Optimal fluid resuscitation in trauma: type, timing, and total

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Purpose of review

This review article explores the recent literature regarding the optimal type and amount of intravenous fluids for the trauma patient from the time of injury through their ICU stay. It discusses damage control principles as well as targeted resuscitation utilizing new technology.

Recent findings

In the prehospital arena, intravenous fluids have been associated with worse patient outcomes due to increased coagulopathy and time to definitive care. Once in the trauma bay, damage control resuscitation principles apply to the severely injured patient. Large volume crystalloid infusion increases mortality. The best patient outcomes have been found with transfusion of blood products in a ratio that closely mimics whole blood. Thrombelastography is a useful adjunct in resuscitation and can help guide the judicious use of blood products. New technology can help providers ascertain when a patient is appropriately resuscitated by determining adequate global and regional perfusion.

Summary

During the resuscitation of the acutely injured patient, crystalloids should be limited in favor of blood components. Damage control principles apply until definitive hemostasis is obtained, at which point the focus should change to targeted resuscitation using traditional global endpoints of resuscitation in conjunction with determinants of regional perfusion.

Keywords

fluid resuscitation, hemorrhage, shock, trauma

INTRODUCTION

Intravenous (i.v.) fluid resuscitation has maintained a prominent position in any algorithm for care of the trauma patient. Historically, i.v. fluids were used to return patients to hemodynamic normality; currently, the focus has shifted toward achieving appropriate end points of resuscitation. Many options exist for fluid resuscitation, and this manuscript will review the recent literature regarding type, timing, and total amounts of fluid to administer to trauma patients.

Intravenous fluid options

Although many types of i.v. fluids exist (Table 1), crystalloids remain the predominant, first-line fluid used for trauma resuscitation. The American College of Surgeons' Advanced Trauma Life Support (ATLS) course recommends using isotonic crystalloids for initial resuscitation of trauma patients, recognizing that they only transiently increase intravascular volume [1]. When isotonic fluids are administered, only one-third of the volume remains extracellular, and of that, one-fourth remains intravascular. The remainder becomes interstitial, disturbing cell volumes, disrupting regulatory mechanisms, and propagating the inflammatory cascade. This increases tissue edema and injury and can lead to abdominal compartment syndrome (ACS), acute respiratory distress syndrome (ARDS), and other potentially devastating complications. Hypertonic saline and colloid solutions appear to remain in the intravascular space for a longer period and, therefore, may require less overall volume of delivery. These fluids

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KEY POINTS

- Crystalloids should be limited in trauma patients.
- Damage control resuscitation with blood products that approximate whole blood is the current best practice for acutely injured patients until bleeding is controlled.
- Thrombelastography can help guide the use of blood products to ensure judicious administration.
- Targeted resuscitation using global and regional endpoints should be employed once hemostasis is achieved.

exist in the trauma provider's arsenal, but must be employed in an evidence-based manner.

Physiology of a trauma patient

The severely injured multitrauma patient has a significant systemic inflammatory response, which contributes to the lethal triad: hypothermia, coagulopathy, and acidosis. Studies have shown that coagulopathy on admission is associated with a 25–40% mortality in the trauma population [2,3▪,4]. Early dysfunction and decrease in activity of clotting factors is, in part, due to hemodilution. It is postulated that decreasing the amount of crystalloid administration early in trauma can help prevent this phenomenon [5]. In fact, investigators have suggested that much of the decrease in coagulopathy and mortality from hemorrhage attributed to massive transfusion protocols and higher plasma and platelet ratios is actually a result of a decrease in early crystalloid volumes [6,7▪,8▪▪]. Trauma-induced coagulopathy has also been linked to inflammation, prompting the study of medications which impact inflammatory profiles. Statins have been found to be associated with lower mortality in injured patients [9]. A recent systematic review suggested that 'there is some evidence that preinjury statin use and postinjury statin treatment may have a beneficial effect' in trauma patients [10▪]. Additional attempts to improve the coagulation profile of these patients have focused on delivery of nonsteroidal anti-inflammatory drugs (NSAIDs) in the prehospital arena [11▪].

