Published in final edited form as:

J Trauma Acute Care Surg. 2018 February ; 84(2): 350–357. doi:10.1097/TA.0000000000001730.

Hypertonic saline resuscitation following emergent laparotomy and temporary abdominal closure

Tyler J. Loftus, MD, Philip A. Efron, MD, FACS, FCCM, Trina M. Bala, ARNP, Martin D. Rosenthal, MD, Chasen A. Croft, MD, FACS, R. Stephen Smith, MD, FACS, Frederick A. Moore, MD, FACS, MCCM, Alicia M. Mohr, MD, FACS, FCCM, and Scott C. Brakenridge, MD, MSCS

University of Florida Health, Department of Surgery and Sepsis and Critical Illness Research Center in Gainesville, Florida

Abstract

Background—Our objective was to establish the safety of 3% hypertonic saline (HTS) resuscitation for trauma and acute care surgery patients undergoing emergent laparotomy and temporary abdominal closure (TAC) with the hypothesis that HTS administration would be associated with hyperosmolar hyperchloremic acidosis, lower resuscitation volumes, and higher fascial closure rates, without adversely affecting renal function.

Methods—We performed a retrospective cohort analysis of 189 trauma and acute care surgery patients who underwent emergent laparotomy and TAC, comparing patients with normal baseline renal function who received 3% HTS at 30 mL/h ($n=36$) to patients with standard resuscitation ($n=153$) by baseline characteristics, resuscitation parameters, and outcomes including primary fascial closure and KDIGO stages of acute kidney injury.

Results—HTS and standard resuscitation groups had similar baseline illness severity and organ dysfunction, though HTS patients had lower serum creatinine at initial laparotomy (1.2 vs. 1.4 mg/dL, $p=0.078$). Forty-eight hours after TAC, HTS patients had significantly higher serum sodium (145.8 vs. 142.2 mEq/L, $p<0.001$), chloride (111.8 vs. 106.6 mEq/L, $p<0.001$), and osmolality (305.8 vs. 299.4 mosm/kg, $p=0.006$), and significantly lower arterial pH (7.34 vs. 7.38, $p=0.011$). HTS patients had lower intravenous fluid volumes within 48 hours of TAC (8.5 vs. 11.8 L, $p=0.004$). Serum creatinine, urine output, and kidney injury were similar between groups. Fascial closure was achieved for 92% of all HTS patients and 77% of all standard resuscitation patients ($p=0.063$). Considering all 189 patients, higher IVF resuscitation volumes within 48 hours of TAC were associated with decreased odds of fascial closure (OR 0.90, 95% CI 0.83–0.97, $p=0.003$).

Conclusions—HTS resuscitation was associated with the development of a hypernatremic, hyperchloremic, hyperosmolar acidosis and lower total IVF resuscitation volumes, without

Please address correspondence to: Scott C. Brakenridge, MD, MSCS, University of Florida Health, Gainesville, FL, 1600 SW Archer Road Room M-602, Gainesville, FL, 32610-3003, 972-415-2447, Scott.Brakenridge@surgery.ufl.edu.

The authors have no relevant conflicts of interest.

This work has not been presented at any meetings and has never been submitted elsewhere.

adversely affecting renal function. These findings may not be generalizable to patients with baseline renal dysfunction and susceptibility to hyperchloremic acidosis-induced kidney injury.

Keywords

Laparotomy; open abdomen; temporary abdominal closure; hypertonic saline; resuscitation

Introduction

For patients undergoing emergent laparotomy, damage control surgery and temporary abdominal closure (TAC) may be used for patients with severely deranged physiology. Rather than performing all indicated procedures and then closing the abdominal fascia, TAC allows the surgeon to quickly address life-threatening conditions, place a temporary dressing over the open abdomen, and transfer the patient to an intensive care unit (ICU) for continued resuscitation, rewarming, and physiologic optimization. This approach gained prominence in 1983 when Stone and colleagues (1) described abbreviated laparotomy for 31 patients with coagulopathy and exsanguinating hemorrhage. Since that time, damage control surgery and TAC have become important strategies for managing trauma patients with the bloody vicious cycle of hypothermia, acidosis, and coagulopathy, patients with intra-abdominal sepsis for whom TAC allows diagnosis and treatment of residual sources of infection at re-laparotomy as well as deferral of anastomosis until physiologic optimization, and patients with vascular emergencies and refractory abdominal compartment syndrome (2–8). Although TAC offers potential advantages for select patients who are not suitable candidates for immediate fascial closure following emergent laparotomy, the open abdomen is also associated with increased risk for intestinal fistula formation and prolonged requirements for ICU resources and mechanical ventilation, especially when early primary fascial closure cannot be achieved (9–11). Therefore, better strategies are needed to promote early fascial closure among TAC patients.

An initial assessment of patients who underwent emergent laparotomy and TAC for trauma or sepsis at our institution found that primary fascial closure was achieved in only 71% of all patients (12). Harvin and colleagues (13) reported 100% fascial closure (n=23/23) within one week of TAC for severely injured trauma patients who received 3% hypertonic saline (HTS) at 30 mL/hour (discontinued at fascial closure or postoperative day 3, whichever came first) following initial laparotomy, compared to 76% fascial closure within one week for a control group of 54 patients who received standard resuscitation. Patients in the HTS group had lower crystalloid resuscitation volumes but did not have significant differences in serum creatinine, urine output, or acute kidney injury compared to the standard resuscitation group. The observed lack of adverse effects on renal function was critically important. Hypertonic saline may have beneficial effects attributable to decreasing resuscitation volumes, creating an osmotic gradient to move fluid from the interstitial to the intravascular space, decreasing bowel edema, and modulating the inflammatory in the context of intestinal ischemia (14–18), but may also increase risk for hyperchloremic acidosis and kidney injury among postoperative and critically ill patients (19–22).

