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Prevalence and Implications of Frailty in Older Adults with Incident Inflammatory Bowel Diseases: a Nationwide Cohort Study

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Conflicts of Interest

BK: Served on an advisory board for Pfizer, Inc
JJ: Nothing to declare
JS: Nothing to declare
CSR: Nothing to declare
JFL: coordinates a study on behalf of the Swedish IBD quality register (SWIBREG), which received funding from Janssen
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Data Availability: All data used can be requested from the Swedish National Board of Health and Welfare and Statistics after ethical approval from the Swedish Ethical Review Authority.

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Abstract

Aims: We aimed to compare the risk of frailty in older adults with incident inflammatory bowel disease (IBD) and matched non-IBD comparators and assess the association between frailty and future hospitalizations and mortality.

Methods: In a cohort of patients with incident IBD ≥60 years from 2007–2016 in Sweden identified using nationwide registers, we defined frailty using Hospital Frailty Risk Score (HFRS). We compared prevalence of frailty in patients with IBD to age, sex, place-of-residency and calendar-year matched population comparators. In the IBD cohort, we used Cox proportional hazards modeling to examine the associations between frailty risk and hospitalizations or mortality.

Results: We identified 10,590 patients with IBD, 52% female with a mean age of 71 years, matched to 103,398 population-based comparators. Among patients with IBD, 39% had no risk for frailty, 49% had low risk and 12% had higher risk for frailty. Mean HFRS was 1.9 in IBD and 0.9 in matched-comparators ($p<0.01$). Older adults with IBD at higher risk for frailty had a 20% greater risk for mortality at 3 years compared with those who were not frail. Compared to non-frail older patients with IBD, patients at higher risk for frailty had increased mortality (HR:3.22, 95%confidence interval (CI): 2.86–3.61), all-cause hospitalization (HR:2.42,95%CI: 2.24–2.61) and IBD-related hospitalization (HR: 1.50,95%CI: 1.35–1.66). These associations were not attenuated after adjusting for comorbidities.

Conclusion: Frailty is more prevalent in older adults with IBD than matched comparators. Among older patients with IBD, frailty is associated with increased risk for hospitalizations and mortality.

Keywords

geriatric; Crohn’s disease; ulcerative colitis; aging

INTRODUCTION

One-quarter of incident IBD diagnoses are in adults ≥60 years.[1, 2] With more effective treatments and decreased disease fatality, the number of people who are aging with IBD is also increasing.[3] It is important to understand geriatric constructs in older patients with IBD. To date, chronologic age and co-morbidity are the most studied geriatric constructs in IBD.[4] However, it is increasingly recognized that age and co-morbidity do not fully approximate risks for adverse outcomes in older adults.[5] Frailty is an age-related decline in multiple physiologic systems that confers significant vulnerability to health-related changes, but does not have a linear relationship with chronologic age.[6] Frailty-related constructs are used to risk stratify patients in fields such as oncology.[7] Frailty is a predictor of outcomes in other chronic inflammatory conditions.[8, 9]

A study in an electronic health record based database demonstrated that frailty was associated with an increased risk for mortality in IBD.[10] However, the studies published to date assess frailty in IBD patients of all ages,[11, 12] without a focused assessment of frailty in older adults. As frailty is an aging-related concept that is more applicable to older adults, describing the prevalence and implications of frailty in older adults with IBD is needed. Furthermore, to date no study has compared the prevalence of frailty in patients with IBD to matched population controls.

We used a nationwide, population-based cohort, to estimate the prevalence of frailty in patients with IBD and compared it with matched adults. We also examined the association between frailty and adverse outcomes, specifically hospitalizations and mortality in older patients with IBD.

METHODS

Data Source

We used the Swedish Patient Registers to achieve our aims. Please see supplemental methods for details.

Cohort

Patients with IBD—We identified patients ≥60 years of age with incident IBD between January 1, 2007 – December 31, 2016 to allow for ≥1 full year of follow-up time in the cohort. We defined IBD by those with ≥2 records in the Nationwide Patient Register (NPR), which has a positive predictive value (PPV) of 93%,[13] or 1 record for IBD in the NPR with a biopsy suggestive of IBD from the ESPRESSO cohort, which improves the definition.[14] This combined definition was used in recent studies of IBD in the Swedish Registers (list of codes in Supplementary Appendix A).[15, 16] Follow-up started at the date of the second code for IBD or pathology.

Matched General Population Comparators—We matched incident IBD cases with up to 10 population-based comparators according to age, sex, place of residence and calendar year to account for demographic contributors to frailty and variations in coding practice.

Frailty

We defined frailty using the Hospital Frailty Risk Score (HFRS).[17] Please see supplemental methods for more details. If the HFRS was 0, subjects were determined to be non-frail. Based on validated cut-offs of 0 - < 5 and ≥ 5, patients were designated to be at low and higher risk for frailty, respectively.

