Traitements Inotropes du choc cardiogénique

Yoann Zerbib
Desc réanimation
Rouen 18/12/2014

Definition

Table 2 Terminology and common clinical and haemodynamic characteristics

Clinical status	Heart rate	SBP mmHg	CI L/min/m^2	PCWP mmHg	Congestion Killip/ Forrester	Diuresis	Hypoperfusion	End organ hypoperfusion
I Acute decompensated congestive heart failure	+/−	Low normal/ High	Low normal/ High	Mild elevation	K II/F II	+	+/−	−
II Acute heart failure with hypertension/hypertensive crisis	Usually increased	High	+/−	>18	K II-IV/FII-III	+/−	+/−	+, with CNS symptoms
III Acute heart failure with pulmonary oedema	+	Low normal	Low	Elevated	KIII/FII	+	+/−	−
IVa Cardiogenic shock*/ low output syndrome	+	Low normal	Low, <2.2	>16	K III-IV/F I-III	low	+	+
IVb Severe cardiogenic shock	>90	<90	<1.8	>18	K IV/F IV	Very low	++	+
V High output failure	+	+/−	+	+/−	KII/FI-II	+	−	−
VI Right sided acute heart failure	Usually low	Low	Low	Low	F I	+/−	+/−, acute onset	+/−

There are exceptions; the above values in table II are general rules.
*The differentation from low cardiac output syndrome is subjective and the clinical presentation may overlap these classifications.
SBP = systolic blood pressure; CI = cardiac index; PCWP = pulmonary capillary wedge pressure; CNS = central nervous system.

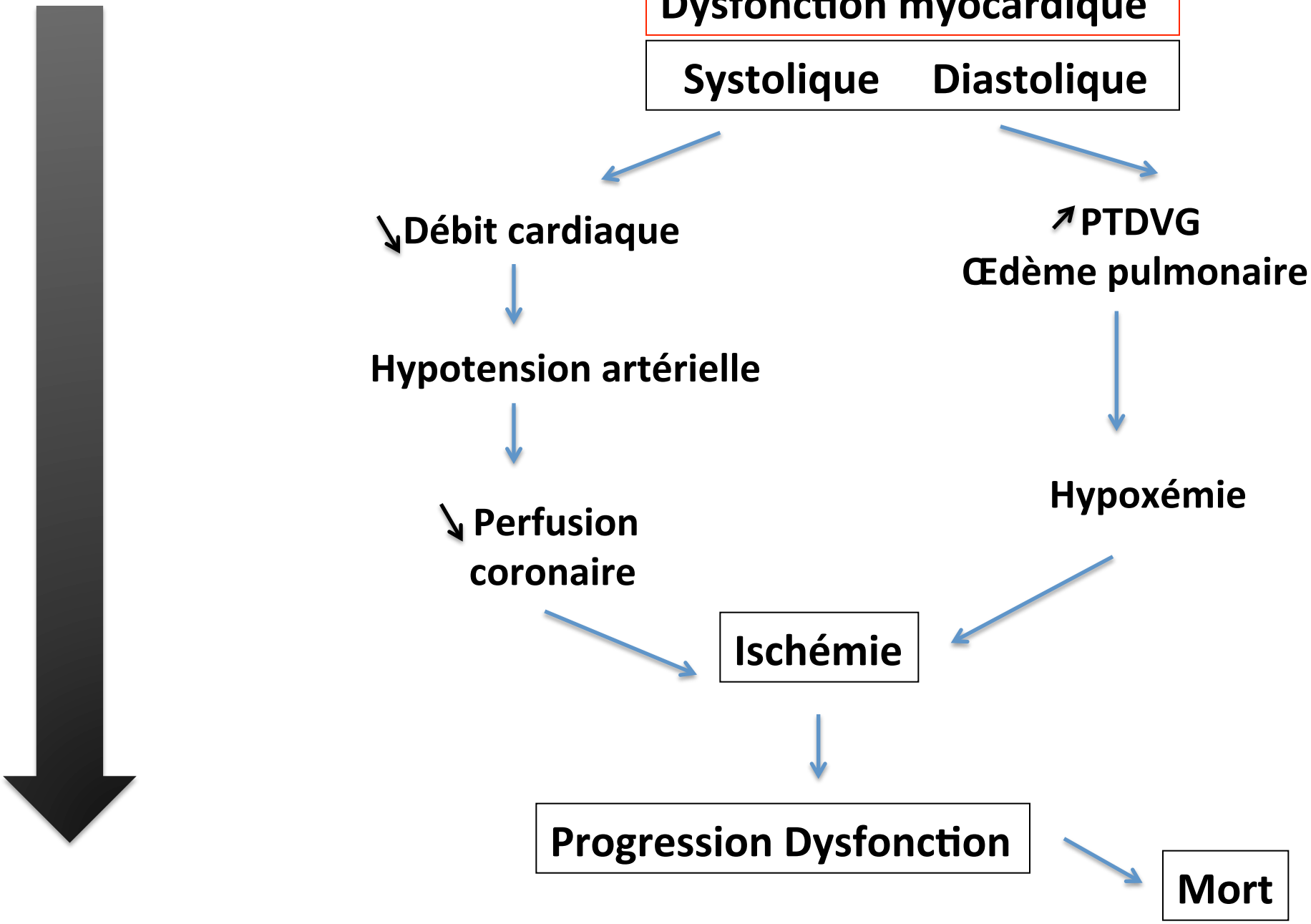
Hypotension Artérielle

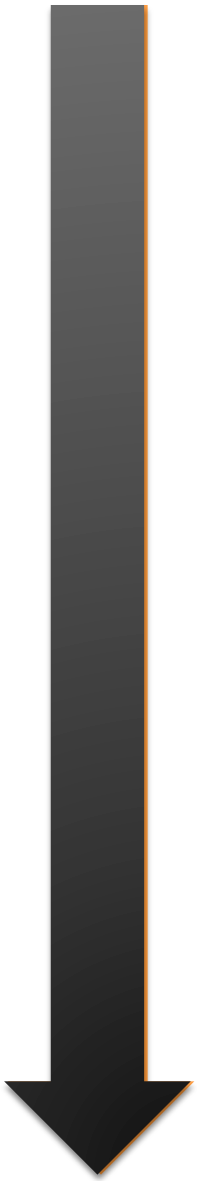
➔ PAS < 90 mmHg, Diminution PAm > 30 mmHg