Therefore, resuscitating TAC patients with HTS is a promising strategy, but requires further study to characterize the risks and benefits. After the pioneering work of Dr. Harvin and colleagues was published (13), we began to administer 3% hypertonic saline (HTS) at 30 mL/hour following TAC for trauma and emergency general surgery patients with normal baseline renal function at the discretion of the operating surgeon. The purpose of this study was to establish the safety of 3% HTS resuscitation for trauma and acute care surgery patients undergoing emergent laparotomy and TAC by characterizing resuscitation parameters, serum osmolality, hyperchloremic acidosis, renal function, and outcomes for the first 36 TAC patients who underwent HTS resuscitation at our institution compared with 153 TAC patients who received standard resuscitation during the same time period. We hypothesized that HTS administration would be associated with hyponatremia, hyperosmolality, hyperchloremic acidosis, decreased resuscitation volumes, and higher fascial closure rates compared to standard resuscitation, without adversely affecting renal function.

Methods

Study design

We performed a retrospective cohort analysis of 189 consecutive adult trauma and emergency general surgery patients who underwent emergent laparotomy and TAC at our institution during a 30-month period ending April 2017. The University of Florida Institutional Review Board approved this study. Derivation of the study population is illustrated in Supplementary figure 1. Our institutional data registry was searched for adult (age ≥ 18 years) patients with survival for ≥ 48 hours and Current Procedural Terminology (CPT) codes for re-laparotomy or laparotomy with CPT modifiers for planned or unplanned reoperation. Deaths prior to 48 hours were excluded because these patients may not have had an opportunity for relaparotomy and fascial closure, and 48 hours was the first of several time-points at which outcomes were assessed. Other exclusion criteria were initial laparotomy at an outside facility, pre-existing intestinal fistula, and conditions for which resuscitation strategies should be tailored to individual patient physiology: complicated pancreatitis (n=25), cirrhosis (n=11), or end-stage renal disease (n=9). Patients with traumatic brain injury were eligible for inclusion. There were no patients in the study population who received 23% HTS. Both trauma and emergency general patients were included in the analysis because both were eligible for hypertonic saline resuscitation during the study period, and we sought to determine whether this strategy would be generalizable to both populations. Patients who received 3% hypertonic saline at 30 mL/hour following TAC were allocated to the HTS group (n=36); all other patients were allocated to the standard resuscitation without HTS group (n=153). At our institution during the study period, accepted indications for exploratory laparotomy and TAC in trauma patients included hypothermia with temperature <35°C, acidosis with arterial pH <7.20, coagulopathy, massive visceral edema, administration of at least 10 units of packed red blood cells, administration of at least 15 liters of crystalloid fluid, inability to close the fascia, impending abdominal compartment syndrome, or surgeon discretion for elective TAC to defer the creation of an anastomosis or to reassess bowel viability. Similar criteria were applied to

patients with intra-abdominal sepsis, with the addition of septic shock requiring vasopressors.

Hypertonic saline administration

At the beginning of the study period, HTS was administered at the discretion of the operating surgeon to patients with normal baseline renal function. During the final eight months of the 30-month study period, there was agreement that HTS would not be administered to patients with any of the following criteria: serum sodium >155 mEq/L, serum chloride > 115 mEq/L, arterial pH < 7.10, chronic kidney disease stage 3 (23), acute kidney injury stage 2 (24), nephrectomy at initial laparotomy, or cirrhosis. Patients receiving HTS at 30 mL/hour also received isotonic fluid boluses or diuresis as necessary to maintain euvoolemia at the discretion of the surgical and critical care teams. Patients who underwent standard resuscitation with no HTS also received isotonic fluid boluses or diuresis as necessary to maintain euvoolemia at the discretion of the surgical and critical care teams. Hypertonic saline was discontinued following primary fascial closure or postoperative day 3, whichever occurred first, consistent with methods from Harvin et al. (13). Direct peritoneal resuscitation was not employed during the study period.

Operative technique

Following TAC with a negative pressure wound therapy (NPWT) dressing, planned re-laparotomy was performed at 24–48 hour intervals until fascial closure was achieved or a planned ventral hernia was created. At each re-laparotomy, continuous fascial traction and sequential closure were attempted by placing figure-of-eight sutures to approximate the fascia at the superior and inferior aspects of the fasciotomy until undue tension was exerted on the fascia or airway pressures were pathologically increased. If fecal diversion was required, a loop ostomy was created in a far lateral position, so that the ostomy would not violate fascia that would be used for midline fascial closure, and so that interval ostomy takedown could be performed without the need for a laparotomy.

Data collection

Data regarding patient demographics, baseline characteristics, illness severity, resuscitation parameters, operative management, and outcomes were collected by query of our institutional research database and by retrospective review of the electronic medical record. Patients characteristics included age, sex, American Society of Anesthesiologists physical status classification (25), Charlson comorbidity index (26), body mass index, the reason for initial laparotomy, vital signs and laboratory values at the time of initial laparotomy, and sequential organ failure assessment (SOFA) scores (27). The Charlson comorbidity index was used as a general indicator of comorbid disease burden that is commonly used in a variety of practice settings. Resuscitation parameters included total intravenous fluid (IVF) administration (including maintenance crystalloid fluids, bolus crystalloid fluids, piggyback fluids for medication administration, and parenteral nutrition), blood product administration, urine output, and NPWT output. Serum sodium, chloride, osmolarity, anion gap, creatinine, and arterial pH were measured on admission, at initial laparotomy, and following initial laparotomy at 48 hours, 96 hours, and 7 days. Peak values of sodium, chloride, and creatinine during admission were also assessed to establish context for interpreting acute

changes following laparotomy and TAC. Outcomes included acute kidney injury per Kidney Disease: Improving Global Outcomes (KDIGO) definitions (24), primary fascial closure, days to primary fascial closure, fascial dehiscence, intra-abdominal abscess formation, length of stay, days on mechanical ventilation, and discharge disposition.

