Prevalence and Impact of Late Defecation in the Critically Ill, Thermally Injured Adult Patient

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The aim of this study was to determine the prevalence of late defecation (absence of laxation for more than 6 days after admission) as an indicator of lower-gastrointestinal (GI) tract dysfunction in burn patients. In addition, the authors wanted to determine whether the addition of polyethylene glycol 3350 to the standard bowel regimen led to improvement in markers of lower-GI function and outcomes. The authors conducted a retrospective chart review of patients admitted to the burn intensive care unit during a 26-month period. Inclusion criteria were 20% or more TBSA burn, requirement for mechanical ventilation, and age over 18 years. Of 83 patients included, the prevalence of late defecation was 36.1% (n = 30). There was no association between late defecation and mortality. Patients with late defecation had more frequent episodes of constipation after first defecation (*P* = .03), of feeding intolerance (*P* = .007), and received total parenteral nutrition more frequently (*P* = .005). The addition of polyethylene glycol to the standard bowel regimen did not affect markers of lower-GI function. Late defecation occurs in more than one third of critically ill burn patients. Late defecation was associated with ongoing lower-GI dysfunction, feeding intolerance, and the use of total parenteral nutrition. The causal relationship between these problems has not been determined. A prospective study at the authors' institution is currently planned to attempt to validate late defecation as a marker of lower-GI tract dysfunction, determine its relationship to various outcomes, and determine risk factors for its development. (J Burn Care Res 2014;35:e224–e229)

The gastrointestinal (GI) tract consists of multiple, anatomically distinct organs in series from the mouth to anus. In addition, there are a myriad of complex functions the GI tract must perform to maintain homeostasis to include: motility, absorption, endocrinologic aspects, immunologic aspects, barrier to bacteria and their constituents, and maintenance of flora. Dysfunction of the GI tract has long been speculated to be associated with the systemic inflammatory response and adverse outcomes in injured and critically ill patients. However, direct correlation of GI tract dysfunction with worse outcomes is lacking for several reasons. Arguably the main issue with correlating GI dysfunction with these adverse outcomes is the lack of an accurate, meaningful definition of GI tract dysfunction and failure in critical illness.[1,2] The benefits of early enteral nutrition in the critically ill adult have been well established, and current guidelines advocate beginning enteral feeding within 24 to 48 hours of admission.[3,4] Because of this, the most of the focus of motility research has been on the upper-GI tract. Only recently, however, has the importance of the proper function of the lower-GI tract been realized.

As an indicator of lower-GI tract function, constipation is difficult to define; patients may report constipation based on consistency, frequency, or pain with bowel movements (BM). The Rome III criteria are the latest attempt to standardize how constipation is defined in the outpatient setting.[5] Constipation in the

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intensive care unit (ICU) setting has been defined by some as the absence of a BM for 3 or more consecutive days.[6] Van der Spoel et al[7] have dichotomized lower-GI dysfunction in critically ill patients, defining late defecation as that prolonged by more than 6 days. Largely because of the variability in definition, the prevalence of constipation in critically ill adult patients varies between 5 and 83%.[6] In observational studies, prolonged ICU length of stay (LOS), difficulty weaning from mechanical ventilation (MV), intolerance of enteral feeds, and increased mortality have been associated with constipation in critical illness.[7,8] A more recent prospective observational cohort study again showed a high incidence of constipation (58%), as well as association of constipation with increased ICU LOS and prolonged weaning from MV.[9]

We could find no reports describing the prevalence of late defecation in critically ill burn patients. Our hypothesis is that late defecation is common among severely burned adults admitted to an ICU. The objective of this study is to determine the prevalence and association of late defecation with various outcomes in this population.

METHODS

Study Design

This study was conducted under a protocol reviewed and approved by the U.S. Army Medical Research and Materiel Command Institutional Review Board, and in accordance with the approved protocol. The records of all patients admitted to the U.S. Army Burn Center ICU between April 2009 and June 2011 were retrospectively screened for study enrollment. Patients were entered into the study if they had sustained a TBSA burn of greater than or equal to 20% and required MV. Patients were excluded if they were less than 18 years of age, had a prior colectomy for any reason, had a preexisting GI motility disorder, or if they were moribund on presentation to the ICU.

