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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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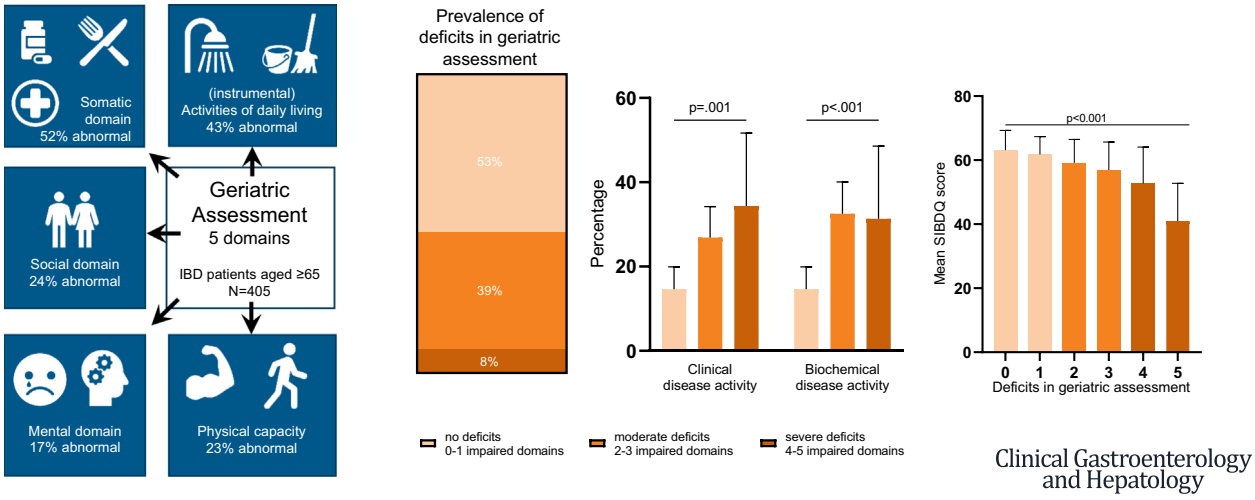

BACKGROUND & AIMS: We aimed to perform geriatric assessment in older patients with inflammatory bowel disease (IBD) to evaluate which IBD characteristics associate with deficits in geriatric assessment and the impact of deficits on disease burden (health-related quality of life).

METHODS: A prospective multicenter cohort study including 405 consecutive outpatient patients with IBD aged ≥65 years. Somatic domain (comorbidity, polypharmacy, malnutrition), impairments

Abbreviations used in this paper: ADL, activities of daily living; CD, Crohn's disease; CI, confidence interval; CRP, C-reactive protein; FCP, fecal calprotectin; HBI, Harvey Bradshaw Index; HRQoL, health-related quality of life; IBD, inflammatory bowel disease; IBD-U, IBD-unclassified; IQR, interquartile range; LUMC, Leiden University Medical Centre; pMS, partial Mayo score; sIBDQ, short Inflammatory Bowel Disease Questionnaire; UC, ulcerative colitis.

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in (instrumental) activities of daily living, physical capacity (handgrip strength, gait speed), and 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 deficits and 4–5 severe deficits. Clinical (Harvey Bradshaw Index >4/partial Mayo Score >2) and biochemical (C-reactive protein ≥10 mg/L and/or fecal 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. A total of 160 (39.5%) patients had moderate deficits in their geriatric assessment; 32 (7.9%) severe. Clinical and biochemical disease activity associated with deficits (clinical: adjusted odds ratio, 2.191; 95% confidence interval, 1.284–3.743; $P = .004$; biochemical: adjusted odds ratio, 3.358; 95% confidence interval, 1.936–5.825; $P < .001$). Deficits in geriatric assessment independently associate with lower health-related quality of life.**

CONCLUSION: **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 health-related quality of life, indicating higher disease burden. Prospective data validating impact of frailty and geriatric assessment on outcomes are warranted to further improve treatment strategies.**

Keywords: Crohn's Disease; Ulcerative Colitis; Elderly; Geriatric Assessment; Frailty.

Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), is a chronic immune-mediated disease characterized 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 patients with IBD.[2] Older patients form a challenging patient population due to heterogeneity in somatic, functional, mental, and social abilities compared with 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 patients with cancer, 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 patients with IBD.[7] However, 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 patients with IBD 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).

Methods

Study Design and Population

This study reports the baseline data of a prospective multicenter cohort study performed in the outpatient departments and infusion centers of 6 hospitals in the Netherlands. In the Leiden University Medical Centre (LUMC, Leiden), patients were included from November 2016 to February 2020; in the Haga Teaching Hospital (HagaZiekenhuis, The Hague), patients were included from December 2017 to July 2018; in the Haaglanden Medical Centre (The Hague), patients were included from March 2019 to February 2020; in the Maastricht University Medical Centre (Maastricht), patients were included from April 2019 to May 2019; in the Alrijne Hospital (Alrijne, Leiden, and Leiderdorp), patients were included from November 2019 to February 2020; and in the Groene Hart Ziekenhuis (Gouda), patients were included from October 2019 to February 2020.

