Inflammatory Bowel Disease and the Elderly: A Review

Sasha Taleban, Jean-Frederic Colombel, M. Jane Mohler, Mindy J. Fain

Abstract
Inflammatory bowel disease among the elderly is common, with growing incident and prevalence rates. Compared with younger IBD patients, genetics contribute less to the pathogenesis of older-onset IBD, with dysbiosis and dysregulation of the immune system playing a more significant role. Diagnosis may be difficult in older individuals, as multiple other common diseases can mimic IBD in this population. The clinical manifestations in older-onset IBD are distinct, and patients tend to have less of a disease trajectory. Despite multiple effective medical and surgical treatment strategies for adults with Crohn's disease and ulcerative colitis, efficacy studies typically have excluded older subjects. A rapidly ageing population and increasing rates of Crohn's and ulcerative colitis make the paucity of data in older adults with IBD an increasingly important clinical issue.

Keywords: Elderly; older; inflammatory bowel disease

1. Introduction
Inflammatory bowel disease (IBD), a chronic inflammatory condition involving the gut, comprises two main subtypes, ulcerative colitis (UC) and Crohn's disease (CD). Long believed to be a disease of the young, 10–30% of patients living with inflammatory bowel disease are over the age of 60, either having aged with IBD or developing it as an older adult. Various definitions are used to describe older patients with IBD. More recently, elders with IBD have been defined as patients ≥ 60 years old. Additionally, there are two distinct groups of older IBD patients: 1) those that transition to older age with IBD after obtaining their diagnosis at a younger age; and 2) individuals diagnosed at a late age [≥ 60 years old]. Older-onset IBD may be associated with less progression of their disease, raising the question as to whether or not IBD across the age spectrum has distinct pathogenesis. Although these two sets of patients are not always separately examined in research studies, a distinction between the two groups is likely indicated. This approach is recommended for two reasons: 1) to assure that variation in tolerance and response to IBD treatments are evaluated; and 2) to identify age-related differences in the clinical course of older-onset IBD that would impact on approach to management and treatment.

Clinical challenges exist in the diagnosis and treatment of older-onset IBD. Studies examining management of IBD in older adults have focused more on the adverse events of therapy, potentially limiting beneficial treatment options for older adults. In this review, we characterise IBD in the elderly and discuss its management.

2. Epidemiology
Approximately 10–15% of IBD in the USA is diagnosed after the age of 60. This incidence rate is conservative, since the true incidence of older-onset IBD can be difficult to determine due to greater difficulty in diagnosing these patients and the methodology of current epidemiological studies.

Older-onset UC is more common than CD, with rates higher in elderly men than women. The worldwide incidence of IBD varies by region, typically highest in Westernised nations and lowest in
developing countries. The US incidence of CD and UC is 4/100,000/year and 6–8/100,000/year, respectively, in individuals > 60 years old. Among older patients worldwide, the incidence among CD and UC is 3/100,000 and 3–11/100,000, respectively, in Europe, and 0.4–6/100,000 and 0.1–1/100,000, respectively, in Asia. In Asia, approximately 15% of newly diagnosed IBD cases are > 60 years of age. When examining the largest cohort of older-onset IBD patients to date, being > 60 years old at diagnosis represented 1/20 and 1/8 of all incident CD and UC cases, respectively. IBD incidence decreases with each subsequent decade after age 60, with 25% of individuals being diagnosed in their 70s and 10% being diagnosed in their 80s.

Though the incidence and prevalence of adult IBD may be stable in several developed countries, the rates are increasing in Asia and parts of Europe among both genders and across all age groups, with the exception of the very young and those > 80. The underlying reasons for this trend may be a combination of increased urbanisation, greater awareness of IBD among providers, better access to care and colonoscopy, and advancements in diagnostic methods. Because mortality in IBD is only very mildly elevated and the disease is most often diagnosed in the young, its overall prevalence among older individuals is expected to grow substantially.

3. Pathophysiology

IBD is believed to develop in genetically susceptible individuals who develop an aberrant immune system that reacts inappropriately to gut organisms and their by-products. Environmental factors can play a role at various stages in this process but have not been specifically studied in older IBD patients. Genetics appear to be less important in older-onset IBD as opposed to patients diagnosed at an earlier age. In CD, 16% of patients < 17 years old had a family history of IBD versus 7% of those > 60 years of age, whereas in UC, 13% of patients < 17 years old had a family history of IBD compared with only 3% of those > 60 years old.

