Published in final edited form as:

J Trauma Acute Care Surg. 2019 April ; 86(4): 670–678. doi:10.1097/TA.0000000000002170.

The impact of standardized protocol implementation for surgical damage control and temporary abdominal closure after emergent laparotomy

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

^aUniversity of Florida Health, Department of Surgery, Gainesville, Florida

^bUniversity of Florida Health, Sepsis and Critical Illness Research Center, Gainesville, Florida

Abstract

Background: To standardize care and promote early fascial closure among patients undergoing emergent laparotomy and temporary abdominal closure (TAC), we developed a protocol addressing patient selection, operative technique, resuscitation strategies, and critical care provisions. We hypothesized that primary fascial closure rates would increase following protocol implementation with no difference in complication rates.

Study Design: We performed a retrospective cohort analysis of 138 adult trauma and emergency general surgery patients who underwent emergent laparotomy and TAC, comparing protocol patients (n=60) to recent historic controls (n=78) that would have met protocol inclusion criteria. The protocol includes low volume 3% hypertonic saline resuscitation, judicious wound vacuum fluid replacement, and early relaparotomy with sequential fascial closure. Demographics, baseline characteristics, illness severity, resuscitation course, operative management, and outcomes were compared. The primary outcome was fascial closure.

Results: Baseline characteristics, including age, ASA class and postoperative lactate levels were similar between groups. Within 48 hours of initial laparotomy and TAC, protocol patients received significantly lower total intravenous fluid resuscitation volumes (9.7 vs. 11.4 L, $p=0.044$) and exhibited higher serum osmolality (303 vs. 293 mosm/kg, $p=0.001$). The interval between abdominal operations was significantly shorter following protocol implementation (28.2 vs. 32.2 hours, $p=0.027$). The incidence of primary fascial closure was significantly higher in the protocol group (93% vs. 81%, $p=0.045$, number needed to treat: 8.3). Complication rates were similar between groups.

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

Author contribution statement

TJL, PAE, TMB, FAM, AMM, and SCB contributed to the literature review and study design. TJL and TMB contributed to data collection and analysis. TJL drafted the manuscript. All authors contributed to protocol design, protocol implementation, data interpretation, and provision of critical revisions.

Conclusions: Protocol implementation was associated with lower crystalloid resuscitation volumes, a transient hyperosmolar state, shorter intervals between operations, and higher fascial closure rates with no difference in complications.

Level of Evidence: Therapeutic study, level IV

Keywords

Damage control laparotomy; open abdomen; temporary abdominal closure; trauma; acute care surgery; fascial closure

Introduction

For patients with severely deranged physiology undergoing emergent laparotomy, surgical damage control and temporary abdominal closure (TAC) with a negative pressure wound therapy (NPWT) dressing allows the surgeon to quickly address life-threatening surgical conditions, place a temporary dressing over the open abdomen, and transfer the patient to an intensive care unit for continued resuscitation, rewarming, and physiologic optimization. In 1983, Stone et al. (1) described abbreviated laparotomy for 31 trauma and emergency general surgery patients with coagulopathy and exsanguinating hemorrhage. “Damage control surgery” and TAC are now the standard surgical approach for managing trauma patients with hemorrhagic shock, hypothermia, acidosis, coagulopathy, and massive visceral edema. Subsequently, the utilization of the surgical damage control and TAC approach was extrapolated to patients with intra-abdominal sepsis to remove cytokine-rich peritoneal fluid, diagnose and treat residual sources of infection at relaparotomy, and to decrease surgical complications by deferring anastomosis until after physiologic optimization. TAC has also been employed for patients with intra-abdominal vascular emergencies and abdominal compartment syndrome. Regardless of the indication for TAC, patients with an open abdomen are at increased risk for intestinal fistula formation, especially when early primary fascial closure cannot be achieved (2–4). One method for avoiding these morbid complications is to perform fascial closure at the initial laparotomy, avoiding TAC and associated complications (5, 6). However, among patients for whom surgical damage control and TAC is necessary due to severely deranged physiology, massive visceral edema, or the need for interval intra-abdominal evaluation, better strategies are needed to assure definitive fascial closure.

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 (7). Concurrent with this finding, we noted that resuscitation strategies and operative techniques were highly variable, beyond what may be expected for personalized management strategies tailored to individual patient physiology. To standardize care and promote early fascial closure, we developed a protocol standardizing patient selection, operative technique, resuscitation strategies, and critical care provisions. Because the protocol includes administration of 3% hypertonic saline (HTS) intravenous fluid, which may increase risk for hyperchloremic acidosis and kidney injury among postoperative and critically ill patients (8, 9), protocol inclusion requires the absence of criteria which may increase vulnerability to the adverse effects of HTS ($\text{Na} > 155 \text{ mEq/L}$, $\text{Cl} > 115 \text{ mEq/L}$, pH

<7.10, acute kidney injury stage 2, chronic kidney disease stage 3, nephrectomy, or cirrhosis). Harvin et al. (10) were the first to demonstrate the safety and efficacy of 3% HTS for trauma patients managed by emergent laparotomy and TAC. To ensure that this strategy was generalizable to patients undergoing laparotomy and TAC for intra-abdominal sepsis, we performed a safety study of 36 trauma and emergency general surgery patients who received 3% HTS resuscitation at our institution, and found that its use was associated with the development of a moderate hyperosmolar, hypernatremic, hyperchloremic acidosis and lower total intravenous fluid resuscitation volumes with no adverse effects on renal function (11).