Description of Nutrition Support

Our protocol for feeding is initiation of nasogastric feeds when there is no concern for occult or overt GI mucosal ischemia. Markers used to indicate ischemia include, but are not limited to: rising lactate, increased bladder pressure, intolerance of gastric feeds during burn shock or sepsis, the use of multiple pressors for shock. Gastric feeds can typically be initiated within 48 hours of thermal injury. Caloric needs are determined by calculating the patient's resting energy expenditure using the Carlson or Milner equation or indirect calorimetry along with the use of an activity factor of 1.2 to 1.4.[10,11] The inclusion of activity factors has been found to maximize lean body mass retention and maintain weight.[12] The enteral feeding formula we provide is high in protein and carbohydrate and low in fat. Nutritional adequacy is evaluated by determining caloric deficits and nitrogen balance, with a goal of avoiding >10 wt% loss and promoting a positive nitrogen balance. We do not routinely follow nutritional markers such as prealbumin; a practice consistent with current guidelines.[4] When patients demonstrate recurrent intolerance of gastric feeds and have no concern for occult or overt GI mucosal ischemia, we attempt to pass a postpyloric nasoenteral tube for feeding access. Our practice also includes the use of enterally administered naloxone when a patient has an isolated feeding residual more than 500 ml or two sequential residuals more than 300 ml because of its benefits in critically ill patients receiving narcotics who demonstrate gastric motility issues.[11] Naloxone is administered enterally at a dose of 2 mg every 6 hours. No other promotility agents are used in our burn ICU. Consistent with American Society for Parenteral and Enteral Nutrition guidelines and U.S. practice, when adult burn patients in our ICU demonstrate significant caloric deficit approaching 7 days, the attending intensivist, burn surgeon, and dietician will consider initiation of total parenteral nutrition (TPN).[4,13,14]

On the basis of the work by van der Spoel et al,[7] two groups were generated for comparison based on time to first BM after admission to the ICU: early defecation was defined as at least one BM within 144 hours (6 days) of ICU admission; late defecation was defined as absence of defecation within 144 hours (6 days) of ICU admission.[7] The primary objective of the study was to determine the prevalence of late defecation in severely burned adults. We also sought to determine the association of late defecation with various outcomes. At the study midway point, a performance improvement (PI) project was initiated. It involved the addition of 17 g of polyethylene glycol (PEG) 3350 twice daily to our standard bowel regimen of 100 mg of docusate sodium twice daily, both of which are initiated simultaneously with enteral nutrition. Two analyses were performed: one to assess the difference between the early-defecation and late-defecation groups, and the other to assess the effect of the PEG 3350 intervention.

Data Collection

Demographic data collected for all patients meeting study criteria included age, sex, percentage TBSA burned, percentage of full-thickness burned area, presence of inhalation injury, injury severity score (ISS), and morphine equivalents administered during ICU stay. Morphine equivalents were calculated by adding total parenteral narcotic usage while in the ICU, with 1 mg of hydromorphone held equivalent to 7 mg of morphine, and 100 mcg of fentanyl held equivalent to 1 mg of morphine.[15,16] As our facility is the only department of defense center for the care of burned military personnel, we also included combat casualties evacuated from the theaters of operation in Iraq and Afghanistan. These casualties typically sustain combined traumatic and thermal injuries and require lengthy evacuation times to reach our definitive treatment center. Secondary outcomes included ICU and hospital LOS, ICU- and 28-day mortality, ventilator-free ICU days, amount of times patients had residual gastric volumes of more than 300 ml, use of TPN, hours to initiation of first enteral feed, hours to first stool after initiation of enteral feeds, the frequency and type of abdominal complications, documented episodes of bacteremia during ICU stay, use of any adjuncts (magnesium citrate, magnesium hydroxide, continuous enteral infusion of Golytely [Braintree Laboratories, Braintree, MS] for markedly delayed laxation, suppositories, enemas, other laxatives or cathartics), use of a fecal management system (FMS) to control loose stool output, and evaluation of stool for presence of *Clostridium difficile* toxin. As an indicator of ongoing lower-GI tract dysfunction, episodes of constipation after the first BM were defined as 72 or more consecutive hours without defecation after first BM. Such episodes were recorded as a secondary outcome. The presence of abdominal complications was determined by query of the electronic medical record and radiology results; complications included ileus, obstruction, pneumatosis intestinalis, and perforation.

