Which vasopressor to improve renal outcomes?

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Disclosures

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- Société Française d’Anesthésie-Réanimation (SFAR)
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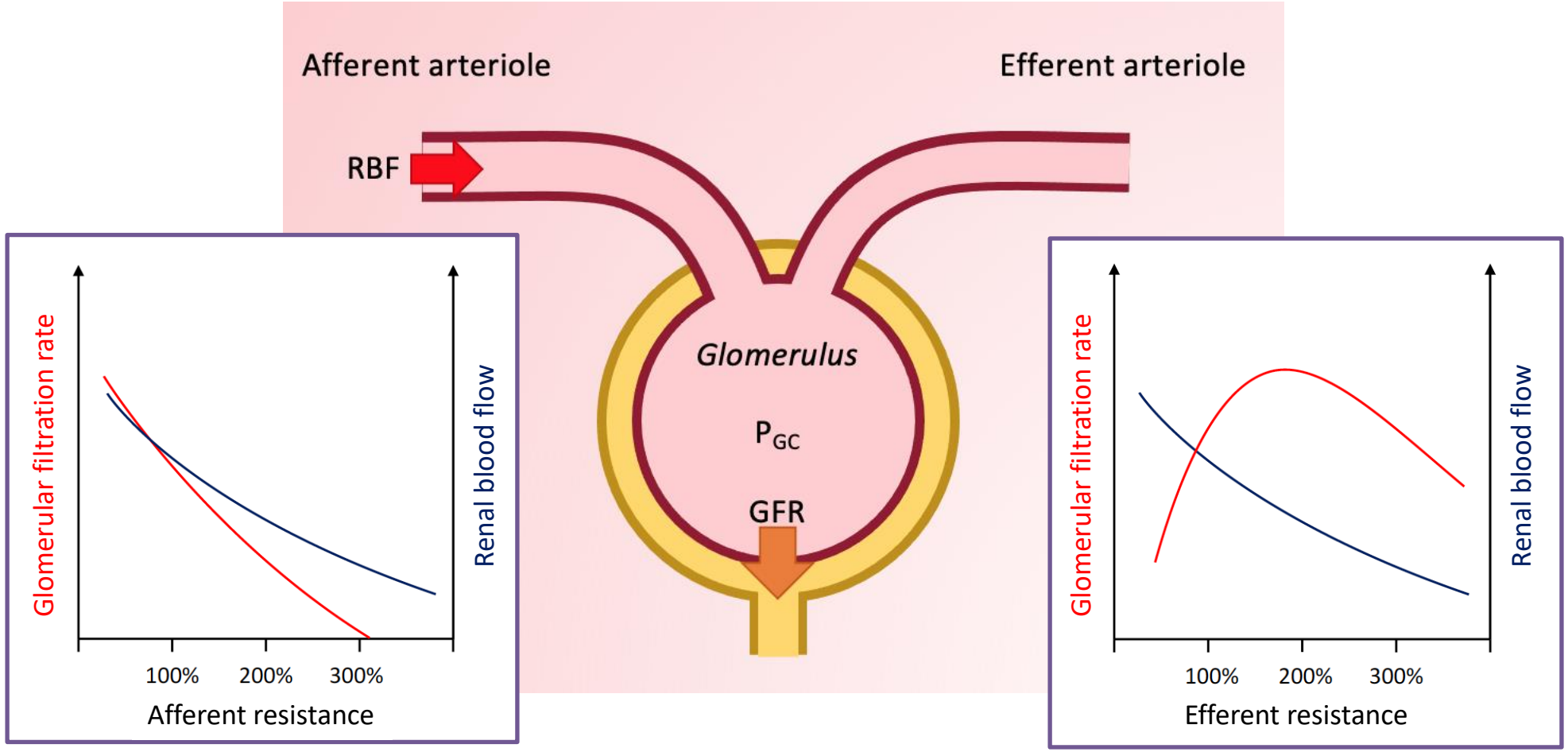
- 4TEEN4 Pharmaceuticals
- Zoll Fondation

