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A Comprehensive Systematic Review of The Role of Vasopressors in Early Management of Hemorrhagic Shock

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ABSTRACT

Introduction: The role of vasopressors in the early management of hemorrhagic shock remains controversial, with conflicting evidence from observational studies and randomized controlled trials. This systematic review aims to evaluate the efficacy and safety of early vasopressor administration in adult patients with hemorrhagic shock.

Methods: A systematic review was conducted screening studies based on predefined criteria: adult patients with hemorrhagic shock from any cause, evaluation of any vasopressor agent within the first 24 hours, comparative study designs reporting clinically relevant outcomes. Fifty-eight sources were identified including randomized controlled trials, observational studies, and systematic reviews. Data were extracted on patient populations, vasopressor interventions, mortality outcomes, hemodynamic effects, fluid requirements, and adverse events.

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Results: Randomized controlled trials demonstrated that low-dose norepinephrine (<0.3 µg/kg/min) concurrent with fluid resuscitation significantly reduced 24-hour mortality (3% vs 13%, p<0.05) and in-hospital mortality (9% vs 21%, p<0.05) (Mohamed et al., 2024). The AVERT-Shock trial found no mortality difference with low-dose vasopressin but showed reduced blood product requirements (1.4 L vs 2.9 L, p=0.01) (Sims et al., 2019). Observational studies consistently associated vasopressor use with increased mortality (Aoki et al., 2018; Plurad et al., 2011; Fisher et al., 2020), though propensity-score analyses attenuated this association (Gauss et al., 2018). Vasopressors consistently achieved hemodynamic stabilization with improved mean arterial pressure and reduced fluid requirements. Adverse event profiles were similar between groups, with vasopressin associated with fewer deep venous thromboses (Sims et al., 2019).

Discussion: The apparent contradiction between observational and randomized evidence is explained by confounding by indication, where sicker patients preferentially receive vasopressors. Context-dependent effects, agent-specific considerations, and timing of administration significantly influence outcomes. Low-dose vasopressors appear safe when used as adjuncts to—not replacements for—hemorrhage control and volume resuscitation.

Conclusion: Early low-dose vasopressor administration, particularly norepinephrine and vasopressin, may be beneficial in selected patients with hemorrhagic shock, improving hemodynamic stability and reducing transfusion requirements without increasing mortality. Further research is needed to optimize agent selection, dosing strategies, and timing of initiation.

Keywords: Hemorrhagic shock, vasopressors, norepinephrine,

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vasopressin, resuscitation, mortality, fluid therapy

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INTRODUCTION

Background

Hemorrhagic shock remains a leading cause of preventable death in trauma, surgical, obstetric, and gastrointestinal bleeding patients worldwide (Claes et al., 2024). The traditional approach to hemorrhagic shock management has emphasized rapid hemorrhage control and volume resuscitation with crystalloids and blood products, while vasopressors have been relatively contraindicated due to theoretical concerns that vasoconstriction may exacerbate bleeding by increasing hydrostatic pressure at injury sites and compromising tissue perfusion (Beloncle et al., 2013; Dutton, 2007). However, this paradigm has been increasingly challenged as accumulating evidence suggests that excessive fluid resuscitation may itself be harmful, contributing to coagulopathy, dilutional anemia, and tissue edema (Tubert et al., 2024).

The pathophysiology of hemorrhagic shock involves complex neurohormonal responses, including endogenous vasopressin release, which is often depleted in prolonged or severe shock states (Holmes and Walley, 2004; Morales et al., 2000). This observation has generated interest in exogenous vasopressor support as a potential adjunct to resuscitation, particularly in patients who remain hypotensive despite adequate volume replacement (Strohmenger et al., 2003; Wenzel et al., 2008).

Research Gap

Despite decades of clinical experience, the role of vasopressors in early hemorrhagic shock management remains poorly defined. A fundamental disconnect exists between observational studies consistently demonstrating increased mortality associated with vasopressor use (Aoki et al., 2018; Plurad et al., 2011; Fisher et al., 2020) and emerging randomized controlled trials suggesting potential benefit or neutrality (Mohamed et al., 2024; Sims et al., 2019). This discrepancy has created clinical uncertainty, with practice patterns varying widely across institutions and providers (Gao et al., 2025; Hylands et al., 2017b).

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Furthermore, significant heterogeneity exists in how "early" vasopressor administration is defined, ranging from prehospital initiation to within 24 hours of hospital arrival (Lienhart et al., 2007; Anand et al., 2024). Optimal agent selection, dosing strategies, timing relative to fluid resuscitation, and identification of patients most likely to benefit remain unresolved questions (Ragoonanan and Friedman, 2021; Stampfl and DeBlieux, 2024).

Novelty

This systematic review provides a comprehensive synthesis of the available evidence spanning 2000-2025, uniquely integrating findings from randomized controlled trials, observational studies, and meta-analyses to reconcile apparent contradictions. Unlike previous reviews that have focused on specific agents or patient populations, this review examines the full spectrum of vasopressor agents across all causes of hemorrhagic shock, with particular attention to the critical distinction between confounding by indication and true treatment effects. The inclusion of recent high-quality propensity-score analyses (Gauss et al., 2018) and the latest randomized trial evidence (Mohamed et al., 2024; Cucci et al., 2025) provides an up-to-date evidence synthesis.

Research Objectives

This systematic review aims to:

1. Evaluate the effect of early vasopressor administration on mortality in adult patients with hemorrhagic shock
2. Assess hemodynamic responses and tissue perfusion indicators following vasopressor initiation
3. Examine the impact of vasopressors on blood product and fluid resuscitation requirements
4. Characterize adverse event profiles associated with different vasopressor agents
5. Identify context-dependent factors that may modify treatment outcomes
6. Synthesize evidence to provide clinically applicable recommendations

Hypotheses

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Based on the available evidence, we hypothesize that:

1. The apparent harm of vasopressors in observational studies is primarily attributable to confounding by indication rather than direct treatment toxicity
2. Low-dose vasopressor administration, when used as an adjunct to appropriate volume resuscitation, may improve hemodynamic stability without increasing mortality
3. Vasopressin and norepinephrine have distinct safety and efficacy profiles that may favor their use in specific clinical contexts
4. Early vasopressor administration may reduce total fluid resuscitation requirements

Benefits of the Study

This review aims to provide clinicians with evidence-based guidance for vasopressor use in hemorrhagic shock, potentially reducing inappropriate therapeutic inhibition in patients who might benefit while preventing unnecessary exposure in those unlikely to derive advantage. For researchers, this synthesis identifies critical knowledge gaps and informs future trial design. For guideline developers, this comprehensive evidence integration supports the refinement of resuscitation algorithms.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the role of vasopressors in early management of hemorrhagic shock.

