https://doi.org/10.31925/farmacia.2026.1.16 **ORIGINAL ARTICLE**

CLINICAL BIOMARKER PROFILES SUPPORTING THE DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE IN GERIATRIC PATIENTS IN A ROMANIAN TERTIARY CENTER

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Abstract

Inflammatory bowel diseases (IBD), represented by ulcerative colitis (UC) and Crohn's disease (CD), have distinct histopathological and clinical features. Disease activity is influenced by patients' biological age; therefore, evaluation of clinical biomarkers may improve assessment in older adults. We conducted a longitudinal observational study including 60 older adult patients diagnosed with IBD. Medical, laboratory, and imaging records were reviewed over a 6-month period. All patients were admitted to the Gastroenterology and Hepatology Clinic of the Fundeni Clinical Institute and underwent imaging and laboratory testing at the same institution. Diagnostic approaches varied across the cohort, combining imagistic investigations with histology and inflammatory biomarkers. The most frequently used biomarkers were fecal calprotectin and C-reactive protein (CRP). At 6 months, fecal calprotectin levels decreased in patients with UC, while CRP levels decreased in patients with CD. Including clinical biomarkers into the diagnostic algorithm for IBD in older adults as a gold standard may enable earlier detection of disease activity, support timely prevention of complications, and improve clinical outcomes in this particularly frail population of affected older patients.

Rezumat

Bolile inflamatorii intestinale (BII), reprezentate de colita ulcerativă (CU) și boala Crohn (BC), au caracteristici histopatologice și clinice distincte. Activitatea bolii este influențată de vârsta biologică a pacienților, prin urmare, măsurarea biomarkerilor clinici poate îmbunătăți evaluarea la vârstnici. Am efectuat un studiu observațional longitudinal care a inclus 60 de pacienți vârstnici diagnosticați cu BII. Dosarele medicale, de laborator și imagistice au fost evaluate timp de 6 luni. Toți pacienții au fost evaluați în Clinicile de Gastroenterologie și Hepatologie ale Institutului Clinic Fundeni și au fost supuși imagisticii și testelor de laborator în aceeași instituție. Abordările diagnostice au variat în cadrul cohortei, combinând investigațiile imagistice cu histopatologia și biomarkerii inflamatori. Biomarkerii cei mai frecvent utilizați au fost calprotectina fecală și proteina C reactivă (CRP). La 6 luni, nivelurile de calprotectinei fecale au scăzut la pacienții cu CU, în timp ce nivelurile de CRP au scăzut la pacienții cu BC. Includerea biomarkerilor clinici în algoritmul de diagnostic pentru bolile inflamatorii intestinale (BII) la vârstnici, ca standard în practica medicală, poate permite detectarea mai timpurie a activității bolii, poate susține prevenirea la timp a complicațiilor și poate îmbunătăți rezultatele clinice la această populație fragilă de pacienți vârstnici.

Keywords: older adults, clinical biomarkers, inflammatory bowel disease

Introduction

Inflammatory bowel disease (IBD) is represented by Crohn's disease (CD) and ulcerative colitis (UC), each having different histological aspects and clinical manifestations, which highlights the need for a targeted molecular diagnosis (1).

A particular aspect of IBD in older adults is related to the sometimes-silent clinical manifestation (2). Some studies (3,4) have shown that older Romanian adults diagnosed with IBD had a higher prevalence of one type of IBD compared to younger adults. Thus, grouping older adults with IBD into age groups and place of residence will facilitate a more comprehensive approach and better patient management.

Clinical biomarkers were shown to be useful in older adults for monitoring disease activity, as well as to determine treatment effectiveness (5,6). Studies have shown that the use of C-reactive protein (CRP) and fecal calprotectin as inflammatory biomarkers

has shown a possibility for the use of less invasive monitoring and diagnostic techniques, especially in frail older adults (7,8).

Nationwide population studies have shown a multimodal distribution of people aged 65 or older, predominantly in rural areas, prior to the Coronavirus disease-19 (COVID-19) pandemic. After the pandemic and the period of national quarantine, the elderly were relocated to urban areas by caregivers (children, grandchildren, social workers), which led to a possible increase in social anxiety and the desire for social isolation. But the relocation of this population group has facilitated faster access to diagnosis and treatment. These results favor a discussion related to the treatment compliance of these patients, together with a thorough investigation of the effects of social isolation on neurocognitive function, mood disorders, and the evolution of IBD (3).

Two prospective studies (9,10) conducted over a period of 12 years, evaluated the epidemiology, trends, phenotypes, and treatment among patients with IBD in Romania, including patients in Romania diagnosed with IBD, and grouped them according to clinical, radiological, endoscopic, and histological features of IBD. They also carried out the division of the country into eight regions: West (W), North-east (NE), Northwest (NW), Southeast (SE), Southwest (SW), South (S), Central (C) and Bucharest-Ilfov (B) to facilitate the analysis of the geographical distribution, phenotype and epidemiological trends of IBD patients in Romania. The same study showed that in the NE there were the most cases of IBD, and in the SV region the fewest cases. Patients diagnosed with UC were mainly distributed in the NE, NV, and C areas, while patients with CD were more numerous in regions B, V, S, and SE. In the south, the proportion of UC and CD was equal.

The geographical distribution of patients with IBD is of importance when considering the accessibility of those patients to an organic diet, because those living in rural areas grow their own produce, and those living in urban areas cannot have access to organic produce so easily due to increased costs (11,12). The type of diet can influence the time of diagnosis; therefore, a correct assessment of the type of diet and how it has changed since diagnosis and over the course of the disease might provide valuable insights into the diagnosis and treatment of IBD.

