

ORIGINAL ARTICLE

# A comparison of diverticulitis in Crohn's disease versus ulcerative colitis

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Crohn's disease, diverticulitis, inflammatory bowel disease, ulcerative colitis.

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**Abstract**

**Background and Aim:** Inflammatory bowel disease (IBD) and diverticulitis both increase morbidity, especially when associated with in-patient hospitalization. This study aimed to evaluate whether hospitalization burden differs for diverticulitis in patients with a history of Crohn's disease (CD) compared to ulcerative colitis (UC).

**Method:** All patients hospitalized for acute diverticulitis with pre-existing UC or CD in 2014 were selected using the national in-patient sample. Cases were identified using the International Classification of Diseases, Ninth Edition codes. Primary outcomes were mortality, cost of admission, length of stay (LOS), and colectomy.

**Results:** A total of 1815 patients were admitted with diverticulitis, and those with CD had a hospitalization associated with decreased cost (aOR -14 537, 95% CI -27 316 to -1758;  $P = 0.026$ ) and LOS (aOR -1.31, 95% CI -2.41 to -0.208;  $P = 0.02$ ) compared to UC. A second analysis comparing diverticulitis hospitalization between those with CD and those with the absence of IBD showed no significant difference in mortality (aOR 2.47, 95% CI 0.59 to 10.36;  $P = 0.22$ ), LOS (aOR 0.03, 95% CI -0.47 to 0.54;  $P = 0.92$ ), or cost of admission (aOR -2196, 95% CI -6933 to 2539;  $P = 0.36$ ) between the cohorts.

**Conclusion:** Patients with UC have worsened hospitalization outcomes when being treated for diverticulitis compared to CD. While the findings may be a result of a difference in colectomy rates, the etiology may also be multifactorial. These conclusions have not been previously described, and further investigations would better characterize these associations.

**Introduction**

Inflammatory bowel disease (IBD) and diverticulitis are both inflammatory conditions of the bowel that lead to increased morbidity and mortality in patients. In industrialized regions, diverticular disease is a relatively common condition, with a prevalence ranging from 7 to 45%, but predominantly occurs in those older than 60 years of age.<sup>1-3</sup> Moreover, a nationwide study in the United States showed a 26% increase in hospital admissions from 1998 to 2005 due to diverticular disease.<sup>4</sup> Diverticulosis occurs where the vasa recta enters the muscle layer of the colon, leading to mucosal herniation through areas of colonic weakness.<sup>5</sup> Diverticulitis ensues when a diverticulum undergoes micro or macroscopic perforations, leading to inflammation, usually as a result of increased intraluminal pressures.<sup>1,6</sup>

Crohn's disease (CD) is characterized by transmural inflammation that can involve any part of the gastrointestinal tract.<sup>7,8</sup> In contrast, ulcerative colitis (UC) is characterized by mucosal layer inflammation that occurs from the rectum and can extend proximally through the colon in a contiguous manner. Perianal disease and endoscopic examination of cobblestoning,

aphthous ulcerations, and biopsies showing granulomas, usually differentiate diverticulitis from CD.<sup>8,9</sup> However, segmental colitis associated with diverticula (SCAD), described in the literature as inflammation in the interdiverticular mucosa without involving the orifices, has been occasionally associated with both UC and CD.<sup>10,11</sup>

Interestingly, a prospective study showed that the prevalence of diverticular disease in UC was found to be lower than controls.<sup>12</sup> On the other hand, CD has been associated with a higher incidence of diverticulitis than would be expected in a population with non-IBD diverticular disease.<sup>8,13</sup>

Moreover, each of these conditions is associated with a substantial financial burden. For example, hospitalization for UC is estimated to be between \$19 000 and \$29 000, depending on the severity of illness,<sup>14</sup> while treatment of CD flares typically costs closer to \$25 000, contingent on the need for surgery.<sup>15</sup> In addition, the average cost of diverticulitis hospitalization has been estimated to be around \$5000.<sup>16</sup> This study aims to evaluate whether hospitalization outcomes differ for patients with acute diverticulitis and a history of CD compared to UC.

