

Clinical usefulness of fecal calprotectin in assessing disease activity and endoscopic remission in intestinal Behçet's disease

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Background/Aims: Intestinal Behçet's disease (BD) is a manifestation of BD involving the gastrointestinal tract. Although fecal calprotectin (FC) is a useful inflammatory marker, its role in intestinal BD is unclear. **Methods:** We retrospectively analyzed 78 patients with intestinal BD to evaluate correlations between FC levels and the Disease Activity Index for Intestinal Behçet's Disease (DAIBD), C-reactive protein (CRP), and erythrocyte sedimentation rate. FC and CRP levels were compared between patients in endoscopic remission and those with active disease. Receiver operating characteristic (ROC) curve analysis was used to evaluate FC's ability to predict endoscopic activity and ulcer size. **Results:** FC levels significantly correlated with DAIBD scores ($r=0.253$, $P=0.025$) and CRP ($r=0.227$, $P=0.046$). Patients with endoscopically active disease had higher FC ($1,124 \pm 1,957$ $\mu\text{g/g}$ vs. $367 \pm 1,208$ $\mu\text{g/g}$; $P<0.001$) and CRP levels (16.0 ± 23.7 mg/L vs. 14.4 ± 46.5 mg/L ; $P=0.027$) than those in remission. Patients with larger ulcers (≥ 30 mm) had higher FC levels than those with smaller ulcers ($2,212 \pm 2,609$ $\mu\text{g/g}$ vs. $962 \pm 1,822$ $\mu\text{g/g}$; $P=0.034$). An FC cutoff level of 176 $\mu\text{g/g}$ discriminated active endoscopic disease (sensitivity 59.3%, specificity 83.3%), with an area under the ROC curve (AUC) of 0.724 (95% confidence interval, 0.605–0.843; $P=0.002$), outperforming CRP (AUC, 0.657). **Conclusions:** FC levels correlated with DAIBD scores and endoscopic inflammation in intestinal BD. FC outperformed CRP in detecting endoscopic activity, supporting its use in disease management. (Intest Res, Published online)

Key Words: Behcet syndrome; Gastrointestinal diseases; Leukocyte L1 antigen complex; Inflammation; Biomarkers

INTRODUCTION

Behçet's disease (BD) is a chronic multi-systemic inflammatory disorder characterized by recurrent oral and genital ulcers, uveitis, and skin lesions.¹ In some patients, BD affects the gastrointestinal tract, a manifestation referred to as intestinal BD.

Intestinal BD is defined by the presence of gastrointestinal symptoms and characteristic ulcerative lesions on endoscopy that most often affect the ileocecal region. Patients with intestinal BD commonly present with abdominal pain, diarrhea, and hematochezia and may develop serious complications such as perforation or massive hemorrhage. Although intestinal involvement is relatively uncommon in BD, it significantly affects the patient's prognosis and quality of life.² The prevalence of BD varies geographically, from 0.64 to 420 cases per 100,000 people,³ and is highest in regions along the historical Silk Road, extending from the Mediterranean to East Asia.⁴ Conversely, it has a relatively low prevalence in the Nordic countries and North America.⁵ Gastrointestinal manifesta-

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tions of BD occur more frequently in East Asian nations such as the Republic of Korea and Japan.⁶

Intestinal lesions in BD are typically large (>1 cm in diameter), deep round, or ovoid ulcers with well-demarcated borders.⁷ Despite these distinctive features, intestinal BD can be difficult to distinguish from Crohn's disease (CD). Both diseases often involve the ileocecal region and present with similar symptoms. Intestinal BD usually presents as solitary or large focal ulcers, whereas CD is characterized by multiple linear or serpiginous ulcers, cobblestone mucosa, and the potential to affect any part of the gastrointestinal tract.^{8,9} Given these overlaps, reliable biomarkers are needed to assess intestinal disease activity in BD and guide management.

