Day-by-Day Management of the Inpatient With Moderate to Severe Inflammatory Bowel Disease

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Abstract: Hospitalization for inflammatory bowel disease is common and requires coordination of care. The goals of hospitalization are to markedly improve symptoms, transition management to an outpatient regimen, and prevent complications. Initially, providers should determine the phenotype and severity of disease flare and provide optimal medical salvage therapy for induction of disease remission. In addition, complications of Crohn's disease and ulcerative colitis should be addressed with testing for *Clostridioides difficile* and cytomegalovirus infections and pharmacologic venous thromboembolism prophylaxis, and early enteral feeding should be encouraged to optimize nutritional status. A standardized daily assessment to determine response to treatment should be performed. Objective measures of response to disease treatment that are measured within 3 to 4 days of hospitalization can predict which patients will benefit from either second-line rescue therapy or surgical intervention. These same measures can be used to determine readiness for hospital discharge. Safe discharge can be optimized with thorough patient education and a comprehensive outpatient follow-up plan.

Inflammatory bowel disease (IBD), specifically ulcerative colitis (UC) and Crohn's disease, is a chronic inflammatory condition of the intestinal tract characterized by abdominal pain, diarrhea, blood in stool, and mucosal ulceration. In at least 20% of patients, a flare necessitates hospitalization and initiation of intravenous corticosteroids.[1,2] Hospitalization is a high-stakes and vulnerable event for patients that carries an increased risk of IBD-related complications and surgery. Despite advances in medical management with biologic therapy, the rate of IBD-associated hospitalization has not uniformly fallen.[3] *Clostridioides difficile* infection, cytomegalovirus infection, toxic megacolon, bowel perforation, venous thromboembolism, malnutrition, and opiate dependence in the setting of

Table 1. Hospital Admission Checklist for the First Day of Admission

History and physical examination

- ❑ IBD history (including initial diagnosis and extent of disease)
- ❑ Current symptoms
- ❑ Medical history (including mental health)
- ❑ Surgical history
- ❑ Family history (focusing on IBD and colorectal cancer)
- ❑ Social history (including smoking, insurance, and employment status)
- ❑ Medication review (including over-the-counter medications, supplements, and recent mesalamine use)

Laboratory evaluation

Assess for disease severity:

- ❑ Complete blood count with differential
- ❑ Complete metabolic panel
- ❑ Erythrocyte sedimentation rate
- ❑ C-reactive protein
- ❑ Albumin

Measure nutritional status:

- ❑ Prealbumin
- ❑ Vitamin D
- ❑ Vitamin B12
- ❑ Iron studies, including ferritin

Evaluate for infection:

- ❑ *Clostridioides difficile* testing
- ❑ Stool culture, stool ova, and parasite testing (or stool PCR-based infectious studies)

Preparation for rescue therapy

- ❑ Place PPD test
- ❑ Obtain hepatitis B virus serologies (surface antigen, surface antibody, core antibody)
- ❑ Obtain TPMT enzyme (if considering thiopurine therapy)
- ❑ Obtain cholesterol panel, pregnancy test, and magnesium (if considering cyclosporine)
- ❑ Weigh patient

Radiographic evaluation

- ❑ Obtain abdominal radiograph at a minimum
- ❑ Obtain CT/MR enterography if there is concern for small bowel Crohn's disease pathology
- ❑ Obtain MR imaging of the pelvis if there is concern for pelvic abscess

Medication review

- ❑ Avoid opiates and anticholinergic medications
- ❑ Order and administer daily pharmacologic venous thromboembolism prophylaxis

Initiation of medical treatment

- ❑ Intravenous methylprednisolone daily (40-60 mg) once infection is ruled out
- ❑ Antibiotics for intra-abdominal or perirectal abscess; interventional consultation for percutaneous drainage
- ❑ Oral vancomycin for *C difficile* infection

CT, computed tomography; IBD, inflammatory bowel disease; MR, magnetic resonance; PCR, polymerase chain reaction; PPD, purified protein derivative; TPMT, thiopurine methyltransferase.

poorly controlled pain are all potential complications.[4,5] Both gastroenterologists and inpatient providers will need to care for these patients with regularity.

