

ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

Section Editor: Stephen B. Hanauer, MD

Pharmacoequity in Older Patients With Inflammatory Bowel Disease



Bharati D. Kochar, MD, MS
Assistant Professor
Harvard Medical School
Massachusetts General Hospital
Boston, Massachusetts

G&H Currently, how common is inflammatory bowel disease in older adults?

BK Inflammatory bowel disease (IBD) has traditionally been thought of as a disease of younger adults. There has been a lot of focus on IBD in the pediatric cohort for a number of reasons, including the identification of several genes and IBD's significant effects on growth. The most recent and robust epidemiologic update on IBD was published recently in *Gastroenterology* and showed that the overall prevalence of IBD was 0.7% in the United States.

... fewer than 1% of patients in clinical trials of medications approved to treat IBD that were published after the year 2000 were 65 years and older.

When looking at different age cohorts, older adults, defined in this paper as those 65 years and older, have the highest prevalence of IBD at 1.7%. Similarly, a recent Canadian epidemiologic update showed that older adults have the highest prevalence of IBD in terms of age categories. Part of this is because people are living longer with IBD, which is a sign that treatment has improved and that the disease is not resulting in premature mortality as

it used to previously. There is likely some detection bias, as people who are 60 years and older are obtaining more and better care resulting in diagnoses of IBD.

G&H What are the main challenges or barriers that older patients with IBD face with regard to pharmacoequity?

BK A term coined relatively recently by Dr Utibe Essien, pharmacoequity refers to the concept of ensuring that individuals of all types of diversity have access to the same and ideally highest-quality medications to address the needs of their health overall. Essentially, the term refers to equity in the pharmacologic prescriptions that physicians provide in medicine. Pharmacoequity is a specific issue for older adults because IBD studies worldwide typically include patients who have a median age in the late 30s or early 40s. Many clinical trials have upper age category restrictions, which exclude a number of older people, so clinicians do not have clinical trial information for these patients. My colleagues and I performed an analysis that showed that fewer than 1% of patients in clinical trials of medications approved to treat IBD that were published after the year 2000 were 65 years and older. When 25% to 30% of patients with IBD are 60 to 65 years and older, this is a large discrepancy. Additionally, clinical trials often have arbitrary comorbidity exclusions, which disproportionately affect older adults. An example is excluding an IBD patient who has chronic obstructive pulmonary disease (COPD) from a clinical trial of a biologic agent. There has been no suggestion that COPD will alter the way the biologic agent will work in this patient with IBD, so having this disease-based exclusion criterion is

arbitrary. IBD clinical trials also do not consider function either as an inclusion criterion, which can allow many older adults to participate in clinical trials, or as an outcome. As clinicians, we should naturally have some hesitancy for prescribing any of the newer agents that we use liberally in younger patients because we do not have the clinical trial and real-world data to support the safety and efficacy of these new agents in older patients. The lack of equitable information to support prescription of novel therapies in older patients with IBD is a significant barrier to achieving pharmacoequity.

A more uniquely US angle is that when patients in the United States turn 65 years, they become eligible for Medicare. This program was designed to be an inpatient insurance plan with the assumption that older patients will naturally have more hospitalizations. Therefore, inpatient-type services such as infusion-based therapies and hospitalizations are well covered, but the therapies that keep patients out of the hospital are not as well covered. Medicare policies have not considered the increase of immune-mediated conditions that require novel therapeutics beyond corticosteroids. Instead, these policies are designed for chronic diseases that older people traditionally have, such as high blood pressure and diabetes. It becomes difficult to care for patients with immune-mediated conditions using novel therapeutic medications when they are on Medicare primarily and do not have the same type of prescription coverage as patients who do not have Medicare, resulting in inherent inequity.

G&H Do older IBD patients themselves also tend to have more hesitancy for prescriptions, especially for newer agents?

BK I think the hesitancy works both ways. I discussed provider hesitancy, and there is a nice international study that surveyed more than 400 gastroenterologists that showed that newer biologic agents were much less likely to be prescribed to older patients because of the hesitancy of gastroenterologists. On the other hand, older patients with IBD, especially those who have aged with the disease, may have had a good experience with older IBD medications, such as corticosteroids, thiopurines, or mesalamine. These medications still have a role in the treatment of IBD, but may carry a slightly less favorable safety profile, especially for patients at older ages. However, if patients have historically had a good experience with such agents and are struggling to obtain insurance approval and pay out-of-pocket costs for novel therapeutics, they will likely want to stay with their older medications. There is definitely a comfort with what is well known. I have also seen hesitancy on the patient side because of the systematic exclusion of older patients from clinical trials. Patients

may be concerned that newer agents may not work for them because the clinical trials did not include older patients like themselves.

