Review Article

Management of inflammatory bowel disease in the elderly: A review

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A B S T R A C T

The burden of Inflammatory Bowel Disease (IBD) is increasing worldwide, with a particular increase in the prevalence in the elderly population, due to the ageing of young-onset IBD as well as to the increasing incidence in elderly patients.

Elderly IBD patients present specific challenges to the treating physician, as they have comorbidities, lower functional reserves, and higher risk of treatment-related complications. The diagnosis of IBD in the elderly may be difficult due to a more subtle disease presentation and to a wide range of differential diagnosis. Moreover, as these patients are often excluded from clinical trials, there is a lack of high-quality evidence to inform on the most appropriate management.

Despite an increasing prevalence, the management of IBD in the elderly is still hindered by frequent misconceptions by physicians treating these patients. Due to a erroneous notion of a milder disease course and fear of adverse events, elderly IBD-patients are managed with frequent and continuous use of steroids and undertreated with effective medical therapies.

In this review, we describe the principles of management of IBD in the elderly, which is a topic of increasing importance to IBD clinics, that will have to progressively adapt to care for an ageing population.

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1. Introduction

Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC) is a global disease with an increasing burden worldwide [1].

While newly industrialized countries in Latin America and Asia are currently experiencing a rapidly rising incidence of IBD but still have a low prevalence, in the Western world IBD is in the "Compounding Prevalence" epidemiological stage. The incidence of the disease is stabilizing, but prevalence is increasing [1,2], which is explained by the chronic and, for now, incurable nature of IBD associated with a relatively low mortality rate [3]. This means that, while IBD is typically thought of as a disease of the young, soon IBD populations will be increasingly comprised of an ageing population with longstanding disease [1]. In fact, presently, approximately 25 to 30% of the IBD population consists of patients >60 years [4] and in a recent nationwide study conducted in Canada, Coward et al. estimated an increase in prevalence from 0.7% to 1.0% in 2030, most evident in the elderly population [5].

Besides patients diagnosed earlier in life who later transition to old-age ("non-elderly onset IBD") one should consider a specific group diagnosed at an older ager ("late-onset" or "elderly-onset" IBD) [6,7]. There is no consensus on the definition of "elderly", and definitions vary between studies from patients over the age of 60, 65, 70 or even 75 [4,6,8]. In a recent European Crohn's and Colitis (ECCO) Topical Review [4], elderly-onset IBD was defined as disease-onset at an age of 60 years or older. Approximately 10 to 20% of new IBD diagnosis are reported in this group of patients, and these numbers are expected to be greater with progressive ageing societies [4,6,9–12] (Fig. 1). According to a recent systematic review of 68 population-based studies evaluating the worldwide incidence of elderly-onset IBD, one in 8600 older adults are diagnosed annually with UC and one in 22.000 with CD, on average, in the Western world [13].

Even though elderly-onset and non-elderly-onset are often grouped together in studies evaluating older IBD patients, the distinction between these two groups is important, as they might have different epidemiology, phenotypes, outcomes, and specific safety concerns with the available treatments. One aspect that emphasizes the differences between these groups is the likely
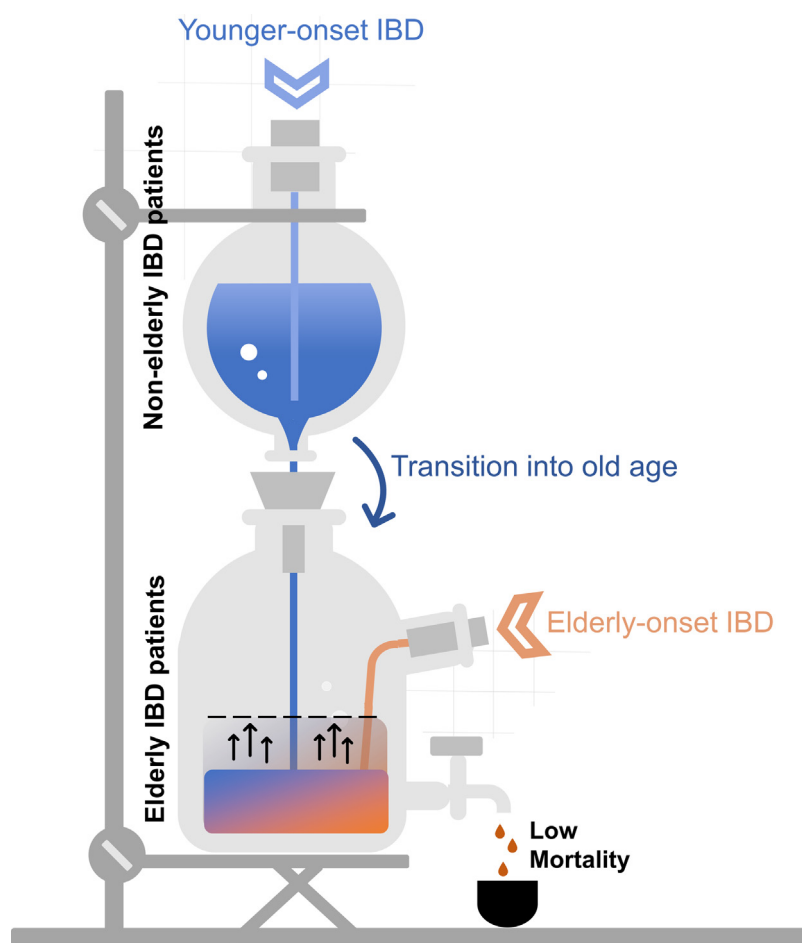

