Crystalloids After Primary Colon Resection and Anastomosis at Initial Trauma Laparotomy: Excessive Volumes Are Associated With Anastomotic Leakage

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Background: Recognition of preventable risk factors for suture line failure after colon anastomosis is important for optimizing anastomotic healing. The purpose of this study was to investigate the impact of crystalloids on the occurrence of anastomotic leakage after traumatic colonic injuries.

Methods: Retrospective review from January 2005 to August 2009 of severely injured patients who underwent primary colocolonic anastomosis and intensive care unit (ICU) admission for ≥72 hours. Demographics on hospital and ICU admission, amount of crystalloids, and blood component transfusions within the first 72 hours were assessed by multivariate analysis to explore independent associations with anastomotic leakage.

Results: Of a total of 123 patients with primary colocolonic anastomosis, 7 died within 72 hour and 24 were discharged before 72 hour from the ICU. The remaining 92 patients required ICU admission for ≥72 hour. Their mean Injury Severity Score was 20.8 ± 10.7, and they were 29.9 years ± 13.0 years old. Twelve patients (13.0%) developed an anastomotic leak. Demographics on hospital and ICU admission, intraoperative blood loss, and the volume of intraoperative fluids given did not differ statistically between patients with or without anastomotic leakage. However, the cumulative amount of crystalloids given over the first 72 hours significantly predicted anastomotic leakage (area under the receiver operating characteristic curve: 0.758 [95% confidence interval 0.592–0.924], $p = 0.009$). By multivariate analysis, ≥10.5 L of crystalloids given over the first 72 hours was independently associated with anastomotic breakdown (odds ratio [95% confidence interval]: 5.26 [1.14–24.39], $p = 0.033$). In addition, increasing age, hemorrhagic shock on admission, and a concomitant stomach injury were independent risk factors for an anastomotic leak ($R^2 = 0.396$).

Conclusion: Increased use of crystalloids after primary colocolonic anastomosis at initial trauma laparotomy is associated with anastomotic leakage. A threshold of 10.5 L of crystalloid fluid infused over the first 72 hours is associated with a 5-fold increased risk for colocolonic suture line failure. The impact of crystalloid restriction on anastomotic failure in trauma patients warrants prospective investigation.

Key Words: Trauma, Colon, Anastomosis, Hollow viscus injury, Crystalloid, Postoperative management.

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Primary anastomosis in traumatic colon injuries has been shown to be safe and feasible in a wide range of trauma patients. However, anastomotic leakage rates of up to 16% have been reported.[1–10] Advancing patient age,[11] hypotension on admission,[3,12] high abdominal trauma index (ATI),[3] left-sided colonic injury,[3] >4 units of packed red blood cell (PRBC) transfusions within the first 24 hours,[1] >6 units of PRBC intraoperatively,[13] number of suture lines,[14] abdominal compartment syndrome,[11] the need for vasopressors,[15] and intensive care unit (ICU) length of stay[11] have been found to be independently associated with anastomotic failure. Although the initial injury is not modifiable, recognition of potentially preventable risk factors during the postoperative phase may facilitate anastomotic healing.

There is Level 1 evidence that after elective colon resections, the perioperative restriction of crystalloids decreases the anastomotic leak rate.[16] The effect of salt and water overload may cause splanchnic edema, increased intra-abdominal pressure and thus decreased mesenteric flow leading to decreased tissue oxygenation and intramucosal acidosis. As a direct consequence, increased gut permeability and impaired wound healing with anastomotic dehiscence may result.[17,18]

In trauma patients sustaining colonic injury, the initial resuscitation is primarily guided by the patient's hemodynamic status, with a goal of maintaining a perfusing blood pressure (BP). After the initial stabilization and surgical management, however, the role of crystalloid restriction in an attempt to prevent anastomotic leakage is unknown in the trauma patient. Therefore, this study was conducted to assess the impact of crystalloids after the initial resuscitation and treatment phase on the occurrence of anastomotic leakage.

METHODS

After institutional review board approval, the Los Angeles County + University of Southern California Medical Center trauma registry was queried, and patients who had sustained a colon injury from January 2005 to August 2009 were identified using the International Classification of Diseases-9th Edition codes. Patient data were collected using a computerized spreadsheet (Microsoft Excel 2003, Microsoft Corporation, Redmond, WA) and included demographics and clinical data on hospital and ICU admission. All trauma patients who underwent colonic resection with primary colocolonic or colorectal anastomosis at the initial trauma laparotomy and were admitted for ≥72 hours to the ICU were included for analysis. Patients who underwent damage control laparotomies with delayed colocolonic anastomosis were excluded from the analysis.

Intraoperative variables abstracted from the anesthesiology notes and operative reports included estimated blood loss, total amount of crystalloids, colloids, and blood component transfusions (PRBC, fresh frozen plasma [FFP], and platelets).

Data collected from the electronic ICU records at 24 hours, 48 hours, and 72 hours included total amount of crystalloids/colloids/PRBC/FFP/platelets, urine output, and vasopressors. In addition, the first arterial blood gas analysis on ICU admission, the first Acute Physiology and Chronic Health Evaluation (APACHE) II score, and the highest APACHE II score within 72 hours after ICU admission were documented. Anastomotic leakage was defined as a suture line failure visualized at unplanned relaparotomy or feculent drain discharge in combination with a gas-containing fluid collection next to the anastomosis on the computed tomographic scan.

Continuous variables, times, and categorical variables are reported as mean ± standard error of the mean or standard deviation, mean ± interquartile (IQ) range, and percentage, respectively; *p* values were obtained from χ^2 or Fisher's exact test for proportions and from Mann-Whitney *U* test for continuous variables.

