Indications for blood transfusion following trauma - a pilot study

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ABSTRACT

Background: Indications for blood transfusion during trauma resuscitation remain poorly understood. This study aimed to objectively determine the range of factors that lead to initiation of blood transfusion during trauma resuscitation.

Design and method: This was a prospective, observational pilot study. A questionnaire was distributed to all clinicians following any transfusion of packed red blood cells during trauma resuscitation. The questionnaire focused on the clinicians’ opinion regarding the indication for red cell transfusion.

Results: Complete data on 37 individual episodes of transfusion initiation in the Emergency Department were collected. The most commonly used pre-hospital factors that influenced initiation of transfusion was a pre-hospital systolic blood pressure (SBP) of \( \geq 100 \) mm Hg (65%), pre-hospital tachycardia (38%) or estimated blood loss of \( >1 \) L (30%) by paramedics. On arrival to hospital, the activation of a massive transfusion protocol was the commonest indication for transfusion, followed by a positive FAST examination (43%), low systolic blood pressure (35%), tachycardia (32%) or pallor (35%). Blood tests to guide initiation of transfusion were less commonly used with 9 (24%) patients transfused for a low haemoglobin level and 6 (16%) patients transfused for coagulopathy.

Conclusions: A combination of objective pre- and in-hospital vital signs, together with subjective indicators such as pallor and estimation of blood loss guided initiation of transfusion following injury.

Keywords: trauma, transfusion, indication, resuscitation, red cell
INTRODUCTION

Urgent replacement of circulatory volume may be essential to maintain tissue perfusion prior to haemostasis. In the presence of ongoing haemodynamic instability after 2 L of crystalloid resuscitation, volume replacement with blood products is currently recommended.\textsuperscript{1–3}

However, the physiological basis of such guidelines remains poorly understood. The amount of blood loss corresponds poorly with routinely used physiological parameters of heart rate, blood pressure and the Glasgow Coma Scale (GCS). A low blood pressure is a late and insensitive finding of haemorrhage and shock, with trauma patients presenting with a median initial systolic blood pressure (SBP) of 90 mm Hg experiencing mortality of 65%.\textsuperscript{4–6} In addition, correction of SBP does not appear to correlate with improved outcome with patients hypotensive (<90 mm Hg) in the pre-hospital setting but normotensive in the ED experiencing a two-fold higher mortality.\textsuperscript{7}

The understanding that tachycardia develops to maintain cardiac output in traumatic hypovolemia is too simplistic. It has been observed that in the setting of massive blood loss, bradycardia may develop.\textsuperscript{8,9} There are many other influences on heart rate and blood pressure in trauma patients apart from blood loss, including age, anxiety, pain, medication and the cardiovascular effects of raised intracranial pressure and spinal cord injury. Interpretation of vital signs must therefore take these factors into consideration.

Tissue injury and the physiological derangements coupled by pathophysiological inflammatory responses and therapeutic confounders further complicate decision making for acute transfusion.\textsuperscript{10} In addition, the initial haemoglobin level that guides transfusion among other critically ill patients, unless very low, is unreliable in the initial stages of trauma resuscitation. The ability to predict which haemorrhaging patients will ultimately require a blood transfusion or massive transfusion continues to be an area of active interest.\textsuperscript{11}

The overarching aim of this research is to understand indications for transfusion during trauma resuscitation with a view to limit potentially avoidable transfusions. In this study we have sought to explore factors as to why clinicians transfuse red cells during trauma resuscitation. It was expected that the range of factors could inform further research options to develop objective clinical guidelines to initiate transfusion.

METHODS

A prospective, observational pilot study was conducted over an eight-month period between August 2012 and March 2013 and all cases that received a blood transfusion in the ED after injury were eligible for inclusion. Immediately after reception and resuscitation of an injured patient who was transfused, the team leader of the resuscitation team—usually an emergency or trauma physician (the attending or consultant physician)—were asked to fill out a questionnaire to determine the reason for the transfusion. The exclusion criteria for patients at the time of enrolment included a burn injury or a prior blood transfusion either at the scene or en-route to hospital. In order to minimise recall bias, clinicians were asked to fill out the survey within an hour of the patient being discharged from the emergency department.

It was estimated that about 150 patients would receive a transfusion post-trauma at The Alfred Emergency & Trauma Centre, Melbourne, Australia during the study period. In this pilot study, we aimed to include 50 trauma transfusion episodes. This number was selected as a pragmatic estimation of surveys that would be returned based on low response rates of medical surveys\textsuperscript{12} coupled with the relatively low priority for research during a trauma resuscitation. As such, it was deemed a convenience sample. In addition to data collected on transfusion decision prospectively, demographic, management and outcome data on patients were extracted from The Alfred Trauma Registry.