## Methods

**Data source.** The national in-patient sample (NIS) represents 20% of all nonfederal hospitals in the United States. This large database was queried for demographic information of the population admitted for acute diverticulitis using the International Classification of Diseases-Ninth Edition Revision-Clinical Modification (ICD-9 CM). The NIS is a product of the Agency for Healthcare Research and Quality and contains patient information that has been deidentified. This is a nationally representative subset acquired through hospital discharge records and is the largest in-patient database currently available in the United States. While a proportion of the national population has been sampled, yearly sampling weights are applied, which then provide national estimates.<sup>17</sup> Years of data and a multitude of works have verified the value of this sampling tool, and thus, it has been utilized for this study.

**Study design and inclusion criteria.** This is a cross-sectional study and includes all patients  $\geq 18$  years old with a primary diagnosis of acute diverticulitis in 2014. The ICD-9 CM codes used were 56 211, 56 201, 56 213, and 56 203. The database was then queried to include all patients with prior diagnosis of CD (5559, 555, 5550, 5551) or UC (5569, 556, 5568, 5565, 5566). Patients included in the study were required to have a primary diagnosis of acute diverticulitis with a prior diagnosis of either UC or CD. Primary study outcomes included mortality, cost of hospitalization, and length of stay (LOS) for diverticulitis with either UC or CD. A second comparison was made between those with CD and those without IBD. Various patient demographics (age, race, gender, income, and insurance status), comorbidities, and hospital characteristics (region and size) were obtained. The severity of the co-morbidities was analyzed via the Deyo modification of the Charlson comorbidity index (CCI). This index measures 17 common medical conditions and assigns different weights to compile a score from 0 to 33, which correlates with overall severity of illness.

**Statistical analysis.** Stata IC version 13 (StataCorp LP, College Station, TX, USA) was used for all statistical analyses. Specifically, the svy suite of commands was the extension package that was utilized. Categorical variables were analyzed with the  $\chi^2$  test, while continuous variables were analyzed with the adjusted Wald's test. Hypothesis testing was two-sided. A multivariate logistic regression model was designed to investigate the association between acute diverticulitis and either UC or CD. The hierarchical model included both hospital-level characteristics (hospital teaching status, bed size, region) and patient-level characteristics (age, race, gender, comorbidities) and the CCI. To eliminate the effect of confounders, this was the primary means by which adjustments were made in the data for patient- and hospital-level characteristics. Univariate analysis was first conducted on all of the above factors and comorbidities that could affect diverticulitis hospitalization. Age, race, hospital location, hospital teaching status, and CCI were included in the final multivariate logistic regression model as  $P < 0.05$ , indicating statistical significance on univariate analysis. In the second comparison, between those with CD and those without IBD, age, gender, race,

hospital location, hospital region, hospital size, CCI, diabetes mellitus type 2, congestive heart failure, chronic lung disease, and renal failure were included in the final multivariate logistic regression model as  $P < 0.05$  was statistically significant on univariate analysis.

**Ethical considerations.** The data in the NIS are publicly available, and as a retrospective study, no patients were actively involved in the data collection process. Thus, it was not subject

