

FECAL CALPROTECTIN AS A NON-INVASIVE MARKER OF ENDOSCOPIC ACTIVITY IN INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE STUDY

Boutayna ELRHAFFOULI^{*1}, Hicham EZ-ZAIDI¹, Aziza HAMI¹

¹ Parasitology Laboratory, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco

Corresponding author: Boutayna Elrhaffouli

Email: b.elrhaffouli@ump.ac.ma

Phone: +212 645 424 283

Article history:

Received: 9 October 2026 Revised: 25 October 2026 Accepted: 28 October 2026 Published online: 01 November 2026

Abstract

Introduction: Inflammatory bowel disease (IBD) is a chronic, relapsing–remitting inflammatory disorder of the gastrointestinal tract. Its monitoring relies mainly on endoscopy and on clinical scores, which are partly subjective. Fecal and blood biomarkers are increasingly used to reduce the need for endoscopy.

Objective: To assess the correlation of fecal calprotectin (FC), C-reactive protein (CRP), hemoglobin and platelet count with clinical and endoscopic activity, and to compare the diagnostic performance of FC and CRP for detecting endoscopic activity.

Methods: We conducted a retrospective study of IBD patients who underwent FC testing between July 2021 and July 2023 at Mohammed VI University Hospital, Oujda, Morocco. A total of 235 assessments from 155 patients were analyzed; the number of assessments varied by analysis according to data availability (137 with an endoscopic score, 132 with a classifiable endoscopic activity). Disease activity was defined using GETAID-recommended scores: Harvey-Bradshaw Index and CDEIS in Crohn's disease (CD), Mayo score and UCEIS in ulcerative colitis (UC). Correlations were assessed using Spearman's coefficient (ρ), and diagnostic performance using receiver operating characteristic (ROC) curves. Disease-specific analyses were considered primary and pooled analyses exploratory. Sensitivity analyses accounted for repeated assessments from the same patients and for censored FC values.

Results and discussion: The cohort included 101 patients with CD, 33 with UC and 21 with unclassified or undocumented IBD; 54.8% were women and the mean age was 37.8 years. Median FC was 78 $\mu\text{g/g}$ and median CRP 4.39 mg/L. In CD, FC correlated weakly with the CDEIS ($\rho = 0.30$, $p = 0.003$, $n = 97$) and the HBI ($\rho = 0.18$, $p = 0.022$, $n = 155$), as did CRP (CDEIS: $\rho = 0.21$, $p = 0.039$; HBI: $\rho = 0.17$, $p = 0.039$); no significant correlation was found in UC. In CD, the AUC for endoscopic activity was 0.723 (95% CI: 0.619–0.827) for FC and 0.659 (95% CI: 0.542–0.776) for CRP. In the exploratory pooled analysis, the AUC was 0.667 (95% CI: 0.567–0.767; $p = 0.001$) for FC and 0.603 (95%

CI: 0.493–0.712; $p = 0.07$) for CRP; the difference was not significant ($p = 0.35$). Clinical and endoscopic activity were not correlated ($\rho = 0.01$, $p = 0.89$). At $\geq 354 \mu\text{g/g}$, FC had a specificity of 90.9% for endoscopic activity. The association of FC with endoscopic activity persisted when restricted to one assessment per patient (CD: $\rho = 0.41$, AUC 0.782), with patient-level cluster bootstrap and with alternative handling of censored values, whereas its weak correlation with clinical activity did not.

Conclusion: FC was the only marker with a significant AUC for endoscopic activity in the pooled analysis, with a better performance in CD, where CRP also had a significant AUC, and high FC values were highly specific for endoscopic inflammation. However, its correlations with disease activity were weak, its advantage over CRP was not significant, and clinical scores did not reflect endoscopic activity. FC is a useful complementary tool to select patients for endoscopy, but it cannot replace endoscopy.

Keywords: Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Fecal calprotectin; C-reactive protein; Endoscopy; Biomarkers

INTRODUCTION

Inflammatory bowel disease (IBD), which includes

Crohn's disease (CD) and ulcerative colitis (UC), is a chronic and destructive inflammatory disease of the gastrointestinal tract. Its main complications, such as stenosis, perforation and failure of medical treatment, are frequent, may lead to surgery, and can make endoscopic examination difficult or even impossible [1,2].

Relapses are detected either clinically, using activity scores, or by endoscopy, which remains the reference examination for IBD [3]. However, clinical scores are subjective, and endoscopy is invasive, costly and not always well tolerated. Alternative approaches include cross-sectional imaging, which is expensive and does not always allow an accurate

Elrhaffouli, B., Ez-zaidi, H., Hami, A.

assessment of inflammatory activity, and biological or fecal markers such as CRP and fecal calprotectin [3,4].

