



Pressing Matters: Vasopressors in Trauma Resuscitation

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Abstract

Purpose of Review This goal of this review is to examine the evolving role of vasopressors in trauma resuscitation, with a particular interest in patients with penetrating trauma, hemorrhagic shock, and refractory hypotension. We evaluate the physiologic basis, current evidence, and clinical scenarios in which vasopressors may be beneficial.

Recent Findings Traditional trauma resuscitation guidelines have consistently discouraged vasopressor use. However, there is emerging literature supporting the selective use of vasopressors to improve hemodynamic stability during trauma resuscitation efforts. Clinical studies support improved blood pressure and reduced transfusion requirements; however definitive mortality benefits have not been established.

Summary Current evidence does not support routine vasopressor use in trauma resuscitation. Nevertheless, vasopressors may serve as important adjunct to a balanced trauma resuscitation plan in select patients and clinical scenarios. Future large multicenter randomized control trials are needed to help define optimal patient selection, timing of intervention, and outcome benefits to vasopressors in trauma resuscitation.

Keywords Trauma · Resuscitation · Hemorrhagic Shock · Vasopressors · Norepinephrine · Vasopressin

Introduction

Trauma and related injuries represent a major global public health challenge, accounting for approximately 4.4 million deaths annually and nearly 8% of all deaths worldwide [1]. Looking closer, for individuals ranging from ages 5–29 years, trauma and associated injuries remain one of the leading causes of death [1]. Among these, there is a disturbing trend of penetrating trauma becoming an increasingly common occurrence in modern trauma care [2, 3]. This trend is particularly concerning within urban settings where firearm and stab related injuries continue to rise [2, 4]. This growing prevalence has placed a substantial burden on emergency

departments, surgical teams, and intensive care units, further bringing to the forefront the major associated health-care concern [2, 4].

Examining further, several social and environmental factors have contributed to this rise in penetrating trauma. Among them, increasing interpersonal violence, socioeconomic disparities, and greater access to firearms continue to drive an increase in the global burden of trauma [2, 4, 5]. This trend became even more apparent following the COVID-19 pandemic, in which many institutions documented further increases in gunshot related injuries and violent assaults [6–8]. When compared to blunt trauma injuries, penetrating injuries often produce more severe damage to tissues and blood vessels, thus leading to rapid blood loss, emergency surgery, massive transfusion, and early mortality [3, 9, 10]. Due to the high level of acuity, increasing burden, and large impact factor, it is essential to continue to study current guidelines, recommendations, and areas to help improve our management of trauma related injuries [9, 10].

The purpose of this narrative review is to offer an updated view on the use of vasopressors in within the setting of trauma resuscitation. Conventional teaching during trauma resuscitation is to “never use vasopressors” in trauma due to concerns of worsening hemorrhage and tissue ischemia

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[11–13]. After looking at the history of trauma management and identification of main causes of trauma induced shock, we hope to convey a framework of the unique profiles of different vasopressors along with identification of clinical scenarios where they may offer positive effects.

Brief History of Trauma Management

Further broken down, hemorrhagic shock remains one of the leading preventable causes of death following penetrating trauma [9, 14, 15]. Most early deaths in this population occur secondary to uncontrolled bleeding and subsequent inadequate tissue perfusion prior to definitive hemorrhage control [14, 15]. Looking closer into the evolution of trauma resuscitation, gives further insight into points of intervention that may lead to survival after a traumatic injury. Early 20th century resuscitation focused primarily on controlling hemorrhage surgically and replacing lost blood volume [16]. Starting during World War I, whole blood quickly became the primary resuscitation method used for resuscitation of injured US combatants [17]. Moving into World War II, freeze-dried plasma was introduced as resuscitation method as it was portable and stable at ambient temperatures [18]. However, this quickly fell out of favor as concerns arose over hepatitis transmission associated with pooled plasma [18]. A major shift occurred during the Vietnam War, where the introduction of crystalloids became the primary method of resuscitation [19, 20]. During this era, the increased risk of transfusion-associated infections along with research suggesting interstitial space needed resuscitation for trauma drove resuscitation to large volumes of crystalloids [19, 20]. The belief that rapid normalization of blood pressure would help with end organ perfusion drove this major shift and was later incorporated into early trauma protocols and Advanced Trauma Life Support (ATLS) training [20, 21]. Fortunately, the civilian sector quickly transitioned away from large volume crystalloid resuscitation, and by the 1990s it was widely held that excessive crystalloid use was found to precipitate acute respiratory distress syndrome, compartment syndrome, multi-organ dysfunction, and worsen dilutional coagulopathy [22–24]. By the early 2000s, Damage-Control Resuscitation (DCR) came to the forefront as the leading model for trauma care [25, 26]. DCR places an emphasis on early hemorrhage control, permissive hypotension, reduced crystalloid administration, and Massive Transfusion Protocols (MTPs) using individual units of plasma, platelets, and packed red blood cells in balanced proportions became the standard across major trauma centers [25–28]. Multiple studies demonstrated improved outcomes when balanced ratios of these individual units were used during massive transfusion resuscitation [27–29]. Moving to the present, trauma resuscitation developed further to include individualized