When exposed to antigens in the gut, the intestine has to distinguish innocuous from detrimental antigens. This distinction is aided by an intact and functional intestinal epithelium, the innate immune system, and an adaptive immune system consisting of primarily B and T cells, which respond to foreign antigens. In ageing, a reduction in the number of naive T cell precursors and an impaired ability of virtual memory T cells contribute to reduced T cell responses. This age-related immunosenescence is associated with changes in intestinal microbiota composition, increasing the risk of an aberrant immune system and development of IBD.

The effect of ageing on the human gut microbiota and its balance with the host’s immune system may be related to the progression of geriatric syndromes and diseases in the elderly population. Major physiological changes impact on the composition and function of the intestinal microbiota in older adults, including decreased intestinal motility, prolonged transit time, faecal retention, nutritional changes associated with decreased sense of smell and taste, dental decay, and dysphagia. Furthermore, the increased use of medications including laxatives and antibiotics also affects the gut microbiota. The composition of bacteria changes in the elderly, with a decrease in anaerobes [e.g. *Bifidobacteria*] in both abundance and species diversity, and an increase in facultative anaerobes, including streptococci, staphylococci, enterococci, and enterobacteria, a balance that is associated with IBD. Frailty, a geriatric syndrome characterised by restricted physiological reserves and an impaired resistance to stressors, may be associated with a more profound gut dysbiosis. Van Tongeren *et al.* found that frail elderly have up to 26-fold less anaerobes and 10-fold more enterobacteria than healthy or less frail elderly.

4. Differential diagnosis and clinical presentation

Establishing a definitive diagnosis of IBD in older adults can be challenging. Illness in older adults is often complicated by the physical changes of ageing, associated comorbidities, and atypical presentations. The unreliability of physical examination findings, and lack of sensitivity of laboratory testing are commonly encountered, and further complicate the diagnostic process. In addition, even with advancements in diagnostic tools, intestinal inflammation from various causes can mimic IBD.

The clinical presentation of IBD upon diagnosis differs between older and younger patients. When compared with younger patients, older-onset IBD more frequently presented with isolated colonic inflammation and perianal fistulas, and less small bowel and upper gastrointestinal disease. Clinically, older-onset CD presents more often with rectal bleeding, and less often with diarrhoea, abdominal pain, and weight loss. Additionally, older-onset CD is more frequently associated with an inflammatory phenotype rather than fistulising disease. In UC, older-onset CD is more often complicated by perianal disease and upper gastrointestinal symptoms.

### Table 1. Differential diagnosis of inflammatory bowel disease in the elderly

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clinical characteristics</th>
<th>Distinguishing findings</th>
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<tbody>
<tr>
<td>Infectious colitis</td>
<td>Diarrhoea with possible blood, fever, dysentery</td>
<td>Pseudomembranes on endoscopy with <em>Clostridium difficile</em>, positive stool studies</td>
</tr>
<tr>
<td>NSAID-induced enterocolitis</td>
<td>Diarrhoea with possible blood, iron deficiency anaemia, obstruction, perforation</td>
<td>Diaphragm-like small bowel stricture, elderly especially at risk</td>
</tr>
<tr>
<td>Ischaemic colitis</td>
<td>Acute onset of abdominal pain followed by bloody diarrhoea</td>
<td>Segmental area of injury, rectal sparing, abrupt transition between normal and affected mucosa</td>
</tr>
<tr>
<td>Segmental colitis associated with diverticula [SCAD]</td>
<td>Bloody stools, diarrhoea, abdominal pain</td>
<td>Inflammation in and around diverticulum only</td>
</tr>
<tr>
<td>Radiation colitis</td>
<td>Bloody diarrhoea, urgency, tenesmus, occur weeks to years after abdominal/pelvic radiation</td>
<td>Histologically, fibrosis and capillary telangiectasia</td>
</tr>
<tr>
<td>Diversion colitis</td>
<td>Occurs in surgically diverted bowel loop, most asymptomatic but can have abdominal pain and bloody/mucous discharge</td>
<td>Histologically, prominent lymphoid hyperplasia</td>
</tr>
<tr>
<td>Solitary rectal ulcer syndrome</td>
<td>Rectal bleeding, straining, pelvic fullness</td>
<td>Histologically, thickened mucosal layer and crypt architectural distortion, smooth muscle and collagen replace lamina propria</td>
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</table>
Ultimately, the patient’s preferences, values and goals of care must help guide therapy, and in many older adults, the presence of age-related conditions, geriatric syndromes such as cognitive impairment, and other functional impairments affect goals of care and treatment options.