Power analysis

In a retrospective review of trauma patients who had TAC following damage control laparotomy, Harvin et al. (13) detected statistically significant differences in resuscitation volumes and primary fascial closure rates when comparing 23 patients who received 3% HTS to 54 patients who had standard resuscitation with isotonic fluids at 125 mL/hour. Because our study was designed to assess similar outcomes in a more heterogeneous patient population including patients with intra-abdominal sepsis and abdominal compartment syndrome, we selected a larger population including 36 patients who received 3% HTS and 153 patients who underwent standard resuscitation without HTS during the same time period.

Statistical analysis

Statistical analysis was performed with SPSS (version 24, IBM, Armonk, NY). To compare HTS and standard resuscitation groups, differences between continuous variables were assessed by the Kruskal-Wallis test and reported as median [interquartile range], and differences between discrete variables were assessed by Fisher's Exact test and reported as *n* (%). Trends in serum sodium, chloride, osmolality, anion gap, creatinine, and arterial pH were illustrated in GraphPad Prism (version 6.05, GraphPad Software, La Jolla, CA) as mean values with 95% confidence intervals and compared by one-way analysis of variance. The impact of resuscitation parameters on acute kidney injury and primary fascial closure was assessed in the entire study population by univariate logistic regression. Stage 2 or 3 acute kidney injury (24) within seven days of TAC was used as an outcome in this analysis based on previous observations that stage 2 or 3 acute kidney injury is an independent predictor of increased mortality among TAC patients (28).

Results

Patient characteristics

Patient characteristics are listed in Table 1. The HTS group included more male patients (72% vs. 52%, $p=0.027$) and trauma patients, though the difference in percentage of trauma patients was not statistically significant (44% vs. 28%, $p=0.072$). ASA class was 4.0 in both groups, Charlson comorbidity index was 1.0 in both groups, and there were no significant differences in admission vital signs or SOFA scores (9.0 vs. 9.0, $p=0.653$) between groups. There were 47 blunt trauma patients (80% of all trauma patients) and 12 penetrating trauma patients (20% of all trauma patients). Trauma patients subjected to emergency laparotomy and TAC were severely injured with injury severity score 31 [17–40].

Management and resuscitation parameters

Trends in serum sodium, chloride, osmolality, anion gap, creatinine, and arterial pH are illustrated in Figure 1. There were no significant differences between groups at the time of

initial laparotomy for any of these parameters. Forty-eight hours following TAC, the HTS group had significantly higher sodium (145.8 vs. 142.2 mEq/L, $p < 0.001$), chloride (111.8 vs. 106.6 mEq/L, $p < 0.001$), and osmolality (305.8 vs. 299.4 mosm/kg, $p = 0.006$), as well as significantly lower arterial pH (7.34 vs. 7.38, $p = 0.011$) compared to the standard resuscitation group. Anion gap was similar between groups at all time points. Standard resuscitation patients had higher serum creatinine at the time of initial laparotomy, though the difference was not statistically significant (1.39 vs. 1.18, $p = 0.078$), and followed a similar downward trend in both groups.

Management and resuscitation parameters are listed in Table 2. The median number of abdominal operations performed in both groups was two, and 44% of all patients required more than two operations. The HTS group had significantly lower total IVF volumes within 48 hours of TAC (8.5 vs. 11.8 L, $p = 0.004$), and had lower NPWT output, though the difference was not statistically significant (1.2 vs. 1.5 L, $p = 0.068$). Urine output was similar between groups at all time points.

Outcomes

Outcomes are listed in Table 3. Fascial closure rates were higher in the HTS group, though the difference was not statistically significant (92% vs. 77%, $p = 0.063$). Peak sodium, chloride, and creatinine levels during admission were similar between groups. Fascial dehiscence and intra-abdominal abscess occurred in 5% and 13% of all patients, respectively, with no significant differences between HTS and standard resuscitation groups. Hospital length of stay, ICU length of stay, and days on mechanical ventilation were also similar between groups. There were 33 inpatient mortalities in the entire population of 189 patients (17%), and only 69 patients (37%) were discharged to their home.

Acute kidney injury

Trends in stages of acute kidney injury over time are illustrated in Figure 2. There were no significant differences between groups in the percentage of patients with acute kidney injury at any time point when classifying by stage 1, stage 2, or stage 3. The incidence of kidney injury peaked 48 hours following initial laparotomy in both groups, and then decreased gradually over time. In each group, 47% of all patients had stage 2 or 3 kidney injury within seven days of TAC.

Associations between resuscitation parameters, kidney injury, and fascial closure

To assess the impact of resuscitation parameters on acute kidney injury and primary fascial closure independent of group allocation, the entire study population was included in a regression analysis to assess associations between resuscitation parameters and two different outcomes: primary fascial closure, and stage 2 or 3 acute kidney injury within seven days of TAC. Results of this analysis are listed in Table 4.

HTS administration was not associated with acute kidney injury (OR 1.01, 95% CI 0.49–2.08, $p = 0.986$), and was associated with greater odds of primary fascial closure, though the effect was not statistically significant (OR 3.26, 95% CI 0.94–11.28, $p = 0.062$). Total IVF volumes, sodium, chloride, and osmolality were not associated with kidney injury at any

time points. Higher NPWT output was associated with increased odds of kidney injury for the 48–96h range (OR 1.23, 95% CI 1.01–1.51, $p=0.040$) and the 96h–7d range (OR 1.24, 95% CI 1.02–1.50, $p=0.034$).

