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Alimentary Tract

Development and validation of the IBD frailty score in a multicenter prospective cohort of IBD outpatients

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ABSTRACT

Background: Frailty is a multidimensional syndrome associated with poor outcomes and increased vulnerability, yet its assessment in inflammatory bowel diseases (IBD) remains challenging due to the absence of disease-specific tools.
Aims: This study aimed to develop and validate the IBD Frailty Score, a tailored instrument for evaluating frailty in patients with Crohn disease (CD) and ulcerative colitis (UC).
Methods: In the development phase, 28 categorical items were included in the IBD Frailty Score. This tool was tested in an exploratory cohort of 121 IBD outpatients and later validated in a prospective multicenter cohort of 512 patients across four tertiary centers. Predictive factors of frailty were identified through univariate and multivariate analyses.
Results: The IBD Frailty Score was feasible, with an average administration time of ~2 minutes. It correlated positively with the Fried Frailty Phenotype, IBD Disability Index, and Charlson Comorbidity Index and showed good reproducibility (rho = 0.78) and strong diagnostic accuracy (AUC = 0.79). A cut-off score of 4 reliably distinguished fit from frail patients. Increasing age, polypharmacy, history of extraintestinal manifestations, and higher disease activity were independent risk factors for frailty.
Conclusions: The IBD Frailty Score is the first validated, disease-specific tool for assessing frailty in IBD. It is practical, reproducible, and correlates well with established measures.

1. Introduction

Approximately, 15% of inflammatory bowel disease (IBD) cases are diagnosed in patients over 65 [1], and with improved survival, the number of older adults with Crohn's disease (CD) and ulcerative colitis (UC) is expected to rise [2]. Consequently, more older IBD patients will require treatment. Although definitions vary, a threshold of 60 years is commonly used to classify "older adults" [3]. Advanced age is linked to poorer outcomes but does not reliably predict adverse events, particularly in those receiving corticosteroids, small molecules, or biologics, underscoring the need for more precise prognostic tools [4].

Frailty is a multidimensional syndrome marked by reduced physiological reserve and increased vulnerability [5], and in the

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general population it is associated with negative outcomes [6,7]. Common tools to assess frailty include the Fried Frailty Phenotype [8] (based on five physical performance criteria) and the Hospital Frailty Risk Score (HFRS) [9], derived from 109 ICD-10 codes and categorizing patients into low, intermediate, and high frailty risk. Retrospective IBD studies show that frailty independently increases the risk of hospitalizations, surgeries, infections, and mortality [10–14]. Using the Fried phenotype, we recently found that ~20% of IBD patients are frail, with higher rates in active disease [15] and partial reversibility in those achieving remission [16]. However, existing frailty tools were developed in geriatric cohorts, raising concerns about applicability to the broader IBD population, where disease-related factors (e.g., activity, subtype, hospitalizations, extraintestinal manifestations, corticosteroid use) may also contribute [17,18,10].

This study aimed to develop and validate the IBD Frailty Score, a disease-specific frailty assessment tool, and to identify predictors of frailty in a large multicenter IBD cohort.

2. Materials and methods

2.1. Development phase of the IBD frailty index

We first conducted a literature review to identify existing frailty tools used in IBD, searching PubMed with terms related to IBD, frailty, scores, and indexes. Based on these findings, a steering group of four IBD specialists defined the key domains for the new score: social, disability, physical, psychological, intestinal disease, and comorbidity. Twenty-eight categorical items were initially selected, avoiding most IBD-related symptoms to prevent bias related to disease type or activity; only fecal incontinence was retained within the disease domain due to its substantial impact on quality of life. Generic questions covering each domain were drafted and redundant items removed. The final 28 items were reviewed to ensure clarity, affirmative phrasing, equal weighting, and binary yes/no responses, and included medical history, relevant comorbidities, daily functional abilities, and an objective handgrip strength measurement [19]. To assess acceptability, feasibility, construct validity, test-retest reliability, and preliminary performance, the score was first tested in an internal cohort of IBD outpatients during routine follow-up visits.