5.1. Mesalazine
First-line therapy for mild to moderate UC, mesalazine is prescribed in 84% of UC patients > 60 years old [Figure 1]. Studies of mesalazine use in mild to moderate CD have been conflicting, though CD patients with colitis may benefit from its use. 27 Still, among older-onset CD, 80% are prescribed mesalazine, probably due to a combination of a lack of treatment options for mild-moderate CD and hesitancy in advancing to immunosuppressant therapy. Topical mesalazine therapies include suppositories, for disease in the distal 10 cm of the rectum, and enemas, which can potentially treat inflammation up to the splenic flexure. In patients with ulcerative proctitis, a combination of oral and topical mesalazine is more effective than either alone. 28

Several factors contribute to significant mesalazine non-adherence in the elderly, including pill sixe, dosing frequency, polypharmacy, financial factors, and perceived risk of side effects. Though serious adverse events are rare, adherence rates are 40–60% based on self-reporting and urinary drug measurements. 29, 30 Once-daily dosing has been shown to increase compliance and decrease pill burden. 28 Collaboration between patients, pharmacists, pharmaceutical companies, and physicians before and during therapy may help address some of these challenges.

Age-associated conditions can increase the difficulty of administering topical agents. Impaired functional status, common in the geriatric population, may prohibit self-administration of rectal suppositories or enemas. Faecal incontinence, common in the elderly, may limit the ability to retain topical agents. Impaired functional status, common in the elderly, may limit the ability to retain topical agents. 31 These patients may benefit from using a hydrocortisone foam preparation, especially if they have more distal disease.

Although, overall, 5-aminosalicylates [5-ASAs] are generally considered safe and efficacious, there are important side effects and drug interactions that occur. The most common adverse reactions include nausea and vomiting, headache, abdominal pain, and rash. 29 Also, a paradoxical worsening of colitis can occur. 32 Nephrotoxicity is a potentially rare but significant outcome in patients on mesalazine with a mean occurrence of 0.26% per patient-year. The incidence does not appear to be related to timing, dosing, or formulation of the 5-ASA. 28 Therefore, caution should be taken in patients with underlying kidney disease, and renal function should be checked before and during therapy. Leukopenia can occur when mesalazine agents are used in combination with thiopurines, due to an increase in 6-thioguanine levels, the active metabolite of azathioprine and 6-mercaptopurine [6-MP]. 33

5.2. Antibiotics
Various anti-microbial agents have been studied in CD and UC, with mixed results. 34 Antibiotics may work best in patients with mild-moderate CD restricted to the colon and have to be used over a prolonged period to maintain efficacy. Ciprofloxacin and metronidazole, typically used in combination, are the most commonly used antibiotics in IBD. Fluoroquinolones are commonly associated with Clostridium difficile colitis, which can have a more severe course in the elderly. 35 Ciprofloxacin can lead to central nervous system abnormalities including a decrease in seizure threshold, which may be caused by decreasing phenytoin levels in patients with a known
seizure disorder. Additionally, elderly on ciprofloxacin may be at particular risk for tendon rupture and QT prolongation. Both ciprofloxacin and metronidazole can interact with warfarin to prolong the prothrombin time. Metronidazole use, especially at higher doses, is associated with peripheral neuropathy. Nausea, anorexia, and a metallic taste in the mouth also can occur with metronidazole. These adverse effects can rapidly impair the nutritional status in the frail patient.

5.3. Steroids
Corticosteroids are effective in establishing but not maintaining remission in moderate to severe IBD. Long-term corticosteroid use comes at the risk of significant systemic side effects including an increased risk of osteoporosis, opportunistic infection and death [Figure 2]. There is an increased risk of osteoporosis and osteonecrosis with higher cumulative doses of corticosteroids. The risk for hip fracture is highest in patients over the age of 60. Long-standing use can lead to uncontrolled or new-onset diabetes, predispose patients to cataracts and glaucoma, worsen pre-existing hypertension, and exacerbate previous psychiatric diagnoses, particularly in elderly patients.

Budesonide is primarily used for inducing remission in CD patients with right colonic and distal small bowel inflammation. A new multi-matrix release formulation has been approved for use in mild to moderate extensive UC. Budesonide, because of high first-pass metabolism, has less systemic absorption, which may lead to fewer side effects.