The hospital is an adult major trauma centre in the state of Victoria, Australia. The state is serviced by one paediatric and two adult Major Trauma Services (MTS) located within metropolitan Melbourne. Major trauma triage guidelines direct approximately 85% of major trauma patients to a MTS for definitive treatment. The Alfred Emergency & Trauma Centre receives in excess of 2000 trauma patients per year with over 1300 patients having an injury severity score of >15. Pre-hospital times for major trauma cases transferred directly from the scene are usually under one hour.\textsuperscript{13}

The study aimed to include any episode that required a blood transfusion during trauma resuscitation, regardless of the need for a massive transfusion. At the discretion of the resuscitation team during the study period, a massive transfusion protocol (MTP) was available to clinicians that commenced transfusion with four units of packed red cells, two units of fresh frozen plasma and one
pool (five units) of platelets. Cryoprecipitate, calcium and tranexamic acid were available according to clinician discretion. Activation of the MTP was based on clinician Gestalt. The shock index was defined by heart rate divided by systolic blood pressure. Continuous data are presented as mean (standard deviation), while ordinal data are presented using median (inter-quartile ranges). Continuous and ordinal data within the subgroups were compared using the Wilcoxon rank-sum test, the chi-squared test was used for comparing variables presented as proportions, with the Fisher’s exact test used when a value in a cell was less than five. A p-value of < 0.05 was considered to be statistically significant. All analyses were undertaken using Stata/IC version 11.0 (College Station, Texas, USA). The Alfred Hospital Research and Ethics Committee approved the study prior to its commencement.

RESULTS
There were 49 questionnaires returned of which, complete data were available for 37 transfusion episodes. There were 12 cases excluded from analysis due to missing data on timing of submission of questionnaire, designation of clinician or ambiguity on boxes being ticked. Demographics and initial clinical variables of included cases are listed in Table 1, sub-grouped by activation of the MTP. Patients who had a massive transfusion protocol initiated had significantly higher shock indices pre-hospital and on arrival to the ED. They also presented with a lower GCS and were more likely to be thrombocytopenic and acidaemic. Clinician responses to primary drivers of transfusion are listed in Table 2. A massive transfusion protocol initiated was more common in the presence of hypotension, a positive Focused Assessment with Sonography in Trauma (FAST) and pallor.

Table 1. Demographics and clinical variables sub-grouped by activation of massive transfusion protocol.

| Variable                      | Overall          | MTP (n = 20) | No MTP (n = 17) | p     |
|-------------------------------|------------------|--------------|-----------------|-------|
| Age, years (SD)               | 45.8 (22.5)      | 45.9 (22.5)  | 45.6 (23.1)     | 0.87  |
| Penetrating trauma, n (%)     | 6 (15.8%)        | 3 (15.0%)    | 3 (17.6%)       | 0.83  |
| ISS (IQR)                     | 29 (24-41)       | 35 (23-42)   | 25 (17-33)      | 0.14  |
| Pre-hospital initial SBP, mm Hg (SD) | 95.9 (25.1)      | 112.1 (22.1) | 85.4 (23.9)     | 0.06  |
| Pre-hospital initial HR, b/min (SD) | 105.6 (29.9)     | 114.1 (32.7) | 95.5 (23.4)     | 0.07  |
| Pre-hospital initial GCS (IQR) | 14 (12-14)       | 14 (7-14)    | 14 (13-15)      | 0.14  |
| Pre-hospital Shock Index (SD) | 1.17 (0.5)       | 1.2 (0.4)    | 0.9 (0.4)       | 0.04  |
| Arrival SBP, mm Hg (SD)       | 97.2 (44.3)      | 85.4 (33.9)  | 112.1 (22.1)    | 0.06  |
| Arrival HR, b/min (SD)        | 106.8 (28.8)     | 99.8 (50.7)  | 96.0 (24.7)     | 0.26  |
| Arrival GCS (IQR)             | 12 (3-16)        | 3 (3-4)      | 5 (5-15)        | 0.02  |
| Arrival temperature, C (SD)   | 35.7 (1)         | 35.7 (1.4)   | 35.8 (0.9)      | 0.99  |
| Arrival Shock Index (SD)      | 1.0 (0.7)        | 1.2 (0.5)    | 0.9 (0.4)       | 0.02  |
| Haemoglobin in g/L (SD)       | 105 (34.4)       | 100.8 (39.3) | 109.9 (27.9)    | 0.34  |
| Platelet count x 10^9 (SD)    | 162.2 (77.4)     | 137.7 (78.5) | 191.1 (67.4)    | 0.04  |
| INR (SD)                      | 2.4 (3.3)        | 3.0 (4.4)    | 1.7 (3.0)       | 0.27  |
| APTT in seconds (SD)          | 65.9 (69.3)      | 78.0 (80.2)  | 51.5 (52.6)     | 0.11  |
| pH (SD)                       | 7.2 (0.2)        | 7.1 (0.39)   | 7.3 (0.11)      | 0.03  |
| Lactate in mmol/L (SD)        | 5.1 (4.9)        | 7.0 (6.3)    | 3.0 (4.7)       | 0.07  |
| Massive transfusion administered | 20 (54.0%)      | 14 (70.0%)   | 6 (35.2%)       | 0.03  |