\+ **Signes d'hypoperfusion tissulaire**

Avec ou sans signes congestifs

ESC guidelines 2005


Dysfonction myocardique
Systolique
Diastolique
↘Débit cardiaque
↗PTDVG
Œdème pulmonaire
Hypotension artérielle
↘ Perfusion coronaire
Hypoxémie
Ischémie
Progression Dysfonction
Mort



Dysfonction myocardique

Systolique Diastolique

↘Débit cardiaque

↗PTDVG

Œdème pulmonaire

Hypotension artérielle

↘ Perfusion coronaire

Hypoxémie

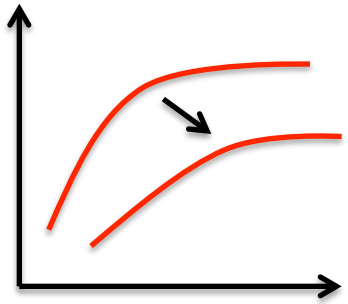
Ischémie

Progression Dysfonction

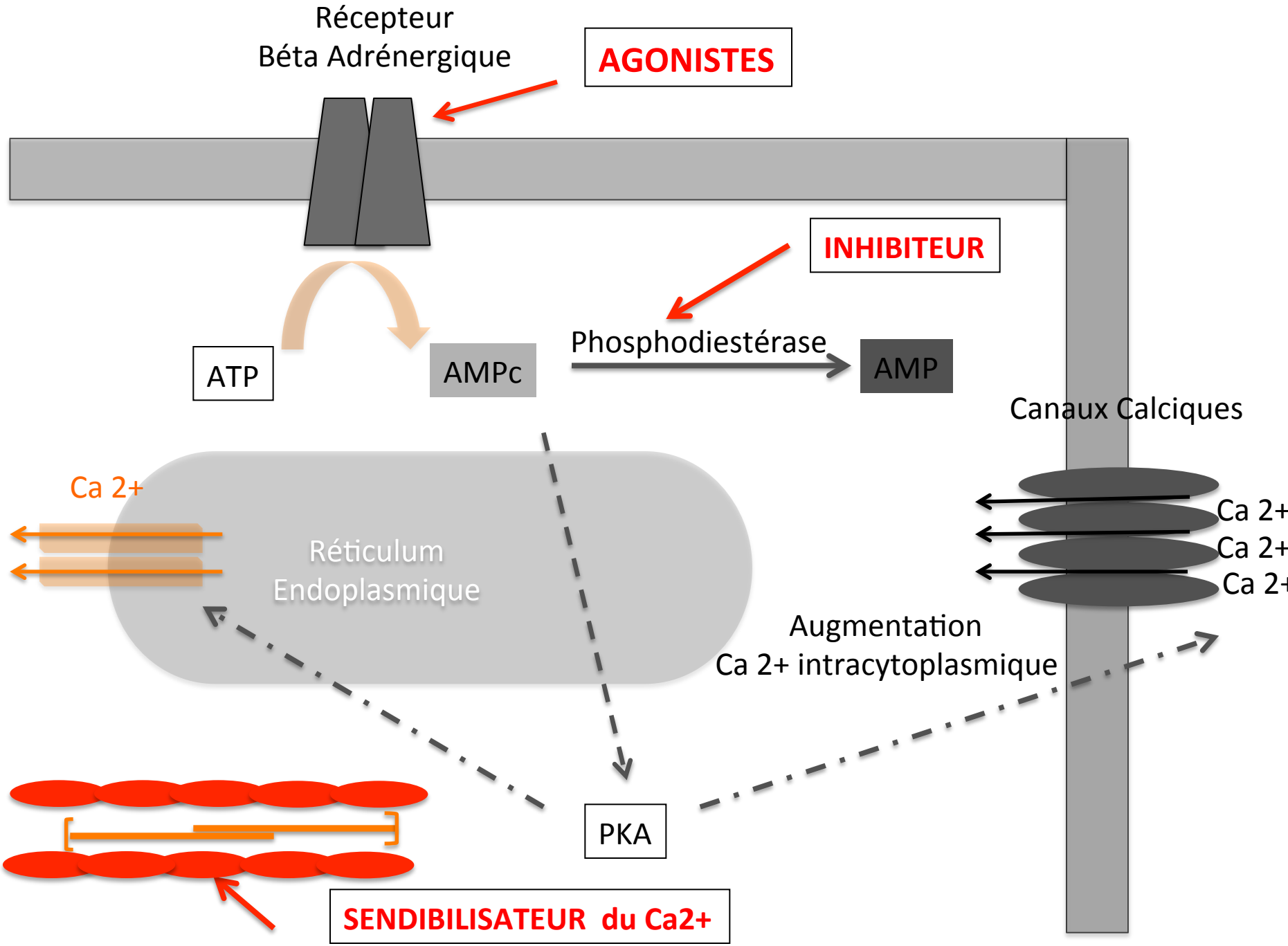
Mort

Traitement Etiologique → **Revascularisation**

Traitement symptomatique



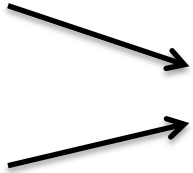
- **Expansion volémique**
- Contrôle de **fréquence** cardiaque
- **Ventilation mécanique** → Précharge/postcharge Hypoxémie
- Traitement **Inotropes et vasopresseurs**
- Assistance circulatoire


