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Effect of constipation on outcomes in mechanically ventilated patients

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ABSTRACT

Constipation can be a significant clinical challenge that can compromise management plans and prolong hospital stays. Our goal was to examine the effects of constipation on mechanically ventilated patients, with outcomes related to inpatient stays. We retrospectively analyzed critically ill patients hospitalized with constipation in the 2016 to 2019 National Inpatient Sample (NIS) database. Constipation was defined using Rome IV criteria. Critically ill patients were defined as mechanically ventilated from admission day 1. Our primary outcome was length of stay (LOS) and total hospital charge. Secondary outcomes included predictors of mortality in critically ill patients with constipation. The study included 2,351,119 weighted discharges of mechanically ventilated patients in the NIS database. Of these, 3.7% had constipation. The adjusted LOS was 3.4 days longer in patients with constipation vs those without it ($P < 0.001$). The adjusted inpatient hospital cost was $31,762 higher in patients with constipation ($P < 0.001$). Men had higher LOS and inpatient costs. Constipation was not associated with increased inpatient mortality ($P < 0.001$). Several conditions increased mortality in critically ill patients with constipation, including peritonitis, fecal impaction, and bowel obstruction.

KEYWORDS Constipation; critically ill; mechanical ventilation; National Inpatient Sample

Motility disorders and problems associated with constipation are often regarded as a major concern in intensive care units (ICUs). ICU patients often describe constipation as one of their most distressing symptoms.[1] It is more frequent for ICU staff to record gastric aspirate output and bowel movements, but the absence of them is less reported. Furthermore, a combination of long work hours and multiple staff members taking care of the same patient may lead to miscommunication, resulting in an inaccurate report of constipation; as a result, its occurrence and effects on critically ill patients are often overlooked. It is well known that constipation is a problem among hospitalized patients, but its burden among mechanically ventilated patients has been poorly researched.[2–4] According to a few small single-center studies, constipation occurs in up to 83% of patients on mechanical ventilation.[4] Constipation results in delayed weaning from mechanical ventilation by up to 43% and affects outcomes such as length of stay (LOS). This study examined data from the National Inpatient Sample (NIS) to explore the burden of constipation in mechanically ventilated patients. We conducted an in-depth analysis on the impact of constipation among these patients, as it is one of the most prevalent motility disorders. Constipation is a complication that occurs in critically ill patients that can be treated or, even better, prevented if we have a better understanding of its prevalence and consequences.

METHODS

We conducted a retrospective cohort study of critically ill ICU patients between 2016 and 2019 in hospitals across the

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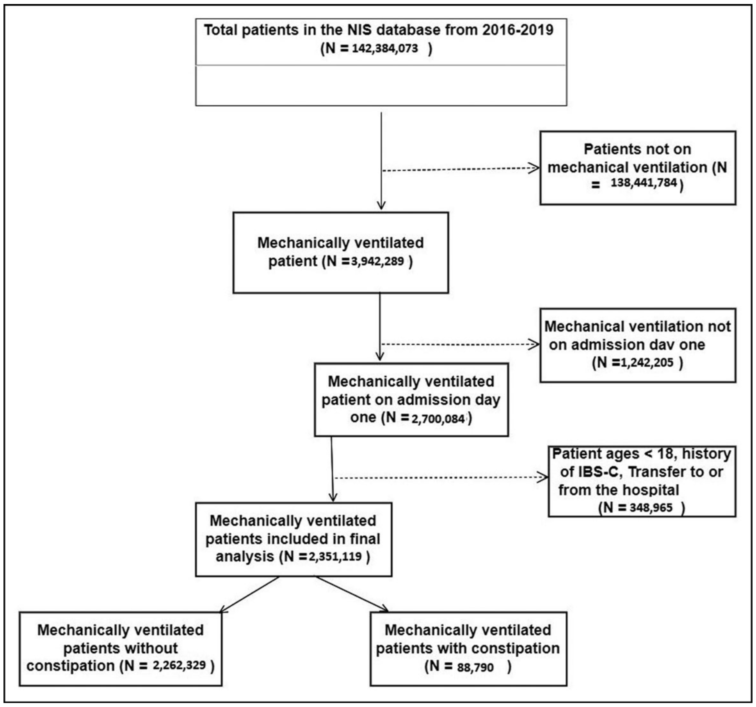

Figure 1. Flowsheet for patient selection using weighted counts from the National Inpatient Sample, 2016 to 2019.

