JOURNAL OF SURGICAL RESEARCH • MARCH 2020 (247) 350–355

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# Aggressive Crystalloid Resuscitation Outcomes in Low-Severity Pediatric Trauma

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## ARTICLE INFO

*Article history:*
Received 22 April 2019
Received in revised form 20 September 2019
Accepted 1 October 2019
Available online 30 October 2019

*Keywords:*
Fluid resuscitation
Pediatrics
Trauma outcomes
ICU length-of-stay

## ABSTRACT

*Background:* Trauma is the leading cause of death among children. Studies have found that insufficient intravenous (IV) fluid resuscitation contributes significantly to morbidity and mortality in pediatric trauma. While large-volume resuscitation represents a potential solution, overly aggressive fluid management may complicate hospitalizations and recovery. Through this study, we aim to evaluate the impact of aggressive fluid resuscitation on outcomes in pediatric trauma.

*Materials and methods:* This is a retrospective review utilizing our level I trauma center registry for pediatric patients aged <16 y admitted from 2014 to 2017. Patients transferred from our center within 24 h and those who arrived from outside hospitals were excluded. Patients who received blood product transfusions were excluded. Included patients were divided into two crystalloid groups: <60 mL/kg/24 h and ≥60 mL/kg/24 h. Outcome measures included ICU length-of-stay, length-of-hospitalization, complications, and mortality rate.

*Results:* Study sample included 320 patients (<60 mL/kg/24 h = 219; ≥60 mL/kg/24 h = 101). The ≥60 mL/kg/24 h group was younger (9.95 *versus* 5.27, $P = 0.0001$). There were no significant differences in GCS on arrival, injury severity score, Abbreviated Injury Scale, Revised Trauma Scores, traumatic brain injury, and operative intervention between groups. Outcome measures showed there was no significant difference in 30-day readmission rate, complications, or mortality. Large-volume crystalloid resuscitation was associated with longer mean ICU length-of-stay (1.5 d *versus* 0.8 d, $P = 0.004$).

*Conclusions:* In this single-institution retrospective database analysis, large-volume crystalloid resuscitation (≥60 mL/kg) was associated with a significant increase in ICU length-of-stay without survival benefit. More research in the form of randomized trials will help determine the optimal rate for fluid resuscitation in pediatric trauma patients while weighing potential critical care complications.



The abstract leading to this article was presented at the American College of Surgeons 2019 Clinical Congress in San Francisco, CA October 27-31, 2019.

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0022-4804/$ – see front matter 
https://doi.org/10.1016/j.jss.2019.10.009

## Introduction

Trauma is the leading cause of death among children aged 1-18 y in the United States.[1] Those who manage pediatric trauma patients recognize fluid administration as a cornerstone of resuscitation. Isotonic crystalloid boluses with normal saline or Ringer's lactate have long been the fluids of choice for volume expansion in trauma.[2] Previous studies identified limited intravenous (IV) access and inadequate volume resuscitation as the leading cause of preventable trauma-related mortality in children.[3,4] In response, management algorithms reflected that "more is better" with respect to fluids, especially considering the prevailing thought that most children are healthy and can tolerate large-volume resuscitation.[5,6]

Although large-volume fluid boluses can restore perfusion in patients with circulatory collapse, there is a growing literature on adverse outcomes associated with overly aggressive large-volume fluid administration. These complications arise from the principle that only one-quarter to one-third of an isotonic fluid bolus remains intravascular. Most of the bolus redistributes to the interstitial space where it does not contribute to hemodynamic support. Adult studies have described the development of acute respiratory distress syndrome (ARDS), compartment syndromes (both abdominal and/or extremity), acute renal failure, and multiorgan failure, all of which may be attributable to interstitial edematous changes from large-volume crystalloid resuscitation.[7] In addition to increased hydrostatic forces and decreased plasma oncotic pressure driving the development of interstitial edema during crystalloid fluid resuscitation, increased physiologic stress in trauma also propagates proinflammatory cascades.[8] Displaced intracellular contents from cytolysis in trauma also activate neutrophils, contributing to endothelial damage and perpetuating systemic vascular leakage.[9]

Some surgeons previously hypothesized that complications from fluid overload are less common in children because they infrequently have underlying cardiovascular and renal pathology.[7] Aside from fewer medical comorbidities, some have discussed how children are physiologically distinct from adults and compensate differently when exposed to physical trauma.[10]

Evidence that hypovolemia is detrimental in pediatric trauma patients is juxtaposed with research, albeit in adults, that shows increased morbidity with overly aggressive fluid resuscitation. Historically, guidelines in pediatric trauma have developed based on principles in adults. Given the prevailing thought that children are physiologically distinct from adults, there should be further study on the effects of aggressive fluid resuscitation in pediatric trauma. Accordingly, we conducted a retrospective observational study to investigate the effects of aggressive fluid resuscitation on complications and outcomes in pediatric trauma patients. We aim to better understand any potential disadvantages with aggressive fluid measures and gauge steps for refining a safe and effective fluid resuscitation protocol for pediatric trauma patients.

