REVIEW

Inflammatory Bowel Disease of the Elderly: Frequently Asked Questions (FAQs)

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The growing recognition of the older inflammatory bowel disease (IBD) patient is heightened by the entry of the 77.2 million baby boomers who will turn 65 beginning of 2011. It is anticipated that this will occur at a rate of 10,000 per day or 4 million per year for the next 19 years. The management of IBD in this population is complex because of problems with co-morbidities, polypharmacy, impaired mobility, and cognition, as well as difficult social and financial issues. This review focuses on the older IBD patient's unique concerns and provides guidance in their diagnosis and management.

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INTRODUCTION

Inflammatory bowel disease (IBD) is generally thought to be primarily a condition of young individuals. However, a significant proportion of new cases of IBD is diagnosed in older individuals, and given the negligible impact of IBD on mortality, younger patients with IBD will contribute to an increasing pool of "elderly" IBD patients as they age.

Physicians caring for this population are faced with multifaceted problems of (i) mimics of IBD, (ii) misdiagnoses, (iii) managing comorbid diseases, and (iv) polypharmacy with multiple drug interactions. Further difficulty exists in extrapolating data and experience from clinical trials, which often exclude the elderly, and patients with significant comorbidities, which are so prevalent in the older population. For example, several studies of adalimumab in Crohn's disease set an upper age limit for study eligibility at 75 years of age. Other recent trials did not set an upper age limit for eligibility, but the median age in most studies was in the 30s, with very few patients included above the age of 60 years. Guidelines are often drawn from heterogeneous populations with different definitions of end points and limited duration of follow-up. This highly selected population and short scope of drug intervention must be weighed against the impact of IBD as a lifetime disease experience.

In this article, we will address questions that commonly arise in the care of older IBD patients.

WHAT IS THE INCIDENCE OF IBD IN THE ELDERLY?

Conflicting data from heterogeneous populations, inconsistent definitions of IBD, and misdiagnoses create confusion with acute self-limited infectious colitides, ischemia, or nonsteroidal anti-inflammatory drug (NSAID)-related bowel changes, and therefore can confound studies on the epidemiology of IBD in the elderly.

Approximately 10–30% of the IBD population is over the age of 60 years, with a male-to-female ratio that is equal (1–3). The incidence of IBD decreases with advancing age, with 65% of elderly cases aged 60–70 years, 25% aged 70–80 years, and 10% over 80 years (3,4). It is now believed that one-third of all new cases of Crohn's disease occur in the elderly population (1,2).

Some studies show a bimodal distribution of IBD incidence, with the expected incidence rise from ages 20 to 39 and another peak at age 60, although this second peak is not seen in all studies (3–6). For example, in a California managed-care group, Crohn's disease appeared to show a bimodal peak, yet this was not true for ulcerative colitis (7).

There are regional differences in the incidence of IBD of the elderly. For example, Crohn's disease incidence rate of 4/100,000 and ulcerative colitis at 6–8/100,000 in the United States can be compared with the European incidence of 8–10/100,000 for both ulcerative colitis and Crohn's disease over the age of 60 years (8,9). These rates are higher in northern than southern Europe (10).

WHAT IS THE SIGNIFICANCE IN DIAGNOSING IBD LATER IN LIFE?

Misdiagnosis at the initial presentation is more common in elderly IBD patients (60% compared with 15% of the younger population) (11,12). There is a delay in the diagnosis up to 6 years in the elderly compared with 2 years in the younger IBD patients

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(12,13). These findings are likely explained by the higher prevalence of IBD-like conditions in the elderly (e.g., ischemic colitis, diverticulitis, NSAID enterocolitis, and so on) and a lack of appreciation of the possibility of a new diagnosis of IBD in an older patient. The elderly suffer worse outcomes because of increased comorbid conditions (13), missed diagnoses and delayed presentation (13), and in some series increased mortality with a greater incidence of deep vein thromboses (13). The latter is presumed because of the hypercoagulability of IBD patients superimposed on dehydration, decreased mobility, or coexistence of colorectal cancer (13), all of which are more common in older patients.

IS THE DISEASE COURSE OF IBD DIFFERENT IN THE ELDERLY?

