Inflammatory bowel disease in older patients: from gut feeling towards evidence-based medicine

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Deficits in geriatric assessment associate with disease activity and burden in older patients with inflammatory bowel disease

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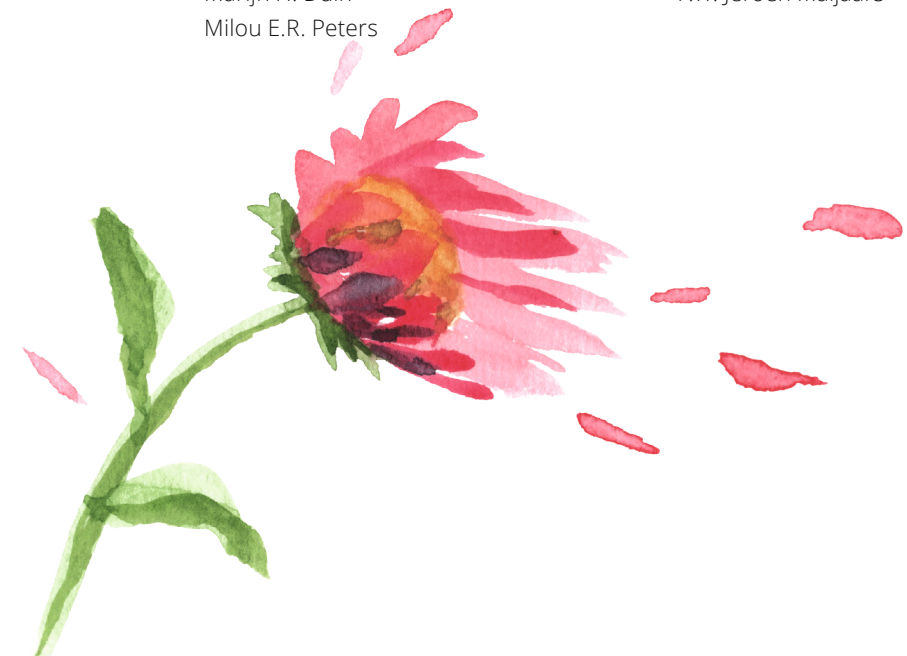

ABSTRACT

Background & aims We aimed to perform geriatric assessment in older inflammatory bowel disease (IBD) patients to evaluate which IBD characteristics associate with deficits in geriatric assessment and the impact of deficits on disease burden (health-related quality of life (HRQoL)).

Methods A prospective multicenter cohort study including 405 consecutive outpatient IBD patients aged ≥65 years. Somatic domain (comorbidity, polypharmacy, malnutrition), impairments in (instrumental) activities of daily living, physical capacity (handgrip strength, gait speed), mental (depressive symptoms, cognitive impairment), and social domain (life-partner) were assessed. Deficits in geriatric assessment were defined as ≥2 abnormal domains; 2-3 moderate and 4-5 severe deficits. Clinical (Harvey Bradshaw Index >4/partial Mayo Score >2) and biochemical (C-reactive protein ≥10 mg/L and/or calprotectin ≥250 µg/g) disease activity and disease burden (short Inflammatory Bowel Disease Questionnaire) were assessed.

Results Somatic domain (51.6%) and activities of daily living (43.0%) were most frequently impaired. 160 (39.5%) patients had moderate deficits in their geriatric assessment, 32 (7.9%) severe. Clinical and biochemical disease activity associated with deficits (clinical: aOR 2.191, 95% CI 1.284-3.743, p=.004, biochemical: aOR 3.358, 95% CI 1.936-5.825, p<.001). Deficits in geriatric assessment independently associate with lower HRQoL.

Conclusions Deficits in geriatric assessment are highly prevalent in older patients with IBD. Patients with active disease are more prone to deficits, and deficits associate with lower HRQoL, indicating higher disease burden. Prospective data validating impact of frailty and geriatric assessment on outcomes are warranted to further improve treatment strategies.

INTRODUCTION

Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), is a chronic immune-mediated disease characterised by a relapsing and remitting course.[1] The incidence and prevalence of IBD in older patients is rising, it has been estimated that in the next decade older patients with IBD will represent more than one-third of all IBD patients.[2] Older patients form a challenging patient population due to heterogeneity in somatic, functional, mental, and social abilities compared to younger patients.[3] These geriatric domains are measured by a geriatric assessment and then integrated into an overall level of frailty. Research on geriatric impairments in older patients is gaining attention. In older cancer patients for example, frailty is associated with poor functioning and high symptom burden during and following treatment, independent of disease-related factors.[4] Also, in adult patients with liver cirrhosis, physical frailty is associated with waitlist mortality, regardless of ascites or hepatic encephalopathy.[5] More recently, Kochar et al. found frailty to be associated with infections in adult patients with IBD receiving immunosuppressive medication,[6] and with mortality in all IBD patients.[7] However, up until now, no evidence is available on the prevalence of deficits in geriatric assessment in older patients with IBD and no prospective studies have been performed on their impact on adverse health outcomes or quality of life.[8]

Therefore, we aimed to assess the prevalence of deficits in geriatric assessment in older IBD patients and to evaluate which IBD disease characteristics associate with these deficits. Furthermore, we will evaluate the impact of deficits in geriatric assessment on health-related quality of life (HRQoL).

MATERIALS AND METHODS

Study design and population

This study reports the baseline data of a prospective multicentre cohort study performed in the outpatient departments and infusion centres of six hospitals in the Netherlands. In the Leiden University Medical Centre (LUMC, Leiden), patients were included from November 2016 - February 2020, in the Haga Teaching Hospital (HagaZiekenhuis, The Hague) patients were included from December 2017 – July 2018, in the Haaglanden Medical Centre (HMC, The Hague) from March 2019 – February 2020, in the Maastricht University Medical Centre (MUMC, Maastricht) from April 2019 – May 2019, in the Alrijne Hospital (Alrijne, Leiden and Leiderdorp) from November 2019 – February 2020 and in the Groene Hart Ziekenhuis (GHZ, Gouda) from October 2019 – February 2020.

