

Advancing transmural remission as a treatment target in Crohn's disease: The future of tight-control strategy?

Crohn's disease (CD), a chronic inflammatory bowel disease (IBD), is an ongoing clinical challenge. Tight disease monitoring is increasingly recognized as a key strategy to achieve optimal disease control.¹ In addition, therapeutic goals in CD have evolved greatly in recent decades to include not only clinical remission but also endoscopic mucosal healing, and more recently even transmural healing (TH).^{2,3} Indeed, considering that transmural damage constitutes a hallmark of CD, it might be more suitable to target TH as assessed through intestinal ultrasonography (IUS) or magnetic resonance enterography (MRE) rather than mere mucosal healing. Of note, TH is emerging as a promising benchmark associated with improved patient outcomes,² including reduced hospitalizations, surgeries, steroid dependency, and treatment escalation.^{4–6} Unfortunately, a commonly validated definition of TH is not yet available. To overcome this limitation, an expert consensus on behalf of the International Bowel Ultrasound [IBUS] Group proposed a definition of TH including bowel wall thickness ≤ 3 mm and the absence of vascular signals on Doppler.⁷ Achieving transmural remission has proven challenging, with no more than 50% of CD patients reaching this milestone, even after advanced therapies,^{8,9} and less than 30% in real-life studies. A recent study by Fernandes et al.¹⁰ takes a significant step in elucidating the potential of a tight-control strategy to optimize CD management to achieve TH. The study underscores that a "tight control" strategy, guided by fecal calprotectin (FC) monitoring and reactive treatment escalation, significantly enhances the rates of transmural remission. The robustness of the study is bolstered by the concurrent use of various investigative modalities, including colonoscopy, MRE, and FC. Patients who experienced an augmented rate of treatment escalation following abnormal FC results were significantly more likely to achieve TH. This implies that adopting a proactive approach to monitoring and adapting treatment in response to biomarker fluctuations may lead to improved clinical outcomes. Notably, the study highlights the importance of early intervention. Patients with early-stage CD, defined as a disease duration of less than 18 months without prior treatment with immunomodulators and biologics, benefited most from this tight-control strategy.¹¹ Implementing a tight-control strategy necessitates frequent assessments of FC and other imaging investigations, possibly incurring additional costs. However, while

this approach may entail elevated monitoring and treatment costs in the short term, it has the potential to yield substantial cost savings by preventing disease progression and complications in the long run.¹² Indeed, these upfront costs should be juxtaposed with the potential benefits. The primary benefit of the tight-control strategy lies in its capacity to promptly identify disease flares and inflammation. Timely intervention enables clinicians to arrest disease progression and mitigate the necessity for more intensive treatments, hospitalizations, and surgeries. The economic benefits associated with averting these severe consequences can be substantial. Moreover, when disease activity is closely monitored, treatment adjustments can be tailored to the patient's immediate needs curtailing the unnecessary use of medications and healthcare resources. Beyond cost considerations, patient-centered outcomes such as improved quality of life, reduced disease burden, and increased productivity should be included in the overarching societal cost-benefit assessment. While considering the advantages of a tight-control strategy based on TH, it is imperative to acknowledge its limitations. Various tools allow the evaluation of TH including MRE, IUS, and computed tomography (CT) scans. Comparative studies showed that IUS and MRE have comparable accuracy while avoiding the radiation risk associated with CT scans.^{13,14} However, there is no evidence comparing the outcomes of patients monitored closely using different tools. Importantly, IUS could be the most appropriate method for this approach. IUS stands out as a patient-centric, user-friendly, noninvasive, real-time tool ideally suited for clinical decision-making in IBD practice.¹⁵ IUS not only allows the assessment of disease activity and response to treatment but also predicts long-term endoscopic activity of disease.¹⁶ Furthermore, its diagnostic accuracy approaches that of more elaborate conventional radiological examinations like MRE.^{17,18} It is worth noting that other studies have already demonstrated the efficacy of clinical decision-making involving IUS findings in reducing inflammation in patients with IBD,¹⁹ and IUS is increasingly finding application in CD management,^{20–22} underscoring its potential utility as a pivotal tool in striving for transmural remission. Inflammatory bowel disease gastroenterologists should be encouraged to consider transmural remission as a viable treatment goal for CD management. A close monitoring strategy including tight monitoring and prompt

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treatment adjustment could lead to more favorable long-term outcomes. Nevertheless, discrepancies exist between clinical, endoscopic, and transmural activity in patients with CD.²³ For this reason, as also hypothesized in ulcerative colitis, the achievement of an increasingly deep remission that simultaneously includes clinical, endoscopic, and transmural disease activity could be associated with improved disease control and patients' quality of life.²⁴


KEYWORDS

Crohn's disease, inflammatory bowel disease, intestinal ultrasound, tight control, transmural remission

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

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DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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