Statistical Analysis

Continuous data are presented as medians with interquartile ranges. Comparisons between groups were performed using Wilcoxon or Student's *t*-tests where appropriate. Categorical data are reported as proportions and, where appropriate, were tested for significance using χ^2 or Fisher's exact tests.

RESULTS

During the 26-month study period, 117 patients were admitted to the burn ICU; 83 patients met the inclusion criteria. Table 1 lists the demographics and outcomes for the patients. Of these patients, 53 (63.9%) had a BM within 6 days of admission to the unit, making up the early-defecation group. The remaining 30 patients (36.1%) were placed into the late-defecation group. Table 2 compares demographics, injury severity, and outcomes between the early- and late-defecation groups. Note that demographics, median ISS, and most outcomes including 28-day and in-hospital mortality were similar between the two groups. Patients with late defecation had longer ICU LOS, more frequent constipative episodes after first BM, had more feeding intolerance (gastric residuals more than 300 mL), and received TPN more frequently.

Table 1. Patient demographics (N = 83)

Age (yr)	46 (33.5–57.8)
Male sex, %	80.5
% TBSA	34.4 (4.6–51.8)
% FT	12 (2.3–24.8)
Inhalational injury, %	32.5
Combat casualties evacuated from Iraq/Afghanistan, %	9.6
ISS	25 (16–32.8)
24-hr resuscitation volume (ml)	13,734 (9,974–17,946)
ICU morphine equivalents (mg)	1,414 (764–2,380)
28-Day mortality (%)	14.5
ICU mortality (%)	30.1
ICU LOS (days)	26 (14–56)
Hospital LOS (days)	38 (27–74)
ICU ventilator-free days	11 (3–23)
Constipation episodes after first BM, n	2 (1–4)
Gastric residuals >300 ml, n	0 (0–3)
Abdominal complications (%)	38.6
Use of TPN (%)	10.8
Bacteremia (%)	56.6
Hours to first enteral feed	27 (17–40.3)

ISS, injury severity score; *ICU*, intensive care unit; *LOS*, length of stay; *TPN*, total parenteral nutrition; *FT*, full thickness.
Continuous data are presented as medians (interquartile range).

Table 3 compares demographics and outcomes between the PEG 3350 group and historical controls. An analysis of outcomes after the addition of PEG 3350 as a PI project did not positively affect any marker of lower-GI tract function, outcome, or complication. The only statistically significant finding between the two groups was that the PEG 3350 group had placement of an FMS more frequently than did the non-PEG 3350 group.

DISCUSSION

This report is the first to define the prevalence of late defecation as a marker of lower-GI tract dysfunction in critically ill burned adults. More than one third

Table 2. Early vs late defecation groups

	Early defecation (N = 53)	Late defecation (N = 30)	*P* Value
Age (yr)	48 (33.8–57)	45.5 (31.8–62)	.819
Male sex, %	74	87	.109
% TBSA	33.9 (27–51.1)	39 (28.1–53.2)	.631
% FT	10.9 (1.3–23)	21.6 (4.6–36.4)	.146
Inhalational injury, n	19	8	.397
ISS	25 (16–29)	25 (16.5–34)	.173
Combat casualties evacuated from Iraq/Afghanistan (%)	9.4	10	.93
24-hr resuscitation volume (ml)	12,381 (9,609–16,711)	15,246 (11,603–18,582)	.14
ICU morphine eq (mg)	1,159 (722.2–2,448)	1,661 (880.8–2,315)	.164
28-Day mortality (%)	15.1	13.3	.829
ICU mortality (%)	28.3	33.3	.636
ICU LOS (days)	21 (12–41)	36.5 (18.8–65)	.05
Hospital LOS (days)	35 (26–55)	51.5 (33.8–76)	.087
ICU ventilator-free days	10 (2–18)	12.5 (5.5–35)	.067
Constipation episodes after first BM	2 (1–3)	3 (2–6)	.03
Gastric residuals >300 ml	0 (0–2)	0 (0–6)	.007
Abdominal complications (%)	39.6	36.7	.793
Use of TPN (%)	3.8	23.3	.005
Bacteremia (%)	49.1	70	.066
Hours to first enteral feeding	26 (15.75–41)	30 (24–35)	.691

ISS, injury severity score; *ICU*, intensive care unit; *LOS*, length of stay; *TPN*, total parenteral nutrition; *BM*, bowel movement; *FT*, full thickness.

of patients demonstrated late defecation, defined as first BM more than 6 days after ICU admission for thermal injury. Late defecation was associated with significantly more episodes of enteral feeding intolerance, episodes of constipation after initial laxation, and use of TPN compared with early defecation. The interim addition of PEG 3350 as an adjunct for laxation at the midway point of the study did not improve markers of lower-GI tract function or other measured outcomes.