Récepteur
Béta Adrénergique
AGONISTES
INHIBITEUR
ATP
AMPc
Phosphodiestérase
AMP
Canaux Calciques
Ca 2+
Réticulum
Endoplasmique
Ca 2+
Ca 2+
Ca 2+
Augmentation
Ca 2+ intracytoplasmique
PKA
SENDIBILISATEUR du Ca2+

Médicaments disponibles

Table 21 Drugs used to treat acute heart failure that are positive inotropes or vasopressors or both

	Bolus	Infusion rate
Dobutamine	No	2–20 µg/kg/min (β+)
Dopamine	No	<3 µg/kg/min: renal effect (δ+)
Milrinone	25–75 µg/kg over 10–20 min	0.375–0.75 µg/kg/min
Enoximone	0.5–1.0 mg/kg over 5–10 min	5–20 µg/kg/min
Levosimedan[a]	12 µg/kg over 10 min (optional)[b]	0.1 µg/kg/min, which can be decreased to 0.05 or increased to 0.2 µg/kg/min
Norepinephrine	No	0.2–1.0 µg/kg/min
Epinephrine	Bolus: 1 mg can be given i.v. during resuscitation, repeated every 3–5 min	0.05–0.5 µg/kg/min

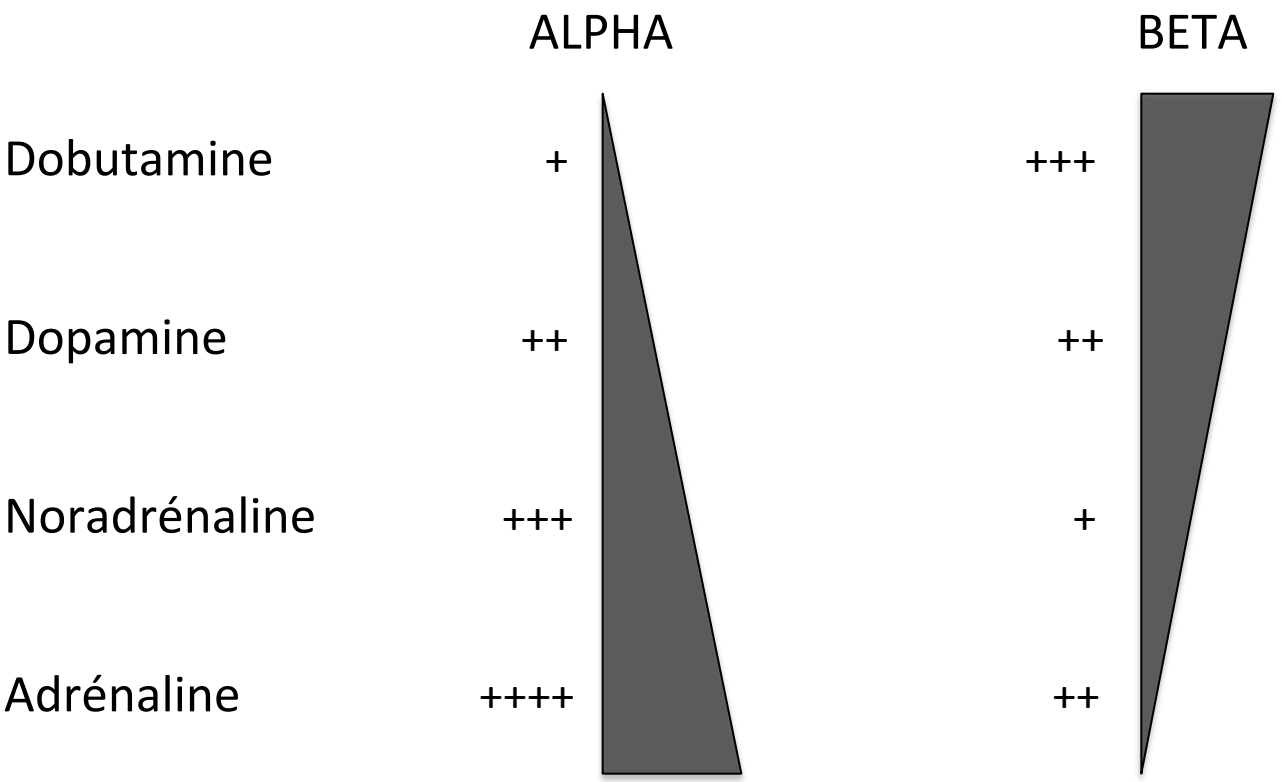


Inhibiteurs de la Phosphodiestérase

Sensibilisateur Calcique

ESC Guidelines, European Heart Journal, 2012

Agonistes adrénergiques



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*

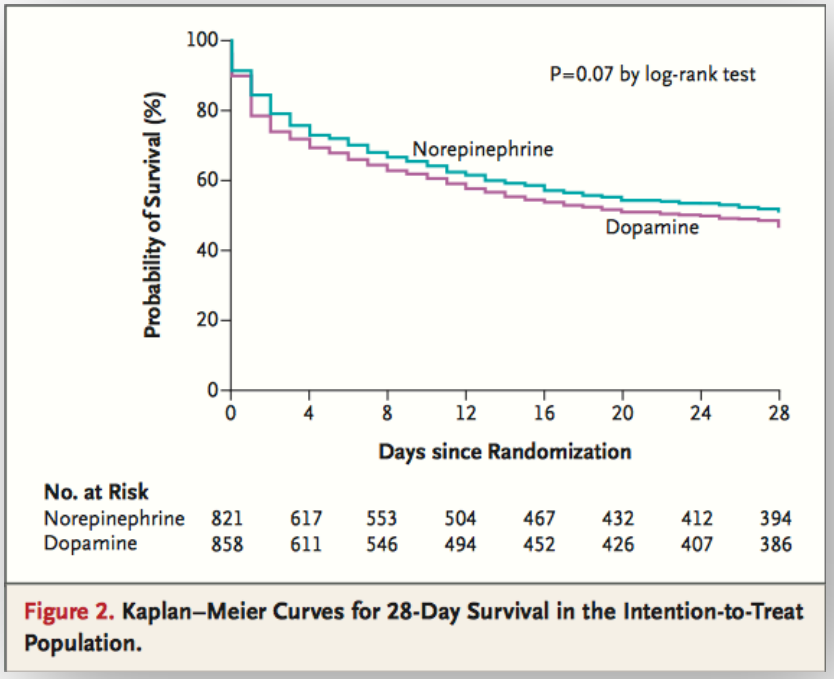
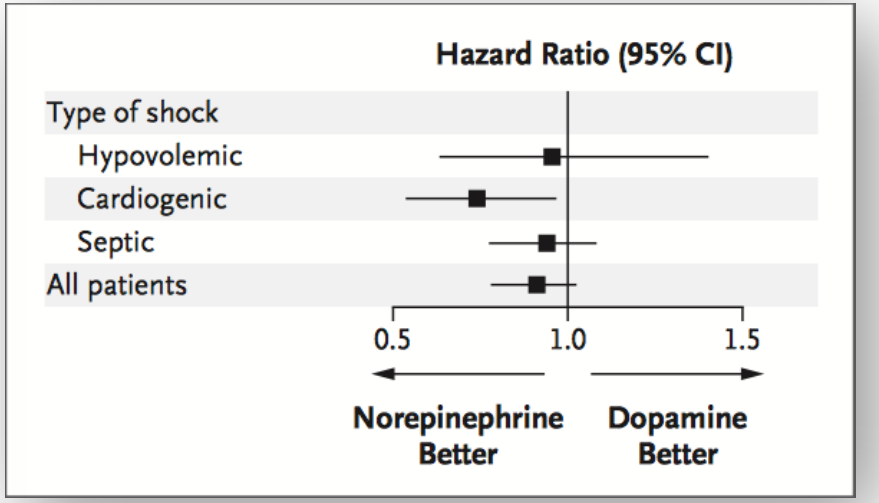


Figure 2. Kaplan–Meier Curves for 28-Day Survival in the Intention-to-Treat Population.