Patient selection

Eligible patients were asked to participate during their regular visit. Inclusion criteria were an age of 65 years or older and a confirmed clinical, endoscopic and/or histological diagnosis

of CD, UC or IBD-Unclassified (IBD-U). Exclusion criteria were inability or unwillingness to participate or sign informed consent and the presence of a language barrier (no Dutch or English). The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines were followed.[9]

Data collection

Study data were collected face-to-face and a geriatric assessment (see below) was performed by trained medical students. Assessments approximately took between 15 to 45 minutes per patient. Demographic and IBD characteristics included age, sex, weight, height, disease type, disease duration and disease behaviour and location according to the Montreal classification[10] (maximum extent at inclusion), current and previous IBD medications and prior IBD-related surgery. Educational level was noted, high educational level was defined as higher vocational or university. Previous hospitalizations (both all-cause and IBD-related) occurring three years prior to the inclusion date were noted. All patient characteristics were verified using the electronical medical record. Clinical disease activity was measured through the Harvey Bradshaw Index (HBI) for CD patients[11] and partial Mayo score (pMS)[12] for UC or IBD-U patients. Active disease was defined by a HBI of >4 or a pMS >2. Laboratory values (Hemoglobin (Hb) and C-reactive protein (CRP)) and fecal calprotectin (FCP) were extracted from the electronical medical record if tests were performed within three months of baseline. Blood Hb levels were divided by lower limit of normal (LLN): 7.5 mmol/L for female and 8.5 mmol/L for male sex. Biochemical disease activity was defined by either a CRP ≥10 mg/L or FCP ≥250 µg/g. To further specify biochemical disease activity, elevated FCP levels were reported separately as well. Endoscopic data were used if endoscopy was performed within 6 months of baseline. IBD-related disability was measured with the IBD Disability Index (IBD-DI).[13] HRQoL was assessed using the short Inflammatory Bowel Disease Questionnaire (sIBDQ)[14] (low score equals low HRQoL).

Geriatric assessment

The purpose of a geriatric assessment is to systematically explore geriatric domains as a reflection of patients' health: the somatic, functional, mental and social domain.[15] In this study, the functional domain was further specified in activities of daily living and physical capacity, resulting in an overall of five different domains. A domain was deemed abnormal when one or more components of a domain were abnormal. To compare patients with deficits in geriatric assessment to patients without deficits, we divided our population in no deficits, moderate deficits and severe deficits. Moderate deficits was defined as two or three impaired domains, severe deficits as four or five impaired domains.

The somatic domain comprises the presence of multiple comorbidities, polypharmacy or malnutrition. Comorbidity was assessed using the Charlson Comorbidity Index (CCI), a weighted index taking into account the number and severity of 16 predefined comorbidities.[16] Age was not included in the CCI. The presence of multiple comorbidities was defined as a CCI ≥3. Polypharmacy was defined as the use of five or more non-IBD prescription medications.[17]

Malnutrition was assessed using the Mini Nutritional Assessment (MNA) short form. Patients are categorized as being at *no risk of malnutrition (*>11 points), *at risk of malnutrition (*8-11 points) or *malnutrition* (≤7 points). Both at risk of malnutrition and malnutrition were considered abnormal.[18]

The functional domain includes activities of daily living and physical capacity. Activities of daily living were assessed by the Katz Index of Independence in Activities of Daily Living (ADL) which consists of six items, each scored with zero, one or two points[19] and the Lawton Instrumental Activities of Daily Living (IADL) with eight items, each scored with one to three points.[20] Patients were defined as impaired in ADL when a score of ≥1 was reached. IADL scores were sex-adjusted: questions on food preparation, housekeeping and laundry were not taken into account for the male sex. A total IADL score for both sexes of ≥1 was considered abnormal. Physical capacity was measured by handgrip strength and gait speed. A JAMAR hand dynamometer (Patterson Medical, Warrenville, IL) was used to assess isometric handgrip strength. Patients were instructed to sit in an upright position, with the elbow of the dominant hand flexed at 90°, and forearm and wrist in neutral position.[21] Grip strength was measured three times on the dominant hand in the second handle setting. The mean value of three measurements was thereafter stratified by sex and body mass index (BMI), according to Fried et al.[22] Gait speed was assessed with a 4-meter gait speed test at usual pace.[23] Gait speed was stratified by sex and height, according to Fried et al.[22]

The mental domain comprises depression and cognitive function. Depression was assessed by the Geriatric Depression Scale (GDS-15) ranging from 0-15 points. A score of ≥6 points was considered indicative of depression.[24] Cognitive function was assessed using the Six Item Cognitive Impairment Test (6-CIT)[25], a short cognition test with a maximum score of 28 points. A score of ≥8 points is indicative of cognitive impairment. The 6-CIT has been validated against the Mini-Mental State Examination (MMSE) and has been demonstrated to have high diagnostic accuracy.[25] The social domain was considered impaired when patients did not have a life-partner, as the presence of a partner indicates a high chance of loneliness and social isolation and provides social support which has been hypothesised to buffer effects of stressful events.[26, 27]

Statistical analyses

Data analyses were performed using IBM SPSS Statistics for Windows, version 25. Continuous variables are presented as mean with standard deviation (SD) or as median with interquartile range (IQR) and compared using an independent T-test or Mann Whitney U test. Categorical variables are presented as numbers and percentages and compared using a chi-square test. Logistic regression was performed to assess factors associated with geriatric deficits. Linear regression was used to evaluate the association between the number of impaired geriatric domains, IBD disease activity and HRQoL (measured by sIBDQ). A sensitivity analysis was added using the sIBDQ while excluding three questions regarding 'fatigue', 'depression' and 'relaxing' as these questions are less IBD-specific. All regression

analyses were performed as complete case analyses. Potential confounders were agreed upon beforehand (age, sex, IBD type (CD versus UC/IBD-U), educational level). As no data were available on prevalence of geriatric deficits in older patients with IBD no sample size calculation was performed. We aimed to include as many patients as possible. A p-value of <.05 was considered statistically significant.

Ethical considerations

The study protocol was declared not subjective to the medical research involving human subjects act by the Committee on Research Involving Human Subjects at the LUMC and was approved in all participating centers. All patients provided written informed consent.

RESULTS

Overall, 547 patients were approached for participation. Out of these, 405 were included (figure 1). Overall median age was 70 years (IQR 67-74) at baseline, 191 patients (47.0%) were diagnosed with CD. Eighty-five (21.7%) patients had clinical disease activity, 93 (26.7%) biochemical disease activity (elevated CRP or FCP) and 68 (29.7%) an elevated FCP (table 1). Biochemical disease activity was available in 348 patients, FCP in 229 and endoscopic disease activity in 141 patients. Patients included in a referral hospital (LUMC or MUMC) did not differ significantly from patients included in a general hospital regarding disease activity or frailty status.