Elderly IBD patients are prone to similar medical and surgical interventions as younger patients (12,13). The first attacks may be particularly severe in older patients, leading to surgery, yet several studies revealed a lower surgical rate for elderly patients with Crohn's disease (14,15).

Generally, it can be expected that once surviving an initial severe attack, a less severe disease course with fewer relapses and hospitalizations occurs in elderly patients with ulcerative colitis but not Crohn's disease (12,16). Response to medical therapy is seen in 80% of the elderly (17). Maintenance of remission occurs less commonly in single elderly patients with Crohn's disease (13.4% vs. 86.1% of patients in a relationship) (18). In ulcerative colitis, colectomy rates are lower in the elderly (1.9% vs. 4.3% in younger patients) (19), who also have a lesser incidence of proximal extension over time (11.3% in elderly patients vs. 19.4% in younger patients) (19). However, disease course was otherwise comparable to the younger patients (19).

ARE THERE DIFFERENCES IN THE CLINICAL PRESENTATION OF IBD IN THE ELDERLY?

Colonic Crohn's disease is more common than small bowel or ileocolonic disease, and is less severe in the elderly with a lower incidence of fistula or stricture formation but with a greater component of inflammatory disease (13,15,19). Elderly IBD patients are less likely to report abdominal pain or weight loss, and less likely to have anemia (12,13,15). More frequent symptoms in this age group include diarrhea, and a paradoxical constipation as distal ulcerative colitis is more common than pancolitis (4,20,21).

Initial ulcerative colitis attacks in the elderly may be more severe (21). Elderly patients have a lower incidence of a family history of IBD, but greater risk of osteoporosis. Extraintestinal manifestations of IBD were similar in both groups (12).

WHAT ARE THE RISKS AND OUTCOME OF SURGERY IN THE ELDERLY IBD PATIENTS?

Because of the higher risk of having a severe initial presentation, ulcerative colitis surgery occurs earlier in the disease course in the elderly, but tends to lessen with longer disease duration compared with the younger patients (14). Predictors of poor outcome of surgery in the elderly include the need for urgent surgery, and hypoalbuminemia but not advanced age, sex, or disease extent (14).

Ileal pouch-anal anastomosis (IPAA) surgery can be successful in the elderly, provided the patient retains good anal sphincter function (22). Interestingly, pouch failure rates do not differ between the young or older IBD patients (23). Fecal incontinence after IPAA is more common in older patients (22), and thus a history of incontinence preoperatively would ordinarily contraindicate pouch surgery (24). Careful patient selection with good anal sphincter function and adequate cognitive ability will lead to greater tolerance of IPAA. In fact, although one study showed a slight decrease in quality of life in older patients after IPAA compared with younger patients, the older patients were just as likely to undergo the operation if they had to choose again, and just as likely to recommend it to a friend (22). The incidence of anastomotic leaks is comparable to that seen in the younger patients. Dysplasia is a more common indication for such surgery in the older patients. If needed, a prostate biopsy would preferably be done by transperineal route rather than risk a complication compromising the ileal-anal pouch by the transanal route (25).

Surgery-associated adverse outcomes have decreased significantly over time in the elderly, from 50% to 27% in a retrospective analysis over 40 years (26). In this review, the factors associated with poor outcome included advanced age, male gender, and low albumin levels (26). In severe ulcerative colitis, early surgery has been recommended for elderly patients because complications such as toxic megacolon, perforation, massive hemorrhage, and mortality are more common in the elderly when surgery is delayed, and outcomes are worse when surgery is performed when patients are critically ill (27).

If IPAA is not performed, a proctocolectomy or subtotal colectomy and end ileostomy is often done (26). There are limited outcome data on how well elderly patients tolerate having an ileostomy. One study indicated that older veterans were less likely to have problems such as leakage or adjusting to the ileostomy than younger veterans (28). Another study showed that older patients were more likely to have difficulty in the daily management of their stoma, although quality of life overall was equal to or better than younger patients with ileostomies (29). Preoperative use of certain medications, like steroids and infliximab, can affect surgical outcomes (30,31), including the risk of infectious complications.