Fig. 1. Compounding Prevalence and Ageing of the Inflammatory Bowel Disease (IBD) population. Elderly IBD patients, who constitute 25 to 30% of the IBD population, include elderly-onset IBD patients (~10–20% of new IBD diagnosis) and patients diagnosed earlier in life that later transition into old age. In the Western World, IBD is in the "Compounding Prevalence" epidemiological stage, as the incidence of the disease is stabilizing but prevalence is increasing due to a low mortality rate. As such, the number of elderly-IBD patients is expected to increase, also as a result of ageing of the population.

weight of genetic factors on the pathophysiology of IBD, which seem to be greater in non-elderly onset IBD [6]. This is derived from the observation that older patients are less likely to have a family history of IBD [14,15], with a possible higher importance of environmental factors on its aetiology [16]. On the other hand, overall risk factors seem to be the same as in non-elderly-onset IBD, with the caveat of limited data, as most results were obtained in younger patients [4,16].

In the past, the recognition of the particularities of paediatric-onset IBD led to the subcategorization of the age of onset of CD with an A1 category for those with an age of diagnosis of 16 or younger [17]. The current A3 category includes a broad group of patients diagnosed over the age of 40 which does not consider the specificities and challenges of elderly-onset IBD. In this review, we discuss the particularities of the management of IBD in the elderly, as IBD clinics will have to adapt and evolve their models of care to an ageing IBD population.

2. Challenges in the elderly population

Older patients with IBD are a real challenge to the clinician throughout all phases of the disease, as there are still uncertainties regarding clinical presentation, diagnosis, disease course, and treatment considerations in this population (Fig. 2). In the following sections, we review the main challenges and points to consider in the management of elderly IBD patients.

2.1. Clinical presentation and diagnosis

Establishing a diagnosis of IBD in the elderly is hampered by a wide list of differential diagnosis of disorders that may be more frequent in this age group than IBD. As a practical exercise, faced with a patient with rectal bleeding and anaemia, IBD would have a very different likelihood of diagnosis in a 30-year-old as opposed to a 70-year-old patient. The differentials list includes, amongst others, infections, cancer, diverticular disease, ischaemic colitis, and drug-induced colitis [4]. Due to the possible confusion with more common disorders, the rate of misdiagnosis at presentation is greater in this population (60%) when compared to younger-onset IBD (15%) [6,18,19]. The unawareness of the possibility of IBD diagnosis in the elderly may also account for the diagnostic delay which is significantly greater in this age group (6 years vs 2 years in the younger population) [6,18]. Despite the difficulties, clinicians should have the same approach in the diagnostic work-up in the elderly with an appropriate anamnesis, ileocolonoscopy and histology [4].

