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The Risk of Mortality in Geriatric Patients with Emergent Regional Enteritis is 12-fold Greater than that in Adult Patients: Female Sex, Hospital Length of Stay and Surgery As other Risk Factors of Mortality

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Abstract

Background:The purpose of this study was to identify the risk factors associated with mortality in patients with regional enteritis.

Methods: This retrospective cohort study analyzed patients emergently admitted with the primary diagnosis of regional enteritis, using the National Inpatient Sample 2005-2014 database. Factors associated with mortality in patients who underwent an operation and patients who did not were determined using a multivariate logistic regression model.

Results: A total of 75,550 adult (ages 18-64 years) and 10,520 elderly (ages 65+ years) patients were studied. The mean (SD) ages for adult males and females were 36.95(12.35) and 38.93(12.42) years, respectively (P<0.001). The mean (SD) ages for elderly males and

females were 73.77 (6.80) and 74.55 (7.15) years, respectively.Among adults, the average hospital length of stay (HLOS) was 4.90 (5.44) days in the surviving and 20.13 (24.25) days in the deceased (P<0.001). Within the elderly population, the mean HLOS was 5.78 (5.91) days in the surviving and 16.41 (13.22) days in the deceased (P<0.001). Mortality rates were significantly higher in both adult (0.4%) and elderly patients (4.2%) who underwent an operation when compared to their non-operative counterparts (0.1% and 0.7%, respectively, P<0.001).Among all patients included in this study, age (95% CI of OR 1.03-1.05), female sex (95% CI of OR 1.08-1.95), presence of surgical procedure (95% CI of OR 1.25-2.51), increasing HLOS(95% CI of OR 1.00-1.02), bacterial infections (95% CI of OR 2.28-4.68), respiratory diseases (95% CI of OR 3.69-7.57), cardiac diseases (95% CI of OR 2.35-4.64), genitourinary system diseases (95% CI of OR 1.15-2.15), fluid and electrolyte disorders (95% CI of OR 1.00-1.90), platelet and white blood cell diseases(95% CI of OR 1.07-2.25), trauma, burns, and poisons (95% CI of OR 2.53-5.39) were found to be significant risk factors of mortality.

Conclusion:The overall proportion of mortality within elderly patients was 12 times that of adults. The elderly death rate was 10.5 times that of adults for patients that underwent surgery.Among all patients emergently admitted with the primary diagnosis of regional enteritis, age, female sex, presence of surgical procedure, increasing HLOS, bacterial infections, respiratory diseases, cardiac diseases, genitourinary system diseases, fluid and electrolyte disorders, platelet and white blood cell diseases, trauma, burns, and poisons were found to be significant risk factors of mortality.

Keywords: Regional Enteritis; Hospital Length of Stay; Emergency Admission Mortality; Geriatric

Introduction

Inflammatory bowel disease (IBD) includestwo major types of chronic inflammatory intestinal disorders: regional enteritis,otherwiseknown as Crohn's disease (CD), and ulcerative colitis (UC). This study focuses specifically on patients emergently admitted with the primary diagnosis of CD. Although the exact cause of CD is not known, more and more data points to CD being a result of a disruption in the intricate interplay between the immune system, gut microflora, and environmental factors.[1] The immunological nature of disease is becoming more apparent as many studies have recently investigated the systemic immunological implications of CD.[1–11] Increasing attention is being brought to this topic as the incidence of CD has been increasing over the last century, particularly in Europe and North America,[12] with a total annual treatment cost of $3.1 billion in the United States alone.[13] While many studies have investigated the systemic complications of CD, information on the associated risk factors of mortality is scarce. This study aims to shine a light on the relationships between different characteristics of CD patients and their association with mortality.

Methods

This retrospective cohort study was done using the 2005-2014 National Inpatient Sample (NIS) data on adult (ages 18-64) and elderly (ages 65+) patients emergently admitted with a primary diagnosis of regional enteritis. The following characteristics were gathered and analyzed for the purposes of this study: age, gender, race, income quartile, insurance status, hospital location, comorbidities (AIDS, alcohol abuse, deficiency anemias, rheumatoid arthritis, chronic blood loss, congestive heart failure, chronic pulmonary disease, coagulopathy,depression, uncomplicated diabetes, chronic complicated diabetes, drug abuse, hypertension,hypothyroidism, liver disease, lymphoma, fluid/electrolyte disorders, metastatic cancer, other neurological disorders, obesity, paralysis, peripheral vascular disease, psychoses, pulmonary circulation disorders, renal failure, solid tumor, peptic ulcer, valvular disease, weight loss), location of enteritis (unspecified site, small intestine, large intestine), invasive diagnostic procedures, surgical procedures, time to invasive diagnostic procedures, time to surgical procedures, hospital length of stay (HLOS), and total hospital charges. A 5-item modified frailty index was constructed to account for functional health status not being included in NIS data. The index ranges from 0 (most healthy/least frail) to 5 (most frail) and was created using cancer, renal failure,paralysis, coagulopathy or weight loss as characteristics representing partial or total loss offunctional health status.The International Classification of Diseases (ICD-9) codes, based on the World Health Organization's Ninth Revision, were used to identify patients with regional enteritis. The ICD-9 codes of surgical and invasive diagnostic proceduresare presented in Table 1.

Table 1. ICD -9 codes for procedures on emergently admitted patients with the primary diagnosis of regional enteritis

Digestive Surgical Procedure (ICD 9)
Operations on Esophagus (42.01-42.19, 42.31-42.99)
Operations on Stomach (43.0-44.03, 44.21-44.99)
Operations on Intestine (45.00-45.03, 45.30-46.99)
Operations on Appendix (47.01-47.99)
Operations on Rectum, Rectosigmoid, and Perirectal Tissue (48.0-48.1, 48.31-48.99)
Operations on Anus (49.01-49.12, 49.31-49.99)
Operations on Liver (50.0, 50.21-50.99)
Operations on Gallbladder and Biliary Tract (51.01-51.04, 51.21-51.99)
Operations on Pancreas (52.01-52.09, 52.21-52.99)
Operations on Hernia (53.00-53.9)
Operations on Other Operations on Abdominal Region (54.0-54.19, 54.3-54.99)
Digestive Invasive Diagnostic Procedure (ICD 9)
Invasive Diagnostic Procedure on Esophagus (42.21-42.29)
Invasive Diagnostic Procedure on Stomach (44.11-44.19)
Invasive Diagnostic Procedure on Intestine (45.11-45.29)
Invasive Diagnostic Procedure on Rectum, Rectosigmoid, and Perirectal Tissue (48.21-48.29)
Invasive Diagnostic Procedure on Anus (49.21-49.29)
Invasive Diagnostic Procedure on Liver (50.11-50.19)
Invasive Diagnostic Procedure on Gallbladder and Biliary Tract (51.10-51.19)
Invasive Diagnostic Procedure on Pancreas (52.11-52.19)
Invasive Diagnostic Procedure on Other Operations on Abdominal Region (54.21-54.29)

Statistical analysis

Statistical examinationwas utilized to describe the numerical findings. For everynumerical variable, the average, standard deviation (SD), and confidence interval (CO) at 95% were determined. Chi-square tests were used to compare the categorical variablesand t-tests employed for continuous variables. Multivariable logistic regression analysis was used to examine the relationship between different variables and mortality. P-values smaller than 0.05 were deemedsignificant. All calculationswere doneutilizingthe SPSS software version 24 (SPSS Inc., Chicago, IL) and R statistical software (Foundation for Statistical Computing, Vienna, Austria).

Results

Sex Categories

A total number of 75,550 adult patients (ages 18-64 years) who were emergently admitted with regional enteritis was included in the study. Within this population, there were 33,557 males and 41,993 females. The mean (SD) age for adult males in the study was 36.95 (12.35) years and the mean age (SD) for adult females was 38.93 (12.42) years. 10,520 elderly (ages 65+) patients were also included in this study. Within the elderly population, there were 3,800 males with mean (SD) age of 73.77 (6.80) years and 6,720 females with mean (SD) age of 74.55 (7.15) years. The first stratified analysis based on sex categories is present in Table 2.

