Fluid resuscitation in trauma patients: what should we know?

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Purpose of review
Fluid resuscitation in trauma patients could reduce organ failure, until blood components are available and hemorrhage is controlled. However, the ideal fluid resuscitation strategy in trauma patients remains a debated topic. Different types of trauma can require different types of fluids and different volume of infusion.

Recent findings
There are few randomized controlled trials investigating the efficacy of fluids in trauma patients. There is no evidence that any type of fluids can improve short-term and long-term outcome in these patients. The main clinical evidence emphasizes that a restrictive fluid resuscitation before surgery improves outcome in patients with penetrating trauma. Fluid management of blunt trauma patients, in particular with coexisting brain injury, remains unclear.

Summary
In order to focus on the state of the art about this topic, we review the current literature and guidelines. Recent studies have underlined that the correct fluid resuscitation strategy can depend on the type of trauma condition: penetrating, blunt, brain injury or a combination of them. Of course, further studies are needed to investigate the impact of a specific fluid strategy on different type and severity of trauma.

Keywords
blunt trauma, colloids, crystalloids, fluid resuscitation, penetrating trauma

INTRODUCTION

Traumatic death is the main cause of life years lost worldwide [1]. Hemorrhage is responsible for almost 50% of deaths in the first 24 h after trauma [2,3].

Volume therapy can influence the early and late outcome; however, the ideal fluid resuscitation in trauma is still debated [4▪,5].

The aim of this clinical review is to present the state of the art about fluid resuscitation in trauma patients focusing on three topics: type of fluid, volume strategy and endpoints in the different traumatic settings. The use of blood products will not be discussed in this work because we decided to focus our attention on clinical fluid management before blood components availability.

WHICH TYPE OF FLUIDS?

The goal of fluid resuscitation is to reduce organ failure because of hypoperfusion of peripheral tissues. It represents a temporary strategy, when life-threatening uncontrolled bleeding exists, until blood components are available and hemorrhage is controlled.

In the literature, there is little evidence that one type of fluid compared with another can improve survival or can be more effective [4▪,6]. Few randomized controlled trials investigating safety and efficacy of fluids in trauma patients exist (Table 1).

Briefly, we present an overview of available fluids for a pragmatic resuscitation strategy: crystalloids, colloids and hypertonic solutions.

Crystalloids

Crystalloids are the initial volume expanders in patients with estimated blood loss of at least 15–30% [5].

Physiological saline is the most commonly used crystalloid solution [7▪] with equal concentration of

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KEY POINTS

- In trauma patients, the goal of fluid resuscitation is the restoration of hemodynamic parameters to maintain a transient increase in perfusion pressure to reduce organ failure because of hypoperfusion of peripheral tissues, until blood components are available and hemorrhage is controlled.
- Studies have demonstrated that hypotensive resuscitation in penetrating trauma causes less bleeding and maintains organ perfusion, improving the outcome.
- Controversies still remain in the fluid management of patients with multisystem blunt injury in particular in presence of traumatic brain injury.
- In patients with traumatic brain injury, hypotonic fluids should be avoided to reduce the risk of cerebral edema.

sodium and chloride; it is isotonic compared with extracellular fluid. Crystalloids with a chemical composition more similar to the extracellular fluid are termed 'balanced' solutions (Hartmann's and Ringer's solutions). Indeed, they are relatively hypotonic because of their lower sodium concentration.

Ringer's solution and physiological saline are commonly used in trauma patients. However, balanced solutions are increasingly recommended as first-line resuscitation fluids in this setting [8].

Isotonic saline seems to modulate the hypercoagulable state and lead to increased blood loss compared with lactated Ringer's solution [9]. Moreover, better effects of lactated Ringer's solution on pH, blood pressure and extravascular lung water index were found in a similar animal model of hemorrhagic shock [10].

On the contrary, any crystalloid solution can initially worsen a preexisting metabolic acidosis because of the lack of bicarbonate [11]. This effect is more evident with isotonic saline because of its strong ion difference zero that results in hyperchloremic acidosis with adverse effects: renal and immune dysfunction [12]. Differently, the balanced solutions contain anions metabolized by liver and kidney to generate bicarbonate that can partially buffer the lactic acidosis caused by hypoperfusion.

