OPTIMAL VASOPRESSOR USE IN CARDIOGENIC SHOCK

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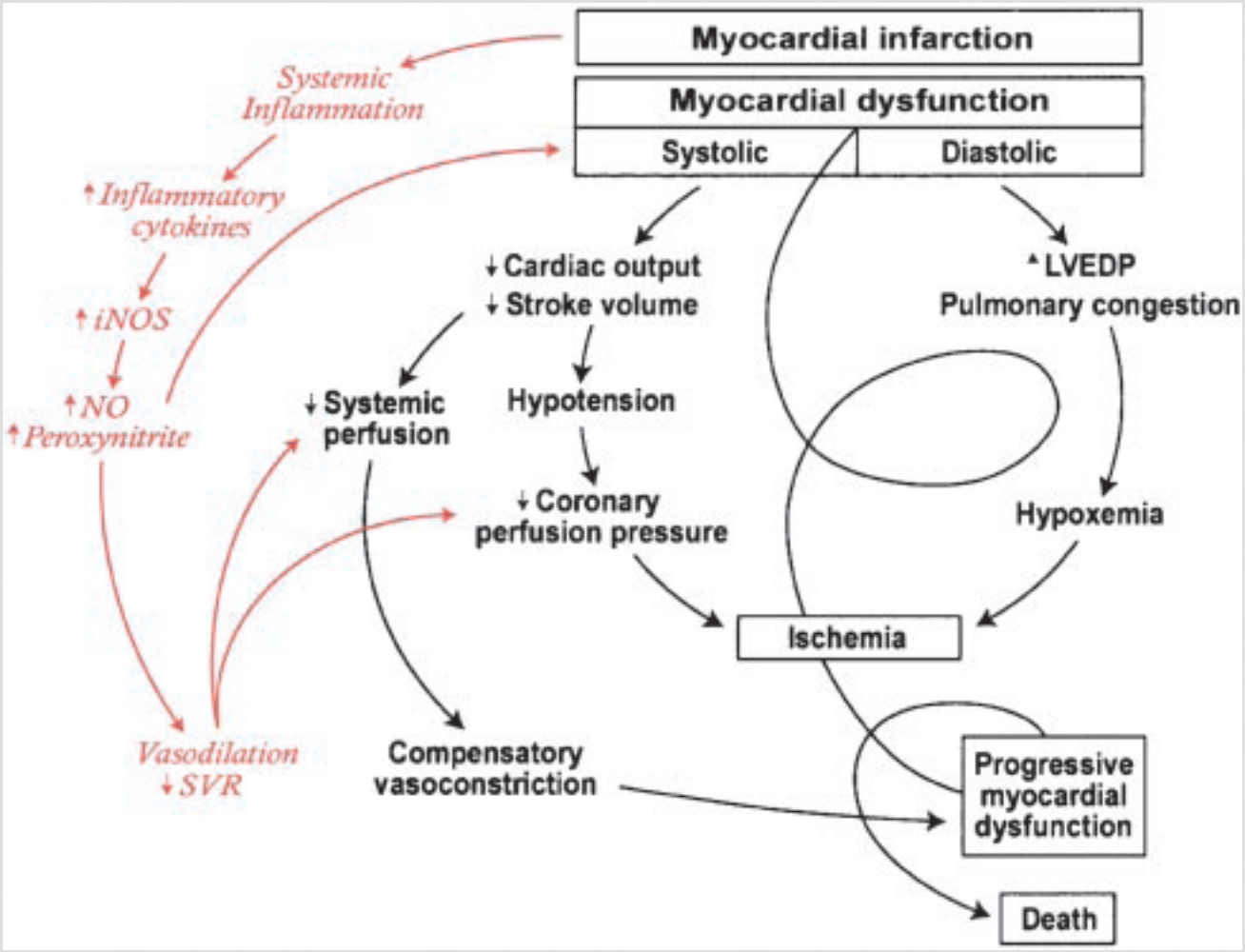
CARDIOGENIC SHOCK

- Low cardiac output
  - Decrease in left/right ventricular function
  - Increase in preload (liver failure)
- Low arterial pressure
  - Decrease in vascular responsiveness to vasopressor
  - Decrease in organ perfusion pressure
- Myocardial ischemia
  - Low coronary perfusion pressure
- Compensatory tachycardia

Cardiogenic Shock Complicating Acute Myocardial Infarction

Expanding the Paradigm

Judith S. Hochman, MD



POTENTIAL PROBLEMS WITH VASOPRESSOR

- Excessive increase in afterload
  - Further decrease in flow
  - Excessive increase in peripheral resistances
  - Further decrease in perfusion pressure at the organ level
- Risk of ischemia exacerbation
- Excessive tachycardia
  - Increase in MVO_2
  - Decrease in diastolic time
- Cellular increase in calcium
  - arrhythmias