Patient Selection

Eligible patients were asked to participate during their regular outpatient visit. Inclusion criteria were an age of 65 years or older and a confirmed clinical, endoscopic, and/or histologic 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 and 45 minutes per patient. Demographic and IBD characteristics included age, sex, weight, height, disease type, disease duration, and disease behavior 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 3 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 patients with CD[11] and partial Mayo score (pMS)[12] for patients with UC or IBD-U. Active disease was defined by a HBI of >4 or a pMS >2. Laboratory values (hemoglobin and C-reactive protein [CRP]) and fecal calprotectin (FCP) were extracted from the electronical medical record if tests were performed within 3 months of baseline. Blood hemoglobin levels were divided by the lower limit of normal: 7.5 mmol/L for female patients and 8.5 mmol/L for male patients. 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.[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 domains.[15] In this study, the functional domain was further specified in activities of daily living and physical capacity, resulting in an overall 5 different domains. A domain was deemed abnormal when 1 or more components of a domain were abnormal. To compare patients with deficits in geriatric assessment with patients without deficits, we divided our population into those with no deficits, moderate deficits, and severe deficits. Moderate deficits were defined as 2 or 3 impaired domains, and severe deficits were defined as 4 or 5 impaired domains.

The somatic domain comprises the presence of multiple comorbidities (Charlson Comorbidity Index),[16] ≥3 points abnormal, age not included), polypharmacy (≥5 non-IBD medications[17]), or malnutrition (Mini Nutritional Assessment),[18] ≤11 points abnormal). Activities of daily living (ADL) comprises Katz Index of Independence in Activities of Daily Living[19] (≥1 points abnormal) and Lawton Instrumental Activities of Daily Living[20] (≥1 points abnormal, corrected for sex). Physical capacity comprises hand grip strength[21] (stratified by sex and body mass index)[22] and 4-meter gait speed[23] (stratified by sex and height).[22] The mental domain comprises depression (Geriatric Depression Scale,[24] ≥6 points abnormal) and cognitive function (Six-Item Cognitive Impairment Test,[25] ≥8 points abnormal). Social domain was considered impaired when patients did not have a life-partner.[26,27] A detailed description of the geriatric assessment performed is presented in the Supplementary Methods.

What You Need to Know

Background

Current evidence points towards an association between retrospectively assessed frailty and negative health outcomes in inflammatory bowel disease (IBD). However, there is a large need for prospective evidence on frailty and geriatric assessment in older patients with IBD.

Findings

In a cohort of 405 older patients with IBD, a geriatric assessment including 5 geriatric domains was performed. Of these 405 patients, 39.5% had a moderate number of deficits (2–3 domains) in their geriatric assessment, and 7.9% severe (4–5 domains). The presence of deficits (≥2 domains) was associated with IBD disease activity and with a higher disease burden.

Implications for patient care

Prevalence of deficits in geriatric domains is high in older patients with IBD, especially in patients with active disease. A multidisciplinary approach towards geriatric impaired older patients with IBD could improve symptom burden and reduce negative health outcomes.

Statistical Analyses

Data analyses were performed using IBM SPSS Statistics for Windows, version 25. Continuous variables are presented as mean with standard deviation 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 χ^2 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 3 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 vs 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. Of these, 405 were included (Figure 1). The overall median age was 70 years (IQR, 67–74 years) at baseline; 191 patients (47.0%) were diagnosed with CD. Eighty-five patients (21.7%) had clinical disease activity, 93 patients (26.7%) had biochemical disease activity (elevated CRP or FCP), and 68 patients (29.7%) had an elevated FCP (Table 1). Biochemical disease activity was available in 348 patients, FCP in 229 patients, and endoscopic disease activity in 141 patients. Patients included in a referral hospital (LUMC or Maastricht University Medical Centre) did not differ significantly from patients included in a general hospital regarding disease activity or deficits in geriatric domains.

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). One hundred ninety-two patients (47.4%) had geriatric deficits, 160 patients had moderate deficits (2–3 deficits), and 32 patients had 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