and physiologic based resuscitation. The inclusion of viscoelastic coagulation testing, low-titer type-O whole blood transfusions, and inclusion of anti-fibrinolytic medications such as tranexamic acid (TXA) have all been integrated along with rapid hemorrhage control as further refinements to improve trauma resuscitation [30–33].

Over the past 100 years, trauma resuscitation, like most things in the field of medicine, has undergone tremendous development and changes in management. However, through these shifts, the use of vasopressors for trauma resuscitation has largely remained a controversial treatment methodology [11–13]. Conventional teaching states that although many vasopressor agents may help to maintain blood pressure and subsequent end organ perfusion in patients with severe hypotension, they can also worsen tissue ischemia [11, 12]. Increases in blood pressure are thought to increase bleeding if administered prior to definitive hemorrhage control being achieved [11, 34]. Furthermore, excessive vasopressors are thought to impair microcirculatory blood flow leading to reduced oxygen delivery to vital organs through supraphysiologic vasoconstriction [12, 34]. Despite these long-standing views, there is emerging evidence that vasopressors may prove to be a beneficial adjunct in selected trauma patients, particularly in refractory hypotension, vasoplegia, traumatic brain injury, and neurogenic shock [9, 11, 35].

The aim of this review is to delve into the current role of vasopressors during the resuscitation of trauma patients. A particular focus will be on those trauma patients in the setting of hemorrhagic shock and accompanying refractory hypotension. We will discuss the pathophysiology of trauma induced shock, examine the physiological rationale for vasopressor administration, identify specific trauma scenarios where vasopressors may play a significant role, analyze current clinical evidence with regards to vasopressor use in trauma, and conclude with future directions for vasopressor use and study in penetrating trauma resuscitation.

Pathophysiology of Trauma Induced Shock

Prior to looking at the use of vasopressors as a treatment in trauma resuscitation, it is important to have a basis in the pathophysiology of trauma induced shock. Most trauma-induced shock occurs secondary to severe blood loss combined with tissue injury leading to inadequate circulating volume and diminished oxygen delivery to tissues [10, 14, 15]. Consequently, impaired end organ perfusion leads to cellular hypoxia, anaerobic metabolism, metabolic acidosis, and ultimately organ dysfunction [10, 14]. Initially a sympathetic response from the nervous system is activated with a subsequent catecholamine release to maintain blood pressure and perfusion [36, 37]. Dysfunction of this sympathetic response occurs in the setting of prolonged shock leading to

systemic inflammation, endothelial dysfunction, coagulopathy, and metabolic acidosis [17, 34, 38]. Eventually, microcirculatory failure, organ dysfunction, and death can occur if definitive hemorrhage control and adequate resuscitation are not achieved [10, 14, 15].