VISIBLE/INVISIBLE EFFECTS OF CATECHOLAMINES

Pre/post load and frequency dependant parameters

- Increase in heart rate.
- Increase in arterial pressure/afterload
- Variable effects on cardiac index/SVO2
- Variable effects on pulmonary pressure

Less visible parameters

- Intrinsic cardiac function
- MVO_2
- Calcium load
- Heart structure
- Immunologic

CATECHOLAMINE INDUCED CARDIOMYOPATHY

- Pheochromocytoma, acute emotional stress, intracranial bleeding, head trauma, ischemic stoke.
- Acute medical illness including sepsis.
- Exogenous catecholergic agents
  - inhaled beta-agonist, epinephrine, amphetamines, cocaine

MECHANISMS

Stimulation of adrenoreceptor in the myocardium

- Local release of NE by sympathic nerve terminal directly innervating the myocardium +++
- Diffusion of circulating catecholamine from the coronary circulation
- Differential effects of NE and E
  - NE is inotropic and lusitropic at low and high concentrations
  - E increases inotropism at low concentration and decreases it at high concentration
  - Explained by a different action on beta-2 receptor
    - Both Gs and Gi Pathways are stimulated by E and only Gs by NE

NOT ONLY ADRENORECEPTOR BINDING

- Catecholamine induced deleterious effects through oxidative mechanisms
  - Oxydation leads to aminochromes and free radical production
  - Intracellular calcium overload
  - Myocardial cell damage (contraction band necrosis)

THE QUESTIONS?

- Which vasopressor?
- Alone or in combination with inotropes?
- Mean arterial pressure level?
- Cardiac index/SVO_2 level?
- Monitoring?
- Timing and indication : vasopressor versus ECMO?

CARDIOGENIC SHOCK HEART AND VESSELS : A DIFFICULT COUPLING

The Direct Effects of Norepinephrine, Epinephrine, and Methoxamine on Myocardial Contractile Force in Man

By Leon I. Goldberg, Ph.D., M.D., Robert D. Bloodwell, M.D., Eugene Braunwald, M.D., and Andrew G. Morrow, M.D.

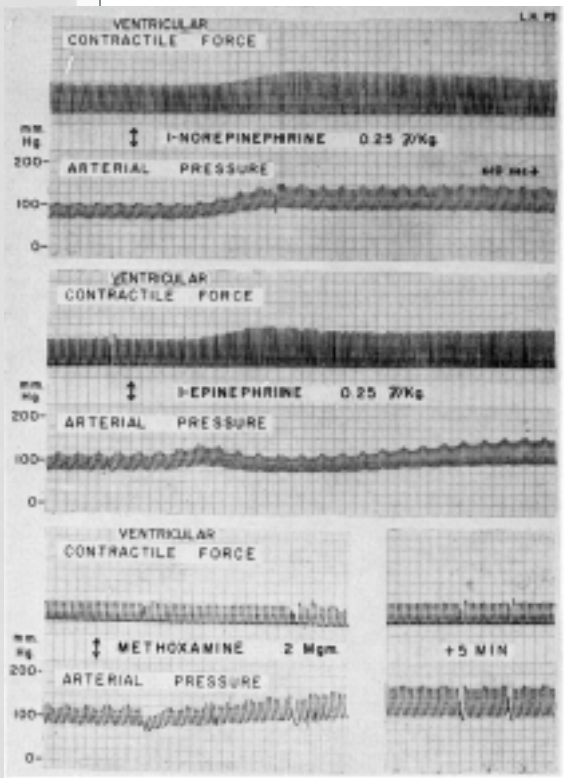


Figure 2

The effects of 0.25 μg./Kg. of norepinephrine and epinephrine and of 2 mg. (34 μg./Kg.) of methoxamine on right ventricular contractile force and arterial pressure in a 39-year-old patient with pulmonary stenosis.

- An old question…
- Aviado and Selzer and Rytand concluded that more definitive studies of these agents in man were needed in order to permit their rational clinical use (1959).

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Comparison of Dopamine and Norepinephrine in the Treatment of Shock

Daniel De Backer, M.D., Ph.D., Patrick Biston, M.D., Jacques Devriendt, M.D., Christian Madl, M.D., Didier Chochrad, M.D., Cesar Aldecoa, M.D., Alexandre Brasseur, M.D., Pierre Defrance, M.D., Philippe Gottignies, M.D., and Jean-Louis Vincent, M.D., Ph.D., for the SOAP II Investigators*

