



Use of Hypertonic Saline After Damage Control Laparotomy to Improve Early Primary Fascial Closure

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USE OF HYPERTONIC SALINE AFTER DAMAGE CONTROL LAPAROTOMY TO IMPROVE EARLY PRIMARY FASCIAL CLOSURE

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14. ABSTRACT- The inability to close the abdominal wall following an initial damage control laparotomy (DCL) has led to new challenges. Purpose: This project aims to test hypertonic saline (HTS) use after DCL to reduce bowel edema and resuscitation volume, leading to successful and faster primary fascial closure (PFC). Our primary objective is to determine if there is a higher rate of PFC in patients who undergo DCL when using HTS versus crystalloid resuscitation. Method: The protocol design was a multi-institutional (5 sites), prospective, double-blind, randomized controlled trial of 195 patients who underwent DCL for abdominal trauma requiring temporary abdominal closure and return to the operating room for definitive treatment. All facilities were Level I Trauma Centers. Results: There were no differences in rates of primary facial closure between the two groups or for time in hours until closure. The HTS group had less fluids daily over 72 hours and over the 72-hour period. The complication rate was higher in all categories except abdominal compartment syndrome in the normal saline group. Mortality in the normal saline group was double that of the HTS group. Finally, coagulation, pH, and lactate did not significantly differ between the two groups throughout the 72-hour evaluation. Conclusion: Finally, our results found an increase in inflammatory markers with the HTS cohort that does not support previously published studies, demonstrating the incompletely understood interaction between trauma and inflammation, as well as the interplay of HTS. This analysis was part of the larger multicenter trial investigating infection rates and organ dysfunction and may necessitate more extensive studies investigating the effects of inflammatory cytokine levels on trauma patient outcomes.					
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1.0 EXECUTIVE SUMMARY

The inability to close the abdominal wall following an initial damage control laparotomy (DCL) has led to new challenges. Hypertonic saline (HTS) use after DCL may reduce bowel edema and resuscitation volume, leading to successful and faster primary fascial closure (PFC). Our primary objective is to determine if there is a higher rate of PFC in patients who undergo DCL when using HTS versus crystalloid resuscitation.

2.0 INTRODUCTION

Damage control laparotomy (DCL) has proven to be a successful means to improve survival in severely injured patients.¹⁻⁵ These patients often require significant resuscitation with crystalloid and blood products which can lead to bowel and retroperitoneal edema, abdominal compartment syndrome, continued acidosis, and coagulopathy.⁶⁻⁷ Ultimately, these factors contribute to difficulties closing the abdominal wall following the initial DCL and have led to new challenges. Delays in primary fascial closure (PFC) contribute to increased fluid losses, higher nutritional demands,⁸⁻⁹ abdominal wall hernias, enterocutaneous fistula, and intra-abdominal infections.¹⁰⁻¹³ Current efforts utilizing negative pressure wound dressings and sequential closure devices¹⁴⁻¹⁶ do not address the underlying intestinal and retroperitoneal edema resulting from resuscitation and inflammation.⁶ From the literature and our experience, approximately 25% laparotomies in trauma result in temporary abdominal closure (TAC) with 24-40% unable to achieve primary fascial closure (PFC).^{17,18} Injury severity is not associated with failure to achieve PFC.¹⁹

Hypertonic saline (HTS) use after DCL has been suggested to reduce bowel edema, and resuscitation volumes, thus allowing for a shorter time to PFC.¹⁴ We randomized patients to receive either HTS or standard crystalloid solutions after DCL. Our primary objective is to determine if there is a higher rate of PFC among patients who undergo DCL and temporary abdominal closure when using HTS versus standard crystalloid resuscitation. For secondary measures, we will determine if faster PFC reduces ICU, ventilator and hospital days, and changes in morbidity to include enterocutaneous fistula (ECF), intra-abdominal abscess (IAA), abdominal wall hernia, and anastomotic failure. Hypertonic saline use in the postoperative period following damage control laparotomy and resuscitation is a feasible practice change due to the readily available intravenous solution that could have a profound impact in the field of trauma and acute care surgery. We believe we can improve PFC rates using hypertonic saline. The use of HTS after DCL may decrease the time to PFC and reduce the number of complications associated with an open abdomen.

