

Periodic cross-sectional imaging (CTE, MRE) may be considered in monitoring response to therapy in certain patients with small bowel Crohn's disease (Summary Statement).

MR inflammatory scores have been developed that may allow for serial MRI to determine response to therapy (127,128). Improvement in MR inflammatory scores correlates with clinical improvement in patients treated with infliximab (129). It has also been demonstrated that an improvement in MRE and CTE inflammatory parameters is associated with a decrease in hospitalizations, surgery, and steroid requirements in patients with small bowel CD (98). The ability to examine the entire bowel wall for changes associated with inflammation is advantageous in populations of patients who cannot be assessed endoscopically (e.g., patients with primarily small intestinal involvement). Small bowel ultrasound has been used largely outside the United States for evaluation of CD. It has been used to assist in the diagnosis of CD, for detection of extramural complications, for the detection and evaluation of stenotic strictures, and for follow-up of the disease course.

Mucosal healing as determined by endoscopy is a goal of therapy (Summary Statement).

- *Endoscopic scores have been developed that are reliable in measuring degree of mucosal healing and may be used to monitor response to therapy.*
- *Evaluation of the ileum for postoperative endoscopic recurrence by colonoscopy within a year after ileocolonic resection may help guide further therapy.*

Mucosal healing has become an important target in assessing efficacy of treatment for IBD. In patients with CD, mucosal healing is defined as an absence of ulceration and endoscopic scoring systems have been developed to quantify degree of ulceration and inflammation in patients with CD within the reach of the colonoscope (130). There are a limited number of studies that have examined the long-term impact of mucosal healing on the clinical course of disease. In patients with early-stage CD, complete mucosal healing after 2 years of therapy predicts sustained steroid-free, clinical remission 3 and 4 years out from initiation of treatment (131). Other clinical outcomes associated with mucosal healing in CD have been decreased surgery and hospitalizations (132). The SES-CD (57) scoring system has been used prospectively to assess mucosal healing in patients treated with anti-tumor necrosis factor (anti-TNF) therapy as well as with anti-TNF/thiopurines combination therapy, demonstrating that changes can be measured; furthermore, there is a strong correlation between improvement in the SES-CD (mucosal) healing and clinical remission (133,134). In the patient who has undergone an ileocolonic resection, assessment of endoscopic lesions just proximal to the anastomosis appears to identify patients who are likely to have a clinical recurrence of CD (135). This endoscopic activity score is known as the Rutgeerts' score and has become widely used in the assessment of postoperative patients (136) (**Supplementary Information** online).

Disease modifiers

Recommendations

6. Nonsteroidal anti-inflammatory drugs (NSAIDs) may exacerbate disease activity and should be avoided when possible in patients with Crohn's disease (strong recommendation, low level of evidence).

There are numerous case reports and observational studies that suggest that use of NSAIDs in patients with CD are associated with IBD flares. NSAIDs have been documented to damage the mucosa of the small intestine distal to the duodenum with ulcerations, erosions, and webs. Mucosal permeability is increased with NSAID therapy leading to increased exposure to luminal toxins and antigens (137). In a comparison study of acetaminophen, naproxen, nabumetone, nimesulide, and aspirin, there was a 17–28% relapse rate of quiescent IBD within 9 days of therapy with the nonselective NSAIDs (naproxen and nabumetone) (138). Recent NSAID use has been associated with an increased risk of emergency admission to the hospital for patients with IBD (139,140). There have been other studies that have not found this association (141). Selective cyclooxygenase-2 inhibitors in short-term therapy have not been shown to exacerbate ulcerative colitis, but similar studies have not been performed in CD (142).

Recommendations

7. Cigarette smoking exacerbates disease activity and accelerates disease recurrence and should be avoided. Active smoking cessation programs should be encouraged (strong recommendation, low level of evidence).

Cigarette smoking has been shown in multiple clinical situations to have an adverse effect on disease activity in CD. There is an increased rate of surgical intervention, incidence of IBD hospitalizations, and peripheral arthritis in patients with CD who smoke as compared with those who do not smoke (143,144). Active smoking has been associated with a penetrating phenotype in CD (145). Active smoking increases the risk of relapse after discontinuation of anti-TNF therapy (146). Patients with CD who stop smoking have decreased flares in disease activity and a decreased need for steroids and immunomodulatory therapy (147).

Recommendations

8. Usage of antibiotics should not be restricted in Crohn's disease patients in order to prevent disease flares (Conditional recommendation, very low level of evidence).

The intestinal microbiome is thought to play a role in the pathogenesis of IBD. Disruption of the intestinal microbiota or dysbiosis may be detrimental in terms of stimulation of the immune system in patients with IBD. It has been shown that dysbiosis is associated with increased intestinal inflammation (148). Antibiotic effects on the gut often lead to symptoms that are indistinguishable from IBD, including diarrhea and abdominal cramping (137). In a large case–crossover study using the General Practice Research Database from 1989 to 1997, exposure to antibiotics within 60 days was