AER
ACTUALITÉS EN RÉANIMATION

21 - 22 NOVEMBRE 2024

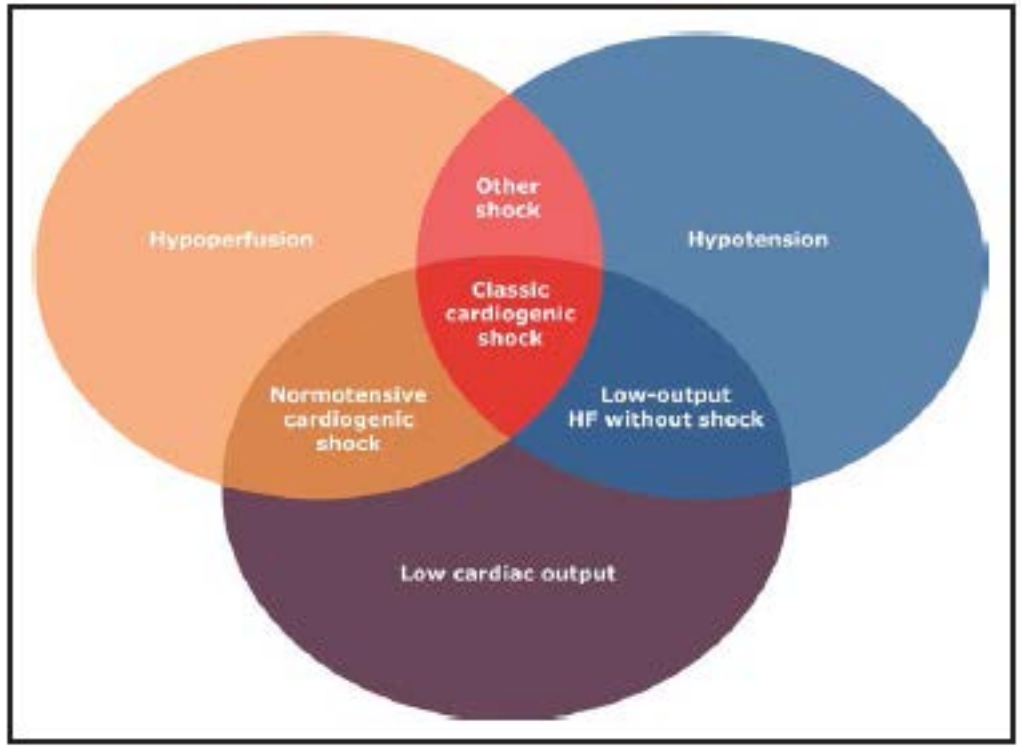
CITÉ CENTRE DE CONGRÈS DE LYON
50, quai Charles de Gaulle
69006 Lyon

Choc cardiogénique vasopresseurs et/ou inotropes

Pr Bruno Levy
Service de Réanimation et Médecine Intensive Brabois
CHRU de Nancy
blevy5463@gmail.com

Définitions

- Pression artérielle systolique < 90 mmHg pendant plus de 30 min
- Vasopresseur pour pour obtenir une pression artérielle systolique ≥ 90 mmHg
- Index cardiaque <1,8 l/min/m^2 ou l'utilisation de vasopresseur/inotropes
- Une augmentation des pressions de remplissage ventriculaire gauche
- Altération de la perfusion tissulaire:
  - Trouble de conscience
  - Oligurie
  - Extrémités froides
  - Augmentation du lactate



Contents lists available at ScienceDirect

Journal of the Society for Cardiovascular Angiography & Interventions

journal homepage: www.jscai.org

Standards and Guidelines

SCAI SHOCK Stage Classification Expert Consensus Update: A Review and Incorporation of Validation Studies

This statement was endorsed by the American College of Cardiology (ACC), American College of Emergency Physicians (ACEP), American Heart Association (AHA), European Society of Cardiology (ESC) Association for Acute Cardiovascular Care (ACVC), International Society for Heart and Lung Transplantation (ISHLT), Society of Critical Care Medicine (SCCM), and Society of Thoracic Surgeons (STS) in December 2021.

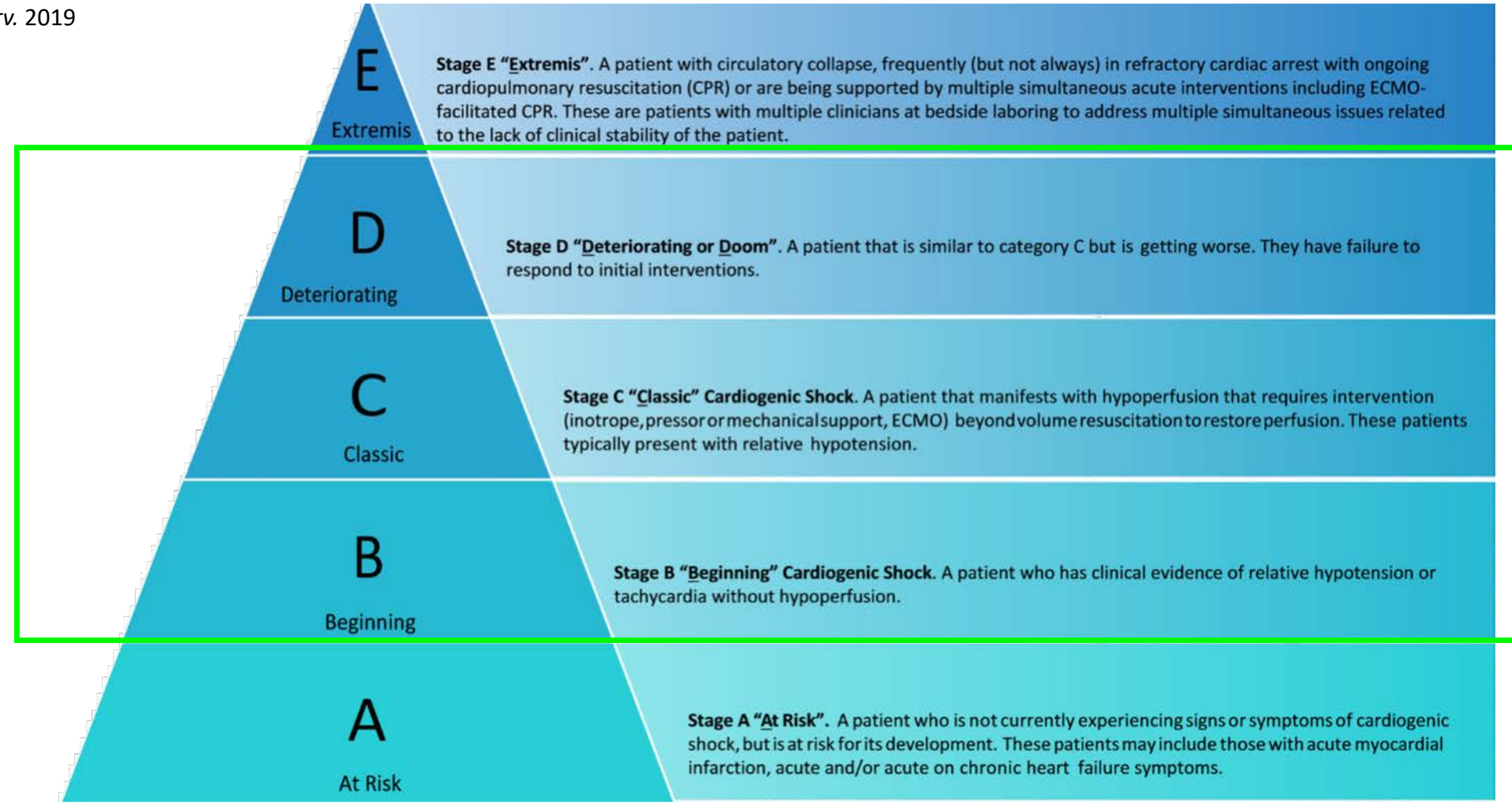
Srihari S. Naidu, MD, FSCAI [a,*], David A. Baran, MD, FSCAI [b], Jacob C. Jentzer, MD [c], Steven M. Hollenberg, MD [d,1], Sean van Diepen, MD, MSc [e,2], Mir B. Basir, DO, FSCAI [f], Cindy L. Grines, MD, MSCAI [g], Deborah B. Diercks, MD, MSc, FACEP [h,3], Shelley Hall, MD [i], Navin K. Kapur, MD, FSCAI [j], William Kent, MD, MSc [k,4], Sunil V. Rao, MD, FSCAI [l,5], Marc D. Samsky, MD [l,5], Holger Thiele, MD, FESC [m,6], Alexander G. Truesdell, MD, FSCAI [n,7], Timothy D. Henry, MD, MSCAI [o]

Definition du choc cardiogénique

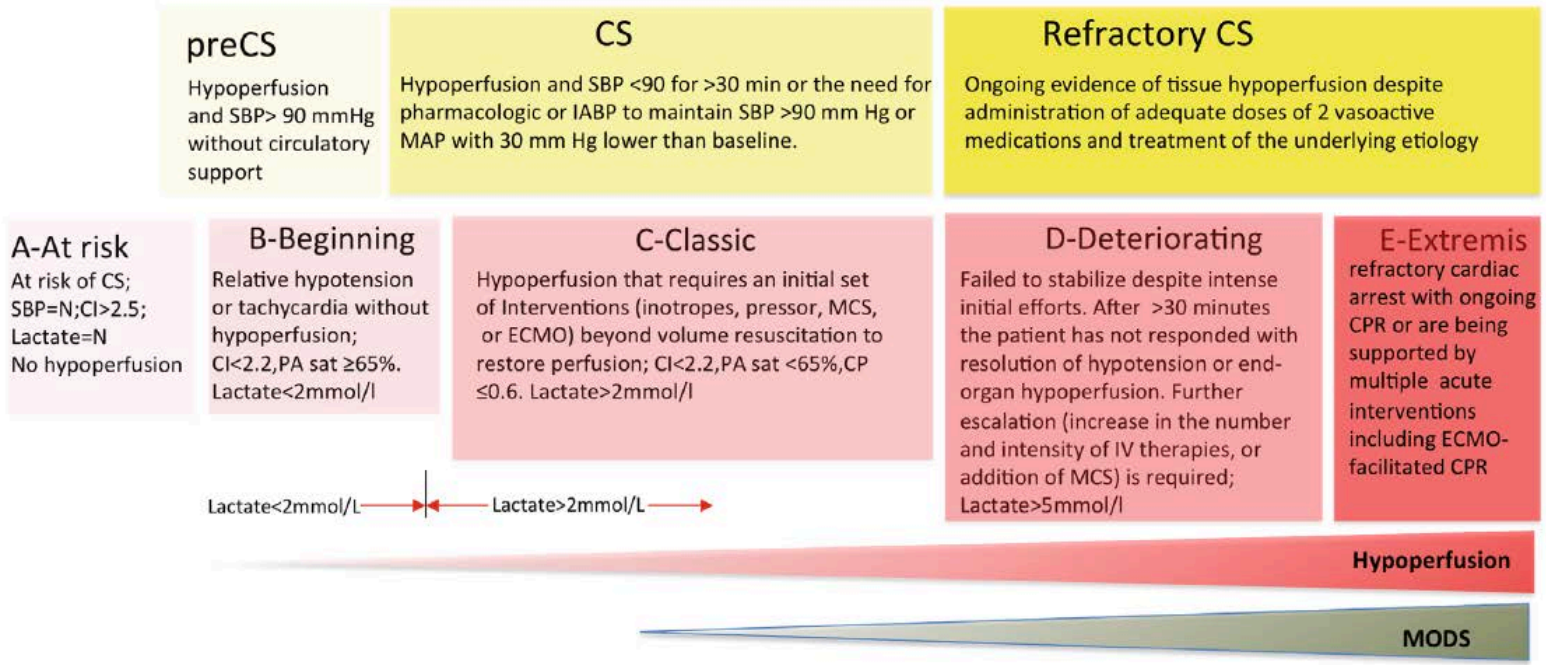
Baran D.A.et al. *Catheter Cardiovasc Interv.* 2019

