Minireview

Peculiarities of the Diagnosis and Treatment of Inflammatory Bowel Diseases in Elderly Patients

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Abstract

Inflammatory bowel diseases (IBD) are chronic inflammatory diseases with increasing prevalence in elderly patients. Multiple comorbidities associated with polypharmacy are to be considered in such patients and impose some limitations in the diagnosis and treatment of IBD. This literature minireview has the purpose of highlighting the particularities of the diagnosis and treatment of IBD in elderly patients. Frailty and sarcopenia are key findings in the geriatric population and need careful consideration and proper therapeutic approach when constructing the diagnosis protocol and treatment regimen in elderly patients with IBD. Considering that the treatment options for IBD in elderly patients are quite extensive, adherence to treatment is expected to be attained. Diagnosing this pathology in the elderly patients' group poses a great responsibility in weighing the risks and benefits of the procedures, as well as costs of hospitalization and comorbidities that can impede a timely diagnosis.

Keywords: inflammatory bowel disease, elderly adults, treatment, diagnosis, peculiarities.

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INTRODUCTION

Inflammatory bowel diseases (IBD), represented by Crohn's disease (CD) and ulcerative colitis (UC), have an important impact on the quality of life (QoL) of elderly adults. Elderly patients with IBD pose additional problems, related to timely diagnosis and treatment adherence. Elderly adults associate numerous comorbidities which can be mistaken for complications of IBD, thus delaying the diagnosis.

Polypharmacy is one of the most important challenges in elderly patients, because of drug-drug interactions and the risk of renal and hepatic injuries.

Environmental factors are thought to play a key role, due to the rising incidence of IBD. In the second half of the twentieth century, the increase in IBD incidence was seen, following the historically highest incidence in Western European, as well as Northern American population[1].

Frailty and sarcopenia are key findings in the geriatric population and need careful consideration and proper therapeutic approach when constructing the diagnosis protocol and treatment regimen in elderly patients with IBD.

MATERIALS AND METHODS

We have reviewed 200 articles, following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. We have accessed online databases such as PubMed, Elsevier, Google Scholar, and Web of Science with geographic restrictions to Europe, all articles being published in English.

Data mining was performed according to the study plan, by three independent authors, according to data search criteria and pre-determined inclusion criteria. Eligible studies were identified, based on several criteria: study population (continent, number of subjects, age, diagnosis of IBD), study design, diagnosis of CD and UC in elderly adults, methods of diagnosis, treatment options.

The following keywords were used: "IBD", "Crohn's", "ulcerative colitis", "elderly", "histopathology", "treatment", "imaging", "complications", "polypharmacy", "comorbidities", "quality of life", single and in combination.

Inclusion criteria: study design (prospective/retrospective study, clinical trials, meta-analyses, systematic reviews), patients who were diagnosed with IBD, patients aged 65 years or over, patients residing in Europe.

Exclusion criteria: patients aged less than 64 years, unconfirmed IBD diagnosis, patients residing outside of Europe.