For the adult patient population, sex differences were observed for race, income quartile, insurance, hospital location, comorbidities, and location of enteritis. The same differences were observed in the elderly population, however there was no significant sex difference in hospital location. Both adult and elderly males and females were more likely to be White. Elderly males and females were most commonly in income Quartile 4 and income Quartile 2, respectively. Adult males and females were least likely to be in income quartile 4. In the adult population, private insurance was the most common method of payment while Medicare was most common in the elderly. For both adult and elderly females, the following comorbidities were more likely to be seen compared to their male counterparts: deficiency anemias, rheumatoid arthritis, depression, hypertension, hypothyroidism, and fluid/electrolyte disorders. Within the adult population, females were observed to have more cases of congestive heart failure, chronic pulmonary disease, diabetes without complications, obesity, neurological disorders, peripheral vascular disorders, psychoses, and valvular disease. Elderly females had more cases of weight loss than elderly males. For both adult and elderly populations, males were observed to have more cases of alcohol abuse and renal failure than females. Adult males had more cases of AIDS, drug abuse, paralysis, and weight loss than adult females while elderly males had more cases of diabetes (with and without complications) and solid tumors than elderly females. For both adult and elderly populations, males had more cases of enteritis of the small intestine when compared with females. Females had more cases of enteritis of the large intestine or an unspecified site when compared with males. Adult and elderly female patients had more invasive

diagnostic procedures compared to their male counterparts. Adult and elderly males had more surgical procedures than their female counterparts. Adult females had a higher modified frailty index score than adult males while elderly males had a higher modified frailty index score than elderly females. Adult females had a longer time to invasive diagnostic procedure and time to surgical procedure than their male counterparts. Both adult and elderly females had a longer HLOS than males. Higher total charges were noted in adult males.

Table 2. Characteristics of emergency admitted patients with the primary diagnosis of regional enteritis stratified according to sex categories, NIS 2005-2014.

		Adult, N (%)			Elderly, N (%)		
		Male	Female	p	Male	Female	p
All Cases		**33,557 (44.4%)**	**41,993 (55.6%)**		**3,800 (36.1%)**	**6,720 (63.9%)**	
Race	**White**	21,113 (73.4%)	26,673 (74.6%)	**<0.001**	2,858 (86.9%)	4,970 (85.5%)	**0.004**
	Black	4,367 (15.2%)	5,964 (16.7%)		150 (4.6%)	362 (6.2%)	
	Hispanic	2,015 (7.0%)	1,858 (5.2%)		162 (4.9%)	311 (5.4%)	
	Asian/Pacific Islander	358 (1.2%)	308 (0.9%)		38 (1.2%)	63 (1.1%)	
	Native American	118 (0.4%)	154 (0.4%)		14 (0.4%)	13 (0.2%)	
	Other	794 (2.8%)	776 (2.2%)		67 (2.0%)	91 (1.6%)	
Income Quartile	**Quartile 1**	8,087 (24.6%)	10,792 (26.2%)	**<0.001**	779 (21.0%)	1,545 (23.4%)	**0.034**
	Quartile 2	8,270 (25.2%)	10,522 (25.5%)		967 (26.0%)	1,713 (25.9%)	
	Quartile 3	8,381 (25.5%)	10,422 (25.3%)		964 (25.9%)	1,643 (24.9%)	
	Quartile 4	8,090 (24.6%)	9,494 (23.0%)		1,007 (27.1%)	1,708 (25.8%)	
Insurance	**Private Insurance**	17,200 (51.4%)	21,949 (52.4%)	**<0.001**	427 (11.3%)	591 (8.8%)	**<0.001**
	Medicare	4,274 (12.8%)	6,045 (14.4%)		3,285 (86.6%)	6,022 (89.7%)	
	Medicaid	5,308 (15.9%)	8,682 (20.7%)		32 (0.8%)	46 (0.7%)	
	Self-Pay	4,487 (13.4%)	3,395 (8.1%)		11 (0.3%)	16 (0.2%)	
	No Charge	520 (1.6%)	368 (0.9%)		4 (0.1%)	7 (0.1%)	
	Other	1,670 (5.0%)	1,454 (3.5%)		36 (0.9%)	35 (0.5%)	
Hospital Location	**Rural**	3,119 (9.3%)	4,406 (10.5%)	**<0.001**	517 (13.6%)	906 (13.5%)	0.700
	Urban: Non-Teaching	12,831 (38.2%)	16,563 (39.4%)		1,746 (45.9%)	3,144 (46.8%)	
	Urban: Teaching	17,607 (52.5%)	21,024 (50.1%)		1,537 (40.4%)	2,670 (39.7%)	
Comorbidities	**AIDS**	73 (0.2%)	21 (0.1%)	**<0.001**	0 (0%)	1 (0.0%)	0.999
	Alcohol Abuse	942 (2.8%)	409 (1.0%)	**<0.001**	63 (1.7%)	37 (0.6%)	**<0.001**
	Deficiency Anemias	6,758 (20.1%)	11,259 (26.8%)	**<0.001**	925 (24.3%)	1,877 (27.9%)	**<0.001**
	Rheumatoid Arthritis	833 (2.5%)	1,581 (3.8%)	**<0.001**	108 (2.8%)	340 (5.1%)	**<0.001**
	Chronic Blood Loss	997 (3.0%)	1,319 (3.1%)	0.180	170 (4.5%)	289 (4.3%)	0.680
	Congestive Heart Failure	267 (0.8%)	405 (1.0%)	**0.014**	345 (9.1%)	602 (9.0%)	0.840
	Chronic Pulmonary Disease	2,626 (7.8%)	5,175 (12.3%)	**<0.001**	758 (19.9%)	1,423 (21.2%)	0.140
	Coagulopathy	536 (1.6%)	668 (1.6%)	0.940	154 (4.1%)	193 (2.9%)	**0.001**
	Depression	3,268 (9.7%)	7,708 (18.4%)	**<0.001**	320 (8.4%)	972 (14.5%)	**<0.001**
	Diabetes, Uncomplicated	1,553 (4.6%)	2,556 (6.1%)	**<0.001**	762 (20.1%)	1,130 (16.8%)	**<0.001**
	Diabetes, Chronic Complications	198 (0.6%)	261 (0.6%)	0.580	111 (2.9%)	146 (2.2%)	**0.017**

