[Short title + Author Name - P&H title] 11 (2021) 152–157

Contents lists available at ScienceDirect

African Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/afjem

Original article

# Association between volume resuscitation & mortality among injured patients at a tertiary care hospital in Kigali, Rwanda

Catalina González Marqués [a,b,*], Katelyn Moretti [a,b], Siraj Amanullah [a,b], Chantal Uwamahoro [c,d], Vincent Ndebwanimana [c,d], Stephanie Garbern [a], Sonya Naganathan [a], Kyle Martin [a], Joseph Niyomiza [c,d], Annie Gjesvik [b], Menelas Nkeshimana [c,d], Adam C. Levine [a], Adam R. Aluisio [a]

[a] Department of Emergency Medicine, Brown University Warren Alpert Medical School, Providence, USA
[b] Department of Epidemiology and Pediatrics Brown University School of Public Health, Providence, USA
[c] Department of Anaesthesia, Emergency Medicine and Critical Care, College of Medicine & Health Sciences, University of Rwanda, Kigali, Rwanda
[d] Department of Accident and Emergency, University Teaching Hospital of Kigali, Rwanda

ARTICLE INFO

*Keywords:*
Rwanda
Injury care
Resuscitation
Global health
Low- & middle-income countries

ABSTRACT

*Background:* Injuries cause significant morbidity and mortality in sub-Saharan African countries such as Rwanda. These burdens may be compounded by limited access to intravenous (IV) resuscitation fluids such as crystalloids and blood products. This study evaluates the association between emergency department (ED) intravenous volume resuscitation and mortality outcomes in adult trauma patients treated at the University Teaching Hospital-Kigali (UTH- K).

*Methods:* Data were abstracted using a structured protocol for a random sample of ED patients treated during periods from 2012 to 2016. Patients under 15 years of age were excluded. Data collected included demographics, clinical aspects, types of IV fluid resuscitation provided and outcomes. The primary outcome was facility-based mortality. Descriptive statistics were used to explore characteristics of the population. Kampala Trauma Scores (KTS) were used to control for injury severity. Magnitudes of effects were quantified using multivariable regression models adjusted for gender, KTS, time period, clinical interventions, presence of head injury and transfer to a tertiary care centre to yield adjusted odds ratios (aOR) with 95% confidence intervals (CI).

*Results:* From the random sample of 3609 cases, 991 trauma patients were analysed. The median age was 32 [IQR 26, 46] years and 74.3% were male. ED volume resuscitation was given to 50.1% of patients with 43.5% receiving crystalloid and 6.4% receiving crystalloid and packed red blood cell (PRBC) transfusions. The median KTS score was 13 [IQR 12, 13]. In multivariable regression, mortality likelihood was increased in those who received crystalloid (aOR = 4.31, 95%CI 1.24, 15.05, $p = 0.022$) and PRBC plus crystalloid (aOR = 9.97, 95%CI 2.15,46.17, $p = 0.003$) as compared to trauma patients not treated with IV resuscitation fluids.

*Conclusions:* Injured ED patients treated with volume resuscitation had higher mortality, which may be due to unmeasured confounding or therapies provided. Further studies on fluid resuscitation in trauma populations in resource-limited settings are needed.

## African relevance

- Injuries cause significant morbidity and mortality in sub-Saharan African countries such as Rwanda.
- Setting-specific, evidence-based improvements to care for injured patients can significantly reduce preventable death and disability.
- Volume resuscitation is one strategy used in the care of injured patients, but there is a paucity of mortality outcome data in Sub-Saharan Africa.

## Introduction

Injuries account for a large proportion of the global burden of

* Corresponding author.
*E-mail address:* cgonzalez-marques@bwh.harvard.edu (C.G. Marqués).

https://doi.org/10.1016/j.afjem.2020.09.014
Received 23 May 2020; Received in revised form 26 July 2020; Accepted 21 September 2020
Available online 5 November 2020

disease, resulting in about five million deaths annually [1–6]. Almost 90% of deaths due to injuries occur in low- and middle-income countries (LMIC) [1,6]. Their impact is estimated to account for 38 million disability-adjusted life-years [1]. Geographically, injuries cause significant morbidity and mortality in sub-Saharan African countries such as Rwanda. The World Health Organization estimates that injuries from road traffic accidents will rise to the third most common cause of morbidity with Sub-Saharan Africa suffering a disproportionate number of these fatalities [2]. These burdens may be compounded by limited access to treatments during the acute and emergent periods of care [5,7]. A frequently used and important treatment approach in acute injury care is intravenous (IV) volume resuscitation with crystalloids fluids and blood products.