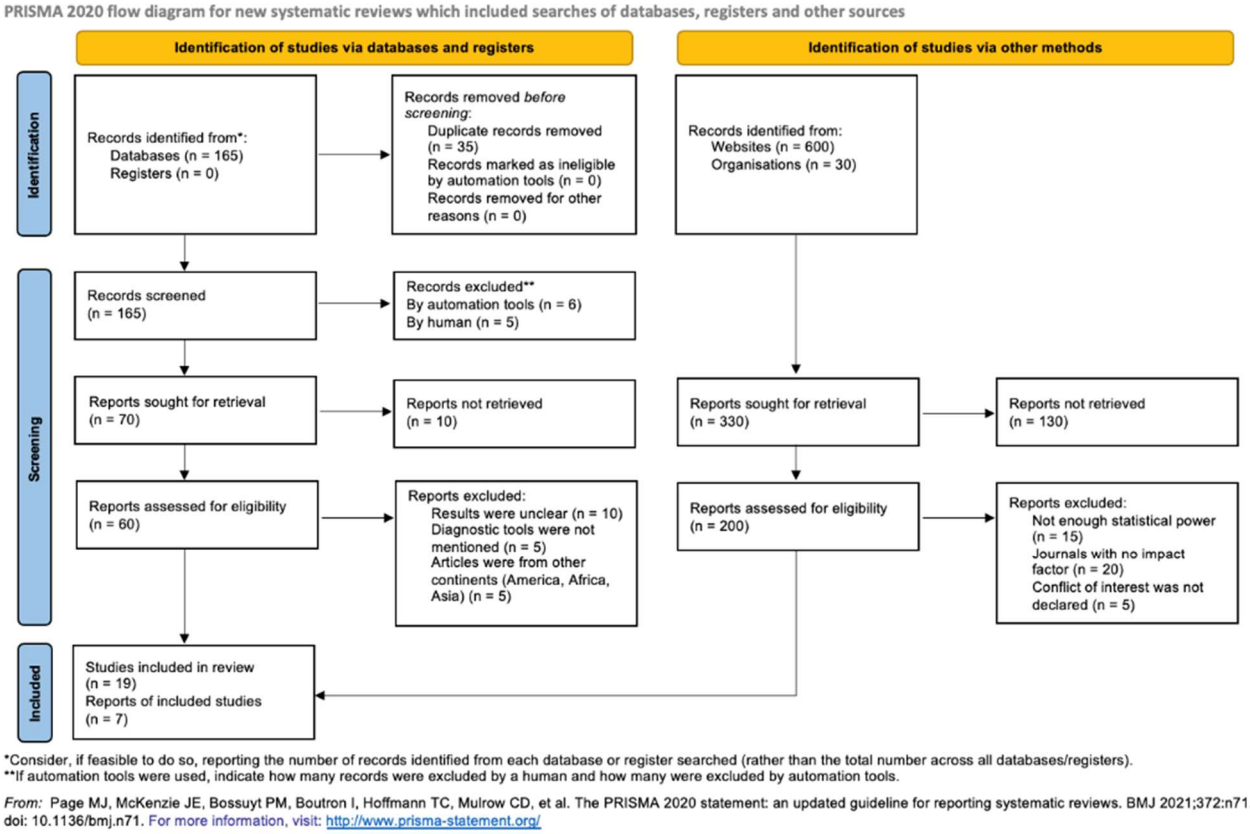
After a careful study of the articles found in the beforementioned databases, we have excluded those who did not meet the criteria for this review.

On PubMed, 130 articles resulted after applying the filter: "abstract", "free full text", "all article types", "less than five years", "inflammatory bowel disease", "older adults", "treatment", "diagnosis", "frailty", of which only 10 were relevant to the topic. Furthermore, selecting "clinical trials" to the article type, only 15 results were found, two articles resulted for "randomized controlled trial", 30 articles for "systematic review" and 5 articles for "meta-analysis". On Elsevier, 30 articles were found by applying the keywords "IBD", "elderly", "diagnosis", "treatment", and on Web of Science 5 articles. On Journal of Crohn's and Colitis, 600 articles were found by applying the filter "elderly", "ulcerative colitis", "Crohn's disease" and sorted by "date-newest first", from which only 30 articles were relevant to the topic.

CROHN'S DISEASE IN THE ELDERLY

CD onset in older patients has shown a lower incidence than in UC for the same population group in Eastern European countries compared to Western countries[2]. Due to a higher inflammatory status in older adults, the disease presents less often with strictures and penetration of the bowel wall. Thus, the characteristic presentation of CD in elderly is highlighted by inflammation of the bowel wall[3]. The incidence of CD has seen a stable increase after World War II in North America and in North European industrialized countries[4].

A study reviewing the literature regarding research done on mouse models has concluded that the development of CD occurs in three stages: the ingress of bacteria and antigenic material into the bowel wall, followed by a weak acute inflammatory response that results in impaired clearance of this material, culminating with chronic granulomatous inflammation and adaptive immune responses. These stages are relevant for diagnosing and treating CD, targeting the changes that appear in the bowel wall[5].



ULCERATIVE COLITIS IN THE ELDERLY

Extraintestinal manifestations are the hallmark of UC, thus conveying a myriad of possibilities for sarcopenia to install in these patients. Sarcopenia is a pathology related to the skeletal muscles and it is characterized by diminished muscle mass, muscle strength, and overall physical performance. This associated disease is strongly related to a lower quality of life due to functional impairment, making sarcopenia an important factor in considering mortality rate in UC patients[6].

