Early fluid resuscitation in severe trauma

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Trauma is a global health problem that affects patients in both rich and poor countries and accounts for 10,000 deaths each day. \(^1\) \(^2\) Trauma is the second leading cause of death after HIV/AIDS in the 5-45 year old age group. \(^1\) \(^2\)

Early triage and resuscitation decisions affect outcome in trauma situations. \(^3\) \(^4\) \(^5\) \(^6\) The two leading causes of mortality in trauma are neurological injury and blood loss. \(^3\) \(^4\) \(^5\) \(^6\) There has been considerable improvement in our understanding of trauma resuscitation in the past 20 years, and data from databases and observational trials suggests outcomes are improving. \(^3\) \(^4\) \(^5\) \(^6\) For patients with severe traumatic injuries (defined as <15 by the injury severity score, an anatomical scoring system), the high volume fluid resuscitation promoted by early advanced trauma life support manuals, \(^3\) \(^4\) \(^5\) \(^6\) followed by definitive surgical care, has given way to a damage control resuscitation (DCR) strategy (box).

This DCR approach has seen a fall in the volume of crystalloid delivered in the emergency department and an associated fall in mortality. \(^3\) \(^4\) \(^5\) \(^6\) In this review, we summarise the evidence guiding the initial period of resuscitation from arrival in the emergency department to transfer to intensive care or operating theatre, focusing on trauma in critically injured adults. This article emphasises newer developments in trauma care. There is debate on whether patients with brain injury should be resuscitated to higher blood pressures, which is briefly discussed later in the text.

**How can patients who need DCR be identified?**

A DCR strategy applies to patients who present with suspected major haemorrhage. While many definitions exist, the most practical in the acute trauma setting is for estimated blood transfusion volumes of over four units in the initial 2-4 h. Identifying these patients can be a challenge because they are often young with good physiological reserve and may have no physiological evidence of hypovolaemic shock. \(^3\) A number of tools have been developed to identify this group of patients; however, physician decision and experience have been found to be just as accurate. \(^6\) \(^7\) \(^8\) Failure to identify these patients early and to apply DCR is associated with excess mortality. \(^8\)

**How can trauma patients in shock be identified?**

Shock may be defined as a life threatening condition characterised by inadequate delivery of oxygen to vital organs in relation to their metabolic requirements. \(^9\) A systolic blood pressure of 90 mm Hg is commonly used to define both hypotension and shock; however, oxygen delivery depends on cardiac output rather than blood pressure. Homeostasis with peripheral vasconstriction acts to preserve blood pressure even as circulating volume is lost. In patients who have had trauma, adequate cardiac output cannot be inferred from blood pressure. Only when blood loss approaches half the circulating volume or occurs rapidly is there a relation between the cardiac output and blood pressure. \(^10\) Patients presenting with hypotension, tachycardia, and obvious blood loss are readily identified as being in a state of haemorrhagic shock. However, many patients will maintain their pulse and blood pressure even after massive blood loss and tissue hypoxia. This condition is termed cryptic shock and is associated with increased mortality. \(^11\) \(^12\)

The role of basic physiological parameters to estimate the severity of blood loss has been popularised in the advanced trauma life support course and manuals. \(^1\) These materials describe physiological deterioration with increasing

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**SUMMARY POINTS**

- Critically injured trauma patients may have normal cardiovascular and respiratory parameters (pulse, blood pressure, respiratory rate), and no single physiological or metabolic factor accurately identifies all patients in this group.
- Initial resuscitation for severely injured patients is based on a strategy of permissive hypovolaemia (hypotension) (that is, fluid resuscitation delivered to increase blood pressure without reaching normotension, aiming for cerebration in the awake patient, or 70-80 mm Hg in penetrating trauma and 90 mm Hg in blunt trauma) and blood product based resuscitation.
- This period of hypovolaemia (hypotension) should be kept to a minimum, with rapid transfer to the operating theatre for definitive care.
- Crystallloid or colloid based resuscitation in severely injured patients is associated with worse outcome.
- Once haemostasis has been achieved, resuscitation targeted to measures of cardiac output or oxygen delivery or use improves outcome.
- Tranexamic acid administered intravenously within 3 h of injury improves mortality in patients who are thought to be bleeding.

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**SOURCES AND SELECTION CRITERIA**

We searched Medline, Embase, the Cochrane database, and Google for randomised controlled trials, meta-analyses, and peer reviewed articles, limiting the search to adults. The search was performed once by the lead author (TH) and once by a professional librarian. All articles were shared and supplemented by the author's own libraries. The main search terms used were “trauma,” “resuscitation,” “fluid,” and “goal directed therapy.” Ongoing studies were identified from www.clinicaltrials.gov.

