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Navigating Complex Gastrointestinal Pathologies in the Aging Population: Therapeutic Paradigms for Inflammatory Bowel Disease and Hepatocellular Carcinoma

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Abstract

Background: The global demographic shift towards an aging population has precipitated a rise in geriatric gastrointestinal disorders. Specifically, the management of Inflammatory Bowel Disease (IBD) and Hepatocellular Carcinoma (HCC) in the elderly presents unique clinical challenges due to immunosenescence, comorbidities, and polypharmacy.

Methods: We conducted a comprehensive review of current literature regarding therapeutic safety and efficacy in elderly patients (>60 years) with IBD and HCC. The analysis focused on the transition from conventional thiopurines to biological agents in IBD, and the evolution of systemic therapies in HCC, alongside surveillance strategies.

Results: In late-onset IBD, phenotypes often present with less extensive disease but higher mortality risk due to complications. Evidence suggests that while thiopurines remain in use, their safety profile in the elderly is compromised by increased risks of lymphoproliferative disorders and bone marrow suppression. Conversely, biological therapies and newer small molecules show promise but are frequently underprescribed due to infection fears. Regarding HCC, the epidemiological landscape is shifting towards non-viral etiologies. Systemic therapies have evolved, yet elderly patients often receive suboptimal surveillance.

Conclusion: Management of GI pathologies in the elderly requires a paradigm shift from standard protocols to personalized, geriatric-focused care. There is a critical need to include older adults in clinical trials to establish robust safety data for biologics and novel HCC treatments.

Keywords: Geriatric Gastroenterology, Inflammatory Bowel Disease, Hepatocellular Carcinoma, Thiopurines, Immunosenescence, Biologics, Polypharmacy.

Introduction

The field of gastroenterology is currently facing a demographic imperative often described as the "Silver Tsunami." As life expectancy increases globally, the prevalence of chronic gastrointestinal pathologies in the elderly population—defined generally as individuals over the age of 60 or 65—is rising concurrently. This demographic shift necessitates a fundamental re-evaluation of therapeutic paradigms, particularly for complex, chronic conditions such as Inflammatory Bowel Disease (IBD) and Hepatocellular Carcinoma (HCC). While these two disease states represent distinct pathophysiological processes, they converge in the geriatric patient through shared challenges: the decline of physiological reserve (frailty), the phenomenon of immunosenescence, and the complexities of polypharmacy.

Inflammatory Bowel Disease, comprising Crohn's disease (CD) and ulcerative colitis (UC), was historically conceptualized as a disease of young adulthood. However, recent epidemiological data indicates a bimodal age distribution, with a significant secondary peak in incidence occurring in the sixth and seventh decades of life [1]. Furthermore, as the prevalent population of young IBD patients ages, the total burden of geriatric IBD is expanding rapidly. Taleban et al. highlight that the management of this cohort is complicated not only by the disease itself but by the rigorous demands of immunosuppressive therapies on an aging immune system [1].

Simultaneously, Hepatocellular Carcinoma remains a leading cause of cancer-related mortality worldwide. In regions like Taiwan and increasingly in the West, the epidemiology of HCC is shifting. While viral hepatitis (HBV, HCV) has historically driven incidence, the rise of metabolic dysfunction-associated steatotic liver disease (MASLD) is creating a new cohort of elderly HCC patients [12, 14]. These patients often present with multiple metabolic comorbidities, making surgical or systemic interventions riskier.

A critical barrier to optimizing care for these populations is the systematic exclusion of older adults from randomized clinical trials (RCTs). Vieujean et al. issue a "call for action," noting that strict inclusion/exclusion criteria regarding age and comorbidities render trial results largely inapplicable to the real-world geriatric population [2]. Consequently, clinicians are often forced to extrapolate safety and efficacy data from younger cohorts, a practice fraught with risk. The physiological handling of drugs—pharmacokinetics and pharmacodynamics—changes drastically with age, altering the therapeutic index of potent agents like thiopurines, anti-TNF biologics, and tyrosine kinase inhibitors.

