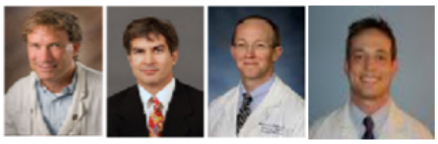
critical care perspectives in emergency medicine



Early Vasopressors or Fluids for Septic Shock?

Key Article

- *Vasopressors or Fluids in Early Septic Shock. The ARISE FLUIDS Investigators, the ANZICS Clinical Trials Group, and the ACEM Clinical Trials Network. New Engl J Med. 2026; published June 11.*

Background

- The optimal approach to IVF administration and timing of vasopressor initiation in patients with early septic shock is unknown.
- The SSC guidelines provide a weak recommendation for IVFs at a dose of at least 30 ml/kg within the first 3 hours of recognition of sepsis-induced hypotension.
- The European Society of Intensive Care Medicine guidelines make a similar recommendation.
- Neither guideline makes specific recommendations regarding the timing of vasopressor initiation.
- As such, there is significant practice variation in the management of septic shock
- The largest randomized trial to evaluate restrictive fluid strategy for early septic shock was stopped for futility and showed no benefit regarding mortality (CLOVERS).
- Some small single enter trials suggest benefit with early vasopressor initiation, however, more evidence is needed.
- Thus, these investigators conducted the Australasian Resuscitation in Sepsis Evaluation: Fluid or Vasopressors in Emergency Department Sepsis (ARISE FLUIDS) trial…

Objective

- To test whether a strategy of restricted fluid volume and early vasopressors, as compared with a strategy of greater fluid volume and later vasopressors, would increase the number of days alive and out of the hospital at day 90

Methods

- Investigator-initiated, open-label, RCT
- 51 sites across 3 countries
- Patients - Included
    - Adults with clinically suspected infection
    - Who had an SBP of < 90 mm Hg, or MAP < 65 mm Hg, despite receiving at least 1 L of IVFs (including IVFs administered in prehospital setting)
    - A lactate > 2 mmol/L
    - Began receiving treatment with an IV ABX
- Patients – Excluded
    - Receipt of > 2 L of IVFs
    - More than 6 hours since ED arrival
    - Need for immediate surgery
    - Clinician determined unsuitability
    - Care limitations

- Randomization
    - Within the first 6 hours of meeting inclusion criteria
    - 1:1 to Vasopressor Group or Fluids Group
    - Intervention delivered for a minimum of 6 hours up to 24 hours
    - Vasopressor Group
        - IVF resuscitation ceased after randomization
        - Vasopressor therapy commenced
        - Vasopressor type, route, dose adjustment, and target MAP were according to clinician preference
        - Fluid boluses of 250 ml were permitted if indicated – refractory hypotension, persistent hypoperfusion, lactate > 4 mmol/L, persistent tachycardia, and oliguria
    - Fluids Group
        - Initial IVF bolus of up to 1 L infused within 60 minutes administered after randomization
        - Additional 500 ml boluses were administered for persistent hypotension or hypoperfusion
        - Unless contraindicated, 30 ml/kg within 3 hrs were recommended
        - Fluid type, method of assessing fluid responsiveness, maintenance fluids, and target MAP were determined by clinician preference
        - Treatment with vasopressors was initiated if the target MAP was not achieved and the clinician determined that the fluid level was restored or the patient's arterial pressure was not responding to fluid resuscitation
- Primary Outcome
    - Days alive and out of the hospital from randomization to follow-up at day 90
- Secondary Outcomes
    - 28-day mortality
    - 90-day mortality
    - Survival from randomization at 90 days
    - Days alive and free from organ support at day 28
- Tertiary Outcomes
    - Time to ED DC
    - Time to ICU DC
    - Time to hospital DC
    - In-hospital mortality

Results

- A total of 1,000 patients underwent randomization. Informed consent not provided for 37 patients, which left **963 patients** in the ITT population
    - Vasopressor Group: 481 patients
    - Fluids Group: 482 patients
- Baseline characteristics
    - Similar in the two groups
    - Prerandomization median fluid volume:
        - Vasopressor Group: 1500 ml
        - Fluids Group: 1500 ml
    - Treatment with vasopressors before randomization

        - Vasopressor Group: 12%
        - Fluids Group: 8.5%
    - Number of patients who underwent source control
        - Vasopressor Group: 16.4%
        - Fluids Group: 19.5%
    - Most common source of infection
        - Respiratory and urinary tract in both groups
- Interventions
    - Percent of patients receiving a vasopressor infusion within 24 hours of randomization
        - Vasopressor Group: 86.5%
        - Fluids Group: 67.6%
    - Median time to vasopressor initiation
        - Vasopressor Group: 0.4 hours
        - Fluids Group: 1.4 hours
    - Median fluid volume received in the first 6 hours after randomization
        - Vasopressor Group: 500 ml
        - Fluids Group: 1500 ml
    - Median fluid volume by 24 hours after randomization
        - Vasopressor Group: 1140 ml
        - Fluids Group: 2248 ml
    - Patients admitted to the ICU
        - Vasopressor Group: 76.5%
        - Fluids Group: 67.8%
    - Patients receiving mechanical ventilation
        - Vasopressor Group: 15.4%
        - Fluids Group: 15.1%
    - Protocol violations
        - Patients receiving intervention for < 6 hours
            - Vasopressor Group: 5.7%
            - Fluids Group: 6.5%
        - Vasopressor Group: 14.8% of patients received a fluid bolus > 250 ml
- Primary Outcome – median number of days alive and out of the hospital at day 90
    - Vasopressor Group: 76 days
    - Fluids Group: 76 days
    - No difference
    - No difference in any prespecified subgroup: age, sex, baseline lactate, APACHE II score, infection source
- Secondary Outcomes
    - No difference in 90-day mortality
    - Median time to ICU discharge
        - Vasopressor Group: 59.3 hours
        - Fluids Group: 69 hours
- Safety Outcomes
    - Pulmonary edema
        - Vasopressor Group: 0.6%
        - Fluids Group: 5%

Limitations Identified by Authors

- Resuscitation targets nor specific measures of responsiveness to fluids were specified
- Unblinded trial
- Intervention limited to first 24 hours – did not control for subsequent hospitalization, including DC decisions
- Clinicians excluded a sizeable proportion of patients with treatment limitations (2080 eligible patients)
    - Patients with preexisting conditions and fluid restriction (i.e., cardiac failure) and patients who received > 2 L before screening were excluded

Take Home Points

- Administration of a restricted volume of IVFs and early vasopressors did not improve the number of days alive and out of the hospital 90-days when compared to a greater volume of fluids and later vasopressor administration in ED patients with septic shock.