Glomerular hemodynamics

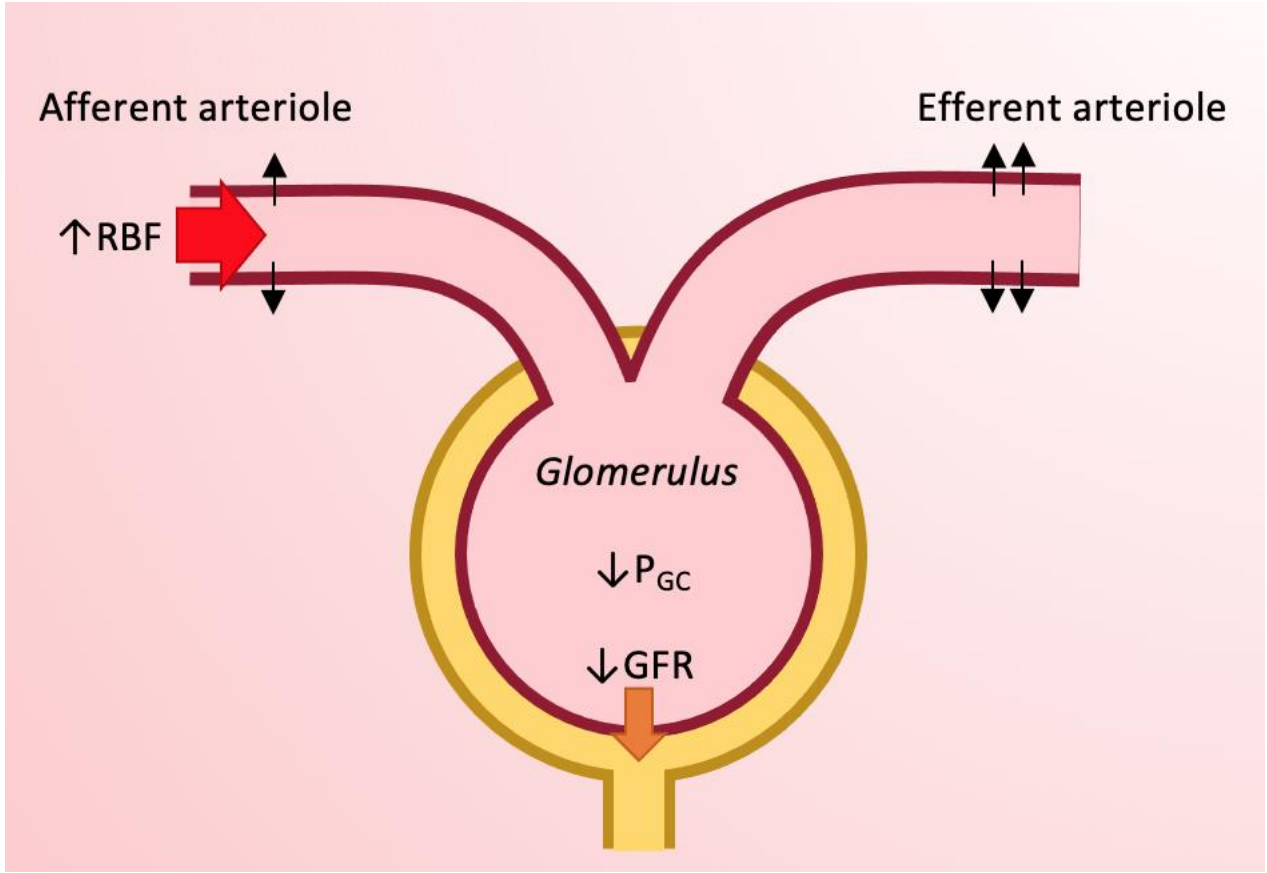


Picod *et al.*, Ann Intensive Care 2024

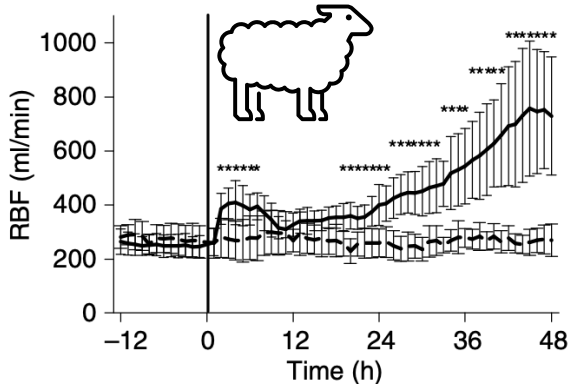
Glomerular hemodynamics: Vasodilatory shock (septic shock-associated AKI)

Renal plasma flow 171 %

Rector et al., Ann Surg 1973

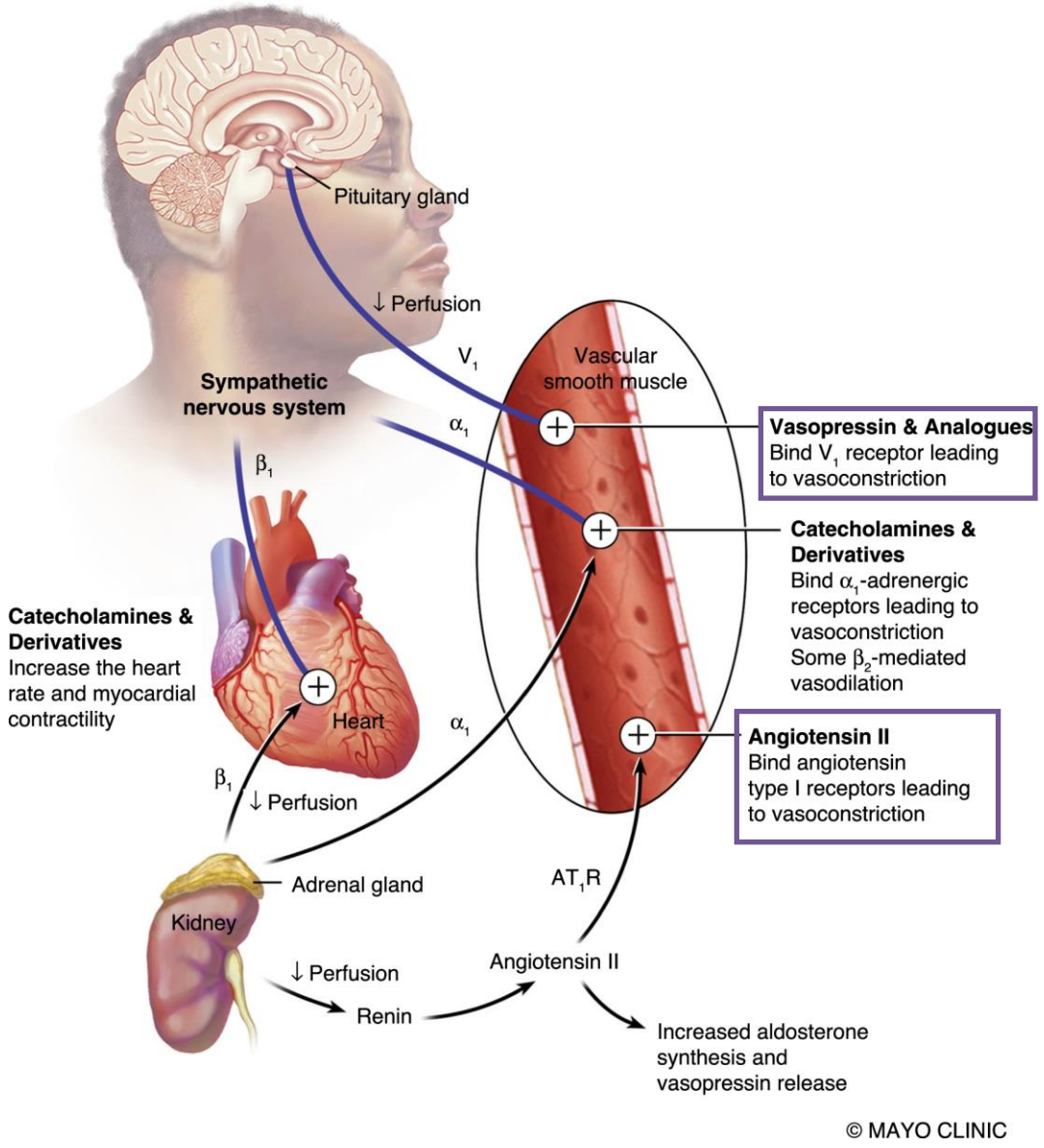


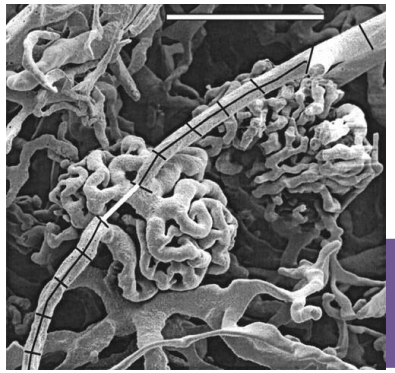
Low pressure – high flow



Langeberg *et al.*, Kidney Int 2006

Vasopressors





Edwards *et al.*, Am J Physiol 1983
Edwards *et al.*, Am J Physiol 1989
Denton *et al.*, Am J Physiol 2000

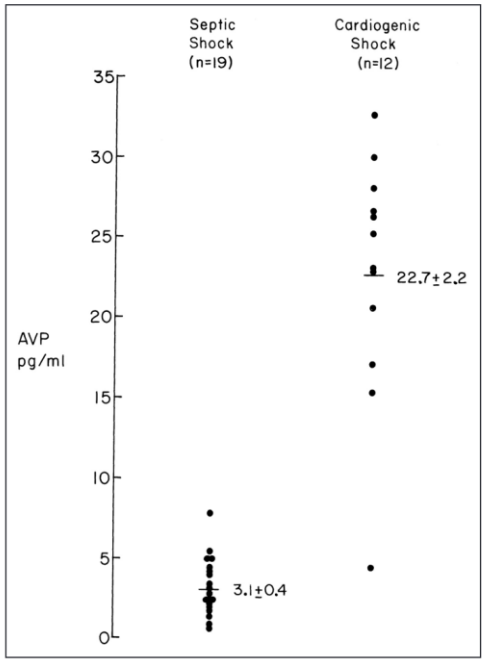
	Afferent vasoconstriction	Efferent vasoconstriction
Norepinephrine	+	+
Vasopressin	+	++
Angiotensin II	+	++