The literature on the clinical presentation of elderly-onset IBD is limited and heterogeneous, but most reports describe a different phenotypic pattern in elderly onset-IBD. Patients with CD may have a more subtle presentation, with symptoms of abdominal pain, weight loss and fever reported as less likely. In opposition, rectal bleeding may be more frequent, which is likely associated to the different disease location in the elderly. More frequently,
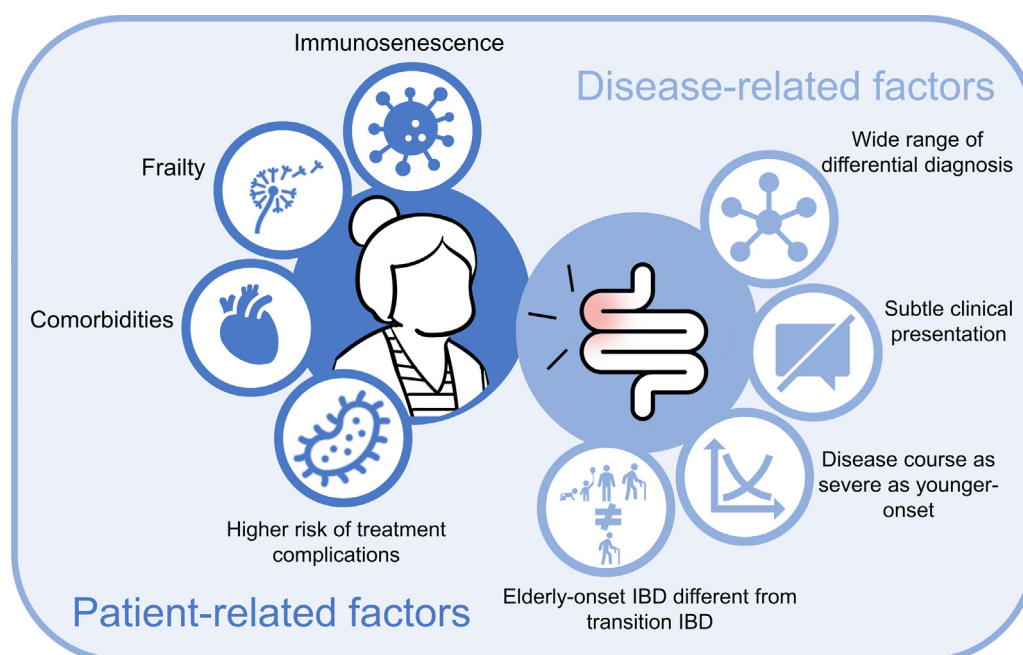
Fig. 2. Specific patient and disease-related challenges of the management of Inflammatory Bowel Disease in the elderly.

elderly-onset CD seems to have an isolated colonic distribution and a predominantly inflammatory behaviour, while perianal involvement is less common [6,12,20,21]. However, these reports are not consistent between studies, and a population-based study described a higher proportion of ileal CD and stricturing phenotype in elderly-onset CD in China [12]. Other reports from Asia also describe a higher frequency of ileal location across all age groups, including the elderly, suggesting the possibility of different phenotypes between Western and Asian populations [22]. On the other hand, elderly-onset UC seems to be more like younger-onset IBD in terms of both symptoms and location, notwithstanding a more subtle clinical presentation and a slightly higher probability of left-side colitis as opposed to extensive colitis [6,10,21,23].

2.2. Natural history

Data on disease course of IBD in the elderly is scarce, heterogeneous and limited by several factors, since, as opposed to disease phenotype, the definition of natural history may be affected by variables other than the biological evolution of the disease. A lower use of immunomodulators and biologics in the elderly is frequently reported [6,9,10,12,21,24–26] and often used as a marker of a milder severity of the disease. Still, this is contraposed by a higher rate of hospitalisations [6,12] and surgery (particularly for UC) [11,21,27] than non-elderly IBD patients. Using rates of medical treatment as a proxy for disease course in the elderly is misleading, as it may reflect physician's reluctance to start immunosuppressants or patient acceptance of treatment rather than a true benign course of the disease [11,21]. In fact, in two multicentre retrospective Italian studies that evaluated medical treatment in the elderly based on disease patterns and behaviour, the authors reported a frequent undertreatment of elderly-onset UC and CD with a more aggressive course, suggesting that treatment decisions may be more influenced by comorbidities rather than disease severity [24,25].

Another limiting factor when evaluating natural history of IBD in the elderly is that patients with elderly-onset IBD are often grouped together with younger-onset IBD as they progress into old age [21]. Rozich et al. hypothesize that the latter group, with a longer standing diagnosis, may have already adapted to cope with IBD as they age, building up adequate biological and functional reserve [28]. On the contrary, as IBD is often more aggressive within the first year of onset [29], and the risk of treatment-related infections is highest within the first months of treatment [30], diagnosis at an older age may contribute to frailty and worse outcomes [28]. As such, disease course and prognosis in these two groups may be very different. In a retrospective comparison of patients over 60 years with adult-onset IBD with patients with elderly-onset IBD, disease-related complications (assessed by a composite variable incorporating IBD-related surgery, all cause hospitalization, treatment escalation, clinical flare or disease complications) were similar between these groups [28]. However, risk of IBD-related surgery was higher in the elderly-onset population, as were treatment-related complications (a composite of malignancy, death, and serious infections).