		Adult, N (%)			Elderly, N (%)		
		Male	Female	p	Male	Female	p
All Cases		**33,557 (44.4%)**	**41,993 (55.6%)**		**3,800 (36.1%)**	**6,720 (63.9%)**	
Comorbidities	**Drug Abuse**	2,356 (7.0%)	2,038 (4.9%)	**<0.001**	26 (0.7%)	44 (0.7%)	0.860
	Hypertension	5,658 (16.9%)	8,087 (19.3%)	**<0.001**	2,259 (59.4%)	4,205 (62.6%)	**0.002**
	Hypothyroidism	512 (1.5%)	2,618 (6.2%)	**<0.001**	321 (8.4%)	1,362 (20.3%)	**<0.001**
	Liver Disease	856 (2.6%)	1,033 (2.5%)	0.430	107 (2.8%)	174 (2.6%)	0.490
	Lymphoma	57 (0.2%)	63 (0.2%)	0.500	32 (0.8%)	48 (0.7%)	0.470
	Fluid/Electrolyte Disorders	9,235 (27.5%)	15,114 (36.0%)	**<0.001**	1,518 (39.9%)	3,243 (48.3%)	**<0.001**
	Metastatic Cancer	48 (0.1%)	78 (0.2%)	0.150	41 (1.1%)	64 (1.0%)	0.530
	Other Neurological Disorders	922 (2.7%)	1,524 (3.6%)	**<0.001**	221 (5.8%)	401 (6.0%)	0.750
	Obesity	1,094 (3.3%)	2,817 (6.7%)	**<0.001**	181 (4.8%)	375 (5.6%)	0.070
	Paralysis	111 (0.3%)	102 (0.2%)	**0.024**	41 (1.1%)	50 (0.7%)	0.080
	Peripheral Vascular Disorders	260 (0.8%)	390 (0.9%)	**0.023**	287 (7.6%)	477 (7.1%)	0.390
	Psychoses	1,491 (4.4%)	2,201 (5.2%)	**<0.001**	76 (2.0%)	168 (2.5%)	0.100
	Pulmonary Circulation Disorders	112 (0.3%)	166 (0.4%)	0.170	63 (1.7%)	108 (1.6%)	0.840
	Renal Failure	610 (1.8%)	592 (1.4%)	**<0.001**	535 (14.1%)	630 (9.4%)	**<0.001**
	Solid Tumor	100 (0.3%)	120 (0.3%)	0.760	105 (2.8%)	85 (1.3%)	**<0.001**
	Peptic Ulcer	46 (0.1%)	50 (0.1%)	0.490	3 (0.1%)	10 (0.1%)	0.400
	Valvular Disease	242 (0.7%)	513 (1.2%)	**<0.001**	177 (4.7%)	361 (5.4%)	0.110
	Weight Loss	3,247 (9.7%)	3,692 (8.8%)	**<0.001**	419 (11.0%)	884 (13.2%)	**0.001**
Regional Enteritis	**Unspecified Site**	18,975 (56.5%)	24,166 (57.5%)	**<0.001**	1,760 (46.3%)	3,120 (46.4%)	**<0.001**
	Small Intestine	9,394 (28.0%)	10,358 (24.7%)		1,201 (31.6%)	1,675 (24.9%)	
	Large Intestine	5,188 (15.5%)	7,469 (17.8%)		839 (22.1%)	1,925 (28.6%)	
Invasive Diagnostic Procedure		8,569 (25.5%)	11,465 (27.3%)	**<0.001**	1,202 (31.6%)	2,271 (33.8%)	**0.023**
Surgical Procedure		4,508 (13.4%)	4,611 (11.0%)	**<0.001**	602 (15.8%)	855 (12.7%)	**<0.001**
Invasive or Surgical Procedure		11,653 (34.7%)	14,490 (34.5%)	0.530	1,533 (40.3%)	2,750 (40.9%)	0.560
Deceased		39 (0.1%)	41 (0.1%)	0.430	56 (1.5%)	67 (1.0%)	**0.029**
		Mean (SD)	**Mean (SD)**	**p**	**Mean (SD)**	**Mean (SD)**	**p**
Age, Years		36.95 (12.35)	38.93 (12.42)	**<0.001**	73.77 (6.80)	74.55 (7.15)	**<0.001**
Modified Frailty Index Score		0.44 (0.70)	0.51 (0.75)	**<0.001**	1.41 (1.05)	1.37 (1.01)	**0.037**
Time to Invasive Diagnostic Procedure, Days		2.60 (2.94)	2.73 (2.82)	**0.003**	2.71 (2.75)	2.90 (2.94)	0.080
Time to Surgical Procedure, Days		3.30 (4.92)	3.52 (4.58)	**0.039**	3.46 (4.23)	3.62 (4.26)	0.500
Length of Stay, Days		4.83 (5.52)	4.99 (5.52)	**<0.001**	5.75 (6.31)	5.99 (6.06)	**0.048**
Total Charges, Dollars		29,155 (45,779)	28,372 (39,866)	**0.014**	34,393 (51,734)	34,111 (49,557)	0.790

Mortality

In the adult sample, 75,490 (99.9%) of patients survived while 80 (0.1%) expired. The mean (SD) age of adult patients in the survivor group was 38.03 (12.42) years while mean (SD) age of those within the deceased group was 49.53 (11.87) years. The mean (SD) age of elderly patients in the survivor group was 74.24 (7.02) years while that of those in the deceased group was 76.32 (7.56) years. The overall rate of mortality among the elderly population (1.2%) was 12 times higher than the rate of mortality among adult patients (0.1%). Among both adult and elderly populations, deceased patients were observed to have more of the following comorbidities than surviving patients: congestive heart failure, coagulopathy, fluid/electrolyte disorders, metastatic cancer, pulmonary circulation disorders, renal failure, and weight loss. In the adult population, deceased patients had more chronic blood loss, diabetes (uncomplicated), liver disease, peripheral vascular disorders, and peptic ulcer. In the elderly population, depression and hypertension were seen more in the surviving group compared to the deceased. In all patients, surgical or invasive procedures were more often seen in the deceased groups compared to surviving groups. In the adult population, invasive diagnostic procedures were more prevalent in the deceased sample than in the surviving sample. Age, modified frailty index score, time to invasive diagnostic procedure, time to surgical procedure, HLOS, and total charges were significantly higher in the deceased contrasted to the surviving group within all patient populations. These characteristics are presented, and other analysis based on outcome categories are presented in Table 3.

Table 3. Characteristics of patients with the primary diagnosis of regional enteritis admitted emergently classified based on survival status, NIS 2005-2014.

		Adult, N (%)			Elderly, N (%)		
		Survived	Deceased	p	Survived	Deceased	p
All Cases		**75,490 (99.9%)**	**80 (0.1%)**		**10,393 (98.8%)**	**123 (1.2%)**	
Sex, Female		**41,938 (55.6%)**	**41 (51.2%)**	**0.430**	**6,648 (64.0%)**	**67 (54.5%)**	**0.029**
Race	**White**	47,719 (74.1%)	49 (80.3%)	0.470	7,731 (86.0%)	94 (93.1%)	0.180
	Black	10,321 (16.0%)	6 (9.8%)		505 (5.6%)	6 (5.9%)	
	Hispanic	3,871 (6.0%)	2 (3.3%)		473 (5.3%)	0 (0%)	
	Asian/Pacific Islander	665 (1.0%)	1 (1.6%)		101 (1.1%)	0 (0%)	
	Native American	272 (0.4%)	0 (0%)		27 (0.3%)	0 (0%)	
	Other	1,567 (2.4%)	3 (4.9%)		157 (1.7%)	1 (1.0%)	
Income Quartile	**Quartile 1**	18,853 (25.5%)	24 (30.4%)	0.440	2,300 (22.5%)	24 (20.0%)	0.870
	Quartile 2	18,760 (25.4%)	22 (27.8%)		2,643 (25.9%)	34 (28.3%)	
	Quartile 3	18,786 (25.4%)	20 (25.3%)		2,576 (25.2%)	29 (24.2%)	
	Quartile 4	17,604 (23.8%)	13 (16.5%)		2,683 (26.3%)	33 (27.5%)	
Insurance	**Private Insurance**	39,130 (52.0%)	41 (51.2%)	0.190	1,005 (9.7%)	13 (10.6%)	0.180
	Medicare	10,299 (13.7%)	17 (21.3%)		9,198 (88.6%)	105 (85.4%)	
	Medicaid	13,979 (18.6%)	14 (17.5%)		77 (0.7%)	1 (0.8%)	
	Self-Pay	7,883 (10.5%)	4 (5.0%)		26 (0.3%)	1 (0.8%)	
	No Charge	885 (.2%)	2 (2.5%)		11 (0.1%)	0 (0%)	
	Other	3,116 (4.1%)	2 (2.5%)		68 (0.7%)	3 (2.4%)	
Hospital Location	**Rural**	7,511 (9.9%)	6 (7.5%)	0.750	1,411 (13.6%)	11 (8.9%)	0.270
	Urban: Non-Teaching	29,367 (38.9%)	31 (38.8%)		4,830 (46.5%)	57 (46.3%)	
	Urban: Teaching	38,612 (51.1%)	43 (53.8%)		4,152 (39.9%)	55 (44.7%)	

