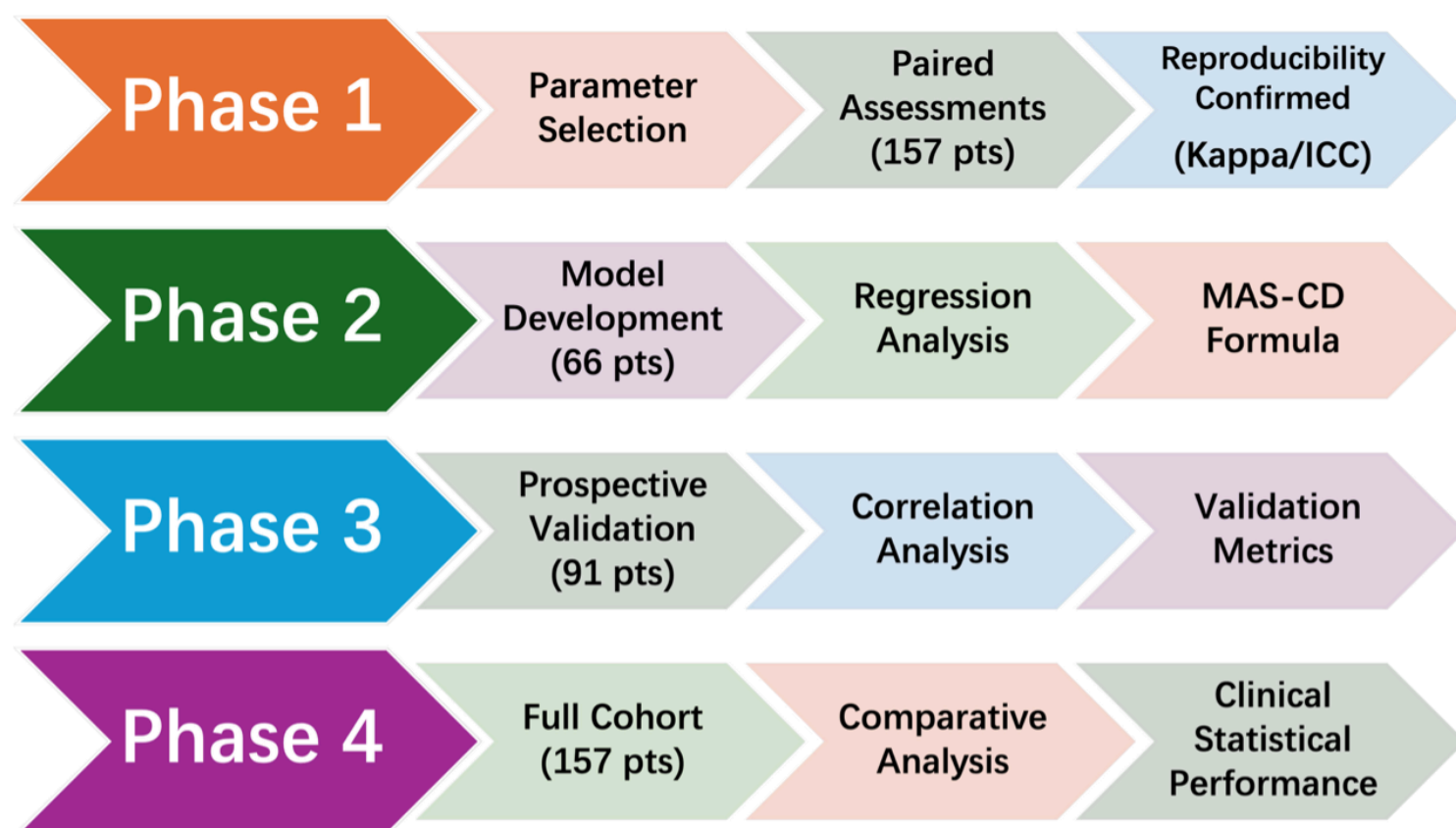


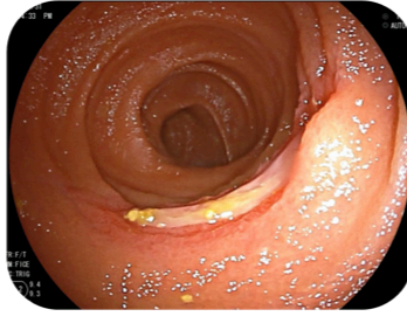
Figure 1

### Research Flowchart

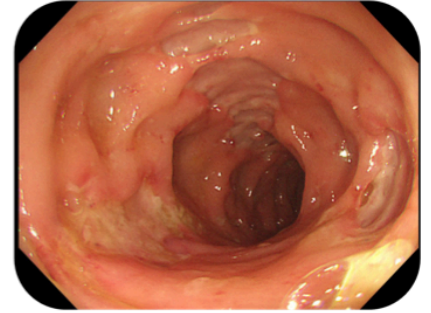
## Ulcer size



Score 1  
0–0.5 cm

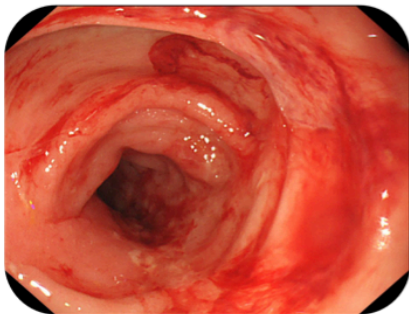


Score 2  
0.5–2 cm

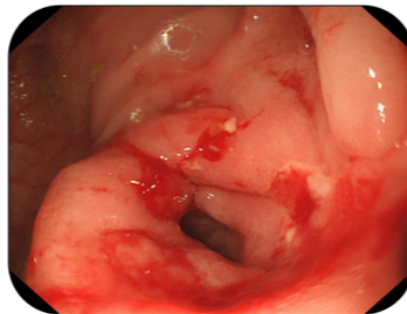


Score 3  
>2 cm

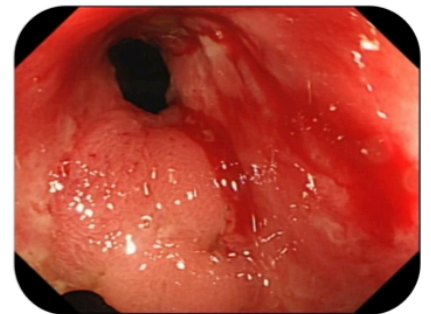