With the knowledge that 3% HTS may be safely administered to both trauma and emergency general surgery patients, we have continued to employ this strategy as part of a comprehensive protocol for managing TAC patients, and now seek to compare protocol patients to pre-implementation historical controls that would have qualified for the protocol. We hypothesized that primary fascial closure rates would increase following protocol implementation with no difference in complication rates.

Methods

Study design

We performed a retrospective cohort analysis of 138 adult acute care surgery (trauma and emergency general surgery) patients who underwent emergent laparotomy and TAC at our institution during a 3-year period ending December 2017, including populations before and after implementation of a standardized protocol for emergent laparotomy and temporary abdominal closure. Patients who were managed by the protocol (n=60) were compared to recent historical controls (2015–2016) who would have qualified for the protocol (n=78). Exclusion criteria were factors which would disqualify patients from initiating the protocol (Na >155 mEq/L, Cl <115 mEq/L, pH <7.10, acute kidney injury stage 2, chronic kidney disease stage 3, nephrectomy, or cirrhosis; n=105), patients with a pre-existing intestinal fistula (n=5), patients with complicated pancreatitis (n=11), patients whose initial laparotomy occurred at an outside facility (n=4), and patients who survived <48 hours and therefore may not have had the opportunity to achieve fascial closure (n=9). Derivation of the study population is illustrated in Supplementary Figure 1, illustrating that these exclusion criteria eliminated nearly half of all patients managed with temporary abdominal closure during the study period.

The University of Florida Institutional Review Board approved this study.

Protocol patient selection

The TAC protocol is illustrated in Figure 1. We based criteria for protocol inclusion were on previous work suggesting that TAC is most appropriate for patients with severely deranged physiology, and for whom definitive fascial closure is difficult or impossible due to massive visceral edema (12). Although the protocol recognizes that the operating surgeon may occasionally perform elective TAC for a “second look” at bowel viability or to defer anastomosis until physiologic resuscitation is complete, there is agreement among the

authors that use of TAC for such patients should be avoided, if possible, in recognition of the morbidity associated with failure to achieve abdominal closure (13). Although open abdomen trauma patients and open abdomen emergency general surgery patients are distinct and unique populations, both were included in this study because hypertonic saline resuscitation appears to be safe and effective in both populations, and inclusion of both populations was intended to increase the generalizability of our findings (7, 11). Based on the effect size reported in a previous study (11), the current study would be adequately powered to detect a difference in primary fascial closure rates with 60 patients receiving HTS resuscitation and 78 patients receiving standard resuscitation given unequal sample sizes in a 1.3:1.0 standard resuscitation to HTS resuscitation ratio (14). There were no observed protocol deviations.

Interventions during initial laparotomy

At the time of initial damage control laparotomy and TAC, a central venous catheter is introduced (an institutional policy requirement for administration of >2% HTS), a nasojejunal enteric feeding tube is placed, and NPWT is performed with continuous pressure at -75mmHg, consistent with recommendations from an international NPWT panel (15). Although higher pressures appear to be more effective in draining fluid, there is experimental evidence suggesting that higher pressures may also reduce intestinal blood flow (16, 17). The modality for NPWT included either the Abthera VAC system (KCI, San Antonio, TX) or a Barker-type TAC technique (18), at the discretion of the operating surgeon. Although fascial traction techniques have demonstrated safety and efficacy in achieving fascial closure for open abdomen patients, level I evidence supporting their use is currently lacking, and so we have not yet adopted these techniques (19, 20). In recognition of the possibility of developing abdominal compartment syndrome in the setting of an open abdomen managed with TAC (21), we measured bladder pressures every four hours. Previous work suggests that high NPWT output is associated with acute kidney injury and failure to achieve primary fascial closure and that low ratios of intravenous fluid administration to NPWT output may be responsible for this effect (22). Therefore, we replaced NPWT output with an intravenous fluid bolus equaling 0.5 mL isotonic fluid for every 1.0 mL NPWT output exceeding 500 mL during a 12-hour shift.

Resuscitation

Post-operatively, we initiated 3% HTS at 30mL/hr via central venous catheter in lieu of standard isotonic maintenance fluid administration. To ensure that HTS would not be administered to patients at increased risk for hyperchloremic metabolic acidosis and kidney injury, we excluded patients with any one of the following criteria from receiving hypertonic saline: serum sodium >155 mEq/L, serum chloride >115 mEq/L, blood pH <7.10, acute kidney injury stage 2 or greater as defined by KDIGO criteria (23), nephrectomy, chronic kidney disease stage 3 or greater (24), or cirrhosis. In addition, patients receiving HTS also received isotonic fluid boluses as necessary to achieve and maintain euvolemia. Because clinical definitions and physiologic evidence of euvolemia are the topic of ongoing debate, the maintenance of euvolemia was at the discretion of the treating clinician, who was at liberty to guide therapy using physiologic parameters that seemed most appropriate for each individual patient. At our institution, bedside transthoracic echocardiography is commonly

employed to guide resuscitation. During HTS therapy, we measured serum sodium levels every 6 hours, and discontinued HTS infusion if serum sodium reached >155 mEq/L. Alternatively, we discontinued HTS administration after achieving primary fascial closure or postoperative day 3 (whichever occurred first), consistent with methods from Harvin et al. (10), or if the patient developed stage 2 acute kidney injury (23).

