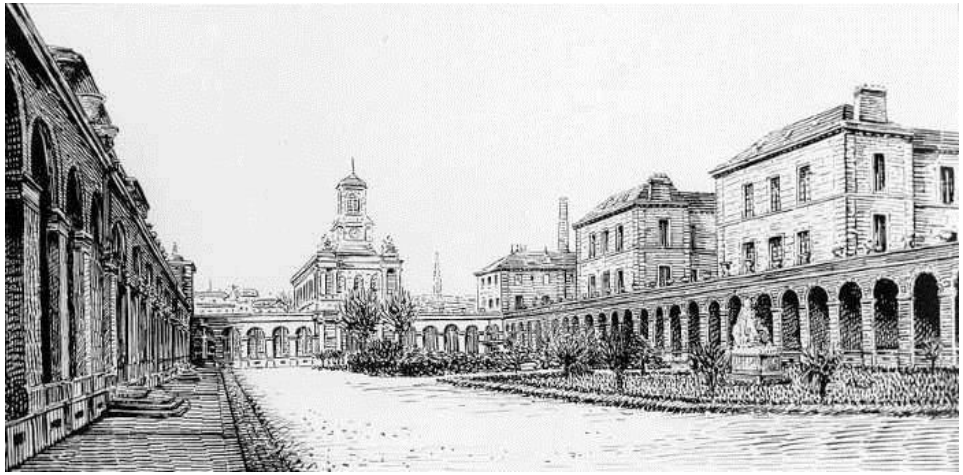
Le choc cardiogénique, pas si simple …:
dobutamine, noradrénaline ou adrénaline ?



Alexandre Mebazaa

Département d'Anesthésie-Réanimation

Hôpitaux Universitaires Saint Louis – Lariboisière

Université Paris 7; INSERM – UMR 942

Conflicts of interest

Honorarium for lectures

- Orion, Abbott, Novartis, Roche

Consultant:

- BMS, Cardiorentis, Novartis, Sphingotec, Sanofi

Messages principaux

- **ICA sans choc:**
  - *Mécanisme* : « congestion »
  - *Traitement initial* : Diurétiques/dérivés nitrés pas d'inotropes

- **Choc cardiogénique**
  - 1) **si bas débit cardiaque + infarctus du myocarde/Post-Arrêt cardiaque**
    - Premier médicament : norépinéphrine +/- inotrope si besoin
  - 2) **si insuffisance ventriculaire droite**
    - Premier médicament : norépinéphrine +/- inotrope si besoin
  - 3) **pas d'adrénaline : dans tous les cas!**

Intensive Care Med
DOI 10.1007/s00134-015-3659-7

Mattia Arrigo
Alexandre Mebazaa

Understanding the differences among inotropes

	Dobutamine	Adrenaline	Milrinone	Levosimendan
Substance class	Catecholamines	Catecholamines	PDE III inhibitor	Calcium sensitizer
Mechanism of inotropic effect	Beta-adrenergic receptor-mediated increase of cAMP synthesis	Beta-adrenergic receptors-mediated increase of cAMP synthesis	Decreased breakdown of cAMP through inhibition of PDE III	Enhanced troponin C sensitivity to intracellular calcium
Half-life	2–3 min	2 min	2 h	1 h, metabolite (OR-1896) up to 80 h
Common IV infusion (mcg/kg/min)	2–20	0.01–0.10	0.375–0.750	0.05–0.20
Frequent adverse effects	Hypotension (14 %), ventricular arrhythmia (7 %), chest pain (7 %), atrial fibrillation (6 %) [15]	Supraventricular tachycardia (12 %), ventricular arrhythmia (7 %), acute coronary events (3 %) [12]	Hypotension (7 %), atrial fibrillation (3 %), ventricular arrhythmia (2–4 %); increased events in ischaemic heart disease [3]	Hypotension (15 %), atrial fibrillation (9 %), ventricular arrhythmia (8 %), headache (8 %) [15]

Arrigo M & Mebazaa A; Intensive Care Med, 2015; 5: 912-915

Intensive Care Med
DOI 10.1007/s00134-015-4041-5

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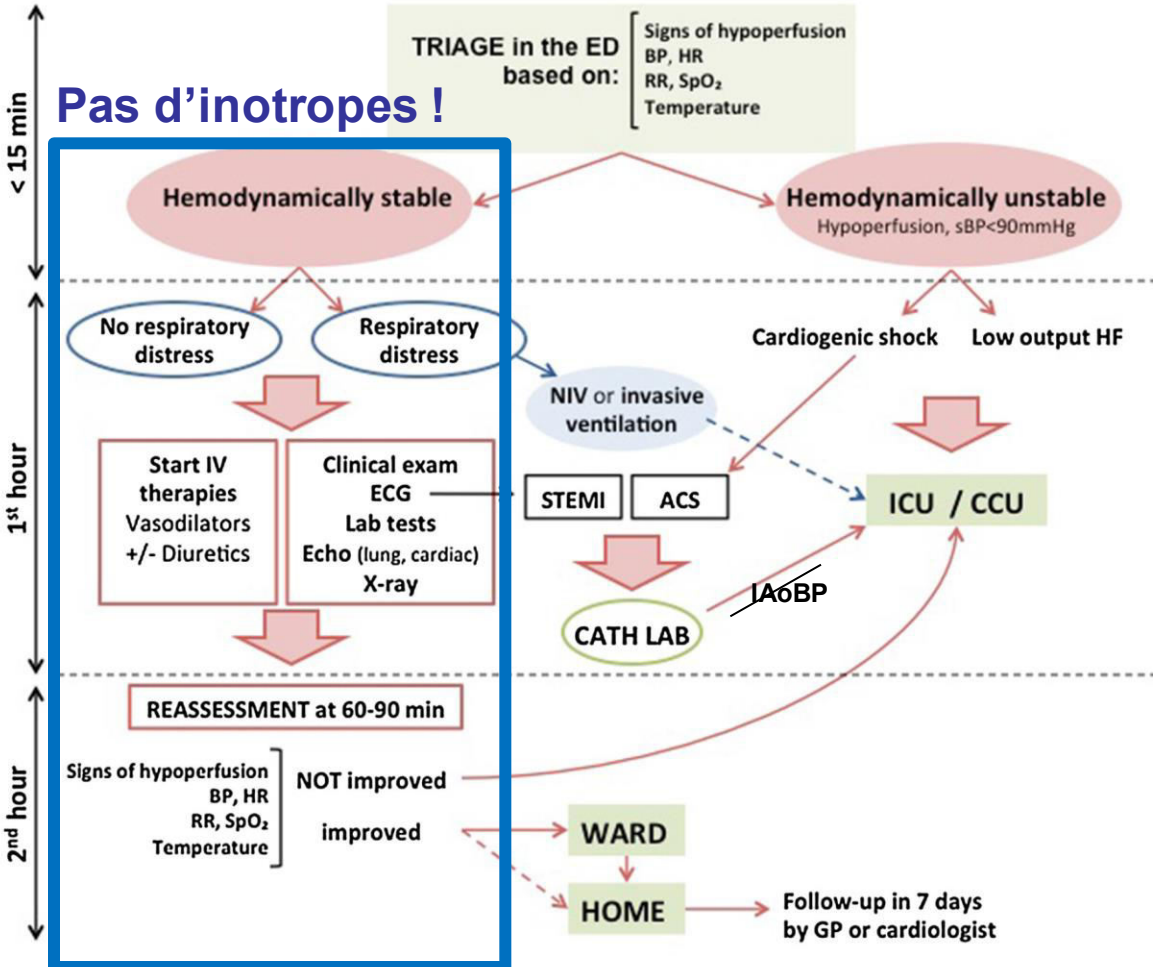
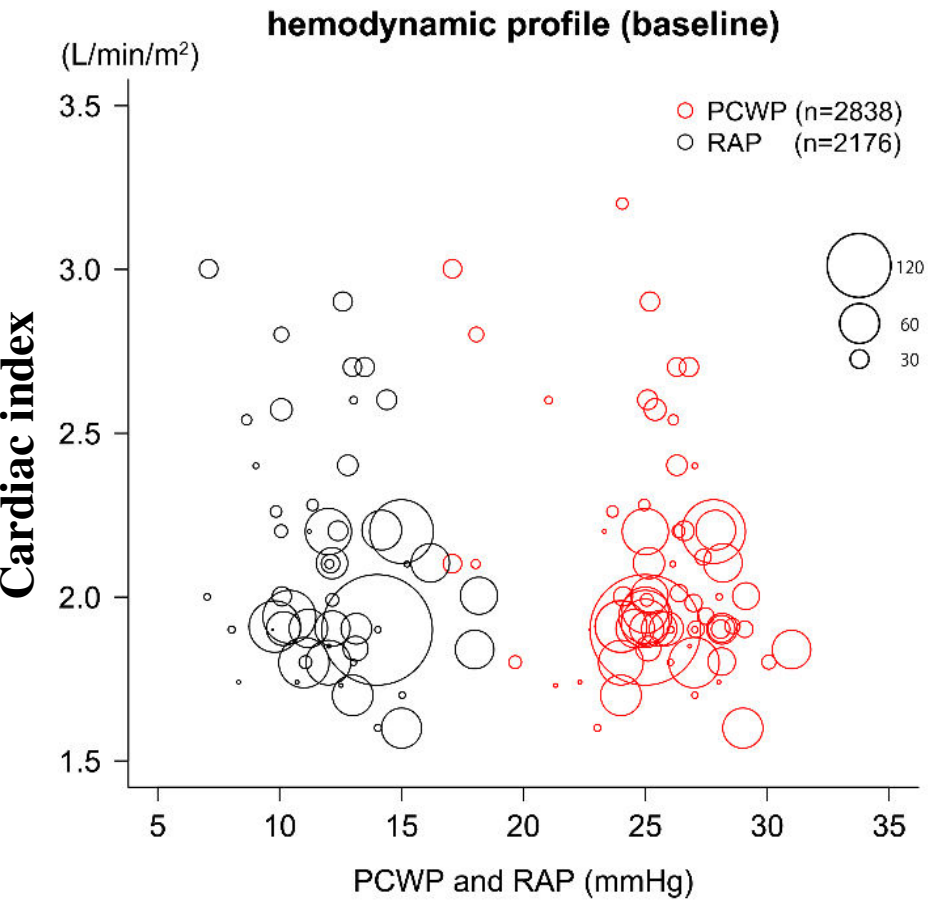
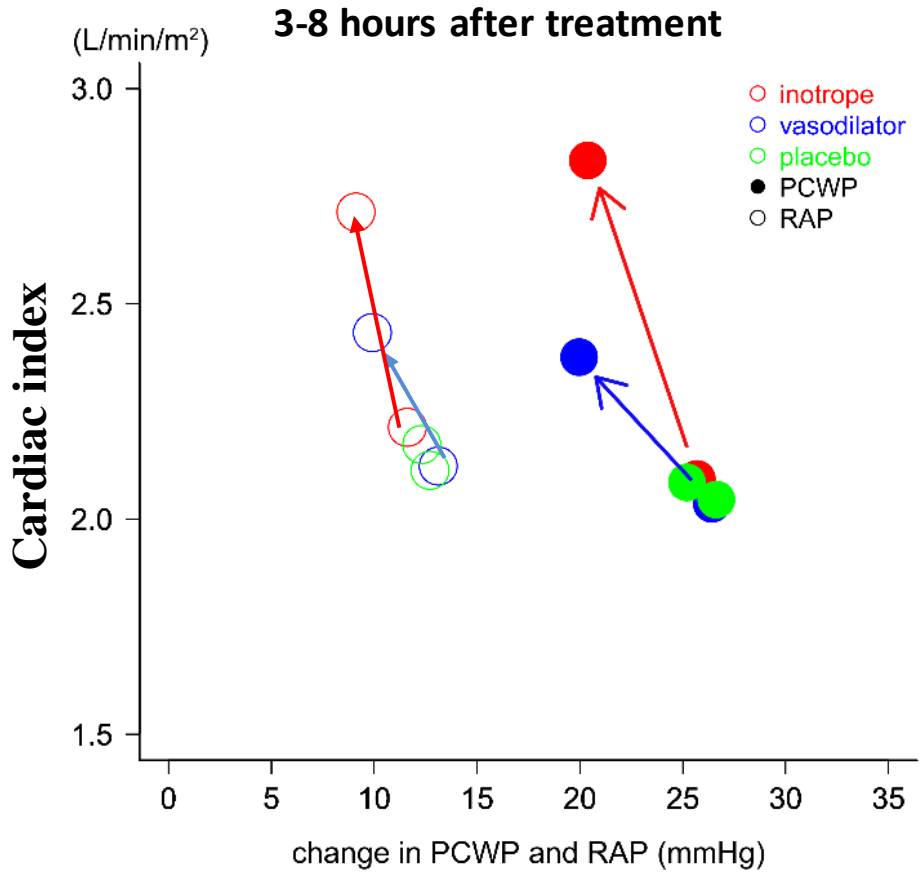
Acute heart failure and cardiogenic shock: a multidisciplinary practical guidance