## Stenosis



Score 1  
single, passable



Score 2  
multiple, passable



Score 3  
impassable

Figure 2

## Schematic Diagram of MAS-CD Scoring

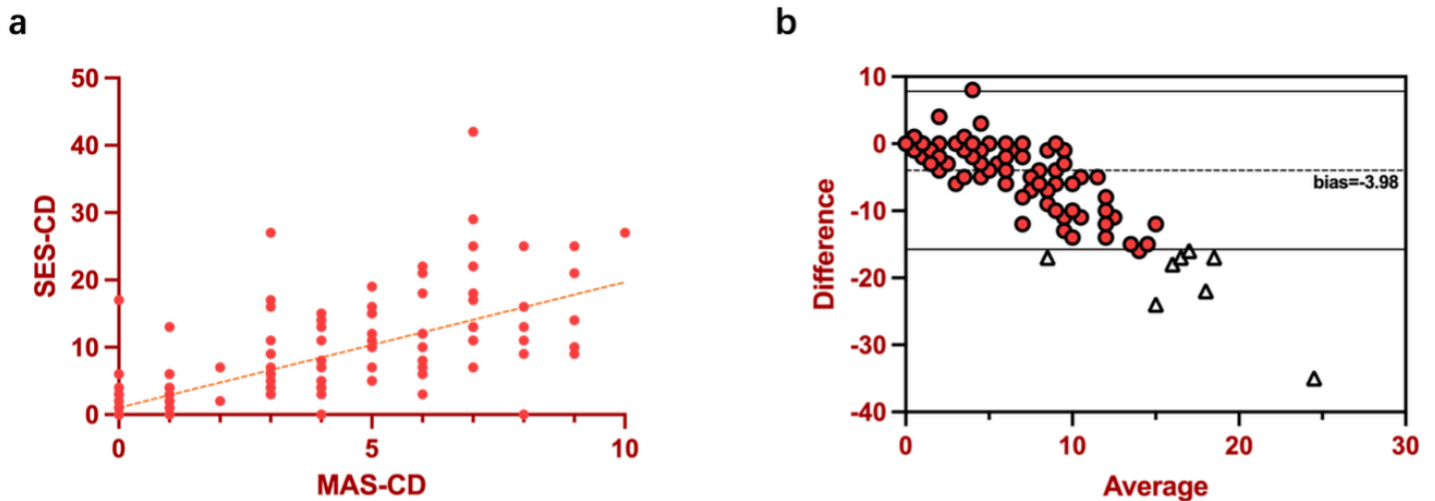


Figure 3

Scatter diagram(a) and Bland-Altman plot(b) of correlation between SES-CD and MAS-CD (157 colonoscopic examinations).

