Chasing 100%: The use of hypertonic saline to improve early, primary fascial closure after damage control laparotomy

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BACKGROUND: Failure to achieve fascial closure after damage control laparotomy (DCL) is associated with increased morbidity and long-term disability. In addition, early closure is associated with reduces infectious, wound, and pulmonary complications. We hypothesized that hypertonic saline (HTS), which attenuates resuscitation-induced intestinal edema in animals, would improve early primary fascial closure (EPFC) rates.

METHODS: This is a retrospective study of trauma patients undergoing DCL, from January 2010 to July 2011. Patients in the HTS group had 30 mL/h of 3% sodium chloride as maintenance fluids while the fascia was open. Patients in the cohort group had isotonic fluids (125 mL/h). The primary outcome, EPFC, was defined as primary fascial closure by postinjury day 7.

RESULTS: Seventy-seven patients underwent DCL (23 received HTS and 54 received isotonic fluids). There were no differences in demographics, injury severity, or pre–intensive care unit vitals, laboratories, fluids, or transfusions. Median fluids in the first 24 hours were lower in the HTS group (3.9 vs. 7.8 L, $p < 0.001$). Times to fascial closure were shorter in those receiving HTS (34 vs. 49 hours, $p < 0.001$), as were the rates of closure at first take back (78% vs. 53%, $p = 0.036$). The primary outcome of EPFC was higher in the HTS group compared with standard fluids (100% vs. 76%, $p = 0.010$). At discharge, the HTS group had a 96% primary fascial closure rate compared with 80% with standard fluids.

CONCLUSION: The use of 3% HTS as maintenance fluids after DCL was associated with 100% EPFC. HTS may be used as an adjunct to facilitate fascial closure in patients undergoing DCL. (*J Trauma Acute Care Surg*. 2013;74: 426–432. Copyright © 2013 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: Diagnostic study, level III.

KEY WORDS: Hypertonic saline; open abdomen; damage control laparotomy; fascial closure.

BACKGROUND

The use of damage control laparotomy (DCL) in patients with severe traumatic injuries to attenuate or avoid the "bloody vicious cycle" of acidosis, coagulopathy, and hypothermia has been associated with improved survival.[1–8] Failure to achieve early fascial closure (within the first 7 days) may result from intestinal and/or retroperitoneal edema, recurrent abdominal compartment syndrome, and continued coagulopathy, acidosis, or hypothermia.[9,10] Unfortunately, failure to achieve fascial closure after DCL is not uncommon and carries a tremendous economic and morbidity burden. The open abdomen has multiple physiologic implications, including increased insensible losses, protein losses, and nutritional demands.[11,12] The open abdomen also may result in significant morbidity, including, but not limited to, incisional hernias, gastrointestinal fistulae, intra-abdominal infections, anastomotic leakage, and sepsis/infections.[13–16]

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To date, efforts to improve fascial closure rates have been composed of laparotomy wound management (i.e., negative pressure therapy) and sequential closure techniques or devices.[17–19] These pathways attempt to prevent or reclaim abdominal domain loss and exert sustained pressure on the intra-abdominal contents, possibly reducing intestinal or retroperitoneal edema. Without a doubt, these adjuncts to fascial closure are important and improve fascial closure rates. Yet, their mechanism of action works primarily on a symptom and not the true problem: resuscitation induced intestinal and retroperitoneal edema and capillary leakage because of a patient's inflammatory state.

Extensive research from our institution has demonstrated that hypertonic saline (HTS) not only prevents but also reverses resuscitation-induced intestinal edema in animal models.[20–22] HTS has also been shown to mitigate the systemic inflammatory response secondary to intestinal ischemia-reperfusion injury in rat models.[23–25] We hypothesized that the use of HTS (3%) as maintenance intravenous fluids after DCL would decrease the time to primary fascial closure and increase the percentage of patients achieving primary fascial closure (EPFC).

METHODS

This study began as a performance improvement project, with subsequent approval of the institutional review boards of the University of Texas Health Science Center–Houston and the Memorial Hermann Hospital for retrospective analysis. We

analyzed all adult trauma patients who underwent DCL between January 2010 and January 2012 at the Texas Trauma Institute (Houston, TX). Patients who were younger than 18 years, pregnant, or incarcerated were excluded. In addition, in an effort to focus on the potential of HTS to facilitate early closure, those patients who died before the first take back (after the initial damage control procedure) were excluded.