## Methods

We designed a retrospective cohort study utilizing our level 1 trauma center pediatric trauma data registry. The study population included patients aged <16 y who were admitted from years 2014 through 2017. Patients were excluded if they were transferred from outside hospitals because we could not consistently determine their fluid management before arrival at our center. Patients transported out of our center in less than 24 h after arrival were also excluded because we could not follow their intake volume and outcome measures. Patients who received blood product transfusions were excluded as well.

Patients who met inclusion and exclusion criteria were divided into two groups based on the crystalloid volume administered during the first 24 h of their care. Nonaggressive IV fluid resuscitation (control group) was defined as <60 mL/kg/d. Aggressive IV crystalloid resuscitation (study group) was defined as ≥60 mL/kg/d. We included all IV fluids given, regardless of location, during the first 24 h. No patients in our study received intraosseous fluids. Surgeons at our institution have discretion with fluid management but generally follow standards outlined by the American College of Surgeons Advanced Trauma Life Support (ATLS) manual.[11] During our 2014-2017 study period, ATLS ninth edition served as the standard.

Study outcome variables included intensive care unit (ICU) admission, ICU length of stay (LOS), hospital LOS, complication rate, and mortality rate. Complications included in the study design were wound infection, urinary tract infection (UTI), deep venous thrombosis (DVT), pulmonary embolism (PE), and sepsis. IBM SPSS statistics software version 22 was used for data analyses with chi-square testing, two-tailed t-testing, and analysis of variance. Significance was defined as $P < 0.05$. This research was conducted in compliance with ethical standards, reviewed by our institutional review board and was determined to be exempt.

## Results

The study included 320 pediatric trauma patients between ages 0 and 15 y who were brought directly to our level I trauma center (Table 1). Between groups, 219 patients received <60 mL/kg/24 h crystalloids and 101 patients received ≥60 mL/kg/24 h crystalloids. Most patients were male with 86.5% and 62.4% of the <60 mL/kg/24 h group and ≥60 mL/kg/24 h group, respectively ($P = 0.28$). The mean age was 9.95 y in the <60 mL/kg/24 h group and 5.27 y in the ≥60 mL/kg/24 h group ($P \leq 0.0001$). Stratification by injury severity score (ISS) separated patients into three subgroups with ISS <9, ISS 9-14, and ISS ≥15. The intergroup ISS distributions were comparable ($P = 0.07$). Mean ISS and standard deviation for the <60 mL/kg/24 h group and ≥60 mL/kg/24 h group was 4.23 (3.7) and 5.06 (4.4), respectively ($P = 0.08$).

Blunt mechanism of injury accounted for most cases with 91% and 89% of the <60 mL/kg/24 h and ≥60 mL/kg/24 h

**Table 1 – Demographic characteristics comparing pediatric trauma population receiving nonaggressive *versus* aggressive fluid resuscitation within 24 h after arrival (2014-2017).**