Although current treatment guidelines address management of IBD across the entire spectrum of disease, specific recommendations for the management of hospitalized IBD patients are limited.[6-8] Practice patterns for the care of hospitalized IBD patients vary widely.[9] This article provides context on reasons for hospitalization and measures of disease severity and includes a standardized day-by-day workflow and primer for hospitalized patients with moderate to severe IBD.

Reasons for Hospitalization and Measures of Disease Severity

Acute severe UC is a life-threatening condition for which inpatient management is advised.[10] The relevant parameters for making this determination can be summarized in the Truelove and Witts criteria and include more than 6 bowel movements per day, frequent blood in stool, elevated body temperature, tachycardia (>90 beats/min), decreased hemoglobin (<75% normal value), and elevated erythrocyte sedimentation rate (>30 mm/hr), with clinical features such as bowel wall changes or dilation on abdominal radiographs and abdominal tenderness or distension on physical examination.[11] The Simple Clinical Colitis Activity Index can be assessed daily, is entirely based on patient symptoms (daytime and nighttime bowel frequency, urgency, blood in stool, general well-being, and presence of extraintestinal manifestations), and may also be used to assess severity of disease.[12]

The reasons for hospital admission for patients with Crohn's disease are more varied due to the heterogeneous nature of the disease. The Montreal Classification of Crohn's Disease Behavior provides a framework for understanding common reasons for hospitalization for Crohn's disease, such as inflammatory enteritis or colitis, stricturing or obstructive disease, and penetrating complications (eg, intra-abdominal or perianal abscesses, fistulas).[13] The Crohn's Disease Activity Index, which is used to gauge disease activity and severity, may be challenging to use in the inpatient setting, as it requires a recall of symptoms over the last 7 days. The Harvey-Bradshaw Index is a simpler tool that can assess daily symptoms and has good correlation with the Crohn's Disease Activity Index.[14]

Day 1 Recommendations

History and Physical Examination

A careful patient history should include a review of the initial diagnosis, extent of disease, and current symptoms (including all components of the Truelove and Witts score for UC and the Harvey-Bradshaw Index for Crohn's disease). Additional information regarding all medical comorbidities (including mental health), surgical history, and family history focusing on IBD and colorectal cancer, should be obtained. A complete social history, including smoking status and insurance and employment status, is also essential. Lastly, a full medication list review (including herbal supplements and over-the-counter medications) should be performed for medications that may exacerbate IBD.[15] In particular, attention should be paid to recent initiation of 5-aminosalicylic acid products, as these can cause a paradoxical worsening in a small proportion of patients (Table 1).[16]

Physical examination should assess for signs of systemic inflammatory response syndrome (eg, tachycardia, hypotension, fever), hypovolemia, and signs of extraintestinal manifestations (eg, arthritis, rash, asymmetric leg swelling consistent with deep vein thrombosis). Abdominal examination should include assessment of bowel sounds, tenderness to palpation, distension, and the presence of an abdominal mass. Abdominal findings may be masked by administration of opiates; therefore, opiates should be avoided in the acute setting if at all possible. In patients with established or suspected Crohn's disease, a perianal and rectal examination should be performed to assess for perianal abscesses and fistulizing disease.

Laboratory Evaluation

Initial laboratory evaluation should include assessment for disease severity (complete blood count with differential, complete metabolic panel, erythrocyte sedimentation rate, C-reactive protein, and albumin), measures of nutritional status (prealbumin; vitamin D; vitamin B12; and iron studies, including ferritin), and evaluation for infection (infectious stool studies, including testing for *C difficile*; blood cultures if suspicion for abscess is high).