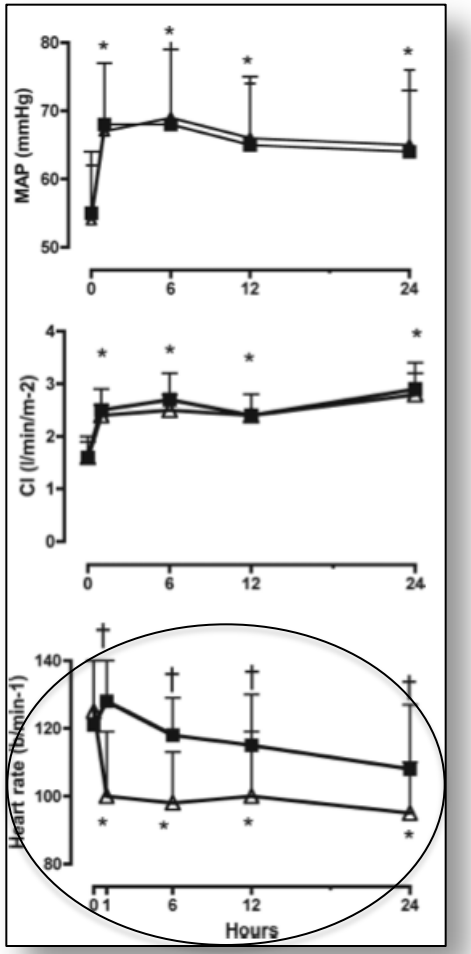
Choc Cardiogénique n= 145 n= 135

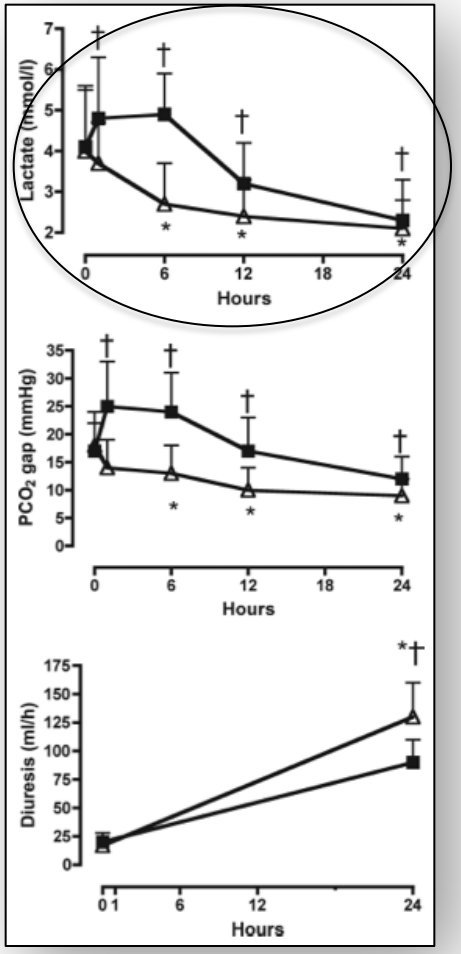


Plus d'arythmies chez les patients traités par dopamine