Higher IVF resuscitation volumes were associated with decreased odds of fascial closure for the 0–48h range (OR 0.90, 95% CI 0.83–0.97, $p=0.003$) and the 48–96h range (OR 0.88, 95% CI 0.80–0.97, $p=0.007$). During the resuscitation phase, sodium and osmolality levels were not associated with fascial closure, but higher chloride levels 48 hours after TAC were associated with increased odds of fascial closure (OR 1.11, 95% CI 1.03–1.19, $p=0.006$). Seven days after TAC, lower serum sodium and osmolality were associated with primary fascial closure, likely representing an effect rather than cause, as the median time to fascial closure was 1.6 days.

Discussion

In this study, HTS resuscitation for TAC patients was associated with the development of a hypernatremic, hyperchloremic, hyperosmolar acidosis, but did not significantly impact renal function. HTS administration was associated with lower total IVF volumes and an increase in fascial closure rates that was not statistically significant, but may be clinically significant on a larger scale. Although HTS patients had higher peak sodium and chloride levels within seven days of TAC, peak levels during the entire admission were similar between groups, suggesting that a short period of 3% HTS administration may not significantly impact overall risk for hyperchloremic acidosis and kidney injury among TAC patients with prolonged periods of critical illness and ventilator support. Importantly, because HTS was administered to patients with normal baseline renal function, these findings may not be generalizable to patients with baseline kidney disease. This is especially germane to septic TAC patients, who are at increased risk for kidney injury due to their underlying disease process (28–30). However, in select TAC patients, the adverse effects were minimal, and there is potential for significant benefit. Although arterial pH was significantly lower 48 hours following TAC in the HTS group, the similar rates of acute kidney injury between groups suggests that HTS may be reasonable for patients with pH <7.15. However, we have insufficient evidence to support this hypothesis. Although this study was not designed to assess whether HTS decreased bowel edema or exerted the anti-inflammatory effects that have been previously reported (15, 17, 18, 31), the observed higher serum osmolality, lower resuscitation volumes, and trends toward lower NPWT output and higher fascial closure rates suggest that HTS resuscitation may be a useful strategy for TAC patients with normal baseline renal function.

Harvin et al. (13) reported similar findings, with a few important differences, some which may be attributable to differences in study design. The Harvin study included only trauma patients, measured resuscitation parameters for a 72 hour period following TAC, and used RIFLE criteria to describe kidney injury; our study population was composed primarily of patients with intra-abdominal sepsis, resuscitation parameters were measured for a 7 day period following TAC, and KDIGO criteria were used to describe kidney injury. In the Harvin study, 96% ($n=22/23$) of all HTS patients were discharged with primary fascial closure intact, compared to 92% ($n=33/36$) of all HTS patients in our study. Patients

undergoing TAC for sepsis may have lower fascial closure rates than trauma patients (12, 32, 33), which may partially explain our lower fascial closure rates compared to that of Harvin and colleagues. Although hypertonic resuscitation has been associated with significantly higher primary fascial closure rates among trauma patients as described by Harvin et al, the higher primary fascial closure rates among HTS patients in this study did not reach statistical significance. This may also be attributable to differences in study populations, particularly the large proportion of septic patients in our study population (62%), who may have greater ongoing fluid resuscitation requirements and visceral edema secondary to persistent inflammation. The observed lack of statistical significance in primary fascial closure rates between groups may represent a type II error, as this study may have been underpowered to detect a statistically significant difference in fascial closure rates for patients with intra-abdominal sepsis. The interval between initial laparotomy and fascial closure in HTS groups was similar (33 hours in the Harvin study, 36 hours in our study). IVF resuscitation volumes within 48 hours of TAC were similar for the standard resuscitation groups (median 11.2 L in the Harvin study, 11.8 L in our study), but resuscitation volumes in the HTS group were higher in our study (8.5 vs. 6.3 L). Observed differences in resuscitation volumes between HTS groups may be partly attributable to more frequent administration of isotonic fluid boluses in our study. In addition, although 3% HTS at 30 mL/hour was intended to be administered in lieu of isotonic maintenance intravenous fluids, the authors observed that providers would occasionally administer 3% HTS at 30 mL/hour in addition to isotonic maintenance intravenous fluids at 100–150mL/hour, particularly when the protocol was first introduced, diluting the impact of low volume HTS resuscitation. Together, these factors may also explain why peak sodium levels during HTS administration were higher in the Harvin study (148 vs. 146 mEq/L). In both studies, there were no significant differences in serum creatinine levels, urine output, or acute kidney injury between HTS and standard resuscitation groups. Therefore, our findings suggest that administration of HTS to trauma TAC patients, as described by Harvin and colleagues, may be generalized to non-trauma emergency general surgery TAC patients, with similar effects.

This study was limited by its retrospective design, small sample size, baseline differences between HTS and standard resuscitation groups, variability in selecting patients for HTS resuscitation, and relative paucity of prior studies for purposes of comparison and power analysis. Selection bias inherent to retrospective studies was limited by including all consecutive patients meeting inclusion and exclusion criteria. The only previously published study of HTS following TAC (13) included fewer patients and detected clinically meaningful differences in resuscitation parameters and outcomes, suggesting that our study was adequately powered to address our hypothesis. To account for baseline differences between HTS and standard resuscitation groups, a regression analysis was performed for the entire study population to identify associations that were independent of group assignment. A larger cohort of HTS patients would allow for a propensity-matched or risk-adjusted analysis, and this will be an important next step in characterizing the safety and efficacy of HTS for a heterogeneous population of TAC patients. Efforts to further mitigate the dilutional effects of isotonic fluids, including the use of early enteral feeds, are warranted (34, 35). For trauma TAC patients, 3% HTS resuscitation is currently being investigated in a multicenter double blind randomized control trial (NCT02297659).