The need for surgery in Crohn's disease is less frequent in the elderly, occurs more often with ileocolonic disease, and there is a higher recurrence rate (15,32). A higher mortality and perioperative problems in elderly Crohn's disease patients can be anticipated with greater comorbid disease. Reports of a "shorter time to surgery" in elderly Crohn's disease may be related to the clinician's anxiety to exclude malignancy in this age group (12,17). Worse outcomes can always be anticipated in a critically ill elderly Crohn's disease patient compared with a younger patient (28). Indeed, one study did substantiate greater postoperative complications, and longer length of stay and operating time in the elderly IBD patients (33), even after adjusting for comorbidity and immunosuppressive therapy.

However, in an older patient with an IBD flare, the increased risk of surgery must be considered in relation to an increased risk of complications from medical therapy, such as corticosteroids, immunomodulators, and antitumor necrosis factor-α biologic antibodies, as discussed below. Thus, as is true for younger patients, surgery has a role in the management of an older patient with IBD, and the treating physician and surgeon must have a thorough knowledge of the indications, risks, and efficacy of these alternatives in older patients.

WHAT ARE THE CHALLENGES WITH MEDICAL THERAPY IN THE ELDERLY?

Generally, the treatment of IBD in the elderly is similar to that in younger patients, with a few exceptions. Important considerations in choosing a therapeutic agent include the location of inflammation, severity of disease, disease behavior (inflammatory, penetrating, stricturing), extraintestinal manifestations, comorbid conditions, and use of other medications. Indeed, in a study of 150 elderly Crohn's disease patients (mean age 73.2 years), polypharmacy was common, with a mean of 6.6 drugs per patient (34).

The benefits of using highly potent agents earlier in IBD treatment, especially in Crohn's disease, are becoming more widely accepted. However, there are relatively little data on this strategy in elderly patients. Treatment with immune modulators and biologic therapy confers a risk of infection and possible malignancy that may be even more pertinent in older patients. On the other hand, underutilization of immunomodulators and biologics may be associated with poorer outcomes in the elderly (34).

Mild-to-moderate distal colitis can be effectively treated and maintained by topical (enema or suppository) aminosalicylate (ASA) therapy. Topical corticosteroids or oral ASA are used if topical ASA is ineffective, although corticosteroids are not used for maintenance therapy. Combined therapy of topical and oral therapy is more effective than oral therapy alone (35). Difficulty with using topical therapy arises with physical limitations and anal sphincter incompetence in the elderly, which is especially common in hospitalized patients. Retention of the enema fluid is further lessened in the presence of active inflammation. This obstacle can be met by either a reduction in enema volume or using an alternative formulation such as hydrocortisone foam.

Forgetting to take the medication secondary to frequent dosing is reported to be the most frequent reason for noncompliance. In elderly patients, polypharmacy and complex dosing regimens add to the noncompliance rate (34). Thus, single daily dosing should improve compliance and reduce the chance of recurrence.

DO PHARMACOKINETICS DIFFER IN THE ELDERLY AND WITH WHAT CONSEQUENCES?

Although the half-life of 5-ASA is 0.5–2 h, depending on intestinal and hepatic acetylation, the elimination of sulfasalazine in the elderly is considerably slower, related to a decreased glomerular filtration rate with a lower renal clearance (36). This aging effect on renal function is magnified in the presence of renal stones. Corticosteroid clearance (renal and nonrenal) is also decreased in the elderly (37). Budesonide undergoes a first-pass metabolism with a systemic bioavailability of 10–15%, although its clearance is unknown in the elderly, who may have a higher blood flow or decreased hepatic metabolism, resulting in greater bioavailability and thereby greater systemic adverse events (37). It should be remembered that 25% of the 60 mg hydrocortisone acetate enema is systemically absorbed and corresponds to the ingestion of 3 mg of prednisone (9).

There are little data on whether the metabolism of infliximab is altered in the elderly.

HOW DOES THE CLINICIAN BALANCE THE RISKS VS. BENEFITS WITH THE OVERRIDING SPECTER OF COMORBID DISEASES AND MULTIDRUG INTERACTIONS?