Massive transfusion protocol (MTP); Standard deviation (SD); Glasgow Coma Score (GCS); Interquartile Range (IQR); Shock Index (SI); Systolic Blood Pressure (SBP); International Normalised Ratio (INR); Heart Rate (HR); Activated Partial Thromboplastin time (APTT).

Pre-hospital factors that influenced transfusion on arrival were a pre-hospital SBP of < 100 mm Hg (65%), pre-hospital tachycardia (38%) or estimated blood loss > 1 L (30%) by the paramedic. On arrival to hospital, the activation of a massive transfusion protocol was the commonest indication for transfusion, followed by a positive FAST (43%), low SBP (35%), tachycardia (32%) or pallor (35%).

The mean initial haemoglobin (Hb) was 105 (34.4) g/L. There were 9 (24%) patients with Hb of < 100 g/L and 6 (16%) patients with an initial INR > 1.5. Blood tests to guide initiation of transfusion were less commonly used with 9 (24%) transfused for a low Hb level and 6 (16%) transfused for coagulopathy.

There were 20 (54%) patients that received a massive transfusion. There were 7 (18.9%) deaths at hospital discharge, of which five patients had received a massive transfusion. Mean length of hospital...
stay was 18.7 (17.6) days. There were 22 patients who were mechanically ventilated with mean ventilated hours of 152.2 (270.1) hours.

DISCUSSION

On arrival to the ED, blood transfusion post-trauma was initiated most commonly based on pre-hospital signs. This highlights the need for accurate estimation of pre-hospital blood loss. In addition, clinician Gestalt at estimation of blood loss using blood pressure and pallor or expectation of further loss appears to drive transfusion rather than objective markers or rules. Such practice is markedly different from transfusion in other areas of critical care medicine, such as in intensive care, that rely on haemoglobin levels to guide transfusion.18

Previous authors have attempted to determine factors associated with the initiation of transfusion after trauma.19 This study differs in approach by exploring a combination of quantitative factors and those that are non-objectively assessed by clinicians such as pallor or estimation of blood loss. Quantitative factors associated with initiation of transfusion were similar to those found in the study conducted by Sisak et al., with ongoing bleeding, low haemoglobin, hypotension and tachycardia. However, we have also attempted to gain some insight into additional qualitative factors that influence a clinician to commence blood transfusion in trauma resuscitation, such as a patient appearing pale, other known comorbidities and being requested to commence a transfusion by a different clinician.

It is important that transfusion is initiated based on accurate data so inappropriate transfusions are avoided.20 Blood is an expensive and precious resource. In addition, adverse outcomes have been associated with even small volumes of transfusion after trauma.21 This has to be balanced against prompt delivery of blood and blood products to appropriately treat the exsanguinating, potentially coagulopathic patient.

A number of prediction scores for transfusion and massive transfusion are available but appear to be used uncommonly in clinical practice and were not used by participants in this study. These models are most often developed based on an initial deliberate broad selection of potential predicting variables.22 It seems justifiable, based on our findings, to include pre-hospital clinical variables into a multivariate logistic regression when such future efforts are undertaken. It appears unlikely that one single variable that adequately predicts critical bleeding exists, the need to combine as much information as possible is obvious.

To achieve this practically, the aid from computer technology both in gathering and handling information is needed. Pre-hospital heart rate patterns23 have been shown to be associated with haemorrhage and it has been suggested that pre-hospital data should be systematically gathered and analysed to serve in the initial development of future predictive models. Once pre-morbid data can be reliably included, interpretation of the true physiological impact of the injury can be further enhanced.