Conclusions

HTS resuscitation for a heterogeneous population of TAC patients was associated with the development of a hypernatremic, hyperchloremic, hyperosmolar acidosis, but did not adversely affect renal function. HTS administration was also associated with lower total IVF volumes during the initial resuscitation period. Because HTS was administered to patients with normal baseline renal function, these findings may not be generalizable to patients with acute or chronic kidney disease and susceptibility to hyperchloremic acidosis-induced kidney injury. Future research should seek to validate these findings with a larger sample size, methodologic or statistical control for baseline differences in patient characteristics, and a robust comparison of risks and benefits of HTS resuscitation for TAC patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank Peggy Marker, Paul Nickerson, and Lauren Ochoa for their assistance with protocol implementation and data management. The authors were supported in part by grants R01 GM113945-01 (PAE), R01 GM105893-01 (AMM), and P50 GM111152-01 (PAE, FAM, AMM, SCB) awarded by the National Institute of General Medical Sciences (NIGMS). TJL was supported by a post-graduate training grant (T32 GM-008721) in burns, trauma and perioperative injury by NIGMS.

References

1. Stone HH, Strom PR, Mullins RJ. Management of the major coagulopathy with onset during laparotomy. *Ann Surg.* 1983; 197(5):532–5. [PubMed: 6847272]
2. Burch JM, Ortiz VB, Richardson RJ, Martin RR, Mattox KL, Jordan GL Jr. Abbreviated laparotomy and planned reoperation for critically injured patients. *Ann Surg.* 1992; 215(5):476–83. discussion 83–4. [PubMed: 1616384]
3. Rotondo MF, Schwab CW, McGonigal MD, Phillips GR 3rd, Fruchterman TM, Kauder DR, Latenser BA, Angood PA. 'Damage control': an approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma.* 1993; 35(3):375–82. discussion 82–3. [PubMed: 8371295]
4. Diaz JJ Jr, Cullinane DC, Dutton WD, Jerome R, Bagdonas R, Bilaniuk JW, Collier BR, Como JJ, Cumming J, Griffen M, et al. The management of the open abdomen in trauma and emergency general surgery: part 1-damage control. *J Trauma.* 2010; 68(6):1425–38. [PubMed: 20539186]
5. Moore EE, Thomas G. Orr Memorial Lecture. Staged laparotomy for the hypothermia, acidosis, and coagulopathy syndrome. *Am J Surg.* 1996; 172(5):405–10. [PubMed: 8942535]
6. Waibel BH, Rotondo MF. Damage control in trauma and abdominal sepsis. *Crit Care Med.* 2010; 38(9 Suppl):S421–30. [PubMed: 20724875]
7. Perez D, Wildi S, Demartines N, Bramkamp M, Koehler C, Clavien PA. Prospective evaluation of vacuum-assisted closure in abdominal compartment syndrome and severe abdominal sepsis. *J Am Coll Surg.* 2007; 205(4):586–92. [PubMed: 17903734]
8. Sartelli M, Abu-Zidan FM, Ansaloni L, Bala M, Beltran MA, Biffi WL, Catena F, Chiara O, Coccolini F, Coimbra R, et al. The role of the open abdomen procedure in managing severe abdominal sepsis: WSES position paper. *World J Emerg Surg.* 2015; 10:35. [PubMed: 26269709]
9. Dubose JJ, Scalea TM, Holcomb JB, Shrestha B, Okoye O, Inaba K, Bee TK, Fabian TC, Whelan J, Ivatury RR, et al. Open abdominal management after damage-control laparotomy for trauma: a prospective observational American Association for the Surgery of Trauma multicenter study. *J Trauma Acute Care Surg.* 2013; 74(1):113–20. discussion 1120–2. [PubMed: 23271085]