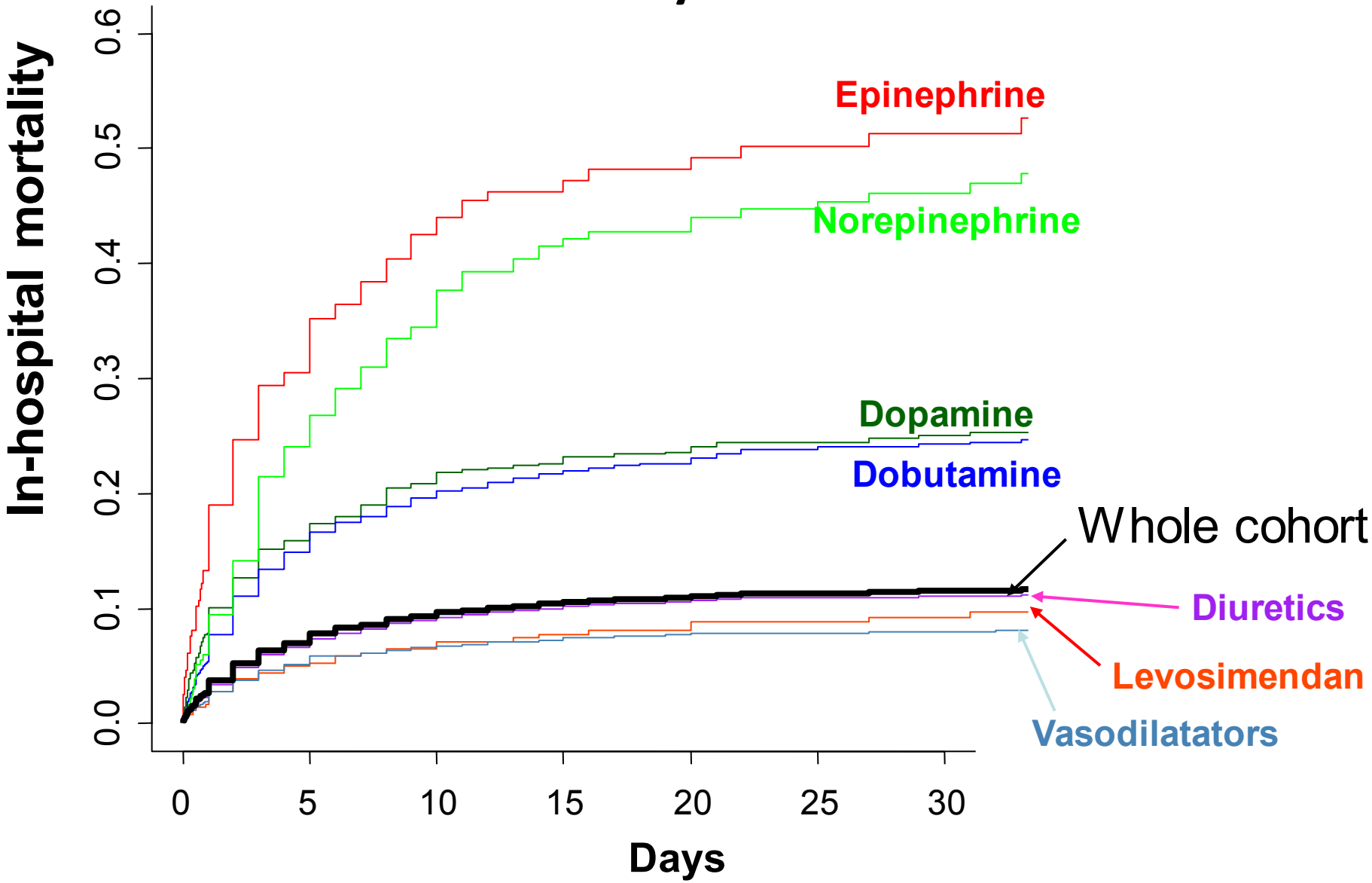
Invasive hemodynamics at baseline and after treatment in AHF: results of a meta-analysis





Ishihara et al Clin Res Cardiol 2016.

Effect of IV drugs in-hospital mortality: propensity score analysis



Mebazaa et al Intensive Care Medicine 2011

EUROPEAN SOCIETY OF CARDIOLOGY®

European Journal of Heart Failure (2017)
doi:10.1002/ejhf.991

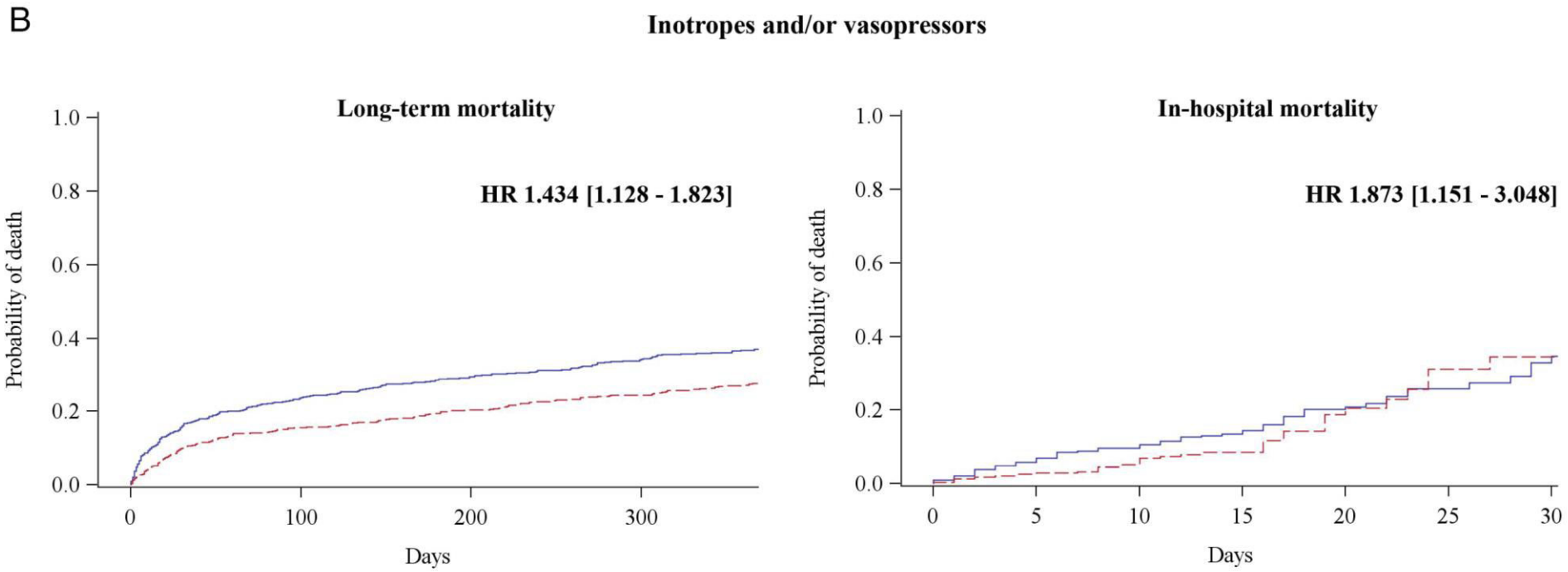
RESEARCH ARTICLE

Long-term safety of intravenous cardiovascular agents in acute heart failure: results from the European Society of Cardiology Heart Failure Long-Term Registry