2.2. Prospective validation phase

The validation study was conducted across four tertiary IBD centers, enrolling adult patients (≥18 years) with confirmed CD or UC during routine visits. Exclusion criteria were age <18, inability to complete assessments, or refusal of consent. At baseline, all participants completed validated frailty, disability, and comorbidity tools: the IBD Frailty Score, Fried Frailty Phenotype, Hospital Frailty Risk Score, IBD Disability Index, and Charlson Comorbidity Index [20]. Because these tools are not self-administered, questionnaires were completed in person by a physician independent from the clinical assessor. Demographic and clinical data collected included age, sex, smoking and alcohol use, BMI, polypharmacy (≥5 drugs/day), IBD type and Montreal phenotype, disease activity (HBI for CD, pMayo for UC), inflammatory markers, disease duration, extra-intestinal manifestations, IBD-related surgeries or hospitalizations, steroid dependence or resistance, prior and current biologic or immunosuppressive therapies, and comorbidities including psychiatric disorders.

2.3. Statistical analysis

Following Riley et al. [21], a validation cohort of 500 patients with an expected frailty prevalence of 20%[17,16] provides a 95% CI of ±4% around this estimate. Categorical variables were compared with the Chi-square test, and continuous variables with the Mann-Whitney test. Internal consistency and construct validity were assessed through correlations between the IBD Frailty Score and other frailty, disability, and comorbidity tools using Spearman coefficients. Reproducibility was tested in a subgroup of 20 patients retested after 1 week [22]. Test performance was evaluated using ROC curves, with the Fried Frailty Phenotype as the gold standard. We also assessed which of the 28 items correlated most strongly with frailty using item-level Spearman analyses. Finally, univariate and multivariate models identified predictors of frailty in the validation cohort. Analyses were performed with SPSS v26 and R v4.1.2 (MatchIt package).

3. Results

3.1. Demographic and clinical characteristics of IBD patients of the exploratory cohort

Between April and October 2023, a total of 121 consecutive IBD outpatients were enrolled at the University Hospital “Tor Vergata” in Rome, Italy. Of these, 76 (62.8%) were male, with a median age of 47 years (range: 18–92 years), and 29 (24%) were aged ≥60. Seventy-one patients had UC (58.7%), and the median disease duration for the entire cohort was 108 months (range: 2–946 months). A clinically active disease was diagnosed in 31 patients (25.6%), while elevated fecal calprotectin levels (>250 µg/g) were found in 20 patients (16.5%). A history of steroid dependence or resistance was reported in 29 patients (23.9%), and 37 (30.6%) were receiving advanced therapies (Table 1).

3.2. Preliminary assessment of the IBD frailty score in the exploratory cohort

In this initial assessment, the IBD Frailty Score proved to be easy to administer, with an average completion time of 2 minutes and 19 seconds, making it feasible for both patients and clinicians. This was comparable to the Fried Frailty Phenotype, which had an average administration time of 2 minutes and 11 seconds. The Hospital Frailty Risk Score required significantly less time, with a mean administration time of just 38 seconds. According to the Fried Frailty Phenotype, 52 out of 121 patients (43%) were classified as frail, while 62 (51.2%) were considered fit, and 7 (5.8%) were pre-frail. The median IBD Frailty Score was 3 (range: 0–15). The median Hospital Frailty Risk Score was 1 (range: 0–11). Since IBD affects not only the physical but also the psychological health of patients, as well as their social, family, and work dimensions, disability is a crucial factor to consider in clinical studies involving this population. The IBD Disability Index is one of the most widely used tools to assess this condition [23]. It is a self-administered questionnaire that provides a score ranging from 0 to 100, with values above 50 indicating severe disability. The median score of the IBD Disability index was 24 (range: 0–70), while the median Charlson Comorbidity Index was 1 (range: 0–7).

The IBD Frailty Score had a positive correlation with the Fried Frailty Phenotype (rho = 0.55, $p < 0.0001$) the Hospital Frailty Risk Score (rho = 0.35, $p < 0.0001$), the IBD Disability Index (rho = 0.60, $p < 0.001$), and the Charlson Comorbidity Index (rho = 0.44, $p < 0.0001$).

A subgroup of 20 IBD patients underwent repeat frailty assessment one week after baseline, demonstrating value stability and good test reproducibility (rho = 0.78, $p < 0.0001$).

Furthermore, we tested the preliminary performance of the IBD Frailty Score using the Fried Frailty Phenotype as the gold standard, due to its conceptual similarity to our tool. Performance was evaluated using a ROC curve analysis, which yielded an area under the

Table 1
Demographic and clinical characteristics of the exploratory cohort (BMI: body mass index, ISS: immunosuppressants). Fecal calprotectin values were available for 93/121 patients (77%) and CRP values for 104/121 patients (86%).

