Damage Control Management in the Polytrauma Patient

Second Edition

Hans-Christoph Pape
Andrew B. Peitzman
Michael F. Rotondo
Peter V. Giannoudis
Editors

Springer

Damage Control Resuscitation

6

Eric J. Voiglio, Bertrand Prunet, Nicolas Prat, and Jean-Stéphane David

6.1 Introduction

Damage control resuscitation (DCR) for trauma, initially described to address the entire lethal triad immediately upon admission to a combat hospital before damage control surgery (DCS) [1], is now accepted as part of an integrated approach DCR-DCS from point of wounding to definitive treatment [2]. Therefore, DCR can be divided in two steps: while bleeding is ongoing and once bleeding has been stopped.

6.1.1 Physiological Bleeding Control

When bleeding occurs, the baroreceptors located in the aortic arch and carotid sinus detect the drop in arterial pressure. This information is transmitted to the brain stem, which immediately increases sympathetic tone [3]. This increased sympathetic tone causes tachycardia (oxygen transportation is ensured by less blood that circulates faster) and vasoconstriction which favours the blood circulation of the heart and brain at the expense of all other organs and tissues (gut, kidney, muscle and skin). Vasoconstriction at the bleeding site decreases bleeding flow and allows platelets and the activated coagulation factors to seal the leak by a vascular clot [4] (Fig. 6.1). Fibrinolysis regulates coagulation [5] and prevents vascular occlusion. In favourable cases, the bleeding has stopped or slowed. In unfavourable cases, because the vascular breach is too large or the bleeding sites are multiple, the trauma patient is in a situation where the coagulation factors have been consumed, fibrinolysis is activated [6], a large volume of blood has been lost, tachycardia and vasoconstriction are not sufficient to compensate for blood loss and therefore the

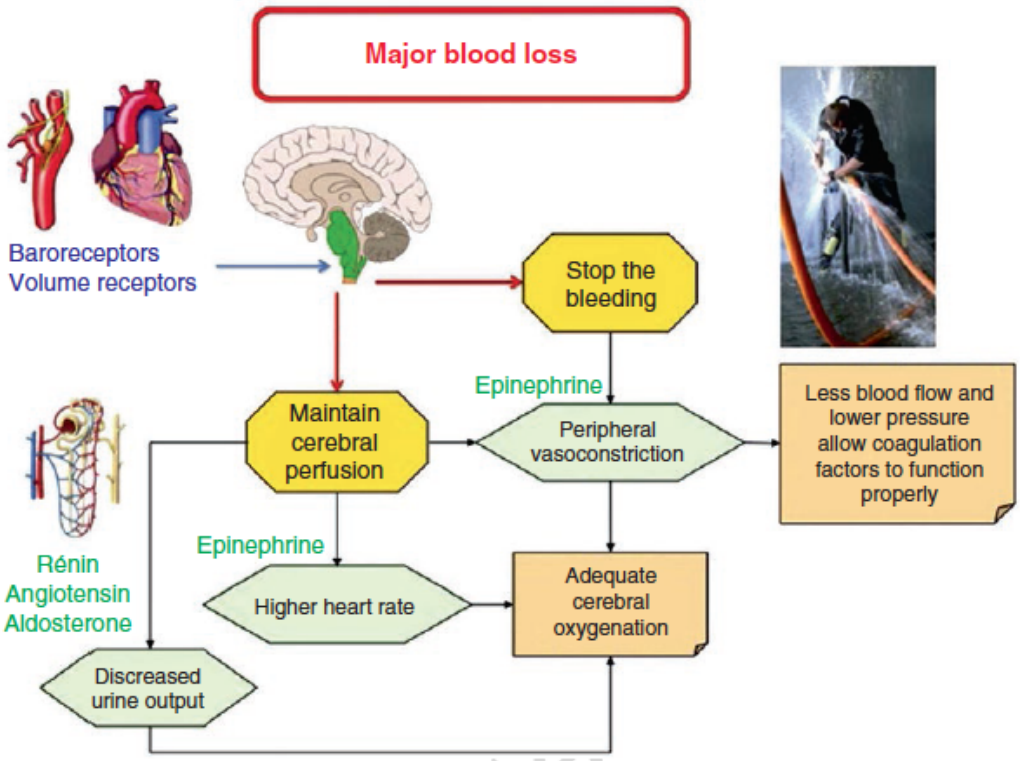
AU1 E.J. Voiglio, MD, PhD, FACS, FRCS, FEBSEmSurg (✉)
University Hospitals of Lyon, Unit of Emergency Surgery, Centre Hospitalier Lyon-Sud, 69495 Pierre-Bénite, France
e-mail: eric.voiglio@chu-lyon.fr

B. Prunet, MD, PhD
Department of Anesthesiology – Intensive Care – Burn Unit, Sainte Anne Military Teaching Hospital, Boulevard Sainte Anne, 83000 Toulon, France
e-mail: bertrand.prunet@intradef.gouv.fr

N. Prat, MD, PhD
War-Related Trauma Unit, French Armed Forces Institute of Biomedical Research, 91220 Bretigny sur Orge, France
e-mail: nicolas-j.prat@intradef.gouv.fr

J.-S. David, MD, PhD
Department of Anesthesiology and Critical Care Medicine, Centre Hospitalier Lyon Sud, Faculté de Médecine Lyon Est, Université Claude Bernard Lyon 1, 69495 Pierre-Bénite, France
e-mail: js-david@univ-lyon1.fr

H. Pape et al. (eds.), *Damage Control Management in the Polytrauma Patient*,
DOI 10.1007/978-3-319-52429-0_6



AU4 **Fig. 6.1** Simplified pathophysiology of bleeding. Bleeding induces hypovolaemia and low blood pressure that trigger volume and baroreceptors which, in turn, transmit the information to the central nervous system [3]. This results in increased sympathetic vascular tone with the double role of maintaining cerebral transfusion and stopping the bleeding. Vasoconstriction in the entire organism (except the heart and brain) deviates the blood supply to the brain, while decreasing blood loss by decreasing the flow and pressure at the level of the vascular injury leaves time for clot formation [4]. Increased heart rate allows partial compensation of the loss of oxygen transportation by increasing the rapidity of red blood cell circulation. At the same time, urine output is decreased by activation of the renin-angiotensin-aldosterone complex with the goal of compensating hypovolemia (E. Voiglio et al. *J Visc Surg*. 2016,153,13–24)

oxygen carrying capacity continues to decrease while the bleeding goes on.

6.1.2 The Lethal Triad: Hypothermia, Acidosis and Coagulopathy

Blood loss causes hypothermia, as the blood plays, among others, the role of a heat transfer liquid. In the cells of a bleeding trauma patient, because of oxygen deficiency, glycolysis stops at the step of pyruvate, which, instead of being consumed by the Krebs cycle, feeds lactate production [7]. Therefore bleeding trauma patient develops lactic acidosis. Coagulation proteins are enzymes that function at 37 °C and pH greater than 7.2. Under hypothermic and acidotic conditions, the coagulation factors have decreased activity [8]. Being the blood hypocoagulable, the bleeding continues later exacerbating hypothermia and acidosis which themselves exacerbate coagulopathy: the haemorrhagic vicious circle [9] is constituted which leads to the death of the trauma patient by exsanguination (Fig. 6.2).

