Clinical Pathway: Vasopressin Use in Traumatic Hemorrhagic Shock

Purpose

The purpose of this clinical pathway is to reduce blood product utilization during resuscitation of adult trauma patients with hemorrhagic shock through the early administration of low-dose arginine vasopressin (AVP) in conjunction with standard damage-control resuscitation (DCR) and the Massive Transfusion Protocol (MTP). Hemorrhage accounts for approximately 72% of trauma-related deaths within the first 24 hours after injury. Patients requiring massive transfusion are at particular risk for endogenous vasopressin deficiency due to hormone loss in shed blood, its short half-life (10–35 minutes), and dilution from crystalloid and blood product administration (Sims et al., 2019).

Physiologic Rationale

Low-dose vasopressin supplementation (≤0.04 units/min) replaces deficient endogenous hormone rather than functioning solely as a pharmacologic vasoconstrictor (LaGrone et al., 2024; Sims et al., 2019). Vasopressin exerts several beneficial physiologic effects during hemorrhagic shock, including activation of vascular smooth muscle V1 receptors independent of α-adrenergic stimulation, attenuation of vasoplegia through inhibition of ATP-sensitive potassium channels and nitric oxide-mediated vasodilation, enhancement of renal perfusion at low doses, promotion of hemostasis through von Willebrand factor release and platelet-dependent thrombin generation, and conservation of intravascular volume through renal V2 receptor activation.
Preclinical evidence supports these mechanisms. A meta-analysis of 15 randomized animal studies involving 433 animals demonstrated significantly improved survival with vasopressin or terlipressin compared with standard resuscitation (mortality 15% vs. 63%; OR 0.09, 95% CI 0.05–0.15; $P < .001$) (Cossu et al., 2014).

Clinical Pathway

Step 1. Patient Identification

Use of vasopressin is an optional strategy implemented at the discretion of the treating physician. Patients may be considered candidates when all of the following criteria are present:

- Adult trauma patient (≥18 years of age)
- Hemorrhagic shock
- Mean arterial pressure (MAP) <65 mmHg despite initial volume resuscitation
- Requirement for ≥6 units of blood products within 12 hours of arrival

Precautions
Central venous access is strongly recommended for vasopressin administration. Use caution in patients with ischemic heart disease, left ventricular dysfunction, pulmonary hypertension with right ventricular failure, significant atherosclerotic disease, or renal dysfunction because of the potential risks of increased afterload, coronary vasoconstriction, fluid retention, and hyponatremia. Reported adverse effects include decreased cardiac output, bradycardia, tachyarrhythmias, mesenteric ischemia, distal limb ischemia, and hyponatremia. During pregnancy, vasopressin should generally be considered a second-line vasopressor and used only when the anticipated maternal benefit outweighs the theoretical fetal risk.

Step 2. Standard Damage-Control Resuscitation

Standard damage-control resuscitation should continue concurrently with consideration of vasopressin therapy and includes:

- Rapid hemorrhage control (operative, endovascular, or temporizing measures)
- Balanced blood product resuscitation (target 1:1:1 PRBC:FFP)
- Tranexamic acid administration within three hours of injury
- Calcium replacement to maintain ionized calcium ≥1.0 mmol/L
- Active temperature management with maintenance of normothermia
- Laboratory-guided resuscitation using thromboelastography (TEG) or rotational thromboelastometry (ROTEM), when available

Step 3. Vasopressin Initiation

Initiate vasopressin only after all of the following conditions have been met:

- Massive Transfusion Protocol has been activated.
- Blood product resuscitation is underway.
- Hemorrhage control has been achieved or is actively being secured.
- Persistent hypotension (MAP <65 mmHg) remains despite adequate volume resuscitation.

Dosing

- IV Bolus: 4 units
- Continuous Infusion: Start at 0.04 units/minute.
- Titrate between 0 and 0.04 units/minute to maintain a target MAP of ≥65 mmHg.