The potentially deleterious effects of crystalloids aggressive administration are the development of tissue edema and coagulopathy. Crystalloids can shift into the extracellular space within minutes, so only 25% of the infused solution remains in the intravascular space [13]. As known, in trauma conditions, there is an endothelial direct injury that increases permeability and the dilution of plasma proteins because of crystalloid infusion

Table 1. Randomized controlled trials investigating safety and efficacy of fluids that enrolled patients with trauma

Study, year	Enrolled patients (*n*)	Trauma patients (*n*)	Crystalloids versus colloids		Primary outcome results
SAFE, 2004	ICU patients (6997)	Trauma (1287)	0.9% Saline	4% Albumin	28-day mortality: similar
SAFE TBI, 2007	TBI patients enrolled in SAFE study (460): post hoc study	TBI (460)	0.9% Saline	4% Albumin	24-month mortality: higher in albumin group
FIRST, 2011	Penetrating and blunt trauma (115)	Penetrating trauma (70), blunt trauma (45)	0.9% Saline	HES 130/0.4	Volume need: higher in P-sal gastrointestinal function: similar 30-day mortality: similar Adverse events: lower lactate levels in P-HES Renal injury: less in P-HES
CHEST, 2012	ICU patients (7000)	Trauma (532), TBI (58)	0.9% Saline	6% HES 130/0.4	90-day mortality: similar
CRYSTAL, 2013	Hypovolemic ICU patients (2857)	Hypovolemic shock trauma (177)	Crystalloids	Colloids	28-day mortality: similar

HES, hydroxyethyl starch; n, number of patients; P-HES, penetrating trauma patients enrolled in Colloids group; P-sal, penetrating trauma patients enrolled in Saline group; TBI, traumatic brain injury.

can aggravate the 'systemic inflammatory response syndrome' and the interstitial edema formation [14]. Clinical implications of crystalloids overload might include acute respiratory distress syndrome, brain edema and the development of intra-abdominal hypertension [15–18].

Coagulation can also be impaired for the hemodilution of clotting proteins and for the disruption of thrombus formation worsening the post trauma coagulopathy.

An overview of potential adverse effects of crystalloids large infusion is presented in Fig. 1.

Colloids

Colloids are suspension of molecules that cannot cross the cellular membrane because of their molecular weight [7▪]. Their property to remain inside the intravascular space is responsible for the volume-sparing effect. In fact, a 1 : 3 ratio of colloids to crystalloids is considered necessary to achieve an equivalent plasma expansion. However, a crystalloid-to-colloid ratio of approximately 1.5 has been recently demonstrated to be closer to reality [19]. Colloids are mainly divided into human (e.g. 4–5% of albumin) [20] and synthetic (dextrans, gelatins, hydroxyethyl starches), hypooncotic (gelatins, 4–5% of albumin) and hyperoncotic (dextrans, hydroxyethyl starches, and 20–25% of albumin).

Dextran, a glucose polymer, should be avoided for fluid resuscitation because of the risk for anaphylactoid reactions, negative effects on renal function and coagulation [21].

Gelatins, modified beef collagens with short half-life for their low molecular weight and their rapid renal excretion, are the least effective colloids. They are well tolerated in terms of coagulation and renal effects despite the highest rate of allergic reactions [22]. Hydroxyethyl starch (HES), a high-polymeric glucose produced by hydroxyethyl substitution of amylopectin, is protected against hydrolysis by nonspecific plasmatic amylases. This feature not only increases the intravascular expansion but also its toxic effects on kidney, liver, bone marrow and skin. HES with a high molecular weight of 200 kDa and a substitution degree of more than 0.4 can cause acute kidney failure in patients with severe sepsis [23–25] and can impair coagulation