IV volume resuscitation of injured patients presents a challenge in that recommendations for use and choice of resuscitation fluids are being constantly reviewed and debated [8–10]. Although care guidelines from high-income countries (HIC) advocate for initial use of judicious crystalloids followed by blood products, crystalloid is often still recommended in LMIC settings in favour of blood due to relatively limited access to blood products [9,10]. Furthermore, in LMIC settings, choice of volume resuscitation fluid may be restricted by availability; wherein, the fluid available does not necessarily equate to the best fluid for the patient [8]. Setting-specific, evidence based improvements to the quality and processes of care for the injured can significantly reduce preventable death and disability. In comparison to HICs, there is substantially less research published from LMICs pertaining to the treatment of injured patients with volume resuscitation approaches. This study evaluates the association between volume resuscitation with crystalloid fluid and packed red blood cells (PRBCs) on mortality outcomes in injured patients who presented to the University Teaching Hospital Emergency Department in Kigali, Rwanda (UTH—K).

## Methods

### *Study design, setting and population*

This retrospective study was conducted at the UTH—K, Rwanda. The UTH-K is the primary trauma centre for the city of Kigali with an estimated population of over 1 million, and also serves as the academic referral centre for the entire country. The UTH-K is a >500 bed tertiary care teaching hospital with surgical and specialty consulting services as well as the nation's sole emergency medicine training program [11]. The UTH-K ED has routine access to crystalloid fluids and access to blood products is reserved for emergent transfusion. If blood products are not available in the hospital blood bank, physicians can request blood products from the external National Centre for Blood Transfusion, located adjacent to the hospital.

The database analysed consisted of a random sample of all UTH-K Emergency Department (ED) cases from two time periods (November 2012 through October 2013 and August 2015 through July 2016). As described previously, data from a random sampling of ED cases was queried from institutional records via protocolised methods [11]. All patients >15 years old presenting with an injury to the UTH-K ED were eligible for inclusion. Patients <15 years of age and without identifiable medical records or lacking ED documentation for the encounter of interest were excluded. Data collected included patient demographics, prior medical history, clinical presentation, ED care, surgical interventions, transfer status from other facilities, injury diagnoses, length of stay, and ED and inpatient outcomes. Clinical presentation data included triage vital signs and documented mental status. Case types were coded as injury or medical cases. This study was approved by the UTH-K ethics committee and the institutional review board of Rhode Island Hospital.

### *Data management*

The primary predictor variable was volume resuscitation during the ED care. Volume resuscitation was defined as receiving crystalloid fluids (normal saline or Ringer's lactate), receiving both crystalloid and PRBCs or receiving no resuscitation fluid. No patients received PRBCs alone. The primary outcome was facilities-based mortality, aggregated across ED and inpatient care.

Clinical characteristics of presentation, vital signs and mechanism of injury were categorized based on the validated Kampala Trauma Score (KTS). The KTS utilizes age, blood pressure, respiratory rate and neurological status as well as injury severity [12–15]. KTS has been found to be an adequate predictor of injury severity and prognosis in LMICs with a lower score (≤12) indicating a moderate to severe injury and a higher score (≥13) indicating a less severe injury state [12–15]. ED interventions including needle chest decompression, thoracostomy, haemorrhage control and pericardiocentesis were analysed in aggregate as major clinical interventions and coded as binary. All forms of surgical interventions were aggregated for analysis. Data was coded as missing in the database, however for variables in which it would be unlikely to have no record of the intervention, including intubation, operating room-based procedures or transfer events, missing data was recoded as not performed.

