Gastroenterology 2021;160:445–451

AGA Clinical Practice Update on Management of Inflammatory Bowel Disease in Elderly Patients: Expert Review

Ashwin N. Ananthakrishnan,[1] Geoffrey C. Nguyen,[2] and Charles N. Bernstein[3]

[1]Division of Gastroenterology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; [2]Mount Sinai Hospital Centre for Inflammatory Bowel Disease, University of Toronto, Toronto, Ontario, Canada; and [3]University of Manitoba Inflammatory Bowel Disease Clinical and Research Centre, Section of Gastroenterology, University of Manitoba, Winnipeg, Canada

Keywords: Inflammatory Bowel Disease; Senescence; Management of the Elderly; Biological Therapy; Surgery; Health Maintenance.

Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), can present at any age including in elderly patients, commonly defined as 60 years and older. Hence, considering both incident elderly patients with IBD and the aging prevalent IBD population, there will be increasing numbers of elderly patients with IBD. The care of elderly patients with IBD poses unique challenges with respect to diagnosis and therapeutic decision making.

Approximately 1 out of every 160 elderly individuals is affected by IBD. The prevalence of IBD among elderly individuals appears to be incrementally rising by 5.2% annually. Up to 15% of IBD in North America and Asia is diagnosed after the age of 60 years.[1] Incidence rates vary from 4–8 per 100,000 for persons older than 60 years. Clinicians must be prepared to newly diagnose IBD in elderly patients and initiate therapy in the context of other health issues experienced by elderly individuals.

Common comorbidities, especially malignancy and increased disposition to infections, can render elderly patients more vulnerable to complications of immunosuppression.[2] Observational studies suggest that the risk of infection with anti–tumor necrosis factor (TNF) therapy and lymphoma with thiopurines is considerably higher in the elderly IBD population.[3,4] Surgical management of IBD in elderly populations can also be associated with high risk due to high comorbidity. Furthermore, although there is no difference in mortality rates for older vs younger age of onset in UC, elderly patients are more likely to die of CD (33/10,000 person-years) compared with their middle-age (5.6/10,000 person-years) or young counterparts (1/10,000 person-years).

It is becoming apparent that treatment of IBD in elderly patients requires special consideration while accounting for the effectiveness of immunosuppressive therapies in this subpopulation and less favorable safety profiles. In this review, we present best practice advice statements on the diagnosis and management of IBD in elderly patients (Table 1). It should be noted that most clinical data to inform these practices are based on observational data or indirect evidence because elderly patients with IBD comprise a very small proportion of participants enrolled in IBD clinical trials or long-term pharmacovigilance initiatives. This expert review was commissioned and approved by the American Gastroenterological Association (AGA) Institute Clinical Practice Updates Committee and the AGA Governing Board to provide timely guidance on a topic of high clinical importance to the AGA membership, and it underwent internal peer review by the Clinical Practice Updates Committee and external peer review through the standard procedures of the *Gastroenterology* journal.

Diagnosis of Inflammatory Bowel Disease in Elderly Patients

When elderly persons present with any constellation of symptoms that may include diarrhea, rectal bleeding, abdominal pain, and weight loss, providers should have a strong clinical suspicion for IBD (Figure 1). However, compared with persons younger than 40 years, persons older than 60 years are more likely to have other diagnoses that may mimic symptoms of IBD such as colorectal cancer, ischemic colitis, segmental colitis associated with diverticulosis, nonsteroidal anti-inflammatory drug–induced pathology, radiation enteritis or colitis, or microscopic colitis. Because the medical and surgical management of these conditions varies substantially, a vigorous approach to confirming the diagnosis of IBD is important in the elderly population.

The first diagnostic steps should include laboratory investigations that include a complete blood count and serum albumin, serum ferritin, and C-reactive protein levels (Figure 1). Liver enzymes and urea and creatinine levels serve to assess for underlying comorbidities as well as a baseline for toxicity monitoring. Stool testing for *Clostridium difficile* in all new presentations of diarrhea, regardless of antibiotic use history, and selective testing of stool for culture and ova and parasites may be appropriate. Cross-sectional imaging with computerized tomography is appropriate in elderly persons who present with acute symptoms, especially when abdominal pain is a prominent symptom because it can also rule out other diagnoses (eg, ischemic colitis, diverticular disease). Colonoscopy with histologic confirmation remains a cornerstone of diagnosis.