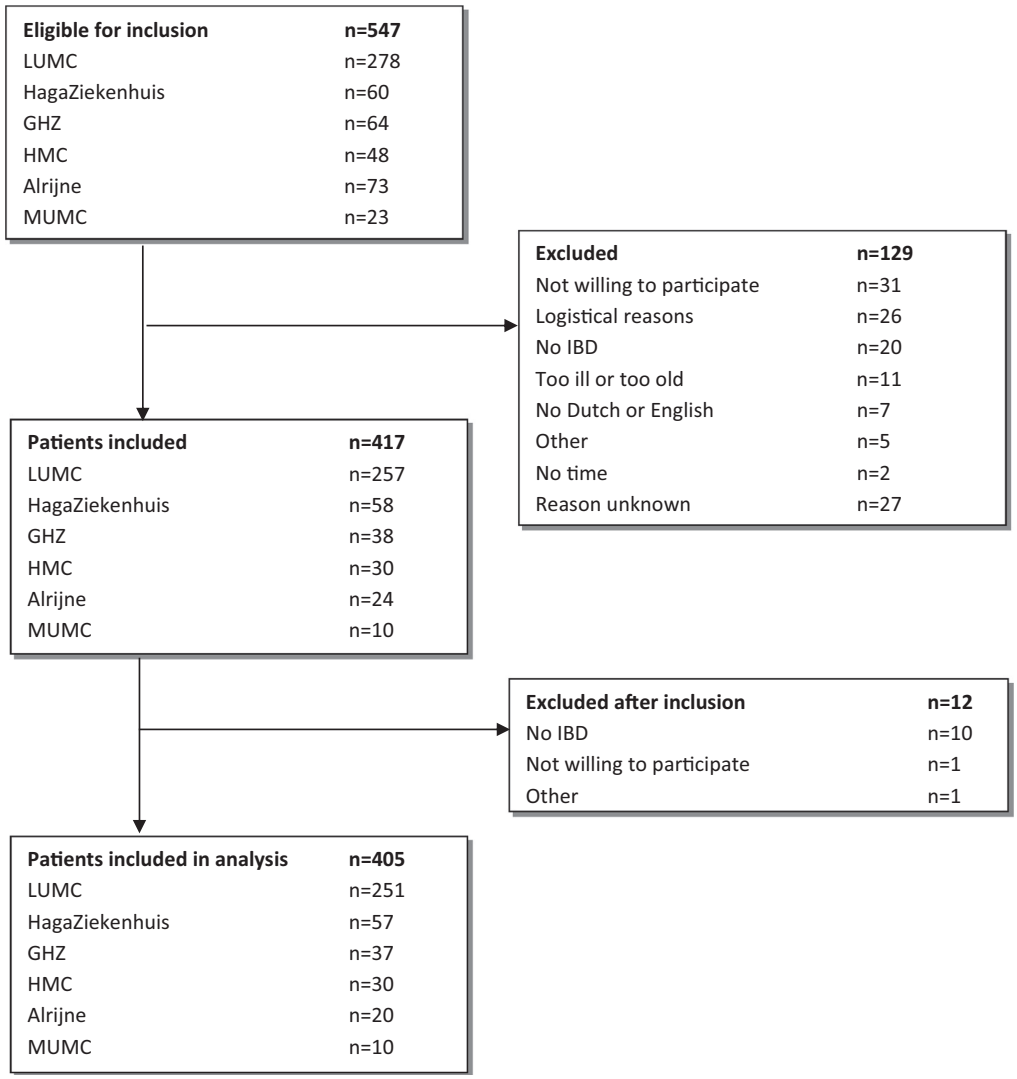

Figure 1. Flowchart patient inclusion. Logistical reasons are researcher- or hospital-related logistical reasons such as no consulting room available or due to different hospital locations. No time means patient had no time; too ill or too old means patient thinks he or she is too ill or too old to participate.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

Table 1. Characteristics of Older Patients With Inflammatory Bowel Disease With Deficits in Geriatric Assessment

	No deficits in geriatric assessment (0–1) (n=213) n (%)	Moderate deficits in geriatric assessment (2–3) (n=160) n (%)	Severe deficits in geriatric assessment (4–5) (n=32) n (%)	*P* value
Median age at baseline, *y* (IQR)	69.0 (67.0-72.0)	71.0 (68.0-75.0)	72.5 (70.3-79.8)	<.001
Sex (female)	82 (38.5)	81 (50.6)	25 (78.1)	<.001
Mean BMI, kg/m^2 (SD)	25.9 (3.5)	26.1 (5.0)	27.1 (5.8)	.378
Educational level (high)[a]	75 (36.1)	45 (29.6)	1 (3.6)	.002
Current smoker	20 (9.4)	11 (8.8)	5 (15.6)	.435
IBD type				.029
CD	85 (39.9)	86 (53.8)	20 (62.5)	
UC	121 (56.8)	69 (43.1)	12 (37.5)	
IBD-U	7 (3.3)	5 (3.1)	0 (0.0)	
Current ostomy				.132
No ostomy	200 (93.9)	148 (92.5)	26 (81.3)	
Ileostomy	11 (5.2)	10 (6.3%)	5 (15.6)	
Colostomy	2 (0.9)	2 (1.3)	1 (3.1)	
Previous all-cause hospitalization[b]	56 (26.3)	62 (38.8)	19 (59.4)	<.001
Previous IBD-related hospitalization	20 (9.4)	18 (11.3)	12 (37.5)	<.001
Median disease duration, *y* (IQR)	21.0 (8.0-39.0)	24.0 (6.0-40.8)	15.5 (7.3-43.8)	.964
Older-onset IBD	64 (30.0)	58 (36.3)	14 (43.8)	.213
Age at diagnosis, *y*				.908
≤16	5 (2.3)	3 (1.9)	1 (3.1)	
17-40	79 (37.1)	58 (36.3)	10 (31.3)	
>40	129 (60.6)	99 (61.9)	21 (65.5)	
Disease location (CD)				.623
Ileum	23 (27.1)	25 (29.1)	3 (15.0)	
Colon	18 (21.2)	13 (15.1)	4 (20.0)	
Ileocolonic	44 (51.8)	48 (55.8)	13 (65.0)	
Upper GI involvement (CD)	6 (7.1)	4 (4.7)	1 (5.0)	.818
Disease behavior (CD)				.718
Inflammatory	39 (45.9)	32 (37.2)	8 (40.0)	
Stricturing	24 (28.2)	30 (34.9)	5 (25.0)	
Penetrating	22 (25.9)	24 (27.9)	7 (35.0)	
Peri-anal disease (CD)	24 (28.2)	19 (22.1)	3 (15.0)	.432
Disease location (UC/IBD-U)				.281
Proctitis	19 (14.8)	10 (13.5)	2 (16.7)	
Left-sided colitis	40 (31.3)	29 (39.2)	7 (58.3)	
Pancolitis	69 (53.9)	35 (47.3)	3 (25.0)	
Mean Hb, *mmol/L* divided by LLN (SD)[c]	1.06 (0.11)	1.05 (0.13)	1.07 (0.13)	.313
Median CRP, *mg/L* (IQR)	3.0 (1.7-4.0)	3.0 (2.0-6.0)	3.0 (2.0-9.6)	.027
Median FCP, *μg/g* (IQR)	82.0 (26.3-187.5)	172 (51.0-484.0)	108 (32.0-244.0)	.004
Elevated FCP (FCP ≥250 μg/g)	23 (21.3)	41 (40.2)	4 (21.2)	.007
Biochemical disease activity (CRP ≥10 mg/L or FCP ≥250 μg/g)	31 (17.1)	52 (37.7)	10 (34.5)	<.001
Clinical disease activity (HBI >4/pMS >2)	31 (14.9)	43 (27.7)	11 (39.9)	.001
Median HBI (IQR)	2.0 (1.0-3.0)	3.0 (2.0-5.0)	3.0 (2.0-7.0)	.003
Median pMS (IQR)	0.0 (0.0-1.0)	1.0 (0.0-2.0)	1.0 (0.0-2.5)	.010
Endoscopic disease activity	35 (46.7)	24 (42.9)	6 (60.0)	.627

