



# Použití vazopresorů – současný stav poznání

M. Matějovič



CHEST

Postgraduate Education Corner

CONTEMPORARY REVIEWS IN CRITICAL CARE MEDICINE

## Hemodynamic Evaluation and Monitoring in the ICU\*

*Michael R. Pinsky, MD, FCCP*

### *Hemodynamic Monitoring Truths*

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Tachycardia is never a good thing.

Hypotension is always pathologic.

There is no such thing as normal cardiac output.

Central venous pressure is only elevated in disease.

Peripheral edema is of cosmetic concern.

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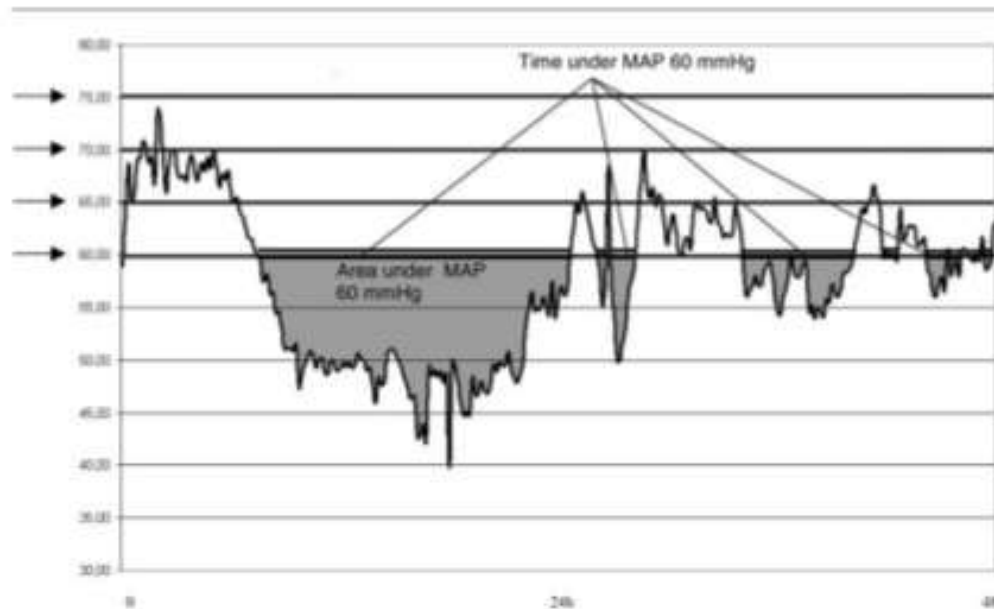
# Nejsilnější prediktor mortality

Intensive Care Med (2005) 31:1066–1071  
DOI 10.1007/s00134-005-2688-z

ORIGINAL

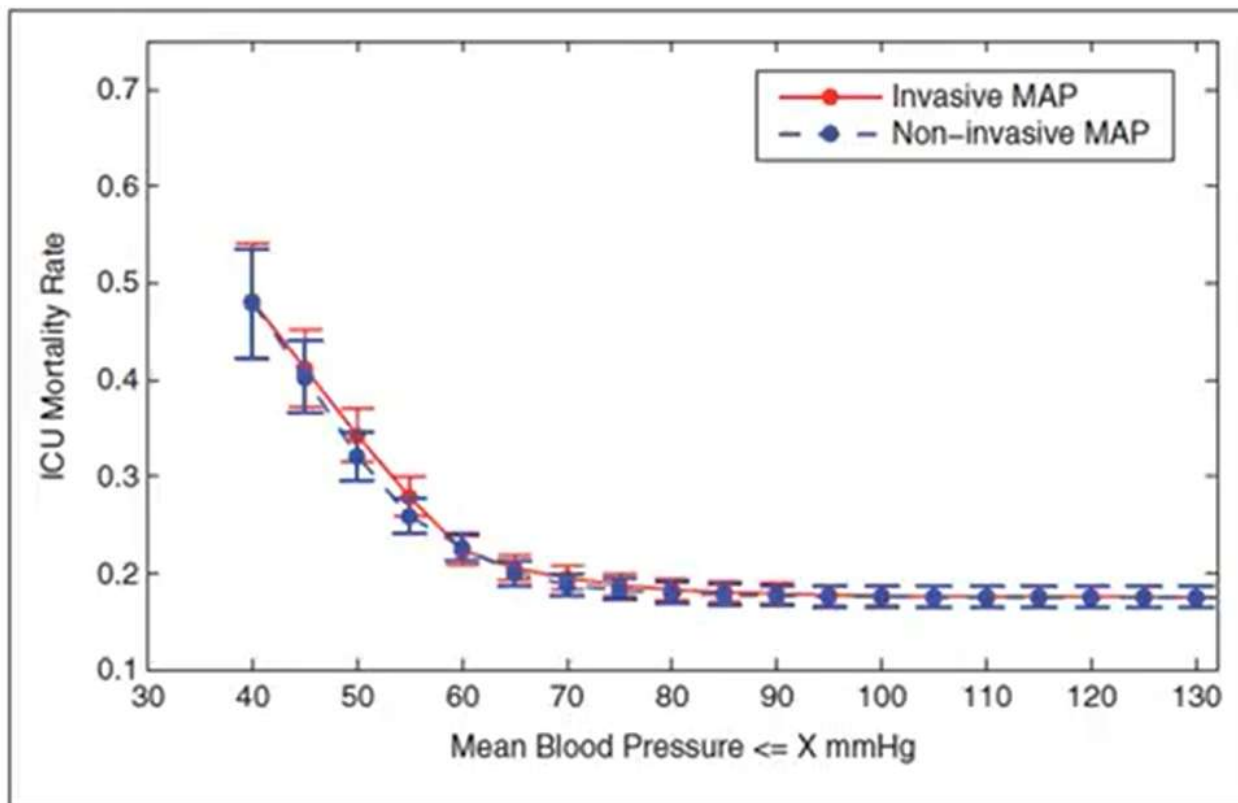
Marjut Varpula  
Minna Tallgren  
Katri Saukkonen  
Liisa-Maria Voipio-Pulkki  
Ville Pettilä