Finally, data on the natural history of elderly patients with IBD are often derived from studies from referral centres or single regions, which may not be truly representative of elderly-onset IBD. In many of these studies, IBD in the elderly is described as having a milder course [15,21,23]. In this regard, data from population-based studies from unselected cohorts may be more illustrative of the phenotype and clinical course of the elderly IBD population. A recent systematic review based on population-based cohorts that compared the natural history and outcomes of elderly-onset IBD to adult-onset IBD found similar risks of surgery, hospitalization and corticosteroid exposure between these groups, suggesting a similar disease course [9]. A population-based study from China reported similar results, suggesting that elderly-onset IBD is at least as complicated as adult-onset IBD [12].

Even with the limitations of the available data, it seems likely that elderly-onset IBD is not milder than younger-onset disease. Both patients and physicians should be aware of the possibility of an aggressive behaviour even later in life, and should make appropriate treatment decisions based on the potential implications of active disease on health-related quality of life, associated comorbidities and disease complications.

2.3. Patient-related challenges

Other than disease-specific factors, there are unique characteristics of elderly patients that influence their management, which include comorbidities, drug interactions, immunological dysfunction, and somatic, cognitive, and social abilities [6,31].

Ageing is associated with progressive physiological and pharmacokinetic changes that can complicate drug metabolism, efficacy, and safety [32,33]. Impaired mobility, incontinence and coordination skills may also hinder the administration of rectal therapies [4].

Additionally, the occurrence of other chronic conditions is common in the elderly [34–36]. In an American study, more than half of geriatric IBD patients had a Charlson comorbidity index equal or superior to 4 [35]. The most frequent comorbidities were cardiovascular, respiratory, and diabetes mellitus. Kariywasam et al. [37] reported that comorbidities rather than age at diagnosis were the main drivers of delayed immunomodulator use in both CD and UC. As comorbidities were more frequent in elderly-onset IBD patients, immunomodulator use was lower in this age group. Indeed, comorbidities may increase the risk of treatment-related complications [28] and preclude the use of certain treatments, as it is the case of anti-TNF and advanced heart failure [26]. Cognitive deficit and depression, which are common disorders in the elderly, may also complicate the management of IBD patients [4].

In accordance with frequent comorbidities, polypharmacy (defined as the simultaneous use of ≥ 5 drugs) is common in IBD patients, particularly in those older than 62 years old where the prevalence may reach 48% [34]. On average, older IBD patients were regularly taking 7 drugs in a retrospective observational study [35]. Polypharmacy may have a potential impact on drug adherence and drug interactions, and should be a variable to consider when selecting a treatment for an IBD patient [4,38]. For example, steroids can interfere with the efficacy of antiepileptics. Moreover, not only steroids, but also azathioprine and 5-aminosalicylates alter the action of anticoagulants [4].

Immunosenescence is an impairment of the innate and adaptive immune systems that occurs with age, and that may promote an aberrant immune response to environmental antigens [39]. The relative immunodeficiency of the elderly may be responsible for an increased infection risk, and older patients are more vulnerable to opportunistic infections and *C. difficile* [6]. Along with cardiovascular complications, serious infections are one of the most common reasons for hospitalization in the elderly with IBD [12,40]. Hospitalized older IBD patients are at higher risk of in-hospital mortality, and age is an independent risk factor for mortality even after adjusting for comorbidity [6,41,42]. In comparison with the general population, older IBD patients may have an increased risk of several types of cancer [6,12,43], which underline the importance of excluding malignancy before starting immunosuppressive treatments.

2.4. Impact of functional status

Despite the focus on chronological age to define IBD in the elderly, there is an increased recognition that biological age and functional status may be a more important determinant of health outcomes and more appropriate as clinical risk stratification tools [4,44–46].

Frailty is a state of increased vulnerability where a relatively minor insult may cause a dramatic and disproportionate change in health status, with a poor resolution of homoeostasis [47]. It is related to an accelerated decline in physiological reserve as a consequence of a deterioration in multiple physiological systems [47]. The first formal frailty score was the "Frailty phenotype" [48], which determined the presence or absence of five physical

criteria (unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity). Later, a model based on an accumulation of deficits was developed, including both physical and psychosocial elements of frailty [49,50]. In addition to these scores, surrogate markers of frailty have also been evaluated. These include sarcopenia (defined as the reduction of lean muscle mass), malnutrition and disability. While these entities are associated with frailty, these terms are not interchangeable [49].