| Demographic characteristics | <60 mL/kg/ first 24 h | ≥60 mL/kg/ first 24 h | P |
|---|---|---|---|
| Total patients (*n*) | 219 | 101 | — |
| Male | 150 (86.5%) | 63 (62.4%) | 0.28 |
| Female | 69 (13.5%) | 38 (37.6%) | |
| Mean age [SD] | 9.95 [4.5] | 5.27 [4.2] | <0.0001 |
| Race | | | |
| White | 165 (75%) | 74 (73%) | |
| African-American | 34 (16%) | 16 (16%) | 0.89 |
| Other | 20 (9%) | 11 (11%) | |
| Ethnicity | | | |
| Hispanic | 118 (54%) | 52 (51.5%) | 0.69 |
| Non-Hispanic | 101 (46%) | 49 (48.5%) | |
| Mean GCS on arrival [SD] | 14.8 [1.1] | 14.6 [1.1] | 0.14 |
| Mean ISS [SD] | 4.23 [3.7] | 5.06 [4.4] | 0.08 |
| ISS < 9 | 192 (87.7%) | 79 (78.2%) | |
| ISS 9-14 | 21 (9.6%) | 19 (18.8%) | 0.07 |
| ISS ≥ 15 | 6 (2.7%) | 3 (3.0%) | |
| Revised Trauma Score (RTS) | 7.71 | 7.63 | 0.14 |
| Mean AIS scores by region [SD] | | | |
| Head | 1.86 [0.99] | 1.83 [0.96] | |
| Neck | 1 [0] | 1.5 [0.71] | |
| Thorax | 1.73 [0.98] | 1.82 [0.98] | |
| Abdomen | 1.25 [0.44] | 1.67 [0.87] | 0.89 |
| Spine | 2 [0.58] | 1 [0] | |
| Upper extremity | 1.54 [0.54] | 1.58 [0.55] | |
| Lower extremity | 1.57 [0.73] | 1.71 [0.85] | |
| Mechanism of injury | | | |
| Blunt | 199 (91%) | 89 (88%) | 0.57 |
| Penetrating | 20 (9%) | 12 (12%) | |
| Isolated TBI | 91 (41.5%) | 40 (39.6%) | 0.74 |
| Operative intervention | | | |
| Yes | 107 (48.9%) | 53 (52.5%) | 0.63 |
| No | 112 (51.1%) | 48 (47.5%) | |
| Comorbidities | | | |
| 0 | 161 (73.5%) | 83 (82%) | |
| 1 | 46 (21%) | 14 (14%) | 0.26 |
| 2 | 11 (5%) | 4 (4%) | |
| 3 | 1 (0.50%) | 0 (0%) | |

groups, respectively (P = 0.57). Revised Trauma Score (RTS) was similar between groups (7.71 *versus* 7.63, P = 0.14). Abbreviated Injury Scale (AIS) scoring across anatomic regions (head, neck, thorax, abdomen, spine, upper extremity, lower extremity) were similar between groups (P = 0.89). Isolated traumatic brain injuries occurred at similar rates between groups (41.5% *versus* 40%, P = 0.74). Over three-quarters of all patients in the study had no medical comorbidities. Those with comorbidities included asthma, attention-deficit hyperactive disorder, obesity, and diabetes mellitus, with no differences between groups (P = 0.26). Patients underwent operative intervention for their injuries at similar rates between groups, 48.9% and 52.5% (P = 0.63).

**Table 2 – Outcome measures comparing pediatric trauma population receiving nonaggressive *versus* aggressive fluid resuscitation within 24 h after arrival (2014-2017).**

| Outcome measures | <60 mL/kg/ 24 h | ≥60 mL/kg/ 24 h | P |
|---|---|---|---|
| ICU stay | | | |
| Yes | 77 (35.2%) | 52 (51.5%) | 0.008 |
| No | 142 (64.8%) | 49 (48.5%) | |
| Mean ICU LOS [SD] (d) | 0.8 [1.1] | 1.5 [1.1] | 0.004 |
| Mean total hospitalization [SD] (D) | 1.8 [1.2] | 2.6 [1.9] | 0.013 |
| 30-day readmission rate | | | |
| Yes | 3 (1.4%) | 3 (3%) | 0.59 |
| No | 216 (98.6%) | 98 (97%) | |
| Complication rates | | | |
| Wound infection | 2 (0.91%) | 0 (0%) | |
| UTI | 1 (0.46%) | 0 (0%) | 0.17 |
| DVT | 0 | 0 | |
| PE | 0 | 0 | |
| Sepsis | 0 | 0 | |
| Mortality rate | 1 (0.46%) | 0 (0%) | 0.68 |

Outcome measures (Table 2) demonstrated no significant difference in 30-day readmission rate, complications, or mortality rate. Large-volume fluid resuscitation was associated with a significantly longer mean ICU LOS, 1.5 d *versus* 0.8 d (P = 0.004), and longer mean total hospital LOS (2.6 *versus* 1.8 d, P = 0.013). Subgroup analysis for ISS (Table 3) demonstrated longer ICU-LOS for ≥ 60 mL/kg/d patients with ISS <9 (0.92 *versus* 0.57 d, P = 0.013). Analysis of ICU LOS with respect to operative intervention (Table 4) revealed that the ≥60 mL/kg/d group had longer ICU LOS for both operative patients (1.88 *versus* 0.57 d, P = 0.0013) and nonoperative patients (1.85 *versus* 1.03 d, P = 0.0001).