Prehospital care

Injured patients are often first encountered by emergency medical services (EMS) providers. Paramedics have the ability to obtain i.v. access, begin fluid resuscitation, and administer medications. Traditionally, 1 to 2 l of i.v. crystalloid was administered to hypotensive trauma patients in the field. However, data have called into question whether or not these interventions improve patient outcomes. In the mid-1990s, the idea of early fluid resuscitation for victims of penetrating trauma was challenged. The concept of hypotensive resuscitation was suggested to avoid 'popping the clot' prior to definitive hemostasis, which was most often surgical control of bleeding. In a classic 1994 article, Bickell *et al.* [12] determined that early aggressive i.v. fluid resuscitation should be avoided in patients with penetrating torso trauma until operative control of bleeding was established. In spite of multiple additional studies confirming these findings in the prehospital setting [13–15], administration of large fluid volumes by EMS remains a common practice throughout the country. The Eastern Association for the Surgery of Trauma published an evidence-based guidelines pertaining to i.v. access and fluid resuscitation for prehospital providers [16]. After reviewing the literature, the following recommendations were made: placement of vascular access at the scene should be avoided (level 2); if placing an i.v., consider intraosseus if there are two failed peripheral i.v. attempts (level 2); avoid giving fluids in patients with penetrating torso injuries (level 2); if giving fluids, titrate to palpable radial pulse instead of a predetermined amount (level 3); all fluid types are equivalent in the prehospital setting (level 1); and avoid the use of rapid infusers (level 3). Since these guidelines were published, additional studies have become available which

Table 1. Fluid comparison chart

Solution	Glucose	Na^+	K^+	Ca^{++}	Cl^-	Lactate	Acetate	Gluconate	Mg^{++}	pH
D5W	50	0	0	0	0	0	0	0	0	5.0
NS	0	154	0	0	154	0	0	0	0	5.5
D5½NS	50	77	0	0	77	0	0	0	0	5.5
3% NS	0	513	0	0	513	0	0	0	0	5.0
LR	0	130	4	3	109	28	0	0	0	6.5
Plasmalyte	0	140	5	0	98	0	27	23	3	7.4

both confirm and challenge these findings. Haut *et al.* [17] studied over 750 000 patients in the American College of Surgeons' National Trauma Data Bank and determined that prehospital i.v. fluid administration was associated with increased mortality for all subsets of trauma patients. Duke *et al.* [18] postulated that not all early i.v. fluids were harmful. The authors determined that a restrictive fluid strategy (arbitrarily determined as less than 150 ml prior to operative intervention) with the goal of maintaining end-organ perfusion resulted in decreased hospital length of stay, along with improvements in both operating room and ICU mortality. A 2013 study by Hampton *et al.* [19▪] confirmed these findings in prospectively evaluated data from 10 level 1 trauma centers in which patients who received prehospital i.v. fluids (700 ml) had lower in-hospital mortality than those who did not. Although a definitive cut-off amount is yet to be determined, aggressive i.v. fluid resuscitation in the prehospital setting should be avoided, with studies suggesting that a restrictive fluid strategy should be employed.

Controversy still remains on the use of i.v. fluids in patients with traumatic brain injury (TBI). As even a single episode of hypotension can lead to worse outcomes in head-injured patients, maintaining cerebral perfusion pressure is essential. The mainstay of treatment of TBI patients is to avoid a secondary brain injury either from hypotension or from hypoxia. Hypertonic saline has been looked at as a therapeutic option for TBI patients. It has been shown to restore the normal function of polymorphonuclear lymphocytes which is often deranged after TBI [20,21▪]. Hypertonic saline has the ability to expand intravascular volume with less fluid than isotonic solutions, theoretically decreasing the coagulopathy associated with aggressive fluid resuscitation in trauma patients. Despite these promising findings, the use of hypertonic saline has not been found superior to resuscitation with isotonic fluids in trauma patients with respect to survival or long-term functional outcomes. Isotonic fluids remain the recommended fluid for patients with TBI, with isotonic saline preferred over lactated Ringers [22]. No studies have looked at patients with combined penetrating torso injuries as well as head injury. In those instances, the provider's best judgment must be used to weigh the risks and benefits of fluid administration.