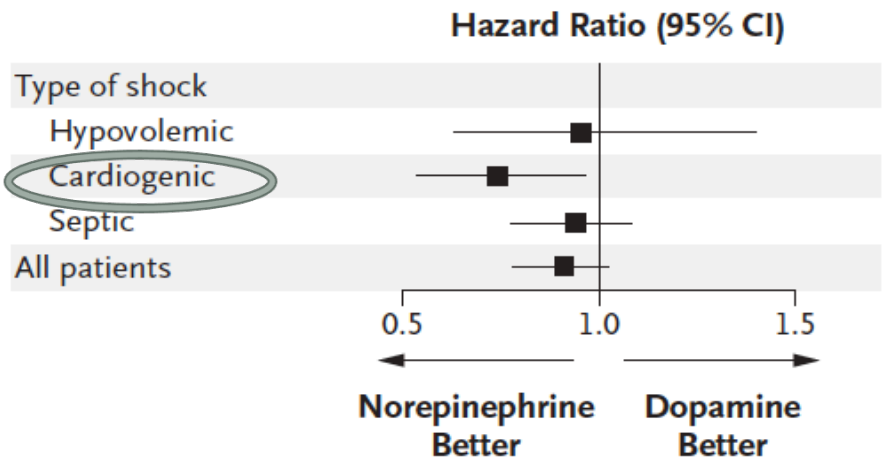


Figure 3. Forest Plot for Predefined Subgroup Analysis According to Type of Shock.

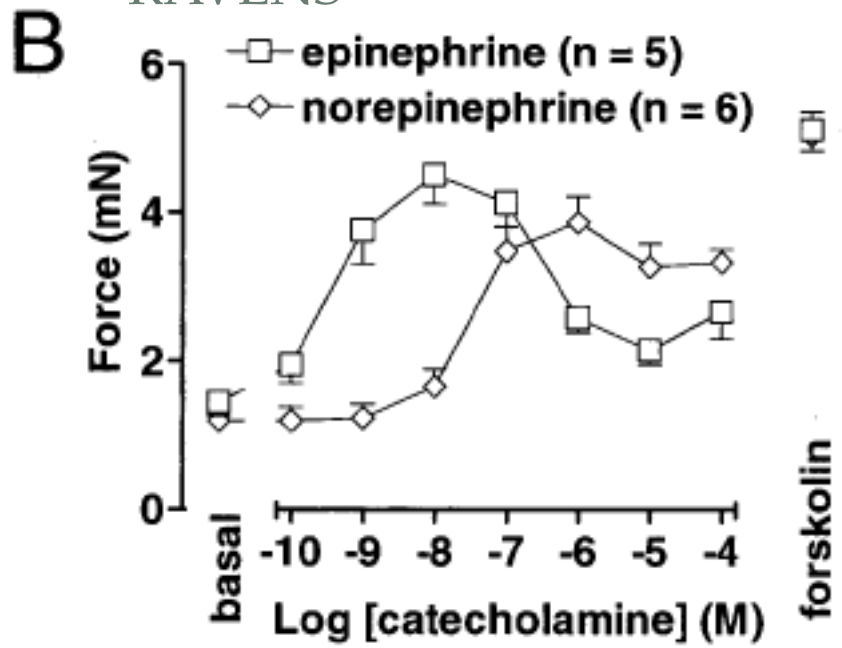
A total of 1044 patients were in septic shock (542 in the dopamine group and 502 in the norepinephrine group), 280 were in cardiogenic shock (135 in the dopamine group and 145 in the norepinephrine group), and 263 were in hypovolemic shock (138 in the dopamine group and 125 in the norepinephrine group). The P value for interaction was 0.87.

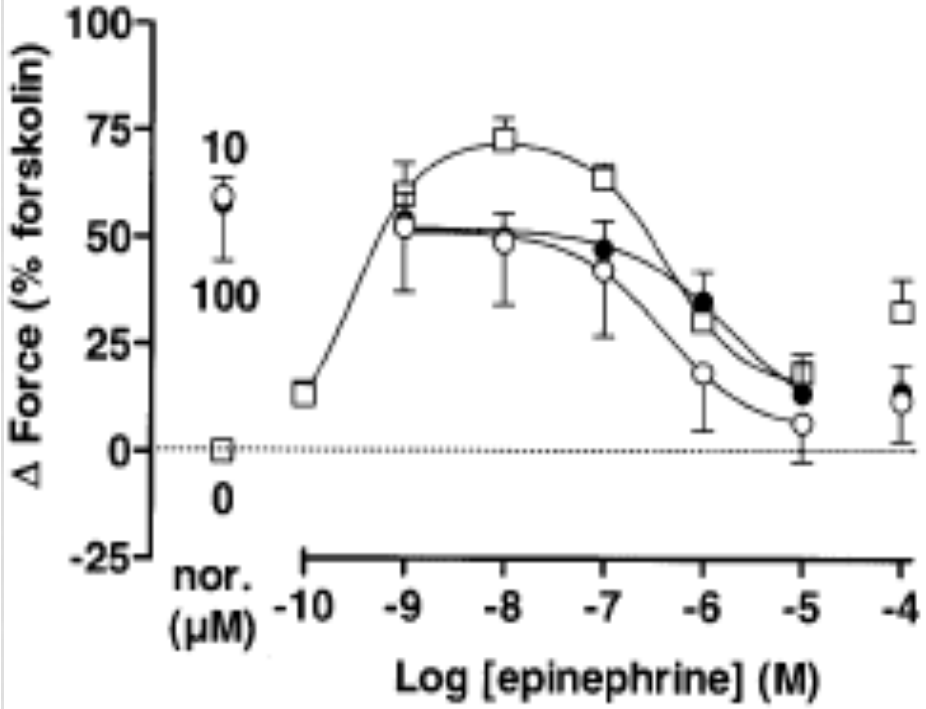
EPINEPHRINE VERSUS NOREPINEPHRINE

Epinephrine Activates Both G_s and G_i Pathways, but Norepinephrine Activates Only the G_s Pathway through Human β_2-Adrenoceptors Overexpressed in Mouse Heart