		Adult, N (%)			Elderly, N (%)		
		Survived	Deceased	p	Survived	Deceased	p
All Cases		**75,490 (99.9%)**	**80 (0.1%)**		**10,393 (98.8%)**	**123 (1.2%)**	
Sex, Female		**41,938 (55.6%)**	**41 (51.2%)**	**0.430**	**6,648 (64.0%)**	**67 (54.5%)**	**0.029**
Comorbidities	**AIDS**	93 (0.1%)	1 (1.3%)	0.100	1 (0.0%)	0 (0%)	0.999
	Alcohol Abuse	1,344 (1.8%)	3 (3.8%)	0.170	99 (1.0%)	1 (0.8%)	0.999
	Deficiency Anemias	17,993 (23.8%)	19 (23.8%)	0.990	2,775 (26.7%)	26 (21.1%)	0.170
	Rheumatoid Arthritis	2,407 (3.2%)	5 (6.3%)	0.120	445 (4.3%)	1 (0.8%)	0.070
	Chronic Blood Loss	2,311 (3.1%)	6 (7.5%)	**0.021**	453 (4.4%)	6 (4.9%)	0.780
	Congestive Heart Failure	667 (0.9%)	5 (6.3%)	**<0.001**	901 (8.7%)	46 (37.4%)	**<0.001**
	Chronic Pulmonary Disease	7,782 (10.3%)	13 (16.3%)	0.080	2,153 (20.7%)	28 (22.8%)	0.580
	Coagulopathy	1,177 (1.6%)	26 (32.5%)	**<0.001**	328 (3.2%)	19 (15.4%)	**<0.001**
	Depression	10,964 (14.5%)	7 (8.8%)	0.140	1,285 (12.4%)	5 (4.1%)	**0.005**
	Diabetes, Uncomplicated	4,096 (5.4%)	10 (12.5%)	**0.005**	1,876 (18.1%)	16 (13.0%)	0.150
	Diabetes, Chronic Complications	458 (0.6%)	1 (1.3%)	0.390	257 (2.5%)	0 (0%)	0.080
	Drug Abuse	4,387 (5.8%)	3 (3.8%)	0.630	70 (0.7%)	0 (0%)	0.999
	Hypertension	13,710 (18.2%)	26 (32.5%)	**<0.001**	6,401 (61.6%)	61 (49.6%)	**0.007**
	Hypothyroidism	3,127 (4.1%)	3 (3.8%)	0.999	1,671 (16.1%)	12 (9.8%)	0.060
	Liver Disease	1,883 (2.5%)	6 (7.5%)	**0.004**	277 (2.7%)	4 (3.3%)	0.570
	Lymphoma	120 (0.2%)	0 (0%)	0.999	80 (0.8%)	0 (0%)	0.999
	Fluid/Electrolyte Disorders	24,288 (32.2%)	52 (65.0%)	**<0.001**	4,684 (45.1%)	75 (61.0%)	**<0.001**
	Metastatic Cancer	124 (0.2%)	2 (2.5%)	**0.008**	96 (0.9%)	9 (7.3%)	**<0.001**
	Other Neurological Disorders	2,440 (3.2%)	4 (5.0%)	0.330	609 (5.9%)	12 (9.8%)	0.070
	Obesity	3,907 (5.2%)	4 (5.0%)	0.999	553 (5.3%)	3 (2.4%)	0.220
	Paralysis	212 (0.3%)	1 (1.3%)	0.200	89 (0.9%)	2 (1.6%)	0.290
	Peripheral Vascular Disorders	647 (0.9%)	3 (3.8%)	**0.032**	754 (7.3%)	10 (8.1%)	0.710
	Psychoses	3,679 (4.9%)	7 (8.8%)	0.110	239 (2.3%)	4 (3.3%)	0.370
	Pulmonary Circulation Disorders	269 (0.4%)	7 (8.8%)	**<0.001**	162 (1.6%)	9 (7.3%)	**<0.001**
	Renal Failure	1,193 (1.6%)	8 (10.0%)	**<0.001**	1,139 (11.0%)	25 (20.3%)	**<0.001**
	Solid Tumor	220 (0.3%)	0 (0%)	0.999	188 (1.8%)	2 (1.6%)	0.999
	Peptic Ulcer	93 (0.1%)	2 (2.5%)	**0.005**	13 (0.1%)	0 (0%)	0.999
	Valvular Disease	753 (1.0%)	1 (1.3%)	0.550	529 (5.1%)	9 (7.3%)	0.270
	Weight Loss	6,899 (9.1%)	36 (45.0%)	**<0.001**	1,254 (12.1%)	49 (39.8%)	**<0.001**

		Adult, N (%)			Elderly, N (%)		
		Survived	Deceased	p	Survived	Deceased	p
All Cases		**75,490 (99.9%)**	**80 (0.1%)**		**10,393 (98.8%)**	**123 (1.2%)**	
Sex, Female		**41,938 (55.6%)**	**41 (51.2%)**	**0.430**	**6,648 (64.0%)**	**67 (54.5%)**	**0.029**
Regional Enteritis	**Unspecified Site**	43,096 (57.1%)	51 (63.7%)	0.470	4,825 (46.4%)	53 (43.1%)	0.430
	Small Intestine	19,745 (26.2%)	17 (21.3%)		2,834 (27.3%)	40 (32.5%)	
	Large Intestine	12,649 (16.8%)	12 (15.0%)		2,734 (26.3%)	30 (24.4%)	
Invasive Diagnostic Procedure		20,009 (26.5%)	30 (37.5%)	**0.026**	3,436 (33.1%)	36 (29.3%)	0.370
Surgical Procedure		9,080 (12.0%)	39 (48.8%)	**<0.001**	1,395 (13.4%)	61 (49.6%)	**<0.001**
Invasive or Surgical Procedure		26,098 (34.6%)	51 (63.7%)	**<0.001**	4,207 (40.5%)	75 (61.0%)	**<0.001**
		Mean (SD)	**Mean (SD)**	**p**	**Mean (SD)**	**Mean (SD)**	**p**
Age, Years		38.03 (12.42)	49.53 (11.87)	**<0.001**	74.24 (7.02)	76.32 (7.56)	**0.001**
Modified Frailty Index Score		0.48 (0.73)	1.33 (0.82)	**<0.001**	1.38 (1.02)	1.87 (1.16)	**<0.001**
Time to Invasive Diagnostic Procedure, Days		2.66 (2.77)	13.33 (17.98)	**0.008**	2.80 (2.78)	6.35 (8.10)	**0.035**
Time to Surgical Procedure, Days		3.38 (4.65)	10.26 (13.78)	**0.004**	3.42 (4.05)	6.76 (6.85)	**<0.001**
Length of Stay, Days		4.90 (5.44)	20.13 (24.25)	**<0.001**	5.78 (5.91)	16.41 (13.22)	**<0.001**
Total Charges, Dollars		28,560 (41,674)	183,200 (228,408)	**<0.001**	32,865 (45,755)	148,799 (163,818)	**<0.001**

Operation Status

Statistical analysis based on operation status is present in Table 4. In the adult population, 9,122 (12.1%) patients underwent an operation while 66,492 (87.9%) patients did not. In the elderly population, 1,457 (13.8%) patients underwent surgery while 9,064 (86.2%) patients did not. Among patients that underwent surgery, mortality rate was 10.5 times greater in the elderly (4.2%) compared to adults (0.4%). Among all patients included in this study, patients in both the surgical and non-surgical groups were more likely to be White. Among adult patients, income Quartile 1 was most common in the non-operative group while income Quartile 3 was most common in the operative group. Private insurance was the most common method of payment for adults in both surgical and non-surgical groups. Among the adult population, urban teaching hospitals were the most common hospital location for patients in both surgical and non-surgical groups. Both adult and elderly surgical groups had a higher proportion of patients with the following comorbidities: chronic blood loss, congestive heart failure, coagulopathy, pulmonary circulation disorders, and weight loss. Adults in the surgical group included a higher proportion of patients with deficiency anemias, metastatic cancer, peripheral vascular disorders, solid tumor, and peptic ulcer. Rheumatoid arthritis, depression, diabetes (uncomplicated) hypertension, and neurological disorders were observed more commonly in the non-operative group within both adult and elderly populations. Drug abuse, hypothyroidism, liver disease, and psychoses were observed more commonly in the non-surgical group within the adult population. The most observed description of the location of regional enteritis was unspecified for the adult surgical and adult non-surgical. The most common location of regional enteritis within the elderly surgical group was the small intestine. Among all patients in the study, there were more invasive diagnostic procedures and deaths observed in patients who underwent surgery. Furthermore, all patients who had an operation generally had a higher modified frailty index, time to invasive diagnostic procedure, HLOS, and total charges.

Table 4. Characteristics of emergency admitted patients with the primary diagnosis of regional enteritis. Data was stratified according to operation status, NIS 2005-2014.