Patient demographics; injury characteristics; prehospital vital signs and fluids; emergency department (ED) vital signs, laboratory values, and fluids; operating room (OR) vital signs, laboratory values, fluids, and procedure information; and intensive care unit (ICU) vital signs, laboratory values, fluids, and serum sodium levels were recorded. Fluid administration (24, 48, and 72 hours) and urine output were measured. Time to closure, mortality, and morbidities were also noted. The primary outcome, EPFC, was defined as primary fascial closure within 7 days.[26]

Two groups of patients were compared: those who received HTS as maintenance intravenous fluids after DCL and those who received "standard" maintenance intravenous fluids. As this was an observational study, the use of HTS was left solely to the discretion of the attending trauma surgeon. HTS patients received 3% sodium chloride at 30 mL/h in the ICU immediately after DCL. This rate was not titrated; the HTS maintenance fluids were started after DCL and continued until postoperative day 3 or fascial closure, whichever occurred sooner. Additional resuscitation with crystalloid, colloid, plasma, platelets, or red blood cells was given as dictated by the patient's clinical condition. The rate and concentration of HTS was chosen based on the approximation of volume for 3% sodium chloride compared with 0.9% sodium chloride (100 mL/h or 3.33 = 30 mL). Standard maintenance (STD) fluids after DCL consisted of isotonic (0.9% sodium chloride) or hypotonic crystalloid (lactated Ringer solution) at 125 mL/h.

The choice of laparotomy coverage was not controlled; however, because of institutional practices, a negative pressure wound V.A.C. (Kinetic Concepts, Inc., San Antonio, TX) was used exclusively during the study period.

Continuous data are presented as medians with 25th and 75th interquartile range (IQR) with comparisons between groups performed using the Wilcoxon rank sum (Mann–Whitney *U* test). Categorical data are reported as proportions and, where appropriate, tested for significance using χ^2 or Fisher exact tests. All statistical tests were two tailed with $p < 0.05$ set as significant.

Purposeful regression modeling was then used to construct a multivariate linear and a multivariate logistic regression model evaluating the time to fascial closure and predicting EPFC.[27] This was performed using the technique of purposeful selection of covariates described by Hosmer and Lemeshow.[28] In an effort to minimize the risk of falsely identifying significant results with multiple comparisons, all variables were prespecified and judged *a priori* to be clinically sound. These independent variables included age, sex, Injury Severity Score (ISS), ED vitals and laboratories, prehospital and hospital fluid administration, and transfusions. After this, the variables were entered into stepwise regression that generated five variables of significance (mechanism of injury, severity of anatomic injury [ISS], severity of physiologic injury [arrival systolic blood pressure], and severity of shock [arrival base excess]). These were then applied to a multivariate regression analysis evaluating these variables and HTS. Stata Statistical software (version 10.1; Stata Corp, College Station, TX) was used for analysis.

RESULTS

Univariate Analysis

Demographics, Injury Characteristics, and Initial Resuscitation

Four-hundred thirty-eight patients underwent emergent laparotomy during the study period, with 119 (27%) undergoing DCL. Forty-two patients (35%) were excluded, 21 patients died before first take back, 19 patients were younger than 18 years, 2 patients were pregnant, and 1 patient was incarcerated. Seventy-seven patients met inclusion criteria, of which 23 received HTS and 54 received STD fluids. The demographics and injury characteristics of the two groups were similar (Table 1).

Prehospital fluids (median, 500 mL; IQR, 110 and 1,300 vs. median, 550 mL; IQR, 50 and 950; $p = 0.705$) and transfusions (median, 0 U; IQR, 0 and 0 vs. median, 0 U; IQR, 0 and 0; $p = 0.133$) between STD and HTS were similar. ED laboratory values, fluid administration, and transfusion volume were also similar (Table 2).

No differences in OR arrival vital signs and laboratory values were seen (Table 3). In addition, OR fluid administration and transfusion volumes were equivalent between the two groups. Median operative times were similar between STD (median, 115 min; IQR, 90 and 204) and HTS groups (median, 148 min; IQR, 119 and 206). ICU arrival vital signs and laboratory values were also similar between groups.