### *Data analysis*

STATA Version 15.0 (Stata Corp; College Station, USA) was used for all analyses. The study population was stratified based on the exposure of interest as having been treated in the ED with crystalloid fluids, crystalloid fluids and PRBCs and those who received neither. KTS was treated as binary in order to categorize those observations with moderate and severe injury (KTS 0–13) versus those with less severe injuries (KTS ≥14). Variables were described using frequencies with percentages or medians with associated interquartile ranges (IQR). Characteristics based on the exposure categories were compared using Pearson $X^2$ tests for categorical variables and by Mann-Whitney or *t*-tests for non-normally and normally distributed continuous variables, respectively.

Univariate regression was performed for patient characteristics to evaluate differences between those who received crystalloid fluids, crystalloid fluids and blood and those who did not receive any resuscitation fluids for the primary outcome, all-cause facilities-based mortality. Magnitudes of effects were quantified using regression models to yield unadjusted and adjusted odds ratios (aOR) with 95% confidence intervals (CI). Gender, KTS score and time period were included a priori based on prior literature [11,12,14,15]. Transfer status, intubation, presence of head trauma, surgical and ED interventions were included given their effect on the outcome of mortality document in acute care settings [16,17,18]. As volumes of fluid varied among patients, a sensitivity analysis was run evaluating the association between total volume of fluid received and mortality.

## Results

Among the random sample of 3609 cases, 1322 (36.6%) were ≥ 15 years and seeking care for injuries. Three-hundred and thirty-one patients meeting inclusion criteria did not have complete data for this analysis. Resultantly, 991 patients were analysed (Fig. 1).

The median age was 32 [IQR 26, 46] years with a male predominance (74.3%). The median KTS was 13 [IQR 12, 13]. Among included patients, 43.1% were transferred to UTH-K from outside facilities for higher level of care. Thirty-nine percent ($n = 394$) of the patients had a documented head injury and 33.7% ($n = 334$) underwent a surgical intervention. Facilities-based mortality occurred in 7.1% ($n = 70$) of the cohort. ED volume resuscitation with fluids was given to 50.1% of patients. Of those who received volume resuscitation, 43.6% ($n = 432$) received crystalloid and 6.5% ($n = 64$) crystalloid and PRBC transfusion