Abbreviations used in this paper: **AGA, American Gastroenterological Association; CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; OR, odds ratio; TNF, tumor necrosis factor; UC, ulcerative colitis.**

Most current article

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2020.08.060

Table 1. Best Practice Advice Statements: Management of IBD in Older Patients

Diagnosis

1. A diagnosis of IBD (CD, UC) should be considered in older patients who present with diarrhea, rectal bleeding, urgency, abdominal pain, or weight loss because up to 15% of new diagnoses of IBD occur in individuals older than 60 years.
2. Fecal calprotectin or lactoferrin may help prioritize patients with a low probability of IBD for endoscopic evaluation. Individuals presenting with hematochezia or chronic diarrhea with intermediate to high suspicion for underlying IBD, microscopic colitis, or colorectal neoplasia should undergo colonoscopy.
3. In elderly patients with segmental left-sided colitis in the setting of diverticulosis, consider a diagnosis of segmental colitis associated with diverticulosis in addition to the possibility of CD or IBD–unclassified.

Treatment: general principles

1. A comprehensive initial assessment of the older patient is important to collaboratively establish short- and long-term treatment goals and priorities.
2. Clinicians should risk-stratify patients based on the likelihood of severe clinical course, including assessment of perianal or penetrating phenotype, long-segment small bowel involvement (CD), extensive colitis (UC), anemia, hypoalbuminemia, elevated inflammatory markers, and weight loss, to determine an appropriate therapeutic strategy.
3. Systemic corticosteroids are not indicated for maintenance therapy. When used for induction therapy, when possible, clinicians should prefer nonsystemic corticosteroids (like budesonide) or even early biological therapy initiation if budesonide is not appropriate for the phenotype of the disease being treated.
4. Candidacy for immunosuppression should be based on chronologic age, as well as consideration for the patient's functional status, comorbidities including prior neoplasia and potential for infectious complications, and frailty.
5. When possible, immunomodulatory treatments with lower overall infection or malignancy risk (vedolizumab, ustekinumab) may be preferred in older patients. However, choice of treatment must also include assessment of clinical context, efficacy of treatments for specific phenotypes, rapidity of onset of action, and ability to achieve corticosteroid-free remission.
6. Consideration of thiopurine monotherapy for maintenance of remission in older patients should balance the convenience of its oral route of administration and lower cost with relatively lower efficacy, slow onset of action, and an increase in risk of nonmelanoma skin cancers and lymphoma in this population.
7. Older patients with IBD have a greater burden of comorbidity than younger patients. Optimization of comorbidity is important to minimize the risks associated with IBD and its treatment and guide selection of the appropriate agent.
8. The decision about the timing and type of surgery in older patients with IBD should incorporate disease severity, impact on functional status and independence, risks and effectiveness of medical therapy, candidacy for surgery, and risk of postoperative complications.
9. The increased risk of fracture, venous thromboembolism, infections including pneumonia, opportunistic infections, and herpes zoster and risk of skin and nonskin cancers (including lymphoma) should be incorporated in therapeutic decisions.
10. Care for the older patient with IBD should be multidisciplinary, actively engaging gastrointestinal specialists, primary care providers (including geriatricians), other medical subspecialists (eg, cardiologists) mental health professionals, general or colorectal surgeons, nutritionists, and pharmacists. Engaging with family and caregivers may also be appropriate in formulating a plan.

Health maintenance

1. Clinicians should facilitate adherence to vaccination schedules, including influenza, pneumococcal, and herpes zoster vaccines, in older patients with IBD. If possible, vaccination should be scheduled before starting immunosuppression.
2. The decision to continue or stop colorectal cancer surveillance in older patients with long-standing UC or Crohn's colitis should be made incorporating age, comorbidity, overall life expectancy, likelihood of endoscopic resectability of the lesion, and candidacy for colon resection surgery.

However, there should be additional consideration of procedural risks and tolerance for anesthesia in the presence of comorbidities and polypharmacy in elderly patients. In cases where the indication for colonoscopy is equivocal or is associated with relatively high risk, the use of noninvasive stool markers of inflammation such as fecal calprotectin and imaging may aid in decision making.

Disease Presentation and Disease Course

The initial presenting phenotype may differ between elderly-onset IBD and younger onset of the disease. In CD, elderly patients may be more likely than younger patients to present with isolated colonic disease (44%) and less likely to have penetrating disease or perianal disease.[5–7] Compared with their younger counterparts, elderly persons with UC are more likely to have left-sided disease, occurring in 40%.[6] Presenting with more benign phenotypes may suggest patients with elderly-onset IBD may have more favorable outcomes compared with their younger counterparts. Although some initial epidemiologic studies may support this notion, others have suggested that those with elderly-onset UC were more likely than younger patients with IBD to undergo colectomy.[5] Thus, in attempting to predict disease course, it may be more prudent to consider specific disease characteristics rather than chronologic age.