Calprotectin is a calcium- and zinc-binding heterodimer of the S100A8 and S100A9 proteins. It accounts for up to 60% of the cytosolic proteins of neutrophils and is also expressed by monocytes and macrophages; it has antibacterial and antifungal properties [5]. The migration of neutrophils into the inflamed intestinal mucosa and lumen allows calprotectin to be measured in stool (fecal calprotectin, FC), making it a biomarker of intestinal inflammation and a predictor of clinical relapse in IBD [6]. FC is not specific to IBD: it also increases in other inflammatory and infectious conditions (bacterial enteritis, diverticulitis, autoimmune enteropathy, intestinal polyps, colorectal cancer) and with the use of non-steroidal anti-inflammatory drugs (NSAIDs) [5]. FC is resistant to degradation by intestinal enzymes and remains stable in stool for several days at room temperature. Blood markers such as CRP an acute-phase protein synthesized by hepatocytes [7] hemoglobin and platelet count can also reflect inflammatory flares, but they are not specific to intestinal inflammation [7,8].

The aim of this study was to evaluate the correlation of FC with endoscopic and clinical activity, to compare it with other inflammatory markers (CRP, hemoglobin, platelet count), and to assess its diagnostic performance using ROC curve analysis.

MATERIALS AND METHODS

Study design and population

We conducted a retrospective study of IBD patients who underwent FC testing, together with CRP and complete blood count, between July 2021 and July 2023 at Mohammed VI University Hospital, Oujda, Morocco. Each FC measurement with its concomitant blood tests and clinical and/or endoscopic evaluation was considered an assessment; patients could contribute several assessments during follow-up.

Inclusion criteria were an established diagnosis of IBD based on standard clinical, endoscopic, radiological and histological criteria and at least one FC measurement with concomitant blood tests. Exclusion criteria were: suspected concomitant gastrointestinal infection, gastrointestinal malignancy, pregnancy, and current use of antibiotics, cytotoxic drugs, NSAIDs or alcohol.

The study was conducted in accordance with the Declaration of Helsinki. Data were collected retrospectively from medical and laboratory records and anonymized before analysis. Owing to the retrospective design and the use of anonymized data, the study was exempt from ethics committee approval, and the requirement for informed consent was waived.

Assessment of disease activity

Disease activity was assessed using the scores and thresholds recommended by the GETAID (Groupe d'Étude Thérapeutique des Affections Inflammatoires du Tube Digestif) [9]. In CD, clinical activity was assessed using the Harvey-Bradshaw Index (HBI), which includes general well-being, abdominal pain, number of liquid stools, abdominal mass and extra-intestinal complications [10]; clinical

remission was defined as $HBI \leq 4$, mild activity as 5–7, moderate as 8–16 and severe as > 16 [11]. In UC, clinical activity was assessed using the Mayo score (UC-DAI) [12]: ≤ 2 , inactive disease; 3–5, mild; 6–10, moderate; ≥ 11 , severe [9].

CD patients underwent ileocolonoscopy and UC patients complete colonoscopy. Endoscopic lesions were scored using the Crohn's Disease Endoscopic Index of Severity (CDEIS) [13] and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) [14], using the GETAID scoring forms [9]. The CDEIS is based on elementary lesions (non-ulcerated lesions, superficial and deep ulcerations) and their extent in five segments (ileum, right colon, transverse colon, left colon and rectum), with additional points for ulcerated and non-ulcerated stenosis; it ranges from 0 to 44 [13]. The UCEIS is based on three descriptors vascular pattern (0–2), bleeding (0–3) and erosions/ulcers (0–3) and ranges from 0 to 8 [14]. Endoscopic remission was defined as $CDEIS < 3$ in CD and $UCEIS \leq 1$ in UC; higher values were considered endoscopically active [15,16]. Scores outside the possible range of each index (one Mayo score of 15 and one UCEIS of 10) were considered data-entry errors and excluded.