Enteral nutrition

Unless surgically contraindicated, we placed a nasojejunal feeding tube at the conclusion of the index surgical procedure, and initiated enteral nutrition as soon as clinically appropriate and possible (25). The enteral nutrition formula and instillation rate is dictated by existing nutrition protocols which stipulate that immunomodulating enteral feeds (IPMACT®, Nestle, Rosslyn, VA) are used for trauma patients unless sepsis develops or is suspected (26). Enteral feeds are limited at 10 mL/hour for patients at increased risk for non-occlusive bowel necrosis (e.g. active resuscitation, sustained hypotension, vasopressin use, high-dose vasopressor use, paralytic use). For patients with intestinal continuity or an ostomy and low risk for non-occlusive bowel necrosis, enteral feeds are systematically advanced to meet calculated nutritional goals.

Technical considerations

At each relaparotomy, we attempt to achieve continuous fascial traction and sequential closure by placing 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 are adversely affected. Undue tension on the fascia was determined by tactile judgement of the surgeon and visual inspection of the fascia for shearing and tearing at suture lines. If fecal diversion is required, a loop ostomy is created lateral to the rectus muscles, so that the ostomy does not violate fascia that would eventually be used in a midline fascial closure, and so that interval ostomy takedown can be performed without violation of the previously closed midline fascia. For patients in whom primary fascial closure seems unlikely, but skin closure appears possible, we consider developing skin flaps in preparation for placement over a biologic mesh fascial bridge. For large fascial defects without possibility of skin closure due to massive visceral edema or loss of abdominal domain, we utilize a polyglactin mesh bridge closure. In order to minimize risk of enteroatmospheric fistula formation, we perform split thickness skin grafting as soon as possible following polyglactin bridge closure based on tissue granulation and adequate nutritional status. Following planned ventral hernia formation, we consider abdominal wall reconstruction by components separation with mesh reinforcement after 6–12 months, with resolution of inflammation and non-adherences of to the skin graft (3, 27).

Data collection

We collected data regarding patient demographics, baseline characteristics, illness severity, resuscitation course, operative management, and outcomes by query of our institutional database and by retrospective review of electronic medical records. Patient characteristics included age, sex, American Society of Anesthesiologist physical status class, Charlson comorbidity index, body mass index, reason for laparotomy, vital signs, laboratory values, performance of solid organ and hollow viscous resection or repair procedures, blood product

administration, urine output, NPWT output, performance and timing of fascial closure, intestinal fistula formation, surgical site infections, peak sodium, chloride, and creatinine levels, initiation of dialysis, length of stay in the hospital, in the intensive care unit (ICU), and on mechanical ventilation, the performance of tracheostomy, inpatient mortality, and discharge disposition. All resuscitation parameters were assessed on admission and at 48–72 hour intervals for one week following initial laparotomy and TAC.

Statistical analysis

We performed all statistical analysis with SPSS version 24 (IBM, Armonk, NY). We compared continuous variables by the Kruskal-Wallis test and reported as median [interquartile range]. Discrete variables were compared by Fisher's Exact test and reported as number and frequency (n, %). Achievement of fascial closure over time was also compared by the Mantel-Cox log-rank test. Significance was set at an alpha level of less than 0.05. Absolute risk reduction was calculated to determine the number needed to treat with protocol inclusion to achieve fascial closure for one additional patient.

Results

Patient characteristics are listed in Table 1. Baseline characteristics were similar between groups before and after protocol implementation. For the entire study population, median age was 55, ASA class was 4.0, and Charlson comorbidity index was 1.0. Fifty-nine percent of all patients (n=81) underwent initial laparotomy and TAC for intra-abdominal sepsis. The etiology of intra-abdominal sepsis was bowel ischemia in 38 patients, hollow viscous perforation in 29 patients, anastomotic leak in two patients, and other sources of inflammation or infection in 12 patients. The remaining patients required laparotomy due to trauma (35%) or non-traumatic hemorrhage (7%). Vital signs and laboratory values were also similar between historic control and protocol groups (Table 1). Approximately two thirds of all patients underwent hollow viscous resection or repair at initial laparotomy and approximately one-third underwent solid organ resection or repair, with no significant differences between groups.

