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Inflammatory Bowel Disease in the Elderly

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Introduction

The incidence of inflammatory bowel disease (IBD) among the elderly in Canada has increased from 1 out of 160 seniors in 2018, to 1 out of 88 seniors in 2023, representing 1.14% of the senior population.[1] It is thought that more than one-third of all IBD patients will be over 60 years of age in the next decade.[2] The prevalence is expected to increase due to a combination of new diagnoses as well as the aging of younger people already living with IBD.

Elderly persons with IBD face unique challenges that younger people with IBD often do not, such as co-existing comorbidities, frailty, polypharmacy, and an increased risk of infections and cancer. While the therapeutic management of elderly persons with IBD is similar to that of younger people with IBD, it requires careful consideration of many different factors, and special attention is needed when weighing the risks and benefits of medical therapy.

Clinical Presentation

Elderly-onset Crohn's disease (CD) is more frequent in females, while elderly-onset ulcerative colitis (UC) is more common in males.[3,4]

Elderly persons with IBD can present with different symptoms compared to younger people with IBD. In UC, weight loss is more commonly reported, while rectal bleeding and abdominal pain are less commonly reported.[3] Left sided disease is the most common presentation. Additionally, the cumulative 5-year risk of surgery is 7.8%, which is similar to that of adults with IBD.[5] Compared with younger individuals with CD, elderly people are more likely to have isolated colonic disease, as well as fibrostenosis, while penetrating or perianal disease is rare.[5,6] Rectal bleeding, diarrhea, abdominal pain, and weight loss are all less common.[3] The cumulative 5-year risk of surgery for those over the age of 60 with CD is 22.6%.[5] Rates of primary sclerosing cholangitis and dermatologic manifestations of IBD are similar between elderly persons and younger adults,

with elderly persons having higher rates of ocular manifestations of IBD, and lower rates of arthritis.[7]

In addition, the risk of post-operative mortality is higher in elderly persons with IBD compared to younger people, with rates of 6.1% versus 0.7% in UC and 4.2% versus 0.3% in CD. The risk of non-fatal post-operative complications is similarly higher for elderly people with both CD and UC.[8]

It is important to consider other causes of intestinal inflammation in elderly people, as the differential diagnosis can be broad. This includes conditions such as infectious colitis, microscopic colitis, ischemic colitis, segmental colitis associated with diverticulosis, radiation colitis, and malignancy.[9] For this reason, elderly people can often be misdiagnosed,[10] which can lead to delays in receiving appropriate treatment.

Comorbidities in the Elderly

Persons with IBD are at an increased risk of developing osteoporosis, a risk that cannot be solely attributed to corticosteroid use.[11] A population-based study in Manitoba showed that people over the age of 65 years with IBD have an increased risk of cerebrovascular disease (hazard ratio [HR] 1.19, 95% confidence interval [CI] 1.01–1.40), cardiac disease (HR 1.24, 95% CI 1.07–1.43), peripheral vascular disease (HR 1.36, 95% CI 1.14–1.62), cancer (HR 1.21, 95% CI 1.04–1.40), and other comorbidities.[12] A large US study assessing a nationwide database found that persons with IBD over the age of 65 are more likely to be hospitalized with serious infections and cardiovascular complications compared to individuals aged 40–64 and those younger than 40.[13]

Disease Related Complications

Ananthakrishnan et al. showed that older persons with IBD (65 years or older) who are hospitalized for their condition have an increased mortality compared to those with IBD aged 19–64 years (odds ratio [OR] 3.91, 95% CI 2.50–6.11). This mortality risk is even higher when compared to just those aged 19–35 years (OR 17.42, 95% CI 8.92–33.99).[14] A large US cohort study found that the risk of herpes zoster was higher in those with IBD treated with 5-ASA only compared to persons without IBD (adjusted HR [aHR] 1.72, 95% CI 1.51–1.96). Within the IBD cohort, age was identified as a risk factor for becoming infected.[15] A retrospective study that included[13] hospitals in Hong Kong showed that elderly-onset persons with IBD have a higher risk of developing herpes zoster (OR 2.42, 95% CI 1.22–4.80), cytomegalovirus colitis (OR 3.07, 95% CI 1.92–4.89), all-cancer development (OR 2.97, 95% CI 1.84–4.79), and IBD-related hospitalizations (OR 1.14, 95% CI 1.09–1.20) compared with those with adult-onset IBD.[6]