Laboratory measurements

Stool samples were collected avoiding contamination with water or urine; the first morning stool was preferred. Approximately 1g of stool was sent to the laboratory. FC was measured using a quantitative lateral-flow immunochromatographic assay (Quantum Blue® Calprotectin High Range, Bühlmann Laboratories, Schönenbuch, Switzerland). In this sandwich immunoassay, a monoclonal capture antibody specific for calprotectin is coated on the test line, and a second monoclonal detection antibody conjugated to colloidal gold is present on the conjugate release pad. After addition of the extracted and diluted stool sample, calprotectin-conjugate complexes bind to the test line, while unbound conjugate binds to a goat anti-mouse antibody on the control line. The signal is read with a dedicated reader. Results were reported as < 30 , < 100 or $> 1,800 \mu\text{g/g}$ when outside the quantification range (93, 32 and 8 assessments, respectively; one further result was reported as $< 35 \mu\text{g/g}$). The normal value in our laboratory was $< 80 \mu\text{g/g}$; because some results were only reported as $< 100 \mu\text{g/g}$, FC was considered positive at $\geq 100 \mu\text{g/g}$.

CRP, hemoglobin and platelet count were measured on blood samples collected at the time of the assessment. CRP was considered positive above 5 mg/L.

Statistical analysis

Continuous variables are presented as mean (range) or median (interquartile range, IQR), and categorical variables as numbers and percentages. Analyses were performed on available data without imputation; the number of assessments contributing to each analysis therefore varies according to the availability of clinical scores, endoscopic scores and biomarker values, and is detailed in Table 4.

Because CD and UC were assessed with different, non-interchangeable scores, disease-specific analyses were

Elrhaffouli, B., Ez-zaidi, H., Hami, A.

considered primary: biomarkers were correlated with the HBI and CDEIS in CD, and with the Mayo score and UCEIS in UC. Pooled analyses, which also included patients with unclassified IBD, were considered exploratory. For pooled ROC analyses, endoscopic activity was first dichotomized using the validated threshold of each index (CDEIS ≥ 3 , UCEIS ≥ 2), so that the outcome was expressed on a common scale; pooled Spearman correlations of raw scores are reported for descriptive purposes only.

Because clinical and endoscopic scores are ordinal and FC values were censored and non-normally distributed, correlations were assessed using Spearman's rank correlation coefficient (ρ). The diagnostic performance of FC and CRP for endoscopic activity was evaluated by ROC curve analysis; AUCs with 95% confidence intervals were calculated, optimal cut-offs were determined by the Youden index, and the AUCs of FC and CRP were compared on paired assessments by bootstrap resampling (2,000 replicates).

FC values outside the quantification range were assigned the limit value ($< 30 \mu\text{g/g} = 30$, $< 35 \mu\text{g/g} = 35$, $< 100 \mu\text{g/g} = 100$ and $> 1,800 \mu\text{g/g} = 1,800 \mu\text{g/g}$). Because Spearman's correlation and ROC analysis depend only on ranks, this is equivalent to treating results $< 30 \mu\text{g/g}$ as tied at the lowest rank and results $> 1,800 \mu\text{g/g}$ as tied at the highest rank, whatever the value assigned. In contrast, results reported only as $< 100 \mu\text{g/g}$ cannot be ranked relative to quantified values between 30 and $100 \mu\text{g/g}$, and assigning them $100 \mu\text{g/g}$ may rank them above lower quantified values. Results reported as $< 100 \mu\text{g/g}$ were considered negative (below the positivity threshold of $100 \mu\text{g/g}$). The influence of this censoring was assessed in sensitivity analyses in which results $< 100 \mu\text{g/g}$ were (i) assigned the lowest rank (tied with results $< 30 \mu\text{g/g}$) or (ii) excluded.

Because patients could contribute several assessments, which are not independent observations, two further sensitivity analyses were performed: (i) restriction to one assessment per patient (the first assessment with an endoscopic evaluation for endoscopic analyses, and the first assessment with a clinical score for clinical analyses); and (ii) estimation of the 95% CIs of ρ , of the AUCs and of the FC-CRP AUC difference by patient-level cluster bootstrap (2,000 replicates, resampling patients with all their assessments). All tests were two-sided, and $p < 0.05$ was considered significant. Analyses were performed using SPSS software (IBM Corp., Armonk, NY, USA) and Python.

RESULTS

Study population

A total of 235 assessments from 155 patients were analyzed (Table 1). The cohort included 101 patients with CD (163 assessments), 33 with UC (48 assessments) and 21 with unclassified or undocumented IBD (24 assessments). Patients contributed a median of 1 assessment (range 1–5); 53 patients (34.2%) contributed more than one assessment. Women accounted for 54.8% of patients ($n = 85$). The mean age was 37.8 years (range 4–74): 36.4 years (range 15–74) in CD and 42.2 years (range 15–64) in UC. For patients with unclassified IBD, disease activity was taken as recorded in the medical file.