Patients presenting with acute abdomen have shown a more difficult diagnosis of severe UC because of the distinctive physiology of this age group, but severe UC should always be considered when an older adult complains of abdominal pain[7].

The most common clinical presentation of older-onset UC is the left-sided colitis, but rectal bleeding, abdominal pain, and extraintestinal manifestations are more often seen in younger-onset UC. A similarity between UC in elderly and adult-onset UC is represented by the disease course[8].

DIAGNOSTIC TOOLS IN ELDERLY WITH IBD

According to the American Gastroenterological Association guidelines, the first diagnostic steps are laboratory investigations that include a complete blood count and serum albumin, serum ferritin, and C-reactive protein levels[9].

LABORATORY TESTING

Underlying comorbidities and toxicity monitoring are evaluated through liver enzymes and urea and creatinine levels. Stool testing for Clostridium difficile in all new presentations of diarrhea, regardless of antibiotic use history, and selective testing of stool for culture and ova and parasites may be

appropriate to exclude any other pathologies that can mimic IBD[9].

IMAGING STUDIES

Cross-sectional imaging with computed tomography is appropriate in elderly persons who present with acute symptoms, especially when abdominal pain is a prominent symptom, because it can also exclude ischemic colitis and diverticular disease. Colonoscopy with histologic confirmation remains a cornerstone of diagnosis. However, there should be additional consideration of procedural risks and tolerance for anesthesia in the presence of comorbidities and polypharmacy in elderly patients. In cases where the indication for colonoscopy is equivocal or is associated with relatively high risk, the use of noninvasive stool markers of inflammation such as fecal calprotectin and imaging may aid in decision making[9].

One study shows that video capsule endoscopy (VCE) can be safely performed in elderly because some of these patients can have unsuspected small intestine CD, despite negative conventional bidirectional gastrointestinal endoscopies, thus changing the course of treatment. Further studies in this particular age group would help identify clinical and biochemical parameters for stratifying the risks[10].

TREATMENT OPTIONS IN ELDERLY WITH IBD

One study suggests that a better efficacy was seen in patients with active UC when fecal microbiota transplantation was delivered via the colonic route. There are signals linking gut microbial diversity and biological classification of organisms belonging to Clostridia (short chain fatty acid producers) with clinical response, calprotectin and a shift towards an immunoregulatory phenotype[11].

MONOCLONAL ANTIBODIES

Another study shows that the fecal loss of Infliximab was associated with increased markers of systemic and luminal inflammation, making this biological treatment option a useful tool for measuring disease severity, treatment response and clinical outcomes. Due to the small population sample of this study, an ideal treatment plan with Infliximab could not be set[12].

Ustekinumab and vedolizumab were researched for their effectiveness in extraintestinal manifestations of patients with IBD as a good therapy option. However, the study showed that there was no difference in therapeutical outcome between the two biological agents at the 52 weeks follow-up[13].

Ustekinumab, a humanized monoclonal antibody, was shown by a study that it achieved clinical response in almost three-quarters of elderly patients, with the same rate of infections and other adverse effects, with the exception of de novo neoplasms[14].

A retrospective study done on 1090 elderly patients with IBD indicated that biological drugs have response rates like those of young and adult population, golimumab being the drug that had to be discontinued most frequently due to ineffectiveness in the older adult population[15].

THIOPURINES

Even though thiopurines treatment may lead to appearance of lymphoproliferative disorders, one study shows that there was no risk of developing such disorders in IBD patients undergoing treatment with thiopurines[16].

ANTI-INFLAMMATORY THERAPY

Conventional non-steroidal anti-inflammatory drugs (NSAIDs) have shown in a study that in approximately 20% of IBD

patients relapse has installed, which was thought to be caused by the dual inhibition of the cyclooxygenase (COX) enzymes, though a number of COX-2-selective NSAIDs appeared to be safe[17].