Aminosalicylates

The 5-aminosalicylates are the "workhorse" for inducing and maintaining remission in ulcerative colitis and appear comparable in efficacy in both young and older patients (36). In Crohn's disease, the benefit of aminosalicylates is not clear. Although cases of 5-ASA nephrotoxicity and interstitial nephritis are reported (36), the risk is quite low. Interstitial nephritis is an idiosyncratic effect that is unpredictable and cannot necessarily be related to the 5-ASA dose or length of usage. There is a divisive literature regarding the renal impact of 5-ASA, and it is unknown whether the risk of nephrotoxicity is related to age.

Important 5-ASA drug interactions include:

(a) An increase in the international normalized ratio when given with warfarin (particularly with olsalazine) (9,38).
(b) Increased levels of 6-thioguanine metabolite of 6-mercaptopurine (6-MP) or azathioprine (AZA) in a dose-dependent manner (39). This interaction may be put to advantage by using lower doses of 6-MP given with 5-ASA to reach therapeutic levels (39).

Corticosteroids

Patients with ulcerative colitis who do not respond to ASA, and those with severe colitis, often require oral corticosteroids. In mild-to-moderate ileal or ileocecal Crohn's disease, induction therapy with budesonide is usually recommended. AZA and 6-MP have been used for maintenance therapy for steroid-refractory disease and to avoid long-term steroid use. Budesonide interferes with bone metabolism less than conventional steroids (40), although long-term use may cause steroid-related side effects, the risk of which may be increased in the elderly as noted above. In elderly patients, there is a higher incidence of corticosteroid dependence leading to increased requirement for immunosuppressive therapy (41).

Although elderly IBD patients may initially benefit from corticosteroids, adverse events are more frequent and more severe, including longer hospitalizations, osteoporotic-related fractures, altered mental status, and precipitating or exacerbating diabetes mellitus and hypertension (42). Osteoporotic-related fractures and osteonecrosis have been especially common in the elderly IBD

population, approaching a 15% prevalence (43). Early bone density testing with repeated annual exams and limiting corticosteroid use in both duration and dosage and always creating an exit strategy are considered mandatory (44). The fracture rate in the elderly increases with cyclosporine (45) and methotrexate, which are superimposed on the impact of inflammatory cytokines of active IBD. Coexistent malabsorption or nutritional deprivation of vitamin D and calcium occurs frequently in the elderly; e.g., 55% of hospitalized elderly are protein malnourished (46), with 21% ingesting < 50% of their maintenance nutritional requirements (47).

Corticosteroid drug interactions include phenytoin, phenobarbital, ephedrine, and rifampin, all of which accelerate steroid metabolism and thereby lessen its systemic activity (9).

Immunomodulators

Methotrexate, 6-MP, and AZA are the most commonly used in this group for their steroid-sparing properties. Allopurinol use is hazardous for its propensity for increased myelotoxicity when given with 6-MP or AZA, but this interaction potentially has a benefit in reducing the 6-MP/AZA dose (48). This is particularly true if abnormal liver functions supervene with the continued use of these immunomodulators. Once introduced, improved liver functions have been recorded without altered 6-MP/AZA efficacy. However recent concerns have arisen that concomitant use of immunomodulators and allopurinol increases the incidence of infection in older patients. Those with high body mass index and high thiopurine dosage had lower absolute lymphocyte counts, which predicted such infection (49). Other important drug interactions with 6-MP and AZA include a possible decrease in the anticoagulation effect of warfarin (50).

Methotrexate depends upon renal excretion; therefore, the lower glomerular filtration rate in the aged population will have an impact on this drug's clearance (9). Its capability for bone marrow suppression, hepatic fibrosis, and alopecia is well recognized, as is the need for supplemental folate when administering this drug (9). NSAIDs and 5-ASA will inhibit the renal excretion of methotrexate and may increase its toxicity (9). Tetracycline inhibits methotrexate absorption and penicillin decreases its renal clearance (9). Methotrexate also alters the clearance of theophylline.

Cyclosporine is sometimes used in IBD patients who need immunosuppression, although fewer clinicians are as experienced with this drug as with corticosteroids and infliximab. Furthermore, the risk of side effects with cyclosporine is higher in older patients than younger patients. Cyclosporine requires CYP3A4 metabolism. Age does not impact the peak plasma concentrations of cyclosporine or the half-life (51).