ICU Resuscitation Volumes

The STD fluid group received significantly higher volumes of crystalloid compared with the HTS group at 24, 48, and 72 hours (Table 4). The STD group received a median of

TABLE 1. Demographic and Injury Characteristics of STD and HTS Fluid Groups

	STD (n = 54)	HTS (n = 23)	*p*
Median age, years	34 (23–51)	31 (23–48)	0.528
Male gender, %	72	86	0.147
White race, %	56	52	0.749
Median BMI	26 (24–31)	29 (24–32)	0.522
Blunt mechanism, %	72	60	0.291
Median head AIS	0 (0–3)	0 (0–1)	0.214
Median chest AIS	3 (0–3)	3 (0–3)	0.966
Median abdomen AIS	4 (3–4)	4 (3–4)	0.794
Median extremity AIS	0 (0–3)	2 (0–3)	0.150
Median ISS	29 (18–41)	25 (19–34)	0.418

All continuous values are presented as median (25th–75th IQR).

AIS, Abbreviated Injury Scale; BMI, body mass index; HTS, hypertonic saline; ISS, Injury Severity Score; STD, standard fluids.

TABLE 2. ED Vital Signs, Laboratory Values, and Resuscitation Fluids

	STD (n = 54)	HTS (n = 23)	*p*
Initial ED vital signs, laboratory values, and resuscitation volumes			
Median SBP, mm Hg	92 (80 to 119)	102 (80 to 121)	0.473
Median pulse, beats/min	105 (84 to 128)	119 (93 to 145)	0.146
Median hemoglobin, g/dL	12.5 (11.1 to 14.1)	12.6 (11.4 to 14.0)	0.975
Median INR	1.2 (1.1 to 1.4)	1.3 (1.1 to 1.6)	0.921
Median base value, mmol/L	−7 (−10 to −3)	−8 (−13 to −5)	0.303
Median crystalloids, mL	1,000 (0 to 1,450)	1,000 (0 to 1,000)	0.330
Median RBC, U	1 (0 to 3)	1 (0 to 3)	0.932
Median plasma, U	1 (0 to 2)	1 (0 to 2)	0.713

All continuous values are presented as median (25th–75th IQR).

INR, international normalized ratio; GCS, Glasgow Coma Scale; HTS, hypertonic saline; PT, prothrombin time; PTT, partial thromboplastin time; RBC, red blood cells; SBP, systolic blood pressure; STD, standard fluids; w-RTS, weighted revised trauma score; k/mm^3, 1,000 cells per cubic millimeter.

3,955 mL more crystalloid for 24 hours, a median of 4,890 mL more crystalloid for 48 hours, and a median of 5,260 mL more crystalloid than the HTS group for 72 hours. However, the red blood cell, plasma, and platelet transfusion volumes between the two groups were similar.

ICU Renal Function and Electrolyte Changes

With respect to renal function, the STD group had lower peak sodium in the first 72 hours compared with the HTS patients (Table 4). No differences were seen in peak creatinine, change of sodium from admission (delta sodium), or change of creatinine from admission (delta creatinine) in the first 72 hours. Only one patient was continued on HTS greater than 72 hours. The need for renal replacement therapy was similar between the STD and the HTS groups (5% vs. 8%; $p = 0.609$). No statistically significant difference in the median 24-, 42-, and 72-hour urine output was observed between the two groups.

