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# Beyond mucosal healing: fecal calprotectin and the path toward histologic remission in ulcerative colitis

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**Article:** Predictive accuracy of fecal calprotectin for histologic remission in ulcerative colitis **(Intest Res 2025;23:144-156)**

Ulcerative colitis (UC) management has evolved with increasing emphasis on achieving not only symptomatic control but also endoscopic remission, which is currently recognized as a formal therapeutic target.[1] According to the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE)-II recommendations, treatment targets in UC should be viewed as a continuum encompassing short-term (symptomatic response/remission), intermediate (normalization of inflammatory biomarkers such as C-reactive protein and fecal calprotectin [FC]), and long-term goals (endoscopic healing and restoration of quality of life).[1] Although histologic healing is not yet established as a routine clinical endpoint, it is increasingly regarded as an important target due to its association with reduced relapse rates, lower corticosteroid use, and fewer long-term complications.[2,3] While there are no randomized controlled trials specifically evaluating treat-to-target strategies in UC, indirect evidence from Crohn's disease—notably the CALM study—demonstrates that a tight control strategy incorporating both symptoms and biomarkers is more effective than symptom-driven care alone in achieving deep remission. This, in turn, leads to a lower risk of complications, surgery, and hospitalization.[4] However, the degree of correlation among clinical symptoms, biomarkers, and endoscopic healing remains uncertain. Also, in routine clinical practice, repeated endoscopic assessments are invasive, costly, and may be impractical. Therefore, there is an important need to determine whether noninvasive biomarkers can serve as accurate and reliable surrogates for mucosal inflammation, and be suitable for implementation in UC care pathways.[5]

Among noninvasive biomarkers, FC has demonstrated reasonable utility in predicting mucosal healing, especially at levels below 150 μg/g.[6] However, the optimal cutoff for predicting histologic remission remains undefined. Furthermore, among the various histologic indices used in UC—such as the Geboes Score (GS), Nancy Index (NI), and Robarts Histopathology Index (RHI)—it is not yet clear which best correlates with clinical symptoms, endoscopic findings, or biomarkers.[3,7]

In the current issue of *Intestinal Research*, Singh et al.[8] evaluated the predictive performance of FC for histologic remission in a prospective cohort of 347 patients with UC. The authors compared four histologic scoring systems—GS, continuous GS, NI, and RHI—and found high concordance among them. Importantly, they demonstrated that FC levels below 100 μg/g predicted histologic remission with ≥85% accuracy across all indices. This study provides robust evidence supporting the role of FC as a surrogate marker for histologic remission, particularly when applying stringent thresholds. The strength of correlation between FC and histologic indices was stronger than that with clinical or endoscopic measures, echoing findings from prior meta-analyses.[9] Notably, the data also suggest that histologic remission may precede endoscopic healing,

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challenging the traditional concept of mucosal healing hierarchy and underscoring the need for further longitudinal validation.[10]

By validating FC thresholds against multiple histologic indices, this study strengthens the role of FC as a key component of treat-to-target strategies in UC,[1] particularly by supporting its use as a surrogate marker for histologic remission. Such an approach may reduce the need for frequent invasive assessments and help advance a more patient-centered, efficient UC management paradigm. While the single-center design and the lack of longitudinal follow-up are limitations, the clinical implications are compelling. Future studies should aim to validate these findings in multicenter, longitudinal cohorts and evaluate their relevance in predicting long-term outcomes such as relapse, hospitalization, and colectomy.[9]

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