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ORIGINAL ARTICLE

Estimated injury-associated blood loss versus availability of emergency blood products at a district-level public hospital in Cape Town, South Africa



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ABSTRACT

Introduction: International guidance suggests that injury-associated haemorrhagic shock should be resuscitated using blood products. However, in low- and middle-income countries resuscitation emphasises the use of crystalloids – mainly due to poor access to blood products. This study aimed to estimate the amount of blood loss from serious injury in relation to available emergency blood products at a secondary-level, public Cape Town hospital.

Methods: This retrospective, cross-sectional study included all injured patients cared for in the resuscitation area of Khayelitsha Hospital's emergency centre over a fourteen-week period. Injuries were coded using the Abbreviated Injury Scale, which was then used to estimate blood loss for each patient using an algorithm from the Trauma Audit Research Network. Descriptive statistics were used to describe blood volume lost and blood units required to replace losses greater than 15% circulating blood volume. Four units of emergency blood are stored in a dedicated blood fridge in the emergency centre. Platelets and fresh plasma are not available.

Results: A total of 389 injury events were enrolled of which 93 were excluded due to absent clinic data. The mean age was 29 (\pm 10) years. We estimated a median of one unit of blood requirement per week or weekend, up to a maximum of eight or six units, respectively. Most patients (n = 275, 94%) did not have sufficient injury to warrant transfusion. Overall, one person would require a transfusion for every 15 persons with a moderate to serious injury.

Conclusion: The volume of available emergency blood appears inadequate for injury care, and doesn't consider the need for other causes of acute haemorrhage (e.g. gastric, gynaecological, etc.). Furthermore, lack of other blood components (i.e. plasma and platelets) presents a challenge in this low-resourced setting. Further research is required to determine the appropriate management of injury-associated haemorrhage from a resource and budget perspective.

African relevance

- Emergency blood products have limited availability in low-resourced, African emergency centres.
- Most injury-related transfusions in these settings are not directly dispensed from a blood bank.
- There is a high burden of injury-related blood loss in these settings.
- More effective ways of dealing with haemorrhagic shock are required in low-resourced settings.

Introduction

South Africa has one of the highest injury burdens in the world; accounting for a homicide-related mortality rate eight times, and road-traffic mortality rate twice the global rate [1,2]. In fact, South Africa has one of the highest injury-related mortality rates globally [1,2]. Local research done in Cape Town revealed an initial injury diagnosis in 26% of all presentations with most victims between the ages of 20 and 40 living within 15 km of the emergency centre (EC) they attended [3]. As observed elsewhere, the incidence of injury is higher in urban compared to rural areas; however, given such a large burden and few

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dedicated trauma centres that are often geographically removed from where injury primarily occurs, initial injury care often falls to ECs at secondary-level hospitals (hospitals with generalist specialist care, but no super-specialty care) [3,4]. This is also the case in Cape Town [3,4].

Crystalloids have been the mainstay for resuscitating injured patients for decades and have been similarly advocated by the Advanced Trauma Life Support course [5]. This has mainly to do with crystalloids being cheap, readily available and relatively good volume expanders, rather than being an evidence-based resuscitation treatment for injuryassociated haemorrhagic shock [6-9]. Indeed, recent work suggests that over-aggressive crystalloid resuscitation is associated with substantial morbidity in a variety of clinical areas [6]. It also appears to be associated with prolonged ventilation time. Intensive Care Unit (ICU) and hospital stay, as well as increased complication rates, including acute lung injury, coagulopathy, abdominal compartment syndrome and surgical site infections [6]. Decreased use however, appears to have the opposite effect [7]. A 50% mortality decrease involving critically injured soldiers was observed to be associated with a 61% reduction in crystalloid use amongst a number of variables in a retrospective analysis [7]. Taking this one step further, reduced crystalloid use upfront, followed by replacing blood loss with blood products in specific ratios, by using so-called massive transfusion protocols, have led to further improved outcomes [8-10].

According to the University of South Africa Institute for Social and Health Sciences health review in 1999, it was approximated that the cost to the South African public health sector from severe road traffic accidents and gunshot injuries could amount up to R10,000 (or \$2890 converted using purchasing power parity index) per day - which comes to R26,000 (or \$4360) per day in today's terms - through prolonged ICU admission, hospital stay and rehabilitation [11]. Given the high level of injury seen in Cape Town's mid-level ECs, restricted access to blood products would likely encourage the use of crystalloids, possibly contributing to the associated morbidity and thereby increasing costs. So whilst the advantages of using blood products compared to crystalloids have seen crystalloid use de-emphasised in high resource settings, it is still recommended in low-resourced settings [12-16]. It is possible that a primary intervention, or investment such as appropriate, early use of emergency blood products may have a positive economic impact on downstream care as described elsewhere [16].