Table 3. Non-PEG 3350 vs PEG 3350 groups

	Non-PEG 3350 (N = 36)	PEG 3350 (N = 47)	*P* Value
Median age (yr)	44 (34–54)	49 (30.3–61)	.593
Male sex (%)	84	76.6	.532
% TBSA	29.8 (26.3–48)	38.1 (28.9–52)	.221
% FT	10.9 (2.1–23)	15.4 (2–3.4)	.3
Inhalation injury	8	19	.058
ISS	25 (16–25)	25 (25–34)	.021
ICU morphine eq (mg)	1150 (813–2571)	1634 (754–2315)	.618
28-Day mortality (%)	8.3	19.2	.144
ICU mortality (%)	25	34	.308
ICU LOS (days)	27 (8.8–63)	25 (17–52)	.186
Median hospital LOS (days)	35 (26–78)	45.5 (28.5–68)	.272
ICU ventilator-free days	7 (2–22)	12.5 (6.3–23)	.182
Additional constipation episodes	2 (1.8–4)	2 (1–4)	.415
Gastric residuals >300 mL	0 (0–0)	0 (0–3)	.519
Abdominal complications (%)	30.6	44.7	.142
Use of TPN (%)	16.7	6.4	.162
Bacteremia (%)	66.7	48.9	.179
Hours to first enteral feed	27 (17.8–45)	27.5 (17–35)	.259
Use of FMS (%)	72	94	.001
Evaluation for *Clostridium difficile*, %	30.6	27.7	.885

PEG, polyethylene glycol; *FT*, full thickness; *ISS*, injury severity score; *LOS*, length of stay; *TPN*, total parenteral nutrition; *FMS*, fecal management system; *ISS*, injury severity score; *ICU*, intensive care unit.

In their randomized study in critically ill adults requiring MV and circulatory support comparing lactulose, PEG, and placebo, van der Spoel et al[7] determined the prevalence of late defecation to be 32.1% (van der Spoel JI, personal communication, September 2012). Several factors may have contributed to the unique prevalence of late defecation in our patients. Enrollment in van der Spoel's prospective study occurred if patients had not defecated by the third day of ICU admission, whereas our retrospective study evaluated all patients from time of admission; not specifically those demonstrating initial lower-GI tract dysfunction. If similar enrollment criteria were used in the van der Spoel study, their prevalence can be assumed to have been much lower than reported. As the pathogenesis of constipation/late defecation in ICU patients includes sepsis-associated motility dysfunction, GI hypoperfusion caused by hypotension, hypovolemia and vasoactive drugs, and the negative impact of narcotics on motility, severely burned patients are arguably at much higher risk for all of these processes than a general ICU population.[7–9] These cumulative and more severe GI inhibitory factors likely contributed to our higher prevalence of late defecation in severely burned adults included in our study.

Opiods have well-established GI motility inhibitory effects. Because of high narcotic requirements, our patients receive the opioid antagonist naloxone enterally dosed at 2 mg every 6 hours at the first sign of motility dysfunction. Surprisingly, ICU morphine equivalents received were not significantly different between the early- and late-defecation groups, suggesting other factors for late defecation. Gacouin et al[9] showed an association between vasopressor use, applied positive end expiratory pressure (PEEP), hypotension, and severity of hypoxemia with delayed bowel function in mechanically ventilated patients. These factors may have contributed to the delayed laxation in more than one third of our patients. In contrast to findings of previous studies, we did not find an association between lower-GI tract dysfunction and ventilator-free days, increased ICU mortality, or 28-day mortality when compared with those patients who had a BM within 6 days of ICU admission.[7,9] In the prospective observational study by Gacouin et al,[9] there was an association between those patients with constipation and a higher incidence of bacterial infections. We examined the incidence of bacteremia, but did not find a difference when comparing late with early BM (21 vs 26 episodes; $P = .06$).