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Screening

We screened in sources based on their abstracts that met these criteria:

- **Population - Hemorrhagic Shock**: Does this study include patients diagnosed with hemorrhagic shock from any cause (trauma, surgical, gastrointestinal bleeding, obstetric hemorrhage, etc.)?
- **Intervention - Vasopressor Use**: Does this study evaluate the use of any vasopressor agent (norepinephrine, epinephrine, dopamine, vasopressin, phenylephrine, etc.) as a therapeutic intervention?
- **Timeframe - Early Management**: Does this study focus on vasopressor use within the first 24 hours of hemorrhagic shock recognition or during the acute resuscitation phase?
- **Study Design - Comparative**: Does this study include a comparison group (control, placebo, standard care, or alternative vasopressor)?
- **Study Population - Human Subjects**: Is this study conducted in human subjects (not animal or in-vitro studies)?
- **Population Age - Adult Patients**: Does this study focus on patients 16 years and older (not exclusively pediatric populations under 16 years)?
- **Outcomes - Clinical Relevance**: Does this study report at least one clinically relevant outcome such as mortality, hemodynamic parameters, organ function, length of stay, or adverse events?
- **Study Design - Adequate Methodology**: Is this study one of the following designs: randomized controlled trial, non-randomized controlled trial, cohort study, case-control study, systematic review, or meta-analysis (not a case report, case series, conference abstract, or unpublished study)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

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The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Hemorrhagic Shock	Vasopressors	Standard Resuscitation	Mortality
Keyword 2	Traumatic Hemorrhage	Norepinephrine	Fluid Therapy Alone	Hemodynamic Stability
Keyword 3	Major Bleeding	Vasopressin	Conventional Care	Transfusion Requirements
Keyword 4	Acute Blood Loss	Early Vasoactive Support	No Early Vasopressors	Adverse Events

The Boolean MeSH keywords inputted on databases for this research are: *("Hemorrhagic Shock" OR "Traumatic Hemorrhage" OR "Major Bleeding" OR "Acute Blood Loss") AND ("Vasopressors" OR "Norepinephrine" OR "Vasopressin" OR "Early Vasoactive Support") AND ("Standard Resuscitation" OR "Fluid Therapy Alone" OR "Conventional Care" OR "No Early Vasopressors") AND ("Mortality" OR "Hemodynamic Stability" OR "Transfusion Requirements" OR "Adverse Events")*

Data extraction

- **Patient Population**:

  Extract characteristics of hemorrhagic shock patients, including:

  - Type of hemorrhagic shock (traumatic, surgical, gastrointestinal, etc.)
  - Severity indicators (blood pressure, shock index, blood loss volume, transfusion requirements)
  - Demographics (age, gender) if relevant to outcomes
  - Underlying cause/mechanism of injury

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- Exclusion criteria that might affect generalizability

- **Vasopressor Intervention**:

  Extract all details about vasopressor use in hemorrhagic shock management, including:

  - Specific vasopressor agent(s) used (norepinephrine, epinephrine, vasopressin, dopamine, phenylephrine, etc.)
  - Dosing regimen (initial dose, titration, maximum dose)
  - Route of administration
  - Duration of treatment
  - Combination therapies (multiple vasopressors, other agents)

- **Early Management Definition**:

  Extract how 'early management' is defined and operationalized, including:

  - Time window for vasopressor initiation (e.g., within 24 hours, within 6 hours, etc.)
  - Reference point for timing (arrival at ED, hospital admission, recognition of shock)
  - Any distinction made between immediate, early, and late vasopressor use
  - Sequence relative to other interventions (before/after fluid resuscitation, surgery, etc.)

- **Mortality Outcomes**:

  Extract all mortality-related findings for early vasopressor use in hemorrhagic shock, including:

  - Primary mortality endpoint (in-hospital, 30-day, 24-hour, etc.)
  - Mortality rates in vasopressor vs. control groups
  - Adjusted and unadjusted mortality risk (odds ratios, hazard ratios, relative risk with confidence intervals)

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- Time-to-death data if available
- Factors that modified mortality risk

- **Hemodynamic Effects**:

  Extract hemodynamic responses to early vasopressor use in hemorrhagic shock, including:

  - Blood pressure response (systolic, diastolic, mean arterial pressure)
  - Heart rate changes
  - Cardiac output or stroke volume effects
  - Tissue perfusion indicators (lactate, base deficit, organ function)
  - Time to hemodynamic stabilization
  - Vasoconstriction effects on bleeding control

- **Fluid Resuscitation Context**:

  Extract details about concurrent fluid management with early vasopressor use, including:

  - Volume of fluids administered (crystalloids, colloids, blood products)
  - Timing of fluid vs. vasopressor administration
  - Volume status assessment (central venous pressure, hypovolemia indicators)
  - Comparison of outcomes based on volume status
  - Fluid resuscitation strategy (aggressive vs. restrictive)
  - Blood transfusion requirements and timing

- **Adverse Effects**:

  Extract complications and negative effects specifically associated with early vasopressor use in hemorrhagic shock, including:

  - Cardiovascular complications (arrhythmias, myocardial ischemia, cardiac arrest)
  - Tissue ischemia or necrosis

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- Renal dysfunction
- Increased bleeding or worsened hemorrhage
- Limb or digit ischemia
- Any dose-dependent adverse effects
- Comparison of adverse event rates between vasopressor and control groups

- **Study Design**:

  Extract study methodology information essential for interpreting vasopressor findings, including:

  - Study type (RCT, cohort, case-control, case series)
  - Sample size and power considerations
  - Control group characteristics (standard care, placebo, no vasopressor)
  - Primary and secondary endpoints
  - Follow-up duration
  - Key confounding variables controlled for
  - Statistical methods used for analyzing vasopressor effects

