The utility of a shock index $\geq 1$ as an indication for pre-hospital oxygen carrier administration in major trauma

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**A B S T R A C T**

**Introduction and aims:** The use of intravenous oxygen carriers (packed red blood cells (PRBC), whole blood and synthetic haemoglobin (HBOCs) for selected pre-hospital trauma resuscitation cases has been reported, despite a lack of validated clinical indications. The aim of this study was to retrospectively identify a sub-group of adult major trauma patients most likely to benefit from pre-hospital oxygen carrier administration and determine the predictive relationship between pre-hospital shock index (SI) [pulse rate/systolic blood pressure] and haemorrhagic shock, blood transfusion and mortality.

**Methods:** A retrospective review of adult major trauma patients recorded in The Alfred Trauma Registry was conducted. Patients were included if they received at least 1 L of pre-hospital crystalloid and spent over 30 min in transit. The association of shock index and transfusion was determined. Patients were further sub-grouped by mode of transport to determine the population of trauma patients who could be included into prospective studies of intravenous oxygen carriers.

**Results:** There were 1149 patients included of whom 311 (21.9%) received an acute blood transfusion. The SI correlated well with transfusion practice. A SI $\geq 1.0$, calculated after at least 1 L of crystalloid transfusion, identified patients with a high specificity (93.5%; 95% CI: 91.8–94.8) for receiving a blood transfusion within 4 h of hospital arrival. While patients transported by helicopter had higher injury severity and blood transfusion requirement, there were no difference in physiological variables and outcomes when compared to patients transported by road car.

**Conclusions:** A shock index $\geq 1.0$ is an easily calculated variable that may identify patients for inclusion into trials for pre-hospital oxygen carriers. Shocked patients have high mortality rates whether transported by road car or by helicopter. The efficacy of pre-hospital intravenous oxygen carriers should be trialled using a shock index $\geq 1.0$ despite fluid resuscitation as the clinical trigger for administration.

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**Introduction**

Worldwide injury mortality has shown substantial decline secondary to improved outcome among transport-related injuries. Addressing modifiable risk factors including speed, alcohol and other drugs, fatigue, the wearing of seatbelts or helmets, vehicle overcrowding and road conditions have been shown to be key contributory factors. There is also evidence that the implementation of organised trauma systems reduces mortality, shortens hospital stay, and decreases the number of intensive care unit admissions. Despite these changes, mortality in patients with massive haemorrhage has remained high, with recent reports of mortality rates up to 40% in patients receiving massive transfusions in advanced trauma systems.

Trauma systems have designated receiving hospitals, with pre-hospital providers bypassing non-designated sites. This has contributed to increased pre-hospital times, but associated with significant mortality benefits. In a recent meta-analysis of US trauma centres, average pre-hospital times from injury to hospital were in excess of 30 min for road ambulances and over 60 min for helicopter transports. Pre-hospital care occupies most of the ‘golden hour’ of trauma resuscitation and for many trauma patients, the initial life- and limb-saving care is now being achieved in the pre-hospital phase. Resuscitation interventions available in this phase, however, remain limited. The intravascular volume expansion strategy adopted in most pre-hospital services is crystalloid administration, despite emerging evidence on the adverse effects of high volume crystalloid resuscitation prior to definitive control of haemorrhage.
Conventional management of traumatic shock involves haemorrhage control, fluid resuscitation and administration of blood and blood component therapy. Packed red blood cells (PRBC) or red cell concentrates are commonly used, with the use of whole blood uncommon and yet to be adopted in the civilian setting. Synthetic haemoglobin based oxygen carriers (HBOCs) have shown promise, eliminating the need for allogenic blood transfusions in 59% of patients. However, their use remains limited due to availability, potential adverse effects and a lack of adequate clinical trials.

Regardless of the type of oxygen carrier used, routine pre-hospital transfusions to date have not demonstrated improvements in outcome, while presenting substantial logistic and cost challenges. A particular challenge is reliably identifying patients who will require transfusion, with current clinical prediction rules demonstrating limited applicability.

A simple predictive indicator, the shock index (SI) [pulse rate divided by systolic blood pressure], has shown promise as a clinical indicator of traumatic shock and may be suited for this use in the pre-hospital phase. Therefore, using a retrospective review of trauma registry data, we aimed to:

1. Identify the sub-group of trauma patients who could potentially benefit from pre-hospital oxygen carrier administration.
2. Validate the utility of the SI for predicting transfusion in this group of patients.
3. Describe the association between mode of pre-hospital transport, haemorrhagic shock and blood transfusion.