Vasopressin deficiency in septic shock

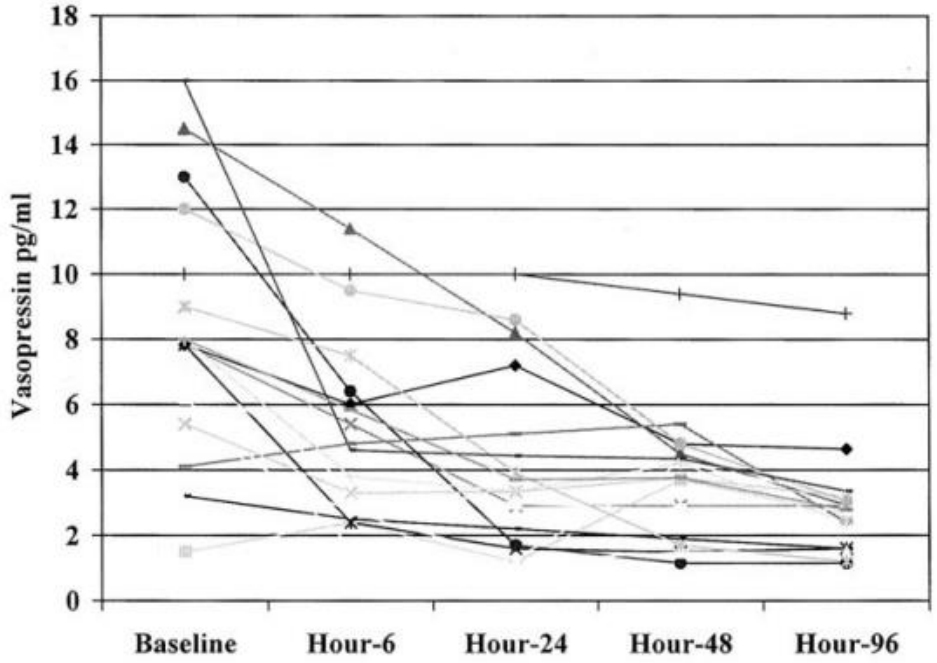
ARTICLE

Vasopressin Deficiency Contributes to the Vasodilation of Septic Shock

Donald W. Landry, Howard R. Levin, Ellen M. Gallant, Robert C. Ashton, Susan Seo, David D'Alessandro, Mehmet C. Oz, and Juan A. Oliver



Landry *et al.*, Circulation 1997



Circulating vasopressin levels in septic shock

Tarek Sharshar, MD; Anne Blanchard, MD, PhD; Michel Paillard, MD; Jean Claude Raphael, MD; Philippe Gajdos, MD; Djillali Annane, MD, PhD

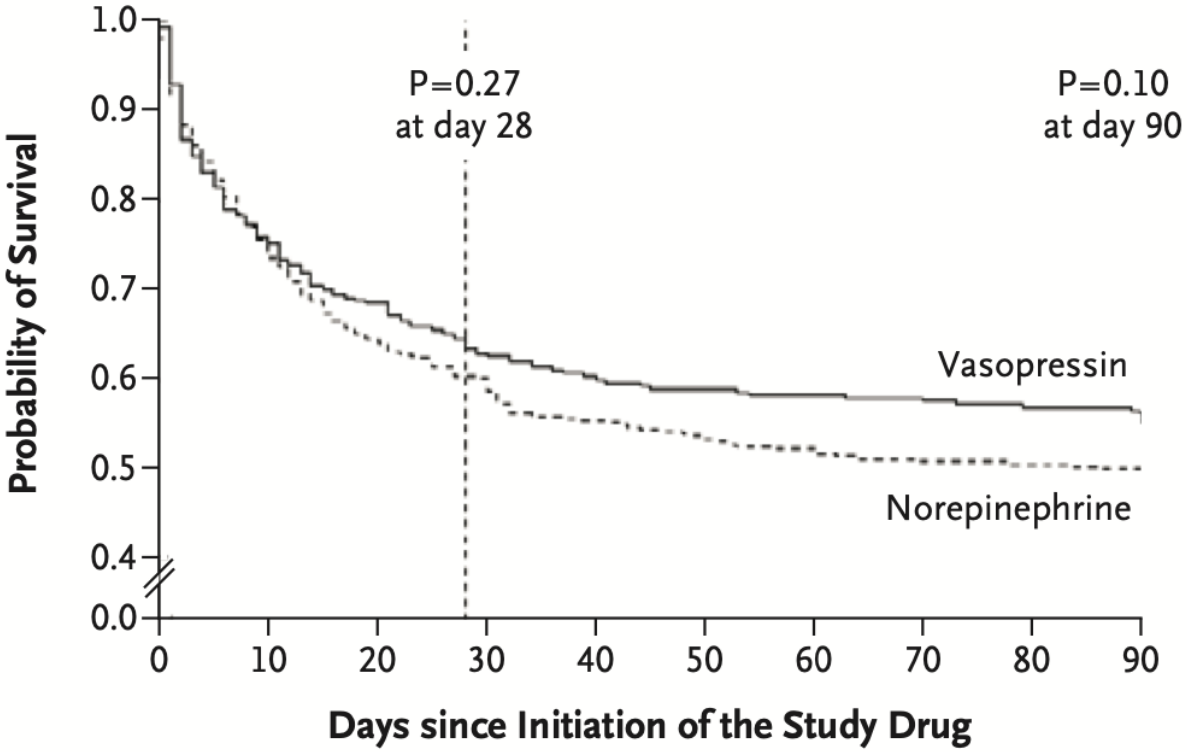
Sharshar *et al.*, Crit Care Med 2003

VASST Trial

Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock

N = 778

Septic shock with ≥ 5µg/min norepinephrine
Randomization: **Vasopressin (0.01 to 0.03 U/min**) vs norepinephrine



Renal	18.5 (3–28)	21.5 (4–28)	0.54
Renal-replacement therapy	23 (5–28)	25 (6–28)	0.64

Stratum	Norepinephrine Group	Vasopressin Group	P Value†	Absolute Risk Reduction (95% CI)	Relative Risk (95% CI)
	no./total no. (%)			%	
More severe septic shock					
28-day mortality	85/200 (42.5)	88/200 (44.0)	0.76	−1.5 (−11.2 to 8.2)	1.04 (0.83 to 1.3)
90-day mortality	105/199 (52.8)	103/199 (51.8)	0.84	1.0 (−8.8 to 10.8)	0.98 (0.81 to 1.18)
Less severe septic shock	NE < 15µg/min				
28-day mortality	65/182 (35.7)	52/196 (26.5)	0.05	9.2 (−0.1 to 18.5)	0.74 (0.55 to 1.01)
90-day mortality	83/180 (46.1)	69/193 (35.8)	0.04	10.4 (0.4 to 20.3)	0.78 (0.61 to 0.99)