To assess the impact of the volume of crystalloids, PRBC, and FFP administered on anastomotic leakage, area under the receiver operating characteristic curves were calculated. Furthermore, to explore a critical threshold for the volume of crystalloids given within 72 hours in relation to the development of an anastomotic leak, a cutoff analysis was performed using repeated multivariate analysis exploring increasing volumes beginning at 5,000 mL in 500 mL steps. The highest R^2 defined the best cutoff. A similar cutoff analysis was performed for transfused units of PRBC within 72 from admission, beginning with the first unit in 1 unit steps.

To detect potential risk factors for the development of an anastomotic leakage, demographics on admission, intraoperative fluids and ICU data at 24 hours, 48 hours, and 72 hours were compared using univariate analysis. Subsequently, multivariate analysis, adjusting for the significant differences ($p < 0.05$), was used to detect independent associations. In addition, all differences ($p < 0.2$), including the critical cutoff values for the 72-hour-volume of crystalloids and transfused PRBC units, were entered into a forward logistic regression model to identify independent risk factors for the development of an anastomotic leakage.

All statistical analysis were performed using the Statistical Package for Social Sciences (SPSS Windows), version 16.0 (SPSS, Chicago, IL).

RESULTS

During the 56-month study period, 152 patients with colonic injuries requiring resection were admitted. Of those patients, 16 underwent damage control laparotomy with fecal diversion and 13 underwent ileocecal resection with ileocolic anastomosis and were excluded (Fig. 1). The remaining 123 patients (80.9%) underwent primary colocolonic anastomosis. Of those, 7 patients died within the first 72 hours and 24 were admitted to the floor or to the ICU for <72 hours (Fig. 1).

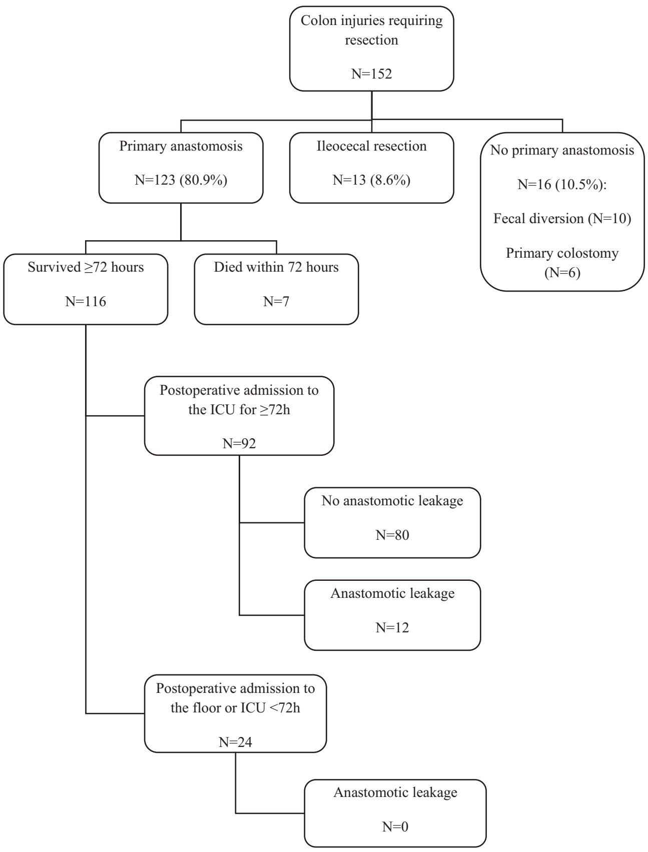

Figure 1. Outline of the study population.

The remaining 92 patients were admitted to the ICU for ≥72 hours and were further analyzed. The mean Injury Severity Score (ISS) for these patients was 20.8 ± 10.7, and they were 29.9 years ± 13.0 years old (Table 1). Their mean ICU length of stay was 9.4 (IQ range, 3.5–9.5) days. In 16 of these 92 patients (17.4%), the abdominal fascia was not closed at the initial operation. A delayed abdominal fascial closure was then performed. A total of 12 patients (13.0%) developed an anastomotic dehiscence. In eight cases, the suture line failure was found at reoperation because of fascial dehiscence with feculent discharge (n = 4) or abdominal distension with increasing signs of sepsis (n = 4). In four cases, feculent discharge from the drains and the computed tomographic scan findings of gas-containing fluid collections next to the anastomosis led to the diagnosis of anastomotic failure. These four patients underwent conservative treatment with prolonged antibiotic treatment and computed tomography-guided drainage of fluid pockets. The average time of failure was 12.0 days (IQ range, 7.0–14.0 days) after admission. These patients were significantly more often in hemorrhagic shock on admission (systolic BP <90 mm Hg) and had sustained significantly more often a concomitant stomach injury compared with the patients without leakage (Table 1). The ATI score and the location of the colocolonic anastomo-

TABLE 1. Univariate Analysis of the Demographic Differences Between Patients With No Leak and Leak

