


Association between C-Reactive Protein, Fecal Calprotectin, and Endoscopic Disease Activity in Patients with Inflammatory Bowel Disease

Samia Bentabet^{1,2}, Oumaima El Abed^{1,2}, Mounia El Yousfi^{1,2}, Mohammed El Abkari^{1,2}, Sidi Adil Ibrahim^{1,2}, Nada Lahmidani^{1,2}

¹Department of Hepato-Gastroenterology, Hassan II University Hospital, Fez, Morocco

²Faculty of Medicine and Pharmacy, Sidi Mohammed Ben Abdellah University, Fez, Morocco

Email: samia.bentabet@usmba.ac.ma

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Abstract

Background: Endoscopic evaluation is considered the reference method for assessing inflammatory activity in inflammatory bowel disease (IBD) [1]. Nevertheless, the invasive nature and cost of repeated endoscopic procedures limit their use for frequent monitoring in routine clinical practice [2]. In this context, non-invasive biomarkers such as C-reactive protein (CRP) and fecal calprotectin (FC) have been increasingly used to estimate intestinal inflammatory activity [3]. **Aim:** To examine the relationship between CRP, fecal calprotectin, and endoscopic disease activity in patients with IBD, and to determine the diagnostic performance of their combined use. **Methods:** This cross-sectional observational study included 180 adult patients with confirmed IBD who underwent recent endoscopic evaluation along with concomitant measurements of CRP and fecal calprotectin. Endoscopic activity was assessed using the Simple Endoscopic Score for Crohn's Disease (SES-CD) for Crohn's disease and the Mayo endoscopic subscore for ulcerative colitis. Associations between biomarker levels and endoscopic scores were analyzed using Spearman's rank correlation coefficient. **Results:** A total of 180 patients were included, of whom 120 had Crohn's disease, and 60 had ulcerative colitis. Fecal calprotectin demonstrated strong correlations with endoscopic activity in Crohn's disease ($r = 0.74$, $p < 0.001$) and ulcerative colitis ($r = 0.69$, $p < 0.001$). In comparison, CRP showed moderate correlations with endoscopic severity ($r = 0.48$ and $r = 0.42$, respectively). The combined evaluation of CRP and fecal calprotectin improved the identification of moderate-to-severe endoscopic inflammation, with a sensitivity of 88% and a specificity of 76%. **Conclusion:** Fecal calprotectin shows a strong association with endoscopic disease activity and appears to be more informative than CRP for reflecting mucosal inflammation in patients with IBD.

Keywords

Inflammatory Bowel Disease, Crohn's Disease, Ulcerative Colitis, Fecal Calprotectin, C-Reactive Protein, Endoscopic Activity

1. Introduction

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory conditions characterized by alternating periods of remission and relapse. Continuous assessment of disease activity is essential for guiding therapeutic decisions and optimizing patient outcomes [1]. In recent years, mucosal healing has become a central therapeutic objective because it is associated with lower relapse rates, reduced hospitalization, and improved long-term prognosis [2] [3].

Endoscopic evaluation remains the reference method for directly assessing intestinal inflammation and mucosal lesions in patients with IBD [4]. However, repeated endoscopic procedures are invasive, costly, and sometimes poorly tolerated by patients, which limits their use for frequent monitoring during routine follow-up [5].

For this reason, increasing attention has been directed toward the use of non-invasive biomarkers to evaluate intestinal inflammatory activity. C-reactive protein (CRP) is widely used as a marker of systemic inflammation, although its ability to reflect intestinal disease activity is variable [6]. In contrast, fecal calprotectin, a neutrophil-derived protein released into the intestinal lumen during inflammation, has emerged as a sensitive and specific marker of mucosal inflammatory activity in IBD [7]-[10].

Several studies have reported strong associations between fecal calprotectin levels and endoscopic disease activity and have highlighted its potential value for predicting relapse and monitoring response to therapy [11]-[14]. Furthermore, recent international recommendations emphasize the role of biomarker-based monitoring strategies as part of treat-to-target approaches in the management of inflammatory bowel disease [15]-[19].

The aim of the present study was to evaluate the relationship between CRP, fecal calprotectin, and endoscopic disease activity in patients with inflammatory bowel disease, and to assess the diagnostic performance of their combined use.