Trauma resuscitation bay

Previous editions of ATLS teach that fluid resuscitation in the trauma bay should start with warmed isotonic i.v. fluids. A 1–2 l initial bolus (or 20 ml/kg for pediatric patients) is recommended, which includes any fluids given prior to arrival in the trauma bay, followed by titration of fluid based on patient response [1]. The cut-off of 2 l is based more on expert opinion than evidence-based medicine. In fact, the data that ATLS referenced for this state that 1 to 2 l of crystalloid may be given while 'awaiting the availability of whole blood' [23]. From the data published, large volumes of crystalloid infusion appear to be detrimental to trauma patients. These fluids increase blood loss in patients with an uncontrolled bleeding source, and lead to increased coagulopathy in the general trauma population. Ley *et al.* [24] examined prospectively gathered data in an attempt to define an appropriate amount of crystalloid infusion in the trauma bay. They determined that volume of crystalloid up to 1 l did not negatively affect patients, whereas infusions of 1.5 l or more in the emergency department had a two-fold increase in mortality. Additionally, isotonic saline can cause a hyperchloremic metabolic acidosis, and lactated Ringers can theoretically contribute to lactic acidosis in large volumes. Plasma-lyte, a calcium-free, balanced crystalloid solution with a neutral pH, has been shown to improve acid-base status and hyperchloremia at 24 h after injury compared with isotonic saline. However, there is currently no evidence that this results in improved long-term outcomes [25▪].

With high volumes of crystalloid attributed to worse patient outcomes, there has been a push to determine what type of fluid resuscitation is best in the trauma bay. Colloid solutions offer another reasonable alternative, but are difficult to study rigorously as this encompasses such a heterogeneous collection of fluids. Albumin and hydroxyethyl starch (HES) are two common colloids investigated in the published literature. In 2007, the Saline versus Albumin Fluid Evaluation (SAFE) trial showed that albumin was detrimental to patients with severe head injuries and it stopped being used for this purpose. Further investigation revealed that albumin use was associated with increased intracranial pressure in TBI patients and was the likely cause of the increased mortality [26▪]. Although HES, like other colloid solutions, has the theoretical benefit of sustained intravascular volume expansion with less fluid administration than crystalloids, the potential for inducing renal failure and causing or worsening coagulopathy has led it to fall out of favor with trauma practitioners [27▪]. Blood products have become the mainstay of early resuscitation in the trauma bay. Patients who have hypotension secondary to exsanguination do better with resuscitation with blood than crystalloids. Combat medicine has shown that patients transfused with whole blood have improved outcomes over patients given individual components [28]. Because of this finding, massive transfusion protocols were developed with the intention of getting all blood components to the patient in a timely manner (termed hemostatic resuscitation). Although many authors suggest a 1 : 1 : 1 ratio of packed red blood cells, plasma and platelets [29,30], research is still being conducted as to the most effective combination [8▪▪,31▪▪]. Interestingly, although outcomes are better with hemostatic resuscitation than with traditional methods, it does not seem to correct hypoperfusion or coagulopathy during acute traumatic hemorrhage. Lactate levels remain elevated and coagulopathy parameters remain deranged until bleeding is controlled. These findings underscore the importance of promptly getting trauma patients to definitive management [32▪]. Additional studies have shown beneficial effects of plasma as a resuscitative fluid in place of crystalloids. Plasma, whether dried or thawed, reverses endothelial cell permeability and improves the inflammation associated with injury [33▪,34▪]. It also improves platelet function and clot strength in animal models of hypovolemic shock associated with multisystem trauma [35▪].