NEJM, mars 2010

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

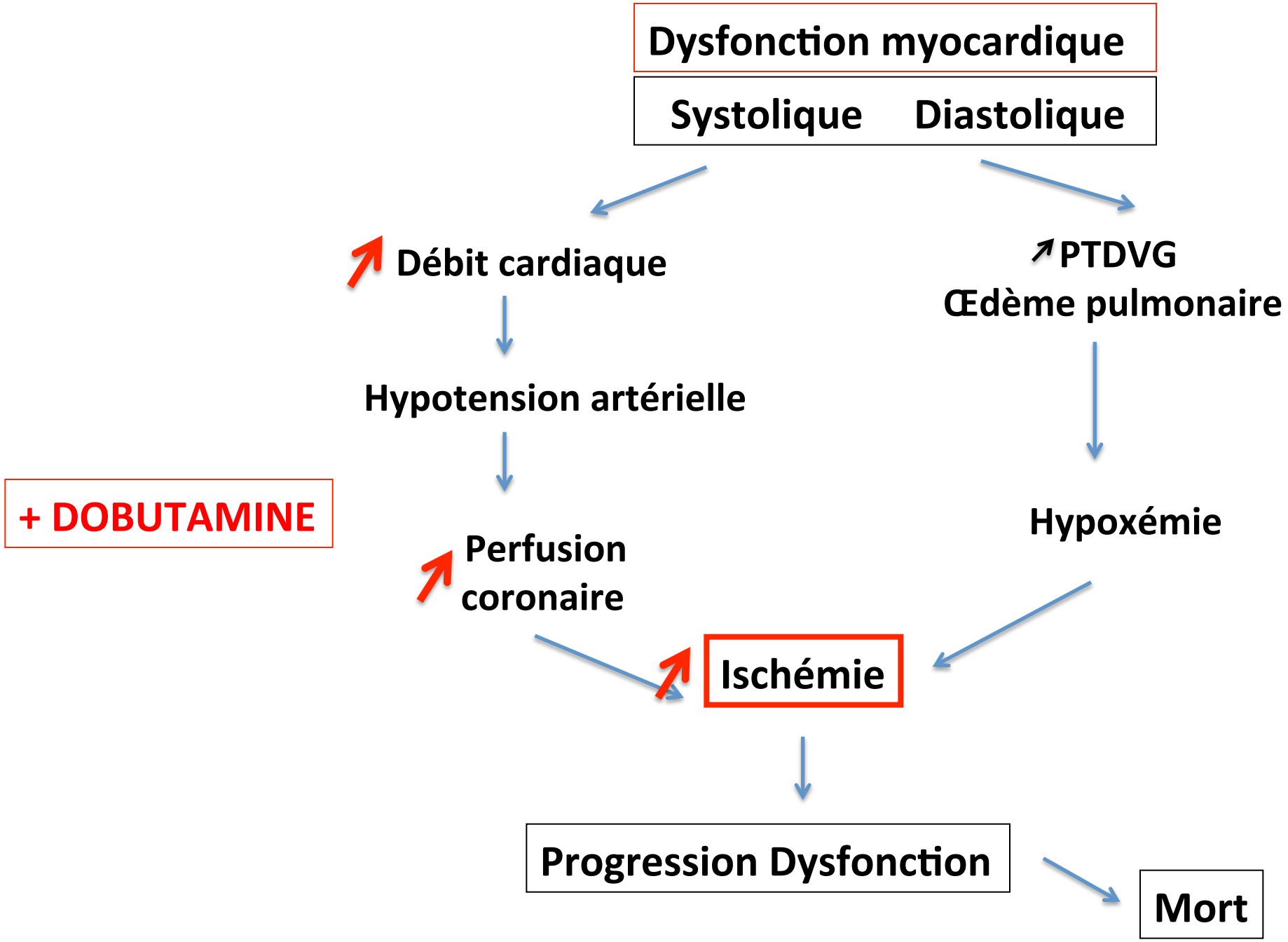




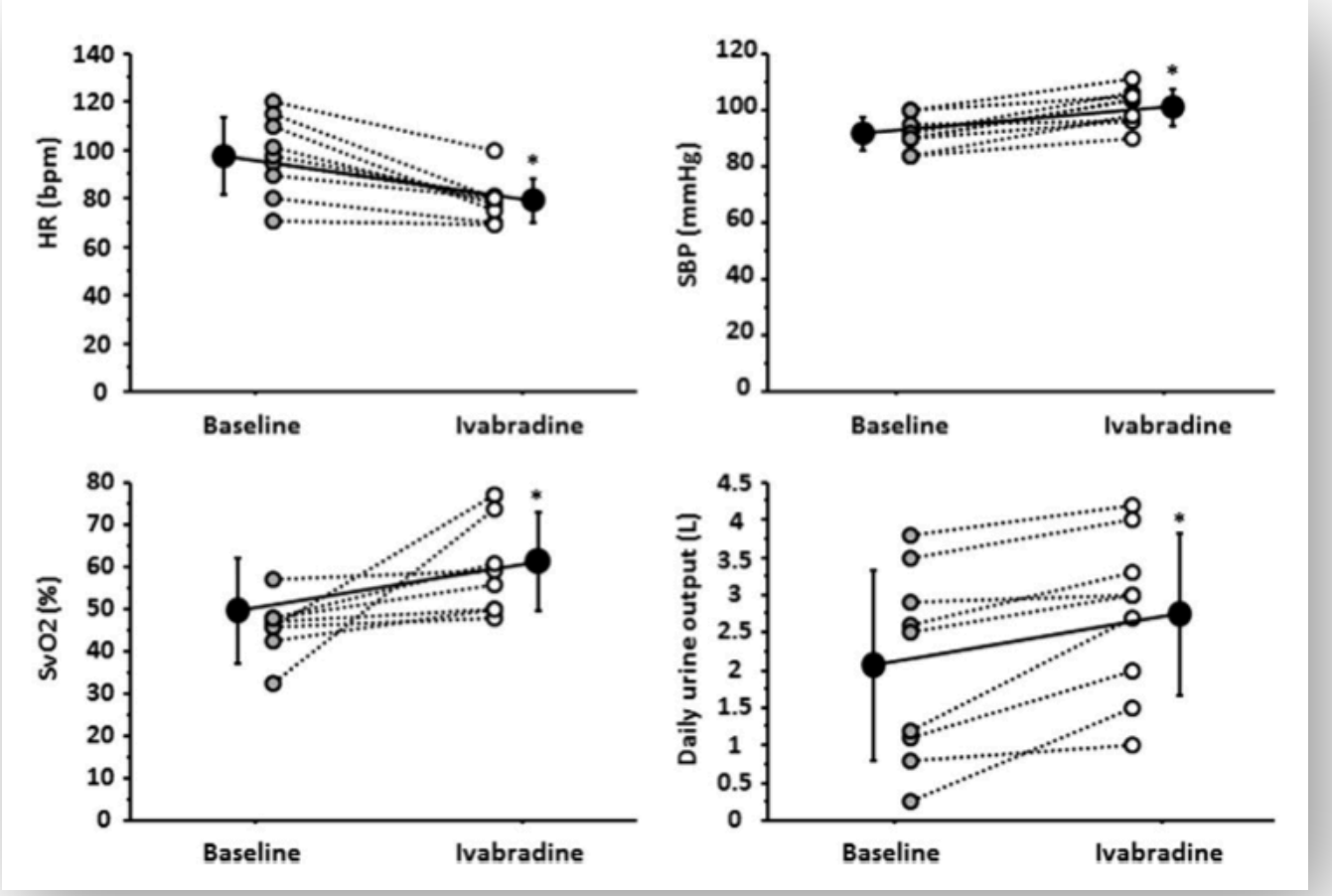
n = 15 dans chaque bras.