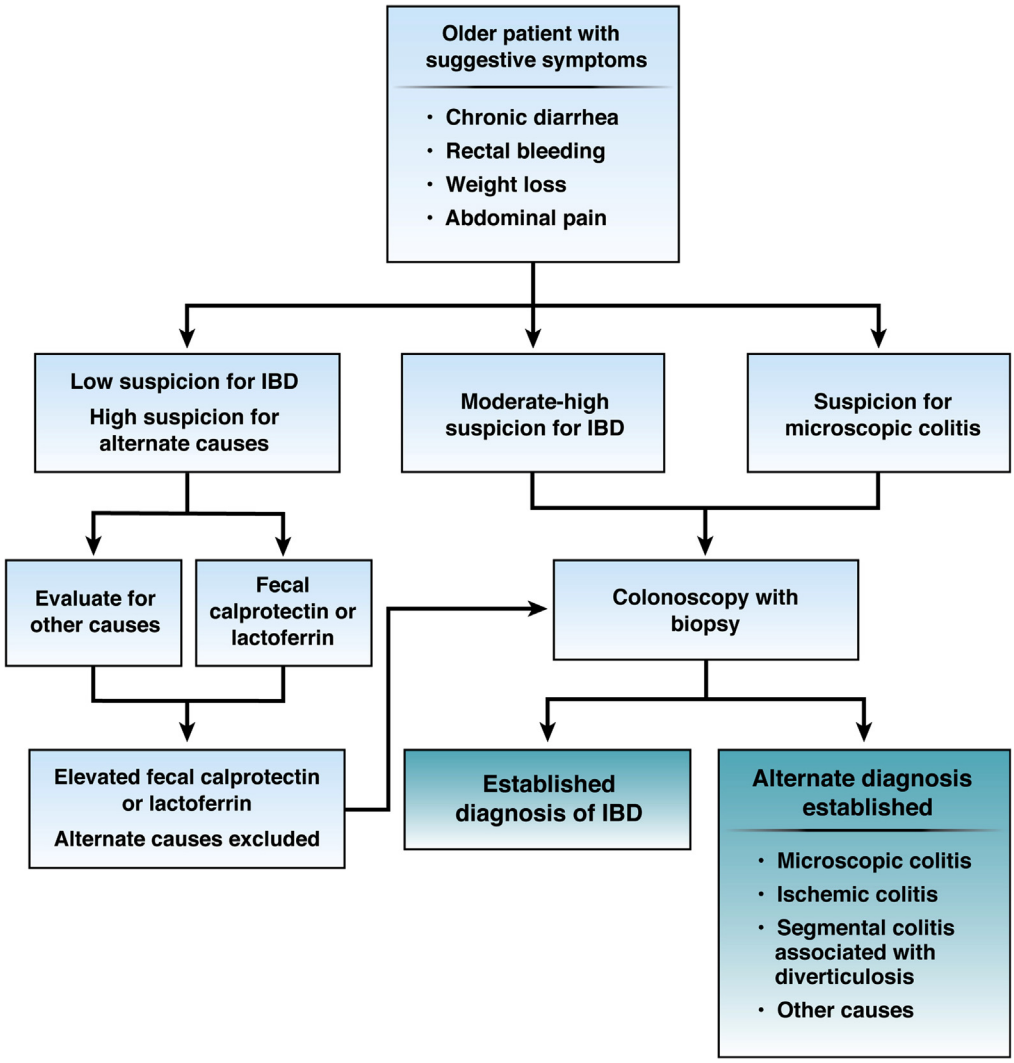

Figure 1. Diagnostic algorithm for elderly patients with inflammatory bowel disease.

Multidisciplinary Approach to Management

Managing an older individual diagnosed with IBD warrants a multidisciplinary approach. In a sample from the National Social Life Health and Aging Project, nearly a third (29%) of persons aged 57–85 years were using at least 5 prescription drugs, and 4% of this elderly cohort were at risk of major drug-drug interactions, emphasizing the importance of pharmacist support. Multiple coexisting chronic diseases may warrant comanagement with a geriatrician to integrate frequently complex care and polypharmacy. Moreover, access to mental health providers may be helpful because of the high prevalence of depression and other mental health disorders in the elderly population. Because physical and cognitive decline can increase with age, social workers or health care navigators may work closely with health providers to enable reliable access to care and supportive care at home.

Medical Therapy in Elderly Patients With Inflammatory Bowel Disease

The principles behind the selection of optimal medical therapy in elderly patients with IBD based on disease presentation and prognostic factors is similar to that of the general population (Figure 2). Although there is little evidence for age-related differences in efficacy of various therapeutic agents, there are safety considerations that may be warranted given the higher frequency of malignancy and the effects of immunosenescence among elderly individuals. Unfortunately, safety data among elderly people are relatively sparse because this population is underrepresented in clinical trials and registries. In addition to chronologic age, clinicians should also assess overall fitness and frailty when considering the selection of treatments. Pretreatment frailty was associated with an increased risk of infections after immunomodulator or anti-TNF treatment or after surgery.[8] Interventions aimed to ameliorate physical and nutritional