### Table 2. Indications for initiation of transfusion

| Indication                              | Overall (n = 37) | MTP (n = 20) | No MTP (n = 17) | P     |
|-----------------------------------------|-----------------|-------------|----------------|------|
| Pre-hospital blood pressure < 100 mm Hg| 24 (65%)        | 16 (80%)   | 8 (47%)        | 0.05 |
| ED systolic blood pressure < 100 mm Hg | 24 (65%)        | 16 (80%)   | 8 (47%)        | 0.05 |
| MTP* activated                          | 20 (54%)        | 20 (100%)  | -              |      |
| Appeared pale                           | 19 (51%)        | 14 (70%)   | 5 (29%)        | 0.02 |
| Positive FAST*                          | 16 (43%)        | 13 (65%)   | 3 (18%)        | <0.01|
| Pre-hospital heart rate > 100 b/min    | 14 (38%)        | 8 (40%)    | 6 (35%)        | 0.99 |
| ED systolic blood pressure < 90 mm Hg  | 12 (32%)        | 10 (50%)   | 2 (12%)        | 0.02 |
| ED heart rate > 100 b/min              | 12 (32%)        | 9 (45%)    | 3 (18%)        | 0.09 |
| Haemoglobin < 100 g/L                   | 9 (24%)         | 3 (15%)    | 6 (35%)        | 0.25 |
| Pre-arrival estimated blood loss > 1 L  | 8 (22%)         | 6 (30%)    | 2 (12%)        | 0.25 |
| Ongoing exsanguination                 | 8 (22%)         | 5 (25%)    | 3 (18%)        | 0.70 |
| ED heart rate > 120 b/min              | 8 (22%)         | 6 (30%)    | 2 (12%)        | 0.25 |
| Wide pulse pressure                    | 7 (19%)         | 6 (30%)    | 1 (6%)         | 0.10 |
| Pelvic trauma                          | 7 (19%)         | 4 (20%)    | 3 (18%)        | 0.99 |
| Anticoagulant/antiplatelet use          | 6 (16%)         | 4 (20%)    | 2 (12%)        | 0.67 |
| Haemoglobin < 80 g/L                    | 6 (16%)         | 4 (20%)    | 2 (12%)        | 0.67 |
| Coagulopathy                           | 6 (16%)         | 5 (25%)    | 1 (6%)         | 0.19 |
| Someone else told me to do it          | 4 (11%)         | 2 (10%)    | 2 (12%)        | 1.00 |
| Past history of coagulopathy           | 1 (3%)          | 1 (5%)     | 0              |      |

*Massive Transfusion Protocol; ^Focused Assessment with Sonography in Trauma.
Additional pre-hospital data such as pre-hospital hypotension may also enhance predictability, as even if corrected prior to arrival to the ED, has been previously associated with the need for emergent, therapeutic interventions. Pre-hospital ultrasound was not available in our setting, but may hasten diagnosis and prediction of transfusion, as an in-hospital positive FAST was commonly used as an indication for transfusion initiation. Effectiveness of pre-hospital ultrasound in the trauma setting has not been established to date, but further research is indicated.

With the assistance of computer technology and machine learning, accuracy can improve further. Mina et al. reported an area under the receiver operating curve (AUROC) of 96% for detection of MT (≥10 units in 24 hours) with the use of their smartphone application which utilised advanced computing and resampling of data over 500 iterations. For detecting the need for any “life saving interventions,” machine learning of HR, GCS, and heart rate complexity, Liu et al. reported an AUROC of 99%. Such prediction tools have performed substantially more superior to the Trauma Associated Severe Hemorrhage (TASH) score—the best current predictor of transfusion requirement after injury without the explicit need of computer assistance—with an AUROC between 0.889 and 0.905 in its development population and similar accuracy in Australia.

Qualitative estimation of blood loss, such as pallor or pre-hospital estimation was also identified a factor in clinical decision making for initiation of transfusion. However, there is some conjecture regarding accuracy of parametric estimation of blood loss. It has been estimated that only 24% of paramedics were within 50% of the actual volume of blood loss but accuracy has been shown to be higher in other studies. A visual analog scale, a bleed being suspected as arterial or venous, surrogate markers of perfusion, point of care haemoglobin or other scoring systems that include various markers from all these observations, may improve estimation of pre-hospital blood loss.

This study is limited in being a pilot study but provided an indication on the range of quantitative and qualitative factors that determine initiation of blood transfusion on arrival to hospital. Only a small proportion of the accessible sample filled out the questionnaire and selection bias is a possibility. A relatively large proportion of cases had to be excluded due to improper completion of the data sheet. Considering indications for the activation of the massive transfusion protocol would add strength to further studies. Non-parametric tests of statistical significance were limited by the small sample size, and in this pilot study, the effect size may be a better indicator of clinical significance. Future directions outlined by this study involve improving accuracy of estimation of blood loss. Using objective measures of estimation of blood loss, it would be useful to extend such investigations to include a larger sample across multiple centres. Such data may inform evidence-based guidelines towards indications for initiation of blood transfusion after trauma.

CONCLUSIONS

Following injury, initiation of blood transfusion was undertaken for a variety of reasons, the most common being based on pre-hospital shock. Subjective measures of blood loss such as pallor and estimation of external loss also continued to be used. Improved accuracy at estimation of pre-hospital blood loss should focus on improving accuracy of such clinical indicators.

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