Covariates

Pertinent covariates were age, sex, type of IBD, IBD medications, health care utilization, country of birth, level of education and geographic location. Please see supplemental methods for more details.

Outcomes

The primary outcome was mortality. Mortality was ascertained from the Causes of Death Register which is 99% complete.[18] Underlying causes of death were defined by ICD codes (listed in Supplementary Appendix E).[19] A secondary outcome was hospitalizations, all-cause hospitalizations and IBD-related, determined by the primary diagnosis code for the hospitalization in the NPR.[20]

Statistical Analysis

We constructed Cox proportional hazard models to estimate hazard ratios (HRs) for the outcomes comparing IBD patients according to risk for frailty (no risk, low risk and higher risk). The models were adjusted for age, sex, calendar year, country of birth and education level prior to diagnosis. We also presented adjusted HRs (aHR) for the following pre-specified sub-groups: sex, age in categories, type of IBD, Charlson Co-morbidity Index (CCI) and medications used to treat IBD at the time of diagnosis. We constructed age and sex-weighted Kaplan-Meier curves to determine time to the outcomes by severity of frailty in patients with IBD. For the cause of death analysis, we constructed a competing risk model using the primary cause of death with all the other causes of death as a competing risk. All analyses were conducted in SAS v9.4 (Cary, NC) and Stata v16.0 (College Station, TX).

RESULTS

We identified 10,590 adults ≥60 years with incident IBD between 2007 and 2016 (Table 1). Patients with IBD had a mean age of 71 years (range: 60–96 years) and were 52% female. Among patients with IBD, 27% had CD, 59% had UC and 13% had IBD-U. Mean CCI was 0.6 with 16% having a CCI of ≥2. Mean HFRS was 1.9. When examining the severity of frailty, 39% of patients with IBD had a risk score of 0 at diagnosis. Nearly half (49%) were at low risk for frailty and 12% were at higher risk for frailty.

We matched the patients with IBD on age, sex, place of residency and calendar year, to 103,398 non-IBD comparators (Table 1). In the non-IBD cohort, mean CCI was 0.4 and mean HFRS was 0.9. The majority of non-IBD comparators (73%) were non-frail, 21% were at low risk for frailty and 6% were at higher risk for frailty.

Mean follow-up in the cohort was 5 years. IBD patients with higher risk for frailty were more likely to be older, female and have less education (Table 2). Mean CCI and healthcare use increased with frailty. Immunosuppression use was the highest in patients with IBD who were at low risk for frailty (Table 2).

Non-frail patients with IBD had a mortality rate of 30/1,000 person-years (P-Y), whereas patients with IBD at low risk for frailty had a mortality rate of 51/1,000 P-Y and those at higher risk for frailty had a mortality rate of 153/1,000 P-Y. Incidence rates by sub-groups are presented in Supplemental Table 1. Risk differences for mortality between those at higher risk for frailty and non-frail older adults with IBD was 20% at 3 years and 30% at 6 years. After adjusting for all covariates, patients with IBD who were at higher risk for frailty had >3 times the risk of mortality compared with non-frail patients (aHR: 3.22, 95% CI: 2.86–3.61, Table 3). Frailty was more strongly associated with mortality in patients

with IBD aged 60–69 years (aHR: 5.55, 95% CI: 4.44–6.93) than in those ≥80 years (aHR: 2.07, 95% CI: 1.73–2.47) (p-interaction <0.01). HRs did not markedly vary by strata such as sex, IBD type and CCI. Increasing risk of frailty was associated with a shorter time to all-cause mortality (Figure 1a). Additionally, older adults with IBD had a greater risk for all-cause mortality compared with matched non-IBD comparators even when stratified by frailty (Supplemental Table 3).

In a competing risk model, higher risk for frailty resulted in statistically significant increases in risk of death from digestive diseases, infections, hematologic conditions, respiratory diseases, endocrine, nutrition and metabolic diseases, diseases of the circulatory system, trauma and diseases of the nervous system compared with those without frailty (Figure 2). Lower risk for frailty only conferred increased risk of death from digestive respiratory and cardiovascular diseases compared with older IBD patients without frailty. Notably the risk of death from malignancies was not significantly elevated in frail patients ≥60 years with incident IBD.

The risk differences for all-cause hospitalization between those who are at higher risk for frailty and non-frail older adults with IBD was 31% at 3 years and 24% at 6 years. Older patients with incident IBD who were at higher risk for frailty had a significantly increased risk for all-cause hospitalization (aHR: 2.42, 95% CI: 2.24–2.61) and IBD-specific hospitalization (aHR: 1.50, 95% CI: 1.35–1.66). Frailty was more strongly associated with all-cause hospitalization in patients with IBD aged 60–69 years (aHR: 2.90, 95% CI: 2.57–3.29) than in those ≥80 years older (aHR: 1.73, 95% CI: 1.48–2.02) (p-interaction: <0.01). The relationship between frailty and hospitalizations did not differ by number of serious comorbidities (Table 4 & Supplemental Table 2). After weighting for the covariates, being at higher risk for frailty resulted in a decreased time to all-cause hospitalization and IBD related hospitalization (Figures 1b & 1c).