Recently, the treat-to-target strategy has been increasingly emphasized in the management of intestinal BD, as in inflammatory bowel disease (IBD).^{10,11} In this context, achieving endoscopic remission has been proposed as an important therapeutic goal rather than relying solely on symptom control. A previous longitudinal study demonstrated that the presence of endoscopic mucosal healing at clinical remission independently predicted a favorable long-term prognosis in patients with intestinal BD.¹² Furthermore, recent clinical practice guidelines for intestinal BD have also highlighted endoscopic assessment and remission as key components of disease monitoring and therapeutic targets.¹³

Fecal calprotectin (FC) is a calcium-binding protein derived predominantly from neutrophils, which is released into the intestinal lumen during active inflammation.¹⁴ FC is widely used as a noninvasive biomarker for intestinal inflammation in IBD, including CD, ulcerative colitis and intestinal BD.¹⁵⁻¹⁹ Stool FC concentrations correlate with neutrophil migration to the gut mucosa and, thus, reflect mucosal inflammatory activity.²⁰ In clinical practice, FC is useful for distinguishing IBD from other functional disorders, such as irritable bowel syndrome, and for monitoring disease activity in IBD.²¹ FC analysis also offers several advantages over endoscopy; it is noninvasive, reproducible, cost-effective, and stable in stool samples at room temperature for several days.^{14,22} Nevertheless, FC is not entirely specific to IBD; elevated FC levels can be observed in infections, colorectal neoplasia, and nonsteroidal anti-inflammatory drug-induced enteropathy.²³ In addition, FC is less sensitive in isolated small bowel CD, where neutrophil infiltration of the colon is minimal.²⁴ Although FC is an established marker of IBD, its application in intestinal BD remains underexplored. A few studies have suggested that fecal, but not serum, calprotectin levels correlate with active intestinal BD and

the presence of intestinal ulcers. However, robust data and validated cutoff values for FC in intestinal BD are lacking, and its clinical utility for assessing disease activity and endoscopic remission in BD has not been well defined.²⁵ Therefore, we aimed to investigate the clinical usefulness of FC in intestinal BD. Specifically, we evaluated the relationship between the FC level and disease activity indices (clinical, laboratory, and endoscopic) in patients with intestinal BD. Additionally, we examined whether FC can serve as a noninvasive marker of endoscopic remission by correlating it with endoscopic findings and sought to identify FC cutoff values that predict endoscopic disease activity and ulcer severity. We aimed to determine whether FC is a reliable biomarker for monitoring intestinal inflammation and guiding treatment decisions in patients with intestinal BD.

METHODS

1. Study Design and Patients

This retrospective single-center study was conducted at the Inflammatory Bowel Disease Center of Severance Hospital (Seoul, Republic of Korea). Medical records from August 2014 to September 2023 were reviewed to identify patients diagnosed with intestinal BD who underwent both colonoscopy and FC testing within a 3-month interval. Intestinal BD was diagnosed based on clinical criteria and endoscopic findings of characteristic intestinal ulcers in patients with BD.²⁶ A total of 78 patients met the inclusion criteria and were enrolled. Inclusion criteria were as follows: (1) a confirmed diagnosis of intestinal BD regardless of patient age, and (2) availability of at least 1 colonoscopy and 1 quantitative FC measurement within a 3-month period of each other. We excluded patients who only had qualitative (positive/negative) FC results without a numeric value, those who lacked relevant laboratory data (such as C-reactive protein [CRP] or erythrocyte sedimentation rate [ESR]) within 3 months of colonoscopy, and those without available clinical follow-up records around the time of sampling.

2. Disease Activity Assessment

Disease activity was evaluated in 3 domains: clinical, laboratory, and endoscopic. Clinical activity was assessed using the Disease Activity Index for Intestinal Behçet's Disease (DAIBD). The DAIBD is a validated index that scores intestinal BD activity based on symptoms and clinical parameters, with higher scores indicating a more active disease. For descriptive purposes, DAIBD scores were categorized as remission and mild,

moderate, or severe disease activity according to established cutoffs.²⁷ Laboratory activity was assessed by indicators such as FC level, serum CRP level, and ESR, measured on the same day or within a few days of colonoscopy. Endoscopic activity was determined based on colonoscopy findings. Endoscopic remission was defined as complete mucosal healing (no visible ulcers) of the terminal ileum or the colon. Endoscopically active disease was defined as the presence of any ulcer (aphthous or deep ulcers) in the terminal ileum and/or any segment of the colon on colonoscopy. The size, number, and location of intestinal ulcers were recorded for each colonoscopy. Ulcer size was typically measured using open biopsy forceps. For analysis, ulcers were classified into large (≥ 30 mm in diameter) and small (< 30 mm) categories. This cutoff was selected based on its optimal statistical performance in discriminating FC levels. The ulcer location was classified as affecting the small intestine or colon (including the cecum and more distal colonic segments).