Patients in the late BM group had a longer ICU LOS, although overall hospital LOS was not affected. It is possible that those patients with late defecation represented a more ill cohort of patients with more severe organ dysfunction and thus had longer ICU LOS, as it has been shown that constipation is a marker of illness severity.[7,9] Although a comparison of ISS scores between the groups (Table 2) would indicate that this is not the case, there are multiple variables that are not accounted for in ISS scoring that, if recorded, may have shown the higher acuity of the delayed laxation group. Also, despite similar injury severity demographics at admission, organ function may have deteriorated more severely in the late-defecation cohort as critical illness evolved. Important questions to consider include whether earlier laxation would affect upstream motility and potentially global GI tract function and would this improve our ability to administer adequate enteral calories? Late defecation could reflect global GI tract motility dysfunction as it was associated with foregut dysmotility and ongoing hindgut dysmotility. It is also possible that late defecation contributed to the inability to administer adequate enteral nutrition, and improvement in this endpoint may have prevented the severe caloric deficit in patients who received TPN. As of now the answer to these questions remain elusive and are hypothesis generating.

We conducted a PI project at the midway point of the study that involved the addition of 17 g of PEG 3350 twice daily to our standard bowel regimen. Despite previous reports of PEG 3350 resulting in earlier laxation, our experience was not consistent with this.[7] There were no significant differences in markers of lower-GI function between the PEG and non-PEG groups. The study by Van der Spoel et al[7] compared two agents with a placebo; we did not have a placebo control, but rather a standard bowel regimen with docusate sodium twice daily. It is possible that the dose of PEG 3350 was too low to positively affect laxation. However, the increased use of an FMS in the PEG 3350 group may indicate that stool output, when it occurred, tended to be more liquid.

The greatest impact this study provides is opening the door for future characterization of GI dysfunction in arguably the most severely ill population of adult ICU patients. The GI tract has long been speculated to be the source of inflammatory mediators, nosocomial infections including ventilator-associated pneumonia, bacteremia, and even mortality in critical illness.[1,2,17,18] Despite speculation of the relationship between GI dysfunction and outcomes in critical illness, precise definition of abnormal function, failure, and correlation with GI tract outcomes and morbidity and mortality is lacking.[1,2] Confounding this paucity of data is the fact that the multiple anatomically distinct portions of the GI tract demonstrate normal function and dysfunction/failure very differently. In addition, when considering the global function of the GI tract, one must take into consideration the multiple, interrelated aspects of its function; namely, motility, absorption, immunologic, barrier, secretion/endocrine. To say the least, the GI tract represents one of the most complex organ systems affected by critical illness and one of the most poorly studied; the least studied segment in critical illness being the hindgut. The best data to date on the subject of colonic motility in the ICU is the previously discussed report by van der Spoel et al.[7] We have chosen to maintain consistency by using the same terminology: late defecation, to describe lower-GI motility dysfunction in our adult burn population. The retrospective findings of this study are hypothesis generating and meaningful to our institution and to the broader burn community as this problem has not been described previously and is likely extremely common and potentially associated with worse outcomes. Whether lower-GI tract dysfunction is causally related to the morbidities discussed in this and previous studies is debatable. Our institution is actively involved in organ function research including GI function. We are currently in the process of prospective validation of late defecation as a marker of lower-GI dysfunction, its association with outcomes, and determining risk factors associated with its development. In addition, we are planning a prospective observational study to determine the prevalence of various markers of GI tract dysfunction in critically ill burn patients; late defecation is one marker to be evaluated in this planned study.

Our study has several limitations. It is retrospective in nature and suffers from the limitations inherent in such reviews. Though we collected data during a 2-year period, our sample size is small. No attempt was made to standardize triggers for TPN initiation. In addition, validated organ function scores were not measured; this would be useful in future research to correlate late defecation with global scores of organ dysfunction and failure.

CONCLUSION

We have demonstrated that more than one third of critically ill, severely burned adults admitted to an ICU are found to have late defecation. This delay in laxation is associated with continued lower-GI tract dysfunction, enteral feeding intolerance, and the use of TPN. A prospective study at our institution is currently planned to attempt to validate late defecation as a marker of lower-GI dysfunction, determine its relationship to various outcomes, and determine risk factors for its development.

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