## Discussion

Resuscitation protocols in trauma have adapted in recent years toward a balance between restoring perfusion while limiting complications from interstitially distributed IV fluids.[12] In 2013, the ninth edition of ATLS[5] reduced their crystalloid recommendation from 2 L to 1 L in adult trauma based on evidence from studies that demonstrated increased morbidity with large-volume crystalloid fluids. Despite more conservative crystalloid fluid trends in adults, the ATLS ninth edition advocated for up to three 20 mL/kg isotonic crystalloid boluses in pediatric patients. Recommendations from the

**Table 3 – ICU length-of-stay between groups stratified by injury severity score (ISS).**

| ICU length of stay | ICU length-of-stay (d) | | |
|---|---|---|---|
| | <60 mL/kg/d | ≥60 mL/kg/d | P |
| ISS < 9 | 0.57 | 0.92 | 0.013 |
| ISS 9-14 | 2.67 | 3.05 | 0.73 |
| ISS ≥ 15 | 2.0 | 7.0 | 0.10 |

2010 Pediatric Advanced Life Support (PALS) also expressed that a bolus sum of 60 mL/kg is appropriate for volume resuscitation.[6] Furthermore, children who require a third fluid bolus to restore perfusion may also receive blood products with the third bolus. Discrepancies between adult and pediatric recommendations were largely based on limited literature and evidence in children.

Al-sharif *et al.* addressed IV fluid volumes in pediatric trauma with a retrospective study in 2012.[13] They noted ascites (8%) and pleural effusions (9%) throughout their study population ($n = 139$) with those who received larger resuscitation volumes.[13]

In 2014, Acker *et al.* studied the relationship between crystalloid volume and clinical outcomes in pediatric trauma.[14] They found that, as with adults, excessive crystalloid resuscitation (>60 mL/kg/24 h) in children with severe blunt injuries is associated with increased in-hospital mortality, hospital LOS, discharge to a rehabilitation facility and need for mechanical ventilation. Interestingly, the children in their study did not develop ARDS, multiorgan failure, compartment syndrome, or acute renal failure, all of which are mediated by systemic inflammation and previously documented in adult studies. Although large crystalloid volumes were associated with complicated hospitalizations, they concluded that "trauma and resuscitative fluids in children do not lead to the same degree of activation of the systemic inflammatory response syndrome that is seen in adults".[14]

Military experience with pediatric trauma during conflicts in the Middle East also contributed to our understanding of massive fluid resuscitation in children.[15] In 2015, Edwards *et al.* conducted a retrospective analysis with the U.S. Department of Defense Trauma Registry. They primarily sought to study outcomes with balanced fresh frozen plasma and packed red blood cell (pRBC) transfusions, but additionally found that patients who received large volumes of crystalloids (as much as 150 mL/kg/24 h) had longer ventilator times, ICU LOS, and length of total hospitalization.[16]

Major guidelines soon began to acknowledge recent studies with respect to aggressive fluid resuscitation. The 2015 PALS update[17] discussed potential risks in children, but did not provide concrete recommendations or distinguish the fluid management of pediatric hemorrhage from other trauma groups. As of 2016, Advanced Paediatric Life Support, the United Kingdom PALS equivalent, gave quantifiable recommendations for smaller boluses of 10 mL/kg and advocated for blood product transfusion in initial resuscitation, even as early as the first bolus.[18] ATLS released its tenth edition in 2018 and updated its approach to fluids in pediatric trauma. They recommend pRBC transfusion as early as the second bolus, as compared with after the third bolus previously. In damage control resuscitation, ATLS commented on the "move toward limiting crystalloid resuscitation" in massive transfusion protocols by giving 10-20 mL/kg pRBC transfusion after only one 20 mL/kg isotonic crystalloid bolus.[11] The ATLS decision toward limiting crystalloids in pediatric resuscitation was likely driven by adult literature more than the nascent pediatric literature.[19]

The aforementioned developments with observational studies and guideline shifts influenced our interest in studying the outcomes of aggressive fluid resuscitation in pediatric trauma patients. We chose to track crystalloid fluids within the first 24 h of patient presentation because we wanted to account for fluids given in the operating room, ICU, and hospital floors. By contrast, one systematic review only discussed fluids given during resuscitation in the first hour of arrival.[20] Patients who receive repeated boluses during initial resuscitation can accrue 40-60 mL/kg IV fluid before admission. In addition, some formula express pediatric fluid requirements with a graduated, weight-based "4-2-1" rule. These guides provide only an estimate for fluid rates and can contribute to fluid overload in pediatric trauma patients who have altered fluid distributions and have already received multiple boluses.[3]