One of the major areas of dysfunction in trauma induced shock comes from trauma induced vasoplegia [13, 39, 40]. This is characterized by profound vasodilation in response to hemorrhagic shock and severe injuries, despite adequate crystalloid and colloid resuscitation [13, 39]. The pathophysiology is thought to result from as a systemic inflammatory response leading to excessive nitric oxide production along with depletion of endogenous vasoconstrictors such as Endothelin-1 (ET-1), Angiotensin II (Ang II), Norepinephrine, and Vasopressin [39–42]. Thus, a significant vasoplegic event can result, with the decreased mean arterial pressure leading to further impaired microcirculatory perfusion [13, 39, 40]. Endothelial dysfunction is another factor contributing to trauma-induced shock [38, 43]. This occurs in the setting of hemorrhagic shock leading to tissue hypoperfusion, inflammation, and ischemia-reperfusion injuries preceding a disruption of the vascular endothelial glycocalyx with subsequent increased capillary permeability [17, 18, 43]. Again, this feedback response to hemorrhagic shock can contribute to microcirculatory impairment, tissue edema, and worsening organ dysfunction [43–44]. One of the final areas contributing to pathophysiology of trauma-induced shock comes from endogenous catecholamines released in response to the activation of the sympathetic nervous system (SNS) [36, 37]. Hypoperfusion associated with hemorrhagic shock leads to the activation of the SNS and hypothalamic-pituitary-adrenal axis [36, 45]. This activation leads to increased release and circulating levels of endogenous catecholamines to help maintain blood pressure and organ perfusion [45]. However, in the setting of prolonged shock, catecholamine depletion can quickly occur, leading to refractory hypotension and resultant circulatory collapse [39, 41, 45]. After breaking down the underlying

pathophysiology of trauma-induced shock, potential areas of intervention with vasopressors start to appear.

Vasopressors in Trauma

When talking about vasopressors in trauma, it is very easy to just focus on the generic term of pharmacologic agents that increase blood pressure by causing vasoconstriction and, in some cases, enhance cardiac output [13]. While true, the multitude of different vasopressors possess different attributes that favor a certain agent for a specific clinical scenario or patient population. Table 1 provides a succinct summary of these different mechanisms of action along with key clinical effects. One of the mainstays in treatment of trauma-associated hypotension after resuscitation is norepinephrine [13, 24, 46]. It normally functions as an endogenous catecholamine that primarily functions on α 1-adrenergic receptors to produce peripheral vasoconstriction and increased systemic vascular resistance [24, 46]. Additionally, it has a moderate level of β 1-adrenergic activity that can augment myocardial contractility without significant chronotropic effect [24]. When exogenous supplementation is added, the combined effects of vasoconstriction and increased inotropy function to make norepinephrine a frequent first line treatment for refractory hypotension in many shock states [24, 46]. Epinephrine is another endogenous catecholamine with a strong inotropic and vasopressor effect with effects on combined effects on α 1-, β 1-, and β 2-adrenergic receptors [24, 47]. At lower supplementation doses, more potent β -adrenergic effects predominate, increasing both inotropy and chronotropy to increase heart contractility and rate. Escalating to higher doses, α 1 receptor activation produces significant vasoconstriction [24, 47]. Vasopressin functions as a non-catecholamine vasopressor through activation of V1 receptors on vascular smooth muscle [23, 24]. This allows it to function to increase vasoconstriction independent of adrenergic receptor responsiveness [20, 24]. The alternative pathway to vasoconstriction makes vasopressin especially important

Table 1 Pharmacology of vasopressors

Vasopressor	Primary receptor action	Cardiovascular effects	Key clinical effects	Major considerations
Norepinephrine	Strong α 1, moderate β 1	$\uparrow$ SVR, $\uparrow$ MAP, mild $\uparrow$ contractility	First-line in distributive shock; improves perfusion pressure	Preferred in trauma-associated hypotension after resuscitation
Epinephrine	α 1, β 1, β 2	$\uparrow$ HR, $\uparrow$ contractility, $\uparrow$ SVR (dose-dependent)	Strong inotropic and vasopressor effect	Can increase lactate; higher arrhythmia risk
Vasopressin	V1 receptor agonist	$\uparrow$ SVR independent of adrenergic system	Restores vascular tone in catecholamine-resistant shock	Useful in vasoplegia; may reduce norepinephrine requirements
Phenylephrine	Pure α 1 agonist	$\uparrow$ SVR, reflex bradycardia	Raises MAP via vasoconstriction only	May reduce cardiac output; limited use in trauma
Dopamine	Dose-dependent D1, β 1, α 1	$\uparrow$ CO (low–moderate dose), $\uparrow$ SVR (high dose)	Variable effects depending on dose	Higher arrhythmia risk; largely replaced in modern practice
Angiotensin II	AT1 receptor agonist	$\uparrow$ SVR, $\uparrow$ aldosterone release	Potent vasoconstriction in refractory shock	Used in catecholamine-resistant vasodilatory shock