IBD being a chronic disease, thus needing frequent follow-up routines for older adults, research towards the discovery of new, less invasive, and cost-effective diagnostic methods has been encouraged. In light of these challenges, a molecular diagnostic method has been used, namely autologous white blood cell scintigraphy (WBCS) with 99-tecnetium-hexamethylpropylenamine oxime (99mTc-HMPAO), a very sensitive and specific method that can be used to determine the extent of gastrointestinal tract involvement, disease severity, and response to treatment (13). Another imaging investigation is positron emission tomography/computed tomography (PET/CT) with fluorodeoxyglucose F 18 (18F-FDG), used to highlight intestinal inflammation in children and adults, the benefits of the evaluation and therapeutic response in UC and CD being highlighted by a literature review article (14).

This study aimed to highlight the importance of evaluating treatment possibilities in older adults with IBD and the probability of using less invasive diagnostic methods for this patient population.

Materials and Methods

Study Design

We conducted a longitudinal observational study from September 2023 to February 2024 at the Gastroenterology and Liver Diseases Departments of the Fundeni Clinical Institute (ICF) in Bucharest, Romania. Data was collected from electronic health records, laboratory and imaging databases, and patients' discharge papers. Follow-up duration was six months, with a window of delay between visits of ± 1 week.

The primary objective of this study was to highlight the importance of pharmacological intervention follow-up through non-invasive procedures, such as clinical biomarkers. The desired outcomes of this study were to highlight the potential of using clinical biomarkers to monitor disease progression and to minimize the use of invasive procedures (*e.g.*, colonoscopy, endoscopy, CT, MRI, *etc*.).

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of ICF Bucharest, Romania (Ethical Committee Approval Number 21545 from 26 April 2023). All patients have signed a consent form to be included in this study.

Study Population

Our total source population comprised 60 patients (n = 60), grouped by place of residence and age (65-74 and 75-86 years), with the oldest patient being 86 years old at the time of recruitment for this study.

As inclusion criteria, we considered patients diagnosed with IBD, patients over 65 years of age, place of residence (urban or rural), and patients admitted to an ICF.

Our criteria for exclusion from the study included: patients without a diagnosis of "ulcerative ileocolitis (chronic)", "other UC", "proctitis due to irradiation", "CD not specified", "ulcerative rectosigmoiditis (chronic)", "CD small intestine", "ulcerative enterocolitis (chronic)", "CD large intestine" or "UC not specified"; patients under 65 years old.

We have defined older patients as people 65 years and older, as recommended by the American Geriatrics Society (15).

Diagnostic confirmation was obtained through colonoscopy or superior digestive endoscopy, with biopsy and histopathological examination. Criteria used to confirm the diagnosis of IBD were applied according to the Montreal phenotypic classification, clinical examination (history of the patient, past treatment regimens, physical examination), detection of *Clostridioides difficile* infection (for differential diagnosis and complications analysis), and histopathology examination for treatment efficiency assessment (16).

Clinical Data Collection

The patients were recruited during their admissions to the Gastroenterology and Liver Diseases Department at ICF, and follow-up was conducted either at the Department or by phone or e-mail, depending on the patient's functional independence.

After carefully sorting and applying filters regarding patient record number, age, sex, and place of residence, a supplementary filter for the DRG code was applied (17) at hospital discharge was applied. To clarify stratification, we analyzed the distribution of older patients with IBD by imaging diagnostic method and medication use in both CD and UC. Diet intervention was prescribed by the physician at hospital discharge, according to the ESPEN guidelines (18,19) and adherence assessment was done by testing the nutritional status through the Mini-Nutritional Assessment (MNA) questionnaire (20).

Comorbidities were not the focus of this study, as the main aim was to assess the potential use of biomarkers to detect treatment efficacy, not disease activity, which comorbidities may influence.

Treatment categories were defined based on the primary pharmacologic or surgical intervention recorded during each patient's observation period: combination therapy (two or more medication classes) and monotherapy (a single medication class).

Biomarker Measurements and Diagnostic Procedures

Measurements from patients with ulcerative colitis were extracted from the study dataset, including baseline and follow-up values for each treatment group. For each patient, the change in fecal calprotectin was calculated as the difference between baseline and follow-up measurements, and the values were grouped by treatment. According to the American Gastroenterology Association (AGA) (21), fecal calprotectin is a highly specific biomarker for inflammatory activity in UC (22), but with a lower specificity for CD. Values of $\geq$ 123 μg/g for fecal calprotectin predict endoscopic activity, while values $\geq$ 80 μg/g indicate histological inflammation (23).

C-reactive protein is a widely used inflammatory marker due to its high specificity and sensitivity to the degree of inflammation present in the body, due to its synthesis in the hepatocytes, with a plasma cut-off value of < 0.5 μg/mL (< 5 mg/L) (24,25). In IBD, CRP is particularly useful for quantifying the degree of inflammation, as well as disease activity (5), for both types of IBD.

The older adult patients in our study cohort were diagnosed using imaging techniques and clinical biomarkers. Patients with UC were mainly diagnosed through colonoscopy with biopsy. Additional investigations used in a smaller proportion of cases included superior digestive endoscopy (SDE), abdominal computed tomography (CT), entero-CT, and CT of the thorax, abdomen, and pelvis (CT-TAP), each of them used either alone or as complementary assessments. Colonoscopy with biopsy was also the main diagnostic method in patients with CD. Other imaging techniques used were CT-TAP, as the only diagnostic tool in a minority of older adults, SDE, abdominal CT, and entero-CT. Surgical biopsy was performed exclusively in CD cases in patients undergoing surgery for complications prior to diagnosis. Magnetic resonance imaging (MRI) was additionally referenced as part of the imaging approaches used for CD.