10. Jernigan TW, Fabian TC, Croce MA, Moore N, Pritchard FE, Minard G, Bee TK. Staged management of giant abdominal wall defects: acute and long-term results. *Ann Surg.* 2003; 238(3): 349–55. discussion 55–7. [PubMed: 14501501]
11. Bradley MJ, Dubose JJ, Scalea TM, Holcomb JB, Shrestha B, Okoye O, Inaba K, Bee TK, Fabian TC, Whelan JF, et al. Independent predictors of enteric fistula and abdominal sepsis after damage control laparotomy: results from the prospective AAST Open Abdomen registry. *JAMA Surg.* 2013; 148(10):947–54. [PubMed: 23965658]
12. Loftus TJ, Jordan JR, Croft CA, Smith RS, Efron PA, Mohr AM, Moore FA, Brakenridge SC. Temporary abdominal closure for trauma and intra-abdominal sepsis: Different patients, different outcomes. *J Trauma Acute Care Surg.* 2017; 82(2):345–50. [PubMed: 27787442]
13. Harvin JA, Mims MM, Duchesne JC, Cox CS Jr, Wade CE, Holcomb JB, Cotton BA. Chasing 100%: the use of hypertonic saline to improve early, primary fascial closure after damage control laparotomy. *J Trauma Acute Care Surg.* 2013; 74(2):426–30. discussion 31–2. [PubMed: 23354234]
14. Rizoli SB, Rhind SG, Shek PN, Inaba K, Filips D, Tien H, Brenneman F, Rotstein O. The immunomodulatory effects of hypertonic saline resuscitation in patients sustaining traumatic hemorrhagic shock: a randomized, controlled, double-blinded trial. *Ann Surg.* 2006; 243(1):47–57. [PubMed: 16371736]
15. Attuwaybi B, Kozar RA, Gates KS, Moore-Olufemi S, Sato N, Weisbrodt NW, Moore FA. Hypertonic saline prevents inflammation, injury, and impaired intestinal transit after gut ischemia/reperfusion by inducing heme oxygenase 1 enzyme. *J Trauma.* 2004; 56(4):749–58. discussion 58–9. [PubMed: 15187737]
16. Gonzalez EA, Kozar RA, Suliburk JW, Weisbrodt NW, Mercer DW, Moore FA. Conventional dose hypertonic saline provides optimal gut protection and limits remote organ injury after gut ischemia reperfusion. *J Trauma.* 2006; 61(1):66–73. discussion -4. [PubMed: 16832251]
17. Radhakrishnan RS, Radhakrishnan HR, Xue H, Moore-Olufemi SD, Mathur AB, Weisbrodt NW, Moore FA, Allen SJ, Laine GA, Cox CS Jr. Hypertonic saline reverses stiffness in a Sprague-Dawley rat model of acute intestinal edema, leading to improved intestinal function. *Crit Care Med.* 2007; 35(2):538–43. [PubMed: 17205008]
18. Radhakrishnan RS, Xue H, Moore-Olufemi SD, Weisbrodt NW, Moore FA, Allen SJ, Laine GA, Cox CS Jr. Hypertonic saline resuscitation prevents hydrostatically induced intestinal edema and ileus. *Crit Care Med.* 2006; 34(6):1713–8. [PubMed: 16625118]
19. Toyonaga Y, Kikura M. Hyperchloremic acidosis is associated with acute kidney injury after abdominal surgery. *Nephrology (Carlton).* 2017; 22(9):720–7. [PubMed: 27312130]
20. Suetrong B, Pisitsak C, Boyd JH, Russell JA, Walley KR. Hyperchloremia and moderate increase in serum chloride are associated with acute kidney injury in severe sepsis and septic shock patients. *Crit Care.* 2016; 20(1):315. [PubMed: 27716310]
21. Noritomi DT, Soriano FG, Kellum JA, Cappi SB, Biselli PJ, Liborio AB, Park M. Metabolic acidosis in patients with severe sepsis and septic shock: a longitudinal quantitative study. *Crit Care Med.* 2009; 37(10):2733–9. [PubMed: 19885998]
22. Yunos NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. *JAMA.* 2012; 308(15):1566–72. [PubMed: 23073953]
23. Stevens PE, Levin A. Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group M. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Ann Intern Med.* 2013; 158(11):825–30. [PubMed: 23732715]
24. Palevsky PM, Liu KD, Brophy PD, Chawla LS, Parikh CR, Thakar CV, Tolwani AJ, Waikar SS, Weisbord SD. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. *Am J Kidney Dis.* 2013; 61(5):649–72. [PubMed: 23499048]
25. Haynes SR, Lawler PG. An assessment of the consistency of ASA physical status classification allocation. *Anaesthesia.* 1995; 50(3):195–9. [PubMed: 7717481]

26. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987; 40(5):373–83. [PubMed: 3558716]
27. Vincent JL, de Mendonca A, Cantraine F, Moreno R, Takala J, Suter PM, Sprung CL, Colardyn F, Blecher S. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med.* 1998; 26(11):1793–800. [PubMed: 9824069]
28. Loftus TJ, Bihorac A, Ozrazgat-Baslanti T, Jordan JR, Croft CA, Smith RS, Efron PA, Moore FA, Mohr AM, Brakenridge SC. Acute Kidney Injury Following Exploratory Laparotomy and Temporary Abdominal Closure. *Shock.* 2017; 48(1):5–10. [PubMed: 28009772]
29. Bagshaw SM, Uchino S, Bellomo R, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, et al. Septic acute kidney injury in critically ill patients: clinical characteristics and outcomes. *Clin J Am Soc Nephrol.* 2007; 2(3):431–9. [PubMed: 17699448]
30. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med.* 2001; 29(7):1303–10. [PubMed: 11445675]
31. Aggarwal A, Ong JP, Younossi ZM, Nelson DR, Hoffman-Hogg L, Arroliga AC. Predictors of mortality and resource utilization in cirrhotic patients admitted to the medical ICU. *Chest.* 2001; 119(5):1489–97. [PubMed: 11348958]
32. Quyn AJ, Johnston C, Hall D, Chambers A, Arapova N, Ogston S, Amin AI. The open abdomen and temporary abdominal closure systems--historical evolution and systematic review. *Colorectal Dis.* 2012; 14(8):e429–38. [PubMed: 22487141]
33. Bruhin A, Ferreira F, Chariker M, Smith J, Runkel N. Systematic review and evidence based recommendations for the use of negative pressure wound therapy in the open abdomen. *Int J Surg.* 2014; 12(10):1105–14. [PubMed: 25174789]
34. Duchesne JC, Simms E, Guidry C, Duke M, Beeson E, McSwain NE, Cotton B. Damage control immunoregulation: is there a role for low-volume hypertonic saline resuscitation in patients managed with damage control surgery? *Am Surg.* 2012; 78(9):962–8. [PubMed: 22964205]
35. Burlew CC, Moore EE, Cuschieri J, Jurkovich GJ, Codner P, Nirula R, Millar D, Cohen MJ, Kutcher ME, Haan J, et al. Who should we feed? Western Trauma Association multi-institutional study of enteral nutrition in the open abdomen after injury. *J Trauma Acute Care Surg.* 2012; 73(6):1380–7. discussion 7–8. [PubMed: 22835999]

Figure 1.