	Total (N = 92)	Leak (N = 12)	No Leak (N = 80)	p*
Age (yr)	29.9 ± 13.0	38.4 ± 15.7	28.6 ± 12.1	*0.024*
Male	83 (90.2)	12 (100.0)	71 (88.8)	0.221
ISS	20.8 ± 10.7	23.2 ± 10.4	20.4 ± 10.8	0.284
ISS ≥16	67 (72.8)	11 (91.7)	56 (70.0)	0.116
Systolic BP <90 mm Hg on admission	10 (10.9)	4 (33.3)	6 (7.5)	*0.007*
GCS score ≤8	3 (3.3)	0 (0.0)	3 (3.8)	0.495
Penetrating injury	68 (73.9)	10 (83.3)	58 (72.5)	0.425
AIS head ≥3	11 (12.0)	1 (8.3)	10 (12.5)	0.678
AIS chest ≥3	27 (29.3)	4 (33.3)	23 (28.8)	0.745
AIS extremity ≥3	16 (17.4)	2 (16.7)	14 (17.5)	0.943
Site of colon injury				
Left colon	40 (43.5)	6 (50.0)	34 (42.5)	0.214
Right colon	31 (33.7)	2 (16.7)	29 (36.3)	0.325
Transverse colon	17 (18.5)	3 (25.0)	14 (17.5)	0.689
Rectum	2 (2.2)	0 (0.0)	2 (2.5)	1.000
Multiple, requiring subtotal colectomy	2 (2.2)	1 (8.3)	1 (1.3)	0.245
Concomitant injury				
Liver	9 (9.8)	0 (0.0)	9 (11.3)	0.221
Spleen	11 (12.0)	1 (8.3)	10 (12.5)	0.678
Pancreas	4 of 88 (4.3)	1 (8.3)	3 (3.8)	0.468
Kidney	12 (13)	3 (25.0)	9 (11.3)	0.187
Abdominal vascular injury	12 (13)	3 (25.0)	9 (11.3)	0.187
Stomach	9 (9.8)	4 (33.3)	5 (6.3)	*0.003*
Small bowel	49 (53.3)	4 (33.3)	45 (56.3)	0.138
Perforation of diaphragm	9 (9.8)	1 (8.3)	8 (10.0)	0.856
ATI	29.8 ± 8.4	28.9 ± 9.4	30.0 ± 8.3	0.547
Delayed abdominal closure	16 (17.4)	4 (33.3)	12 (15)	0.118
Hours to OR <6 h	11 (88.0)	11 (91.7)	70 (87.5)	0.678
Units PRBC within the first 24 h	6.0 ± 6.8	8.0 ± 9.6	5.6 ± 6.0	0.316
≥4 U PRBC within 24 h	29 (31.5)	4 (33.3)	25 (31.3)	0.885

GCS, Glasgow Coma Scale; AIS, Abbreviated Injury Scale; OR, odds ratio.
* Mann-Whitney *U* test, χ^2 test, or Fisher's exact test.
Values are presented as mean ± standard deviation or N (%).

TABLE 2. Comparison of the Intraoperative Estimated Blood Loss and Fluids Administered Between Patients With Leak and No Leak (Mean ± Standard Error of the Mean)

	Total (N = 92)	Leak (N = 12)	No Leak (N = 80)	p*
Estimated blood loss (mL)	1,186 ± 147	1,750 ± 615	1,108 ± 144	0.229
Crystalloids (L)	4.8 ± 0.3	5.1 ± 0.9	4.8 ± 0.3	0.829
PRBC (U)	3.6 ± 0.6	6.0 ± 2.4	3.2 ± 0.5	0.391
FFP (U)	2.0 ± 0.4	3.3 ± 1.9	1.8 ± 0.4	0.487
Platelets (U)	0.3 ± 0.1	0.6 ± 0.4	0.3 ± 0.1	0.345
Albumin (mL)	322 ± 56	464 ± 138	303 ± 60	0.229
Hespan (mL)	116 ± 41	214 ± 149	103 ± 42	0.306

* Mann-Whitney *U* test.

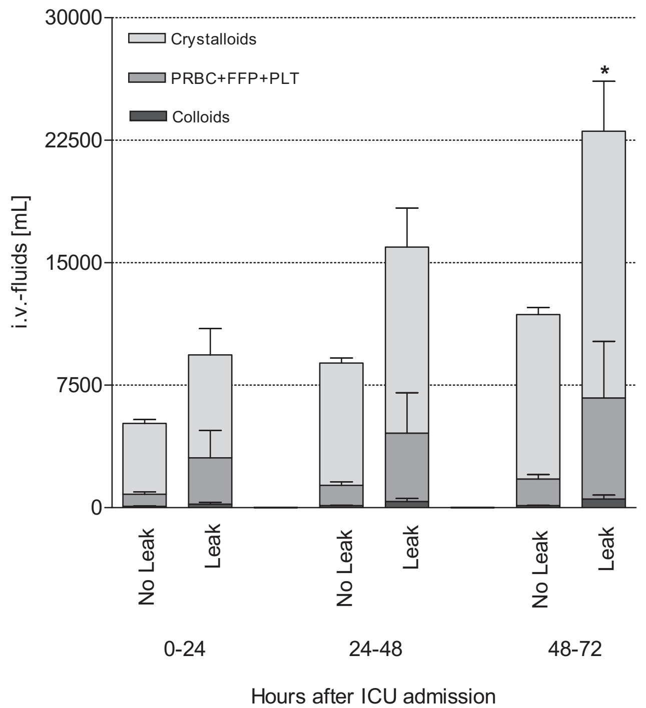

Figure 2. Cumulative amount of crystalloids, colloids, and blood transfusions at 24 hours, 48 hours, and 72 hours in patients with colonic anastomosis who developed an anastomotic leak or not (mean ± standard error of the mean) *Cumulative amount of fluids for patients with leak vs. no leak, $p = 0.023$, Mann-Whitney *U* test.

sis were similar for both groups (Table 1). Intraoperative blood loss, crystalloid, and blood component requirements were not statistically different between patients with or without anastomotic leakage (Table 2).

