Injury, Int. J. Care Injured 45 (2014) 1296–1300

Contents lists available at ScienceDirect

Injury

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

Massive blood transfusions post trauma in the elderly compared to younger patients

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ARTICLE INFO

Article history:
Accepted 17 January 2014

Keywords:
Wounds and injuries
Trauma
Elderly
Blood product transfusion
Fresh frozen plasma
Resuscitation

ABSTRACT

Introduction: Older age and blood transfusion have both been independently associated with higher mortality post trauma and the combination is expected to be associated with catastrophic outcomes. Among patients who received a massive transfusion post trauma, we aimed to investigate mortality at hospital discharge of patients ≥65 years old and explore variables associated with poor outcomes.
Methods: A retrospective review of registry data on all major trauma patients presenting to a level I trauma centre between 2006 and 2011 was conducted. Mortality at hospital discharge among patients ≥65 years old was compared to the younger cohort. A multivariable logistic regression model was constructed to determine independent risk-factors for mortality among older patients.
Results: There were 51 (16.4%) patients of age ≥65 years who received a massive transfusion. There were 20 (39.2%) deaths, a proportion significantly higher than 55 (21.1%) deaths among younger patients ($p < 0.01$). Pre-hospital GCS, the presence of acute traumatic coagulopathy and higher systolic blood pressure on presentation were independently associated with higher mortality. Age and volume of red cells transfused were not significantly associated with higher mortality.
Conclusions: Survival to hospital discharge was demonstrated in elderly patients receiving massive transfusions post trauma, even in the presence of multiple risk factors for mortality. Restrictive resuscitation or transfusion on the basis of age alone cannot be supported. Early aggressive resuscitation of elderly trauma patients along specific guidelines directed at the geriatric population is justified and may further improve outcomes.

Introduction

Transfusion of red blood cells is a key component in the resuscitation of massively haemorrhaging patients post injury. The volume of red cells transfused, however, has been associated with increased mortality and morbidity, independent of injury or shock severity [1–3]. Large volumes of red cell transfusion have been associated with multiple adverse effects. Acute complications include hypothermia, dilutional coagulopathy, hypocalcaemia, hypomagnesaemia, citrate toxicity, lactic acidosis and air embolism. Volume overload may occur in the very young, the elderly and in patients with cardiovascular disease. Transfusion associated sepsis has been reported to occur in at least 1:500,000 red cell transfusions [4]. Transfusion-associated graft-versus-host disease occurs more frequently in certain immune-compromised patient groups. The incidence of transfusion related immunomodulation remains unknown, but is associated with multiple organ failure and mortality [5].

Outcomes post massive transfusion among injured patients has been improving [6]. When compared to younger patients, trauma in older patients has been associated with higher mortality with less severe injury [7–9]. Age as young as 56 years old has been associated with higher mortality post injury, with an incremental increasing effect with advanced age, independent of injury severity [10]. The combination of massive transfusion and older age is therefore expected to be associated with catastrophic outcomes. Transfusion of over 12 units of red cells post trauma to patients over the age of 75 years has been argued be futile [11] and the multitude of adverse events has been the focus of a more restrictive transfusion policy for older patients [12]. However, survival among

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http://dx.doi.org/10.1016/j.injury.2014.01.016

the elderly receiving a massive transfusion post trauma was also observed [13].

We aimed to compare mortality at hospital discharge between older and younger sub-groups of patients who received a massive transfusion post trauma. Secondarily, among older trauma patients who received massive transfusions, we aimed to outline clinical signs and initial investigation results associated with higher mortality.

Methods

Setting

The state of Victoria, Australia has one paediatric and two adult Major Trauma Services (MTS) located within metropolitan Melbourne. Major trauma triage guidelines direct 85% of major trauma patients to a MTS for definitive treatment. [Name blinded] trauma registry prospectively records pre-hospital and hospital data on all major trauma patients, defined as having an Injury Severity Score (ISS) greater than 15, requiring urgent surgery or Intensive Care Unit admission, or dying in hospital. In August 2008, during the study period, a massive transfusion guideline was introduced for trauma resuscitation. This guideline recommended high volume red blood cells (RBC):fresh frozen plasma (FFP) at a ratio at 4:2 units, high volume PRBC:platelets at a ratio of 1:1 units and cryoprecipitate when fibrinogen levels were measured to be <1.0 g/L.

Patient selection

The older population was defined by age ≥65 years [14–16]. This was a retrospective review of data in the [Name blinded] trauma registry. All patients included in the [Name blinded] trauma registry, presenting between January 2006 and December 2011 and receiving a massive transfusion, defined as 5 or more RBC units transfused in the first 4 h from hospital arrival, were included [17]. The traditional definition of massive transfusion (10 units in 24 h) was not used as an inclusion criteria as it excludes patients who die early receiving <10 units of red cells and may include patients who do not require blood transfusions on presentation to the ED. In addition, we believe half a person's blood volume (approximated as 5 units of RBC units in a 70 kg male) may be considered as substantial haemorrhage. Pre-hospital transfusions were included to calculate total volumes of RBCs. Acute traumatic coagulopathy (ATC) was defined as an INR ≥ 1.5 or aPTT > 60 s on the first sample of blood taken on presentation to hospital [18]. Pupil abnormality (dilated and/or unreactive, unilaterally or bilaterally) was used as an additional surrogate sign of severe head injury.