2. Materials and Methods

2.1. Study Design and Setting

This cross-sectional observational study was conducted at the Department of Hepato-Gastroenterology, Hassan II University Hospital, Fez, Morocco.

2.2. Study Population

A total of 180 adult patients with confirmed inflammatory bowel disease were in-

cluded between January 2019 and January 2025, comprising:

- 120 patients with Crohn's disease.
- 60 patients with ulcerative colitis.

All patients were enrolled consecutively at the Department of Hepato-Gastroenterology of Hassan II University Hospital, Fez, Morocco.

The maximum allowed interval between endoscopic assessment and biomarker measurement (CRP and fecal calprotectin) was 14 days. Only patients with both evaluations performed within this timeframe were included to ensure temporal consistency.

Inclusion Criteria

Patients were eligible if they met the following criteria:

- Age \geq 18 years.
- Confirmed diagnosis of Crohn's disease or ulcerative colitis.
- Recent colonoscopy or rectosigmoidoscopy.
- Concurrent measurement of CRP and fecal calprotectin.

Exclusion Criteria

Included patients with acute infections, recent gastrointestinal surgery (<3 months), known colorectal cancer, use of nonsteroidal anti-inflammatory drugs within the previous 2 weeks, or incomplete clinical or biological data.

2.3. Endoscopic Activity Definitions

In Crohn's disease, endoscopic activity was assessed using the Simple Endoscopic Score for Crohn's Disease (SES-CD), with moderate-to-severe activity defined as SES-CD \geq 7.

In ulcerative colitis, endoscopic activity was assessed using the Mayo endoscopic subscore, with moderate-to-severe activity defined as a Mayo score \geq 2.

2.4. Biomarker Assessment

Elevated CRP was defined as >5 mg/L, and elevated fecal calprotectin (FC) as >250 μ g/g.

The combined CRP + FC test was considered positive when both markers were elevated simultaneously.

2.5. Endoscopic Assessment

Endoscopic disease activity was evaluated using:

- SES-CD for Crohn's disease.
- Mayo endoscopic subscore for ulcerative colitis.

Moderate-to-severe activity was defined as:

- SES-CD \geq 7.
- Mayo score \geq 2.

2.6. Biomarker Measurement

CRP levels were measured in serum, with elevated levels defined as >5 mg/L.

Fecal calprotectin was measured using standardized assays, with elevated levels defined as $>250 \mu\text{g/g}$.

The combined CRP + FC test was considered positive when both markers were elevated.

2.7. Statistical Analysis

Continuous variables were expressed as mean \pm standard deviation. Correlations between biomarkers and endoscopic scores were evaluated using Spearman's rank correlation coefficient. Statistical analyses were performed using SPSS software. A two-sided p -value < 0.05 was considered statistically significant.

3. Results

3.1. Patient Characteristics

A total of 180 patients with confirmed inflammatory bowel disease were included in the study. The mean age of the study population was 34.2 years, with a predominance of female patients (58%). Crohn's disease represented the majority of cases, accounting for 120 patients (66.7%), whereas 60 patients (33.3%) were diagnosed with ulcerative colitis.

The baseline characteristics of the study population are summarized in **Table 1**.

Table 1. Baseline characteristics of the study population.

Variable	Value
Total patients	180
Mean age	34.2
Female	105 (58%)
Male	75 (42%)
Crohn's disease	120 (66.7%)
Ulcerative colitis	60 (33.3%)

Among patients with Crohn's disease, ileal involvement (L1) was observed in 38%, colonic involvement (L2) in 27%, and ileocolonic disease (L3) in 35% of cases.

In patients with ulcerative colitis, left-sided colitis represented the most frequent disease extent (41%), followed by pancolitis (37%) and proctitis (22%).

3.2. Biomarker Levels according to Endoscopic Activity

Crohn's Disease: In patients with Crohn's disease, Active endoscopic inflammation (SES-CD ≥ 7) was associated with significantly higher levels of inflammatory biomarkers compared with inactive disease.

Mean CRP levels were 26.4 mg/L in patients with active disease compared with 8.2 mg/L in those with inactive disease. Similarly, fecal calprotectin concentrations

were markedly elevated in active disease (780 µg/g) compared with inactive disease (190 µg/g).