In IBD, at least 10% of patients over the age of 65 years have a frailty associated diagnosis [45]. Frailty was demonstrated to be an important determining factor of outcomes such as hospital readmission, length of hospital-stay, treatment-related complications, perioperative IBD outcomes and mortality, independently of age, comorbidity, and disease severity [8,45,46,51–53]. In geriatric assessment, deficits in various domains are highly prevalent in elderly IBD patients and are associated with lower health-related quality of life [31]. This underlines the importance of systematic assessment of frailty in IBD patients. Despite the existence of numerous frailty indexes for both clinical and research purposes [54], a simple and validated IBD-specific frailty score useful for clinical practice is not yet available [44].

3. Management of IBD in the elderly

3.1. General principles

Although no specific guidelines are currently available, the principles of IBD treatment in the elderly should be similar to the younger population, with the consideration of the specific challenges aforementioned [4] (Fig. 3). According with this view, therapy should be focused on inducing and maintaining remission, preventing disease-related complications and improving quality of life. Endoscopic remission should be considered the ideal treatment target according to current guidelines [55,56], but in elderly population, physicians may opt to tolerate mild endoscopic activity in view of the perceived lower long-term risks of IBD-related complications, resulting from a relatively shorter lifespan compared to the younger population [57,58]. Still, one of the most important factors to evaluate in elderly-IBD is patients' desires and treatment expectations. With patient-reported outcomes, which are more often used in the elderly, patients are directly involved in choosing the management strategy with their physician [59].

The choice of the most appropriate therapeutic approach in older patients should be driven by balancing potential benefits and risks on an individual basis [59]. If the risks of IBD-related complications prevail, or in case of a fit old patient, a top-down approach could be cautiously considered, as it has been demonstrated that early combined immunosuppression had similar efficacy in older and younger CD patients, and was more effective than conventional treatment in lowering disease-related complications [60]. Conversely, in a frail patient, the risks of treatment-related complications could induce clinicians to opt for a more conservative step-up approach. Still, one should consider that a flare of IBD in a frail patient with diminished functional reserves may have very deleterious effects on the patient health status [4,42] and that refraining from the use of the most effective drugs may induce an increased risk of surgery [59]. Additionally, both severe disease activity and steroids use are factors greatly associated with serious infections in IBD [60]. Notably, a recent study showed that an effective use of anti-TNF drugs was able to improve frailty in elderly IBD patients, with a greater impact on patients with higher pre-treatment frailty [44]. As such, treating physicians should consider the possibility of frailty improvement with IBD treatment during the risk-benefit assessment for each individual patient.
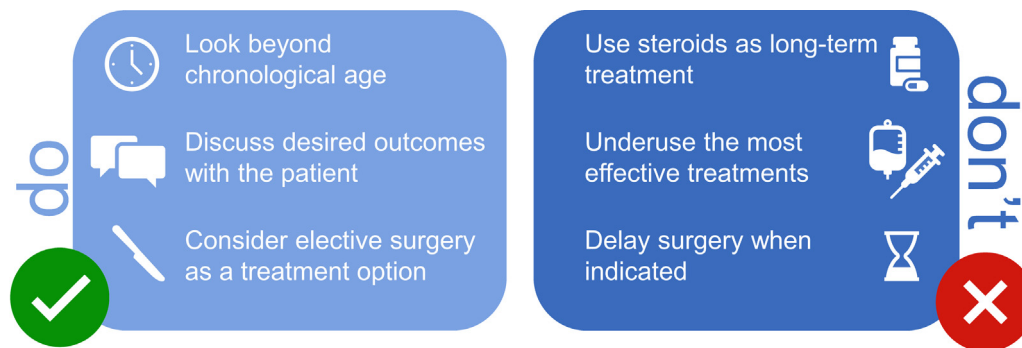
Fig. 3. Common mistakes and principles of management of Inflammatory Bowel Disease in the elderly.

A key principle of management is to avoid undertreating patients, a common mistake in clinical practice, where physicians rely on the frequent use of steroids and delay treatment escalation. The underuse of the most effective therapies in elderly IBD could have several explanations including, (i) the misperception of a milder course of disease in this population [21]; (ii) a false perception of the safety and convenience of steroids instead of steroid-sparing therapies [61,62]; (iii) the fear of adverse events (as suggested by an international survey) [63]; or (iv) concerns about a reduced efficacy of immune-modulating therapies due to immunosenescence, although no clear data are currently available [57].

A major limitation in choosing an appropriate treatment strategy and target in the elderly with IBD is that elderly patients are often excluded from clinical trials as many factors serving as barriers for recruitment are more likely to affect this age group (such as comorbidities and malignancies) [64]. This limits the generalization of their RCT results to guide treatment in the elderly. In a systematic review of inclusion of older adults in the randomized controlled trials (RCT) of approved drugs to treat IBD, Kochar et al. found that less than 1% of participants were ≥ 65 years [64].