Statistical Analysis

The initial search results were manually filtered by reviewing the patient's discharge documents and speaking with patients to identify those eligible for the study. Then, patients were sorted by IBD type, gender, place of residence, diagnostic method, and year of diagnosis using an Excel spreadsheet. The graphs were made using the Excel program (Microsoft Office®, Albuquerque, NM, USA), and the statistical analysis was done using the data analysis software of the same program, alongside IBM SPSS version 30.0 software, for descriptive analysis of our study lot, and a two-tailed t-test for testing statistical significance of the results.

For each disease group, CD and UC, biomarker concentrations (fecal calprotectin and CRP) were measured at diagnosis and again 6 months later in the same individuals. Because the two measurements were obtained from the same participants, a two-tailed paired t-test ($\alpha = 0.05$) was performed to assess changes for each patient over this period.

The variables extracted for analysis included baseline CRP, follow-up CRP, treatment regimen, and information used for diagnosis confirmation. CRP change was calculated as the difference between follow-up and baseline measurements and further summarized descriptively across the different treatment regimens.

For fecal calprotectin, the mean change was calculated for each treatment group, and descriptive statistics were used to compare average calprotectin change across treatment categories, while analyzing the therapies received in both CD and UC patients.

Results and Discussion

Unspecified UC accounts for the highest proportion, at 35%, as shown in Figure 1. This suggests that more than one-third of cases fall into this general category, in which specific details about ulcerative colitis are unavailable. The second most common diagnosis in this age group was chronic ulcerative enterocolitis (21%), similar to CD of the large intestine, indicating a significant prevalence of CD localized to the large intestine. CD of the small intestine accounts for 12% of cases, indicating a smaller but notable number of cases. The least represented diagnosis (6%) in the "young"-old patients were: unspecified CD and chronic ulcerative rectosigmoiditis.

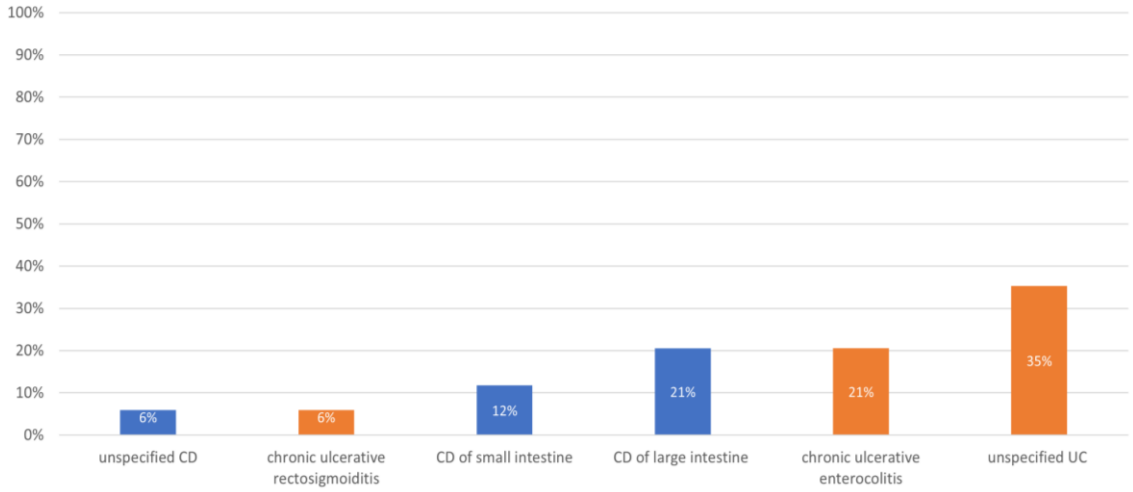


Figure 1.
Patients in the age group 65-74 years, diagnosed with IBD, irrespective of place of residence

Unspecified UC accounts for 55%, making it the most common diagnosis among old-old patients, as shown in Figure 2. This suggests that more than half of the cases in this age group involve ulcerative colitis without further specification. CD of the large intestine accounts for 20%, the second most prevalent diagnosis in this age group, and is a significant condition in this age group. The least prevalent diagnoses (5%) were represented by: chronic ulcerative ileocolitis, chronic ulcerative rectosigmoiditis, other UC, CD of the small intestine, and chronic ulcerative enterocolitis. Each of these represents a small proportion of the cases, highlighting a diverse but less common range of IBD diagnoses in this population.