Alexandre Mebazaa[1,2,3]*, Justina Motiejunaite[1,2,4], Etienne Gayat[1,2,3], Maria G. Crespo-Leiro[5], Lars H. Lund[6], Aldo P. Maggioni[7], Ovidiu Chioncel[8], Eiichi Akiyama[1,9], Veli-Pekka Harjola[10], Petar Seferovic[11], Cecile Laroche[12], Marisa Sanz Julve[13], Eulalia Roig[14], Frank Ruschitzka[15], and Gerasimos Filippatos[16], on behalf of the ESC Heart Failure Long-Term Registry Investigators

Mebazaa A et al Eur J Heart Failure 2017

Heart Failure Association:ESC-Long term registry: propensity matching



Mebazaa A et al Eur J Heart Failure 2017

All catecholamines are not equal!

Table 3 Duration and dosage of treatment with intravenous inotropes and/or vasopressors and their association with long-term all-cause death

Inotrope/vasopressor (whole cohort, *n* = 833)	**Dobutamine (*n* = 354)**	**Dopamine (*n* = 206)**	**Levosimendan (*n* = 109)**	**Norepinephrine (*n* = 45)**	**Epinephrine (*n* = 14)**
Hours of treatment					
Mean ± SD	42.5 ± 29.9	43.4 ± 32.3	24.8 ± 6.3	40.2 ± 28.3	37.6 ± 41.7
Median (IQR)	36.0 (23.0–72.0)	36.0 (20.0–72.0)	24.0 (24.0–24.0)	35.0 (17.0–60.0)	22.0 (1.0–72.0)
Long-term all-cause death, %	37.9	49.0	38.5	55.6	64.3
Inotrope/vasopressor (matched cohort, *n* = 606)	**Dobutamine (*n* = 512)**	**Dopamine (*n* = 314)**	**Levosimendan (*n* = 168)**	**Norepinephrine (*n* = 36)**	**Epinephrine (*n* = 16)**
HR (95% CI) for long-term all-cause death	1.055 (0.727–1.531)	**1.628 (1.031–2.572)**	1.229 (0.618–2.445)	3.762 (0.903–15.663)	NA

Mebazaa A et al Eur J Heart Failure 2017

Intensive Care Med
DOI 10.1007/s00134-015-4041-5

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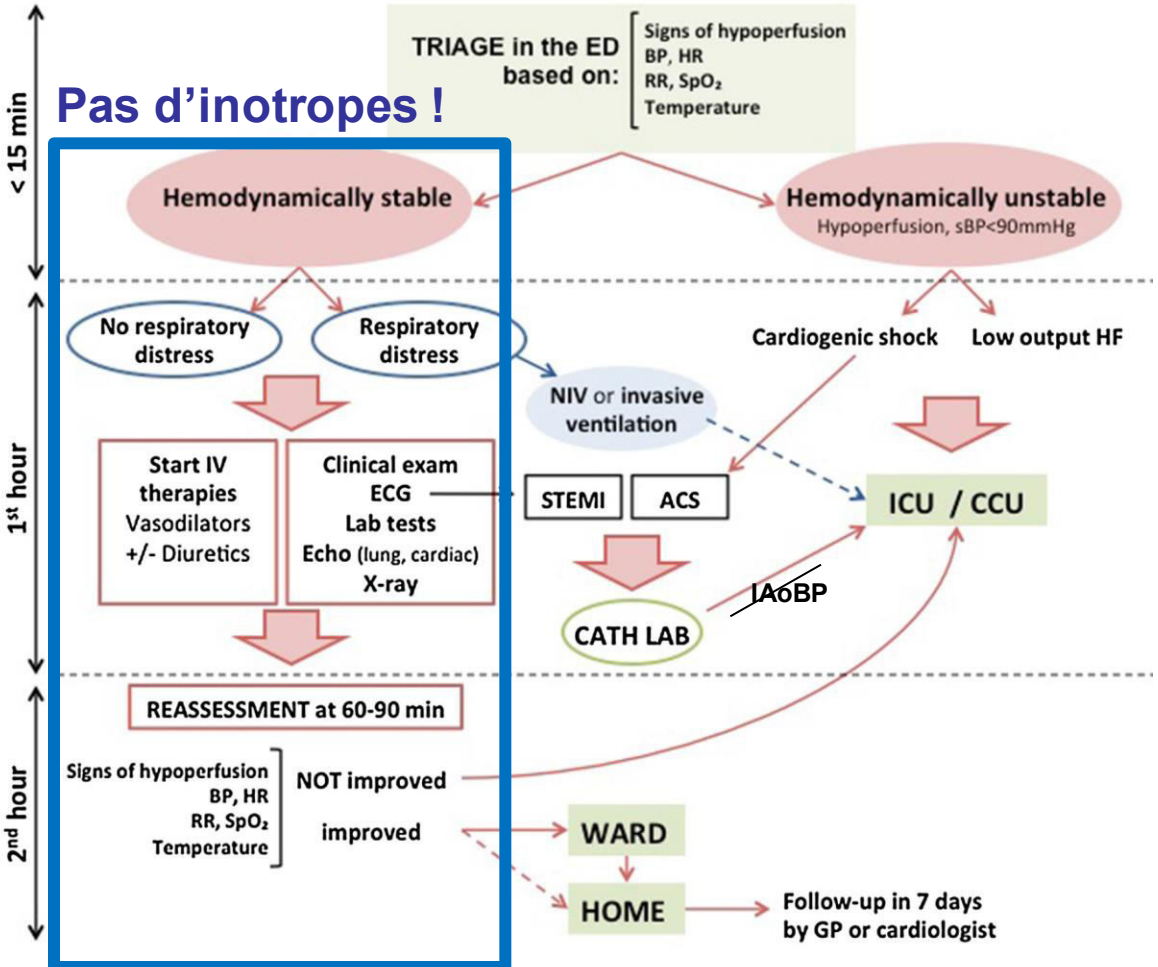
Acute heart failure and cardiogenic shock: a multidisciplinary practical guidance



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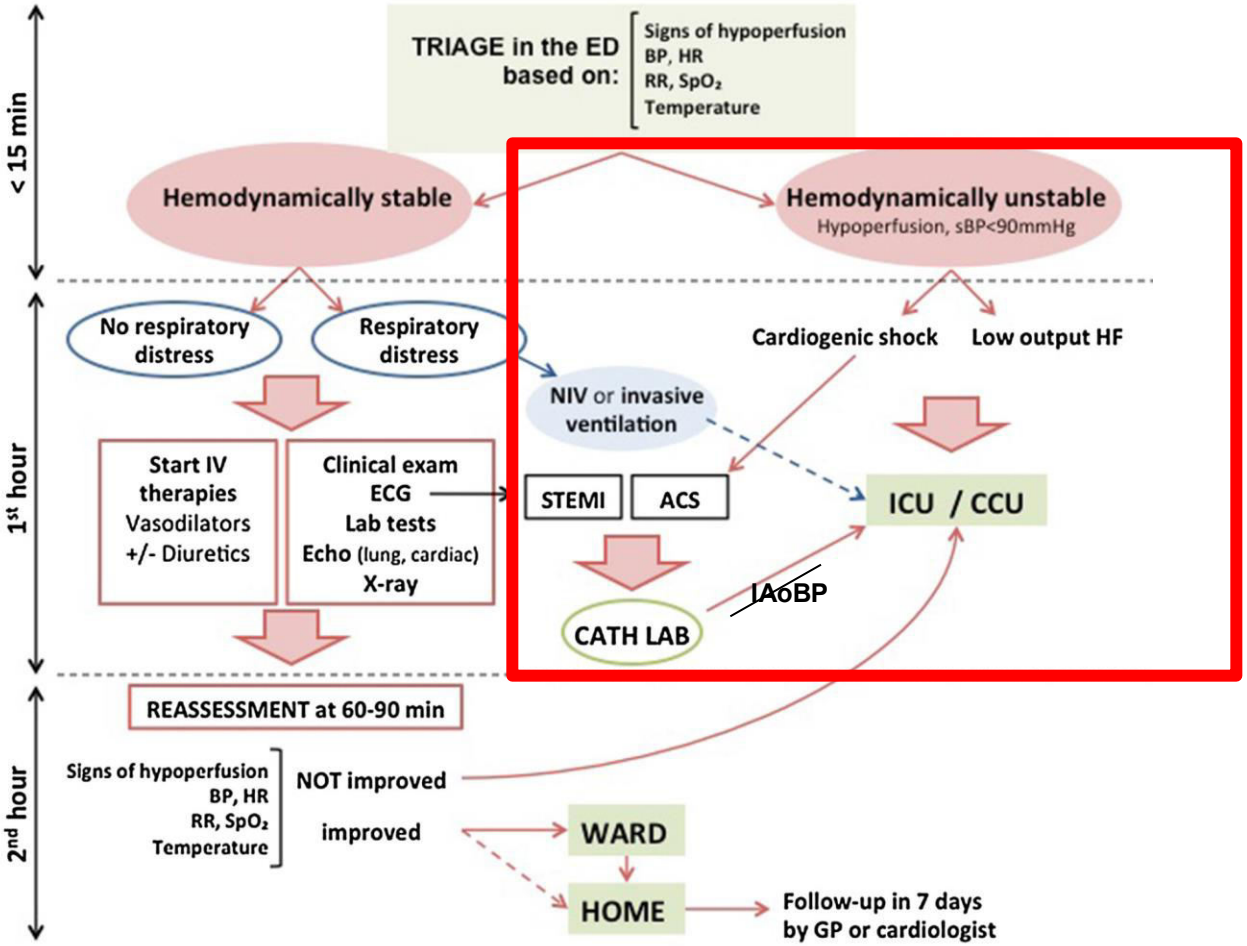