3.2. Drug efficacy in the elderly

Overall, current literature did not demonstrate differences of efficacy of medical treatment in elderly patients [4], as it was shown for corticosteroids [65] and thiopurines [66]. Methotrexate is not widely used in elderly patients, but a retrospective study showed similar outcomes in these patients compared to a younger cohort [67].

Biological agents in the elderly IBD population are rarely utilized, with rates as low as 2% in UC patients and 6% in CD patients at 5 years following date of diagnosis, compared to 7% and 20% in the adult population [68]. Data from the large TARGET-IBD multicenter cohort indicated that older patients with IBD were prescribed more aminosalicylate monotherapy and less anti-TNF therapy compared with younger patients [26]. The underuse of biological therapies in elderly-onset IBD may lead to increasing rates of surgery in UC [11,69].

Concerning the efficacy of anti-TNF drugs in the elderly, available data is conflicting. A pooled analysis of RCT comparing patients >60 years with younger ones showed that they had similar rates of clinical remission after both induction (OR, 0.78; 95% CI, 0.51–1.19) and maintenance (OR, 0.65; 95% CI, 0.41–1.06) [70]. These results were confirmed in a real-life setting [71]. There are, however, other reports demonstrating a lower efficacy of anti-TNF treatment in bio-naïve elderly IBD patients [72], and higher risk of anti-TNF treatment discontinuation, due to both the increased risk of adverse events and the lower rate of response [73]. However, elderly patients may need more time to obtain remission after starting anti-TNF treatment, suggesting that pharmacokinetic mechanisms could play a role [74,75].

Regarding vedolizumab, data are more homogeneous, indicating that drug efficacy is similar in elderly and in young patients [76–78]. Interestingly, a large multicenter Italian study showed that vedolizumab effectiveness in elderly UC patients may be reduced in terms of treatment persistence, clinical and biochemical remission, while no age-dependant effect on effectiveness was observed in CD [78].

Limited data are available for ustekinumab, with only one study in IBD setting showing a similar rate of clinical response in elderly and young patients, but the first group was less likely to achieve complete clinical remission [79].

An early identification of patients responding to biological therapies could have a significant impact in clinical management of elderly IBD patients. Unfortunately, the most used biomarkers in IBD setting, such as C-reactive protein (CRP) or faecal calprotectin (FC) have a significantly lower reliability in the elderly population, mainly due to their low specificity [80,81]. Indeed, both CRP and FC could be increased by several non-IBD conditions and by several drugs, such as proton pump inhibitors and nonsteroidal anti-inflammatory drugs, which are commonly used in the elderly population [57,80]. A recent study pointed out that the serum triiodothyronine-to-thyroxine (T3/T4) ratio before starting a biological therapy in elderly IBD patients could predict therapeutic outcome in terms of mucosal healing at one year [82]. Interestingly, T3/T4 ratio could be considered as an independent biomarker of frailty in elderly patients regardless of disease [83]. If the results of this study would be confirmed in future larger studies, the assessment of T3/T4 ratio could help clinicians in identifying patients with higher probability of therapeutic response, maximizing the results, and reducing the rate of treatment-related complications.

3.3. Drug safety in the elderly

Safety profile should be considered as a significant issue in the elderly IBD population for almost all therapeutic agents, as elderly IBD patients seem to have higher risks of treatment-related complications, especially those with elderly-onset IBD [28].

Aminosalicylates and sulfasalazine are undoubtedly drugs with a good safety profile, but they are associated with an increased risk of nephrotoxicity, particularly in patients with concomitant renal dysfunction or heart failure [84], comorbidities that are more frequent in elderly patients [36].

Corticosteroid treatment is clearly associated with higher risks of complications in elderly patients as compared with younger ones, especially in case of a prolonged use [4]. The TREAT registry highlighted that age, use of corticosteroids and narcotics were independent predictors of mortality, whereas mortality rates were similar between infliximab- and non-infliximab-treated patients

[85]. In fact, most studies agree that infections, and particularly serious infections, are more common in elderly IBD patients, especially in those receiving corticosteroids [6,85–87]. Corticosteroids are also associated with other complications, such as osteoporosis, alteration in mental status, fluid retention, ocular problems, and drug interactions [88]. Given all of these risks, corticosteroids in the elderly should be initiated with an appropriate 'exit strategy', planning a transition to a safer maintenance therapy [89].

