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Effects of inflammatory bowel disease on in-hospital outcomes in patients with congestive heart failure: A retrospective national inpatient sample study

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Congestive heart failure (CHF) is defined as a complex clinical syndrome stemming from structural or functional factors that impair ventricular filling or ejection. It is a significant cause of hospitalization, mortality and healthcare expenditure, especially in the aging population. There are around 5 million individuals in the United States with CHF [1]. Inflammatory bowel disease (IBD) is an idiopathic multi-system inflammatory disorder that involves chronic intestinal inflammation interspersed with episodes of flares. The umbrella term mainly describes two main entities- Ulcerative colitis and Crohn's disease. It's a global disease with a prevalence of 0.3% and incidence of 280–320 per 100,000 people in North America [2]. The chronic inflammatory state associated with IBD is a significant risk factor predisposing to a prothrombotic state and increased mortality from coronary artery disease (CAD) as well as CHF [3]. There is a scarcity of literature regarding outcomes of CHF patients with IBD. To our best knowledge, there have been a couple of studies in Denmark and the United States evaluating the incidence of Ischemic Heart Diseases (IHD) in IBD patients [4,5]. There is not much information on long-term outcomes in CHF patients with IBD. We, therefore, undertook this study to evaluate how IBD affected the outcomes in patients admitted for heart failure treatment in an American nationwide cohort.

In this study, we have used the most recent 2016 NIS database. We included all the patients of CHF with and without IBD by using the respective ICD-10 codes. Primary outcomes of interest were mortality, cardiogenic shock, cardiac arrest, stroke, acute kidney injury (AKI), length of stay and cost of care. Multivariate logistic regression was used for adjustment of potential confounders including age, gender, race, socioeconomic status, diabetes, hypertension, smoking, alcohol use, chronic kidney disease, obesity, dyslipidemia, Charlson Comorbidity Index, hospital location, hospital region, teaching status, and hospital size. STATA/IC 15.1 was used for statistical analysis.

In the year 2016, we found 3,053,738 patients admitted for heart failure. Of these patients, 8685 had an established diagnosis of IBD (group A), and 3,045,053 did not have IBD (group B). The mean age in group A was 72.4 years (71.8–73) and that in group B was 72 years (71.8–72.1). Comorbidities like diabetes (20.3%), dyslipidemia (43.8%), obesity (18%), and chronic kidney disease (37.4%) were significantly less common in CHF patients with IBD as compared to those without IBD. The average cost of hospitalization for group A was significantly higher [$84,562 (77,622–91,502), $p < 0.05$]. The average length of stay was also longer for group A as compared to group B (8.2 vs. 6.4 days) with p-value < 0.05. Upon ethnic consideration, it was found that most patients in group A were white (84.4% vs. 71%). The incidence of AKI was significantly higher in group A as compared to group B in both univariate (OR, 1.25; 95% CI, 1.14–1.4, p value < 0.001) and multivariate analysis (OR, 1.3; 95% CI, 1.16–1.4; p-value < 0.001). There was no difference in mortality, cardiogenic shock, cardiac arrest, and stroke (Table 1).

The elevated levels of inflammatory cytokines in IBD may affect the arterial endothelium. A major contributor for this is the C-reactive protein, which is increased several folds in IBD patients. Among the other inflammatory mediators, tumor necrosis factor alpha (TNF-α), vascular endothelial growth factor (VEGF) and interleukin-6 (IL-6) also play a significant role in promoting cardiovascular risk. It has been observed that an acute phase reactant calprotectin is elevated in IBD. These mediators lead to arterial damage, chronic ischemic changes of the myocyte and eventually act as an additive factor in the pathogenesis of CHF [6]. Besides CHF, IBD has an important association with other cardiovascular effects. There is a growing body of evidence to show that individuals with IBD are predisposed to ischemic cerebrovascular diseases, atrial fibrillation, peripheral artery disease, venous thrombosis,

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Table 1

Patients with congestive heart failure (CHF) with and without inflammatory bowel disease (IBD).