The results of the geriatric assessment are presented in table 2. To visualize the number of impaired geriatric domains, we plotted the number of patients against the number of impaired geriatric domains per patient (figure 2). 192 patients (47.4%) had geriatric deficits, 160 patients moderate (2-3 deficits) and 32 severe deficits (4-5 deficits). Several differences were noted between these patients, as displayed in table 1.

Disease activity

Active disease, when assessed by clinical indices, was more often present in patients with geriatric deficits (14.9% in patients without deficits, 27.7% in patients with moderate and 39.9% in patients with severe deficits, p=.001)) and when assessed by biochemical disease indices (17.1% (31/181) versus 37.7% (52/138) and 34.5% (10/29), p<.001). An elevated FCP was also more often present in patients with geriatric deficits (table 1).

A higher frequency of impaired somatic domain (69.9% versus 45.1%, p<.001) was observed in biochemically active IBD, also when all three components (comorbidity, polypharmacy and (risk of) malnutrition) were analysed separately. An impaired physical capacity (30.1% versus 19.6%, p=0.038) was mainly observed in patients with biochemically active disease, which was mainly explained by a difference in abnormal gait speed (30.1% versus 19.6%, p=.023, supplementary figure 1). To further explore differences between active and non-

active IBD patients regarding impairments in geriatric domains we performed a sub-analysis by defining elevated FCP as ≥50 instead of ≥250 µg/g. Especially polypharmacy (44.9% versus 27.8%, p=.014), abnormal IADL (27.8% versus 15.3%, p=.038) and abnormal gait speed (9.2% versus 1.4%, p=.031) were more often present in patients with FCP ≥50 µg/g (supplementary figure 1).

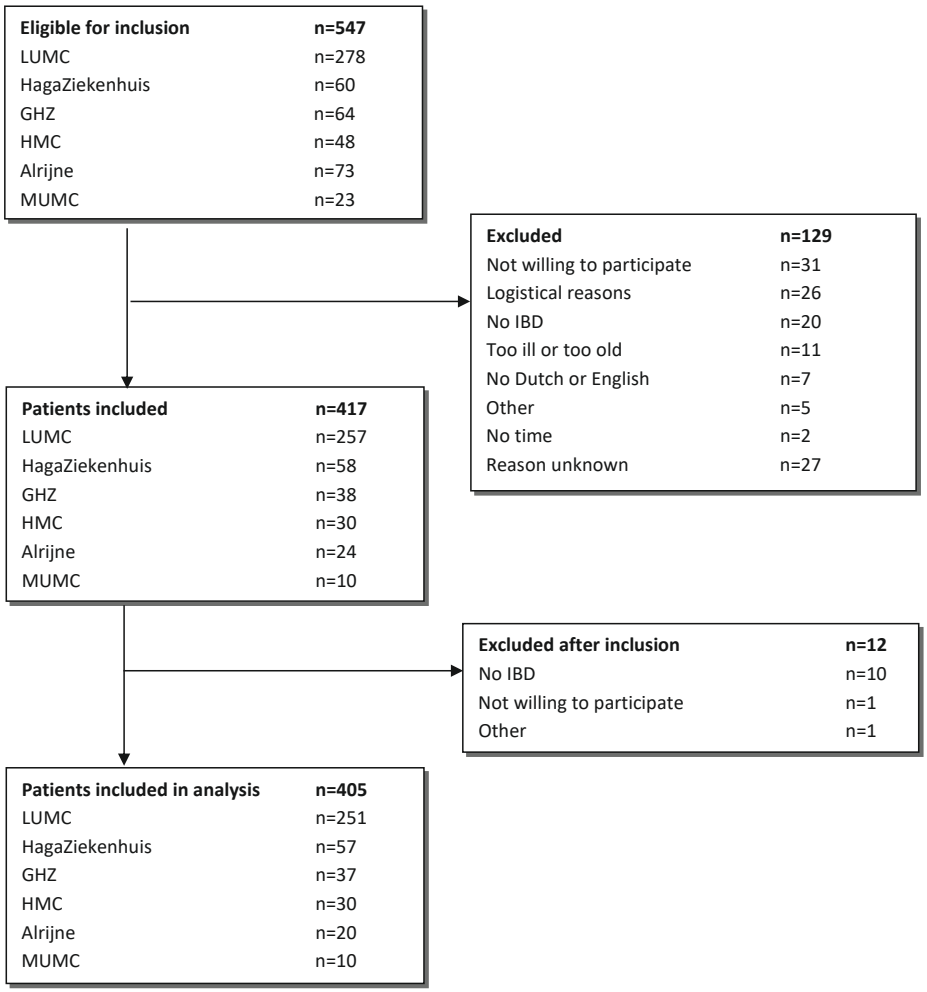

Figure 1. Flowchart patient inclusion. Logistical reasons are researcher- or hospital-related logistical reasons such as no consulting room available or due to different hospital locations. No time means patient had no time; too ill or too old means patient thinks he or she is too ill or too old to participate. GHZ, Groene Hart Ziekenhuis; HMC, Haaglanden Medical Centre; LUMC, Leiden University Medical Centre; MUMC, Maastricht University Medical Centre.

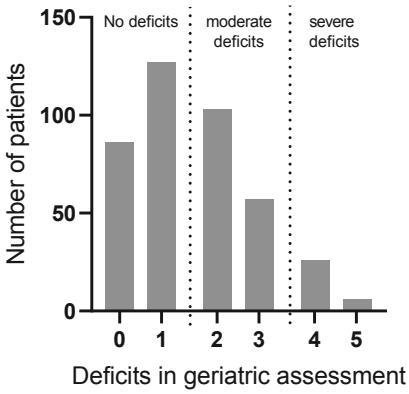

Figure 2. Prevalence of the number of deficits in geriatric assessment.