This article aims to synthesize current evidence regarding the management of these complex GI pathologies in the aging population. We will first examine the therapeutic landscape of IBD, contrasting the traditional use of thiopurines with emerging biological strategies, specifically addressing the safety concerns raised by Strigáč et al. and others [4, 5]. Subsequently, we will explore the evolving management of HCC, focusing on surveillance and systemic therapy in the context of an aging liver. By integrating these perspectives, we aim to provide a comprehensive overview of the challenges and opportunities in geriatric gastroenterology.

Methods

To construct this narrative review, we employed a comprehensive literature search strategy focusing on pivotal studies, systematic reviews, and clinical guidelines published primarily between 2012 and 2024. The search was targeted at identifying high-quality evidence regarding the management of IBD and HCC specifically in elderly populations.

The primary inclusion criteria for the selected literature were: (1) Study population defined as "elderly," "geriatric," or "older onset," typically categorized as age >60 or >65 years; (2) Focus on pharmacological interventions (thiopurines, biologics, small molecules for IBD; systemic therapies for HCC) or clinical outcomes (safety, efficacy, mortality); and (3) Publication in peer-reviewed gastroenterology or oncology journals. We prioritized systematic reviews and meta-analyses, such as those by Ananthakrishnan et al. [3], to ensure the data presented reflects broad clinical trends rather than isolated case reports.

Data extraction focused on key thematic areas: phenotypic presentation differences between young and old cohorts, adverse event rates (specifically infection and malignancy), and clinician prescribing patterns. For HCC, we focused on epidemiological shifts and adherence to surveillance guidelines as outlined by the Taiwan Liver Cancer Association and other international bodies [15]. This review synthesizes these findings to generate clinical insights relevant to the practicing gastroenterologist.

Results

The Inflammatory Bowel Disease Landscape in the Elderly

Shutterstock Phenotype and Clinical Presentation

The clinical presentation of late-onset IBD differs significantly from that of early-onset disease. Ananthakrishnan et al., in a systematic review, demonstrate that older-onset Crohn's disease is more likely to present as colonic disease rather than ileal or penetrating disease [3]. This "inflammatory" rather than "fistulizing" phenotype might suggest a milder disease course; however, the mortality rate in this group is paradoxically higher.

This excess mortality is not necessarily driven by IBD activity alone but by the interplay between active inflammation and comorbid conditions such as cardiovascular disease and diabetes. Furthermore, the diagnosis is often delayed in the elderly because symptoms like diarrhea or rectal bleeding are frequently misattributed to diverticular disease, ischemic colitis, or colorectal cancer [1].

Therapeutic Efficacy and Safety: The Thiopurine Debate

For decades, thiopurines (azathioprine and 6-mercaptopurine) served as the backbone of steroid-sparing maintenance therapy. However, their role in the elderly is increasingly scrutinized. Warner et al. provide a practical guide to prescribing, noting that while effective, thiopurines require rigorous monitoring for myelosuppression, which occurs more frequently in older patients due to reduced bone marrow reserve [7].

More concerning is the signal regarding malignancy. Singh et al. highlight that the risk of lymphoproliferative disorders (specifically non-Hodgkin's lymphoma) associated with thiopurines increases with age [8]. In young patients, this risk is statistically low, but in the elderly, the absolute risk increase becomes clinically significant. Strigáč et al. reinforce this, suggesting that the safety profile of thiopurines in elderly patients is inferior to that of newer agents, necessitating a careful risk-benefit calculation [4]. Despite this, thiopurines remain widely prescribed, often due to their low cost and oral formulation, which supports adherence in a population burdened by polypharmacy.

The Shift to Biologics and Small Molecules

The introduction of biological therapies (anti-TNF agents like infliximab and adalimumab, and gut-selective agents like vedolizumab) revolutionized IBD care. However, adoption in the elderly has been slow. Chan et al. surveyed gastroenterologists and found a pervasive "risk perception" bias: clinicians are often more afraid of the infectious complications of biologics in the elderly than the complications of untreated disease or corticosteroids [11].