Access to Care

It has been reported that technology literacy decreases with age,[16] making it difficult for elderly persons with IBD to access their gastroenterologist, particularly as more health care providers have been incorporating virtual care into their practices since the COVID-19 pandemic. Additionally, research has shown that elderly persons with IBD who are treated by a gastroenterologist, or are part of a network with more gastroenterologists, experience better outcomes. These patients are more likely to be prescribed a biologic or immunomodulator compared with those who are not treated by a gastroenterologist.[17]

Frailty

Frailty describes a state where one has a decreased physiologic reserve in response to a stressor, which is often not related to chronologic age, but more to biologic age. Although frailty can theoretically occur at any age, it is more common in the elderly. Frailty has been shown to be related to low-grade inflammation with elevated levels of c-reactive protein (CRP), tumor-necrosis factor-alpha (TNF-alpha), and interleukin-6.[18] It has been shown that fecal calprotectin levels can be elevated in various diseases such as ischemic colitis, neoplasm, and even diverticulitis, as well as with certain therapies such as non-steroidal anti-inflammatory drugs and proton pump inhibitors.[19] Since these are more common in the elderly, biomarkers such as CRP and fecal calprotectin may be less specific for disease activity in the elderly with IBD. Studies reveal that frailty is present in 5–33% of persons with IBD,[20-22] and is more common in older persons with IBD compared to those without IBD.[23] The presence of frailty in persons with IBD is associated with an increase in adverse outcomes, including prolonged hospitalization, readmission to hospital

for IBD, and mortality.[22,24] One study also showed that the presence of pre-treatment frailty was associated with an increased risk of infections in those receiving immunomodulators and anti-TNF therapy.[25]

Polypharmacy

Polypharmacy, often defined as the use of 5 or more medications, is a concern in the elderly, as it can lead to non-adherence with IBD therapies. In people 65 years or older, polypharmacy has been associated with adverse outcomes including drug interactions, falls, urinary incontinence, and cognitive decline.[26] In addition, it poses a risk of flaring in those with IBD (OR 4.0, 95% CI 1.66–1.92).[27] A study of senior persons with IBD showed that each individual had on average 9 prescribed medications, and 40% of them had a potential drug interaction involving one of their IBD therapies.[28] A retrospective study of persons with IBD aged 60 years or older showed that almost three-quarters of the patients experienced polypharmacy. Severe polypharmacy, defined as taking 10 or more medications, was associated with an increased risk of hospitalization (aHR 2.16, 95% CI 1.37–3.43).[29]

Deficits

Geriatric deficits are more common in elderly persons with IBD, and those with active disease are more likely to have deficits compared to those without.[30] The same study also found that elderly persons who were diagnosed with IBD at age 60 or later are more likely to experience cognitive impairment, reduced handgrip strength, and slower gait speed. These deficits are also associated with a lower health-related quality of life.

Treatment and Safety

While therapeutic efficacy for elderly persons with IBD is mostly similar to that of younger patients, there are potential complicating factors to consider. These include increased risks of infection and malignancy, and the potential for drug-drug interactions.

Corticosteroids remain effective for induction therapy and for rapidly improving symptoms in persons with IBD. A systematic review and meta-analysis showed that the use of corticosteroids in persons with IBD over 60 years of age is similar to their use in those younger than age 60, however, the study also showed that the use of immunomodulators and biologics is lower among elderly persons with IBD.[5]

Oral 5-ASA therapies are an effective and safe therapy for inducing and maintaining remission for mild-to-moderate UC, and despite its lack of evidence for their use in CD, they remain widely used.[3] Thiopurines continue to be effective treatments for both UC and CD. A cohort study following elderly persons with IBD has shown that one-fifth of patients were exposed to thiopurines within 5 years of their diagnosis.[31] Thiopurine use, however, can increase the risk of infections,[32] non-melanoma skin cancers in persons over 65,[33] and lymphoproliferative disorders in those over 50.[34] In elderly patients with IBD who start a thiopurine over 60, they are at an increased risk of adverse events including infections, neoplasms, and hematologic abnormalities compared to those who are less than 50 who start a thiopurine.[35]