		Adult, N (%)			Elderly, N (%)		
		No Operation	Operation	p	No Operation	Operation	p
All Cases		**66,492 (87.9%)**	**9,122 (12.1%)**		**9,064 (86.2%)**	**1,457 (13.8%)**	
Sex, Female		**37,382 (56.3%)**	**4,611 (50.6%)**	**<0.001**	**5,865 (64.7%)**	**855 (58.7%)**	**<0.001**
Race	**White**	41,884 (73.8%)	5,904 (76.4%)	**<0.001**	6,770 (86.1%)	1,058 (85.5%)	**0.001**
	Black	9,248 (16.3%)	1,083 (14.0%)		444 (5.6%)	68 (5.5%)	
	Hispanic	3,490 (6.1%)	383 (5.0%)		420 (5.3%)	53 (4.3%)	
	Asian/Pacific Islander	585 (1.0%)	81 (1.0%)		82 (1.0%)	19 (1.5%)	
	Native American	239 (0.4%)	33 (0.4%)		17 (0.2%)	10 (0.8%)	
	Other	1,326 (2.3%)	244 (3.2%)		129 (1.6%)	29 (2.3%)	
Income Quartile	**Quartile 1**	16,803 (25.8%)	2,085 (23.3%)	**<0.001**	1,988 (22.5%)	326 (22.8%)	0.560
	Quartile 2	16,487 (25.3%)	2,312 (25.8%)		2,295 (25.8%)	385 (26.9%)	
	Quartile 3	16,455 (25.2%)	2,360 (26.4%)		2,243 (25.2%)	364 (25.5%)	
	Quartile 4	15,429 (23.7%)	2,190 (24.5%)		2,361 (26.5%)	355 (24.8%)	
Insurance	**Private Insurance**	33,849 (51.0%)	5,345 (58.8%)	**<0.001**	873 (9.6%)	145 (10.0%)	0.910
	Medicare	9,434 (14.2%)	886 (9.7%)		8,026 (88.6%)	1,282 (88.0%)	
	Medicaid	12,494 (18.8%)	1,504 (16.5%)		64 (0.7%)	14 (1.0%)	
	Self-Pay	7,048 (10.6%)	840 (9.2%)		23 (0.3%)	4 (0.3%)	
	No Charge	768 (1.2%)	120 (1.3%)		10 (0.1%)	1 (0.1%)	
	Other	2,726 (4.1%)	402 (4.4%)		61 (0.7%)	10 (0.7%)	
Hospital Location	**Rural**	6,891 (10.4%)	636 (7.0%)	**<0.001**	1,241 (13.7%)	182 (12.5%)	0.270
	Urban: Non-Teaching	26,263 (39.5%)	3,153 (34.6%)		4,222 (46.6%)	668 (45.8%)	
	Urban: Teaching	33,338 (50.1%)	5,333 (58.5%)		3,601 (39.7%)	607 (41.7%)	
Comor-bidities	**AIDS**	80 (0.1%)	12 (0.2%)	0.400	1 (0.0%)	0 (0%)	0.999
	Alcohol Abuse	1,208 (1.8%)	143 (1.6%)	0.090	81 (0.9%)	19 (1.3%)	0.130
	Deficiency Anemias	15,508 (23.3%)	2,511 (27.5%)	**<0.001**	2,385 (26.3%)	417 (28.6%)	0.060
	Rheumatoid Arthritis	2,213 (3.3%)	201 (2.2%)	**<0.001**	402 (4.4%)	46 (3.2%)	**0.025**
	Chronic Blood Loss	2,005 (3.0%)	312 (3.4%)	**0.035**	377 (4.2%)	82 (5.6%)	**0.011**
	Congestive Heart Failure	573 (0.9%)	99 (1.1%)	**0.033**	790 (8.7%)	157 (10.8%)	**0.011**
	Chronic Pulmonary Disease	6,901 (10.4%)	901 (9.9%)	0.140	1,853 (20.4%)	328 (22.5%)	0.070
	Coagulopathy	945 (1.4%)	259 (2.8%)	**<0.001**	280 (3.1%)	67 (4.6%)	**0.003**
	Depression	9,946 (15.0%)	1,031 (11.3%)	**<0.001**	1,144 (12.6%)	148 (10.2%)	**0.008**
	Diabetes, Uncomplicated	3,708 (5.6%)	401 (4.4%)	**<0.001**	1,668 (18.4%)	224 (15.4%)	**0.005**
	Diabetes, Chronic Com-plications	404 (0.6%)	55 (0.6%)	0.960	219 (2.4%)	38 (2.6%)	0.660
	Drug Abuse	4,031 (6.1%)	363 (4.0%)	**<0.001**	61 (0.7%)	9 (0.6%)	0.810

		Adult, N (%)			Elderly, N (%)		
		No Operation	Operation	p	No Operation	Operation	p
All Cases		**66,492 (87.9%)**	**9,122 (12.1%)**		**9,064 (86.2%)**	**1,457 (13.8%)**	
Sex, Female		**37,382 (56.3%)**	**4,611 (50.6%)**	**<0.001**	**5,865 (64.7%)**	**855 (58.7%)**	**<0.001**
Comorbidities	**Hypertension**	12,247 (18.4%)	1,499 (16.4%)	**<0.001**	5,615 (61.9%)	849 (58.3%)	**0.007**
	Hypothyroidism	2,832 (4.3%)	299 (3.3%)	**<0.001**	1,463 (16.1%)	220 (15.1%)	0.310
	Liver Disease	1,709 (2.6%)	180 (2.0%)	**<0.001**	243 (2.7%)	38 (2.6%)	0.870
	Lymphoma	105 (0.2%)	15 (0.2%)	0.880	75 (0.8%)	5 (0.3%)	**0.048**
	Fluid/Electrolyte Disorders	21,625 (32.5%)	2,728 (29.9%)	**<0.001**	4,067 (44.9%)	694 (47.6%)	**0.049**
	Metastatic Cancer	97 (0.1%)	29 (0.3%)	**<0.001**	91 (1.0%)	14 (1.0%)	0.880
	Other Neurological Disorders	2,223 (3.3%)	223 (2.4%)	**<0.001**	554 (6.1%)	68 (4.7%)	**0.030**
	Obesity	3,476 (5.2%)	435 (4.8%)	0.060	474 (5.2%)	82 (5.6%)	0.530
	Paralysis	186 (0.3%)	27 (0.3%)	0.780	72 (0.8%)	19 (1.3%)	0.051
	Peripheral Vascular Disorders	539 (0.8%)	111 (1.2%)	**<0.001**	649 (7.2%)	115 (7.9%)	0.320
	Psychoses	3,335 (5.0%)	357 (3.9%)	**<0.001**	202 (2.2%)	42 (2.9%)	0.120
	Pulmonary Circulation Disorders	198 (0.3%)	80 (0.9%)	**<0.001**	136 (1.5%)	35 (2.4%)	**0.012**
	Renal Failure	1,069 (1.6%)	133 (1.5%)	0.280	1,024 (11.3%)	141 (9.7%)	0.070
	Solid Tumor	182 (0.3%)	38 (0.4%)	**0.018**	157 (1.7%)	33 (2.3%)	0.160
	Peptic Ulcer	78 (0.1%)	18 (0.2%)	**0.044**	12 (0.1%)	1 (0.1%)	0.999
	Valvular Disease	649 (1.0%)	106 (1.2%)	0.090	451 (5.0%)	87 (6.0%)	0.110
	Weight Loss	5,293 (8.0%)	1,647 (18.1%)	**<0.001**	970 (10.7%)	333 (22.9%)	**<0.001**
Regional Enteritis	**Unspecified Site**	39,007 (58.7%)	4,169 (45.7%)	**<0.001**	4,421 (48.8%)	460 (31.6%)	**<0.001**
	Small Intestine	16,408 (24.7%)	3,364 (36.9%)		2,272 (25.1%)	604 (41.5%)	
	Large Intestine	11,077 (16.7%)	1,589 (17.4%)		2,371 (26.2%)	393 (27.0%)	
Invasive Diagnostic Procedure		17,041 (25.6%)	3,010 (33.0%)	**<0.001**	2,826 (31.2%)	647 (44.4%)	**<0.001**
Deceased		41 (0.1%)	39 (0.4%)	**<0.001**	62 (0.7%)	61 (4.2%)	**<0.001**
		Mean (SD)	**Mean (SD)**	**p**	**Mean (SD)**	**Mean (SD)**	**p**
Age, Years		38.05 (12.37)	37.98 (12.87)	0.600	74.31 (7.08)	74.01 (6.70)	0.120
Modified Frailty Index Score		0.47 (0.73)	0.54 (0.74)	**<0.001**	1.37 (1.02)	1.45 (1.02)	**0.010**
Time to Invasive Diagnostic Procedure, Days		2.54 (2.36)	3.49 (4.84)	**<0.001**	2.72 (2.47)	3.34 (4.27)	**0.001**
Length of Stay, Days		4.12 (3.60)	10.73 (10.93)	**<0.001**	4.98 (4.47)	11.64 (10.53)	**<0.001**
Total Charges, Dollars		22,787 (24,974)	71,775 (91,334)	**<0.001**	26,894 (32,729)	79,711 (96,127)	**<0.001**

Risk Factors of Mortality

The multivariable logistic regression model with mortality as the dependent variable was built separately for all patients emergently admitted with a primary diagnosis of regional enteritis. (Table 5) Among all patients, age, female sex, presence of surgical procedure, increasing HLOS, bacterial infections, respiratory diseases, cardiac diseases, genitourinary system diseases, fluid and electrolyte disorders, platelet and white blood cell diseases, trauma, burns, and poisons were deemed significantly correlated with mortality.