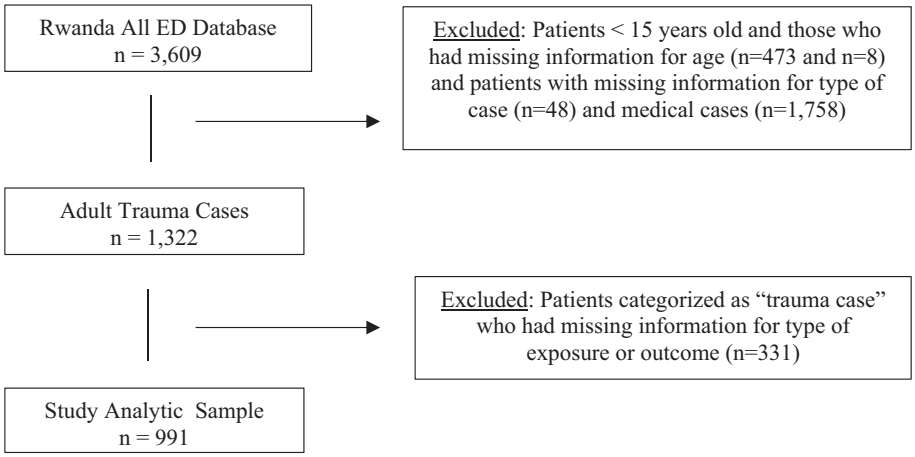


**Fig. 1.** Study flow diagram.

**Table 1**
Characteristics of study population stratified by volume resuscitation treatments.

| | No IVF | Crystalloid | Blood + crystalloid |
|---|---|---|---|
| | n = 495 | n = 432 | n = 64 |
| | n, (%) | n, (%) | n, (%) |
| **Outcome** | | | |
| Lived | 481(97.17%) | 384 (88.89%) | 56 (87.50%) |
| Died | 14 (2.83%) | 48 (11.11%) | 8 (12.50%) |
| **Gender** | | | |
| Male | 342 (69.09%) | 346 (80.09%) | 48 (75.00%) |
| Female | 152 (30.71%) | 86 (19.91%) | 16 (25.00%) |
| **Age** | | | |
| Age 15–55 | 407 (82.22%) | 387 (89.58%) | 56 (87.50%) |
| Age > 55 | 88 (17.78%) | 45 (10.42%) | 8 (12.50%) |
| **Systolic blood pressure** | | | |
| >89 | 318 (64.24%) | 379 (87.73%) | 48 (75.00%) |
| ≤89 | 8 (1.62%) | 12 (2.78%) | 10 (15.60%) |
| Missing | 169 (34.14%) | 41 (9.49%) | 6 (9.40%) |
| **Operative interventions** | | | |
| No | 340 (68.69%) | 287 (66.44%) | 30 (46.88%) |
| Yes | 155 (31.31%) | 145 (33.56%) | 34 (53.12%) |
| **Intubation** | | | |
| No | 485 (97.98%) | 385 (89.12%) | 59 (91.19%) |
| Yes | 10 (2.03%) | 47 (10.88%) | 5 (7.81%) |
| **ED interventions** (non-operative) | | | |
| No | 31.92% (158) | 34.72 (150) | 39.06% (25) |
| Yes | 68.08% (337) | 65.28% (282) | 60.94% (39) |
| **Head trauma** | | | |
| No | 351 (70.91%) | 205 (47.45%) | 41 (64.06%) |
| Yes | 144 (29.09%) | 227 (52.55%) | 23 (35.94%) |
| **Kampala Trauma Score** | | | |
| KTS ≥ 13 | 78 (15.76%) | 188 (43.52%) | 24 (37.50%) |
| KTS ≤ 12 | 121 (24.44%) | 124 (28.70%) | 13 (20.31%) |
| Missing | 296 (59.80%) | 120 (27.78%) | 27 (42.19%) |
| **Transferred to UTH-K** | | | |
| No | 321 (64.85%) | 218 (50.46%) | 25 (39.06%) |
| Yes | 174 (35.15%) | 214 (49.54%) | 39 (60.94%) |

**Table 2**
Unadjusted and adjusted odds of mortality among injured patients receiving fluid resuscitation ($n = 991$).

| | Odds ratio, 95% CI | Adjusted odds ratio, 95% CI |
|---|---|---|
| **Intravenous fluid resuscitation** | | |
| None | Ref | Ref |
| Crystalloid | 4.29 [2.33, 7.91] | 4.31 [1.24, 15.05] |
| Crystalloid & Blood | 4.91 [1.97, 12.21] | 9.96 [2.15, 46.17] |
| **Gender** | | |
| Male | Ref | Ref |
| Female | 0.92 [0.58, 1.62] | 2.15 [0.95, 4.70] |
| **Kampala Trauma Score** | | |
| KTS ≥ 13 | Ref | Ref |
| KTS Score ≤ 12 | 0.29 [0.14, 0.61] | 0.71 [0.30, 1.67] |
| **Time period** | | |
| Nov 2012- Oct 2013 | Ref | Ref |
| During residency | 0.48 [0.29, 0.82] | 0.53 [0.25, 1.12] |
| **Operative intervention** | | |
| No | Ref | Ref |
| Yes | 0.56 [0.32, 0.99] | 0.30 [0.12, 0.73] |
| **Head injury** | | |
| No | Ref | Ref |
| Yes | 2.95 [1.78, 4.89] | 1.00 [0.44, 2.30] |
| **Intubation** | | |
| No | Ref | Ref |
| Yes | 19.04 [10.56, 24.30] | 12.48 [4.89, 31.86] |
| **ED intervention (non-operative)**[a] | | |
| No | Ref | Ref |
| Yes | 1.11 [0.66, 1.88] | 1.08 [0.51 2.32] |
| **Transferred to UTH-K** | | |
| No | Ref | Ref |
| Yes | 2.91 [1.74, 4.87] | 1.39 [0.66,2.94] |

[a] ED non-operative interventions were defined as needle decompression, chest thoracostomy, haemorrhage control, wound debridement.

(Table 1). The crystalloid fluid received by patients in this study was 0.9% normal saline or Ringer's lactate. No patients in the study population received PRBCs only.

Covariates associated with a significant increase in the unadjusted odds of mortality were head injury, intubation, receiving an ED intervention and having been transferred (Table 2). Conversely, covariates associated with a significant decrease in the unadjusted odds of mortality included surgical interventions and being treated during the 2015–16 time period when formal emergency medicine training was in place at the study site (Table 2).