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Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	*("Hemorrhagic Shock" OR "Traumatic Hemorrhage" OR "Major Bleeding" OR "Acute Blood Loss") AND ("Vasopressors" OR "Norepinephrine" OR "Vasopressin" OR "Early Vasoactive Support") AND ("Standard Resuscitation" OR "Fluid Therapy Alone" OR "Conventional Care" OR "No Early Vasopressors") AND ("Mortality" OR "Hemodynamic Stability" OR "Transfusion Requirements" OR "Adverse Events")*	24
Semantic Scholar	*("Hemorrhagic Shock" OR "Traumatic Hemorrhage" OR "Major Bleeding" OR "Acute Blood Loss") AND ("Vasopressors" OR "Norepinephrine" OR "Vasopressin" OR "Early Vasoactive Support") AND ("Standard Resuscitation" OR "Fluid Therapy Alone" OR "Conventional Care" OR "No Early Vasopressors") AND ("Mortality" OR "Hemodynamic Stability" OR "Transfusion Requirements" OR "Adverse Events")*	250
Springer	*("Hemorrhagic Shock" OR "Traumatic Hemorrhage" OR "Major Bleeding" OR "Acute Blood Loss") AND ("Vasopressors" OR "Norepinephrine" OR "Vasopressin" OR "Early Vasoactive Support") AND ("Standard Resuscitation" OR "Fluid Therapy Alone" OR "Conventional Care" OR "No Early Vasopressors") AND ("Mortality" OR "Hemodynamic Stability" OR "Transfusion Requirements" OR "Adverse Events")*	99
Google Scholar	*("Hemorrhagic Shock" OR "Traumatic Hemorrhage" OR "Major Bleeding" OR "Acute Blood Loss") AND ("Vasopressors" OR "Norepinephrine" OR "Vasopressin" OR "Early Vasoactive Support") AND ("Standard Resuscitation" OR "Fluid Therapy Alone" OR "Conventional Care" OR "No Early Vasopressors") AND ("Mortality" OR "Hemodynamic Stability" OR "Transfusion Requirements" OR "Adverse Events")*	393
Wiley Online Library	*("Hemorrhagic Shock" OR "Traumatic Hemorrhage" OR "Major Bleeding" OR "Acute Blood Loss") AND ("Vasopressors" OR "Norepinephrine" OR "Vasopressin" OR "Early Vasoactive Support") AND ("Standard Resuscitation" OR "Fluid Therapy Alone" OR "Conventional Care" OR "No Early Vasopressors") AND ("Mortality" OR "Hemodynamic Stability" OR "Transfusion Requirements" OR "Adverse Events")*	68

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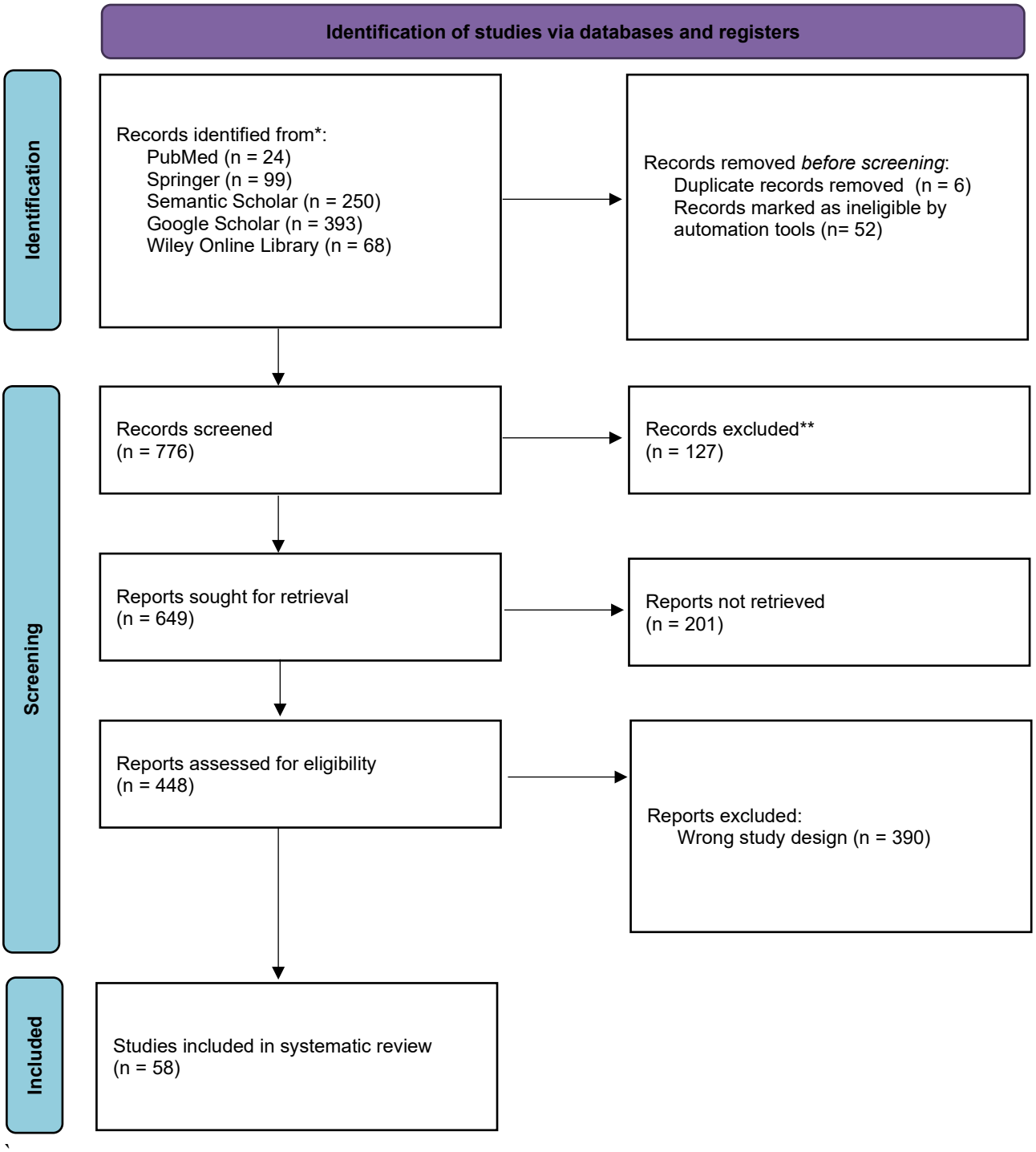


Figure 1. Article search flowchart

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RESULTS

Characteristics of Included Studies

The following table presents all 58 sources identified for this systematic review, encompassing randomized controlled trials, observational studies, systematic reviews, and narrative reviews examining vasopressor use in hemorrhagic shock.

Study	Patient Population	Vasopressor(s) Studied	Primary Focus
H. Lienhart et al., 2007	Traumatic hemorrhagic shock, SBP <90 mmHg	Vasopressin 10 IU IV	Hospital admission rate
R. M. Mohamed et al., 2024	Traumatic, MAP 65-75 mmHg, n=200	Norepinephrine <0.3 µg/kg/min	24-hour mortality
Carrie A Sims et al., 2019	Traumatic, ≥6 U blood products, n=100	AVP bolus 4 U, infusion ≤0.04 U/min	Blood product transfusion volume
Tadaharu Shiozumi et al., 2025	Traumatic hemorrhagic shock, adults	Noradrenaline, vasopressin	Mortality, organ dysfunction
M. Hylands et al., 2017	Acute traumatic injury	Multiple agents	Short-term mortality
M. Cucci et al., 2025	Traumatic, ISS 26, n=37	Vasopressin, norepinephrine	28-day vasopressor-free days