On ICU admission, the APACHE II score tended to be higher in patients who later developed a leakage compared with those who did not (25.1 ± 8.4 vs. 20.3 ± 9.5, $p = 0.103$). Hemoglobin levels and base deficit on ICU admission were similar for both groups (11.2 ± 2.9 mg/dL vs. 12.1 ± 2.3 mg/dL, $p = 0.379$ and 4.6 ± 7.0 vs. 3.8 ± 4.0, $p = 0.648$). However, during the next 72 hours, the highest APACHE II score was significantly higher for patients with anastomotic leak compared with those without (29.2 ± 12.2 vs. 22.0 ± 9.1, $p = 0.019$). In addition, patients with a leak required vasopressors for ≥12 hours significantly more often than those without leak (25% [3 of 12] vs. 3.8% [3 of 80], $p = 0.005$). Cumulative urine output tended to be lower in patients with leakage compared with those without (5,663 ± 683 vs. 7,467 ± 377 within 72 hours, $p = 0.082$). However, all patients had urine production within normal limits.

The Role of Crystalloids

At 24 hours, 48 hours, and 72 hours in the ICU, patients with anastomotic leakage received more overall fluids than those without a leak (Fig. 2). The differences at 24 hours and 48 hours

TABLE 3. Comparison of Crystalloids and Blood Transfusions Administered Within the First 72 h Between Patients With and Without Colonic Leakage

	Total (N = 92)	Leak (N = 12)	No Leak (N = 80)	p*
Crystalloids (L)	10.9 ± 0.6	16.3 ± 3.1	10.1 ± 0.4	*0.009*
PRBC (U)	7.4 ± 0.8	9.6 ± 4.0	3.9 ± 0.7	0.284
≥12 U PRBC within 72 h	12 (13.0)	4 (33.3)	8 (10.0)	*0.025*
FFP (U)	3.8 ± 0.7	6.2 ± 3.3	3.5 ± 0.6	0.365
Platelets (U)	5.1 ± 1.9	8.8 ± 3.1	3.1 ± 1.0	0.313
Colloids (mL)	173 ± 44	531 ± 248	119 ± 31	*0.047*

* Mann-Whitney *U* test, χ^2 test.
Values are presented as mean ± standard error of the mean or N (%).

TABLE 4. Area Under the ROC for the 72-h Amount of Crystalloids, PRBC, and FFP to Predict an Anastomotic Dehiscence

	Area Under the ROC (95% CI)	Standard Error	p
Crystalloid	0.758 (0.592–0.924)	0.085	*0.009*
PRBC	0.647 (0.444–0.849)	0.103	0.138
FFP	0.619 (0.424–0.813)	0.099	0.231

were statistically not significant, but at 72 hours, this discrepancy became significant (23.2 ± 5.8 L vs. 11.9 ± 0.6 L, $p = 0.023$). All types of fluids increased in a collinear fashion in patients who developed an anastomotic dehiscence (Table 3). However, in contrast to PRBC and FFP, only the volume of crystalloids significantly predicted anastomotic leakage with an area under the receiver operating characteristic curve of 0.758 ([95% confidence interval {CI} 0.592–0.924], $p = 0.009$) (Table 4). Furthermore, all types of fluids (crystalloids, colloids, PRBC, FFP, and platelets) were examined by a forward logistic regression model. Only the volume of crystalloids given in the first 72 hours was independently associated with the development of an anastomotic leakage ($p = 0.037$, $R^2 = 0.616$). The volumes of transfused PRBC, FFP, and platelets within the first 72 hours and the volume of colloids transfused dropped out from this forward logistic regression model.

With increasing amounts of crystalloids, the incidence of anastomotic leakage increased (Fig. 3). A cutoff of ≥10.5 L of crystalloids within the first 72 hours was found to be the critical threshold for the development of an anastomotic dehiscence. Thirty of 92 patients (32.6%) got ≥10.5 L of crystalloids within 72 hours. These "high-volume" patients were at a significantly higher risk of an anastomotic leakage when compared with those patients who received <10.5 L crystalloids within 72 hours (26.7% vs. 6.5%, odds ratio [95% CI]: 5.27 [1.44–19.28], $p = 0.007$). The sensitivity, specificity, and positive and negative predictive value at this

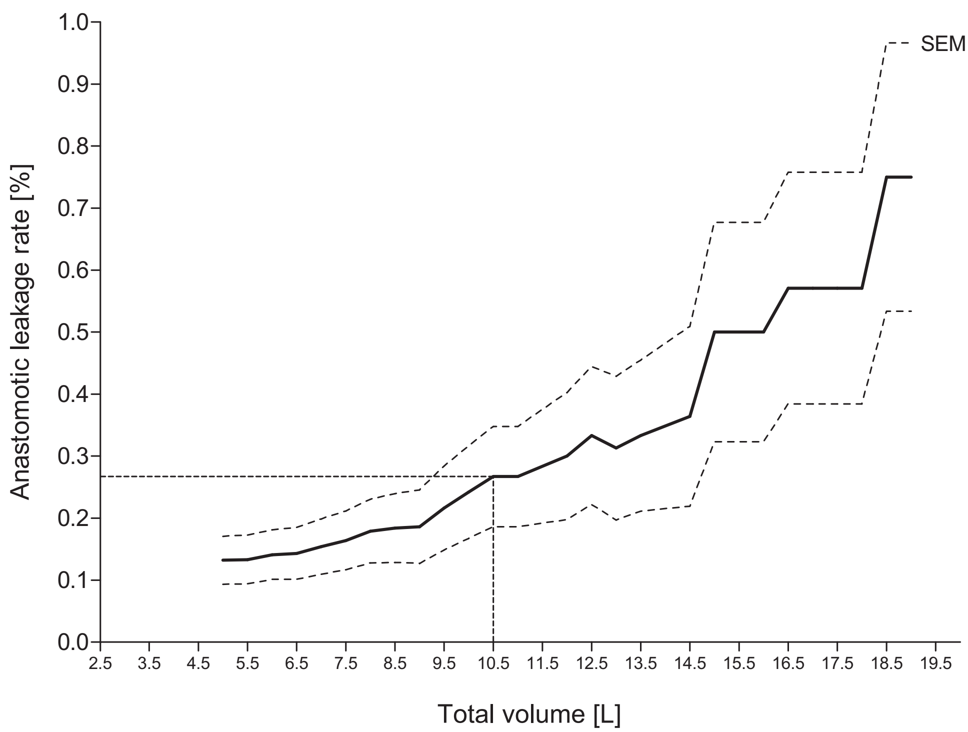

Figure 3. Cutoff analysis for the amount of crystalloids (total volume [L] within the first 72 hours postoperatively) to develop an anastomotic leakage in trauma patients who underwent colonic resection and primary anastomosis. *Dotted line* indicates cutoff at 10.5 L of crystalloids within 72 hours, which was the critical threshold associated with failure of the colon anastomosis.