Russell *et al.*, New Eng J Med 2008

VANISH Trial

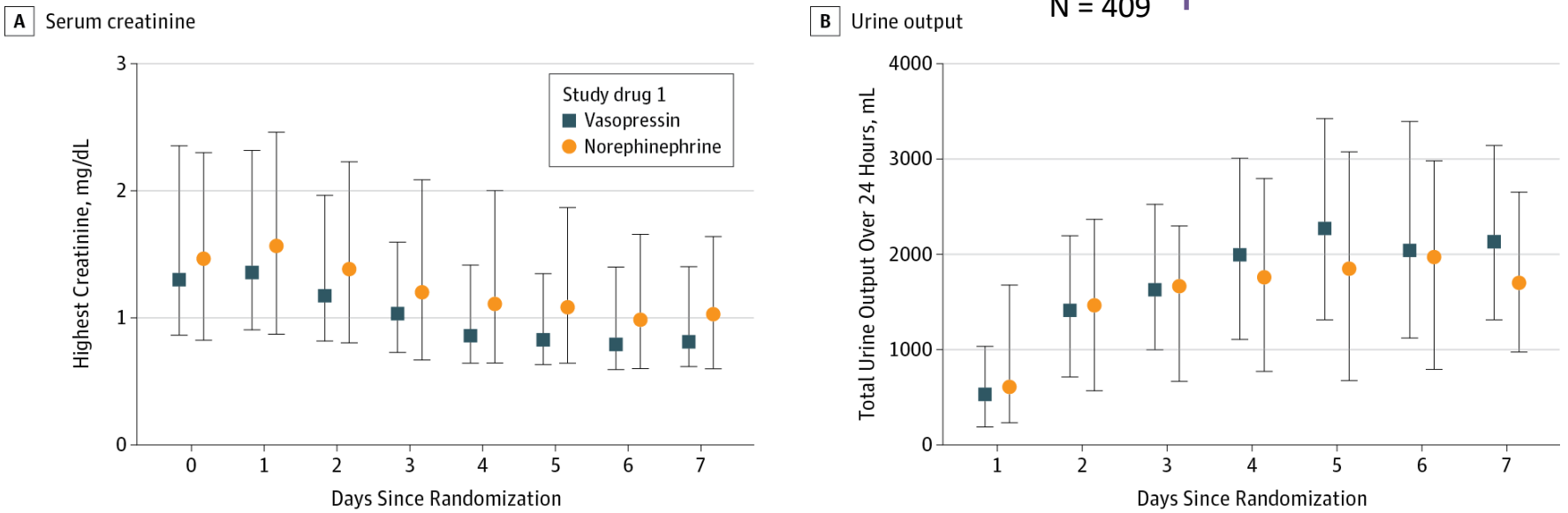
JAMA | Original Investigation

Effect of Early Vasopressin vs Norepinephrine on Kidney Failure in Patients With Septic Shock

The VANISH Randomized Clinical Trial

N = 409

Septic shock requiring vasopressors
Randomization: **Vasopressin (0.01 to 0.06 U/min)** vs norepinephrine



- No significant difference in the distribution of kidney failure–free days between vasopressin and norepinephrine groups ($p = 0.88$)
- Decreased need for RRT: 25.4% in the vasopressin arm and 35.3% in the norepinephrine group (OR 0.40 [0.20-0.73])

Gordon *et al.*, JAMA 2016

Vasopressin in septic shock

SYSTEMATIC REVIEW

Vasopressin in septic shock: an individual patient data meta-analysis of randomised controlled trials

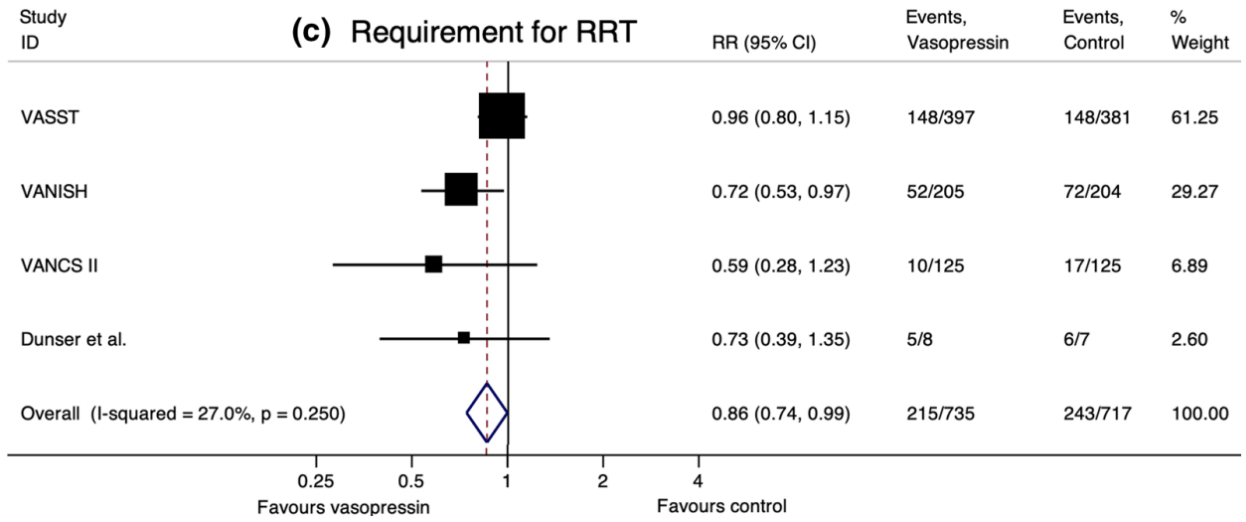
Check for updates

4 RCTs
1453 patients

- VASST
- VANISH
- VANCS II
- Dunser *et al.*

- No effect of vasopressin on 28-day mortality - RR [0.86-1.12] or serious adverse events - RR 1.02 [0.82-1.26]

- Vasopressin reduced the requirement for renal replacement therapy - RR 0.86 [0.74-0.99]



Nagendran *et al.*, Intensive Care Med 2019

VANCS Trial

Vasopressin *versus* Norepinephrine in Patients with Vasoplegic Shock after Cardiac Surgery

