

Supplement Article

The Impact of Inflammatory Bowel Disease in Canada 2018: IBD in Seniors

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Abstract

Approximately one in every 160 seniors live with IBD. Due to the fact that IBD has no known cure, and thus patients diagnosed at younger ages will carry their disease with them into their senior years, the number of senior IBD patients is rising significantly in Canada. Seniors with IBD present unique challenges for care. Patients with IBD will experience greater comorbid conditions resulting from their advancing age and longer disease duration. Risks associated with IBD-related surgeries and complications from other illnesses associated with age and their medications further complicate treatment options and may lead to higher healthcare utilization. Healthcare providers need to be prepared to work in multidisciplinary teams with other specialists in order to address the complexity and comorbidities of seniors with IBD.

Highlights

1. Approximately one out of every 160 individuals over the age of 65 in Canada is living with IBD.
2. The rising prevalence of IBD in seniors results from new diagnoses and advancing age of previously diagnosed patients with IBD.
3. Patients with IBD will experience greater comorbid conditions resulting from their advancing age and longer disease duration.
4. As the IBD population ages, the proportion of seniors with IBD will increase in gastroenterology clinics.
5. The care of seniors with IBD brings unique challenges with respect to therapeutic decision-making.

Key Summary Points

1. Approximately 0.6% of seniors in Canada live with IBD.
2. In Ontario, the prevalence of IBD among seniors increased by 5.2% per year, which outpaced the 3.9% per year rise observed in nonseniors.

Received: 24 July 2018; Accepted: 6 September 2018

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3. Approximately 15% of IBD patients are newly diagnosed after the age of 65 years.
4. The incidence of IBD in seniors ranged from 16.5 to 18.9 per 100,000 in Canada.
5. In Ontario, the diagnosis of ulcerative colitis in seniors was double that of Crohn's disease.
6. Clinical presentation of seniors with Crohn's disease is unique with a higher likelihood to present with isolated colonic disease without fistulizing disease or extra-intestinal manifestations as compared with those diagnosed at a younger age.
7. Seniors with IBD are less likely to have outpatient visits relating to their IBD as compared with younger patients with IBD.
8. Among individuals diagnosed over the age of 65, the 10-year risk of intestinal surgery was 7% to 19% for ulcerative colitis and 31% for Crohn's disease.
9. Seniors who undergo intestinal resections for their IBD have significantly higher postoperative complications and mortality as compared with younger IBD patients undergoing surgery.
10. The use of anti-TNF agents in seniors is lower for Crohn's disease (4.0%) and ulcerative colitis (2.3%) as compared with younger individuals with IBD. However, the rate of use of biologics is increasing over time.
11. Therapeutic decision-making in seniors with IBD is challenging due to their comorbid conditions.
12. Seniors who use thiopurines have a higher risk of lymphoma (5.4 per 1000 person-years) as compared with IBD patients younger than 50 (0.37 per 1000 person-years) exposed to thiopurines.
13. Newer gut-selective $\alpha 4\beta 7$ integrin inhibitors may be a safer choice for seniors due to potentially lower risk of infection and cancer.
14. Due to multiple comorbidities, seniors with IBD may struggle with polypharmacy that can lead to drug interactions and reduced medication adherence.
15. Persons between 65 and 79 of age with IBD on average cost the healthcare system \$5298 per year, which is higher than age-matched controls.

Gaps in Knowledge and Future Directions

1. Administrative healthcare databases are more likely to misclassify senior patients with IBD. Future research is necessary to improve the identification of senior patients with IBD in databases.
2. Gastroenterologists will need to contend with an older IBD population with greater comorbidities. Research focusing on defining the burden of comorbidities in senior IBD patients is needed for healthcare resource utilization planning.
3. The use of anti-TNF in senior patients is lower than in younger individuals with IBD. Future research should evaluate trends in using biologics in the senior population with the advent of newer biologics such as integrin and other cellular adhesion molecule inhibitors.
4. Polypharmacy is a challenge for senior IBD patients. Future research should focus on interventions to simplify drug regimens and administration for senior patients.
5. Senior individuals with IBD cost the healthcare system more than age-matched controls. However, research is necessary to establish the IBD-attributable cost to the healthcare system and the indirect cost to society.

