Hemorrhagic Shock

95

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Case Presentation

A 22-year-old woman was transported to the trauma bay following a motorcycle crash. She was immobilized on a spine board with a cervical collar in place. A single large bore intravenous catheter was placed pre-hospital and a crystalloid bolus was initiated. She was able to speak, and she had bilateral breath sounds. There were no external signs of bleeding. Her pulse was 142 beats/min and thready. Her right chest and abdomen were tender, and her pelvis was mechanically unstable. She had deformity of her right femur and left foot. She was placed on the monitor and noted to have an axillary temperature of 96 °F, blood pressure of 75/38 mmHg, respiratory rate of 36, and oxygen saturation of 90%. Her chest x-ray showed multiple right-sided rib fractures but a normal mediastinal contour, and her pelvic x-ray demonstrated a 3 cm pubic symphyseal diastasis. She had a positive focused assessment with sonography in trauma (FAST) exam in the right upper quadrant and around the bladder. Point of care venous blood gas testing indicated a pH of 7.28 with a lactate of 6 mg/dL and a base deficit of 12.

Question

What are the treatment priorities for this patient in hemorrhagic shock?

Answer Patients in hemorrhagic shock need early blood product resuscitation and hemorrhage control to interrupt and reverse the cycle of hypothermia, coagulopathy, and acidosis that are the hallmark of this condition (Fig. 95.1). This patient's assessment of blood consumption (ABC) score was 3 on presentation; so emergency release blood products were taken from the trauma bay refrigerator, and the institution's massive transfusion protocol was initiated. During this resuscitation, equal parts packed red blood cells, fresh frozen plasma, and platelets were given as concurrently as possible. After applying a pelvic binder, a femoral arterial catheter was placed percutaneously. Because the chest x-ray demonstrated a normal mediastinal width, there were no clear contraindications to resuscitative endovascular balloon occlusion of the aorta (REBOA). With ongoing hypotension and a positive FAST exam, a REBOA catheter was advanced into the distal thoracic aorta (Zone 1) and inflated. The patient was taken emergently to the operating room for abdominal exploration, pre-peritoneal pelvic packing and pelvic external fixation. Over the next 6 h she received 10 units of packed red blood cells, 10 units of plasma and 2 units of apheresis platelets. Care was taken to include empiric calcium chloride administration during blood product transfusion. Thromboelastography (TEG) also indicated a need for cryoprecipitate and demonstrated increased fibrinolysis; so tranexamic acid (TXA) was also given. Post-operatively, her hemodynamics improved, her lactate rapidly cleared, and her TEG normalized.

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Principles of Management

Diagnosis of Hemorrhagic Shock

Like other forms of shock, early recognition of hemorrhagic shock is key to patient survival since the median time from onset to death is between 1 and 2 h [1, 2]. Clinical indicators of hemorrhagic shock include tachycardia, hypotension,