3. Outcomes

The primary objective was to examine the association between FC levels and disease activity in intestinal BD. This included the correlation of FC level with the DAIBD clinical score and inflammatory markers (CRP level and ESR), as well as a comparison of FC levels between patients in endoscopic remission and those with endoscopically active disease. The secondary objective was to evaluate the usefulness of FC as a predictive biomarker of endoscopic outcomes. We aimed to determine whether FC could predict (1) the presence of active mucosal disease on colonoscopy (ulcers vs. no ulcers) and (2) the presence of large ulcers (≥ 30 mm) among those with active disease. For comparison, we also assessed the performance of CRP level and ESR in predicting endoscopic outcomes.

4. Statistical Analysis

Pearson correlation analysis was used to assess the linear relationship between the 2 quantitative variables. The mean values were compared using the Mann-Whitney *U* test, Kruskal-Wallis test, or Student *t*-test, as appropriate. Categorical variables were analyzed using the chi-square test or Fisher exact test. A receiver operating characteristic (ROC) curve was constructed to determine the optimal cutoff value by plotting the true positive rate (sensitivity) against the false positive rate (1-specificity) across various thresholds. The optimal cutoff value was determined using the Youden index. The cutoff point with the high-

est Youden index was selected as the optimal threshold. The diagnostic test accuracy was evaluated using the area under the ROC curve (AUC). In all analyses, a complete case analysis was performed, and patients with missing data of relevant variables were excluded from the corresponding analyses. All statistical analyses were performed using the IBM SPSS Statistics for Windows (version 27.0; IBM Corp., Armonk, NY, USA). Statistical significance was set at a two-tailed *P*-value < 0.05 .

5. Ethical Considerations

The study protocol was approved by the Institutional Review Board of Severance Hospital (IRB No. 4-2025-0427). Given the retrospective design and the use of anonymized clinical data, the requirement for informed consent was waived by the IRB. The study was conducted in accordance with the principles of the Declaration of Helsinki and the applicable regulations for studies involving human subjects.

RESULTS

1. Baseline Characteristics

Between August 2014 and September 2023, 78 patients with intestinal BD who met the inclusion criteria were enrolled at the IBD Center of Severance Hospital in Seoul, Republic of Korea. The baseline characteristics of the patients at sampling for FC are summarized in Table 1. Of these, 32 patients (41.0%) were men, the mean age at diagnosis of intestinal BD was 39.9 ± 16.6 years (median, 41 years; range 3–74 years), and the mean disease duration was 6.4 ± 7.8 years (median, 2 years; range 0–29 years). The mean body mass index at sampling was 21.9 ± 3.7 kg/m². The mean DAIBD score was 55.6 ± 46.4 , and 25.6%, 11.5%, 37.2%, and 25.6% of patients were classified as having remission and mild, moderate, and severe clinical disease activity at sampling, respectively. Of the 78 patients with intestinal BD, 53 (67.9%) received 5-aminosalicylic acid; 27 (34.6%), corticosteroids; 25 (32.1%), immunomodulators; and 13 (16.7%), biologic agents. Additionally, 20 patients (25.6%) had a history of intestinal surgery. The mean white blood cell level was $6,666 \pm 2,540/\mu\text{L}$; hemoglobin, 12.4 ± 2.0 g/dL; albumin, 4.2 ± 0.6 g/dL; FC, $891 \pm 1,788$ $\mu\text{g/g}$; CRP, 15.5 ± 32.1 mg/L; and ESR, 28.6 ± 31.0 mm/hr.

2. Relationship between the FC Level and the DAIBD Score

A statistically significant correlation was identified between the DAIBD scores and FC levels ($r = 0.253$, $P = 0.025$) (Fig. 1A).