While it is very difficult to take out a trauma patient from this vicious circle, it is very easy to drive him there. It is sufficient to delay the time of haemostasis by a superfluous 'equipment' and unnecessary imaging investigations (further

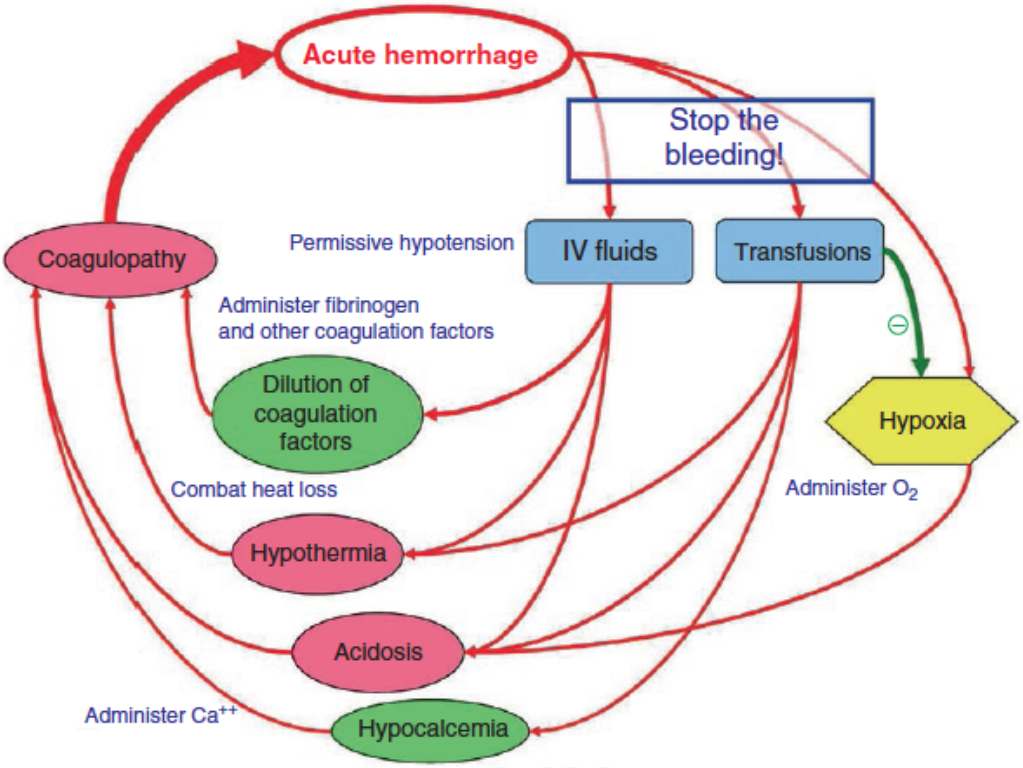


Fig. 6.2 Simplified bloody vicious circle. Acute bleeding triggers cellular hypoxia resulting in metabolic acidosis (lactic acid) [7] and hypothermia (decreased metabolism, loss of heat transport by hypovolaemia). Hypothermia and acidosis lead to coagulopathy because the coagulation factors are enzymes that do not work efficiently below 34 °C and or pH <7.25 [8]. Coagulopathy exacerbates bleeding. Crystalloid volume resuscitation results in dilution of the coagulation factors, cooling and induction of acidosis by dilution and hyperchloraemia. Transfusions add to the deleterious effect of perfusions via the citrate anticoagulants added to PRBC (acidosis and hypocalcaemia) [10]; conversely, transfusions can decrease cell hypoxia by improving oxygen transportation. The only way to interrupt the vicious circle is to stop the bleeding [11]. Administration of oxygen, and limiting IV fluid volume, the strategy of permissive hypotension, combating hypothermia, early transfusion of packed red cells, correction of coagulation disorders by supplying the necessary factors and correction of hypocalcaemia can slow down the vicious circle and buy the time necessary to obtain haemostasis (E. Voiglio et al. *J Visc Surg*. 2016,153,13–24)

haemorrhage), to dilute his/her blood with perfusions (hypothermia, dilution acidosis, anaemia, dilution of coagulation factors, hypocoagulability induced by hydroxyethyl starch [12]) and to rely on a misleading 'haemodynamic stability' artificially achieved by administration of vasopressors (lactic acidosis from visceral and peripheral ischaemia). It has been demonstrated for patients with severe injury of the abdomen and hypotensive at admission that the probability of death increases by 1% every 3 min spent in the shock room [13]. Medico-surgical procrastination is a great provider of haemorrhagic vicious circle.

6.2 Damage Control Resuscitation Before Bleeding Is Stopped

6.2.1 Initial Assessment: Advanced Trauma Life Support (ATLS) Protocol

The treatment of bleeding is to stop the bleeding [11]. *Damage control resuscitation* is a management strategy of which goal is to enable survival of the trauma patient until bleeding is controlled while keeping the risk of iatrogenicity to a minimum. *Damage con-*

trol resuscitation is part of ATLS ABCDE protocol [14] that ensures oxygenation of the cells:

- Airway: airway is most often secured by orotracheal intubation. When orotracheal intubation is impossible and airway has to be secured, cricothyroidotomy is a DC procedure [15]. C-spine is protected by a cervical collar.
- Breathing: trauma patient is given 100% O_2. The SaO_2 is monitored. If a pleural effusion (pneumo- and/or haemothorax) is present, a chest tube is placed. A sucking thoracic wound is treated by a vented chest seal [16].
- Circulation: control of bleeding is initially achieved, depending on situations, by direct pressure eventually enhanced by haemostatic dressings [17], by tourniquet placement [18] or by placement of a pelvic sling [19]. ECG and blood pressure are monitored non-invasively. Two large-bore intravenous lines or one intraosseous line is placed. Crystalloid perfusion is started. In case of haemorrhagic shock, permissive hypotension and transfusion of red blood cell unit (RBC) (O Rh- then type specific) and early plasma administration are recommended [14]. A FAST echography is performed to look for intraperitoneal bleeding and cardiac tamponade [20].
- Disability: GCS score is calculated, pupillary reactivity and symmetry are checked, and focal neurological deficits are searched.
- Exposure: patient's dresses are removed, and a logroll is performed to allow complete examination including the back. Body temperature is monitored.

Whenever a patient presents haemorrhagic shock by an active bleeding that cannot be controlled by external manoeuvres, *damage control* resuscitation is indicated as long as haemostasis has not been achieved most often by surgery, sometimes by interventional radiology.

6.2.2 Targeted Blood Pressure with Permissive Hypotension and Restrictive Fluid Administration

Traditional fluid resuscitation in the polytrauma patient involved rapid infusion of large volumes of clear fluids in an attempt to rapidly restore circulating blood volume and blood pressure. It has become apparent that this approach has several potentially detrimental consequences. The premise of permissive hypotension is to keep the blood pressure low enough to avoid exacerbating haemorrhage by hydrostatic clot disruption while maintaining adequate end-organ perfusion [21]. The concept of damage control resuscitation aims to achieve a lower than normal blood pressure, also called 'permissive hypotension', and thereby avoid the adverse effects of early aggressive resuscitation using high doses of fluids while there is a potential risk of tissue hypoperfusion during short periods [22]. Permissive hypotension and restrictive fluid administration are therefore reciprocal components of this approach; initial fluid administration is delayed or minimized, and less aggressive resuscitative end points are used. A targeted systolic blood pressure (SBP) of 80–90 mmHg is recommended until major bleeding has been stopped in the initial phase following trauma without brain injury [23]. In patients with severe traumatic brain injury (GCS $\leq$8), maintenance of a mean arterial pressure $\geq$80 mmHg is recommended [23]. This approximately equates to aiming for the restoration of a palpable radial pulse. A restrictive fluid administration strategy is recommended to achieve target blood pressure until bleeding can be controlled [23]. Such an approach decreases both the severity and incidence of dilutional coagulopathy and as such complements a strategy of haemostatic resuscitation. Second, this reduces fluctuations in, and elevation of, systolic blood pressure which may disrupt the premature blood clot forming in areas of injury causing further bleeding. Therefore, it would appear that restricting initial IV fluid administration in the severely injured should have advantages, and the

infusion of large volumes of crystalloid is no longer appropriate. In specific situations, permissive hypotension may also be of benefit, particularly in patients with severe haemorrhage from an arterial source. Great caution should be taken in those with concomitant head injury, and further work is required to clearly delineate which patients might benefit the most from this approach [24].