Clinical management parameters are listed in Table 2. The median number of abdominal procedures for both groups was two operations. The median interval between all abdominal operations was significantly shorter following protocol implementation (28.2 vs. 32.2 hours, $p=0.027$). Within 48 hours of initial laparotomy and TAC, protocol patients received significantly lower total intravenous fluid resuscitation volumes (9.7 vs. 11.4 L, $p=0.044$). Urine output volumes were similar between groups at all time periods. NPWT output was similar between groups within 96 hours of TAC. NPWT output was significantly lower in the protocol group from 96 hours to seven days following TAC. This difference was primarily attributable to persistent NPWT output among patients who had not achieved fascial closure within four days, a phenomenon which was more common prior to protocol implementation.

To illustrate the safety profile of HTS resuscitation in this patient population, serum sodium, chloride, osmolarity, and creatinine trends are illustrated in Figure 2. Baseline levels on admission and at the time of initial laparotomy and TAC were similar between groups.

Forty-eight hours following initial laparotomy, the protocol cohort had higher serum sodium (145 vs. 142 mEq/L, $p<0.001$), chloride (111 vs. 106 mEq/L, $p<0.001$), and osmolarity (303 vs. 293 mosm/kg, $p=0.001$), but similar blood urea nitrogen (15.5 vs. 14.0 mg/dL, $p=0.119$) and serum glucose (129 vs. 120 mg/dL, $p=0.186$). A similar pattern was observed 96 hours following initial laparotomy for sodium (146 vs. 143 mEq/L, $p=0.012$), chloride (109 vs. 106 mEq/L, $p=0.001$), and osmolarity (305 vs. 299 mosm/kg, $p=0.041$), but similar blood urea nitrogen (17.0 vs. 15.0 mg/dL, $p=0.213$) and serum glucose (127 vs. 122 mg/dL, $p=0.212$). Seven days following initial laparotomy, serum chloride remained significantly higher among protocol patients (105 vs. 103 mEq/L, $p=0.039$); sodium and osmolarity were similar between groups. Serum creatinine levels were similar between groups at all time points. There were two instances in which a patient receiving HTS developed serum sodium >155 mEq/L prior to planned discontinuation of the HTS infusion.

Clinical outcomes are listed in Table 3. The incidence of primary fascial closure during the index hospital admission was significantly higher in the protocol group (93% vs. 81%, $p=0.045$). The percentage of patients with an open abdomen over time is illustrated in **Figure 3**, also favoring the protocol group ($p=0.005$). The absolute risk reduction for failure to achieve fascial closure by protocol utilization was 12%. Therefore, 8.3 patients must be managed by the TAC protocol to achieve one fascial closure for one additional patient. Complications were similar between groups, with fascial dehiscence in 4% of all patients, intestinal fistula formation in 3%, and surgical site infection in 21%. Peak sodium and chloride during admission were both higher in the protocol group (151 vs. 147 mEq/L, $p=0.001$ and 116 vs. 111 mEq/L, $p<0.001$, respectively). There were no significant differences between groups in lengths of stay, ventilator days, or performance of tracheostomy. Only 38% of all patients were discharged home. Inpatient mortality and discharge to hospice rates were similar between pre- and post-protocol groups (mortality: 10% vs. 13%, $p=0.601$; hospice: 8% vs. 2%, $p=0.138$).

Discussion

We observed that protocol implementation was associated with lower early intravenous fluid resuscitation volumes, a transient hyperosmolar state, shorter intervals between laparotomies, and significantly higher fascial closure rates, without observable adverse effects. The comprehensive and multi-faceted nature of the protocol hinders our ability to understand which aspects of the protocol impacted fascial closure rates. Based on available evidence, several factors likely contributed.

The hypernatremic, hyperchloremic, hyperosmolar state and lower early resuscitation volumes may be attributable to the provision of 3% hypertonic saline in lieu of isotonic maintenance intravenous fluid. Lower resuscitation volumes may also be partly attributable to earlier and more frequent fascial closure in the protocol group, though it is not possible to establish causality with available data. In addition to reducing resuscitation volumes, hypertonic saline creates an osmotic gradient in the intravascular space and protects against bowel wall edema and gut ischemia-induced systemic inflammation, as observed in rat models of mesenteric venous hypertension (28, 29) and intestinal ischemia (30, 31), providing another mechanism by which protocol patients may have benefited from HTS

resuscitation. Among trauma patients, Harvin et al. (10) found that 3% hypertonic saline administration was associated with reduced total resuscitation volumes without affecting peak creatinine, change in creatinine, or the requirement for renal replacement therapy, compared to patients who were resuscitated with lactated Ringer solution at 125 mL/hr. All 23 patients who received 3% HTS at 30 mL/hour achieved primary fascial closure, though one patient was ultimately discharged with a planned ventral hernia.