Jürgen F. Heubach, Ursula Ravens, and Alberto J. Kaumann

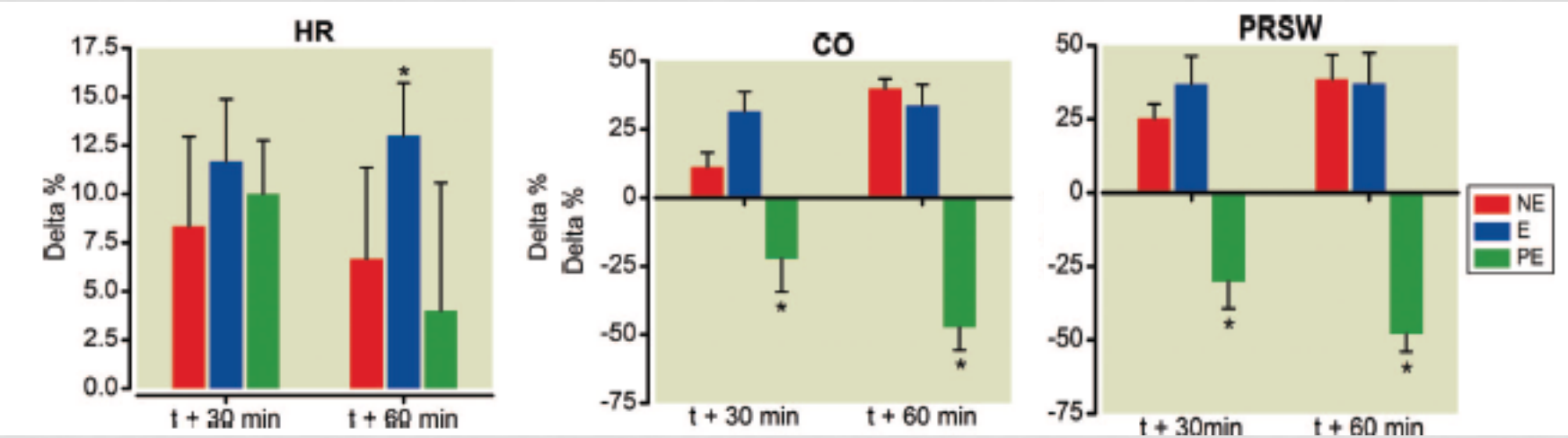
RAVENS





Comparison of Equipressor Doses of Norepinephrine, Epinephrine, and Phenylephrine on Septic Myocardial Dysfunction

Nicolas Ducrocq, M.D.,* Antoine Kimmoun, M.D.,* Anna Furmaniuk, M.Sc.,† Zerin Hekalo, M.Sc.,† Fatiha Maskali, Ph.D.,‡ Sylvain Poussier, Ph.D.,‡ Pierre-Yves Marie, M.D., Ph.D.,§ Bruno Levy, M.D., Ph.D.‖



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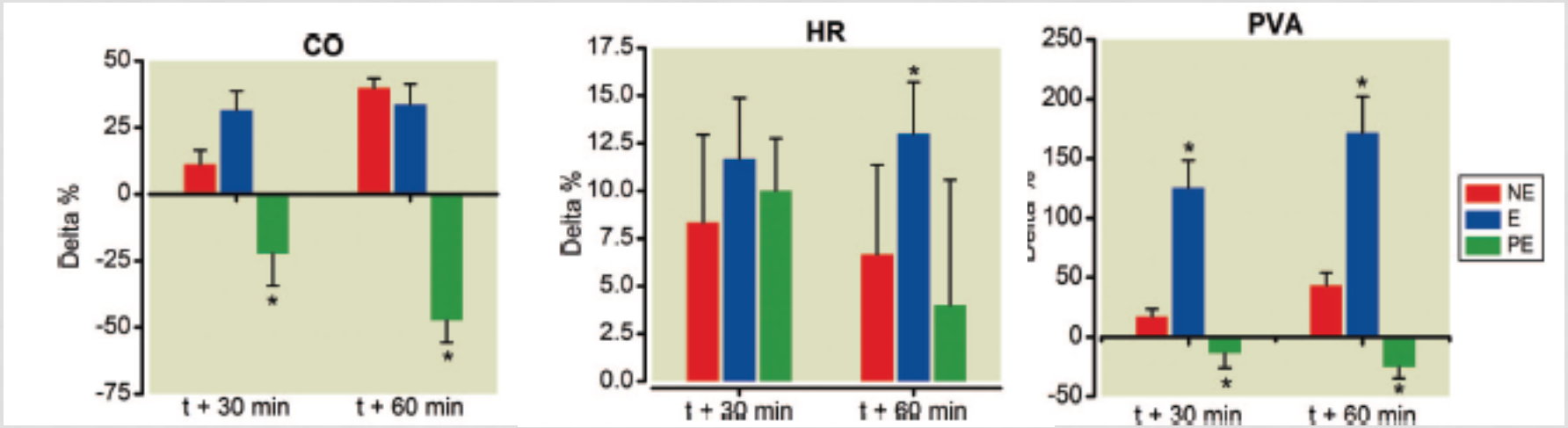