Older-onset

Thirty percent of patients had older-onset IBD, defined as an age of onset ≥60 years. Older-onset patients had a higher age at cohort entry (71.5 (68-76) versus 70 (67-72), p<.001) and more often biochemical disease activity (44.6% (52/118) versus 17.8% (41/230), p<.001), elevated FCP (48.2% (41/85) versus 18.8% (27/144), p<.001) and endoscopic disease activity (61.5% (32/52) versus 37.1% (33/89), p=.005). Older-onset patients were more often impaired in mental domain, mainly cognitive impairment (16.9% versus 6.7%, p=.001), and in their physical capacity, both handgrip strength (24.3% versus 16.4%, p=.048) and gait speed (11.8% versus 3.0%, p<.001, supplementary figure 2). This difference between older-onset and non-older onset remained present when analysing biochemically active and biochemically inactive patients separately. In patients with biochemically inactive disease, older-onset patients had a higher rate of cognitive impairment (16.7% versus 6.3%, p=.012), abnormal handgrip strength (22.7% versus 15.3%, p=.134) and abnormal gait speed (9.1% versus 2.6%, p=.027, supplementary figure 2). HRQoL did not differ between older-onset and non-older-onset patients.

Factors associated with deficits in geriatric assessment

A multivariate analysis was performed to assess factors associated with deficits in geriatric assessment (table 3). IBD disease activity, as assessed using clinical disease indices, biochemical disease indices or elevated FCP, was independently associated with the presence of deficits. Also, being female and having a previous all-cause hospitalization was associated with the presence of deficits.

Impact of deficits in geriatric assessment on HRQoL

Both clinical and biochemical disease activity and the number of deficits in geriatric assessment were associated with a lower HRQoL (supplementary figure 3, supplementary table 1). Elevated FCP and endoscopic disease activity did not associate with HRQoL (supplementary figure 4, supplementary table 1). Both clinical disease activity and the

number of deficits in geriatric assessment were also independently associated with a lower HRQoL (table 4). The association between deficits in geriatric assessment and HRQoL did not change when clinical disease activity was replaced by biochemical disease activity or by elevated FCP alone. After excluding the questions regarding fatigue, depression and relaxing from the sIBDQ, the number of deficits in geriatric assessment remained associated with a lower HRQoL. Four out of five geriatric domains impacted HRQoL independent of clinical disease activity: mental domain (B -6.810, 95% CI -8.847, -4.772, p=.000), somatic domain (B -3.182, 95% CI -4.653, -1.711, p=.000), activities of daily living (B -2.787, 95% CI -4.363, -1.210, p=.001) and physical capacity (B -2.544, 95% CI -4.401, -.686, p=.007).

DISCUSSION

In this study, we provide the first prospective data on geriatric assessment in older patients with IBD. Almost fifty percent had two or more deficits in geriatric assessment.. Active IBD was associated with the presence of deficits in geriatric assessment and additionally, number of deficits independently associated with a lower HRQoL, demonstrating a higher IBD symptom burden in patients with geriatric deficits.

Older patients form a challenging patient population due to heterogeneity in geriatric assessment. Impairments in geriatric assessment reflect the overall level of frailty.[28] Recently published studies provide evidence for an association between the presence of frailty and negative health outcomes.[6 7 29] However, in these retrospective studies, frailty is measured by ICD codes and, while malnutrition[6 7] and comorbid conditions[29] are the defining domains in those studies, other geriatric domains are not well represented. Frailty is defined as a state of increased vulnerability to poor resolution of homeostasis following a stressor[28] and comprises a spectrum which is best measured by a comprehensive geriatric assessment.[15] The most frequently abnormal domains in our study were the somatic domain, especially polypharmacy, and activities of daily living. In total, almost half of all assessed IBD patients had two or more deficits in their geriatric assessment. No other evidence on the prevalence of deficits in geriatric assessment in older IBD patients is currently present. Frailty rates in IBD patients have been described by Kochar et al. (5-7%)[6 7] and Qian et al (32.7%).[29] However, in these papers frailty is described in a retrospective manner by using ICD codes and in IBD patients of all ages. By using a geriatric assessment, we not only detected already established diagnoses, but also discovered new deficits. This finding further stresses the importance of prospective research on frailty in older patients with IBD by using a geriatric assessment.

Disease activity, both clinical and biochemical (CRP or FCP) was independently associated with geriatric deficits. Although CRP corresponds with disease activity and is therefore frequently used as an inflammatory marker during IBD treatment,[30] it is linked to many diseases and correlates with frailty, poor physical activity and cognitive decline.[31] For this reason, we

performed the analyses on biochemical disease activity separately for FCP alone and found an association between elevated FCP and geriatric deficits. The association between IBD disease activity and geriatric deficits could be explained by several mechanisms. Patients with polypharmacy or malnutrition have a higher chance of developing an IBD-flare.[17 32] The association between depression and disease activity has been established before,[33] but a link between IBD disease activity and cognitive function has also been described previously.[34] Also, mechanisms related to inflammation contribute to muscle wasting .[35] In addition, as ADL comprise stool incontinence, disease activity including frequent bowel movements, could easily cause impairments in ADL. The association between active inflammation and frailty in older patients has also been confirmed in RA.[36]

Older-onset patients had more deficits in geriatric assessment, mainly in physical capacity and cognition. It could be hypothesized that the recent inflammatory state in patients with older-onset IBD, contributes to triggering or exaggerating underlying geriatric deficits.

Furthermore, we found that female sex was predictive of deficits in geriatric assessment. This has also been found in earlier studies[22 29] and could be due to a higher symptom reporting or poorer perceived health and greater vulnerability to frailty via extrinsic effects on sarcopenia.[22 37 38]

We found an independent association between an increasing number of deficits in geriatric assessment and a decreasing HRQoL. This finding suggests that geriatric impaired and therefore frail older patients with IBD experience a higher disease burden, independent of present disease activity. In patients with cancer, this association has also been found.[4]

One of the strengths of this study is that we included IBD patients in tertiary, peripheral and teaching hospitals. However, as we aimed to conduct a study with as little study burden as possible, biochemical and endoscopic data of patients were extracted from the electronical medical record and not performed for study purposes. Therefore, no firm conclusions can be drawn on the association between endoscopic disease activity and outcomes of interest due to lower data availability. However, because of this low study burden, we created a low barrier for patients to participate and therefore generated a representative cohort.