G&H Could you discuss any other research on the likelihood of older patients accessing advanced therapies or surgery for IBD?

BK Recently, two very nice studies from the Danish National Patient Register showed that older patients with IBD are much more likely to receive corticosteroids and mesalamine, less likely to receive modern therapeutic agents such as biologics, and still more likely to undergo surgery, which is an important consideration as well. It has been known for a while in the literature that older patients with IBD appear to have higher rates of surgery. It is not entirely clear why this is the case based on existing retrospective studies where we cannot determine why surgery was chosen. In clinical practice, sometimes my patients go to surgery because the latest medications that may have prevented their disease progression were not affordable because of out-of-pocket costs, especially since patients with Medicare are not eligible for pharmaceutical prescription assistance programs due to anti-kick-back legislation. Alternatively, a surgical option is often selected for more definitive treatment that averts the need for medical therapy. Older patients have a higher rate of complications with IBD surgery, which is to be expected because older adults have a higher rate of complications with any type of intervention, compared with younger patients.

G&H What other effects might result from lack of pharmacoequity in older patients with IBD?

BK The lack of pharmacoequity in older patients with IBD specifically has the potential to be a large societal problem. Although IBD is not lethal, it is debilitating. The occurrence of disability at older ages has more significant consequences than at younger ages when disability is more likely reversible.

Disabling older people who were otherwise likely to be healthy has societal ramifications. I have had many patients in their 60s and 70s who had to retire early because their IBD was becoming difficult to control.

Additionally, there have been cases when older people with IBD were living independently, being productive, contributing members of the community but, with a significant flare of their IBD, ended up in an assisted living facility. For diseases that affect quality of life, effective treatment is very important, especially at older ages. Thus far, the focus has been on trying to address acute care needs such as heart attacks and cancers of older patients.

There also needs to be a shift in focus to quality-of-life care in older patients with any type of chronic condition to extend care to all members of society.

G&H What steps can be taken to achieve pharmacoequity in older patients who have IBD?

BK That is the million-dollar question. There are a number of steps that could be taken in a multipronged approach. First of all, prospective investigation is needed. Thus far, many of the studies have been retrospective, looking back at data that have already been collected. It is important to have some prospective investigation, looking forward at current patients to understand the contributors to these disparities and outcomes seen in older patients. Better understanding what contributes to the disparities in receiving treatments and treatment outcomes is important to achieving equity.

Improvements are also needed in clinical trial analytics. Realistically, it does not make sense to run clinical trials specifically in older patients with IBD, but it does make sense to use advanced analytics on subgroups of older patients to better understand treatment efficacy. Additionally, increasing access to novel, high-cost therapeutics for older patients is important for generating real-world effectiveness data.

Medicare policy needs to be updated to reflect the rapidly advancing fields that are immune-mediated inflammatory disorders. Recently, there was an expansion of the prescription drug law. Ustekinumab (Stelara, Janssen) is now on the top 10 list of highest-cost medications for Medicare, so it will be covered more favorably than other biologic agents. This happened around the same time that SEQUENCE trial results came out, which showed that risankizumab (Skyrizi, AbbVie) had a faster onset of action than ustekinumab for the treatment of patients with Crohn's disease. Furthermore, from a policy standpoint, having robust prescription assistance programs for high-cost medications for older adults is critical. Anti-kickback legislation is important, but there probably needs to be some legislative modifications to better achieve the intent of the law and not affect patients directly. Increased resources to counsel older adults transitioning to Medicare on how to select a plan based on existing and future conditions are important as well.

Another major Medicare-based inequity is the lack of appropriate nutrition and mental health counseling. In IBD, it is well established that these multidisciplinary aspects of care are critical, yet if patients have primary Medicare insurance, they only have access to a nutritionist if they have chronic kidney disease or diabetes.

This results in lower-quality care for older people who have IBD.