Thrombelastography (TEG) has become increasingly available in the trauma bay. TEG evaluates the viscoelastic properties of whole blood as it clots (Figs. 1 and 2) [36]. It gives information regarding clot formation, strength and dissolution, and can be used as a point-of-care test because results are available in minutes [37]. Although only a few major trauma centers have incorporated TEG into their resuscitation algorithms, a growing body of evidence suggests that TEG-guided resuscitation can improve patient outcomes while decreasing blood product waste [38▪,39▪].

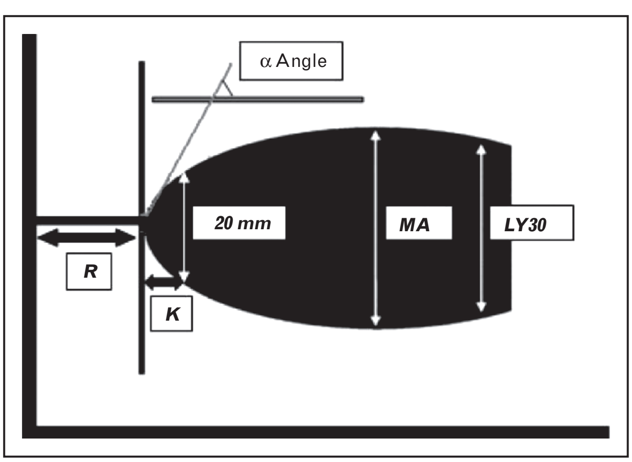

FIGURE 1. Signature waveform of a normal TEG tracing. Reproduced from [36].

The operating room and beyond

In addition to the complications of fluid resuscitation caused by third spacing, trauma patients are at high risk of surgical complications. Excessive i.v. crystalloids are associated with intestinal edema, inability to close the abdominal fascia, and postoperative ACS. Over-aggressive fluid resuscitation has also been shown to increase anastomotic leak rates. Schnuriger *et al.* [40] showed that administration of more than 10.5 l of i.v. fluids within the first 72 h of admission (less than 4 l per day) increased the risk of failure of colo-colonic anastomoses performed at initial laparotomy in trauma patients.

After the acute traumatic injury has been addressed, the focus should change from damage control resuscitation to goal-directed fluid administration. Establishing and maintaining adequate tissue perfusion and oxygenation is the objective of all goal-directed resuscitation strategies (Table 2). The trauma team should avoid both over and under-resuscitation and can use specific targets to guide administration of fluids. Basic endpoints of resuscitation often consist of mental status, heart rate, blood pressure, and urine output. Providers can also measure end-organ perfusion via laboratory values (that is lactate, base deficit, bicarbonate) or tissue hemoglobin oxygen saturation at the level of microcirculation (St02 monitor). Other advanced methodologies directly measure cardiac function or volume status via echocardiography and ultrasound [41], esophageal Doppler, stroke volume, central venous pressure, and/or pulmonary artery occlusion pressures. No single target is sufficient alone to use

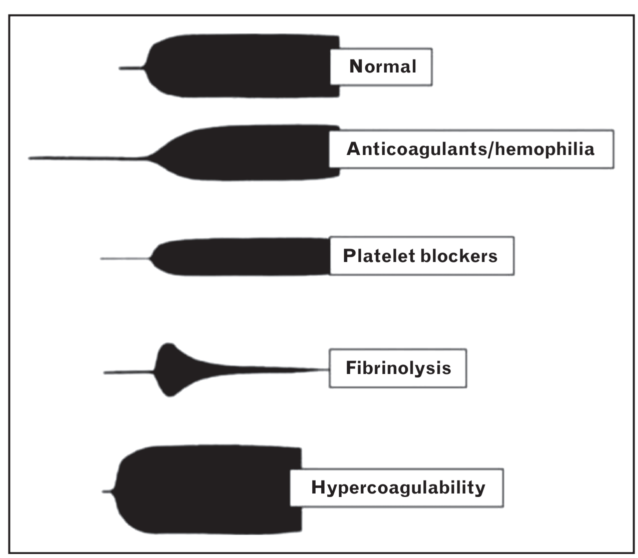

FIGURE 2. Examples of normal and abnormal tracings on TEG. Reproduced from [36].