The VANCS Randomized Controlled Trial

N = 330

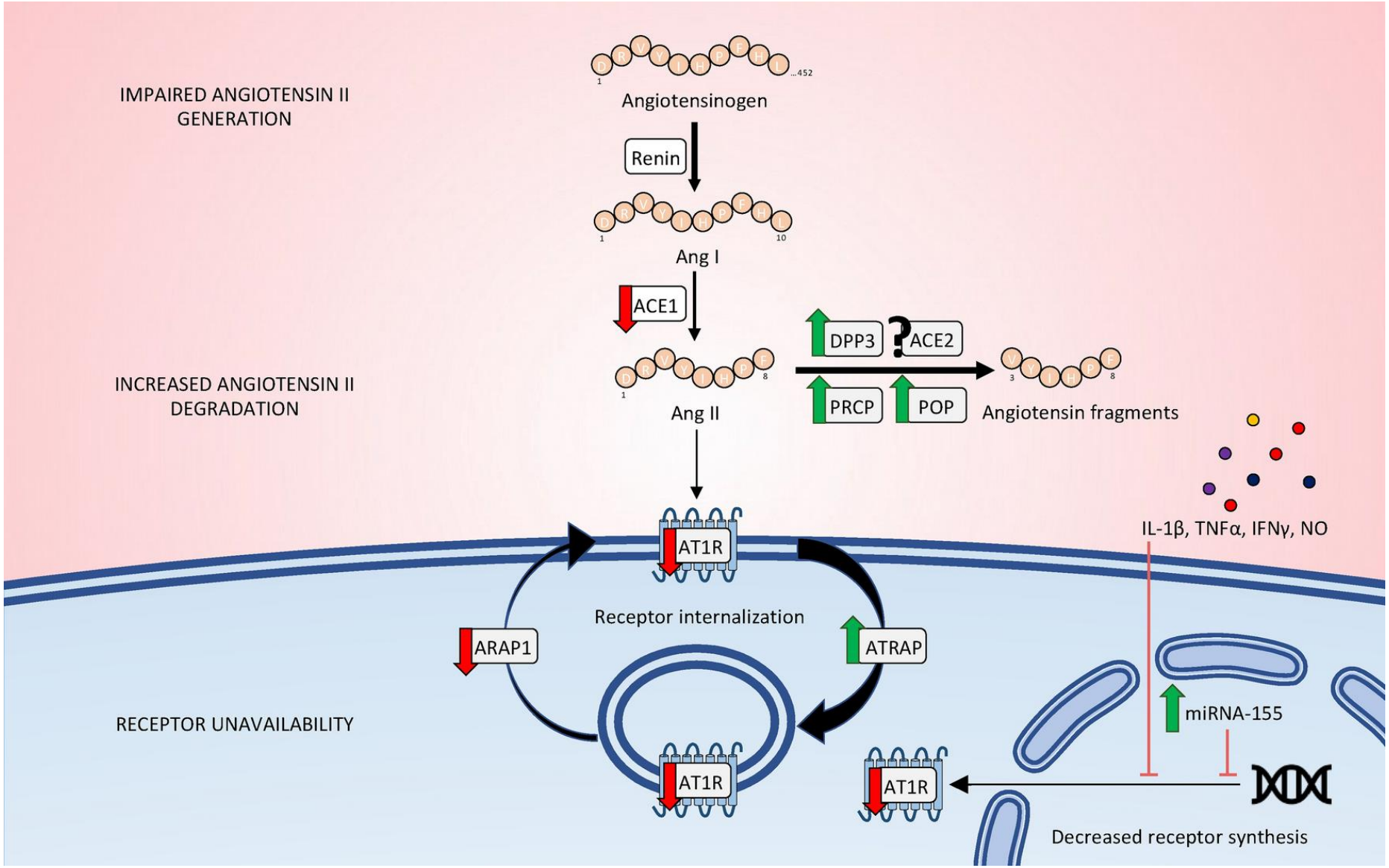
Vasodilatory shock after cardiac surgery requiring vasopressors
Randomization: **Vasopressin (0.01 to 0.06 U/min**) vs norepinephrine

Table 2. Primary and Secondary Outcomes in the Two Groups

Variable	Norepinephrine (n = 151)	Vasopressin (n = 149)	Unadjusted Odds Ratio or Hazard Ratio or Between-group Difference (95% CI)	*P* Value	Adjusted* Odds Ratio or Hazard Ratio or Between-group Difference (95%CI)	*P* Value
Primary outcome, n (%)	74 (49.0)	48 (32.2)	0.55 (0.38 to 0.80)	0.0014	0.52 (0.36 to 0.75)	0.0005
30-d mortality	24 (15.9)	23 (15.4)	0.99 (0.56 to 1.76)	0.98	1.11 (0.62 to 1.96)	0.73
MV > 48 h	13 (8.6)	8 (5.4)	0.62 (0.26 to 1.49)	0.28	0.62 (0.26 to 1.51)	0.30
Sternal wound infection	15 (9.9)	7 (4.7)	0.46 (0.19 to 1.13)	0.09	0.48 (0.19 to 1.18)	0.11
Reoperation	10 (6.6)	10 (6.7)	0.8 (0.52 to 1.23)	0.31	0.79 (0.51 to 1.22)	0.28
Stroke	4 (2.6)	4 (2·7)	1.03 (0.26 to 4.11)	0.97	1.08 (0.27 to 4.39)	0.91
Acute renal failure	54 (35.8)	15 (10.3)	0.26 (0.15 to 0.46)	< 0.0001	0.26 (0.15 to 0.46)	< 0.0001
Secondary outcomes, n (%)						
Infection	23 (15.2)	16 (10.7)	0.67 (0.34 to 1.33)	0.25	0.71 (0.35 to 1.42)	0.33
Septic shock	13 (8.6)	9 (6.0)	0.68 (0.28 to 1.65)	0.40	0.73 (0.3 to 1.81)	0.50
Atrial fibrillation	124 (82.1)	95 (63.8)	0.38 (0.22 to 0.65)	0.0004	0.37 (0.22 to 0.64)	0.0004
Ventricular arrhythmias	32 (21.2)	27 (18.1)	0.82 (0.46 to 1.46)	0.50	0.8 (0.45 to 1.43)	0.45
Length of ICU stay (d), median (IQR)	6 (4 to 9)	5 (4 to 7)	–2.42 (–4.11 to –0.73)	0.0050	–2.28 (–3.94 to –0.62)	0.0071
Length of hospital stay (d), median (IQR)	13 (10 to 20)	10 (8 to 12)	–3.76 (–6.1 to –1.42)	0.0016	–3.66 (–6.01 to –1.32)	0.0022

Hajjar *et al.*, Anesthesiology 2017

Angiotensin II deficiency in septic shock

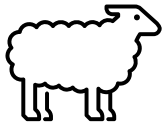


Picod *et al.*, Ann Intensive Care 2024

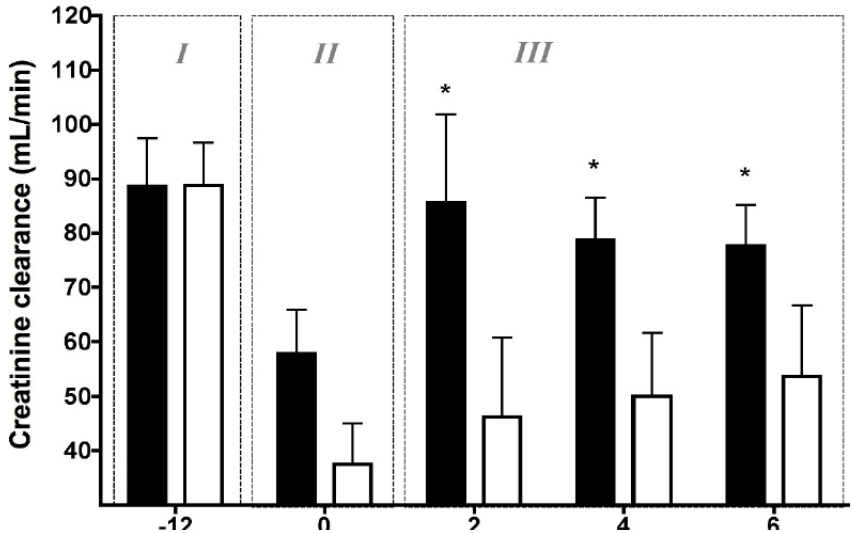
Angiotensin II in experimental sepsis-associated AKI