in patients with catecholamine-resistant shock states [20, 23]. Phenylephrine functions through $\alpha 1$ -adrenergic receptor stimulation to increase arterial and venous vasoconstriction [24, 47]. Pure $\alpha 1$ effects, in conjunction with a lack of β stimulation, can lead to reflex bradycardia and despite a higher MAP, can reduce cardiac output [24]. As the third key endogenous catecholamine, dopamine functions on multiple different sites including dopaminergic, α , and β receptors [24, 48]. Supplementation with exogenous dopamine initially leads to effects primarily on dopaminergic receptors, originally thought to increase renal perfusion, although this has largely been disproven [48, 49]. At escalating doses, first $\beta 1$ -adrenergic stimulation takes place to increase cardiac output followed by $\alpha 1$ -adrenergic receptor stimulation to increase vasoconstriction [24]. Despite the broad receptor activation, dopamine has multiple negative effects including increasing risk of precipitating arrhythmias and less predictable hemodynamic effects that have caused it to fall out of favor as a first line vasopressor [24, 48].

Consideration of the unique profiles of the different vasopressors can lead to their selection in certain clinical scenarios. Despite the seemingly broad ranging positive effects these vasopressors may provide, it is important to balance this along with the important risks they also convey. As previously described, excessive vasoconstriction can dramatically reduce microcirculatory blood flow, especially in the setting of hemorrhagic shock. Resultant impaired oxygen delivery at the microcapillary and tissue level can occur despite a seemingly normal mean arterial pressure (MAP) [11, 12, 34]. This impairment can lead to hypoxia on a cellular level thus leading to organ dysfunction and eventual failure. Coming from another direction, despite the seemingly beneficial effect of vasopressors increasing the MAP, early vasopressor use prior to adequate hemorrhage control can be detrimental by exacerbating bleeding through raising the blood pressure at sites of uncontrolled hemorrhage [11, 22]. The disruption of thrombus by a higher MAP can also precipitate bleeding with consumption of platelets and coagulation factors, further worsening coagulopathy [34]. Another concerning factor is that ongoing vasopressor use may conceal ongoing hypovolemia leading to inadequate resuscitation [11, 12]. On an organ system level, vasopressors are associated with increased myocardial oxygen demand, which in vulnerable populations can precipitate myocardial ischemia [24]. This same vasoconstriction can also affect renal, splanchnic, and gut perfusion leading to further end organ ischemia [24–47]. At higher levels, certain vasopressors and inotropes can precipitate arrhythmias which can have lethal consequences in patients in hypovolemic shock [48]. Vasopressors may artificially raise mean arterial pressure; however, this number may give a false sense of security in the trauma resuscitation algorithm. Despite a

seemingly normal MAP, there is no actual measurement of cardiac output and consequently inadequate tissue perfusion may be hidden.