Detailed biomarker levels according to endoscopic activity are presented in **Table 2**.

Table 2. Biomarker levels according to endoscopic activity.

Disease	Endoscopic Activity	CRP (mg/L)	Fecal Calprotectin (µg/g)
Crohn's disease	Active	26.4	780
Crohn's disease	Inactive	8.2	190
Ulcerative colitis	Active	12.8	720
Ulcerative colitis	Remission	5.6	210

These findings indicate that patients with active mucosal inflammation present markedly higher biomarker levels compared with those in endoscopic remission.

3.3. Correlation between Biomarkers and Endoscopic Activity

Correlation analysis demonstrated a significant association between biomarker levels and endoscopic disease severity in both Crohn's disease and ulcerative colitis.

The correlation coefficients between biomarkers and endoscopic activity scores are summarized in **Table 3**.

Table 3. Correlation between biomarkers and endoscopic activity scores.

Biomarker	Crohn's Disease (SES-CD)	Ulcerative Colitis (Mayo score)
Fecal calprotectin	$r = 0.74$ ($p < 0.001$)	$r = 0.69$ ($p < 0.001$)
C-reactive protein	$r = 0.48$ ($p < 0.001$)	$r = 0.42$ ($p = 0.002$)

Fecal calprotectin demonstrated strong correlations with endoscopic disease activity in both disease phenotypes. In Crohn's disease, the correlation between fecal calprotectin and SES-CD score was $r = 0.74$, whereas CRP showed a moderate correlation ($r = 0.48$).

Similarly, in ulcerative colitis, fecal calprotectin showed a strong correlation with the Mayo endoscopic score ($r = 0.69$), while CRP demonstrated a weaker correlation ($r = 0.42$).

Overall, fecal calprotectin showed consistently stronger correlations with endoscopic disease severity than CRP, suggesting that fecal calprotectin more accurately reflects intestinal inflammatory activity.

3.4. Ulcerative Colitis

In patients with ulcerative colitis, active disease (defined as Mayo score 2 - 3) was associated with higher biomarker levels compared with patients in endoscopic remission (Mayo score 0 - 1).

Mean CRP levels were 12.8 mg/L in active disease compared with 5.6 mg/L in remission. Fecal calprotectin concentrations were also significantly higher in active disease (720 µg/g) compared with remission (210 µg/g), as shown in **Table 2**.

These findings further support the role of fecal calprotectin as a marker of mucosal inflammation in ulcerative colitis.

3.5. Combined Diagnostic Performance

The combined evaluation of CRP and fecal calprotectin improved the detection of clinically significant endoscopic inflammation.

The diagnostic performance of the combined biomarker approach for identifying moderate-to-severe endoscopic activity showed:

- Sensitivity: 88%.
- Specificity: 76%.

These results suggest that the combined use of CRP and fecal calprotectin may improve the identification of patients with active intestinal inflammation and may help guide decisions regarding the need for endoscopic reassessment.

4. Discussion

The present study demonstrates that fecal calprotectin is strongly associated with endoscopic disease activity in patients with inflammatory bowel disease and shows a stronger correlation with mucosal inflammation than C-reactive protein. These findings support the growing evidence that fecal calprotectin represents a reliable non-invasive biomarker for assessing intestinal inflammatory activity in both Crohn's disease and ulcerative colitis.

Fecal calprotectin is a calcium-binding protein predominantly derived from neutrophils and released during intestinal inflammation. Because it directly reflects neutrophil migration into the intestinal lumen, its concentration in stool correlates closely with the degree of mucosal inflammatory burden [6] [7]. In contrast, CRP is a systemic acute-phase reactant produced by hepatocytes in response to inflammatory cytokines such as interleukin-6. Although CRP is widely used in clinical practice due to its accessibility and low cost, it may underestimate localized intestinal inflammation, particularly in ulcerative colitis, where inflammation is often limited to the mucosal layer [5] [20].