Comparison of norepinephrine-dobutamine to epinephrine for hemodynamics, lactate metabolism, and organ function variables in cardiogenic shock. A prospective, randomized pilot study*

Bruno Levy, MD, PhD; Pierre Perez, MD; Jessica Perny, MD; Carine Thivilier, MD; Alain Gerard, MD

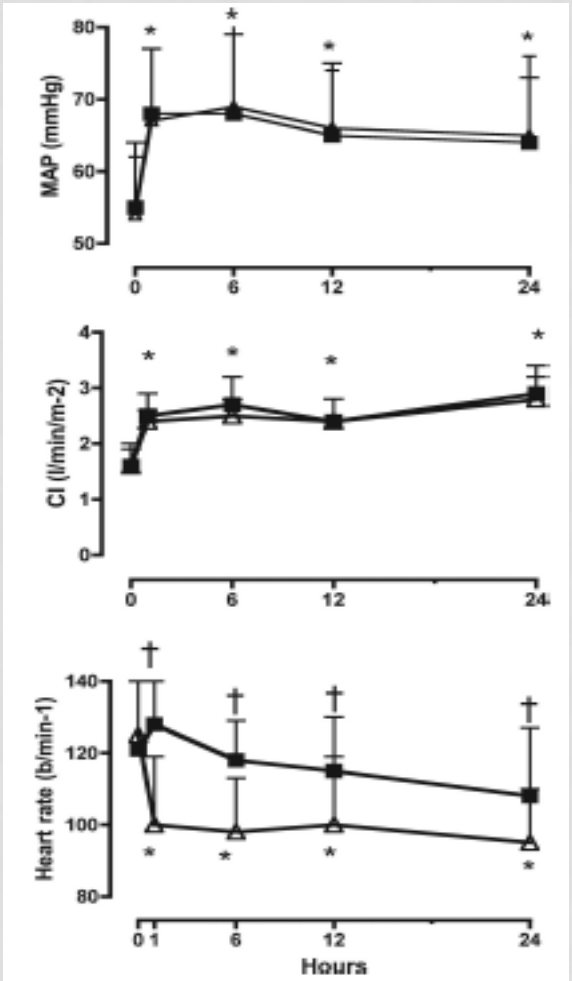
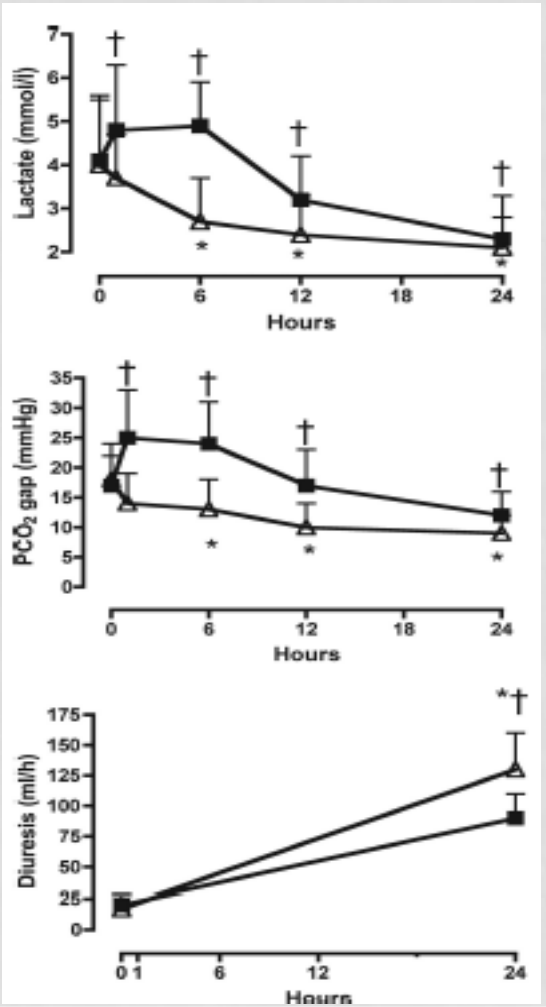