TABLE 3. OR and ICU Vital Signs, Laboratory Values, and Resuscitation Fluids

	STD (n = 54)	HTS (n = 23)	*p*
Initial OR vital signs, laboratory values, and resuscitation volumes			
Median SBP, mm Hg	111 (90 to 135)	100 (90 to 120)	0.417
Median pulse, beats/min	110 (97 to 130)	120 (90 to 138)	0.768
Median base value, mmol/L	−7 (−10 to −4)	−8 (−13 to −5)	0.556
Median crystalloids, mL	2,500 (1,250 to 3,150)	1,700 (1,200 to 3,000)	0.337
Median RBC, U	5 (2 to 9)	6 (3 to 12)	0.735
Median plasma, U	4 (1 to 8)	6 (2 to 13)	0.269
Median platelet, U	0 (0 to 6)	3 (0 to 6)	0.301
Initial ICU vital signs and laboratory values			
Median SBP, mm Hg	137 (119 to 162)	141 (120 to 161)	0.651
Median pulse, beats/min	103 (85 to 116)	96 (90 to 110)	0.494
Median temperature, °F	94.5 (92.9 to 96.8)	94.8 (93.4 to 97.0)	0.805
Median base value, mmol/L	−3 (−5 to −1)	−2 (−6 to 0)	0.527
Median hemoglobin, g/dL	11.6 (10.1 to 13.0)	11.2 (10.4 to 12.3)	0.588
Median INR value	1.3 (1.2 to 1.4)	1.3 (1.1 to 1.4)	0.063

All continuous values are presented as median (25th–75th IQR).

HTS, hypertonic saline; ICU, intensive care unit; INR, international normalized ratio; k/mm^3, 1,000 cells per cubic millimeter; OR, operating room; PT, prothrombin time; PTT, partial thromboplastin time; RBC, red blood cells; SBP, systolic blood pressure; STD, standard fluids.

TABLE 4. Cumulative 24-, 48-, and 72-Hour Resuscitation Fluids and Renal Function

	STD (n = 54)	HTS (n = 23)	*p*
24-hour fluids and blood products			
Median crystalloids, mL	7,825 (5,600–10,235)	3,870 (2,770–6,770)	<0.001
Median RBC, U	10 (3–16)	9 (4–17)	0.776
Median plasma, U	9 (2–16)	8 (2–12)	0.775
Median platelet, U	3 (0–6)	3 (0–9)	0.646
48-hour fluids and blood products			
Median crystalloids, mL	11,180 (9,200–13,890)	6,290 (4,300–9,495)	<0.001
Median RBC, U	10 (4–17)	9 (4–18)	0.721
Median plasma, U	10 (2–17)	8 (2–12)	0.616
Median platelet, U	6 (0–9)	3 (0–12)	0.631
72-hour fluids and blood products			
Median crystalloids, mL	13,890 (11,350–17,630)	8,630 (6,770–13,655)	<0.001
Median RBC, U	11 (4–17)	10 (5–18)	0.743
Median plasma, U	10 (2–17)	8 (2–13)	0.599
Median platelet, U	9 (0–9)	3 (0–12)	0.673
Renal function at 72 hours			
Median peak sodium, mEq/L	146 (143–148)	148 (146–152)	0.037
Median delta sodium, mEq/L	5 (2–7)	7 (3–11)	0.073
Median peak creatinine, mg/dL	1.3 (1.1–1.7)	1.4 (1.1–1.6)	0.562
Median delta creatinine, mg/dL	0.0 (0.0–0.2)	0.0 (0.0–0.2)	0.245
Median RIFLE score	0 (0–2)	0 (0–1)	0.388

**All continuous values presented as median (25th–75th IQR).

HTS, hypertonic saline; RBC, red blood cells; STD, standard fluids.

Closure Times and Rates

As to the primary outcome, although only 76% of STD fluid patients achieved (EPFC), 100% of HTS patients achieved EPFC. The STD group underwent primary fascial closure in a median of 50 hours after DCL compared with only 33 hours in the HTS group (Table 5). The STD group underwent a median of one relaparotomy (IQR, 1 and 3) compared with a median of one relaparotomy (IQR, 1 and 1) in the HTS group ($p = 0.001$). Eight percent of STD patients died with an open abdomen compared with 0% of HTS patients ($p = 0.167$). Although 20% of the STD fluid group was discharged with an open abdomen, only 4% (one patient) of the HTS group was discharged open ($p = 0.070$).