TABLE 5. Independent Risk Factors for Leakage (in the Order of the R^2)

	Odds Ratio (95% CI)	p	R^2
Crystalloids within 72 h ≥10.5 L	5.26 (1.14–24.39)	0.033	0.141
Age	1.06 (1.01–1.12)	0.019	0.097
Systolic BP <90 mm Hg on admission	8.00 (1.07–45.45)	0.043	0.093
Concomitant gastric injury	5.62 (1.00–31.25)	0.050	0.065

Forward logistic regression; variables in the equation: ISS ≥16, age, concomitant gastric/kidney/vascular/small bowel injury, systolic BP <90 mm Hg on admission, delayed abdominal closure, APACHE II score on admission and highest APACHE II score within the first 72 h, vasopressors ≥12 h, PRBC ≥4 U within 24 h, PRBC ≥12 U within 72 h, crystalloids ≥10.5 L in the first 72 h in the ICU, and amount of colloids within 72 h.

threshold to predict an anastomotic leakage were 66.7%, 72.5%, and 26.7% and 93.5%, respectively.

By multivariate analysis, including 15 potential risk factors, it was found that the threshold of ≥10.5 L of crystalloids within 72 hours was independently associated with anastomotic leakage (odds ratio [95% CI]: 5.26 [1.14–24.39], $p = 0.033$). Additional independent risk factors were increasing age, hemorrhagic shock on admission, and a concomitant stomach injury ($R^2 = 0.396$) (Table 5).

Outcomes

Patients with anastomotic leakage had significantly longer ICU and hospital lengths of stay (17.8 ± 17.6 days vs. 8.1 ± 10.9 days, adjusted $p = 0.091$ and 54.4 ± 55.0 days vs. 18.8 days ± 15.6 days, adjusted $p < 0.001$). Mortality in patients with anastomotic failure was higher when compared with those without anastomotic failure; however, after adjustment for demographic variations, this difference did not reach statistical significance (16.7% vs. 1.3%, adjusted $p = 0.524$, adjusted for age, systolic BP <90 mm Hg on admission, stomach injury, highest APACHE II within the first 72 hours, ≥12 units of PRBC within 72 hour, and vasopressors ≥12 hours).

DISCUSSION

A large number of studies, including a Cochrane review,[19] demonstrated that primary repair or anastomosis of colon injuries is the preferred management option and that fecal diversion or colostomy even after destructive colon injuries is associated with an overall higher complication rate.[1,4,7–10] As a direct consequence of this, primary anastomosis is performed more liberally in a growing number of trauma patients with increasing injury severity.[2] Similarly, this study cohort consisted of trauma patients with a mean ISS of 21 and a mean ATI of 30 and 11% had a systolic BP <90 mm Hg on admission. In addition, all patients required postoperative ICU admission for ≥72 hours. In this group of severely injured patients, anastomotic leakage occurred in 13%, which is within the reported range of 7% to 14% of comparable studies dealing with unselected patients sustaining destructive colon injuries requiring resection.[1,3,13]

This paradigm shift results in an increasing number of severely injured patients admitted to the ICU with primary colon anastomosis. Recognition of potentially preventable or modifiable risk factors during the postoperative phase is important for optimizing anastomotic healing. The relationship between increasing amounts of crystalloids and increasing incidence of anastomic leakage has been demonstrated for patients undergoing elective intestinal resections.[16,20–22] However, the impact of crystalloid infusion in traumatic colon resections is less clear. This is a particularly important issue for injured patients, because the volume of crystalloids infused is expected to be much higher than in elective surgery because of the role of fluids in the acute resuscitation phase of care. The intent of this study was not to question this initial fluid administration but rather to assess the impact of the volumes given postoperatively on the rate of anastomotic failure.

On ICU admission, arterial blood gases, hemoglobin, and APACHE II scores were similar in patients who developed an anastomotic leak and those who did not. This indicates that the patients arrived in a similar physiologic condition to the ICU. However, with increasing time in the ICU, the discrepancy between the volumes of crystalloids given to patients with and without a leak increased and became significant at 72 hours. At this time, in contrast to PRBC and FFP, the administered crystalloid volume significantly predicted anastomotic leakage. This relationship was independent, and a critical threshold of 10.5 L of crystalloids within 72 hours was found. In these patients, on average, 3.5 L of crystalloids were given daily, and this was associated with a 5-fold increased risk for suture line failure.

It is unclear from this dataset why some patients received more crystalloids than others. The increased amounts may be a surrogate marker for worsening physiologic status during the initial phase in the SICU. The significantly higher APACHE II score within the first 72 hours may be an indicator for this; however, this was dropped by the regression model. The crystalloids were, however, all prescribed at the discretion of the surgical team, and this could not be addressed by the model. In addition, there might be other variables, which were not captured by the present multivariate analysis that could have influenced these results. Although the ISS was entered into the equation, the overall severity and characteristics of the initial injury burden could still have been underestimated.