EUROPEAN SOCIETY OF CARDIOLOGY®

European Journal of Heart Failure (2015) **17**, 501–509
doi:10.1002/ejhf.260

Clinical picture and risk prediction of short-term mortality in cardiogenic shock

Veli-Pekka Harjola[1*,†], Johan Lassus[2†], Alessandro Sionis[3], Lars Køber[4], Tuukka Tarvasmäki[5], Jindrich Spinar[6], John Parissis[7], Marek Banaszewski[8], Jose Silva-Cardoso[9], Valentina Carubelli[10], Salvatore Di Somma[11], Heli Tolppanen[2], Uwe Zeymer[12], Holger Thiele[13], Markku S Nieminen[2], and Alexandre Mebazaa[14], for the CardShock study investigators and the GREAT network

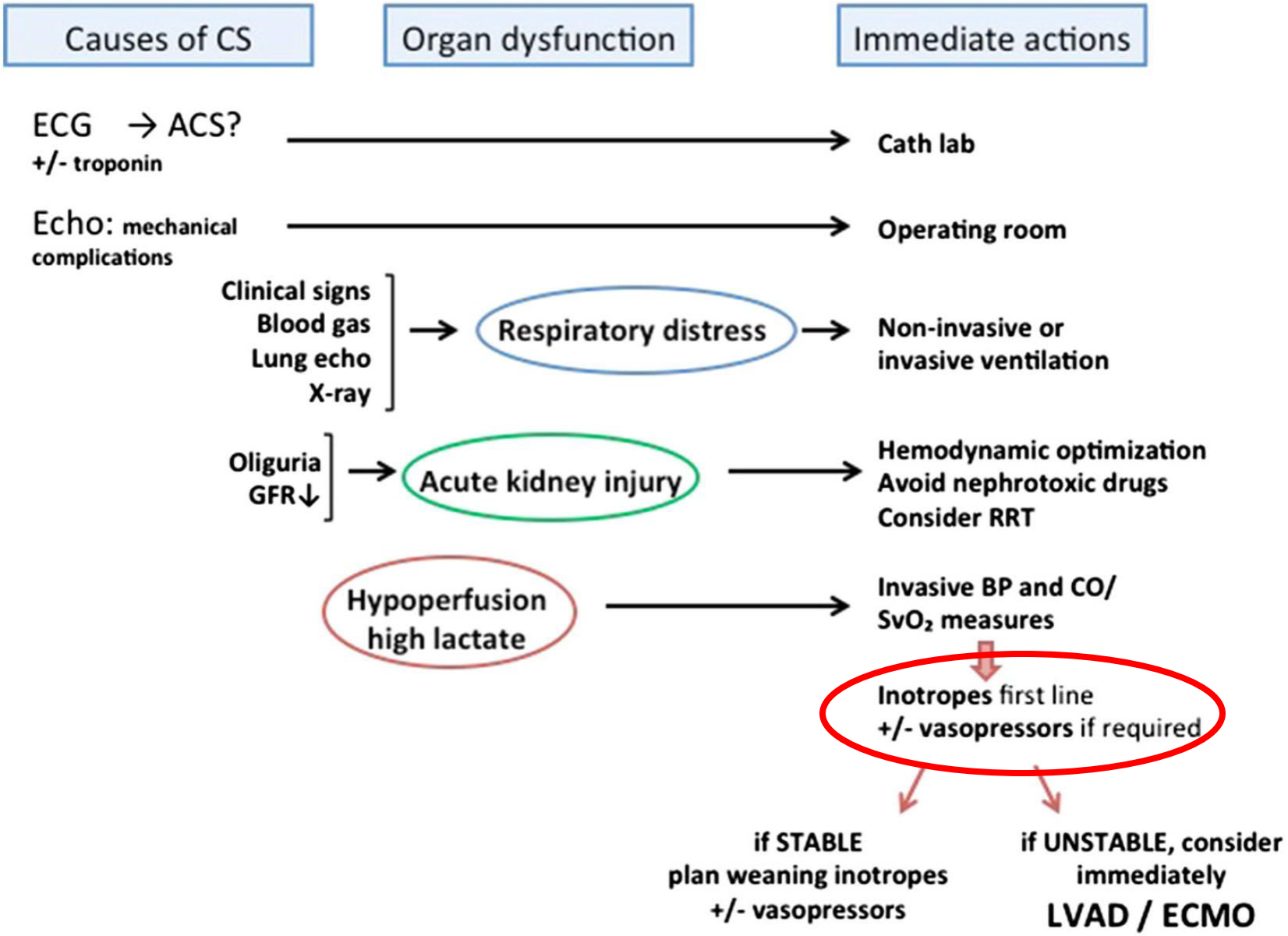
VP Harjola et al, Eur J Heart Failure 2015

CardShock: patients characteristics

Characteristic	All ($n = 219$)
Systolic blood pressure, mmHg	78 (14)
Diastolic blood pressure, mmHg	47 (10)
Mean arterial pressure, mmHg	57 (11)
Heart rate, b.p.m.	90 (28)
Sinus rhythm	170 (78)
Clinical findings, *n* (%)	
Cold periphery	207 (95)
Confusion	148 (68)
Oliguria	121 (55)
Lactate >2 mmol/L	155 (71)

VP Harjola et al, Eur J Heart Failure 2015

CARDIOGENIC SHOCK (CS)



Mebazaa et al. Intensive Care Medicine 2016

HF guidelines 2016

Inotropic agents – dobutamine, dopamine, levosimendan, phosphodiesterase III (PDE III) inhibitors
Short-term, i.v. infusion of inotropic agents may be considered in patients with hypotension (SBP <90 mmHg) and/or signs/ symptoms of hypoperfusion despite adequate filling status, to increase cardiac output, increase blood pressure, improve peripheral perfusion and maintain end-organ function.
An intravenous infusion of levosimendan or a PDE III inhibitor may be considered to reverse the effect of beta-blockade if beta-blockade is thought to be contributing to hypotension with subsequent hypoperfusion.
Inotropic agents are not recommended unless the patient is symptomatically hypotensive or hypoperfused because of safety concern.
Vasopressors
A vasopressor (norepinephrine preferably) may be considered in patients who have cardiogenic shock, despite treatment with another inotrope, to increase blood pressure and vital organ perfusion.
It is recommended to monitor ECG and blood pressure when using inotropic agents and vasopressors, as they can cause arrhythmia, myocardial ischaemia, and in the case of levosimendan and PDE III inhibitors also hypotension. In such cases intra-arterial blood pressure measurement may be considered.