DISCUSSION

In a nationwide, population-based cohort of >10,000 older adults with incident IBD, we demonstrated for the first time that frailty is more prevalent in older adults with IBD than in matched comparators without IBD. Additionally, our data demonstrate that older patients with IBD at higher risk for frailty were significantly more likely to experience adverse outcomes including mortality and hospitalization. Our findings suggest that frailty is a pertinent concept to explore further as a risk stratification modality in patients with IBD. As the population with IBD is rapidly aging, there is a greater need to develop accurate models for risk stratification to inform shared decision making.

Frailty, function and multi-morbidity are overlapping but distinct geriatric entities, all of which confer increased risk for adverse events, especially to older people.[5] Physical function is difficult to accurately determine using health services data.[21] Comorbidity has long been studied in IBD and recent studies conclude that comorbidity is a better predictor for adverse events than chronologic age alone.[22] Despite overlap and proposed etiologic bi-directionality, frailty and comorbidity are not fully overlapping constructs.[23] Frailty has been recognized in recent guidelines on multi-morbidity as a critical aspect that confers increased

risk for adverse events associated with multi-morbidity.[24] Initial retrospective studies of frailty in IBD also demonstrate that frailty is associated with an increased risk for serious adverse outcomes.[10, 11, 25] Our robust analyses extend prior work by demonstrating the frailty is strongly associated with adverse outcomes even after accounting for comorbidity.

Frailty and functional status have been used to risk stratify older adults with cancer requiring chemotherapy.[26] Similar to oncology, immunosuppressive therapies are the mainstays of modern IBD treatment.[27, 28] As with chemotherapy, age-related changes may impact the tolerance of immunosuppression and shift the risk-benefit ratio for treatment modalities.[29] Our data support the need to evaluate frailty in a prospective manner to determine its utility as a risk stratification modality and decision making tool for patients with IBD.

In Canadian and Swedish studies assessing causes of death in older adults with IBD, malignancy was a leading cause of death.[19, 30] Unexpectedly, when stratified by frailty and assessed in a competing risk model we demonstrate that frail older patients with IBD did not have significantly increased risk of death from malignancies. As expected, however, higher risk for frailty increased the risk of death. What may be more notable, however, is that even a lower risk of frailty significantly increased the risk of death from digestive, respiratory and cardiovascular diseases compared with non-frail older patients with incident IBD. Better elucidating how frailty influences cause of death in frail IBD patients may help tailor early interventions for pre-frail older adults with IBD.

Corticosteroid use is known to result in adverse outcomes related to frailty including decreased muscle mass, bone density and even mortality in patients with IBD.[31, 32] Despite this, 39% of older patients with IBD were treated with systemic corticosteroids in the first year after diagnosis. It is not known if corticosteroids are immediately useful to ameliorate the frailty syndrome by treating inflammation or if they are worsening frailty. Future studies of frailty in IBD will benefit from assessing trajectories of frailty longitudinally. This will result in better understanding the role of steroid-sparing IBD therapy in modulating frailty.

Our study has a number of strengths. This is the first study of frailty in IBD in a population-based cohort allowing for true comparisons for the prevalence of frailty in unselected cohorts and mitigating selection bias. The cohorts and variables used have been previously validated in a robust manner with excellent test characteristics. Our study has a number of limitations as well. This study does not allow for granular disease level information and markers of inflammation to inform the analyses. Additionally, the use of ICD codes to define frailty likely results in a bias including those with more co-morbidities and fewer functional limitations; however, the HFRS was previously used in studies of frailty in other disease processes, including IBD. It is possible that a healthcare system such as the Swedish one (with universal tax-financed coverage and drug use subsidized by the state) may be influencing prescription patterns and outcomes. This needs to be taken into account when trying to generalize these findings to IBD patients in countries.

In conclusion, in a large nationwide-study of older people, we demonstrate for the first time that frailty is more prevalent in older adults with IBD than population-matched comparators. We also demonstrate that frailty is strongly associated with hospitalizations and mortality in

older adults with incident IBD, even after accounting for comorbidities. Understanding the relationship between frailty at diagnosis with medications used to treat IBD will improve the quality of life and overall health of older patients with IBD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What You Need to Know

Background:

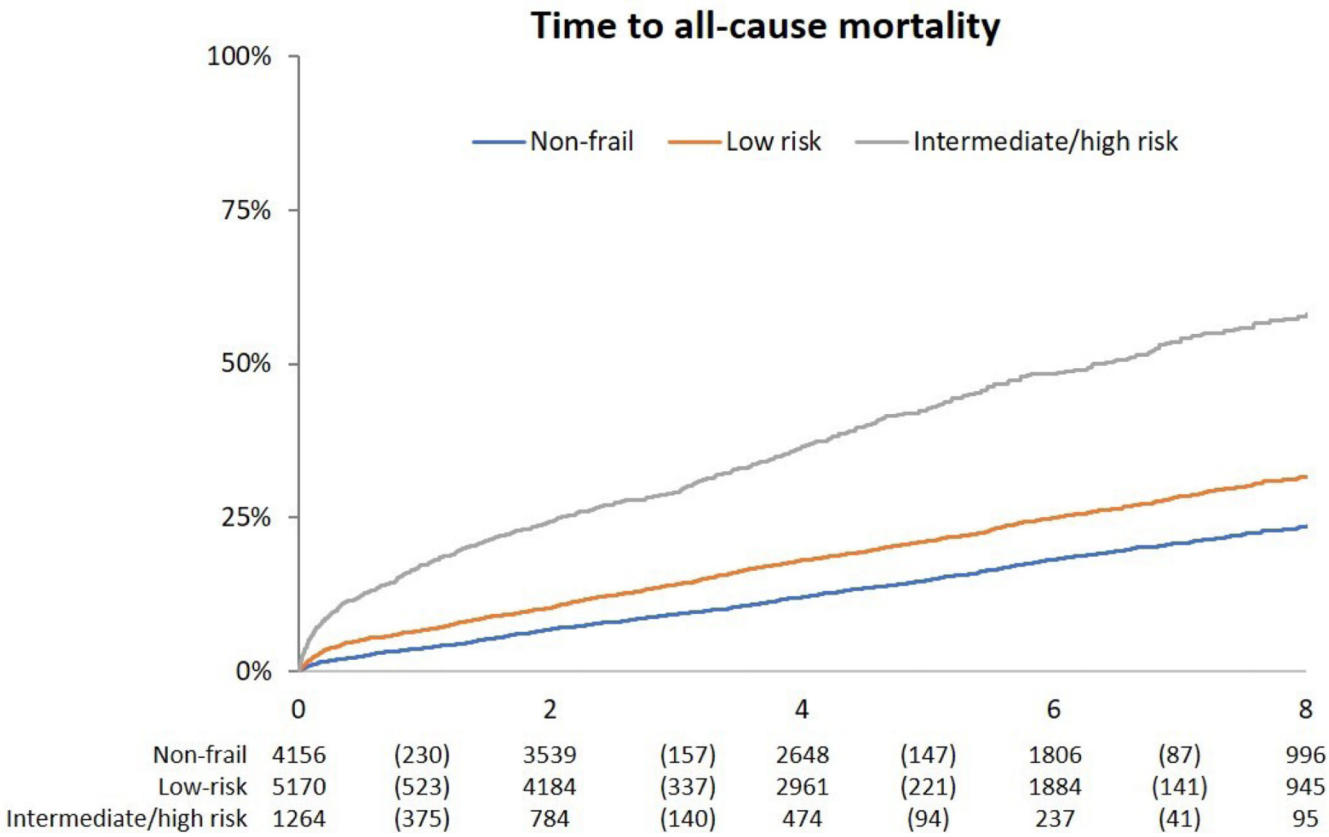
Frailty is associated with re-admissions, infections after immunosuppression and mortality in adults of all ages with IBD.