## Hemodynamic variables related to outcome in septic shock



The highest AUC values were found for hypotension area under 65 mmHg (AUC 0.853, 95% CI 0.772–0.934)

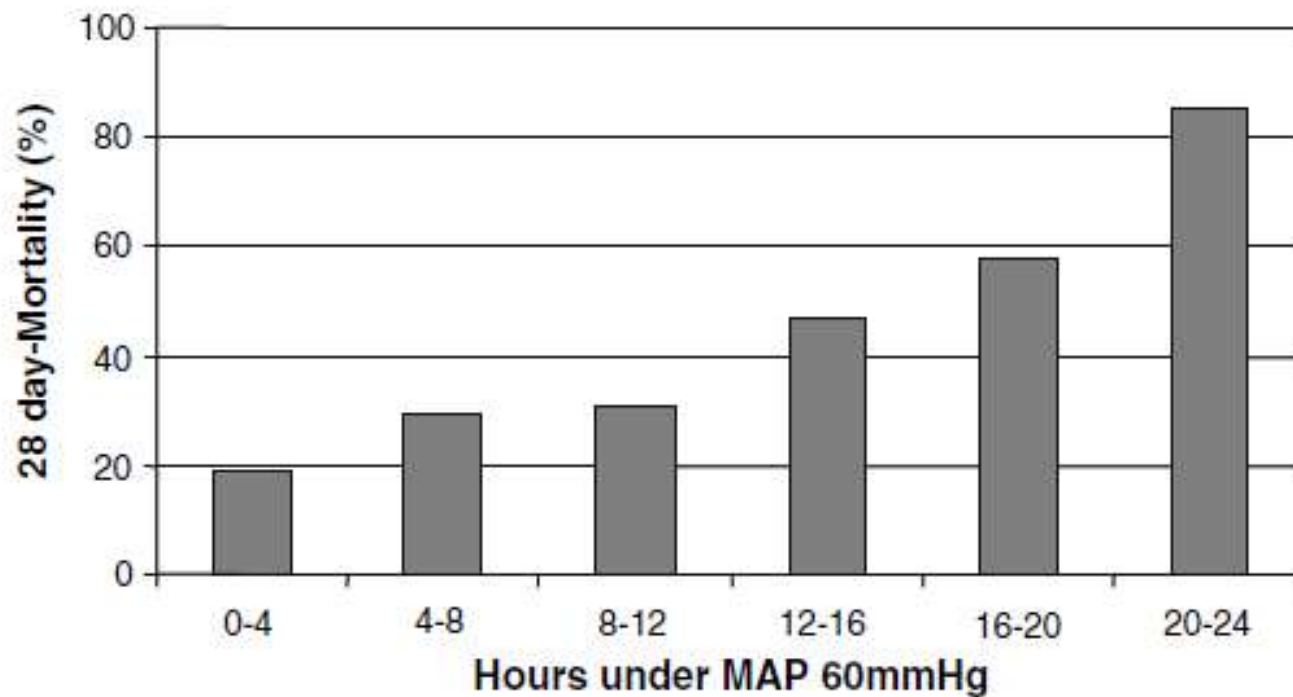
Li-wei H. Lehman, PhD<sup>1,2</sup>; Mohammed Saeed, MD, PhD<sup>1,2,3</sup>; Daniel Talmor, MD<sup>4</sup>;  
Roger Mark, MD, PhD<sup>1,2</sup>; Atul Malhotra, MD<sup>5</sup>



Crit Care Med 2013; 41:34

# Arterial blood pressure during early sepsis and outcome

Intensive Care Med (2009) 35:1225–1233





**Závažnost** i **délka** trvání hypotenze jsou spojeny se špatnou prognózou



Mean Arterial Pressure (MAP)



55 mmHg

Mean Arterial Pressure (MAP)



60 mmHg

Mean Arterial Pressure (MAP)



68 mmHg



Mean Arterial Pressure (MAP)



