

Supplementary Online Content

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 Surg*. Published online August 28, 2019. doi:10.1001/jamasurg.2019.2884

eFigure 1. 48-Hour Cumulative Blood Products for Per-Protocol Analysis

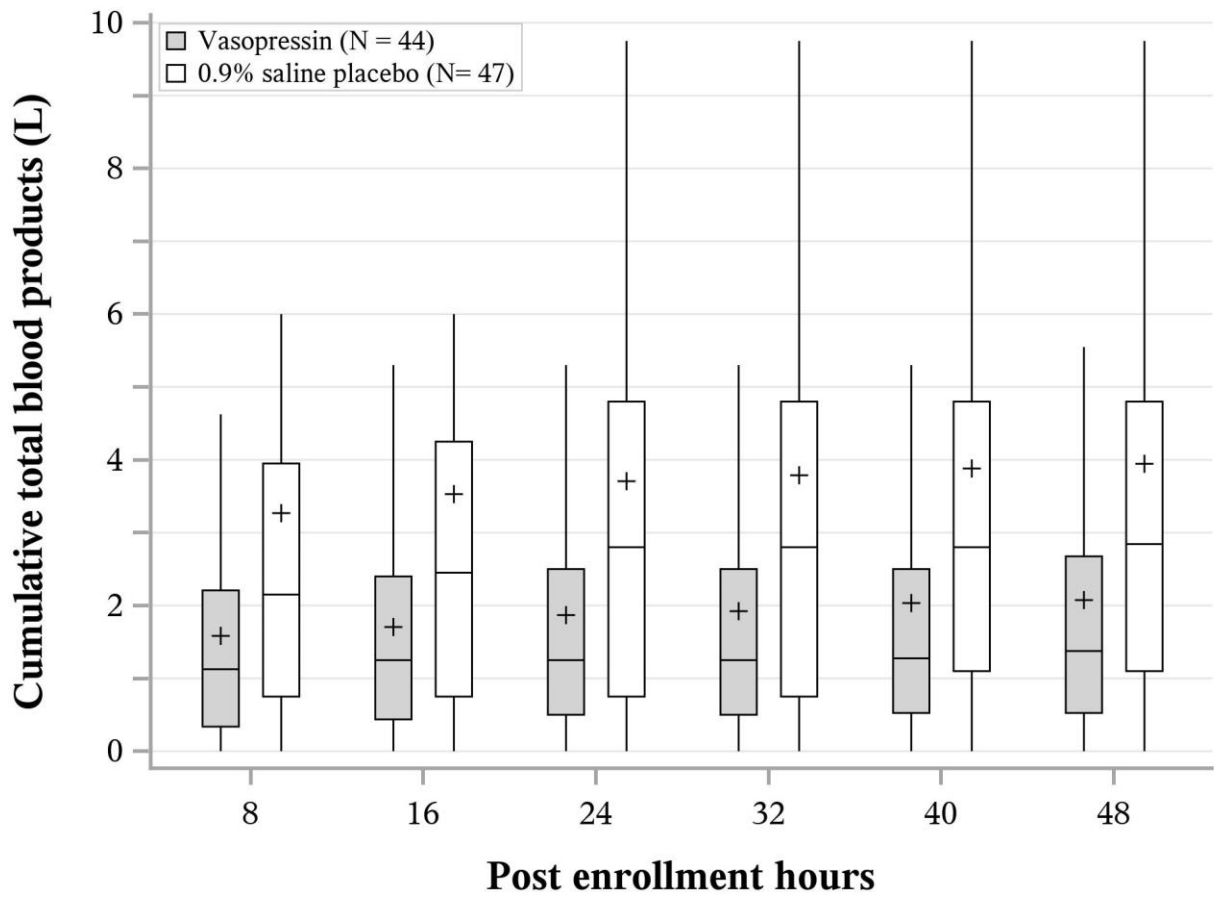
eFigure 2. Vital Signs and Urine Output for Each 8-Hour Period