Current evidence suggests this fear may be partially misplaced, or at least requires nuance. While anti-TNF agents are associated with an increased risk of severe infections (pneumonia, sepsis) in older adults compared to younger cohorts, they may still be safer than prolonged corticosteroid use, which is associated with high rates of fracture, diabetes destabilization, and delirium. LeBlanc et al. review the updated therapeutic landscape, advocating for a "safety-first" approach that may favor gut-selective biologics (vedolizumab) or interleukin inhibitors (ustekinumab) over systemic anti-TNFs in frail elderly patients, although head-to-head trials in this specific demographic are lacking [5].

Diagnostic Nuances: Fistulizing Disease

While less common in the elderly, fistulizing Crohn's disease requires precise imaging for management. Ni et al. demonstrated the utility of Computed Tomography Enterography (CTE) in predicting perianal fistulas [6]. In the elderly, where invasive examination under anesthesia carries higher risk, high-resolution cross-sectional imaging becomes a vital tool for surgical planning and disease monitoring.

The Hepatocellular Carcinoma Landscape in the Elderly

Epidemiological Evolution

Parallel to the IBD challenge, the management of HCC in the elderly is evolving. Lai and Chung report on the epidemiology of HCC in Taiwan, a region with historically high prevalence [12]. The data indicates a shift: as vaccination and antiviral programs successfully reduce HBV and HCV burdens, the average age of HCC diagnosis is rising. We are increasingly seeing HCC in septuagenarians and octogenarians, often driven by metabolic factors. Huang et al. emphasize the global rise of NAFLD/MASLD-related HCC, which disproportionately affects older adults with long-standing metabolic syndrome [14].

Surveillance and Treatment

Surveillance for HCC in the elderly is controversial. While guidelines generally recommend ultrasound screening every six months for cirrhotic patients, adherence drops significantly with age. Teng et al., in the 2023 update for HCC management, underscore the importance of continuing surveillance in fit elderly patients who would be candidates for treatment [15].

The evolution of systemic therapy, as reviewed by Finn and Zhu, has moved from sorafenib to immune checkpoint inhibitors (ICIs) and combination therapies [16]. A critical finding in geriatric oncology is that chronological age alone should not preclude systemic therapy. Elderly patients with preserved liver function (Child-Pugh A) often tolerate these newer therapies well, provided their performance status is adequate.

Discussion

Comparative Safety Analysis and Immunosenescence

The central tension in geriatric gastroenterology lies in the balance between disease control and iatrogenic harm. This balance is fundamentally altered by immunosenescence—the gradual deterioration of the immune system brought on by natural age advancement. This biological reality provides the context for why the "start low and go slow" mantra is insufficient; it must be replaced with "start smart and monitor closely."

Our review of the data suggests a diverging safety profile between thiopurines and biologics that contrasts with historical prescribing habits. Traditionally, clinicians viewed thiopurines as the "conservative" choice and biologics as "aggressive." The evidence provided by Strigáč et al. [4] and Singh et al. [8] flips this narrative. The mechanism of action of thiopurines—generalized DNA synthesis inhibition in replicating cells—is inherently toxic to the aging bone marrow. The association with Epstein-Barr Virus (EBV) related lymphomas is particularly pertinent in the elderly, who likely harbor latent EBV. Conversely, targeted biologics, while carrying infection risks, do not possess the same mutagenic potential. Therefore, for a 75-year-old patient with moderate-to-severe Crohn's disease, a gut-selective biologic might actually represent the "conservative" (i.e., safer) option compared to a systemic thiopurine.

However, the "infectious risk" remains the primary barrier. Juneja et al. note that geriatric IBD patients have higher hospitalization rates for infections [10]. This necessitates a rigorous vaccination strategy (influenza, pneumococcal, zoster) prior to initiating therapy, a step often missed in the rush to treat active flares.

The Comorbidity Conundrum and Polypharmacy

The management of IBD cannot occur in a vacuum. The presence of comorbidities significantly influences therapeutic choices. Juneja et al. highlighted that elderly IBD patients have a high burden of cardiovascular and metabolic disease [10]. This creates direct contraindications; for example, the use of JAK inhibitors (a newer class of small molecules) is currently cautioned in patients with major cardiovascular risk factors—a description that fits a large portion of the geriatric IBD population.

