JAMA Clinical Guidelines Synopsis

Diagnosis and Management of Crohn Disease

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GUIDELINE TITLE ACG Clinical Guideline: Management of Crohn's Disease in Adults

RELEASE DATE March 27, 2018

PRIOR VERSION February 2009

DEVELOPER American College of Gastroenterology (ACG)

FUNDING SOURCE ACG

TARGET POPULATION Adult patients with Crohn disease

MAJOR RECOMMENDATIONS

- Fecal calprotectin should be considered to help differentiate the presence of inflammatory bowel disease from irritable bowel syndrome (strong recommendation; moderate level of evidence).
- Oral mesalamine should not be used to treat patients with active Crohn disease (strong recommendation; moderate level of evidence).
- Anti–tumor necrosis factor (TNF) agents (infliximab, adalimumab, certolizumab pegol) should be used to treat Crohn disease that is resistant to treatment with corticosteroids or requires ongoing steroid therapy (strong recommendation; moderate level of evidence).
- Combination therapy of infliximab with immunomodulators (thiopurines) is more effective than treatment with either immunomodulators alone or infliximab alone in patients who have not received these agents in the past (strong recommendation; high level of evidence).
- For patients with moderately to severely active Crohn disease and objective evidence of active disease, anti-integrin therapy (with vedolizumab) with or without an immunomodulator should be considered to induce remission (strong recommendation; high level of evidence).

Summary of the Clinical Problem

Crohn disease is a chronic inflammatory disease that can affect any portion of the gastrointestinal tract. The incidence and prevalence of Crohn disease is increasing worldwide and will result in an increase in the number of primary care physicians who will provide care for patients with this condition. There are also new diagnostic tools, better understanding of factors that modify disease activity, and novel therapeutics available to treating physicians.

Characteristics of the Guideline Source

This guideline was developed and funded by the ACG.[1] The ACG commissioned a task force of 6 board-certified gastroenterologists with expertise in diagnosis and management of Crohn disease in adults, 5 of whom disclosed potential conflicts of interest, which did not prevent participation in the writing process. The literature searches used to support the guideline were limited to primary clinical trials, meta-analyses, systematic reviews, and prior guidelines. A GRADE approach was used to assess the quality of the evidence. Limitations of available research were discussed and incorporated into the strength of the recommendation (**Table**).

Evidence Base

This guideline has 60 graded recommendations based on clinical trial data and 53 summary statements (provided when trial data were not available). The recommendations covered in this synopsis were chosen for their broad clinical relevance. The guideline suggests that fecal calprotectin is useful for diagnosing Crohn disease among patients in whom both inflammatory bowel disease and irritable bowel syndrome are being considered. A recent meta-analysis reported a pooled fecal calprotectin sensitivity of 93% (95% CI, 0.85%-0.97%) and specificity of 96% (95% CI, 0.79%-0.99%).[2]

The guidelines suggest that oral mesalamine should not be used to treat patients with active Crohn disease because of lack of empirical evidence supporting its efficacy. A 2011 meta-analysis of 4 randomized clinical trials did not demonstrate a benefit of mesalamine over placebo (relative risk [RR], 0.91; 95% CI, 0.77-1.06).[3] The authors of the guidelines also do not recommend use of mesalamine as a long-term treatment in patients with Crohn disease as it has not been shown to be effective for maintenance of remission.

This guideline recommends the use of anti-TNF agents to treat corticosteroid-resistant Crohn disease. A meta-analysis of 9 studies found that infliximab maintains clinical remission (RR, 2.50; 95% CI, 1.64-3.80) and leads to a clinical response (RR, 1.66; 95% CI, 1.00-2.76) in patients with a response to infliximab induction therapy vs

Table. Guideline Rating

Standard	Rating
Establishing transparency	Good
Management of conflict of interest in the guideline development group	Fair
Guideline development group composition	Fair
Clinical practice guideline–systematic review intersection	Fair
Establishing evidence foundations and rating strength for each of the guideline recommendations	Good
Articulation of recommendations	Good
External review	Good
Updating	Good
Implementation issues	Good

those who did not receive infliximab. Similarly, the meta-analysis found that adalimumab and certolizumab also maintain clinical remission in patients who had responded to these therapies (RRs, 2.86 [95% CI, 2.01-4.02] and 1.68 [95% CI, 1.30-2.16], respectively).[4] Combination therapy with anti-TNF agents and immunomodulators (thiopurines) is preferred for patients who do not have risk factors precluding their use, as studies have shown that combination therapy reduces immunogenicity.[5]

The guideline makes a strong recommendation, based on a high level of evidence, that anti-integrin therapies (such as vedolizumab) be considered for patients with moderately to severely active Crohn disease. A recent randomized trial conducted in 39 countries found that 39% of patients assigned to vedolizumab every 8 weeks were in clinical remission at week 52 vs 21.6% in the placebo group ($P < .001$).[6] However, the study also found that serious adverse effects and infections were more common in the vedolizumab group.

Benefits and Harms

The updated guideline has the potential to promote use of more accurate diagnostic tools, evidence-based treatments, and improved health outcomes for patients. The guideline authors discourage use of therapies lacking high-quality evidence, potentially reducing costs and adverse effects related to use of ineffective medications. The potential harms of this guideline include promotion of expensive therapies that may be unavailable to some patients. The novel agents, including the anti-TNF agents, vedolizumab, and ustekinumab, that are supported in this guideline also have the potential to cause harm. The medications discussed above have been associated with both rare (lymphoma, progressive multifocal leukoencephalopathy, and opportunistic infections) and more common (upper respiratory tract infections, urinary tract infections, and infusion reactions) adverse events.

Discussion

Management of Crohn disease has evolved substantially since the last ACG guideline was issued in 2009. Previously, Crohn disease treatment involved a step-up model in which patients were first prescribed a corticosteroid, then an immune modulator, and finally a biologic agent if previous steps failed. Up to 30% of patients with Crohn disease have mild disease that will not progress and do not need a biologic agent. The current treatment recommendations are limited because the comparative efficacy of various treatments, including the novel interleukin 12 and 23 inhibitor ustekinumab, is not known.

Areas in Need of Future Study or Ongoing Research

This guideline acknowledges the difficulty of predicting which patients will respond to specific treatments. The ability to use risk factors and biomarkers to predict response could result in improved outcomes and more cost-efficient care. Further research is needed focusing on the role of the microbiome in Crohn disease and whether fecal microbiota transplants are effective therapy.[7] As novel therapies are developed, the importance of tailoring treatment algorithms will become even greater, highlighting the need for testing the comparative efficacy of the various treatments.

Related guidelines

American Gastroenterological Association Institute Guideline on the Management of Crohn's Disease After Surgical Resection

ECCO-ESGAR Guideline for Diagnostic Assessment in IBD

ARTICLE INFORMATION

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Correction: This article was corrected on May 30, 2019, for incorrect comma placement in a sentence.

Conflict of Interest Disclosures: None reported.

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