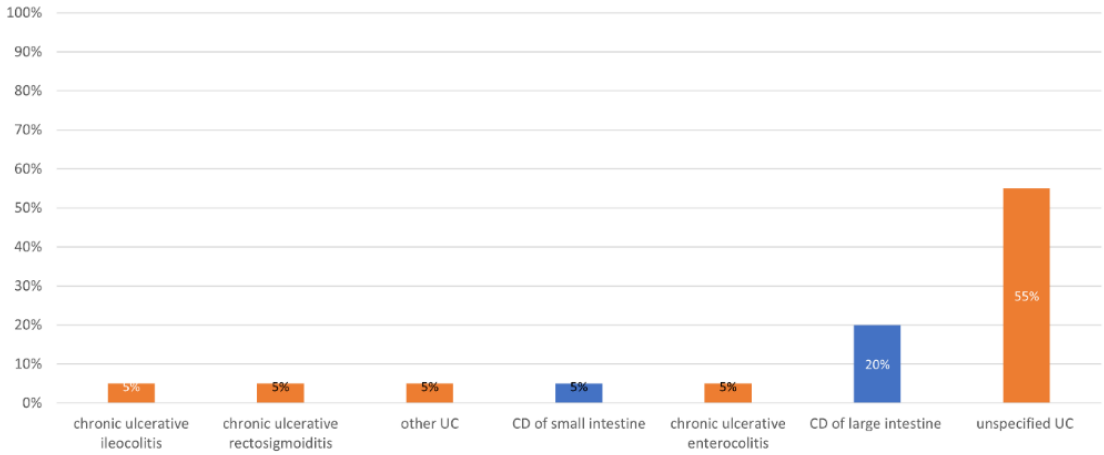
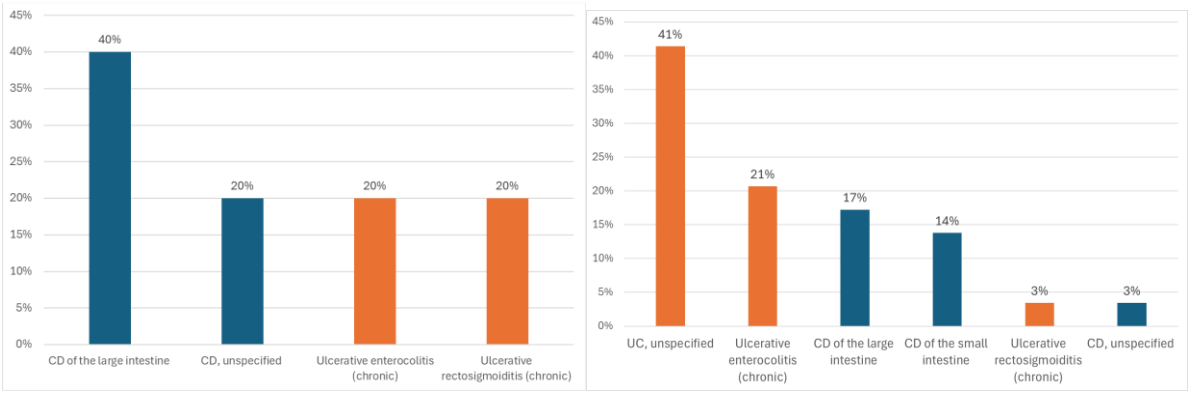


Figure 2.
Patients in the age group 75-86 years, diagnosed with IBD, irrespective of place of residence and diagnostic methods used

We have found an equal prevalence of 20% for the diagnosis of unspecified CD, chronic ulcerative enterocolitis, and chronic ulcerative rectosigmoiditis for older adults in the age group 65-74 residing in rural areas. Within the same age group, a prevalence of 40% was observed among patients diagnosed with

CD localized to the large intestine, as shown in Figure 3a.

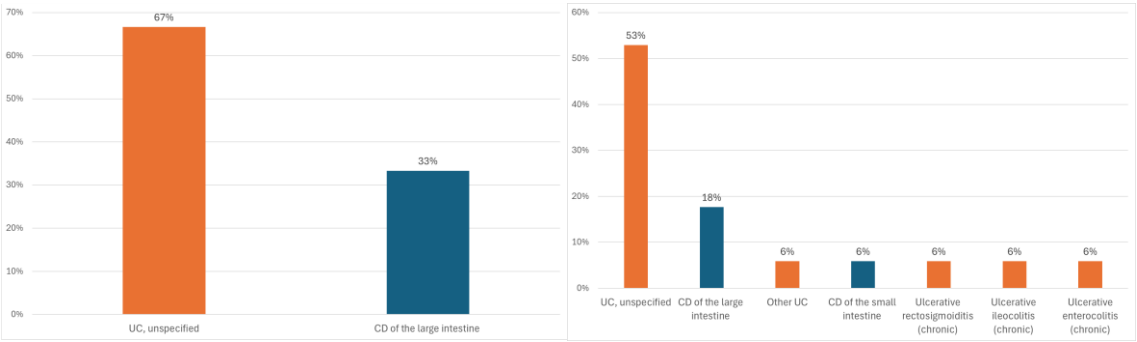
Figure 3b represents graphically that the patients aged 75-86 residing in the urban area had the least prevalent type of IBD (3%), represented by unspecified CD and chronic ulcerative rectosigmoiditis. The next least prevalent type of IBD (14%) in this age group is CD localized to the small intestine. Moreover, 17% of our study participants were diagnosed with CD of the large intestine. Of the "young"-old patients diagnosed with UC and residing in the urban area, 21% had chronic ulcerative enterocolitis and 27% had an unspecified type of UC.



(a) (b)

Figure 3.
Patients in the age group 65-74 years diagnosed with IBD, residing in rural (a) and urban areas (b)

Figure 4 shows that patients in the old-old cohort residing in the rural area had a higher prevalence of unspecified UC (67%). In comparison, 33% had CD localized to the large intestine, as highlighted in Figure 4a. This is important as defining the location of the lesions in the case of both IBD influences the treatment outcome and possible changes in diet and general lifestyle greatly. From our study lot, those belonging to the 75-86 age group had a more diverse representation of IBD diagnoses, as shown in Figure 4b. We have observed an equal representation (6%) of patients diagnosed with chronic ulcerative ileocolitis, chronic ulcerative rectosigmoiditis, chronic ulcerative enterocolitis, other types of UC, and CD of the small intestine. The same population has exhibited a prevalence of 18% for CD of the large intestine and 53% for unspecified UC.