6.2.3 Vasopressor Agents

Vasopressors may be required transiently to sustain life and maintain tissue perfusion in the presence of life-threatening hypotension, even when fluid expansion is in progress and hypovolaemia has not yet been corrected [23]. If used, it is essential to respect the recommended objectives for SBP (80–90 mmHg) in patients without traumatic brain injury [23]. Norepinephrine is the agent of choice to restore and maintain target arterial pressure in haemorrhagic shock. Although it has some β-adrenergic effects, it acts predominantly as a vasoconstrictor. Arterial α-adrenergic stimulation increases arterial resistance and may increase cardiac afterload; norepinephrine exerts both arterial and venous α-adrenergic stimulation. Indeed, in addition to its arterial vasoconstrictor effect, norepinephrine induces venoconstriction at the level of the splanchnic circulation in particular, which increases the pressure in capacitance vessels and actively shifts splanchnic blood volume to the systemic circulation [25]. This venous adrenergic stimulation may recruit some blood from the venous unstressed volume. Moreover, stimulation of β2-adrenergic receptors decreases venous resistance and increases venous return [25]. Animal studies that investigated uncontrolled haemorrhage have suggested that norepinephrine infusion reduces the amount of fluid resuscitation required to achieve a given arterial pressure target, is associated with lower blood loss and significantly improved survival [26, 27].

Furthermore, because vasopressors may increase cardiac afterload if the infusion rate is excessive or left ventricular function is already impaired, an assessment of cardiac function during the initial ultrasound examination is essential. Cardiac dysfunction could be altered in the trauma patient following cardiac contusion, pericardial effusion or secondary to brain injury with intracranial hypertension. The presence of myocardial dysfunction requires treatment with an inotropic agent such as dobutamine or epinephrine. In the absence of an evaluation of cardiac function or cardiac output monitoring, cardiac dysfunction must be suspected in the presence of a poor response to fluid expansion and vasopressor.

6.2.4 Red Blood Cell Transfusion

Blood's main duty is to carry and deliver oxygen to tissues. During bleeding, this capacity is degraded due to two principal phenomena: drop in local blood flow and loss of oxygen carrier, haemoglobin. As seen in the previous section, local blood flow can be restored at least temporarily by fluid infusion and vasopressors use. This fluid infusion, combined with the physiological response to blood loss leading to fluid transfers from cellular and interstitial compartments to the vascular bed, causes the dilution of the haemoglobin and the drop in haemoglobin level (Hb). However, because the relationship between Hb and adverse outcomes in patient with haemorrhagic shock has not been assessed yet [28], it is not possible to determine with certitude the optimal Hb in trauma patients.

Because no artificial oxygen carrier is available so far, the only way to restore the capability of blood to carry oxygen to the tissues is to transfuse RBCs. RBCs are available as packed RBCs (PRBCs) from blood banks. The shelf storage time is limited to about 40 days at 4 °C, but the longer the storage, the more lysed RBCs release intracellular toxic content as potassium or free haemoglobin. This is why a LIFO (last in, first out) procedure for PRBCs release from blood banks needs to be implemented for severely injured patients [29].

In the *European* guidelines, the Hb threshold for PRBCs transfusion is set to 7–9 g/dL [23] where in US guidelines Hb is set to 7 g/dL [30]. These recommendations are based on studies showing that PRBCs transfusions can be associated with increased mortality, lung injury, increased infection rate and renal failure in injured patients and mainly on the *Transfusion Requirements in Critical Care* (TRICC) study demonstrating no efficacy of liberal approach (Hb threshold of 10–12 g/dL) versus restricted approach (7–9 g/dL) on mortality [31]. For patients with concomitant haemorrhagic shock and traumatic brain injury, recent studies demonstrate no beneficial effect of a higher Hb threshold for RBCs transfusion on mortality or neurological outcomes but a higher risk of thromboembolic events [32, 33], even if a higher Hb improves local cerebral oxygenation [34].

RBCs play also a major role in haemostasis. Circulating RBCs marginate the platelets close to the endothelium, enhancing their adhesion capabilities [35], and support thrombin generation providing interactions with coagulation factors on their cellular surfaces [36].

6.2.5 Fibrinolysis Prevention

Fibrinolysis is a key component of the physiological haemostasis system. It mainly involves the tissue plasminogen activator (tPA) and its inhibitors, the plasminogen activator inhibitors (PAI1 and 2) to regulate the activation of the plasminogen into plasmin, responsible for fibrin binding and degradation. However, a huge stimulation of the coagulation system after severe trauma and activated protein C (aPC) system activation by tissue hypoperfusion [37] can lead to an exacerbation of the fibrinolysis. This hyperfibrinolysis is an essential part of the ACoT and is associated with a mortality rate of nearly 90% [38].

The best way to assess hyperfibrinolysis in trauma patients is to use viscoelastic tests. However, the low sensitivity of this method does not allow to detect low increases in fibrinolytic activity, still accountable for ACoT [39].

Hyperfibrinolysis contribution to ACoT can be lower by the use of an antifibrinolytic agent. The CRASH-2 study [40] assessed the systematic injection of tranexamic acid (TXA) in trauma patients with or at risk of severe bleeding. The competitive binding of the plasminogen/plasmin site on the fibrin allows the TXA to inhibit the fibrinolysis. The injection of a loading dose of 1 g of TXA over 10 min followed by the infusion of 1 g over 8 h led to a significant reduction in mortality from bleeding without an increase in thromboembolic events rate. From that same trial, a deeper analysis showed that TXA lowers the risk of death by bleeding by 2.5% if given less than 1 h after trauma and by 1.3% if given between 1 and 3 h after trauma. However, the risk is increased by 1.3% if the TXA is given more than 3 h after trauma [41]. The MATTERs study conducted in military setting later consolidated these conclusions [42]. Based on these results, European guidelines recommend the systematic injection of TXA (1 g/10 min, 1 g/8 h) as soon as possible, within the 3 h after the injury [23].

6.2.6 Plasma and Platelet Transfusion in Haemostatic Resuscitation

Coagulation factors and platelets can be shed, consumed, diluted or inactivated in severe trauma patients. Even if they play only a partial role in the ACoT, their replacement is crucial to restore the haemostasis. Standard available fresh frozen plasma (FFP) contains all the major coagulation factors in proportions close to the physiological levels and seems to have anti-inflammatory property while lessening the endothelial hyperpermeability after haemorrhagic shock [43]. Its transfusion should be initiated as soon as possible to avoid iatrogenic or physiological dilutional coagulopathy during a balanced resuscitation with PRBCs. However, the optimal ratio of FFP to PRBCs remains of debate. Some studies showed a potential benefit of an FFP-PRBCs ratio close to 1:1 [44, 45]. However, these results were discussed and potentially flawed by survival bias (i.e. less severe patients survive longer

enough to get more plasma, thawed plasma being available later than PRBCs) [46]. The recent PROPPR randomized clinical trial [47] compared 1:1:1 FFP-PLT-PRBCs ratio to 1:1:2 in severe trauma patients without survival bias. Unfortunately, the results showed a nonstatistically significant reduction in mortality for the 1:1:1 ratio group, letting the question open. European guidelines propose to transfuse 1 FFP every two PRBCs during the initial management of patients with expected massive haemorrhage, continued with goal-directed therapy based on standard laboratory (PT or aPTT inferior to 1.5 times the normal controls) and/or viscoelastic tests [23]. To resolve the delay in availability of the FFP, plasma can be stored as thawed plasma or liquid (fresh nonfrozen) plasma. But in this form, labile coagulation factors like FVIII can be depleted [48]. Lyophilized plasma provided by the *French* military is a nice option. Available in 10 min, stable at room temperature and universal, it offers a great alternative to FFP [49].