A key problem in Cape Town secondary-level hospital ECs is the lack of direct access to a blood bank; emergency blood products required in these ECs tend to be restricted to a fixed number of units kept in a dedicated blood refrigerator for emergencies and replenished after use from an off-site blood bank. A recent study by Morris et al. considered the indications for use of emergency blood from the blood refrigerator [17]. Emergency blood transfusions occurred mainly in the EC and this was mostly for injury-associated haemorrhage [17]. Other causes included upper gastro-intestinal haemorrhage, early pregnancy complications, anaemia and perioperative complications [17]. Yet, the study did not tell us whether there was sufficient emergency blood stock available for the intended indications, nor whether use was appropriate – only that emergency blood was used.

The number of blood products allocated to each EC are predetermined by the off-site blood bank based on past use; it includes packed red cells, but not plasma or platelets. Only Cape Town's tertiary hospitals have direct access to a 24-h blood bank. Given the high local injury burden and limited blood available in emergency blood refrigerators, it is important to quantify the requirement for emergency blood to be kept on site. To date, there has been no modelling applied to estimate the required volume of blood products needed for evidence-based injury care in secondary-level ECs across South Africa.

The aim of this study was to retrospectively estimate the amount of blood loss from serious injury in relation to the availability of emergency blood products at Khayelitsha Hospital, a secondary-level public Cape Town hospital with no on-site blood bank service.

Methods

We used a retrospective, cross-sectional design for this study. Study subjects were limited to injured patients of all ages that were triaged for care to the resuscitation area of Khayelitsha Hospital's EC. Khayelitsha Hospital, in Cape Town, South Africa has a 47-bed EC which forms part of a 230-bed secondary-level, public referral hospital. It provides a 24-h EC, as well as inpatient paediatrics, obstetrics, gynaecology, surgery, and medicine of which all but the EC, medicine and paediatrics were family medicine run at the time of the study. The EC sees around 3000 new patients per month with a reported inpatient bed occupancy level at around 131% [18]. The EC has a poverty-related burden of disease that ranges from penetrating injuries to infective diseases (including HIV and tuberculosis) [18]. The EC keeps four units of emergency blood (two units each of group O negative and positive) in a dedicated emergency blood fridge in the EC. Fresh plasma and platelets are not stored on site, although freeze dried plasma is available. In order to maintain safe stock levels, emergency blood is replenished directly after use. The nearest blood bank is at Tygerberg Hospital which is approximately 25 km away. A one-way trip would take between 35 min to an hour depending on time of day and city traffic [19]. Although no exact figure exists, the time to replenish EC emergency blood stock is estimated to be around two hours.

Patients with isolated burns or a head injury, or patients that were not managed in the resuscitation area were excluded. Subjects were first identified as injured patients that attended to the resuscitation area of the EC using the electronic Khayelitsha Hospital EC resuscitation database. This sample was then cross-checked with the hard-copy resuscitation register to ensure a complete sample. The electronic database has captured all patients managed within the resuscitation area since 1 November 2014 and has previously been described [20]. Data from eligible patients were selected from fourteen randomly selected weeks between 1 November 2014 and 30 November 2015, allowing evaluation of the ebb and flow on different days of the week whilst not over-representing busy times such as holidays, end of month, etc. We made use of the randomisation function of Office Excel (Microsoft, Redmond, US) to select the weeks included. Given an estimate of approximately 20-30% data corruption (within the database and clinical record), and approximately 21-24 injured patients with complete records seen per week in the EC's resuscitation area, fourteen weeks would result in approximately 294-336 complete data sets. We therefore set out to collect a sample of 294 injury events with complete data sets. This sample would account for just over three months' worth of moderate to severe injury data. We felt that since the study did not involve inferential statistics that rely on a predefined sample size, and the relative novelty of the study, that this convenience sample was iustified.