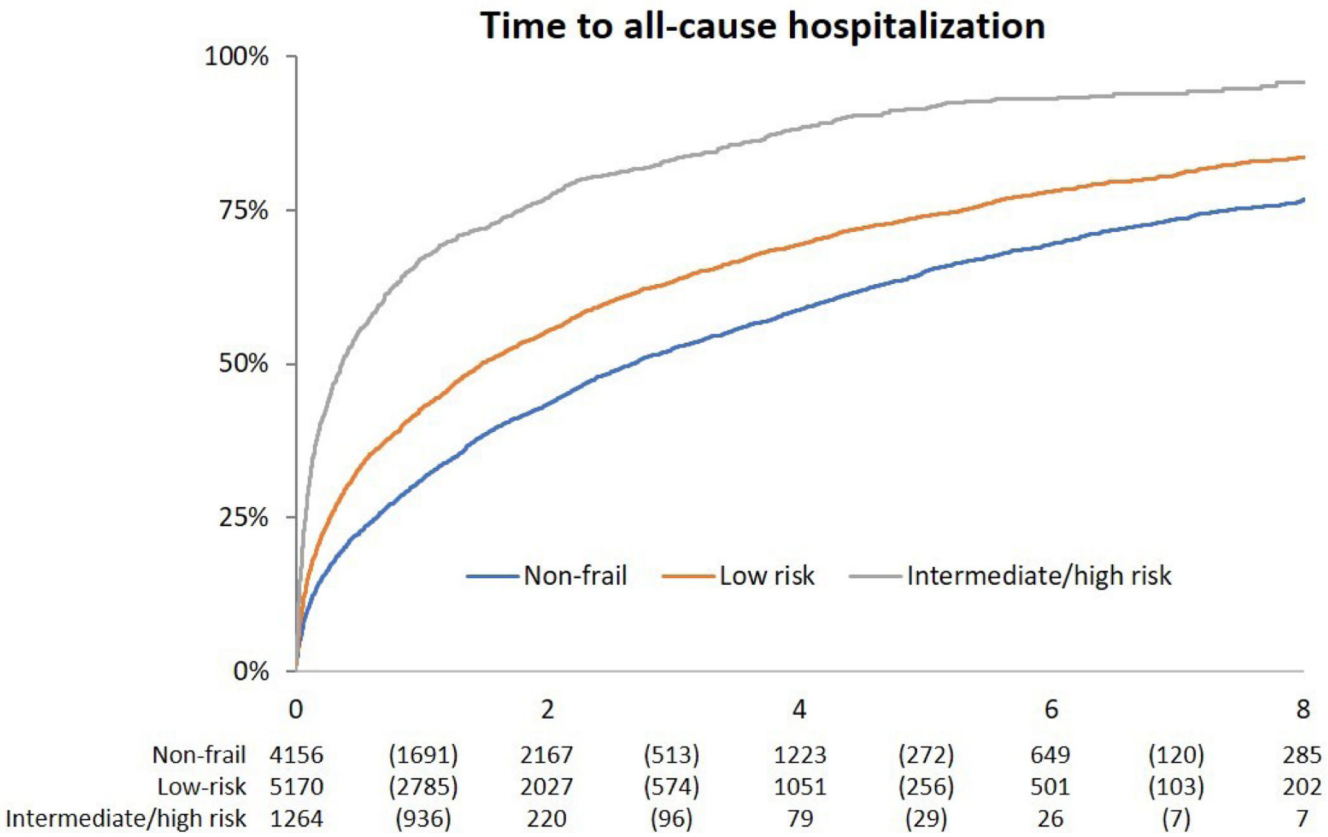
Findings:

Adults ≥60 years with incident IBD have a higher prevalence of frailty compared with matched population-based comparators (61% versus 27%). Frailty in older adults with incident IBD is strongly associated with increased risks for mortality and hospitalizations, independent of comorbidities. Frailty is associated with a significantly increased risk of death from digestive, respiratory and cardiovascular diseases.

Implications for Patient Care:

These findings support the need to better understand the relationship between frailty and IBD outcomes and to develop a tailored frailty assessment tool that can be implemented in an efficient manner in IBD clinic to risk stratify older patients.





Non-frail	4156	(1691)	2167	(513)	1223	(272)	649	(120)	285
Low-risk	5170	(2785)	2027	(574)	1051	(256)	501	(103)	202
Intermediate/high risk	1264	(936)	220	(96)	79	(29)	26	(7)	7