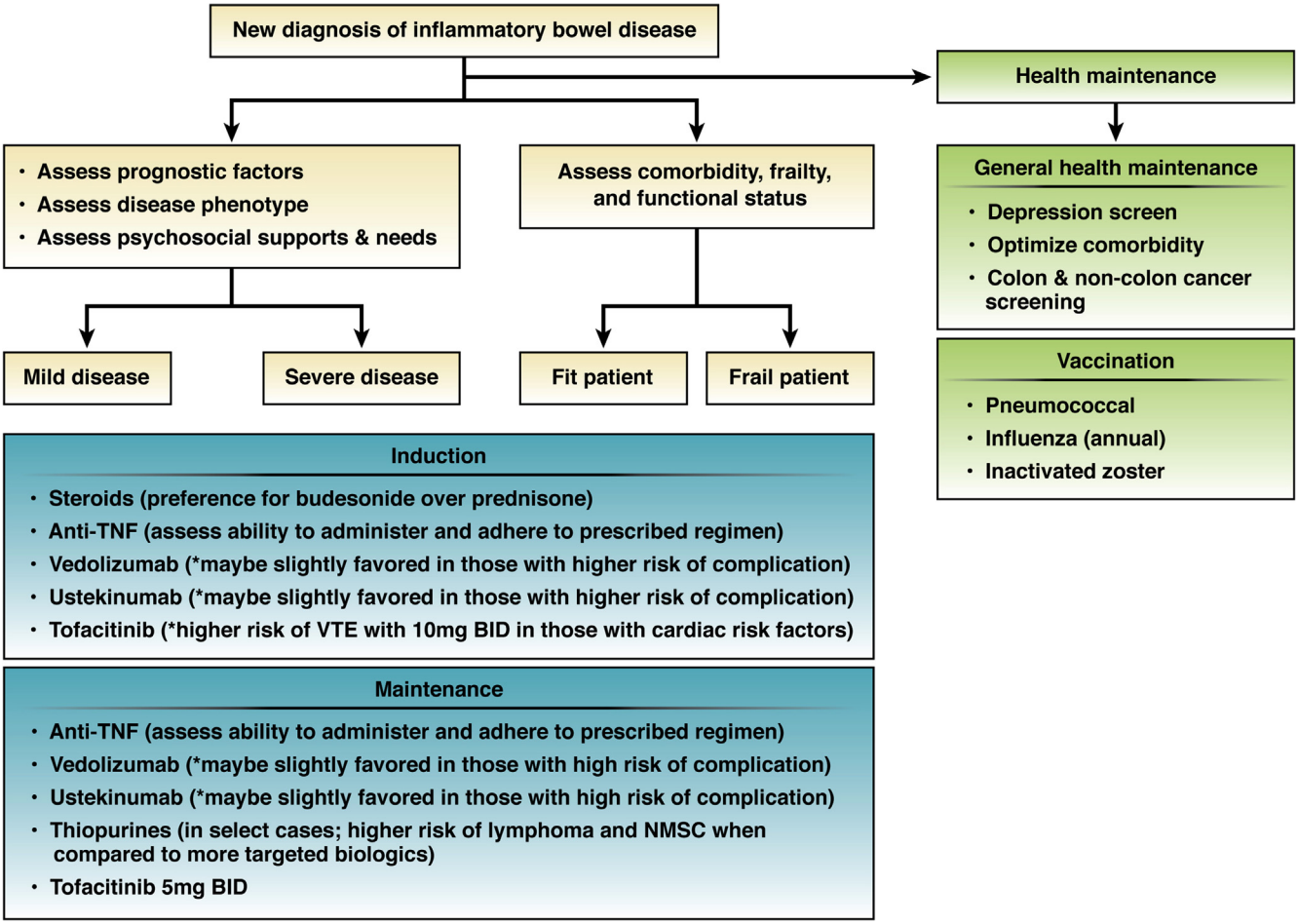

Figure 2. Treatment algorithm for elderly patients with inflammatory bowel disease. BID, twice daily; VTE, venous thromboembolism.

frailty, including physical therapy and nutritional support, may thus be an important part of care of older patients with IBD. Screening before the initiation of medical therapy for IBD including assessment of hepatic and renal function, presence of latent tuberculosis or hepatitis B infection, and assessment of thiopurine methyl transferase status before thiopurine use is similar in older patients with IBD as in younger patients. Despite the potential risks for immunomodulatory therapy in elderly patients, therapy choices should not be delayed and/or corticosteroid therapy prolonged out of concerns for immune therapy–associated risks.