After identification of the sample, a full list of injuries from the injury event were identified from multiple sources, including the electronic database, electronic clinical record, transfusion register and the electronic radiology record. We also included the following variables: gender, age, date and time of injury and triage priority. Injuries were then coded using the Abbreviated Injury Scale (AIS) and the Injury Severity Score (ISS) were calculated to describe injury severity. The AIS were then securely transferred to the Trauma Audit and Research Network (TARN) to derive the predefined, approximated blood volume loss using the TARN's injury-to-blood-loss tool. The TARN developed this injury-to-blood-loss tool using consensus methodology. Although the tool itself, or its methodology have not been published or externally validated it has been used in publication [21]. The tool provides the proportional circulating blood volume loss of an injury, as described by individual AISs. Using the various AISs that contribute to a patient's injuries as a guide, one can calculate the proportional circulating blood volume loss of all injuries. This data collection process and proportional circulating blood volume loss estimation is graphically described in

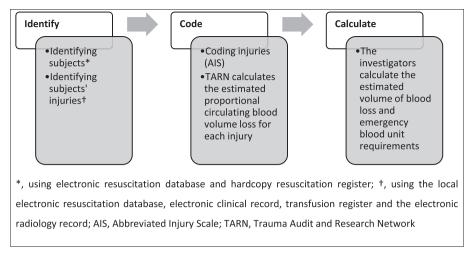


Fig. 1. Study design and flow.

Descriptive statistics were used to describe overall, week (Monday to Thursday) and weekend (Friday to Sunday) volumes of blood loss (median and interquartile range, IQR) and the ISS. Estimated blood loss from injury was expressed as a proportion of circulating blood volume (approximated to 5000 mL) and from there calculated to units of whole blood (approximated to 450 mL representing one unit). Using the Advanced Trauma Life Support classification of haemorrhage, we used proportional circulating blood volume loss of more than 15% (or more than 750 mL) to describe haemorrhage that would hypothetically require replacement. Our calculations for emergency blood replacement assumed that circulating blood volume needs only be restored back to this level. Calculations were based on one unit of packed red cells, replacing one unit of whole blood lost. As a unit of emergency blood can only be used for one patient, we did not report on these in decimals (e.g. 1.6 units), but rounded units required up to the nearest full unit of emergency blood (e.g. 2 units). The difference between the volume of packed red cells and whole blood loss was, for simplicity's sake, not corrected. The cohort estimated to require massive transfusion is also described. We used the Western Province Blood Transfusion Service. Clinical guidelines for the use of blood products in South Africa to define massive blood loss; defined as more than 50% blood volume loss within three hours [22]. The study received ethics approval through the University of Cape Town (670/2015). A STROBE checklist was used to structure the final report (https://strobe-statement.org/).

Results

A total of 389 injury events were identified from the database of which 95 were excluded due to insufficient clinical detail. An additional two subjects were identified as extreme outliers: the first case required an estimated 11 units and the second required an estimated nine units of blood. Although these values fell well beyond the interquartile range it was decided not to exclude it from main calculations (see discussion). The majority of patients were male (n = 257, 87.4%). The mean age was 29 years \pm a standard deviation of 10 years. Demographics are described in Table 1. The main findings of the study are presented in Table 2. Table 3 provides the findings as it pertains to the week (Monday to Thursday) and weekend (Friday to Sunday).

The overall estimated weekend proportion blood loss of circulating volume was 2.7 times more than in the week ($50,000\,\mathrm{mL}/18,450\,\mathrm{mL}$); the proportion blood loss of circulating volume was more than 15%. The estimated weekend volume loss was 2.2 times more than in the week ($19,000\,\mathrm{mL}/8450\,\mathrm{mL}$). This would equate to 1.8 times more units of blood required over weekends ($22\,\mathrm{units}/12\,\mathrm{units}$). Over the $14\,\mathrm{week}$ study period, this would equate to a mean of $1.6\,\mathrm{units}$ of blood per weekend and $0.7\,\mathrm{units}$ of blood per week. Fig. $2\,\mathrm{graphically}$ describes

Table 1 Sample demographics, overall and for cohort estimated to not require transfusion (\leq 15% blood loss) and cohort estimated to require transfusion (>15% blood loss).

Variable	All	≤15% blood loss	> 15% blood loss
n	294	275	19
Age (mean ± SD)	29 ± 10 years	29 ± 10 years	29 ± 7 years
Male (n, %)	257, 87.4	239, 86.9	18, 94.7
ISS (median, IQR)	5, 4–10	5, 3–9	14, 12–19

SD, standard deviation; ISS, Injury Severity Score; IQR, interquartile range.

Table 2 The overall proportional and volume of blood loss descriptors for the sample (n = 294).