**Table 1** Unadjusted baseline characteristics of diverticulitis in Crohn's disease versus ulcerative colitis

Variable	Crohn's disease (n = 1090)	Ulcerative colitis (n = 725)	P value
Age (SEM)	59.59 (1.06)	65.3 (1.32)	0
Female (%)	8251 (57)	486 (67)	0.08
Race			0.7
Caucasian (%)	943 (86.5)	607 (83.7)	
Black (%)	65 (5.97)	20 (2.76)	
Hispanic (%)	60 (5.47)	57 (7.86)	
Asian (%)	6 (0.5)	41 (5.66)	
Other (%)	16 (1.5)	0%	
COPD (%)	225 (20.64)	109 (15.86)	0.25
ESRD (%)	95 (8.72)	45 (6.21)	0.38
CHF (%)	65 (5.96)	55 (7.59)	0.54
Liver Disease (%)	55 (5.05)	10 (1.38)	0.07
DMcx (%)	25 (2.29)	10 (1.38)	0.53
HTN (%)	600 (55.05)	400 (55.17)	0.98
CCI (%)			0.88
0	652 (59.82)	405 (55.86)	
1	198 (18.8)	160 (22.07)	
2	135 (12.4)	85 (11.72)	
3	105 (9.63)	75 (10.34)	
Hospital size			0.3
Small (%)	61 (5.56)	58 (8.01)	
Medium (%)	61 (5.56)	139 (19.20)	
Large (%)	968 (88.9)	528 (72.8)	
Hospital region			0.71
Northeast (%)	225 (20.64)	175 (24.14)	
Midwest (%)	250 (22.94)	165 (22.76)	
South (%)	460 (42.2)	265 (36.55)	
West (%)	155 (14.22)	120 (16.55)	
Insurance			0.06
Northeast (%)	473 (43.4)	373 (51.45)	
Midwest (%)	93 (8.49)	68 (9.42)	
South (%)	427 (39.15)	266 (36.70)	
West (%)	97 (8.90)	18 (2.48)	
Income			0.3
Medicare (%)	253 (23.20)	153 (21.13)	
Medicaid (%)	289 (26.51)	255 (35.20)	
Private insurance (%)	310 (28.44)	158 (21.83)	
Self-pay (%)	238 (21.8)	159 (21.93)	

Values are % except for age (mean + standard error mean).

CCI, Charlson comorbidity index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DMcx, complicated diabetes mellitus type 2; ESRD, end-stage renal disease; HTN, hypertension.

to Institutional Review Board approval, and informed consent was not needed.<sup>18</sup>

## Results

In this study, we examined the population of those hospitalized for acute diverticulitis with prior diagnosis of IBD. There were 1815 patients meeting inclusion criteria, and 60% had CD, as shown in Table 1. The populations were largely similar in terms of age ( $60 \pm 1.06$  years old in CD vs  $65 \pm 1.32$  years old in UC,  $P = 0.0$ ), were predominantly female (57% in CD vs 67% in UC,  $P = 0.08$ ), and were primarily Caucasian (87% in CD vs 84% in UC,  $P = 0.70$ ). Comparing CD to UC, comorbidities that were most prevalent include hypertension (55% vs 55%,  $P = 0.98$ ), followed by chronic obstructive pulmonary disease (20.64% vs 15.86%,  $P = 0.25$ ), end-stage renal disease (8.72% vs 6.21%,  $P = 0.38$ ), and congestive heart failure (5.96% vs 7.59%,  $P = 0.54$ ). Among the two cohorts, there were no statistically significant differences with regard to comorbidities.

However, hospital measures showed that UC incurred a much heavier hospitalization burden, as seen in Table 2. LOS in the UC cohort was markedly increased compared to the CD cohort ( $6.4 \pm 0.53$  days vs  $4.7 \pm 0.24$  days,  $P < 0.00$ ), while the cost of hospitalization proportionally rose in the UC cohort compared to the CD cohort ( $\$51\,923 \pm \$6615$  vs  $\$36\,140 \pm \$2245$ ,  $P = 0.02$ ). There were also 20 colectomies documented in the UC cohort, while none were documented in the CD cohort. Age, race, hospital location, hospital teaching status, and CCI were included in the logistic regression model, which confirmed that CD was associated with a decrease in the cost (OR  $-15\,783$ , 95% CI  $-29\,475$  to  $-2091$ ,  $P = 0.02$ ; aOR  $-14\,537$ , 95% CI  $-27\,316$  to  $-1758$ ,  $P = 0.03$ ) and LOS (OR  $-1.70$ , 95% CI  $-2.85$  to  $-0.55$ ,  $P = 0.37$ ; aOR  $-1.31$ , 95% CI  $-2.41$  to  $-0.21$ ,  $P = 0.02$ ) of hospitalization (Table 3). Moreover, there was an observed difference in mortality comparing CD to UC (OR 0.44, 95% CI 0.07 to 2.66,  $P = 0.37$ ; aOR 0.90, 95% CI 0.10 to 7.87,  $P = 0.92$ ), although this was not statistically significant.