In elective surgery, it has been shown that perioperative restriction of crystalloids decreases the anastomotic leakage rate.[16,20,21,23] The effect of salt and water overload may cause splanchnic edema, increased intra-abdominal pressure and thus decreased mesenteric flow leading to decreased tissue oxygenation and intramucosal acidosis. As a direct consequence, increased gut permeability and impaired wound healing with anastomotic dehiscence may result.[17,18] Therefore, abdominal pressures should be routinely monitored postoperatively, and in high-risk patients, delayed abdominal closure should be considered.

In addition to the proposed mechanism of fluid sequestration into the interstitial space and subsequent edema, a direct modulation of the inflammatory response by crystalloids might impair anastomotic healing. Previous research has shown that crystalloids given during the resuscitation phase of trauma patients can directly modulate inflammation and vascular permeability seen after traumatic hemorrhage.[24–27] Ex vivo and in vivo, it has been shown that crystalloids causes neutrophil activation and increased expression of neutrophil adhesion molecules in a dose-responsive fashion.[28,29]

Increasing age, shock on admission, and associated gastric injuries were also found to be independently associated with anastomotic suture line failure. Increasing age and shock on admission has been found previously to be associated with suture line failure.[3,11,12] However, concomitant gastric injury has never been described as an independent risk factor for leakage, although the combination of a colon and gastric injury may be synergistic with respect to intra-abdominal infections.[30,31] In patients with these risk factors, a more liberal approach to damage control principles including fecal diversion with delayed colocolonic anastomosis may be of benefit.

CONCLUSION

Increased use of crystalloids over the first 72 hours is associated with anastomotic leakage in patients undergoing primary colocolonic anastomosis at initial trauma laparotomy. In contrast to the volume of blood component transfusions, crystalloid volumes significantly predicted anastomotic dehiscence. A threshold of 10.5 L within the first 72 hours was independently associated with a 5-fold increased risk for suture line failure. The impact of crystalloid restriction on anastomotic failure in trauma patients warrants prospective investigation.

REFERENCES

1. Demetriades D, Murray JA, Chan L, et al. Penetrating colon injuries requiring resection: diversion or primary anastomosis? An AAST prospective multicenter study. *J Trauma.* 2001;50:765–775.
2. Kashuk JL, Cothren CC, Moore EE, Johnson JL, Biffl WL, Barnett CC. Primary repair of civilian colon injuries is safe in the damage control scenario. *Surgery.* 2009;146:663–668; discussion 668–670.
3. Murray JA, Demetriades D, Colson M, et al. Colonic resection in trauma: colostomy versus anastomosis. *J Trauma.* 1999;46:250–254.
4. Gonzalez RP, Merlotti GJ, Holevar MR. Colostomy in penetrating colon injury: is it necessary? *J Trauma.* 1996;41:271–275.
5. Demetriades D, Murray JA, Chan LS, et al. Handsewn versus stapled anastomosis in penetrating colon injuries requiring resection: a multicenter study. *J Trauma.* 2002;52:117–121.
6. Vertrees A, Wakefield M, Pickett C, et al. Outcomes of primary repair and primary anastomosis in war-related colon injuries. *J Trauma.* 2009; 66:1286–1291; discussion 1291–1283.
7. Stone HH, Fabian TC. Management of perforating colon trauma: randomization between primary closure and exteriorization. *Ann Surg.* 1979;190:430–436.
8. Ivatury RR, Gaudino J, Nallathambi MN, Simon RJ, Kazigo ZJ, Stahl WM. Definitive treatment of colon injuries: a prospective study. *Am Surg.* 1993;59:43–49.
9. Chappuis CW, Frey DJ, Dietzen CD, Panetta TP, Buechter KJ, Cohn I Jr. Management of penetrating colon injuries. A prospective randomized trial. *Ann Surg.* 213:492–497, 1991; discussion 497–498.
10. Sasaki LS, Allaben RD, Golwala R, Mittal VK. Primary repair of colon injuries: a prospective randomized study. *J Trauma.* 1995;39:895–901.
11. Behrman SW, Bertken KA, Stefanacci HA, Parks SN. Breakdown of intestinal repair after laparotomy for trauma: incidence, risk factors, and strategies for prevention. *J Trauma.* 1998;45:227–231; discussion 231–223.
12. Shannon FL, Moore EE. Primary repair of the colon: when is it a safe alternative? *Surgery.* 1985;98:851–860.
13. Stewart RM, Fabian TC, Croce MA, Pritchard FE, Minard G, Kudsk KA. Is resection with primary anastomosis following destructive colon wounds always safe? *Am J Surg.* 1994;168:316–319.
14. Miller PR, Fabian TC, Croce MA, et al. Improving outcomes following penetrating colon wounds: application of a clinical pathway. *Ann Surg.* 2002;235:775–781.
15. Zakrison T, Nascimento BA Jr, Tremblay LN, Kiss A, Rizoli SB. Perioperative vasopressors are associated with an increased risk of gastrointestinal anastomotic leakage. *World J Surg.* 2007;31:1627–1634.
16. Brandstrup B, Tonnesen H, Beier-Holgersen R, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Ann Surg.* 2003;238:641–648.
17. Marjanovic G, Villain C, Juettner E, et al. Impact of different crystalloid volume regimes on intestinal anastomotic stability. *Ann Surg.* 2009;249: 181–185.
18. Lobo DN. Fluid, electrolytes and nutrition: physiological and clinical aspects. *Proc Nutr Soc.* 2004;63:453–466.
19. Nelson R, Singer M. Primary repair for penetrating colon injuries. *Cochrane Database Syst Rev.* 2003:CD002247.
20. Nisanevich V, Felsenstein I, Almogy G, Weissman C, Einav S, Matot I. Effect of intraoperative fluid management on outcome after intraabdominal surgery. *Anesthesiology.* 2005;103:25–32.
21. MacKay G, Fearon K, McConnachie A, Serpell MG, Molloy RG, O'Dwyer PJ. Randomized clinical trial of the effect of postoperative intravenous fluid restriction on recovery after elective colorectal surgery. *Br J Surg.* 2006;93:1469–1474.
22. Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *Lancet.* 2002;359:1812–1818.
23. Rahbari NN, Zimmermann JB, Schmidt T, Koch M, Weigand MA, Weitz J. Meta-analysis of standard, restrictive and supplemental fluid administration in colorectal surgery. *Br J Surg.* 2009;96:331–341.
24. Watters JM, Tieu BH, Todd SR, et al. Fluid resuscitation increases inflammatory gene transcription after traumatic injury. *J Trauma.* 2006; 61:300–308; discussion 308–309.
25. Rizoli SB, Rhind SG, Shek PN, et al. The immunomodulatory effects of hypertonic saline resuscitation in patients sustaining traumatic hemorrhagic shock: a randomized, controlled, double-blinded trial. *Ann Surg.* 2006;243:47–57.
26. Bulger EM, Cuschieri J, Warner K, Maier RV. Hypertonic resuscitation modulates the inflammatory response in patients with traumatic hemorrhagic shock. *Ann Surg.* 2007;245:635–641.
27. Makley AT, Goodman MD, Friend LA, et al. Resuscitation with fresh whole blood ameliorates the inflammatory response after hemorrhagic shock. *J Trauma.* 2010;68:305–311.
28. Rhee P, Wang D, Ruff P, et al. Human neutrophil activation and increased adhesion by various resuscitation fluids. *Crit Care Med.* 2000;28:74–78.
29. Alam HB, Stanton K, Koustova E, Burris D, Rich N, Rhee P. Effect of different resuscitation strategies on neutrophil activation in a swine model of hemorrhagic shock. *Resuscitation.* 2004;60:91–99.
30. Croce MA, Fabian TC, Patton JH Jr, et al. Impact of stomach and colon injuries on intra-abdominal abscess and the synergistic effect of hemorrhage and associated injury. *J Trauma.* 1998;45:649–655.
31. Salim A, Teixeira PG, Inaba K, Brown C, Browder T, Demetriades D. Analysis of 178 penetrating stomach and small bowel injuries. *World J Surg.* 2008;32:471–475.