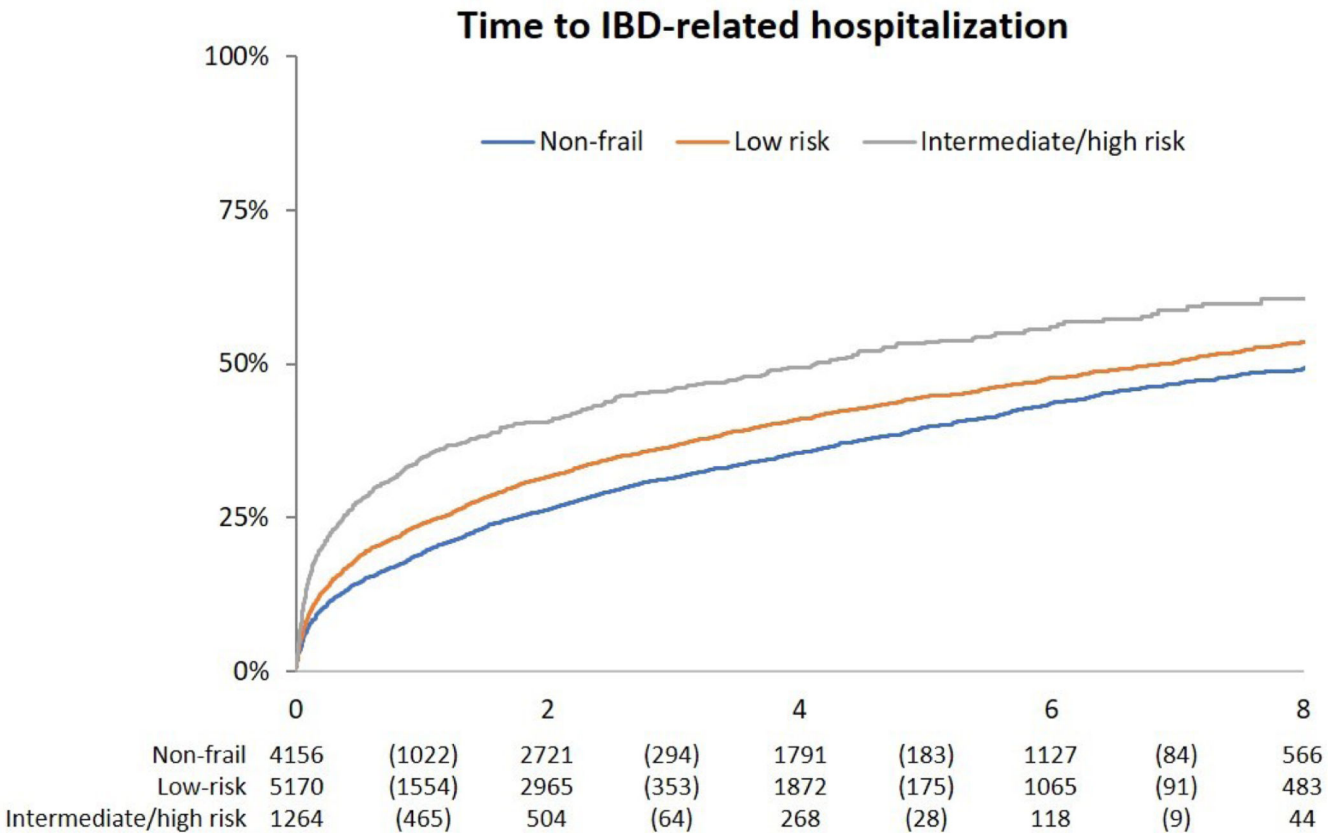


Figure 1:

Kaplan-Meier failure curves weighted for age and sex for (A) all-cause mortality (B) all-cause hospitalizations and (C) inflammatory bowel disease (IBD)-related hospitalizations for patients ≥60 years with incident IBD in Sweden

Mortality	N Events (%)			Adjusted Hazard Ratio* (95% CI)	
	Non-Frail	Low Risk of Frailty	Higher Risk of Frailty	Low Risk of Frailty vs Non-Frail	Higher Risk of Frailty vs Non-Frail
All causes	676 (16.3%)	1 295 (25.0%)	667 (52.8%)	1.48 (1.35-1.63)	3.22 (2.86-3.61)
Cause Specific Mortality					
Hematologic Diseases and Conditions	1 (0.0%)	1 (0.0%)	4 (0.3%)	0.69 (0.04-12.13)	13.55 (1.09-168.71)
Infectious Diseases	16 (0.4%)	41 (0.8%)	38 (3.0%)	1.70 (0.95-3.02)	5.60 (2.84-11.08)
Endocrine, Nutritional and Metabolic Diseases	17 (0.4%)	39 (0.8%)	25 (2.0%)	1.66 (0.92-2.99)	4.18 (1.93-9.09)
Respiratory diseases	40 (1.0%)	118 (2.3%)	64 (5.1%)	2.17 (1.51-3.12)	3.79 (2.44-5.88)
Digestive Diseases	61 (1.5%)	131 (2.5%)	79 (6.3%)	1.51 (1.11-2.05)	3.18 (2.17-4.64)
Circulatory and Cardiovascular Diseases	193 (4.6%)	413 (8.0%)	248 (19.6%)	1.48 (1.25-1.76)	2.90 (2.34-3.60)
Trauma and External Causes	20 (0.5%)	36 (0.7%)	19 (1.5%)	1.27 (0.73-2.20)	2.89 (1.33-6.30)
Disease of Nervous System and Sense Organs	28 (0.7%)	41 (0.8%)	25 (2.0%)	1.09 (0.66-1.79)	2.34 (1.19-4.58)
Urinary diseases	13 (0.3%)	29 (0.6%)	14 (1.1%)	1.39 (0.72-2.67)	2.24 (0.83-6.04)
Musculoskeletal and Connective Tissue Diseases	7 (0.2%)	11 (0.2%)	7 (0.6%)	0.96 (0.35-2.64)	1.65 (0.38-7.26)
Malignant Neoplasms	239 (5.8%)	347 (6.7%)	107 (8.5%)	1.13 (0.95-1.33)	1.23 (0.95-1.60)
Psychiatric Disorders	25 (0.6%)	48 (0.9%)	20 (1.6%)	1.20 (0.72-1.99)	1.17 (0.58-2.38)

Figure 2:

Forrest-Plot for risk of main cause-specific mortality by frailty in Swedish patients ≥60 years with incident inflammatory bowel diseases (IBD) between 2007–2016

Table 1:

Baseline characteristics of Swedish patients ≥60 years with incident inflammatory bowel disease (IBD) and matched population-based comparators between 2007–2016