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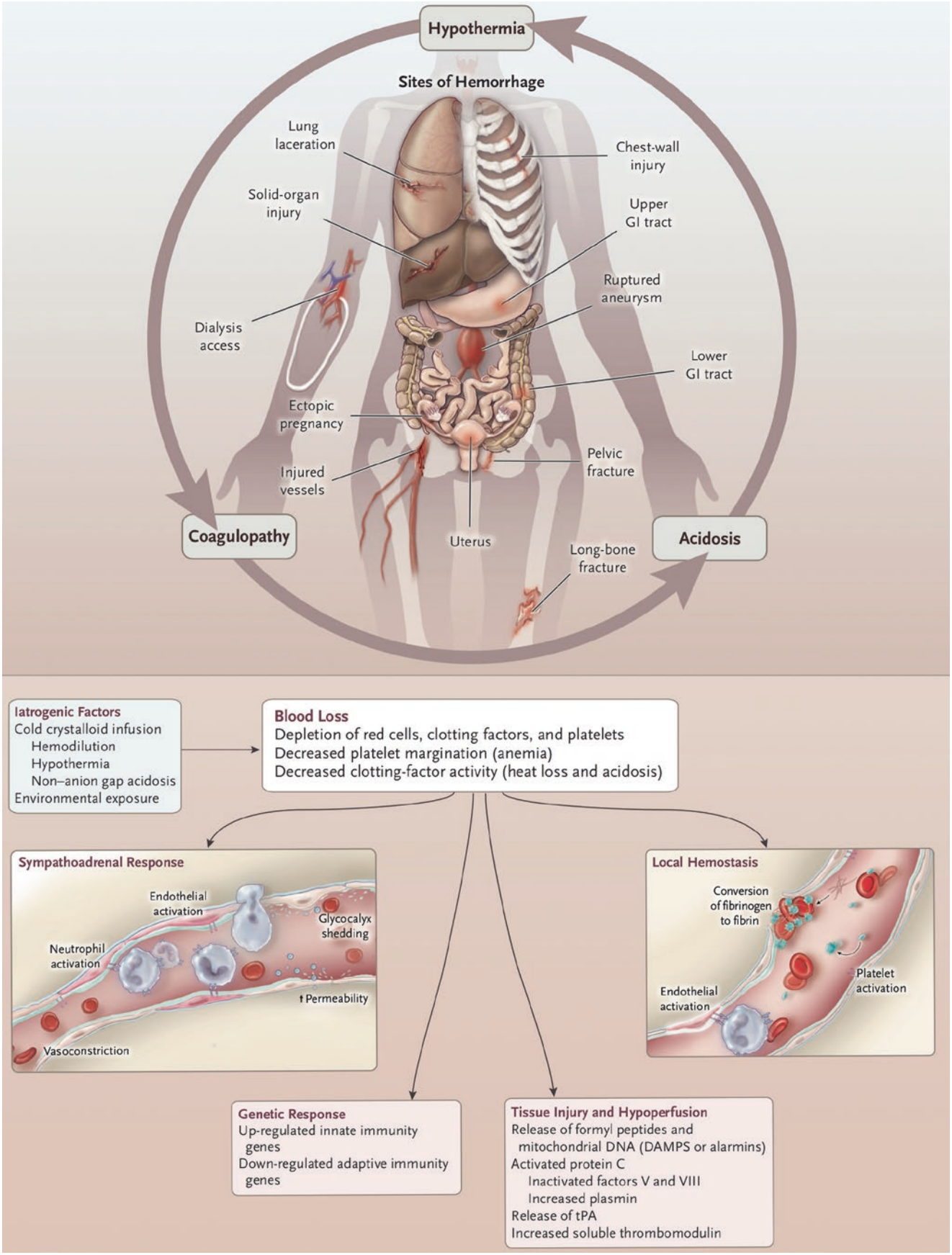

Fig. 95.1 In hemorrhagic shock, the combined effects of intravascular volume depletion, loss of red-cell mass and procoagulant elements, simultaneous activation of the hemostatic and fibrinolytic systems, compensatory mechanisms, and iatrogenic factors contribute to the phenotype of coagulopathy, hypothermia, and progressive acidosis. This so-called "bloody vicious cycle" ultimately leads to death if not prevented or corrected. Reproduced from Cannon JW. Hemorrhagic Shock. N Engl J Med 2018;378:370–379

narrowed pulse pressure, increased respiratory rate, altered mental status, and low urine output [3]. While many of these are nonspecific a thorough history and physical exam will aid in determining the cause of shock. It is key to note that while diagnostic studies are being performed to determine the source of bleeding, prompt, empiric blood product resuscitation should be performed simultaneously. Early surgical consultation is also recommended in all cases of hemorrhagic shock as the most common causes of death from hemorrhage include trauma, abdominal aortic aneurysm, gastrointestinal sources, and maternal hemorrhage [4, 5].

In acutely bleeding trauma patients, the most likely source of hemorrhage must be rapidly identified. In addition to the physical exam, useful diagnostic studies include plain films, ultrasound, and occasionally diagnostic peritoneal aspiration. For penetrating trauma patients, a similar approach is used to determine the most likely trajectory and, thus, which organs and/or blood vessels may be bleeding. While CT has become the primary tool for elucidating injuries in stable patients, it should rarely be used in patients who present in hemorrhagic shock.

