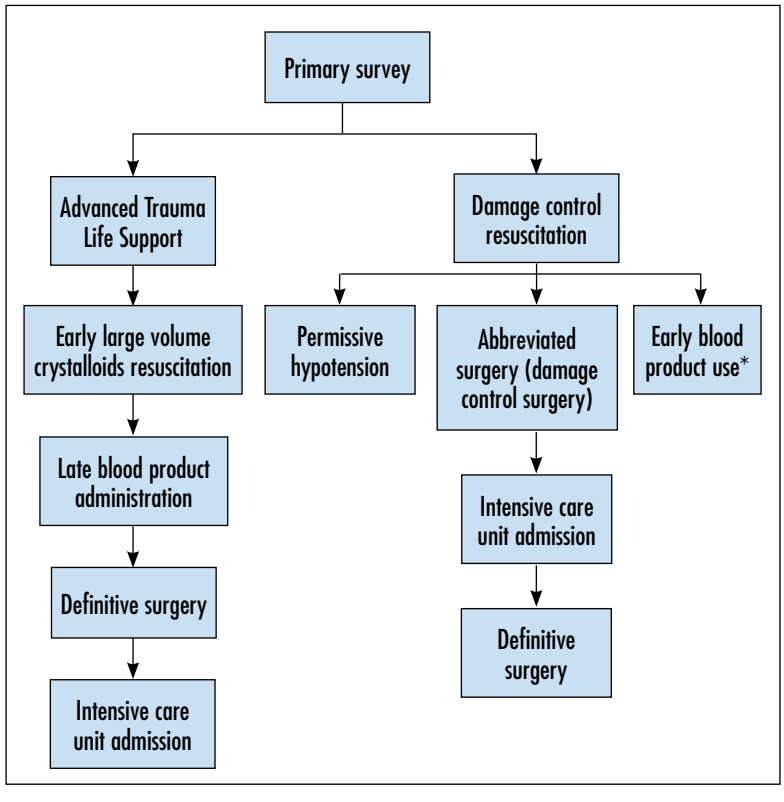
Resuscitation beyond Advanced Trauma Life Support: damage control

This article describes the general principles of the damage control concept in the management of the haemorrhaging multiply injured patient in a civilian setting. Military practice, head injuries and burns as well as trauma in paediatric and elderly patients and pregnant women will not be covered.

The damage control model is based on two principles: damage control resuscitation and damage control surgery. These two arms of damage control are often illustrated separately to aid understanding of complex resuscitation efforts, but they occur simultaneously and are aimed at saving the trauma patient from deranged physiology.

Damage control resuscitation uses three key concepts: permissive hypotension, early use of blood products as primary resuscitation fluids, and early and rapid correction of coagulopathy (Duchesne et al, 2010; Dutton, 2012) (*Figure 1*). Damage control surgery focuses on the haemorrhage and contamination control (Schreiber, 2012).

Figure 1. Traditional aspects of Advanced Trauma Life Support trauma care vs the damage control concept. * = 1:1:1 red blood cells:fresh frozen plasma:platelets.



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Permissive hypotension

The circulatory system can be viewed as an electrical circuit (P=F x R) in which F is blood flow, P represents the pressure difference between the two ends of the vessel and R is the vascular resistance (Guyton and Hall, 2006). The end point of resuscitation is when adequate blood flow is established to provide sufficient oxygen to the tissues. However, aggressive resuscitation with large volumes of intravenous fluids may inadvertently lead to more blood loss, as the increased pressure in damaged blood vessels disrupts the formed blood clot. Therefore, in 1994 Bickell et al introduced the concept of deliberate hypotensive resuscitation, which aims to keep the blood pressure low enough to avoid exsanguination while maintaining perfusion of the vital organs. This team randomized patients with penetrating chest trauma into two groups, one which received conventional fluid management and one group which did not receive any intravenous fluid in the pre-hospital phase or in the emergency department. This trial demonstrated significantly improved outcomes (62% *vs* 70% mortality, and shorter hospital stays) in the group with no fluids given.

However, there are several restrictions to applying this concept. First, the patients in this trial sustained penetrating injuries while blunt trauma is the main mechanism of injury in a civilian setting. Also, permissive hypotension was only used in the emergency department – in theatres all patients received aggressive fluid resuscitation. Furthermore, it is unclear how long permissive hypotension can be used for, but this can be used in patients who have suffered catastrophic haemorrhage (Harris et al, 2012). Once blood loss is controlled or excluded administration of appropriate amounts of intravenous fluids or blood products is central to management thereafter.