Variable	Median (IQR)	Maximum range	Sum	
Circulating blood volume loss per patient (%)*	0 (0–10)	80	-	
Blood volume loss (mL)**	0 (0-500)	4000	68,450	
> 15% blood loss cohort (n = 19)				
Variable	Median (IQR)	Maximum range	Sum	
		. 0		
Circulating blood volume loss per patient (%)*	23 (23–23)		-	
ě .	23 (23–23) 1150 (1150–1150)	4000	- 27,450 (40% of total)	

IQR, interquartile range.

- * Estimation by TARN.
- ** Calculated from% circulating volume blood loss per subject assuming circulating volume is 5000 mL.
- $\,$ *** Calculated to restore circulating blood volume to at least 85% of circulating volume.

the ratio of patients not requiring transfusion versus those that do.

The vast majority of patients were estimated to not have injuries severe enough to mandate transfusion (n=275, 93.5%). Of the 19 patients that were estimated to require transfusion, 15 (57.9%) would have needed only one unit. There were four patients that were estimated to require more than one unit. Of these, two patients were estimated to have suffered massive blood loss (more than 50% circulation blood volume). One was on a Wednesday (estimated to require eight units) and the other on a Friday (estimated to require six units), not in

Table 3The proportion and volume of blood loss descriptors for the weekend and weekly sample.

Variable	Weekend (n = 195)		Week (n = 99)			
	Median (IQR)	Maximum range	Sum	Median (IQR)	Maximum range	Sum
Circulating blood volume loss per patient (%)* Blood volume loss (mL)** > 15% blood loss cohort	0 (0–10) 0 (0–500)	68 3400	- 50,000	0 (0-5) 0 (0-250)	80 4000	- 18,450
Variable	Weekend (n = 14)			Week $(n = 5)$		
	Median (IQR)	Maximum range	Sum	Median (IQR)	Maximum range	Sum

IQR, interquartile range.

the same week. These two patients' transfusion requirements would have outstripped local resources.

Discussion

The vast majority of patients who presented with injuries to the resuscitation area of the EC were estimated to have lost less than 15% of circulating blood volume and thus per our definition did not require transfusion. Only one in 15 was estimated to have lost more than 15% of circulating blood volume, and of those one unit would have sufficed

in nearly two-thirds of cases. Other local research has shown that a mean of 1.6 units of emergency blood is required for patients requiring blood products due to injury, fairly close to our estimated median of one unit [17].

It is important however, to consider that haemorrhagic shock is not managed with statistics, but blood requirements as indicated through clinical assessment (a transfusion of 0.6 units would be an unusual one in an adult). The absolute numbers are therefore more useful as this provides us with a practical number of estimated units of blood; as four units of emergency blood is stored in the blood fridge at Khayelitsha

Overall:	Massive blood loss:	Mondays to	Fridays to Sundays:
One in every 15	One in every 9 persons	Thursdays:	One in every 14
persons with a	requiring transfusion	One in every 20 persons	persons with a
moderate to serious	will require more	with a moderate to	moderate to serious
injury will require	blood than what is	serious injury will	injury will require
transfusion	locally available	require transfusion	transfusion
TATA	TAN	WWW	TAT
***	*	***	*

Fig. 2. Visual representation of need for blood products overall, for massive blood loss, during the week and over weekends.

^{*} Estimation by TARN.

^{**} Calculated from% circulating volume blood loss per subject assuming circulating volume is 5000 mL.

^{***} Calculated to restore circulating blood volume to at least 85% of circulating volume.

hospital EC, sufficient supplies already exist to deal with the majority of patients estimated to require emergency blood for injury.

A key element in considering emergency blood stock is to take the variability of need and the time it takes to replenish stocks into account. Weekends saw more patients that required emergency blood compared to the week, although this did not occur in our injury sample, patients requiring emergency blood in short succession will quickly outstrip availability. We know from the same local research cited earlier that injury only accounts for approximately 26% of emergency blood use from the EC stock [17]. Although this measured value cannot be directly applied to our estimated value, it would suggest that at least two to three times more emergency blood is required for other indications [17]. Morris et al. included indications such as early pregnancy complications, ruptured ectopic pregnancy, postpartum haemorrhage, symptomatic anaemia, and upper or lower gastrointestinal haemorrhage [17]. Furthermore, massive blood loss occurred in one out of every nine patients estimated to require emergency blood. The need for six or eight units of blood is substantially more than what is available on site. What is clear is that at least one to two units should be available at all times for injury-related haemorrhagic shock, and that this does not take into account the blood needed for other indications or occasional patients that will need very large transfusions.