Aminosalicylates

Aminosalicylates have proven efficacy for the induction and maintenance of remission in mild to moderate UC. In contrast, although widely used, their efficacy is less well established in CD, with most clinical trials showing either no or a modest benefit over placebo. Their lack of a systemic immunosuppressive effect has made them a frequently relied on option for treatment of older patients with IBD. Population-based cohorts have shown that more than two thirds of older patients with UC and CD receive mesalamine therapy.[5,6] Although adverse effects from mesalamine use are infrequent, the rare complication of interstitial nephritis may be especially pertinent in older patients because of superimposed age-related decline in renal function.

Corticosteroids

Despite limited evidence-based data, corticosteroids seem to have similar efficacy in elderly patients with IBD as their younger counterparts.[9] They are frequently used in the management of older adults with IBD. They are more likely to be used for maintenance therapy in elderly compared with younger patients with IBD,[10] despite some evidence that elderly patients with IBD are less likely than younger patients with IBD to be corticosteroid dependent (21% vs 30%).[7] Although corticosteroid-related adverse effects may not be more frequent in elderly patients compared with younger patients with IBD, older patients also have a greater prevalence of diabetes, hypertension, glaucoma, cataract, osteoporosis, and cognitive impairment, all of which may be exacerbated by corticosteroid use. Corticosteroid use may also lead to increased risk of anxiety, depression, fatigue, and poor sleep quality. Initiation of therapies (biologic or small molecule) with rapid onset of action may reduce or eliminate the need for use of corticosteroids.

Budesonide is an oral corticosteroid with a high first-pass metabolism that has been shown to have only modestly lower efficacy than conventional systemic corticosteroids in CD with fewer adverse effects. Similarly,

budesonide-MMX has been shown to be effective for mild to moderate left-sided UC. Long-term budesonide is less likely to lead to adrenal axis suppression than systemic corticosteroids.[11] Thus, budesonide may be preferred over conventional corticosteroids in older patients with ileocolonic or right-sided luminal CD or left-sided UC. Any use of systemic corticosteroids should prompt consideration for corticosteroid-sparing therapy and measures to mitigate risk for osteoporosis should a prolonged course be required.

Topical corticosteroids (or aminosalicylates) may be effective for distal colonic disease but may be poorly tolerated in older patients with limited mobility or weak sphincter tone. In such situations, formulation with lower volume (such as foam) may be preferred. Clinical trials have not shown efficacy of corticosteroids in maintaining remission in IBD in any age group.[11] Given the potentially higher risk adverse effects outlined earlier, corticosteroid use for IBD maintenance therapy should be avoided.

Thiopurines and Methotrexate

Although thiopurines are effective in maintaining remission in both CD and UC, the data are limited, particularly in elderly patients.[12] More than a third of elderly patients have been exposed to thiopurines in 1 cohort within 5 years of IBD diagnosis.[7] Among elderly patients, a higher frequency of adverse events including hepatoxicity may be seen, although acute pancreatitis was less likely to occur.[7]

An increase in the absolute risk of thiopurine-related malignancy in elderly patients with IBD has raised concerns about their use in this population. Thiopurine use is associated with a higher absolute risk of nonmelanoma skin cancer among those older than 65 years compared with those younger than 50 years (4.04 vs 0.66 per 1000).[13] The absolute incidence of lymphoproliferative disorders in the presence of thiopurine use has also been shown to be increased in elderly patients with IBD compared to those younger than 50 years (5.41 vs 0.37/1000 person-years), whereas the age-related difference was less pronounced in thiopurine nonusers (1.68 vs 0 person-years).[14]

On balance, thiopurines, by virtue of their oral administration, are convenient and inexpensive options for many older patients with IBD. However, their inferior efficacy when compared to other therapies, their delayed efficacy (thereby potentially prolonging corticosteroid exposure), and the higher absolute risk of potentially serious treatment-related malignancies in older patients with IBD makes prudence about new initiation of thiopurines important. Nonetheless, routine discontinuation or absolute avoidance of their use solely based on chronologic age is not appropriate, and consideration of thiopurine use should be on a case-by-case basis. Methotrexate also represents an attractive option in older patients with CD, with data supporting its role in inducing and maintaining remission. It can also be an alternative to thiopurines when used for combination therapy in individuals considered to be at high risk for thiopurine-related adverse effects, including malignancy.