But when does the actual hypotension begin? Clinicians often refer to hypotension as a systolic blood pressure ≤90 mmHg (Eastridge et al, 2007; Harris et al, 2012), but this appears to be an arbitrary cut off with little data to support this. Eastridge et al (2007) provided data from 870 634 patient records from the National Trauma Data Bank and analysed first measurement of systolic blood pressure in the emergency department relative to mortality. They found that for every 10 mmHg drop in the systolic blood pressure

below 110 mmHg, the mortality was increased by 4.8%. Furthermore, there was 26% mortality at a systolic blood pressure of 60 mmHg. However, these findings should not be confused with systolic blood pressure being an end point of resuscitation. The systolic blood pressure is a diagnostic tool, and should be interpreted along with other markers of organ perfusion to guide management. Hypotensive patients with rising lactate acid levels, decreasing urine output and deteriorating Glasgow Coma Scale score may need to return to theatre or the angiography suite to control ongoing haemorrhage.

Fluid resuscitation strategies

For many years management of trauma patients was based on the belief that the use of large volumes of intravenous crystalloid lead to the best outcomes. However, this is harmful because it exacerbates the lethal triad (Dutton, 2012; Harris et al, 2012) and the shock-induced inflammatory response. This leads to profound systemic and cellular complications, which cause systemic inflammatory response syndrome, adult respiratory distress syndrome, multi-organ dysfunction syndrome and death (Moore et al, 2004).

Crystalloids

Isotonic crystalloids, like Hartmann's solution and isotonic saline 0.9%, are frequently used during resuscitation. However, Hartmann's solution has been found to be less harmful than isotonic saline 0.9%, which causes hyperchloraemic metabolic acidosis as a result of its high sodium load and chloride load (Duchesne et al, 2010). Isotonic saline 0.9% also acts as a procoagulant at lower dilution levels and an anticoagulant at higher volumes (Coats et al, 2006; Todd et al, 2007).

Hypertonic solutions

A compelling new option is hypertonic saline (3.5% or 7.5%), which can increase the blood pressure with lower volumes (250 ml) as a result of rapid shifts of fluid between the cellular and interstitial spaces (Duchesne et al, 2010). Under normal conditions, Starling forces lead to balanced fluid movement across the capillary membranes (Guyton and Hall, 2006). By providing additional osmotic pressure, sodium shifts the physiological balance in favour of reabsorption (Guyton and Hall, 2006). In effect, increased intravascular volume leads to an increase in blood pressure. Hypertonic saline is also useful in patients with head injuries and is associated with fewer complications, such as adult respiratory distress syndrome or sepsis (Shackford et al, 1998; Duchesne et al, 2010). On the other hand, high sodium load and raised oncotic pressure can lead to cellular dehydration.

Another option is hypertonic saline combined with dextran which, with its potent osmotic effect, provides additional volume expansion (Krausz, 2006). Krausz (2006) suggested that a small bolus of hypertonic saline combined with dextran can be beneficial in haemorrhagic shock, but Moore et al (2004) found that it is associated with a risk of inducing splanchnic ischaemia. Current evidence shows that hypertonic saline combined with dextran solutions can improve blood pressure and reduce intracranial pressure. Unfortunately, no survival or outcome benefit has been associated with the use of either hypertonic saline or hypertonic saline combined with dextran. A lack of well-designed double blinded randomized control trials makes it impossible to draw definitive conclusions and further research is needed (Strandvik, 2009; Rossaint et al, 2010). Therefore, the European guideline on management of bleeding and the National Institute for Health and Clinical Excellence suggests the use of small boluses (250 ml) of crystalloids as primary resuscitation fluids (National Institute for Health and Clinical Excellence, 2004; Rossaint et al, 2010).

Colloids

Evidence from a meta-analysis showed an increased risk of death in trauma patients resuscitated with colloids (Rossaint et al, 2010). When compared with isotonic saline 0.9%, Coats et al (2006) found that large volumes of gelofusine may be associated with a profound anticoagulant effect.

Blood products

Patients who suffer from catastrophic haemorrhage are at risk of coagulopathy and require transfusion to restore blood volume. In such circumstances, blood products should be used as primary resuscitation fluids as early as possible (Rossaint et al, 2010). Transfusion of red blood cells alone is not free of consequences and can exacerbate the dilutional coagulopathy further (Todd et al, 2007). These findings led to the introduction of massive transfusion protocols proving that the deranged coagulation system could be corrected by the use of high ratios of fresh frozen plasma:red blood cells:platelets (1:1:1) (Rossaint et al, 2010). Although Borgman et al (2007) showed that massive transfusion protocols are associated with lower mortality rates, there is an increased risk of serious complications including lung injury, multi-organ dysfunction syndrome, sepsis and mortality as high as 50% (Malone et al, 2003).