Figure 2. Evolution of mean arterial pressure



NOREPINEPHRINE IS AN INOTROPE

SHOCK, Vol. 41, No. 4, pp. 269–274, 2014

INCREASING MEAN ARTERIAL PRESSURE IN CARDIOGENIC SHOCK SECONDARY TO MYOCARDIAL INFARCTION: EFFECTS ON HEMODYNAMICS AND TISSUE OXYGENATION

Pierre Perez,* Antoine Kimmoun,*†‡ Vincent Blime,* and Bruno Levy*†‡

**CHU Nancy, Service de Réanimation Médicale Brabois, Pole Cardiovasculaire et Réanimation Médicale, Hôpital Brabois; and †INSERM, Groupe Choc, U1116, Faculté de Médecine, Vandoeuvre-les-Nancy; and ‡Université de Lorraine, Nancy, France*

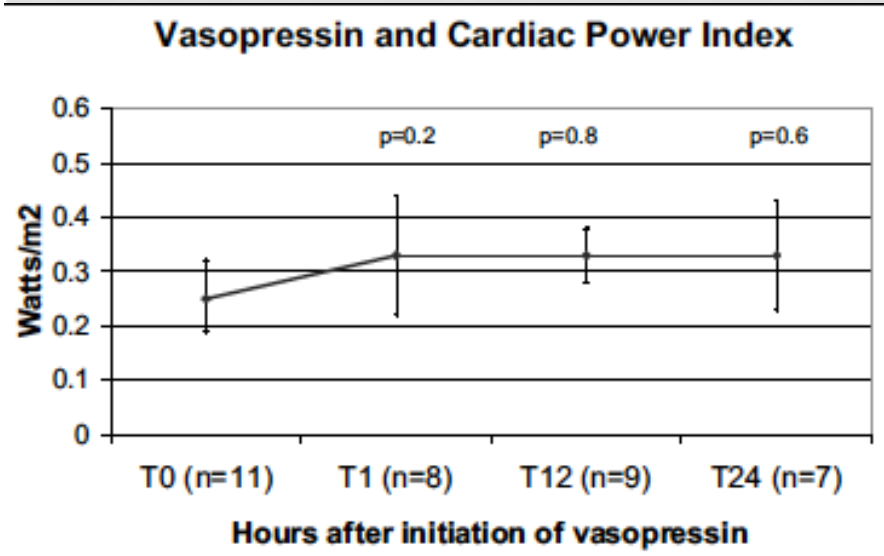
NOREPINEPHRINE AS AN INOTROPE

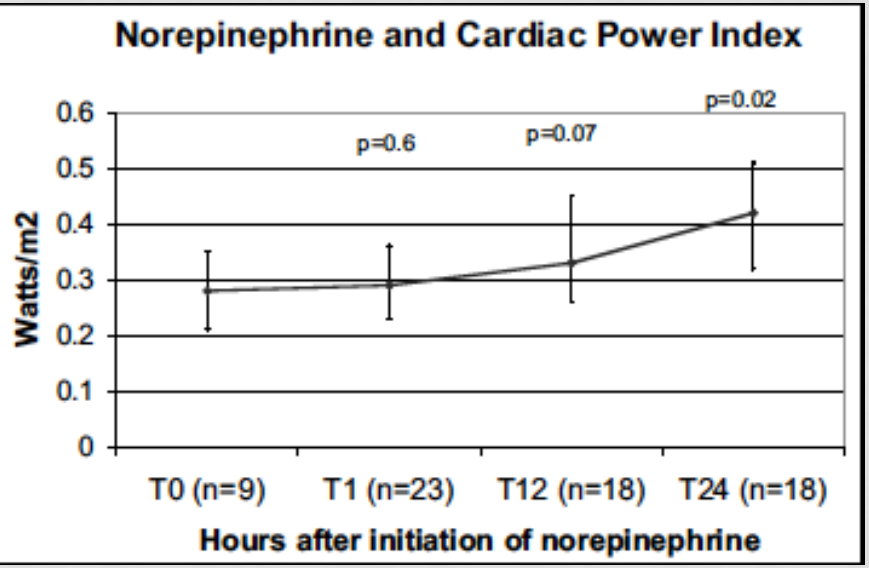
	MAP 65 mmHg	MAP 85 mmHg	p=
Heart rate (bpm)	102 +/- 8	105 +/- 7	p > 0,05
CI (l/min/m²)	2,3 +/- 0,4	2,8 +/- 0,3	p < 0,05
CPI (watt/m²)	0,38 +/- 0,03	0,58 +/- 0,04	p < 0,01
SVO_2 (%)	73 +/- 2	79 +/- 2	p < 0,05

Effect of *Vasopressin* on Hemodynamics in Patients With Refractory Cardiogenic Shock Complicating Acute Myocardial Infarction