82 mmHg

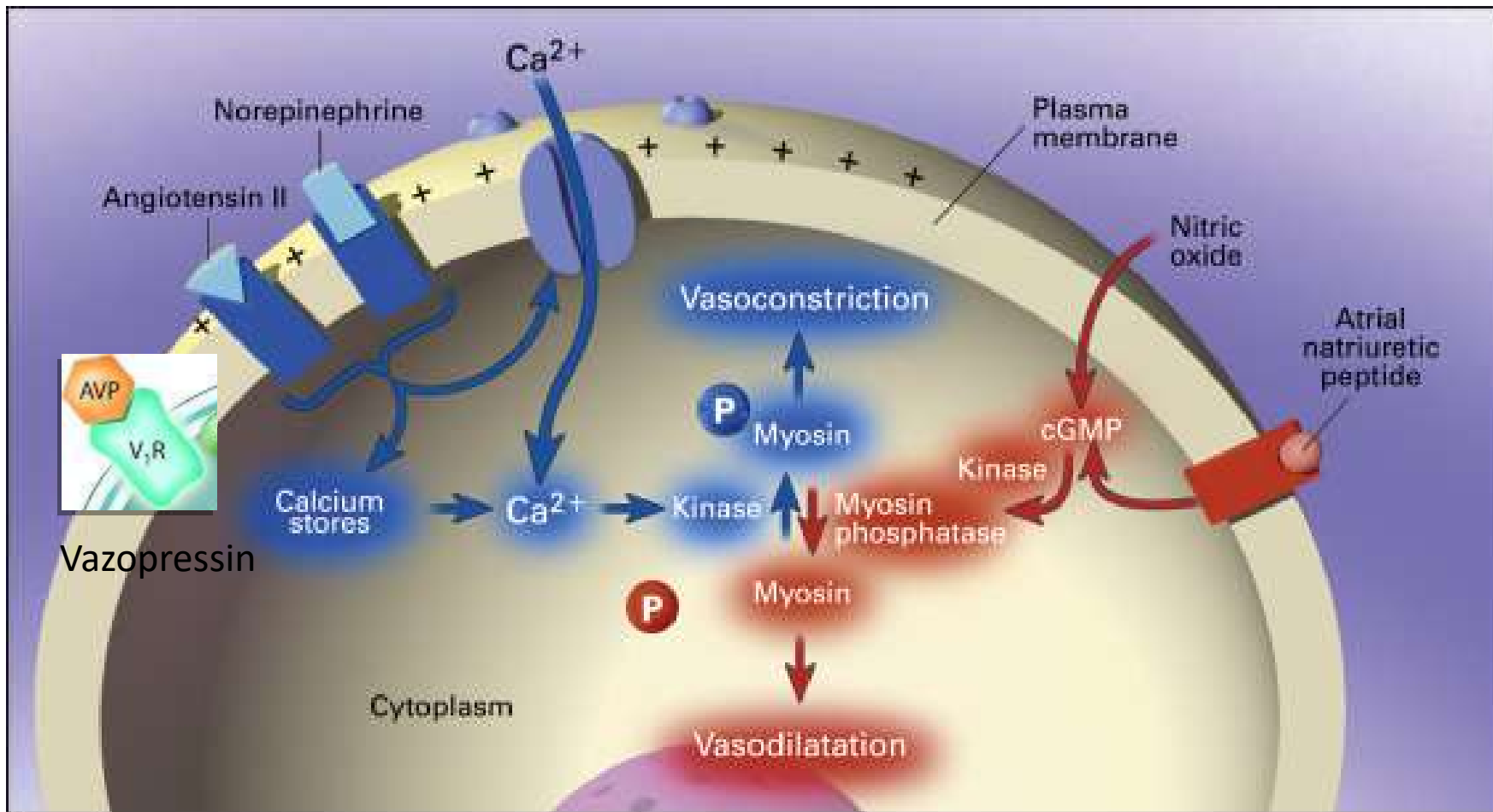
# Pooled analysis of higher versus lower blood pressure targets for vasopressor therapy in septic and vasodilatory shock

François Lamontagne<sup>1,2\*</sup>, Andrew G. Day<sup>3</sup>, Maureen O. Meade<sup>4,5</sup>, Deborah J. Cook<sup>4,5</sup>, Gordon H. Guyatt<sup>5</sup>, Mathieu Hylands<sup>6</sup>, Peter Radermacher<sup>7</sup>, Jean-Marie Chrétien<sup>8</sup>, Nicolas Beaudoin<sup>9</sup>, Paul Hébert<sup>10</sup>, Frédérick D'Aragon<sup>1,2</sup>, Ferhat Meziani<sup>11</sup> and Pierre Asfar<sup>12</sup>

## Take-home message:

In this individual patient-data meta-analysis, higher blood-pressure targets—i.e. more aggressive use of vasopressors - were associated with an increased risk of death in patients enrolled >6 h after initiation of vasopressors. Lower blood-pressure targets were not associated with patient-important adverse events in any subgroup, including chronically hypertensive patients.





N Engl J Med. Landry, D., Oliver J. Pathogenesis of Vasodilatory Shock. 345;588-595

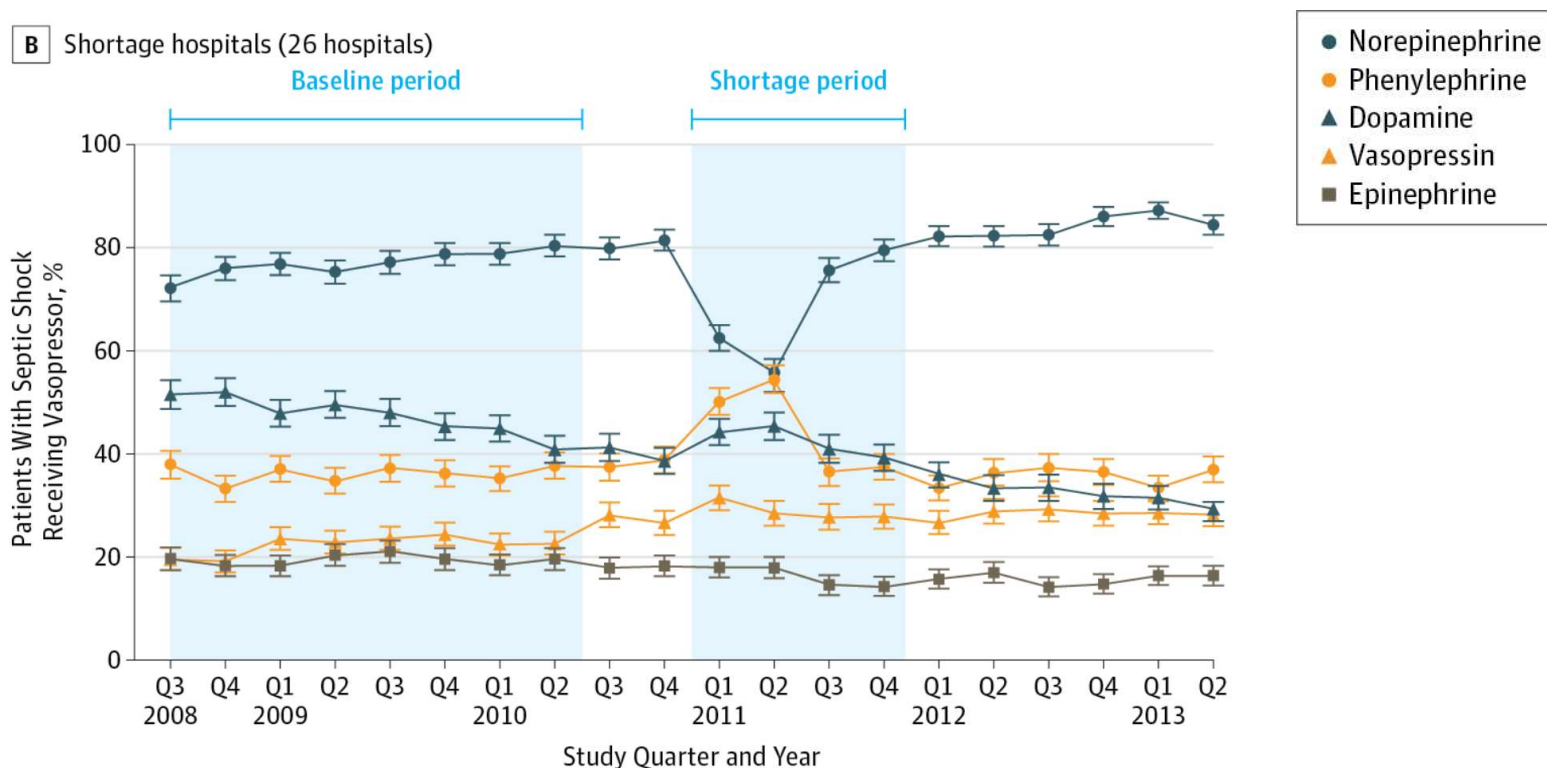
## Který z vazopresorů má nejpříznivější vztah k mortalitě u septického šoku