Preparation for Rescue Therapy

Patients with inflammatory disease (eg, acute severe UC, Crohn's colitis, Crohn's ileitis) will likely require corticosteroids as mainstay therapy; however, 30% to 40% of patients with acute severe UC will fail to respond and require second-line or rescue therapy (eg, infliximab, cyclosporine).[17] In preparation for initiation of rescue therapy, testing should be obtained as soon as possible for tuberculosis with a tuberculin skin test (or with quantiFERON [Qiagen] if the turnaround time is <48 hr or if the patient was previously exposed to the Bacillus Calmette–Guérin vaccine); hepatitis B surface antigen, surface antibody, and core antibody; thiopurine methyltransferase enzyme (if thiopurine therapy is being considered); and pregnancy test, cholesterol, and magnesium (if cyclosporine is being considered). If tuberculosis and hepatitis B virus testing

Table 2. Assessment and Plan for Day 2 and Beyond of Hospital Admission

Daily Assessment		
History and physical examination ❑ Assess daytime and nocturnal bowel frequency, urgency, presence of blood in stool, abdominal pain, general well-being ❑ Assess for extraintestinal manifestations, abdominal distension or mass; assess percutaneous drain output daily (if present)		
Laboratory evaluation ❑ Obtain complete blood count, chemistry panel plus albumin, erythrocyte sedimentation rate, C-reactive protein ❑ Follow up with outstanding laboratory results ordered on day of admission. Ensure tuberculin skin test is placed.		
Medication review ❑ Ensure opiates and anticholinergics are minimized ❑ Ensure active pharmacologic venous thromboembolism prophylaxis order and confirm patient received ordered dose		
Nutritional assessment ❑ Encourage oral intake and enteral supplementation as needed ❑ Consider total parenteral nutrition in setting of prolonged bowel obstruction, short gut syndrome, high-output enteral fistula, or perioperative nutritional optimization		
Day 2	**Day 3**	**Day 4 and Beyond**
Perform daily assessment	**Perform daily assessment**	**Perform daily assessment**
Medical treatment ❑ Give second dose of intravenous corticosteroids or continue antibiotics	**Medical treatment** ❑ Give third dose of intravenous corticosteroids or continue antibiotics	**Medical treatment** ❑ Give fourth dose of intravenous corticosteroids or continue antibiotics ❑ Initiate rescue therapy (eg, infliximab, cyclosporine)
Endoscopic evaluation *Ulcerative colitis:* ❑ Perform flexible sigmoidoscopy with biopsy (confirm flare and rule out cytomegalovirus infection) *Crohn's colitis/ileitis without stricturing:* ❑ Perform full colonoscopy if inflammation is distributed beyond reach of sigmoidoscopy	**Assess response to medical treatment** *Ulcerative colitis:* ❑ Calculate Travis and Ho indices *Stricturing Crohn's disease:* ❑ Assess resolution of obstruction by history (tolerating oral intake, passing flatus/stool) *Intra-abdominal/perianal abscess:* ❑ Monitor for decreasing drain output, improved inflammatory laboratory markers, and resolution of sepsis physiology	Continue surgical consultation if patient is not responding to medical rescue therapy
Nutrition ❑ Obtain nutritional consultation ❑ Encourage early enteral feeding	**Preparation for rescue therapy** ❑ Obtain colorectal surgery consultation ❑ Review contraindications and treatment considerations for medical rescue therapy ❑ Discuss risks and benefits of rescue therapy options with patient and initiate if high risk for treatment failure	
Pain management ❑ Discuss strategies for pain management with patient (control inflammation, prescribe acetaminophen or tramadol as needed) ❑ Consider pain consultation for opiate-sparing agents for severe pain		

has been performed in the last 12 months, and the patient has no new risk factors, repeat testing is not needed.[18] A detailed clinical history of tuberculosis risk factors augments tuberculosis screening, as immunosuppression (eg, high-dose corticosteroids) may decrease the precision of tuberculosis testing.[19] The patient should also be weighed for accurate weight-based medication dosing.