An additional analysis was conducted with acute diverticulitis but comparing CD to the population without IBD. There

were 219 815 patients in this cohort, with a median age of  $60 \pm 1.06$  years in CD versus  $60.4 \pm 0.09$  years without IBD ( $P = 0.41$ ), with Caucasian prevalence (87% in CD vs 77% without IBD,  $P = 0.70$ ) and slight female predominance (57% in CD vs 58% without IBD,  $P = 0.73$ ). As in the previous cohort, the most common comorbidities are hypertension (55% in CD vs 54% without IBD,  $P = 0.67$ ), chronic obstructive pulmonary disease (21% in CD vs 16% without IBD,  $P = 0.09$ ), and end-stage renal disease (8.7% in CD vs 7% without IBD,  $P = 0.31$ ) (Table 4). In terms of hospital measures, there was an interesting contrast to the prior set of hospital outcomes. Comparing the population with CD to those without IBD, there was negligible difference between the mortality rates (0.9% vs 0.42%), and both the hospital LOS ( $4.73 \pm 0.24$  days vs  $4.70 \pm 0.03$  days,  $P = 0.90$ ) and the cost of hospitalization ( $\$36\,140 \pm \$2245$  vs  $\$38\,793 \pm \$442$ ,  $P = 0.28$ ) were nearly identical (Table 2). Between the cohort with CD and those without IBD, multivariate logistic regression also reflected these findings, showing no difference in mortality (OR 2.22, 95% CI 0.55 to 9.05,  $P = 0.26$ ; aOR 2.47, 95% CI 0.59 to 10.36,  $P = 0.22$ ), LOS (OR 0.03, 95% CI  $-0.45$  to 0.51;  $P = 0.90$ ; aOR 0.03, 95% CI  $-0.47$  to 0.54,  $P = 0.91$ ), and cost of admission (OR  $-2438$ , 95% CI  $-6865$  to 1989,  $P = 0.28$ ; aOR  $-2196$ , 95% CI  $-6933$  to 2539,  $P = 0.36$ ) (Table 5).

## Discussion

Diverticula typically present around the sigmoid colon, and when this is accompanied by left-sided IBD, the conditions may coexist.<sup>8</sup> Patients can have a history of IBD with subsequent development of diverticulitis, as well as a history of IBD with induction of inflammation in asymptomatic diverticula.<sup>11,19</sup> However, the hospital burden of diverticulitis with pre-existing IBD has not been previously reported. There were 1815 patients admitted nationally for acute diverticulitis with pre-existing IBD in 2014. There were 33.5% more admissions for CD compared to UC, which is consistent with trends in the literature.<sup>8,12,13</sup> Mucosal scarring in some UC patients may reduce the ability to form diverticula and could account for the decreased frequency of

**Table 2** Hospital outcome measures

Outcome	Ulcerative colitis	Crohn's disease	No IBD	<i>P</i> value (CD vs UC)	<i>P</i> value (CD vs No IBD)
Died (%)	15 (2.1)	10 (0.9)	914 (0.42)		
Mean LOS (SEM)	6.4 (0.53)	4.73 (0.24)	4.70 (0.03)	<0.00	0.9
Cost of hospitalization (SEM)	\$51 923 (\$6615)	\$36 140 (\$2245)	\$38 793 (\$442)	0.02	0.28
Colectomy (%)	20 (2.8)	0	985 (0.45)		

Mean reported  $\pm$  SEM.

CD, Crohn's disease; IBD, inflammatory bowel disease; LOS, length of stay; UC, ulcerative colitis.