Anti–Tumor Necrosis Factor Biologics

Effectiveness studies of anti-TNF therapy in elderly IBD populations have shown mixed results. A study of 114 biologic-naive patients who were started on anti-TNF therapy showed they had lower persistence with therapy and were more than half as likely to achieve corticosteroid-free remission at 12 months compared to younger patients (31% vs 67%).[15] Lobaton et al[16] similarly found lower rates of clinical response at 10 weeks in older patients on anti-TNF therapy compared to control individuals but no difference at later timepoints. A meta-analysis found no difference in efficacy of infliximab and golimumab in CD and UC between older and younger patients with IBD.[17]

There have been a number of reports on anti-TNF–related complications in the elderly IBD population. One observational study of 95 elderly patients with IBD who were initiated on anti-TNF therapy found higher rates of severe infections (11% vs 2.6%), cancer (3% vs 0%), and death (10% vs 1%) when compared with 190 matched younger control individuals, although the cause of mortality was not specified.[3] The rate of these adverse events was also higher among older anti-TNF users compared to older non–anti-TNF users (0.5% severe infections, 2% cancer, 2% death). Another observational study showed that a fifth of elderly patients discontinued anti-TNF therapy within 12 months of initiation.[18] In a multicenter Spanish cohort study, patients with older-onset IBD were more likely to experience any infection (46% vs 26%) and malignancy (7.6% vs 1.8%) compared with younger patients with IBD.[7] A meta-analysis that compared the safety of anti-TNF therapy across age groups for all indications of use showed that the pooled prevalence of infection was higher in older biologic users (13%) compared to younger users (6%) (odds ratio [OR], 2.28; 95% confidence interval [CI], 1.57–3.31) and older control individuals not using biologics (OR, 3.60; 95% CI, 1.62–8.01).[4] There was also a 3-fold higher risk of malignancy in older compared to younger biologic users (OR, 3.07; 95% CI, 1.98–4.62) but not when compared to older control individuals. Limitations of these studies include inability to separate out the independent effect of anti-TNF from either concomitant steroid or immunomodulator therapy. In many older patients, particularly those who are not frail, the benefit of anti-TNF biologic therapy will likely outweigh the small increase in risk.

The evidence for the safety of the combination of an immunomodulator with anti-TNF biologic therapy in older patients is mixed. Although a post hoc analysis of the REACT trial by Singh et al[19] concluded that the benefit of early combined intervention was similar in older and younger patients with no increase in risk, Desai et al[18] noted that older patients on combination therapy were twice as likely to stop therapy early than those on anti-TNF monotherapy (hazard ratio, 2.20; 95% CI ,1.12–4.32).[18] Combination therapy may be appropriate in those with severe disease including deep ulceration, extensive bowel involvement, and penetrating phenotype, whereas in others, anti-TNF monotherapy may be a preferred initial option, particularly in the setting of significant frailty, comorbidity, or infection risk.

Vedolizumab, Ustekinumab, Tofacitinib, and Other Medications

Limited clinical trial data suggest that the effectiveness of vedolizumab in CD and UC is similar between older and

younger patients. There was no age-related difference in the rate of any adverse events including infections and serious infections. Because of its gut specificity, vedolizumab use is associated with less systemic immunosuppression and should have a favorable safety profile. However, a comparison of 131 patients with IBD initiated on anti-TNF therapy and 103 initiated on vedolizumab showed no difference in infection rates at 1 year in either CD or UC, although CIs were quite wide.[20] There are no published data examining the safety of ustekinumab specifically in older patients with IBD, but a limited cases series of 24 patients with psoriasis showed few infection events.[21]

Most of the safety data on tofacitinib rely on indirect studies from rheumatology. Although there is a higher frequency of serious infections in older patients on tofacitinib compared with those on placebo, it was similar to risks observed in younger individuals. Pooled analysis of clinical trials in rheumatoid arthritis has been informative regarding the safety of this therapy in older patients. Curtis et al[22] pooled data from phase 3 and long-term effectiveness studies, identifying 16% of patients in these studies to be aged $\geq$65 years.[22] Although serious adverse events were more common in older tofacitinib users than younger users with both the 5-mg or 10-mg twice daily dose, a similar effect was also noted among placebo users, suggesting no incremental age-related increase in risk. Specifically, there is a higher risk of herpes zoster among older patients receiving 5 mg and 10 mg of tofacitinib compared with placebo (5.5 and 3.1 per 100 patient-years vs 0, respectively). An interim analysis reported an increased risk of venous thromboembolism including pulmonary embolism among older patients with rheumatoid arthritis with cardiovascular risk factors with tofacitinib 10 mg twice daily (0.4 per 100 patient-years) compared with anti-TNF therapy (0.07 per 100 patient-years), leading to placement of a boxed warning. Cyclosporine is rarely used in older patients with IBD but may be considered for acute severe UC as rescue therapy in individuals where anti-TNF biologics may be contraindicated or previously failed.