In those receiving IV volume resuscitation, 11.1% ($n = 48$) died in the crystalloid only group 12.5% ($n = 8$) in the crystalloid and PRBC group compared to 2.8% ($n = 14$) mortality in those who received no volume resuscitation (Fig. 2). Both crystalloid volume resuscitation and volume resuscitation with crystalloid and PRBCs had increased odds of mortality compared to the cases that did not receive fluid resuscitation. With those who received crystalloid having a 4.19 [95% CI 2.33, 7.91, $p$-value <0.001] increased odds of mortality and those receiving

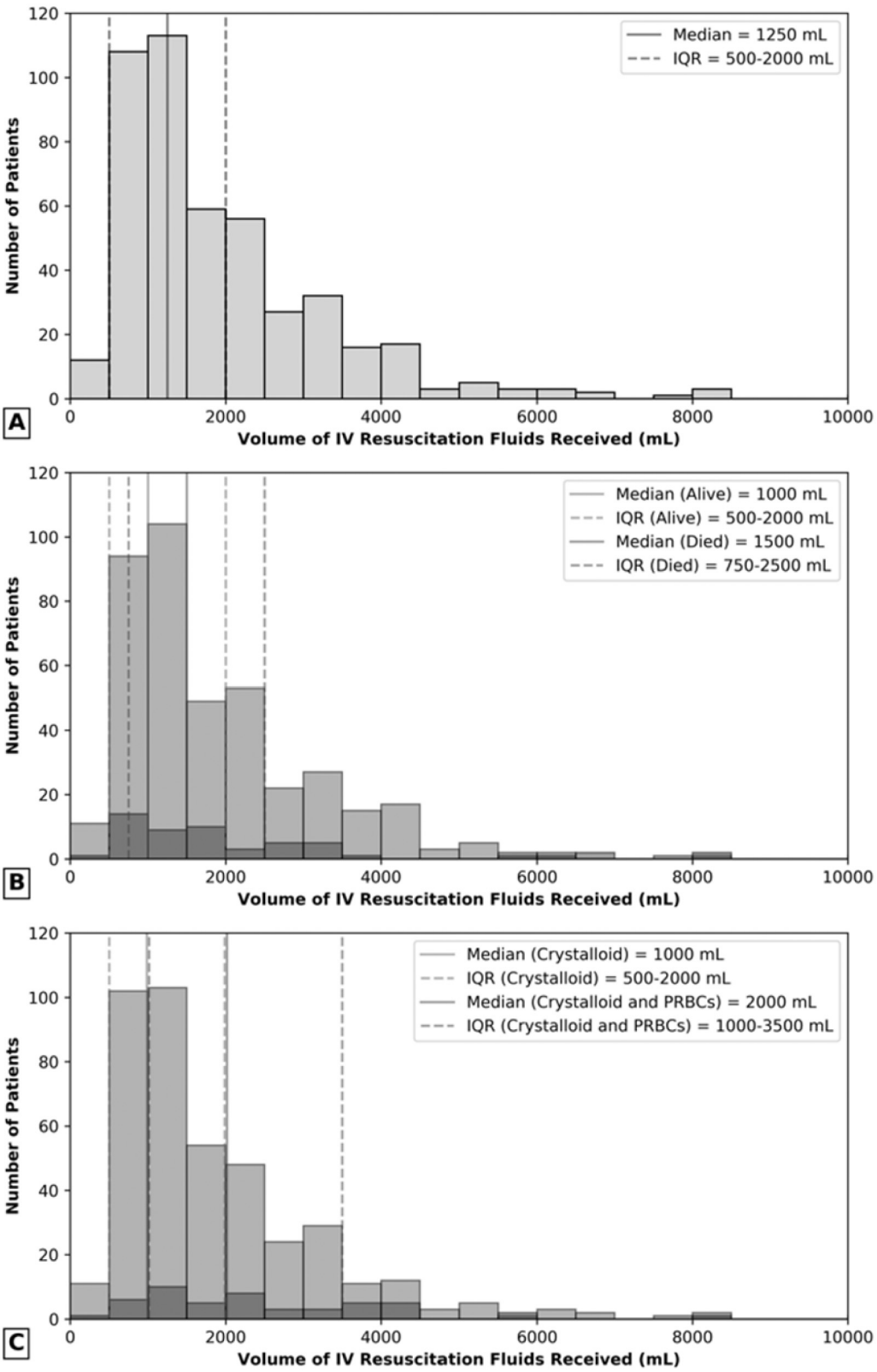


**Fig. 2.** Volume of IV resuscitation fluid received among study population
**A:** IV resuscitation fluid volumes received among all patients who received fluid resuscitation.
**B:** IV resuscitation fluid volumes among patients who survived (light gray) compared to patients who died (dark gray).
**C:** IV resuscitation fluid volumes among patients who received crystalloid fluid only (light gray) compared to patients who received crystalloid fluid with pRBCs (dark gray).

crystalloid and PRBCs having a 4.91 [95% CI 1.97, 12.2, p-value 0.001] increased odds (Table 2). In multivariable analysis, the adjusted odds of mortality were increased in those that received crystalloid (aOR = 4.39, 95% CI 1.26, 15.31 $p < 0.001$) and crystalloid with PRBCs (aOR = 10.48, 95%CI 2.27,48.29, $p = 0.002$) as compared to injured patients not treated with IV resuscitation fluids.

Sensitivity models were conducted, controlling for volumes of ED crystalloids given. For both patients who received crystalloid and patients who received crystalloid with PRBCs, the majority of patients received <1000 ml of resuscitation fluids. While the median fluid volume for crystalloid with PRBC infusion (2000 ml) was higher than the median volume for crystalloid infusion (1000 ml), this difference was

not significant ($P = 0.672$, Fig. 2C). The sensitivity models demonstrated that in those observations that received IV crystalloid fluids there was no significant impact on facilities-based mortality. This was true for both those that received between 1000 ml–2000 ml ($P = 0.445$) and the group that received ≥2000 ml ($P = 1.62$) as compared to cases that were treated with <1000 ml of IV crystalloid fluids in the ED (Table 3).