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Study	Patient Population	Vasopressor(s) Studied	Primary Focus
Tobias Gauss et al., 2018	Traumatic HS, ≥4 RBC units, n=518	Noradrenaline	In-hospital mortality
M. Aoki et al., 2018	Traumatic HS, SBP <90 mmHg, n=3,551	Not specified	In-hospital mortality
M. Hylands et al., 2017a	Traumatic, adults	Multiple agents	Short-term mortality
H. Lienhart et al., 2008	Traumatic, uncontrolled	Arginine vasopressin 10 IU	Not specified
Highlights. (2019)	Traumatic, n=100	Vasopressin	Blood product use
F. Beloncle et al., 2013	Traumatic (polytrauma)	Norepinephrine, vasopressin	Literature synthesis
K. Uchida et al., 2020	Blunt trauma, n=40	Not specified	Mortality risk factors
D. Plurad et al., 2011	Critical injury, n=1,349	Multiple agents	Mortality
Andrew D. Fisher et al., 2020	Combat wounded, n=28,222	Not specified	Survival
T. Anand et al., 2024	Traumatic, SBP <90, n=1,049	Not specified	24-hour and in-hospital mortality
Robert M. Van Haren et al., 2014	Emergency surgery patients, n=746	Multiple agents	Mortality

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Study	Patient Population	Vasopressor(s) Studied	Primary Focus
B. Claes et al., 2024	Not specified	Multiple agents	Literature synthesis
M. Hylands et al., 2017b	Traumatic, n=111	Multiple agents	Hemodynamic management patterns
V. Wenzel et al., 2008	Uncontrolled HS	Arginine vasopressin	Literature synthesis
Emma G. Burke et al., 2025	Traumatic	Not specified	Literature synthesis
Bradley J Haan et al., 2020	Distributive and hemorrhagic shock, n=245	Vasopressin, norepinephrine	Time to shock reversal
S. Grmec et al., 2008	Blunt trauma with PEA arrest, n=31	Arginine vasopressin 40 U IV	ROSC and 24-hour survival
Cole Bird et al., 2025	Burn patients ≥20% TBSA	Not specified	Clinical severity indicators
David Leon et al., 2025	Traumatic	Arginine vasopressin	Literature synthesis
S. Smith et al., 2020	Shock patients, n=162	Angiotensin II	MAP response
M. Harrison et al., 2019	Traumatic	Arginine vasopressin	Blood product transfusion

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Study	Patient Population	Vasopressor(s) Studied	Primary Focus
Wolfgang G. Voelckel et al., 2025	Traumatic	Arginine vasopressin	Literature synthesis
H. Strohmenger et al., 2003	Various shock states	Vasopressin	Literature synthesis
M. Ng et al., 2017	Traumatic, n=552	Multiple agents	Mortality
J. Marshall et al., 2019	ED shock patients, n=2,581	Multiple agents	In-hospital mortality
H. Raab et al., 2008	Uncontrolled traumatic HS	Arginine vasopressin	Literature synthesis
Mathew Geevarghese et al., 2023	Hypovolemic/hemorrhagic shock	Centhaquine	Survival and hemodynamics
N. Tyagi et al., 2023	Septic shock (not HS)	Not applicable	Not applicable
M. Renberg et al., 2025	Porcine model, n=16	AVP 40 U IM	Hemodynamic stabilization
P. C. M. C. Michael White et al., 2023	Septic shock (not HS)	Vasopressin	Renal outcomes
Guinot Pierre-Grégoire et al., 2025	Mixed cardiogenic-vasodilatory shock	Vasopressin	Renal outcomes
M. Aoki et al., 2017	Traumatic	Not specified	Mortality

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Study	Patient Population	Vasopressor(s) Studied	Primary Focus
Matthew Stampfl et al., 2024	Various shock states	Multiple agents	Clinical guidance
Perrine Tubert et al., 2024	Traumatic	Multiple agents	Fluid resuscitation strategies
K. Stadlbauer et al., 2005	Traumatic	Vasopressin	Bleeding control mechanisms
P. Fangio et al., 2005	Pelvic fracture, n=311	Not specified	Hemorrhage management
J. Jentzer et al., 2018	Refractory vasodilatory shock	Multiple agents	Clinical guidance
Ross E Orpet et al., 2024	Trauma patients	Not specified	Clinical recommendations
E. Laou et al., 2023	Hemorrhagic shock, n=179 (clinical)	Vasopressin receptor agonists	Mortality
D. Ragoonanan et al., 2021	Various shock states	Multiple agents	Dosing guidance
Luis D. Pacheco et al., 2024	Obstetric patients	Norepinephrine	Peripheral administration safety
D. Lindberg et al., 2019	Traumatic	Arginine vasopressin	Blood product requirements

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Study	Patient Population	Vasopressor(s) Studied	Primary Focus
Michael Hessler et al., 2017	Vasodilatory shock, n=321	Angiotensin II	MAP response
A. Patel et al., 2019	Various shock states	Multiple agents	Clinical guidance
D. Dries et al., 2006	Septic shock (primarily)	Dopamine, norepinephrine, vasopressin	Clinical guidance
Hans Gao et al., 2025	EMS patients, n=1,212	Multiple agents	Vasopressor utilization patterns
C. L. Holmes et al., 2004	ICU patients	Vasopressin	Clinical guidance
R. Dutton et al., 2007	Traumatic	Not specified	Hemorrhagic shock management
E. Bassi et al., 2013	Refractory shock	Norepinephrine, AVP, terlipressin	Therapeutic strategies
Robbie Ley Greaves et al., 2024	Prehospital patients	Not specified	Safety of peripheral vasopressors
M. Sanui et al., 2004	Traumatic	Arginine vasopressin	Literature synthesis
D. Morales et al., 2000	Vasodilatory shock	Arginine vasopressin	Therapeutic rationale

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The included sources represent a heterogeneous body of literature spanning from 2000 to 2025. The evidence base comprises 4 completed randomized controlled trials with clinical data, several RCT protocols, numerous retrospective cohort studies, and reviews providing clinical context. Full text was available for 18 sources, while 40 were abstract-only. Notably, several sources addressed septic shock rather than hemorrhagic shock and were included for contextual comparison of vasopressor mechanisms.

Effects on Mortality

Mortality Outcomes from Randomized Controlled Trials

Study	Vasopressor	Mortality Endpoint	Vasopressor Group	Control Group	Effect Estimate	p-value
R. M. Mohamed et al., 2024	Norepinephrine	24-hour mortality	3%	13%	Not reported	<0.05
R. M. Mohamed et al., 2024	Norepinephrine	In-hospital mortality	9%	21%	Not reported	<0.05
Carrie A Sims et al., 2019	AVP	30-day mortality	12% (6/49)	12% (6/51)	No difference	P=0.94
S. Grmec et al., 2008	AVP + HHS	24-hour survival	62% (8/13)	11% (2/18)	Significantly higher survival	P=0.001

The RCT evidence presents a mixed picture. Mohamed et al. demonstrated that early low-dose norepinephrine (<0.3 µg/kg/min) concurrent with resuscitative fluids significantly reduced

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both 24-hour mortality (3% vs 13%) and in-hospital mortality (9% vs 21%). In contrast, the AVERT-Shock trial by Sims et al. found no mortality difference with low-dose vasopressin supplementation, with identical 30-day mortality rates of 12% in both groups. Grmec et al. reported markedly improved 24-hour survival (62% vs 11%) in blunt trauma patients with pulseless electrical activity treated with vasopressin combined with hydroxyethyl starch solution, though this population represented cardiac arrest rather than hemorrhagic shock per se.