- a) DOPAMIN
  - b) NORADRENALIN
  - c) ADRENALIN
  - d) VAZOPRESIN
  - e) Jiný
- } Adrenergní
- } Non- adrenergní

**Noradrenalin je první volbou u všech typů šokových stavů**

From: Association Between US Norepinephrine Shortage and Mortality Among Patients With Septic Shock

JAMA. 2017;317(14):1433-1442. doi:10.1001/jama.2017.2841



[35.9%] vs [39.6%], absolute mortality difference = 3.7% [95% CI, 1.5%-6.0%];

Změna z NOR na Dopa + Phenylephrine byla spojena se zhoršením mortality

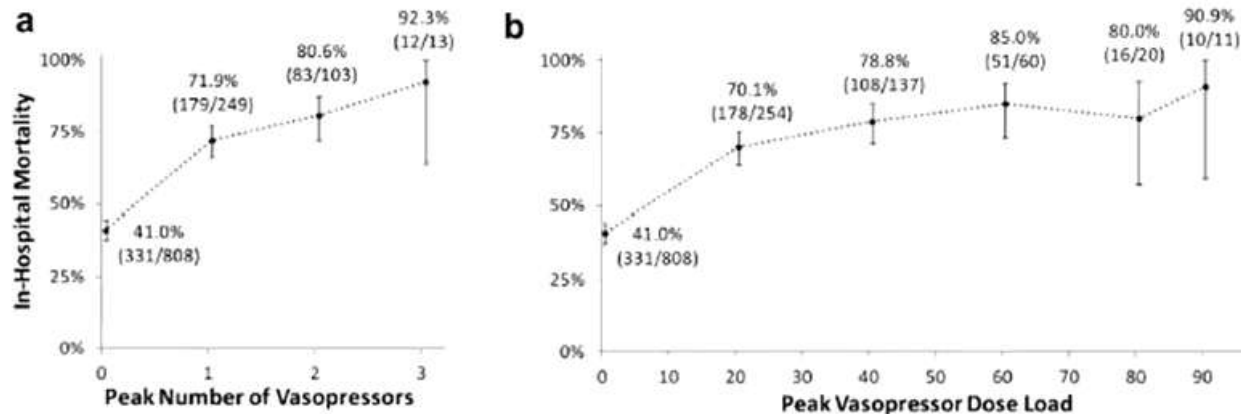
# Je dávka vazopresorů důležitá?

## Co je „refrakterní šok“ a je důležité to rozlišovat?

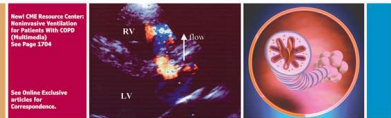
### Intensity of Vasopressor Therapy for Septic Shock and the Risk of In-Hospital Death



Donald A. Brand, PhD, Patricia A. Patrick, DrPH, Jeffrey T. Berger, MD, Mediha Ibrahim, MD, Ajsza Matela, MD, Shweta Upadhyay, MD, and Peter Spiegler, MD



**Dávka vazopresoru je prediktorem  
prognózy**



# Ekvivalence vazopresorů

**Table 1.** Converting Vasopressor Doses to Norepinephrine Equivalents<sup>4-6,8,10,12,23,24,26,27</sup>

Drug	Dose	Norepinephrine Equivalent
Epinephrine	0.1 mcg/kg/min	0.1 mcg/kg/min
Dopamine	15 mcg/kg/min	0.1 mcg/kg/min
Norepinephrine	0.1 mcg/kg/min	0.1 mcg/kg/min
Phenylephrine	1 mcg/kg/min	0.1 mcg/kg/min
Vasopressin	0.04 U/min	0.1 mcg/kg/min

Jentzer JC, Vallabhajosyula S, Khanna AK, Chawla LS, Busse LW, Kashani

KB, Management of Refractory Vasodilatory Shock, *CHEST* (2018), doi: 10.1016/j.chest.2017.12.021.