Radiographic Evaluation

Patients hospitalized with IBD will often receive radiographic evaluation, usually due to the severity of abdominal pain or concerning findings on physical examination. Relevant findings on a computed tomography scan or plain-film abdominal radiograph include bowel obstruction, dilatation, or free air. In patients with well-established UC without prior concern for indeterminate colitis, a plain-film abdominal radiograph is all that is needed. A computed tomography scan or magnetic resonance imaging can identify intra-abdominal abscesses, fistulizing disease, or stricturing disease.[20,21] Lastly, if a pelvic abscess is suspected, magnetic resonance imaging of the pelvis provides detailed anatomic delineation of the anal sphincter complex to guide further management.[22]

Medication Review

Inpatient medications should be reviewed. In patients with inflammatory disease, opiates and anticholinergic medications should be avoided, as they can increase bowel dilation and precipitate toxic megacolon. Opiates and anticholinergics can mask symptoms and examination findings, making it more difficult to assess the patient's clinical status day by day. Initiation or escalation of opiates in the hospital may also predispose the patient to long-term opiate use and associated morbidity and mortality.[23] Prophylaxis for venous thromboembolism is recommended for all hospitalized patients with IBD, even if rectal bleeding is present (hemorrhagic shock or transfusion dependence being the exceptions).[24,25]

Initiation of Medical Treatment

If infection has been ruled out, initiation of intravenous corticosteroids (equivalent to 40-60 mg of intravenous methylprednisolone)[6,7] is recommended. Broad-spectrum antibiotics should be prescribed for intra-abdominal or perirectal abscesses, and consideration of percutaneous drainage should be pursued. Oral vancomycin should be prescribed for *C difficile* infection when present.

Day 2 Recommendations

Endoscopic Evaluation

All patients with UC or Crohn's colitis or ileitis should undergo endoscopic evaluation with a flexible sigmoidoscopy (UC) or colonoscopy (Crohn's in the absence of stricture) to confirm disease severity and to obtain a biopsy for cytomegalovirus (Table 2).[26]

Nutrition

Malnutrition in hospitalized IBD patients is associated with increased mortality and length of stay.[27] Nutritional consultation should be provided early and consistently throughout the patient's stay to ensure nutritional needs are being met. Early enteral feeding should be pursued, if possible.[28] If patients are considered to be at high nutritional risk and are unable to maintain adequate oral intake on their own, enteral supplementation should be considered.[29] Although enteral feeding is preferred, parenteral nutrition may be needed in the settings of obstructive bowel with inability to place the feeding tube distal to the obstruction, short gut syndrome resulting in severe malabsorption, high-output enteric fistula, or perioperative nutritional optimization.[30]

Daily Assessment of Response

Daily documentation of the variables in the Simple Clinical Colitis Activity Index or Harvey-Bradshaw Index provides an objective measure of disease activity progression over a 24-hour period.

Daily Medication Administration Record Review

The medication administration record and active medication orders should be reviewed to ensure that venous thromboembolism prophylaxis is not only being ordered but is also being received by the patient. The medication administration record should also be reviewed to ensure that opiates, anticholinergics, and nonsteroidal anti-inflammatory drugs are not ordered inappropriately.

Pain Management Options

The mainstay of pain management in IBD is control of the underlying cause of pain: inflammation, stricture, or abscess. Initiation or escalation of chronic opiates should be avoided. Additional pain management with acetaminophen or tramadol (a partial μ opioid agonist) may be tried. In cases where pain control is challenging, consultation with an acute pain management service may be needed for initiation of opiate-sparing medications such as low-dose intravenous ketamine.[31]

Day 3 Recommendations

After 72 hours in the hospital on appropriate medical treatment, the patient's clinical trajectory should start to become apparent. In UC, a number of scores have been developed to predict the risk of colectomy in hospitalized patients with acute severe UC.[32] The Travis[33] and Ho[34]

indices, calculated after 3 days of intensive treatment, are useful to predict failure of corticosteroids and need for colectomy and/or rescue therapy (Table 2). For Crohn's enteritis and colitis, a similar approach may be used, although no predictive scores for hospitalized Crohn's disease patients have been similarly validated.