Ponikowski P et al, Heart Failure Guidelines, Eur Heart J, 2016

Tarvasmäki *et al. Critical Care* (2016) 20:208
DOI 10.1186/s13054-016-1387-1

Critical Care

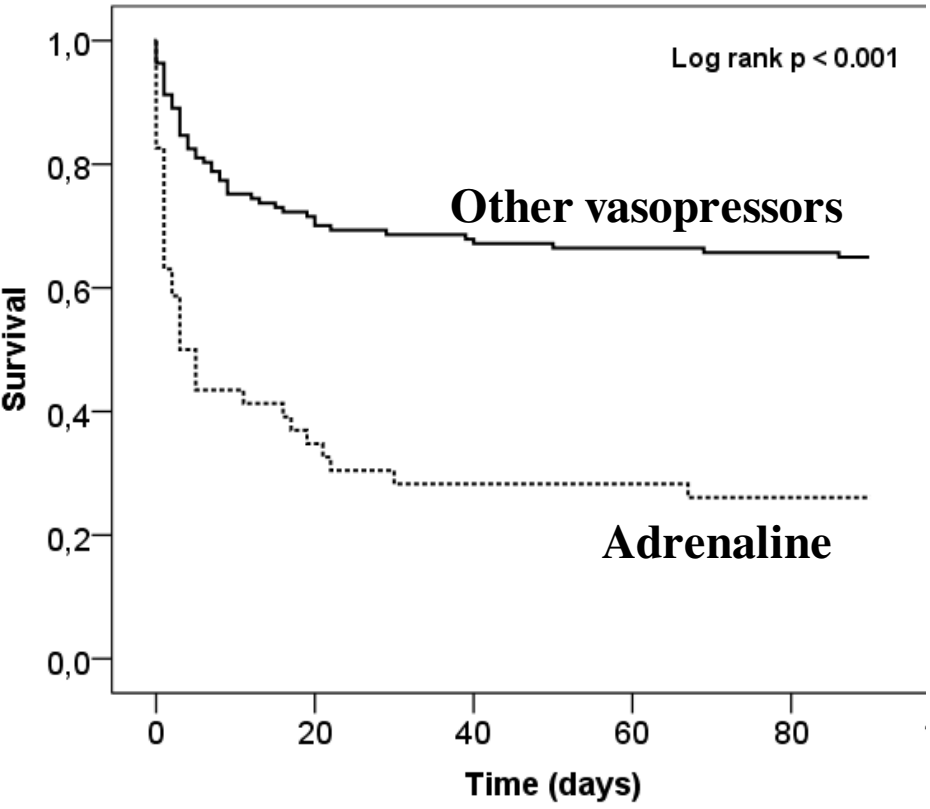
RESEARCH Open Access

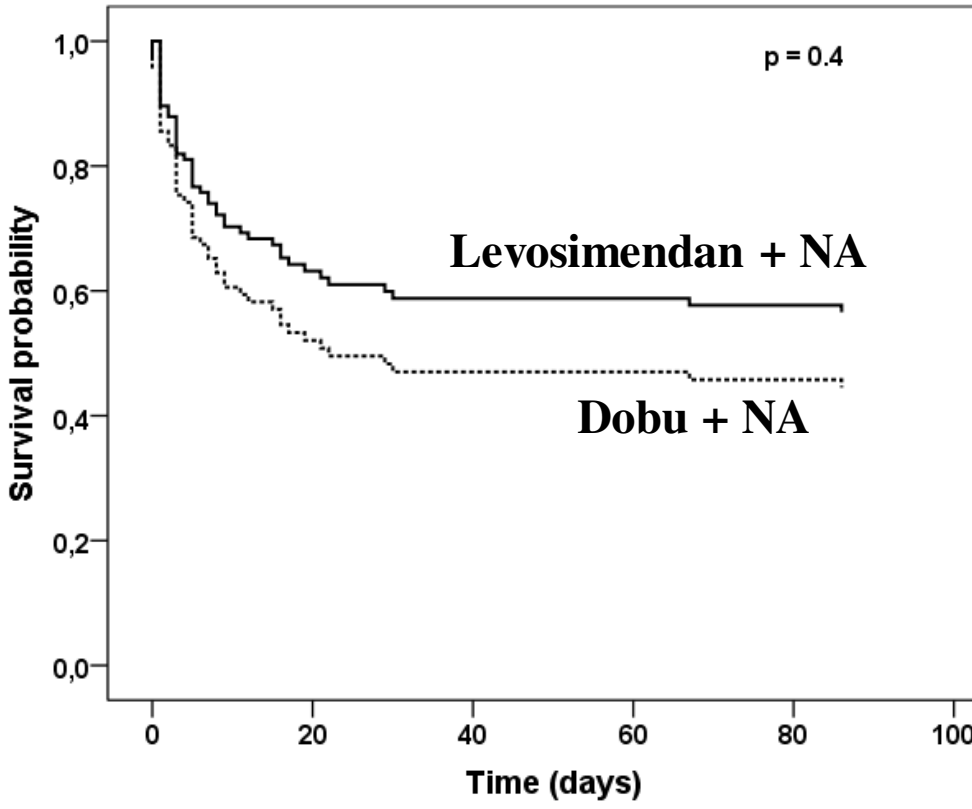
Current real-life use of vasopressors and inotropes in cardiogenic shock - adrenaline use is associated with excess organ injury and mortality

Tuukka Tarvasmäki[1*], Johan Lassus[2], Marjut Varpula[2], Alessandro Sionis[3], Reijo Sund[4], Lars Køber[5], Jindrich Spinar[6], John Parissis[7], Marek Banaszewski[8], Jose Silva Cardoso[9], Valentina Carubelli[10], Salvatore Di Somma[11], Alexandre Mebazaa[12], Veli-Pekka Harjola[1] and for the CardShock study investigators

Tarvasmäki T et al. Crit Care 2016

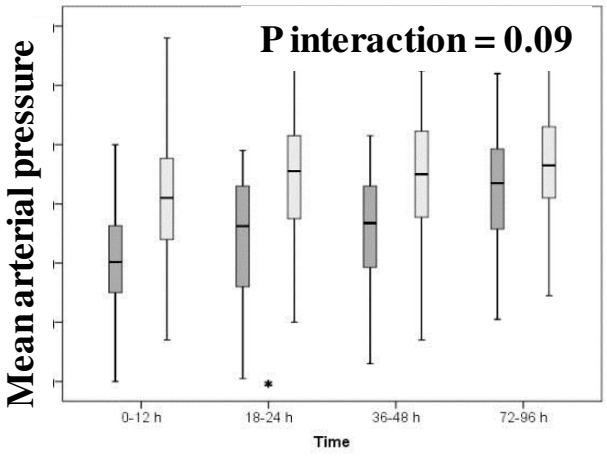
CardShock: Adrenaline is the worse vasopressor in cardiogenic shock secondary to ACS

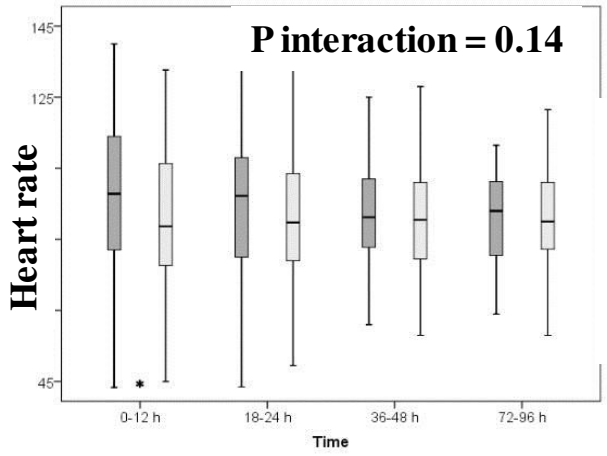


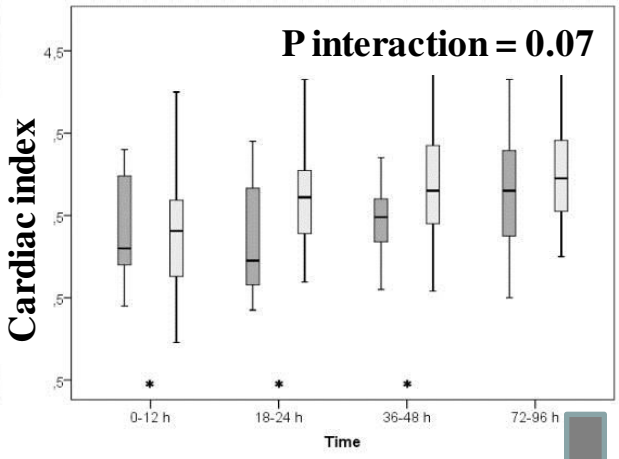


Tarvasmäki T et al. Crit Care 2016

CardShock: Detrimental effect of adrenaline on organ function (regardless to resuscitation)







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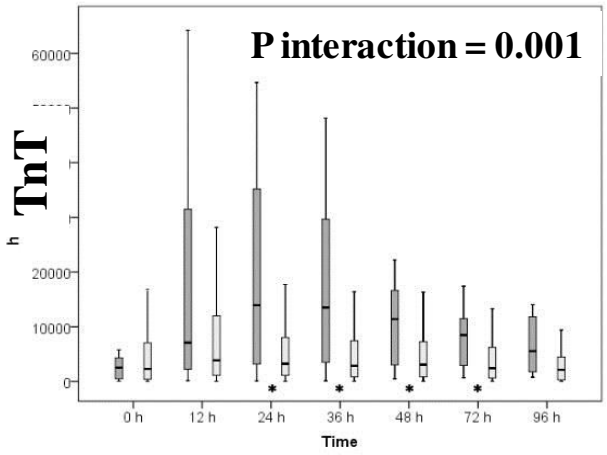
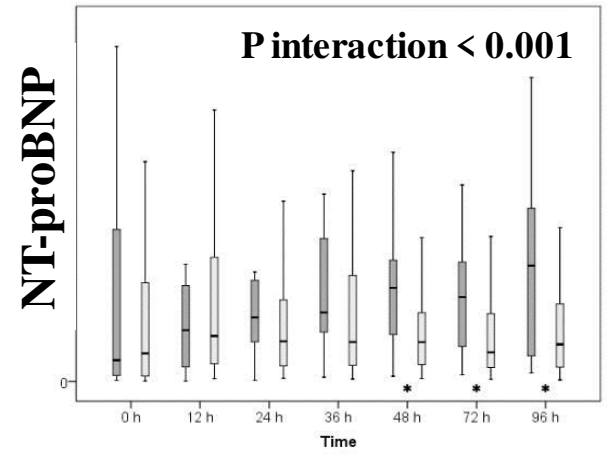
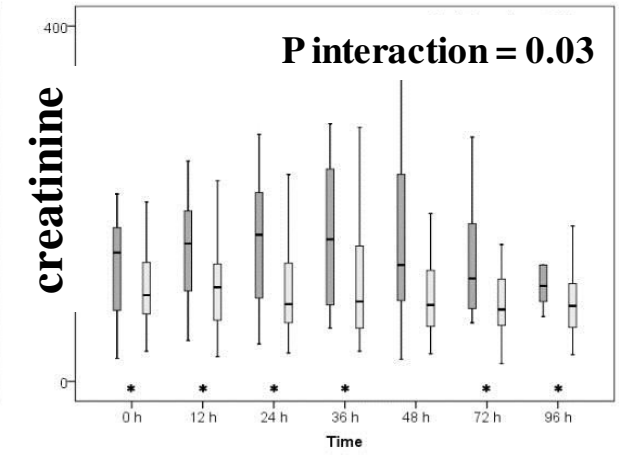