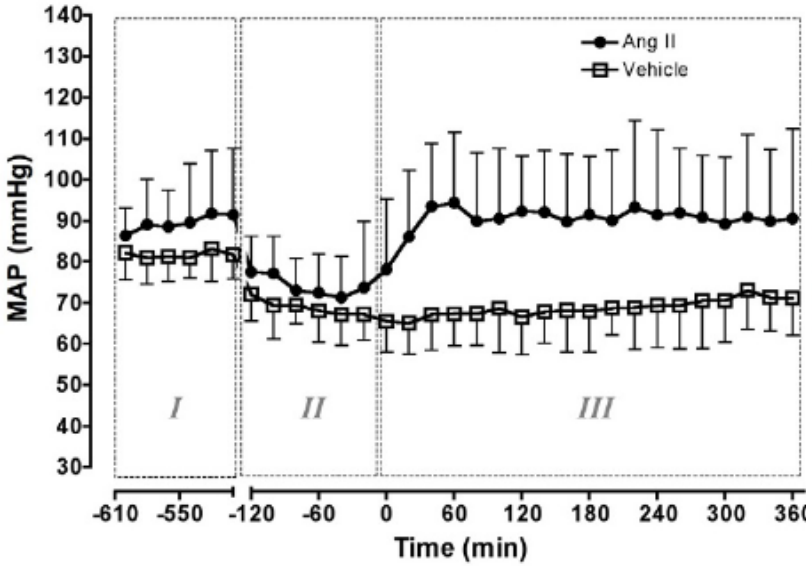
Research

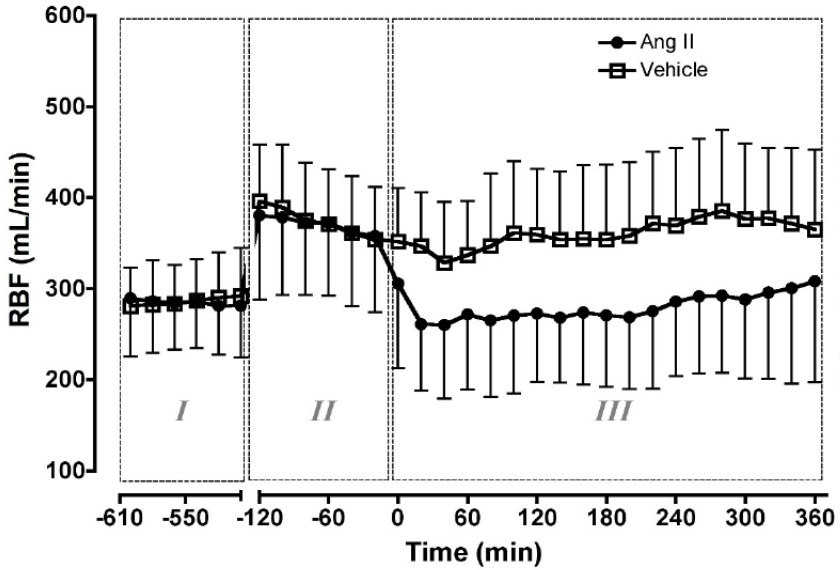
Angiotensin II in experimental hyperdynamic sepsis

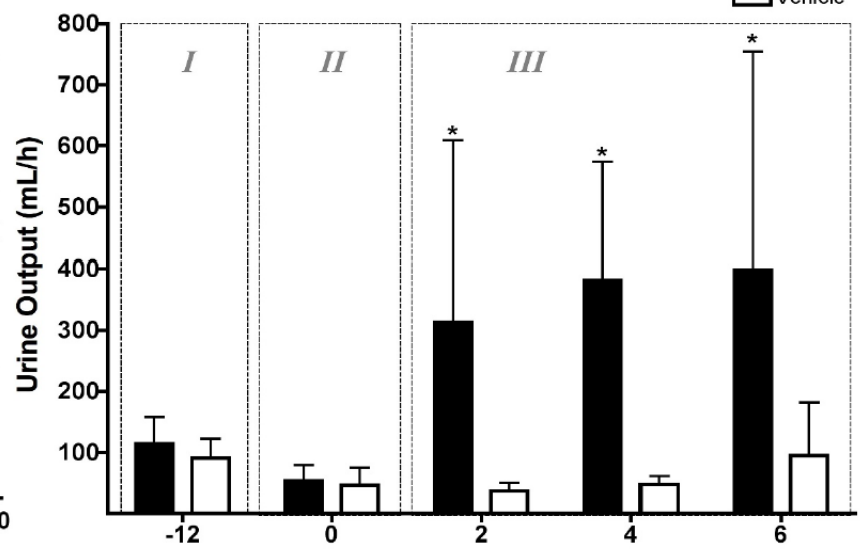


E. Coli infusion
Randomization: **Ang II** vs vehicle









Wan *et al.*, Crit Care 2009

ATHOS 3 Trial

Angiotensin II for the Treatment of Vasodilatory Shock

N = 220

Vasodilatory shock with ≥ 0.2µg/kg/min norepinephrine-equivalent
Randomization: **Ang II (20 to 200 ng/kg/min**) vs placebo