Gastrointestinal bleeding can typically be localized using a stepwise approach [1] although the diagnostic algorithm may vary slightly depending on local resources [6]. Table 95.1 for patients with significant hemorrhage, options include endoscopy (both lower and upper), computed tomography (CT) angiography, or conventional angiography. While endoscopy allows for direct visualization of the bleeding source with the ability to intervene there can be wide local variability with comfort level in regards to endoscopy in critically ill patients as well as availability of endoscopic services after business hours. Computed tomography (CT) with intravenous contrast is fast and highly specific; however sensitivity is not as high as with endoscopy or a bleeding scan [7]. In select patients, CT angiography can be used to direct subsequent selective embolization as either a temporizing measure or even as definitive therapy.

Resuscitation

Resuscitation in hemorrhagic shock should be initiated expeditiously first and foremost with blood products. A massive transfusion protocol should be initiated promptly and the tenets of damage control resuscitation should be followed [8]:

- Avoid or correct hypothermia
- Apply direct pressure or a tourniquet proximal to sites of hemorrhage in extremities
- Delay fluid administration until time of definitive hemostasis in penetrating trauma
- Minimize crystalloid infusions (<3 L in first 6 h)
- Use a massive transfusion protocol to ensure that sufficient blood products are rapidly available
- Avoid delays in definitive surgical, endoscopic, or angiographic hemostasis
- Minimize imbalances in plasma, platelet, and red-cell transfusions
- Obtain functional laboratory measures of coagulation (TEG or ROTEM)
- Selectively administer pharmacological adjuncts to reverse any anticoagulant medications and to address persistent coagulopathy

Table 95.1 Diagnostic modalities for gastrointestinal bleeding

Modality	Minimum rate of bleed	Intervention capable
Endoscopy	0 (stigmata of recent hemorrhage)	Clip, epinephrine injection, band
CT	0.5 mL/min	None
Interventional radiology	0.5–1 mL/min	Embolization
Tagged red blood cell scan	0.05–0.1 mL/min	None

Vascular Access

Obtaining vascular access for a patient in hemorrhagic shock is essential. ATLS guidelines indicate vascular access should be obtained during the "C" phase of a primary survey of the "ABCs" of trauma. Short, large bore peripheral venous catheters are preferred as this will allow for rapid transfusion of large volumes of blood products. However, peripheral access can be challenging in hypovolemic patients; thus other forms of intravenous access are commonly used. These include intraosseous catheters, rapid infusion catheters, and central venous catheters. There remains controversy as to the optimal access sites and the approach that affords the most rapid access with the complications [9–11]. There should be at least two sites used when obtaining vascular access. For patients with traumatic hemorrhage, sites should be chosen that are away from potential venous injuries. Last, the use of a rapid infuser for blood products with warming capabilities is highly recommended (e.g. Belmont® Rapid Infuser, Belmont Medical Technologies, Billerica, MA).

Massive Transfusion

Massive transfusion has traditionally been defined as receipt of 10 units or more red cell products in a 24-h period. An alternative definition for identifying patients with massive hemorrhage is 3 or more units of packed red blood cells given in 1 h [12]. For patients with massive bleeding, every minute of delay in mobilizing a massive transfusion protocol (MTP) significantly increases mortality. However, early identification of patient who will require massive transfusion often proves difficult [13]. A number of different scoring systems have been developed to aid in the identification of

massively bleeding patients [3] including the Assessment of Blood Consumption (ABC) score which assigns a single point for each of the following: penetrating mechanism, HR > =120, SBP < =90, and positive FAST [14]. An ABC score of 2 or greater is commonly used as a trigger for activating the MTP as 45% of these patients ultimately receive a massive transfusion.