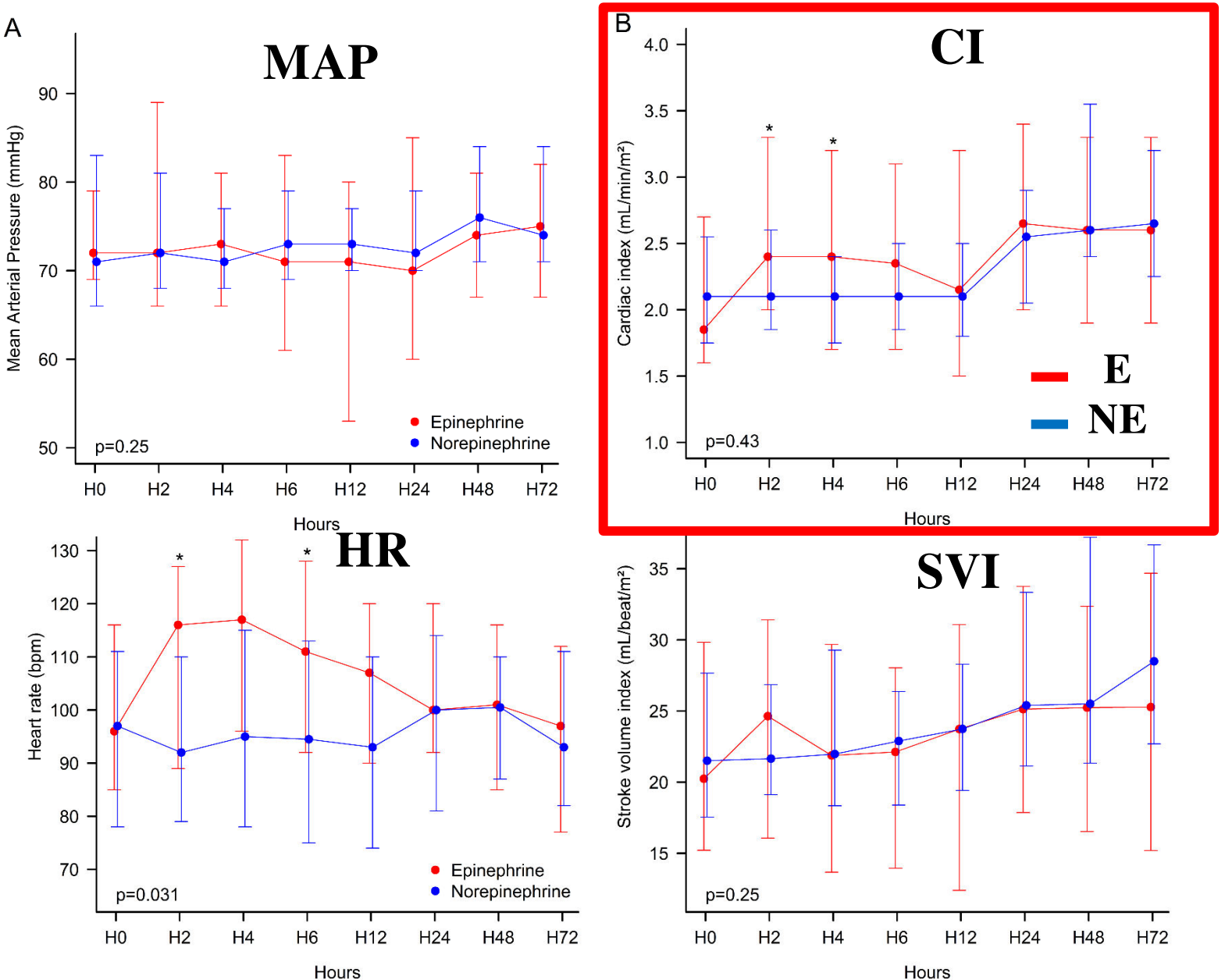




Tarvasmäki T et al. Crit Care 2016

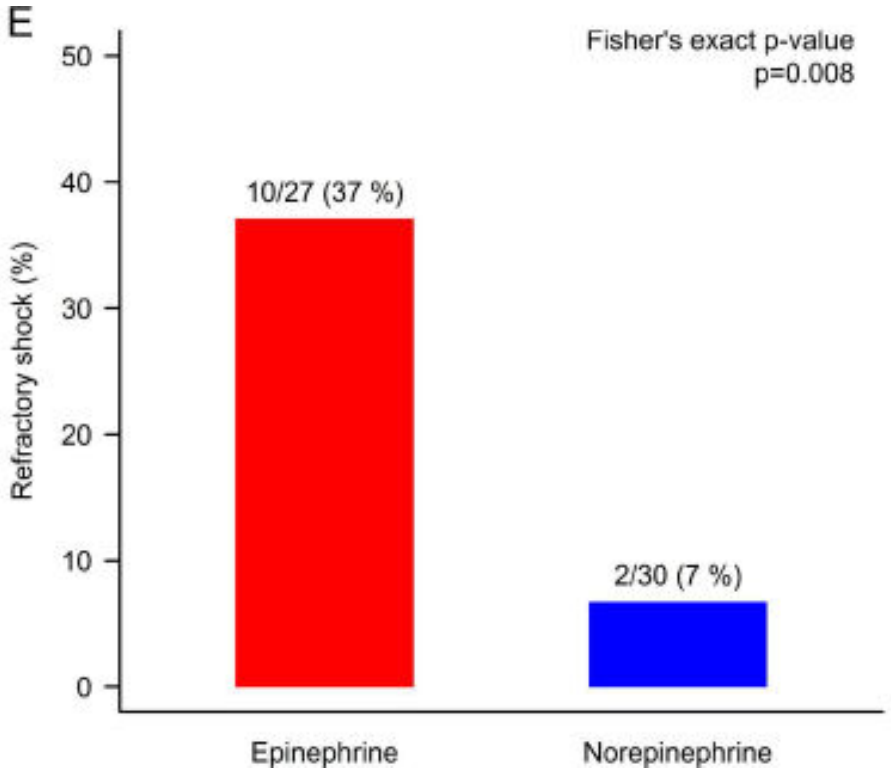
Epinephrine vs NE in CS: primary endpoint