Keywords: *Crohn's disease; Ulcerative colitis; Elderly; Epidemiology; Healthcare utilization*

Though IBD is commonly diagnosed in young adulthood, it can present at any age. As the IBD population ages, there will be an increasing number of IBD patients who are senior (commonly defined as age 65 years or older). The care of senior IBD patients brings unique challenges with respect to diagnosis and therapeutic decision-making. The frequent coexistence of comorbid conditions may influence the choice of therapeutic

strategies. The IBD clinic of the future will be populated with older patients with longer disease durations and higher risks of comorbid conditions. This section of the report will characterize the unique considerations and challenges for care of seniors with IBD. A complete overview of the objectives, working committees and methodology of creating the report can be found in online supplemental file, Technical Document.

EPIDEMIOLOGY

Approximately one out of every 160 senior individuals in Canada is affected by IBD. The prevalence of IBD among seniors is rising. Epidemiologic data from Ontario suggest that the prevalence of IBD increased by 5.2% annually among seniors between 1999 and 2008, higher than that observed in nonseniors (3.9% annual increase) (1). The increase in prevalence was similarly observed in both Crohn's disease and ulcerative colitis. The incidence of IBD in Canada varies by province and the age cutoff used to define senior, but it has been reported to be as high as 18.9 per 100,000 for Crohn's disease and 16.5 per 100,000 in ulcerative colitis, with the highest rate of IBD noted in Quebec (2). In Ontario, the incidence of ulcerative colitis (12.4 per 100,000) was nearly twice that of Crohn's disease (6.6 per 100,000) in seniors. A similar predominance of ulcerative colitis among newly diagnosed IBD cases among seniors was also reported in Manitoba, where the incidence was 16.5 per 100,000 for ulcerative colitis compared with 10.7 per 100,000 for Crohn's disease (3). The rising prevalence of IBD in seniors is a result of new diagnoses made in this population and advancing age of previously diagnosed patients with IBD with long disease duration.

DISEASE PRESENTATION

Senior patients with longstanding IBD who were diagnosed in younger adulthood may be clinically distinct from those with senior-onset IBD. As many as 15% of IBD patients are diagnosed after 65 years of age. The diagnosis of IBD in seniors can be challenging, and misdiagnosis can occur in up to 60% of the cases due to other conditions that can mimic IBD (4). These other conditions include some that occur more frequently in the senior population such as microscopic colitis, diverticular disease, ischemic colitis, infectious colitis and malignancy. Moreover, the presentation of IBD can be more subtle in seniors. In ulcerative colitis, rectal bleeding and abdominal pain are less common, and weight loss is more commonly seen (5). Similarly, diarrhea, rectal bleeding, abdominal pain and weight loss are all less commonly seen in senior-onset Crohn's disease than in disease presenting at younger ages (5).

With respect to disease characteristics, seniors with Crohn's disease are more likely than their younger counterparts to have isolated colonic disease. They are also less likely to present with perianal fistulizing disease and extra-intestinal manifestations. On disease presentation, senior ulcerative colitis patients are more likely to have left-sided disease. Family history of IBD is less common among senior patients (5).

Inflammatory bowel disease often follows a more benign disease course when presenting in seniors. For Crohn's disease, there is less frequent development of fibrostenotic or penetrating disease phenotype. In ulcerative colitis, there is less frequent extension of colitis (proximal to the splenic flexure) compared

with younger-onset ulcerative colitis (5, 6). A large French cross-sectional study of IBD patients suggests that older age (>60 years) is not associated with worse quality of life, fatigue or disability (7).

HEALTHCARE UTILIZATION

While seniors, in general, see physicians and other healthcare providers more often, those with IBD may not see physicians more often for IBD-related reasons. Nguyen et al. determine that healthcare visits for IBD among Ontarians diagnosed after age 65 are significantly lower than for those diagnosed prior to age 65 (8). This observation holds true both for the first year after diagnosis and into the third year of disease. The same pattern is seen when comparing visits to the emergency department. This may be due to the lower acuity of senior-onset IBD when compared with nonsenior onset IBD or may also be related to senior outpatient visits being more focused on diseases of higher morbidity, such as cardiovascular disease.

In the first year after diagnosis, the hospitalization rate with a primary diagnosis of IBD for senior-onset IBD was 357 per 1000 person-years for Crohn's disease and 247 per 1000 person-years for ulcerative colitis. During the fifth year after diagnosis, these rates decreased substantially to 48 and 25 per 1000 person-years, respectively. Ananthakrishnan et al. find that hospitalization rates in the United States are not different between senior and nonsenior IBD patients. However, the case fatality rate of IBD is four times higher than among younger hospitalized patients, and the duration of the hospital stay is an average of two days longer (9).