US. Patients were selected from the NIS database, a publicly available inpatient database maintained by the Agency for Healthcare Research and Quality.[5] NIS has been developed as a stratified probability sample to represent all nonfederal hospitals nationwide. Detailed information on its design and sampling methods is available at https://www.hcup-us.ahrq.gov. As NIS contains deidentified patient data, it was deemed exempt from review by East Carolina University. Patient consent was waived due to the public availability of data.

Critically ill patients were defined as those on mechanical ventilation within 1 day of admission. The *International Classification of Diseases, Tenth Revision, Clinical Modification Procedure Codes* (ICD-10-CM-PCS) system does not have a unified code for mechanical ventilation. Our study included patients with a principal ICD-10-CM-PCS diagnosis specific to mechanical ventilation: 5A1945Z, 5A1935Z, and 5A1955Z. These patients were further stratified to those who were intubated on admission using the variable PRDAYn available in the NIS database. The day on which the procedure is performed (PRDAYn) is calculated from the procedure date (PRDATEn) and the admission date (ADATE). The Rome IV criteria define constipation as having two of the following for at least 3 months: (1) hard stools in at least 25% of defecations; (2) straining in at least 25% of defecations; (3) a sensation of incomplete evacuation in at least 25% of defecations; (4) less than three bowel movements per week; and (5) use of manual measures to help move or remove the stools from the rectum.[6,7] Therefore, ICD-10-CM diagnosis codes based on these definitions were used for constipation, including K5900, K5901, K5903, K5904, and K5909.

The primary outcome measures of this study were LOS and total charge (inpatient costs) in critically ill patients with constipation. Secondary outcomes included factors affecting inpatient mortality in critically ill patients with constipation. Other covariates of interest included patient age, gender, race, annual income, and health insurance, as well as hospital location, bed size, and teaching status. We used the Elixhauser list of 31 comorbidities for case-mix adjustment, a well-validated algorithm for predicting in-hospital mortality caused by various conditions, and utilized ICD diagnosis codes.[8] Inclusion criteria consisted of adults $\geq$ 18 years of age and mechanical ventilation on day 1 of admission. Exclusion criteria included a history of irritable bowel disease, related constipation, and transfers in or out of the hospital (to limit confounding regarding the LOS). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed for reporting data[9]; the checklist is available in the Supplementary Material. The flowsheet for patient selection is shown in *Figure 1*.

We built a hierarchical multivariate linear and logistic regression model to adjust for the confounding variables by using only variables associated with the outcome of interest on univariable regression analysis at $P < 0.2$ or known potential confounders despite a P value indicating no significance. Continuous variables were compared using the Student t test, and categorical variables were compared using the chi-square test. Our analysis used 0.05 as the threshold for statistical significance, and all P values were two-sided. All outcomes were adjusted for patient and hospital-level characteristics, including age, race, sex, insurance type, residential region, Elixhauser Comorbidity Index score, hospital teaching status, and hospital bed size, as previous studies have utilized them as well.[10] We also adjusted for constipation-related sequela such as diverticulosis, diverticulitis, fecal