	IBD n (%)	Non-IBD Comparator n (%)
n	10,590	103,398
Female	5,522 (52)	54,014 (52)
Mean age in years (SD)	71 (±8)	71 (±8)
Range of age in years	60–96	60–96
Age in Categories:		
60–69 years	5,425 (51)	53,487 (52)
70–79 years	3,510 (33)	34,277 (33)
≥80 years	1,655 (16)	15,634 (15)
Education Level:		
≤9 years	4,027 (38)	37,340 (36)
10 – 12 years	4,259 (40)	40,788 (39)
>12 years	2,171 (21)	23,979 (23)
Mean follow-up in years (SD)	5 (±3)	5 (±3)
IBD Type:		
Crohn's disease (CD)	2,887 (27)	N/A
Ulcerative colitis (UC)	6,289 (60)	N/A
IBD-unclassified	1,414 (13)	N/A
CD Montreal Classification		
L1/L3/LX	2,422 (84)	
L2	448 (16)	
UC Montreal Classification		
E1/E2	2,665 (42)	
E3	817 (13)	
EX	2,807 (45)	
Mean number of outpatients visits / year (SD)[#]	3.3 (±6.7)	1.7 (±3.6)
Mean number of hospitalizations / year (SD)[#]	0.7 (±1.1)	0.3 (±0.7)
IBD Medications at Index Date		
Local corticosteroids	934 (9)	
Systemic corticosteroids	1,745 (17)	
Systemic 5-ASAs[^]	2,792 (26)	
Immunomodulators or Anti-TNF agents	275 (3)	
IBD Medications in the Year after Diagnosis		
Local corticosteroids	2,055 (19%)	113 (0.1%)
Systemic corticosteroids	4,106 (39%)	8,602 (8%)
Systemic 5-ASAs[^]	5,621 (53%)	300 (0.3%)
Immunomodulators	1,365 (13%)	1,496 (1%)

	IBD n (%)	Non-IBD Comparator n (%)
Anti-TNF agents	224 (2%)	105 (0.1%)
Charlson Co-morbidity Index (CCI):		
Range of CCI	0–13	0–15
0	6,462 (61)	79,300 (77)
1	1,515 (14)	9,117 (9)
≥2	2,613 (25)	14,981 (15)
Mean Frailty Risk Score (Range)	1.9 (0–41)	0.9 (0–34)
Severity of Frailty[$]:		
Non-frail	4,156 (39)	75,806 (73)
Low risk for frailty	5,170 (49)	22,071 (21)
Higher risk for frailty	1,264 (12)	5,521 (6)

Comparators are matched on age, sex, place of residence and calendar year

SD: Standard deviation

[#]In the 3 years prior to diagnosis

TNF: Tumor Necrosis Factor

[^]5-aminosalicylates

[$]Non-frail: frailty risk score of 0, low risk: frailty risk score of >0 – <5, higher risk: ≥5

Table 2:

Characteristics of Swedish patients ≥60 years with incident inflammatory bowel disease (IBD) between 2007–2016, stratified by frailty

	Non-frail n (%)	Low risk of Frailty n (%)	Higher Risk of Frailty n (%)
n	4,156	5,170	1,264
Female	1,999 (48)	2,796 (54)	727 (58)
Mean age in years (SD)	70 (±7)	71 (±8)	75 (±8)
Age in Categories:			
60–69 years	2,439 (59)	2,596 (50)	390 (31)
70–79 years	1,264 (30)	1,781 (34)	465 (37)
≥80 years	453 (11)	793 (15)	409 (32)
Education Level:			
≤9 years	1,433 (35)	2,037 (39)	557 (44)
10 – 12 years	1,712 (41)	2,061 (40)	486 (38)
>12 years	959 (23)	1,012 (20)	200(16)
Mean follow-up in years (SD)	6 (±3)	5 (±3)	4 (±3)
IBD Type:			
Crohn's disease	1,079 (26)	1,424 (28)	384 (30)
Ulcerative colitis	2,883 (69)	2,801 (54)	605 (48)
IBD-unclassified	194 (5)	945 (18)	275 (22)
CD Montreal Classification			
L1/L3/LX	910 (84)	1,181 (83)	331 (86)
L2	157 (15)	238 (17)	53 (14)
UC Montreal Classification			
E1/E2	1,400 (49)	1,066 (38)	199 (33)
E3	333 (12)	412 (15)	72 (12)
EX	1,150 (40)	1,323 (47)	334 (55)
Mean number of outpatients visits / year (SD)[#]	1.8 (±2.1)	3.6 (±5.7)	7.1 (±14.3)
Mean number of hospitalizations / year (SD)[#]	0.2 (±0.4)	0.7 (±0.9)	2.2 (±1.9)
IBD Medications at Index Date			
Local corticosteroids	374 (9)	452 (9)	108 (9)
Systemic corticosteroids	662 (16)	881(17)	202 (16)
Systemic 5-ASAs[^]	1,372 (33)	1,250 (24)	170 (13)
Immunomodulators or Anti-TNF agents	89 (2)	153 (3)	33 (3)
IBD Medications in the year after diagnosis			
Local corticosteroids	781 (19%)	1,024 (20%)	250 (20%)
Systemic corticosteroids	1,432 (35%)	2,187 (42%)	502 (40%)
Systemic 5-ASAs[^]	2,472 (60%)	2,722 (53%)	427 (34%)
Immunomodulators	526 (13%)	741 (14%)	98 (8%)