**KEY COMPONENTS OF DCR**

- Permissive hypovolaemia (hypotension) (see summary points)
- Haemostatic transfusion (resuscitation)—that is, fresh frozen plasma, platelets, or packed red blood cells, and tranexamic acid. Avoidance of crystalloids (normal saline, Hartmann’s, Ringer’s lactate solutions), colloids (a substance microscopically dispersed evenly throughout another substance; with resuscitation fluids, this term refers to larger molecules dispersed most usually in normal saline, such as gelofuson, haemaccel, or volulyte), and vasopressors.
- Damage control surgery or angiography to treat the cause of bleeding.
- Restore organ perfusion and oxygen delivery with definitive resuscitation.
volumes of blood loss, and categorise four stages of shock. But data from a 1989-2007 analysis of the United Kingdom Trauma Audit Research Network database suggest that this model is not reflected in practice. Patients with progressive levels of blood loss to stage 4 haemorrhagic shock (equating to >2 L blood loss) were found to increase their pulse rates from 82 to 95 beats per minute, not to change respiratory rates or Glasgow coma scale, and maintain systolic blood pressures above 120 mm Hg. Although an important part of the initial assessment, physiological derangement alone is neither sensitive nor specific as a tool to identify shock in trauma patients.

There is observational evidence from large datasets in the UK and United States that mortality increases in trauma patients in both blunt and penetrating trauma, while systolic blood pressure falls below 110 mm Hg. A US review of 870,634 sets of trauma records identified that for every 10 mm Hg below 110 mm Hg, mortality increased by 4.8%. Shock index does not improve after risk stratification of trauma patients.

Metabolic assessment with lactate and base excess also predicts blood loss and mortality. Furthermore, these parameters may be increased from exercise around the time of injury (running, fighting) or may be (false)low if the hypoxic tissues are not being perfused sufficiently to wash anaerobic products into the circulation (for example, when a tourniquet is applied). For patients in whom central access is obtained, mixed venous oxygen saturation is also a good indicator of blood loss, with levels below 70% suggesting inadequate oxygen delivery.

Estimated injuries and associated blood loss are an important part of the initial trauma assessment. Clinical examination is augmented by focused ultrasound assessment of the chest, pericardium, and peritoneal cavity (extended focused assessment with sonography in trauma (eFAST), a specific but insensitive test for blood loss); and computed tomography (a sensitive and specific test for blood loss).

**What is permissive hypotension (hypovolaemic) resuscitation?**

Permissive (hypotension) hypovolaemic resuscitation is used to describe a process that minimises administration of fluid resuscitation until haemorrhage control has been achieved, or is deemed unnecessary on definitive imaging. Resuscitation is the restoration of oxygen delivery and organ perfusion to match requirements. In the 1960s and 1970s, a strategy of high volume crystalloid resuscitation in a ratio of 3 mL per 1 mL of blood loss was promoted, which was thought to replace intravascular and interstitial losses and reduce the risk of organ failure. However, vigorous fluid resuscitation increases blood pressure, the effect of which increases hydrostatic forces on newly formed clot, dilutes clotting factors and haemoglobin, and reduces body temperature. These effects could promote further bleeding. In permissive hypotension, definitive resuscitation is deferred until haemostasis is obtained. It is now recognised that aggressive crystalloid resuscitation also impairs organ perfusion.

**What evidence do we have for hypovolaemic resuscitation?**

Considerable animal work has informed our understanding of hypovolaemic resuscitation. In summary, this research found that withholding fluid resuscitation from animals with critical blood loss (about half their circulating volume) was associated with death, whereas animals with less severe blood loss had a lower mortality with no fluid resuscitation.

The table summarises three randomised controlled trials exploring the risks and benefits of hypovolaemic resuscitation. These trials provide evidence of a mortality advantage in favour of this resuscitation strategy for truncal penetrating trauma and evidence of no harm in blunt trauma.

The National Institute for Health and Clinical Excellence has recommended that in older children and adults with blunt trauma, no fluid be administered in the prehospital resuscitation phase if a radial pulse can be felt, or for penetrating trauma if a central pulse is palpable. In the absence of this, 250 mL crystalloid fluid boluses are administered and the patient is reassessed until these pulses, as described, return.

Much of the evidence for hypovolaemic resuscitation was developed before the advent of haemostatic resuscitation, as described below. This period of hypovolaemic resuscitation is maintained for as short a period as possible, until the injury complex is defined and any sites of blood loss treated surgically or embolised.