eTable. Laboratory Values on Postoperative Days 1 and 2

eMethods. Pennsylvania Trauma Outcomes Study Definitions of Complications

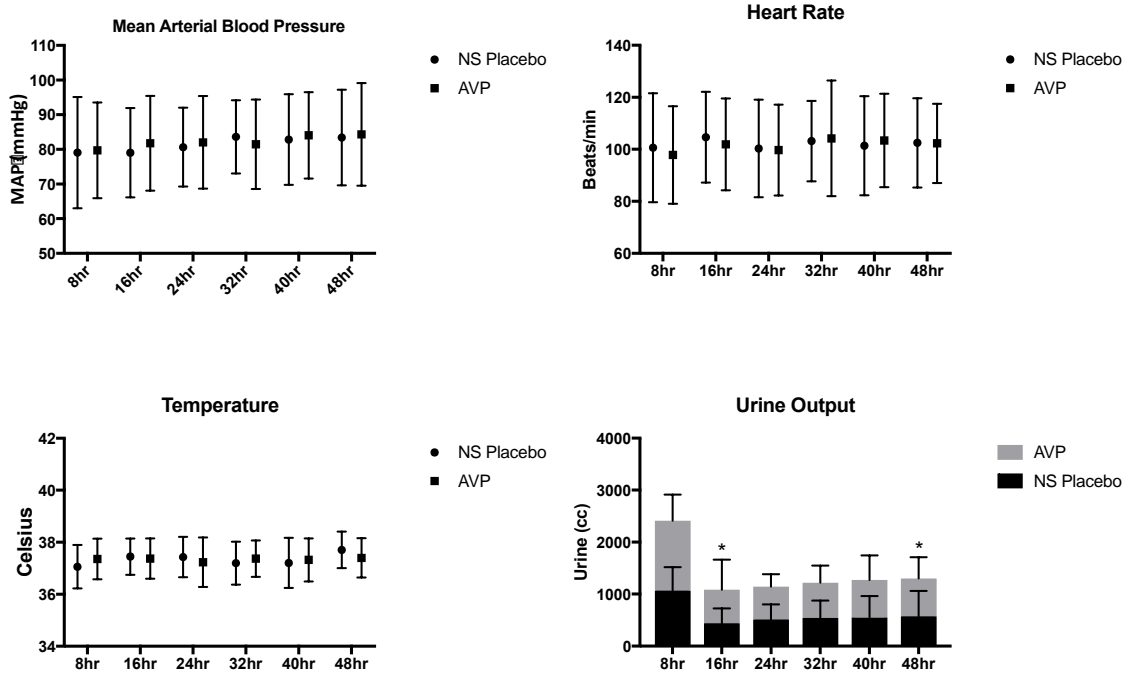
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. 48-hour Cumulative Blood Products for Per-Protocol Analysis



Boxplots comparing randomized groups for cumulative total blood products from enrollment to 48 hours postoperatively. The box represents the interquartile range, the horizontal line is the median, the whiskers extend to high and low values within 1.5 interquartile ranges of the box, and the plus symbol represents the mean.

eFigure 2. Vital Signs and Urine Output for Each 8-Hour Period



Data are represented as means \pm SD. Urine output is represented by median \pm IQR. Groups were analyzed at each time point with students t test or Kruskal Wallis as appropriate with $p < 0.05$ considered significant.

eTable. Laboratory Values on Postoperative Days 1 and 2

Lab Value	Day 1			Day 2		
	NS Placebo	AVP	P Value	NS Placebo	AVP	P Value
Sodium	141 ± 3	140 ± 4	0.42	139 ± 3	138 ± 17	<0.05
Chloride	109 ± 3	107 ± 16	0.31	109 ± 5	107 ± 13	0.05
CO2	22 ± 5	23 ± 5	0.22	25 ± 3	24 ± 4	0.56
BUN	15 ± 5	13 ± 4	0.09	14 ± 7	12 ± 5	0.27
Creatinine	1.39 ± 0.55	1.24 ± 0.47	0.14	1.25 ± 0.56	1.13 ± 0.47	0.30
Hemoglobin	10.1 ± 2.2	10.2 ± 2.3	0.85	9.6 ± 2.2	9.4 ± 2.2	0.69
Platelets	115 ± 40	128 ± 54	0.22	104 ± 33	113 ± 40	0.27
INR	1.4 ± 0.3	1.4 ± 0.4	0.82	1.4 ± 0.3	1.4 ± 0.3	0.32
PTT	36 ± 8	42 ± 24	0.18	37 ± 7	35 ± 8	0.18
Lactate	4.7 [2.8, 8]	4.6 [2.5, 8]	0.50	2.4 [1.5, 3.2]	2.3 [1.2, 3.4]	0.53

Values represent the highest sodium, chloride, BUN , creatinine, INR, PTT, and lactate as well as the lowest hemoglobin and platelets available on postoperative day 1 and 2. Groups were analyzed with students t test or Kruskal Wallis as appropriate with p <0.05 considered significant.

eMethods. Pennsylvania Trauma Outcomes Study Definitions of Complications

Deep venous thrombosis: The formation, development, or existence of a blood clot or thrombus within the vascular system, which may be coupled with inflammation. This diagnosis may be confirmed by a venogram, ultrasound, or CT. The patient must be treated with anticoagulation therapy and/or placement of a vena cava filter or clipping of the vena cava.