In conclusion, our findings underline the importance of assessing the presence of frailty in older patients with IBD, as the prevalence of geriatric deficits we found is high. Patients with active disease were more prone to geriatric deficits and patients with geriatric deficits had a higher symptom burden. Prospective data validating the influence of frailty and geriatric deficits on negative health outcomes are warranted. As the population ages, we should strive to work towards a multidisciplinary evaluation of older patients with IBD to aim for the best possible treatment goals, while accounting for biological age based risk factors.

Table 1. Characteristics of older inflammatory bowel disease patients with deficits in geriatric assessment.

		No deficits in geriatric assessment (0-1) (n=213)	Moderate deficits in geriatric assessment (2-3) (n=160)	Severe deficits in geriatric assessment (4-5) (n=32)	P-value
Age at baseline	Median (IQR)	69.0 (67.0-72.0)	71.0 (68.0-75.0)	72.5 (70.3-79.8)	<.001
Sex (Female)	N (%)	82 (38.5)	81 (50.6)	25 (78.1)	<.001
BMI	Mean (SD)	25.9 (3.5)	26.1 (5.0)	27.1 (5.8)	.378
Educational level (high)	N (%)	75 (36.1)	45 (29.6)	1 (3.6)	.002
Current smoker	N (%)	20 (9.4)	11 (8.8)	5 (15.6)	.435
IBD Type					.029
CD	N (%)	85 (39.9)	86 (53.8)	20 (62.5)	
UC	N (%)	121 (56.8)	69 (43.1)	12 (37.5)	
IBD-U	N (%)	7 (3.3)	5 (3.1)	0 (0.0)	
Current ostomy					.132
No ostomy	N (%)	200 (93.9)	148 (92.5)	26 (81.3)	
Ileostomy	N (%)	11 (5.2)	10 (6.3%)	5 (15.6)	
Colostomy	N (%)	2 (0.9)	2 (1.3)	1 (3.1)	
Previous all-cause hospitalization	N (%)	56 (26.3)	62 (38.8)	19 (59.4)	<.001
Previous IBD-related hospitalization	N (%)	20 (9.4)	18 (11.3)	12 (37.5)	<.001
Disease duration	Median (IQR)	21.0 (8.0-39.0)	24.0 (6.0-40.8)	15.5 (7.3-43.8)	.964
Older-onset	N (%)	64 (30.0)	58 (36.3)	14 (43.8)	.213
Age at diagnosis					.908
≤16 years	N (%)	5 (2.3)	3 (1.9)	1 (3.1)	
17-40 years	N (%)	79 (37.1)	58 (36.3)	10 (31.3)	
>40 years	N (%)	129 (60.6)	99 (61.9)	21 (65.5)	
Disease location (CD)					.623
Ileum	N (%)	23 (27.1)	25 (29.1)	3 (15.0)	
Colon	N (%)	18 (21.2)	13 (15.1)	4 (20.0)	
Ileocolonic	N (%)	44 (51.8)	48 (55.8)	13 (65.0)	
Upper GI involvement (CD)	N (%)	6 (7.1)	4 (4.7)	1 (5.0)	.818
Disease behaviour (CD)					.718
Inflammatory	N (%)	39 (45.9)	32 (37.2)	8 (40.0)	
Stricturing	N (%)	24 (28.2)	30 (34.9)	5 (25.0)	
Penetrating	N (%)	22 (25.9)	24 (27.9)	7 (35.0)	

Table 1. Continued.

		No deficits in geriatric assessment (0-1) (n=213)	Moderate deficits in geriatric assessment (2-3) (n=160)	Severe deficits in geriatric assessment (4-5) (n=32)	P-value
Peri-anal disease (CD)	N (%)	24 (28.2)	19 (22.1)	3 (15.0)	.432
Disease location (UC/IBD-U)					.281
Proctitis	N (%)	19 (14.8)	10 (13.5)	2 (16.7)	
Left-sided colitis	N (%)	40 (31.3)	29 (39.2)	7 (58.3)	
Pancolitis	N (%)	69 (53.9)	35 (47.3)	3 (25.0)	
Hb (mmol/L divided by LLN)	Mean (SD)	1.06 (0.11)	1.05 (0.13)	1.07 (0.13)	.313
CRP (mg/L)	Median (IQR)	3.0 (1.7-4.0)	3.0 (2.0-6.0)	3.0 (2.0-9.6)	.027
FCP (µg/g)	Median (IQR)	82.0 (26.3-187.5)	172 (51.0-484.0)	108 (32.0-244.0)	.004
Elevated FCP (FCP ≥250 µg/g)	N (%)	23 (21.3)	41 (40.2)	4 (21.2)	.007
Biochemical disease activity (CRP≥10 mg/L or FCP≥250 µg/g)	N (%)	31 (17.1)	52 (37.7)	10 (34.5)	<.001
Endoscopic disease activity	N (%)	35 (46.7)	24 (42.9)	6 (60.0)	.627
HBI	Median (IQR)	2.0 (1.0-3.0)	3.0 (2.0-5.0)	3.0 (2.0-7.0)	.003
pMS	Median (IQR)	0.0 (0.0-1.0)	1.0 (0.0-2.0)	1.0 (0.0-2.5)	.010
Clinical disease activity (HBI>4/pMS>2)	N (%)	31 (14.9)	43 (27.7)	11 (39.9)	.001
No current IBD therapy	N (%)	38 (17.8)	40 (25.0)	8 (25.0)	.216
Current mesalamine	N (%)	101 (47.4)	58 (36.3)	11 (34.4)	.066
Current prednisone or budesonide	N (%)	14 (6.6)	19 (11.9)	6 (18.8)	.036
Current immunomodulatory therapy	N (%)	36 (16.9)	38 (23.8)	7 (21.9)	.263
Current biological therapy	N (%)	50 (23.5)	51 (31.9)	6 (18.8)	.113
Prior IBD-related surgery	N (%)	77 (36.2)	63 (39.4)	16 (50.0)	.317
SIBDQ	Mean (SD)	62.3 (5.8)	58.4 (4.9)	50.7 (12.1)	<.001
IBD-DI	Mean (SD)	13.8 (10.3)	22.7 (13.8)	31.2 (19.5)	<.001

No deficits: 0-1 deficits in geriatric assessment, moderate deficits: 2-3 deficits in geriatric assessment, severe deficits: 4-5 deficits in geriatric assessment. High educational level: higher vocational or university level.