The number of assessments included in each analysis is detailed in Table 4. A clinical score was available for 214 assessments (155 CD, 47 UC, 12 unclassified IBD), of which 206 could be classified as inactive ($n = 170$) or active ($n = 36$), and an endoscopic score for 137 assessments (97 CD, 33 UC, 7 unclassified IBD), of which 132 could be classified as in remission ($n = 33$) or active ($n = 99$). The 8 clinical and 5 endoscopic assessments that could not be classified all belonged to patients with unclassified IBD for whom no activity status was recorded, so that no disease-specific threshold could be applied. The median FC level was $78 \mu\text{g/g}$ (IQR 30–151), and FC was below $100 \mu\text{g/g}$ in 125 assessments (53.2%). The median CRP level was 4.39 mg/L (IQR 1.35–10.48).

Correlation analyses

Correlations are summarized in Table 2. In disease-specific analyses, FC correlated with the CDEIS ($\rho = 0.30$, $p = 0.003$, $n = 97$) and with the HBI ($\rho = 0.18$, $p = 0.022$, $n = 155$) in CD, whereas no significant correlation was found in UC (UCEIS: $\rho = 0.12$, $p = 0.51$, $n = 33$; Mayo score: $\rho = 0.25$, $p = 0.10$, $n = 47$). In the exploratory pooled analysis, FC showed a weak correlation with endoscopic activity ($\rho = 0.27$, $p = 0.002$, $n = 137$) and with clinical activity ($\rho = 0.21$, $p = 0.002$, $n = 214$).

In CD, CRP correlated weakly with the CDEIS ($\rho = 0.21$, $p = 0.039$, $n = 94$) and with the HBI ($\rho = 0.17$, $p = 0.039$, $n = 148$), whereas no correlation was found in UC (UCEIS: $\rho = 0.14$, $p = 0.44$; Mayo score: $\rho = -0.09$, $p = 0.54$). In the pooled analysis, CRP correlated weakly with endoscopic activity ($\rho = 0.24$, $p = 0.006$, $n = 133$) but not with clinical activity ($\rho = 0.11$, $p = 0.10$, $n = 206$). Hemoglobin and platelet count were not significantly correlated with clinical or endoscopic scores in CD or UC; in the pooled analysis, platelet count correlated weakly with clinical activity ($\rho = 0.16$, $p = 0.025$) but not with endoscopic activity ($\rho = 0.13$, $p = 0.13$), and hemoglobin was not correlated with clinical ($\rho = -0.09$, $p = 0.17$) or endoscopic activity ($\rho = -0.12$, $p = 0.17$). Clinical activity was not correlated with endoscopic activity in CD ($\rho = 0.05$, $p = 0.62$), in UC ($\rho = 0.04$, $p = 0.83$) or overall ($\rho = 0.01$, $p = 0.89$).

Positivity of biomarkers according to disease activity

FC ($\geq 100 \mu\text{g/g}$) was positive in 44.4% (44/99) of endoscopically active assessments and negative in 75.8% (25/33) of assessments in endoscopic remission. In clinically active assessments, FC was positive in 41.7% (15/36) and negative in 65.3% (111/170) of clinically inactive assessments.

CRP ($> 5 \text{ mg/L}$) was positive in 57.1% (56/98) of endoscopically active assessments and negative in 58.1% (18/31) of assessments in endoscopic remission. It was positive in 45.7% (16/35) of clinically active assessments and negative in 50.0% (82/164) of inactive ones.

ROC curve analysis

ROC analyses were performed on assessments with both a biomarker value and a classifiable endoscopic activity (132 for FC, 129 for CRP) (Table 3). In CD, the AUC for endoscopic activity was 0.723 (95% CI: 0.619–0.827; $p < 0.001$, $n = 97$) for FC and 0.659 (95% CI: 0.542–0.776; $p = 0.008$, $n = 94$) for CRP. In UC, only 4 assessments were in endoscopic remission, which did not allow a reliable ROC analysis. In the exploratory pooled analysis, the AUC was 0.667 (95% CI: 0.567–0.767; $p = 0.001$) for FC and 0.603 (95% CI: 0.493–0.712; $p = 0.07$) for CRP; the difference between the two markers was not statistically significant ($\Delta\text{AUC} = 0.062$; 95% CI: -0.075 to 0.184 ; $p = 0.35$).

The optimal FC cut-off identified by the Youden index in the pooled analysis was 31 $\mu\text{g/g}$ (sensitivity 76.8%, specificity 57.6%), i.e. close to the lower limit of quantification of the assay; because it lies below the value of results reported only as $< 100 \mu\text{g/g}$, this cut-off should be interpreted with caution. At the laboratory positivity threshold of 100 $\mu\text{g/g}$, sensitivity was 44.4% and specificity 75.8%; at 354 $\mu\text{g/g}$, sensitivity was 24.2% and specificity 90.9%. For CRP, the optimal cut-off was 2.13 mg/L (sensitivity 75.5%, specificity 45.2%).