(a) (b)

Figure 4.
Patients in the age group 75-86 years, diagnosed with IBD, residing in rural area (a) and urban area (b)

There is a predominance of UC diagnoses, including unspecified UC, chronic ulcerative ileocolitis, chronic ulcerative rectosigmoiditis, and other localisations of UC, which together make up 65% of the cases in our studied population. This indicates the predominance of UC over CD in this group. On the one hand, the high percentage of unspecified UC (55%) might indicate challenges with detailed classification or incomplete documentation of UC in older patients. On the other hand, CD, especially in the small and large intestine, is found in 25% of patients, with most cases (20%) localized to the large

intestine. These findings are congruent with other studies in the scientific literature (1,26).

There is a clear preference for colonoscopy with biopsy for both IBD types, with a prevalence of 45% for patients diagnosed with UC and 20% for patients diagnosed with CD, irrespective of age group and place of residence. This is sustained by the scientific literature, as the guidelines for diagnosis of IBD recommend colonoscopy with biopsy in both older adults and younger adults as a diagnostic tool (1).

Our studies have shown that there were other types of diagnostic methods used for older adults with IBD, but with a lower prevalence than the ones mentioned previously. Computed tomography of the thorax, abdomen and pelvis (CT TAP) was used as a sole diagnostic tool in older adults with IBD only in 2% of patients with CD, but it was not used to diagnose UC. Superior digestive endoscopy (SDE) is another diagnostic tool that was used as the only means of diagnosing IBD in our studied population, but also in combination with others (colonoscopy and CT TAP). Surgery with biopsy was used only in CD patients (5%), but the diagnostic purpose of this method was secondary, as these patients had suffered complications of IBD before being diagnosed with IBD. In some patients, colonoscopy with biopsy was completed by other types of investigations: abdominal CT (2%), entero-CT (2%), SDE (2%), CT TAP (2%).

UC is mostly (45% of cases) diagnosed by histology, which reflects the pathology's characteristics of mucosal involvement, whereas CD involves deeper tissue layers and requires more advanced imaging (CT, MRI) and sometimes surgery.

Table I shows that the disease duration had a mean of 13.7 years and a variance of 109.5, and that fecal calprotectin levels were markedly increased at diagnosis (mean = 653.6 µg/g; variance = 532704.3). A decrease in calprotectin levels was observed six months after treatment and dietary changes, with a mean of 143.8 µg/g and a greatly decreased variance of 38847.5. In the same table, the CRP showed a similar pattern to the fecal calprotectin, with an average baseline CRP of 47.7mg/L (variance = 2155.8), while CRP values after six months declined to 11 mg/L (variance = 272.4).

Table I

Summary statistics (count, sum, mean, and variance) for disease duration and inflammatory biomarkers at diagnosis and after six months of dietary intervention

Groups	Count	Sum	Average	Variance
Disease duration (years)	60	823	13.71667	109.5285
Calprotectin level (µg/g) at diagnosis	60	39213.72	653.562	532704.3
Calprotectin level (µg/g) after 6 months of treatment and diet change	60	8625.8	143.7633	38847.53
C-reactive protein (mg/L) at diagnosis	60	2863.48	47.72467	2155.844
C-reactive protein (mg/L) after 6 months of treatment and diet change	60	657.48	10.958	272.3948

In CD, both biomarkers demonstrated a consistent decline from baseline to 6 months. For fecal calprotectin, the reduction was statistically significant ($p = 0.003$, $p < 0.05$), as well as for CRP, which also showed a significant decrease over the same interval ($p = 0.001$, $p < 0.05$). These findings indicate measurable changes for each patient in both clinical biomarkers during the first 6 months following diagnosis.

In UC, both biomarkers exhibited decreasing trends over time, but neither change reached statistical significance. For fecal calprotectin, the decrease was not statistically significant ($p = 1.08$, $p > 0.05$). Similarly, CRP showed a statistically nonsignificant decrease ($p = 3.7$, $p > 0.05$). Thus, no meaningful biomarker modulation for each individual was detected in this disease group over the studied period.

The significant reductions observed in both biomarkers tested (fecal calprotectin and CRP) within CD patients may indicate that biological processes in this group are comparatively more stable, allowing modest changes for each individual to become detectable over the considered 6-month period. In contrast, although both biomarkers showed a downward trend in patients diagnosed with UC, the absence of statistical significance should be interpreted cautiously. UC is characterized by higher inflammatory activity and more rapid clinical progression, factors that can introduce substantial variability in the patterns of these biomarkers. This biological unpredictability may obscure short-term changes, even when the overall direction of effect is similar.

Intrinsically, the differing statistical outcomes between UC and CD patients may reflect underlying pathophysiological differences rather than true differences in treatment response, as we have found to be mentioned in the literature (27). From a clinical perspective, these findings suggest that biomarker monitoring strategies may need to be tailored to the biological behavior of each disease subtype (28).

Following six months of pharmacological and dietary intervention, a differential pattern in fecal

calprotectin concentrations was observed between CD and UC, as highlighted by Figure 5. The average fecal calprotectin level among older persons with CD was 153.40 µg/g, whereas individuals with UC demonstrated a lower mean level of 138.95 µg/g.

This difference between CD and UC in fecal calprotectin levels after 6 months of treatment and diet change further emphasizes the specificity and sensitivity of this biomarker in diagnosing IBD, making it a less invasive tool for this particularly frail population.

