



Vasopressor Therapy in Sepsis

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Objectives

- After completion of this module, participants will:
 - Compare catecholamine and vasopressors for patients with septic shock
 - Describe the initial vasopressor of choice for patients with septic shock
 - Explain the literature for vasopressor therapy in patients with septic shock



New Definitions

Sepsis

- Life-threatening organ dysfunction caused by a dysregulated host response to infection
- Defined by qSOFA + SOFA scores
- Emphasizes organ dysfunction
- De-emphasizes nonspecific systemic inflammation
- No more “severe sepsis”

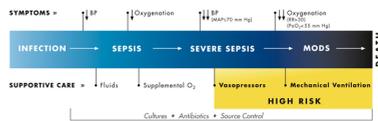
Septic shock

- Persistent hypotension requiring vasopressors AND lactate > 2
- A subset of sepsis in which underlying circulator and cellular/metabolic abnormalities are profound enough to substantially increase mortality
- Hypotension = MAP < 65
- Combination of ↓ BP and ↑ lactate:
 - » Significantly higher risk-adjusted mortality for combo (42.3%) vs. for pressors alone (30.1%), lactate > 2 alone (25.7%)

Singer M, et al. JAMA 2016;315(8):801-810.



Time and Terminology Matters



Vasopressors / Inotropics

Agent	α ₁	β ₁	β ₂	DA ₁	DO ₂	VO ₂	pH _i
Dopamine							
1-3 mcg/kg/min	0	+	0	++++	↑	↑	↑↓
3-10 mcg/kg/min	0/±	++++	+++	++++			
10-20 mcg/kg/min	+++	++++	+	0			
Norepinephrine							
2-200 mcg/min (0.05-3 mcg/kg/min)	++++	++	0	0	↑	↑	↑
Phenylephrine							
10-77 mcg/min (0.5-3 mcg/kg/min)	++++	0	0	0	↑	↑	NA
Epinephrine							
0.01-0.05 mcg/kg/min	++	++++	++	0	↑	↑	↑↓
>0.05 mcg/kg/min	++++	++++	+	0			
Vasopressin							
0.04 Units/min	0	0	0	0	↑	↑	NA
Dobutamine							
2-10 mcg/kg/min	+	+++	++	0	↑	↑	↑
>10-20 mcg/kg/min	++	++++	++++	0			



Sepsis Occurrence in Acutely Ill Patients (SOAP)

SOAP study evaluated the epidemiology of sepsis in Europe

- P, MC, observational study
- Objective
 - Whether dopamine administration influenced outcome in septic shock in the SOAP cohort
- Included adult patients admitted from 5/1 – 5/15/2002
- Evaluated all vasopressors, alone and in combination
- Baseline characteristics similar with exception of increased HF in dopamine group
- 1058 patients (14.7% septic shock)
 - 375 – dopamine
 - 683 – No dopamine

Saiki, et al. Crit Care Med 2005;34:989-997



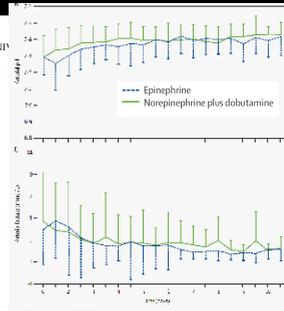
Mortality

	Epinephrine (n=165)	Norepinephrine plus dobutamine (n=159)	p
At day 7	40 (25%)	34 (20%)	0.30
At day 14	55 (35%)	44 (26%)	0.08
At day 28	64 (40%)	58 (34%)	0.31
At discharge from intensive care	75 (47%)	75 (44%)	0.69
At discharge from hospital	84 (52%)	82 (49%)	0.51
At day 90	84 (52%)	85 (50%)	0.73

Data are number of deaths (%).

Table 3: All-cause mortality rates

Annemans D, et al. *Lancet*. 2008;372:2226-2234.



Annemans D, et al. *Lancet*. 2008;372:2226-2234.