The vasopressin bolus and infusion may be ordered through the institution's Vasopressin Traumatic Hemorrhage order panel.

Step 4. Hemodynamic Targets

The primary hemodynamic goal is maintenance of a mean arterial pressure of 65 mmHg or greater. If adequate blood pressure is not achieved despite the maximum vasopressin infusion (0.04 units/min), norepinephrine is the preferred additional vasopressor. Catecholamines should be discontinued before tapering vasopressin whenever possible. Should vasopressor therapy become necessary again, vasopressin should be restarted before additional catecholamines are initiated.

Step 5. Monitoring

Continuous monitoring should include:

- Mean arterial pressure
- Heart rate
- Vasopressor requirements
- Hourly urine output

Laboratory evaluation should be performed every 4–6 hours, or more frequently as clinically indicated, and should include:

- Complete blood count
- Lactate
- Comprehensive metabolic panel
- PT/INR
- Fibrinogen
- Ionized calcium

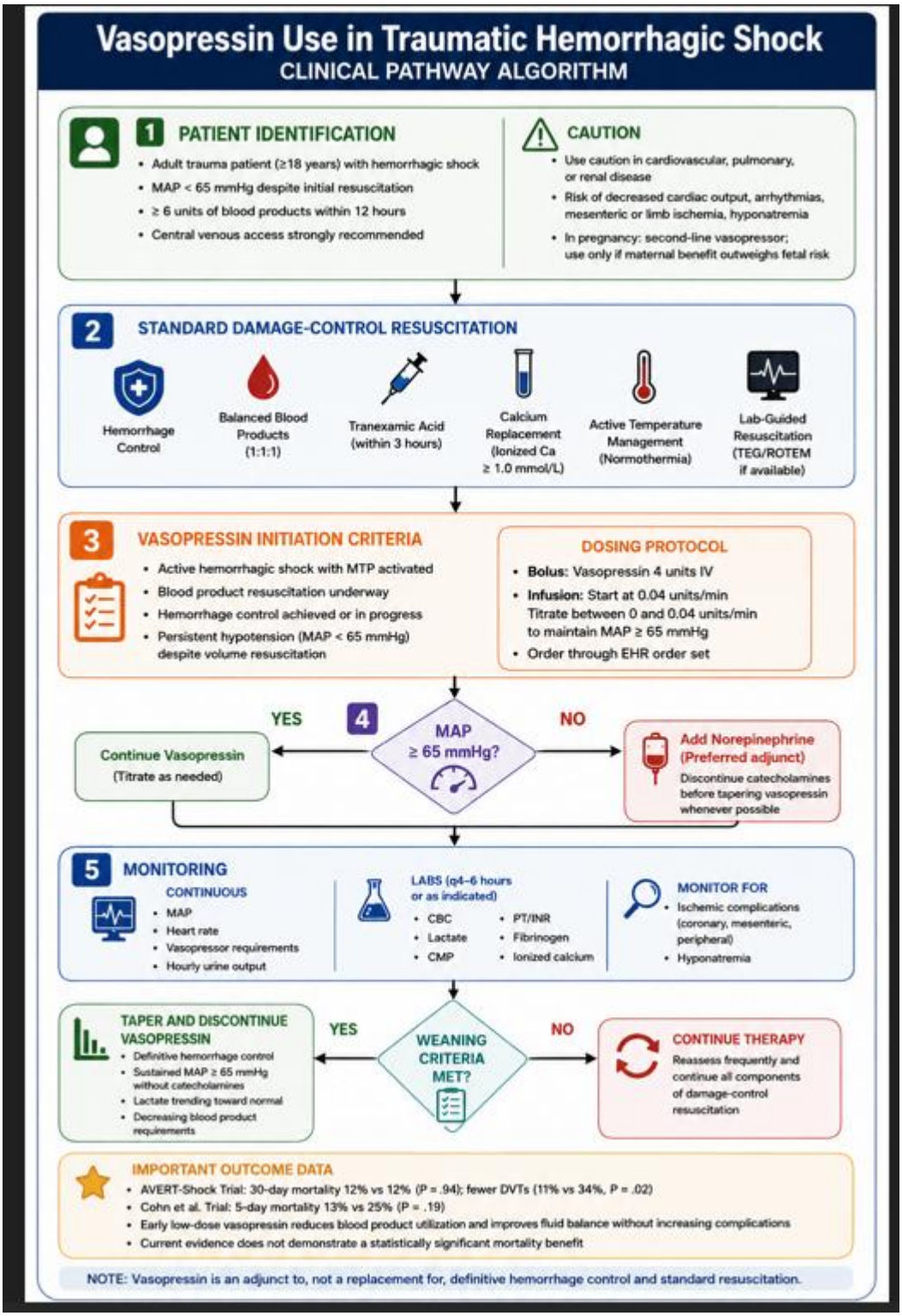
Patients should also be monitored closely for ischemic complications (coronary, mesenteric, or peripheral) and hyponatremia.

