

# RESEARCH LETTER

## Frailty and Inflammatory Bowel Disease: A Nationwide Assessment



Frailty is a complex syndrome in older patients caused by several social and clinical factors resulting in worse patient outcomes including falls, incident disability, hospitalization, and mortality.<sup>1–4</sup> With the current aging inflammatory bowel disease (IBD) population,<sup>5</sup> it is expected that the number of frail individuals with IBD will continue to increase. Previous studies showed that frail individuals with IBD had a 2- to 3-fold increase in readmission mortality compared to nonfrail IBD individuals.<sup>6,7</sup> However, there is a lack of U.S. data on the inpatient mortality, morbidity, and hospital utilization associated with the presence of frailty in this patient population.

We conducted a retrospective study using the National Inpatient Sample (NIS) databases from 2016 to 2020. The NIS, developed for the Healthcare Cost Utilization Project, is the largest public all-payer database in the U.S., providing regional and national estimates of inpatient hospital admissions, with a 20% sample from nonfederal acute care hospitals.<sup>8</sup> The data within the NIS is deidentified and publicly available, eliminating the need for an institutional review board.<sup>8</sup>

The Hospital Frailty Risk Score (HFRS) was developed in 2018 in England,<sup>9</sup> and is derived from a list of 109 International Classification of Diseases, Tenth Revision, Clinical Modification codes found to be over-represented in a subset of individuals with higher hospital use and resource utilization. Each code is associated with a set number of points; [Table A1](#). Scores <5 were defined as low frailty scores (LFS), while scores of 5 to 15 and ≥15 were defined respectively as intermediate (IFS) and high frailty scores (HFS).

We included individuals ≥18 year old hospitalized for IBD between 2016 and 2020. A primary IBD-related hospitalization was defined as a hospitalization in which IBD was listed as the primary diagnosis. Our primary outcomes were the inpatient mortality and morbidity among Crohn's disease (CD)- and ulcerative colitis (UC)-related hospitalizations with IFS and HFS as compared to LFS. Complications included sepsis, *Clostridioides difficile* infection (CDI), acute respiratory failure, acute kidney injury, and secondary vascular events (eg, cerebrovascular events, acute coronary syndromes, deep vein thrombosis, pulmonary embolism, and portal vein thrombosis); [Table A2](#). Secondary outcomes included length of stay, and total health-care charges.

Baseline characteristics were compared using a *t* test for continuous variables and a chi-square test for categorical variables. A multivariate logistic regression analysis was then applied to estimate the mortality and morbidity and the adjusted odds ratios (aORs) with 95% confidence intervals (CIs), among patients with IFS and HFS as compared to LFS. We analyzed weighted samples from the NIS database using the Stata/SE Version 17.0 software (StataCorp, College Station, Texas).

A total of 148,583,219 hospitalizations were recorded from 2016 to 2020, including 455,655 (0.3%) IBD-related hospitalizations. Among these, 282,805 (0.2%) were CD-related, 172,850 (0.1%) were UC-related. Within IBD-related hospitalizations, 358,995 had LFS (CD—229,995; UC—129,000), 95,210 had IFS (CD—52,210; UC—43,000), and 1450 had HFS (CD—600; UC—850). Overall, frail IBD individuals were more likely to have a Charlson Comorbidity Index ≥ 3 (LFS—5%, IFS—19%, HFS—47%, *P* < .01, *P* < .01), and a lower-than-normal body mass index (LFS—17%, IFS—20%, HFS—23%, *P* < .01); [Table 1](#).

Frail individuals with IBD exhibited a 5- to 9-fold increase in mortality (IFS: aOR = 5.41, 95% CI: 2.70–10.84; HFS: aOR = 9.04, 95% CI: 2.25–36.41) as compared to those with LFS; [Table 2](#). This was largely driven by frail individuals with UC, who had up to a 10-fold increase in mortality (HFS: aOR = 10.36, 95% CI: 2.24–47.95); [Tables A3](#) and [A4](#). Furthermore, frail IBD individuals had higher odds of sepsis (IFS: aOR = 8.32, 95% CI: 6.19–10.84; HFS: aOR = 27.16, 95% CI: 13.64–54.08) and CDI (IFS: aOR = 2.25, 95% CI: 1.87–2.72; HFS: aOR = 4.73, 95% CI: 2.12–10.53); [Table 2](#). While frail individuals with UC had a 17-fold higher odds of acute respiratory failure (HFS: aOR = 16.68, 95% CI: 6.05–45.38), those with CD had a 9-fold increase in acute kidney injury (HFS: aOR = 8.66, 95% CI: 3.94–19.03); [Tables A3](#) and [A4](#). Lastly, frail individuals with IBD were at increased odds of secondary vascular events; [Table 2](#).