Table 5. Backward logistic regression analysis evaluating the associations between mortality, the dependent variable, and various risk factors in patients emergently admitted with a primary diagnosis of regional enteritis (NIS 2005-2014).

Patients' Characteristics	Mortality	
	N = 86,019	R^2 = 0.368
	OR (95% CI)	P
Number of Events	N = 203	
Age, Years	1.04 (1.03, 1.05)	<0.001
Surgical Procedure	1.78 (1.25, 2.51)	0.001
Hospital Length of Stay, Days	1.01 (1.00, 1.02)	0.003
Sex, Female	1.45 (1.08, 1.95)	0.014
Bacterial Infections (Other than Tuberculosis)	3.26 (2.28, 4.68)	<0.001
Respiratory Diseases	5.28 (3.69, 7.57)	<0.001
Cardiac Diseases	3.31 (2.35, 4.64)	<0.001
Genitourinary System Diseases	1.57 (1.15, 2.15)	0.005
Fluid and Electrolyte Disorders	1.38 (1.00, 1.90)	0.047
Platelet and White Blood Cell Diseases	1.56 (1.07, 2.25)	0.019
Trauma, Burns, and Poisons	3.69 (2.53, 5.39)	<0.001
Coagulopathy	Removed Via Stepwise Backward Elimination	
Regional Enteritis Location		
Invasive Procedure		
Peripheral Vascular Diseases		
Liver Diseases		
Neoplasms		
Neurological Diseases		
Cerebrovascular Diseases		
Tuberculosis		
Nonbacterial Infections		
Anemia and/or Hemorrhage	Removed Via Stepwise Backward Elimination	
Digestive Diseases other than Liver		
Diabetes		
Drug Abuse/Withdrawal/ Dependence		
Alcohol Abuse/Withdrawal/ Dependence		
Tobacco Use		
Hypertension		
Endocrine Diseases		
Nutritional/Weight Disorders		
Musculoskeletal System and Connective Tissue Diseases		
Psychiatric Diseases		
Skin Diseases		
Long Term Medication Usage		
Diseases of Oral Cavity, Salivary Glands, and Jaw		
Sleep Disorders		
Lack of Physical Evidence		
Inappropriate Diet and Eating Habits		
High Risk Lifestyle Behaviors		
Social Factors		

Table 6: Secondary diagnoses of patients emergently admitted with a primary diagnosis of regional enteritis (NIS 2005-2014). Data was stratified according to survival status

	Adult, N (%)			Elderly, N (%)		
Comorbidities and Secondary Diagnoses (ICD-9 Codes)	**Survived**	**Deceased**	**p-value**	**Survived**	**Deceased**	**p-value**
Observations	**75,490 (99.9)**	**80 (0.1)**		**10,393 (99)**	**123 (1)**	
Tuberculosis (010.0-018.96)	38 (0.1)	1 (1.3)	**<0.001**	0 (0)	0 (0)	
Bacterial Infections Other than Tuberculosis (020.0-041.9, 790.7)	3,138 (4)	43 (54)	**<0.001**	696 (7)	53 (43)	**<0.001**
Nonbacterial Infections (042, 795.71, V08, 045.0-139.8, 790.8, and/or presence of Comorbidity of AIDS)	3,792 (5)	23 (29)	**<0.001**	466 (5)	14 (11)	**<0.001**
Diabetes (250.0-250.93, V58.67, and/or presence of Comorbidity of Diabetes Uncomplicated or Diabetes Chronic Complications)	4,595 (6)	11 (14)	**0.004**	2,141 (21)	16 (13)	**0.038**
Hypertension (401.0-405.99, 796.2, and/or presence of Comorbidity of Hypertension)	13,896 (18)	26 (33)	**0.001**	6,420 (62)	61 (50)	**0.006**
Anemia and/or Hemorrhage (280.0-285.9, 784.7, 784.8, and/or presence of Comorbidity of Anemia)	22,459 (30)	44 (55)	**<0.001**	3,821 (37)	53 (43)	0.150
Respiratory Diseases (415.0-417.9, 460-519.9, 784.91, 786, and/or presence of Comorbidity of COPD, ILD or Pulmonary Circulation Disease)	11,608 (15)	61 (76)	**<0.001**	3,024 (29)	98 (80)	**<0.001**
Coagulopathy (286.0-286.9, 790.92, V58.61, V58.63, and/or presence of Comorbidity of Coagulopathy)	2,465 (3)	27 (34)	**<0.001**	1,024 (10)	26 (21)	**<0.001**
Cardiac Diseases (391.X, 392.0, 393.398.99, 410.0-414.9, 420.0-429.9, 794.3X, 785.XX, and/or presence of Comorbidity of CHF or Valvular Diseases)	7,357 (10)	52 (65)	**<0.001**	4,157 (40)	93 (76)	**<0.001**
Cerebrovascular Diseases (325, 430-438)w	238 (0.3)	3 (4)	**<0.001**	255 (3)	6 (5)	0.090
Peripheral Vascular Diseases (440-457.9, and/or presence of Comorbidity of Peripheral Vascular Disorders)	5,442 (7)	15 (19)	**<0.001**	1,757 (17)	24 (20)	0.440
Liver Diseases (570-573.9, 790.4, 794.8, and/or presence of Comorbidity of Liver Diseases)	2,940 (4)	14 (18)	**<0.001**	420 (4)	6 (5)	0.640
Diseases of Digestive System other than Liver (530.00-569.9, 574.0-579.9, 787, 001.0-009.3, and/or presence of Comorbidity of Peptic Ulcer)	49,335 (65)	65 (81)	**0.003**	8,071 (78)	103 (84)	0.110
Diseases of Oral Cavity, Salivary Glands, and Jaws (520-529)	585 (1)	0 (0)	0.430	57 (0.5)	1 (0.8)	0.690
Nutritional/Weight Disorders (260-273.9, 275.XX,277.0-278.8, 783.XX, 799.3-799.4, and/or presence of Comorbidity of Weight Loss)	19,533 (26)	49 (61)	**<0.001**	5,215 (50)	69 (56)	0.190
Endocrine Diseases (240.0-259.9, 991.0-992.9, and/or presence of Comorbidity of Endocrine Diseases)	8,641 (11)	17 (21)	**0.006**	3,621 (35)	31 (25)	**0.026**
Genitourinary System Diseases (580.0-629.9, 403.XX, 791.XX, 788.XX, and/or presence of Comorbidity of Renal Diseases)	13,882 (18)	50 (63)	**<0.001**	3,946 (38)	73 (59)	**<0.001**