Cyclosporine drug interactions include:

(a) Increased nephrotoxicity when given with certain antibiotics such as gentamicin, tobramycin, vancomycin, ketoconazole, ciprofloxacin, and trimethoprim–sulfamethoxazole. Other drug interactions occur with NSAIDs, melphalan, and histamine-2 receptor antagonists such as cimetidine (9,51).
(b) The *P*450 cytochrome inhibitors decrease the metabolism of cyclosporine, thereby increasing its blood levels, particularly in the elderly. Examples include diltiazem, nicardipine, verapamil, metoclopramide, allopurinol, amiodarone, and macrolide antibiotics such as azithromycin, clarithromycin, and erythromycin (9,51).
(c) Reduced cyclosporine blood levels can occur with accelerated hepatic metabolism when given with phenytoin, rifampin, and carbamazepine (9,51).

Antibiotics

Antibiotics are used primarily to treat fistulizing Crohn's disease and other infectious complications. The role of antibiotics in the primary treatment of IBD is controversial. Antibiotics have many potential side effects, including diarrhea and an increased risk of *Clostridium difficile* infection. Metronidazole and ciprofloxacin are commonly used in IBD patients. The side effects and drug interactions of metronidazole include:

(a) Cytochrome inhibition resulting in increased levels of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-coA) reductase inhibitors such as simvastatin, sildenafil, and calcium channel blockers (52).
(b) Potentiation of warfarin, thereby prolonging the international normalized ratio (9,38).
(c) Antabuse (disulfiram) reaction with alcohol ingestion (52).
(d) Neuropathy may be particularly marked in the elderly as well as the associated nausea and metallic taste (9,52).
(e) Increased elimination by phenytoin or phenobarbital.

Ciprofloxacin decreases theophylline clearance with the potential for significant central nervous system side effects (53). It also reduces caffeine clearance (53), may alter serum phenytoin levels (9), and increases warfarin levels, resulting in an increased international normalized ratio (38,53).

WHAT IS THE ROLE OF BIOLOGIC THERAPY IN THE ELDERLY?

Biologic therapy is well recognized as a breakthrough in the management of IBD, yet there is a paucity of data involving its use in the elderly IBD patients. However, much can be gleaned from experience with biological use in other populations. In 7 of 13 rheumatoid arthritis and/or psoriasis studies and 2 IBD studies using biologic agents in the elderly, differences in efficacy or safety were seen in elderly patients when compared with younger patients (**Table 1**).

Infliximab was the first anti-tumor necrosis factor antibody approved for use in Crohn's disease, followed by adalimumab and certolizumab. Infliximab is also approved for use in ulcerative colitis. There are little data on the efficacy of these agents in the elderly. An Italian study of elderly IBD patients treated with an anti-tumor necrosis factor antibody (68 infliximab and 13 adalimumab) when followed at 26 months revealed a remission rate of 65% in Crohn's disease and 61% in ulcerative colitis (54).

The main concern for toxicity with biologic therapy is with infections, although in a large postmarketing study, the risk of serious

Table 1. Summary of literature on biologic therapy in the elderly: adverse events vs. efficacy

	Age effect
In RA, age was a predictor of SI, especially tuberculosis (84)	+
In RA treated with etanercept, age was not associated with SAEs (85)	=
In psoriasis treated with etanercept, AEs were more common in young and SI more common in elderly (86)	±
In elderly RA patients (4 RCT, 2 open label), similar AEs with etanercept and placebo (87)	=
In RA, no safety differences between age groups (88)	=
In RA, no difference in drug discontinuation rates, and HAQ improved less in the elderly (89)	±
In RA, age was not a predictor of infection (90)	=
In RA, age was a predictor of SI (91)	+
In RA, comorbidities were a predictor of SI, age±risk (92)	±
In RA treated with MTX vs. MTX and biologic therapy, age was not predictive of efficacy (93)	=
In elderly RA patients treated with biologics and DMARDs, steroids doubled the SI risk (94)	±
In RA and psoriasis treated with infliximab, no difference in efficacy by age, but SAE increased in patients >65 years old (95)	+
In elderly RA patients treated with biologics and DMARDs, age was associated with SAEs (96)	+
In IBD patients treated with infliximab or adalimumab, age was associated with AE, SAE, and SI (56)	+
In IBD patients treated with anti-TNF biologics, age was associated with SI and mortality (54)	+