Characteristics	IBD patients (N = 121)
Age in years, median [range]	47 [18-92]
Gender, n (%)	
Male	76 (62.8)
Female	45 (37.2)
BMI in kg/m^2, n (%)	
≤18.5	4 (3.4)
18.5-25	63 (52)
≥25	54 (44.6)
Smoking habits, n (%)	
Never	68 (56.2)
Current	18 (14.9)
Former	34 (28.1)
Missing	1 (0.8)
IBD, n (%)	
Crohn disease	50 (41.3)
Ulcerative colitis	71 (58.7)
Duration of disease in months, median [range]	108 [2-946]
History of Extra-Intestinal Manifestations, n (%)	14 (11.6)
Previous surgery for IBD, n (%)	30 (24.8)
Steroid-dependence/resistance, n (%)	29 (23.9)
Clinically active IBD, n (%)	31 (25.6)
Fecal Calprotectin > 250 mg/kg, n (%)	20 (16.5)
Increased values of CRP (mg/L), n (%)	17 (14)
Current therapy, n (%)	
5-ASA	86 (71)
Advanced therapies	37 (30.6)
ISS	5 (4)
Antibiotics	8 (6.6)
Steroids	9 (7.4)
Polypharmacy, n (%)	11 (9)
IBD Frailty Score, median [range]	3 [0-15]
Fried Frailty Phenotype, n (%)	
Frail	52 (43)
Pre-frail	7 (5.8)
Fit	62 (51.2)
Hospital Frailty Risk Score, median [range]	1 [0-11]
Charlson's Comorbidity Index, median [range]	1 [0-7]
IBD Disability Index, median [range]	24 [0-70]

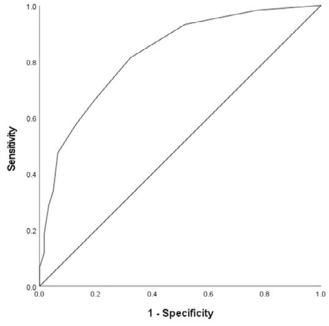

Fig. 1. Receiver Operating Characteristic (ROC) curve for IBD Frailty Score based on the Fried Frailty values at baseline for the exploratory cohort.

curve (AUC) of 0.83 (95% CI: 0.75–0.90; Fig. 1). Using a cutoff value of 4, the IBD Frailty Score demonstrated a sensitivity of 66.1% and a specificity of 80.6% in distinguishing between fit and frail patients.

3.3. Demographic and clinical characteristics of IBD patients of the validation cohort

From September 2024 to April 2025 a total of 512 patients with IBD were enrolled, of which 149 (29%) were from the investigating center, 200 (38%) from the University Hospital Policlinico Magna Graecia of Catanzaro, 100 (19%) from the University Hospital Campus Biomedico of Rome and 71 (14%) from the University Hospital Gemelli of Rome. The characteristics of the patients at baseline are reported in Table 2. The median age of the patients was 48 years (range: 19-87); 126 out of 512 (24.6%) were older than 60 years, 261 (51%) were male, 280 (54.7%) had a diagnosis of UC, 182 (35.5%) had clinically active disease, and 277 (54%) were taking biologics or small molecules. Ninety-five out of 512 patients (18.6%) had a history of extra-intestinal manifestations, 110 (21.5%) were steroid-dependent or resistant, and 119 (23.2%) had taken 5 or more drugs (defined as polypharmacy).

Table 2
Demographic and clinical characteristics of the validation cohort (BMI: body mass index, ISS: immunosuppressants). Fecal calprotectin values were available for 342/512 patients (67%) and CRP values for 485/512 patients (95%).

Characteristics	IBD patients (N = 512)
Age in years, median [range]	48 [19-87]
Gender, n (%)	
Male	261 (51.0)
Female	251 (49.0)
BMI in kg/m^2, n (%)	
≤18.5	12 (2.3)
18.5-25	78 (15.3)
≥25	422 (82.4)
Smoking habits, n (%)	
Never	350 (68.4)
Current	97 (18.9)
Former	63 (12.3)
Missing	2 (0.4)
IBD, n (%)	
Crohn disease	232 (45.3)
Ulcerative colitis	280 (54.7)
Duration of disease in months, median [range]	108 [1-768]
History of Extra-Intestinal Manifestations, n (%)	95 (18.6)
Previous surgery for IBD, n (%)	113 (22)
Steroid-dependence/resistance, n (%)	110 (21.5)
Clinically active IBD, n (%)	182 (35.5)
Fecal Calprotectin > 250 mg/kg, n (%)	95 (18.6)
CRP (mg/L), median [range]	3 [0.07-9.7]
Current therapy, n (%)	
5-ASA	209 (40.8)
Advanced therapies	277 (54)
ISS	20 (3.9)
Steroids	38 (7.4)
Polypharmacy, n (%)	119 (23.2)
IBD Frailty Score, median [range]	4 [0-15]
Fried Frailty Phenotype, median [range]	1 [0-5]
Fried Frailty Phenotype, n (%)	
Frail	112 (22)
Pre-frail	268 (52)
Fit	132 (26)
Hospital Frailty Risk Score, median [range]	0 [0-7]
Charlson's Comorbidity Index, median [range]	0 [0-22]
IBD Disability Index, median [range]	29 [0-97]