**Table 3** Effect of Crohn's disease versus ulcerative on diverticulitis hospitalization

	Unadjusted odds ratio	95% CI	<i>P</i> value	Adjusted odds ratio	95% CI	<i>P</i> value
Died	0.44	0.07 to 2.66	0.37	0.90	0.102 to 7.87	0.92
Length of stay (days)	-1.70	-2.85 to -0.55	<0.00	-1.31	-2.41 to -0.21	0.02
Cost of hospitalization	-15 783	-29 475 to -2091	0.02	-14 537	-27 316 to -1758	0.03

CI, confidence interval.

**Table 4** Unadjusted baseline characteristics of diverticulitis in Crohn's disease *versus* absence of IBD

Variable	Crohn's disease (n = 1090)	No IBD (n = 218 725)	P value
Age (SEM)	59.59 (1.06)	60.4 (0.09)	0.41
Female (%)	8251 (57)	126 860 (58)	0.73
Race			
Caucasian (%)	943 (86.5)	168 200 (76.9)	0.7
Black (%)	65 (5.97)	18 592 (8.5)	
Hispanic (%)	60 (5.47)	24 060 (11)	
Asian (%)	6 (0.5)	2056 (0.94)	
Other (%)	16 (1.5)	787 (0.36)	
COPD (%)	225 (20.64)	35 280 (16.13)	0.09
ESRD (%)	95 (8.72)	15 376 (7.03)	0.31
CHF (%)	65 (5.96)	10 914 (4.99)	0.49
Liver Disease (%)	55 (5.05)	7, 655 (3.5)	0.2
DMcx (%)	25 (2.29)	3981 (1.82)	0.6
HTN (%)	600 (55.05)	117, 324 (53.64)	0.67
CCI (%)			0.23
0	652 (59.82)	130 119 (59.5)	
1	198 (18.8)	49 125 (22.46)	
2	135 (12.4)	20 035 (9.15)	
3	105 (9.63)	19 446 (8.89)	
Hospital size			0.34
Small (%)	61 (5.56)	48 607 (22.22)	
Medium (%)	61 (5.56)	70 305 (32.14)	
Large (%)	968 (88.9)	99 811 (45.63)	
Hospital region			0.75
Northeast (%)	225 (20.64)	47 748 (21.83)	
Midwest (%)	250 (22.94)	49, 738 (22.74)	
South (%)	460 (42.2)	85 390 (39.04)	
West (%)	155 (14.22)	35 849 (16.39)	
Insurance			0.06
Northeast (%)	473 (43.4)	93 439 (42.7)	
Midwest (%)	93 (8.49)	20 691 (9.46)	
South (%)	427 (39.15)	93 898 (42.93)	
West (%)	97 (8.90)	10 697 (4.89)	
Income			0.62
Medicare (%)	253 (23.20)	54 134 (24.75)	
Medicaid (%)	289 (26.51)	60 368 (27.60)	
Private insurance (%)	310 (28.44)	53 216 (24.33)	
Self-pay (%)	238 (21.8)	51 007 (23.32)	

Values are % except for age (mean + standard error mean).

CCI, Charlson comorbidity index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DMcx, complicated diabetes mellitus type 2; ESRD, end stage renal disease; HTN, hypertension; IBD, inflammatory bowel disease.

diverticulitis seen in the study.<sup>20</sup> With regard to baseline characteristics, age was significantly different, while female gender and race were similar between the cohorts (Table 1).

Interestingly, there was a 26.5% increase in median LOS and 30.4% increase in cost of hospitalization with UC compared to CD. In addition, there were 50% more deaths with UC *versus* CD, which may be a result of emergent surgery.<sup>11</sup> Overall, UC compared to CD was also associated with worse hospitalization outcomes on multivariate logistic regression. However, there was no significant difference in mortality.