Patients who received 3% hypertonic saline (HTS, n=36) intravenous fluids had a hypernatremic, hyperchloremic, hyperosmolar acidosis 48 hours following emergency laparotomy and temporary abdominal closure (TAC). Patients who received HTS had slightly lower serum creatinine levels at the time of TAC, and had a similar trend in creatinine over time compared to patients who did not receive HTS (n=153). Data are presented as mean values with 95% confidence intervals, * $p < 0.05$ between groups.

Figure 2.

Stages of acute kidney injury following emergent laparotomy and temporary abdominal closure (TAC), comparing patients who received 3% hypertonic saline (HTS, n=36) resuscitation to patients who had standard resuscitation with no HTS (n=153). Kidney injury was characterized by Kidney Disease: Improving Global Outcomes (KDIGO) definitions. There were no significant differences between groups in the percentage of patients with acute kidney injury at any time point when classifying by stage 1, stage 2, or stage 3.

Table 1

Characteristics of patients who received 3% hypertonic saline (HTS) intravenous fluids following emergency laparotomy and temporary abdominal closure compared to patients who had standard resuscitation without HTS.

Patient characteristics	All patients n = 189	HTS n = 36	No HTS n = 153	p
Age (years)	57 [45–70]	49 [36–65]	61 [48–71]	0.082
Male	105 (56%)	26 (72%)	79 (52%)	0.027
ASA physical status class	4.0 [3.0–4.0]	4.0 [3.0–4.0]	4.0 [3.0–4.0]	0.436
Charlson comorbidity index	1.0 [0.0–3.0]	1.0 [0.0–2.0]	1.0 [0.0–3.0]	0.136
Body mass index (kg/m ²)	28.1 [24.2–34.8]	29.6 [24.5–34.8]	27.7 [23.7–34.9]	0.475
Reason for laparotomy				
Sepsis	118 (62%)	19 (53%)	99 (65%)	0.188
Trauma	59 (31%)	16 (44%)	43 (28%)	0.072
Non-trauma hemorrhage	10 (5%)	1 (3%)	9 (6%)	0.690
ACS	2 (1%)	0 (0%)	2 (1%)	>0.999
At initial laparotomy				
Temperature (°C)	36.8 [36.3–37.3]	37.1 [36.5–37.5]	36.8 [36.3–37.3]	0.235
Heart rate	102 [90–115]	103 [95–119]	102 [88–115]	0.256
Systolic blood pressure (mmHg)	123 [104–142]	124 [104–143]	122 [103–142]	0.850
Mean arterial pressure (mmHg)	82 [71–95]	81 [71–94]	86 [74–98]	0.264
Lactic acid (mmol/L)	2.3 [1.2–3.7]	2.5 [1.1–3.5]	2.2 [1.2–3.8]	0.933
Base deficit (mEq/L)	4.3 [2.1–7.6]	3.6 [1.4–7.0]	4.5 [2.2–8.1]	0.260
International normalized ratio	1.4 [1.2–1.6]	1.4 [1.2–1.5]	1.4 [1.2–1.7]	0.200
SOFA score	9.0 [7.0–10.0]	9.0 [8.0–10.0]	9.0 [7.0–10.5]	0.653

ASA: American Society of Anesthesiologists, ACS: abdominal compartment syndrome, SOFA: sequential organ failure assessment score.

Data are presented as median [interquartile range] or n (%).

Table 2

Management and resuscitation parameters for patients who received 3% hypertonic saline (HTS) intravenous fluids following emergency laparotomy and temporary abdominal closure (TAC) compared to patients who had standard resuscitation without HTS.

Management and resuscitation parameters	All patients n = 189	HTS n = 36	No HTS n = 153	p
Abdominal operations	2.0 [2.0–3.0]	2.0 [2.0–3.0]	2.0 [2.0–3.0]	0.091
Required >2 operations	84 (44%)	12 (33%)	72 (47%)	0.191
0–48h following TAC				
Total IVF ^a administration (L)	11.6 [8.0–14.3]	8.5 [6.3–13.1]	11.8 [8.7–14.7]	0.004
PRBC administration (units)	2.0 [0.0–4.0]	1.0 [0.0–4.0]	2.0 [0.0–5.0]	0.069
Plasma administration (units)	0.0 [0.0–3.0]	0.0 [0.0–2.0]	1.0 [0.0–3.0]	0.189
Total urine output (L)	2.8 [1.9–3.9]	2.8 [2.3–4.1]	2.8 [1.9–3.9]	0.425
Total NPWT output (L)	1.4 [0.9–2.2]	1.2 [0.6–1.9]	1.5 [1.0–2.3]	0.068
48–96h following TAC				
Total IVF ^a administration (L)	6.5 [4.3–9.1]	5.8 [4.6–7.3]	6.6 [4.0–9.7]	0.133
Total urine output (L)	3.0 [2.0–4.6]	3.1 [2.2–4.4]	3.0 [2.0–4.8]	0.933
Total NPWT output (L)	0.2 [0.0–1.4]	0.1 [0.0–1.0]	0.3 [0.0–1.6]	0.126
96h–7d following TAC				
Total IVF ^a administration (L)	6.0 [3.2–8.8]	5.0 [1.8–8.0]	6.1 [3.4–8.9]	0.165
Total urine output (L)	5.5 [3.6–7.7]	5.7 [4.1–8.5]	5.3 [3.6–7.7]	0.256
Total NPWT output (L)	0.0 [0.0–0.7]	0.0 [0.0–0.2]	0.0 [0.0–0.7]	0.159

IVF: intravenous fluid, PRBC: packed red blood cell, NPWT: negative pressure wound therapy abdominal dressing.