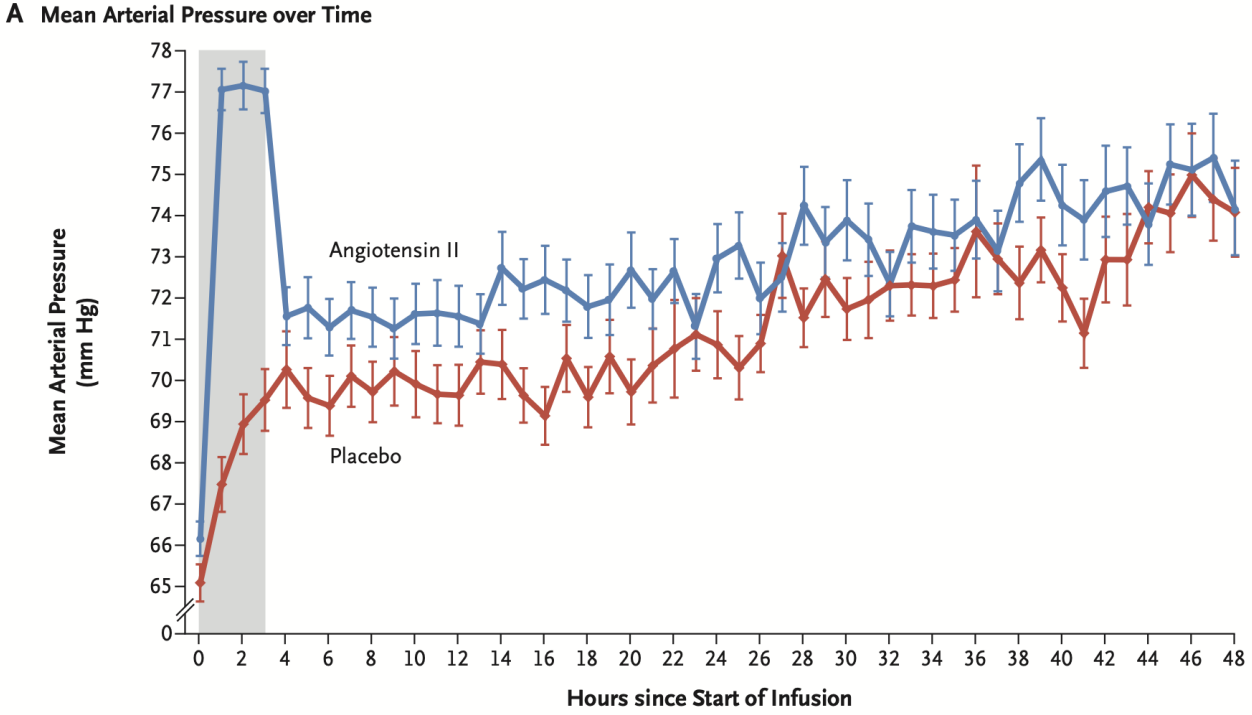


Table 2. Primary and Secondary End Points.*

End Point	Angiotensin II (N=163)	Placebo (N=158)	Odds or Hazard Ratio (95% CI)	P Value
Primary efficacy end point: MAP response at hour 3 — no. (%)†	114 (69.9)	37 (23.4)	Odds ratio, 7.95 (4.76–13.3)	<0.001
Secondary efficacy end points				
Mean change in cardiovascular SOFA score at hour 48‡	−1.75±1.77	−1.28±1.65		0.01
Mean change in total SOFA score at hour 48§	1.05±5.50	1.04±5.34		0.49
Additional end points				
Mean change in norepinephrine-equivalent dose from baseline to hour 3¶	−0.03±0.10	0.03±0.23		<0.001
All-cause mortality at day 7 — no. (%)	47 (29)	55 (35)	Hazard ratio, 0.78 (0.53–1.16)	0.22
All-cause mortality at day 28 — no. (%)	75 (46)	85 (54)	Hazard ratio, 0.78 (0.57–1.07)	0.12

Khanna *et al.*, New Eng J Med 2017

Post hoc analyses of ATHOS 3

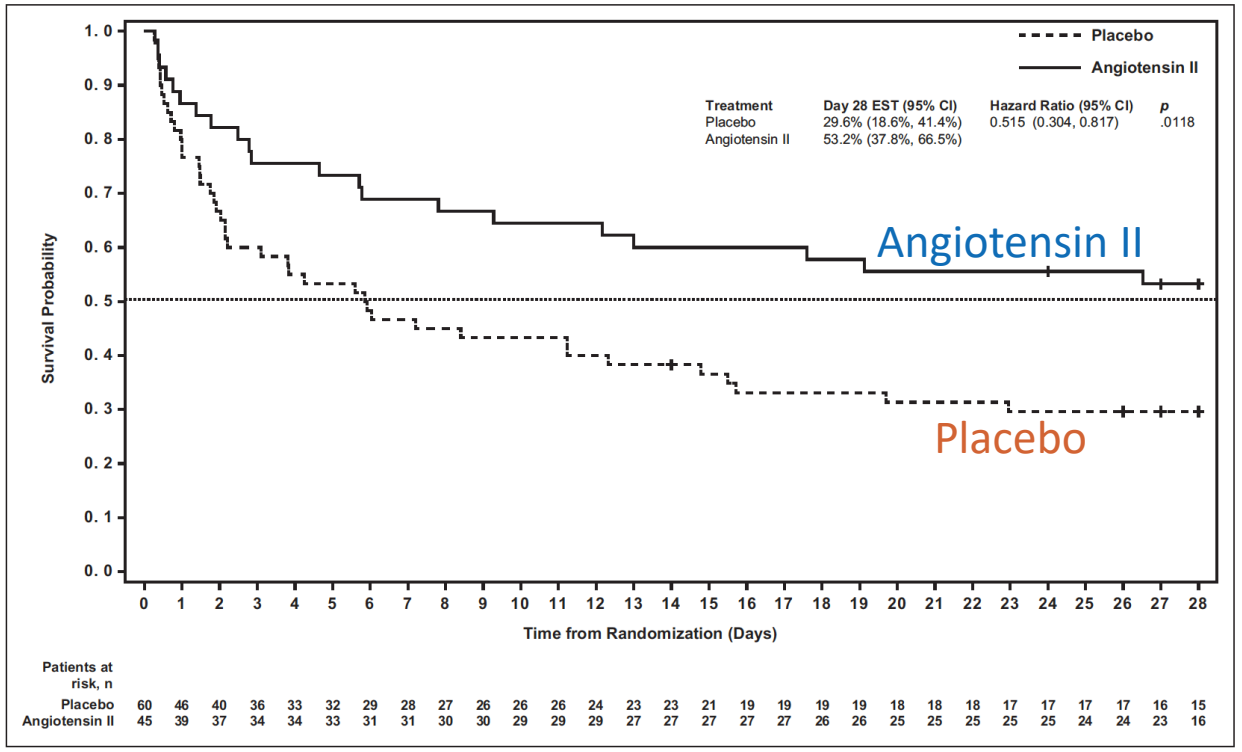
Outcomes in Patients with Vasodilatory Shock and Renal Replacement Therapy Treated with Intravenous Angiotensin II