Coagulopathy

Traditional understanding of coagulopathy is based on several mechanisms including loss of coagulation factors as a result of haemorrhage, dilution from intravenous fluid administration including red blood cells, hypothermia and acidosis (*Figure 1*). These mechanisms imply that coagulopathy develops following an injury and is the result of ongoing haemorrhage. Consequently empirically delivered massive transfusion protocols aim to correct

this 'late' coagulopathy, but fail to address endogenous acute coagulopathy of trauma shock, which is initiated by the injury and tissue hypoperfusion (Frith and Brohi, 2010).

At present coagulopathy is monitored by standard laboratory tests, including prothrombin time and activated partial thromboplastin time, which describe only an isolated part of the complex coagulation pathway not affected by resuscitation fluids (Coats et al, 2006; Johansson et al, 2008). Furthermore, the results are only available after 45–60 minutes, at which point they may not reflect the patient's condition, making prothrombin time and activated partial thromboplastin time tests unreliable.

These limitations have led to the development of viscoelastic haemostatic assays such as thromboelastography and thromboelastometry, which allow graphic illustration of clot formation in whole blood (Johansson et al, 2008; Stahel et al, 2009). Johansson et al (2008) showed that thromboelastography-guided transfusion therapy for massively bleeding patients led to normalization of their haemostasis. However, the small study sample size (n=10) makes it difficult to draw definite conclusions. As yet there have been no randomized controlled studies in this area. Future techniques may solve current deficiencies in the management of coagulopathy by providing more robust measures of whole blood at the bedside.

Pharmacological haemostatic agents

Haemostatic agents include cryoprecipitate, recombinant activated factor VIIa, tranexamic acid and prothrombin complex concentrate.

Cryoprecipitate consists of fibronectin, von Willebrand factor, factor VIII, factor XIII and most importantly fibrinogen, which is essential to the clot's quality. Fibrinogen levels can be lowered by haemodilution, but it remains controversial whether or not cryoprecipitate should be routinely used as a fibrinogen supplement during damage control resuscitation (Lier et al, 2008; Duchesne et al, 2010).

Recombinant activated factor VIIa is indicated in uncontrolled haemorrhage which has failed to respond to appropriate surgical and non-surgical haemostasis (Thomas et al, 2007; Hauser et al, 2010). It reduces the requirement for blood products in patients who sustained blunt trauma, by increasing thrombin generation at the platelet surface (Boffard et al, 2005). Unfortunately, the use of recombinant activated factor VIIa is associated with increased risk of arterial thromboembolic events, such as cardiovascular accidents or mesenteric ischaemia. Therefore, recombinant activated factor VIIa is not currently licensed for use and should be administered with expert guidance (Thomas et al, 2007; Rossaint et al, 2010).

The CRASH-2 study showed that administration of tranexamic acid, a safe and inexpensive synthetic lysine analogue, significantly reduces all-cause mortality in trauma patients with severe haemorrhage (Shakur et al, 2010). Tranexamic acid inhibits fibrinolysis and thereby reduces blood loss as well. More importantly CRASH-2 showed that there is no increased risk of thromboembolic events and current guidelines support the use of tranexamic acid in trauma patients (Rossaint et al, 2010).

Prothrombin complex concentrate, containing natural anticoagulants (protein C and S) and coagulation factors (II, VII, IX, X), can be rapidly administered irrespective of blood type (Marietta et al, 2010). Infusion of prothrombin complex concentrate with fibrinogen can avoid traditional administration of fresh frozen plasma and platelets (Schochl et al, 2010). However, these retrospective studies have many deficiencies and the current lack of randomized control trials means that their results must be interpreted with caution.

Damage control surgery

Damage control laparotomy

Damage control surgery is an essential part of damage control resuscitation and follows a sequential process of restoring physiology and then correcting anatomy later. The principles of damage control surgery are to control haemorrhage, prevent sepsis and preserve organ perfusion (Nunez et al, 2010). It is necessary to keep the patient warm and the operating time short, because prolonged surgery exacerbates already disturbed immune and physiological systems. Patients can lose on average 4.6°C per hour during laparotomy which can further exacerbate bleeding (Duchesne et al, 2010).

During the initial operation, bleeding and contamination are controlled using temporary measures, including packing, ligation or shunting of major vessels, and limited resection with stapling of the segments which are the source of contamination (Nunez et al, 2010). Temporary abdominal closure excluding fascia helps to avoid abdominal compartment syndrome, and drains may be left in situ (Jansen et al, 2009). Subsequently the patient is transferred to intensive care unit where further resuscitation aims to correct exhausted physiology by addressing all three components of the lethal triad (Jansen et al, 2009; Nunez et al, 2010). On restoration of normal physiology reconstructive surgery and abdominal closure can be performed.