Un syndrome, plusieurs définitions

Baran D.A.et al. *Catheter Cardiovasc Interv.* 2019

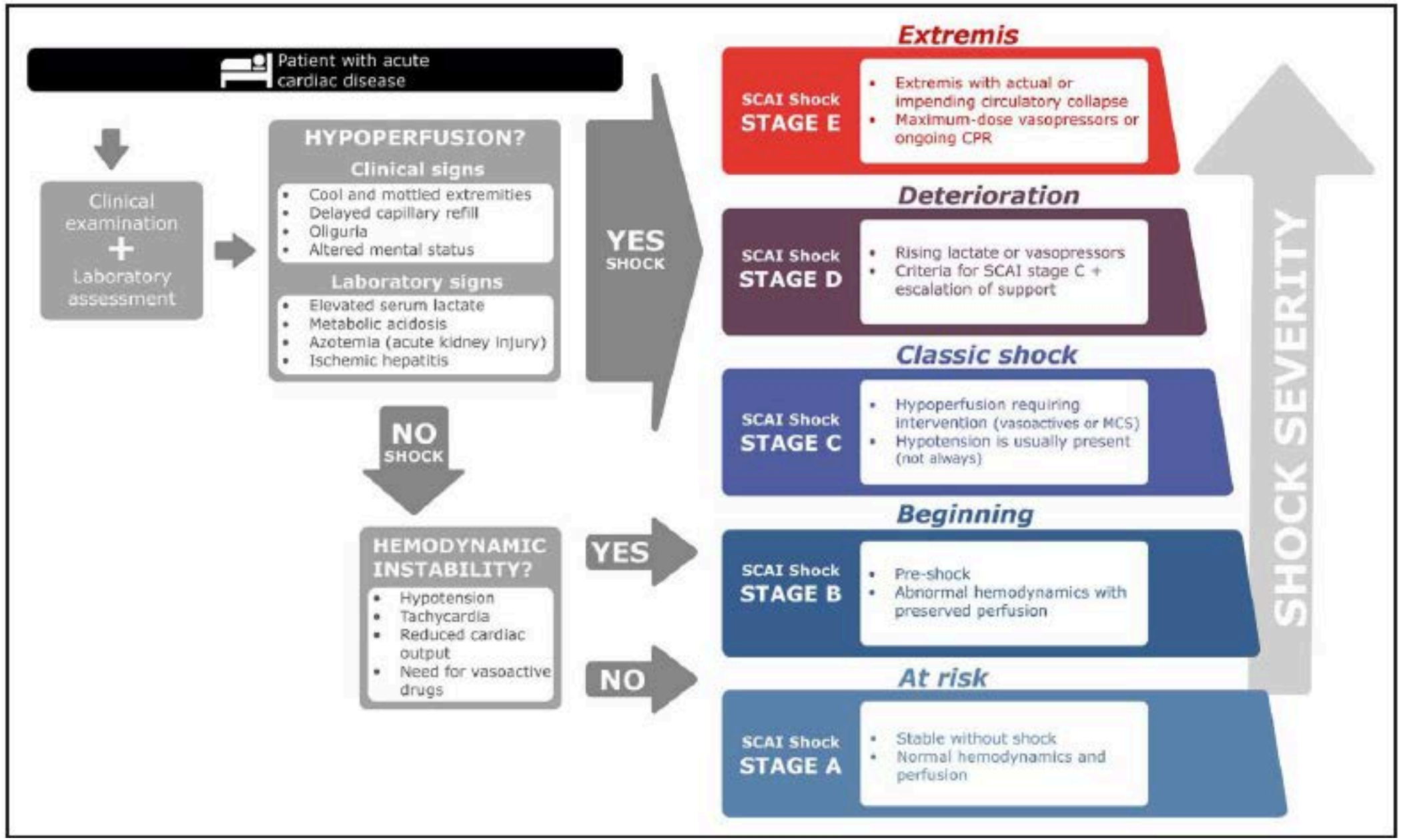


A Clinical classifications of CS



B Hemodynamic classification of CS

SVR ↓;PCWP N ↓;CVP N ↓ **"warm-dry"**	SVR ↓;PCWP ↑;CVP ↑ **"warm-wet"**
SVR ↑;PCWP N ↓;CVP N ↓ **"cold-dry"**	SVR ↑;PCWP ↑;CVP ↑ **"cold-wet"**



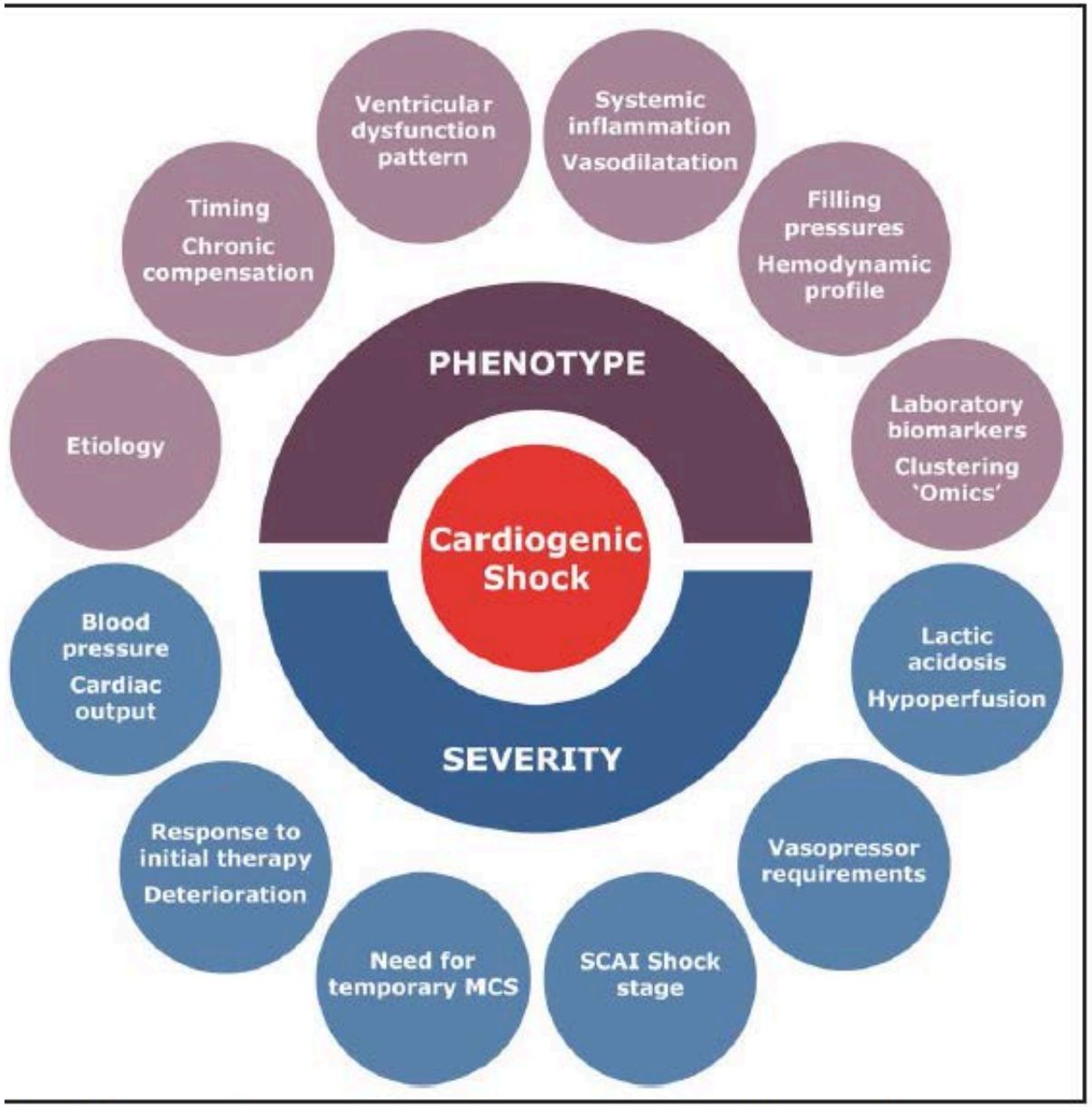
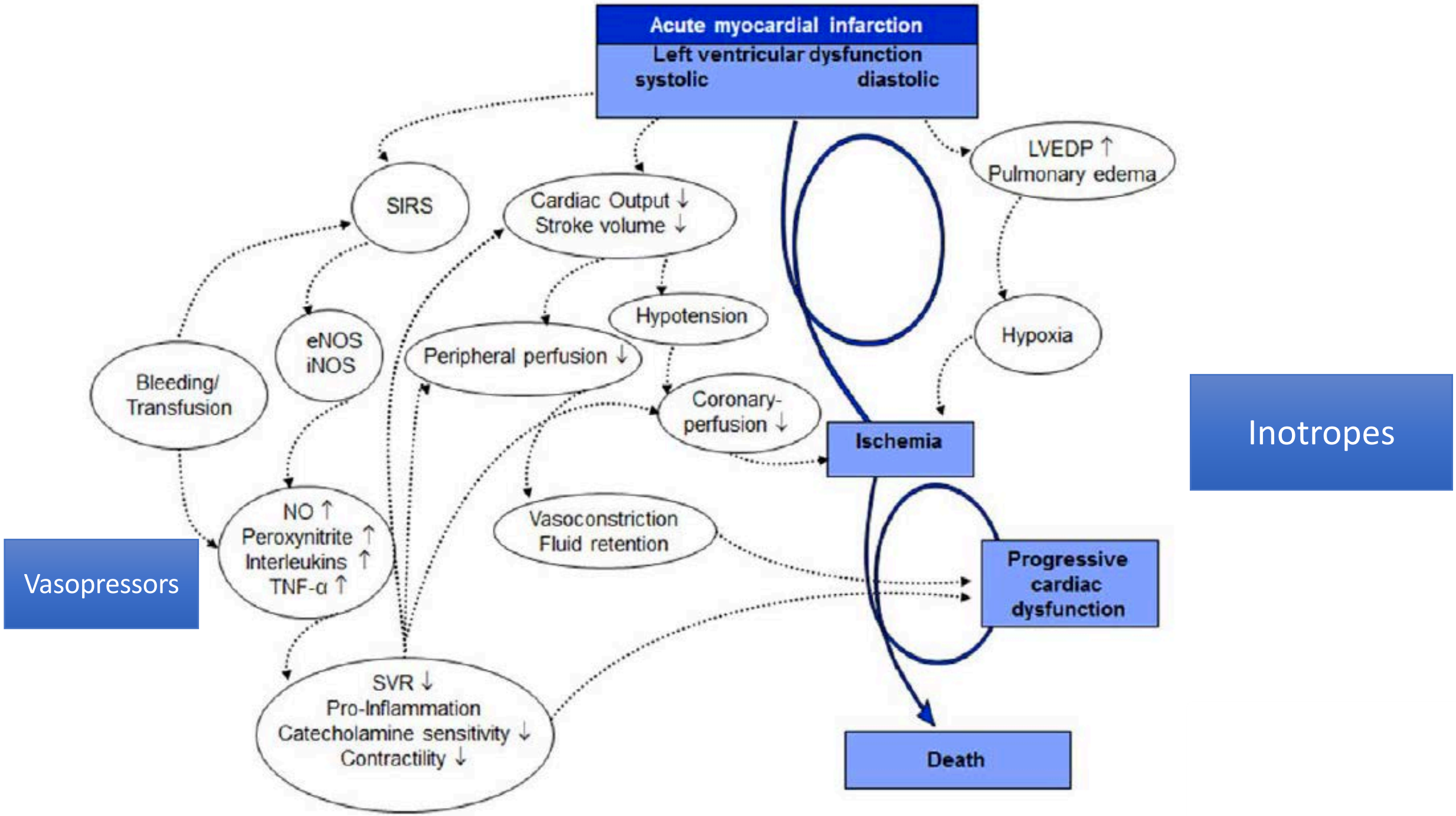