Current evidence supports a balanced resuscitation strategy for patients in hemorrhagic shock. This approach emphasizes higher ratios of plasma and platelets given earlier in resuscitation [15] with a goal of achieving 1:1:1 (plasma: platelets: packed red blood cells) [16–18]. Any patient requiring massive transfusion should have calcium given empirically since the anticoagulant citrate is found in all blood products and can lead to further coagulopathy in the exsanguinating patient [19].

Crystalloid

In the mid-1980's the concept of restoring the interstitial volume with crystalloid resuscitation emerged [20]. This approach was never intended to replace blood product administration for hemorrhagic shock; however, the mis-application of this literature resulted in over-reliance on crystalloid therapy. This approach resulted in abdominal compartment syndrome, acute respiratory distress syndrome, coagulopathy, hypoxemia, and decreased survival [21]. Thus, crystalloid solutions should be used sparingly in patients with hemorrhagic shock (no more than 3 L in 6 hours) and should not replace blood products [22]. Additionally, albumin should not be used in trauma patients [23]. Finally, hypertonic saline has also shown little benefit and perhaps even harm [24].

Vasopressors

Because hemorrhagic shock is a form of hypovolemia rather than vasoplegia or cardiac dysfunction, vasopressors have a very limited role. One single-center randomized trial demonstrated an early survival benefit to vasopressin repletion in hemorrhagic shock; however there was no long-term survival benefit [25]. Another recently concluded single center randomized trial further demonstrated decreased blood product administration with vasopressin use (NCT01611935). Nonetheless, we acknowledge there are some cases in which the etiology of shock is unknown and the urgency of the situation warrants simultaneous management with both volume administration and empiric vasopressor use. Once it is determined that hemorrhage is the cause of shock, transfusion should continue even as vasopressors are titrated off.

Laboratory Results

Several laboratory results are useful in both identifying patients in shock and for guiding resuscitation although clinical indicators of hemorrhage shock should be used primarily to determine need for transfusion as described above.

Hematology Labs

Laboratory data indicating adequate hemoglobin, coagulation profile, and platelet count may not accurately reflect the degree of blood loss or coagulopathy especially early after severe blood loss. Conversely, minor abnormalities in these values can herald life-threatening hemorrhage. Thus, transfusion should continue until hemostasis is achieved and any derangements in key laboratory indicators have resolved.

Chemistries

Several electrolytes should also be assessed for derangement including calcium, potassium, and in some cases magnesium. During massive transfusion calcium is often found to be low as the excess citrate in blood products binds calcium [19]. Calcium is an important clotting cofactor, integral to the coagulation cascade and essential for normal cardiac function. Thus, it is imperative that both hypocalcemia be avoided during resuscitation. Calcium chloride administration is the preferred method for calcium correction. In regards to potassium, blood banks typically dispense products that will be expiring soon rather than freshly acquired blood products [26]. Packed red blood cells in particular are prone to hyperkalemia due to red cell lysis with increased age. This can lead to high serum potassium levels during massive transfusion and must be monitored closely. Finally, citrate can also bind magnesium leading to severe hypomagnesemia resulting in QT prolongation during massive resuscitation [26]. Intermittent monitoring and even empiric administration with any ECG changes should be considered during massive resuscitation. Finally, while coagulation studies such as prothrombin and partial thromboplastin time may be helpful [27], viscoelastic assays allow for more targeted management of coagulopathies arising from massive transfusion.

Endpoints of Resuscitation

Once definitive hemostasis has been achieved, the rate of blood product infusion should be slowed and care should be taken to avoid over-resuscitation. A combination of laboratory data and vital signs can guide the decision to stop blood product infusion entirely. Correction of coagulopathy with use of thromboelastography will aide in the decision for additional plasma, platelets or cryoprecipitate. Lactate and base deficit should normalize as the patient emerges from a state of oxygen deficit and the oxygen debt is repaid [28–30]. Electrolyte levels should be assessed and any abnormalities again corrected. Bedside echocardiography can be used to evaluate intravascular volume status as well as following urine output [31, 32]. In regards to vital signs, a goal mean

arterial pressure (MAP) of 65 mm Hg is safe as there is no evidence of the benefit for prolonged "hypotensive resuscitation." [33]