IQR=Interquartile range; SD=standard deviation; BMI=Body Mass Index; IBD=Inflammatory Bowel Disease; CD=Crohn's disease; UC=ulcerative colitis; IBD-U=IBD-Unclassified; Hb=hemoglobin; mmol/L, millimole per liters; LLN=lower limit of normal; CRP=c-reactive protein; FCP=fecal calprotectin; HBI=Harvey-Bradshaw Index; pMS=partial Mayo Score; sIBDQ=short IBD questionnaire (health-related quality of life); IBD-DI=IBD-disability index.

Previous hospitalization: in 3 years before inclusion. Only oral IBD therapy was noted. Male LLN Hb: 8.5 mmol/L, female 7.5 mmol/L.

Valid percentages are reported, missing data: BMI 1; educational level 17; Hb 68; CRP 81; FCP 176; Biochemical disease activity 57; endoscopic disease activity 264; clinical disease activity 14; sIBDQ 6.

Table 2. Geriatric characteristics of older patients with inflammatory bowel diseases

Impaired in somatic domain	**N (%)**	**209 (51.6)**
Comorbidity	N (%)	56 (13.8)
Polypharmacy	N (%)	163 (40.2)
Nutritional status		
-at risk of malnutrition	N (%)	73 (18.1)
-malnutrition	N (%)	8 (2.0)
Impaired in activities of daily living	**N (%)**	**174 (43.0)**
Impaired in ADL	N (%)	121 (29.9)
Impaired in IADL	N (%)	94 (23.2)
Impaired in physical capacity	**N (%)**	**92 (22.7)**
Low handgrip strength	N (%)	77 (19.9)
Low gait speed	N (%)	24 (6.0)
Impaired in mental domain	**N (%)**	**67 (16.5)**
Cognitive impairment	N (%)	41 (10.1)
Depressive symptoms	N (%)	35 (8.7)
Impaired in social domain	**N (%)**	**96 (23.7)**
No life-partner	N (%)	96 (23.7)

Comorbidity defined by Charlson Comorbidity Index ≥3; Polypharmacy defined as ≥5 non-IBD medications; Nutritional status defined as 'at risk of malnutrition' (Mini Nutritional Assessment (MNA) 8-11) or 'malnutrition' MNA≤7; Impaired in Activities of Daily Living (ADL) defined as ADL ≥1; Impaired in Instrumental Activities of Daily Living (IADL) ≥1, corrected for sex. Low handgrip strength corrected for sex and body mass index (Fried criteria); Low gait speed in m/s corrected for sex and height (Fried criteria). Cognitive impairment defined as 6-Cognitive Impairment Test ≥8; Depressive symptoms defined as Geriatric Depression Scale-15 ≥6;
Valid percentages are reported: missing data: nutritional status 2; handgrip strength: 18; gait speed 7; cognition 1, depressive symptoms 1; partner: 3.

Table 3. Univariable and multivariable logistic regression analyses on factors associated with deficits in geriatric assessment in older patients with inflammatory bowel diseases

	Univariable analyses			Multivariable analyses		
Covariate	**Odds of frailty**	**95% CI**	**P-value**	**Adjusted odds of frailty †**	**95% CI**	**P-value**
Age in years	1.115	1.067-1.165	.000	1.107	1.056-1.160	.000
Sex (female)	1.969	1.325-2.927	.001	1.939	1.263-2.978	.002
Crohn's disease	1.856	1.250-2.755	.002	1.799	1.179-2.743	.006
Educational level (high)	.609	.393-.944	.027	.730	.459-1.162	.185
Clinical disease activity	2.390	1.455-3.927	.001	2.192	1.284-3.743	.004
Biochemical disease activity	2.857	1.736-4.702	.000	3.358	1.936-5.825	.000
Elevated FCP	2.188	1.213-3.948	.009	2.721	1.376-5.379	.004
Endoscopic disease activity	.952	.490-1.850	.885	.907	.427-1.919	.799
Previous all-cause hospitalization	2.046	1.346-3.109	.001	1.994	1.267-3.137	.003
Previous IBD-related hospitalization	1.787	.978-3.266	.059	1.551	.800-3.006	.194
Previous IBD-related surgery	1.235	.827-1.844	.303	.963	.573-1.617	.886
IBD therapy						
-Corticosteroid use	2.034	1.018-4.063	.044	1.876	.905-3.887	.091
-Immunomodulator use	1.458	.889-2.392	.135	1.316	.761-2.274	.326
-Biological use	1.275	.812-2.000	.291	1.463	.875-2.448	.147

Deficits in geriatric assessment: ≥2 deficits in geriatric assessment, high educational level: higher vocational or university level. Biochemical disease activity=C-reactive protein ≥10 mg/L and or fecal calprotectin ≥250 µg/g. FCP=fecal calprotectin; IBD=inflammatory bowel disease

† Each covariate adjusted for age, sex, Crohn's disease and educational level.

Analyses were performed as complete case analysis

Table 4. Multivariable regression analysis of the association between number of deficits in geriatric assessment and the short Inflammatory Bowel Disease Questionnaire in older patients with inflammatory bowel disease

		Unstandardized coefficient B	**95% Confidence Interval**	**P-value**
Age in years		.189	.035, .342	.016
Sex (female)		-1.854	-3.303, -.404	.012
Educational level (high)		-1.085	-2.596, .425	.158
IBD type (CD)		-.849	-2.248, .551	.234
Clinical disease activity		-5.360	-7.065, -3.656	.000
Number of impaired geriatric domains				
	0	*Reference*		
	1	-1.078	-3.011, .856	.274
	2	-2.908	-4.992, -.825	.006
	3	-6.001	-8.491, -3.511	.000
	4	-8.638	-12.259, -5.017	.000
	5	-19.666	-26.549, -12.782	.000

Deficits in geriatric assessment: ≥2 deficits in geriatric assessment, clinical disease activity : Harvey Bradshaw index >4 or partial Mayo Score >2, high educational level: higher vocational or university level. Analysis performed as complete case analysis, 375 patients were included in multivariable analysis. CD=Crohn's disease.