Among IBD-related hospitalizations, we found that frail individuals stayed on average 3 to 10 days longer than those with LFS (IFS: adjusted mean difference (aMD) = 3.36, 95% CI: 3.01–3.71; HFS: aMD = 9.75, 95% CI: 6.18–13.31), and had significantly higher total hospital expenditures (IFS: aMD = \$29,582, 95% CI: 24,331–34,834; HFS: aMD = \$74,452, 95% CI: 41,143–107,760).

Our study is the first to assess the relationship between the HFRS and the inpatient outcomes in over 450,000 IBD-related hospitalizations. We found that higher frailty scores were associated with proportionately higher inpatient mortality and morbidity. Notably, significantly increased odds of sepsis (up to 35-fold), and a 2- to 6-fold increase in CDI were seen in frail IBD patients in comparison to their nonfrail counterparts. A previous study found that frail IBD patients had a 17% increase in the risk of infection after immunomodulator therapy.<sup>10</sup> These findings hold particular significance, as CDI has been associated with increased odds of IBD-related mortality, urgent

**Table 1.** Baseline Characteristics When Evaluating IBD-Related Hospitalizations Stratified by the HFRS Groups

Baseline characteristics	Low Frailty score Percentage (no.)	Intermediate Frailty score Percentage (no.)	High Frailty score Percentage (no.)	P
Age (y)				<.01
18–39.9	66.8% (239,890)	42.6% (40,530)	16.6% (240)	
40–59.9	14.5% (51,950)	16.8% (15,945)	11.0% (160)	
≥60	18.7% (67,155)	40.7% (38,735)	72.4% (1050)	
Sex				<.01
Male	48.3% (173,455)	38.7% (36,860)	36.9% (535)	
Female	51.7% (185,434)	61.3% (58,330)	63.1% (915)	
Race				<.01
Non-Hispanic White	72.7% (253,085)	75.5% (70,130)	74.4% (1060)	
Non-Hispanic Black	14.0% (48,830)	14.1% (13,115)	14.0% (200)	
Hispanic	8.5% (29,670)	6.6% (6140)	8.1% (115)	
Others	4.8% (16,600)	3.8% (3520)	3.2% (50)	
BMI				<.01
<19 kg/m <sup>2</sup>	17.4% (12,070)	20.2% (5790)	23.3% (120)	
19–24.9 kg/m <sup>2</sup>	28.2% (19,590)	34.6% (9940)	40.8% (210)	
25–29.9 kg/m <sup>2</sup>	11.5% (7965)	11.9% (3420)	13.6% (70)	
≥30 kg/m <sup>2</sup>	42.9% (29,745)	33.3% (9570)	40.1% (115)	
Insurance status				<.01
Medicare	22.1% (62,990)	45.1% (33,505)	73.0% (825)	
Medicaid	19.8% (56,645)	17.4% (12,915)	15.5% (175)	
Private insurance	52.0% (148,650)	32.2% (24,705)	11.1% (125)	
Self-pay	6.1% (17,405)	4.3% (3190)	0.4% (5)	
Median household income				<.01
Lowest quartile	25.1% (88,835)	27.1% (25,370)	32.3% (460)	
Second quartile	25.1% (88,805)	26.8% (25,195)	21.8% (310)	
Third quartile	25.8% (91,315)	24.9% (23,360)	25.6% (365)	
Highest Quartile	24.0% (84,830)	21.3% (19,970)	20.4% (290)	
Hospital region				<.01
Northeast	21.9% (78,500)	19% (18,000)	17.9% (260)	
Midwest	24.2% (86,730)	24.2% (23,005)	27.9% (405)	
South	37.7% (135,165)	39.7% (37,810)	42.8% (620)	
West	16.3% (58,600)	17.2% (16,395)	11.4% (165)	
Hospital teaching status				<.01
Teaching	74.2% (220,445)	71.6% (54,780)	71.6% (830)	
Nonteaching	25.8% (76,615)	28.4% (21,745)	28.5% (330)	
Hospital size				<.01
Small	19.8% (71,079)	19.9% (18,900)	17.6% (255)	
Medium	27.3% (98,115)	29.1% (27,660)	31.7% (460)	
Large	52.9% (189,800)	51.1% (48,650)	50.7% (735)	
Comorbidities				<.01
0	71.0% (255,035)	45.6% (43,360)	12.4% (180)	
1	18.6% (66,905)	22.3% (21,230)	19.7% (285)	
2	5.9% (21,000)	13.4% (12,750)	21.4% (310)	
≥3	4.5% (16,055)	18.8% (17,870)	46.6% (675)	