Hemostatic Adjuncts

TXA

Tranexamic Acid (TXA) is a drug that was first used in the 1960s in both medical and surgical applications to reduce bleeding. It is a synthetic derivative of the amino acid lysine that inhibits fibrinolysis by blocking the lysine binding sites on plasminogen. Not unlike other therapies, the interest in trauma stemmed from its ability to reduce blood loss and transfusion requirements in the liver transplant and cardiopulmonary bypass population (i.e. other high volume transfusion populations) [34]. The CRASH-2 randomized, placebo-controlled trial demonstrated a small but statistically significant mortality benefit [35]. A caveat to TXA use in hemorrhagic shock (off-label use) is that it must be administered early—within 3 hours of injury - as mortality sharply increases if used outside this window [36]. Two ongoing studies are now investigating the potential benefit to TXA in the pre-hospital environment (NCT02086500 and NCT02187120).

Early Hemorrhage Control

The median time to death for a trauma patient is 1 to 2 hours and hence the "golden hour" trauma surgeons rely upon to steer the team towards expeditious hemorrhage control [37]. As pre-hospital treatment algorithms improve and pre-hospital transport times are shortened (e.g. by minimizing pre-hospital interventions or by promoting police transport of select patients), more patients with hemorrhagic shock will arrive to hospital-level care alive [38]. Improved in-hospital resuscitation practices—including all the principles of damage control resuscitation—further increase survival probability in these patients when combined with rapid definitive hemostasis in the operating room or angiography suite [16, 17].

Surgical Hemostasis

With few exceptions, surgical hemostasis is the gold standard for any patient in hemorrhagic shock. Once a diagnosis has been ascertained (see Diagnosis section) a reasonable surgical plan can be expeditiously made. For trauma patients, once in the operating room a wide preparation is recommended to include the neck to the knees with both arms extended. This allows access to the neck, chest, abdomen and major arterial structures of the upper and lower extremities. If the most likely source of hemorrhage cannot be ascertained prior to operative intervention, a laparotomy should be performed as the first intervention [39, 40].

Once in the abdomen, if this is determined to be the source, then typically a damage control operation is performed. The principals of damage control operation are to first stop life-threatening bleeding and second to control any contamination [41, 42]. Care should be taken in patient selection, as more liberal use of this technique is not without risks such as hernias, fistulas, and infection. Thus, this type of procedure should be reserved for those patients with profound derangements in physiology or who require a necessary/planned second look (e.g. mesenteric ischemia) [43–45].

If the source of bleeding is determined to be in the abdomen, then an expeditious laparotomy should be performed with packing in all quadrants. During the packing open dialogue between the surgeon and anesthesia provider should be maintained to determine the trajectory of the resuscitation. Anesthesia may need time to "catch-up" after the packing is completed. The packs should then be removed in an orderly fashion to determine the location of bleeding. Vascular injury to the viscera and solid organs should be assessed followed by an evaluation of the retroperitoneum. Major vascular trauma of the central blood vessels can be ruled out with a right medial visceral rotation (i.e. Cattell-Braasch) and a left medial visceral rotation (i.e. Mattox) if indicated based on mechanism, hematoma location (zone I, zone II, or zone III), and whether or not the hematoma is expanding.

Angiographic Hemostasis

As implied earlier, there are cases in which angiography is necessary to control bleeding. These include blunt injury to the pelvis with retroperitoneal bleeding, liver bleeding, and splenic bleeding. There are various algorithms for control of bleeding from pelvis injuries that include a combination of operative pre-peritoneal packing and interventional radiology**.** Some algorithms combine both methods in sequence or concomitantly in hybrid operating rooms [46]. Non-traumatic hemorrhage from the liver, spleen and gastro-intestinal sources are also typically good candidates for angiographic embolization. In all cases the hemodynamic stability of the patient will dictate whether or not they are suitable for the angiography suite since a hemodynamically unstable patient should only be in the operating room.