AE, adverse event; DMARD, disease-modifying antirheumatic drug; HAQ, Health Assessment Questionnaire; IBD, inflammatory bowel disease; MTX, methotrexate; RA, rheumatoid arthritis; RCT, randomized controlled trial; SAE, serious adverse event; SI, serious infection; TNF, tumor necrosis factor. Age effect: +, age associated with worse outcome; ±, association with age was mixed or unclear; =, no association between age and outcomes.

infection was not as marked as that seen with corticosteroids and narcotics (55). On the other hand, in the Italian study of elderly IBD patients, 10% had severe infections, two developed neoplasms (rectal and prostate), and there were nine deaths (54). A Mayo Clinic study of elderly IBD patients given biologic therapy revealed greater adverse events in older patients compared with a matched cohort of younger patients on similar therapy, when adjusted for disease extent, severity, and comorbidities (56). In another study of 500 patients with Crohn's disease treated with infliximab, there were five deaths possibly related to infliximab, and four of these deaths were in patients over the age of 65 years (57). However, many of the older patients in this study had comorbidities and many were on concomitant immunomodulator therapy, such that the independent contribution of age was not clear (57). Nonetheless, significant hepatic disease, congestive heart failure, concomitant infections, or bone marrow depression should contraindicate the use of biologic therapy. Live vaccines must be avoided when using these, or any other, immune-suppressing medications.

DOES ANTICOAGULATION/ANTIPLATELET THERAPY AFFECT IBD MANAGEMENT IN THE ELDERLY?

Despite the fear of worsening IBD in patients given antiplatelet or anticoagulation therapy, a study of this issue in 90 elderly Crohn's disease patients showed that aspirin and warfarin use was not associated with increased Crohn's disease activity (58). Similarly, the Lenox Hill Hospital experience with 41 IBD patients on aspirin and clopidogrel for coronary artery disease (CAD) showed no change in the frequency of IBD flares in most patients on antiplatelet therapy when compared with a control group not on such therapy (59). Interestingly, an 11% reduction in IBD flares occurred in patients on antiplatelet therapy (59).

Another study of aspirin use in "geriatric" Crohn's disease patients with vascular disease showed no difference in hospitalizations whether taking ASA or not (60). However, the cardiovascular risk in the elderly with selective Cox II inhibitors such as rofecoxib merited its withdrawal from the market. Celecoxib remains in the market, but is still a concern. This becomes a difficult problem in the elderly IBD patients with arthralgias/arthritis.

As noted above, many drugs that are used in treating IBD can interfere with warfarin metabolism (38), and potential interactions should be considered in any patient taking warfarin when a new IBD medication is begun.

WHAT ARE THE CLUES IN THE DIFFERENTIAL DIAGNOSIS OF THE ELDERLY IBD PATIENTS?

In the elderly, an appropriate differential diagnosis needs to be considered before making a definite diagnosis, as several other conditions can present with symptoms that mimic IBD, including complicated diverticular disease (diverticulitis and diverticular bleeding), ischemic colitis, medication-associated diarrhea (NSAIDs, antibiotics, others), microscopic colitis, radiation colitis, and infectious diarrhea. These conditions are relatively common in older subjects and, for some, a delay in diagnosis or the institution of inappropriate treatment can lead to grave complications.

Infectious colitis presents a particular difficulty when bloody diarrhea is the presenting complaint (61). *C. difficile* is a common threat whereas organisms such as *Shigella*, *Campylobacter*, *Escherichia coli 0157:H7*, and *Yersinia* are often of shorter duration, resolving within 1 to 2 weeks (61). Nevertheless, *Yersinia* causes ileitis and the extraintestinal manifestations that mimic Crohn's disease. These infections are often identified by culture in the realm of acute self-limited colitis with comparable findings on endoscopic biopsy. *C. difficile* is no longer restricted as a nosocomial infection, but is now also recognized as a community-acquired infection. This is particularly true in patients over 65 years of age who may be infected with a virulent strain that can cause a prolonged hospitalization and greater mortality (62).