Mortality Outcomes from Observational Studies

Study	Sample Size	Vasopressor Mortality	Control Mortality	Adjusted OR/HR (95% CI)	Key Findings
M. Aoki et al., 2018	3,551	43%	16%	OR 2.172 (1.666–2.833)	Increased mortality with vasopressors
M. Aoki et al., 2018 (PSM)	Matched	Not reported	Not reported	OR 2.168 (1.442–3.320)	Persistent association after matching
D. Plurad et al., 2011	1,349	43.6%	4.2%	OR 17.60 (12.10–25.60)	Strong association with mortality
Tobias Gauss et al., 2018	518	Not reported	Not reported	HR 0.95 (0.45–2.01)	No adverse effect after PSM

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Study	Sample Size	Vasopressor Mortality	Control Mortality	Adjusted OR/HR (95% CI)	Key Findings
Andrew D. Fisher et al., 2020	28,222	Survival 71.3%	Survival 94.3%	Adjusted OR 0.32 (0.18–0.56)	Lower survival with vasopressors
K. Uchida et al., 2020	40	Not reported	Not reported	OR 21.32 (3.71–121.6)	Vasopressor use associated with death
T. Anand et al., 2024	1,049	24-h: 19%	In-hosp: 33%	aOR 0.65 per hour delay	Earlier use associated with worse outcomes

Observational data consistently demonstrate an association between vasopressor use and increased mortality. The large Japanese nationwide cohort (n=3,551) by Aoki et al. found vasopressor use associated with an adjusted odds ratio of 2.172 for in-hospital mortality, which persisted in propensity score-matched analyses (OR 2.168). Plurad et al. reported even more striking findings with mortality of 43.6% in vasopressor-treated patients versus 4.2% in controls. Fisher et al. found prehospital vasopressor use in combat casualties associated with lower odds of survival that persisted after adjustment (OR 0.32).

However, Gauss et al.'s propensity-score analysis of 518 patients with traumatic hemorrhagic shock found no association between early noradrenaline use and 24-hour mortality (HR 0.95, 95% CI 0.45-2.01), suggesting that when adequately controlling for confounding, the apparent harm may be attenuated.

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Meta-Analytic Evidence

The systematic review and meta-analysis by Laou et al. pooling available clinical studies found no statistically significant difference in mortality risk between patients receiving vasopressin receptor agonists versus those not treated with such agents (RR 1.17, 95% CI 0.67-2.08; p=0.562). The systematic review by Hylands et al. found that across observational studies, unadjusted risk ratios for mortality ranged from 2.31 to 7.39, but these were considered very low quality evidence due to significant confounding by indication.

Dose-Response and Timing Relationships

Study	Finding	Implication
M. Ng et al., 2017	Mortality: 1 vasopressor 5.1%, 2 vasopressors 18.9%, 3 vasopressors 32.4%, 4 vasopressors 80%	Dose-dependent mortality increase
T. Anand et al., 2024	Each hour delay in vasopressor initiation: aOR 0.65 for 24-h mortality	Earlier initiation associated with worse outcomes
K. Uchida et al., 2020	Early administration OR 10.56 (1.90–58.5)	Early and high-dose use linked to death
Robert M. Van Haren et al., 2014	Epinephrine independently associated with mortality (OR 6.88)	Agent-specific effects

The number of vasopressors required appears strongly correlated with mortality, with Ng et al. demonstrating a stepwise increase from 5.1% with one vasopressor to 80% with four vasopressors. Anand et al. found that each one-hour delay in vasopressor administration beyond the

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first hour was independently associated with decreased odds of 24-hour mortality (aOR 0.65), suggesting that the need for earlier vasopressors indicates more severe illness. Van Haren et al. identified epinephrine as independently associated with mortality (OR 6.88) during emergency trauma surgery, while other vasopressors showed no independent association when epinephrine users were excluded.

Effects on Blood Product and Fluid Requirements

Study	Vasopressor	Blood Product Volume (Vasopressor)	Blood Product Volume (Control)	p-value	Additional Findings
Carrie A Sims et al., 2019	AVP	Median 1.4 L (IQR 0.5-2.6)	Median 2.9 L (IQR 1.1-4.8)	P=0.01	Crystalloid requirement not different
R. M. Mohamed et al., 2024	Norepinephrine	4.39 ± 1.15 L total fluids	6.03 ± 1.43 L total fluids	<0.001	Blood product units similar between groups
M. Hylands et al., 2017	Various	3.8 ± 5.0 L	5.4 ± 6.6 L	Not reported	Lower volumes in vasopressor group in RCT

A consistent finding across studies is the potential fluid-sparing effect of vasopressors. The AVERT-Shock trial demonstrated that patients receiving low-dose AVP required significantly less blood products at 48 hours (1.4 L vs 2.9 L, p=0.01), though crystalloid requirements were similar

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(9.9 L vs 11.0 L). Mohamed et al. found significantly reduced total fluid resuscitation requirements in the norepinephrine group (4.39 L vs 6.03 L). The systematic review by Hylands et al. noted lower blood transfusion volumes in the vasopressor group in the single included RCT.

Hemodynamic Effects

Study	Vasopressor	Blood Pressure Response	Other Hemodynamic Parameters
R. M. Mohamed et al., 2024	Norepinephrine	MAP significantly higher at 30, 45, 60, 90 min	HR significantly higher; lactate levels lower at 6, 12 h
S. Grmec et al., 2008	AVP	MAP 100.4 ± 11.4 vs 80.3 ± 12.4 mmHg	Higher PETCO2 suggesting better tissue perfusion
S. Smith et al., 2020	Angiotensin II	MAP increase 9.3 mmHg (h0 to h3)	Median time to MAP ≥65: 16 minutes
M. Renberg et al., 2025	AVP (IM)	SAP +33.5 mmHg, MAP +33.0 mmHg	CI +19.2%, SV +32.1% at 90 min

Vasopressors consistently achieve hemodynamic stabilization. Mohamed et al. demonstrated significantly higher MAP at multiple time points with early norepinephrine. Grmec et al. found vasopressin produced higher mean arterial pressure compared to epinephrine (100.4 vs 80.3 mmHg). The experimental study by Renberg et al. showed intramuscular AVP increased systolic arterial pressure by 33.5 mmHg and cardiac index by 19.2%, though effects were transient.