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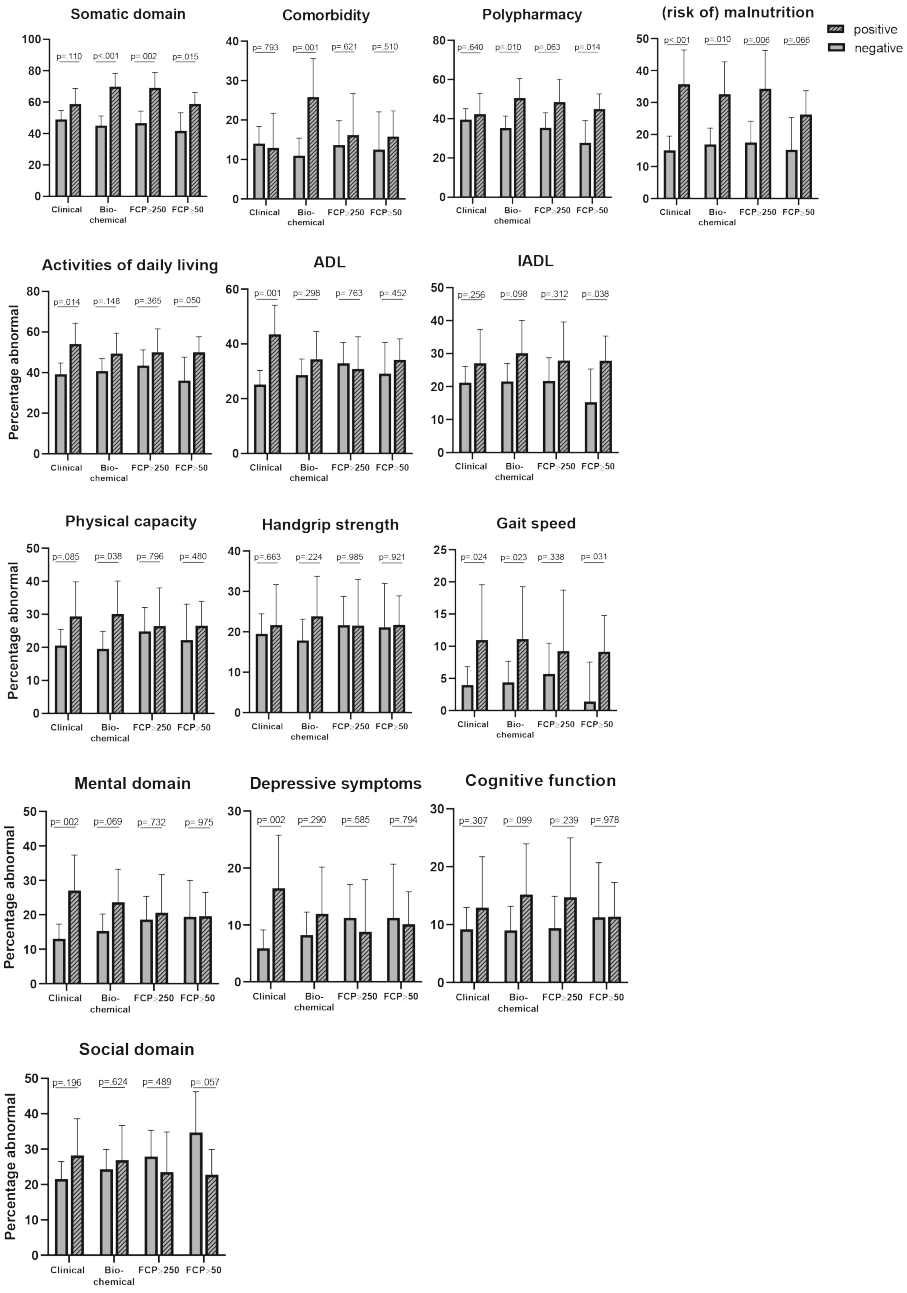
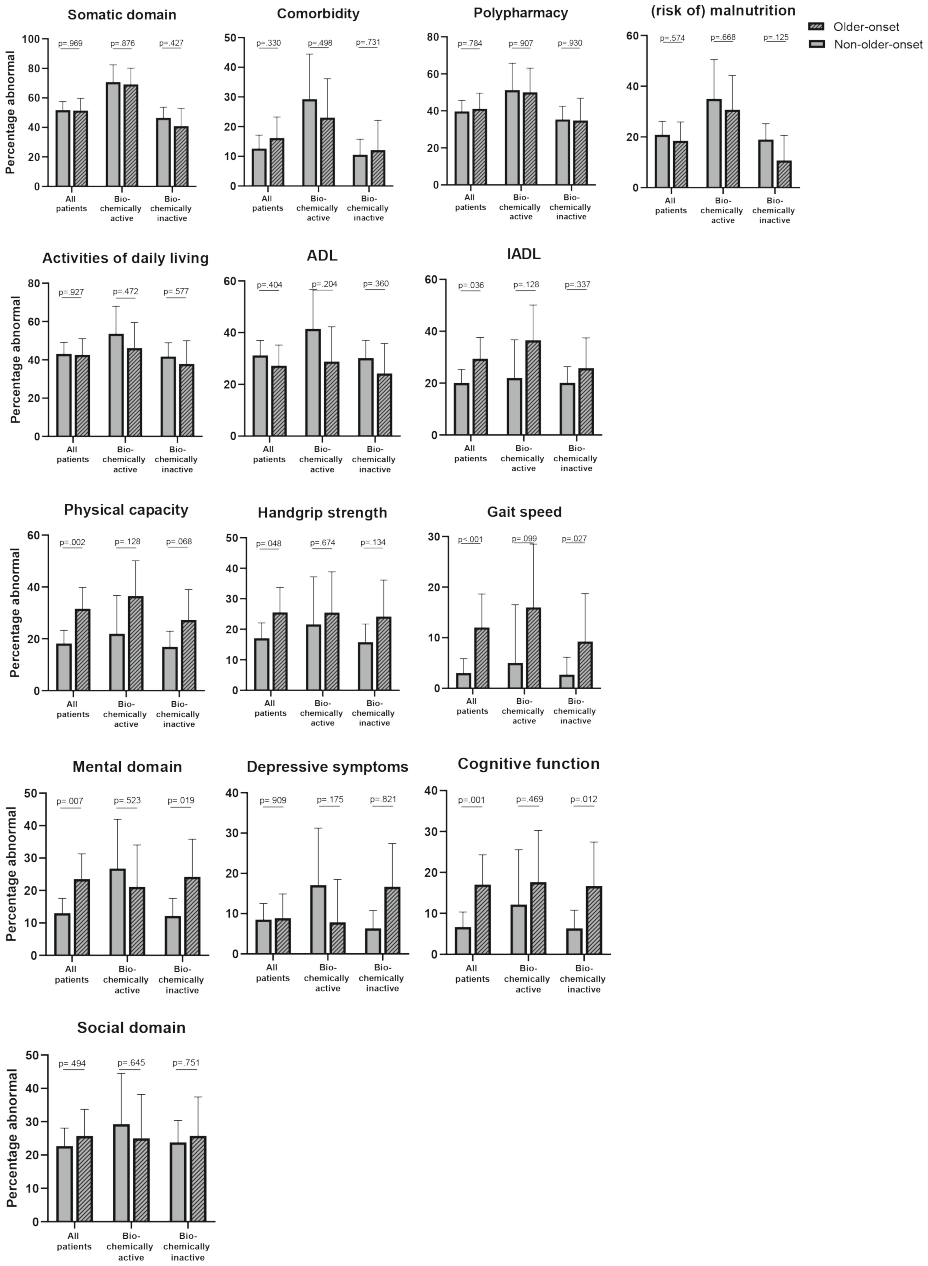
Supplementary table 1: Univariable regression analyses of the association between number of deficits in geriatric assessment and short Inflammatory Bowel Disease Questionnaire.