NSAID-induced ulcerations, strictures, and even perforation may mimic IBD or complicate the management of an IBD patient (63). Relapses of ~20% in patients of their IBD have been reported because of NSAID use, especially the nonselective inhibitors (64). This was not seen with selective COX II inhibitors or aspirin, a COX I inhibitor, or acetaminophen (65). However, the University

of Pittsburgh's experience did not correlate NSAID use with rates of IBD activity over an 18-month period (18).

Ischemic colitis in the elderly IBD patient occurs with segmental involvement leading to confusion with Crohn's disease (66). The classic abrupt onset of severe pain and subsequent bloody stools suggests this diagnosis. The history, biopsy, and subsequent course, and less often imaging studies, can usually distinguish this diagnosis from Crohn's disease.

Microscopic colitis frequently mimics irritable bowel syndrome with diarrhea, and occurs most commonly in mid- to later-age women (67). Given the normal-appearing mucosa, this diagnosis should not typically be confused with IBD. The diagnosis requires biopsy confirmation to detect either collagenous or lymphocytic colitis. Interestingly, 10% of such patients may also have celiac disease (67). The response to budesonide has been most favorable and rarely requires systemic corticosteroids (67). Patients in the older age range may also undergo spontaneous remission or require a lower drug dosage.

Radiation-induced injury may also mimic IBD or complicate the management of the elderly patients with IBD. This injury occurs most commonly with gynecologic, rectal, and prostate cancers, and represents a formidable management problem (68). The mucosal appearance may be similar to IBD, although biopsies can often distinguish these diagnoses. Topical 4% formalin solution applied to the affected area can be helpful, but more than half of the patients will require repeated treatments. Rarely is colorectal resection needed (68).

Diverticulosis is common in the elderly, with 35–60% of people over age 60 years affected (69). In one population-based cohort, diverticula were found in 46% of patients with IBD who were ≥60 years old at the time of diagnosis (70). Diverticulitis and diverticular bleeding are the most common complications, and can mimic symptoms of IBD. Diverticulitis can be difficult to distinguish from Crohn's disease, especially when there is perforation and abscess formation or fistulization. In most cases, management of these complications is the same irrespective of whether they are because of Crohn's disease or diverticulitis, and in a patient without known Crohn's disease, mucosal biopsies may help make the distinction based on the presence or absence of chronic architectural changes.

Diverticular colitis, also known as segmental colitis associated with diverticula, can mimic Crohn's disease of the colon (71). This condition may be associated with granulomata on sigmoid biopsies, and may respond to oral mesalamine, although occasionally corticosteroids are required (71).

Other confounding diagnoses include lymphoma, carcinoid syndrome, vasculitis, and amyloidosis.

IS IBD-RELATED COLORECTAL CANCER SURVEILLANCE DIFFERENT IN THE ELDERLY?

Surveillance guidelines are based on duration of colitis, and recommendations are not different for the elderly, with the exception that surveillance should only be done in patients whose life expectancy is such that they would be expected to benefit, and in those who are healthy enough to undergo colectomy should dysplasia be found. There is considerable anxiety regarding risks of colorectal cancer in the elderly IBD patients, especially with prolonged disease duration and extent (72). This is heightened by the coincident increase in sporadic cancers with advanced age (73), as well as from precancerous lesions in the flat mucosa that may escape colonoscopic detection. Conceivably, simple polypectomy may be adequate if accompanied by the absence of dysplasia in four quadrant biopsies at the base of the excised polyp (74). This is particularly true if the polyp was distant from the site of colitis and was pedunculated with a short duration of disease and absent primary sclerosing cholangitis. However, this advice is still based on limited experience. Even with the use of chromoendoscopy or confocal endoscopy (75), managing colonic polyps in the long-standing IBD patient requires a lengthy discussion with the patient regarding the risks and benefits of repeated surveillance vs. that patient's candidacy for surgery.

There is evidence from the Cleveland Clinic that the cumulative incidence of pouch neoplasia increases in time, to 5.1% at 25 years after surgery. The major risk factor was preoperative ulcerative colitis-related dysplasia or cancer. Interestingly, mucosectomy, which is often touted as a benefit in preventing cancer over the stapled anastomosis, was not protective. As the elderly patient is particularly prone to neoplasia, this IPAA population requires greater scrutiny and surveillance (76).