Safety problems are significant in case of immunosuppressive treatment with thiopurines. Their use increases the risk of infections, nonmelanoma skin cancers and lymphoproliferative disorders, particularly in elderly patients [90–94]. The CESAME study [91] indicated that older age is an independent risk factor for the development of lymphomas. Even though azathioprine therapy increases life expectancy in patients with CD, the incremental gain in life expectancy decreases with increasing patients' age due to the increasing risk of lymphoma [95]. Notably, the risk of malignancies seems to be significant even after the discontinuation of thiopurine therapy [96], suggesting a long-term monitoring of elderly IBD patients treated with these drugs. Moreover, the ENEIDA registry showed that patients starting thiopurines after 60 years had higher rates of myelotoxicity, digestive intolerance and hepatotoxicity [97]. For these reasons, ECCO suggests that the use of thiopurines in the elderly needs careful consideration and monitoring [4]. Thiopurines should be avoided in the case of chronic renal disease and lower renal clearance, in those with a history of neoplasms or lymphoma, and in patients requiring the use of xanthine oxidase inhibitors [97].

Biological agents seem to have a safer profile in comparison with thiopurines, although all the immune-suppressive therapies could increase the risks of infections and cancer [98]. The ENEIDA registry showed that elderly patients with IBD have a similar risk of developing infliximab-related adverse events in comparison with younger patients [99]. In a pooled analysis of data from RCT, even though elderly UC patients had an increased baseline risk of serious adverse events, no increase in risk could be attributed to anti-TNF therapy [70]. Conversely, Desai et al. [73] observed a threefold risk of discontinuation of anti-TNF treatment in patients starting the therapy over the age of 60. On the same line, an Italian multicenter study showed that elderly IBD patients treated with anti-TNFs displayed an increased risk of infections (particularly respiratory infections) malignancy and mortality when compared to a younger group or to elderly patients treated with other drugs [100]. These findings were confirmed by a more recent study that took into consideration all serious adverse events, which were significantly higher in patients >65 years treated with anti-TNF as compared to younger ones [74]. The IBDREAM registry confirmed these data, indicating that older patients treated with anti-TNF have higher rates of treatment discontinuation, although the concomitant use of thiopurines at baseline was associated with lower failure rates, but with higher risk of serious adverse events and infections [101].

A recent survey indicated that vedolizumab is the preferred treatment option of the gastroenterologists in elderly IBD patients [63]. This could be related to its gut-selectivity, which a perceived lower risk of adverse events. Indeed, a post-hoc analysis of GEM-INI trials showed no age-related differences in the incidence of adverse haematological events, malignancy, or death [76]. These results were confirmed in a recent, large real-life study [78]. Accordingly, Kochar et al. observed that older IBD patients treated with vedolizumab had a lower risk of infection-related hospitalization compared with those initiating anti-TNF therapies [102]. Conversely, Adar et al. [71] reported an increased risk of pneumonia in elderly IBD patients treated with vedolizumab, similar to the rates obtained in patients treated with anti-TNF. A larger subsequent study of 3 population-based cohorts confirmed that the risk

of serious infections was not decreased with vedolizumab versus anti-TNF in patients with CD, whereas it decreased of 32% in patients with UC, suggesting that the disease phenotype could play a role in the development of infections in vedolizumab-treated patients [103].

Fewer data are currently available for ustekinumab. UNITI-1 and UNITI-2 registration trials found that the proportion of patients who developed infections was similar between those treated with ustekinumab and those treated with placebo [104,105], and a recent meta-analysis confirmed these reassuring findings, but patients were not stratified by age [106]. However, a real-life study showed no significant differences in infusion reactions, infection, or postsurgical complications in patients stratified by age category (>65 vs <65 years old) [79].

Despite the notion that newer biologics may have better safety profiles, in a recent meta-analysis evaluating safety of biologics in elderly-IBD, the rate of adverse events and infections was not different between the investigated biologics [107]. The authors concluded that data was still lacking to propose sequencing of biologics in the elderly based on safety, and that larger studies are needed.

Tofacitinib is a Janus kinase (JAK) inhibitor, a small molecule with proven efficacy in IBD. However, as increasing age seems to be a risk factor for adverse events reported with this drug (namely a higher risk of infections and of thrombotic events), its use in the elderly should be carefully considered [108].