Sensitivity analyses

Results of the sensitivity analyses are shown in Supplementary Table S1. When restricted to the first assessment with endoscopy of each patient (124 patients, including 87 with CD), the associations of FC with endoscopic activity were maintained and slightly stronger: in CD, $\rho = 0.41$ ($p < 0.001$) with the CDEIS and $\text{AUC} = 0.782$ (95% CI: 0.686–0.879); in the pooled analysis, $\text{AUC} = 0.727$ (95% CI: 0.631–0.822; $n = 119$), and the difference from CRP remained non-significant ($\Delta\text{AUC} = 0.074$; 95% CI: -0.075 to 0.210 ; $p = 0.27$). In contrast, the correlation of FC with clinical activity was no longer significant (pooled: $\rho = 0.14$, $p = 0.10$, $n = 138$; CD: $\rho = 0.11$, $p = 0.29$, $n = 95$). With patient-level cluster bootstrap, the 95% CIs were 0.11–0.47 for ρ (FC–CDEIS in CD), 0.607–0.825 for the AUC of FC in CD, 0.555–0.775 for the pooled AUC of FC and -0.075 to 0.196 for the FC–CRP difference ($p = 0.34$). When results $< 100 \mu\text{g/g}$ were assigned the lowest rank, ρ (FC–CDEIS) was 0.28 ($p = 0.005$) and the AUC of FC was 0.689 in CD and 0.635 overall; when they were excluded, ρ was 0.34 ($p = 0.002$, $n = 81$) and the AUC 0.740 in CD and 0.676 overall. The associations of FC with endoscopic activity were therefore not materially affected by repeated measurements or by censoring.

DISCUSSION

IBD causes significant morbidity and requires endoscopy for diagnosis and follow-up [3]. In recent years, FC has been increasingly used as a non-invasive marker for monitoring IBD [3,4].

In this study, FC was weakly correlated with endoscopic activity, more clearly in CD ($\rho = 0.30$) than in UC, and it was the only marker with an AUC significantly greater than 0.5 for detecting endoscopic inflammation in the pooled analysis

(0.667 overall and 0.723 in CD; in CD, CRP also had a significant AUC of 0.659). However, the strength of these associations was limited: CRP was also weakly correlated with endoscopic activity, and the difference between the AUCs of FC and CRP was not significant.

Previous studies have reported FC thresholds of 50–100 $\mu\text{g/g}$ for detecting intestinal inflammation and have shown that FC increases with the severity of inflammation [17,18]. In our study, clinical activity was not correlated with endoscopic findings, confirming that symptoms alone do not reliably reflect mucosal inflammation and that objective markers are needed.

In a meta-analysis, FC was more sensitive than CRP for detecting endoscopic activity in IBD [4]. In UC, FC correlated with clinical and endoscopic activity more closely than CRP [19], and several studies have shown that FC correlates well with endoscopic and histological activity [17,18]. Patients in sustained remission have very low FC levels (median $< 40 \mu\text{g/g}$), whereas those who relapse have significantly higher levels [20].

The correlations observed in our study were weaker than in most published series. Several factors may explain this: the retrospective design; the different endoscopic scales used in CD and UC (CDEIS and UCEIS), which is why disease-specific analyses were prioritized; the small number of UC assessments, with very few in endoscopic remission; the high proportion of FC results reported only as below the quantification limit (53.2%), which reduces the information available for rank-based analyses; the inclusion of repeated assessments, as associations were slightly stronger when only one assessment per patient was analyzed; and the possible delay between stool sampling and endoscopy.

Treatment targets in IBD now include endoscopic remission, and FC is used as a monitoring target. Published cut-offs vary: a threshold of 56 $\mu\text{g/g}$ has been reported to predict sustained remission [21], and 250 $\mu\text{g/g}$ was proposed in a study of 123 UC patients [22]. In our study, the Youden-optimal cut-off was low (31 $\mu\text{g/g}$), favoring sensitivity, whereas a value $\geq 354 \mu\text{g/g}$ had a specificity of 90.9%. In practice, a high FC value strongly suggests endoscopic activity, whereas a low value does not exclude it.

Distinguishing symptoms of irritable bowel syndrome from active IBD remains challenging, and such symptoms may lead to unnecessary escalation of IBD therapy, with potential side effects [23,24]. A simple, inexpensive non-invasive marker such as FC can help in this setting.