EDITORIAL COMMENT

Although the untoward effects of excessive crystalloid administration have been most commonly described in the scenario of cyclical hyperresuscitation, coagulation defects, and abdominal compartment syndrome,[1,2] Schnuriger et al.[3] present initial evidence for another worrisome association: anastomotic leakage after primary colon resection and anastomosis performed during initial trauma laparotomy. Furthermore, although primary resection and anastomosis have been well accepted as a treatment strategy at the time of standard laparotomy, the application of this procedure in the damage control scenario has been recently debated, although our results in Denver suggested that it can be safely applied.[4]

The authors retrospectively evaluated 92 patients who underwent primary colon resection and anastomosis at initial laparotomy and were admitted to the intensive care unit for at least 72 hours. Patients with leakage received more overall fluids, and only the volume of crystalloids significantly predicted leakage. Despite including colloids, packed red blood cells < fresh frozen plasma, and platelets in their logistic regression model, a cut off >10.5 L seemed to be the critical threshold for dehiscence.

The authors are to be congratulated, and their data certainly give us pause as we continue to rethink many of our resuscitation strategies for trauma. However, the authors do identify a number of limitations that must be addressed before reaching definitive conclusions. First, multiple variables could have influenced their results. Although Injury Severity Score was entered into the equation, the overall severity and characteristics of the initial injury burden could have been underestimated. Second, during the time frame of their study, the authors did not have an established policy of damage control, and many would argue that the most severely injured patients should undergo delayed anastomosis after initial resection and stabilization. This study excluded 16 patients who underwent damage control laparotomy with fecal diversion and did not include any patients with delayed anastomosis in the damage control scenario. Accordingly, a more liberal approach to damage control and delayed anastomosis might have reduced the dehiscence rates attributed to excess crystalloid administration. Furthermore, given the retrospective nature of this study, one also could argue that increased crystalloid administration represents a surrogate marker of worsening physiologic status during the initial 72 hour time frame. Finally, the crystalloids were administered at the discretion of the surgical teams, and no uniform policy of administration was in place during the time of the study.

Despite these limitations, the author's findings of an association between excess crystalloid administration and anastomotic dehiscence are notable and deserve further investigation. With many centers currently altering their resuscitation strategies to further reduce crystalloid administration during initial resuscitation, the current findings could suggest that curtailment of crystalloid use should be extended to the postoperative time frame as well. We look forward to further prospective data and further applications of restrictive crystalloid policies in the damage control scenario to help elucidate the ideal management strategy for this challenging group of patients.

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REFERENCES

1. Brandstrup B, Tønnesen H, Beier-Holgersen R, et al; Danish Study Group on Perioperative Fluid Therapy. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Ann Surg.* 2003;238:641–648.
2. Gonzalez E, Pieraci F, Moore EE, Kashuk J. Coagulation abnormalities in the trauma patient: the role of point of care thrombelastography. *Semin Thromb Hemost.* 2010;36:723–737.
3. Schnüriger B, Inaba K, Wu T, Eberle BM, Belzberg H, Demetriades D. Crystalloids after primary colon resection and anastomosis at initial trauma laparotomy: excessive volumes are associated with anastomotic leakage. *J Trauma*. 2011;70:603–610.
4. Kashuk JL, Cothren CC, Moore EE, Johnson JL, Biffl WL, Barnett CC. Primary repair of civilian colon injuries is safe in the damage control scenario. *Surgery.* 2009;146:663–668.