SURGERY

Targownik et al. determine that persons who have ulcerative colitis diagnosed after age 65 have a 3.1% risk of requiring a colectomy within 90 days compared with a 1.6% risk of those diagnosed under age 65 (10). However, among those over the age of 65, the risk of requiring surgery was lower over time, with the colectomy rates at five years for those diagnosed over age 65 being approximately 7% at 10 years post-diagnosis compared with 10% for those between 25 to 64 years of age at diagnosis and 17% for those diagnosed under age 25. By contrast, Nguyen et al. report that persons with senior-onset ulcerative colitis have a higher rate of IBD-related surgery, with 19% of senior and 13% of younger adults undergoing IBD-related surgery within 10 years of diagnosis (11). Persons with ulcerative colitis and higher levels of comorbidity are twice as likely to require surgical management. Among persons with Crohn's disease, Nguyen et al. report a rate of surgical management of 31% over 10 years, which is not different from the surgical rate of persons not diagnosed as a senior (11). In a large population-based French cohort of persons with senior-onset Crohn's disease (defined as those diagnosed over the age of 60), the rates of

surgical management by one and ten years was found to be 18% and 32%, respectively (5).

The risk of postoperative morbidity and mortality is increased among seniors requiring intra-abdominal surgery (12). Moreover, the 30-day postoperative mortality risk is approximately 10-fold higher for senior IBD patients compared with nonsenior Crohn's disease (4.2% versus 0.3%) and ulcerative colitis (6.1% versus 0.7%) patients. Adjusted risk of postoperative complications was similarly higher. Nonfatal postoperative complications were similarly 1.4-fold and 1.7-fold higher for senior patients with Crohn's disease and ulcerative colitis, respectively (12).

DRUG UTILIZATION

Therapeutic decision-making in seniors with IBD is challenging. Seniors with IBD often have comorbid conditions related to their IBD (e.g., venous thromboembolism) or as a product of aging (e.g., cardiovascular disease and cancer). Consequently, the impact of adverse events associated with IBD treatments is amplified in seniors.

Benchimol et al. assess drug prescription and utilization rates among senior Ontarians with Crohn's disease and ulcerative colitis between 2006 and 2009. While use of 5-ASA was gradually decreasing, immunomodulator and corticosteroid utilization remained stable, and the use of biologic therapies rose (13). More recent data from Manitoba show that in 2014, approximately 7% of all persons with IBD were using an immunomodulator, compared with 4% in 2004. A rapid rise in the prevalence of anti-TNF use in this population was also found. In 2010, 3.0% of Crohn's disease patients and 0.7% of ulcerative colitis patients over age 65 were actively using anti-TNFs. By 2014, the prevalence of anti-TNF use in seniors had risen to 4.0% and 2.3% in Crohn's disease and ulcerative colitis, respectively. These anti-TNF rates are lower than what has been observed for younger IBD patients. While we do not yet have any data on the utilization of vedolizumab in seniors, we anticipate that it may be more readily used because of its perceived lack of systemic immunosuppression.

Targownik et al. (2012) report that within the first year of diagnosis, at most 11% of persons over age 65 had an active dispensation for corticosteroids. However, later in the course of disease, the point prevalence of corticosteroid use ranged from 3% to 5%. Over the first five years following diagnosis, persons over 65 years old have a significantly decreased risk of being dispensed corticosteroids compared with persons aged 25 to 64 at diagnosis (HR 0.82; 95% CI, 0.71–0.95) (14). These data highlight important differences in prescribing patterns among seniors with IBD compared with younger IBD patients, though it is unclear whether this is due to seniors having less severe acute flares of IBD or a recognition on the part of clinicians of the unfavourable side effect profile of corticosteroids.

MANAGEMENT OF IBD IN SENIORS

The medical and surgical management of IBD in seniors is influenced by unique challenges. Physiological changes that occur with age, including immunosenescence and decline in renal function, and the higher frequency of comorbidities, including cancer and cardiovascular disease, can alter the risk-benefit ratio of many medical therapies. Polypharmacy is an important consideration. A cohort study of 190 senior IBD patients revealed that they had, on average, nine routinely prescribed medications. Forty percent had a drug interaction that involved one of their IBD medications (15). This finding emphasizes the importance of receiving all medications from a single pharmacy in order to check for interactions. Polypharmacy may also influence adherence. Strategies such as simplifying drug regimens (e.g., 5-ASA to once-daily regimens) and using convenient pill packaging may improve challenges faced by the senior population.