## Discussion

This study identified a possible association between receiving IV resuscitation fluids and PRBCs and overall facilities-based mortality in the Rwandan injured population. While the association may be due to unmeasured confounding factors not controlled for or properties of the therapies involved, patient severity was controlled for via KTS score and mechanism of injury. Given the retrospective design of this research, it is hypothesis generating and further study regarding volume resuscitation with crystalloid fluids and PRBCs in trauma populations in Rwanda and similar limited resource settings is needed.

There are heavy burdens of injury related morbidity and mortality in LMICs, for which the evidence base on the treatment of injuries suffers from a paucity of data. These injured patients are high-risk and are commonly treated in EDs in LMICs [3]. As such, understanding the impacts of IV resuscitation provided in ED settings in LMICs is of key importance as there is little definitive research in this subject area. Although multivariable analyses performed controlled for injury severity, emergent treatments and temporal factors, unmeasured confounders such as availability of additional treatments and procedural services, prolonged transfer times, delayed presentation and disease specific characteristics were not controlled for. Findings of poor outcomes with IV resuscitation treatments may be influenced by these unmeasured confounders. The driving influences on mortality in injured patients, in this setting, are likely multifactorial and further prospective studies are greatly needed to inform care given the large burden of care from injuries in sub-Saharan Africa.

Maintaining adequate organ perfusion is the goal of resuscitation of the acutely injured patient [8]. In limited resource settings, IV crystalloid solutions are often utilized until scarce blood products are attainable [8]. Results of this study suggest volume resuscitation may be of limited benefit in this population. Similar associations between volume resuscitation with IV fluids and mortality have been demonstrated in sepsis populations in sub-Saharan Africa through the FEAST trial group [19,20]. Another study in Zambia comparably found that septic adults receiving aggressive fluid resuscitation and blood products had increased mortality [21]. However, the pathophysiological mechanisms at work in resuscitation of sepsis and traumatic injury differ. Further studies in adult populations with injuries in LMICs are still needed to further evaluate the association of IV fluids and mortality.