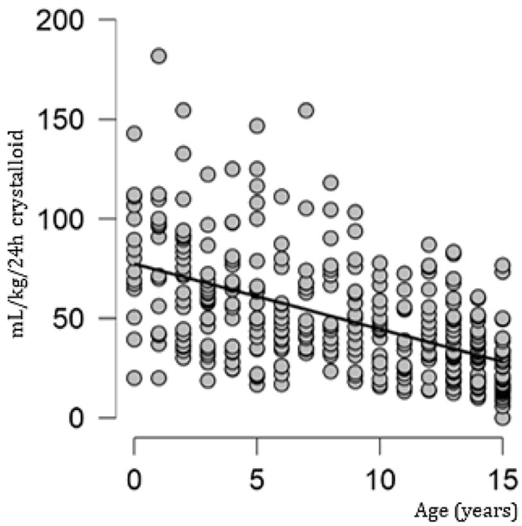
Our study's two fluid volume-defined groups had similar baseline characteristics with no statistically significant differences in gender proportions, race, ethnicity, GCS, mean ISS, mean RTS, AIS, traumatic mechanism (blunt *versus* penetrating), presence of isolated traumatic brain injury, or preexisting comorbidities. The proportion between males and females in our study groups resembled demographics reported across the pediatric trauma literature. We utilized RTS as a metric that accounts for vital signs and hemodynamic stability on arrival to the trauma center. AIS scoring was used to demonstrate injury severity across anatomic regions and assess the prevalence of multisystem trauma.

Patients who received large volumes of crystalloid fluids during the first 24 h had longer ICU stays (1.5 d *versus* 0.8 d, $P = 0.004$) and longer hospitalizations altogether (2.6 d *versus* 1.8 d, $P = 0.013$). ICU LOS was not influenced by whether or not patients underwent operative intervention. Regardless of whether patients were taken to the operating room or not, those in the ≥60 mL/kg/d group had longer ICU LOS (Table 4). With the large-volume crystalloid group being younger, we investigated further to evaluate if age contributed to ICU LOS (Figure). The age differential between our study groups had only a weak correlation with ICU LOS ($r = 0.06$, $P = 0.235$). Given this weak age–ICU LOS correlation, we hold confidence in our outcomes analysis and do not believe that age was a significant source of confounding for longer ICU LOS in the ≥60 mL/kg/24 h group.

With respect to additional outcome measures, there were no statistically significant differences in mortality rate or 30-day readmission rate between the two cohorts in our study.

**Table 4 – ICU length-of-stay between groups among operative and nonoperative patients.**

| ICU length of stay | ICU length-of-stay (d) | | |
|---|---|---|---|
| | <60 mL/kg/d | ≥60 mL/kg/d | P |
| Operative | 0.57 | 1.88 | 0.0013 |
| Nonoperative | 1.03 | 1.85 | 0.0001 |




| | Pearson correlation coefficient (r) | p |
|---|---|---|
| Age—mL/kg/first 24h | -0.55 | <0.001 |
| Age—ICU-length-of-stay | 0.06 | 0.235 |

**Fig – Relationship between crystalloid fluid administration and age. When comparing the age distribution between our two crystalloid groups, the ≥60 mL/kg/24 h group was considerably younger on average. This is consistent with the principle that smaller children have higher fluid demands per kilogram. Correlation analysis (Fig. 1) demonstrated a moderate correlation ($r = -0.55$, $P \leq 0.001$) that aligns with this principle. Further analysis revealed that the age differential between our study groups had only a weak correlation with ICU length-of-stay ($r = 0.06$, $P = 0.235$). Given this weak age–ICU length-of-stay correlation, we hold confidence in our outcomes analysis.**

Complication rates with wound infection, UTI, DVT, PE, and sepsis were low and not statistically significant between study groups.

Our historical cohort study bears resemblance to three other outcomes studies: Acker *et al.*,[14] Edwards *et al.*,[16] and Coons *et al.*[21] All the three studies were retrospective chart reviews like our present study. Acker *et al.* and Coons *et al.* studied populations at urban level I trauma centers similar to our study population, whereas Edwards *et al.* studied military data from foreign war zones where injuries were of higher severity on average. We conducted a search on clinicaltrials.gov and were unable to locate any upcoming, ongoing, or completed clinical trials related to IV fluid volume in pediatric trauma resuscitation.