EDITORIAL COMMENT

The admonition of Moore and Shires[1] "The objective of (peri-operative) care is restoration to normal physiology and normal function of organs…… This can never be achieved by inundation" was all but ignored during the last 20 years. This period witnessed a strong belief that resuscitation was not optimal till supranormal end points were achieved. This "more of a good thing is better" philosophy leads to undesirable consequences. Some examples are secondary abdominal compartment syndrome and intra abdominal hypertension (IAH),[2] sometimes "hyper acutely" within the first few hours of resuscitation,[3] increasing the need for open abdomens; unrecognized extremity compartment syndrome culminating in amputation[4]; and iatrogenic pulmonary edema resulting in increased ventilator days and greater need for tracheostomy.[5] Other similar side effects of overzealous resuscitation created an unfortunate cycle of more interventions leading to even more complications.

A decade ago, Pruitt[5] coined the term "fluid creep" to describe excessive crystalloid resuscitation of burn patients. He warned of the need to push back the pendulum to avoid poor outcomes. It is now apparent that this "fluid creep" is not only limited to burn resuscitation but also extends to elective operations and trauma management. In this decade, more and more discerning clinicians have reassessed and recalibrated their resuscitation practices, because of accumulating evidence of increased complications with perioperative positive fluid balance and improved outcomes with a restrictive fluid administration. Lobo et al.[6] and subsequently Brandstrup et al.,[7] in a randomized study, noted that patients who received liberal amounts of fluid after colonic operations experienced more cardiopulmonary, gastric, and tissue-healing complications than those who received a "restricted" regimen. Similar findings, emphasizing avoidance of fluid overload, were noted by Kologlu et al.[8] in 1999 and Nisanevich et al.[9] in 2005. In 2009, Marjanovic et al.[10] showed that intraoperative fluid overload in a rat model of an ileoileal anastomosis can impair anastomotic healing by resulting in intestinal wall edema, lower anastomotic bursting pressure, and reduced hydroxyproline concentration. Excessive resuscitation volumes may also lead to IAH that causes splanchnic hypoperfusion, gut mucosal acidosis, anastomotic edema, and break down.[11] Increased gut permeability from IAH also leads to more ascites that exacerbates IAH and the cycle perpetuates itself.[12]

All these factors may be at play for the retrospective observations of Schnüriger et al.[13] in this issue of *J Trauma*. They analyzed 92 intensive care unit patients with primary colocolostomy after penetrating trauma. Twelve patients (13.0%) developed an anastomotic leak. The authors noted that the cumulative amount of crystalloids (≥10.5 L) given over the first 72 hours was independently associated with anastomotic breakdown (odds ratio, 5.26 [1.14–24.39]; $p = 0.033$). This seems to be the first report analyzing the effect of the inevitable "fluid creep" and the cumulative fluid balance on the healing of colocolostomy in severely injured penetrating trauma patients. This important communication should be noted and the hypothesis studied prospectively with careful monitoring and collection of vital data such as: anatomic and physiologic injury severity, resuscitation end points, abbreviated versus definitive laparotomy, grading of colon injury and its management, postoperative monitoring of intra abdominal pressures, and most importantly, precise type and amount of fluids and packed cells. Many of these issues remain unclear in present article including why some patients received more crystalloids than others. Were these patients sicker? Could that be the explanation for the leaks?

In summary, Dr. Pruitt's "fluid creep" may very well be relevant in resuscitation after penetrating trauma. The pendulum needs to swing back, again!

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REFERENCES

1. Moore FD, Shires G. Moderation. *Ann Surg.* 1967;166:300–301.
2. Balogh Z, McKinley BA, Cocanour CS, et al. Supranormal trauma resuscitation causes more cases of abdominal compartment syndrome. *Arch Surg.* 2003;138:637–642.
3. Rodas EB, Malhotra AK, Chhitwal R, Aboutanos MB, Duane TM, Ivatury RR. Hyperacute abdominal compartment syndrome: an unrecognized complication of massive intra-operative resuscitation for extra-abdominal injuries. *Am Surg.* 2005;71:977–81.4.
4. Tremblay LN, Feliciano DV, Rozycki GS. Secondary extremity compartment syndrome. *J Trauma.* 2002;53:833–837.
5. Pruitt BA Jr. Protection from excessive resuscitation: "pushing the pendulum back." *J Trauma.* 2000;49:567–568.
6. Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomized controlled trial. *Lancet.* 2002;359:1812–1818.
7. Brandstrup B, Tonnesen H, Beier-Holgersen R, et al; Danish Study Group on Perioperative Fluid Therapy. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Ann Surg.* 2003;238:641–648.
8. Nisanevich V, Felsenstein I, Almogy G, Weissman C, Einav S, Matot I. Effect of intraoperative fluid management on outcome after intraabdominal surgery. *Anesthesiology.* 2005;103:25–32.
9. Kologlu M, Sayek I, Kologlu LB, Onat D. Effect of persistently elevated intraabdominal pressure on healing of colonic anastomoses. *Am J Surg.* 1999;178:293–297.
10. Marjanovic G, Villain C, Juettner E. Impact of different crystalloid volume regimes on intestinal anastomotic stability. *Ann Surg.* 2009;249:181–185.
11. Ivatury RR, Cheatham ML, Malbrain M, Sugrue M. *Abdominal Compartment Syndrome.* Austin, TX: Landes Publishers; 2006.
12. Lobo DN. Fluid overload and surgical outcome: another piece in the jigsaw. *Ann Surg.* 2009;249:186–188.
13. Schnüriger B, Inaba K, Wu T, et al. Crystalloids after primary colon resection and anastomosis at initial trauma laparotomy: excessive volumes are associated with anastomotic leakage. *J Trauma.* 2011;70:603–610.