5.4. Immune-modifying agents
Older patients with mesalamine resistance or corticosteroid requirement may benefit from 6-MP, azathioprine, or methotrexate for maintenance therapy in IBD, and cyclosporine for rescue therapy in severe UC. 6-MP and azathioprine are effective in maintaining remission in UC and CD, whereas intramuscular methotrexate is effective in moderate to severe CD. There does not appear to be any difference in efficacy of immune-modifying agents between those aged > 60 years and younger patients. However, in a retrospective analysis of IBD patients ≥ 65 years old, whereas a third of patients were on long-term corticosteroids, only 6% were on 6-MP or azathioprine, and just 1% were on methotrexate, suggesting these agents are being underused in the elderly.

The hesitation to initiate immune-modifying agents likely is associated with the potential for adverse reactions [Figure 2]. The thiopurines, 6-MP and azathioprine, can lead to leukopenia and transaminitis and therefore monitoring complete blood counts and liver enzymes is essential in the elderly. Testing for thiopurine methyltransferase genetics and enzyme activity can help prevent toxicity by identifying those at risk for myelosuppression. Acute pancreatitis occurs in 3% of patients, typically within the first weeks after starting thiopurines. Nausea and dyspepsia without pancreatic inflammation are the most common adverse events. These potential adverse events are similar across all age groups. The rate of non-Hodgkin lymphoma increases with thiopurine use and appears to further increase with duration of use, concomitant anti-tumour necrosis factor [anti-TNF] inhibitors, and advancing age. Additionally, 6-MP and azathioprine are associated with an increased risk of non-melanoma skin cancer and therefore these patients should undergo an annual skin examination.

Methotrexate can be associated with nausea, fatigue, stomatitis, and rash. Concomitant use of folic acid can improve or prevent these adverse events. There is no known increased risk of lymphoma with the use of methotrexate. Cyclosporine can worsen hypertension and renal insufficiency, common medical problems in the elderly, so caution should be used in this age group.

Allopurinol and angiotensin-converting enzyme [ACE] inhibitors may enhance the myelosuppressive effects of thiopurines. Whereas azathioprine and 6-MP interfere with the metabolism of warfarin to decrease its anticoagulation qualities, methotrexate can increase its anticoagulation properties. Non-steroidal anti-inflammatory drugs [NSAIDs] can increase concentrations of methotrexate. Loop diuretics and methotrexate mutually can alter the concentration of one another.
5.5. Anti-TNF agents

Anti-TNF agents are an option in moderate to severe CD and UC, especially in steroid-dependent or steroid-resistant patients. Monoclonal antibodies to TNF-α are effective in inducing clinical and histological remission, improving quality of life, and decreasing rates of hospitalisation and surgery.\(^\text{28,39}\) Compared with younger adults, studies on anti-TNF use among the elderly are conflicting. An Italian study, comparing patients > 65 years old with younger counterparts, found clinical remission rates of 59% in UC and 65% in CD in older patients after approximately 2 years of treatment on infliximab or adalimumab, similar to rates in younger patients.\(^\text{59}\) Another study from Belgium revealed that the long-term clinical response to anti-TNF agents was similar between those initiating the drug before and after age 65.\(^\text{60}\) A retrospective US study found that younger IBD patients had a higher response rate than older patients and were three times less likely to stop therapy.\(^\text{61}\) However, none of these studies differentiated between incident and prevalent cases of IBD at an advanced age. Additionally, disease duration, a known predictor of anti-TNF response, was longer in the older patients in these studies,\(^\text{60,61}\) suggesting that response rates may actually have been underestimated in the elderly. Despite these findings in the elderly, anti-TNF maintenance therapy is used in just 9% of older CD and 1% of older UC patients [Figure 1].