Fibrinogen, a key component in the coagulation cascade, is the first and most depleted factor in haemorrhagic trauma patients [50]. However, FFP concentration in fibrinogen is not high enough to restore fibrinogen levels with only FFP transfusion [51], and it may be required to administered fibrinogen through cryoprecipitate or fibrinogen concentrate.

Platelet depletion or dysfunction [52] in trauma patients needs to be addressed by platelet transfusion. Platelets are available as platelet concentrate (PLT) or apheresis platelets (aPLT) containing approximately six times more platelets and plasma. *European* guidelines [44] propose to transfuse platelets if platelet count is less than 50.10^9/L in trauma patients or less than 100.10^9/L in case of ongoing bleeding or traumatic brain injury.

The best way to replace shed whole blood after or during haemorrhage would be to use whole blood, in replacement for component therapy. Even if used and authorized in remote military setting when blood products are lacking and needs for transfusion surge [53, 54], this technique has not reached the routine clinical practices because of some misconceptions (necessity for whole blood to be ABO specific, impossibility to obtain leucoreduced whole blood while maintaining platelets and loss of platelet function caused by cold storage) [55].

6.2.7 Viscoelastic Techniques and Administration of Concentrated Factors

Standard coagulation tests are of little use for haemorrhagic shock management because they generally require more than an hour, and urgent corrective action may not be delayed that long. To adapt the treatment of haemostasis after the initial phase, viscoelastic techniques (VETs) may be very useful. VETs have been developed for several years and represent a comprehensive assessment of clot formation based on the mechanisms originating coagulopathy, including, in a second stage, inflammatory phenomena [56, 57]. It is possible to obtain a faster and more accurate evaluation of haemostasis through the use of activator or inhibitor which allows to distinguish phenomena occurring during ongoing bleeding such as fibrinogen deficit and hyperfibrinolysis. Identifying deficits makes possible to intervene specifically with clotting factor concentrates, avoiding the use of labile blood products (LBP), and, although this remains to be demonstrated formally, reduce morbidity related to the use of the LBP (multiple organ failure, infection, ARDS, TRALI and TACO) [58–60]. According to the latest European guidelines, VETs are accepted as alternative to standard coagulation tests to guide the treatment of posttraumatic coagulopathy (grade 1C) [23].

6.2.7.1 Principles of Clot Viscoelastic Property Studies

Clot formation is assessed with ROTEM® (Tem GMBH, Munich, Germany) or with TEG® (Haemoscope Corporation, Niles, Illinois, USA). These tools explore dynamics of clot development, stabilization and dissolution (fibrinolysis) [60–64]. The measured parameters are time (s), amplitude (mm) or angles. The measurements are

made on whole blood collected in a citrated tube. The recalcified blood is then placed in a cuvette heated to 37 °C (or to temperature of the patient), in which a pin is plunged. The speed of rotation thereof will depend on the viscosity of blood. According to the technique, it is either the cuvette which rotates (TEG®) or the pin (ROTEM®). In the latest version of TEG®, measures are made by an electro-optical technique. To accelerate the technical and differentiating phenomena involved in haemostasis disorders, activators are added. They depend on the type of techniques used [60].

ROTEM® analyser uses routinely four channels: INTEM (intrinsic contact activation pathway explored by adding ellagic acid), EXTEM (extrinsic pathway explored by adding tissue factor), FIBTEM (addition of cytochalasin D which blocks the platelets to explore fibrinogen function) and APTEM (addition of aprotinin for inhibiting and therefore exploring fibrinolysis). Two other channels are used in specific circumstances: HEPTEM (INTEM + heparinase to assess heparin effect) and ECATEM (addition of ecarin to detect thrombin inhibitors). In trauma, most useful channels are EXTEM and FIBTEM. Thus, a deficit in prothrombin and in fibrinogen and a low platelet count can be discriminated. As an example, an EXTEM with a short clotting time (thrombin formation correct) and with a diminished maximal clot firmness will suggest low platelet activity if maximal clot firmness is normal with FIBTEM.

TEG® analyser uses generally one single channel after activation by kaolin (equivalent to INTEM). However, it has been shown that platelet and fibrinogen contributions to maximal amplitude could not be differentiated [65]. Therefore TEG® can now be performed with addition of both tissue factor and kaolin (rapid-TEG) to explore the extrinsic pathway, and with addition of abciximab, a potent platelet inhibitor, to explore fibrinogen function [66].

6.2.7.2 Coagulopathy Diagnosis by VETs

At admission, the results of the standard biology are correlated to some ROTEM® parameters, e.g. clotting time (CT) (EXTEM) and PT (prothrombin time) or maximal clot firmness (MCF) (FIBTEM) and level of fibrinogen [67, 68]. Similarly, TEG® R parameter (equivalent to CT) is correlated to PT; correlations were observed between the parameter R (equivalent to CT) and PT [69, 70]. However, this good correlation between standard and viscoelastic techniques at admission may vary during the management [57]. Thus, a CT EXTEM is less correlated to PT after attempt to correct coagulopathy and/or depending to pathophysiological criteria as acidosis and hypothermia [57]. The standard test that estimates the concentration of clotting factors does not take into account the effect of inflammation that develops in the hours following the trauma and activates coagulation. Thus, only VETs that take into account all parameters can provide a fair image of coagulation status [57]. The possibility to predict the need for massive transfusion has been reported with ROTEM® [68, 71, 72] as well as with TEG® (rapid-TEG) [73]. Many algorithms have been proposed to treat bleeding disorders. However these algorithms are specific to either technique and non-interchangeable.

6.2.7.3 VETs and Coagulation Factor Concentrates

Post-traumatic coagulopathy is complex and includes phenomena of coagulation factor loss, dilution, thrombocytopenia, platelet disorders, consumption and fibrinolysis [74]. Fibrinogen deficiency is the most observed among factor deficiencies. The massive release of tissue factor which activates haemostasis and increases thrombin generation is important to consider. Thus, in trauma patients, thrombin generation remains increased as long as factor levels remain >30% [75]. This increase in thrombin generation associated with the frequently observed fibrinogen deficiency suggests the order of administration of haemostatic products. It is thus likely that fibrinogen concentrates have to be administered first, followed in a second phase (ideally according to standard coagulation tests or VETs) by the FFP and the PC (or PCC ? prothrombin complex concentrate) except, of course, situations of severe haemorrhagic shock when fibrinogen FFP and PCC are administered simultaneously. This

method is only valid when fibrinogen concentrates are available (fibrinogen concentrates and/or cryoprecipitate).