This research was undertaken to identify a potential population for future prospective studies on human and synthetic oxygen carriers in pre-hospital trauma resuscitation.

Methods

Setting

The southern Australian state of Victoria has one paediatric and two adult major trauma services (MTS) located within the capital, Melbourne. For this catchment population of 6 million, major trauma triage guidelines direct 85% of major trauma patients to an MTS for definitive treatment. The Alfred Hospital is one of the two adult MTS and receives 55% of the States’ major trauma. The Alfred Trauma Registry captures pre-hospital and hospital data for all major trauma patients. During the time period of this study, inclusion criteria for the database were patients with an ISS >15, or requiring emergency surgery, or >24 h intensive care unit (ICU) admission or death. Data for this study were extracted by trained database managers, blinded to the objectives of the analyses.

The single pre-hospital service, Ambulance Victoria, is staffed by university trained paramedics using Victorian Ambulance Clinical Information System providing evidence-based guidelines to direct decisions.

Patient selection and definitions

The a priori indication for pre-hospital oxygen carriers was determined to be patients in haemorrhagic shock post trauma following at least 1 L of intravenous crystalloid administration. The indications for blood transfusion during trauma resuscitation, let alone in the pre-hospital phase, remain subjective and this indication was based on consensus among trauma clinicians in our centre after reviewing patient outcomes.

Following a previous conclusion of the utility of SI > 0.9 in predicting massive transfusion, we chose a SI ≥ 1.0 as a cut-off point for analysis to select patients for potential oxygen carrier therapy post trauma. This value was chosen for its ease of calculation, better inter-user reliability and high predictive value for massive transfusion.

All patients included in The Alfred Hospital Trauma Registry, presenting between 1 January 2006 and 31 December 2009 and transported to hospital directly from the scene of injury were included in this study (Fig. 1). In this time period there was no provision for pre-hospital blood transfusion (except in exceptional circumstances such as prolonged entrapment). There have been no reported pre-hospital cases of other intravenous oxygen carrier use in Victoria. Patients with missing data on vital signs or transfusion were excluded. Patients who received less than 1 L crystalloid pre-hospital or had a pre-hospital time of less than 30 min were also excluded as it was assumed that in these patients, pre-hospital oxygen carriers would not be indicated.

Shock index (SI) normally ranges from 0.5 to 0.7 in healthy adults. The SI has been suggested to be a better measure of haemodynamic stability in the emergency department (ED) setting than individual vital sign measurements. For this study the SI ‘at scene’ was calculated from the first documented observation by pre-hospital staff. The worst recorded value was used to determine shock index ‘in transit’. The first recorded vital sign on presentation to the ED was used to determine SI post pre-hospital management. This was the most generalisable time-point when pre-hospital data was consistently available. ‘Massive transfusion’ was defined as 5 or more PRBC units transfused in the first 4 h from hospital arrival. Acute traumatic coagulopathy was defined as an INR > 1.5 or an aPTT of >60 s. In-hospital mortality was the primary endpoint. Early death, defined as death within 4 h of presentation to the ED was also reported.

Analysis

Continuous and normally distributed data were presented as means (standard deviation), whereas ordinal or skewed data were presented as medians (interquartile ranges). Missing data were handled by pairwise deletion of the missing variable. All analyses were performed using Stata version 11.0 (Statacorp, College Station, TX, USA).

This study was approved by The Alfred Hospital Research and Ethics Committee.
Results

There were 1419 patients identified by the inclusion criteria of this study (Fig. 1). There were 311 (21.9%) patients who received a blood transfusion in the first 4 h post Trauma Centre arrival and of these 188 (13.2%) patients received a massive transfusion. The association of SI at presentation in these patients with massive transfusion and any transfusion in the first 4 h is presented in Fig. 2.