Table 1. Continued

	No deficits in geriatric assessment (0–1) (n=213) n (%)	Moderate deficits in geriatric assessment (2–3) (n=160) n (%)	Severe deficits in geriatric assessment (4–5) (n=32) n (%)	*P* value
Current IBD therapy				
No current IBD therapy[d]	38 (17.8)	40 (25.0)	8 (25.0)	.216
Current mesalamine	101 (47.4)	58 (36.3)	11 (34.4)	.066
Current prednisone or budesonide	14 (6.6)	19 (11.9)	6 (18.8)	.036
Current immunomodulatory therapy	36 (16.9)	38 (23.8)	7 (21.9)	.263
Current biological therapy	50 (23.5)	51 (31.9)	6 (18.8)	.113
Prior IBD-related surgery	77 (36.2)	63 (39.4)	16 (50.0)	.317
Mean SIBDQ (SD)	62.3 (5.8)	58.4 (4.9)	50.7 (12.1)	<.001
Mean IBD-DI (SD)	13.8 (10.3)	22.7 (13.8)	31.2 (19.5)	<.001

NOTE: No deficits, 0–1 deficits in geriatric assessment; moderate deficits, 2–3 deficits in geriatric assessment; severe deficits, 4–5 deficits in geriatric assessment. 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.

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

[a]High educational level: higher vocational or university.

[b]Previous hospitalization: in 3 years before inclusion.

[c]Male LLN Hb, 8.5 mmol/L; female LLN Hb, 7.5 mmol/L.

[d]Only oral IBD therapy was noted.

(14.9% in patients without deficits, 27.7% in patients with moderate deficits, and 39.9% in patients with severe deficits; P =.001) and when assessed by biochemical disease indices (17.1% [31/181] vs 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% vs 45.1%; P <.001) was observed in biochemically active IBD, also when all 3 components (comorbidity, polypharmacy, and [risk of] malnutrition) were analyzed separately. An impaired physical capacity (30.1% vs 19.6%; P =.038) was mainly observed in patients with biochemically active disease, which was mainly explained by a difference in abnormal gait speed (30.1% vs 19.6%; P =.023) (Supplementary Figure 1). To further explore differences between patients with active and non-active IBD regarding impairments in geriatric domains, we performed a subanalysis by defining elevated FCP as ≥50 μg/g instead of ≥250 μg/g. Polypharmacy (44.9% vs 27.8%; P =.014), abnormal Lawton Instrumental Activities of Daily Living (27.8% vs 15.3%; P =.038), and abnormal gait speed (9.2% vs 1.4%; P =.031) were more often present in patients with FCP ≥50 μg/g (Supplementary Figure 1).