	Adult, N (%)			Elderly, N (%)		
Comorbidities and Secondary Diagnoses (ICD-9 Codes)	**Survived**	**Deceased**	**p-value**	**Survived**	**Deceased**	**p-value**
Observations	**75,490 (99.9)**	**80 (0.1)**		**10,393 (99)**	**123 (1)**	
Neurological Diseases (317.0-326, 330.0-337.9, 340-359.9, 392, 780.0-780.09, 780.2-780.4, 317-319, 290.XX, 294.XX, 781.0-782.0, and/or presence of Comorbidity of Paralysis or Other Neurological Disorders or Paralysis)	6,373 (8)	12 (15)	**0.035**	1,735 (17)	31 (25)	**0.012**
Diseases of the Musculoskeletal System and Connective Tissue (274.XX, 710.0-739, and/or presence of Comorbidity of Rheumatoid Arthritis or Lupus)	12,157 (16)	19 (24)	0.060	3,342 (32)	25 (20)	**0.005**
Fluid and Electrolyte Disorders (275.0-276.9, 458.0-459.9, and/or presence of Comorbidity of Fluid and Electrolyte Disorders)	25,947 (34)	56 (70)	**<0.001**	5,062 (49)	81 (66)	**<0.001**
Neoplasms (140.0-239.9, V10.XX, and/or presence of Comorbidity of Lymphoma, Metastatic Diseases, or Tumor)	4,842 (6)	10 (13)	**0.026**	2,154 (21)	17 (14)	0.060
Platelet and White Blood Cell Diseases (204.0-208.92, 287.0-288.9, 238.71)	7,219 (10)	24 (30)	**<0.001**	979 (9)	19 (15)	**0.023**
Psychiatric Diseases (293.XX, 295.0-302.9, 306.0-316, 780.1, V62.8, V15.4, and/or presence of Comorbidity of Psychoses)	19,490 (26)	19 (24)	0.670	2,050 (20)	13 (11)	**0.011**
Skin Diseases (680.0-709.9, 782.1-782.9)	4,869 (6)	12 (15)	**0.002**	718 (7)	14 (11)	0.053
Trauma, Burns and Poisoning (800-999)	4,043 (5)	45 (56)	**<0.001**	731 (7)	64 (52)	**<0.001**
Drug Abuse/Withdrawal/Dependence (292.0-292.9, 304.0-304.93, 305.2-305.93, and/or presence of Comorbidity of Drug Abuse)	4,449 (6)	3 (4)	0.420	95 (1)	1 (0.8)	0.910
Alcohol Abuse/Withdrawal/Dependence (291.0-291.9, 303.0-303.93, 305.0-305.03, and/or presence of Comorbidity of Alcohol Abuse)	1,344 (2)	3 (4)	0.180	99 (1)	1 (0.8)	0.870
Tobacco Use (305.1)	22,773 (30)	13 (16)	**0.007**	2,243 (22)	17 (14)	**0.037**
Long-Term Medications/Radiotherapy (V58.0-V58-2, V58.62, V58.64-V58.66, V58.68-V58.69)	8,312 (11)	7 (9)	0.520	1,328 (13)	6 (5)	**0.009**
Social Factors (V60.0-V62.6, V63.0-V64.3, V15.81)	5,455 (7)	4 (5)	0.440	308 (3)	1 (0.8)	0.160
Sleep Disorders (327, 780.5, V69.4, V69.5)	2,350 (3)	2 (3)	0.750	433 (4)	3 (2)	0.340
Lack of Physical Exercise (V69.0)	0 (0)	0 (0)		1 (0.0)	0 (0)	0.910
Inappropriate Diet and Eating Habits (V69.1)	2 (0.0)	0 (0)	0.960	0 (0)	0 (0)	
High Risk Lifestyle Behaviors (V69.2, V69.3)	4 (0.0)	0 (0)	0.950	0 (0)	0 (0)	
Body Mass Index of Less than 18.9 (V85.0)	1,276 (30)	9 (64)	**0.018**	179 (29)	4 (57)	0.370
Body Mass Index of 19-24.9 (V85.1)	922 (22)	0 (0)		149 (24)	1 (14)	
Body Mass Index of 25.0-29.9 (V85.21-V85.25)	407 (10)	2 (14)		86 (14)	0 (0)	
Body Mass Index of 30.0 and over (V85.30-V85.45)	1,679 (39)	3 (21)		98 (32)	2 (29)	

Discussion

The purpose of this current study was to analyze the associations between demographics, hospital length of stay (HLOS), comorbidities, surgical status, and mortality in adult and elderly patients admitted to the hospital emergently with a primary diagnosis of regional enteritis. Our results indicate that age, female sex, increasing HLOS, surgical procedures, bacterial infections, respiratory diseases, cardiac diseases, genitourinary system diseases, fluid and electrolyte disorders, platelet and white blood cell diseases, trauma, burns, and poisons were the main predictors of mortality in patients admitted emergently with a leading diagnosis of regional enteritis.

Increasing Age

As expected, increasing age is a significant predictor of mortality in our study. For every year of increasing age, the likelihoodof mortality rose by 4% within all patients. Furthermore, our results indicate that the overall death rate among elderly was 12 times higher when compared to adults.A population-based study of 1595 patients in Scotland found that mortality was lowest in the <30 years age group and highest in the 65+ years age group – this trend was found for all sub-groups based on surgical status.[14] Interestingly, Jess et al. found a significantly increased mortality and standardized mortality ratio in younger women in their 20s and 40s compared to the background population, though these findings were not generalized to the male population.[15] This may be related to the notion that complications of Crohn's Disease(CD) are related to the duration of the disease, rather than the subject's current age.[16,17] In a retroactive cohort study in England, Chu et al. found that the proportion of mortality attributed to neoplasia in CDpatients was almost ten percent higher in peoplewith longstanding (more than 20 years sincediagnosis) CD versus those with less than five years from diagnosis.[18] Canavan et al. did not find an association between disease prolongation and increased mortality.In fact, they found higher death rates in people diagnosed with CD within 5 years - for which most patients died of surgical complications.[19] More research is warranted to investigate the relationship between age, duration of disease, and mortality in patients with CD.

Female Sex

Our study points to female sex as a predictor of mortality because it increased the odds of mortality by 45%. Previous studies have pointed to apossible correlationbetween female sex and mortality in CD, however the exact connection has yet to be established.[15,20–22]Jess et al. concluded that women who were diagnosed with CD before the age of 50 suffered significantly higher mortality associated with advanced disease.15This group proposed a more aggressive disease course in females as a possible explanation for the sex-related difference in mortality.[15]Zhulina et al. had very similar findings and also concluded that earlier diagnostic periods and female sex were independently associated with increased mortality.[21]Contrarily, some studies found that there was a nonsignificant effect of gender on mortality[14,23] – which alludesthat although our findings are statistically significant, they may not be as clinically significant.Within our study, the majority of elderly patients (63.9%) were female. Furthermore, our results showed that adult women had significantly higher rates of congestive heart failure, chronic pulmonary disease, and fluid and electrolyte disorders. Age and the aforementioned comorbidities were also all independently correlatedwith higher rates of death; therefore, the existence of more elderly females in our sampleand the greaterfrequency of significant comorbidities within females may help explain our findings.

Hospital Length of Stay

Our study's results suggest that increasing HLOS is prOur study's results suggest that increasing HLOS is predictor of deathwithin CD patients. The odds of mortalityrose by 1% for every additional day that patients stayed in the hospital. Patients with IBD are thought to be at higher risk of hospital-acquired infections (HAI) due to the systemic nature of the disease and use of immunosuppressive agents;[24] Karagozian et al. found that mortality and HLOS are both increased in IBD patients who develop HAIs.[24] Specifically, they foundthat the median HLOS for patients that acquired HAIs was 22 days while only6 days for those who did not develop HAI. Similarly, our results showed average HLOS to be around 18 days for deceased patients and 5 days for survived patients. The aforementioned study also attributes the vast majority of HAI cases to genitourinary infection,[24] which we found to be an independent predictor of mortality. Several different retrospective studies that also used the 2005-2014 NIS database including similarly emergently admitted patientsconcluded increasing HLOS to be a significant risk factor of

mortality.[25–29]This highlights the need for providers to remain vigilant for the eventualityof nosocomial infections amongst patients admitted for longer than 1 week.

Operational Status

Surgical operationswere a strong predictor of deathamong all patients in this study.Going throughan operation increased the likelihood of mortality by 78%. Specifically, 62% ofall deceased patients in the study underwent an invasive or surgical procedure. This is in stark contrast to the surviving group, of whom only 35% encounteredan invasive or surgical procedure.Among those who underwent surgery,a comparison between age groups showed that mortality was 10.5-fold greater in elderly patients compared to adults. Furthermore, the average HLOS for patients that underwent operations were at least twice that of patients who did not undergo surgery. This is important as our study, along other similar retrospective studies, have found increasing HLOS to be an independent risk factor of mortality.[25–29]Previous studies have also shown that even though mortality rates in patients requiring emergency surgery for CD have decreased over the past decades, they still remain relatively high at 5-10% .[30–32]Medical management is the preferred treatment for CD patients, while surgical management is reserved for patients with progressive disease or life-threatening complications.[33] This suggeststhat surgery can be viewed as an index of disease severity and may help explain our findings.