Tissue perfusion indicators showed improvement with vasopressor use in some studies. Mohamed et al. reported significantly lower serum lactate levels at 6 and 12 hours and lower serum

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creatinine at 6, 12, and 18 hours in the norepinephrine group. The theoretical benefit of vasopressin includes redirecting blood flow away from bleeding sites toward vital organs.

Adverse Effects

Study	Adverse Effect	Vasopressor Group	Control Group	Notes
Carrie A Sims et al., 2019	DVT	11% (5/44)	34% (16/47)	Significantly lower with AVP
Carrie A Sims et al., 2019	Total complications	55% (24/44)	64% (30/47)	No significant difference
M. Cucci et al., 2025	New RRT requirement	14.3%	6.7%	Not significant (p=0.478)
R. M. Mohamed et al., 2024	AKI incidence	No difference	No difference	Similar between groups

Contrary to theoretical concerns, the AVERT-Shock trial found that AVP was associated with significantly fewer deep venous thromboses (11% vs 34%, p=0.02) without increasing total complications. Mohamed et al. found no difference in acute kidney injury incidence between norepinephrine and control groups.

However, potential adverse effects remain a concern. The systematic review protocol by Shiozumi et al. identified theoretical risks including arrhythmias, myocardial infarction, digital or mesenteric ischemia, and acute kidney injury. Excessive vasoconstriction may reduce perfusion to vital organs and potentially exacerbate bleeding by elevating hydrostatic pressure at injury sites. Beloncle et al. noted concerns about disseminated cardiac cell necrosis and severe acute renal dysfunction with high-dose vasopressor therapy. Ragoonanan et al. reported increased risk of digital ischemia with vasopressin doses exceeding 0.06 U/min.

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Definitions of Early Management

The included studies varied considerably in their operational definitions of "early" vasopressor administration:

Study	Time Window	Reference Point	Definition
R. M. Mohamed et al., 2024	Immediate	ED arrival	Concurrent with initial resuscitation
H. Lienhart et al., 2007	Within 10 min of standard treatment	Emergency physician arrival at scene	After failed initial resuscitation
M. Aoki et al., 2018	Within 24 hours	ED arrival	Alongside blood transfusion
T. Anand et al., 2024	Within 6 hours	Hospital admission	Early resuscitation phase
D. Plurad et al., 2011	Within 24 hours	Hospital admission	During ongoing resuscitation
M. Cucci et al., 2025	Within 6 hours	Hospital arrival	Refractory hemorrhagic shock
M. Hylands et al., 2017b	Before surgery or ≤6 hours	Hospital arrival	Early resuscitation period

This heterogeneity in definitions complicates direct comparisons across studies and may partially explain divergent findings.

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Synthesis

Explaining the Apparent Contradiction

The literature presents an apparent paradox: observational studies consistently associate vasopressor use with increased mortality, while randomized trials show either benefit or no harm. This discrepancy can be explained through several mechanisms:

Confounding by Indication: Patients who receive vasopressors are systematically sicker than those who do not. The systematic review by Hylands et al. explicitly identified that "patients who received vasopressors were systematically sicker than patients treated without vasopressors," rendering the risk of bias high in observational studies. When Gauss et al. applied rigorous propensity-score matching, the association between noradrenaline use and mortality disappeared (HR 0.95, 95% CI 0.45-2.01), suggesting that observed associations in unmatched cohorts reflect disease severity rather than treatment harm.

Context-Dependent Effects: The benefit or harm of vasopressors appears dependent on the clinical context:

- In patients with severe traumatic hemorrhagic shock unresponsive to initial fluid resuscitation, low-dose norepinephrine concurrent with resuscitative fluids reduced mortality
- In patients receiving massive transfusion who already received 6+ units of blood products, AVP supplementation did not affect mortality but reduced blood product requirements
- In prehospital combat settings, vasopressor use was associated with worse survival, possibly reflecting resource limitations or different patient populations

Agent-Specific Effects: The choice of vasopressor matters. Van Haren et al. found epinephrine independently associated with mortality (OR 6.88), while excluding epinephrine users eliminated the mortality association with other vasopressors. This may reflect that epinephrine is typically used for cardiac arrest, confounding interpretation. Low-dose vasopressin (≤0.04 U/min)

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appears safer than higher doses and may provide unique benefits including reduced blood product requirements and fewer thrombotic complications.

Timing and Dose Considerations: The dose-response relationship between vasopressor requirements and mortality likely reflects disease severity rather than treatment toxicity. The finding that each hour delay in vasopressor initiation was associated with decreased mortality supports the interpretation that the need for early vasopressors indicates more severe shock states rather than that earlier treatment causes harm.

Conclusions by Clinical Context

Based on the available evidence, the role of vasopressors in hemorrhagic shock can be contextualized as follows:

For patients with traumatic hemorrhagic shock not responding to initial fluid resuscitation: Low-dose norepinephrine (<0.3 μg/kg/min) concurrent with resuscitative fluids may reduce mortality and fluid requirements. This is supported by RCT evidence and consistent with the physiologic rationale of maintaining perfusion pressure while limiting crystalloid dilution of clotting factors.

For patients requiring massive transfusion: Low-dose vasopressin supplementation (4 U bolus, ≤0.04 U/min infusion) does not increase mortality and may reduce blood product requirements. The reduction in deep venous thrombosis suggests potential additional benefits.

For refractory or severe hemorrhagic shock: Vasopressors remain a therapy of last resort when conventional therapies fail. Animal studies and case reports support efficacy in hemodynamic stabilization, but the absence of clear mortality benefit in clinical studies warrants caution.

For patients with concomitant traumatic brain injury: The need to maintain cerebral perfusion pressure may justify earlier vasopressor use despite ongoing hemorrhage, though specific evidence in this subpopulation remains limited.

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The preponderance of evidence suggests that the apparent harm of vasopressors in hemorrhagic shock observed in observational studies reflects confounding by indication. When appropriately applied as adjuncts to—not replacements for—hemorrhage control and volume resuscitation, low-dose vasopressors may improve hemodynamic stability and reduce transfusion requirements without increasing mortality. Current guideline recommendations to titrate fluids and vasopressors to achieve minimum blood pressure targets until hemorrhage is controlled appear consistent with the available evidence, though considerable uncertainty remains regarding optimal agents, doses, and timing.

DISCUSSION

Reconciling the Evidence Paradox

The most striking finding of this systematic review is the fundamental discordance between observational and randomized evidence regarding vasopressor effects on mortality. Observational studies, including large nationwide cohorts (Aoki et al., 2018; Plurad et al., 2011; Fisher et al., 2020), consistently report strong associations between vasopressor use and increased mortality, with adjusted odds ratios ranging from 2.17 to 17.60. In contrast, randomized controlled trials demonstrate either mortality benefit (Mohamed et al., 2024) or neutral effects (Sims et al., 2019; Grmec et al., 2008).