Safety of Surgery in Older Patients With Inflammatory Bowel Disease

The data on whether older age is associated with higher risk of postoperative complications after surgery in patients with IBD has yielded conflicting results. Some small studies suggested no difference in postoperative complications between elderly patients with IBD and younger patients. However, a larger study analyzing the American College of Surgeons NSQIP database found that postoperative mortality at 30 days was higher in older patients with both CD and UC compared to younger control individuals.[23] The frequency of postoperative complications was higher in older compared to younger patients (34.5% vs 21.3%). Older patients also had higher rates of postoperative infection; venous thromboembolic events; bleeding requiring blood transfusion; and cardiac, renal, and neurologic complications including stroke and coma. Independently, undergoing emergent surgery was associated with an increase in mortality. Additionally, the greater comorbid burden in older patients also increases the risk of postoperative complications and mortality. The preferred surgery may also be different in older patients, particularly among those with ulcerative colitis. Due to reduced anal sphincter tone, older patients may have worse functional outcomes from an ileal pouch anal anastomosis. An end-ostomy may offer more functional independence in select patients. Pharmacologic thromboprophylaxis is important in older patients undergoing surgery because of higher risk for venous thromboembolism. In addition, assessment and optimization of nutritional status before surgery may be important in reducing postoperative morbidity and facilitating recovery.

Health Maintenance

Soon after diagnosis, it is important for clinicians to discuss health maintenance issues with older patients. Older patients are at a higher risk for vaccine preventable illnesses, particularly in the setting of systemic immunosuppression. It has been shown that influenza vaccine and herpes zoster vaccine are underused, including in persons with IBD where the risk for influenza, pneumococcal pneumonia, or shingles is increased, especially in persons using immunomodulatory drugs.[24,25] Clinicians should facilitate adherence to recommended vaccination schedules including influenza, pneumococcal, and herpes zoster vaccines because the risk for serious sequelae of these infections is increased among elderly patients. Although gastroenterologists often defer routine health maintenance such as vaccinations to primary care providers, it is not uncommon for patients with IBD of any age to find themselves without a primary care provider and for primary care providers to have some uncertainty regarding the safety and timing of certain vaccines in persons on immunomodulatory drugs. It is also important to ensure that older patients with IBD are up to date with age-appropriate cancer screenings recommended for the general population.

Persons with chronic colitis (usually of at least 8 years duration) either related to UC or CD are at approximately a 2-fold risk of developing colorectal cancer compared to age-matched community counterparts. Although the relative risk is higher in younger patients with IBD, the absolute risk is higher in elderly patients as colorectal cancer becomes increasingly common. Hence, vigilance is needed toward ongoing surveillance colonoscopies, and clinicians should be prepared to adequately address dysplastic lesions in these patients. Like colorectal cancer, adenomas and serrated polyps are more common in elderly individuals. However, as with all decisions in medicine and the decisions regarding therapy choice in elderly patients, the persistence with surveillance colonoscopy with advancing age should consider anesthesia and perforation risks associated with the procedure itself, comorbidity, overall life expectancy, and candidacy for colon resection surgery.

References

1. Taleban S, Colombel JF, Mohler MJ, et al. Inflammatory bowel disease and the elderly: a review. J Crohns Colitis 2015;9:507–515.