Untreated hypovolaemic shock leads to microvascular hypoperfusion and hypoxia, leading to multiorgan failure. Hypovolaemic resuscitation sacrifices perfusion for coagulation and haemorrhage control. The trauma team carefully balances the resuscitation process to maintain organ perfusion but at lower than normal blood pressure to regulate bleeding. Based on the evidence available, we suggest that fluid resuscitation before haemorrhage control should aim to maintain a systolic blood pressure of 80 mm Hg or a

<table>
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<td>Pseudo-randomised controlled trial</td>
<td>No fluid resuscitation before surgical intervention in operating theatre &amp; crystalloid based resuscitation</td>
<td>Penetrating truncal trauma and systolic blood pressure &lt;90 mm Hg (n=598)</td>
<td>Prehospital and in emergency department</td>
<td>Lower mortality in group with no fluid resuscitation than in group with crystalloid based resuscitation (survival 70% vs 62.2%, P=0.04)</td>
<td>Short transport distances, mortality benefit predominantly vascular injuries, young cohort (mean age 31 years), 8% in no fluid group received fluids</td>
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<tr>
<td>Randomised controlled trial</td>
<td>Resuscitation to target systolic blood pressure 100 mm Hg &amp; 70 mm Hg</td>
<td>Blunt or penetrating trauma and systolic blood pressure &lt;90 mm Hg in first hour (n=110)</td>
<td>Urban trauma centre resuscitation room</td>
<td>No mortality difference, low mortality of four (7.3%) patients in each group</td>
<td>Low mortality, study underpowered to show mortality difference; observed systolic blood pressures were 114 mm Hg and 100 mm Hg despite targets</td>
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<td>Randomised controlled trial: interim analysis</td>
<td>Intraoperative resuscitation to mean arterial pressure 50 mm Hg &amp; 65 mm Hg</td>
<td>Traumatic injuries excluding traumatic brain injury with at least one episode of systolic blood pressure &lt;90 mm Hg (n=90)</td>
<td>Operating theatre</td>
<td>No mortality difference</td>
<td>Observed blood pressures did not differ significantly despite targets; results may not translate to preoperative environment</td>
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Severe bleeding in trauma patients can result in disordered blood clotting. Until recently, this effect was thought to be a late phenomenon arising primarily from loss of coagulation factors during haemorrhage and dilution from resuscitation fluids. However, it is now recognised that trauma induced coagulopathy occurs within minutes of injury, and is associated with a fourfold increase in mortality.  The process is multifactorial but is partly due to an endogenous coagulopathy that occurs as a result of tissue damage in severe shock. This understanding has led to changes in the management of trauma haemorrhage.

**Haemostatic resuscitation**

Haemostatic resuscitation is a combination of strategies targeting trauma induced coagulopathy to reduce bleeding and improve outcomes.

**How do blood products aid in resuscitation?**

The main strategy to treat trauma induced coagulopathy is to provide volume replacement that augments coagulation. This replacement has been achieved by the transfusion of fresh frozen plasma, platelets, and packed red blood cells. A retrospective observational study performed on military personnel with similar injuries but differing resuscitation fluid strategies suggested that the use of higher ratios of fresh frozen plasma to packed red blood cells may improve outcomes. Similar results have been seen in other retrospective studies and a few small prospective cohort studies, although the retrospective studies are subject to survival bias.

It is also unclear whether the benefit from these strategies comes from the coagulation factors present in fresh frozen plasma or from reducing the amount of crystalloid and colloid administered. Nevertheless, it seems clear that the usual 1-2 units of plasma previously administered after massive transfusions was insufficient to prevent dilutional coagulopathy. Current consensus is that plasma should be given from the beginning of the resuscitation, alongside transfusions of packed red blood cells, in a ratio of 1 "unit" of plasma for each 1-2 units of packed red blood cells. Very little is known about platelet function in trauma induced coagulopathy or the effectiveness of platelet transfusions. Although these early strategies of blood product in high doses seem effective, they are based on limited evidence. These regimens also place substantial resource demands on blood banks and are logistically difficult to implement owing to the requirements for rapid thawing and delivery.

Research is also being undertaken to look at alternatives to blood component therapy for the management of trauma induced coagulopathy. Fibrinogen is the central substrate of blood clotting, and levels are low in this patient group. Some retrospective evidence suggests that patients who receive more fibrinogen replacement (in the form of cryoprecipitate and plasma) have better outcomes in terms of total use of packed red blood cells and mortality. Fibrinogen is also available as a powdered concentrate and could be a replacement therapy that can be easily administered in trauma induced coagulopathy.
How do I identify patients with trauma induced coagulopathy?  
Standard clotting tests from laboratories such as the prothrombin time do not show any of the key derangements in trauma induced coagulopathy, such as reduced clot strength and fibrinolysis. Furthermore, in a trauma setting, it is impractical to wait for tests that can take up 1 h to process. The point of care versions of these tests (such as the prothrombin time) are prone to be under-read in the presence of low haematocrits. These difficulties have led to a renewed interest in the use of thromboelastography—a point of care assessment of clot generation, strength, and breakdown. This procedure has the potential to provide a rapid assessment of the whole clotting process, but it has not yet been validated in the acute setting. In the absence of a validated diagnostic test at the point of care, management is therefore blind to the status of the coagulation system and relies on clinical judgment and empiric therapy.