The median values of frailty in this population using the IBD Frailty Score, the Fried Frailty Phenotype, or the Hospital Frailty Risk Score were 4 (range: 0-15), 1 (range: 0-5), or 0 (range: 0-7), respectively, while the IBD Disability Index and the Charlson's Comorbidity Index had median values of 29 (range: 0-97) and 0 (range: 0-22), respectively.

3.4. Validation phase

In the validation cohort, the IBD Frailty Score continued to demonstrate feasibility, with a mean administration time of 2 minutes and 7 seconds, comparable to the Fried Frailty Phenotype (1 minute and 52 seconds) and the Hospital Frailty Risk Score (40 seconds). Internal consistency and construct validity were confirmed, as the IBD Frailty Score showed a positive correlation with the Fried Frailty Phenotype (rho = 0.40, $p < 0.0001$). In contrast, a weak negative correlation was found between the IBD Frailty Score and the Hospital Frailty Risk Score (rho = –0.16, $p < 0.0001$).

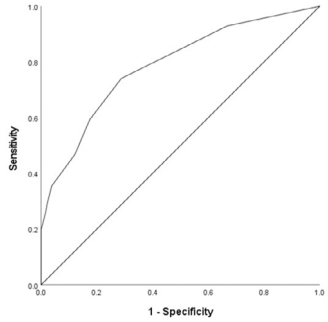

Fig. 2. Receiver Operating Characteristic (ROC) curve for IBD Frailty Score based on the Fried Frailty values at baseline for the validation cohort.

The IBD Frailty Score also correlated with the IBD Disability Index (rho = 0.44, p < 0.001) and the Charlson Comorbidity Index (rho = 0.24, p < 0.001).

Test performance analysis assuming the Fried Frailty Phenotype as gold standard and using a ROC curve yielded an AUC of 0.79 (95% CI: 0.74–0.83; Fig. 2), with a sensitivity of 74.1% and a specificity of 71.2% at a cutoff value of 4, effectively distinguishing between fit and frail patients. Overall, 319 out of 512 patients (62%) had an IBD Frailty Score ≥4 and were classified as frail.

Furthermore, we assessed the contribution of each item of the IBD Frailty Score in detecting frailty. Items 2, 3, 4, 5, 7, 10, and 12 showed the strongest correlations, whereas items 1, 13, 14, 23, and 26 demonstrated weaker correlations with the gold standard (Supplementary Table 1).

3.5. Predictive factors of frailty using the IBD frailty score on the validation cohort

To evaluate the impact of age on the frailty status in our population, we conducted a subgroup analysis. Among the 512 patients in the validation cohort, 126 (24.6%) were aged 60 years or older. No significant difference was observed in terms of median IBD Frailty Score values between patients aged ≥60 and those under 60 (median score 5, range 1–14 vs 4, range 1–15, respectively; p=0.053). Similar findings were observed using the Fried Frailty Phenotype (median 2, range 0–5 vs 1, range 0–5; p=0.14) and the Hospital Frailty Risk Score (median 0, range 0–7 vs 0, range 0–4; p=0.33). Additionally, no significant differences were found in frailty scores between patients with disease duration ≥96 months (286/512; 55.7%) and those with shorter disease duration <96 months (226/512; 44.3%) using the IBD Frailty Score (median 4, range 1–15 vs 4, range 1–14; p=0.12), the Fried Frailty Phenotype (median 1, range 0–5 in both groups; p=0.29), or the Hospital Frailty Risk Score (median 0, range 0–6 vs 0, range 0–7; p=0.29). Given the established role of disease activity as a risk factor for frailty in IBD [13,14,17,18], we explored this aspect and found significantly higher median IBD Frailty scores in patients with active disease (181/512; 35.4%) compared to those in remission (330/512; 64.4%) (median 5, range 1–15 vs 4, range 1–14; p<0.001). Similarly, the frailty score was significantly higher in patients with active disease than in those with inactive disease when assessed by the Fried Frailty Phenotype (median 2, range 0–5 vs 1, range 0–5; p=0.002) but not by Hospital Frailty Risk Score HFRS (median 0, range 0–7 vs 0, range 0–4; p=0.30).