This paradox is best explained by confounding by indication—the phenomenon whereby patients who receive vasopressors are systematically sicker than those who do not. Hylands et al. (2017) explicitly identified that across observational studies, patients receiving vasopressors had greater injury severity, lower blood pressures, and higher transfusion requirements at baseline. When Gauss et al. (2018) applied rigorous propensity-score matching to 518 patients with traumatic hemorrhagic shock, the association between noradrenaline use and mortality completely disappeared (HR 0.95, 95% CI 0.45-2.01), suggesting that observed associations in unmatched cohorts reflect disease severity rather than treatment harm.

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The dose-response relationship further supports this interpretation. Ng et al. (2017) demonstrated a stepwise mortality increase from 5.1% with one vasopressor to 80% with four vasopressors, while Anand et al. (2024) found that each hour delay in vasopressor initiation was paradoxically associated with decreased mortality (aOR 0.65). These findings indicate that the need for earlier and multiple vasopressors serves as a marker of shock severity rather than a cause of poor outcomes.

Agent-Specific Considerations

The choice of vasopressor agent appears to significantly influence outcomes. Van Haren et al. (2014) found that epinephrine was independently associated with mortality (OR 6.88) during emergency trauma surgery, while excluding epinephrine users eliminated the mortality association with other vasopressors. This may reflect that epinephrine is typically reserved for cardiac arrest or agonal states, confounding interpretation, but also raises concerns about potential adverse effects including tachycardia, increased myocardial oxygen demand, and arrhythmogenic potential (Patel and Ackland, 2019).

Norepinephrine has emerged as a favorable first-line agent based on randomized trial evidence. Mohamed et al. (2024) demonstrated that early low-dose norepinephrine (<0.3 µg/kg/min) administered concurrently with resuscitative fluids significantly reduced both 24-hour and in-hospital mortality while achieving superior hemodynamic stabilization and lower lactate levels. The observed fluid-sparing effect (4.39 L vs 6.03 L total fluids) may contribute to these benefits by limiting crystalloid-induced dilutional coagulopathy and tissue edema (Tubert et al., 2024).

Vasopressin offers theoretical advantages in hemorrhagic shock due to its unique mechanism of action. Unlike catecholamines, vasopressin does not increase myocardial oxygen consumption, may preserve or enhance renal blood flow, and has been proposed to redirect blood flow away from non-critical vascular beds toward vital organs (Stadlbauer et al., 2005; Voelckel, 2025). The AVERT-Shock trial (Sims et al., 2019) demonstrated that low-dose vasopressin supplementation (4 U bolus, ≤0.04 U/min infusion) significantly reduced blood product requirements at 48 hours (1.4 L vs 2.9 L, p=0.01) without affecting mortality. Notably, vasopressin

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was associated with significantly fewer deep venous thromboses (11% vs 34%, p=0.02), suggesting potential additional benefits beyond hemodynamic support (Sims et al., 2019).

However, dose-dependent adverse effects remain a concern with vasopressin. Ragoonanan and Friedman (2021) reported increased risk of digital ischemia with doses exceeding 0.06 U/min, while Beloncle et al. (2013) noted concerns about mesenteric ischemia and acute kidney injury with high-dose therapy. The available evidence supports low-dose vasopressin supplementation rather than high-dose rescue therapy.

Angiotensin II represents a newer vasopressor option with limited evidence in hemorrhagic shock. Smith et al. (2020) demonstrated significant mean arterial pressure increases (9.3 mmHg at 3 hours) in shock patients, with a median time to target pressure of 16 minutes. However, its specific role in hemorrhagic shock remains undefined (Hessler et al., 2017).

Timing and Contextual Factors

The definition of "early" vasopressor administration varied considerably across studies, complicating direct comparisons. Time windows ranged from immediate administration concurrent with initial resuscitation (Mohamed et al., 2024) to within 24 hours of admission (Aoki et al., 2018; Plurad et al., 2011). Reference points included emergency department arrival, hospital admission, and recognition of shock. This heterogeneity may partially explain divergent findings and highlights the need for standardized definitions in future research (Shiozumi et al., 2025).

The sequence of vasopressor administration relative to fluid resuscitation appears critical. In the trial by Mohamed et al. (2024), norepinephrine was initiated concurrently with fluids, whereas historical practice has emphasized fluid administration first, with vasopressors reserved for fluid-refractory shock. The concept of "permissive hypotension" with concurrent low-dose vasopressor support may represent an optimal strategy, maintaining minimum perfusion pressures while limiting excessive fluid administration (Beloncle et al., 2013; Burke et al., 2025).

Specific patient populations may derive particular benefit from early vasopressor support. Patients with traumatic brain injury require maintenance of cerebral perfusion pressure, potentially justifying earlier vasopressor use despite ongoing hemorrhage (Leon et al., 2025). Obstetric patients with hemorrhagic shock may benefit from the uterine vasoconstrictive effects of vasopressin,

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potentially reducing pelvic bleeding (Pacheco et al., 2024). Burn patients with hemorrhagic shock appear to have worse outcomes when vasopressors are required, likely reflecting greater shock severity rather than treatment toxicity (Bird et al., 2025).

Hemodynamic Effects and Tissue Perfusion

Vasopressors consistently achieve hemodynamic stabilization across studies. Mohamed et al. (2024) demonstrated significantly higher mean arterial pressure at multiple time points with early norepinephrine, along with lower serum lactate at 6 and 12 hours, suggesting improved tissue perfusion. Grmec et al. (2008) found vasopressin produced higher mean arterial pressure compared to epinephrine (100.4 vs 80.3 mmHg) in blunt trauma patients with pulseless electrical activity, with higher end-tidal CO2 suggesting better tissue perfusion.

Experimental evidence supports these clinical findings. Renberg et al. (2025) showed that intramuscular vasopressin increased systolic arterial pressure by 33.5 mmHg and cardiac index by 19.2% in a porcine hemorrhagic shock model, though effects were transient. The theoretical benefit of vasopressin in redirecting blood flow toward vital organs while reducing bleeding from peripheral vascular beds remains attractive but requires further clinical validation (K. Stadlbauer et al., 2005; Wenzel et al., 2008).

Fluid Resuscitation Context

A consistent finding across studies is the fluid-sparing effect of vasopressors. The AVERT-Shock trial demonstrated significant reduction in blood product requirements with vasopressin (Sims et al., 2019), while Mohamed et al. (2024) found substantially lower total fluid resuscitation volumes with norepinephrine. Hylands et al. (2017) noted lower blood transfusion volumes in the vasopressor group in the single included RCT, though observational studies were confounded by indication.

This fluid-sparing effect may represent a key mechanistic benefit of vasopressors in hemorrhagic shock. Excessive crystalloid administration exacerbates coagulopathy through dilution of clotting factors and fibrinogen, impairs platelet function, and contributes to tissue edema and abdominal compartment syndrome (Tubert et al., 2024). By maintaining perfusion pressure with

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smaller fluid volumes, vasopressors may attenuate these complications while achieving hemodynamic goals.