Recent studies have favoured a more balanced volume resuscitation approach for critically injured patients [22]. However, a majority of the literature available on fluid resuscitation in critically ill patients focuses on sepsis, where the pathophysiological mechanisms suggest a benefit to fluid resuscitation. This is in contrast to trauma-induced and dilutional coagulopathies where the exact pathophysiology is not fully understood but believed to contribute to poorer outcomes [8]. Multicentre prospective studies taking place in LMICs are needed to generate an adequately large sample size and assess the association of IV fluid resuscitation on mortality in traumatically injured patients.

A sensitivity analysis was run evaluating the association between total volume of fluid received and mortality - it was not found to have a significant difference. However, this study was limited by the inability to quantify the amount of crystalloid fluids and PRBCs given to patients over time in the ED. Data was only available for total amount received during their entire ED stay and the exact time over which the resuscitation occurred was unknown. Additionally, due to the retrospective nature of the study, it was unknown if any clinical criteria was applied in order to determine which patients received crystalloid fluids and what criteria determined the amount they received.

Due to the retrospective nature of the study, the analyses were limited to the variables available in the data. In addition, 25.04% ($n = 331$) of cases were ineligible for analysis due to missing data which may have introduced bias in the results. Missing data is not uncommon in research conducted in low- and middle-income countries and resource limited settings as noted in prior studies [23,24]. Although the well validated KTS was used to control for injury severity, it does not take into account the dynamic nature of patient acuity and changes overtime which could confound the present results along with unmeasured variables. While the analysis attempted to control for specific ED and operative interventions and factors noted to increase mortality in injured patient populations, not all possible confounders were not identifiable. Furthermore, due to the study's retrospective nature, causality cannot be inferred, thus limiting the ability to fully determine the effects of IV fluid resuscitation on the outcome of interest. Finally, this was a single centre study conducted at a tertiary care hospital and may not be generalizable to populations and treatment centres with different resource availability.

Another limitation in this study is that only a small proportion of the patients that were treated with blood products in the form of PRBCs. Additionally, none of those patients received PRBCs alone. This is likely related to the limited availability of PRBCs in this setting. Although sub-Saharan African countries have reported improved access to safe and adequate blood supplies, many countries including the current study setting of Rwanda still fall below the WHO target of 10 whole-blood donations per 1000 inhabitants [25]. In these locations there is a high burden of injury-related blood loss and available resources may not be adequate to meet the needs of acutely injured patients [10].

## Conclusions

The presented data suggests an association of increased mortality in injured patients who receive fluid resuscitation. Given the high health burden of traumatic injury in LMICs and resource issues pertaining to blood product accessibility, these findings indicate the need for additional studies. Prospective research evaluating the impacts of resuscitation fluids on mortality via randomized controlled randomized trials would advance the evidence-base and clinical practice and improve care in LMIC settings.

## Dissemination of results

Results from this study were shared with ED staff members at the

**Table 3**
Sensitivity analysis - mortality by volume of fluid received.

| Volume received | Crystalloid (n = 432) | Crystalloid + PRBC (n = 64) | Odds ratio, 95% CI | p-Value | Adjusted odds Ratio, 95% CI[a] | p-Value |
|---|---|---|---|---|---|---|
| <1000 ml | 232 (53.7%) | 31 (48.4%) | Ref | Ref | Ref | Ref |
| 1000-2000 ml | 106 (24.5%) | 12 (18.8%) | 1.36 [0.68, 2.74] | 0.38 | 1.50 [0.18, 12.46] | 0.71 |
| ≥2001 ml | 94 (21.8%) | 21 (32.8%) | 1.62 [0.82, 3.19] | 0.16 | 0.79 [0.10, 6.28] | 0.82 |

[a] Adjusted by gender, KTS, time period, surgical interventions, intubation, presence of head trauma, ED interventions.

data collection site through an informal presentation. Preliminary results from this work were presented at Society for Academic Emergency Medicine Conference 2019, International Conference on Emergency Medicine 2019, and 7th Emergency Medicine Society of South Africa 2019.

## CRediT authorship contribution statement

Authors contributed as follows to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: CGM contributed 40%; KM and ARA 10%; and SA, CU, VN, SG, SN, KM, JN, AG, MN, ACL 4% each. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

## Declaration of competing interest

Funding for data collection was provided through grants from the University Emergency Medicine Foundation, Providence, Rhode Island. The funders had no role in the study design, data collection or reporting processes. The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the views of any academic organizations. The authors declared no conflicts of interest.

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