colectomy, length of hospital stay, and readmissions.<sup>11,12</sup> In fact, in this high-risk population susceptible to organ damage from IBD,<sup>13–15</sup> caution and timely management of frail individuals are warranted to prevent further morbidity and mortality.

This study has certain limitations. Firstly, it relies on ICD codes, which

lack verifiability through manual review. Secondly, the NIS database lacks information on disease activity, indications for colectomy, and readmissions. Lastly, it is important to note that a single individual may account for multiple admissions.

In summary, frailty is associated with increased inpatient mortality,

morbidity, and health-care burden amongst the IBD population. The HFRS is a useful predictive tool which can facilitate identifying individuals at a higher risk of unfavorable outcomes, thereby facilitating targeted interventions to address modifiable components of frailty.

**Table 2.** Outcomes of IBD-Related Hospitalizations Stratified by HRFS

Outcomes	Incidence N (%)			Regression analysis aOR <sup>a</sup> [95% CI]		
	Low score (HFRS <5)	Intermediate (HFRS 5–15)	High score (HFRS >15)	Low score (HFRS <5)	Intermediate (HFRS 5–15)	High score (HFRS >15)
Total primary IBD-related hospitalizations	100% (358,995)	100% (95,210)	100% (1450)	N/A	N/A	N/A
Mortality	0.1% (295)	1.0% (1005)	4.2% (85)	(Ref.)	5.41 [2.70–10.84]	9.04 [2.25–36.41]
Infection related complications						
Sepsis, severe sepsis, and septic shock	0.4% (1420)	4.3% (4075)	13.5% (195)	(Ref.)	8.32 [6.19–11.17]	27.16 [13.64–54.08]
<i>Clostridioides difficile</i> infection	2.0% (7040)	4.6% (4390)	7.9% (115)	(Ref.)	2.25 [1.87–2.72]	4.73 [2.12–10.53]
Organ dysfunction						
Acute respiratory failure	0.2% (830)	2.1% (1965)	11.7% (170)	(Ref.)	5.41 [3.71–7.90]	17.29 [7.71–38.77]
Acute kidney injury	4.9% (17,570)	21.4% (20,390)	40% (580)	(Ref.)	3.39 [2.98–3.86]	6.86 [4.07–11.54]
Vascular events						
Cerebrovascular accident	0.01% (45)	0.3% (300)	4.5% (65)	(Ref.)	6.07 [1.60–23.06]	54.73 [8.97–333.79]
Acute coronary syndrome	0.1% (365)	0.4% (405)	1.4% (20)	(Ref.)	1.42 [0.60–3.41]	7.12 [1.38–36.86]
Deep vein thrombosis	0.8% (2710)	2.5% (2410)	5.5% (80)	(Ref.)	2.26 [1.75–2.93]	2.34 [0.81–6.79]
Pulmonary embolism	0.3% (1075)	1.0% (975)	2.8% (40)	(Ref.)	2.82 [1.85–4.31]	4.38 [0.87–22.10]
Portal vein thrombosis	0.3% (905)	0.3% (320)	1.0% (15)	(Ref.)	0.77 [0.38–1.50]	3.29 [0.38–28.41]

<sup>a</sup>Adjusted for age, race, BMI, comorbidity index, income, insurance status, hospital characteristics, and comorbid conditions.

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## Supplementary Materials

Material associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.gastha.2024.07.003>.

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**Abbreviations used in this paper:** aMD, adjusted mean difference; aOR, adjusted odds ratio; CD, Crohn's disease; CDI, *Clostridioides difficile* infection; CI, confidence interval; HFRS, Hospital Frailty Risk Scores; HFS, high frailty score; IFS, intermediate frailty score; LFS, low frailty score; NIS, National Inpatient Sample; UC, ulcerative colitis



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STROBE.