Furthermore, the intersection with liver disease is critical. As noted in the HCC references [12-16], the prevalence of liver pathology in the elderly is high. Initiating potentially hepatotoxic IBD drugs (including methotrexate or certain biologics that can cause enzyme elevations) requires baseline assessment of liver function. If a patient has underlying NAFLD/MASLD [14], their reserve to handle drug-induced liver injury is reduced.

Polypharmacy serves as a compounding factor. An elderly patient taking antihypertensives, statins, anticoagulants, and oral hypoglycemics is at high risk for drug-drug interactions. Adding a regimen of oral mesalamines or corticosteroids increases the pill burden and the risk of non-adherence. Warner et al. emphasize that simplifying the regimen is crucial for efficacy [7]. This is where the argument for biologics (often administered every 2 to 8 weeks) gains strength—they remove the daily compliance burden, though they introduce the logistical burden of infusions or injections.

Expanded Analysis: The Nuance of "frailty" vs. "Chronological Age" in Therapeutic Decision Making

To fully understand the implications of the data presented, we must expand upon the concept of frailty as a superior predictor of outcomes compared to chronological age. The reliance on birth year as a cutoff for therapeutic eligibility is an antiquated metric in modern gastroenterology. Both the IBD and HCC literature reviewed here point toward a "functional status" approach.

In the context of IBD, Sturm et al. in the ECCO topical review emphasize that "biological age" differs from chronological age [9]. A "fit" 80-year-old with no comorbidities may tolerate anti-TNF therapy better than a "frail" 65-year-old with sarcopenia, diabetes, and heart failure. Frailty affects the pharmacokinetics of drugs—sarcopenia (muscle wasting) alters the volume of distribution for hydrophilic drugs, while changes in albumin levels (often lower in frail states) affect the binding of highly protein-bound drugs like ceftriaxone or, more relevantly, affects the interpretation of drug levels.

When we analyze the reluctance to prescribe biologics identified by Chan et al. [11], it likely stems from an inability to quantify this frailty. If clinicians had access to validated geriatric assessment tools integrated into the IBD clinic (e.g., the Fried Frailty Phenotype or the Rockwood Clinical Frailty Scale), they might feel more empowered to prescribe appropriate aggressive therapy to "fit" elderly patients.

This concept extends seamlessly to the HCC references. Teng et al. [15] and Finn & Zhu [16] discuss systemic therapies like atezolizumab plus bevacizumab. The limiting factor for these potent immunotherapies is often not the liver tumor itself, but the patient's ability to withstand immune-related adverse events (irAEs). A frail immune system may be less prone to autoimmune storms, but a frail body is less able to recover if one occurs. Conversely, in the surgical management of HCC, underlying sarcopenia is a known predictor of poor post-operative outcomes and higher mortality.

Therefore, the "Next Step" in research discussed by Vieujean et al. [2] should not just be "including older adults" in trials, but stratifying them by frailty. A trial that treats all 70-year-olds as a monolith will likely yield "muddy" safety data. A trial that separates "fit" vs. "frail" seniors would likely show that "fit" seniors achieve efficacy rates comparable to younger adults, finally providing the evidence base needed to reduce the therapeutic nihilism currently seen in practice.

Limitations

Our review is limited by the nature of the available data. As noted, most "elderly" data in IBD and HCC comes from subgroup analyses of larger trials or retrospective observational cohorts. These studies are prone to selection bias—the "healthy worker" effect, where only the robust elderly get treated and studied, while the frail are managed palliatively and vanish from the dataset. Additionally, the definition of "elderly" varies between studies (cutoffs of 60, 65, or 75), complicating direct comparisons.

Conclusion

The management of gastrointestinal pathologies in the aging population requires a sophisticated, multidimensional approach that transcends simple symptom control. In Inflammatory Bowel Disease, the therapeutic paradigm is shifting away from broad immunosuppression with thiopurines—which carry elevated risks of malignancy and myelosuppression in the elderly—toward more targeted biological therapies. However, this shift is hindered by clinician hesitation regarding infection risks. In Hepatocellular Carcinoma, the challenge lies in maintaining vigilant surveillance in an aging population increasingly driven by metabolic rather than viral risk factors.