Table 1. Characteristics of patients included in the study

Variables	Constipation No	Constipation Yes	P value
N	2,262,329	88,790	0.001
Male	1,257,939 (56%)	47,245 (53%)	
Female	1,004,389 (44%)	41,545 (47%)	
Mean age (years)	60.6 ± 0.1	62.2 ± 0.14	
Race			0.001
White	1,413,829 (65%)	16,255 (64%)	
Black	393,255 (18%)	16,255 (19%)	
Hispanic	228,924 (10%)	9130 (11%)	
Asian or Pacific Islander	60,814 (3%)	2145 (2%)	
Native American	15,910 (1%)	430 (<1%)	
Other	71,264 (3%)	2790 (3%)	
Elixhauser Comorbidity Index score			0.001
0	44,180 (2%)	565 (1%)	
1	114,134 (5%)	2570 (3%)	
2	204,334 (9%)	6035 (7%)	
≥3	1,900,284 (84%)	79,625 (90%)	
Median annual income in patient's zip code			0.0001
$1–24,999	764,719 (35%)	28,935 (33%)	
$25,000–34,999	578,999 (26%)	19,649 (26%)	
$35,000–44,999	495,439 (22%)	19,649 (23%)	
$45,000 or more	374,249 (17%)	16,370 (19%)	
Insurance			0.001
Medicare	1,192,599 (55%)	15,775 (59%)	
Medicaid	425,349 (19%)	15,775 (18%)	
Private	429,535 (20%)	16,055 (19%)	
Uninsured	134,380 (6%)	3230 (4%)	
Hospital characteristics			
Hospital region			0.001
Northeast	373,180 (16%)	14,315 (16%)	
Midwest	467,690 (21%)	21,715 (24%)	
South	936,410 (41%)	35,840 (40%)	
West	485,654 (21%)	35,840 (19%)	
Hospital bed size			0.007
Small	360,919 (16%)	13,454 (15%)	
Medium	670,934 (30%)	25,670 (29%)	
Large	1,231,080 (54%)	49,670 (56%)	
Hospital status			0.001
Rural	133,399 (6%)	14,565 (5%)	
Urban nonteaching	469,220 (21%)	14,565 (16%)	
Urban teaching	1,660,314 (73%)	69,754 (79%)	
Sepsis	646,289 (29%)	26,830 (30%)	0.001
Urine retention	56,929 (3%)	6395 (7%)	0.001
Fecal impaction	5,730 (<0.01%)	210 (<0.01%)	0.6
Bowel obstruction	18,590 (1%)	1245 (1%)	0.001
Bowel perforation	11,834 (1%)	795 (1%)	0.001
Peritonitis	24,795 (1%)	1350 (2%)	0.001
Diverticulosis	20,290 (1%)	1530 (2%)	0.001
Diverticulitis	8,325 (<0.01%)	600 (1%)	0.001
Vasopressors	185,505 (8%)	7005 (8%)	0.1

impaction, urine retention, peritonitis, bowel perforation, sedative or opiate analgesia use, and vasopressor support. ICD 10 codes are shown in the Supplementary Material.

In addition, we adjusted for the 10 most common principal diagnoses for which patients were admitted in the ICU from 2016 to 2019 in the NIS database (Supplementary Material). Dichotomous variables were consolidated to report adjusted odds ratios (AOR) with 95% confidence intervals (CI) and P value. Continuous data were reported as adjusted standard mean differences for continuous data with P values. Standard errors were reported as ± SE in linear regression outcomes. Analyses were performed using STATA version 16.0.

RESULTS

A total of 2,351,119 weighted discharges from 2016 to 2019 in the NIS database met the study inclusion criteria for patients with mechanical ventilation. Among them, 88,790 (3.7%) had a secondary diagnosis of constipation. Constipation was more prevalent in men than women (53% vs. 47%, $P < 0.001$). Constipation was more prevalent in whites followed by blacks and Hispanics (64%, 19%, and 11%, respectively). Among hospital regions, the distribution of constipation was significantly higher in the South (up to 40%, $P < 0.001$). Critically ill patients with constipation had slightly higher rates of sepsis, peritonitis, and urinary retention; however, rates of diverticulitis, diverticulosis, fecal impaction, bowel obstruction, and perforation were comparable in both groups ($P < 0.001$). Additional characteristics are described in *Table 1*.

The mean LOS of critically ill patients with constipation was 12.3 days vs 8.4 days in those without constipation. On

Table 2. Multivariate linear regression showing inpatient length of stay and charges in critically ill patients with constipation

Outcome	No constipation	Constipation	Difference	
			Crude	Adjusted
Mean length of stay (days) ± SE	8.4 ± 0.03	12.3 ± 0.1	3.9 ± 0.1*	3.4 ± 0.09*
Mean total charge (US$) ± SE	$146,941 ± 1101	$184,051 ± 2104	$37,110 ± 1755*	$31,762 ± 1680*

*$P < 0.001$.