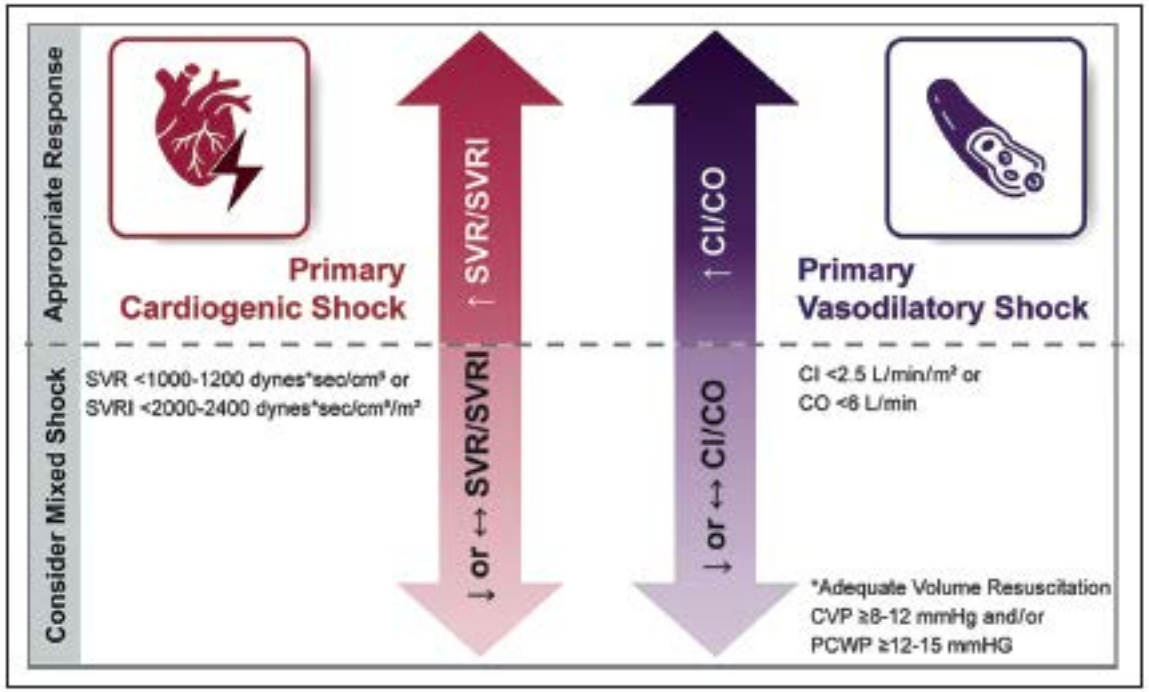
Figure 3. Components to be considered when evaluating the severity and phenotype of patients with cardiogenic shock. Markers of shock severity (*bottom*) are distinct from the assessment of shock phenotype (*top*) (14, 21, 33). MCS = mechanical circulatory support, SCAI = Society for Cardiovascular Angiography and Intervention.

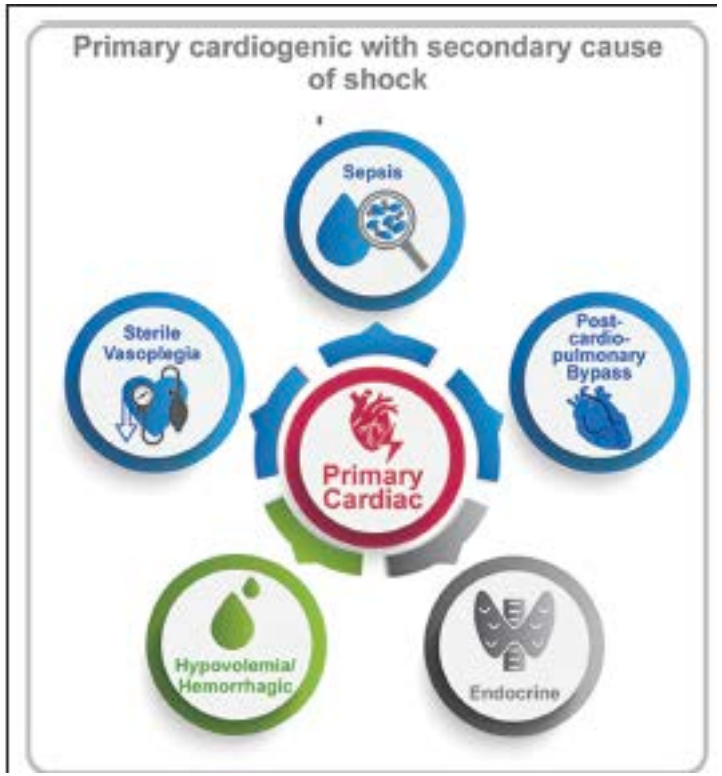
Evaluer la gravité et établir une stratégie


Acute myocardial infarction
Left ventricular dysfunction
systolic
diastolic
LVEDP ↑
Pulmonary edema
SIRS
Cardiac Output ↓
Stroke volume ↓
Hypotension
Hypoxia
eNOS
iNOS
Peripheral perfusion ↓
Bleeding/
Transfusion
Coronary-
perfusion ↓
Ischemia
Inotropes
NO ↑
Peroxynitrite ↑
Interleukins ↑
TNF-α ↑
Vasoconstriction
Fluid retention
Vasopressors
Progressive
cardiac
dysfunction
SVR ↓
Pro-Inflammation
Catecholamine sensitivity ↓
Contractility ↓
Death

Mixed Cardiogenic Shock: A Proposal for Standardized Classification, a Hemodynamic Definition, and Framework for Management

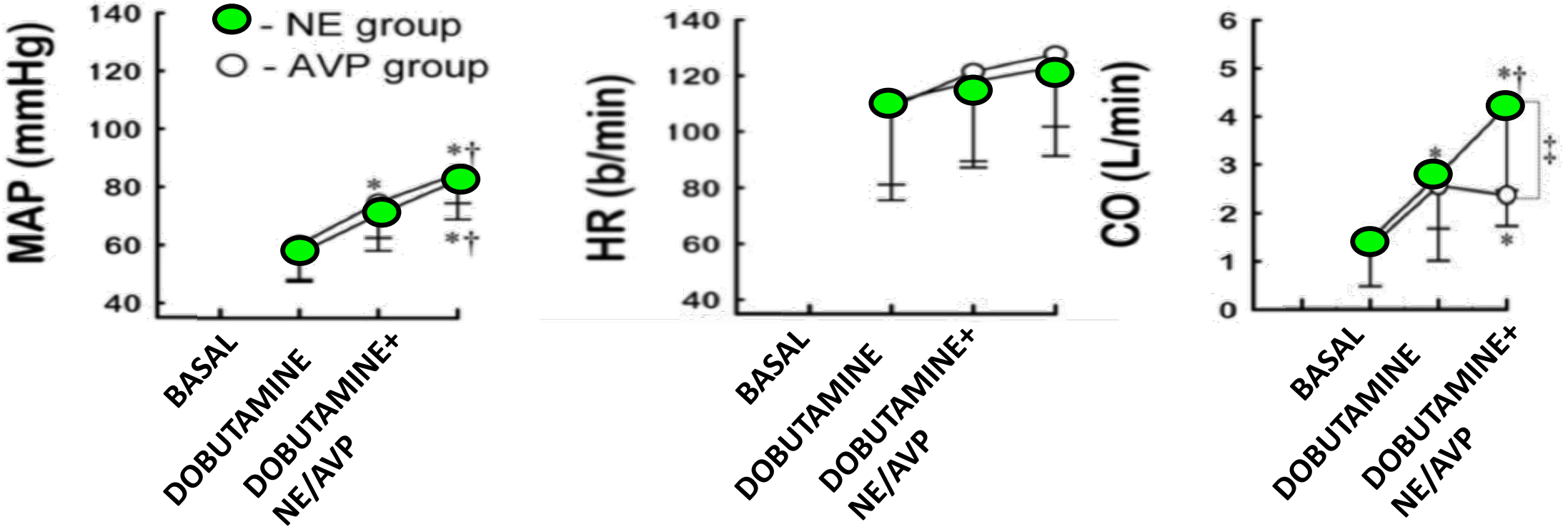
Sean van Diepen, MD, MSc; Janine Pöss, MD; Janek M. Senaratne, MD, MSc; Ann Gage, MD; David A. Morrow, MD, MPH





Débit cardiaque et inopresseurs

How O.J. *Translational Research* 2010



La noradrénaline augmente le débit cardiaque durant le choc cardiogénique

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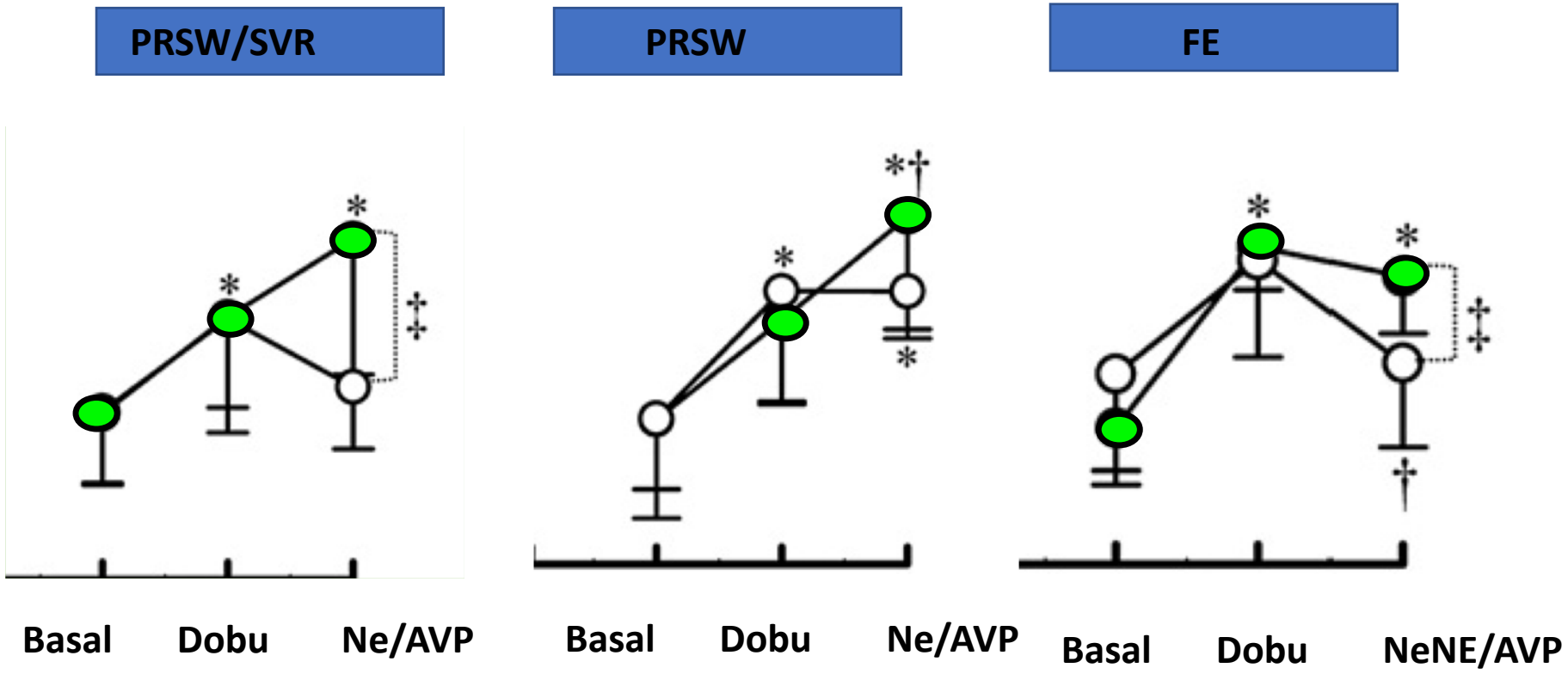
Inopressors improve cardiac function in CS

NE group

AVP group



(How O-J, Translational Research 2010;156:273–281)

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Potential problems with vasopressors/inotropes

Excessive increase in afterload

- Further decrease in flow
  - Excessive increase in peripheral resistances
  - Further decrease in perfusion pressure at the organ level

Excessive tachycardia and risk of ischemia exacerbation

Increase in MVO_2 and decrease in diastolic time

Cellular increase in calcium

Arrhythmias, Tako-Tsubo

Catecholamines

- The use of catecholamines is considered to be the angular stone of hemodynamic cardiogenic shock treatment
- This therapeutic class includes dopamine, epinephrine, norepinephrine and phenylephrine
- From pathophysiological data, the first conclusion is that agents that exhibit both inotropic and vasopressor effects are likely the most indicated in CS treatment.