ROTEM® was evaluated in trauma through retrospective or prospective observational studies. The level of proof thus remains relatively low. Schöchl et al. suggested in a first study that ROTEM®-guided administration of coagulation factors improved patient survival when compared to a predictive mortality score (TRISS) [76]. The same group showed that when comparing patients treated with factor concentrates guided by ROTEM® with patients receiving labile blood components (LBC) guided by the standard biology, they could reduce significantly the use of LBC but also the incidence of multiple organ failure without affecting survival [77]. In a recent study, an Italian team confirmed the reduction of the use of LBC reducing costs significantly by more than 23% but still with no change in survival [78]. The issue with all these studies (however this could also be considered an advantage) is that ROTEM® use is combined with that of factor concentrates making it difficult to know what ultimately is most important [79]. A European randomized study should start soon to compare standard biology and ROTEM® using LBP in the same initial ratio (iTACTIC Study, NCT02593877, trial.gouv).

As regards TEG®, a retrospective study involving 1974 patients showed that TEG® could perfectly replace the standard biological tests [80]. In a recent randomized work, it has been shown that the use of TEG® in comparison with the standard biology could improve patient survival at 28 days without association with a modification of LBP consumption in the first 24 h except for cryoprecipitate (paradoxically greater in the group standard biology). A higher consumption of FFP and PCC was observed in the group standard biology in the early hours [81]. According to the authors, this result was related primarily to a decreased mortality from bleeding and a decreased early mortality by earlier diagnosis of coagulopathy and appropriate action. A reduction of ICU stay length with an increased number of ventilator-free days was also observed.

Finally, in severe trauma, situations of hyperfibrinolysis whose prognosis is catastrophic can be observed. TEG® and ROTEM® allow a rapid and accurate diagnosis of hyperfibrinolyses [82] but will lack sensitivity to assess the intensity of fibrinolysis especially if minor or moderate [39]. Usually thresholds of 3% maximum fibrinolysis (maximum lysis) on TEG® and 15% on ROTEM® are applied to diagnose hyperfibrinolysis. If in Europe, tranexamic acid is widely used since the CRASH-2 trial in severe trauma [40], in North America, the practice is rather to administer tranexamic acid to patients with hyperfibrinolysis documented by VETs [82].

6.3 Damage Control Resuscitation once Bleeding Has Been Stopped

Further resuscitation once haemostasis has been achieved is the intensive care unit resuscitative phase where physiological and biochemical stabilization is achieved and a thorough tertiary examination is performed to identify all injuries (Fig. 6.3) [83]. This step is devoted to reverse the sequelae of hypotension-related metabolic failure and support physiological and biochemical restoration. Simultaneous treatment of all physiological abnormalities is essential, and as a result, the first several hours in the ICU are extremely labour intensive and often require the collaborative efforts of multiple critical care physicians, nurses and ancillary staff [84]. Efforts to warm during surgery, shorten the shock and improve coagulation are pursued. An aggressive approach to correction of coagulopathy is paramount, and procoagulant objectives remain the same. Assessment of visceral dysfunction is achieved (in particular the lung, kidney and liver). One of the keys to physiological restoration is the establishment of adequate oxygen delivery to body tissues. Haemodynamic optimization in this step of major post-shock inflammation often requires a significant fluid volume expansion due to vasodilation. The needs of vasopressors can also be very consequent. Objectives of blood pressure change and aim to restore adequate perfusion of

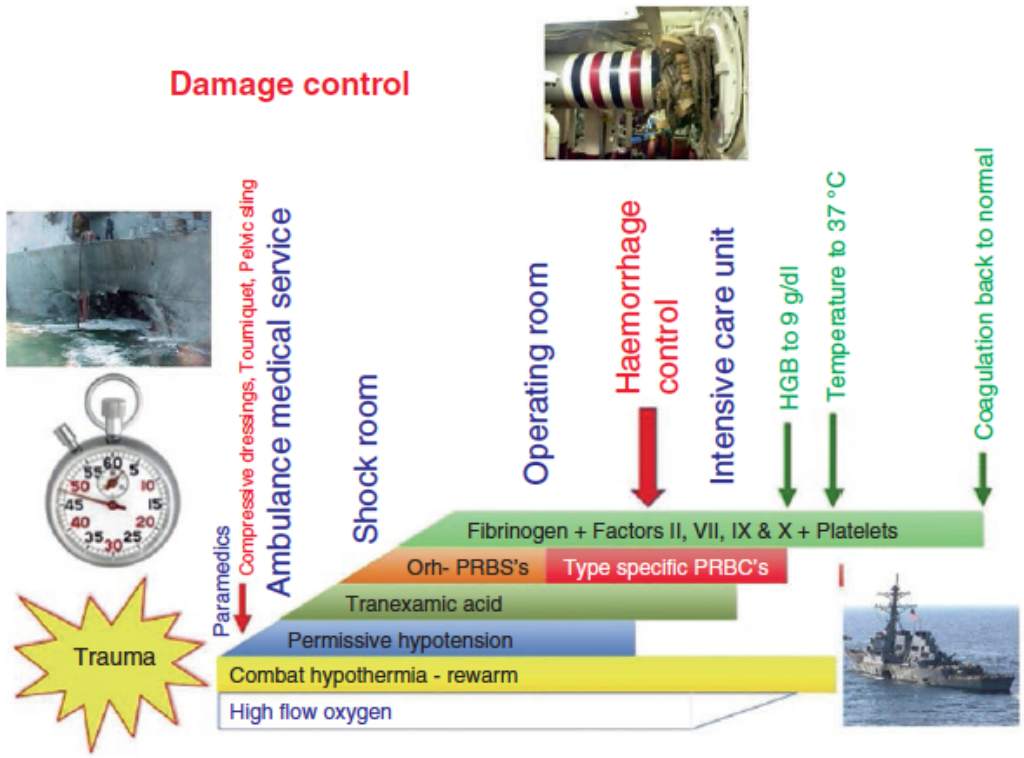


Fig. 6.3 Increasing power of damage control. Damage control should be started in the field by the paramedics who are trained to stop bleeding with local pressure or tourniquets, administer oxygen and combat hypothermia. The race against the clock starts. The emergency team in the field should strive for only minimal vascular filling, the objective being to obtain a systolic blood pressure of 90 mmHg [23]; tranexamic acid should be administered [42]. O-negative and then type-specific PRBC transfusions are started with the objective of obtaining haemoglobin of 9 g/dL (according to European guidelines [23]); coagulation disorders are corrected by administration of fibrinogen [23],coagulation factors [77] and platelet concentrates [23]. The patient is transferred rapidly to the operating room (or angiography suite, as necessary). When bleeding has been arrested, blood pressure should return to normal. Damage control resuscitation should be pursued until preset objectives of haemoglobin, temperature and coagulation parameters are attained. The comparison with naval damage control can be made in that not only should the water inflow be stopped, but the vital functions of the vessel must be restored as well (electricity, communications, propulsion, rudder) (E. Voiglio et al. *J Visc Surg*. 2016,153,13–24)

all organs (MAP = 65 mmHg). Invasive monitoring devices are generally used to guide fluid administration and normalize haemodynamics. Abramson and colleagues did show that serum lactate clearance correlates well with patient survival and that the ability to clear lactate to normal levels within 24 h was paramount to ensuing patient survival [85]. Immediate and aggressive core rewarming not only improves perfusion but also helps reverse coagulopathy. All of the warming manoeuvres initiated in the trauma bay and operating theatre should be duplicated in the intensive care unit. Gentilello showed that failure to correct a patient's hypothermia after a damage control operation is a marker of inadequate resuscitation or irreversible shock [84]. A complete physical examination or 'tertiary survey' of the patient should occur. This should include relevant imaging studies where appropriate, and the patient should also proceed to CT scan to detect occult injuries if stable enough. In cases of blunt trauma, completion of the spinal survey is imperative. Finally, the scheduled revision surgery is the last step of the DC strategy and occurs after 12–48 h (sometimes 72 h) of stabilization. The consensual approach is to consider the second look when lethal triad is under control. It has two objectives: the final repair organs (packings