Table 1. Baseline Characteristics of the Study Patients

Variable	Total (n = 78)	Endoscopic remission group (n = 24)	Endoscopically active group (n = 54)	P-value
Male sex	32 (41.0)	7 (29.2)	25 (46.3)	0.214
Age at diagnosis of intestinal Behçet's disease (yr)	39.9 ± 16.6	37.4 ± 17.9	41.1 ± 16.1	0.370
Disease duration (yr)	6.4 ± 7.8	7.5 ± 6.7	6.0 ± 8.3	0.162
Body mass index (kg/m ²)	21.9 ± 3.7	21.6 ± 3.7	22.0 ± 3.7	0.631
Systemic Behçet's disease	44 (56.4)	15 (62.5)	29 (53.7)	0.621
DAIBD score	55.6 ± 46.4	55.4 ± 48.6	55.7 ± 45.9	0.912
Remission	20 (25.6)	7 (29.2)	13 (24.1)	
Mild	9 (11.5)	1 (4.2)	8 (14.8)	
Moderate	29 (37.2)	10 (41.7)	19 (35.2)	
Severe	20 (25.6)	6 (25.0)	14 (25.9)	
Medication at entry				
5-Aminosalicylic acid	53 (67.9)	18 (75.0)	35 (64.8)	0.439
Corticosteroids	27 (34.6)	8 (33.3)	19 (35.2)	1.000
Immunomodulators	25 (32.1)	6 (25.0)	19 (35.2)	0.439
Biologic agents	13 (16.7)	2 (8.3)	11 (20.4)	0.323
Previous surgery	20 (25.6)	6 (25.0)	14 (25.9)	1.000
Laboratory parameters				
White blood cell count (/ μ L)	6,666 ± 2,540	6,471 ± 2,094	6,752 ± 2,729	0.899
Hemoglobin (g/dL)	12.4 ± 2.0	13.1 ± 1.8	12.1 ± 2.0	0.042
Albumin (g/dL)	4.2 ± 0.6	4.4 ± 0.5	4.2 ± 0.6	0.202
Fecal calprotectin (μ g/g)	891 ± 1,788	367 ± 1,208	1,124 ± 1,957	<0.001
C-reactive protein (mg/L)	15.5 ± 32.1	14.4 ± 46.5	16.0 ± 23.7	0.027
ESR (mm/hr) ^a	28.6 ± 31.0	20.8 ± 27.3	31.9 ± 32.2	0.074

Values are presented as number (%) or mean ± standard deviation.

^aESR data were missing for 1 patient and were excluded from ESR-related analyses; other available data from this patient were included.

DAIBD, Disease Activity Index for Intestinal Behçet's Disease; ESR, erythrocyte sedimentation rate.

P-value for comparing endoscopic remission and active status in patients with intestinal Behçet's disease.