ANTIBIOTICS

One study regarding antibiotic therapy used in elderly patients with IBD has shown the this treatment regimen may induce remission in active CD and UC, although due to a varied number of antibiotics tested the results are inconclusive concerning its efficacy[18].

5-AMINOSALICYLATES

5-aminosalicylates (5-ASAs), such as sulfasalazine and mesalazine, convey a cornerstone in the therapeutic approach to UC in elderly patients. Even though they have a controversial role in CD, in the EPIMAD study, 90% of older patients with CD were on 5-ASAs[19].

CORTICOSTEROIDS

Corticosteroids, even though very widely used as gold standard therapy in IBD due to their high efficacy in inducing remission of this pathology, have numerous contraindications in older adults. The limitations in this age group are related to the effects of corticosteroids on different pathologies that are very common in elderly (heart failure, diabetes, hypertension and osteoporosis, cataract and glaucoma)[20].

METHOTREXATE

Methotrexate and thiopurines are used as therapeutic agents in elderly patients with IBD. In CD, methotrexate is preferred, while thiopurines showed a better clinical outcome in UC[19].

ANTI-TUMOR NECROSIS FACTORS

Anti-tumor necrosis factors (anti-TNFs) are shown to have great results in the induction and maintenance of moderate to severe active IBD in elderly patients, although the adverse effects of this therapeutic regimen outweigh the benefits[21].

ANTI-INTEGRINS

Anti-integrins such as vedolizumab were studied in the landmark GEMINI trials, where their efficacy and safety have appeared to be similar across all age groups, but elderly patients diagnosed with IBD and following this treatment protocol exhibited the lowest rate of severe infections and side effect-related hospitalization[22].

Tofacitinib is a Janus kinase (JAK) inhibitor, an orally administered small molecule, approved by the National Institute for Health and Care Excellence (NICE) in 2018 for moderate to severe active UC, although it is recommended to be used with caution due to its life-threatening risk for pulmonary embolisms, deep vein thrombosis or clotting abnormalities[23].

POSSIBLE COMPLICATIONS IN ELDERLY PATIENTS WITH IBD

Sarcopenia is shown by multiple studies to be an important finding in older adults with IBD[6], [24]. Infections were linked to the presence of sarcopenia in patients with IBD, thus starting new biologic medications requires a thorough overall clinical and laboratory assessment of older adults[24].

IBD patients commonly associate frailty, which greatly increases mortality in these patients, but outcomes can be improved by determining physiologically fitness to withstand immunosuppressive therapies, thus aiding in more effective steroid-sparing treatment regimens[25].

Lymphoproliferative and myeloproliferative disorders are often encountered in patients

with IBD, irrespective of age onset of IBD[16].

The higher hospitalization rate and costs of older patients with IBD were linked to the risk of serious infections and extraintestinal, cardiovascular and respiratory complications, rather than IBD-related complications [26] [27] [28]. In order to aid in lowering the costs and burden of hospitalization of these patients, population health management strategies with active patient engagement, delivery system redesign using health information technology advances are thought to be useful[29].

The limitations of the research are related to the low number of articles regarding IBD in elderly patients, the late diagnosis in this population group, as well as associated cognitive impairment that can often accompany other pathological processes in older adults.

CONCLUSIONS

Even though there are enough diagnostic tools that can be used for elderly patients, there are some limitations regarding associated diseases[9]. One study suggests that if treating IBD may ameliorate the frailty syndrome itself, then adverse outcomes related to frailty can also be reduced [25].

Thus, inflammatory bowel diseases in elderly benefit from various diagnostic tools as well as numerous therapeutical options, aiding in a better management of the polypharmacy and multiple comorbidities that are specific to this age group.

Author Contributions:

A.G.P. conceived the original draft preparation. A.G.P., R.I.D., and L.B.G. were responsible for conception and design of the review. A.G.P., R.I.D., L.B.G., and T.S. were responsible for the data acquisition. A.G.P., was responsible for the collection and assembly of the articles/published data, and their inclusion and interpretation in this review. A.G.P., R.I.D., L.B.G., T.S., M.M.D. contributed equally to the present work. All authors contributed to the critical revision of the manuscript for valuable intellectual content. All authors have read and agreed with the final version of the manuscript.

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