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The effect of perioperative fluid management on postoperative ileus in rectal cancer patients

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Abstract

Background—Postoperative ileus is a common cause of increased morbidity and cost after operative intervention. The aim of this study was to assess how fluid type, volume, and timing may affect incidence of postoperative ileus.

Methods—A retrospective cohort study was performed on patients undergoing operative intervention for rectal cancer from 2008 to 2015 at a single institution. Univariate and multivariate analyses were used to assess the effect of type (crystalloid versus colloid), volume by quartile, and timing (perioperative versus postoperative) on rate of postoperative ileus.

Results—A total of 300 patients were included, and the overall incidence of ileus in our cohort was 30% (n = 90). Both univariate and multivariate analyses showed that increasing volume of crystalloid volume administered was associated with increased postoperative ileus incidence (first quartile: 16.3%; second quartile: 31.5%, third quartile: 34.2%; and fourth quartile: 39.2%; P = .012), and administration of colloid was not shown to correlate. Furthermore, timing was not shown to be associated with the rate of postoperative ileus.

Conclusion—Increased volumes of crystalloid are associated with higher rates of ileus, while administration of colloid is not. Based on this retrospective data, limiting the volume of crystalloid perioperatively may help lower the rate of ileus postoperatively. (*Surgery* 2017;161:1628-32.)

Postoperative ileus (POI) is a common complication following abdominal operation, occurring in approximately 17%–27% of patients undergoing partial colectomy.¹ It not only occurs at high incidence but also has significant consequences for both the patient and the health care system. It has been reported that POI increases the mean hospital duration of stay by nearly 5 days and increases the cost of care by approximately \$8,000 per stay.^{2,3} Other

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analyses have shown higher complication, reoperation, readmission, and mortality rates in patients with ileus.⁴

Thus, a greater understanding of causes and possible preventative strategies has the potential to significantly improve quality and value of care for patients undergoing abdominal operations.^{3–6} While the development of POI can rarely be attributed to a single cause, several management considerations, such as fluid status, use of nasogastric decompression, opioid use, and operative approach have been implicated as potentially modifiable risk factors for POI.^{7,8}

Intravenous fluid (IVF) administration and volume status are clearly associated with POI. Bowel edema secondary to volume overload is associated with delayed recovery of gastrointestinal function and extended hospital stay.⁷ Conversely, relative intraoperative fluid restriction in patients undergoing major intra-abdominal surgery has been shown to shorten the time to recovery of gastrointestinal function.⁹

It remains unclear, however, if the primary effect of IVF administration on bowel function is due to net volume gain, hypoalbuminemia, or both. Studies performed using albumin replacement have not demonstrated any improvement in tolerance of enteral feeding or acceleration in return of bowel function, leaving the role of hypoalbuminemia unclear.^{10,11} While multiple previous studies have compared crystalloid and colloid, none have evaluated POI as an outcome.^{12,13} Furthermore, the timing of IVF administration in the perioperative period as it relates to development of POI has not been investigated previously.

The aim of this study was to characterize the impact of the volume, type, and timing of IVF administration during the perioperative period on risk of POI in patients undergoing surgery for rectal cancer. We hypothesized that greater volume of IVF, crystalloid fluids, and large relative volume administered intraoperatively would all increase the risk for POI.

METHODS

Study population

This study is a retrospective cohort study including all patients with a diagnosis of rectal cancer who underwent proctectomy or proctocolectomy at the University of Wisconsin Hospital from August 2008–June 2015. Patients for whom documentation of perioperative fluid administration was incomplete or unobtainable were excluded. Data were extracted from each subject's electronic medical record. This study was approved by the University of Wisconsin-Madison Institutional Review Board.

Variable definitions and end points

Retrospective chart review was performed to collect patient-, operative-, fluid-, and outcomes-related data for each subject. Patient-related variables included age, body mass index (BMI), ethnicity, American Society of Anesthesiologists (ASA) classification, smoking status (defined as current smoker or past smoker versus nonsmoker), receipt of neoadjuvant chemotherapy, tumor stage, and presence of comorbidities, including diabetes, congestive heart failure, hypertension, chronic obstructive pulmonary disease, and

disseminated cancer. Operation-related variables included operation performed, operative time, operative approach, estimated blood loss, and wound classification.