Older-onset IBD

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

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-

Table 2. Geriatric Characteristics of Older Patients With Inflammatory Bowel Disease

Geriatric characteristic	n (%)
Impaired in somatic domain	209 (51.6)
Comorbidity[a]	56 (13.8)
Polypharmacy[b]	163 (40.2)
Nutritional status[c]	
At risk of malnutrition	73 (18.1)
Malnutrition	8 (2.0)
Impaired in activities of daily living	174 (43.0)
Impaired in ADL[d]	121 (29.9)
Impaired in IADL[e]	94 (23.2)
Impaired in physical capacity	92 (22.7)
Low handgrip strength[f]	77 (19.9)
Low gait speed[g]	24 (6.0)
Impaired in mental domain	67 (16.5)
Cognitive impairment[h]	41 (10.1)
Depressive symptoms[i]	35 (8.7)
Impaired in social domain	96 (23.7)
No life-partner	96 (23.7)

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

cause hospitalization was associated with the presence of deficits.

Impact of Deficits in Geriatric Assessment on Health-Related Quality of Life

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 5 geriatric domains impacted HRQoL independent of clinical disease activity: mental domain (B, −6.810; 95% confidence interval [CI], −8.847 to −4.772; P =.000), somatic domain (B, −3.182; 95% CI, −4.653 to −1.711; P =.000), ADL (B, −2.787; 95% CI, −4.363 to −1.210; P =.001), and physical capacity (B, −2.544; 95% CI, −4.401 to −0.686; P =.007).

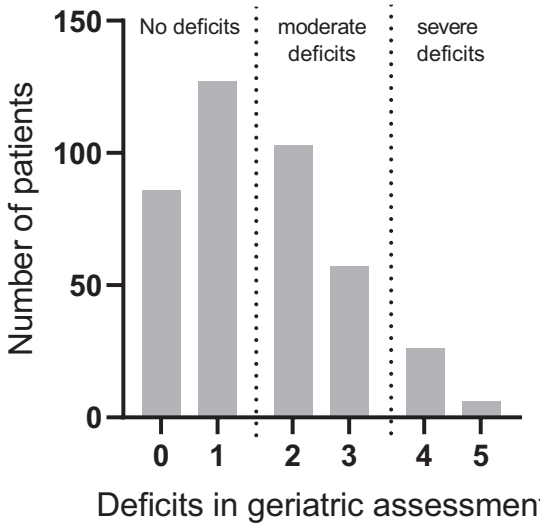

Figure 2. Prevalence of the number of deficits in geriatric assessment.

Discussion

In this study, we provide the first prospective data on geriatric assessment in older patients with IBD. Almost 50% had 2 or more deficits in geriatric assessment. Active IBD was associated with the presence of deficits in geriatric assessment, and additionally, the number of deficits was 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 domains. 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 International Classification of Diseases codes, and, whereas 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 that is best measured by a comprehensive geriatric assessment.[15] The most frequently abnormal domains in our study were the somatic domain, especially polypharmacy, and ADL. In total, almost one-half of all assessed patients with IBD had 2 or

Table 3. Univariable and Multivariable Logistic Regression Analyses on Factors Associated With Deficits in Geriatric Assessment[a] in Older Patients With Inflammatory Bowel Disease

	Univariable analyses			Multivariable analyses		
	Odds of geriatric deficits	95% CI	*P* value	Adjusted odds of geriatric deficits	95% CI	*P* value
Age, *y*	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)[b]	.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[c]	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
Current 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

NOTE: In multivariable analysis, each covariate was adjusted for age, sex, Crohn's disease, and educational level. Analyses were performed as complete case analysis.
CI, Confidence interval; CRP, C-reactive protein; FCP, fecal calprotectin; IBD, inflammatory bowel disease.
[a]Deficits in geriatric assessment: ≥2 deficits in geriatric assessment.
[b]High educational level: higher vocational or university level.
[c]Biochemical disease activity, CRP ≥10 mg/L and/or FCP ≥250 μg/g.

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% CI	*P* value
Age, *y*	.189	.035–.342	.016
Sex (female)	−1.854	−3.303 to −.404	.012
Educational level (high)[a]	−1.085	−2.596 to .425	.158
IBD type (CD)	−.849	−2.248 to .551	.234
Clinical disease activity[b]	−5.360	−7.065 to −3.656	.000
Number of deficits in geriatric assessment			
0	*Reference*		
1	−1.078	−3.011 to .856	.274
2	−2.908	−4.992 to −.825	.006
3	−6.001	−8.491 to −3.511	.000
4	−8.638	−12.259 to −5.017	.000
5	−19.666	−26.549 to −12.782	.000

NOTE: Analysis performed as complete case analysis; 375 patients were included in multivariable analysis.
Lower Short Inflammatory Bowel Disease Questionnaire means lower health-related quality of life.
CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease.
[a]High educational level: higher vocational or university.
[b]Clinical disease activity: Harvey Bradshaw index >4 or partial Mayo Score >2.

more deficits in their geriatric assessment. No other evidence on the prevalence of deficits in geriatric assessment in older patients with IBD is currently present. Frailty rates in patients with IBD have been described in retrospective studies by Kochar et al (5%–7%)[6,7] and Qian et al (32.7%).[29] 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 and/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 comprises 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 rheumatoid arthritis.[36]

Patients with older-onset IBD 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 patients with IBD 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.

Conclusions

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 IBD 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.

Supplementary Material

Note: To access the supplementary material accompanying this article, please click here.

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Conflicts of interest

The authors disclose no conflicts.