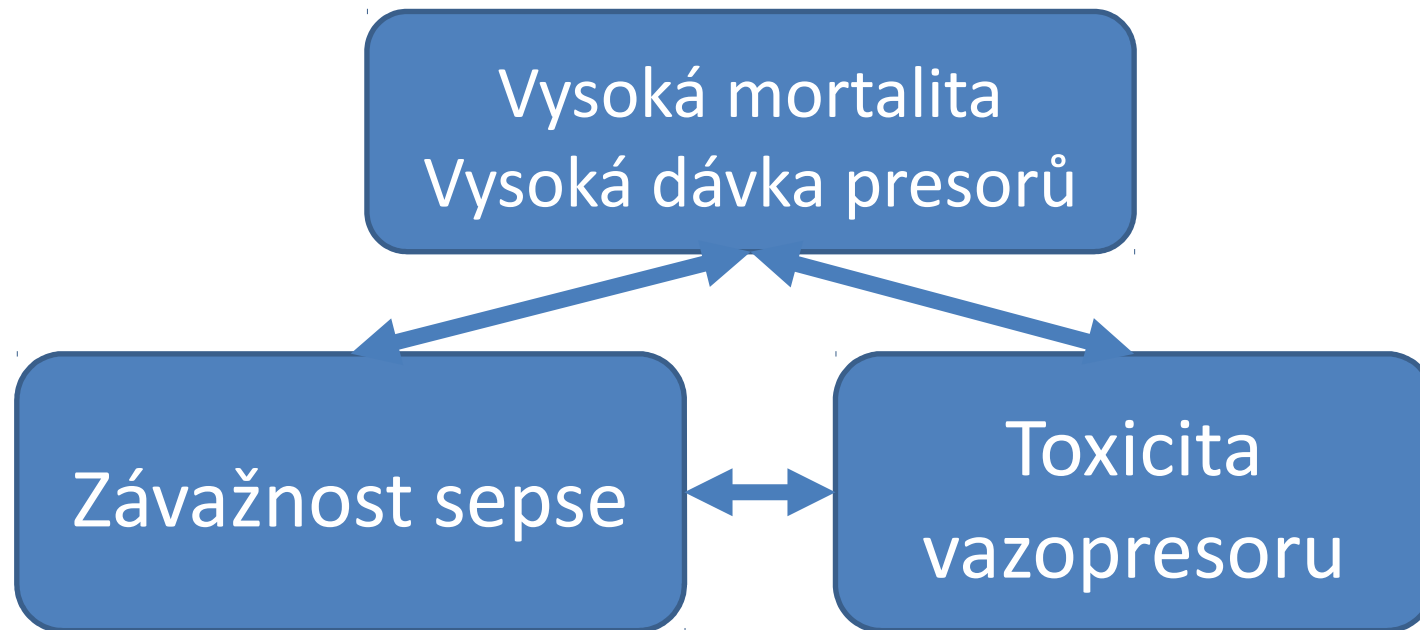
# Existuje „bod zlomu“?



Mortalita (>50%)  
Pokles účinnosti

Cca 0.5  $\mu\text{g}/\text{kg}/\text{min}$

Intenzita vazopresorické podpory



- ★ obvious e.g. tachyarrhythmias, digital ischaemia
- ★ stimulation of bacterial growth
- ★ increased bacterial virulence
- ★ immunosuppression
- ★ metabolic modulation
- ★ decreased bioenergetic efficiency
- ★ altered blood-brain barrier
- ★ increased cardiac work
- ★ ventricular remodelling
- ★ thrombogenic

Singer M. Lancet 2007; 370: 636-7

# Je „bod zlomu“ důvodem k léčebné změně ?



Mortalita (>50%)  
Pokles účinnosti

Cca 0.5  $\mu\text{g}/\text{kg}/\text{min}$

- NOR + normální laktát
- NOR + vysoký laktát
- NOR + MODS

**Intenzita vazopresorické podpory**



# STANOVISKO VÝBORU ČSIM 2017 K POUŽITÍ VASOPRESINU V INTENZIVNÍ PÉČI

- Použití vasopresinu lze zvážit u pacientů se septickým šokem, kde nelze dosáhnout cílových hodnot krevního tlaku i přes použití vysokých dávek noradrenalinu. V těchto případech doporučujeme přidání vasopresinu do maximální dávky 4 IU/h, což odpovídá přibližně 0,04 IU/kg.h, s cílem dosažení cílové hodnoty krevního tlaku nebo snížení dávky noradrenalinu.
- Poznámka: diskuze vasopresin vs terlipresin (plicní hypertenze/pravé srdce, dynamická obstrukce výtokového traktu levé komory srdeční)
- Osobní pohled 😊

A black and white photograph of a person sitting on a rocky shore, looking out over a calm lake. In the background, there are dark, silhouetted mountains under a cloudy sky. The overall mood is contemplative and serene.

**If you want  
to be trusted,  
be honest.**



HIGHER PERSPECTIVE

# Když selhává i druhá volba?

## Vasopressor Use for Adult Septic Shock (with guidance for steroid administration)

Initiate norepinephrine (NE) and titrate up to 35-90  $\mu\text{g}/\text{min}$   
to achieve MAP target 65 mm Hg

MAP target **not** achieved  
and judged  
poorly responsive to NE

Add vasopressin up to  
0.03 units/min to achieve  
MAP target\*

MAP target  
achieved

MAP target  
**not** achieved

- \* Consider IV steroid administration
- \*\* Administer IV steroids
- \*\*\* SSC guidelines are silent on phenylephrine

### Notes:

- Consider dopamine as niche vasopressor in the presence of sinus bradycardia.
- Consider phenylephrine when serious tachyarrhythmias occur with norepinephrine or epinephrine.
- Evidence based medicine does not allow the firm establishment of upper dose ranges of norepinephrine, epinephrine and phenylephrine and the dose ranges expressed in this figure are based on the authors interpretation of the literature that does exist and personal preference/experience. Maximum doses in any individual patient should be considered based on physiologic response and side effects.