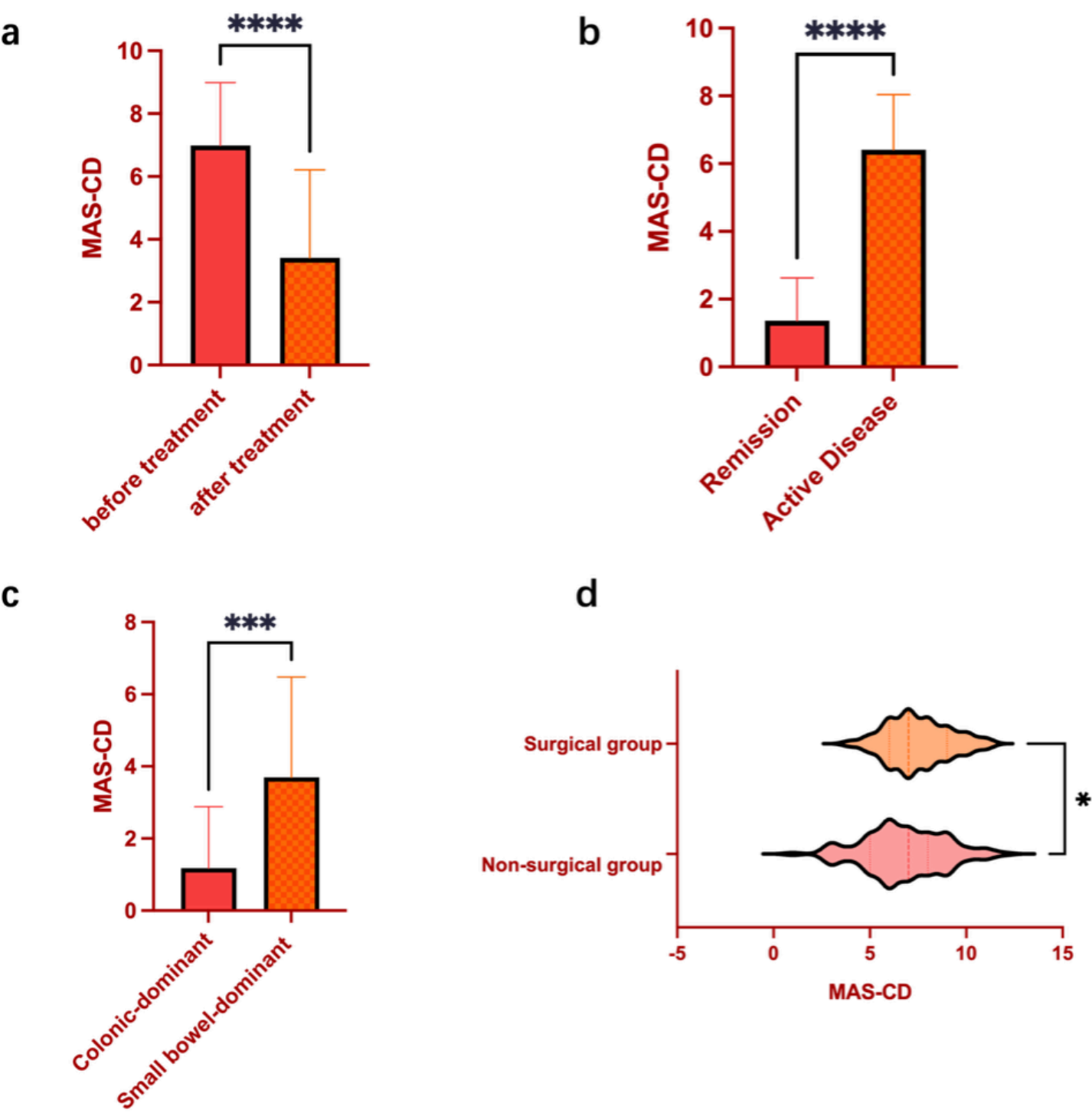


Figure 4

Clinical utility of MAS-CD across diverse scenarios in Crohn's Disease.

(a) Pretreatment vs. post-treatment MAS-CD scores. (b) Significant differentiation between remission and active disease states. (c) Phenotype-specific responses, showing lower MAS-CD in colonic-

dominant versus small bowel-dominant disease. (d) Violin plot with boxplot overlays