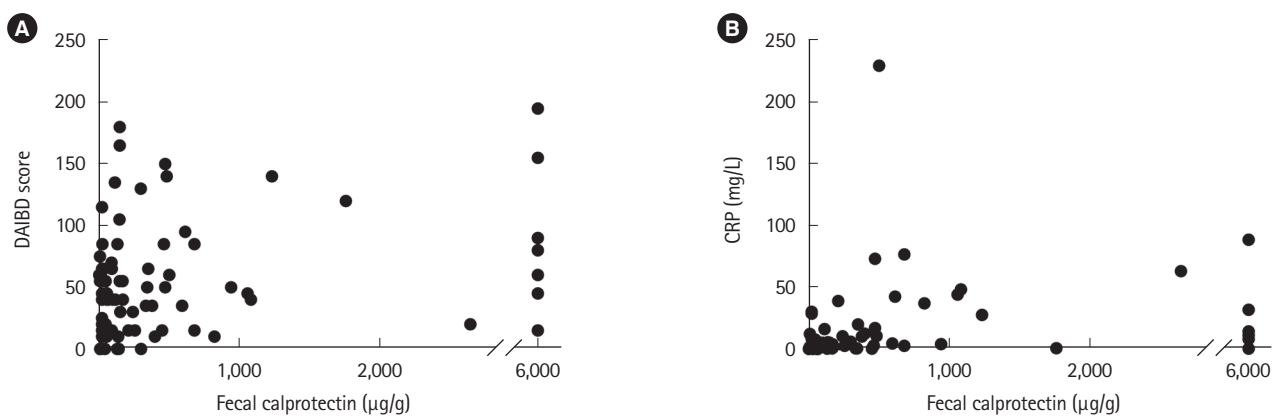


Fig. 1. Correlation between fecal calprotectin levels and clinical parameters in patients with intestinal Behçet's disease. (A) A weak but statistically significant positive correlation was observed between fecal calprotectin levels and Disease Activity Index for Intestinal Behçet's Disease (DAIBD) scores ($r=0.253$, $P=0.025$). (B) Fecal calprotectin levels also showed a significant positive correlation with serum C-reactive protein (CRP) levels ($r=0.227$, $P=0.046$).

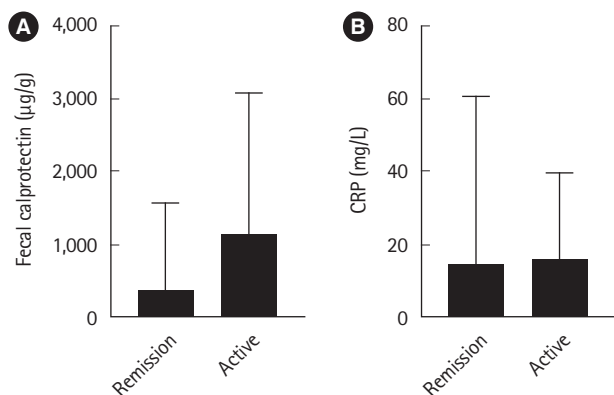


Fig. 2. Comparison of inflammatory markers between patients in endoscopic remission and those with endoscopically active disease. (A) Fecal calprotectin levels were significantly higher in patients with endoscopically active disease than those in remission ($1,124 \pm 1,957 \mu\text{g/g}$ vs. $367 \pm 1,208 \mu\text{g/g}$; $P < 0.001$). (B) Serum C-reactive protein (CRP) levels were also significantly elevated in the endoscopic active group compared to the remission group ($16.0 \pm 23.7 \text{ mg/L}$ vs. $14.4 \pm 46.5 \text{ mg/L}$; $P = 0.027$).

The mean FC levels were $498 \pm 1,315$, 499 ± 825 , $834 \pm 1,812$, and $1,542 \pm 2,326 \mu\text{g/g}$ in the remission, mild, moderate, and severe clinical disease activity groups, respectively; however, no statistical significance was observed among the groups. To further investigate the relationship between clinical disease severity and FC levels, the patients were categorized into 2 groups: non-severe (remission, mild, and moderate disease activity) and severe. The FC level was significantly higher in the severe group compared to that in the non-severe group ($1,542 \pm 2,326$ vs. $666 \pm 1,521 \mu\text{g/g}$; $P = 0.024$).

3. Relationship between FC and CRP Levels

A statistically significant correlation was observed between FC and CRP levels ($r = 0.227$, $P = 0.046$) (Fig. 1B). The mean FC levels were $530 \pm 1,397 \mu\text{g/g}$ and $1,613 \pm 2,247 \mu\text{g/g}$ in the normal and elevated CRP groups, respectively ($P < 0.001$). In contrast, FC and ESR levels were not correlated.

4. Relationship between FC Levels and Colonoscopy Findings

Of the 78 patients, 24 (30.8%) and 54 (69.2%) were in the endoscopic remission and endoscopically active groups, respectively (Table 1). The endoscopically active group had lower hemoglobin levels ($13.1 \pm 1.8 \text{ g/dL}$ vs. $12.1 \pm 2.0 \text{ g/dL}$; $P = 0.042$), higher FC levels ($1,124 \pm 1,957 \mu\text{g/g}$ vs. $367 \pm 1,208 \mu\text{g/g}$; $P < 0.001$), and higher CRP levels ($16.0 \pm 23.7 \text{ mg/L}$ vs. $14.4 \pm 46.5 \text{ mg/L}$; $P = 0.027$) compared to the endoscopic remission group

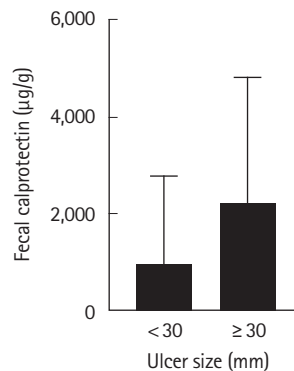


Fig. 3. Fecal calprotectin levels according to ulcer size in endoscopically active disease. Patients with ulcers measuring $\geq 30 \text{ mm}$ had significantly higher fecal calprotectin levels than those with ulcers measuring $< 30 \text{ mm}$ ($2,212 \pm 2,609 \mu\text{g/g}$ vs. $962 \pm 1,822 \mu\text{g/g}$; $P = 0.034$).