**Fig. 3** This figure demonstrates how the guideline recommendations on vasopressor and steroid use can be molded into a flow diagram approach to the management of septic shock

# Když selhává i druhá volba?

## Vasopressor Use for Adult Septic Shock (with guidance for steroid administration)

Initiate norepinephrine (NE) and titrate up to 35-90  $\mu\text{g}/\text{min}$  to achieve MAP target 65 mm Hg

MAP target **not** achieved and judged poorly responsive to NE

Add vasopressin up to 0.03 units/min to achieve MAP target\*

MAP target achieved

MAP target **not** achieved

Add epinephrine up to 20-50  $\mu\text{g}/\text{min}$  to achieve MAP target\*\*

MAP target achieved

MAP target **not** achieved

- \* Consider IV steroid administration
- \*\* Administer IV steroids
- \*\*\* SSC guidelines are silent on phenylephrine

### Notes:

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**Fig. 3** This figure demonstrates how the guideline recommendations on vasopressor and steroid use lead to the management of septic shock





- korekce hypoxémie, těžké anémie, acidózy (CRRT), kalcium?
- potřeba analgosedace?
- dávka vazopresinu? (0.06)
- NO inhibice (metylénová modř, hydroxykobalamin /Cyanokit/
- Thiamin, vitamin C?

# AN ORANGE A DAY KEEPS SEPSIS AT BAY?



Retro, před/po design  
47 pts  
**8.5 vs 40% mortalita**

## Marik Protocol

IV Vitamin C 1.5g q6hr  
x4d or ICU DC

\*

IV Hydrocortisone 50mg q6hr  
x7d or ICU DC + 3d Taper

\*

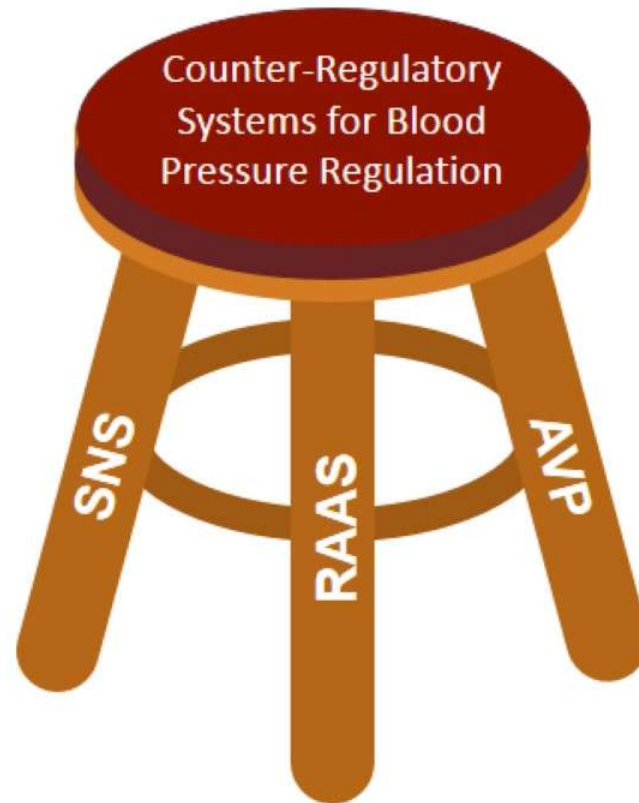
IV Thiamine 200mg q12hr  
x4d or ICU DC





- korekce hypoxémie, těžké anémie, acidózy (CRRT), kalcium?
- potřeba analgosedace?
- dávka vazopresinu? (0.06)
- NO inhibice (metylénová modř, hydroxykobalamin /Cyanokit/
- Thiamin, vitamin C
- Selepresin (selektivní V1a agonista)  
Sepsis-ACT f III. - ukončeno pro futility

# Multimodální léčba vazopresory



**Currently, two classes of drugs are available for treatment of shock: catecholamines and vasopressin<sup>[a]</sup>**





## Clinical Experience with Angiotensin II in the Treatment of Shock

*Francesco del Greco, M.D., and David C. Johnson, M.D., Chicago*

SEVERAL VASOPRESSOR AGENTS have been employed in recent years for treating shock and severe hypotension. The most powerful of these agents, levarterenol bitartrate, is limited in its use because of undesirable side effects.

In 1957, Schwyzer et al.<sup>1</sup> and Bumpus, Schwartz, and Page<sup>2</sup> reported the successful synthesis of a new vasopressor agent, angiotensin II. Extensive physiological and pharmacological studies in animals and man have shown that angiotensin II is considerably more potent than levarterenol.<sup>3, 4</sup> To date, only a few, limited studies concerning the effectiveness of angiotensin II in the treatment of shock in man have appeared, mostly in European literature.<sup>5-8</sup> The present report deals with a clinical evaluation of angiotensin II (valine-5 angiotensin II amide [Hypertensin]) in the treatment of shock due to various etiologies.

The effects of using angiotensin in the treatment of shock from various causes were studied in 21 patients. The blood pressure returned to normal in every instance excepting 6 patients who were moribund when treatment was begun. Of 6 patients who were in advanced bacteremic shock and whose prognosis was considered hopeless, 4 survived as did one with severe shock associated with postoperative intracranial bleeding and two with severe barbiturate poisoning. Angiotensin was also used in treating 10 patients in whom hypotension appeared in the course of dialysis by an artificial kidney. Six survived. In this series of cases angiotensin produced no side effects of any sort.