Limitations. This study has several limitations: its retrospective, single-center design; the limited number of assessments with paired endoscopy ($n = 132$); the inclusion of repeated assessments from the same patients, which are not independent, although the associations with endoscopic activity were consistent in sensitivity analyses restricted to one assessment per patient and using patient-level bootstrap (the weak correlation with clinical activity was not); the presence of patients with unclassified IBD, who were included only in pooled analyses; the censoring of FC values below the quantification limit; and the lack of a standardized interval between stool sampling and endoscopy: only the date of FC measurement was available in the records, so that the

Elrhaffouli, B., Ez-zaidi, H., Hami, A.

interval between stool sampling and endoscopy could not be determined, and inflammatory activity may have changed between the two examinations. Prospective studies, analyzing CD and UC separately, are needed.

CONCLUSION

In our population, FC was the only marker with a significant diagnostic performance for endoscopic activity in the pooled analysis, particularly in CD, where CRP also performed significantly (AUC 0.659), and high FC values were highly specific for endoscopic inflammation. However, its correlations with disease activity were weak and its advantage over CRP was not statistically significant. Clinical scores did not reflect endoscopic activity. FC is therefore a useful complementary tool to select patients for endoscopy, but it cannot replace endoscopy.

DECLARATIONS

Ethics approval: Exempt from ethics committee approval owing to the retrospective, anonymized design; informed consent was waived. **Conflicts of interest:** The authors declare no conflicts of interest. **Funding:** This research received no external funding.

REFERENCES

- Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. *Lancet*. 2017;389(10080):1741-1755.
- Ungaro R, Mehandru S, Allen PB, Peyrin-Biroulet L, Colombel JF. Ulcerative colitis. *Lancet*. 2017;389(10080):1756-1770.
- Maaser C, Sturm A, Vavricka SR, et al. ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: Initial diagnosis, monitoring of known IBD, detection of complications. *J Crohns Colitis*. 2019;13(2):144-164.
- Mosli MH, Zou G, Garg SK, et al. C-reactive protein, fecal calprotectin, and stool lactoferrin for detection of endoscopic activity in symptomatic inflammatory bowel disease patients: a systematic review and meta-analysis. *Am J Gastroenterol*. 2015;110(6):802-819.
- Jukic A, Bakiri L, Wagner EF, Tilg H, Adolph TE. Calprotectin: from biomarker to biological function. *Gut*. 2021;70(10):1978-1988.
- Tibble JA, Sigthorsson G, Bridger S, Fagerhol MK, Bjarnason I. Surrogate markers of intestinal inflammation are predictive of relapse in patients with inflammatory bowel disease. *Gastroenterology*. 2000;119(1):15-22.
- Vermeire S, Van Assche G, Rutgeerts P. Laboratory markers in IBD: useful, magic, or unnecessary toys? *Gut*. 2006;55(3):426-431.
- Ma C, Battat R, Khanna R, Parker CE, Feagan BG, Jairath V. What is the role of C-reactive protein and fecal calprotectin in evaluating Crohn's disease activity? *Best Pract Res Clin Gastroenterol*. 2019;38-39:101602.
- GETAID (Groupe d'Étude Thérapeutique des Affections Inflammatoires du Tube Digestif). Indices et scores [Internet]. Available from: <https://www.getaid.org/scores> (accessed October 2026).
- Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. *Lancet*. 1980;1(8167):514.
- Vermeire S, Schreiber S, Sandborn WJ, Dubois C, Rutgeerts P. Correlation between the Crohn's disease activity and Harvey-Bradshaw indices in assessing Crohn's disease severity. *Clin Gastroenterol Hepatol*. 2010;8(4):357-363.
- Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. *N Engl J Med*. 2005;353(23):2462-2476.
- Mary JY, Modigliani R. Development and validation of an endoscopic index of the severity for Crohn's disease: a prospective multicentre study. Groupe d'Etudes Thérapeutiques des Affections Inflammatoires du Tube Digestif (GETAID). *Gut*. 1989;30(7):983-989.
- Travis SP, Schnell D, Krzeski P, et al. Developing an instrument to assess the endoscopic severity of ulcerative colitis: the Ulcerative Colitis Endoscopic Index of Severity (UCEIS). *Gut*. 2012;61(4):535-542.
- Vuitton L, Marteau P, Sandborn WJ, et al. IOIBD technical review on endoscopic indices for Crohn's disease clinical trials. *Gut*. 2016;65(9):1447-1455.
- Travis SP, Schnell D, Krzeski P, et al. Reliability and initial validation of the ulcerative colitis endoscopic index of severity. *Gastroenterology*. 2013;145(5):987-995.
- Røseth AG, Aadland E, Jahnsen J, Raknerud N. Assessment of disease activity in ulcerative colitis by faecal calprotectin, a novel granulocyte marker protein. *Digestion*. 1997;58(2):176-180.
- D'Haens G, Ferrante M, Vermeire S, et al. Fecal calprotectin is a surrogate marker for endoscopic lesions in inflammatory bowel disease. *Inflamm Bowel Dis*. 2012;18(12):2218-2224.
- Xiang JY, Ouyang Q, Li GD, Xiao NP. Clinical value of fecal calprotectin in determining disease activity of ulcerative colitis. *World J Gastroenterol*. 2008;14(1):53-57.
- De Vos M, Louis EJ, Jahnsen J, et al. Consecutive fecal calprotectin measurements to predict relapse in patients with ulcerative colitis receiving infliximab maintenance therapy. *Inflamm Bowel Dis*. 2013;19(10):2111-2117.
- Mooiweer E, Severs M, Schipper ME, et al. Low fecal calprotectin predicts sustained clinical remission in inflammatory bowel disease patients: a plea for deep remission. *J Crohns Colitis*. 2015;9(1):50-55.
- Lobatón T, Rodríguez-Moranta F, Lopez A, Sánchez E, Rodríguez-Alonso L, Guardiola J. A new rapid quantitative test for fecal calprotectin predicts endoscopic activity in ulcerative colitis. *Inflamm Bowel Dis*. 2013;19(5):1034-1042.
- Halpin SJ, Ford AC. Prevalence of symptoms meeting criteria for irritable bowel syndrome in inflammatory bowel disease: systematic review and meta-analysis. *Am J Gastroenterol*. 2012;107(10):1474-1482.