comparing treatment arms, demonstrating reduced MAS-CD in surgical versus non-surgical cohorts. (\*p<0.05, \*\*p<0.01, \*p<0.001).

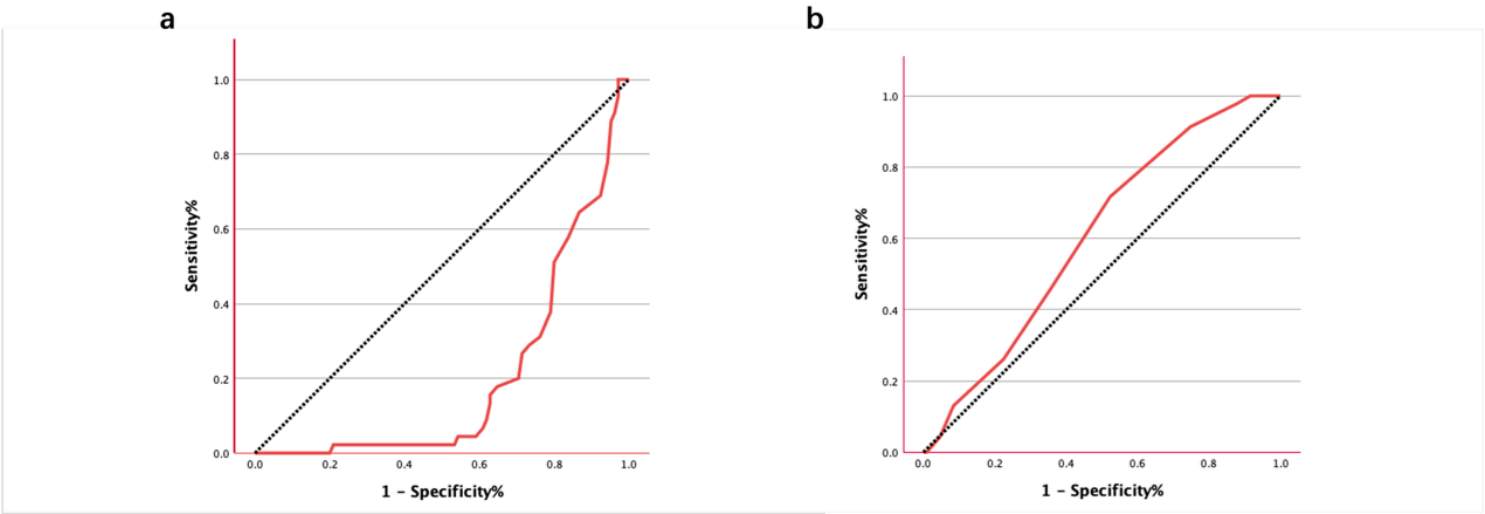


Figure 5

**ROC curves of SES-CD and MAS-CD for predicting clinical outcomes of Crohn’s disease.**

(a) ROC curve for SES-CD, showing an AUC of 0.21(95% CI 0.13–0.27). (b) ROC curve for MAS-CD with an AUC of 0.61(95% CI 0.51–0.70).