The NEW ENGLAND  
JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 3, 2017

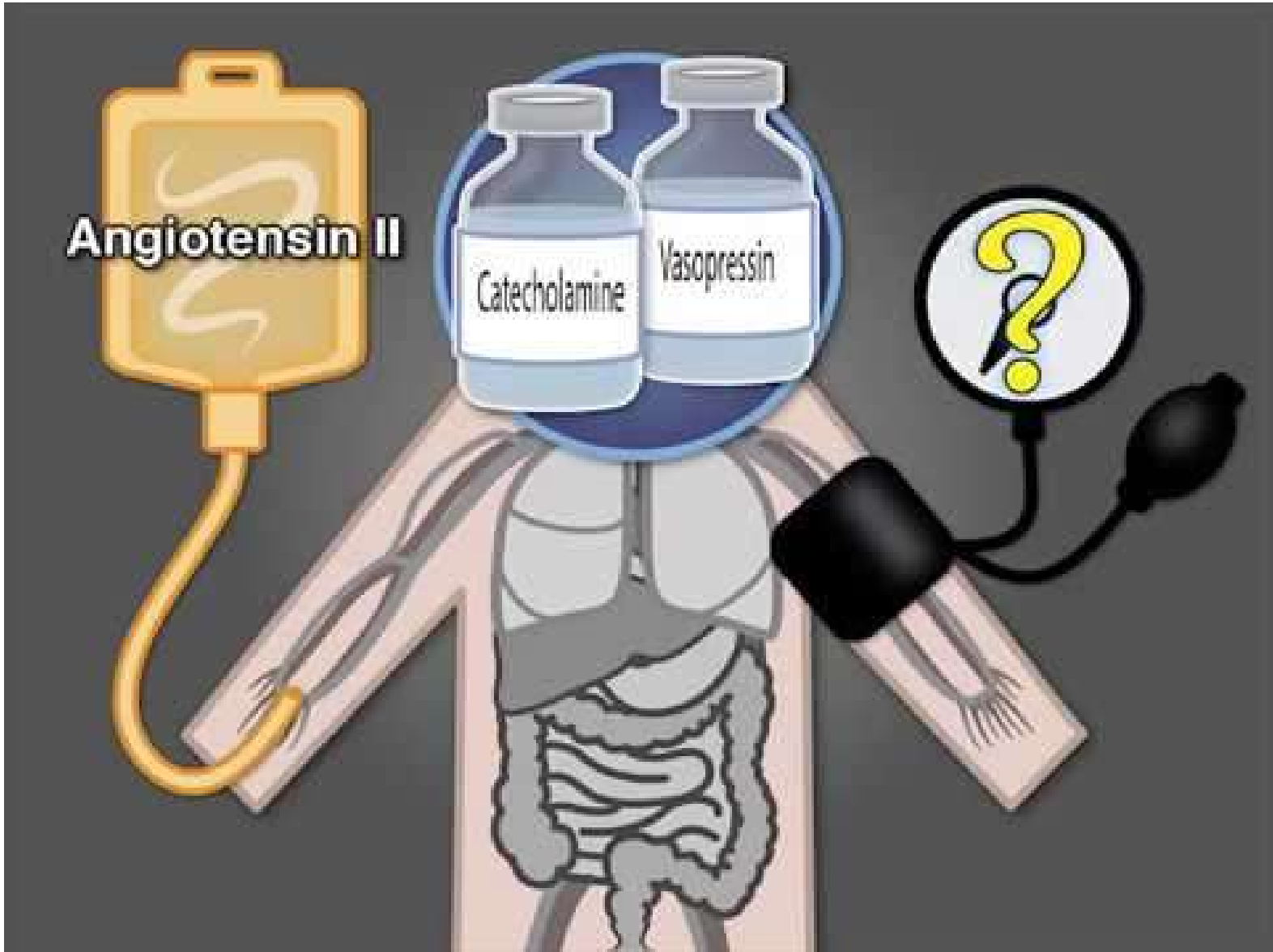
VOL. 377 NO. 5

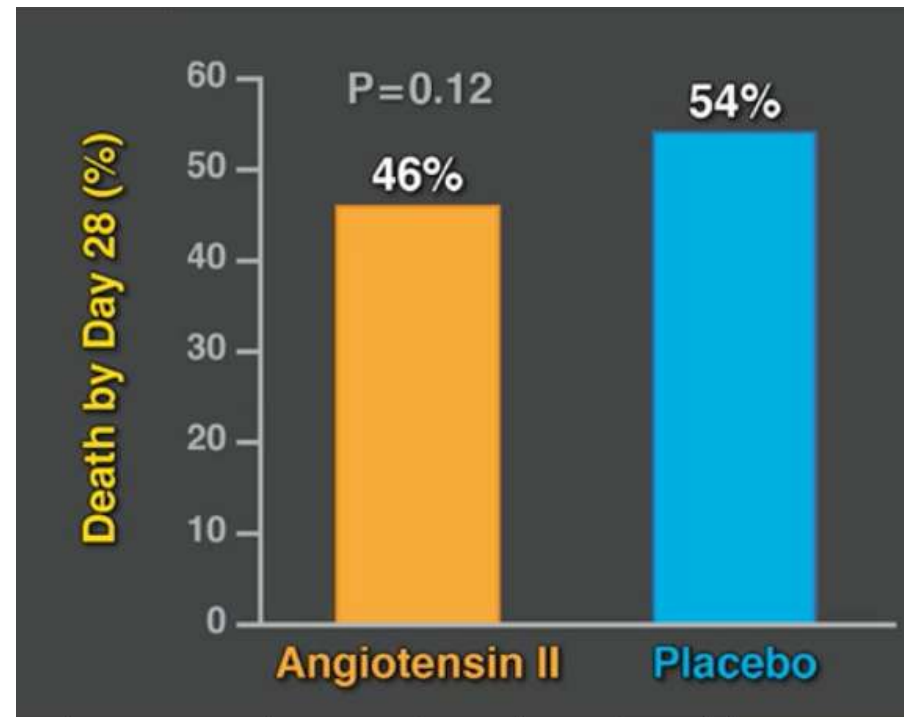
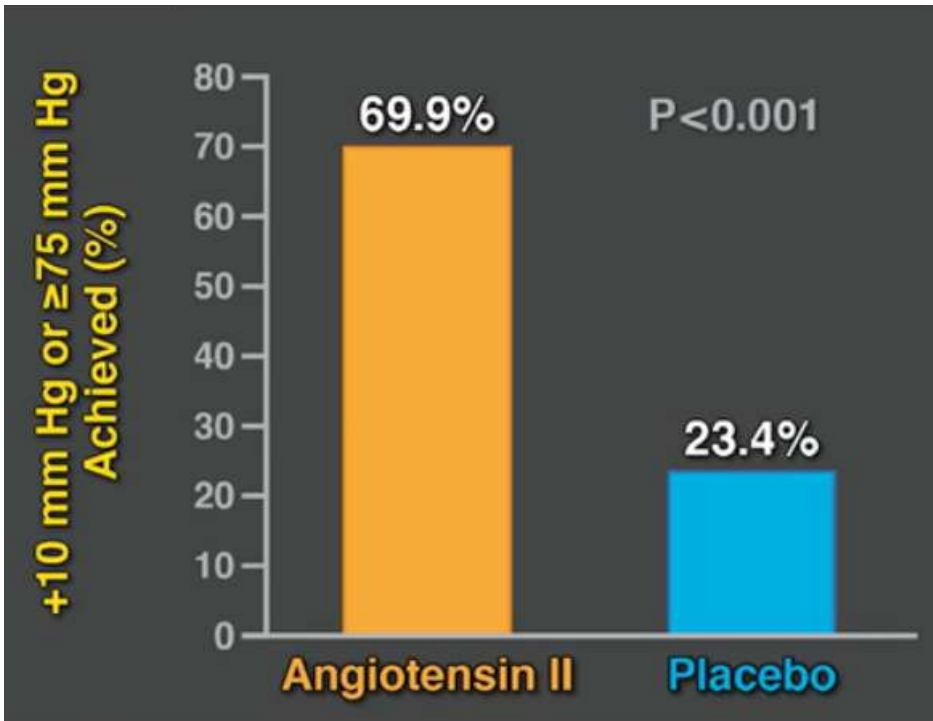
Angiotensin II for the Treatment of Vasodilatory Shock