Multivariate Regression Analyses

After controlling for mechanism of injury, arrival systolic blood pressure, ISS, and base deficit, the use of HTS was

TABLE 5. Primary and Secondary Outcomes between STD and HTS Groups

	STD (n = 54)	HTS (n = 23)	*p*
EPFC, %	76	100	0.010
Median time to fascial closure, hour	50 (35–127)	33 (21–48)	0.001
Median ICU-free days	15 (6–23)	23 (7–26)	0.163
Median ventilator-free days	22 (14–27)	26 (12–28)	0.138
24-hour mortality, %	4.7	0.0	0.290
30-day mortality, %	9.4	8.7	0.923

All continuous values are presented as median (25th–75th IQR).
HTS, hypertonic saline fluids; ICU, intensive care unit; STD, standard fluids.

independently associated with reduced time to fascial closure (coefficient, −139.53; 95% confidence interval, −289.95 to −6.14; $p = 0.039$). In the multiple logistic regression model, the use of HTS perfectly predicted primary fascial closure by day 7 (Table 6).

Because there were no events where the use of HTS did not succeed in achieving the dependent variable of closure at day 7, we used the Fisher exact test logistic regression analysis. Controlling for the same above variables of base deficit, ISS, mechanism, and arrival systolic blood pressure, the use of HTS was associated with an increased likelihood of achieving closure by day 7 (odds ratio, 9.89; 95% confidence interval, 1.521 to infinity; $p = 0.012$).

DISCUSSION

In this observational study, the use of 3% HTS increased the incidence of primary fascial closure by post-DCL day 7 to 100% and decreased time to fascial closure. The results of this study are important for several reasons.

First, we have implemented an inexpensive adjunct to fascial closure that can be combined with any institutionally preferred method of sequential fascial closure or temporary abdominal closure. Indeed, this pathway has been written into a formal protocol and is now standard for all patients undergoing DCL at our institution. Moreover, there was no difference in mortality or renal failure between the groups.

Second, the use of HTS as maintenance fluids after DCL increased the rate of EPFC and reduced the number of planned relaparotomies. This improvement may lead to a decrease in the rate of intra-abdominal infections, gastrointestinal fistulae, incisional hernias, and all other complications associated with an open abdomen. The present study was not powered to definitively these end points, but the assumption is reasonable.

Lastly, by decreasing the number of planned laparotomies after DCL and increasing the rate of discharge with closed fascia, this may lead not only to a lower scar tissue burden but also fewer planned incisional hernia repairs. This makes futures surgeries in a young or old patient easier, safer, and potentially avoids the need for an operation with a not insignificant complication rate. And this may lead to an improved quality of life, as evidenced by the work of Zarzaur et al.[29]

Although the actual mechanism by which HTS may improve fascial closure rates is outside the scope of this clinical outcomes study, multiple potential mechanisms exist. First, the use of HTS may prevent the "fluid creep" that is all too common in any ICU. Certainly in this study, the HTS had significantly lower 24-, 48-, and 72-hour crystalloid administration. Second, the HTS may act in humans as it does in animal models. That is, to change the balance of Starling's forces to shift fluid into the vascular system and out of the interstitium. Third, the HTS may attenuate the patient's inflammatory response to trauma and secondary insults, decrease the capillary leak that occurs, and prevent intestinal edema.[30–33]

The initial finding of 100% primary fascial closure in the HTS should be tempered by the fact that we only had a 96% fascial closure rate at discharge, which neared but did not meet statistical significance compared with the control group. With larger sample sizes, this difference may be statistically significant, but that is unclear at this time. Ultimately, this reflects the reality that even if one is to create the ideal fascial closure algorithm, fascial dehiscences, intra-abdominal infections requiring open drainage, and unplanned relaparotomies are a fact of life in this very seriously injured group of patients. Although 100% fascial closure rate should properly be our goal, it will likely be impossible to attain.

Although we feel that the current data support that HTS be seriously considered in the management of DCL patients, this study has several limitations. First, and most notable, this is not a randomized study. This was an observational study evaluating the differences of fluid management between two groups of faculty at our facility. In addition, although the groups seem similar in all baseline comparisons, differences among the groups, which are not measured or captured in this study, may very well exist. In addition, this was not a multicenter investigation but rather the results from a single institution. Finally, this study is limited to the relatively small sample sizes in each group that might have led to underpowering and a type II error.

