ULCERATIVE COLITIS GUIDELINES (Part 1 of 2)

These guidelines are the preferred approach to the management of adults with ulcerative colitis (UC) and represent the official practice recommendations of the American College of Gastroenterology (ACG).

DIAGNOSIS

- Suspect UC in patients with hematochezia and urgency
- Exclude infectious etiologies at time of diagnosis. Test stool to rule out *C. difficile*
- Confirm diagnosis by obtaining colonoscopy with intubation of the ileum and biopsies of affected and unaffected areas by a trained pathologist[1]
- Determine extent of disease to guide therapy, such as:
  - — proctitis[2]
  - — left-sided colitis[3]
  - — extensive colitis[4]
- Define disease severity (mildly, moderately, or severely active disease) to guide therapy, based on:
  - — patient-reported outcomes (PROs): bleeding and normalization of bowel habits
  - — inflammatory burden (endoscopic assessment, including extent and severity and markers of inflammation)
  - — disease course (need for hospitalization or steroids and failure to respond to medications)
  - — disease impact (functionality and quality of life)
- May use fecal calprotectin (FC) as a noninvasive marker of disease activity and to assess response to therapy and relapse
- Avoid serologic antibody testing to establish or rule out diagnosis of UC or to determine prognosis

GOALS OF MANAGEMENT

- Treat to achieve mucosal healing[5] to increase likelihood of sustained steroid-free remission and prevent hospitalizations and surgery
- Initial treatment should focus on restoration of normal bowel frequency and control of the primary symptoms of bleeding and urgency
- Prevent and monitor for disease-related and drug-related complications
- Establish routine visits to monitor for relapse and address health maintenance needs
- Screen for coexistent anxiety and depressive disorders, and when identified, provide patients with resources to address these conditions

TREATMENT[6]

Mildly Active Disease

Disease extent	Induction[7]	Maintenance[8]
Proctitis	Rectal 5-aminosalicylate (5-ASA) 1g/day	Rectal 5-aminosalicylate (5-ASA) 1g/day
Left-sided colitis	• Rectal 5-ASA ≥1g/day preferred over rectal steroids • Rectal 5-ASA ≥1g/day combined with oral 5-ASA ≥2g/day[9] preferred over oral 5-ASA alone • Intolerant or nonresponsive to oral/rectal 5-ASA: oral budesonide multi-matrix (MMX) 9mg/day	Oral 5-ASA ≥2g/day[9]
Extensive colitis	Oral 5-ASA ≥2g/day[9]	Oral 5-ASA ≥2g/day[9]
UC of any extent with failed response to 5-ASA	Oral systemic corticosteroids[8]	
Failure to reach remission with 5-ASA	Consider alternate therapeutic classes (changing to alternate 5-ASA formulation is not recommended)	
Mildly to moderately active UC nonresponsive to oral 5-ASA	Add budesonide MMX 9mg/day	
With poor prognostic factors[10]	Treat with therapies for moderately to severely active disease	

Moderately to Severely Active Disease[11]

Induction	Maintenance[8,15]
• Moderately active only: — Oral budesonide MMX 9mg/day — 5-ASA[9] could be used as monotherapy • Oral systemic corticosteroids • Anti-TNF therapy:[12,13] adalimumab, golimumab, or infliximab[14] • Vedolizumab • Tofacitinib 10mg orally twice daily for 8wks • Previous failure with anti-TNF therapy: initiate vedolizumab or tofacitinib • Patients with nonresponse or loss of response to therapy should be assessed with therapeutic drug monitoring to identify reason for lack of response and whether to optimize existing therapy or select alternate therapy • Monotherapy with thiopurines or methotrexate not recommended	• Remission after anti-TNF induction: continue adalimumab, golimumab, or infliximab • Remission after vedolizumab induction: continue vedolizumab • Remission after tofacitinib induction: continue tofacitinib • Remission after corticosteroid induction: initiate thiopurines • Patients who have achieved remission but previously failed 5-ASA therapy and are now on anti-TNF therapy, concomitant 5-ASA is not recommended • Methotrexate not recommended • 5-ASA therapy likely not as effective in previously severely active UC compared with previously moderately active