B Levy et al. Epinephrine vs NE in CS. J Am Coll Cardiol, 2018

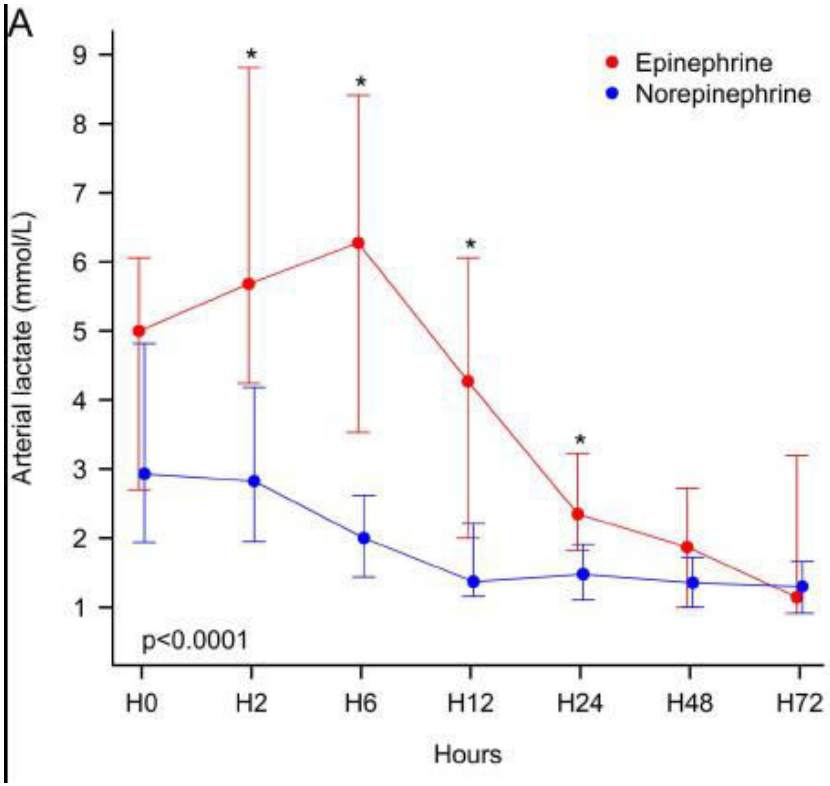


OPTIMA – CC: Epinephrine versus norepinephrine in cardiogenic shock

% Refractory Shock



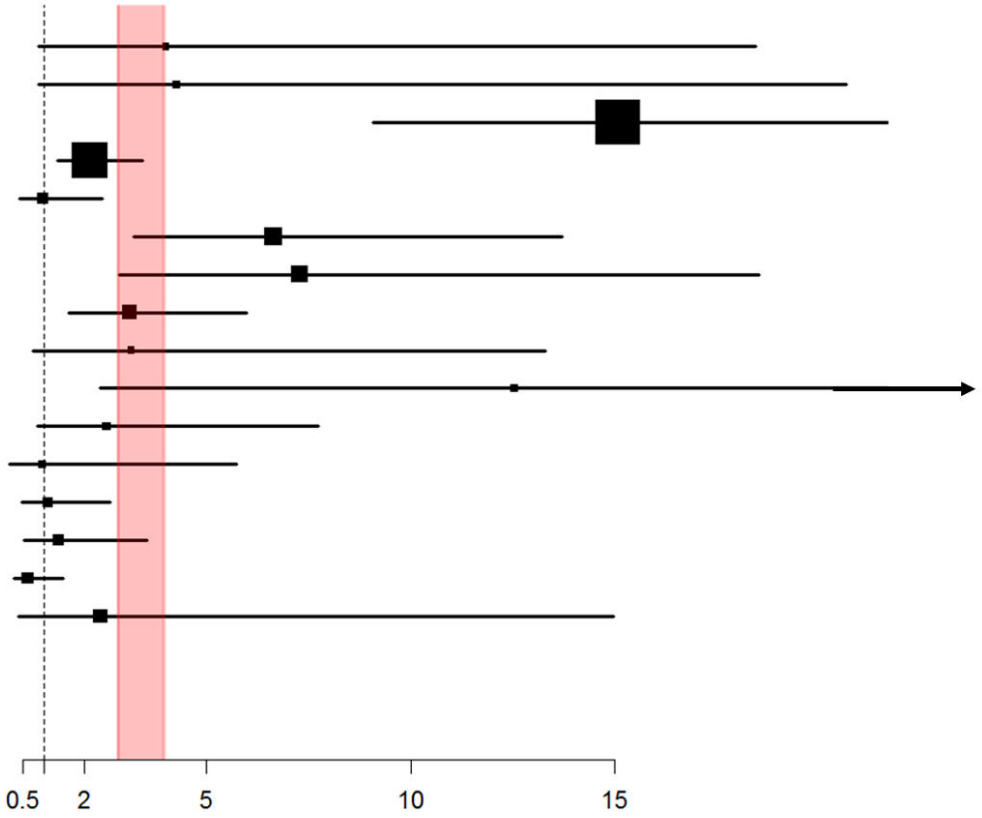
Arterial lactate



Levy B et al, J American Coll Cardiol, 2018

Epinephrine and short-term survival in cardiogenic shock: An individual data meta-analysis of 2,583 patients.

	No. of patients	No. of patients receiving epinephrine	OR for short-term mortality [95% CI]
Adler, 2012	40	10	4.00 [0.87 - 18.45]
Adler,unpublished	47	9	4.27 [0.88 - 20.67]
AHEAD, 2011	674	304	15.08 [9.08 - 25.05]
ALARM, 2011	520	86	2.14 [1.34 - 3.42]
Chua, 2011	105	80	0.99 [0.40 - 2.45]
CARDSHOCK, 2016	219	46	6.64 [3.22 - 13.71]
Champion, 2014	192	130	7.27 [2.85 - 18.54]
EFICA, 2006	158	75	3.10 [1.61 - 5.98]
Gaudard, 2015	40	11	3.15 [0.75 - 13.29]
IMPRESS in Severe Shock, 2017	48	14	12.55 [2.38 - 66.01]
OPTIMA CC, 2018	57	27	2.55 [0.84 - 7.72]
Basir, unpublished	45	8	0.96 [0.16 - 5.73]
Popovic, 2011	86	47	1.11 [0.47 - 2.63]
Simonis, 2012	89	25	1.37 [0.53 - 3.55]
SMASH, 1998	111	41	0.62 [0.26 - 1.47]
Valente, 2011	152	34	2.40 [0.38 - 14.96]
All studies	2583	947	3.33 [2.81 - 3.94]



Levy B et al, J American Coll Cardiol, 2018

Intensive Care Med
https://doi.org/10.1007/s00134-018-5214-9

REVIEW

Management of cardiogenic shock complicating myocardial infarction

Alexandre Mebazaa[1,2,3,4*], Alain Combes[5*], Sean van Diepen[6], Alexa Hollinger[2,3,7], Jaon N. Katz[8], Giovanni Landoni[9,10], Ludhmila Abrahao Hajjar[11], Johan Lassus[12], Guillaume Lebreton[13,14], Gilles Montalescot[14,15], Jin Joo Park[16], Susanna Price[17], Alessandro Sionis[18,19], Demetris Yannopolos[20], Veli-Pekka Harjola[21], Bruno Levy[22,23,24] and Holger Thiele[25*]

Mebazaa… Thiele. Intensive care Medicine 2018

< 2 hours

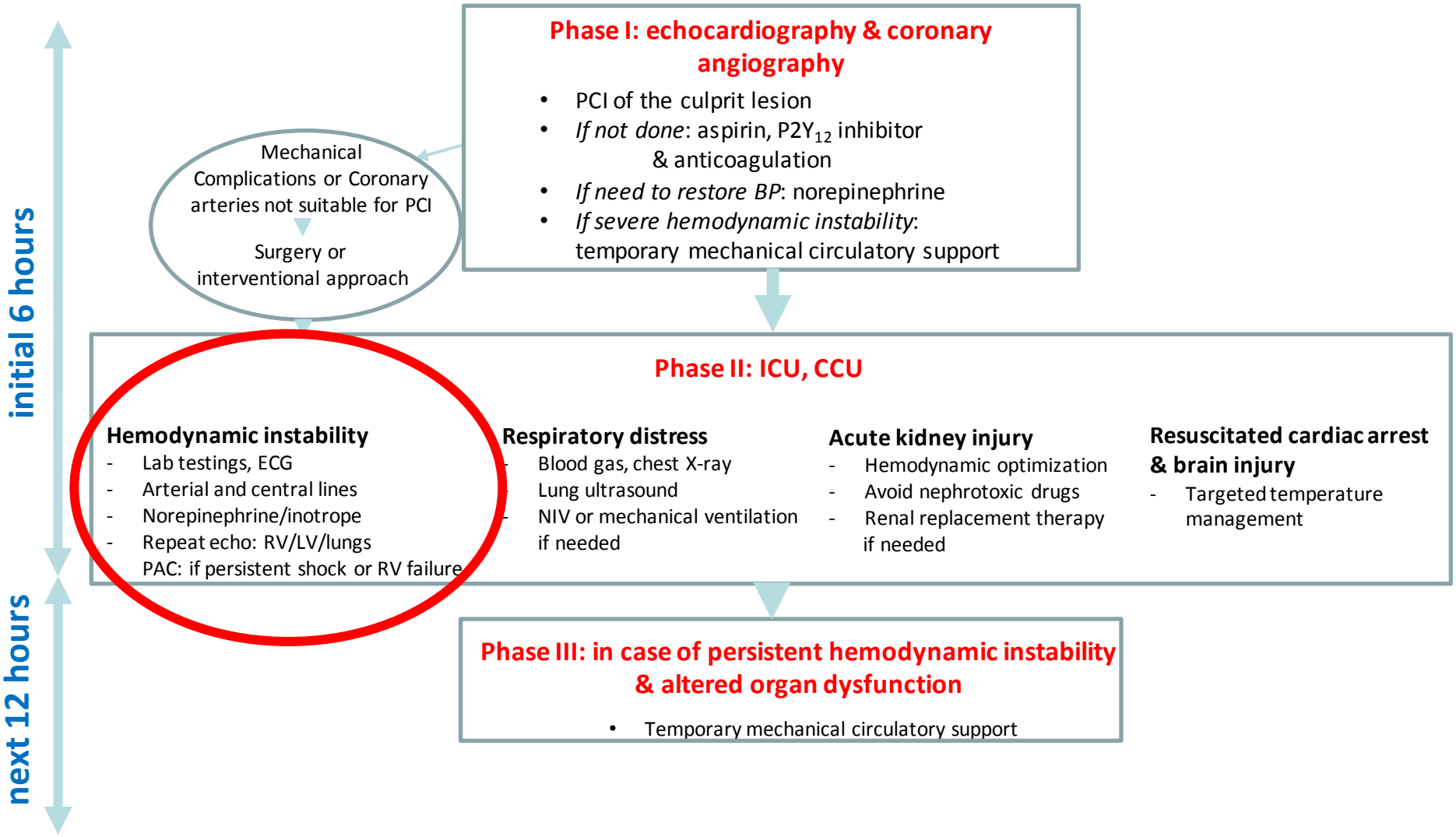
STEMI or high-risk ECG signs or symptoms suggesting AMI, < 3 hours & hemodynamic instability or resuscitated cardiac arrest

PCI should be performed < 120 min: alert & transfer to cardiac shock center for primary PCI