Univariate analysis identified increasing age, BMI, smoking status, polypharmacy, presence of comorbidities, the history of extraintestinal manifestations, and higher disease activity as factors associated with frailty (defined as an IBD Frailty Score ≥4) (Table 3). In multivariate analysis, increasing age (OR 1.01, 95% CI 1.00–1.03), polypharmacy (OR 1.99, 95% CI 1.17–3.40), history of extraintestinal manifestations (OR 2.05, 95% CI 1.17–3.58), and higher disease activity (OR 1.23, 95% CI 1.12–1.35) emerged as independent risk factors for frailty (Table 3).

4. Discussion

Frailty is increasingly recognized in the IBD population. Our group has recently reported a frailty prevalence of approximately 20% among IBD patients and showed that, in a subset of cases, the frail phenotype may be reversible [17,18]. More recent studies have further highlighted the clinical significance of frailty in IBD. A recent meta-analysis encompassing 23 studies and over one million patients confirmed that frailty is common in this population and is associated with a range of IBD-related adverse outcomes, including infection-related hospitalizations after treatment, postoperative complications, and mortality [24]. Despite these interesting observations, there are some concerns that limit the use of the current tools for assessing frailty in IBD. In fact, the tools developed for use in geriatric populations are not ideally suited for IBD, which is primarily a disease of young adults, despite a recognized second incidence peak in older individuals and a growing prevalence among those over 60[2]. Moreover, previous studies have shown that disease-specific factors, such as active inflammation or certain treatments like corticosteroids, can significantly impact frailty status [14,8].

In this study, conducted on a large cohort of IBD patients across four high-volume centres, we demonstrated that the IBD Frailty Score, a specific tool designed to assess frailty in IBD, is feasible to administer within a reasonable time frame and shows positive correlation with established measures of frailty, disability, and comorbidities. The score was originally developed in the Italian language and validated across Italian centers before being translated into English in an outpatient population. Furthermore, test-retest reliability assessed in a subgroup of patients indicated excellent reproducibility of the tool. The IBD Frailty Score showed a strong correlation with the Fried Frailty Phenotype, which is the most widely used tool in the outpatient setting. The weak correlation observed in the validation cohort with the Hospital Frailty Risk Score may be because the target populations of the two scores are quite different, with the Hospital Frailty Risk Score specifically designed for hospitalized patients.

Although the administration times of the IBD Frailty Score are comparable to those of the Fried Frailty Phenotype and longer than those of the HFRS, this index differs from the above-mentioned ones primarily because it allows for a comprehensive assessment of the patient not only with regard to the condition of frailty but also with regard to disability and the burden of comorbidities. Moreover, the fact that it correlates positively with both the IBD Disability Index and the Charlson Comorbidity Index allows the clnicians to make a multidimensional assessment by using a single questionnaire.

In our study population, 64% of patients had an IBD Frailty Score ≥4 and were therefore classified as frail. This high prevalence of frailty may be explained by the score's capacity to identify frailty without an intermediate phenotype, unlike the Fried Frailty Phenotype. Follow-up studies are warranted to explore the possibility of defining an intermediate phenotype by assessing patient outcomes using this score.

Further analysis identified individual items that were strongly associated with frailty, even though further studies are needed to confirm and validate such observations and ascertain whether there are items of the test that may help predict specific IBD-related outcomes (e.g. need of hospitalization and/or surgery).

Our study demonstrate that increasing age, polypharmacy, history of extraintestinal manifestations, and higher disease activity are predictive factors of frailty further indicating the need of an

Table 3
Univariate and multivariate analysis to detect predictive factors fo frailty in the validation cohort (BMI: body mass index, ISS: immunosuppressants).