removal, intestinal anastomoses and definitive vascular repair) and the permanent closure of the abdomen. One should keep in mind that if a patient does not normalize haemodynamically or lactic acid or base deficit fail to improve, the patient should be taken back to the operating theatre earlier for re-exploration. Generally, two subgroups of patients are seen in this step that require 'unplanned' re-operation before physiological restoration. The first is the group of patients who have ongoing transfusion requirements or persistent acidosis despite normalized clotting and core temperature. Monitoring of the clinical (blood pressure, tachycardia, suction drains, dressings) and biological parameters (haemoglobin, lactate level) can lead to the decision to further surgery and/or angiography. These patients are usually found to have ongoing surgical bleeding or a missed visceral injury that was not treated adequately during the initial damage control operation and have a very high mortality rate [86]. The second group requiring unplanned return to the operating theatre have developed abdominal compartment syndrome defined as sustained or repeated intravesical pressure above 20 mmHg in the presence of new single or multiple organ system failure [87]. This could be the consequence of abdominal trauma which is accompanied by a visceral oedema and haematomas but also the use of intra-abdominal packing.

Conclusion

The treatment of bleeding remains to stop the bleeding. DCR is together with DCS part of a global DC strategy. DCR is a potent tool to hinder and even reverse the lethal triad. Delaying bleeding control under the pretext that DCR is available and effective is a fallacious conduct that results in increased morbidity and mortality.

References

1. Holcomb JB, Jenkins D, Rhee P, Johannigman J, Mahoney P, Mehta S, Cox ED, Gehrke MJ, Beilman GJ, Schreiber M, Flaherty SF, Grathwohl KW, Spinella PC, Perkins JG, Beekley AC, McMullin NR, Park MS, Gonzalez EA, Wade CE, Dubick MA, Schwab CW, Moore FA, Champion HR, Hoyt DB, Hess JR. Damage control resuscitation: directly addressing the early coagulopathy of trauma. J Trauma. 2007;62(2):307–10.
2. Fries CA, Midwinter MJ. Trauma resuscitation and damage control surgery. Surgery (Oxford). 2010;28(11):563–7.
3. Heesch CM. Reflexes that control cardiovascular function. Am J Phys. 1999;277:S234–43.
4. Clemetson KJ. Platelets and primary haemostasis. Thromb Res. 2012;129:220–4.
5. Chapin JC, Hajjar KA. Fibrinolysis and the control of blood coagulation. Blood Rev. 2014. pii: S0268-960X(14)00072–1. doi: 10.1016/j.blre.2014.09.003. Epub ahead of print.
6. Hess JR, Brohi K, Dutton RP, et al. The coagulopathy of trauma: a review of mechanisms. J Trauma. 2008;65:748–54.
7. Huckabee WE. Relationship of pyruvate and lactate during anaerobic metabolism. I. Effects of infusion of pyruvate or glucose and of hyperventilation. J Clin Invest. 1958;37:244–54.
8. Martini WZ. Coagulopathy by hypothermia and acidosis: mechanisms of thrombin generation and fibrinogen availability. J Trauma. 2009;67(1):202–8. discussion 208-9
9. Moore EE. Thomas G. Orrr Memorial Lecture. Staged laparotomy for the hypothermia, acidosis, and coagulopathy syndrome. Am J Surg. 1996; 172:405–10.
10. Churchill-Davidson HC. Some problems of massive blood transfusion. Proc R Soc Med. 1968;61:681–2.
11. Boffard KD, Choong PI, Kluger Y, et al. The treatment of bleeding is to stop the bleeding! Treatment of trauma-related hemorrhage. Transfusion. 2009;49:240S–7S.
12. Cabrales P, Tsai AG, Intaglietta M. Resuscitation from hemorrhagic shock with hydroxyethyl starch and coagulation changes. Shock. 2007;28:461–7.
13. Clarke JR, Trooskin SZ, Doshi PJ, et al. Time to laparotomy for intra-abdominal bleeding from trauma does affect survival for delays up to 90 minutes. J Trauma. 2002;52:420–5.
14. ATLS Subcommittee, American College of Surgeons' Committee on Trauma, International ATLS working group. Advanced trauma life support (ATLS®): the ninth edition. J Trauma Acute Care Surg. 2013;74:1363–6.
15. Frerk C, Mitchell VS, McNarry AF, Mendonca C, Bhagrath R, Patel A, O'Sullivan EP, Woodall NM, Ahmad I, Difficult Airway Society intubation guidelines working group. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. Br J Anaesth. 2015;115(6):827–48.
16. Butler FK, Dubose JJ, Otten EJ, Bennett DR, Gerhardt RT, Kheirabadi BS, Gross KR, Cap AP, Littlejohn LF, Edgar EP, Shackelford SA, Blackbourne LH, Kotwal RS, Holcomb JB, Bailey JA. Management of open pneumothorax in tactical combat casualty care: TCCC guidelines change 13-02. J Spec Oper Med. 2013;13(3):81–6.