Taken together, the multitude of potential side effects and associated complications seem to make an easy case that vasopressors in trauma should be avoided with extreme prejudice. Despite this, we hold a position that vasopressors may be deployed with a high level of vigilance to provide potential benefits to a trauma population. One area where vasopressor consideration may hold significant benefit would be in the setting of maintenance of coronary blood flow. As coronary blood flow is highly dependent on the aortic diastolic pressure, especially to the left ventricle, vasopressors can be used to increase systemic vascular tone to continue myocardial oxygen demand [50]. Along with this, a reflex slowing of the heart rate with an augmented MAP can decrease myocardial oxygen demand and increase time in diastole, further increasing myocardial oxygen delivery, and increase heart filling and subsequent cardiac output [50]. As previously described, this needs to be balanced against excessive vasoconstriction which can have the contrary effect of worsening myocardial oxygen demand. Another area of benefit that vasopressors may convey is limitation of excessive crystalloid or blood product administration during damage control surgery [13, 25]. Vasopressors can support blood pressure in the short term with lower fluid administration to avoid potential side effects associated with tissue edema, compartment syndrome, and dilutional coagulopathy [13, 23–25]. As discussed in a recent 2023 European guideline on management of major bleeding and coagulopathy following trauma, vasopressors can serve an important role in the persistently vasoplegic patient despite adequate hemorrhage control along with a balanced blood product administration [9]. Again, despite acknowledging the potential benefit, they again stress the importance of careful titration to avoid impairing microcirculatory blood flow [9]. Vasopressors again have a controversial role as adjunct treatment in damage control resuscitation. As we will look at in the discussion section below, there have not been any large, randomized control studies looking into the survival benefit of vasopressors during trauma stabilization in a pre-hospital, operating room, or ICU setting [12, 13]. Despite this, there may be a place for vasopressors to prevent complete circulatory collapse and temporary stabilization while ongoing hemorrhage control is achieved, and transfusion protocols can be initiated. Adequate MAP is also essential in maintenance of cerebral perfusion pressure (CPP), defined as intracranial pressure subtracted from mean arterial pressure [30, 51]. Although much of this review focuses on penetrating trauma, traumatic brain injury can be closely associated with this patient population, thus supporting of CPP through vasopressor supplementation of MAP can help

to maintain adequate cerebral blood flow [30, 51]. Other special trauma subgroups may also see significant benefit with the use of vasopressors as an adjuvant to their overall treatment plan. Spinal cord injuries (SCIs) are unfortunately a frequent confounding factor of many traumas. Of these, traumatic cervical SCIs often result in neurogenic shock characterized by profound bradycardia, hypotension, and autonomic dysregulation [52, 53]. In this setting, vasopressors can help stabilize both perfusion to the spine in hopes of recovery, but also to stabilize a polytrauma patient suffering from autonomic dysregulation [52, 53].

Clinical Evidence

As previously identified, there are multiple areas of potential benefit of vasopressors in penetrating trauma. Despite this, there is a paucity of actual clinical trials supporting vasopressor use in trauma [12]. Most data are derived from small, randomized trials, observational reviews, and extrapolation of data from non-trauma shock settings [12]. To this point, many studies point to the heterogeneity of trauma patient populations, timing of interventions, and concurrent resuscitation strategies as some of the limiting factors to significant academic findings [12, 13]. Despite the scarcity of high-quality evidence, there seems to be consensus that vasopressin and norepinephrine can function as first-line vasopressors in trauma resuscitation [13, 46].

One of the strongest trauma-specific supporters for the use of vasopressors in trauma comes from a 2011 study by Cohn et al. that found low-dose vasopressin in severely injured patient with hemorrhagic shock reduced fluid requirements and improved early hemodynamic stability when compared to standard resuscitation measures [35]. It is essential to note that this study was underpowered to detect significant mortality differences between the study groups [35]. A subsequent study by Sims et al. with the AVERT Shock trial looked at vasopressin supplementation vs. placebo to find that the vasopressin intervention group had reduced transfusion requirements in selected patients but again was underpowered to identify mortality differences [54]. Together, the Cohn and Sims findings support the identified physiologic rationale that vasopressin can offer benefit in the setting of endogenous vasopressin depletion and subsequent catecholamine-resistant vasodilation [35, 54]. Looking further into the benefit of vasopressin, a randomized control trial by van Haren et al. investigated vasopressin vs. standard vasopressors in patients with severe traumatic brain injury [55]. They found that vasopressin may assist in maintaining cerebral perfusion pressure while reducing catecholamine supplementation [55]. Together, these studies lay the groundwork for vasopressin supporting hemodynamic stability in multiple trauma settings, however, they are also linked in their

limited sample sizes and power to detect differences in mortality outcomes [35, 54, 55].