Damage control orthopaedics

Similarly, damage control orthopaedics is based on the principle of delayed definitive fixation of long bone fractures. Pape et al (2002) randomized patients into two groups, one with primary intramedullary nailing and the other group treated by damage control orthopaedics. Both groups were treated within 24 hours of injury. They found significantly increased levels of the proinflammatory cytokine interleukin-6 in the fracture nailing group with a peak 24 hours after the injury. In contrast, the

damage control orthopaedics group had no increase in interleukin-6 levels following surgery. These findings favour the use of damage control orthopaedics in severely injured patients with a high risk of multi-organ dysfunction syndrome. In contrast, substantial evidence shows that delayed stabilization of long bone fractures is associated with multi-organ dysfunction syndrome and respiratory complications including adult respiratory distress syndrome, hospital-acquired pneumonia and fat embolism (Johnson et al, 1984; Crowl et al, 2000; Grotz et al, 2004).

Johnson et al (1984) favoured immediate fracture stabilization following injury. Their argument was based on the fact that, immediately following injury, patients are in 'the best nutritional condition' and that early definitive fracture stabilization lowers morbidity and mortality. They showed that delay (more than 24 hours post injury) in fracture stabilization leads to a fivefold increase in incidence of adult respiratory distress syndrome. However, the small sample size of this retrospective study and the inclusion of patients with hospital-acquired pneumonia in the adult respiratory distress syndrome group makes it difficult to accept such conclusions.

Reynolds et al (1995) replicated the findings of early femoral fixation (within 24 hours) regarding reduced respiratory complications and mortality. However, when looking closer at the results, patients with an injury severity score >18 had a significantly increased rate of respiratory complications. This indicates that respiratory complications were mainly related to the severity of injury overall rather than the timing of fracture fixation.

This becomes particularly relevant in patients with associated head injuries when early definitive fixation of fractures can add to secondary brain injury by prolonging hypotension and hypoxia (Grotz et al, 2004).

Intensive care unit

Management of patients with haemorrhagic shock does not end in theatre. The patient is subsequently transferred to the intensive care unit where the main goal is to restore severely abnormal physiology by aggressively addressing all three components of the lethal triad (Moore et al, 1998; Jansen et al, 2009; Nunez et al, 2010). This ultimately enables definitive surgery without compromising the patient's physiological status and exacerbating the inflammation cascade. During the intensive care unit phase, the patient's condition is evolving and attention is needed when analysing trends in haemodynamic parameters, such as blood pressure, urine output, saturation, heart and respiratory rates. Also, coagulation profiles, resolution of hypothermia and lactate acid levels are taken into account.

Normalization of the above parameters helps to achieve the most fundamental objective, which is to restore perfusion and subsequent oxygen delivery to the tissues (Blow et al, 1999). Also, monitoring of infection with appropriate use of antibiotics is needed. Polytrauma cases require a multidisciplinary approach and liaison with other medical specialties to aid recovery and rehabilitation.

Definitive surgery

Once the physiology has been corrected the vast majority of patients return to theatre for a definitive procedure, usually within 48 hours of injury. However, some critically ill trauma patients may need to wait more than 48 hours for definitive procedures to be performed. It is essential to recognize that different surgical procedures have a different impact on the patient and some injuries can be left without definitive care for longer than others. However, waiting is not without consequences for a number of reasons.

Lee and Peitzman (2006) showed that patients who return to theatre more than 72 hours post injury have a greater mortality. Deferred abdominal wound closure may require abdominal wall reconstruction at a later stage. Delayed surgery may also be associated with an increased risk of infection. When temporary abdominal packs are still in situ, the risk of infection has to be balanced and occasionally the packs may need changing on intensive care unit. Also, if a temporary external-fixator has been applied following a femoral shaft fracture and a conversion to intramedullary nail is delayed, the risk of local pin site infection is greater (Johnson et al, 1984; Pape et al, 2002).

KEY POINTS

- Prompt haemorrhage recognition and application of the damage control resuscitation concept are the key elements in management of the trauma patient.
- The damage control approach allows normalization of physiological parameters, which increases the survival probability of trauma patients.
- The multidisciplinary trauma team plays a crucial role in the successful outcome of the polytrauma victim from resuscitation to recovery.

Conclusions

The most important end point of damage control resuscitation is oxygen delivery to the tissues, which prevents physiological deterioration and increases the survival probability of trauma patients. This can be achieved by a number of measures including a permissive hypotension strategy, an abbreviated resuscitative surgery, early use of blood products and physiological stabilization on the intensive care unit. However, the key to successful management of the haemorrhage is prompt application of the aforementioned measures by a well-trained trauma team of doctors and nurses who have a clear vision of each step of the resuscitation efforts. Therefore, polytrauma patients should be treated with a holistic approach by the multidisciplinary trauma team from resuscitation until recovery to ensure a successful outcome. **BJHM**

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