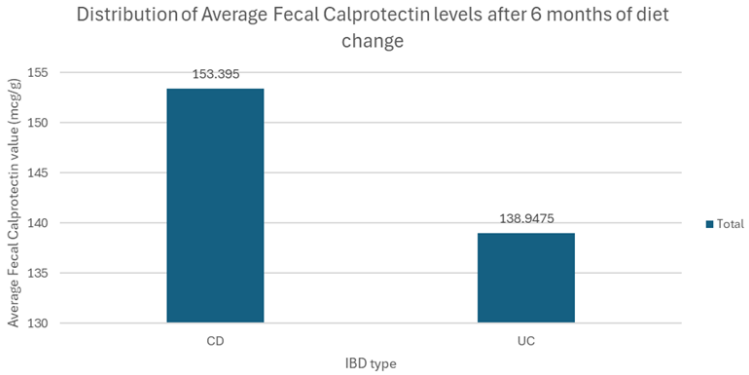


Figure 5.
Distribution by type of IBD of fecal calprotectin levels after 6 months of diet change and therapy introduction in older adults

Figure 6 further highlights the marked decrease in average fecal calprotectin levels in both groups of patients, with CD and UC, suggesting a significant effectiveness of the treatment initiated after diagnosis. Also, the higher initial values in the CD group compared to the UC (761.33 compared to 599.678 µg/g) indicate a more pronounced inflammation in patients with CD at the time of diagnosis.

The differences in absolute values and decreases in fecal calprotectin levels reflect the distinct pathophysiological peculiarities of the two types of IBD, as well as the different responses to directed and specific therapy.

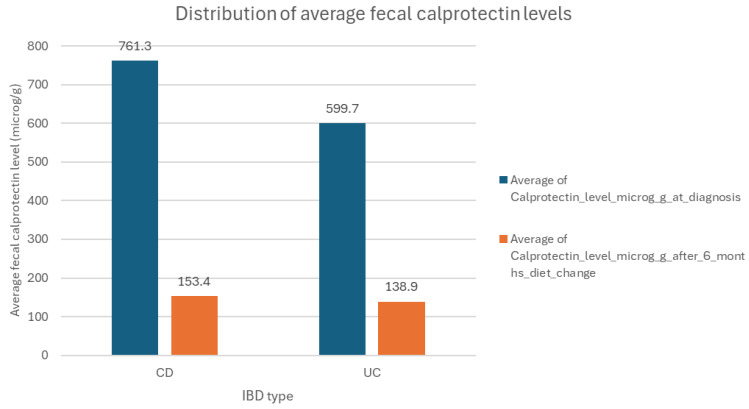


Figure 6.
Distribution of average fecal calprotectin levels (µg/g) according to IBD type, measured at diagnosis and 6 months after diagnosis and diet change, in older adults with IBD

Figure 7 shows the distribution of CRP levels by dosing time, highlighting the evolution of inflammatory status at diagnosis and at 6 months after the diet change and treatment initiation.

Average CRP levels were significantly elevated at diagnosis in both types of IBD (CD=41.7mg/L; UC=50.7mg/L), reflecting increased systemic inflammatory activity. At 6 months from diagnosis, after treatment initiation and diet change, a significant decrease in CRP was observed in both groups (CD=7.3mg/L; UC=12.8mg/L), with a greater percentage reduction in patients with CD (approximately 82.5%) compared to those with UC (approximately 74.8%). These results suggest an effective therapeutic response in both forms of IBD, with a possible difference in the kinetics of the inflammatory response between the two conditions.

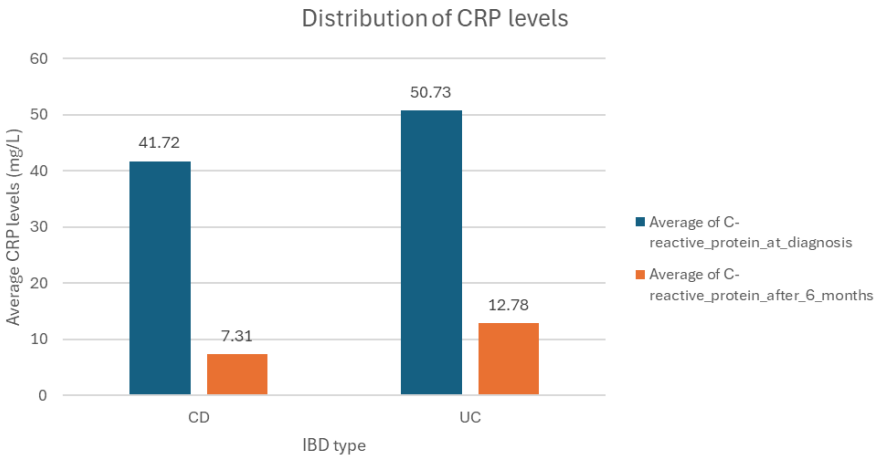


Figure 7.
Distribution of CRP levels (mg/L) in older patients by IBD type and moment of dosing, at diagnosis and 6 months after diagnosis (CRP - C-reactive protein; CD - Crohn's Disease; UC - ulcerative colitis)

Although CD and UC highlight a clear trend towards a decrease in CRP, the rate of reduction is more pronounced in CD, which could reflect a greater efficacy of the treatment used, a greater variability of inflammatory expression in UC, and an increased time until therapeutic response is achieved in UC, which will also require more frequent monitoring.

In pathologies resembling CD, acute biomarker changes may provide useful information about early disease dynamics. However, in more inflammatory and rapidly progressing conditions such as UC, longer observation periods or additional biomarkers may be required to capture meaningful trends (29). Several limitations should be acknowledged, including the relatively small sample size, the 6-month follow-up period, and the reliance on two biomarkers, which may not fully represent the complexity of each disease. These factors may limit the generalizability of the findings, and they also highlight the need for larger, longitudinal studies to validate these observations.