Table 3. Subgroup analysis of primary outcomes among critically ill patients with constipation

Variables	Adjusted difference in length of stay (days)	Adjusted difference in hospital charge
Gender		
Male	#	#
Females	−1.1 ± 0.17	−$19,996 ± 2853*
Race		
White	#	#
Black	1.29 ± 0.24*	$3,686 ± 4097
Hispanic	0.9 ± 0.34*	$33,539 ± 6160*
Asian	3.2 ± 0.9*	$33,475 ± 11,800*
Increasing comorbidities	0.66 ± 0.04*	$9,515 ± 707*
Hospital region		
Northeast	#	#
Midwest	−1.4 ± 0.3*	−$12,319 ± 5426*
South	−0.3 ± 0.3	$14,045 ± 5490*
West	−1.2 ± 0.35*	$82,819 ± 7287*
Hospital status		
Rural	#	#
Urban nonteaching	1.5 ± 0.39*	$57,899 ± 5825*
Urban teaching	2.02 ± 0.24*	$77,366 ± 5042*
Hospital bed size		
Small	#	#
Medium	1.01 ± 0.27*	$15,239 ± 5473*
Large	2.02 ± 0.24*	$37,410 ± 4968*
Insurance type		
Medicare	#	#
Medicaid	3.4 ± 0.37*	$22,846 ± 5188*
Private	0.9 ± 0.25*	$27,718 ± 5188*
Uninsured	1.7 ± 0.53*	$20,737 ± 5188*

*$P < 0.05$.
#indicates the analysis was done against that variable.

crude analysis, constipation increased the LOS by 3.8 ± 0.1 days ($P < 0.001$). After adjusting for potential confounders, the difference in LOS in days was 3.4 ± 0.09 ($P < 0.001$) (*Table 2*). Subgroup analysis revealed women with constipation had a reduced LOS up to 1.1 ± 0.07 days compared to men ($P < 0.01$). Blacks had an increased LOS compared to whites (adjusted mean difference, 1.29 ± 0.24, $P < 0.001$). In Hispanics and Asians, there was also increased LOS compared to whites (adjusted mean difference, 0.9 ± 0.35 days and 3.29 ± 0.35 days, respectively, $P < 0.03$). Vasopressor use also increased LOS independently (adjusted mean difference, 0.8 ± 0.3 days, $P < 0.001$) (results not shown in tables).

The total cost of all critically ill patients in NIS from 2016 to 2019 was $345 billion. The mean hospital charge per patient (inpatient costs) with constipation was $184,051 vs $146,941 in those without constipation. Crude analysis showed that patients with constipation had an increased hospital charge of $37,110 ($P < 0.001$). After adjusting for potential confounders, the increase in total charge was $31,762 ($P < 0.001$) (*Table 2*). Subgroup analysis showed that women had a lower hospital charge than men (adjusted mean difference, −$19,996 ± 5673, $P < 0.01$). There was no significant difference for hospital costs when comparing black race to white race ($P > 0.05$). Both Hispanics and Asians had increased inpatient costs compared to whites (adjusted mean difference, $33,539 ± 6160 and $33,475 ± 11,800, respectively, $P < 0.03$). Vasopressor use also increased LOS independently (adjusted mean difference, 0.8 ± 0.3 days, $P < 0.001$) (results not shown in tables) (*Table 3*).

In critically ill patients, constipation was associated with decreased inpatient mortality (AOR 0.47, 95% CI 0.45–0.5, $P < 0.001$). Subgroup analysis did not reveal any gender or racial disparities in terms of inpatient mortality. Some independent positive predictors of mortality in critically ill patients with constipation were age (AOR 1.03, 95% CI 1.02–1.034, $P < 0.001$), sepsis (AOR 2.6, 95% CI 2.4–2.9, $P < 0.001$), fecal impaction (AOR 2.1, 95% CI 1.05-4.2, $P < 0.001$), vasopressor use (AOR 2.4, 95% CI 2.1–2.7, $P < 0.001$), bowel obstruction (AOR 2.8, 95% CI 2.1–3.7, $P < 0.001$), cardiac arrhythmias (AOR 1.2, 95% CI 1.1–1.3, $P < 0.001$), pulmonary circulation disorders (AOR 1.15,