We also observed shorter intervals between operations in the protocol group. The protocol recommends relaparotomy within 24 hours if possible and within 48 hours at the latest. The optimal timing of relaparotomy remains controversial. The prospective randomized RELAP trial (32) compared planned relaparotomy every 36–48 hours for patients with severe peritonitis to laparotomy on-demand for patients with clinical deterioration (increase ≥ 4 points in the Multiple Organ Dysfunction Score, development of a surgical emergency, or lack of clinical improvement with a likely intra-abdominal source of sepsis). This study found no difference in major morbidity or mortality between groups, but demonstrated a reduction in number of relaparotomies, ICU length of stay, days on mechanical ventilation, and overall hospital length of stay in the on-demand group. A subsequent analysis of RELAP trial data identified six variables associated with necessity for relaparotomy: heart rate > 90 , hemoglobin < 8.1 g/dL, temperature < 35.5 or $> 39.0^{\circ}\text{C}$, no defecation, diffuse contamination at initial laparotomy, and inotrope requirement (33). Regardless of planned or on-demand approaches, TAC patients should undergo relaparotomy within 48 hours. In a review of 105 patients who required relaparotomy for persistent abdominal sepsis, mortality was similar among patients undergoing relaparotomy on-demand and planned relaparotomy (34). However, delay in relaparotomy for more than 48 hours was associated with increased mortality (76.5% vs. 28%, $p=0.0001$). Longer delays between operations may also allow for adhesion formation. In our study, the incidence of organ/space surgical site infections was higher in the protocol group, although the difference was not statistically significant, and the overall surgical site infection rate was slightly lower in the protocol group. It is plausible that a longer duration of open abdomen management allows for more complete source control, though it is difficult to test this hypothesis with available data.

The performance of TAC rather than fascial closure at the time of initial laparotomy is an important subject that requires further investigation. Comparisons between immediate fascial closure and TAC for the septic abdomen have had conflicting results. One prospective randomized trial found that among patients with severe peritonitis undergoing laparotomy, mortality was lower for patients managed with TAC compared with closure at initial laparotomy (11% vs. 41%, $p=0.01$) (35). A retrospective review of critically ill patients with intra-abdominal sepsis managed with TAC and planned relaparotomy versus immediate abdominal closure at initial laparotomy found that ICU and hospital length of stay were significantly longer in the TAC cohort with no difference in mortality (36). Subsequently, a randomized trial of patients undergoing laparotomy for severe secondary peritonitis found that there were no significant differences between TAC and immediate closure in acute renal failure, duration of mechanical ventilation, need for total parenteral nutrition, need for reoperation due to residual infection, or mortality (37). However, this trial was discontinued at the first interim analysis due to findings that the relative risk and odds ratio for death were 1.83 and 2.85 times higher among TAC patients. Notably, TAC was performed by suturing a

polypropylene mesh bridge to the fascia and relaparotomy was performed by incising and then re-closing the mesh. This technique has become less common in modern practice with the adoption of NPWT and dynamic fascial closure strategies, which provide advantages in achieving fascial closure and reducing the incidence of intestinal fistula formation (38–40). More recently, Harvin et al. (5) implemented a formal audit and feedback process for damage control trauma laparotomies performed at their institution, and found that the incidence of damage control laparotomy decreased following implementation of the audit and feedback process. In a subsequent comparison between trauma patients who underwent damage control laparotomy with TAC and matched patients who underwent definitive laparotomy with immediate fascial closure, the incidence of major abdominal complications was higher in the TAC group (56% vs. 19%, $p=0.066$) (13). It remains unknown whether similar effects would be observed among patients with intra-abdominal sepsis. Based on the weight of available evidence, it seems prudent to reserve TAC for patients with severely deranged physiology and patients for whom visceral edema precludes fascial closure at initial laparotomy.

This study was limited by selection bias inherent to retrospective studies and the potential influence of the Hawthorne effect (i.e., clinician behavior may have been influenced by the knowledge that protocol implementation would be accompanied by ongoing assessment of safety and efficacy). Although the Hawthorne effect confounds outcomes research, it may also be good for patient care. In addition, data from a single institution may not be generalizable to other practice settings. We sought to improve the generalizability of these findings by including heterogeneous populations of trauma and emergency general surgery patients undergoing laparotomy and TAC, while recognizing that these patient populations are distinct, with unique pathophysiology and historically higher fascial closure rates among trauma patients (7). Future research should focus on patient selection for TAC versus definitive laparotomy and immediate fascial closure, particularly in the setting of intra-abdominal sepsis.

Conclusions

Following implementation of a protocol for emergent laparotomy and temporary abdominal closure, we observed lower early intravenous fluid resuscitation volumes, a transient hyperosmolar state, shorter intervals between operations, and significantly higher fascial closure rates, without adverse effects. The hypernatremic, hyperchloremic, hyperosmolar state and lower early resuscitation volumes among protocol patients was likely attributable to the provision of 3% hypertonic saline. We also observed shorter intervals between operations in the protocol group, consistent with protocol recommendations for relaparotomy within 24 hours if possible and within 48 hours at the latest. Future research should compare TAC with definitive laparotomy and immediate fascial closure among patients with intra-abdominal sepsis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors thank Peggy Marker, Paul Nickerson, and Lauren Ochoa for their assistance with protocol implementation and data management. The authors have no relevant conflicts of interest. 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.