Pas d'effet sur la MORTALITE
Pas d'effet sur l'index cardiaque

Levy B et al, Crit Care Med, 2011


Dysfonction myocardique
Systolique
Diastolique
↗ Débit cardiaque
↗PTDVG
Œdème pulmonaire
Hypotension artérielle
+ DOBUTAMINE
Hypoxémie
↗ Perfusion coronaire
↗ Ischémie
Progression Dysfonction
Mort

Hemodynamic effects of Ivabradine in addition to dobutamine in patients with severe systolic dysfunction☆



n = 9

Diminution FC
Augmentation PAS
Augmentation ScvO2
Pas de diminution du débit cardiaque

R. Gallet et al. Inter Jour of Cardiology, 2014

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

n = 16

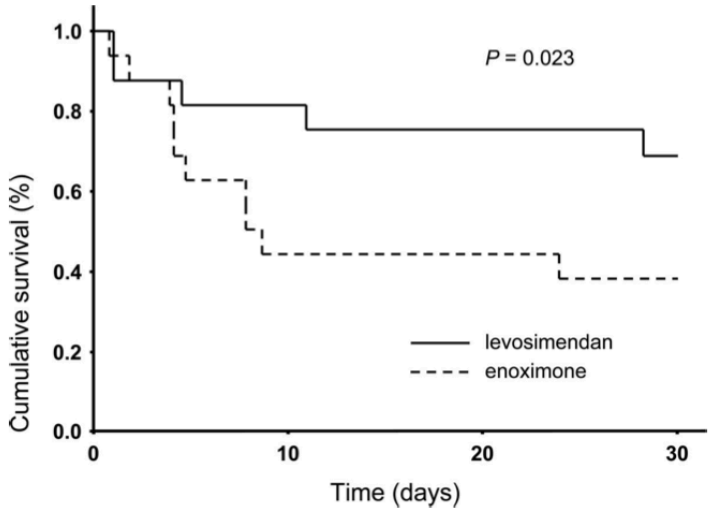


Figure 2. Kaplan-Meier analysis of the 30-day all-cause mortality rate in the levosimendan (*solid line*) and enoximone-treated groups (*broken line*), $p = 0.023$ (log-rank test).

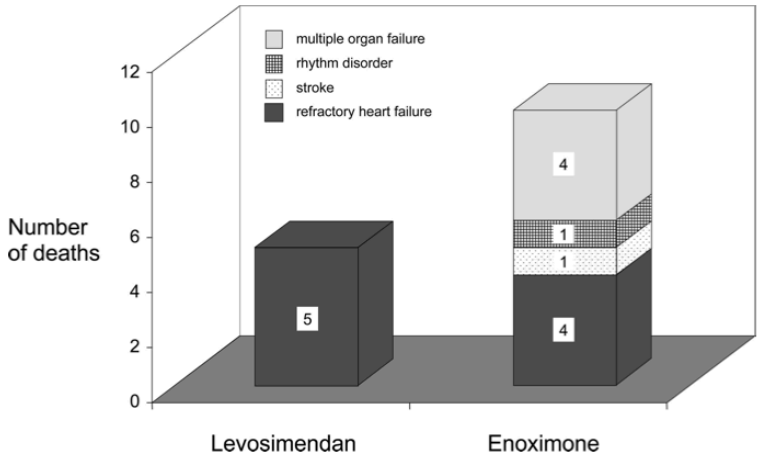


Figure 5. Bar graphs showing causes of death after 30 days in levosimendan- and enoximone-treated patients (refractory heart failure, stroke, rhythm disorder, and multiple organ failure).

Conclusions: **In severe and refractory cardiogenic shock complicating acute myocardial infarction, levosimendan, added to current therapy, may contribute to improved survival compared with enoximone.**

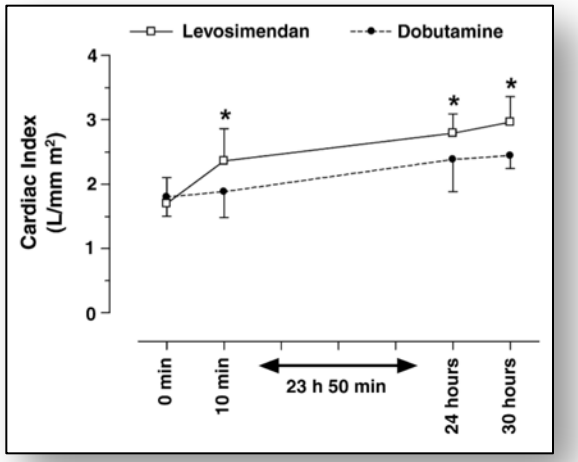
Joerg T et al,Crit Care Med, 2008

Dobutamine Vs Levosimendan

- **Choc cardiogenique. Phase aigue de l'infarctus (n=11)**

  ➔ amélioration de l'index cardiaque

  M.J. Garc´ıa-Gonza´lez et al. / European Journal of Heart Failure 8 (2006)