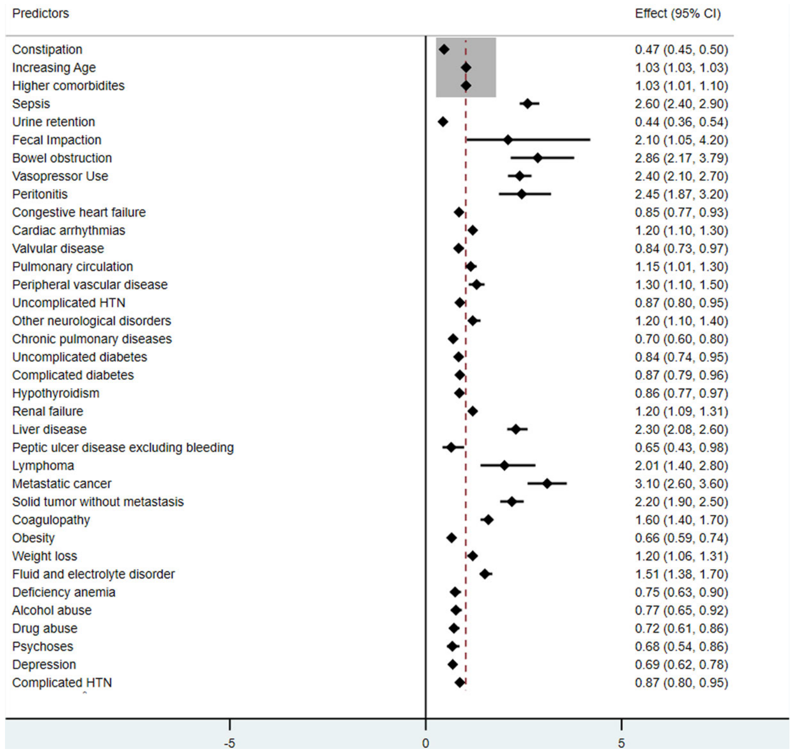

Figure 2. Multivariate logistic regression for predictors of mortality in critically ill patients with constipation.

95% CI 1.01–1.3, $P < 0.001$), peripheral vascular disease (AOR 1.3, 95% CI 1.1–1.5, $P < 0.001$), neurological disorders (AOR 1.2, 95% CI 1.1–1.4, $P < 0.001$), renal failure (AOR 1.2, 95% CI 1.09–1.31, $P < 0.001$), peritonitis (AOR 2.4, 95% CI 1.87–3.2, $P < 0.03$), liver disease (AOR 2.3, 95% CI 2.08–2.6, $P < 0.001$), and fluid and electrolyte disorders (AOR 1.51, 95% CI 1.38–1.7, $P < 0.001$). Diverticulosis, diverticulitis, congestive heart failure, hypothyroidism, and complicated hypertension were not associated with increased mortality in critically ill patients with constipation *(Figure 2)*.

DISCUSSION

This present study utilized a large population-based sample to study the effect of constipation on mechanically ventilated patients. Several factors can influence constipation among patients admitted to ICU, such as shock, the use of pharmacological agents like sedatives or analgesics, a sudden change in electrolyte disturbances, and diet.[4] The traditional definition of constipation is less than three bowel movements per week, feelings of incomplete evacuation, difficulty passing stools, the need for manual maneuvers for defecation, and hard stools.[11] While most of these criteria are subjective, bowel movement frequency is objectively measured and is the primary reporting mechanism of constipation in the ICU. Our study revealed that constipation, defined by Rome IV criteria and coded using ICD 10 diagnosis codes, increases the LOS in mechanically ventilated patients. It tends to affect men more than women in terms of LOS, hence translating into higher inpatient costs. Several factors that affect inpatient mortality in critically ill patients with constipation, and therefore its association with mortality, are debatable.