Acute Severe Disease — hospitalized[16,17]

Induction	Maintenance	Surgery
• Methylprednisolone 60mg/day or hydrocortisone 100mg 3 or 4 times/day • Failure with IV corticosteroids by 3-5 days: initiate medical rescue therapy with infliximab or cyclosporine[18]	• Remission with infliximab induction: continue infliximab • Remission with cyclosporine induction: initiate thiopurines or vedolizumab	Indications for surgery: • Toxic megacolon • Colonic perforation • Severe refractory hemorrhage • Refractoriness to medical therapy

(continued)

NOTES

[1] If terminal ileum is normal, further evaluation of stomach and small bowel by upper endoscopy and cross-sectional imaging is not needed unless there are other symptoms or findings to suggest proximal GI involvement or diagnosis of Crohn's Disease rather than UC.

[2] Within 18cm of anal verge, distal to rectosigmoid junction.

[3] Extending from sigmoid to splenic flexure.

[4] Beyond splenic flexure.

[5] Defined as resolution of inflammatory changes (Mayo endoscopic subscore 0 or 1).

[6] Fecal microbiota transplantation and complementary therapies (eg, probiotics, curcumin) require further study as UC treatment.

[7] Response to induction therapy should be assessed within 6wks.

[8] Systemic corticosteroids are not recommended for maintenance of remission.

[9] Oral 5-ASA agents include mesalamine, olsalazine, sulfasalazine. Low dose (2-2.4 g/day) of 5-ASA is recommended over higher dose (4.8 g/day) as no difference in remission rate is seen. In patients with mildly to moderately active UC of any extent using oral 5-ASA to induce remission, dosing can be either once-daily or more frequently, based on patient preference to optimize adherence, as efficacy and safety are no different.

[10] Poor prognostic factors associated with increased risk of hospitalization or surgery include: age <40yrs at diagnosis, extensive colitis, severe endoscopic disease (Mayo endoscopic subscore 3, UCEIS ≥7), hospitalization for colitis, elevated CRP, low serum albumin. Each prognostic factor carries a different weight and must be discussed in a shared decision-making fashion with patient. The greater the number of factors, the worse the prognosis as measured by the likelihood of colectomy.

[11] Consultation with surgeon to consider colectomy is recommended in patients refractory or intolerant to maximal medical therapy.

[12] Patients who have failed 5-ASA therapy and in whom anti-TNF therapy is initiated for induction, 5-ASA therapy should not be used for added clinical efficacy.

[13] Patients who are primary nonresponders to an anti-TNF (lack of therapeutic benefit after induction despite adequate drug levels) should be considered for alternative therapy class rather than alternating to another anti-TNF drug. However, patients who had an initial response, but subsequently lost efficacy to one anti-TNF therapy, alternate anti-TNF therapy is recommended compared to no treatment. Measuring serum drug levels and antibodies (if there is not a therapeutic level) to assess reason for loss of response is recommended.

[14] Combination therapy with a thiopurine is recommended when infliximab is used for induction.

[15] Budesonide MMX has not been studied for maintenance of remission of previously moderately to severely active UC.

[16] Hospitalized patients with acute severe UC (ASUC) should have stool testing to rule out *C. difficile*. Treat concomitant CDI with vancomycin instead of metronidazole.

[17] Routine use of broad-spectrum antibiotics and use of total parenteral nutrition is not recommended. Avoid NSAIDs, opioids, and anticholinergic agents.

[18] Choice between infliximab and cyclosporine should be based on provider experience, history of previous failure of immunomodulator or anti-TNF therapy, and serum albumin.

REFERENCES

Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J of Gastroenterology* 2019;114:384-413. https://doi.org/10.14309/ajg.0000000000000152; published online February 22, 2019.

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