This work has not been previously presented and this manuscript is not under consideration elsewhere. The authors have no relevant conflicts of interest. This work will be presented at a poster session at the American College of Surgeons Clinical Congress 2018 in Boston, Massachusetts. The authors were supported in part by grants R01 GM113945-01 (PAE), R01 GM105893-01A1 (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. Research reported in this publication was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR001427. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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. 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]
3. 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]
4. 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]
5. Harvin JA, Kao LS, Liang MK, Adams SD, McNutt MK, Love JD, Moore LJ, Wade CE, Cotton BA, Holcomb JB. Decreasing the Use of Damage Control Laparotomy in Trauma: A Quality Improvement Project. *J Am Coll Surg* 2017;225(2):200–9. [PubMed: 28445796]
6. George MJ, Adams SD, McNutt MK, Love JD, Albarado R, Moore LJ, Wade CE, Cotton BA, Holcomb JB, Harvin JA. The effect of damage control laparotomy on major abdominal complications: A matched analysis. *Am J Surg.* 2018;216(1):56–9. [PubMed: 29157889]
7. 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]
8. 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]
9. 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]
10. 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]
11. Loftus TJ, Efron PA, Bala TM, Rosenthal MD, Croft CA, Smith RS, Moore FA, Mohr AM, Brakenridge SC. Hypertonic saline resuscitation after emergent laparotomy and temporary abdominal closure. *J Trauma Acute Care Surg.* 2018;84(2):350–7. [PubMed: 29140948]
12. Roberts DJ, Zygun DA, Faris PD, Ball CG, Kirkpatrick AW, Stelfox HT, Indications for Trauma Damage Control Surgery International Study G. Opinions of Practicing Surgeons on the

Appropriateness of Published Indications for Use of Damage Control Surgery in Trauma Patients: An International Cross-Sectional Survey. *J Am Coll Surg*. 2016;223(3):515–29. [PubMed: 27321388]

13. George MJ, Adams SD, McNutt MK, Love JD, Albarado R, Moore LJ, Wade CE, Cotton BA, Holcomb JB, Harvin JA. The effect of damage control laparotomy on major abdominal complications: A matched analysis. *Am J Surg* 2017.
14. Snedecor GW, Cochran WG. Statistical methods. 7th ed. Ames, Iowa: Iowa State University Press; 1980 104 p.
15. 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]
16. Lindstedt S, Malmjö M, Hansson J, Hlebowicz J, Ingemansson R. Pressure transduction and fluid evacuation during conventional negative pressure wound therapy of the open abdomen and NPWT using a protective disc over the intestines. *BMC Surg*. 2012;12:4. [PubMed: 22443416]
17. Lindstedt S, Hansson J, Hlebowicz J. Comparative study of the microvascular blood flow in the intestinal wall during conventional negative pressure wound therapy and negative pressure wound therapy using paraffin gauze over the intestines in laparostomy. *Int Wound J*. 2012;9(2):150–5. [PubMed: 21985421]
18. Barker DE, Kaufman HJ, Smith LA, Ciraulo DL, Richart CL, Burns RP. Vacuum pack technique of temporary abdominal closure: a 7-year experience with 112 patients. *J Trauma*. 2000;48(2):201–6; discussion 6–7. [PubMed: 10697075]
19. Dennis A, Vizinas TA, Joseph K, Kingsley S, Bokhari F, Starr F, Poulakidas S, Wiley D, Messer T, Nagy K. Not so fast to skin graft: transabdominal wall traction closes most “domain loss” abdomens in the acute setting. *J Trauma Acute Care Surg*. 2013;74(6):1486–92. [PubMed: 23694876]
20. Correa JC, Mejia DA, Duque N, J MM, Uribe CM. Managing the open abdomen: negative pressure closure versus mesh-mediated fascial traction closure: a randomized trial. *Hernia* 2016;20(2):221–9. [PubMed: 26833235]
21. Gracias VH, Braslow B, Johnson J, Pryor J, Gupta R, Reilly P, Schwab CW. Abdominal compartment syndrome in the open abdomen. *Arch Surg*. 2002;137(11):1298–300. [PubMed: 12413323]
22. 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]
23. 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]
24. 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]
25. Bansal V, Coimbra R. Nutritional support in patients following damage control laparotomy with an open abdomen. *Eur J Trauma Emerg Surg*. 2013;39(3):243–8. [PubMed: 26815230]
26. Martindale RG, McClave SA, Vanek VW, McCarthy M, Roberts P, Taylor B, Ochoa JB, Napolitano L, Cresci G, American College of Critical Care M, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition: Executive Summary. *Crit Care Med* 2009;37(5):1757–61. [PubMed: 19373044]
27. Fabian TC, Croce MA, Pritchard FE, Minard G, Hickerson WL, Howell RL, Schurr MJ, Kudsk KA. Planned ventral hernia. Staged management for acute abdominal wall defects. *Ann Surg*. 1994;219(6):643–50; discussion 51–3. [PubMed: 8203973]
28. 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]
29. 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]
 30. 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]
 31. 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]
 32. van Ruler O, Mahler CW, Boer KR, Reuland EA, Gooszen HG, Opmeer BC, de Graaf PW, Lamme B, Gerhards MF, Steller EP, et al. Comparison of on-demand vs planned relaparotomy strategy in patients with severe peritonitis: a randomized trial. *JAMA.* 2007;298(8):865–72. [PubMed: 17712070]
 33. Kiewiet JJ, van Ruler O, Boermeester MA, Reitsma JBA decision rule to aid selection of patients with abdominal sepsis requiring a relaparotomy. *BMC Surg.* 2013;13:28. [PubMed: 23870702]
 34. Koperna T, Schulz F Relaparotomy in peritonitis: prognosis and treatment of patients with persisting intraabdominal infection. *World J Surg* 2000;24(1):32–7. [PubMed: 10594200]
 35. Serclova Z, Ryska O, Dytrych P, Marvan J, Marx K, Konecna E, Miksikova A, Antos F. [Fascial closure of the abdominal wall by dynamic suture after topical negative pressure laparostomy treatment of severe peritonitis--results of a prospective randomized study]. *Rozhl Chir.* 2012;91(1):26–31. [PubMed: 22746075]
 36. Adkins AL, Robbins J, Villalba M, Bendick P, Shanley CJ. Open abdomen management of intra-abdominal sepsis. *Am Surg.* 2004;70(2):137–40; discussion 40. [PubMed: 15011916]
 37. Robledo FA, Luque-de-Leon E, Suarez R, Sanchez P, de-la-Fuente M, Vargas A, Mier J. Open versus closed management of the abdomen in the surgical treatment of severe secondary peritonitis: a randomized clinical trial. *Surg Infect (Larchmt).* 2007;8(1):63–72. [PubMed: 17381398]
 38. Kreis BE, de Mol van Otterloo AJ, RW. Kreis Open abdomen management: a review of its history and a proposed management algorithm. *Med Sci Monit.* 2013;19:524–33. [PubMed: 23823991]
 39. Carlson GL, Patrick H, Amin AI, McPherson G, MacLennan G, Afolabi E, Mowatt G, Campbell B. Management of the open abdomen: a national study of clinical outcome and safety of negative pressure wound therapy. *Ann Surg* 2013;257(6):1154–9. [PubMed: 23478532]
 40. Atema JJ, Gans SL, Boermeester MA. Systematic review and meta-analysis of the open abdomen and temporary abdominal closure techniques in non-trauma patients. *World J Surg* 2015;39(4):912–25. [PubMed: 25446477]

