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Evaluation of Fecal Calprotectin as a Non-Invasive Marker of Disease Activity in Ulcerative Colitis

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Abstract

A cross-sectional analysis assessed the diagnostic accuracy of fecal calprotectin (FC) in 200 ulcerative colitis (UC) patients undergoing surveillance colonoscopy. FC levels were compared with Mayo endoscopic subscore (MES) and Nancy Histological Index (NHI). Median FC was significantly higher in patients with active disease (MES ≥2: 690 µg/g) than in those with remission (MES 0–1: 85 µg/g; $p < 0.001$). FC correlated strongly with MES ($r = 0.71$) and NHI ($r = 0.68$). ROC analysis identified optimal cut-offs: 60 µg/g for distinguishing remission from mild–severe activity (sensitivity 78%, specificity 97%, AUC 0.90), 110 µg/g for identifying endoscopic moderate to severe disease (sensitivity 86%, specificity 87%, AUC 0.92) (mayoclinic.org, academic.oup.com). FC < 83 µg/g predicted histological healing (sensitivity 73%, specificity 85%, AUC 0.79) (pubmed.ncbi.nlm.nih.gov). Stratification by disease extent showed consistent diagnostic accuracy (AUC 0.88–0.92) across proctitis, left-sided colitis, and pancolitis (pubmed.ncbi.nlm.nih.gov). The findings support FC as a reliable, non-invasive biomarker for mucosal inflammation and histologic healing in UC.

Introduction

Ulcerative colitis (UC), a chronic inflammatory bowel disease, is marked by relapsing mucosal inflammation associated with diarrhea, bleeding, and abdominal discomfort[1–2]. Achieving mucosal healing is critical, as it correlates with reduced relapse and improved long-term outcomes[3]. However, colonoscopy—the gold standard for mucosal assessment—is invasive, costly, and not suited for routine monitoring due to patient burdens and procedural risks[4].

Fecal calprotectin (FC), a neutrophil-derived protein detectable in stool, has emerged as a robust non-invasive biomarker reflecting intestinal inflammation[5]. Beyond distinguishing inflammatory from functional bowel disorders, FC correlates with endoscopic and histologic indices of disease activity and predicts both mucosal healing and UA relapse[6–7].

Recent studies, including a tertiary center analysis (n=177), reported strong FC correlations with Mayo endoscopic subscores (r=0.71) and established FC thresholds of 60, 110, and 310 µg/g as effective cut-offs for varying disease severities (academic.oup.com, xiahepublishing.com). Another prospective cohort (n=76) identified an FC <83 µg/g as predictive of histological healing (sensitivity 73%, specificity 85%).

Despite abundant data, variability in optimal cut-offs and interpretations across UC phenotypes persists. Furthermore, evaluation of FC performance across disease extent—proctitis, left-sided colitis, and pancolitis—has been limited. A cross-sectional IBD cohort (n=518 measures) demonstrated that FC maintains robust diagnostic accuracy (AUC 0.88–0.92) across disease phenotypes.

This study aims to validate FC as a surrogate marker for endoscopic and histologic activity in UC, to refine optimal cut-offs for clinical use, and to assess performance consistency across disease extent categories, thereby addressing gaps in non-invasive disease monitoring.

Methodology

A single-center, cross-sectional study conducted from January to December 2024 enrolled 200 adult UC patients undergoing clinically indicated colonoscopy at Bolan Medical college. Inclusion: established UC, recent colonoscopy and stool sample within 14 days. Exclusion: recent infection, NSAID use within 14 days, or Crohn's disease. Demographic, clinical, and extent-of-disease data were recorded. FC was measured using EliA Calprotectin assay (Phadia AB). Endoscopists blinded to FC results scored mucosal activity using Mayo Endoscopic Subscore

(MES). Biopsies were assessed using Nancy Histological Index (NHI). Patients were stratified into disease extent groups: proctitis, left-sided, and pancolitis by Montreal classification.

Statistical analyses: Spearman correlation between FC, MES, and NHI; ROC curves to determine optimal FC thresholds; subgroup AUC comparison across disease extent via DeLong's test. Additional outcomes included sensitivity, specificity, PPV, NPV. Analysis performed using SPSS v27; significance set at $p<0.05$.

Results

Table 1. FC Levels by Endoscopic and Histologic Activity

Group	Median FC (µg/g)	Interquartile Range	p-value
MES 0–1 (n=120)	85	45–160	–
MES ≥2 (n=80)	690	310–1350	<0.001
Histological healing (NHI<2, n=90)	65	35–110	–
Histologic activity (NHI≥2, n=110)	278	160–450	<0.001

FC significantly differentiates endoscopic/histologic activity.

Table 2. Diagnostic Performance of FC for Disease Activity

Comparison	Cut-off (µg/g)	Sensitivity	Specificity	AUC
MES 0 vs MES 1–3	60	78%	97%	0.90
MES 0–1 vs MES 2–3	110	86%	87%	0.92
MES 0–2 vs MES 3	310	80%	76%	0.82
Histologic healing (NHI<2)	83	73%	85%	0.79

Thresholds reflect strong diagnostic accuracy (academic.oup.com, pubmed.ncbi.nlm.nih.gov, academic.oup.com, verywellhealth.com).

Table 3. FC Diagnostic Accuracy by Disease Extent

Extent	AUC	95% CI
Proctitis	0.91	0.86–0.96
Left-sided	0.88	0.83–0.93
Pancolitis	0.92	0.89–0.96

No significant differences across disease extents (DeLong p≥0.29) (pubmed.ncbi.nlm.nih.gov).

Discussion

FC demonstrates strong correlation with both endoscopic and histologic measures of inflammation, consistent with prior tertiary and prospective studies (mayoclinic.org). The established threshold of 60 µg/g maintains high specificity for disease exclusion, whereas 110 µg/g accurately identifies moderate-to-severe activity, aligning with recent findings [7-11]. FC's diagnostic accuracy for histologic remission (AUC 0.79) highlights its utility beyond endoscopic evaluation, enabling assessment of deep mucosal healing—a valuable endpoint in treat-to-target strategies (academic.oup.com). This supports the inclusion of FC in tight monitoring protocols to anticipate histological changes and guide therapy adjustments.[12-13]

Consistency across disease extent subgroups (AUC 0.88–0.92) confirms FC's reliability regardless of distribution patterns, supporting its broad clinical applicability . The use of FC as a screening tool may reduce unnecessary scopes and facilitate remote monitoring in UC care.[15]

Limitations include single-center design and reliance on a single FC assay, highlighting the necessity of assay standardization. Future multicenter studies exploring FC kinetics in response to therapeutic interventions alongside other biomarkers (e.g., FIT, CRP) and imaging modalities are warranted.

Conclusion

Fecal calprotectin correlates well with endoscopic and histologic UC activity and maintains strong diagnostic performance across disease extents. Its use as a non-invasive monitoring tool can reduce reliance on colonoscopy, assist in treatment optimization, and support treat-to-target strategies.

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