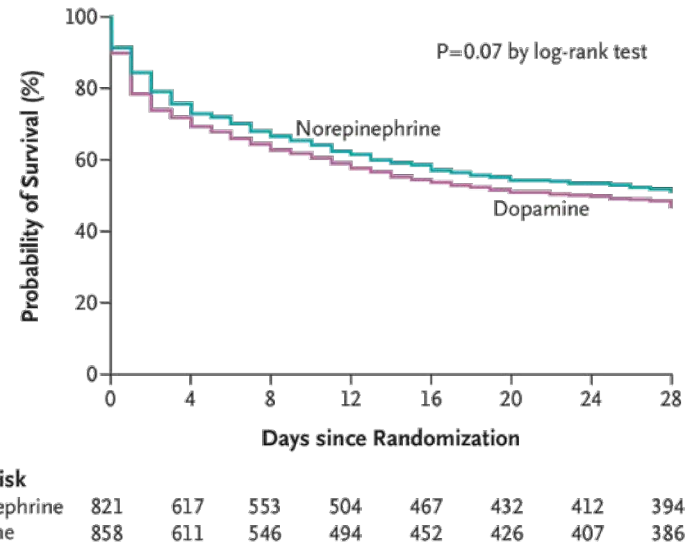
Norepinephrine as a first line-agent.

- Vasoactive trials in CS have historically been difficult to perform
- Therefore, current recommendations are mainly based on meta-analyses and expert opinions.

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*

Phase III, double-blind, 1679 patients



No. at Risk								
Norepinephrine	821	617	553	504	467	432	412	394
Dopamine	858	611	546	494	452	426	407	386

Adverse events			
Arrhythmias — no. (%)	207 (24.1)	102 (12.4)	<0.001
Atrial fibrillation	176 (20.5)	90 (11.0)	
Ventricular tachycardia	21 (2.4)	8 (1.0)	
Ventricular fibrillation	10 (1.2)	4 (0.5)	

Similar mortality

7% of dopamine treated patients were switched to norepinephrine

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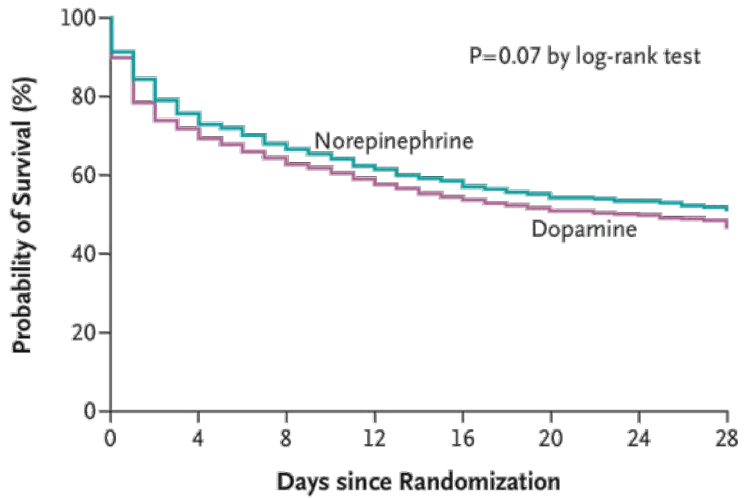

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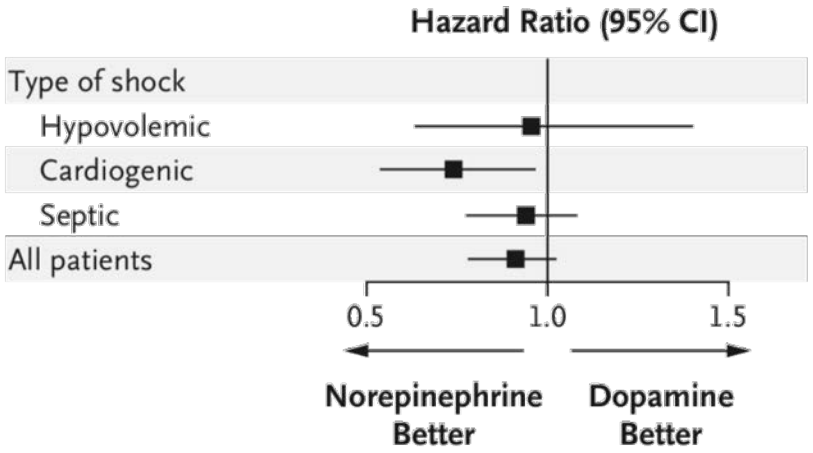

Similar mortality

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Comparison of Dopamine and Norepinephrine in the Treatment of Shock

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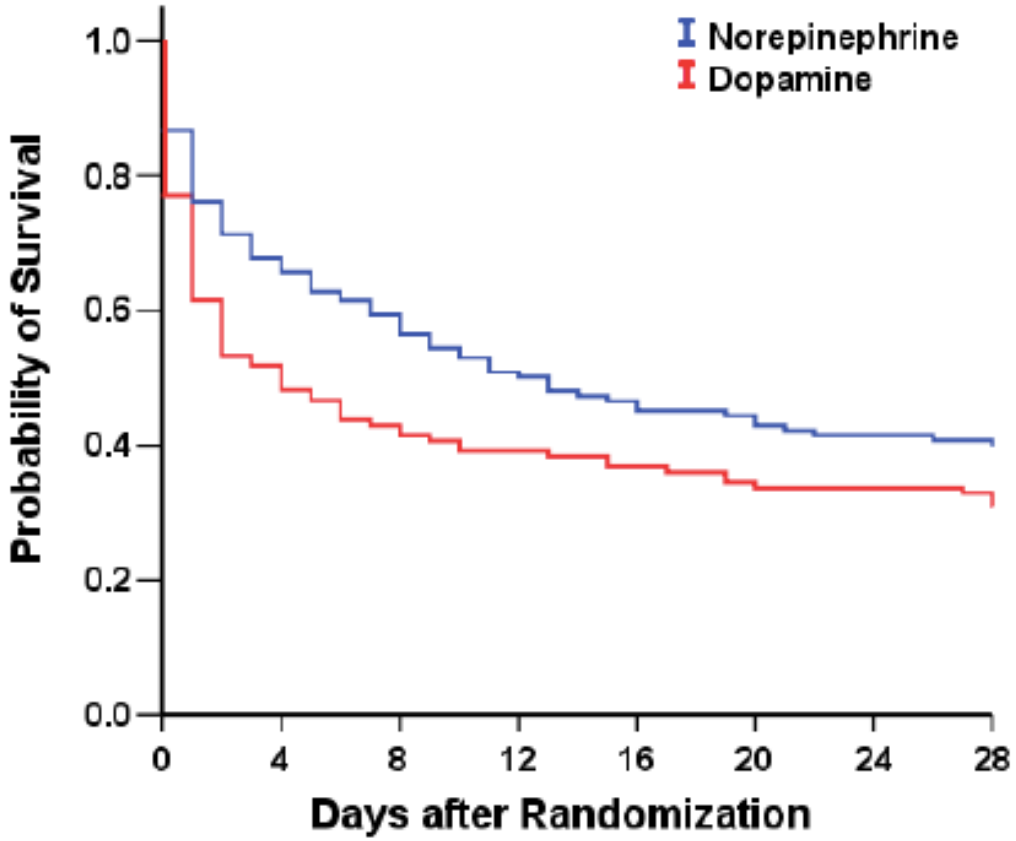

P =0.03

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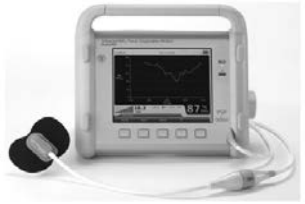
INCREASING MEAN ARTERIAL PRESSURE IN CARDIOGENIC SHOCK SECONDARY TO MYOCARDIAL INFARCTION: EFFECTS ON HEMODYNAMICS AND TISSUE OXYGENATION

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

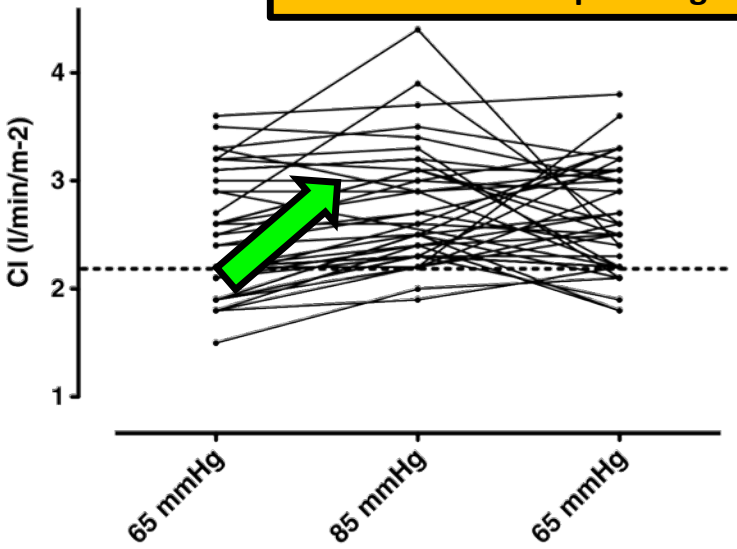
25 chocs cardiogéniques avec syndrome d'ischémie reperfusion, noradrenaline pour augmenter la PAM de 65 à 85 mmHg

	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

Inopresseurs et perfusion tissulaire



25 chocs cardiogéniques avec syndrome d'ischémie reperfusion, noradrenaline pour augmenter la PAM de 65 à 85 mmHg



	MAP = 65 mmHg	MAP = 85 mmHg	Volunteers
St_{O_2}, %	83 ± 6	83 ± 7	80 ± 5
Delta St_{O_2}, %	10 ± 3*	14 ± 4*†	14 ± 5†
St_{O_2} desaturation slope, %/s	−9.2 ± 3.1*	−9.3 ± 3.3*	−15.5 ± 4.5
St_{O_2} recovery slope, %/s	3.0 ± 1.3*	3.6 ± 1.3*†	5.1 ± 1.3†
THI	13 ± 2.9	13 ± 3.1	14.6 ± 1.8

Amélioration du débit cardiaque et des paramètres de perfusion tissulaire sous noradrénaline