What fluids should be used to resuscitate trauma patients who do not need DCR?  
Patients who do not need DCR need no immediate resuscitation until definitive imaging has identified the underlying injuries. These patients should be observed carefully for signs of physiological and metabolic deterioration, consequent on disease progression with blood loss, visceral injury, and pericardial or pleural tamponade. Debate continues on the relative merits of colloid or crystalloid based resuscitation strategies, with a recent Cochrane review concluding that there was no evidence that survival was better with one or the other solution.

However, a subgroup analysis of 460 patients with traumatic brain injury (Glasgow coma scale ≤13) from a large randomised controlled trial comparing the safety of albumin in normal saline with normal saline identified a survival advantage in the crystalloid group (33.2% vs 20.4%, P=0.003).

Hypertonic solutions have been proposed to improve cerebral perfusion and reduce cerebral oedema, and have been advocated for resuscitation of patients with traumatic brain injury. A meta-analysis of eight randomised trials identified a survival advantage in this group, but a randomised controlled trial of 229 patients with hypotension and severe traumatic brain injury (Glasgow coma scale 4–9) who received prehospital resuscitation with hypertonic or normal saline had almost identical survival and neurological function six months after injury. Furthermore, a recent randomised controlled trial of prehospital use of hypertonic solutions was terminated by the data and safety monitoring board after randomisation of 1 331 patients, having met prespecified futility criteria. Among patients with severe traumatic brain injury not in hypovolaemic shock, initial resuscitation with either hypertonic saline or hypertonic saline or dextran, compared with normal saline, did not result in improved neurological outcome or survival at six months. Thus, we suggest the use of crystalloid based fluid administration in this cohort of patients who are less severely injured.

Once haemostasis is achieved, what should be done to ensure adequate resuscitation in severe trauma?  
Once haemostasis has been achieved with surgical intervention, fracture splintage or angiography, or the requirement for these interventions identified as not necessary, then definitive resuscitation is required. If patients are resuscitated to normal blood pressure and pulse without further parameters being used to evaluate for tissue hypoxia, over half of patients would be inadequately resuscitated, with increased morbidity and mortality. Resuscitation to targets of oxygen delivery or use is termed goal directed therapy, and good quality evidence from randomised trials indicates that this approach should be used in trauma; indeed, the original evidence for this approach came from trauma studies.

What other agents should be used in the initial resuscitation period?  
Hyperfibrinolysis is common after trauma, owing to associated hypovolaemic shock and tissue injury. In a recent, large, multinational randomised controlled trial researchers targeted a specific component of trauma induced coagulopathy—hyperfibrinolysis. They showed a reduction in mortality with the use of tranexamic acid, which has anti-fibrinolytic properties (1 g delivered over 15 min, then 1 g over 4 h, commenced within 3 h of injury).

Contributors. TH conceived the review and wrote the introduction, sections of permissive hypovolaemia, resuscitation endpoints, and fluid resuscitation. RT wrote the sections contrasting colloids and crystalloids with hypertonic saline. KB wrote the sections on blood product use and trauma induced coagulopathy. The contributions were correlated by TH, and all authors reviewed the paper. TH is guarantor.

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How do we identify and target trauma induced coagulopathy in the acute phase?  
What is the most effective combination of blood products for initial trauma resuscitation?

Should patients with traumatic brain injury be subject to different initial resuscitation strategies?

Does therapeutic hypothermia have a role in trauma resuscitation or traumatic brain injury in the acute phase?
ANSWERS TO ENDGAMES, p 48

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PICTURE QUIZ

Signs of shock and raised jugular venous pressure

1. The chest radiograph shows a globular cardiac silhouette, possibly as a result of fluid surrounding the heart. The echocardiogram shows a large pericardial effusion (figure).
2. Cardiac tamponade. Electrocardiography classically shows diffuse decreased QRS voltages and may display electrical alternans.
3. In view of the slow onset, associated weight loss, and other systemic symptoms, cancer is the most likely diagnosis. In developing countries tuberculosis should also be considered.
4. Beck’s triad and Kussmaul’s sign were seen in this patient. Pulsus paradoxus could be most likely diagnosis. In developing countries tuberculosis should also be considered.
5. Urgent pericardiocentesis under fluoroscopy or echocardiographic guidance should be

CASE REPORT

Ear pain and facial palsy

1. Necrotising (malignant) otitis externa.
2. The House-Brackmann grading system.
3. Admission for intravenous antibiotics, aural microsuction, eye care, pain management, and occasionally surgical debridement.

STATISTICAL QUESTION

Hazards and hazard ratios

Statements a and d are true, whereas b and c are false.