CONCLUSION

The advent of DCL has resulted in improved rates of survival in patients with severe injury. This life-saving approach comes with the intended consequence of a laparotomy wound (open abdomen). In addition, the open abdomen is

TABLE 6. Multivariate Models Predicting Closure Rates

	Odds ratio	95% CI	*p*
Closure at initial take back			
Blunt mechanism	0.46	0.112–1.885	0.280
ISS	1.01	0.951–1.066	0.817
ED base value	1.07	0.965–1.207	0.298
ED SBP, mm Hg	0.98	0.948–1.004	0.127
HTS infusion	3.87	1.228–14.334	0.022
Closure by day 7			
Blunt mechanism	0.15	0.014–1.556	0.110
ISS	1.00	0.938–1.069	0.959
ED base value	1.05	0.896–1.236	0.538
ED SBP, mm Hg	0.99	0.969–1.103	0.452
HTS infusion	Value for colinearity (i.e., HTS independently predicted closure)		

CI, confidence interval; ED, emergency department; HTS, hypertonic saline; SBP, systolic blood pressure.

associated with unintended increased nutritional demands, fluid losses, and complications. To date, reports of methods to increase the incidence of primary fascial closure rely on protocols for sequential abdominal closure or negative wound therapy, thereby preventing or reclaiming lost abdominal domain. HTS, however, aims at reducing intestinal edema, one of the primary etiologies of this loss of domain and failure to close. In this small, single-center study, the use of 3% HTS as maintenance intravenous fluid after DCL was associated with increased rates of EPFC and shorter times to fascial closure. Given the published morbidity associated with an open abdomen, the use of HTS warrants further study and consideration as an adjunct to achieving fascial closure.

AUTHORSHIP

J.A.H., M.M.M., J.C.D., and B.A.C. designed the study. J.A.H. and B.A.C. conducted the literature search. J.A.H., M.M.M., and B.A.C. collected the data. C.E.W. and B.A.C. analyzed the data. J.C.D., C.S.C., C.E.W., J.B.H., and B.A.C. interpreted the data. All authors participated in the writing, revising and editing of the manuscript.

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DISCLOSURE

The authors declare no conflict of interest.

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DISCUSSION

Dr. Eileen M. Bulger (Seattle, Washington): This report presents provocative data regarding the potential role for hypertonic saline infusion as an adjunct to facilitate delayed fascial closure after damaged control laparotomy.

There is no question that failure to achieve definitive fascial closure results in significant morbidity and mortality and increased resource utilization.

Although limited by a small sample size and a non-randomized design, this report suggests that the continuous infusion of 3 % saline in the post-operative period is safe and may contribute to reduced overall fluid requirements and, thus, early abdominal closure.

My questions for the authors are as follows. The use of hypertonic saline in this study was based on surgeon discretion and was not randomized. This raises the concern that other aspects of patient care may also have varied with the same surgeons.

Can you comment on whether the surgeons who chose to use 3 % saline were also more aggressive about the timing and the frequency of planned re-operations which might have impacted your results?

While it did not reach statistical significance, I note that there is a higher rate of penetrating trauma patients in the hypertonic saline group, 40 % versus 28 % in the standard group.

Victims of penetrating trauma can often return to the operating room sooner due to lack of other significant injuries such as traumatic brain injury which may delay re-operation so please comment on whether these associated injuries among those with blunt trauma in the standard group might have contributed to the delays or the problems with early fascial closure.

How was the rate of 30ccs per hour of hypertonic saline fluid selected? I note that your median peak serum sodium was similar between the groups at 146 and 148.

How often was serum sodium monitored in these patients? And do you have evidence that the patients receiving hypertonic saline had longer periods of hypertonicity than those patients in the control arm?

You mentioned the possibility of a future randomized controlled trial. Do you think that in future studies a fixed rate such as this should be used? Or should we target a specific serum sodium range?

And if you are planning a follow-up randomized controlled trial I would also like you to comment on the issue of blinding.

Blinding can be particularly challenging in hypertonic saline studies because clinicians see the serum sodium and will, therefore, figure out which group their patient is in so in a future trial do you think blinding is important? If so, how would you do it?

Again, I want to congratulate the authors on this provocative data. I think it lends certainly preliminary data that would support future trials. Thank you.

Dr. Rao R. Ivatury (Richmond, Virginia): Enjoyed the paper very much. How did you monitor the intraabdominal pressures? And was there any change of instance of abdominal compartment syndrome?