Perez P et al. *Shock* 2014

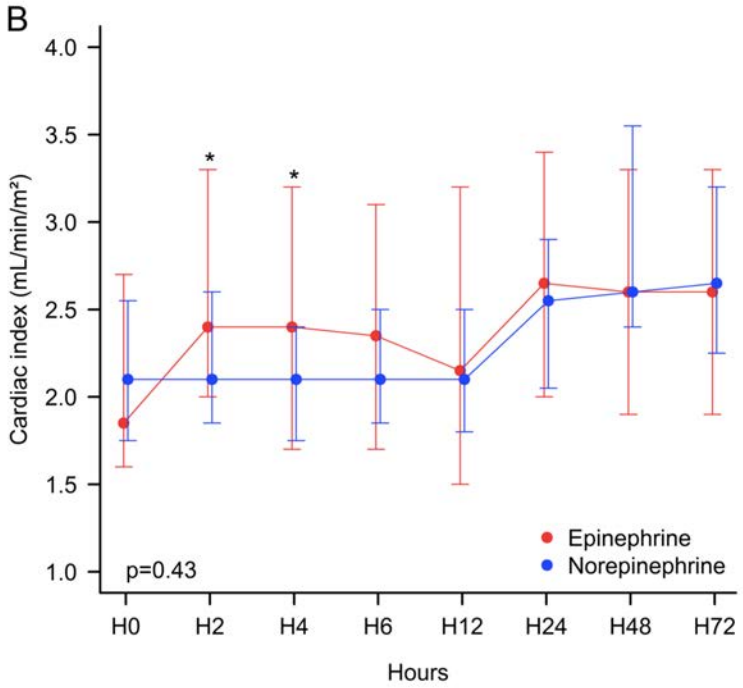
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 72, NO. 2, 2018

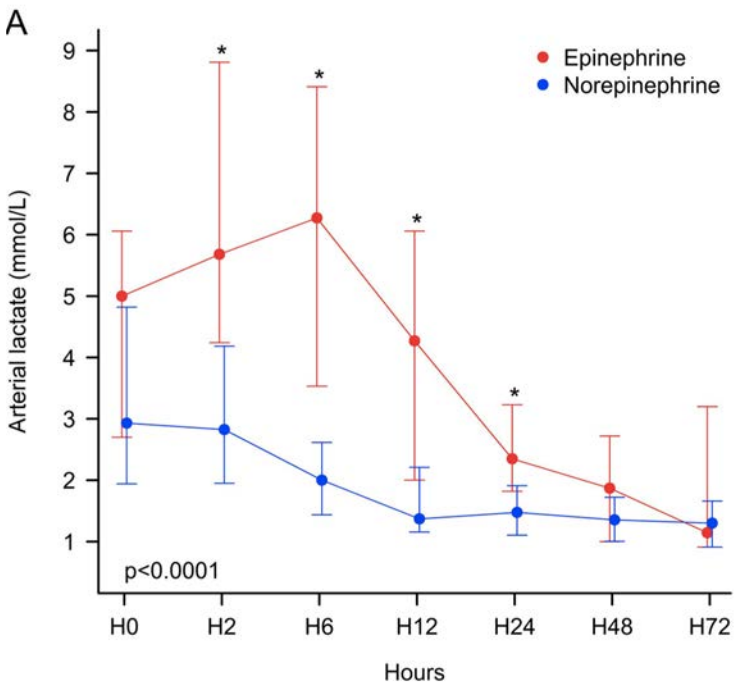
PUBLISHED BY ELSEVIER

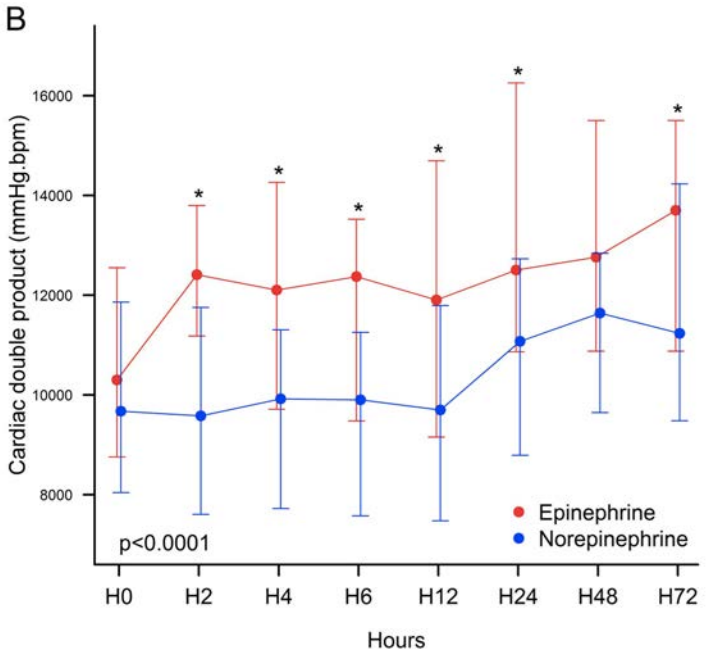
Epinephrine Versus Norepinephrine for Cardiogenic Shock After Acute Myocardial Infarction

Bruno Levy, MD, PhD,[a] Raphael Clere-Jehl, MD,[b] Annick Legras, MD,[c] Tristan Morichau-Beauchant, MD,[d] Marc Leone, MD, PhD,[e] Ganster Frederique, MD,[f] Jean-Pierre Quenot, MD, PhD,[g] Antoine Kimmoun, MD, PhD,[a] Alain Cariou, MD, PhD,[d] Johan Lassus, MD, PhD,[h] Veli-Pekka Harjola, MD, PhD,[h] Ferhat Meziani, MD, PhD,[b] Guillaume Louis, MD,[i] Patrick Rossignol, MD, PhD,[j] Kevin Duarte, PhD,[j] Nicolas Girerd, MD, PhD,[j] Alexandre Mebazaa, MD, PhD,[k] Philippe Vignon, MD, PhD[l]

- No differences in vasopressor and dobutamine doses
- **Higher heart rate in the epinephrine group with a similar cardiac index and similar stroke volume.**
- **Epinephrine induced lactic acidosis**







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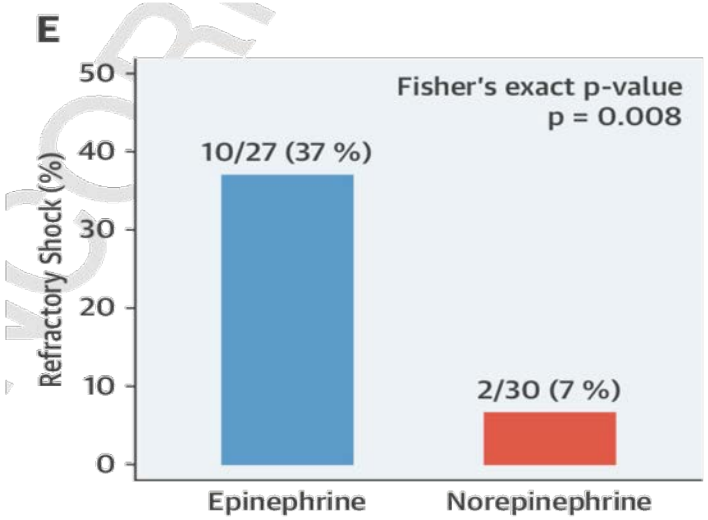
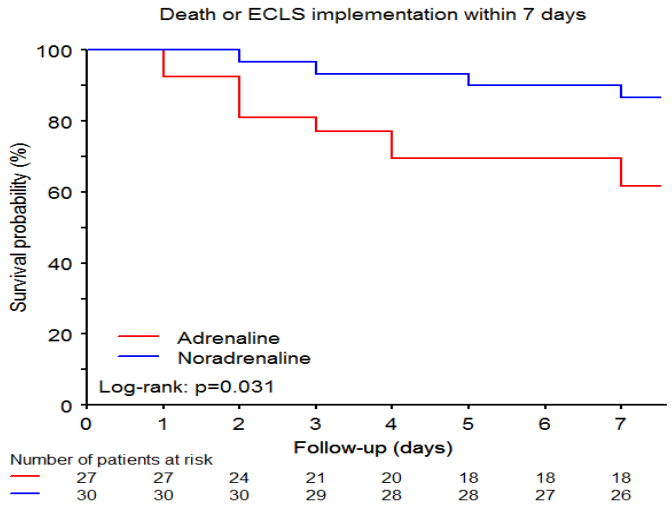


- **More refractory cardiogenic shock in the epinephrine group**
  - Early termination of the study



- **Epinephrine use was associated with a trend of an increased risk of death** (p=0.08) and an increased risk of death plus ECMO (p=0.031) at 7 days. There was a trend of an increased risk of death plus ECMO at J28 (p= 0.064)

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Intensive Care Med
https://doi.org/10.1007/s00134-018-5222-9

SYSTEMATIC REVIEW

Epinephrine and short-term survival in cardiogenic shock: an individual data meta-analysis of 2583 patients

Valentine Léopold[1], Etienne Gayat[1], Romain Pirracchio[2], Jindrich Spinar[3], Jiri Parenica[3], Tuukka Tarvasmäki[4,5], Johan Lassus[4], Veli-Pekka Harjola[4], Sébastien Champion[6], Faiez Zannad[7], Serafina Valente[8], Philip Urban[9], Horng-Ruey Chua[10,11,12,13,14], Rinaldo Bellomo[10,11,12,13], Batric Popovic[15], Dagmar M. Ouweneel[16], José P. S. Henriques[16], Gregor Simonis[17,18], Bruno Lévy[19], Antoine Kimmoun[19], Philippe Gaudard[20], Mir Babar Basir[21], Andrej Markota[22], Christoph Adler[23], Hannes Reuter[23], Alexandre Mebazaa[1,24*] and Tahar Chouihed[1,7,25,26]