Our findings are consistent with several previous investigations demonstrating a strong association between fecal calprotectin levels and endoscopic disease severity in IBD [21]-[24]. In particular, Schoepfer *et al.* [12] showed that fecal calprotectin correlates more closely with endoscopic activity than CRP in patients with ulcerative colitis. Similarly, Sipponen *et al.* [11] reported a significant relationship between fecal calprotectin concentrations and endoscopic lesions in Crohn's disease. Meta-analyses have also confirmed the high diagnostic accuracy of fecal calprotectin for detecting active intestinal inflammation and predicting mucosal lesions [23].

In the present study, fecal calprotectin demonstrated strong correlations with

endoscopic scores in both Crohn's disease and ulcerative colitis. These findings reinforce its role as a surrogate marker of mucosal inflammation. Because fecal calprotectin reflects intestinal neutrophilic inflammation directly at the mucosal level, it provides a more specific indicator of intestinal disease activity than systemic inflammatory markers.

Interestingly, the strength of correlation between fecal calprotectin and endoscopic activity was slightly higher in Crohn's disease compared with ulcerative colitis. This observation may be explained by differences in disease phenotype and inflammatory burden. Crohn's disease is characterized by transmural inflammation and often involves extensive segments of the gastrointestinal tract, which may lead to higher levels of inflammatory biomarkers and stronger correlations with objective measures of disease activity.

Another important finding of this study is the improved diagnostic performance observed when CRP and fecal calprotectin were evaluated together. The combined biomarker strategy achieved a sensitivity of 88% and specificity of 76% for detecting moderate-to-severe endoscopic activity. This suggests that integrating multiple biomarkers may enhance the identification of patients with clinically significant inflammation and support decision-making regarding the need for endoscopic reassessment. Multimarker monitoring strategies have increasingly been proposed to improve disease assessment and guide therapeutic decisions in IBD management [25]-[28].

From a clinical perspective, the use of fecal calprotectin as a non-invasive monitoring tool may help reduce the need for frequent endoscopic procedures, improve patient comfort, and facilitate closer disease surveillance. Biomarker-guided monitoring strategies may also support treat-to-target approaches that aim to achieve mucosal healing and optimize long-term outcomes in patients with IBD [29] [30].

However, several limitations of this study should be acknowledged. First, the cross-sectional design does not allow evaluation of longitudinal changes in biomarker levels or their predictive value for relapse and therapeutic response. Prospective longitudinal studies would be necessary to determine whether fecal calprotectin can reliably predict disease relapse or guide treatment adjustments. Second, although fecal calprotectin is widely used in clinical practice, there is currently no universally standardized cut-off value applicable across different patient populations and assay methods.

Despite these limitations, our study has several strengths. The use of validated endoscopic scoring systems, including the SES-CD for Crohn's disease and the Mayo endoscopic subscore for ulcerative colitis, ensured objective assessment of mucosal disease activity. In addition, biomarker measurements were obtained concurrently with endoscopic evaluation, allowing accurate correlation analysis. Finally, the study was conducted in a real-world tertiary care cohort, reflecting routine clinical practice and enhancing the clinical applicability of the findings.

Overall, our results reinforce the value of fecal calprotectin as a key biomarker for assessing intestinal inflammation in inflammatory bowel disease and support

its integration into non-invasive monitoring strategies.

These findings are consistent with current international treat-to-target strategies for inflammatory bowel disease management. According to the STRIDE-II recommendations, objective assessment of inflammation using biomarkers such as fecal calprotectin is strongly encouraged to guide treatment decisions and monitor therapeutic response.

Recent guidelines from the American Gastroenterological Association further support the use of fecal calprotectin and CRP as non-invasive tools for monitoring disease activity and guiding therapeutic decisions in both ulcerative colitis and Crohn's disease [31] [32].

5. Conclusions

In this study of 180 patients with inflammatory bowel disease, fecal calprotectin showed stronger correlations with endoscopic activity than C-reactive protein in both Crohn's disease ($r = 0.74$ vs 0.48) and ulcerative colitis ($r = 0.69$ vs 0.42). Patients with active disease exhibited markedly higher biomarker levels.

The combined use of fecal calprotectin and CRP improved detection of moderate-to-severe endoscopic activity, with 88% sensitivity and 76% specificity. These findings support fecal calprotectin as a reliable non-invasive biomarker for monitoring intestinal inflammation and optimizing the use of endoscopy in IBD follow-up.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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