Most studies examining anti-TNF use in the elderly focus on potential adverse effects of therapy [Figure 2]. Cottone et al. reported a 12% risk of serious infection in the elderly on anti-TNF agents, including pneumonia and sepsis. Overall, 3% of the patients died from septic shock.\(^\text{62}\) To decrease the risk of infection, guidelines suggest that patients be tested for tuberculosis, hepatitis B, and when appropriate, endemic fungal infections before initiation of biologicals.\(^\text{28,39}\) Biologicals also have been associated with malignancy, particularly lymphoma and melanoma.\(^\text{62}\) However, the risk of developing non-Hodgkin lymphoma while on anti-TNFs is difficult to decipher, as many patients in the studies were also prescribed immune modifying agents.\(^\text{56}\) The Crohn’s Therapy, Resource, Evaluation, and Assessment Tool [TREAT] Registry, a prospective cohort study that examined outcomes of CD treatment regimens in North America, found no increased risk of malignancy in patients exposed to biologicals versus other treatments.\(^\text{27}\) When compared with the background risk of different malignancies according to the Surveillance, Epidemiology and End Results [SEER] database, there continued to be no enhanced malignancy risk with biologicals.\(^\text{27}\) However, current studies only provide short-term data with anti-TNF exposure and longer-term malignancy risk is yet to be defined.

Other potential adverse events with anti-TNF agents include dermatological manifestations, infusion reactions, and neurological sequelae. Anti-TNFs are contraindicated in moderate to severe New York Heart Association class 3 or 4 heart failure.\(^\text{39}\) Psoriasis, psoriasis-form rash, and injection site reactions are the most common skin findings. Since both IBD itself and anti-TNFs are associated with psoriasis, it can be difficult to distinguish the aetiology. Infliximab, especially when it has been discontinued and then restarted, can result in a hypersensitivity infusion reaction that is associated with fever, rash, hives, and dyspnoea. Rarely, biologicals have been associated with demyelinating disease.
5.6. Surgery
Recent studies indicate the risk of surgery among older IBD patients is similar to that in younger patients. A retrospective cohort study of the Nationwide Inpatient Sample found that whereas elderly UC patients were less likely to undergo surgery than younger patients, there was no difference in surgical rates among elderly and younger CD patients. Age is independently associated with postoperative morbidity, with hypertension and dyspnoea serving as the top risk factors. However, the rate of major postoperative complications and death among elderly patients has improved, ranging from 50% in 1960–84 to 27% in 1994–99. The improved complication rate over time suggests the availability of more effective IBD medical management options for the elderly, higher emphasis on improving nutrition, and/or an increased tendency to perform surgery earlier in the course of disease. Also, studies consistently reveal the importance of timing of surgery, with more urgent colectomies, presumably in patients with more significant inflammation, associated with worse outcomes.

Similar surgical rates among younger and older IBD patients may have important implications. These findings may reflect studies suggesting a more severe course of IBD on presentation in some elderly. Additionally, they may suggest that providers are less inclined to prescribe immune suppressive agents and biologicals, and more likely to refer patients to surgery for refractory disease.

In older IBD patients with preserved anal sphincter function undergoing reconstructive proctocolectomy, ileal pouch-anal anastomosis (IPAA) is preferred. Long-term bowel incontinence, nocturnal bowel movement frequency, and daytime bowel movements appear similar across age groups. When compared with younger patients, pouch failure rates in older patients also are similar. Patients who have undergone IPAA continue to be at risk for dysplasia, particularly with the stapled technique which leaves rectal tissue behind. When continence is impaired, ileorectal anastomosis is an acceptable alternative to IPAA.

Following surgery for older-onset CD, disease recurrence appears to be less common than in younger patients [43% versus 64%], but time to relapse can be shorter [3.7 versus 5.8 years]. The improved prognosis may in part derive from the fact that the elderly have less small bowel and penetrating disease than younger patients, a profile that has been associated with decreased risk of disease recurrence.

6. Colorectal cancer surveillance
Colorectal dysplasia and cancer also serve as indications for surgery. Using a SEER-Medicare linkage program database, patients who transition to older age with CD and UC have an odds ratio [OR] of 1.93 [p < 0.001] and 1.45 [p = 0.01], respectively, of developing colorectal cancer. This association in part reflects a longer duration of disease, a known risk factor for development of colorectal dysplasia/cancer. On the other hand, when compared over 6 years with non-IBD patients, older-onset IBD was not associated with an increased risk of intestinal dysplasia or cancer. The lack of an increased colon cancer risk in the elderly may be a reflection of the short follow-up of the study, may suggest that the inflammatory burden in the elderly may not be significant enough to predispose to cancer, or may imply that the biology of colorectal cancer among older IBD patients may be different.

In adults, the surveillance guidelines in IBD are based on the extent and duration of colonic disease. The decision to continue surveillance colonoscopy accounts for patient morbidity and the risk of the procedure. The American Society of Gastrointestinal Endoscopy suggest that elderly undergo colonoscopy if it affects clinical outcome and the benefits outweigh the risks. Age is a known independent factor for complications in colonoscopy. Among inpatient IBD patients, when compared with non-IBD patients, advanced age is associated with colonic perforation, though the absolute risk is small. A careful patient assessment in collaboration with the primary care provider may help in making appropriate surveillance decisions.