17. Granville-Chapman J, Jacobs N, Midwinter MJ. Pre-hospital haemostatic dressings: a systematic review. Injury. 2011;42:447–59.
18. Kragh Jr JF, Walters TJ, Baer DG, et al. Survival with emergency tourniquet use to stop bleeding in major limb trauma. Ann Surg. 2009;249:1–7.
19. Hornez E, Maurin O, Bourgouin S, et al. Management of exsanguinating pelvic trauma: do we still need the radiologist? J Visc Surg. 2011;148:e379–84.
20. Scalea TM, Rodriguez A, Chiu WC, et al. Focused assessment with sonography for trauma (FAST): results from an international consensus conference. J Trauma. 1999;46:466–72.
21. Giannoudi M, Harwood P. Damage control resuscitation: lessons learned. Eur J Trauma Emerg Surg. 2016;42:273–82.
22. Waydhas C, German Society of Trauma Surgery (DGU). Preclinical management of multiples injuries: S3 guideline. Unfallchirurg. 2012;115(1):8–13.
23. Rossaint R, Bouillon B, Cerny V, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition. Crit Care. 2016;20:100.
24. Kaafarani HM, Velmahos GC. Damage control resuscitation in trauma. Scand J Surg. 2014;103(2):81–8.
25. Gelman S, Mushlin PS. Catecholamine-induced changes in the splanchnic circulation affecting systemic hemodynamics. Anesthesiology. 2004;100(2):434–9.
26. Poloujadoff MP, Borron SW, Amathieu R, Favret F, Camara MS, Lapostolle F, et al. Improved survival after resuscitation with norepinephrine in a murine model of uncontrolled hemorrhagic shock. Anesthesiology. 2007;107(4):591–6.
27. Harrois A, Baudry N, Huet O, Kato H, Dupic L, Lohez M, et al. Norepinephrine decreases fluid requirements and blood loss while preserving intestinal villi microcirculation during fluid resuscitation of uncontrolled hemorrhagic shock in mice. Anesthesiology. 2015;122(5):1093–102.
28. Bouglé A, Harrois A, Duranteau J. Resuscitative strategies in traumatic hemorrhagic shock. Ann Intensive Care. 2013;3:1.
29. Spinella PC, Dunne J, Beilman GJ, O'Connell RJ, Borgman MA, Cap AP, Rentas F. Constant challenges and evolution of US military transfusion medicine and blood operations in combat. Transfusion. 2012;52:1146–53.
30. Napolitano LM, Kurek S, Luchette FA, Corwin HL, Barie PS, Tisherman SA, Hebert PC, Anderson GL, Bard MR, Bromberg W, Chiu WC, Cipolle MD, Clancy KD, Diebel L, Hoff WS, Hughes KM, Munshi I, Nayduch D, Sandhu R, Yelon JA. Clinical practice guideline: red blood cell transfusion in adult trauma and critical care*. Crit Care Med. 2009;37:3124–57.
31. McIntyre L, Hebert PC, Wells G, Fergusson D, Marshall J, Yetisir E, Blajchman MJ, Canadian Critical Care Trials Group. Is a restrictive transfusion strategy safe for resuscitated and critically ill trauma patients? J Trauma: Inj Infect Crit Care. 2004;57:563–8. discussion 568
32. Elterman J, Brasel K, Brown S, Bulger E, Christenson J, Kerby JD, Kannas D, Lin S, Minei JP, Rizoli S, Tisherman S, Schreiber MA, Resuscitation Outcomes Consortium Investigators. Transfusion of red blood cells in patients with a prehospital Glasgow Coma Scale score of 8 or less and no evidence of shock is associated with worse outcomes. J Trauma Acute Care Surg. 2013;75:8–14. discussion 14
33. Robertson CS, Hannay HJ, Yamal J-M, Gopinath S, Goodman JC, Tilley BC, Epo Severe TBI Trial Investigators, Baldwin A, Rivera Lara L, Saucedo-Crespo H, Ahmed O, Sadasivan S, Ponce L, Cruz-Navarro J, Shahin H, Aisiku IP, Doshi P, Valadka A, Neipert L, Waguspack JM, Rubin ML, Benoit JS, Swank P. Effect of erythropoietin and transfusion threshold on neurological recovery after traumatic brain injury: a randomized clinical trial. JAMA. 2014;312:36–47.
34. Smith MJ, Stiefel MF, Magge S, Frangos S, Bloom S, Gracias V, Le Roux PD. Packed red blood cell transfusion increases local cerebral oxygenation. Crit Care Med. 2005;33:1104–8.
35. Spann AP, Campbell JE, Fitzgibbon SR, Rodriguez A, Cap AP, Blackbourne LH, Shaqfeh ESG. The effect of hematocrit on platelet adhesion: experiments and simulations. Biophys J. 2016;111:577–88.
36. Peyrou V, Lormeau JC, Hérault JP, Gaich C, Pfliegger AM, Herbert JM. Contribution of erythrocytes to thrombin generation in whole blood. Thromb Haemost. 1999;81:400–6.
37. Brohi K, Cohen MJ, Ganter MT, Matthay MA, Mackersie RC, Pittet J-F. Acute traumatic coagulopathy: initiated by hypoperfusion: modulated through the protein C pathway? Ann Surg. 2007;245:812–8.
38. Heim C, Steurer MP, Brohi K. Damage control resuscitation: more than just transfusion strategies. Curr Anesthesiol Rep. 2016. doi:10.1007/s40140-016-0145-x.
39. Raza I, Davenport R, Rourke C, Platton S, Manson J, Spoors C, Khan S, De'Ath HD, Allard S, Hart DP, Pasi KJ, Hunt BJ, Stanworth S, MacCallum PK, Brohi K. The incidence and magnitude of fibrinolytic activation in trauma patients. J Thromb Haemost. 2013;11:307–14.
40. CRASH-2 trial collaborators, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, Dewan Y, El-Sayed H, Gogichaishvili T, Gupta S, Herrera J, Hunt B, Iribhogbe P, Izurieta M, Khamis H, Komolafe E, Marrero M-A, Mejía-Mantilla J, Miranda J, Morales C, Olaomi O, Olldashi F, Perel P, Peto R, Ramana PV, Ravi RR, Yutthakasemsunt S. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet. 2010;376:23–32.
41. CRASH-2 collaborators, Roberts I, Shakur H, Afolabi A, Brohi K, Coats T, Dewan Y, Gando S, Guyatt G,

Hunt BJ, Morales C, Perel P, Prieto-Merino D, Woolley T. The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. Lancet. 2011;377:1096–101. 1101.e1–2

42. Morrison JJ. Military application of tranexamic acid in trauma emergency resuscitation (MATTERs) study. Arch Surg. 2012;147:113.
43. Peng Z, Pati S, Potter D, Brown R, Holcomb JB, Grill R, Wataha K, Park PW, Xue H, Kozar RA. Fresh frozen plasma lessens pulmonary endothelial inflammation and hyperpermeability after hemorrhagic shock and is associated with loss of syndecan 1. Shock. 2013;40:195–202.
44. Borgman MA, Spinella PC, Perkins JG, Grathwohl KW, Repine T, Beekley AC, Sebesta J, Jenkins D, Wade CE, Holcomb JB. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. J Trauma. 2007;63:805–13.
45. Kashuk JL, Moore EE, Johnson JL, Haenel J, Wilson M, Moore JB, Cothren CC, Biffl WL, Banerjee A, Sauaia A. Postinjury life threatening coagulopathy: is 1:1 fresh frozen plasma:packed red blood cells the answer? J Trauma. 2008;65:261–70. – discussion 270–1
46. Snyder CW, Weinberg JA, McGwin G, Melton SM, George RL, Reiff DA, Cross JM, Hubbard-Brown J, Rue LW, Kerby JD. The relationship of blood product ratio to mortality: survival benefit or survival bias? J Trauma. 2009;66:358–62. discussion 362–4
47. Holcomb JB, Tilley BC, Baraniuk S, Fox EE, Wade CE, Podbielski JM, del Junco DJ, Brasel KJ, Bulger EM, Callcut RA, Cohen MJ, Cotton BA, Fabian TC, Inaba K, Kerby JD, Muskat P, O'Keeffe T, Rizoli S, Robinson BRH, Scalea TM, Schreiber MA, Stein DM, Weinberg JA, Callum JL, Hess JR, Matijevic N, Miller CN, Pittet J-F, Hoyt DB, Pearson GD, Leroux B, van Belle G, PROPPR Study Group. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. JAMA. 2015;313:471–82.
48. Downes KA, Wilson E, Yomtovian R, Sarode R. Serial measurement of clotting factors in thawed plasma stored for 5 days. Transfusion. 2001;41:570.
49. Sailliol A, Martinaud C, Cap AP, Civadier C, Clavier B, Deshayes A-V, Mendes A-C, Pouget T, Demazeau N, Chueca M, Martelet F-R, Ausset S. The evolving role of lyophilized plasma in remote damage control resuscitation in the French Armed Forces Health Service. Transfusion. 2013;53(Suppl 1):65S–71S.
50. Rourke C, Curry N, Khan S, Taylor R, Raza I, Davenport R, Stanworth S, Brohi K. Fibrinogen levels during trauma hemorrhage, response to replacement therapy, and association with patient outcomes. J Thromb Haemost. 2012;10:1342–51.
51. Hagemo JS, Stanworth S, Juffermans NP, Brohi K, Cohen M, Johansson PI, Røislien J, Eken T, Næss PA, Gaarder C. Prevalence, predictors and outcome of hypofibrinogenaemia in trauma: a multicentre observational study. Crit Care. 2014;18:R52.
52. Ramsey MT, Fabian TC, Shahan CP, Sharpe JP, Mabry SE, Weinberg JA, Croce MA, Jennings LK. A prospective study of platelet function in trauma patients. J Trauma Acute Care Surg. 2016;80:726–32. discussion 732–3
53. Sailliol A, Ausset S, Peytel E. Blood transfusion in emergency settings: French military health service experience. Transfus Clin Biol. 2010;17:279–83.
54. Spinella PC, Perkins JG, Grathwohl KW, Beekley AC, Holcomb JB. Warm fresh whole blood is independently associated with improved survival for patients with combat-related traumatic injuries. J Trauma: Inj Infect Crit Care. 2009;66:S69–76.
55. Spinella PC, Pidcoke HF, Strandenes G, Hervig T, Fisher A, Jenkins D, Yazer M, Stubbs J, Murdock A, Sailliol A, Ness PM, Cap AP. Whole blood for hemostatic resuscitation of major bleeding. Transfusion. 2016;56:S190–202.
56. Haas T, Fries D, Tanaka KA, Asmis L, Curry NS, Schochl H. Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: is there any evidence? Br J Anaesth. 2015;114(2):217–24.
57. David JS, Durand M, Levrat A, Lefevre M, Rugeri L, Geay-Baillat MO, et al. Correlation between laboratory coagulation testing and thromboelastometry is modified during management of trauma patients. J Trauma Acute Care Surg. 2016;81:319–27.
58. Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. Am J Hematol. 2014;89(2):228–32.
59. Schochl H, Schlimp CJ. Trauma bleeding management: the concept of goal-directed primary care. Anesth Analg. 2014;119(5):1064–73.
60. Hans GA, Besser MW. The place of viscoelastic testing in clinical practice. Br J Haematol. 2016;173(1):37–48.
61. Luddington RJ. Thrombelastography/thromboelastometry. Clin Lab Haematol. 2005;27:81–90.
62. Perry DJ, Fitzmaurice DA, Kitchen S, Mackie IJ, Mallett S. Point-of-care testing in haemostasis. Br J Haematol. 2010;150(5):501–14.
63. Jackson GN, Ashpole KJ, Yentis SM. The TEG vs the ROTEM thromboelastography/thromboelastometry systems. Anaesthesia. 2009;64(2):212–5.
64. Nielsen VG. A comparison of the Thrombelastograph and the ROTEM. Blood Coagul Fibrinolysis. 2007;18(3):247–52.
65. Larsen OH, Fenger-Eriksen C, Christiansen K, Ingerslev J, Sorensen B. Diagnostic performance and therapeutic consequence of thromboelastometry activated by kaolin versus a panel of specific reagents. Anesthesiology. 2011;115(2):294–302.