When looking at norepinephrine in trauma, most findings are taken from observational studies as opposed to randomized controlled trials [26, 46]. A 2022 cohort study of 2164 patients across the US and France by Gauss et al. investigated early norepinephrine vs. no early vasopressor. Looking at their primary outcome of 24-hour mortality, they found that early norepinephrine was not associated with 24-hour mortality risk [26]. The lack of definitive mortality benefit may be seen as a strike against norepinephrine in trauma cases, however further investigation of the findings described the limitations of retrospective trauma reviews [26, 46]. It points to norepinephrine consistently improving mean arterial pressure and shock reversal, but the absence of mortality benefits could be associated more with the severity of the illness rather than a causal harmful effect [26]. Using a broader search, a South African retrospective ICU study demonstrated that although catecholamine doses were generally associated with higher mortality, trauma patients were an outlying exception [56]. In this patient population, they found survival benefits despite high doses vasopressors. They postulated that this may have been more a reflection of a younger patient population with lower comorbidity burden. However, any survival benefit remains important because it supports the trial of vasopressors in trauma.

Rossaint et al. sought to come out with consensus vasopressor recommendations for major hemorrhagic trauma patients with their 2023 European Trauma Guidelines [9]. They cautiously recommended vasopressors only in an adjuvant role alongside hemorrhage control and blood resuscitation. Emphasis was placed that vasopressors should be reserved for cases of persistent hypotension despite adequate volume resuscitation [9]. Of note, they did identify traumatic brain injury or neurogenic shock as specific physiologic conditions that may benefit from early intervention with vasopressors in a trauma setting [9].

Looking to more recent publications about vasopressors in trauma unfortunately does not provide a more definitive picture than our previous reviews. In 2024, the National Association of Emergency Medical Services Physicians (NAEMSP) came out with recommendations for pre-hospital trauma vasopressor [57]. They concluded that routine vasopressor use in hemorrhagic shock is not supported in the pre-hospital setting [57]. In contrast, a 2025 trauma surgery review by Burke et al. identified a shift away from the old thinking of “never use vasopressors in trauma” towards identification of specific clinical scenarios where selective use may be indicated [58]. These recent opposing conclusions, stemming from a lack of documented superiority of a certain treatment path, further fuel the ongoing controversy of whether vasopressors have a place in trauma resuscitation.

Overall, the evidence in support of vasopressors in trauma is lacking, but a summary of the described studies is shown in Table 2. Most studies point to the heterogeneity of the trauma patient population, confounding resuscitation measures, lack of consistent outcome measures, and timing of interventions as significant barriers to large randomized controlled trials [12, 13]. However, we hold that integration of the evidence available suggests that vasopressors may play an important supportive role in trauma resuscitation. Most of the evidence points to vasopressin offering advantages in vasodilatory states, while norepinephrine is frequently cited as a first line agent for refractory hypotension [9, 13, 46]. The pathophysiology of certain trauma scenarios, spinal cord injury, traumatic brain injuries, along with extrapolation of other study findings to trauma physiology offer a path to possible benefits. As an example, the VANCS trial by Hajjar et al. is often cited as a landmark trial in the treatment of vasoplegic shock after cardiac surgery [33]. In this study, vasopressin was found to have a lower composite outcome of mortality or severe complications when compared to norepinephrine [33]. Studies like this can be extrapolated to identify further areas of study to make a positive impact on morbidity and mortality. However, definitive conclusions on survival benefits associated with vasopressors in trauma patients remain elusive at this time.

Alternative Vasopressors

If we move towards an expansion beyond the textbook definition of vasopressors in trauma patients there is some additional resources available to take advantage of. One such ‘agent’ we can look towards is calcium supplementation [34, 35, 38]. Calcium plays an integral role in cardiovascular function though its action as a mediator of myocardial contractility [59, 60]. Additionally, it has been shown to be a mediator of smooth muscle tone, and coagulation enzyme activity. While not a typical vasopressor, these actions together help to improve hemodynamic status indirectly through increased myocardial contractility and responsiveness to endogenous and exogenous vasopressors [59]. Low ionized calcium levels have been shown to be associated with decreased vasopressor responsiveness and thus worsening shock physiology [61]. Furthermore, hypocalcemia is frequently cited as correlated with increased mortality in trauma populations. This becomes essential information in the setting of massive transfusion protocols as excess citrate binds to ionized calcium quickly leading to a significant lowering of free ionized calcium [34, 60, 61]. Unlike many of the previously mentioned vasopressors, calcium functions as an adjunct to improve arterial pressure and cardiac output without many of the side effects associated with traditional vasopressors [59–61]. There is increasing evidence for its