	Non-frail n (%)	Low risk of Frailty n (%)	Higher Risk of Frailty n (%)
Anti-Tumor Necrosis Factor agents	80 (2%)	127 (3%)	17 (2%)
Charlson Co-morbidity Index:			
0	3,284 (79)	2,914 (56)	264 (21)
1	348 (8)	897(17)	270 (21)
≥2	524 (13)	1,359 (26)	730 (58)

Non-frail: frailty risk score of 0, low risk: frailty risk score of >0 – <5, higher risk: ≥5

SD: Standard deviation

[#] In the 3 years prior to diagnosis

[^] 5-aminosalicylates

Table 3:

Hazard ratios for all-cause mortality in Swedish patients ≥60 years with incident inflammatory bowel disease between 2007–2016

	Adjusted Hazard Ratios* for Mortality (95% CI)	
	Low Risk of Frailty	**Higher Risk of Frailty**
Overall	1.48 (1.35–1.63)	3.22 (2.86–3.61)
Male	1.47 (1.29–1.68)	3.42 (2.90–4.03)
Female	1.49 (1.31–1.71)	3.08 (2.62–3.62)
60–69 years	1.61 (1.35–1.93)	5.55 (4.44–6.93)
70–79 years	1.57 (1.35–1.83)	3.59 (2.99–4.32)
≥80 years	1.28 (1.09–1.51)	2.07 (1.73–2.47)
Crohn's disease	1.39 (1.16–1.66)	2.82 (2.27–3.51)
Ulcerative colitis	1.48 (1.32–1.67)	2.99 (2.56–3.48)
IBD-unclassified	1.89 (1.25–2.86)	5.31 (3.42–8.22)
CCI=0	1.14 (1.00–1.30)	2.10 (1.66–2.65)
CCI=1	1.18 (0.92–1.51)	1.70 (1.27–2.29)
CCI≥2	1.53 (1.28–1.85)	2.83 (2.32–3.44)
Local Corticosteroids *	1.74 (1.20–2.53)	3.15 (1.94–5.13)
Systemic Corticosteroids *	1.37 (1.09–1.73)	3.01 (2.24–4.06)
Systemic 5-ASAs *	1.57 (1.29–1.90)	2.15 (1.58–2.93)
Immunomodulators / Anti-TNF *	1.14 (0.51–2.57)	5.22 (2.06–13.19)

Non-frail: frailty risk score of 0, low risk: frailty risk score of >0 – <5, higher risk: ≥5

Hazard ratios are compared to non-frail IBD patients

CI: Confidence Interval

*At the time of diagnosis

TNF: Tumor Necrosis Factor

All models are adjusted for age, sex, calendar year, country of birth and education prior to diagnosis

Table 4:

Hazard ratios for all-cause hospitalization in Swedish patients ≥60 years with incident inflammatory bowel disease between 2007–2016

	Adjusted Hazard Ratios for Hospitalization (95% CI)	
	Low Risk of Frailty	**Higher Risk of Frailty**
Overall	1.37 (1.30–1.44)	2.42 (2.24–2.61)
Male	1.36 (1.27–1.46)	2.43 (2.17–2.73)
Female	1.38 (1.29–1.49)	2.43 (2.19–2.70)
60–69 years	1.40 (1.30–1.50)	2.90 (2.57–3.29)
70–79 years	1.36 (1.25–1.48)	2.57 (2.27–2.90)
≥80 years	1.31 (1.15–1.49)	1.73 (1.48–2.02)
Crohn's disease	1.25 (1.14–1.37)	2.22 (1.93–2.55)
Ulcerative colitis	1.39 (1.31–1.49)	2.40 (2.16–2.68)
IBD-undetermined	1.21 (1.01–1.46)	2.09 (1.66–2.62)
CCI=0	1.29 (1.21–1.37)	1.85 (1.60–2.14)
CCI=1	1.12 (0.92–1.30)	1.71 (1.40–2.08)
CCI≥2	1.29 (1.15–1.45)	2.20 (1.92–2.52)
Local Corticosteroids *	1.74 (1.20–2.53)	3.15 (1.94–5.13)
Systemic Corticosteroids *	1.37 (1.09–1.73)	3.01 (2.24–4.06)
Systemic 5-ASAs *	1.57 (1.29–1.90)	2.15 (1.58–2.93)
Immunomodulators / Anti-TNF *	1.14 (0.51–2.57)	5.22 (2.06–13.19)

Non-frail: frailty risk score of 0, low risk: frailty risk score of >0 – <5, higher risk: ≥5

Hazard Ratios are compared to non-frail patients with IBD

CI: Confidence Interval

* At the time of diagnosis

TNF: Tumor Necrosis Factor

All models are adjusted for age, sex, calendar year, country of birth and education prior to diagnosis