(Table 1, Fig. 2). Among the 54 patients with endoscopically active disease, ulcers were most commonly located in the ileum (31 patients, 57.4%), followed by the ileocecal valve (19 patients, 35.2%), colon (16 patients, 29.6%), anastomosis site (6 patients, 11.1%), and cecum (5 patients, 9.3%). Regarding the number of ulcers, 32 patients (59.3%) presented with multiple ulcers, while 22 patients (40.7%) had a single ulcer. The mean size of the ulcers in this group was $16.5 \pm 14.8 \text{ mm}$. On categorizing ulcers into 2 groups based on the size, FC level was significantly higher in the group with ulcers measuring $\geq 30 \text{ mm}$ ($2,212 \pm 2,609 \mu\text{g/g}$ vs. $962 \pm 1,822 \mu\text{g/g}$; $P = 0.034$) compared to that in the group with ulcers $< 30 \text{ mm}$ in endoscopically active group (Fig. 3). However, the FC levels did not differ significantly based on the location of the ulcers (small intestine vs. colon), nor was there any correlation with the number of ulcers in the endoscopically active group.

5. Relationship between CRP Levels and Colonoscopy Findings

The CRP levels significantly differed between the groups with ulcers measuring $\geq 30 \text{ mm}$ and $< 30 \text{ mm}$ ($31.1 \pm 30.2 \text{ mg/L}$ vs. $13.8 \pm 22.1 \text{ mg/L}$; $P = 0.037$) in the endoscopically active group, similar to the observation in the FC level. However, unlike FC levels, CRP levels also differed depending on the ulcer location (small intestine vs. colon) ($10.9 \pm 21.9 \text{ mg/L}$ vs. $22.9 \pm 24.7 \text{ mg/L}$; $P = 0.003$) in the endoscopically active group.