ATHOS 3

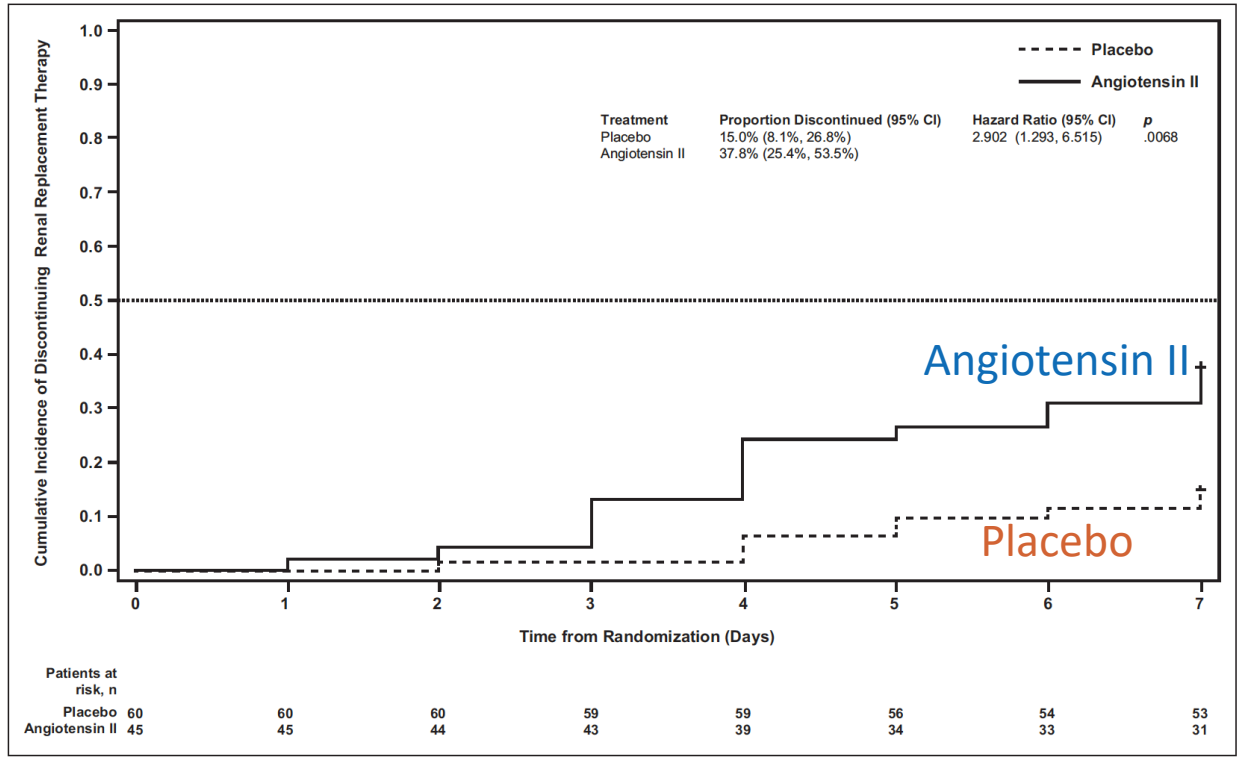
***Post hoc* analysis**

Patients with RRT at randomization

Survival



Liberation from RRT



Tumlin *et al.*, Crit Care Med 2018

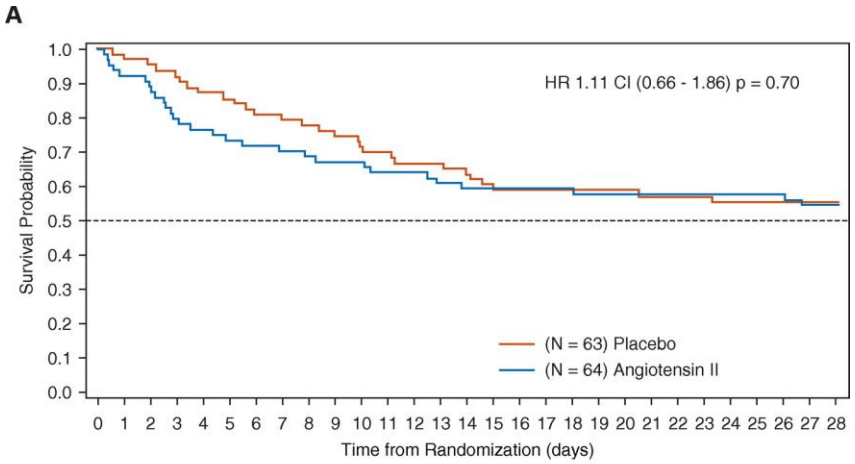
Post hoc analyses of ATHOS 3

Renin and Survival in Patients Given Angiotensin II for Catecholamine-Resistant Vasodilatory Shock
A Clinical Trial

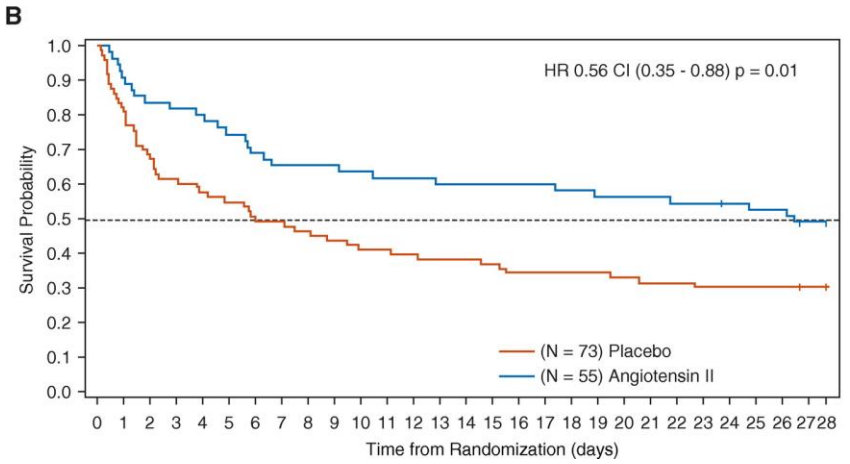
ATHOS 3
***Post hoc* analysis**

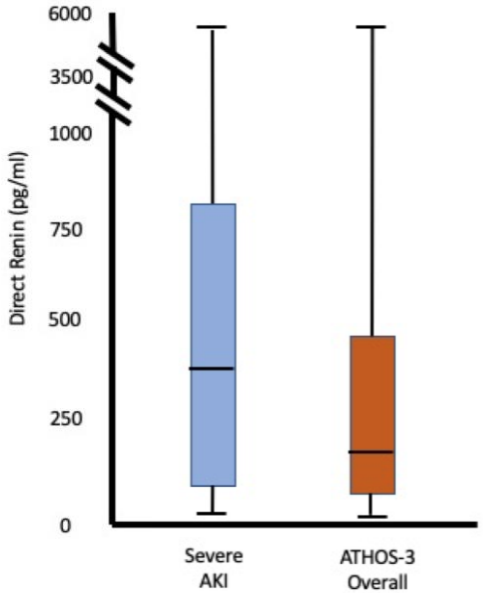
Dichotomization by serum renin (median 172.7 pg/mL)

Low Renin



High Renin





Bellomo *et al.*, Am J Respir Crit Care Med 2020

Conclusion: Which vasopressor to improve renal outcomes?

- At the early phase of vasodilatory shock-associated AKI, renal blood flow is increased due to a preferential efferent arteriole vasodilation.

- **Vasopressin** is associated with a (moderate) reduction of the need for RRT.

- **Angiotensin II** might be associated with improved outcomes in patients with severe AKI.

➢ **We still lack a precise strategy of vasopressor use in vasodilatory shock**

- Timing of each vasopressor
- Potential combinations: **Vasopressin** + **angiotensin II?**

Long term (renal) outcomes?