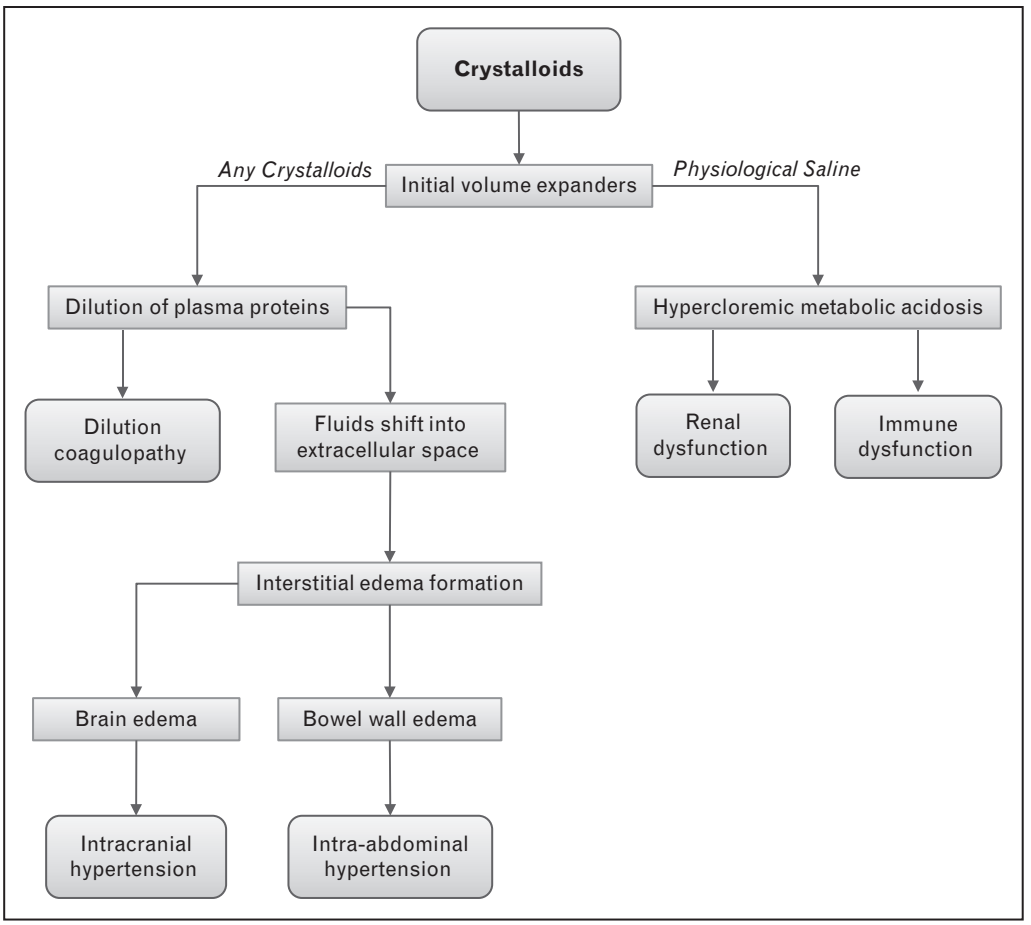

FIGURE 1. Potential adverse effects of crystalloids large infusion.

[26]. These solutions were replaced by HES with lower molecular weight and a lower substitution ratio (HES 130/0.4) with fewer negative effects on coagulation and that can be safely used in the hemorrhagic patient [27]. However, controversies still exist on safety of the latest HES solutions. Recently, 6% HES (130; 0.42) was associated with significant increase of 90-day mortality and renal replacement therapy, in ICU patients with severe sepsis, compared with Ringer's acetate, similarly to 10% HES in previous trials [28]. The contemporary CHEST trial, enrolling 7000 ICU patients, found that 6% HES (130; 0.4) compared with saline solution was associated with similar 90-day mortality but with significant increase in renal replacement therapy. There was no difference in mortality in predefined subgroup of trauma patients with traumatic brain injury [29].

More recently, the CRISTAL trial comparing different colloids versus different crystalloids in ICU patients with hypovolemic shock did not find any difference in 28-day mortality [30▪] also in the subgroup of trauma patients. Because of the relevant differences in terms of method among trials the crystalloid/colloid debate ranges on although a Cochrane Systematic Review concludes that there is no evidence that colloids reduce the mortality risk compared with crystalloids in patients with trauma, burns or following surgery. Then, because colloids are more expensive and one type of colloids (starches) might increase the risk of death, their use can be justified in the context of randomized clinical trials [4▪].

In conclusion, no large-scale clinical trial exists for the treatment of posttraumatic uncontrolled hemorrhagic shock with synthetic colloid administration when liberal infusion is needed.

Hypertonic saline

Hypertonic saline typically consists of 7.2–7.5% saline. It causes a marked osmotic fluid shift from intracellular to extracellular space resulting in less volume requirement [31,32].

It has the following potential beneficial effects:

(1) It reduces the endothelial swelling occurring in the early phases of shock [32].
(2) It reduces plasma viscosity [33], improving the regional blood flow.
(3) It reduces fluid requirement compared with lactated Ringer's infusion as demonstrated in burned patients.

This reduced requirement for fluids has been demonstrated to be associated with less edema formation, lower inspiratory pressure and less incidence of intra-abdominal hypertension during the first day after injury compared with the isotonic resuscitation [14,34].