Fluid type, volume, and day of administration were the primary exposure variables of interest. Fluid type was categorized as crystalloid (including lactated ringers, 0.45% and 0.9% normal saline, dextrose 5%-water) or colloid (including 2.5% or 5% albumin, hetastarch, and packed red blood cells). Fluid timing was categorized as occurring intraoperatively, postoperatively on the day of operation, postoperative day (POD) 1, or POD 2 or later. Volume of fluid received for each time period was recorded separately for crystalloid and colloid fluids.

For analytic purposes, continuous variables were broken into clinically significant groups when possible and into quartiles when no clear clinically significant cutoffs were apparent. Intraoperative crystalloid volume was divided into quartiles, yielding 4 categories with the following cutoffs: 0–2,700 mL, 2,701–3,400 mL, 3,401–4,200 mL, and greater than 4,200 mL. Intraoperative colloid administration was defined as a binary variable based on whether the patient received any colloid versus no colloid fluids. Age was divided into 4 categories (less than 50 years, 50–64 years, 65–79 years, and greater than 80 years); BMI was defined as normal (BMI < 25), overweight (25–29.9), and obese (≥ 30); operative duration was divided into quartiles; and estimated blood loss was divided into categories (0–100 mL, 101–500 mL, 501–1,000 mL, and >1,000 mL).

The primary outcome for this study was occurrence of postoperative ileus, defined using the American College of Surgeons National Surgical Quality Improvement Program definition of presence of nasogastric tube or nil per os (NPO) status on POD 4 or later.

Statistical analysis

We investigated the relationship between perioperative fluid administration and POI. Initial univariate analysis using χ^2 tests was performed to identify patient and operative characteristics associated with the development of POI. Similarly, univariate analysis was used to explore the relationship between fluid volume and type with POI.

Multivariate analysis using binary logistic regression was then performed to examine the independent effect of both fluid volume and fluid type using POI as the outcome. All variables for which there was a statistically significant association with POI on univariate analysis ($P < .05$) were included in the multivariate model: age, BMI, smoking status, and operative approach. Additionally, we adjusted for operative duration and estimated blood loss.

The impact of timing of fluid administration on POI was assessed by comparing the rate of fluid administration intraoperatively (mL/min) to the rate of fluid administered during POD 1 (mL/min). Thus, this value, termed the “rate ratio,” was higher in patients receiving a predominance of their IVF in the operating room and lower in those receiving most of their IVF on POD 1. An independent sample Student *t* test was performed to compare the mean rate ratios between patients with and without POI. All analyses were performed using SPSS software (version 22; IBM Corp, Armonk, NY).

RESULTS

A total of 300 patients were identified for inclusion in this study. The majority of patients in the study underwent a low-anterior resection (66%, $n = 199$) or abdominoperineal resection (25%, $n = 74$), while the remaining 9% ($n = 27$) underwent total proctocolectomy, sigmoid colectomy, or pelvic exenteration. Incidence of POI in our overall cohort was 30.0% ($n = 90$). On univariate analysis, patients developing POI were older (62 years vs 57.5 years; $P = .004$), lost more blood intraoperatively (532 mL vs 344 mL; $P = .002$), were more likely to undergo open operation (76% vs 52%; $P < .001$), and received higher average intraoperative crystalloid fluid volume (3,944 mL vs 3,348 mL; $P < .001$) (Table I).

Additionally, increasing quartile of crystalloid volume administration was associated with a higher incidence of POI (first quartile: 16.3%; second quartile: 31.5%; third quartile: 34.2%; fourth quartile: 39.2%; $P = .012$), while receipt of colloid was not associated with any change in POI incidence.

The multivariate analysis confirmed that volume of IVF administration is an independent predictor of POI, while also showing that receipt of colloid does not predict development of POI (Table II). Additional independent predictors of POI that were identified on multivariate analysis included patient age if older than 80 years (odds ratio [OR]: 6.883; 95% confidence interval [CI]: 1.877–25.239) as well as laparoscopic and robotic approach (OR: 0.392; 95% CI: 0.184–0.836 and OR: 0.236; 95% CI: 0.064–0.0873, respectively) compared to open (Table II). Finally, no difference was seen in the average rate ratio for those who developed POI and those who did not develop POI (ileus: 7.996; no ileus: 6.814; $P = .286$) (Table I).

DISCUSSION

In this single-institution, retrospective analysis of patients undergoing rectal cancer operation, we found that increasing volumes of crystalloid fluid administration was associated with higher incidence of POI, but that colloid fluids did not appear to increase the risk for delayed return of bowel function. While the former finding is consistent with prior studies detailing the success of restricted fluid protocols in lowering POI incidence,^{7,9} the latter has not been described previously to our knowledge. The failure of colloid fluids to increase risk for POI suggests that interstitial, third-spacing of fluid plays an important role and may represent a potential opportunity to modify risk for POI in select patients.