Medicare patients may also face issues involving switching of medications. I have a number of patients who were diagnosed with IBD in their 40s or 50s and have been stable on a biologic agent for 10 years. Once they were on Medicare, however, they had an interruption in their biologic coverage until all of their authorizations were sorted out and they had to deal with out-of-pocket costs in the meantime. Insurance formulary-based medication switches are another major legislative issue that needs to be addressed in Congress.

G&H What research is currently awaited in this area?

BK We have a multicentered prospective cohort funded by the Crohn's & Colitis Foundation and the National Institute of Aging to characterize function in older people. Currently, there is not a robust understanding of the relationship between IBD and aging syndromes. Clinically, it seems like patients with more active IBD have more geriatric syndromes; however, that needs to be more definitively determined.

G&H Are there any misconceptions in this area that you would like to clear up?

BK There is a host of literature showing that older patients have adverse outcomes. Studies showing that older patients with IBD treated with biologic agents have a higher rate of infections, cancers, and hospitalizations than younger patients treated with biologic agents would make a prescriber feel as if they are doing harm to their patients by using novel therapeutic agents. I think that is a large misconception that needs to be predicated on the fact that older people at baseline, even if they are completely healthy, will have a higher likelihood for adverse events such as infections, malignancies, and hospitalizations than someone who is a decade or two younger. Comparing older patients with younger patients is like comparing apples and oranges. What we need to do is compare older patients treated with novel biologic agents with older patients treated with corticosteroids, thiopurines, or mesalamine, and then adverse outcomes should be assessed. One nice analysis demonstrated that older patients treated with biologic agents have a lower rate of adverse outcomes than older patients who are in placebo arms of IBD clinical trials. An important point to drive home is that increased risks for adverse outcomes seen in older patients are because of their increased baseline risk, not necessarily because of a drug-attributable risk.

(Continues on page 503)

(Continued from page 496)

Disclosures

Dr Kochar has served on advisory boards for Pfizer and Bristol Myers Squibb, but all relationships have ended.

Suggested Reading

Ananthakrishnan AN, Nguyen GC, Bernstein CN. AGA clinical practice update on management of inflammatory bowel disease in elderly patients: expert review. *Gastroenterology*. 2021;160(1):445-451.

Bermudez H, Faye AS, Kochar B. Managing the older adult with inflammatory bowel disease: is age just a number? *Curr Opin Gastroenterol*. 2023;39(4):268-273.

Chan W, Kariyawasam VC, Kim S, et al. Gastroenterologists' preference and risk perception on the use of immunomodulators and biological therapies in elderly patients with ulcerative colitis: an international survey. *Eur J Gastroenterol Hepatol*. 2020;32(8):976-983.

Kochar B, Ananthakrishnan AN, Ritchie CS. Pharmacoequity for older adults with inflammatory bowel diseases. *Gastroenterology*. 2024;166(2):235-239.

Kochar B, Kalasapudi L, Ufere NN, Nipp RD, Ananthakrishnan AN, Ritchie CS. Systematic review of inclusion and analysis of older adults in randomized controlled trials of medications used to treat inflammatory bowel diseases. *Inflamm Bowel Dis*. 2021;27(9):1541-1543.

Kochar B, Ufere NN, Ritchie CS, Lai JC. The 5Ms of geriatrics in gastroenterology: the path to creating age-friendly care for older adults with inflammatory bowel diseases and cirrhosis. *Clin Transl Gastroenterol*. 2022;13(1):e00445.

Lewis JD, Parlett LE, Jonsson Funk ML, et al. Incidence, prevalence, and racial and ethnic distribution of inflammatory bowel disease in the United States. *Gastroenterology*. 2023;165(5):1197-1205.e2.

Nordestgaard RLM, Wewer MD, Malham M, Wewer V, Boysen T, Burisch J. Treatment of inflammatory bowel disease with steroid-sparing medications is age-dependent—results from a Danish nationwide cohort study, 2000-2018 [published online June 10, 2024]. *Aliment Pharmacol Ther*. doi:10.1111/apt.18106.

Nørgård BM, Zegers FD, Knudsen T, et al. Patients with elderly onset inflammatory bowel disease have a decreased chance of initiation of all types of medications and increased risk of surgeries—a nationwide cohort study. *Aliment Pharmacol Ther*. 2023;58(1):48-59.