	Univariate analysis		Multivariate analysis	
	or (95% ci)	p value	or (95% ci)	p value
Gender Male (n = 261) Female (n = 251)	0.78 (0.54-1.11)	0.16	not considered	
Age (years)	1.02 (1.01-1.03)	0.001	1.01 (1.00-1.03)	0.038
BMI (kg/cm^2)	1.08 (1.03-1.13)	0.001	–	0.08
Smoking No (n = 415) Yes (n = 97)	1.63 (1.01-2.63)	0.048	–	0.35
Alcohol No (n = 432) Yes (n = 78) Missing (n = 2)	1.54 (0.91-2.59)	0.11	not considered	
Polipharmacy No (n = 391) Yes (n = 119) Missing (n = 2)	2.80 (1.73-4.55)	<0.001	1.99 (1.17-3.40)	0.01
Comorbidities No (n = 239) Yes (n = 267) Missing (n = 6)	2.18 (1.51-3.15)	<0.001	–	0.23
IBD CD (n = 232) UC (n = 280)	1.25 (0.87-1.78)	0.23	not considered	
Perianal disease No (n = 443) Yes (n = 55) Missing (n = 14)	1.24 (0.69-2.26)	0.47	not considered	
Duration of disease (months)	1.00 (1.00-1.00)	0.051	–	0.87
Number of surgeries	0.83 (0.59-1.16)	0.28	not considered	
Number of hospitalizations	1.14 (0.92-1.42)	0.24	not considered	
History of Extraintestinal manifestations No (n = 417) Yes (n = 95)	1.77 (1.08-2.90)	0.022	2.05 (1.17-3.58)	0.012
Steroid-dependence/resistence No (n = 400) Yes (n = 110) Missing (n = 2)	1.26 (0.81-1.97)	0.31	not considered	
Number of previous advanced therapies	1.00 (0.78-1.27)	0.98	not considered	
Current advanced therapy No (n = 234) Yes (n = 278)	0.73 (0.51-1.05)	0.09	–	0.36
Disease activity	1.26 (1.15-1.37)	<0.001	1.23 (1.12-1.35)	<0.001
Fecal calprotectine (> 250 mg/kg)	1.00 (1.00-1.00)	0.048	not considered due to missing values	
CRP (mg/L)	1.04 (1.01-1.07)	0.025	–	0.20

appropriate score for assessing frailty in IBD rather using tools validated in a different clinical setting (i.e., geriatric patients).

This study has several notable strengths. The test is administered by the physician rather than completed autonomously by the patient thus minimizing the risk of potential misinterpretation. Its prospective design, the multicentre approach, and the inclusion of over 500 patients contribute to the robustness and reliability of the findings. Our experience is not unique, as similar efforts have been made in other specialized fields such as rheumatology. Given the specific characteristics of individual diseases, there have been attempts to develop and validate disease-specific tools for assessing frailty in those contexts as well [25]. The potential of a disease-specific tool for accurately assessing frailty is considerable, as it could enable better patient stratification, ideally guiding decisions on whether to initiate pharmacological treatment and determining the most appropriate therapy. The identification of older patients with and without frailty is crucial for several reasons. A substantial proportion of elderly individuals with IBD are not frail, and the use of a dedicated assessment tool allows for individualized treatment strategies. This approach may help reduce undertreatment by optimizing the use of the expanding range of biologics and small molecules, ultimately improving disease control and quality of life in this population. Moreover, stratifying older patients according to frailty status could facilitate their inclusion in clinical trials, thereby improving the evaluation of efficacy and safety of specific therapies in this at risk group. Finally, such a score provides a valuable opportunity to better characterize frailty in IBD, to elucidate its dynamic and longitudinal relationship with disease activity, and to design targeted interventions aimed at reducing the overall burden of frailty in these patients.

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Data availability

Data are available from the corresponding author upon reasonable request.

Authors' contributions

SS: literature search, data collection, data interpretation, writing; CV, EDC, RS, FC, PB, FB, IM, GR, DIL, VC: data collection; DG: data analysis, data interpretation; FS, FL, MC, DDMC, EC, GM: data interpretation, critical revision of the manuscript; IM: study design, data collection, data interpretation, writing.

Declaration of competing interest

IM received fees from Janssen, Galapagos, and AbbVie. GM consulted for First Wave BioPharma and Giuliani SpA, spoke for Takeda, AbbVie, Galapagos, Lilly, and Pfizer, and holds a Smad7 antisense patent. EDC served on an AbbVie advisory board. PB advised for Takeda, Eli Lilly, and AbbVie. FS consulted for Erring and Sandoz. EC advised for Takeda, AbbVie, and Johnson & Johnson and received lecture fees from AbbVie, Johnson & Johnson, Takeda, and Eli Lilly. Other authors report no conflicts.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dld.2026.01.228.

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