Prolonged LOS is associated with poor hospital outcomes and mortality in all patients.[12] Mechanically ventilated patients require continuous sedation and analgesia, which are linked to an increased incidence of constipation in these patients.[13] In our analysis, there was a 79% increased association between sedation and constipation (AOR 1.79, 95% CI 1.4–2.2, $P < 0.001$) (results not shown). In addition to sedative opiates, the use of vasopressors is also associated with constipation in critically ill patients. A possible explanation is that shock requiring vasopressors results in selective intestinal ischemia, and shock itself is associated with decreased gut motility that results in intestinal atony and functional ileus.[14] Our study showed an increased association between vasopressor use and LOS as well (mean difference, 0.8 ± 0.3 days, $P < 0.001$). Van der Spoel et al demonstrated that delayed defecation is associated with the administration of vasopressors; however, it cannot be distinguished whether the constipation is a consequence of the administration of vasopressors or of the severity of illness for which the medication was given in the first place.[15] The use of opiates results in decreased preload and impaired vasoconstriction, which cause a reduction in cardiac output in shock; this leads to diminished gut motility and gut hypoxia. All these factors contribute toward increased constipation and prolonged hospital stays in critically ill patients.[16] Additionally, constipation has been shown to increase abdominal pressure and induce alveolar derecruitment prolonging mechanical ventilation, which leads to longer stays in the hospital.[17,18]

Moreover, there were racial disparities regarding LOS, with blacks, Hispanics, and Asians having increased LOS compared to whites. Previous studies have reported that Hispanics and African Americans have a greater preference for aggressive life-sustaining therapies, despite guarded prognosis.[19,20] Additionally, some studies have suggested a significant mistrust of healthcare among certain races, including African Americans, leading to concerns regarding fear of curative care abandonment.[21,22] The attitude toward unfavorable prognosis among patients of different races may have a cultural component, resulting in an increased LOS in these patients.

ICU-level care is almost four times more expensive than general care on hospital floors, which adds substantially to healthcare costs.[23] In critically ill patients, imaging, laboratory tests, and pharmacological agents are more likely to be required because of the nature of their illness, and constipation can add to this by causing further complications. Constipation is a risk factor for intraabdominal hypertension, leading to subsequent organ dysfunction and inpatient costs.[24] Acquired bacterial infections have been reported in patients with constipation due to fecal stasis, impairing the natural decontamination process of the body.[16] This can result in superimposed infections and prolonged stay, translating into increased hospital costs. Our subgroup analysis revealed that critically ill women with constipation had a lower inpatient cost than men. According to research, male patients have up to 9.7% higher inpatient costs than female patients for certain medical conditions.[25,26] This could be due to the increased cases of mechanical ventilation and comorbidities in men compared to women.[27]

This study reported that constipation did not increase mortality in critically ill patients, which is consistent with a previous report.[4] In critically ill patients with constipation, several comorbidities can increase mortality. Using multivariate logistic regression analysis, it was revealed that constipation-related conditions such as bowel obstruction and fecal impaction significantly increased mortality. However, diverticulitis or diverticulosis had no effect on mortality. This finding is consistent with a previous study that reported a significant impact of fecal impaction on mortality rates, as much as 22%.[28] It is critical to monitor patients with fecal impaction for additional comorbidities outlined above, as they increase inpatient mortality.

Our study has several strengths. NIS allows analysis of a large population, increasing the study's power. Inpatient analyses were generated using data from the four more recent databases within NIS, ensuring national representativeness and providing extensive healthcare data. Various confounding variables were adjusted using univariate and multivariate regressions, minimizing bias in our results. On the other hand, there are several limitations to this study. Since cohorts were identified retrospectively, causality cannot be determined. The study did not have randomization and blinding, affecting the result interpretation. The data extracted were based on ICD-10 codes, and misclassification can lead to bias in data collection. A final limitation is the potential for missing data in the NIS.

In conclusion, constipation contributes to worsening clinical outcomes, thus prolonging hospital stays and incurring additional healthcare costs, but not affecting mortality rates in critically ill patients. Constipation is often neglected in an acute care setting for critically ill patients, but it can delay recovery, increase inpatient stays, and cause debilitation.

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