6. Usefulness of the FC Level as a Predictive Biomarker for Endoscopically Active Disease

While using an FC level cutoff of $\geq 176 \mu\text{g/g}$ to predict endo-

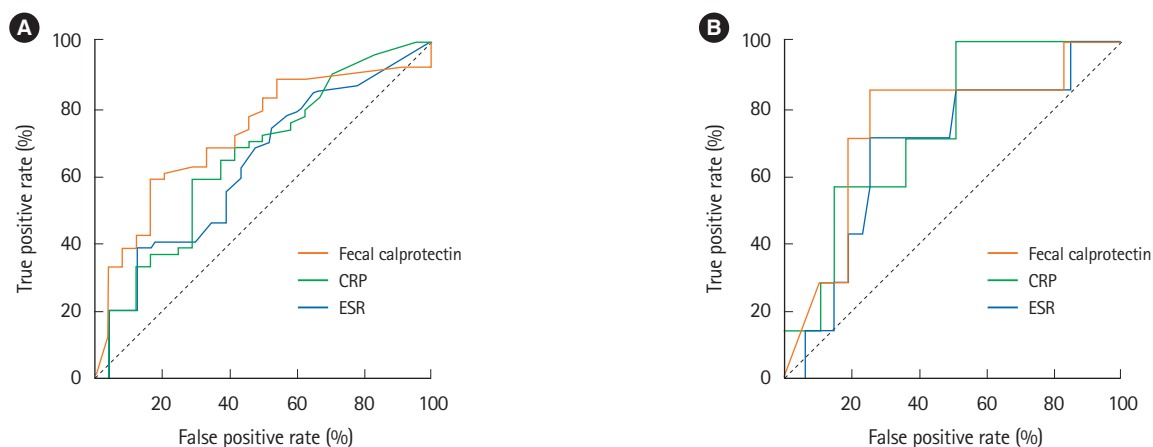


Fig. 4. Receiver operating characteristic (ROC) curves for predicting disease severity in intestinal Behçet's disease. (A) Fecal calprotectin level showed the highest diagnostic performance in predicting endoscopically active disease (area under the ROC curve [AUC] = 0.724, $P=0.002$), compared to C-reactive protein level (CRP; AUC = 0.657, $P=0.028$) and erythrocyte sedimentation rate (ESR; AUC = 0.629, $P=0.074$). (B) Among patients with endoscopically active disease, the fecal calprotectin level demonstrated superior accuracy in predicting large ulcers (≥ 30 mm) (AUC = 0.748, $P=0.036$), compared to the CRP level (AUC = 0.745, $P=0.038$) and ESR (AUC = 0.678, $P=0.132$).

scopically active disease, the sensitivity was 59.3%, and the specificity was 83.3%. The AUC was 0.724 (95% confidence interval [CI], 0.605–0.843; $P=0.002$) (Fig. 4A). In comparison, the CRP level to predict endoscopically active disease yielded an AUC of 0.657 (95% CI, 0.523–0.791; $P=0.028$), whereas ESR had an AUC of 0.629 (95% CI, 0.493–0.766; $P=0.074$). Among these markers, FC had the highest AUC value.

7. Usefulness of the FC Level as a Predictive Biomarker for Ulcer Size in Endoscopically Active Disease

When an FC cutoff of ≥ 543 $\mu\text{g/g}$ was used to predict ulcer sizes measuring ≥ 30 mm in the endoscopically active disease group, the sensitivity and specificity were 85.7% and 74.5%, respectively. The AUC was 0.748 (95% CI, 0.547–0.948; $P=0.036$). In the case of CRP level, the AUC was 0.745 (95% CI, 0.579–0.911; $P=0.038$), lower than that of the FC level (Fig. 4B). However, for ESR, when using ESR to predict ulcer sizes measuring < 30 mm, the AUC was 0.678 (95% CI, 0.472–0.884; $P=0.132$), which was not statistically significant.

DISCUSSION

Our study demonstrated that the FC level is a valuable biomarker of disease activity in patients with intestinal BD. FC levels were significantly correlated with disease activity (DAIBD scores) and CRP levels and were markedly higher in patients with active mucosal ulceration. In contrast, ESR was not significantly associated with endoscopic activity in our

study, underscoring its limited value as a marker of disease activity in intestinal BD. Moreover, FC levels outperformed serum CRP levels in identifying active intestinal lesions, as indicated by a higher AUC in the ROC analysis. These results suggest that FC can serve as a reliable noninvasive surrogate marker for both clinical inflammatory activity and endoscopic severity of intestinal BD.

To the best of our knowledge, this is the first study to propose specific FC cutoff values for predicting endoscopic disease activity and stratifying ulcer severity in intestinal BD. An FC threshold of 176 $\mu\text{g/g}$ best discriminated endoscopically active disease, and FC levels also reflected ulcer size, with levels ≥ 543 $\mu\text{g/g}$ indicating a high likelihood of large destructive ulcers. Defining these objective FC cutoffs is a novel contribution of our study and could be clinically useful for risk stratification. Notably, FC levels did not vary by ulcer location, with similar values observed in patients with small intestinal and colonic ulcers. This suggests that FC levels reflect overall intestinal inflammatory burden regardless of lesion site.

Our findings are consistent with the emerging evidence on the role of FC in intestinal BD. Esatoglu et al.²⁸ reported that fecal (but not serum) calprotectin levels were associated with active gastrointestinal lesions in Behçet's syndrome. Similarly, Özşeker et al.²⁵ noted that patients with BD and subclinical intestinal involvement had higher FC levels than those without gastrointestinal involvement, with FC also correlating with inflammatory markers like CRP and ESR. Our study builds on these observations by quantitatively linking FC level with

graded disease activity and introducing actionable cutoff values for clinical use. Furthermore, when patients were stratified into non-severe (remission, mild, and moderate) and severe disease activity groups, FC levels were significantly higher in the severe group compared to those in the non-severe group ($1,542 \pm 2,326 \mu\text{g/g}$ vs. $666 \pm 1,521 \mu\text{g/g}$; $P=0.024$). This further supports the ability of FC to reflect the clinical disease severity in intestinal BD. The ability of FC levels to reflect the presence and size of ulcers enhances its clinical utility in intestinal BD.