In addition, experimental and clinical studies found that hypertonic saline could exert anti-inflammatory effects especially in traumatic hemorrhagic shock by reducing proinflammatory cytokines and increasing anti-inflammatory interleukins [35], with a lower incidence of acute lung injury [36]. However, there is inconsistent evidence regarding a survival benefit with hypertonic saline versus isotonic crystalloids in hypovolemic trauma patients with blunt or penetrating trauma [37,38].

WHICH FLUID STRATEGY IN WHICH TRAUMA?

The initial assessment of the severity of polytrauma patients remains one of the key aspects. Advanced Trauma Life Support (ATLS) guidelines have defined four classes of hypovolemic shock based on estimated percentage blood loss and on corresponding vital signs [39].

Alternatively, the 'shock index,' the ratio of heart rate to systolic pressure, is a clinical indicator of hypovolemic shock to stratify patients for transfusion requirements and outcomes in the prehospital setting [40,41].

The recommended initial hemodynamic management is based on the infusion of 1–21 of crystalloids [8] to divide hemorrhagic shock patients into fluid-responsive, without active bleeding, and fluid-unresponsive, with uncontrolled hemorrhage. This approach derives from traditional practice rather than scientific evidence.

However, the correct fluid resuscitation strategy depends also on the type of trauma.

Penetrating trauma

Penetrating trauma injuries are due to the energy of the penetrating instrument.

Since 1994, Bickell *et al.* [42] have demonstrated that a prehospital aggressive fluid administration to hypotensive patients with thoracoabdominal penetrating injuries was associated with lower survival and higher complication rate as compared with a fluid therapy started at the time of surgery. Previous animal studies had already hypothesized that an aggressive fluid resuscitation can cause the hydraulic disruption of effective thrombus, the dilution of coagulation factors and the lowering of blood viscosity [43,44] with the risk for re-bleeding [42,44,45].

The restrictive fluid therapy allowing low blood pressure until hemorrhage control and the administration of vasopressors in case of life-threatening

hypotension may be the best choice in a selected patient group (penetrating torso injuries, short transport times). In clinical practice, a prehospital 'scoop and run' strategy in patients with penetrating traumas should be taken, allowing a lower level of systolic blood pressure (70–60 mmHg) [42,46]. Many experimental and clinical studies have demonstrated that hypotensive resuscitation in penetrating trauma causes less intra-abdominal bleeding and maintains equivalent organ perfusion than normotensive resuscitation [42,47–51].

Recently, a randomized controlled trial has investigated the use of crystalloids versus colloid (HES 130/0.4) in patients with blunt and penetrating trauma [52]. Despite significant problems with randomization in the blunt trauma group, in the penetrating trauma group there was a benefit in terms of faster resuscitation without renal injury when HES 130/0.4 was administered [52].

Although nowadays the exact target for blood pressure has not yet been established and may depend on patient comorbidities, the concept of 'permissive hypotension' before surgical bleeding control and the use of hypertonic solutions as an alternative to isotonic crystalloids is underlined in the recent updated version of ATLS guidelines [8,53].

Blunt trauma

Blunt trauma is the consequence of widespread energy transfer to the body after motor vehicle accidents or falls.

It is a complicated clinical condition characterized by numerous sites of hemorrhage. Moreover, patients with blunt trauma can be often affected by traumatic brain injury (TBI), which is very sensitive to hypotension, and also by distinct vascular injuries that should be treated as penetrating trauma to avoid a secondary bleeding [54].

Until now, no large randomized study has been conducted on fluid resuscitation in patients with blunt trauma. Dutton *et al.* [54] in a small study investigated both blunt and penetrating-injured patients with hemorrhagic shock using a fluid resuscitation protocol with a target of a systolic blood pressure (70–80 mmHg) until surgical control. Similar mortality was found, despite a higher injury severity in the low-pressure group, suggesting that this approach should be taken into account.

A recent trial enrolling patients with severe extremity injuries without abdominal trauma found that patients who developed secondary abdominal compartment syndrome had a significantly higher crystalloids administration (9.9 versus 2.7 l) [55]. The concept that a supernormal fluid resuscitation was associated with decreased intestinal perfusion, increased incidence of intra-abdominal hypertension, abdominal compartmental syndrome, multiple organ failure and death [56] has led to investigate the use of vasopressors as an adjunct to crystalloid infusion after major trauma. However, vasopressors' use within 12 h was associated with higher mortality risk in blunt trauma compared with fluid resuscitation [57].