24. Pezzone MA, Wald A. Functional bowel disorders in inflammatory bowel disease. *Gastroenterol Clin North Am.* 2002;31(1):347-357.

Table 1. Characteristics of the study population

Characteristic	Value
Patients / assessments, n	155 / 235
Crohn's disease, n (%)	101 (65.2)
Ulcerative colitis, n (%)	33 (21.3)
Unclassified or undocumented IBD, n (%)	21 (13.5)
Female / Male, n (%)	85 (54.8) / 70 (45.2)
Mean age, years (range)	37.8 (4–74)
Crohn's disease	36.4 (15–74)
Ulcerative colitis	42.2 (15–64)
Median fecal calprotectin, µg/g (IQR)	78 (30–151)
FC < 100 µg/g, n (%) of assessments	125 (53.2)
Assessments per patient, median (range)	1 (1–5)
Median CRP, mg/L (IQR)	4.39 (1.35–10.48)
Clinically active / inactive assessments, n	36 / 170
Endoscopically active / remission assessments, n	99 / 33

Table 2. Spearman correlations between biomarkers, clinical activity and endoscopic activity

Comparison	All IBD ρ (p) [n]	Crohn's disease ρ (p) [n]	Ulcerative colitis ρ (p) [n]
FC vs endoscopic activity	0.27 (0.002) [137]	0.30 (0.003) [97]	0.12 (0.51) [33]
FC vs clinical activity	0.21 (0.002) [214]	0.18 (0.022) [155]	0.25 (0.10) [47]
CRP vs endoscopic activity	0.24 (0.006) [133]	0.21 (0.039) [94]	0.14 (0.44) [33]
CRP vs clinical activity	0.11 (0.10) [206]	0.17 (0.039) [148]	−0.09 (0.54) [47]
Hemoglobin vs endoscopic activity	−0.12 (0.17) [135]	−0.19 (0.067) [96]	−0.11 (0.56) [32]
Hemoglobin vs clinical activity	−0.09 (0.17) [211]	−0.12 (0.15) [153]	−0.15 (0.32) [46]
Platelets vs endoscopic activity	0.13 (0.13) [128]	0.13 (0.22) [91]	0.11 (0.57) [31]
Platelets vs clinical activity	0.16 (0.025) [204]	0.15 (0.067) [148]	0.13 (0.39) [45]
Clinical vs endoscopic activity	0.01 (0.89) [137]	0.05 (0.62) [97]	0.04 (0.83) [33]

ρ , Spearman's correlation coefficient; n, number of assessments. Clinical activity: HBI in CD, Mayo score in UC. Endoscopic activity: CDEIS in CD, UCEIS in UC. Out-of-range scores excluded. Disease-specific analyses (CD, UC) are primary. Pooled analyses (All IBD) combine scores measured on different scales and include unclassified IBD; they are exploratory and descriptive. The number of assessments varies according to data availability (see Table 4).