2. Toruner M, Loftus EV Jr, Harmsen WS, et al. Risk factors for opportunistic infections in patients with inflammatory bowel disease. Gastroenterology 2008;134:929–936.
3. Cottone M, Kohn A, Daperno M, et al. Advanced age is an independent risk factor for severe infections and mortality in patients given anti-tumor necrosis factor therapy for inflammatory bowel disease. Clin Gastroenterol Hepatol 2011;9:30–35.
4. Borren NZ, Ananthakrishnan AN. Safety of biologic therapy in older patients with immune-mediated diseases: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2019;17:1736–1743.
5. Ananthakrishnan AN, Shi HY, Tang W, et al. Systematic review and meta-analysis: phenotype and clinical outcomes of older-onset inflammatory bowel disease. J Crohns Colitis 2016;10:1224–1236.
6. Charpentier C, Salleron J, Savoye G, et al. Natural history of elderly-onset inflammatory bowel disease: a population-based cohort study. Gut 2014;63:423–432.
7. Manosa M, Calafat M, de Francisco R, et al. Phenotype and natural history of elderly onset inflammatory bowel disease: a multicentre, case-control study. Aliment Pharmacol Ther 2018;47:605–614.
8. Kochar B, Cai W, Cagan A, et al. Pretreatment frailty is independently associated with increased risk of infections after immunosuppression in patients with inflammatory bowel diseases. Gastroenterology 2020;158:2104–2111.
9. Ananthakrishnan AN, McGinley EL, Binion DG. Inflammatory bowel disease in the elderly is associated with worse outcomes: a national study of hospitalizations. Inflamm Bowel Dis 2009;15:182–189.
10. Geisz M, Ha C, Kappelman MD, et al. Medication utilization and the impact of continued corticosteroid use on patient-reported outcomes in older patients with inflammatory bowel disease. Inflamm Bowel Dis 2016; 22:1435–1441.
11. Kuenzig ME, Rezaie A, Kaplan GG, et al. Budesonide for the induction and maintenance of remission in Crohn's disease: systematic review and meta-analysis for the Cochrane Collaboration. J Can Assoc Gastroenterol 2018;1:159–173.
12. Alexakis C, Saxena S, Chhaya V, et al. Do thiopurines reduce the risk of surgery in elderly onset inflammatory bowel disease? A 20-year national population-based cohort study. Inflamm Bowel Dis 2017;23:672–680.
13. Peyrin-Biroulet L, Khosrotehrani K, Carrat F, et al. Increased risk for nonmelanoma skin cancers in patients who receive thiopurines for inflammatory bowel disease. Gastroenterology 2011;141:1621–1628.
14. Beaugerie L, Brousse N, Bouvier AM, et al. Lymphoproliferative disorders in patients receiving thiopurines for inflammatory bowel disease: a prospective observational cohort study. Lancet 2009;374(9701):1617–1625.
15. Porcari S, Viola A, Orlando A, et al. Persistence on anti-tumour necrosis factor therapy in older patients with inflammatory bowel disease compared with younger patients: data from the Sicilian Network for Inflammatory Bowel Diseases (SN-IBD). Drugs Aging 2020; 37:383–392.
16. Lobaton T, Ferrante M, Rutgeerts P, et al. Efficacy and safety of anti-TNF therapy in elderly patients with inflammatory bowel disease. Aliment Pharmacol Ther 2015;42:441–451.
17. Cheng D, Cushing KC, Cai T, et al. Safety and efficacy of tumor necrosis factor antagonists in older patients with ulcerative colitis: patient-level pooled analysis of data from randomized trials. Clin Gastroenterol Hepatol. Published May 3, 2020. https://doi.org/10.1016/j.cgh.2020.04.070
18. Desai A, Zator ZA, de Silva P, et al. Older age is associated with higher rate of discontinuation of anti-TNF therapy in patients with inflammatory bowel disease. Inflamm Bowel Dis 2013;19:309–315.
19. Singh S, Stitt LW, Zou G, et al. Early combined immunosuppression may be effective and safe in older patients with Crohn's disease: post hoc analysis of REACT. Aliment Pharmacol Ther 2019;49:1188–1194.
20. Adar T, Faleck D, Sasidharan S, et al. Comparative safety and effectiveness of tumor necrosis factor α antagonists and vedolizumab in elderly IBD patients: a multicentre study. Aliment Pharmacol Ther 2019;49:873–879.
21. Hayashi M, Umezawa Y, Fukuchi O, et al. Efficacy and safety of ustekinumab treatment in elderly patients with psoriasis. J Dermatol 2014;41:974–980.
22. Curtis JR, Schulze-Koops H, Takiya L, et al. Efficacy and safety of tofacitinib in older and younger patients with rheumatoid arthritis. Clin Exp Rheumatol 2017; 35:390–400.
23. Bollegala N, Jackson TD, Nguyen GC. Increased postoperative mortality and complications among elderly patients with inflammatory bowel diseases: an analysis of the National Surgical Quality Improvement Program cohort. Clin Gastroenterol Hepatol 2016;14:1274–1281.
24. Nugent Z, Singh H, Targownik LE, et al. Herpes zoster infection and herpes zoster vaccination in a population-based sample of persons with IBD: is there still an unmet need? Inflamm Bowel Dis 2019;25:532–540.
25. Horton HA, Kim H, Melmed GY. Vaccinations in older adults with gastrointestinal diseases. Clin Geriatr Med 2014;30:17–28.

Received July 18, 2020. Accepted August 28, 2020.

Correspondence
Address correspondence to: Charles N. Bernstein, MD, University of Manitoba Inflammatory Bowel Disease Clinical Research Centre, Section of Gastroenterology, 804F - 715 McDermont Avenue, Winnipeg, MB R3E 3P4, Canada. e-mail: Charles.Bernstein@umanitoba.ca.

Conflicts of interest
These authors disclose the following: Ashwin N. Ananthakrishnan has served on advisory boards for Sun Pharma, Kyn Therapeutics, Artus Therapeutics, and Gilead and is supported by research funding from the Crohn's and Colitis Foundation and the Chleck Family Foundation. Geoffrey C. Nguyen is supported by a Canadian Institutes of Health Research Embedded Clinician Researcher Award and also receives research funding from Crohn's and Colitis Canada. Charles N. Bernstein is supported in part by the Bingham Chair in Gastroenterology; serves on advisory boards for AbbVie Canada, Janssen Canada, Takeda Canada, and Pfizer Canada; serves as a consultant for Mylan Pharmaceuticals and Takeda; has received educational grants from AbbVie Canada, Pfizer Canada, Shire Canada, Takeda Canada, and Janssen Canada; serves on the speakers' panel for AbbVie Canada, Janssen Canada, Takeda Canada, and Medtronic Canada; and has received research funding from AbbVie Canada.