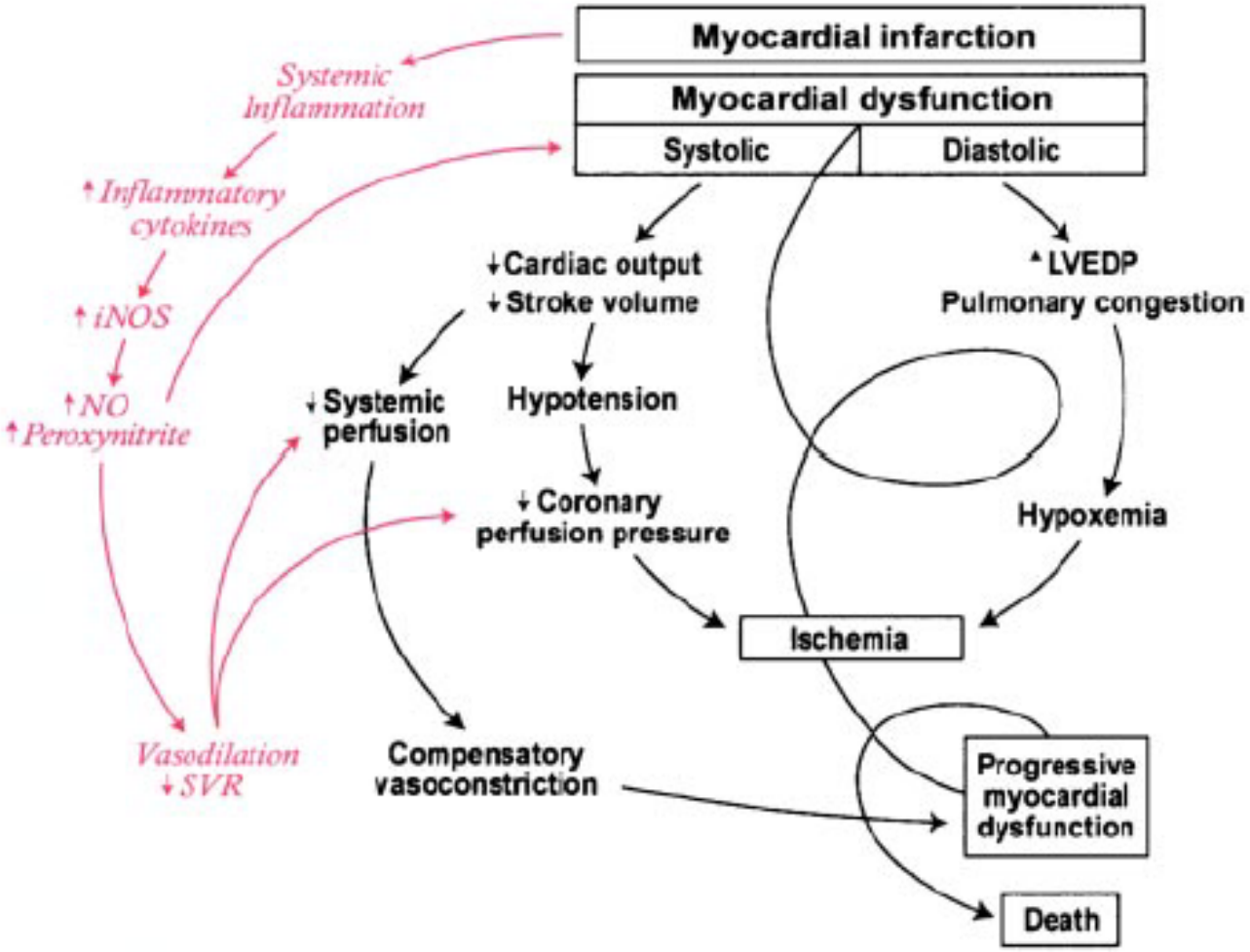
Sanjit Jolly, MD, Gary Newton, MD, Eric Horlick, MD, Peter H. Seidelin, MB, Heather J. Ross, MD, Mansoor Husain, MD, and Vladimir Dzavik, MD*

(Am J Cardiol 2005;96:1617–1620)





THE NEW PARADIGM



Effect of Tilarginine Acetate in Patients With Acute Myocardial Infarction and Cardiogenic Shock