The risk of infections (e.g., pneumonia or urinary tract infections) increases with age and raises the concern of immunosuppressive therapy for IBD. Multicentre, retrospective, cohort data from Europe suggest that senior patients who receive anti-TNF therapy are at considerably higher risk of serious infection (11%) compared with nonsenior IBD patients (2.5%) and senior control patients (0.5%) (16). Mortality is similarly higher in the senior patients taking anti-TNF compared with nonsenior anti-TNF users and senior controls (10% versus 1% and 2%, respectively). Because senior IBD patients are poorly represented in clinical trials, there is sparse data on the efficacy of anti-TNF therapy in seniors. A retrospective observational study suggests that seniors are less likely than nonsenior IBD patients to have a partial or complete response to anti-TNF therapy (61% versus 83%) and are four-fold more likely to stop anti-TNF therapy (17). Despite the risk of infection, anti-TNF therapy remains an important therapeutic option for steroid-refractory or steroid-dependent patients. However, the less favourable risk-benefit profile is an important consideration in determining the appropriate treatment options. Gut-selective biologic therapies such as vedolizumab, which have a lower risk of infection, may be safer in seniors.

Malignancy is more frequent with age and may also impact therapeutic decisions (18). The risk of lymphoproliferative disorders increases with age but especially so in the presence of thiopurine use. Among senior patients (>65 years) who continued to take thiopurines, the risk of lymphoma was 5.41 per 1000 person-years compared with 0.37 per 1000 person-years in IBD patients younger than 50 who were taking the medication (19,20). Thus, the higher absolute risk of lymphoma in the senior associated with thiopurine use is an important consideration.

It is important to keep in mind that surgery remains a therapeutic option and, when performed electively, is associated with considerably lower postoperative mortality and morbidity than when performed emergently (12). A retrospective cohort study suggests that elective colectomy may be associated with greater survival than medical therapy in ulcerative colitis patients older than 50 (21).

COSTS OF CARE FOR SENIORS WITH IBD

Several studies have determined the costs of care among the entire IBD population. However, IBD-specific costs among seniors with IBD or senior-onset IBD are unknown. Bernstein et al. use population-based data to enumerate the total cost of care among all Manitobans with IBD in 2005. Persons aged between 65 and 79 were found to have mean total healthcare costs of \$5298 CAD compared with \$3537 CAD among age-matched controls. The mean difference of \$1761 CAD is slightly lower than the \$2070 CAD difference between that of cases and controls in the overall population (22). However, it is not clear whether the difference in costs between cases and controls is directly related to IBD-specific care. Van der Have et al. study the direct and indirect costs associated with IBD in seniors within a multicentre Dutch cohort. The direct healthcare costs of IBD (converted to 2018 inflation-adjusted Canadian dollars) are estimated at \$535 CAD per quarter year for persons over age 60 compared with \$1440 per quarter year for those under age 60 ($P < 0.001$). The IBD-attributable costs were lower in those 70 years of age or older when compared with those aged 60 to 69 (\$636 versus \$355, $P < 0.0001$). Not surprisingly, productivity losses were significantly lower among seniors (\$175 versus \$21, $P < 0.001$) (23).

CONCLUSION

The Canadian health system must be prepared for a rising number of senior patients living with IBD. Though risk-benefit profiles of various therapeutic interventions may differ in the senior population, it is important to keep in mind that the treatment goals remain the same and should aim for complete steroid-free remission. Inflammatory bowel disease health providers must also be prepared to work in multidisciplinary teams with other specialists to optimize IBD management in the context of other comorbidities.

Acknowledgements

The authors would like to thank Shabnaz Siddiq who acted as a coordinator for this work, and Joseph Windsor and Fox Underwood who edited the articles. This work was funded by Crohn's and Colitis Canada. EB and GN were supported by New Investigator Awards from CIHR, Crohn's and Colitis Canada, and the Canadian Association of Gastroenterology. EB was also supported by the Career Enhancement Program from the Canadian Child Health Clinician Scientist Program. CB was supported in part by the Bingham Chair in Gastroenterology. GN and GK were CIHR Embedded Clinician Research Chairs.

Supplement sponsorship. This article appears as part of the supplement "The Impact of Inflammatory Bowel Disease in Canada 2018," sponsored by AbbVie Corporation and co-sponsored by Crohn's and Colitis Canada.

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