Across all biomarkers in patients with UC, the degree of change from baseline to six months was substantially larger than the variability within each time point, indicating robust differences at the level of the studied population (6). Although disease duration showed considerable variability, its distribution did not mirror the patterns observed in biomarker decline, suggesting that improvements in fecal calprotectin and CRP occurred independently of disease duration.

Figure 8 highlights that among patients with UC, the combination therapy of vedolizumab (VDZ) and 5-aminosalicylic acid (5-ASA) produced the largest average decrease in fecal calprotectin levels, with a mean decline of 710.5 µg/g. In contrast, combination therapy between a corticosteroid and mesalazine (MSZ) showed the smallest improvement, with an average reduction of 47 µg/g.

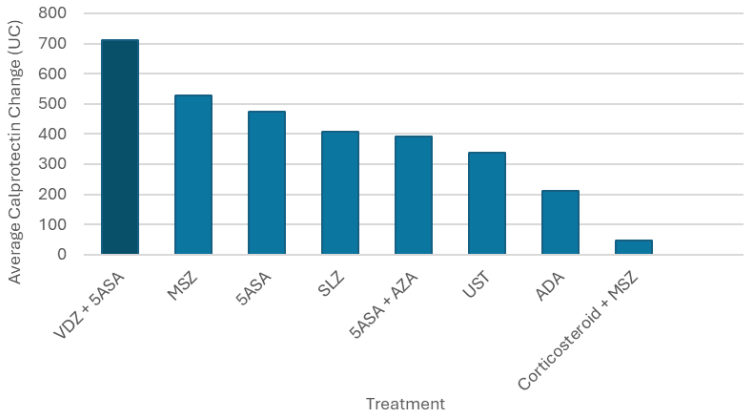


Figure 8.
Change in average fecal calprotectin values (µg/g) over a 6-month period according to treatment used in the UC older patients

A similar trend is shown in Figure 9, where CRP changes varied across treatment regimens for UC patients. The combination of corticosteroids and MSZ showed the largest reduction in CRP, indicating a more pronounced decrease in inflammatory activity. In contrast, adalimumab (ADA) demonstrated the smallest CRP change within the cohort. Other treatment regimens showed intermediate reductions, with sulfasalazine (SLZ) and 5-ASA monotherapy displaying slightly higher CRP changes compared with other monotherapies.

A greater decrease in CRP within the UC patient group may suggest that the corticosteroid and MSZ combination therapy is more effective at reducing inflammatory activity in these patients. On the other hand, the smaller CRP change observed within the group that received ADA may indicate a more limited impact of this substance on the inflammatory activity in this cohort. One possible explanation for the stronger effect of combination therapy is shown in some studies (21,30), highlighting that corticosteroids and MSZ may determine matching or harmonious actions against inflammation. These findings suggest that combination therapy may offer better benefits over the anti-inflammatory response than monotherapy, although confirmation in larger and more diverse patient cohorts is necessary.

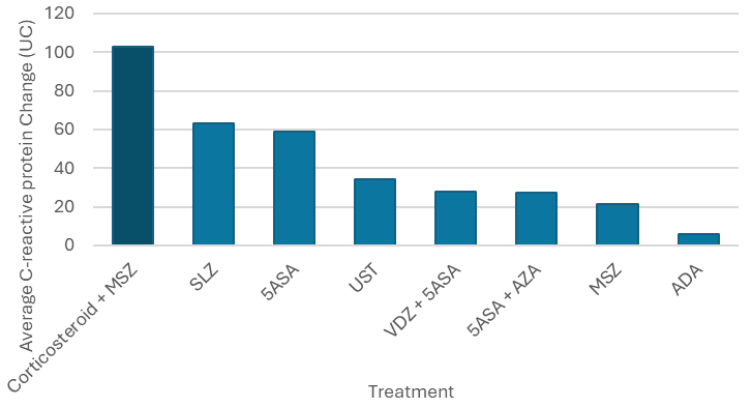


Figure 9.
Average CRP (mg/L) changes in UC patients depending on treatment regimen

Mean fecal calprotectin change varied substantially across treatment groups, with higher positive values indicating greater improvement, as seen in Figure 10. Adalimumab (ADA) demonstrated the biggest average drop, representing the greatest improvement in inflammatory activity over the 6-month interval. Moderate decreases were observed with 5-ASA, ustekinumab (UST), and MSZ monotherapy. Combination therapies, including corticosteroid-based therapies and MSZ with azathioprine (AZA), showed lesser improvements. Infliximab (IFX) and SLZ produced minimal change, while surgical intervention was associated with the smallest overall reduction.

The markedly greater improvement in UC patients observed under VDZ and 5-ASA concomitantly suggests that combination therapy may provide improved anti-inflammatory benefit compared to monotherapy. This pattern may reflect a synergistic effect, in which the action of VDZ that is selectively targeting the colon is completed by the anti-inflammatory properties of 5-ASA at the mucosal level, as some studies have already showcased (31). If confirmed in larger cohorts, these findings suggest that combining VDZ with 5-ASA may offer an important therapeutic advantage for patients with UC who require more vigorous control of mucosal inflammation.

Figure 11 illustrates the trend of variation of the mean CRP change across treatment categories, with higher positive values indicating greater improvement. SLZ demonstrated the largest average reduction in CRP over the studied time interval. Moderate improvements were observed with IFX, UST, and the combination between MSZ-AZA, while minor reductions were associated with 5-ASA, ADA, and corticosteroid-based combination therapies. MSZ monotherapy and the corticosteroid-MSZ combination showed a slight change, while surgical intervention produced only a modest reduction.