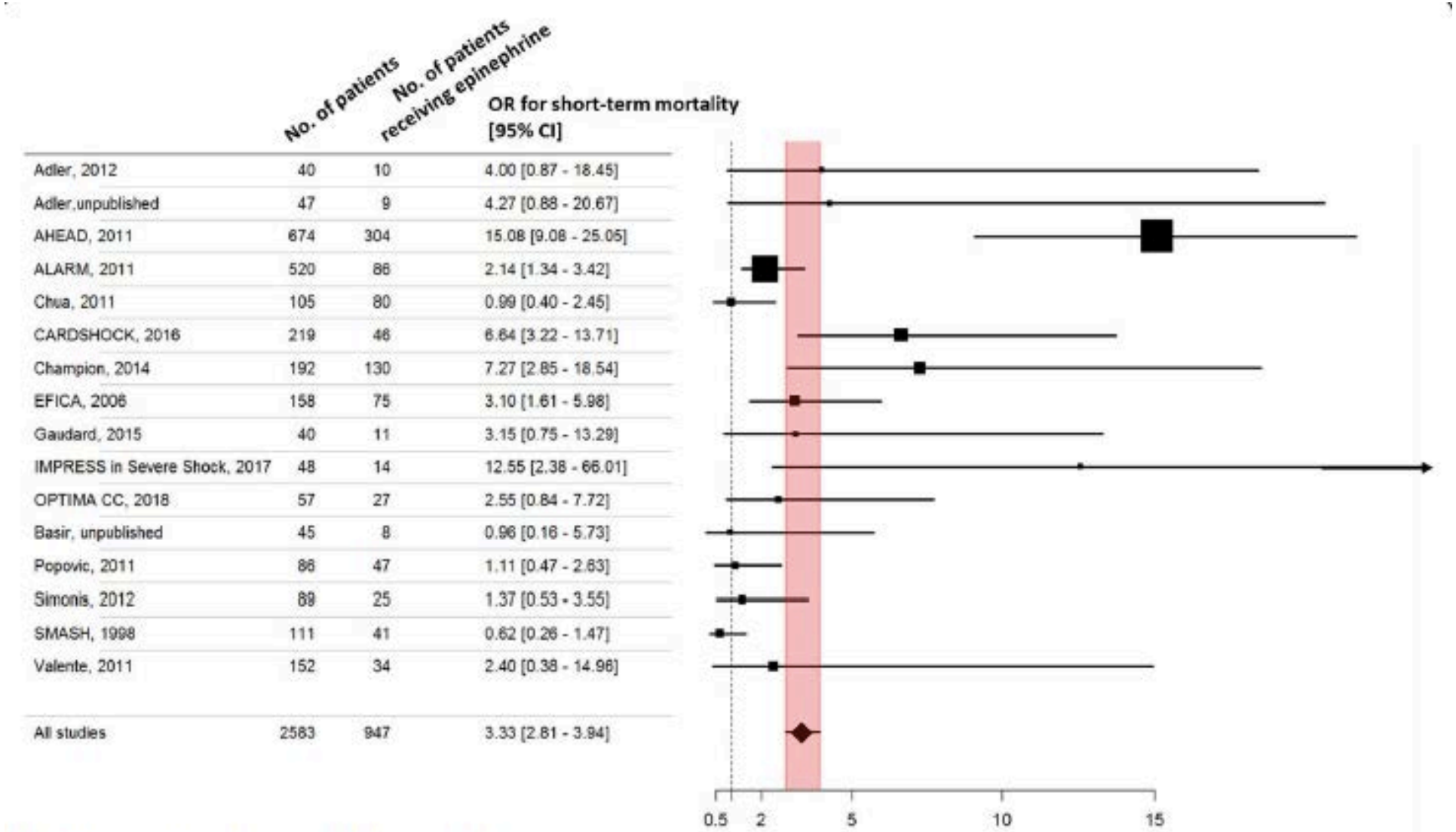
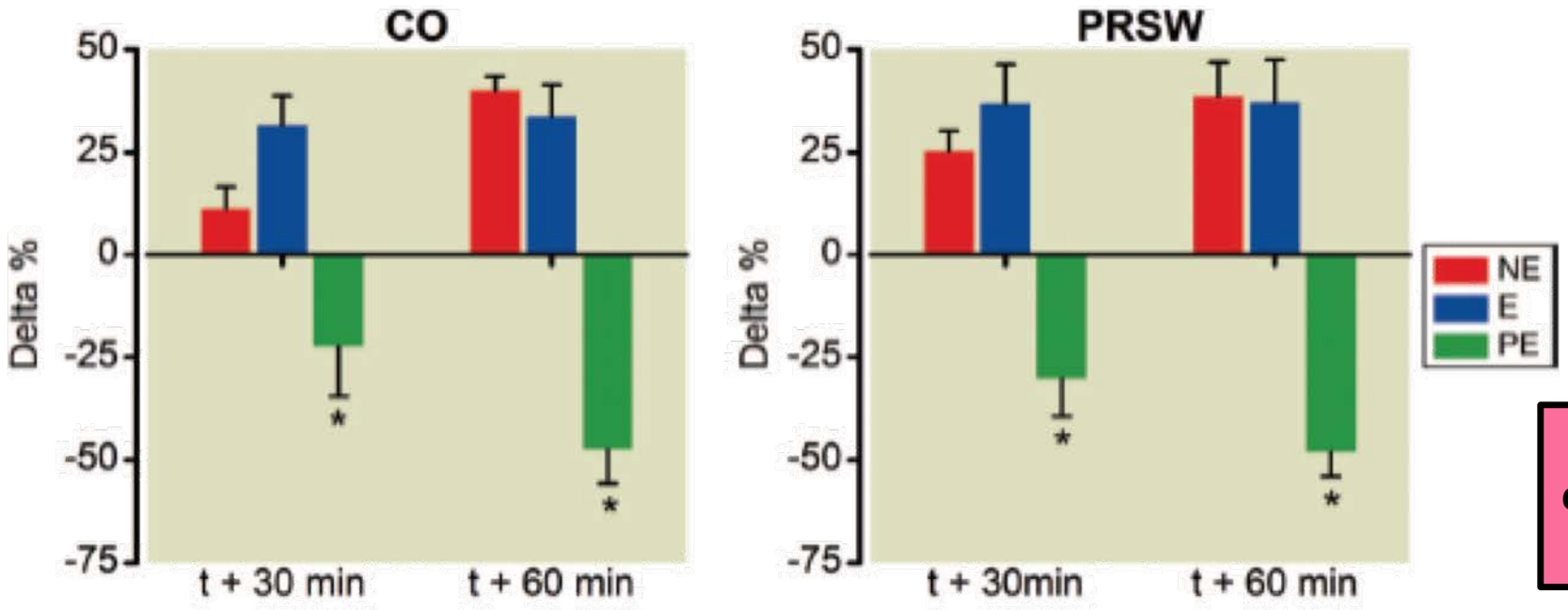


Fig. 3 Forest plot of the meta-analysis of short-term mortality

Phényléphrine

Cardiomyopathie septique expérimentale, comparaison Adrénaline, Noradrénaline, Phényléphrine



La phénylephrine diminue le debit cardiaque

La phénylephrine diminue la reserve d'inotropisme

La phényléphrine semble expérimentalement délétère sur la fonction cardiaque

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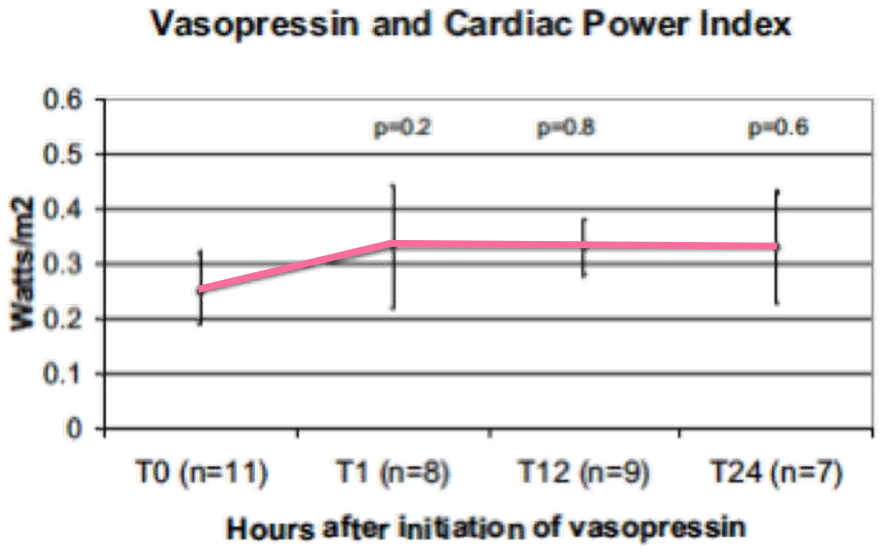
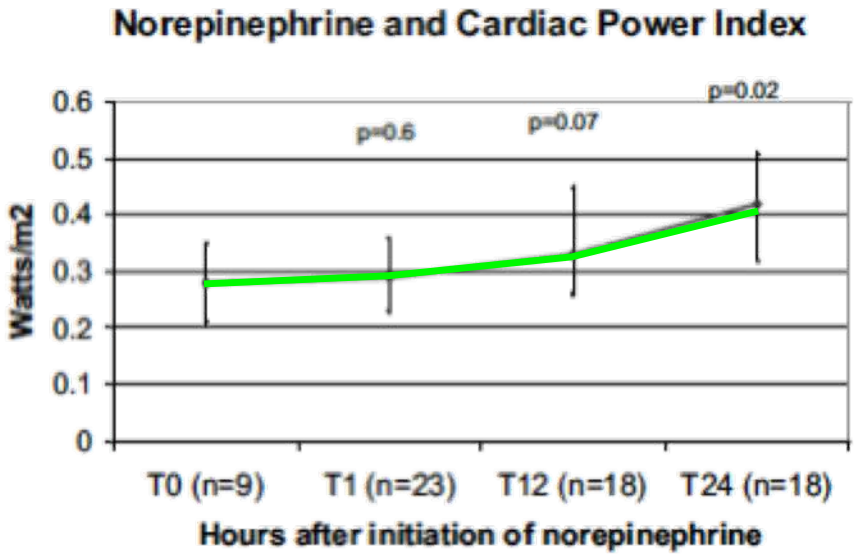
Vasopressine

Jolly S et al. *Am J cardiol* 2005

36 patients en choc cardiogénique, rétrospectif, CPI= CIxPAM/451 (W/m²), N>0.5 W/m²



La vasopressine n'augmente pas le CPI



La noradrénaline augmente le CPI

Dobutamine as a first-line inotrope.

- Studies are scarce comparing pure inotrope or inodilator drugs during cardiogenic shock
  - Dobutamine (beta-1-adrenergic agonist), enoximone (IPDE phosphodiesterase-3 inhibitor) and levosimendan (calcium sensitizer)
  - both dobutamine and milrinone are associated with arrhythmias and systemic hypotension
- ESC, French, German and Scandinavian recommendations favor dobutamine

Milrinone as Compared with Dobutamine in the Treatment of Cardiogenic Shock

N Engl J Med . 2021 Aug 5;385(6):516-525.