Anti-TNF therapies remain an important option for elderly persons with IBD, especially for those who are hospitalized, steroid dependent, or steroid refractory. However, the evidence for anti-TNF efficacy in older people with IBD is conflicting. Some studies show that elderly persons have a lower persistence with anti-TNF therapy and are more likely to experience treatment failure.[36,37] Alternatively, analyses from randomized trials show no difference between the older cohort (60 years old and older) compared with the younger cohort (younger than 60) in terms of inducing and maintaining remission.[38] A pooled analysis from randomized trials assessing anti-TNF found an increased risk of adverse events in people aged over 60 years with UC. However, age was a more significant predictor of these adverse events than the anti-TNF therapy.[38] Persons over 60 with immune-mediated inflammatory diseases who were on biologics had an increased risk of infection compared to both older people not on biologics and younger persons on biologics.[39] One study showed that combination therapy involving anti-TNF and a thiopurine in persons over 60 was associated with an increased risk of herpes zoster infection.[15] However, another study observed no difference in infection risk for those over 60 years on combination therapy compared to those receiving conventional treatment.[40]

Vedolizumab, a gut-specific monoclonal antibody, is effective in the elderly, with an efficacy comparable to younger persons.[41,42]

In a retrospective cohort of persons over 60 assessing vedolizumab and anti-TNF therapy, vedolizumab was discontinued less frequently (25.9% versus 51.9%), and had higher endoscopic remission rates (65.7% versus 45.2%).[43] Vedolizumab is effective in the elderly, and is equally as effective and safe as ustekinumab in elderly persons with CD.[44,45] A retrospective study in Italy showed a higher persistence on vedolizumab in non-elderly persons with UC compared with people over 65 years-old, but this was not seen with CD, although they did not control for prior anti-TNF exposure.[46] Vedolizumab has a lower risk of infectious complications and is considered safe for elderly patients.[47]

Ustekinumab, an anti-IL12/23 antibody, has comparable effectiveness across all age groups.[48] One study showed that rates of mucosal healing were similar in the older (65 years and older) and younger (<65 years) cohorts.[49] It is also considered safe for elderly patients, with no increased risk of infectious complications.[50]

Newer anti-IL23 antibody treatments are also considered equally effective and safe among all age groups, including elderly patients, with no increased risk of infections or malignancy.[51,52]

Advanced oral therapies, including Janus kinase inhibitors (JAKi) (tofacitinib and upadacitinib) and oral S1P receptor modulators (ozanimod and etrasimod), have emerged as therapeutic options in recent years. Clinical trial data assessing etrasimod in UC have shown that outcomes are similar across all age groups, including those over 60.[53] Additionally, safety outcomes are similar across all age groups with no increased risk of infection.[53,54] Tofacitinib has been shown to be effective in treating UC across all age groups. However, age was a significant predictor for herpes zoster infection, malignancies excluding non-melanoma skin cancers (NMSC), and NMSC.[55] Small studies have shown upadacitinib to be effective in older people with UC,[56] and it is also indicated in the treatment of CD. The safety profile of upadacitinib in the elderly is thought to be comparable to younger people[49], though there is an increased risk of herpes zoster infection with JAKi treatment and this risk increases with age.[57] Hence, it is imperative that persons with IBD be vaccinated against herpes zoster regardless of their therapy, but especially if they are starting treatment with a JAKi.

Conclusion

The prevalence of IBD in elderly persons is only increasing, presenting unique challenges for their management. When treating elderly persons with IBD, one must be cognizant of age, comorbidities, polypharmacy, frailty, and access to care. Anti-TNF therapies are potentially associated with an increased risk of infection, therefore, biologics with improved side effect profiles should be considered when appropriate. Owing to the complex medical needs of elderly persons with IBD, a multidisciplinary approach is essential to provide comprehensive care.

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