The distribution of fecal calprotectin level decrease in our older CD patients illustrates a wide range of improvements associated with the treatment regimen within the cohort. Patients under treatment with ADA produced the greatest mean improvement in fecal calprotectin and CRP values, whereas those who received 5-ASA, UST, and MSZ produced moderate decreases in the same biomarkers. When testing for fecal calprotectin changes in patients following a combination therapy and IFX, only mild improvements in fecal calprotectin were observed, while patients who underwent surgery as a

therapeutic regimen showed the least reduction in fecal calprotectin. These findings provide a descriptive overview of improvements in inflammatory activity over the period chosen for this study, depending on the treatment these patients received (32,33).

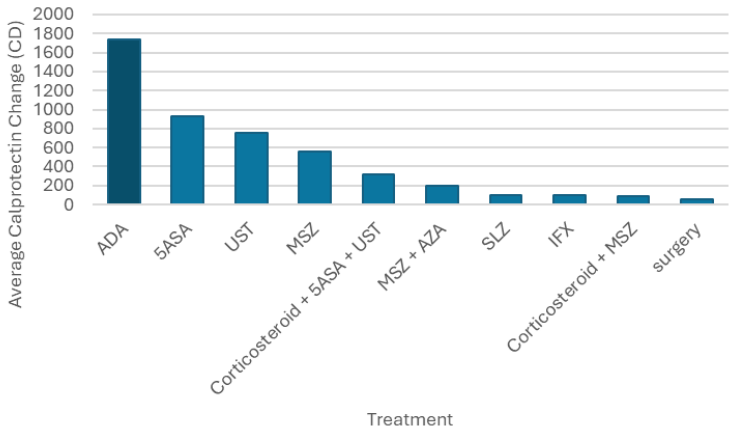


Figure 10.
Average fecal calprotectin change (µg/g) in older patients with CD, according to treatment regimen

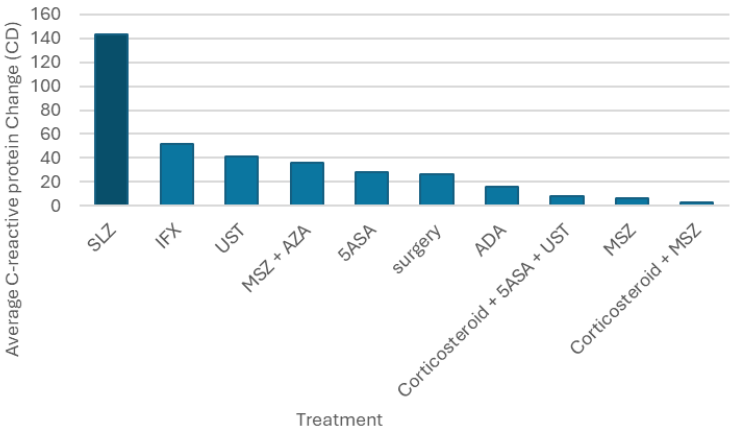


Figure 11.
Average CRP change (mg/L) in older patients with CD when studying therapy options used in this older adult cohort

In the same CD cohort, the distribution of CRP values showed a decrease, which indicates a significant improvement related to the treatment association within the cohort. SLZ produced the greatest average improvement, whereas patients under IFX, UST, and the MSZ-AZA combination had only moderately decreased in this inflammatory marker (32,34,35). More discrete improvements were observed with therapies that had 5-ASA, ADA, and corticosteroid combinations. MSZ monotherapy and the corticosteroid-MSZ combination demonstrated minimal change, while in patients who have undergone a surgical intervention, a modest reduction was seen. Overall, the results provide a descriptive overview of the variance in improvements in CRP over the 6 months, related to the treatment used in these older adults with CD.

In the future, we intend to conduct cross-sectional and prospective studies to analyze other factors that can influence the early diagnosis of this type of gastrointestinal disorder, as well as the modalities of therapeutic management according to various specific parameters unique to these patients (36). We also want to develop a way to carry out a screening for the early identification of these conditions, in which the end user, *i.e.*, the patient, is also involved. Our findings indicate a need for targeted healthcare strategies for managing large intestine-related IBD in older adult populations. Abdominal ultrasound was shown by some studies to help identify relapse episodes (37-39).

A major limitation for the evaluation of older adults diagnosed with IBD is related to the lack of an established database of scheduled appointments for each patient. Thus, a thorough and consistent follow-up of these patients can be challenging. Artificial intelligence can also help in the future with scheduling appointments according to the data

inputs for each patient (frequency of hospital presentations, change in treatment, multiple admissions in a short time), to better predict and prevent future relapses and complications (40-42).

Conclusions

Our study emphasizes the need for improved diagnostic clarity, age-specific therapeutic strategies, and better healthcare infrastructure for managing IBD in older adults. It highlights challenges like diagnostic uncertainty, patient reluctance, and the impact of comorbidities, while advocating for future research to address these gaps. Altogether, biomarkers as diagnostic methods should be the standard of care for older adults with IBD, as they represent a less invasive method, which poses fewer side effects and contraindications. This is of utmost importance as older adults are particularly susceptible to post-procedural complications due to the presence of polypharmacy.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article. The other data generated in the present study may be requested from the corresponding author.

Ethics approval and consent to participate

All experimental procedures were approved by the Committee of ICF Bucharest, Romania (Ethical Committee Approval Number 21545 from 26 April 2023). Informed consent was obtained from all patients included in the study.

AI use disclosure

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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