^aIncluding maintenance crystalloid fluids, bolus crystalloid fluids, piggyback fluids for medication administration, and parenteral nutrition.

Data are presented as median [interquartile range] or n (%).

Table 3

Outcomes for patients who received 3% hypertonic saline (HTS) intravenous fluids following emergency laparotomy and temporary abdominal closure compared to patients who had standard resuscitation without HTS.

Outcomes	All patients n = 189	HTS n = 36	No HTS n = 153	<i>p</i>
Primary fascial closure ^a	151 (80%)	33 (92%)	118 (77%)	0.063
Days to fascial closure	1.6 [1.1–2.8]	1.5 [1.1–2.1]	1.7 [1.1–3.3]	0.202
Peak sodium ^b (mEq/L)	149 [145–153]	150 [147–155]	149 [145–152]	0.093
Peak chloride ^b (mEq/L)	114 [109–117]	115 [111–118]	113 [109–117]	0.134
Peak creatinine ^b (mg/dL)	1.4 [1.0–2.4]	1.3 [1.0–1.8]	1.5 [1.0–2.5]	0.189
Fascial dehiscence	9 (5%)	1 (3%)	8 (5%)	>0.999
Intra-abdominal abscess	24 (13%)	6 (17%)	18 (12%)	0.413
Dialysis during admission	26 (14%)	4 (11%)	22 (14%)	0.790
Discharged on dialysis	22 (12%)	3 (8%)	19 (12%)	0.772
Hospital length of stay (days)	18.8 [11.5–30.7]	19.1 [13.1–31.4]	18.8 [11.1–30.7]	0.834
ICU length of stay (days)	10.0 [4.0–18.0]	11.0 [4.0–18.0]	10.0 [4.0–19.0]	0.988
ICU-free days	7.2 [3.7–14.5]	8.7 [3.6–16.3]	7.2 [3.7–14.1]	0.651
Ventilator days	7.0 [3.0–14.0]	6.0 [3.0–10.5]	7.0 [3.0–16.0]	0.240
Discharge disposition				
Home	69 (37%)	16 (44%)	53 (35%)	0.336
Subacute nursing facility	27 (14%)	6 (17%)	21 (14%)	0.605
Long term care facility	26 (14%)	5 (14%)	21 (14%)	>0.999
Inpatient rehabilitation	12 (6%)	1 (3%)	11 (7%)	0.468
Another hospital	11 (6%)	4 (11%)	7 (5%)	0.226
Hospice	11 (6%)	0 (0%)	11 (7%)	0.128
Inpatient mortality	33 (17%)	4 (11%)	29 (19%)	0.335

ICU: intensive care unit.

^aIntact at the time of discharge.

^bDuring admission.

Data are presented as n (%) or median [interquartile range].

Table 4

Univariate associations between resuscitation parameters, acute kidney injury, and primary fascial closure among patients who underwent emergent laparotomy and temporary abdominal closure (TAC).

Time period	Resuscitation parameters	Acute kidney injury ^a			Primary fascial closure		
		OR	95% CI	p	OR	95% CI	p
POD 0 ^b	3% HTS administration	1.01	0.49–2.08	0.986	3.26	0.94–11.28	0.062
0–48h	IVF ^c administered (L)	1.00	0.94–1.06	0.952	0.90	0.83–0.97	0.003
	NPWT output (L)	1.17	0.96–1.42	0.119	0.72	0.58–0.90	0.003
	Sodium (mEq/L)	1.00	0.94–1.06	0.865	1.03	0.95–1.11	0.454
48h	Chloride (mEq/L)	0.98	0.93–1.03	0.485	1.11	1.03–1.19	0.006
	Osmolarity (mosm/kg)	1.01	0.99–1.04	0.413	1.01	0.98–1.04	0.526
48–96h	IVF ^c administered (L)	1.02	0.95–1.11	0.586	0.88	0.80–0.97	0.007
	NPWT output (L)	1.23	1.01–1.51	0.040	0.62	0.49–0.79	<0.001
96h	Sodium (mEq/L)	0.98	0.94–1.02	0.355	0.98	0.93–1.04	0.555
	Chloride (mEq/L)	0.99	0.94–1.04	0.711	1.00	0.94–1.07	0.973
	Osmolarity (mosm/kg)	0.99	0.98–1.01	0.291	1.00	0.99–1.01	0.495
96h–7d	IVF ^c administered (L)	1.05	0.98–1.13	0.177	0.93	0.85–1.02	0.101
	NPWT output (L)	1.24	1.02–1.50	0.034	0.70	0.57–0.86	0.001
7d	Sodium (mEq/L)	1.02	0.96–1.07	0.555	0.93	0.87–1.00	0.035
	Chloride (mEq/L)	1.03	0.98–1.09	0.242	0.95	0.89–1.02	0.133
	Osmolarity (mosm/kg)	1.01	0.99–1.03	0.176	0.97	0.95–1.00	0.016

OR: odds ratio, CI: confidence interval, HTS: hypertonic saline, IVF: intravenous fluid, NPWT: negative pressure wound therapy. Sodium, chloride, and osmolarity values were measured in serum.

^aStage 2 or 3 acute kidney injury within seven days of exploratory laparotomy and temporary abdominal closure per consensus Kidney Disease: Improving Global Outcomes (KDIGO) definitions.

^bHTS was initiated on postoperative day zero following TAC and continued until fascial closure or postoperative day 3, whichever occurred first.

^cIncluding maintenance crystalloid fluids, bolus crystalloid fluids, piggyback fluids for medication administration, and parenteral nutrition.