Figure 1:
Temporary abdominal closure protocol.

Figure 2:

Patients undergoing emergent laparotomy and temporary abdominal closure (TAC) who were managed on the protocol had higher serum sodium, chloride, and osmolarity 48 and 96 hours following TAC (* $p < 0.05$). Results are illustrated as median values with boxes representing interquartile range and whiskers representing 1.5 times the interquartile range.

Figure 3:

The percentage of patients with an open abdomen decreased at a greater rate in the protocol group.

Table 1:

Summary of patient characteristics at initial laparotomy before and after protocol implementation.

Patient characteristics	All patients n = 138	Before protocol n = 78	After protocol n = 60	p
Age (years)	55 [42–66]	55 [45–68]	50 [35–65]	0.121
Male	82 (59%)	41 (53%)	41 (68%)	0.080
ASA physical status classification	4.0 [3.0–4.0]	4.0 [3.0–4.0]	4.0 [3.0–4.0]	0.117
Charlson comorbidity index	1.0 [0.0–2.3]	0.5 [0.0–2.0]	1.0 [0.0–3.0]	0.173
Body mass index (kg/m ²)	28.5 [23.5–34.3]	28.6 [24.7–35.7]	28.2 [22.7–33.3]	0.441
Reason for laparotomy				
Sepsis	81 (59%)	46 (59%)	35 (58%)	>0.999
Trauma	48 (35%)	24 (31%)	24 (40%)	0.283
Non-trauma hemorrhage	9 (7%)	8 (10%)	1 (2%)	0.077
Temperature (°C)	36.8 [36.4–37.1]	36.7 [36.3–37.1]	36.9 [36.5–37.2]	0.217
Heart rate	105 [90–121]	105 [86–118]	106 [94–123]	0.180
Mean arterial pressure (mmHg)	82 [70–96]	85 [71–98]	81 [69–89]	0.095
pH	7.33 [7.26–7.38]	7.34 [7.29–7.38]	7.30 [7.22–7.37]	0.060
Base deficit (mEq/L)	3.2 [1.3–7.0]	3.2 [1.8–6.1]	3.3 [1.0–7.2]	0.865
Lactic acid (mEq/L)	2.3 [1.2–3.5]	2.3 [1.2–3.5]	2.3 [1.1–3.6]	0.938
Anion gap (mEq/L)	19.1 [16.6–22.2]	19.3 [17.2–22.5]	18.8 [15.9–21.5]	0.151
Sodium (mEq/L)	141 [137–143]	141 [138–144]	140 [137–143]	0.169
Chloride (mEq/L)	104 [100–108]	104 [100–107]	104 [101–108]	0.380
Creatinine (mg/dL)	1.0 [0.7–1.3]	0.9 [0.7–1.2]	1.0 [0.7–1.3]	0.131
Solid organ resection or repair	43 (31%)	20 (26%)	23 (38%)	0.139
Hollow viscous resection or repair	94 (68%)	50 (64%)	44 (73%)	0.274
Bowel resection or repair	87 (63%)	45 (58%)	42 (70%)	0.157

ASA: American Society of Anesthesiologists, SOFA: sequential organ failure assessment. Data are presented as median [interquartile range] or n (%).