WHAT ARE THE ISSUES RELATED TO VACCINATION IN THE ELDERLY IBD PATIENTS?

The vaccination status of the elderly IBD patients is often neglected. The patient's vaccination schedule or antibody titers should be reviewed, and appropriate vaccines administered (77,78), preferably before immunosuppressive therapy is begun, as these medications may blunt the immune response (77,78). Live vaccines are contraindicated in immune-suppressed patients for fear of disseminated infection (79). Immunosuppressed patients must be counseled regarding travel to certain areas if live vaccines (e.g., yellow fever, Bacillus Calmette-Guérin (BCG), oral polio, oral typhoid) are required for travel to those areas (77,78).

Live intranasal flu vaccines should be avoided in immunosuppressed patients, with a preference for the inactivated intramuscular vaccine (80). Pneumococcal vaccine should be given periodically, i.e., the initial dose, and then revaccination in patients over 65 years after 5 years, whether immunosuppressed or not (81).

Hepatitis B serologies should be checked before beginning immunosuppressive therapy. If immunity is not found, the three-dose vaccine should be given, especially before use of anti-tumor necrosis factor biologic agents (82). Suboptimal responses to this vaccine may occur and, if so, revaccination should be considered with the use of a combined hepatitis A and B vaccine, as the hepatitis A component may provoke an adjuvant-like response.

Hepatitis A vaccine should be given to all IBD patients in a two-dose schedule with a booster dose after 10 years (77,78).

Meningococcal vaccine should be given to patients expected to live in a dormitory or barracks-like environment or those who have undergone splenectomy (77,78).

Herpes zoster vaccine is of special concern in the elderly IBD patients. Serologic titers should be drawn before administration of immunomodulators, steroids, or biologics. If needed, the patients should be immunized. Prior varicella history and herpes zoster antibody status are frequently unknown. For patients on immunosuppressive therapy, discontinuation of these medications for a minimum of 4 weeks before vaccination is suggested, and some authorities prefer a 3-month wait. Varicella vaccine may be given to household members of immune-suppressed patients, but if a vaccine-related rash occurs, then contact with the immune-suppressed patients should be avoided (78).

If the MMR vaccine history is unknown, antibody titers should be checked. A minimum of 6 weeks to preclude viremia would be necessary between MMR administration and the use of immunomodulators. However, there is reasonable safety in giving MMR to household contacts of immune-compromised patients (72,73).

IS IBD A SIGNIFICANT RISK FACTOR FOR CAD?

In a study comparing patients with IBD and CAD with age- and sex-matched patients with CAD alone, the Framingham risk score indicated IBD to be an independent risk factor for CAD, after controlling for variables such as hypertension, diarrhea, tobacco use, and serum lipids (83). There were no significant treatment differences between the groups. Whether mucosal inflammation with increased proinflammatory cytokines and adhesion molecules leads to atherosclerosis, altered lipids, and plaque rupture remains speculative.

CONCLUSION

The clinical features and treatment considerations of IBD in the older patients are similar to younger patients, with notable exceptions as discussed above.

In addition, consideration of appropriate differential diagnoses, comorbidities, drug–drug interactions, and concerns about progression to neoplasia is critical in the management of the older IBD patients. With the growth of the elderly IBD patient population, the impact on utilization of available health resources in this group will be considerable.

There has to be a clinical distinction between "fit vs. frail" elderly. The former should not be excluded from newer therapies or clinical trials simply by age discrimination, and more research specifically addressing issues in elderly IBD patients is needed. Clinicians must add concepts of management of the elderly to their deliberative processes. Given emerging data on the risks of aggressive immunosuppressive therapy in the elderly, an approach to drug therapy in this group might be a "start low-go slow" concept, with reassessment for progression to more aggressive therapy if response is inadequate. However, the risk of inadequately treating IBD in terms of disease progression and quality of life needs to be part of the decision-making process. Traditional therapeutic decisions should be coupled with special needs such as social support networks for this highly vulnerable population.

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CONFLICT OF INTEREST

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