Inclusion and exclusion criteria differed among these recent studies. Acker *et al.* capped their age inclusion at 16 y, Coons *et al.* included those up to age 18 y, and Edwards *et al.* included those aged 14 y and younger. Acker *et al.* studied only blunt trauma, but other similar studies included both blunt and penetrating injuries. Coons *et al.* studied fluid resuscitation as long as 48 h after arrival, whereas the other studies, including ours, limited their scope to 24 h. Acker *et al.* uniquely only studied patients with ISS >15 and other observational studies, including this study, acknowledged any ISS. Notably, only a minority of our study population (3.1%) could be considered "severely injured" by an ISS >15. Acker *et al.* also did not exclude patients transported from outside hospitals, a variable excluded by both our study and Coons *et al.* due to inherent difficulty in accurately quantifying fluid the patient's received from EMS and outside hospitals before their arrival.

While Coons *et al.* studied similar variables as us, they demonstrated significant differences in ICU LOS at 48 h after arrival, but not 24 h. Our study population was somewhat larger, $n = 320$ *versus* $n = 200$. They commented that their most critically injured patients were excluded from the study because they arrived from outside hospitals, and we excluded those patients in our study as well. Despite longer mean ICU LOS, we found that large volumes of crystalloids were not associated with medical complications including wound infection, UTI, DVT, PE, and sepsis in our study population. Acker *et al.* similarly noted that children seem physiologically resilient during resuscitation and recovery from trauma.

Our study has a number of limitations. It is a single-institution study with a relatively small sample size which somewhat restricted subgroup analysis. Stratification by ISS and age could not be extended past our defined subgroups due to sample size. Although retrospective cohort studies are useful for correlating exposures with outcomes, causation cannot be implied. Our study included all injured children, rather than just the most severely injured children in whom fluid management may be more challenging. We analyzed whether operative intervention was different between groups and if operative intervention could impact ICU LOS, but we did not account for different types of procedures (e.g., craniotomy, laparotomy, thoracotomy, open reduction, and internal fixation, etc.) Along the same lines, we did not specifically analyze for pleural effusions or ascites, both of which are commonly associated with fluid overload. We included all crystalloids in the form of boluses, maintenance fluids, and carrier fluids for medications. At the same time, we did not explore the impact of colloid fluids, which are typically used in more critical patients, a factor that represents potential confounding. Nonetheless, we controlled for the effect of blood product transfusion by excluding those patients from our study.

We chose to use ICU LOS as an outcome variable that is widely reported in trauma and critical care literature. However, we did not individually account for endotracheal intubation, ventilator days, and prevalence of ARDS across our study population. This decision was made because we believe all of the aforementioned variables contribute toward the overall ICU LOS. Finally, we acknowledge that the difference we found in mean ICU LOS may not be clinically significant in every case. However, small differences are often more appreciable when comparing outcomes at the hospital level when striving to improve the quality of care.

## Conclusion

Aggressive fluid management was a cornerstone of trauma care until recent years. Adult studies were the first to reveal that large volumes of isotonic crystalloid fluid can be associated with a myriad of complications. Some have speculated that children, less often affected by medical comorbidities, are physiologically resilient and able to handle large fluid volumes without decompensating. Despite these perceived differences, the foundation of pediatric trauma protocols lies with evidence and trends from adult studies. Studies with fluid resuscitation in injured children have thus far been observational, with only a handful of studies in the past decade identifying complications specific to pediatric populations.

Our study demonstrated that aggressive IV crystalloid administration is associated with longer ICU stays. Future research in the form of randomized controlled trials may be useful to optimize fluid resuscitation protocols in pediatric trauma. The effects of aggressive IV fluids may not be limited to the initial boluses given in trauma bays and emergency departments. Maintenance IV fluids given during hospitalization, even as early as the first admission day, may impact outcomes in injured children.

## Acknowledgment

Authors' contributions: Study design and conception was contributed by A.E., M.M., D.B., and S.Z. Data collection was carried out by S.Z., A.E., D.B., and J.D.E. Data analysis and interpretation was performed by A.E., M.M., D.B., and J.D.E. Drafting of manuscript was carried out by J.D.E., A.E., and S.Z. Critical revisions of manuscript were done by A.E., M.M., D.B., and J.D.E. Approval of final version of manuscript was done by A.E., M.M., D.B., J.D.E., and S.Z.

## Disclosure

The authors disclose no competing interests.

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