Overall mortality was 8.1% with 31 (2.2%) early deaths. There were 207 (14.6%) patients with a SI ≥ 1 on presentation and with significantly higher mortality (18.3% vs. 6.3%, p < 0.01). Demographics, pre-hospital and hospital presentation characteristics and injury profiles of patients sub-grouped by SI ≥ 1 is presented in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>SI &lt; 1.0 (n = 1212)</th>
<th>SI ≥ 1.0 (n = 207)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)a</td>
<td>41.1 (18.3)</td>
<td>38.5 (18.2)</td>
<td>0.06</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>938 (77.4%)</td>
<td>151 (72.9%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Penetrating trauma (%)</td>
<td>45 (3.7%)</td>
<td>16 (7.7%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Entrapment (%)</td>
<td>274 (22.6%)</td>
<td>58 (28.0%)</td>
<td>0.11</td>
</tr>
<tr>
<td>GCSb</td>
<td>14 (13–15)</td>
<td>14 (6–14)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pre-hospital HR (b/min)a</td>
<td>92.2 (23.2)</td>
<td>112.8 (27.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pre-hospital SBP (mm Hg)a</td>
<td>122.6 (30.9)</td>
<td>101.6 (35.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pre-hospital SBP &lt; 100 mm Hg (%)</td>
<td>241 (19.9%)</td>
<td>95 (45.9%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pre-hospital IV fluids (L)a</td>
<td>2.6 (2.4)</td>
<td>3.3 (2.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>HR on arrival (b/min)b</td>
<td>93.3 (22.8)</td>
<td>123.0 (30.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SBP on arrival (mm Hg)c</td>
<td>146.7 (26.7)</td>
<td>95.9 (32.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ATC (%)</td>
<td>68 (5.9%)</td>
<td>72 (36.5%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HCO3 (mmol/L)d</td>
<td>23.1 (3.3)</td>
<td>19.9 (4.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SBP (mm Hg)e</td>
<td>134.6 (20.4)</td>
<td>112.5 (25.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ISSf</td>
<td>16 (11–22.5)</td>
<td>25 (18–32)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Massive transfusion (%)</td>
<td>98 (8.1)</td>
<td>90 (43.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Any transfusion (%)</td>
<td>175 (14.5)</td>
<td>135 (65.2)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

GCS, Glasgow coma score; ATC, acute traumatic coagulopathy; HCO3−, serum bicarbonate; Hb, haemoglobin.

* Reported as means (standard deviation).

b Reported as medians (interquartile range).

The specificity of SI ≥ 1 for predicting any blood transfusion in the first 4 h of in-hospital resuscitation was 93.5% (95% CI: 91.8–94.8) with a sensitivity of 43.4% (95% CI: 37.8–49.1) and a positive predictive value of 65.2 (95% CI: 58.2–71.6) while the specificity for predicting a ‘massive transfusion’ was 90.5% (95% CI: 88.7–92.0) with a sensitivity of 47.9% (95% CI: 40.6–55.2) and a positive predictive value of 43.5% (36.7–50.5).

The association between SI at scene, in transit and on arrival to the ED is illustrated in Fig. 3. Among included patients with a

![Fig. 2. Transfusion rates by shock index.](image_url)

![Fig. 3. Shock index at scene, in transit and on arrival.](image_url)
SI $\geq 1$, demographics and presenting clinical variables, subgrouped by modality of transport are listed in Table 2. Patients transported by helicopter emergency medical services (HEMS) had a mean pre-hospital time of 88 (45) min, which was significantly longer than those transported by road (34 (SD 28) min; $p < 0.01$). Among patients with a SI $\geq 1$, the presence of severe hypotension (SBP $\leq 100$ mm Hg) was not associated with significantly increased mortality ($p = 0.051$), but was associated with significantly higher massive transfusion rates (54.4% vs. 33.0%, $p < 0.01$).

A significantly higher proportion of patients transported by HEMS were intubated (45.7% vs. 26.9%, $p = 0.01$) and underwent a chest decompression (38.5% vs. 19.2%, $p = 0.04$). Patients transported by HEMS received a significantly higher volume of IV fluids (3.2 (SD 2.5) L vs. 2.4 (SD 2.1) L, $p = 0.02$). There was no significant difference in rates of inotrope use or pre-hospital cardio-pulmonary resuscitation. Hospital outcomes in patients presenting with a SI $\geq 1$ are listed in Table 3, showing no significant difference attributable to modality of transport among patients presenting with a SI $\geq 1$.

### Discussion

This is the first study that investigates the potential utility of the shock index to guide pre-hospital adult trauma resuscitation in the Australian setting. The performance of the SI in predicting transfusion in the Victorian setting is similar to that reported at Birmingham, Alabama and comparable to other predictive scores. A SI of $\geq 1.0$ post crystalloid resuscitation of at least 1.0 L identifies a group of patients with significantly worse physiological variables and higher mortality who may benefit from pre-hospital infusion of oxygen carriers.