$N = 3,053,738$			
Variables	CHF with IBD ($n = 8685$)	CHF without IBD ($n = 3,045,053$)	*p* value
Mean age	72.4 (71.8–73)	72 (71.8–72.1)	0.10
Gender (F)	50.6%	50%	0.70
HTN	33%	34.5%	0.22
DM	20.3%	30.3%	0.000
Smoking	29%	28%	0.37
Dyslipidemia	43.8%	48.3%	0.000
Obesity	18%	21.5%	0.000
CKD	37.4%	41%	0.003
PAD	2.3%	2.6%	0.36
Total charge	84,562 (77,622–91,502)	68,071.6 (66,077.8–70,065.4)	0.000
Length of stay	8.2 (7.7–8.7)	6.4 (6.3–6.43)	0.000
Race			0.000
White	84.4%	71%	
Black	8.6%	17.3%	
Hispanic	3.5%	7%	
Weekend admission	23%	22.8%	0.90
Bed size			0.046
Small	15.6%	18%	
Medium	29.7%	28.5%	
Large	54.6%	53.3%	
Hospital region			0.000
North east	26%	20.4%	
Mid-west	26.7%	24.3%	
South	31%	38.3%	
West	16%	16.4%	
Hospital teaching status			0.000
Rural	6.4%	9.4%	
Urban non-teaching	24%	25.8%	
Urban teaching	69.4%	64.8%	
Insurance			0.000
Medicare	80%	76%	
Medicaid	4.3%	8.9%	
Private including HMO	12.5%	11.3%	

Outcomes	Unadjusted odds ratio (OR)	*p* value	Adjusted odds ratio (OR)	*p* value
Mortality	1.2 (0.97–1.48)	0.09	1.06 (0.84–1.33)	0.61
Cardiogenic shock	1.03 (0.82–1.3)	0.76	0.89 (0.69–1.14)	0.36
Cardiac arrest	0.85 (0.6–1.2)	0.34	0.8 (0.56–1.17)	0.25
Stroke	0.7 (0.45–1.1)	0.13	0.74 (0.46–1.2)	0.20
Acute kidney injury	1.25 (1.14–1.4)	0.000	1.3 (1.16–1.4)	0.000
ICU stay	1.3 (0.56–3)	0.54	1.03 (0.4–2.6)	0.96

Outcomes	β coefficient (95% CI)	*p* value
Length of stay	1.84 (1.4–2.3)	0.000
Cost of care	16,490 (9967.2–23,013.4)	0.000

F- female, HTN- hypertension, DM- diabetes, CKD- chronic kidney disease, PAD- peripheral arterial disease, ICU- intensive care unit, HMO- Health Maintenance Organization.

and thromboembolic events [7,8]. Also, IBD flares are associated with increased systemic translocation of bacterial cell wall components that induce tissue (including myocardial) damage and a procoagulant state [3]. Apart from systemic inflammation, increased risk of atherosclerosis and long-term steroid use in IBD play an essential role in the development of CHF in IBD patients [5]. The study involving 736 individuals in Olmsted County, Minnesota, showed that IBD patients had a lower prevalence of cardiovascular risk factors [5]. In our study, we also observed comorbidities like diabetes, dyslipidemia, obesity, and chronic kidney disease were significantly less frequent in CHF patients with IBD as compared to those without IBD. Hence, the increased risk of IHD, as well as CHF in IBD patients, might be contributed by atherosclerosis as a result of chronic systemic inflammation. A Danish study found that there was a 2.5-fold increase in hospitalization rates for CHF in IBD flares [4]. Similarly, the Minnesota study also found that IBD patients were twice as likely to develop HF as compared to controls, and the incidence was correlated with IBD stage [5]. In our study, we also found that IBD patients were at an increased risk for prolonged hospitalization, more resource utilization. We also demonstrated that there was an increased risk of developing AKI in

CHF patients who had IBD. Renal involvement, including nephrolithiasis, glomerulonephritis, tubulointerstitial nephritis, and secondary amyloidosis, have been found in 4%–23% of patients with IBD [9]. On the other hand, there are evidences that CHF can predispose to AKI due to decreased cardiac output [10]. The increased number of AKI in group A can be due to CHF itself; otherwise, CHF and IBD both might contribute to the pathogenesis simultaneously. The exact mechanism of increased incidence of AKI in the IBD group requires further studies.

Though this retrospective study based on the administrative database has several limitations including inadequate documentation, coding errors, the absence of patient's level information, it showed a fascinating influence of IBD on CHF outcomes. It would also make clinicians aware of the anticipated complications.

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