The incidence of POI in our cohort was 30.0%, which is higher than most of the figures reported in the literature.^{3–5} This is likely related to several reasons. Our cohort consisted of patients undergoing abdominal operations for rectal cancer with a relatively large proportion of open operations. Additionally, diagnosis of POI was ascertained via chart review, which likely has much higher sensitivity than reliance on billing codes, such as the use of the International Classification of Diseases, Ninth Revision codes, as described by Iyer et al.³ Finally, exact definitions of POI vary widely in the literature, using indicators such as nasogastric tube reinsertion, nausea or vomiting, return of flatus or stool, or ability to tolerate food.^{4,5} Our use of the presence of nasogastric tube or NPO status on POD 4 is relatively liberal, likely contributing to our high overall observed POI incidence.

Colloid fluids did not appear to affect the risk of POI in the same way as crystalloid fluids. This finding supports our hypothesis that colloid may have a decreased POI-inducing effect or may have no effect at all. Some studies have found that use of colloid in fluid resuscitation of the critically ill can lead to a modest increase in mortality over the use of crystalloid, but studying how colloid might impact POI is a largely novel area of research.^{12,13} Mechanistically, colloid would be expected to result in less bowel edema than comparable volumes of crystalloid due to the ability of colloid to maintain the colloid osmotic pressure within the vasculature, in contrast to the hemodiluting effects of crystalloid.

Analysis of rate ratios was completed to assess the temporality of fluid administration. It is a rough index that reflects fluid administration in the intraoperative versus the postoperative phase. The ratio uses rates as opposed to absolute volume in order to quickly control for the varying durations of the operations. We observed that those who developed POI had not received a higher rate of fluid intraoperatively than they received postoperatively. This preliminary finding suggests that the bowel is not disproportionately vulnerable to fluid effects in the intraoperative period compared to the postoperative phase of care.

Our study does have several important limitations. First, due to the retrospective and non-randomized design, there are certainly unmeasured differences between the patients comprising each of the intraoperative fluid quartiles and between those receiving just crystalloid or crystalloid/colloid together. We collected data on what we considered to be the most clinically relevant potential confounders and controlled for these variables; however, it is impossible to account for all management decisions with regard to fluid administration in the perioperative period in a nonrandomized and retrospective study.

Many variables, such as preoperative fluid status and the type and route of anesthesia, were not addressed. As such, the results should only be used as a consideration in determining fluid administration. Furthermore, many factors have been shown to contribute to the etiology of POI, and many of these, including medications or administration of TPN, were not analyzed in this study. Future studies focusing on factors that necessitate increased fluid administration would be beneficial in addressing how best to limit the incidence of POI.

Fluid status in a surgical patient is the result of many factors, including operative duration, blood loss, and patient fluid excretion. While these factors likely play a role in POI development, analysis was done on administered fluid, because it is the factor that is most easily adjusted at the time of the operation.

Additionally, given the modest sample size of this study, it may lack the degree of power necessary to detect differences in some subgroups of our analyses. For example, only 108 subjects received colloid, which limited our ability to investigate how volume of colloid administration impacts POI. Instead, we treated colloid administration as a binary variable and compared all colloid recipients to nonrecipients.

Finally, we did not address which, if any, patients may have been intentionally managed on an enhanced recovery protocol. These protocols address preoperative, intraoperative, and postoperative elements of care, including close monitoring and restriction of intravenous

fluids to less than 3,500 mL of fluid for colonic or rectal resection, respectively, on the day of operation.¹⁴ Studies assessing the impact of enhanced recovery protocols for colorectal cancer resection have shown that these protocols improve outcome over traditional protocols for recovery after an operation. Additionally, this literature notes no increase in complications in patients managed on a fluid-restrictive protocol.¹⁴

POI is not the only complication that can occur after major abdominal operation. Theoretically, an excessive restriction of fluid runs the risk of inducing renal insufficiency and a host of other concerns. As mentioned above, studies using an enhanced recovery protocol did not show an increase in complications leading us to believe that fluid restriction does not impact other complications.