Therefore, both the use of vasopressors and the overwhelming fluid resuscitation can be deleterious for blunt trauma patients. The treatment with bolus doses of hypertonic saline in blunt trauma patients with hypovolemic shock has not demonstrated positive effects [37,58].

In conclusion, although in absence of a large randomized study, the preponderance of evidence suggests that a controlled hypotension can be beneficial in blunt trauma patients with uncontrolled bleeding until surgical control [59]. Moreover, a slow infusion seems to be superior to a rapid bolus, in reducing the probability of rebleeding [60].

On the contrary, differently from penetrating trauma, many controversies still remain in the fluid management of patients with multisystem blunt injury in particular in presence of TBI [59].

Traumatic brain injury

In TBI, fluid resuscitation is fundamental to maintain the cerebral perfusion pressure [19] and prevent the secondary brain insult because of hypotension.

Therefore, a mean arterial pressure target of 70 mmHg should be maintained. Differently, the management of multiple trauma patients with concomitant TBI can represent a difficult challenge. In this clinical setting, the positive effects of a restrictive fluid strategy with permissive hypotension should be weighted with the risk of cerebral hypoperfusion. Currently, ATLS guidelines prefer lactated Ringer's solution for the initial trauma resuscitation over physiological saline for the lower risk of hyperchloremic acidosis. However, in patients with TBI, isotonic saline should be preferred over hypotonic fluids because it can reduce the risk of cerebral edema [61]. Under this light, hyperoncotic fluid resuscitation has been investigated. However, the administration of albumin compared with saline was associated with higher mortality rates; the cause was not explained [62].

Beneficial effects of hypertonic saline compared with isotonic crystalloids were found in TBI in terms of control of intracranial pressure and reduced biomarkers expression of neuronal injury [63–65]. Despite this, a recent multicenter clinical trial enrolling patients with hypovolemic shock and

TBI in the prehospital setting was stopped because no significant benefit of hypertonic saline was observed [66].

Currently, there is no evidence to support the use of hyperosmolar crystalloids or colloids over isotonic crystalloids in patients with TBI. Moreover, no adequate models have been developed to study the fluid management of patients with blunt trauma and severe TBI [67].

WHICH ENDPOINTS?

In the early phase of trauma resuscitation, blood pressure and heart rate are used to estimate the severity of blood loss and guide the volume therapy. However, they are not useful to predict organ perfusion [68].

Moving from the recent advances, a general practical rule can be adopted to guide fluid infusion. Three different target systolic blood pressure values can be considered for three different traumatic conditions:

(1) 60–70 mmHg for penetrating trauma
(2) 80–90 mmHg for blunt trauma without TBI
(3) 100–110 mmHg for blunt trauma with TBI.

Lactate and base deficits have been demonstrated useful to predict outcome on hospital admission and to stratify patients who need a larger amount of fluid after the initial resuscitation and the normalization of blood pressure values.

Unfortunately, there is not a parameter to predict fluid responsiveness avoiding fluid overload. In fact, central venous pressure is poorly correlated with total blood volume, whereas the dynamic measures such as pulse pressure variation and stroke volume variation require passive mechanical ventilation and regular cardiac rhythm to be correctly interpreted.

The combined use of different physiological parameters may guide the early phase of trauma resuscitation [69].

CONCLUSION

In trauma patients, fluid resuscitation can prevent multiorgan failure and should be considered as a bridging therapy until blood transfusions and hemorrhage surgical control are ensured. As described, many controversies still exist about which type of fluid and how much of this fluid should be given during trauma resuscitation.

On the contrary, significant advances have been made in the last recent years: what did we learn?

(1) Lactated Ringer's solution is recommended as first-line resuscitation fluid in trauma patients [8].
(2) Permissive hypotension with a restrictive fluid resuscitation before surgery improves outcome in patients with penetrating trauma [42].
(3) Albumin should be avoided in patients with TBI [62].
(4) Recent evidence has shown increasing rationale for the use of hypertonic solutions in trauma but no large-scale clinical studies exist up to now.
(5) Fluid management of blunt trauma patients, in particular with TBI, remains unclear.

In conclusion, further studies are necessary to investigate the impact of a specific fluid resuscitation on different types of trauma (penetrating trauma, blunt trauma with or without head injury) stratified for severity of trauma.

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Conflicts of interest

There are no conflicts of interest.

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