The concept of “treat-to-target” has gained attention in the management of IBD, emphasizing tight control of inflammation with the goal of achieving mucosal healing and improving long-term outcomes.^{29,30} Given the chronic, relapsing nature of intestinal BD and its clinical and endoscopic similarities to CD,⁹ a treat-to-target approach is highly relevant for intestinal BD. In practice, this would entail regular monitoring of disease activity and adjustment of therapy to minimize active inflammation.²⁹ Although endoscopy remains the gold standard for assessing disease activity, its invasiveness and high cost limit its frequent use.³¹ Cross-sectional imaging, such as computed tomography enterography or magnetic resonance enterography, can assess bowel damage and complications but may not reliably detect superficial mucosal inflammation.^{32,33}

In this setting, FC offers distinct advantages as a noninvasive, reproducible, and cost-effective tool that can be measured repeatedly without patient burden. Our findings support its role in capturing mucosal inflammatory activity in intestinal BD, similar to classical IBD; normalization of FC is associated with endoscopic remission in IBD.¹⁷ In our study, the patients in endoscopic remission had low FC levels, whereas those with persistent ulcerations had elevated FC values. This reinforces that FC can serve as a surrogate marker for endoscopic remission and a practical tool for personalizing a treat-to-target strategy in the management of intestinal BD.

Our study has some limitations. First, its retrospective design may have introduced bias in patient selection and data completeness. However, we applied strict inclusion criteria and gathered data in a standardized manner to mitigate this limitation. Second, the sample size (78 patients) was relatively modest, reflecting the rarity of intestinal BD, and the study was conducted at a single tertiary center, which may limit generalizability. Third, the timing of FC measurement relative to endoscopy (within 3 months) may have allowed for changes in disease activity between tests, although we attempted to select the closest possible pairs of colonoscopy and FC measurements. Fourth, unlike CD, there is no validated endoscopic in-

dex—such as the Crohn’s Disease Endoscopic Index of Severity³⁴ or the Simple Endoscopic Scale for Crohn’s Disease³⁵—specifically developed for intestinal BD. Consequently, a direct correlation between FC levels and standardized endoscopic severity scores was not feasible. Finally, longitudinal follow-up data evaluating changes in FC over time in response to treatment or the clinical course were not available. These data could provide further insights into the utility of FC as a monitoring tool for long-term disease management. Despite these limitations, this is the largest study to date evaluating FC in intestinal BD with detailed endoscopic correlation.

In summary, our findings highlight the clinical usefulness of FC as a surrogate marker of disease activity and endoscopic remission in patients with intestinal BD. FC correlates with clinical indices, reflects the presence of active ulcers, and helps gauge ulcer size and severity. Notably, FC showed greater accuracy than CRP in detecting endoscopic activity, emphasizing the value of gut-specific inflammatory markers over traditional systemic markers. Taken together, these results support the incorporation of FC monitoring in the management of intestinal BD to improve disease assessment and guide treatment decisions. Incorporating FC monitoring into the routine care of patients with intestinal BD can aid in the early detection of flares, assessment of endoscopic remission, and adjustment of treatment strategies aimed at achieving remission. The use of FC as part of a treat-to-target approach in intestinal BD has the potential to improve disease control, while reducing the need for frequent invasive evaluations. Future prospective studies with larger cohorts should validate the FC cutoff values identified in this study and determine whether FC-guided therapy can improve long-term outcomes in intestinal BD.

ADDITIONAL INFORMATION

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Conflict of Interest

Park J and Cheon JH are editorial board members of the journal but were not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

Conceptualization: Ahn W, Park J, Cheon JH. Data curation: Choi S, Han SJ, Park SJ, Park JJ, Kim TI. Investigation: all authors. Methodology: all authors. Writing—original draft: Ahn W, Choi S, Han SJ, Park SJ, Park JJ, Kim TI. Writing—review & editing: Ahn W, Park J, Cheon JH. All authors approved the final version for submission.

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