Despite these limitations, we have demonstrated that increasing volumes of crystalloid, but not colloid, increase the risk of POI in patients undergoing operative intervention for rectal cancer. This study is a novel investigation into how crystalloid and colloid administration may alter the risk for POI and is an important step in hopefully identifying potential ways to reduce the risk of this common postoperative complication. Further study, in the form of a randomized prospective trial, would be beneficial for cementing the role that fluid status plays in the etiology of postoperative ileus.

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Table I

Patient, operative, and fluid characteristics of patients with and without ileus

<i>Characteristic</i>	<i>No ileus</i>	<i>Ileus</i>	<i>P value</i>
	<i>(n = 210)</i>	<i>(n = 90)</i>	
	<i>% (n)</i>	<i>% (n)</i>	
Age, mean (y)	57.5	62	.004
Age category			.041
<50 y	24.8 (52)	17.8 (16)	
50–64 y	47.6 (100)	38.9 (35)	
65–79 y	23.3 (49)	33.3 (30)	
>80 y	4.2 (9)	10 (9)	
Sex (% men)	55	63	.17
BMI category			.529
<25	31.9 (67)	28.9 (26)	
25–29	33.8 (71)	30 (27)	
>30	34.3 (72)	41.1 (37)	
ASA class category			.219
1 or 2	61.0 (128)	53.3 (48)	
3 or 4	39.0 (82)	46.7 (42)	
Operation duration, mean (min)	283	304	.111
Operation duration category			.212
<226	26.7 (56)	22.2 (20)	
226–273	24.2 (51)	25.6 (23)	
274–329	27.1 (57)	20.0 (18)	
>329	21.9 (46)	32.2 (29)	
Smoker, %	39	49	.114
Operative approach			.001
Open	52 (110)	75.6 (68)	
Laparoscopic	30.4 (64)	15.6 (14)	
Hand-assisted laparoscopic	5.2 (11)	5.6 (5)	
Robotic	11.9 (25)	3.3 (3)	
Estimated blood loss, mean (mL)	344	532	.002
Estimated blood loss category			.005
0–100	32.4 (68)	21.1 (19)	
101–500	52.9 (111)	46.7 (42)	
501–1,000	9.0 (19)	20.0 (18)	
>1,000	5.7 (12)	12.2 (11)	
Intraoperative crystalloid, mean (mL)	3,348	3,944	<.001
Intraoperative crystalloid quartile			.012
0–2,700	31.9 (67)	14.4 (13)	
2,701–3,400	23.8 (50)	25.6 (23)	
3,401–4,200	22.9 (48)	27.8 (25)	

<i>Characteristic</i>	<i>No ileus</i>	<i>Ileus</i>	<i>P value</i>
	<i>(n = 210)</i>	<i>(n = 90)</i>	
	% (n)	% (n)	
>4,200	21.4 (45)	32.2 (29)	
Intraoperative colloid, mean (mL)	197	245	.25
Intraoperative colloid category			.142
Received colloid	66.7 (140)	57.8 (52)	
Did not receive colloid	33.3 (70)	42.2 (38)	
Fluid rate ratio, mean	7.996	6.814	.286

Table II**Multivariate model predicting postoperative ileus**

<i>Variable</i>	<i>OR (95% CI)</i>	<i>P value</i>
Intraoperative crystalloid (mL)		
0–2,700	Reference	
2,701–3,400	2.884 (1.192–6.979)	.019
3,401–4,200	2.973 (1.191–7.418)	.02
>4,200	3.417 (1.321–8.842)	.011
Intraoperative colloid (mL)		
None	Reference	
Received	0.996 (0.531–1.869)	.99
Age		
<50	Reference	
50–64	0.957 (0.451–2.031)	.908
65–79	1.625 (0.729–3.623)	.235
>80	6.883 (1.877–25.239)	.004
BMI		
<25	Reference	
25–29	0.844 (0.416–1.715)	.639
>30	0.926 (0.462–1.856)	.828
Operation duration		
<226	Reference	
226–273	1.31 (0.568–3.020)	.526
274–329	0.808 (0.334–1.951)	.635
>329	0.236 (0.661–3.848)	.299
Smoking status		
Never smoked	Reference	
Current or past smoker	1.625 (0.910–2.902)	.101
Operative approach		
Open	Reference	
Laparoscopic	0.392 (0.184–0.836)	.015
HALS	0.99 (0.283–3.466)	.987
Robotic	0.236 (0.064–0.873)	.031
Estimated blood loss (mL)		
0–100	Reference	
101–500	0.764 (0.366–1.593)	.473
500–1,000	1.512 (0.565–4.051)	.419
>1,000	1.360 (0.415–4.457)	.612