3.4. Surgery in the elderly

Elderly IBD patients seem to have increased rates of surgery, mainly shortly after diagnosis [10,11,21,27,42,69,109]. This may be caused by an underuse of effective medical therapies with subsequent complications needing a surgical procedure, as previously mentioned. However, it may also be a conscious decision by the physician to avoid medical therapy, as surgery may be seen as a safer alternative to immunosuppressive treatment in patients with comorbidities [11,21]. In fact, in a recent survey [63], the presence of comorbidities was the most important factor influencing gastroenterologists' decision on recommending colectomy in UC patients. However, comorbidities also significantly impact the postoperative outcomes of IBD patients, being associated with an important increase in mortality rate [110]. There are conflicting data on the risk of postoperative complications in elderly IBD patients, but many studies demonstrate a higher risk of complications and mortality [70,111–116]. In a recent systematic review, elderly-onset UC patients had high rates of serious post-operative complications (10%) with a 4% mortality [9].

ECCO recommends that age should not be used as a sole predictor of surgical risk in IBD patients and surgery must not be delayed when clearly indicated [4]. Some groups advocate a timely proctocolectomy rather than combination treatment in elderly-onset UC, particularly due to the potential curative nature of the procedure [10]. Ileal J pouch anal anastomosis is a preferential surgical technique in UC if the patient has good anal sphincter function and no history of faecal incontinence, with a high rate of satisfaction in this group [114]. Patients with diminished anal sphincter function may have superior quality of life with colectomy and ileorectal anastomosis or end-ileostomy surgery [117,118].

The decision of surgery should be balanced against medical treatment, considering patient and disease-associated factors. Since emergency surgery is the main factor accounting for post-operative complications, surgery should preferably be performed in an elective rather than emergent setting [115,119] As such, gastroenterologists and surgeons should work in a multidisciplinary team aiming at avoidance of emergency surgical procedures by adequately

controlling disease activity, whether by an appropriate medical treatment, an elective surgical procedure or a combination of both.

3.5. Health maintenance

Concerning preventive medicine in elderly IBD patients, we refer to the published ECCO guidelines on the prevention and management of infections in IBD [120], and the soon to be updated ECCO guidelines on malignancies [121], as many of the same principles apply to this age group.

Advanced age is an independent risk factor for opportunistic infections [100]. To counteract the increased risk of infections, vaccinations are strongly recommended before starting a biological or immune-suppressive therapy in all IBD patients, and particularly in elderly age [61]. This is particularly important for anti-JAK therapies, which are associated with a significant increased risk of severe herpes zoster infection [122].

Regarding colorectal cancer (CRC) screening, there is some evidence suggesting an increased risk of CRC in elderly-onset IBD, with a recommendation of an earlier start of surveillance in this group. However, other studies have not found an increased risk of CRC in this particular cohort [4,112,123–125]. The continuation of CRC screening in older patients should consider the general health status/frailty of the patient and impact of comorbidities against the potential increasing risks of colonoscopy with age [4,6].

Malnutrition is more frequent in IBD patients >65 years than in younger ones [42]. Malabsorption, increased intestinal loss and decreased food intake play a role in protein-calorie malnutrition with subsequent associated infectious risk [112]. It is recommended an annual review of diet, body weight assessment, and regular evaluation of ferritin, albumin and vitamins D and B12 levels [58].

Osteoporosis and osteoporotic fractures are increased by 40–60% in IBD patients and older IBD patients have a further increased risk due to malnutrition, vitamin D deficiency and reduced physical activity besides age-related bone loss [58]. For this reason, dual energy X-ray absorptiometry screening is recommended amongst older IBD patients with corticosteroid use and/or other risk factors [126] and vitamin D/calcium supplementation and treatment of the underlying disease are mandatory [112].

4. Conclusion

With the ageing of the population, IBD clinics must prepare for the expected increased number of elderly IBD patients. In this review we point out the specific challenges physicians face in the management of this group of patients, such as comorbidities, increased risk of treatment complications, and lack of high-quality evidence to inform clinical practice. Biological age may be more relevant than chronological age, and it is of upmost importance that specific risk stratification tools are developed to help guide treatment options.

The previous notion of a milder course of disease in the elderly was likely a misconception, often defined by a decreased use of immunomodulators and biologics in this age group. Awareness must be raised for the similarity of the disease course of elderly patients with that of adult-onset IBD. The same principles of management must be followed, with the same available treatments – whether medical or surgical – available to be used and obtain an adequate disease control. Newer biologics with maybe better safety profiles may be preferred. Desired outcomes must be individualized and discussed with each specific patient, considering a relatively shorter life expectancy and, consequently, a lower risk of developing long-term complications of both treatments and disease. A personalized management would maximise the benefit/risk ratio, obtaining the best results for patients' quality of life, even in the long-term.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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