7. Immunisations
Immunosenescence makes the elderly more susceptible to infections. Additionally, patients > 60 years old appear to respond less well to vaccinations. The vaccination guidelines for elderly IBD patients are similar to those for patients without CD or UC [Table 3]. In general, patients prescribed biologicals and other immunosuppressants should avoid live vaccines. Guidelines traditionally have

<table>
<thead>
<tr>
<th>Table 3. Immunisation recommendations for inflammatory bowel disease [IBD] patients ≥ 65 years old.</th>
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<tbody>
<tr>
<td><strong>Vaccination</strong></td>
</tr>
<tr>
<td><strong>Influenza</strong></td>
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<tr>
<td><strong>Tetanus, Diphtheria, Pertussis [Tdap]</strong></td>
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<tr>
<td><strong>Varicella</strong></td>
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<tr>
<td><strong>Zoster</strong></td>
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<tr>
<td><strong>Measles, Mumps, Rubella [MMR]</strong></td>
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<tr>
<td><strong>Pneumococcal [PPSV23]</strong></td>
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<tr>
<td><strong>Meningococcal</strong></td>
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<tr>
<td><strong>Hepatitis A</strong></td>
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<tr>
<td><strong>Hepatitis B</strong></td>
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<tr>
<td><strong>Haemophilus influenzae type B [Hib]</strong></td>
</tr>
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</table>

1. Td, Tetanus/diphtheria.
2. Risk factors include travel or reside in areas where the bacterium is endemic.
3. Risk factors include chronic liver disease, travelling to endemic areas, men who have sex with men, and the use of street drugs.
4. Risk factors include persons with multiple sex partners, persons with a sexually transmitted disease, men who have sex with men, injection drug users, household contacts of infected persons, healthcare and public safety workers exposed to blood on the job, haemodialysis patients, residents and staff of facilities for developmentally disabled persons, travellers to regions with intermediate or high rates of hepatitis B [hepatitis B surface Ag prevalence of ≥ 2%].
5. Risk factors include exposure factors [i.e. household crowding, low socioeconomic status] and host factors [i.e. race and chronic disease].
recommended against administering the live herpes zoster vaccine to patients prescribed anti-TNF agents, but more recent data suggest this may be safe.\(^{44}\) The decision to administer the zoster vaccine therefore should be made on a case-by-case basis, accounting for the individual risk of vaccinating versus not vaccinating. Guidelines recommend that appropriate patients > 60 years old receive the zoster vaccine. Patients should receive the 23-valent pneumococcal polysaccharide vaccine [PPSV23 or Pneumovax] once at the age of 65 and the inactivated influenza vaccine annually. Dual therapy with biologicals and thiopurines dampens the response to the Pneumovax.\(^{45}\) A booster for tetanus, diphtheria, and pertussis [Tdap] is given every 10 years.

8. Conclusion

Older-onset IBD is associated with unique pathophysiology, clinical features, and natural history. These features can make the accurate diagnosis and treatment of older patients particularly challenging. Most individuals have mild CD or UC and can be treated without immune suppression. But for many others, in part due to limited clinical drug trials and the increased risks associated with immunosuppression in the elderly, medical treatment of older IBD patients often is not optimised, evidenced by higher than expected chronic corticosteroid use and surgical rates. With an ageing population, further studies are necessary to identify risk factors for more aggressive disease in this group, as well as safety and efficacy of current treatment options, to help determine a balance between the risks and benefits of various therapies.

Conflict of Interest

STaleban, MJM, and MJF have no conflict of interest. J-FC has served as consultant, advisory board member or speaker for Abbvie, ABScience, Amgen, Bristol Meyers Squibb, Celgene, Danone, Ferring, Genentech, Giuliani SPA, Given Imaging, Janssen, Immune Pharmaceuticals, Merck & Co., Millennium Pharmaceuticals Inc., Nutrition Science Partners Ltd, Pfizer Inc., Prometheus Laboratories, Protagonis, Receptos, Sanofi, Schering Plough Corporation, Second Genome, Takeda, Teva Pharmaceuticals, UCB Pharma, Vertex, and Dr. August Wolff GmbH & Co.

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