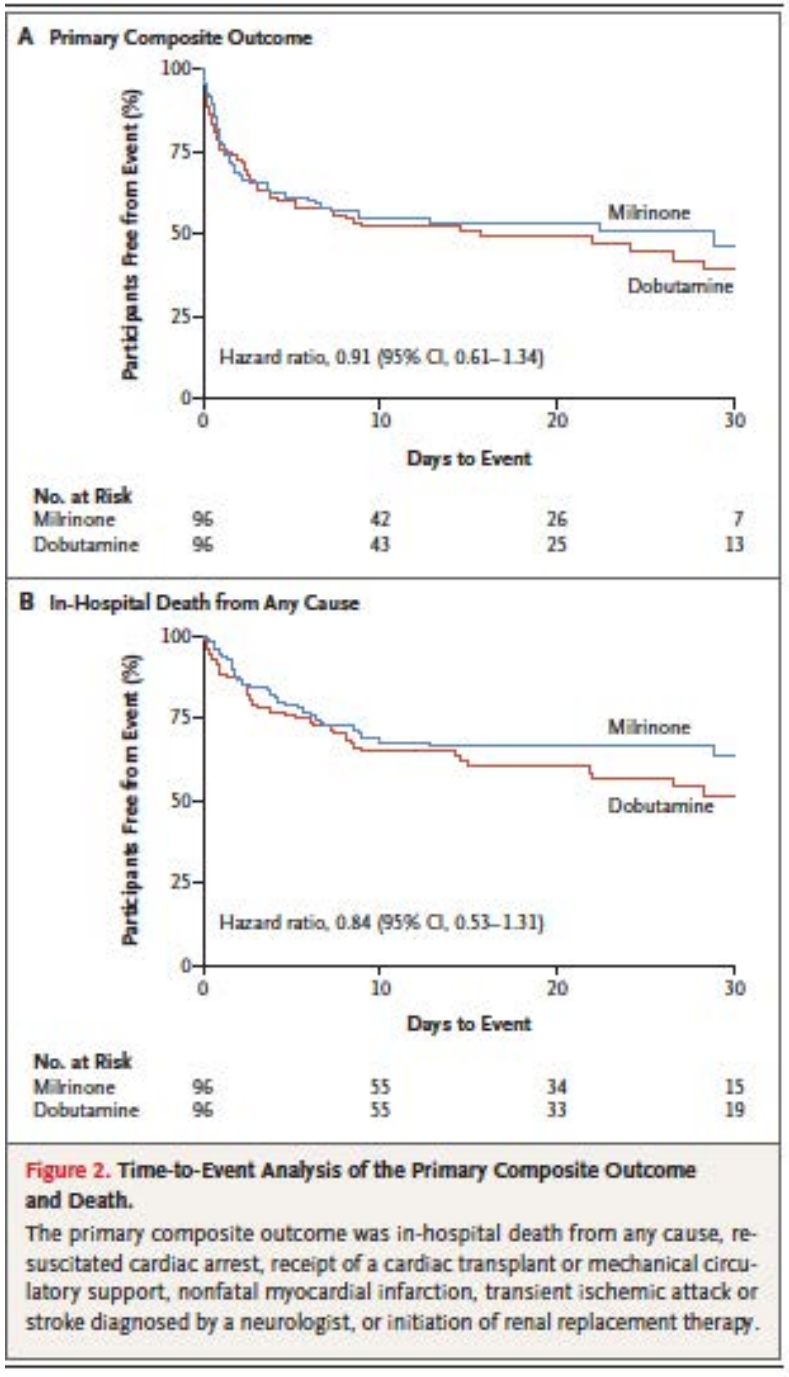
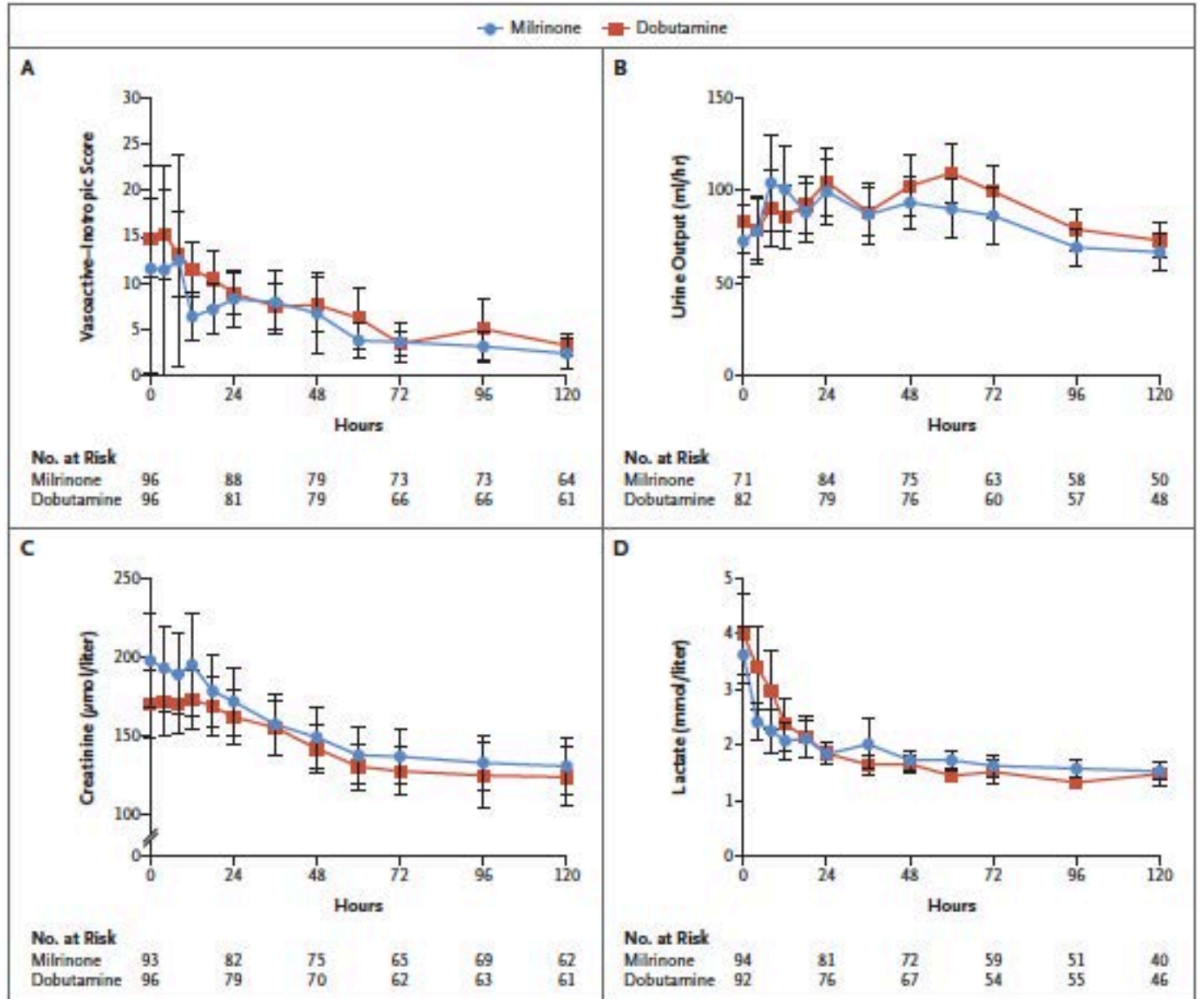


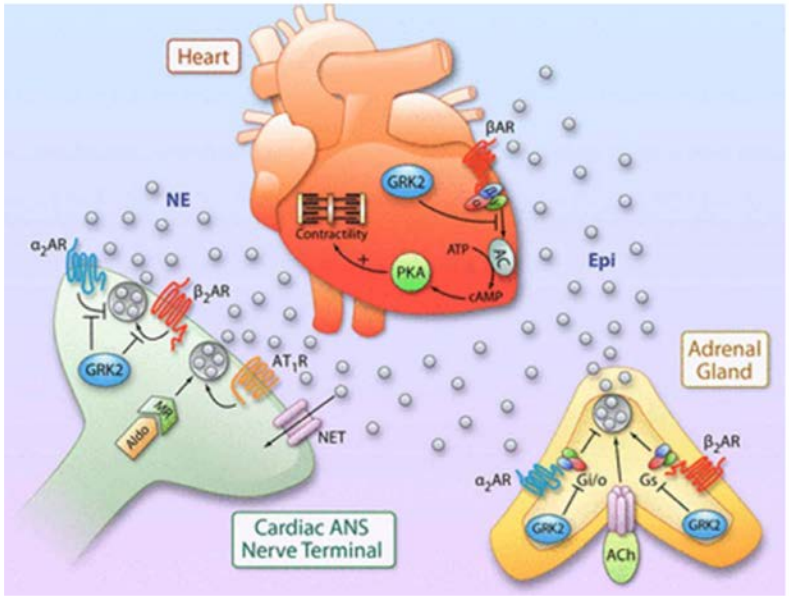
Figure 2. Time-to-Event Analysis of the Primary Composite Outcome and Death.

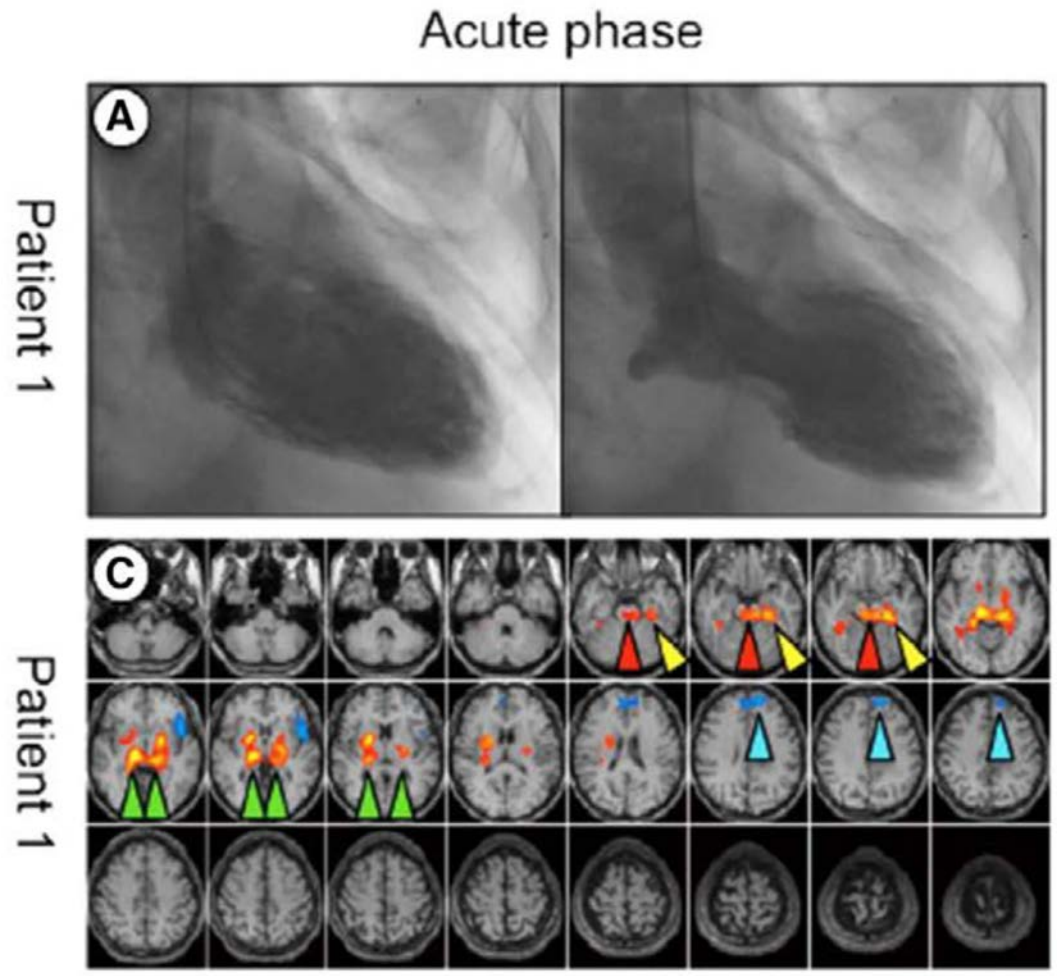
The primary composite outcome was in-hospital death from any cause, resuscitated cardiac arrest, receipt of a cardiac transplant or mechanical circulatory support, nonfatal myocardial infarction, transient ischemic attack or stroke diagnosed by a neurologist, or initiation of renal replacement therapy.



SEVERE TAKOTSUBO

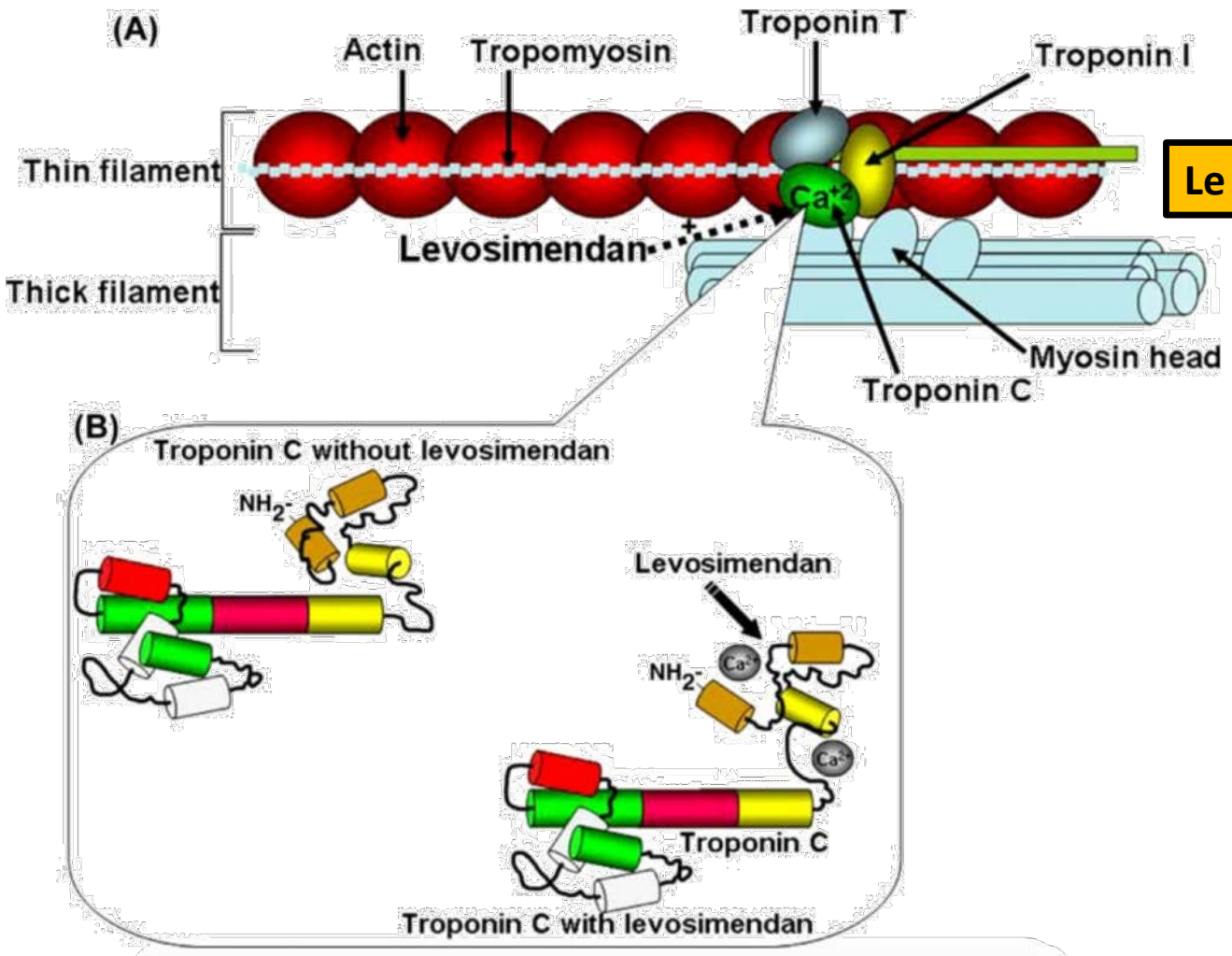
- Catecholamines induced Cardiomyopathy
  - **Cardiogenic shock**
  - 4-20% of the cases
  - Mortality 17-30%