	Unstandardized coefficient B	95% Confidence Interval	p-value
Age in years	.020	-.137, .176	.805
Sex (female)	-2.946	-4.490, -1.402	.000
Educational level (high)	.444	-1.257, 2.145	.608
IBD type (CD)	-1.651	-3.212, -.089	.038
Clinical disease activity	-6.758	-8.553, -4.963	.000
Biochemical disease activity	-4.621	-4.621, -.731	.007
Elevated FCP	-2.038	-4.510, .433	.106
Number of impaired geriatric domains			
0	*Reference*		
1	-1.332	-3.312, .648	.187
2	-3.961	-6.032, -1.889	.000
3	-6.188	-8.603, -3.773	.000
4	-10.409	-13.670, -7.149	.000
5	-22.118	-28.609, -15.627	.000

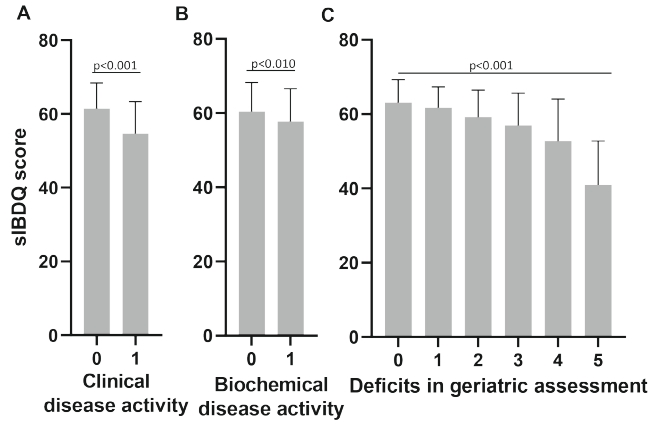
High educational level: higher vocational or university level. Clinical disease activity: Harvey Bradshaw index >4 (Crohn's disease) or partial Mayo Score >2 (ulcerative colitis), biochemical disease activity: CRP≥10 mg/L or FCP≥250 µg/g. CD=Crohn's disease, FCP=fecal calprotectin.



Supplementary figure 1: Prevalence of deficits in geriatric assessment in older patients with inflammatory bowel disease, by clinical disease activity, biochemical disease activity and elevated fecal calprotectin. Percentages and 95% confidence intervals are plotted and groups are compared using a Chi square test. Clinical disease activity : HBI>4 or pMS>2. Biochemically active=c-reactive protein ≥10 mg/L and or FCP ≥250 µg/g); elevated FCP= fecal calprotectin ≥250 µg/g. ADL= Katz Index of Independence in Activities of Daily Living, IADL= Lawton Instrumental Activities of Daily Living



Supplementary figure 2: Prevalence of deficits in geriatric assessment in older patients with inflammatory bowel disease, comparing older-onset with non-older-onset in all patients, biochemically active and biochemically inactive patients Percentages and 95% confidence intervals are plotted and groups are compared using a Chi square test. Biochemically active=C-reactive protein ≥10 mg/L and or fecal calprotectin ≥250 µg/g. ADL= Katz Index of Independence in Activities of Daily Living, IADL= Lawton Instrumental Activities of Daily Living



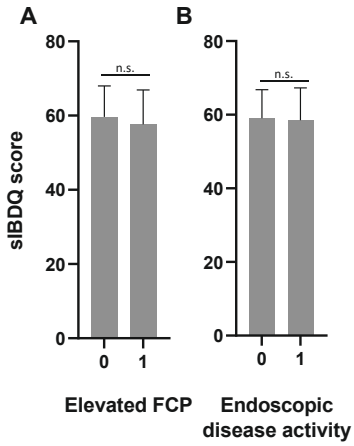
Supplementary figure 3. Health-related quality of life measured by the short Inflammatory Bowel Disease Questionnaire (sIBDQ) in older patients with inflammatory bowel diseases (IBD). Means and standard deviations are plotted.

Means with standard deviations are plotted and groups are compared with an independent samples-T-test (A and B) or one-way ANOVA (C). Clinical disease activity: Harvey Bradshaw Index >4/partial Mayo Score >2, biochemical disease activity: C-reactive protein ≥10 mg/L and/or calprotectin ≥250 µg/g.

A sIBDQ score in older patients with IBD with (1) and without (0) clinical disease activity.

B sIBDQ score in older patients with IBD with (1) and without (0) biochemical disease activity

C sIBDQ score in older patients with IBD with no (0) to five (5) deficits in geriatric assessment



Supplementary figure 4: Health-related quality of life measured by the short Inflammatory Bowel Disease Questionnaire (sIBDQ) in older patients with inflammatory bowel diseases (IBD), by fecal calprotectin (FCP) and endoscopic disease activity.

Means with standard deviations are plotted and groups are compared with an independent samples-T-test. Elevated FCP=fecal calprotectin ≥250 µg/g.

A. sIBDQ score in older patients with IBD with an elevated FCP (1) and with low FCP (0).

B. sIBDQ score in older patients with IBD with endoscopic disease activity (0) and without endoscopic disease activity (0).