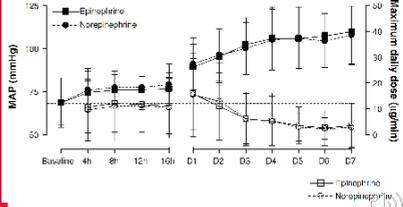
Intensive Care Med. 2008;33:1133-1139
DOI: 10.1177/1422732108321133

ORIGINAL

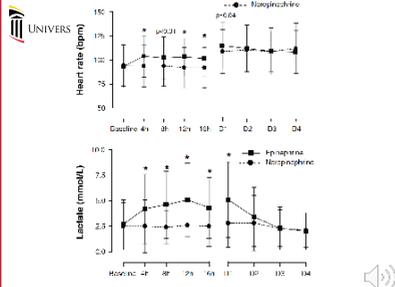
A comparison of epinephrine and norepinephrine in critically ill patients
Lukic A, Mihaljevic M, Jelicic M, et al.

- P, R, MC, DB study septic shock patients
 - Treatment
 - Study drug prepared in identical concentrations
 - Titrated based on goal BP
- Objective
 - Achieve clinician prescribed MAP goal for greater than 24 hours
- 280 enrolled
 - Epi = 140, NE = 140
 - Sepsis: Epi = 76 (54.7%), NE = 82 (59.4%)

Mihaljevic et al. *Intensive Care Med*. 2008;33:2226-2234.



Mihaljevic et al. *Intensive Care Med*. 2008;33:2226-2234.



Mihaljevic et al. *Intensive Care Med*. 2008;33:2226-2234.

Epinephrine

- Can be added to norepinephrine to increase BP or decrease norepinephrine doses
 - Weak recommendation; LQE
- Considered as effective as norepinephrine for BP
- Transient increase in lactate
 - May interfere with lactate clearance
- Increase in HR compared to norepinephrine
- No difference in mortality
- Potential to decrease coronary and mesenteric blood flow

Vasopressin



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Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock

James A. Russell, M.D., Keith P. Walley, M.D., Joel Singer, Ph.D., Anthony C. Gordon, M.B., B.S., M.D., Paul C. Hibberd, M.D., D. James Cooper, B.M., B.S., M.D., Cheryl L. Holmes, M.D., Sangeeta Khanna, M.D., John T. Granton, M.D., Michelle M. Skrobis, B.Sc.N., Deborah J. Cook, M.D., Jeffrey J. Presnell, M.B., B.S., Ph.D., and Ester Ayns, M.Sc. for the SOAP-3 Investigators*

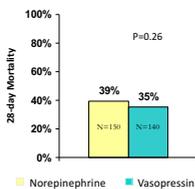
- R, MC, DB study with 778 septic shock patients
 - Treatment
 - VP started at 0.01 units/min titrated to max of 0.03 units/min
 - NE started at 5 mcg/min titrated to > 15 mcg/min
 - VP weaned off 8 hours after catecholamine
- Primary endpoint: 28-day mortality
- 778 enrolled
 - VP = 396, NE = 382

Russell, et al. N Engl J Med. 2008;358:877-887.



VASST – Vasopressin vs Norepinephrine

28-day Mortality

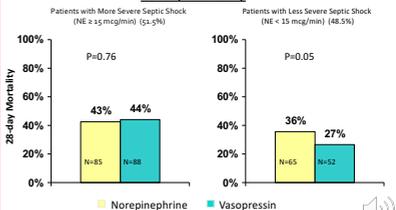


Russell, et al. N Engl J Med. 2008;358:877-887.



VASST – Vasopressin vs Norepinephrine

28-day Mortality



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Vasopressin

- Low-dose vasopressin can be added to norepinephrine to increase MAP and decrease norepinephrine dose
 - Doses up to 0.03 units/min
 - Weak recommendation, LQE
- May decrease CO/CI? (dose related?)
- Potential to decrease coronary and mesenteric blood flow
- Not recommended as single initial agent and doses greater than 0.03-0.04 units/min are considered salvage therapy
 - Higher doses associated with more ADE
- Should be titrated off after catecholamine has been D/C'd



Dobutamine

- Dobutamine can be added to vasopressor
 - Evidence of persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents
 - Weak recommendation, LQE
- Dobutamine should not be used to increase CI to supranormal levels
- Dobutamine may decrease BP due to B2 effects
- Should be titrated to CI or ScvO2
- Max dose 20 mcg/kg/min