Pulmonary embolus: Defined as a lodging of a blood clot in a pulmonary artery with subsequent obstruction of blood supply to the lung parenchyma. The blood clots usually originate from the deep leg veins or the pelvic venous system. Consider the condition present if the patient has a V-Q scan interpreted as high probability of pulmonary embolism or a positive pulmonary arteriogram or positive CT angiogram.

Urinary tract infection: Not present on admission. Clean voided or other catheter urine specimen with > 100,000 organisms/ml on culture. Physician institutes appropriate therapy for a urinary tract infection.

Pneumonia: Hospital acquired or ventilator associated. Chest radiographic examination shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion AND any of the following:

- a. New onset of purulent sputum or change in character or sputum
- b. Organism isolated from the blood
- c. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy
- d. Isolation of virus or detection of viral antigen in respiratory secretions
- e. Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
- f. Histopathologic evidence of pneumonia

Acute respiratory distress syndrome: new (or worsening) respiratory symptoms and impaired oxygenation with PaO₂/FiO₂ >200 but ≤ 300 and PEEP or CPAP ≥ 5 cmH₂O. Chest imaging demonstrates bilateral opacities that are not fully explained by effusions, lobar/lung collapse, or nodules. Respiratory failure cannot be fully explained by cardiac failure or fluid overload with objective assessment (e.g., echocardiography) to exclude hydrostatic edema.

Acute renal failure/Acute kidney injury: an abrupt (within 48 hours) reduction of kidney function defined as: increase in serum creatinine (SCr) of more than or equal to 3x baseline OR; increase in SCr to ≥ 4 mg/dl (≥ 353.3 μmol/l) OR; patients > 18 years with a decrease in eGFR to < 35 ml/min per 1.73 m² OR; reduction in urine output of < 0.3 ml/kg/hr for ≥ 24 hrs OR; anuria for ≥ 12 hrs. OR; requiring renal replacement therapy (e.g., continuous renal replacement therapy (CRRT) or periodic peritoneal dialysis, hemodialysis, hemofiltration, or hemodiafiltration). NOTE: If the patient or family refuses treatment (e.g., dialysis) the condition is still considered to be present if a combination of oliguria and creatinine are present. EXCLUDES patients with renal failure that were requiring chronic renal replacement therapy such as periodic peritoneal dialysis, hemodialysis, hemofiltration, or hemodiafiltration prior to injury.

Gastrointestinal bleeding: blood loss from anywhere in the GI tract, grossly positive nasogastric (NG) aspirate, or grossly positive stool which requires treatment.

Major dysrhythmia: dysrhythmia requiring drugs or defibrillation that does not result in death. Examples include supraventricular tachycardia, rapid atrial fibrillation, sustained ventricular tachycardia, or bradycardia that requires pacing.

Wound infection: drainage of purulent material from a traumatic or incisional wound with active treatment of the wound or administration of antibiotics for the wound.

Sepsis: documented by a physician with at least two or more of the following conditions (which occur at the same time):

1. core temperature of > 38 C or < 36 C
2. white blood cell count > 12,000 or < 4,000 or > 10% immature bands
3. positive blood cultures (excluding contaminants)
4. clinically obvious source of infection

5. heart rate > 90 beats/min or respiratory rate > 20 breaths/min

Extremity Compartment Syndrome: Defined as a condition *not present at admission* in which there is documentation of tense muscular compartments of an extremity through clinical assessment or direct measurement of intracompartmental pressure requiring fasciotomy. Compartment syndromes usually involve the leg but can also occur in the forearm, arm, thigh, and shoulder. Record as a complication if it is originally missed, leading to late recognition, a need for late intervention, and has threatened limb viability.

Coagulopathy: Excludes anticoagulation therapy, coumadin therapy, or underlying hematologic disorders, e.g. hemophilia. Uncontrolled, diffuse bleeding in the presence of coagulation abnormalities, e.g., increased prothrombin time, increased partial thromboplastin time, decreased platelet count, or disseminated intravascular coagulation (DIC) requiring treatment, i.e., transfusion of components such as platelets, clotting factors, FFP.

Soft tissue infection: cellulitis, gas gangrene, necrotizing fasciitis, or myositis requiring treatment.

Ischemia: Decreased tissue oxygen availability due to peripheral vasoconstriction leading to blanching of the skin or necrosis.

Hyponatremia: Serum sodium less than 130 mmol/L.

Urticaria: a skin rash with red, raised, itchy bumps, otherwise, known as hives, diagnosed by the treating team.

Arterial thrombosis: formation of a thrombus within any artery that is documented by treating physician.

Rhabdomyolysis: muscle damage resulting in the release of intracellular muscle constituents. Diagnosis is made in the setting of elevated serum creatinine kinase (>1500 IU/L) and the presence of urine myoglobin.