Dr. Juan A. Asensio-Gonzalez (Valhalla, New York): Thank you. This is indeed a very nice study. I, however, have some questions.

In your presentation, you report admission systolic blood pressures for many of these patients that were consistently over 100. Similarly, your mean intraoperative blood volume replacement for both groups consisted of about 5 to 6 units of packed red blood cells. A significant number of trauma surgeons would not institute damage control on the basis of these findings.

Could you also comment on the types of injuries, for instance vascular, hepatic, and other major injuries that you encountered in your patients? I think this would yield more clarity. Barring absence of this information, I would find it difficult to adopt your approach.

Dr. Joseph DuBose (Baltimore, Maryland): Yes, congratulations to the authors. A question about when was this hypertonic sodium started.

Dr. Steven R. Shackford (San Diego, California): Just one comment: you should really measure osmolarity rather than sodiums because that's really what determines the gradient.

Dr. James W. Davis (Fresno, California): Nice study. I'm a little concerned. Although you said according to protocol that the hypertonic group was to receive 30mls per hour, you actually wound up giving over 160mls an hour according to the abstract and over 325mls an hour in the other group. Can you explain your fluid protocol a little bit more? Thank you.

Dr. Faran Bokhari (Chicago, Illinois): Did you randomize the practitioners as well because I'm not sure that the practice variation does not exist in these circumstances? And were the people that were able to close always the same surgeons?

Dr. Samir M. Fakhry (Charleston, South Carolina): Nice study. Can you tell me whether it's the hypertonic saline that's doing this or is it just not giving as much of the other stuff? Thank you.

Dr. Edward E. Cornwell, III (Washington, D.C.): Thank you. The previous question hit on mine which was how many of the patients from the committed co-authors in the hypertonic group also cared for some of those isotonic patients?

Dr. John Harvin (Houston, Texas): Thank you for those questions and comments.

Dr. Bulger, the perioperative decision to use hypertonic saline was dependent upon the operating surgeon. This may lead to differences in patient care and bias. However, often times the surgeon who operated on the patient initially was not the one who took them back and the ICU attending is different from the operating surgeon. In that context, other than the decisions to use hypertonic saline and to leave the abdomen open, very little would be different in the perioperative care between the standard and hypertonic groups.

We did not specifically look at penetrating versus blunt injury as a mechanism in terms of who would close faster. As you note, we did not see a statistically significant difference between the groups on univariate analysis. That's something that we can certainly build into our multivariate analysis.

We chose 30cc/hr of fluid because we thought that that would be a relatively similar sodium load to isotonic sodium saline at 100cc/hr. Sodium levels were generally checked every 6 hours. We do not have any evidence that there was prolonged hypertonicity in the group.

We are planning a randomized controlled trial. And I agree with you that blinding will be difficult in this patient population. Potentially you could blind the operating surgeon while the ICU team knows who is getting what therapy, but that would be a very difficult thing to do.

Dr. Ivatury, we monitor for abdominal compartment syndrome using bladder pressure measurements. Unfortunately, I do not have the data to compare rates of abdominal compartment syndrome in these patients.

Dr. Asensio, in terms of the amount of blood products given to these patients, I would refer to the Annals of Surgery paper in which, when we implemented all three facets of damage control resuscitation, we showed a significant reduction in the amount of blood products our patients required. In terms of specific injuries, I do not have those numbers to give to you.

Dr. DuBose, the hypertonic saline is started upon arrival to the ICU. In some instances that is not done initially.

Dr. Shackford, thank you for the comment. Measuring osmolarity is a good idea. I'm not sure if that is the mechanism by which this works, but it is certainly information worth having.

Dr. Davis, the extra fluid comes from boluses and drips. We run the hypertonic saline at 30 cc/hr, but patients also have analgesia/sedation drips and IV piggyback medications. Patients also may receive crystalloid boluses as deemed necessary by the ICU physician.

Dr. Bokhari, the practitioners were not randomized and the surgeons who closed the patients were not always the same surgeons that performed the initial laparotomy.

And Dr. Fakhry, how do I think this works? That's a very good question. I think if you ask each author they would give you a different answer. My personal belief is that the improved ability to close patients results from a further reduction in volume administered.

Thank you, again, for the comments and questions.