- **Amélioration fonction diastolique sur des paramètres échographiques (n=11)**

  A. Dominguez-Rodriguez et al. / International Journal of Cardiology 128 (2008)

- **Pas de différence sur la mortalité à long teme (n=11)**

  S. Samimi-Fard et al. / International Journal of Cardiology 127 (2008

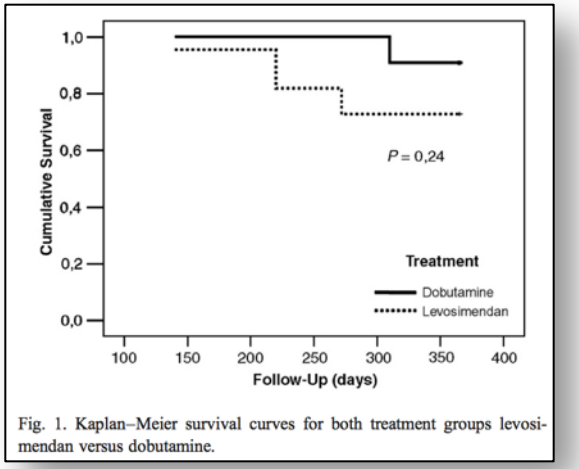


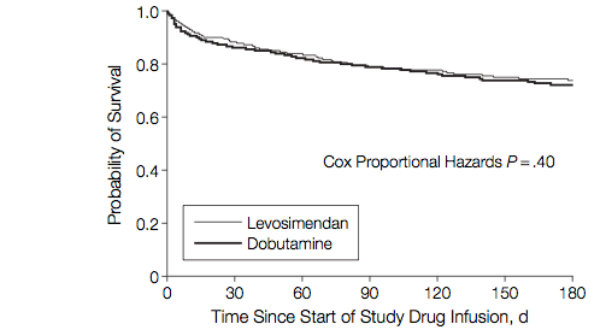
Fig. 1. Kaplan–Meier survival curves for both treatment groups levosimendan versus dobutamine.

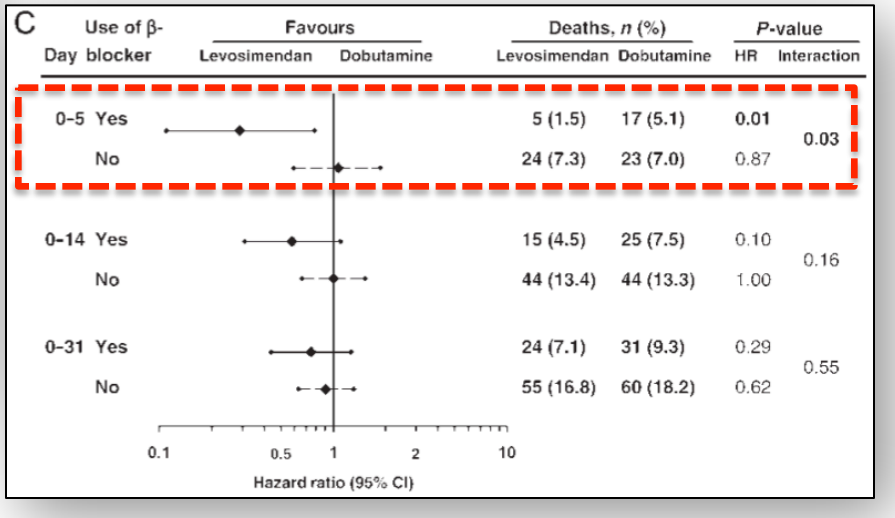
Levosimendan vs Dobutamine for Patients With Acute Decompensated Heart Failure

The SURVIVE Randomized Trial

Alexandre Mebazaa, MD, PhD
Markku S. Nieminen, MD, PhD
Milton Packer, MD
Alain Cohen-Solal, MD, PhD
Franz X. Kleber, MD
Stuart J. Pocock, PhD
Roopal Thakkar, MD
Robert J. Padley, MD
Pentti Põder, MD, PhD
Matti Kivikko, MD, PhD
for the SURVIVE Investigators

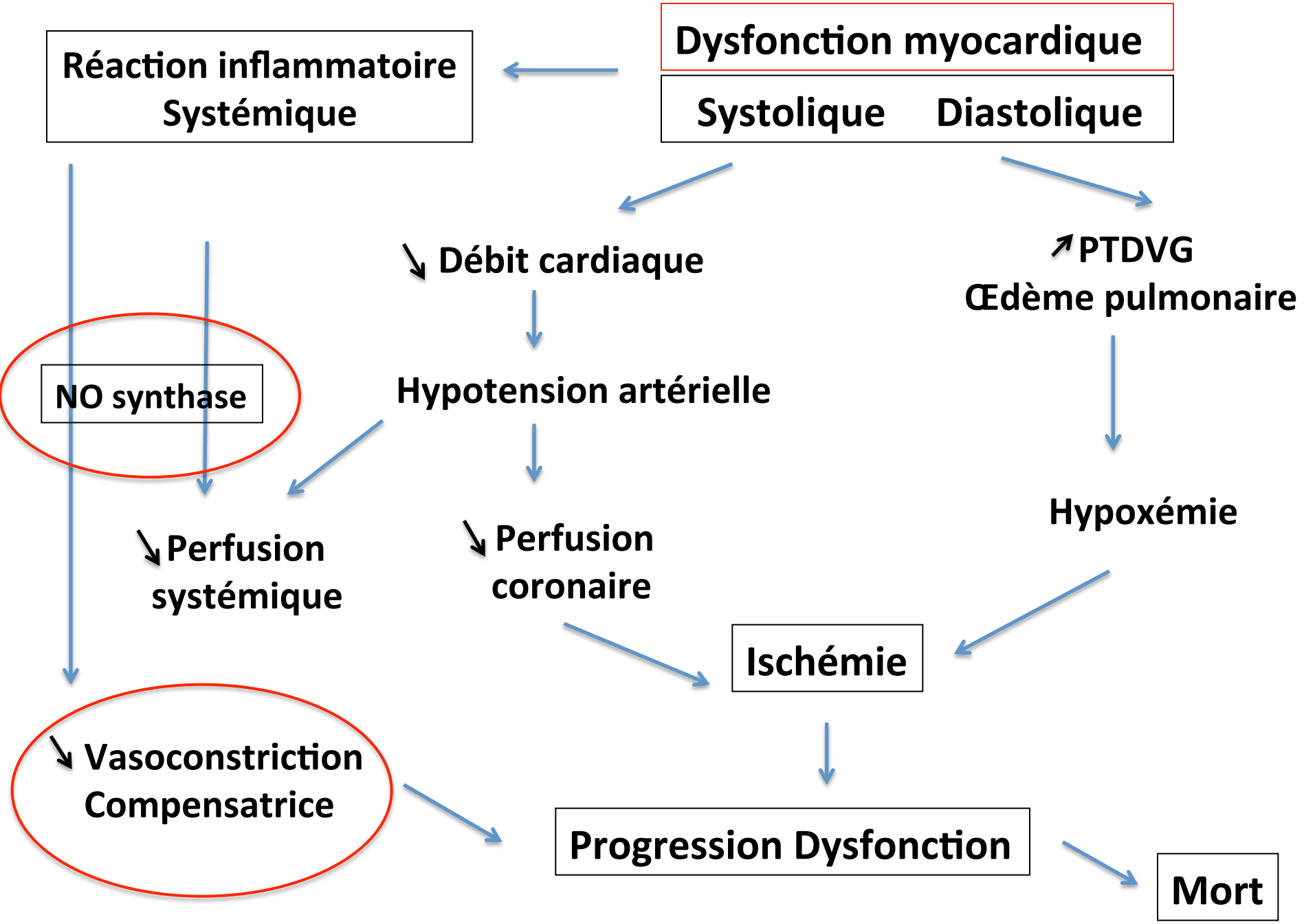
Figure 2. Effect of Dobutamine and Levosimendan Treatment on All-Cause Mortality During 180 Days Following the Start of Study Drug Infusion