3.0 METHODS, ASSUMPTIONS AND PROCEDURES

The inability to close the abdominal wall following an initial damage control laparotomy (DCL) has led to new challenges. Significant resuscitation following trauma using intravenous fluids and blood products can lead to bowel and retroperitoneal edema, abdominal compartment syndrome, continued acidosis, and coagulopathy. This may necessitate either leaving the abdomen open after DCL or performing an operative decompression on someone who did not undergo an initial laparotomy. Delays in primary fascial closure (PFC) contribute to increased fluid losses and nutritional demands, abdominal wall hernias, enterocutaneous fistula, and intra-abdominal infections. Hypertonic saline (HTS) use after DCL has been investigated in animal

models to reduce bowel edema and resuscitation volumes, thus leading to successful PFC and a quicker time to closure. The use of HTS after DCL may decrease the time to PFC and reduce the number of complications associated with an open abdomen. The goals of this study were:

- Determine if there is a higher rate of PFC among patients who undergo DCL and temporary abdominal closure when using HTS versus standard crystalloid resuscitation
- Determine if faster PFC reduces ICU, ventilator and hospital days, and result in lower morbidity to include enterocutaneous fistula (ECF), intra-abdominal abscess (IAA), abdominal wall hernia, and anastomotic failure
- Provide insights into other research areas surrounding an open abdomen in the setting of trauma including Acute Respiratory Distress Syndrome (ARDS), abdominal hypertension, acute kidney injury, coagulopathy, surgical site infections, and immune system effects.

The protocol design was a multi-institutional (5 sites), prospective, double blind, randomized controlled trial of patients who underwent DCL for abdominal trauma requiring temporary abdominal closure and return to operating room for definitive treatment. All facilities were Level I Trauma Centers.

4.0 MAJOR EVENTS/MILESTONES/SUCCESS

In preparation for the execution of this project,

- Kick Off Meeting – Sep 2018
- IRB/IACUC Approval – June 2015
- All experimental procedures completed – Jul 2023
- Data Analysis – Sep 2023
- Poster presentation – provide location and date: see below
- Manuscript submitted to – name of journal and date: see below
- Dissemination of Results – Final report to AFRL attached.

5.0 RISK ASSESSMENT

5.1 Risk Analysis:

There was some risk in meeting schedule and completion date was extended since there had been a delay in providing grant funding to Henry Jackson Foundation to distribute among the additional sites. Second level review took a significant amount of time. The COVID 19 pandemic interrupted enrollment and delayed regulatory processes significantly at all sites. The 6-hour enrollment timeframe also significantly limited some sites. The approval to extend the hours from 6 to 9 for the enrollment window was approved and sites received approval by their IRBs.

5.2 Technical Challenges

The 6-hour enrollment timeframe also significantly limited some sites. The approval to extend the hours from 6 to 9 for the enrollment window was approved and sites received approval by their IRBs. There were some challenges with site data input into the database which were ultimately corrected/resolved and allowed analysis to proceed.

6.0 TRANSITION PLAN

6.1 Military Relevance

Results of this study will provide insights into other research areas surrounding an open abdomen which is common in combat casualty care and damage control surgery. This will include in the setting of trauma including Acute Respiratory Distress Syndrome (ARDS), abdominal hypertension, acute kidney injury, coagulopathy, surgical site infections, and immune system effects.

6.2 Transition Strategy

Transition: Implement hypertonic saline into CPGs to minimize postoperative complications and to improve patient good functional outcomes.

KRL 4 (generates early or very early knowledge for some health-related issue; requires replication) to KRL 7 (conducts early studies adapting KRL 4-6 research-supported applications for use in an identified context)

7.0 RESULTS

There were no differences in rates of primary fascial closure between the two groups or for time in hours until closure. The HTS group had less fluids daily over 72 hours and over the 72-hour period. The complication rate was higher in the normal saline group in all categories except abdominal compartment syndrome. Mortality in the normal saline group was double the HTS group. Finally, coagulation, pH, and lactate did not significantly differ between the two groups over the duration for the 72-hour evaluation.

8.0 CONCLUSION/DISCUSSION

Effort to minimize postoperative complications is paramount for good functional outcome, preventing complications such as fistulae, abscesses, chronic wounds, and ventral hernias. Currently, we show HTS use is safe and is feasible in DCL. While there was no difference in PFC, less fluid and decrease in morbidity and mortality was noted in the HTS group without negative impact on coagulation and resuscitation lab values.

Finally, our results found an increase in inflammatory markers with the HTS cohort that does not support previously published studies, demonstrating the incompletely understood interaction between trauma and inflammation, as well as the interplay of HTS. This analysis was part of the larger multicenter trial investigating infection rates and organ dysfunction and may necessitate larger studies investigating the effects of inflammatory cytokine levels on trauma patient outcomes.

9.0 DELIVERABLES

9.1 Publications:

“Double Blinded Randomized Controlled Trial: Does Hypertonic Saline Resuscitation in Trauma Following Damage Control Laparotomy Attenuate Inflammation?”