Table 2 Summary of key studies evaluating vasopressor use in trauma resuscitation

Study	Design	Population	Intervention	Primary outcome	Key findings
Cohn et al., 2011 [35]	Prospective randomized controlled trial	Severely injured trauma patients with hemorrhagic shock	Low-dose vasopressin vs. standard resuscitation	Fluid requirements and clinical outcomes	Vasopressin reduced fluid requirements and improved early hemodynamic stability. Study was underpowered to detect mortality differences.
Sims et al. (AVERT Shock Trial)	Randomized, placebo-controlled trial	Trauma patients with hemorrhagic shock requiring massive transfusion	Low-dose arginine vasopressin vs. placebo	Blood product transfusion requirements	Vasopressin reduced transfusion requirements and suggested improved hemodynamic control, but no significant mortality benefit was demonstrated.
van Haren et al., 2013 [55]	Pilot randomized controlled trial	Patients with severe traumatic brain injury	Vasopressin vs. standard vasopressor therapy	Cerebral perfusion pressure (CPP) maintenance	Vasopressin maintained CPP while reducing catecholamine requirements, suggesting a potential role in severe TBI resuscitation.
Gauss et al., 2022	Multicenter retrospective cohort study	2,164 patients with blunt trauma and hemorrhagic shock	Early norepinephrine administration vs. no early vasopressor	24-hour mortality	Early norepinephrine was not associated with increased or decreased 24-hour mortality. Improved blood pressure support was observed.
Rossaint et al., 2023 [9]	Evidence-based guideline	Major trauma patients with hemorrhage and coagulopathy	Guideline recommendations for vasopressor use	Consensus recommendations	Vasopressors should be considered only as adjuncts to hemorrhage control and balanced resuscitation in patients with persistent hypotension despite adequate volume replacement.
Tubert et al., 2024	Narrative review	Trauma-induced hemorrhagic shock	Evaluation of fluid resuscitation strategies	Review of contemporary evidence	Highlighted limitations of excessive crystalloid administration and supported physiologically guided resuscitation, including selective vasopressor use in refractory shock states.
Burke et al., 2025 [58]	Contemporary review article	Trauma resuscitation patients	Review of vasopressor utilization in trauma	Synthesis of emerging evidence	Identified a shift away from the dogma of “never use vasopressors in trauma” toward selective use in specific clinical scenarios such as vasoplegia, neurogenic shock, and traumatic brain injury.

integration into massive transfusion protocols for trauma patients in hemorrhagic shock resuscitation strategies.

Other vasopressors, such as Methylene Blue and Angiotensin II have emerged as rescue therapies in cases of refractory shock, acting through non-adrenergic pathways [9, 62–64]. Both have demonstrated hemodynamic benefits in the treatment of distributive shock, but once more without consistent evidence of mortality improvement [62–64]. They may show potential benefit to future trauma resuscitation investigations in treating catecholamine-resistant shock states.

If we expand our review to vasopressors administered by alternative methods, reviews frequently report intracardiac epinephrine as an alternative method of administration [65–67]. In this situation, a high concentration of epinephrine, typically 1:1000 or 1 mg/mL, is administered directly into the left ventricle chamber via a resuscitative thoracotomy during a cardiac arrest [65]. This technique originally developed out of necessity when peripheral or central venous access was difficult to secure. The theoretical advantage comes from the direct α and β -adrenergic stimulation down the coronary arteries to increase myocardial contractility along with peripheral vasoconstriction as a key part of a resuscitation strategy [65, 66]. Despite these hypothetical advantages, modern guidelines discourage this administration in both traumatic and non-traumatic cardiac arrests in favor of IV epinephrine administration [66, 67]. Studies have not proven significant survival benefit when compared to intravenous or intraosseous administration. There are even documented associated risks including coronary artery injury, myocardial laceration, hemopericardium and cardiac tamponade. Despite this, there remain continued published case reports of intracardiac epinephrine being administered in dire resuscitation scenarios as a last resort measure [66, 67].