Bacterial Infections

Bacterial infections, other than tuberculosis, were a significant risk factor within our study, associated with a 3.26-fold increase in the odds of mortality. Specifically, 54% of deceased adults and 43% of deceased elderly patients included in this study suffered from bacterial infections versus only 4% of surviving adults and 7% of surviving elderly. This is not surprising as multiple studies have linked the regional enteritis disease process and the medications used for treatment with increased relative risk of infections.[34,35] Immunosuppressants, including systemic corticosteroids, have historically been the mainstay treatment for CD.[12] Lichtenstein et al. analyzed a large scale prospective cohort and concluded that prednisone use was an independent risk factor for death.[36]On the other hand, a study conducted at the Mayo Clinic analyzed the medical records of 492 patients treated with infliximab for CD, and found a 10-year survival of 94% with only 7% of deaths attributed to infections.[37] Despite the clear benefits of medical management, physicians must be weary of the risks of bacterial infection when managing CD patients with immunomodulating agents.

Trauma, Burns, and Poisons

Trauma, burns, and poisons were strong mortality predictors,creating odds of mortality that was 3.69-fold higher.The mortality rate within those suffering from trauma, burns, and poisons was 2.2%. Furthermore, more than half of all adults and elderly among the deceased groupsuffered from trauma, burns, or poisons. Due to the chronic nature of CD, it has been proposed that repeated bouts of inflammation lead to decreased integrity of the intestinal wall, predisposing regional enteritis patients to severe complications from blunt trauma.[38] While it is plausible that decreased intestinal wall integrity could also leave patients more vulnerable to complications from burns and poisons, more research is needed as literature regarding trauma, burns, and poisons in context of CD is extremely scarce.

Genitourinary Diseases

CD is increasingly considered a systemic disease with numerous extraintestinal manifestations.[4–7,14,39] Genitourinary system complications of CD are considered common.[40]Our results show that the presence of genitourinary disease raised the odds of mortality by 57% in CD patients. Various other studies have similarly reported genitourinary tract diseases causing significantly increased standardized mortality ratios in patients with CD.[15,41–43] Within our study, 10% of the adult deceased group had renal failure versus only 1.6% of the surviving group. Similarly, 20.3% of the deceased elderly had renal failure compared to 11% of living elderly. Ambruzs et. al. concluded significant renal morbidity associated with IBD and suggested a clinically short window of injury reversibility.[44] These results may warrant routine renal monitoring in CD and high index of suspicion for genitourinary disease in patients with CD.

Pulmonary Diseases

Our results indicate that the existenceof lung disease as a comorbidity is the strongest predictor of mortality in CD patients. The presence of pulmonary pathology raised odds of death5.28-fold. Respiratory manifestations of CD, although not as common as other

extraintestinal manifestations of CD, follow an insidious course and may require anincreased vigilance in order to appropriately treat.[5,39] Furthermore, medications used to treat CD have been found to have adverse pulmonary sideeffects.[8] In a Swedish nationwide cohort study, Olen et al. found that lungdisease was the fourth most common cause of death in patients with IBD.[45] In an English cohort study, Chu et al. concluded respiratory and circulatory diseases were the most common cause of mortality in IBD, and also that lung cancer was the most common neoplastic cause of death in CD.[18] Thus, respiratory disease has been shown to be a significant contributor to mortality in context of regional enteritis in at least three different national cohorts. Ekbom et al. suggest a common inflammatory pathway and genetic vulnerability for both chronic obstructive pulmonary disease (COPD) and CD from a large population-based cohort study that found a significant risk in patients with COPD, and their first-degree relatives, for developing CD.[46] Similarly, asthma and bronchitis have both been cited as having significant associations with CD,[47] with a case-control study finding that patients with CD were more likely to present to the hospital with symptoms of breathlessness, sputum production, and cough compared to healthy controls.[48] The insidious nature of respiratory disease in context of CD, the common inflammatory and genetic pathway, and the adverse respiratory effects of medicationused for regional enteritis may help explain the high odds ratio of mortality associated with respiratory diseases within our study, however this topic needs to be investigated further as literature regarding association between pulmonary disease and CD is scarce.

Cardiac Diseases

In our investigation, we found that cardiac disease was a strong predictor of mortality in regional enteritis patients, raising mortality odds by 331%. Multiple studies have previously found increased rates of mortality from cardiac disease in CD.[3,18,45,49] The prevalence of cardiac disease in CD has mostly been attributed to systemic inflammation.[3,4,9,18,45,49,50]Recent studies suggest that IBD patients are more prone to venous thromboembolism,[51] and early atherosclerosis, which has been attributed to greater carotid intimal layer thickness.[52] Studies investigating inflammatory mediators in IBD have concluded that C-reactive protein (CRP) elevation in IBD is associated not only with overall disease severity, but also with increased risk for coronary artery disease (CAD).[3,9] Other inflammatory mediators also raised in CD, such as TNF-a, IL-1, and IL-6 have also shown to cause cardiac myocyte toxicity and can contribute to heart disease.[10]Hasbey et al. concluded that cardiac MRI can be used to track, assess, and monitor myocardial damage caused by systemic inflammation in patients with CD.[49] While the literature seems to concur regarding the increased risk for cardiovascular disease and CD, a few studies show that there is no clear consensus that there is a significant increase in mortality in CD patients with cardiac disease.[50,53] Further work is needed to elucidate the mechanism of cardiovascular mortality in regional enteritis.

Platelet and White Blood Cell Disorders

Due to the inflammatory nature of CD, it is not surprising that platelet and white blood cell disorders were observed to be risk factors of mortality within our study. Platelet and white blood cell diseases independently increased the odds of mortality by 1.56-fold. The overall mortality rate within patients with platelet and white blood cell disorders was 0.5%. Platelet abnormalities in CD were first described in 1968.[54] Reactive thrombocytosis has since then been established as a common occurrence during the active phase of CD and shown to correlate with disease severity.[55–58] This corroborates our findings which showed that 32.5% of adult and 15.4% of elderly patients in the deceased cohort suffered with coagulopathy, while only that of 1.6% of adult and 3.2% of elderly patients in the survived group. Furthermore, Danese et al. concluded that platelets play a significant role in the amplification of gastrointestinal inflammation and should be considered as targets for medical intervention.[55] Similarly, white blood cell disorders in CD patients could also point to more severe disease.[59]More studies are needed to investigate the relationship of IBD and platelet and white blood cell disorders with special focus on common immunological factors.

Fluid and Electrolyte Disorders

Based on the findings presented in this study, fluid and electrolyte disorders were found to bea significant risk factor of mortality in CD patients. Specifically, 65% of adult and 61% of elderly patients were seen to have fluid/electrolyte disturbances in the deceased group, compared to only 32.2% and 45.1% in the adult and elderly survived group, respectively. Furthermore, the prevalence of fluid and electrolyte disorders was greater

in the elderly population (45%) when compared to the adult population (32%). This may help partially explain our findings as age was a predictor of mortality and elderly patients experienced a substantially higher mortality rate.Multiple studies on the relationship between CD and electrolyte disorders have pointed to a change in bidirectional electrolyte flux of electrolytes and water across colonic epithelium brought on by inflammation of mucosa in CD.[11,60–62]Schilli et al. concluded that fecal osmolality was significantly increased in patients with CD compared to normal subjects. [61]Cucino et al. examined comorbid conditions significantly associated with death in CD, stratifying ICD codes into broader categories. In the group of nutritional, volume, and electrolyte disturbances, the most frequent comorbidities, in order, included protein/calorie malnutrition, shock without trauma, anemia, and volume depletion.[63] The authors also suggest CD medications, such as sulfasalazine, corticosteroids, and cholestyramine, aggravate nutritional deficiencies of vitamins, minerals, and trace elements, which are commonly seen in IBD.[63] Our results, together with previous studies, suggest that special attention to the patient's fluid and electrolyte status is required in the context of emergent admissions for CD.

Strengths and Limitations

A large sample size and combined approach to statistical analysis using both logistic regression and generalized additive models were the main strengths of our study. The large sample size and diverse patient population makes our data very generalizable. Our method allowed us to conduct a novel investigation on the wide range of characteristics and factors that can influence mortality rates in patients emergently admitted with CD. Limitations of this study include our inability to ascertain potentially significant information such as severity of comorbidities, cause of death, case complexity, surgeon experience, extent of GI tract involvement and specific locations of enteritis within the GI tract; this additional information can be used to rule out potential confounding variables in future studies.

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Conflict of Interest Disclosure Statement

The authors declare no conflict of interest.

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