Well-established medical rescue therapies for corticosteroid-refractory patients include cyclosporine and infliximab. Cyclosporine is a rapidly acting calcineurin inhibitor that has excellent short-term response rates.[35] Contraindications to cyclosporine use include hypocholesterolemia (risk of seizures) and renal insufficiency.[36] Cyclosporine is associated with nephrotoxicity, anaphylaxis, and opportunistic infections. Cyclosporine is initially given as a continuous infusion at a rate of 2 mg/kg/day, with a target cyclosporine concentration of 150 to 250 ng/mL. If a patient responds within 7 days, he or she should be transitioned to oral cyclosporine as bridging therapy while a thiopurine agent is initiated for long-term maintenance therapy.[37] A novel approach using calcineurin inhibitors in combination with vedolizumab (Entyvio, Takeda) for maintenance therapy has also been described as an effective treatment for achieving corticosteroid-free remission and avoidance of colectomy.[38,39] Due to the nuances of monitoring cyclosporine and toxicities, local expertise in administration and monitoring of cyclosporine is recommended.[5]

Infliximab, a monoclonal antibody to tumor necrosis factor, is also an effective medical rescue therapy for acute severe colitis.[40] Infliximab has the advantage that it may be continued as maintenance therapy without the need to bridge to an alternate agent. The infliximab intravenous induction dosing regimen is 5 mg/kg at weeks 0, 2, and 6. Maintenance dosing can be administered at a dose of 5 to 10 mg/kg every 8 weeks to maintain remission. In patients with severe colitis, the pharmacokinetics of infliximab are altered, with increased drug clearance, lower serum levels, and increased fecal drug loss, and either intensification (10 mg/kg induction dosing) or acceleration (3 doses of infliximab within 2-4 weeks) may improve colectomy-free survival.[41] Contraindications to infliximab use include New York Heart Association Class III/IV heart failure, active or untreated systemic infection, and demyelinating disease.

Tofacitinib (Xeljanz, Pfizer), a rapidly acting oral small molecule Janus kinase inhibitor approved for induction and maintenance of UC, has recently been described in a few small case series as a potential novel alternative rescue therapy for patients who have contraindications to or have already failed infliximab or cyclosporine.[42-44] Comparative studies are needed to further assess the efficacy of tofacitinib as rescue therapy.

Stricturing Crohn's Disease

Patients hospitalized with Crohn's disease–associated small bowel obstruction who are receiving intravenous corticosteroids will typically respond within 72 hours.[45] For patients presenting with small bowel obstruction from Crohn's disease who fail to improve with intravenous corticosteroids in this time frame, anti–tumor necrosis factor therapy may be considered as a surgery-sparing alternative.[46] Surgical resection, especially for purely fibrotic strictures, may ultimately be required.[47] Endoscopic techniques for treatment of strictures, including balloon dilation, stricturotomy, and stent placement, may be considered as surgery-sparing techniques in the appropriate setting (short, nonangulated, endoscopically accessible, and absent penetrating disease).[48]

Crohn's Abscess

Patients with penetrating Crohn's disease and abscesses that are initially amenable to antibiotic therapy and percutaneous drainage should be monitored closely. Within 3 to 5 days, there should be decreased drainage, improvement in symptoms, and resolution of sepsis. If these parameters are not met, then re-evaluation of the percutaneous drain and/or surgical drainage with or without resection should be considered.[49]

Recommendations for Day 4 and Beyond

For patients who fail to respond to medical rescue therapy within 7 days, surgery is likely warranted. Engaging with a consulting surgeon with expertise in colorectal surgery early in the hospital course will help to facilitate timely surgical intervention if indicated and prepare the patient both physically and psychologically for the possibility of surgery (Table 2). Switching to another rescue therapy may induce remission, but the risk of serious adverse events also begins to increase, so this approach often is not recommended.[50,51] Surgery should not be delayed due to recent administration of medical rescue therapy; infliximab and cyclosporine do not increase postoperative complications of colorectal surgery.[52] Nutritional status should be optimized as much as possible prior to surgery; low albumin (<3.5 g/dL) is associated with surgical complications such as anastomotic leak and enterocutaneous fistula.[53] Although enteral nutrition is preferred, some patients may require total parenteral nutrition preoperatively if enteral nutrition is not feasible.