Step 6. Ongoing Assessment and Weaning

Continue vasopressin while hemorrhagic shock persists. Consider tapering vasopressin once all of the following criteria have been achieved:

- Definitive hemorrhage control
- Sustained MAP ≥65 mmHg without catecholamine support
- Lactate trending toward normalization
- Decreasing blood product requirements

Deep venous thrombosis prophylaxis and screening should follow institutional protocols. In the AVERT-Shock trial, vasopressin was associated with fewer deep venous thromboses (11% vs. 34%; $P = .02$).



Key Clinical Outcomes

Current clinical evidence demonstrates that early low-dose vasopressin supplementation significantly reduces blood product utilization during hemorrhagic shock resuscitation. In the AVERT-Shock randomized controlled trial, vasopressin reduced total blood product administration, including packed red blood cells, fresh frozen plasma, platelets, and cryoprecipitate, while improving overall fluid balance without increasing complications.
Similarly, the randomized trial by Cohn and colleagues demonstrated significantly reduced resuscitation fluid requirements and a numerical, though statistically non-significant, reduction in early mortality. The ongoing multicenter CAVALIER trial is expected to further clarify the role of vasopressin in traumatic hemorrhagic shock

resuscitation.

References

1. LaGrone LN, Stein D, Cribari C, et al. American Association for the Surgery of Trauma/American College of Surgeons Committee on Trauma: Clinical Protocol for Damage-Control Resuscitation for the Adult Trauma Patient. *Journal of Trauma and Acute Care Surgery*. 2024;96(3):435-454.
2. Sims CA, Holena D, Kim P, et al. Effect of Low-Dose Supplementation of Arginine Vasopressin on Need for Blood Product Transfusions in Patients With Trauma and Hemorrhagic Shock: A Randomized Clinical Trial. *JAMA Surgery*. 2019;154(11):994-1003.
3. Cohn SM, McCarthy J, Stewart RM, et al. Impact of Low-Dose Vasopressin on Trauma Outcome: Prospective Randomized Study. *World Journal of Surgery*. 2011;35(2):430-439.
4. Jiang S, Chen B, Wang L, et al. Bridging Bench to Bedside: Mechanistic Elucidation and Clinical Translation of Vasopressin and Its Analogues for Hemorrhagic Shock Resuscitation. *Shock*. 2026;65(4).
5. Cossu AP, Mura P, De Giudici LM, et al. Vasopressin in Hemorrhagic Shock: A Systematic Review and Meta-analysis of Randomized Animal Trials. *BioMed Research International*. 2014;2014:421291.
6. De Simone B, Chouillard E, Podda M, et al. The 2023 WSES Guidelines on the Management of Trauma in Elderly and Frail Patients. *World Journal of Emergency Surgery*. 2024;19(1):17.
7. U.S. Food and Drug Administration. Vasopressin Injection Prescribing Information. Accessed July 2026.