Analysis

Normally distributed continuous variables were presented using mean (standard deviation) while ordinal or skewed data were presented using median (inter-quartile range). Student's *t*-test was used to calculate statistical significance between two means, Wilcoxon Rank Sum test was used for difference between two medians, the chi-squared test was used for difference between two proportions or where the count in a two-by-two table cell was less than 5, Fisher's exact test was used. Logistic regression was used to determine univariate associations of variables and mortality recorded at hospital discharge. Variables with missing data were handled by pairwise deletion for univariate analyses and listwise deletion for multivariable analysis. Variables showing any association ($p < 0.10$) with mortality among the older patient sub-group were entered into a multivariable logistic regression model. Results from univariate regression models were reported as unadjusted odds ratios (OR) with 95% confidence intervals, while results from the multivariable regression model were reported as adjusted OR with 95% confidence intervals. A predictive model for death at hospital discharge was developed for elderly patients receiving a massive transfusion and performance of this model reported as area under receiver operating characteristics curve (AUROC) with 95% confidence intervals. A *p*-value of <0.05 was considered to be statistically significant. All analyses were performed using Stata version 11.0 (Statacorp, College Station, TX, USA). This study was approved by [Name blinded] Research and Ethics Committee.

Results

During the study period, 5915 major trauma patients were identified, with 311 patients receiving a massive transfusion. Overall mean age of patients at presentation was 42.4 (19.4) years, and comprised of 51 (16.4%) patients of ≥65 years of age. A comparison of demographics, initial vital signs, blood test results and transfusion practice are presented in Table 1. Initial GCS was significantly lower among younger patients, but rate of pre-hospital intubation was similar-performed on 61 (23.5%) younger patients and 17 (33.3%) older patients ($p = 0.14$). All included patients were received by a trauma team on presentation to the emergency department (ED).

Of the subgroup of older patients, there were 20 (39.2%) deaths, a significantly higher percentage than the 55 (21.1%) deaths among younger patients ($p < 0.01$). Most deaths among the older sub-group occurred early (Fig. 1). Among survivors, hospital length of stay of younger patients was 26.3 (23.5) days, similar to the length of stay of older patients of 26.5 (16.3) days ($p = 0.95$).

The association of injury severity, pre-hospital vital signs, vital signs on presentation, blood test results on presentation, severe head injury and transfusion practice with mortality at hospital discharge are listed in Table 2 (unadjusted) and Table 3 (adjusted). There were 47 cases with complete data available for multivariable logistic regression model. Pre-hospital GCS and acute traumatic coagulopathy on first blood test in hospital were independently

Table 1
Comparison of older (age ≥ 65 years) and younger patients receiving massive transfusions post trauma.

Variable	Young (age < 65 yrs; *n* = 260)	Elderly (age ≥ 65 yrs; *n* = 51)	*p*
Male sex	202 (77.7%)	28 (54.9%)	<0.01
ISS[a]	37 (26–45)	34 (22–43)	0.04
Pre-hospital heart rate (bpm)	109.4 (30.0)	95.4 (26.5)	<0.01
Pre-hospital respiratory rate (bpm)	20.9 (7.4)	23.1 (8.0)	0.08
Pre-hospital systolic blood pressure (mm Hg)	99.2 (35.8)	112.2 (40.9)	0.04
Pre-hospital GCS	13 (4–15)	14 (9–15)	0.04
Temperature (°C)	35.2 (1.5)	35.5 (0.9)	0.25
ED heart rate (bpm)	112.0 (30.9)	95.1 (21.1)	<0.01
ED respiratory rate (bpm)	19.2 (5.5)	19.8 (6.3)	0.64
ED systolic blood pressure (mm Hg)	113.4 (38.1)	114.4 (51.9)	0.87
Abnormal pupils	40 (16.9%)	4 (10.3%)	0.29
Initial haemoglobin (g/L)	10.8 (2.7)	10.0 (2.5)	0.05
Initial lactate (mmol/L)	4.5 (3.1)	4.4 (3.0)	0.78
Initial bicarbonate (mmol/L)	19.3 (4.5)	20.2 (3.7)	0.19
Initial INR	1.7 (0.9)	1.8 (1.3)	0.18
Acute traumatic coagulopathy	109 (45.0%)	22 (43.1%)	0.80
Red cells in 4 h (units)	10 (8–16)	10 (8–18)	0.96
Fresh frozen plasma in 4 h (units)	4 (2–8)	6 (2–8)	0.92
Red cells in 24 h (units)	12 (8–21)	12 (8–23)	0.83
Fresh frozen plasma in 24 h (units)	6 (2–12)	6 (4–10)	0.91

ISS, Injury Severity Score; GCS, Glasgow Coma Scale; ED, emergency department; INR, international normalised ratio.

[a] Calculated using AIS98 scores.