Table 2. Determinants of resuscitation and perfusion

Basic measures of global resuscitation	Advanced measures of global resuscitation	Measures of global perfusion	Measures of regional perfusion
Heart rate	Bedside echocardiography	Initial lactate level	Near-infrared spectroscopy
Shock index	Mixed venous oxygen saturation	Rate of lactate clearance	Sidestream dark field video microscopy
Blood pressure	Pulse pressure variation	Base deficit	Regional capnography
Urine output	Stroke volume variation	Bicarbonate	St02 monitoring
Mental status	Pulmonary artery occlusion pressure	pH	CSF microdialysis
Capillary refill	Central venous pressure		

independently to ascertain the fluid status of the patient. All hemodynamic endpoints speak to global perfusion with no elucidation of regional ischemia [42]. The challenge remains for practitioners to determine if there is ongoing regional ischemia even with normal global hemodynamic parameters. Laboratory values have been extensively studied as perfusion markers. Although initial lactate levels have been correlated with outcomes, trends over time are more predictive of mortality than an isolated measurement. Similarly, base deficit remains a consistent predictor of mortality in trauma patients [43]. Although these laboratory trends are helpful in guiding resuscitation, they still do not differentiate between global and regional derangements in perfusion. Combining laboratory results with hemodynamic parameters can yield a more complete picture of the hemodynamic status of the patient. If lactate levels and base deficit remain abnormal in spite of hemodynamic parameters suggesting adequate resuscitation, there is likely a problem with the oxygen delivery in the microcirculation.

Recent advances in technology have led to the development of more specific means of determining regional perfusion. Gastric mucosal dysoxia, as measured by intramucosal pH and PCO2, has been touted as a predictor of morbidity and mortality in critically ill patients, yet it has fallen out of favor in recent years. Sublingual PCO2 correlates with gastric PCO2 and has been suggested as an easily-applied measure of regional hypoperfusion. In hypotensive trauma patients, this test [44] can predict survival with the equivalent diagnostic ability of lactate and base deficit. Near-infrared spectrometry (NIRS) has also been studied as a noninvasive method of determining tissue oxygenation. A multicenter study [45] of 383 trauma patients confirmed that NIRS-derived muscle tissue oxygen measurements identify poor perfusion as well as base deficit, and can predict the development of multiorgan dysfunction and death. In spite of these promising results, the holy grail of fluid resuscitation targets remains elusive.

CONCLUSION

In spite of a large body of literature investigating optimal fluid resuscitation strategies for trauma patients, much remains unresolved. Limiting prehospital i.v. crystalloids in favor of rapid transport to definitive care at a trauma center appears to be beneficial. The advent of massive transfusion protocols emphasizing early blood component therapy for patients with hypovolemic shock has improved outcomes. Once bleeding is controlled, the focus of fluid administration shifts from damage control resuscitation to goal-directed therapy. Combining both hemodynamic and perfusion-based targets of resuscitation can allow for careful control of the amount and type of fluids provided. Clinicians must continually aim for the ideal balance between over and under-fluid resuscitation in an attempt to obtain the best outcomes and avoid complications for our injured trauma patients.

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Dr Feinman reports no disclosures.

Conflicts of interest

None declared.

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■■ of outstanding interest

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This ongoing multicenter phase III trial is designed to evaluate the difference in 24-h and 30-day mortality among trauma patients predicted to receive massive transfusion. The authors hoped to determine the ideal blood component ratio by comparing a 1 : 1 : 1 (platelets : plasma : PRBCs) resuscitation strategy with a 1 : 1 : 2 (platelets : plasma : PRBCs) administration.

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