Safety Profile

Contrary to theoretical concerns, available evidence does not demonstrate increased complications with low-dose vasopressor therapy in hemorrhagic shock. The AVERT-Shock trial found that vasopressin was associated with significantly fewer deep venous thromboses without increasing total complications (Sims et al., 2019). Mohamed et al. (2024) found no difference in acute kidney injury incidence between norepinephrine and control groups. Cucci et al. (2025) reported no significant difference in new renal replacement therapy requirement (14.3% vs 6.7%, p=0.478) with early vasopressin administration.

However, potential adverse effects remain important considerations. Arrhythmias, myocardial ischemia, digital or mesenteric ischemia, and exacerbation of bleeding through increased hydrostatic pressure at injury sites represent theoretical risks that require ongoing vigilance (Shiozumi et al., 2025; Bassi et al., 2013). The safety of peripheral vasopressor administration in the prehospital setting has been demonstrated (Ley Greaves et al., 2024; Pacheco et al., 2024), supporting feasibility of early initiation.

Limitations of the Evidence

This review is limited by the quality of available evidence. Only four completed randomized controlled trials with clinical data were identified, with small sample sizes and heterogeneous populations. Forty of 58 included sources were abstract-only publications, limiting full methodological assessment. Significant heterogeneity in definitions of "early" administration, vasopressor protocols, and outcome measures precludes meta-analysis for many comparisons.

The predominance of traumatic hemorrhagic shock studies limits generalizability to other etiologies including gastrointestinal bleeding, obstetric hemorrhage, and surgical bleeding. Evidence for specific vasopressor agents beyond norepinephrine and vasopressin remains extremely limited. Long-term outcomes and quality of life measures are rarely reported.

Implications for Clinical Practice

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Despite these limitations, several clinically actionable conclusions emerge. In patients with traumatic hemorrhagic shock not responding to initial fluid resuscitation, low-dose norepinephrine (<0.3 μg/kg/min) concurrent with fluids may reduce mortality and fluid requirements (Mohamed et al., 2024). In patients requiring massive transfusion, low-dose vasopressin supplementation (4 U bolus, ≤0.04 U/min infusion) does not increase mortality and may reduce blood product requirements (Sims et al., 2019). Vasopressors should be viewed as adjuncts to—not replacements for—definitive hemorrhage control and appropriate volume resuscitation (Ross et al., 2024; Dries, 2006).

The choice between norepinephrine and vasopressin may depend on clinical context. Norepinephrine offers extensive clinical experience and proven mortality benefit in a single RCT. Vasopressin offers theoretical advantages in reducing blood product requirements and may be particularly attractive when coagulopathy is a concern or when high-volume resuscitation is anticipated. Epinephrine should be reserved for cardiac arrest or agonal states given its association with worse outcomes in observational studies (Van Haren et al., 2014; Jentzer et al., 2018).

Future Research Directions

Priority areas for future research include adequately powered randomized controlled trials comparing specific vasopressor agents, optimal dosing strategies, and timing relative to fluid resuscitation. Standardized definitions of "early" vasopressor administration are urgently needed. Subgroup analyses should identify patients most likely to benefit, including those with traumatic brain injury, elderly patients, and those with different hemorrhage etiologies (Sanui et al., 2004; Fangio et al., 2005). Long-term outcomes, including quality of life and functional status, should be systematically assessed (Marshall et al., 2019; Lindberg, 2019).

The role of novel vasopressor agents including angiotensin II (Smith et al., 2020) and centhaquine (Geevarghese et al., 2023) requires investigation in hemorrhagic shock populations. Combination strategies, such as norepinephrine plus vasopressin, warrant evaluation. The optimal blood pressure target during active hemorrhage remains incompletely defined and may vary by patient characteristics and injury pattern (Guinot et al., 2025; Michael White, 2023).

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CONCLUSION AND RECOMMENDATIONS

Conclusion

This systematic review synthesizes evidence from 58 sources examining the role of early vasopressor administration in adult patients with hemorrhagic shock. The available evidence resolves the apparent paradox between observational studies suggesting harm and randomized trials demonstrating benefit or neutrality, with confounding by indication emerging as the primary explanation for observed mortality associations in observational research.

Low-dose vasopressor administration, particularly with norepinephrine or vasopressin, appears safe and potentially beneficial when used as an adjunct to appropriate volume resuscitation and definitive hemorrhage control. Norepinephrine (<0.3 μg/kg/min) concurrent with fluid resuscitation may reduce mortality and fluid requirements in traumatic hemorrhagic shock. Vasopressin supplementation (≤0.04 U/min) does not affect mortality but reduces blood product requirements in patients receiving massive transfusion. Both agents achieve hemodynamic stabilization with acceptable safety profiles.

The fluid-sparing effect of vasopressors represents a clinically important benefit, potentially attenuating complications of aggressive crystalloid administration including dilutional coagulopathy and tissue edema. Adverse event rates are similar between vasopressor and control groups, with vasopressin unexpectedly associated with fewer thrombotic complications.

Recommendations

1. **Clinical Practice:** Consider early low-dose norepinephrine (<0.3 μg/kg/min) in adult patients with traumatic hemorrhagic shock who remain hypotensive during initial fluid resuscitation. Consider low-dose vasopressin supplementation (4 U bolus, ≤0.04 U/min infusion) in patients requiring massive transfusion to reduce blood product requirements. Avoid epinephrine except in cardiac arrest or agonal states.

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2. **Timing:** Vasopressors should be initiated concurrently with fluid resuscitation when indicated, not delayed until fluid-refractory shock develops. However, vasopressors must never delay or replace definitive hemorrhage control.

3. **Monitoring:** Patients receiving vasopressors require close monitoring for tissue ischemia, arrhythmias, and adequacy of perfusion. Doses should be titrated to the minimum required to achieve target blood pressures.

4. **Future Research:** Large, pragmatic randomized controlled trials are urgently needed to define optimal agent selection, dosing strategies, timing, and target populations. Standardized definitions of early administration and core outcome sets should be adopted.

5. **Guideline Development:** Current guidelines recommending titrated fluids and vasopressors to achieve minimum blood pressure targets until hemorrhage control are consistent with available evidence and should be maintained while acknowledging remaining uncertainties.

In conclusion, the role of vasopressors in early hemorrhagic shock management is evolving from absolute contraindication toward selective, evidence-based application. When used appropriately in the right patients at the right time with the right agent, vasopressors may improve outcomes by maintaining perfusion while limiting fluid-related complications. The weight of evidence suggests that withholding vasopressors from profoundly hypotensive patients with hemorrhagic shock based on theoretical concerns may be more harmful than their judicious use.

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