Supplementary Methods – Geriatric Assessment

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.[1] Age was not included in the CCI. The presence of multiple comorbidities was defined as a CCI $\geq$3. Polypharmacy was defined as the use of 5 or more non-inflammatory bowel disease (IBD) prescription medications.[2] Malnutrition was assessed using the Mini Nutritional Assessment (MNA) short form. Patients are categorized as being at no risk of malnutrition ($>$11 points), at risk of malnutrition (8–11 points), or malnutrition ($\leq$7 points). Both at-risk of malnutrition and malnutrition were considered abnormal.[3]

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 6 items, each scored with 0, 1, or 2 points,[4] and the Lawton Instrumental Activities of Daily Living (IADL) with 8 items, each scored with 1 to 3 points.[5] Patients were defined as impaired in ADL when a score of $\geq$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 $\geq$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.[6] Grip strength was measured 3 times on the dominant hand in the second handle setting. The mean value of 3 measurements was thereafter stratified by sex and body mass index, according to Fried et al.[7] Gait speed was assessed with a 4-meter gait speed test at usual pace.[8] Gait speed was stratified by sex and height, according to Fried et al.[7]

The mental domain comprises depression and cognitive function. Depression was assessed by the Geriatric Depression Scale, ranging from 0–15 points. A score of $\geq$6 points was considered indicative of depression.[9] Cognitive function was assessed using the Six-Item Cognitive Impairment Test,[10] a short cognition test with a maximum score of 28 points. A score of $\geq$8 points is indicative of cognitive impairment. The Six-Item Cognitive Impairment Test has been validated against the Mini-Mental State Examination and has been demonstrated to have high diagnostic accuracy.[10] 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 hypothesized to buffer effects of stressful events.[11,12]