Table 3. Diagnostic performance of fecal calprotectin and CRP for detecting endoscopic activity (ROC analysis)

Biomarker	n	AUC (95% CI)	p-value	Cut-off	Sensitivity (%)	Specificity (%)
FC – all IBD	132	0.667 (0.567–0.767)	0.001	31 µg/g (Youden)	76.8	57.6
				100 µg/g	44.4	75.8
				354 µg/g	24.2	90.9
FC – Crohn's disease	97	0.723 (0.619–0.827)	<0.001			
CRP – all IBD	129	0.603 (0.493–0.712)	0.07	2.13 mg/L (Youden)	75.5	45.2
CRP – Crohn's disease	94	0.659 (0.542–0.776)	0.008			
FC vs CRP (paired, n = 129)		ΔAUC 0.062 (–0.075 to 0.184)	0.35			

Endoscopic activity: CDEIS ≥ 3 in CD, UCEIS ≥ 2 in UC. AUC, area under the curve; CI, confidence interval (Hanley–McNeil); p-value for AUC > 0.50, and bootstrap comparison (2,000 replicates) for ΔAUC. n, assessments with both a biomarker value and a classifiable endoscopic activity (see Table 4). Pooled analyses are exploratory. CIs accounting for repeated assessments (patient-level cluster bootstrap) are given in Supplementary Table S1.

Table 4. Number of assessments included in each analysis

Analysis	All IBD, n	CD, n	UC, n	Criterion for inclusion
All assessments	235	163	48	FC with concomitant blood tests
FC vs clinical score (Spearman)	214	155	47	HBI (CD) or Mayo score (UC) available
Clinical activity classified (active/inactive)	206	155	47	Clinical score classifiable using GETAID thresholds
FC vs endoscopic score (Spearman)	137	97	33	CDEIS (CD) or UCEIS (UC) available; out-of-range scores excluded
FC ROC analysis (endoscopic activity classified)	132	97	33	Endoscopic activity classifiable (CDEIS ≥ 3 ; UCEIS ≥ 2)
CRP vs endoscopic score (Spearman)	133	94	33	CRP and endoscopic score available
CRP ROC analysis; paired FC-CRP comparison	129	94	33	CRP and classifiable endoscopic activity available
CRP vs clinical score (Spearman)	206	148	47	CRP and clinical score available
Hemoglobin vs endoscopic / clinical score	135/211	96/153	32/46	Hemoglobin and score available
Platelets vs endoscopic / clinical score	128/204	91/148	31/45	Platelet count and score available

All IBD includes assessments of patients with unclassified IBD. Differences between analyses reflect missing clinical scores, endoscopic scores or biomarker values (complete-case analysis). The 8 clinical (214 vs 206) and 5 endoscopic (137 vs 132) assessments that could not be classified belonged to patients with unclassified IBD without a recorded activity status.

Supplementary Table S1. Sensitivity analyses for repeated assessments and censored FC values

Analysis	n (CD / all IBD ROC)	ρ FC–CDEIS, CD (p or 95% CI)	AUC FC, CD (95% CI)	AUC FC, all IBD (95% CI)	ΔAUC FC–CRP, all IBD (95% CI)
Main analysis (all assessments)	97 / 132	0.30 (p = 0.003)	0.723 (0.619–0.827)	0.667 (0.567–0.767)	0.062 (–0.075 to 0.184)
One assessment per patient	87 / 119	0.41 (p < 0.001)	0.782 (0.686–0.879)	0.727 (0.631–0.822)	0.074 (–0.075 to 0.210)
Patient-level cluster bootstrap	97 / 132	0.30 (0.11–0.47)	0.723 (0.607–0.825)	0.667 (0.555–0.775)	0.062 (–0.075 to 0.196)
FC < 100 µg/g assigned the lowest rank	97 / 132	0.28 (p = 0.005)	0.689 (0.580–0.799)	0.635 (0.531–0.739)	0.021 (–0.116 to 0.154)
FC < 100 µg/g excluded	81 / 110	0.34 (p = 0.002)	0.740 (0.631–0.850)	0.676 (0.569–0.783)	0.031 (–0.108 to 0.171)

Main analysis: values from Tables 2 and 3. One assessment per patient: first assessment with an endoscopic evaluation (124 patients). Cluster bootstrap: 2,000 replicates resampling patients with all their assessments (percentile 95% CIs). AUC 95% CIs: Hanley–McNeil except for the cluster bootstrap; ΔAUC 95% CIs: bootstrap (2,000 replicates). ΔAUC computed on assessments with both FC and CRP (n = 129, 116, 129, 129 and 108, respectively).