Further expansion to adjuvant therapies may include the role of low dose steroid supplementation in trauma cases where inotropes or vasopressors are used. Low-dose corticosteroids are not typically recommended in trauma resuscitation, however further study may be warranted if we apply secondary literature. Looking at the surviving sepsis campaign of 2021, IV hydrocortisone for patients in septic shock who have an ongoing vasopressor requirement can accelerate shock reversal [68]. Despite this, there isn't a direct finding in trauma resuscitation, however future studies may demonstrate mortality benefit. However, if the trauma contains trauma including traumatic brain injury steroids have frequently been shown to be harmful as seen in a study by Mass, et al. [69]. These confounding applications further highlight the overall finding of this review that like most things in medicine, the use of specific treatments are closely tied to exact scenario in which they are applied.

Conclusion

The role of vasopressors in trauma resuscitation remains a nuanced and complex one that continues to transform alongside the management of these patients. Currently, there is a paucity of evidence to support the routine use of vasopressors as the standard of care in trauma patients suffering from traumatic hemorrhagic shock. Despite this, for clinical scenarios of refractory hypotension, trauma-induced vasoplegia, traumatic brain injury, or neurogenic shock may benefit from selective administration of vasopressors. Vasopressin and norepinephrine have emerged as the frontrunner agents to improve blood pressure and provide physiologic stability in trauma resuscitation despite not consistently showing a survival benefit. Despite taking the stance that vasopressors can offer benefits to the trauma setting, we acknowledge that they should never be prioritized over prompt hemorrhage control, balanced transfusion resuscitation, and correction of other reversible contributors to shock. Vasopressor use should be balanced based on indication, potential benefit over harm, and with the intention of limiting exposure to the minimal intervention required. Trauma care has continued to undergo rapid development over the past century. In support of this development, large, standardized, multi-center randomized control trials should be prioritized to identify any mortality benefits to vasopressors in trauma resuscitation. Until these findings can be identified, the use of vasopressors must rely on a clinician's ability to balance the potential benefits and risks in adapting to the unique clinical setting of trauma resuscitation. Future studies may find additional benefit and guidance from incorporation of new technologies including transesophageal echo (TEE) or algorithm based cardiac output monitoring to further guide judicious vasopressor use during trauma resuscitation.

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 - This 2011 prospective-randomized clinical trial sought to determine if adding low-dose vasopressin to standard fluid resuscitation in hypotensive trauma patients could reduce fluid requirements and improve outcomes. It is important as it showed that the intervention with low-dose vasopressin improved early hemodynamic stability and reduced

fluid needs. This is one of the early prospective trials that fought the convention of no vasopressors in trauma patients. Despite this, it was not powered to find any definitive mortality benefit, however the non-inferiority helped opposed the conventional thoughts that vasopressors cause harm in trauma resuscitation.

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 - This 2024 narrative review focuses on the current role of crystalloid resuscitation during the treatment of trauma associated hemorrhagic shock. Despite this focus, it does provide a recent framework and summary of situations where vasopressors may fit following hemorrhage control. It is important because in addition to identification of these scenarios, it addresses the increasing interest in vasopressor-supported resuscitation.
- Burke EG, Hartley BW, Succar B, Dumas RP. Re-thinking vasopressor use in the trauma bay: a shifting perspective. *Trauma Surgery & Acute Care Open*. 2025;10(Suppl 1): e001788. doi:<https://doi.org/10.1136/tsaco-2025-001788>.
 - 2025 trauma surgery review identified a shift away from the old thinking of “never use vasopressors in trauma” towards identification of specific clinical scenarios where selective use may be indicated. They pointed to traumatic brain injury, spinal cord injuries, selective hemorrhagic shock patients after adequate resuscitation, and peri-intubation as examples of clinical scenarios where there is potential for vasopressor use. This is one of the most recent examples that challenges the historical teaching of “bleeding patients need blood, not pressors.”

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Conflict of interest I declare that all the authors have no competing interests as defined by Springer, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

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