Supplementary References

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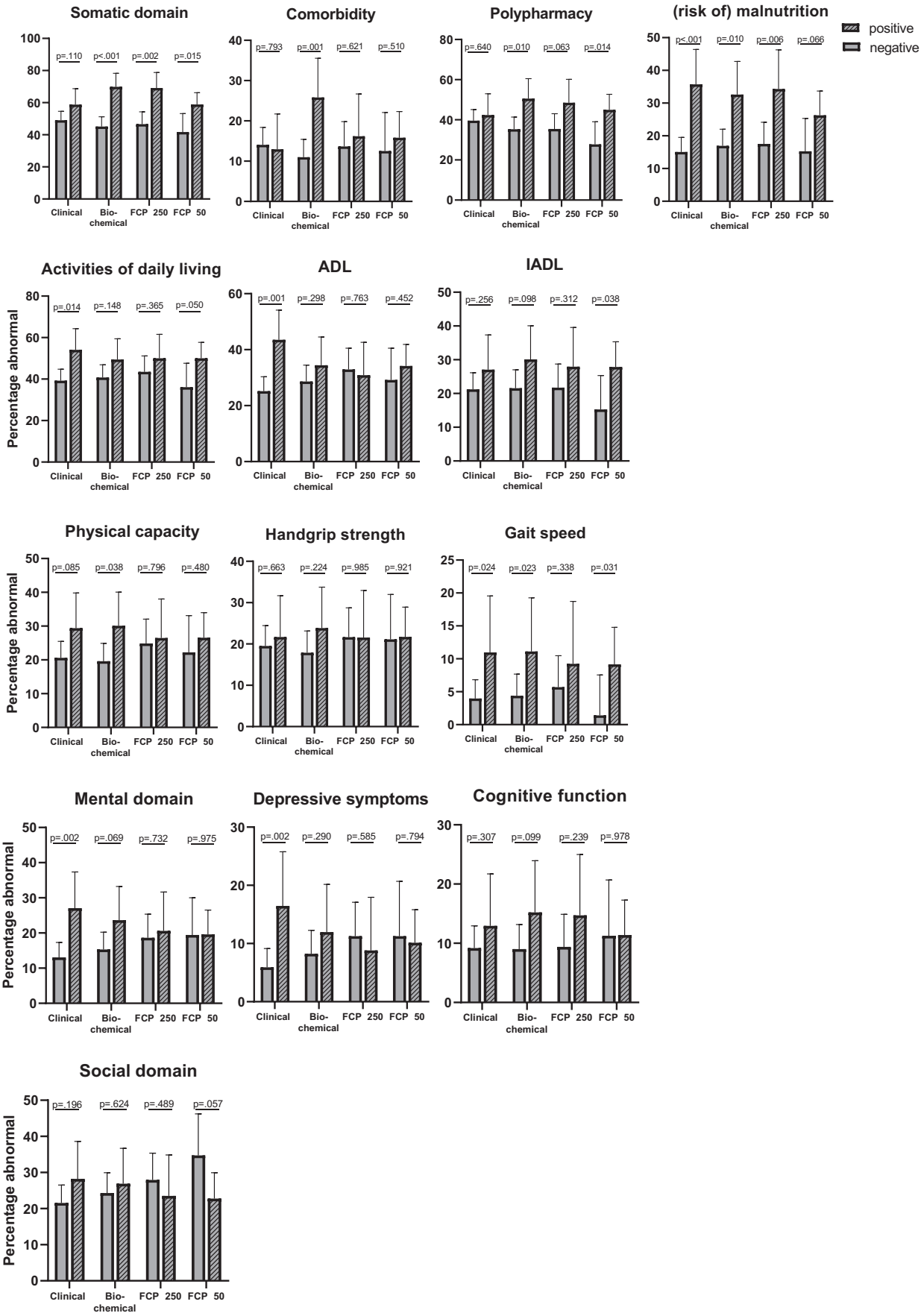
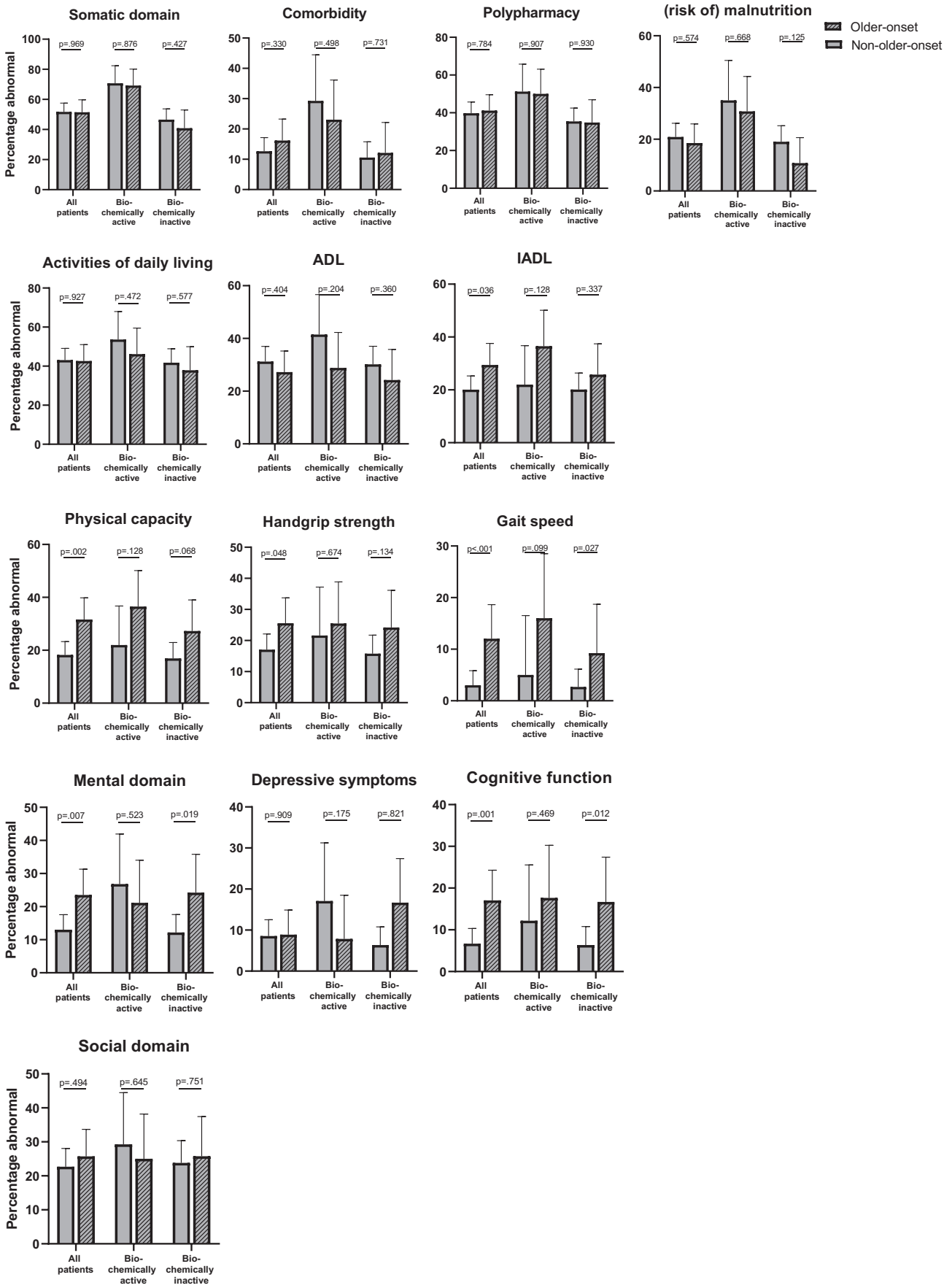
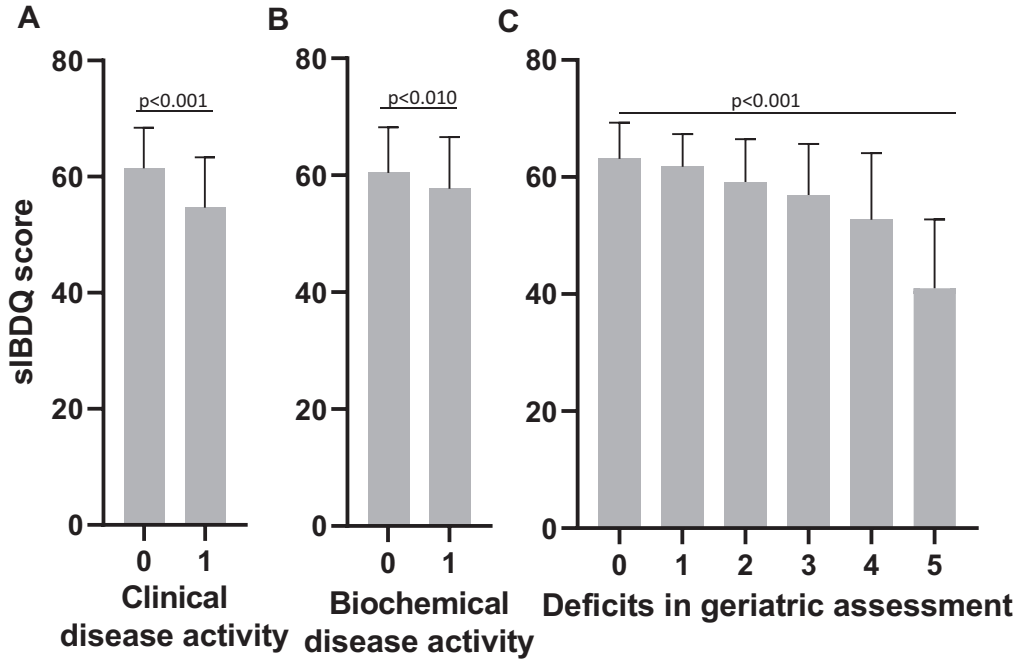