Of the IBD subtypes, CD appears to have the more favorable hospitalization profile. Moreover, despite having 30% fewer patients, the UC cohort had 20 colectomies performed, with a longer and costlier hospital course. The CCI indicates that UC patients are not inherently more ill, and the outcome of this hospitalization is a result of events that occur during the course of the admission. Thus, the colectomies may be a reasonable explanation for the hospital measures seen above as mortality is typically higher in these patients.<sup>11</sup> However, whether these surgeries occurred as a result of severe diverticular disease or UC warrants further investigation as it cannot be determined with the NIS database.

Given the above findings, an alternate analysis was conducted to compare CD hospitalization to the absence of IBD. Despite having 200× more patients, the population without IBD exhibited no significant difference among the LOS or cost of hospitalization. Multivariate logistic regression reflected these outcomes, demonstrating no association between the cohorts and increased mortality or hospitalization burden. There were colectomies performed in 0.5% of the population without IBD, so if this factor contributed to worsened hospitalization outcomes, it did not make as considerable an impact as in the UC cohort.

This is a meaningful study as hospitalization burden with these conditions is quite substantial<sup>14–16</sup> and may differ based on the type of IBD involved. In this work, diverticulitis with simultaneous UC had a greater financial debt compared to a similar cohort with either CD or the complete absence of IBD. Colectomies, performed for severe manifestations of disease, likely have a prominent role in these outcomes. As colectomy is a known treatment in UC, its use as therapy may understandably prolong hospitalization. While it is possible that colectomies were also performed for severe diverticular disease, this information cannot be gathered from these data. It is important to note that the expensive and prolonged hospital course associated with this phenomenon has not been previously investigated in the literature. As such, the utility of this work is twofold: to raise awareness of conditions that may necessitate a higher level of care and the subsequent implications such a study will yield for resource management in hospitals.

**Table 5** Effect of Crohn's disease *versus* absence of IBD on diverticulitis hospitalization

	Unadjusted odds ratio	95% CI	P value	Adjusted odds ratio	95% CI	P value
Died	2.22	0.55 to 9.05	0.26	2.47	0.59 to 10.36	0.22
Length of stay	0.03	−0.45 to 0.51	0.90	0.03	−0.47 to 0.54	0.91
Cost of hospitalization	−2438	−6865 to 1989	0.28	−2196	−6933 to 2539	0.36

CI, confidence interval; IBD, inflammatory bowel disease.

The NIS has several strengths and limitations that warrant consideration. With health-related information from 20% of non-federal hospitals, NIS has amassed a database that enables a representative study of the US population. These sample sizes are typically larger than hospital-funded studies; thus, the trends observed are difficult to dispute and provide a national overview of disease. However, NIS is an administrative database that is susceptible to coding inaccuracies.<sup>14</sup> Indeed, the database is limited to those conditions that possess an ICD-9 code. Without this, there is no definitive way to identify a condition (i.e. Segmental Colitis Associated Disease, SCAD). Moreover, as laboratory values, imaging, and histology are not available, verification of the aforementioned conditions is not possible with this database (i.e. SCAD vs diverticular colitis). Thus, if the World Health Organization originally coded a condition as UC or diverticular colitis, the authors assumed it was an accurate characterization. In addition, the indications for a procedure are not supplied by NIS. Moreover, while multivariate logistic regression did account for most confounders (listed in the methods), there is a possibility that residual confounding still exists. Finally, this database is not designed to determine risk factors or causation. Thus, prospective trials will be necessary to further explore all possible etiologies and clinical applications of these findings.

## Conclusions

In this national study, acute diverticulitis was examined with pre-existing IBD to determine if a difference in hospital outcome exists between UC and CD. There was a greater hospital burden observed in those with UC, which may be attributable to the colectomies that were performed. Moreover, there was a similar hospital burden among both those with CD and those without IBD, although for the latter, colectomies did not comprise as significant a proportion as for UC. The hospitalization outcomes of diverticulitis with concurrent IBD has not been presented in the literature, and this knowledge will assist clinicians in recognizing patients at higher risk of decompensation who will require greater resource utilization.

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