Gastroenterology 2023;165:1367–1399

GUIDELINES

AGA Clinical Practice Guideline on the Role of Biomarkers for the Management of Crohn's Disease

Ashwin N. Ananthakrishnan,[1,*] **Jeremy Adler**,[2,3,*] **Karen A. Chachu**,[4,*] Nghia H. Nguyen,[5] Shazia M. Siddique,[6,7] Jennifer M. Weiss,[8] Shahnaz Sultan,[9] Fernando S. Velayos,[10] Benjamin L. Cohen,[11] and Siddharth Singh,[12,13] on behalf of the AGA Clinical Guidelines Committee*

[1]Division of Gastroenterology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; [2]Division of Pediatric Gastroenterology, C.S. Mott Children's Hospital, Michigan Medicine, University of Michigan, Ann Arbor, Michigan; [3]Susan B. Meister Child Health Evaluation and Research Center, University of Michigan, Ann Arbor, Michigan; [4]Division of Gastroenterology, Department of Medicine, Duke University, Durham, North Carolina; [5]Division of Gastroenterology, Kaiser Permanente Medical Group, Riverside, California; [6]Division of Gastroenterology, Department of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania; [7]Center for Evidence-Based Practice, University of Pennsylvania Health System, Philadelphia, Pennsylvania; [8]Division of Gastroenterology and Hepatology, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin; [9]Division of Gastroenterology, Hepatology, and Nutrition, University of Minnesota, Minneapolis, Minnesota, and Veterans Affairs Healthcare System, Minneapolis, Minnesota; [10]Division of Gastroenterology, Kaiser Permanente Medical Group, San Francisco, California; [11]Division of Gastroenterology, Hepatology, and Nutrition, Digestive Disease Institute, Cleveland Clinic, Cleveland, Ohio; [12]Division of Gastroenterology and Hepatology, University of California San Diego, La Jolla, California; and [13]Division of Biomedical Informatics, Department of Medicine, University of California San Diego, La Jolla, California

BACKGROUND & AIMS: Biomarkers are used frequently for evaluation and monitoring of patients with Crohn's disease (CD). This American Gastroenterological Association (AGA) guideline is intended to support practitioners in decisions about the use of biomarkers for the management of CD. **METHODS:** A multidisciplinary panel of content experts and guideline methodologists used the Grading of Recommendations Assessment, Development and Evaluation framework to formulate patient-centered clinical questions and review evidence on the performance of fecal calprotectin, serum C-reactive protein (CRP), and Endoscopic Healing Index in patients with established CD who were asymptomatic, had symptoms of varying severity, or were in surgically induced remission. Biomarker performance was assessed against the gold standard of endoscopic activity, defined as a Simple Endoscopic Score for Crohn's Disease $\geq$3. The panel used the Grading of Recommendations Assessment, Development and Evaluation Evidence-to-Decision framework to develop recommendations for use of biomarkers in various settings. Implementation considerations were formulated for each recommendation to inform clinical practice. **RESULTS:** The guideline panel made 11 conditional recommendations. In patients with CD in symptomatic remission, the panel suggests use of a biomarker- and symptom-based monitoring strategy over symptoms alone. In patients in symptomatic remission, a fecal calprotectin $<$150 μg/g and normal CRP rules out active inflammation, avoiding endoscopic evaluation for assessment of disease activity. However, elevated biomarkers in this setting merit confirmation with endoscopy before treatment adjustment. In patients with CD with mild symptoms, neither normal nor elevated biomarkers alone are sufficiently accurate to determine endoscopic activity. In patients with CD with moderate to severe symptoms, elevated fecal calprotectin or serum CRP suggests endoscopic activity, precluding routine endoscopic assessment for disease activity. In patients with CD in surgically induced remission in low-risk patients on pharmacologic prophylaxis, a normal fecal calprotectin reliably rules out endoscopic recurrence. In other postoperative settings, the panel suggests endoscopic assessment for establishing postoperative recurrence. **CONCLUSIONS:** In patients with CD, fecal calprotectin and serum CRP can inform disease management in both asymptomatic and symptomatic disease. Discordance between symptom assessment and biomarker value may merit endoscopic evaluation for confirmation of status of disease activity.

Keywords: Inflammatory Bowel Disease; Monitoring; Endoscopic Remission; Treat to Target; Evidence Synthesis.

Inflammatory bowel diseases (IBDs), comprising Crohn's disease (CD) and ulcerative colitis (UC), are rising in incidence and prevalence worldwide.[1,2] They often have an onset in young adulthood and are characterized by a protracted relapsing–remitting course with progressive permanent bowel damage.[3] The therapeutic armamentarium for CD has expanded over the past decade with multiple new mechanisms of action. Despite such progress,

*Authors share co-first authorship.

Abbreviations used in this paper: **AGA, American Gastroenterological Association; AP, abdominal pain; CD, Crohn's disease; CDEIS, Crohn's Disease Endoscopic Index of Severity; CRP, C-reactive protein; EHI, Endoscopic Healing Index; FN, false negative; FP, false positive; GRADE, Grading of Recommendations Assessment, Development and Evaluation; IBD, inflammatory bowel disease; PRO2, 2-item patient-reported outcomes; PRO3, 3-item patient-reported outcomes; RCT, randomized controlled trial; SES-CD, Simple Endoscopic Score for Crohn's Disease; TN, true negative; TP, true positive; UC, ulcerative colitis.**

Most current article

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2023.09.029