Table 2:

Summary of management parameters before and after protocol implementation.

Management	All patients n = 138	Before protocol n = 78	After protocol n = 60	p
Abdominal operations	2.0 [2.0–3.0]	2.0 [2.0–3.0]	2.0 [2.0–3.0]	0.226
Hours between operations	29.2 [23.8–37.0]	32.2 [25.1–41.5]	28.2 [22.5–33.7]	0.027
0–48h following TAC				
Total IVF administration (L)	10.9 [7.9–13.3]	11.4 [8.7–14.2]	9.7 [7.0–13.0]	0.044
RBC administration (units)	2.0 [0.0–4.0]	2.0 [1.0–5.0]	1.0 [0.0–4.0]	0.105
Plasma administration (units)	0.0 [0.0–3.0]	0.0 [0.0–3.0]	0.0 [0.0–2.8]	0.237
Total urine output (L)	3.0 [2.4–3.9]	3.0 [2.3–4.1]	2.9 [2.4–3.6]	0.635
Total NPWT output (L)	1.3 [0.8–2.0]	1.4 [0.9–2.0]	1.2 [0.8–1.7]	0.174
48–96h following TAC				
Total IVF administration (L)	6.5 [4.5–8.7]	6.8 [4.6–9.5]	6.0 [4.4–7.7]	0.192
Total urine output (L)	3.3 [2.2–5.0]	3.3 [2.4–5.2]	3.3 [2.2–4.8]	0.995
Total NPWT output (L)	0.2 [0.0–1.1]	0.2 [0.0–1.4]	0.1 [0.0–0.9]	0.321
96h–7d following TAC				
Total IVF administration (L)	5.2 [2.8–8.1]	5.4 [2.3–8.3]	5.1 [2.8–7.9]	0.954
Total urine output (L)	5.8 [4.1–7.7]	5.8 [4.1–7.5]	5.7 [4.1–8.4]	0.598
Total NPWT output (L)	0.0 [0.0–0.1]	0.0 [0.0–0.5]	0.0 [0.0–0.0]	0.010

TAC: temporary abdominal closure, IVF: intravenous fluid, RBC: red blood cell transfusion, NPWT: negative pressure wound therapy dressing.
Data are presented as median [interquartile range].

Table 3:

Summary of outcomes before and after protocol implementation.

Outcomes	All patients n = 138	Before protocol n = 78	After protocol n = 60	<i>p</i>
Primary fascial closure	119 (86%)	63 (81%)	56 (93%)	0.045
Hours to primary fascial closure	36.8 [25.2–58.5]	41.2 [26.8–65.7]	33.4 [24.4–50.4]	0.139
Fascial dehiscence	5 (4%)	5 (6%)	0 (0%)	0.069
Intestinal fistula formation	4 (3%)	4 (5%)	0 (0%)	0.132
Surgical site infection	29 (21%)	18 (23%)	11 (18%)	0.534
Superficial	4 (3%)	4 (5%)	0 (0%)	0.132
Deep	7 (5%)	6 (8%)	1 (2%)	0.138
Organ/space	18 (13%)	8 (10%)	10 (17%)	0.313
Peak Sodium (mEq/L)	149 [145–153]	147 [144–152]	151 [147–155]	0.001
Peak Chloride (mEq/L)	114 [109–117]	111 [107–116]	116 [112–119]	<0.001
Peak Creatinine (mg/dL)	1.2 [0.9–1.6]	1.2 [0.9–1.5]	1.2 [1.0–1.8]	0.266
Dialysis during admission	9 (7%)	5 (6%)	4 (7%)	>0.999
Discharged on dialysis	8 (6%)	5 (6%)	3 (5%)	>0.999
Hospital length of stay (days)	17.7 [12.4–28.8]	16.7 [9.7–29.4]	19.7 [13.6–28.3]	0.238
ICU length of stay (days)	11.0 [6.0–17.0]	10.0 [5.0–16.3]	12.5 [8.0–18.0]	0.627
ICU-free days	6.4 [2.3–12.8]	6.4 [2.9–12.8]	6.3 [0.9–13.2]	0.090
Days on mechanical ventilation	5.0 [3.0–11.3]	5.0 [3.0–13.0]	6.0 [3.0–9.0]	0.364
Tracheostomy during admission	34 (25%)	21 (27%)	13 (22%)	0.552
Discharge disposition				
Home	53 (38%)	31 (40%)	22 (37%)	0.728
Subacute nursing facility	26 (19%)	12 (15%)	14 (23%)	0.276
Long term care facility	21 (15%)	12 (15%)	9 (15%)	>0.999
Inpatient rehabilitation	7 (5%)	7 (9%)	0 (0%)	0.019
Another hospital	8 (6%)	2 (3%)	6 (10%)	0.078
Hospice	7 (5%)	6 (8%)	1 (2%)	0.138
Inpatient mortality	16 (12%)	8 (10%)	8 (13%)	0.601

ICU: intensive care unit. Data are presented as n (%) or median [interquartile range].