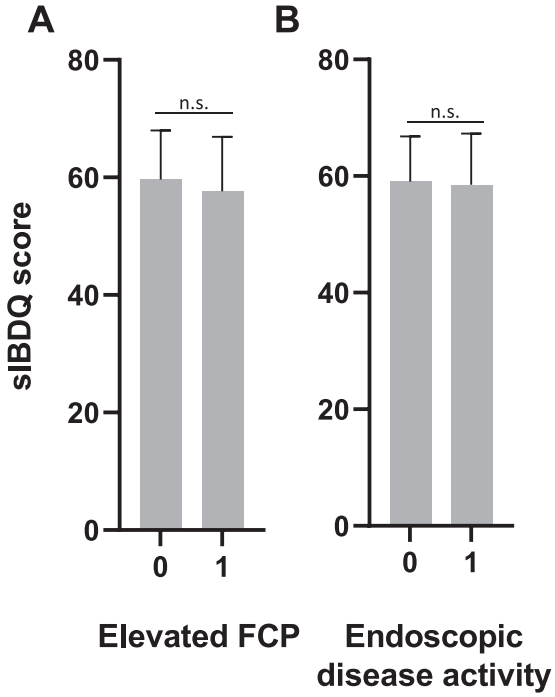
Supplementary Figure 1. Prevalence of deficits in geriatric assessment in older patients with IBD, by clinical disease activity, biochemical disease activity, and elevated FCP. Percentages and 95% confidence intervals are plotted and groups are compared using a χ^2 test. Clinical disease activity: HBI >4 or pMS >2. Biochemically active, CRP $\geq$10 mg/L and/or FCP $\geq$250 μg/g); elevated FCP, fecal calprotectin $\geq$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 IBD, comparing older-onset with non-older-onset in all patients, biochemically active patients, and biochemically inactive patients. Percentages and 95% CIs are plotted and groups are compared using a χ^2 test. Biochemically active, CRP $\geq$10 mg/L and or FCP $\geq$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 sIBDQ in older patients with 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 1-way analysis of variance (*C*). Clinical disease activity, HBI >4/pMS >2; biochemical disease activity, CRP ≥10 mg/L and/or FCP ≥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 sIBDQ in older patients with IBD, by FCP and endoscopic disease activity. Means with standard deviations are plotted, and groups are compared with an independent samples t test. Elevated FCP ≥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).

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, *y*	.020	−.137 to .176	.805
Sex (female)	−2.946	−4.490 to −1.402	.000
Educational level (high)[a]	.444	−1.257 to 2.145	.608
IBD type (CD)	−1.651	−3.212 to −.089	.038
Clinical disease activity[b]	−6.758	−8.553 to −4.963	.000
Biochemical disease activity[c]	−4.621	−4.621 to −.731	.007
Elevated FCP	−2.038	−4.510 to .433	.106
Number of impaired geriatric domains			
0	*Reference*		
1	−1.332	−3.312 to .648	.187
2	−3.961	−6.032 to −1.889	.000
3	−6.188	−8.603 to −3.773	.000
4	−10.409	−13.670 to −7.149	.000
5	−22.118	−28.609 to −15.627	.000

CD, Crohn's disease; FCP, fecal calprotectin; IBD, inflammatory bowel disease.
[a]High educational level: higher vocational or university level.
[b]Clinical disease activity: Harvey Bradshaw Index >4 (CD) or partial Mayo Score >2 (ulcerative colitis).
[c]Biochemical disease activity: C-reactive protein ≥10 mg/L or FCP ≥250 μg/g.