ATHOS-3



THE  
BOTTOM  
LINE





News > Medscape Medical News > FDA Approvals

# FDA Clears Angiotensin II (*Giapreza*) for Septic Shock

Megan Brooks

December 21, 2017



# Timing



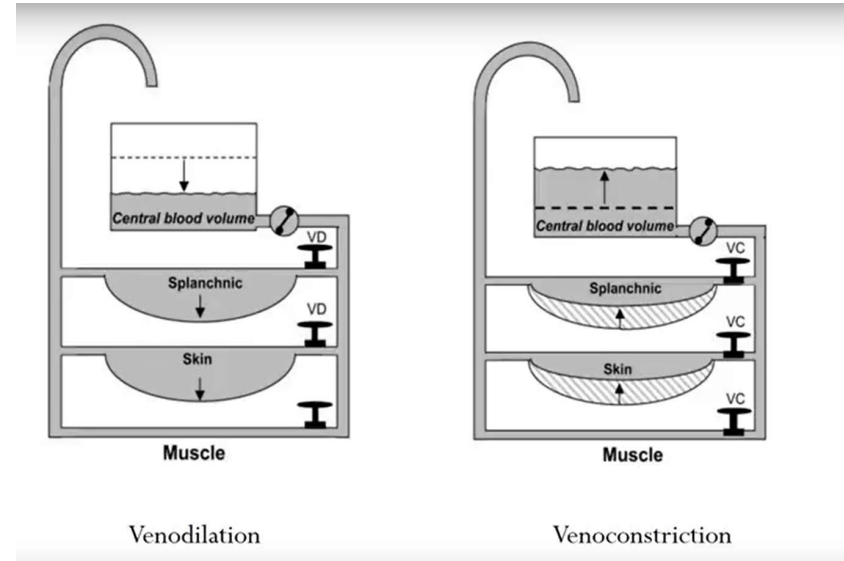
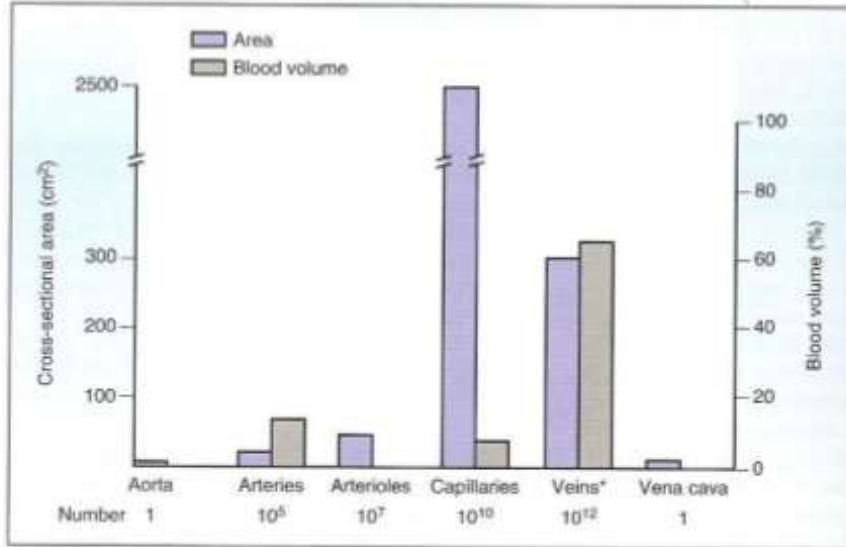
Samotná tekutinová resuscitace nemůže zvrátit septickou vazoplegií a hyporeaktivitu



Venózní kompartment je důležitou součástí septické patofyziologie



# Timing



## Časné zahájení léčby noradrenalinem **společně s** tekutinovou resuscitací u septického šoku:



Může ovlivněním nestresového objemu a vazoplegie snižovat celkovou potřebu tekutin a limitovat tak tekutinové přetížení

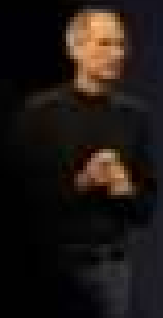


Nemaskuje další potřebu tekutinové resuscitace, ale nesmí být její náhražkou – vždy sleduj důsledky

# Závěr

- Korekce hypotenze bez zbytečného odkladu (MAP  $\approx$  65 mmHg)
- Noradrenalin první volba
- Vasopresin druhá volba
- Slibný angiotensin (ARDS, CPB, ACE..)
- Při limitované odpovědi na jeden lék přidej druhý, ale jiné skupiny spíše než jiný lék stejné skupiny

One more thing...







RED HOT CHILLI PEPPERS