Pelliccia et al. **Circulation** 2017

Levosimendan: action sur le coeur



Le levosimendan se fixe sur la troponine C

⬇

Facilite la fixation du calcium

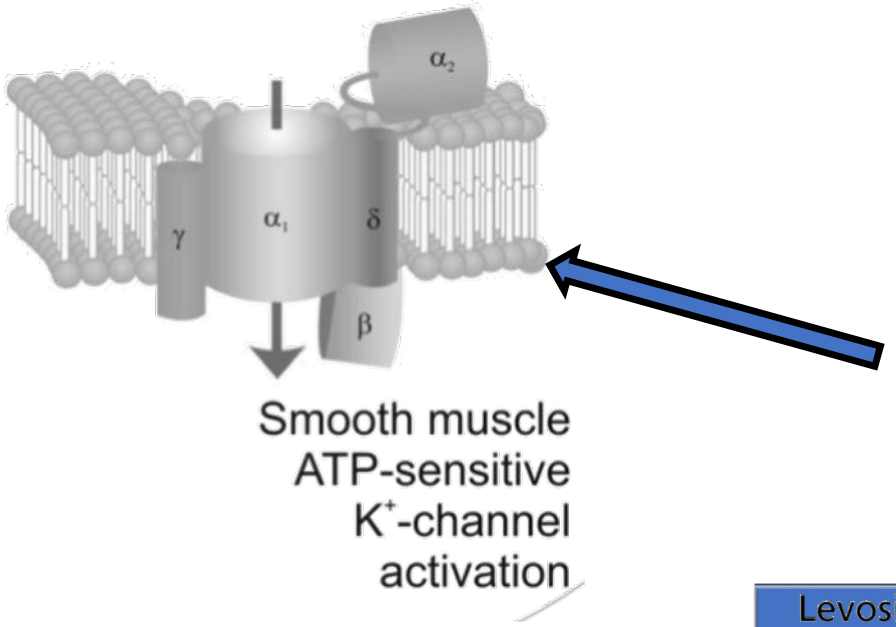
⬇

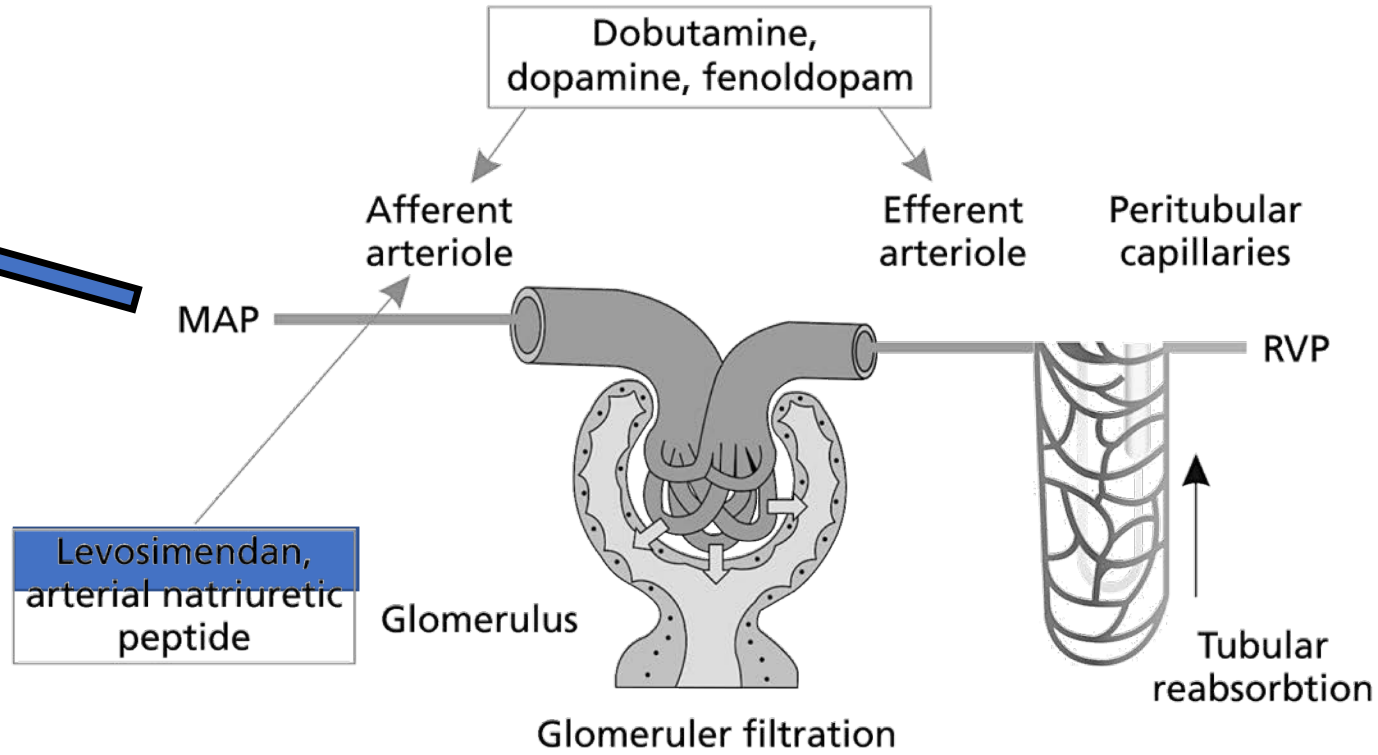
Découvre les sites d'actine

⬇

Augmente la contractilité

Levosimendan : action sur les vaisseaux





Vasodilatation → **Hypotension artérielle**

Bouchez S et al. Cardiovasc Drugs Ther 20184

Levosimendan in cardiogenic shock: Overview of main publications

Clinical Investigations

Crit Care Med 2008 Vol. 36, No. 8

Levosimendan is superior to enoximone in refractory cardiogenic shock complicating acute myocardial infarction*

Joerg T. Fuhrmann, MD; Alexander Schmeisser, MD; Matthias R. Schulze, MD; Carsten Wunderlich, MD; Steffen P. Schoen, MD; Thomas Rauwolf, PhD; Christof Weinbrenner, MD; Ruth H. Strasser, MD

Acute Cardiac Care. 2008; 10: 49–57

informa healthcare

ORIGINAL ARTICLE

Early and sustained haemodynamic improvement with levosimendan compared to intraaortic balloon counterpulsation (IABP) in cardiogenic shock complicating acute myocardial infarction

ARND CHRISTOPH*, ROLAND PRONDZINSKY*, MARTIN RUSS, MATTHIAS JANUSCH, AXEL SCHLITT, HENNING LEMM, SEBASTIAN REITH, KARL WERDAN & MICHAEL BUERKE

Vascular Health and Risk Management

Dovepress

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Levosimendan neither improves nor worsens mortality in patients with cardiogenic shock due to ST-elevation myocardial infarction

Elmir Omerovic
Truls Råmunddal
Per Albertsson
Mikael Holmberg
Per Hallgren
Jan Boren
Lars Grip
Göran Matejka

Same patients in the 3 publications below

ELSEVIER

European Journal of Heart Failure 8 (2006) 723 – 728

The European Journal of Heart Failure

www.elsevier.com/locate/ejheart

Cardiogenic shock after primary percutaneous coronary intervention: Effects of levosimendan compared with dobutamine on haemodynamics

Martín J. García-González [a,*], Alberto Domínguez-Rodríguez [a], Julio J. Ferrer-Hita [a], Pedro Abreu-González [b], Miguel Bethencourt Muñoz [a]

ELSEVIER

International Journal of Cardiology 128 (2008) 214–217

International Journal of Cardiology

www.elsevier.com/locate/ijcard

Effects of levosimendan versus dobutamine on left ventricular diastolic function in patients with cardiogenic shock after primary angioplasty

Alberto Dominguez-Rodriguez [a,*], Sima Samimi-Fard [a], Martin J. Garcia-Gonzalez [a], Pedro Abreu-Gonzalez [b]

ELSEVIER

International Journal of Cardiology 127 (2008) 284–287

International Journal of Cardiology

www.elsevier.com/locate/ijcard

Letter to the Editor

Effects of levosimendan versus dobutamine on long-term survival of patients with cardiogenic shock after primary coronary angioplasty

Sima Samimi-Fard [a], Martín J. García-González [a,*], Alberto Domínguez-Rodríguez [a], Pedro Abreu-González [b]

Conclusions First Part

- In cardiogenic shock complicating AMI, adding levosimendan to standard therapy
  - Improves haemodynamics
  - Seems to be safe
- The current studies are too small to draw conclusions about effects on the incidence of refractory shock, ECMO implantation and survival

Levo-heart shock study

- Effect of early use of levosimendan versus placebo on top of a conventional strategy of inotrope use on a combined morbidity-mortality endpoint in patients with cardiogenic shock
- The study goal is to evaluate the effect of the early use of levosimendan versus placebo on top of a conventional use of inotrope with regard to a composite endpoint of 30-day mortality and/or ExtraCorporeal Life Support (ECLS) requirement and/or dialysis.
- **Experimental group**: patients with cardiogenic shock treated with levosimendan in addition to the conventional strategy.
- **Control group**: Patients with cardiogenic shock treated with placebo for levosimendan in addition to the conventional strategy.
- 610 patients will be included

Take Home Message (1)

- Stabilize arterial pressure with norepinephrine (65-70 mmHg)
- Inotropes : Indication and titration
  - Symptomatic low cardiac output : heart rate, CI/SVO_2, lactate, echo
  - No hypovolemia
  - Dobutamine : start at 2 microgramme/kg/min
  - Levosimendan : no bolus, start at 0.1 microgramme/kg/min puis 0.2 microgramme/kg/min
  - Enoximone no bolus, start at 1 vial//24h
    (2 to 10 microgramme/kg/min)

Take Home Message (2)

Norepinephrine plus dobutamine

Medical treatment

- Contra-indicatio to ECLS
- Improvement on medical treatment

LEVOSIMENDAN?

ECLS/LVAD

- Crash and burn
  - Lactic acidosis, increase in NE, organ failure

Refractory cardiogenic shock