Possible bénéfice du Levosimendan
Chez les patients béta-Bloqués

Mebazza et al, ESC, Eur Jour of Heart Fail, 2009


Dysfonction myocardique
Systolique
Diastolique
Réaction inflammatoire
Systémique
↘ Débit cardiaque
↗ PTDVG
Œdème pulmonaire
NO synthase
Hypotension artérielle
↘ Perfusion
systémique
↘ Perfusion
coronaire
Hypoxémie
Ischémie
↘ Vasoconstriction
Compensatrice
Progression Dysfonction
Mort

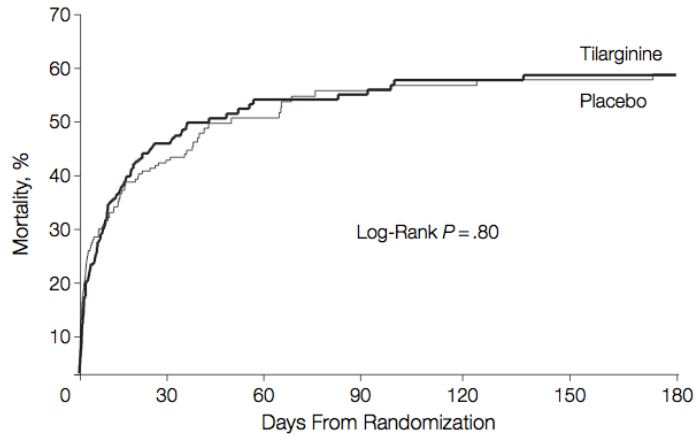
Effect of Tilarginine Acetate in Patients With Acute Myocardial Infarction and Cardiogenic Shock

The TRIUMPH Randomized Controlled Trial

Table 6. Clinical Outcomes at 30 Days

Outcome Overall and by Age*	No./Total (%)		Risk Ratio (95% CI)	*P* Value
	Tilarginine	Placebo		
Mortality at 30 d†	97/201 (48)	76/180 (42)	1.14 (0.92-1.41)	.24
<75 y	57/146 (39)	48/131 (37)	1.06 (0.81-1.37)	
≥75 y	40/54 (74)	27/47 (57)	1.46 (0.97-2.19)	
Mortality at 30 d‡	99/206 (48)	81/190 (43)	1.12 (0.91-1.38)	.28
<75 y	59/150 (39)	51/138 (37)	1.05 (0.82-1.35)	
≥75 y	40/55 (73)	29/50 (58)	1.39 (0.94-2.05)	

Figure 4. Kaplan-Meier Mortality Over 6 Months of Follow-up



No. at Risk							
Tilarginine	204	104	89	86	84	83	78
Placebo	188	106	82	76	73	73	66

The TRIUMPH Investigators, JAMA 2008

Recommandations

ESC Guidelines 2012

GERMAN-AUSTRIAN Guideline 2012

THE COCHRANE COLLABORATION 2014

An i.v. infusion of an inotrope (e.g. dobutamine) should be considered in patients with hypotension (systolic blood pressure <85 mmHg) and/or hypoperfusion to increase cardiac output, increase blood pressure, and improve peripheral perfusion. The ECG should be monitored continuously because inotropic agents can cause arrhythmias and myocardial ischaemia.	IIa	C
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
An i.v. infusion of levosimendan (or a phosphodiesterase inhibitor) may be considered to reverse the effect of beta-blockade if beta-blockade is thought to be contributing to hypoperfusion. The ECG should be monitored continuously because inotropic agents can cause arrhythmias and myocardial ischaemia, and, as these agents are also vasodilators, blood pressure should be monitored carefully.	IIb	C

Possibilité d'utiliser Levosimendan en cas de choc réfractaire

Conclusion

- Mortalité élevée
- Pas de révolution dans les traitements inotropes
- Place du levosimendan à préciser : Myocardite/ TAKO-TSUBO/Dysfonction cardiaque du sepsis
- Interêt du tt étiologique
- Quelle assistance circulatoire….