Discharge Criteria and Planning

For patients who successfully respond to medical therapy, there are no standardized discharge criteria for patients hospitalized with UC or Crohn's disease. For inflammatory Crohn's disease and UC, manageable bowel

Table 3. Checklist for Planning Hospital Discharge

Goals for discharge
❑ Manageable bowel movement frequency (1-4 bowel movements/day)
❑ Minimal rectal bleeding
❑ Ability to tolerate oral nutrition and medications
❑ Adequate pain control
❑ Resolution of sepsis physiology
Medical treatment
❑ Transition to oral prednisone and/or antibiotics
❑ Avoid discharge opiate prescriptions
Vaccinations prior to discharge (if available)
❑ Influenza
❑ Pneumococcal pneumonia
Follow-up education
❑ Arrange outpatient gastroenterologist and primary care physician follow-up appointments
❑ Issue return precautions and anticipatory guidance
❑ Schedule smoking cessation counseling, if needed

movement frequency (1-4 bowel movements/day), minimal rectal bleeding, ability to tolerate an outpatient regimen of medications, and adequate nutrition are reasonable goals. Patients with stricturing Crohn's disease should achieve resumption of bowel function, tolerance of oral nutrition and oral medications, and adequate pain control prior to discharge. Patients on intravenous corticosteroids should be transitioned to an equivalent dose of oral prednisone with a plan for outpatient taper. For patients with penetrating Crohn's disease complicated by intra-abdominal abscess, adequate drainage, resolution of sepsis, and adequate pain control should be achieved prior to transitioning to oral antibiotics and hospital discharge (Table 3).

Discharge planning should ideally begin on the day of admission and continue throughout the hospitalization. Arranging for follow-up care with the primary care provider and outpatient IBD team is associated with a decreased risk of rehospitalization[54] and can help to reinforce the treatment plan and assess for complications. Ongoing tobacco and opiate use are also associated with rehospitalization.[55] Smoking cessation counseling during hospitalization and avoidance of discharge prescriptions for opiates will benefit the patient long term and also may prevent unnecessary rehospitalizations.

Patients with IBD, particularly those receiving immunosuppressive medications, are at increased risk of a variety of opportunistic infections. Vaccination rates for vaccine-preventable illnesses such as influenza and pneumococcal pneumonia in the IBD population are often quite low (<50%), despite guideline recommendations.[56] Systematic reminders to provide vaccinations prior to hospital discharge can increase uptake and provide immunizations to a high-risk population that might not otherwise be vaccinated.[57]

Communication on discharge with the patient is of utmost importance. How and where to obtain discharge prescriptions, including immunomodulator or biologic therapy; contact information for the outpatient gastroenterology team; time and location of follow-up appointments; and anticipatory guidance and education about warning signs to return to medical care should all be clearly provided to the patient.

Conclusion

IBD is a chronic illness with a relapsing and remitting course that may require hospitalization for disease flares or complications. A standardized approach of assessing disease phenotype and severity followed by appropriate medical treatment with either intravenous corticosteroids or antibiotic therapy and supportive care should be provided to all patients. If initial management strategies fail, medical rescue therapy and surgical consultation should be considered. Other steps to minimize disease complications, including appropriate venous thromboembolism prophylaxis, avoidance of opiate medications, and adequate nutrition, should be pursued throughout the hospital stay. Adequate follow-up upon discharge is essential for maintenance of remission and to decrease risk of rehospitalization. Use of standardized care algorithms by both gastroenterologists and hospital medicine providers can reduce care variation and improve adherence to evidence-based guidelines for hospitalized IBD patients.[58]

Disclosures

The authors have no relevant conflicts of interest to disclose.

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