Evidence Contour

REBOA

Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a relatively new technique for achieving temporary proximal vascular control in patients with severe

abdominal, pelvic, or junctional hemorrhage [47, 48]. Aortic occlusion in trauma has traditionally been achieved through an open trans-thoracic or trans-abdominal approach in severely bleeding patients. As endovascular technology has evolved, aortic occlusion can now be achieved by advancing a balloon catheter through a percutaneous femoral arterial approach.

The balloon is used to occlude the distal thoracic aorta (Zone 1) for patients with abdominal hemorrhage. For those with isolated pelvic hemorrhage, occlusion just above the aortic bifurcation (Zone 3) is appropriate. Occlusion directly over the visceral and renal vessels (Zone 2) is generally discouraged. Early clinical studies indicate comparable outcomes to open aortic occlusion when considering a general trauma population with hemorrhagic shock [49, 50] but a distinct survival advantage to REBOA in those with severe shock who have not yet arrested [51].

Whole Blood

Whole blood was transfusion was used beginning as early as the First World War [52]. During the Vietnam War, a transition was made from transfusing whole blood to component therapy. Component therapy is still the mainstay for both civilian and military blood transfusion, but whole blood transfusion saw renewed interest in the early 2000s with the military in the wars in Iraq and Afghanistan [53–55]. Data from these conflicts showed patients that received fresh whole blood had increased 24-hour and 30-day survival. Obtaining fresh whole blood in a civilian setting has obvious difficulties, but stored low titer type O whole blood is being explored as an option for initial resuscitation of acutely bleeding trauma patients [56, 57].

Other Hemostatic Adjuncts

Recombinant factor VII-activated (rVIIa) gained interest in the late 1990s and early 2000s for use in trauma patients suffering hemorrhagic shock (off-label use). Several studies suggested a decrease in requirement for blood product use, but other studies suggested risk of increase in thromboembolic events. Ultimately, use of rVIIa has not demonstrated a mortality benefit [58–60]. Prothrombin concentrate complex (PCC) is a hemostatic adjunct that has been shown to be effective in reversing the effect of vitamin K antagonists for patients in hemorrhagic shock and with intra-cranial hemorrhage. However, there is no proven mortality benefit with PCC use in these situations [61–65]. Fibrinogen concentrate (off-label use) has been used in place of cryoprecipitate in patients undergoing massive transfusion; however this also does not appear to have a mortality benefit [66].

Table 95.2 TEG parameters, clinical indicators, and management for abnormal values

Parameter	Indicator	Treatment
R	Clotting time	Fresh frozen plasma or prothrombin complex concentrate
α angle	Rate of clot formation	Cryoprecipitate or fibrinogen concentrate
K	Rapidity to reach a certain level of clot strength	Cryoprecipitate or fibrinogen concentrate
MA	Platelet number and function	Platelets
LY-30	Clot lysis at 30 min after MA achieved	Tranexamic acid (TXA, if less than 3 h from injury)

Viscoelastic Testing

Viscoelastic testing for clot formation includes both thromboelastography (TEG) and rotational thromboelastometry (ROTEM). These tests identify specific forms of coagulopathy during massive transfusions by analyzing clot dynamics in real-time. Data from this analysis indicates which component (plasma, platelets or cryoprecipitate) or hemostatic adjunct (e.g. TXA) may be needed to correct the patient's coagulopathy (Table 95.2). This approach enables directed transfusion therapy during high volume resuscitation and has been associated with decreased total blood product administration [67] and improved mortality [68]. Recently, these tests have become increasingly popular within both the civilian and military trauma communities [69, 70].

Summary

Early diagnosis, rapid resuscitation, and definitive hemostasis are all essential to improving survival in patients with hemorrhagic shock. Rapid transport to hospital-level care and the appropriate application of the principles of damage control resuscitation further ensure survival in patients with severe hemorrhage. Finally, research exploring new technologies for managing hemorrhagic shock and studies assessing novel hemostatic therapies will enable survival for even more severely bleeding patients in the future.

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