Translating this benefit into statistical significance in prospective trials may be challenging. The current local practice of pre-hospital blood transfusion for shocked patients with long helicopter transport times is based on a legal requisite and not evidence-based medicine. There is no estimate on the degree of mortality benefit of transfusion practice post trauma. Our modelling hypotheses that improved oxygen delivery for shocked pre-hospital trauma patients would provide a measurable clinical benefit. When used in the pre-hospital setting, any changes in mortality, cardiac arrest, anaphylaxis, acute myocardial infarction, cerebrovascular thromboses and renal failure requiring dialysis would need to be explored. On ED arrival, a difference in SI or a difference in venous blood lactate, venous bicarbonate or base deficit or coagulopathy also needs to be adequately investigated. Secondary end-points such as a difference in the use of blood and blood products or a difference in length of stay in ICU and hospital ward may also influence patient and clinician decisions on the use of these products.

There were 38 overall deaths in patients with SI $\geq 1.0$ and 16 early deaths. If we were to generously assume that early, aggressive pre-hospital transfusions while controlling for adverse effects could save 8 lives in the 4 year period, thereby reducing overall mortality from 18.3% to 14.5%, the sample size required to test this hypothesis with 80% power would require 3000 patients. Large multi-centre trials are therefore required. The assumed effect size of transfusion is also limited by its adverse effects. When using PRBCs, the risks of blood transfusion that need to be considered include, but are not limited to volume overload, allergic and allogeneic reactions, dilutional coagulopathy, acute respiratory distress syndrome and multiple organ failure.

In response to a recent coronial directive. Ambulance Victoria Airwing, Australia have introduced the carriage of red cell concentrates on aircraft when the crew receives a call out to all primary cases and selected secondary transfers. However, shocked trauma patients arriving by road car have similarly poor outcomes and in patients with a SI $\geq 1.0$, injury characteristics and physiological variables are similar irrespective of transport mode (Table 2). The option of red cell concentrates is currently not available for road ambulances due to logistical difficulties in storage and transportation of red blood cells in all vehicles. A relatively small number of patients satisfying indications for oxygen carrier transfusion, combined with short shelf life of RBCs and worsening function with ageing raises the issue of potential wastage of a valuable resource.

In the setting of major trauma transport by road cars where PRBCs are not available, the use of synthetic haemoglobin substitutes merit consideration. However, the use of HBOCs has been criticised in a 2008 meta-analysis of data from HBOC trials that demonstrated an increased incidence of myocardial infarction and death in anaemic patients without life-threatening haemorrhagic shock. A 2.7 times increased risk of myocardial infarction was demonstrated but the findings did not consider the 2.3 times increased risk of death in patients with persistent haemorrhagic shock despite fluid resuscitation, as demonstrated in our study. A subsequent series of 54 consenting non-trauma patients with a median haemoglobin level of 40 g/L has demonstrated improved chances of survival with no serious adverse events following HBOC-201 administration.

HBOC-201 has been recently used in Australia via the Therapeutic Goods Administration (TGA)'s Special Access Scheme. It is a modified lactated Ringer’s solution containing 130 g/L of polymerised HB of bovine origin, compatible with all blood types, stable for 3 years when stored at 2–30 °C and stable for 2 years when stored at 40 °C. When fully saturated, HBOC-201 has a similar oxygen-carrying capacity as whole blood with the same haemoglobin concentration. These characteristics make HBOC-201 an appealing alternative when blood is not available. Further
research addressing the safety and efficacy of HBOCs for trauma is required.

This study is limited as it is a retrospective review of pre-hospital data. However, a complete data set of all major trauma patients presenting to a major trauma centre were able to be analysed with a small proportion of patients excluded for missing data. Some of the 136 patients (Fig. 3) may have had a SI ≥ 1.0 after 1.0 L of crystalloid and therefore, potentially benefit from pre-hospital HBOC. Therefore, this retrospective sample of patients with SI ≥ 1.0 on arrival to the ED despite crystalloid resuscitation may underestimate the patient population expected to benefit from pre-hospital HBOC. In addition, as the inclusion criteria was limited in selecting patients with ISS > 15, some shocked trauma patients with single system injuries may have been missed. The exact timing, volume and indications for pre-hospital fluid administration was not available from this hospital based registry. Analyses based on data “in-transit” would therefore have been highly variable and not generalisable. Assumptions on potential benefits are opinion-based, as no reliable data is available for outcome benefits of pre-hospital transfusion.

Conclusions

This study indicates that an easily calculated physiological variable, the SI, may identify the sub-group of adult trauma patients at high risk for transfusion with pre-hospital times greater than 30 min. When calculated to be ≥1.0 despite pre-hospital crystalloid resuscitation, patients had significantly worse physiological variables, injury severity, transfusion requirement and higher mortality than overall major trauma patients. This patient group may benefit from pre-hospital transfusion of oxygen carriers.

Conflict of interest

Nil

Acknowledgements

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References