Draft complete, edits continue for journal submission (Trauma Surgery and Acute Care Open Access)

"Hypertonic Saline After Damage Control Laparotomy to Improve Early Primary Fascial Closure: A Multi-Center Randomized Control Trial"

Manuscript in draft (Journal of Trauma and Acute Care Surgery)

9.2 Presentations:

Presentation Title: Use of Hypertonic Saline after Damage Control Laparotomy to Improve Early Primary Fascial Closure.

Conference: South Texas Chapter ACS, Feb 2015 (Accepted for Podium Presentation- CPT Michelle Buehner)

Conference: SAUSHEC Research Day Apr 2015 (Accepted for GME Podium Presentation- CPT Michelle Buehner)

Presentation Title: Hypertonic Saline Resuscitation in Trauma Following Damage Control Laparotomy: Does it Attenuate Inflammation and Reduce Complications?

Conference: South Texas ACS meeting Feb 2019 (Accepted for Podium Presentation- CPT Patrick McCarthy)

Presentation Title: Use of Hypertonic Saline After Damage Control Laparotomy to Improve Early Primary Fascial Closure: A Single-Center Randomized Controlled Trial

Conference: South Texas ACS meeting Feb 2019 (Accepted for Podium Presentation- 2Lt Ryan Rhie)

Presentation Title: Hypertonic Saline After Damage Control Laparotomy to Improve Early Primary Fascial Closure: A Single-Center Randomized Control Trial.

Conference: USU Research Days May 2019 (Accepted for Poster Presentation- 2Lt Ryan Rhie)

Presentation Title: Double blinded randomized controlled trial: does hypertonic saline resuscitation in trauma following damage control laparotomy attenuate inflammation?

Conference: Alexander Paper competition 1st place clinical science Jan 2020 (Accepted for Podium Presentation- CPT Patrick McCarthy)

10.0 COST

Trauma, Hemostasis & Resuscitation (AFT2R)

Proposal Number AC16OM10

\$682K, all funds expended

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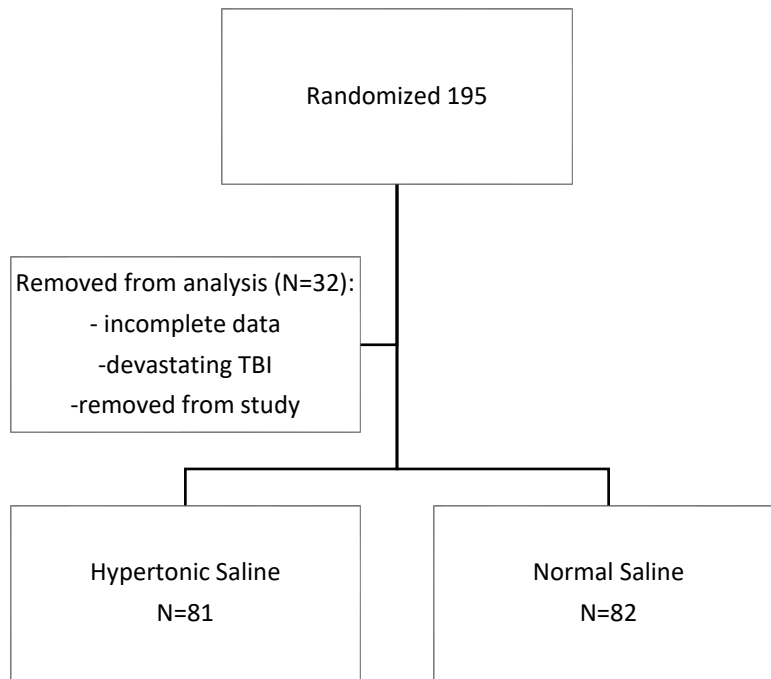
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FIGURES AND TABLES:

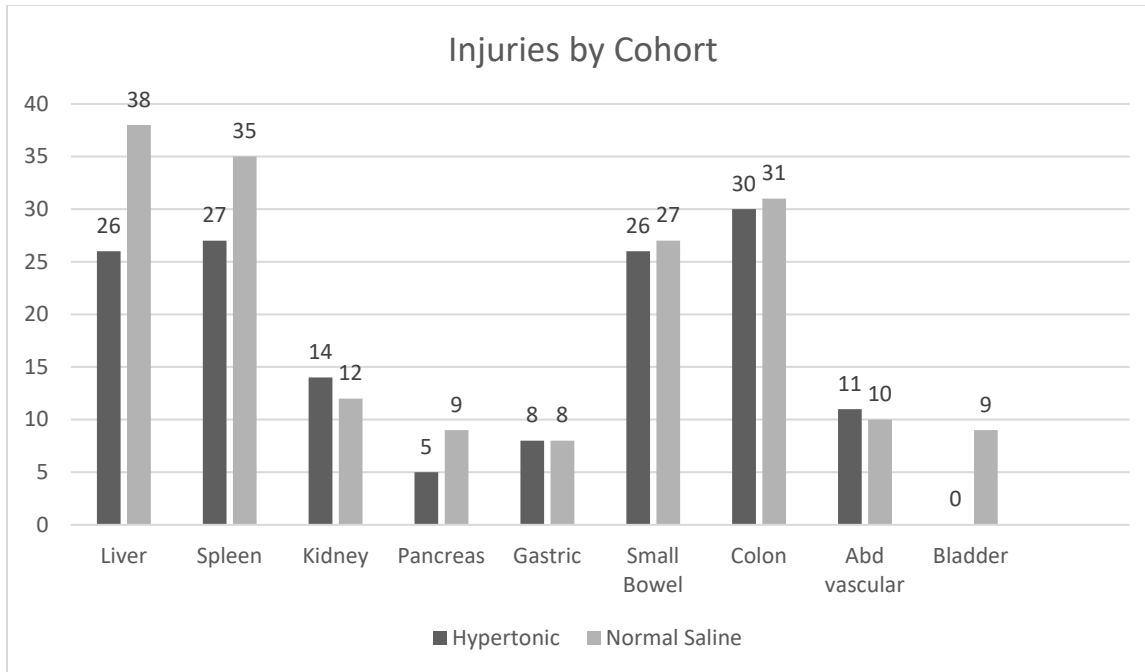
TABLE 1. Definitions

1. Hours to primary fascial closure= time of end of initial OR until end of OR during which fascia is closed, rounded to the nearest 30 minute interval
2. Ventilator associated pneumonia= pneumonia that develops 48 hours or longer after mechanical ventilation defined by at least 2 of the following:
 - a. pulmonary infection: signs include fever, purulent secretions, and leukocytosis
 - b. bacteriologic evidence of pulmonary infection
 - c. radiologic suggestion of pulmonary infection
3. Dehiscence= partial or complete separation of the midline abdominal fascia
4. Surgical site infection= infection occurs within 30 days after exploratory laparotomy defined by at least 2 of the following:
 - a. involves only skin and subcutaneous tissue of the incision
 - b. patient has at least one of the following:
 - i. purulent drainage from the superficial incision.
 - ii. organisms isolated from an aseptically obtained culture from the superficial incision or subcutaneous tissue.
 - iii. superficial incision that is deliberately opened by a surgeon, attending physician or other designee and is culture positive or not cultured
 - c. patient has at least one of the following signs or symptoms: pain or tenderness; localized swelling; erythema; or heat. A culture negative finding does not meet this criterion.
 - d. diagnosis of a superficial incisional SSI by the surgeon or attending physician or other designee.
5. Intra-abdominal abscess= infection occurs within 30 days after the exploratory laparotomy
 - a. infection involves any part of the body deeper than the fascial/muscle layers, that is opened or manipulated during the operative procedure
 - b. patient has at least one of the following:
 - i. purulent drainage from a drain that is placed into the organ/space (e.g., closed suction drainage system, open drain, T-tube drain, CT guided drainage)
 - ii. organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space
 - iii. an abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test
6. Enterocutaneous fistula (ECF)= an abnormal communication between the small or large bowel and the skin or atmosphere.

7. Abdominal compartment syndrome (ACS)= organ dysfunction caused by intra-abdominal hypertension (IAH) as documented by bladder pressure of at least 15cmH₂O.
 8. Hyponatremia= serum sodium level >155
 9. Hyperchloremia= serum chloride level >118
 10. Ventral hernia= incisional hernia of abdominal wall where the fascia does not heal properly.
 11. Anastomotic leak= intestinal wall defect with communication of the intraluminal and extraluminal compartments (at site of anastomosis) that is diagnosed by CT scan as a result of symptoms to include ileus, leukocytosis, fever, vomiting, or diarrhea/constipation.
 12. Acute kidney injury= defined by RIFLE criteria
 13. RIFLE Score: Risk, Injury, Failure, Loss of function, End stage kidney disease (appendix F)
 14. Acute respiratory distress syndrome: Moderate or severe ARDS as defined by the Berlin criteria with a P:F <200
 15. Death (either yes or no), if yes then was it outside of the 72hour study protocol (yes or no) and select only one cause of death.
-



Consort Diagram



Graph 1. Injuries by Cohort

12.0 LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

ARDS Acute Respiratory Distress Syndrome

DCL Damage Control Laparotomy

ECF Enterocutaneous Fistula

HTS Hypertonic Saline

IAA Intra-abdominal Abscess

ICU Intensive Care Unit

IRB Institutional Review Board

KRL Knowledge Readiness Level

PFC Primary Facial Closure

TAC Temporary Abdominal Closure