66. Solomon C, Schochl H, Ranucci M, Schlimp CJ. Can the viscoelastic parameter alpha-angle distinguish fibrinogen from platelet deficiency and guide fibrinogen supplementation? Anesth Analg. 2015;121(2):289–301.
67. Tauber H, Innerhofer P, Breitkopf R, Westermann I, Beer R, El Attal R, et al. Prevalence and impact of abnormal ROTEM(R) assays in severe blunt trauma: results of the 'Diagnosis and Treatment of Trauma-Induced Coagulopathy (DIA-TRE-TIC) study'. Brit J Anaesth. 2011;107(3):378–87.
68. Rugeri L, Levrat A, David JS, Delecroix E, Floccard B, Gros A, et al. Diagnosis of early coagulation abnormalities in trauma patients by rotation thrombelastography. J Thromb Haemost. 2007;5(2):289–95.
69. Kashuk JL, Moore EE, Le T, Lawrence J, Pezold M, Johnson JL, et al. Noncitrated whole blood is optimal for evaluation of postinjury coagulopathy with point-of-care rapid thrombelastography. J Surg Res. 2009;156(1):133–8.
70. Alexander DC, Butt WW, Best JD, Donath SM, Monagle PT, Shekerdemian LS. Correlation of thromboelastography with standard tests of anticoagulation in paediatric patients receiving extracorporeal life support. Thromb Res. 2010;125(5):387–92.
71. Schochl H, Cotton B, Inaba K, Nienaber U, Fischer H, Voelckel W, et al. FIBTEM provides early prediction of massive transfusion in trauma. Crit Care. 2011;15(6):R265.
72. Leemann H, Lustenberger T, Talving P, Kobayashi L, Bukur M, Brenni M, et al. The role of rotation thromboelastometry in early prediction of massive transfusion. J Trauma. 2010;69(6):1403–8.
73. Cotton BA, Faz G, Hatch QM, Radwan ZA, Podbielski J, Wade C, et al. Rapid thrombelastography delivers real-time results that predict transfusion within 1 hour of admission. J Trauma. 2011;71(2):407–14.
74. David JS, Godier A, Dargaud Y, Inaba K. Case scenario: management of trauma-induced coagulopathy in a severe blunt trauma patient. Anesthesiology. 2013;119(1):191–200.
75. Dunbar NM, Chandler WL. Thrombin generation in trauma patients. Transfusion. 2009;49(12):2652–60.
76. Schochl H, Nienaber U, Hofer G, Voelckel W, Jambor C, Scharbert G, et al. Goal-directed coagulation management of major trauma patients using thromboelastometry (ROTEM)-guided administration of fibrinogen concentrate and prothrombin complex concentrate. Crit Care. 2010;14(2):R55.
77. Nienaber U, Innerhofer P, Westermann I, Schochl H, Attal R, Breitkopf R, et al. The impact of fresh frozen plasma vs coagulation factor concentrates on morbidity and mortality in trauma-associated haemorrhage and massive transfusion. Injury. 2011;42(7):697–701.
78. Nardi G, Agostini V, Rondinelli B, Russo E, Bastianini B, Bini G, et al. Trauma-induced coagulopathy: impact of the early coagulation support protocol on blood product consumption, mortality and costs. Crit Care. 2015;19:83.
79. David JS, Marchal V, Levrat A, Inaba K. Which is the most effective strategy: early detection of coagulopathy with thromboelastometry or use of hemostatic factors or both? Crit Care. 2011;15(3):433.
80. Holcomb JB, Minei KM, Scerbo ML, Radwan ZA, Wade CE, Kozar RA, et al. Admission rapid thrombelastography can replace conventional coagulation tests in the emergency department: experience with 1974 consecutive trauma patients. Ann Surg. 2012;256(3):476–86.
81. Gonzalez E, Moore EE, Moore HB, Chapman MP, Chin TL, Ghasabyan A, et al. Goal-directed hemostatic resuscitation of trauma-induced coagulopathy: a pragmatic randomized clinical trial comparing a viscoelastic assay to conventional coagulation assays. Ann Surg. 2016;263(6):1051–9.
82. Levrat A, Gros A, Rugeri L, Inaba K, Floccard B, Negrier C, et al. Evaluation of rotation thrombelastography for the diagnosis of hyperfibrinolysis in trauma patients. Brit J Anaesth. 2008;100:792–7.
83. Lamb CM, MacGoey P, Navarro AP, Brooks AJ. Damage control surgery in the era of damage control resuscitation. Br J Anaesth. 2014;113(2):242–9.
84. Gentilello LM. Practical approaches to hypothermia. Adv Trauma Crit Care. 1994;9:39–79.
85. Abramson D, Scalea TM, Hitchcock R, Trooskin SZ, Henry SM, Greenspan J. Lactate clearance and survival following injury. J Trauma. 1993;35:584–8.
86. Morris JA, Eddy VA, Blinman TA, Rutherford EJ, Sharp KW. The staged celiotomy for trauma. Issues in unpacking and reconstruction. Ann Surg. 1993;217:576–84.
87. Malbrain ML, Cheatham ML, Kirkpatrick A, et al. Results from the international conference of experts on intra-abdominal hypertension and abdominal compartment syndrome. I. Definitions. Intensive Care Med. 2006;32:1722–32.