There is simply not enough information to provide an estimate of an overall emergency blood stock requirement. Perhaps, rather than increase the number of emergency blood units available on site, systems should be put in place to ensure rapid replenishment from the blood bank. Such an approach may at odd times leave the EC vulnerable and would in effect underline the resource restrictions within the local public sector. Alternatively, a case could be made for additional emergency blood units to be available over weekends. These could then be used during the following week in theatre or maternity if unused. Morris et al. showed that 20% of emergency blood was used outside the EC for obstetric emergencies and another 20% during general surgery so the latter remains a valid option [17]. The budget limitations at public hospitals are an additional consideration; blood products are expensive and even more so emergency blood. The question whether to invest at the front end of care, treating haemorrhagic shock with emergency blood products or to shift the cost burden downstream to critical care and rehabilitation is both an interesting and ethical one. A cost analysis of the entire process would be required to answer that question. Although local guidance is clear on the use of crystalloids in the initial resuscitation process, it is at odds with international guidance and a growing evidence base suggesting an association with harm thus leaving local ECs in the challenging position to have to triage patient care to the most available option depending on available resources [12,15].

There were a number of limitations to this study. A large number of patients had to be excluded due to insufficient clinical information. This was mainly due to poor descriptions of injuries. As a result, we were unable to determine the AIS of injuries in these patients and therefore an estimation of the proportion of circulating blood volume loss. This may have likely impacted both on the quality of collected information and the findings overall. It also suggests that the findings of this study may be an underestimate. Safe and appropriate clinical record keeping is a major hurdle to retrospective research in public healthcare facilities in low- and middle-income countries [23]. The study only provides estimates of blood loss and replacement and not actual loss and replacement. Although it may seem simple enough to have included the latter for comparing with estimates, record keeping was simply insufficient to provide a reliable result. The estimation of blood loss from injuries (as per the TARN conversion) is not exact and should not be considered a replacement for prospective research. Some patients would not have needed all the estimated emergency blood as they may have died from their injuries during resuscitation. However, the reverse also applies as at the time of data collection, Khayelitsha Hospital had no full-time surgical services. In essence, this means that more blood

may have been required to stabilise patients as there was no surgical option to control active haemorrhage. In any event, mortality and other outcome measures were not included, mainly as there would have been too many variables to account for in the interpretation. The study did not consider the requirement of other blood products that may be required for haemostatic resuscitation. The South African Blood Transfusion Service recommends the use of fresh frozen plasma and platelets along with blood in a 1:1:1 ratio, but fresh frozen plasma and platelets are not available in most public emergency care settings [22]. The use of freeze dried plasma is not currently considered standard practice as part of haemostatic transfusion and anecdotally, fairly limited stock is available. Including freeze dried plasma alongside a larger volume of emergency blood could present a substantial front-end cost; however, as already stated, it is not known whether such a front-end investment may actually benefit the downstream cost-burden. Finally, the sample size for patients with an estimated blood loss greater than 15% was relatively small which limits any conclusions about this cohort. Local economic impact studies may also be useful to determine the optimal balance between clinical requirement and resource availability. But first, a larger, prospective study powered accordingly and comparing estimates with actual blood products given, should first be considered to provide more clarity on the findings.

The volume of emergency blood available in the EC blood fridge on site for the treatment of injury-associated haemorrhage in the absence of a blood bank appears adequate for the majority of patients with injuries estimated to require transfusion. However, this does not take into account the small but important number of injured patients with massive blood loss, nor patients with non-injury demands for emergency blood. The lack of other blood components presents a challenge within this setting since a change in policy on the volume of blood stock would likely have to go hand-in-hand with the provision of additional resources, such as freeze dried plasma. A cost analysis would likely be premature and more work is first required to determine the appropriate interpretation of the evolving evidence-base surrounding injury-associated haemorrhage and how this intersects with the resource and budget limitations locally.

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Conflicts of interest

SRB is an Editor-in-Chief of the African Journal of Emergency Medicine and was not involved in the peer review or editorial process for this paper. No further conflicts are declared.

Dissemination of results

The results were shared at the 2016 African Conference on Emergency Medicine in Cairo, Egypt as a poster presentation.

Author contributions

HW and SRB conceptualised the idea for the paper. HW, SRB and DJvH designed the study protocol. HW, SRB, DJvH, LH and HL contributed to the acquisition of data. HW, SRB and DJvH analysed and interpreted the data. HW wrote the first draft of the manuscript. HW, SRB, DJvH, LH and HL critically revised subsequent drafts and approved the final version.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.afjem.2018.01.004.

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