The TRIUMPH Randomized Controlled Trial

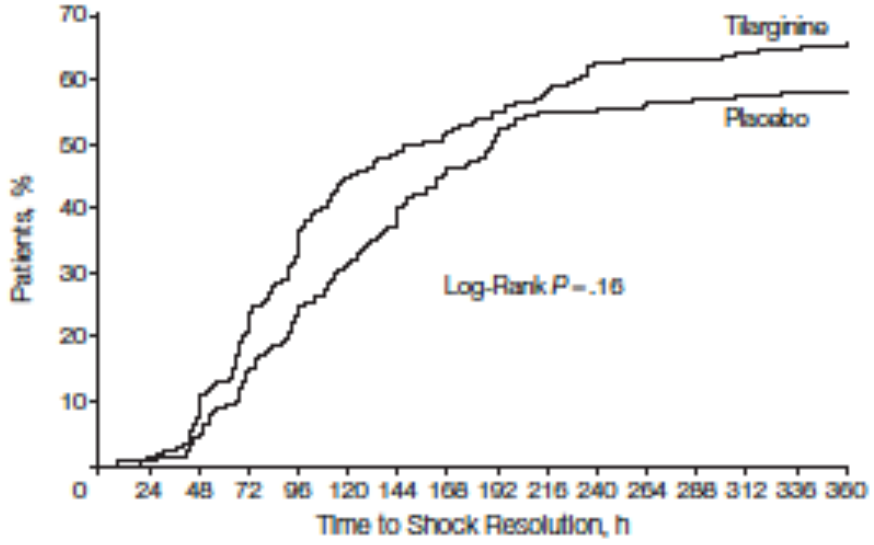
Table 5. Hemodynamic Outcomes

Outcome Overall and by Age*	Tilarginine	Placebo	*P* Value
Two-hour change in SBP, median (IQR), mm Hg (n = 286)†	12.0 (2.5 to 23.0)	7.0 (–2.0 to 17.0)	.001
<75 y (n = 207)	11.0 (2.0 to 22.0)	7.0 (–2.0 to 17.0)	
≥75 y (n = 77)	20.0 (8.0 to 29.0)	3.5 (–3.0 to 15.5)	
Two-hour change in DBP, median (IQR), mm Hg (n = 285)†	5.0 (–4.0 to 11.0)	1.0 (–5.0 to 8.0)	.16
<75 y (n = 206)	5.0 (–3.0 to 10.0)	2.0 (–4.0 to 9.0)	
≥75 y (n = 77)	5.0 (–3.0 to 13.0)	0.0 (–8.0 to 6.5)	
Resolution of shock, No./total (%)	133/201 (66)	110/180 (61)	.31
<75 y	108/146 (74)	89/131 (68)	
≥75 y	24/54 (44)	20/47 (43)	
Duration of shock, median (IQR), h (n = 378)	156 (78 to 759)	190 (100 to 759)	.16
<75 y (n = 275)	123 (73 to 759)	176 (95 to 759)	
≥75 y (n = 100)	759 (96 to 759)	759 (111 to 759)	
Seven-day change in creatinine, mg/dL (n = 107)	0.01 (–0.20 to 0.19)	–0.15 (–0.32 to 0.16)	.16

Effect of Tilarginine Acetate in Patients With Acute Myocardial Infarction and Cardiogenic Shock

The TRIUMPH Randomized Controlled Trial

Figure 2. Kaplan-Meier Curve of Duration of Cardiogenic Shock



No. at Risk						
Tilarginine	201	158	103	84	74	70
Placebo	177	151	108	80	76	74

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

Recommendations	Class[a]	Level[b]	Ref[c]
Patients with hypotension, hypoperfusion or shock			
A vasopressor (e.g. dopamine or norepinephrine) may be considered in patients who have cardiogenic shock, despite treatment with an inotrope, to increase blood pressure and vital organ perfusion. The ECG should be monitored as these agents can cause arrhythmias and/or myocardial ischaemia. Intra-arterial blood pressure measurement should be considered.	IIb	C	–

Cardiogenic Shock Due to Myocardial Infarction: Diagnosis, Monitoring and Treatment

A German-Austrian S3 Guideline

Karl Werdan, Martin Ruß, Michael Buerke, Georg Delle-Karth, Alexander Geppert, Friedrich A. Schöndube

BOX 3

What is new in comparison to the established guidelines?

- Pressure monitoring is not enough for hemodynamic treatment after revascularisation! Additional cardiac output monitoring is mandatory.
- Dobutamine is the inotropic agent of choice; norepinephrine is the vasopressor of choice; levosimendan can be used in addition in patients with catecholamine-refractory shock.
- Even in resuscitated patients, earliest possible PCI should be considered on a case by case basis.
- Intra-aortic balloon counterpulsation (IABP) has been "down-graded."
- If ventilation is needed, it should be invasive and lung-protective.

Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation

The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology:

Treatment of shock (Killip class IV)		
O_2	I	C
Mechanical ventilatory support according to blood gasses	I	C
Haemodynamic assessment with balloon floating catheter	IIb	C
Inotropic agents: dopamine	IIb	B
and dobutamine	IIa	C
Intra-aortic balloon pump	I	C
LV assist devices	IIa	C
Early revascularization	I	B

THE FRENCH RECOMMANDATIONS

- Norepinephrine is the vasopressor of choice
  - Epinephrine is a therapeutic alternative but is associated with tachycardia, hyperlactaemia and arythmia.
- Continuous monitoring of cardiac output and SVO_2 are mandatory
  - Use of Swan-Ganz catheter or transpulmonary thermodilution
- MAP between 65-70 mmHG (more might be discussed)
- NE could be associated to dobutamine
- Always discussed an increase in vasopressor versus an increase in pure inotrope
- Always discuss to switch for ECMO