Ultimately, the chronological age of a patient is less relevant than their biological reserve. Future guidelines must incorporate frailty assessments to guide therapeutic choices. By moving away from ageist exclusion criteria in clinical trials and embracing a personalized, safety-conscious prescribing strategy, gastroenterologists can significantly improve the quality of life for the growing legion of elderly patients navigating these complex chronic diseases.

References

1. Taleban S, Colombel J-F, Mohler MJ, Fain MJ. Inflammatory bowel disease and the elderly: a review. Journal of Crohn's and Colitis. 2015;9(6):507-15.
2. Vieujean S, Caron B, Jairath V, Benetos A, Danese S, Louis E, et al. Is it time to include older adults in inflammatory bowel disease trials? A call for action. The Lancet Healthy Longevity. 2022;3(5):e356-e66.
3. Ananthakrishnan AN, Shi HY, Tang W, Law CC, Sung JJ, Chan FK, et al. Systematic review and meta-analysis: phenotype and clinical outcomes of older-onset inflammatory bowel disease. Journal of Crohn's and Colitis. 2016;10(10):1224-36.
4. Strigáč A, Caban M, Małecka-Wojciesko E, Talar-Wojnarowska R. Safety and effectiveness of thiopurines and small molecules in elderly patients with inflammatory bowel diseases. Journal of Clinical Medicine. 2024;13(16):4678.
5. LeBlanc J-F, Wiseman D, Lakatos PL, Bessissow T. Elderly patients with inflammatory bowel disease: updated review of the therapeutic landscape. World journal of gastroenterology. 2019;25(30):4158.
6. Ni G, Zhao H, Shen H, Li S, Ao W. Prediction of Perianal Fistula in Crohn's Disease by Computed Tomography Enterography. The Turkish Journal of Gastroenterology. 2024;35(3):168.
7. Warner B, Johnston E, Arenas-Hernandez M, Marinaki A, Irving P, Sanderson J. A practical guide to thiopurine prescribing and monitoring in IBD. Frontline Gastroenterology. 2018;9(1):10-5.
8. Singh A, Mahajan R, Kedia S, Dutta AK, Anand A, Bernstein CN, et al. Use of thiopurines in inflammatory bowel disease: an update. Intestinal research. 2022;20(1):11-30.
9. Sturm A, Maaser C, Mendall M, Karagiannis D, Karatzas P, Ipenburg N, et al. European Crohn's and Colitis Organisation topical review on IBD in the elderly. Journal of Crohn's and Colitis. 2017;11(3):263-73.
10. Juneja M, Baidoo L, Schwartz MB, Barrie A, Regueiro M, Dunn M, et al. Geriatric inflammatory bowel disease: phenotypic presentation, treatment patterns, nutritional status, outcomes, and comorbidity. Digestive diseases and sciences. 2012;57:2408-15.
11. Chan W, Kariyawasam VC, Kim S, Pudipeddi AV, Paramsothy S, Shim HH, et al. Gastroenterologists' preference and risk perception on the use of immunomodulators and biological therapies in elderly patients with ulcerative colitis: an international survey. European Journal of Gastroenterology & Hepatology. 2020;32(8):976-83.
12. Lai YW, Chung CH. Epidemiology of hepatocellular carcinoma in Taiwan. Clin Pract. 2024; 14: 570–578.
13. Health Promotion Administration, Ministry of Health and Welfare, Taiwan. Cancer Registry Annual Report, 2019. Taiwan: Health Promotion Administration; 2022. https://www.hpa.gov.tw/File/Attach/14913/File_18302.pdf
14. Huang DQ, El-Serag HB, Loomba R. Global epidemiology of NAFLD-related HCC: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol. 2021; 18: 223–238.

15. Teng W, Wang HW, Lin SM. Management consensus guidelines for hepatocellular carcinoma: 2023 update on surveillance, diagnosis, systemic treatment, and posttreatment monitoring by the Taiwan Liver Cancer Association and the Gastroenterological Society of Taiwan. Liver Cancer. 2024; 13: 468–486.

16. Finn RS, Zhu AX. Evolution of systemic therapy for hepatocellular carcinoma. Hepatology. 2021; 73: 150–157.