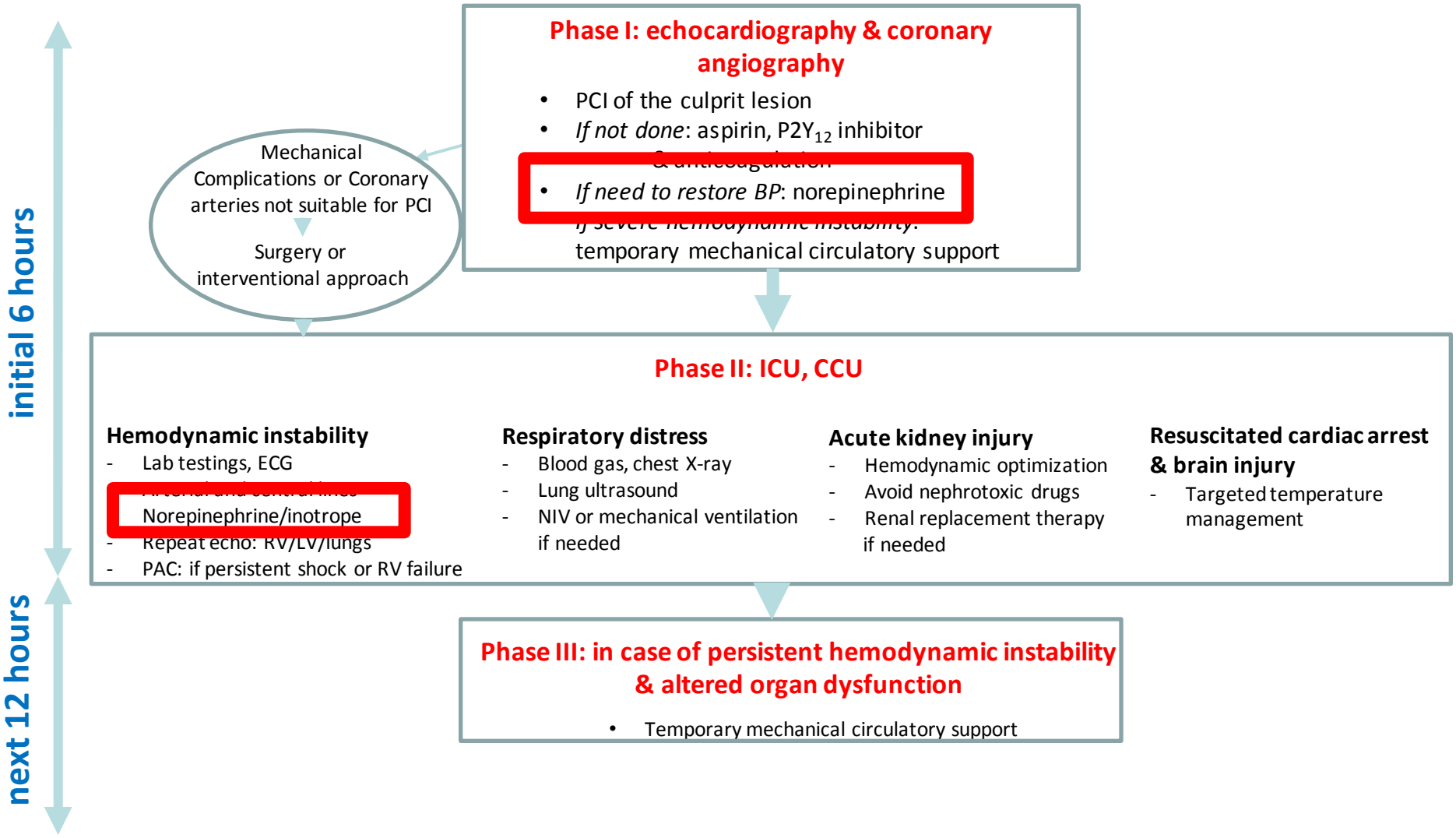
- *During the transport*, start:
  - Aspirin orally or iv
  - Consider potent $P2Y_{12}$ inhibitor (prasugrel or ticagrelor), or clopidogrel if contraindicated, orally
  - Anticoagulation iv
- *If hemodynamic instability*: volume loading < 250 ml & norepinephrine on peripheral line
- *If SpO_2 < 90%:* O_2 therapy

Cardiac Shock Center

Mebazaa… Thiele. Intensive care Medicine 2018



Mebazaa… Thiele. Intensive care Medicine 2018



Mebazaa… Thiele. Intensive care Medicine 2018

In case of severe Right Ventricular dysfunction

Management of Right Ventricular dysfynction

Vasopressors and inotropes	
Noradrenaline, 0.2–1.0 µg/kg.min[30]	Increases RV inotropy, systemic blood pressure, promotes positive ventricular interactions, restores coronary perfusion gradient
Dobutamine, 2–20 µg/kg.min[30]	Increases RV inotropy, lowers filling pressures
Levosimendan, 0.1–0.2 µg/kg.min (6–12 µg/kg bolus over 10 min is optional and not recommended if SBP <90 mmHg). Infusion can be decreased to 0.05 µg/kg.min or increased to 0.2 µg/kg.min)[30]	Combines RV inotropy and pulmonary vasodilation; favourably affects right ventricular–arterial uncoupling

VP Harjola et al. Eur J Heart Failure 2016

Messages principaux

- **ICA sans choc:**
  - *Mécanisme* : « congestion »
  - *Traitement initial* : Diurétiques/dérivés nitrés pas d'inotropes

- **Choc cardiogénique**
  - 1) **si bas débit cardiaque + infarctus du myocarde/Post-Arrêt cardiaque**
    - Premier médicament : norépinéphrine +/- inotrope si besoin
  - 2) **si insuffisance ventriculaire droite**
    - Premier médicament : norépinéphrine +/- inotrope si besoin
  - 3) **pas d'adrénaline : dans tous les cas!**

Choc cardiogénique

Choc cardiogénique : quelle place pour l'assistance circulatoire?

Marina CLEMENT
Paris, FRANCE

Déclaration de conflits d’intérêts

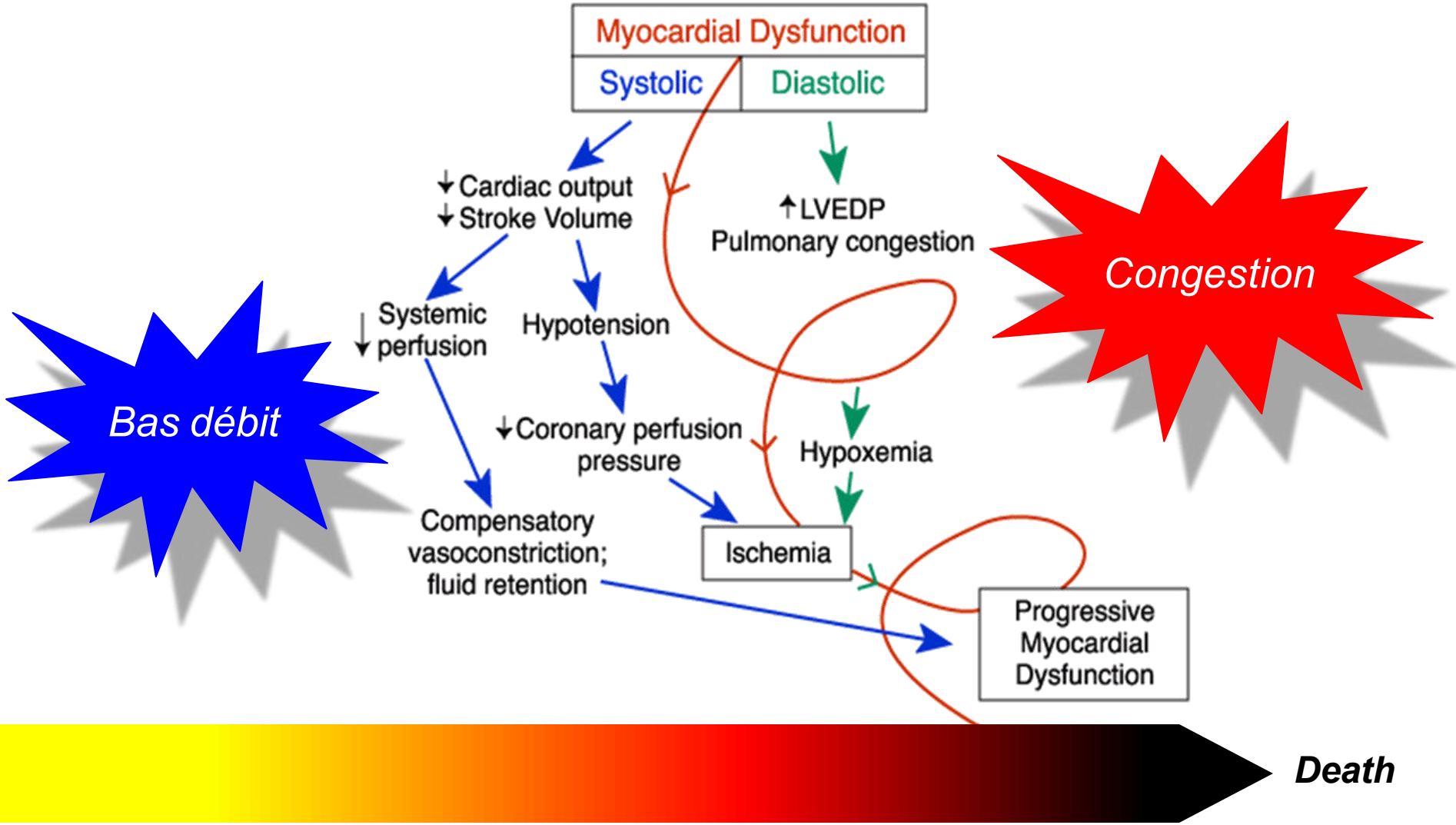
Choc cardiogénique

Définition

- Hypotension systémique persistante
  - PAS < 80 mmHg
  - au moins 30 minutes
- Diminution de la fonction cardiaque
  - Index cardiaque < 1,8 L/min/m^2
- Hypoperfusion tissulaire - anoxie tissulaire
  - Oligurie, extrémités froides, confusion…
- Augmentation de la P de remplissage du VG
  - Pression capillaire pulmonaire > 18 mmHg

Choc cardiogénique

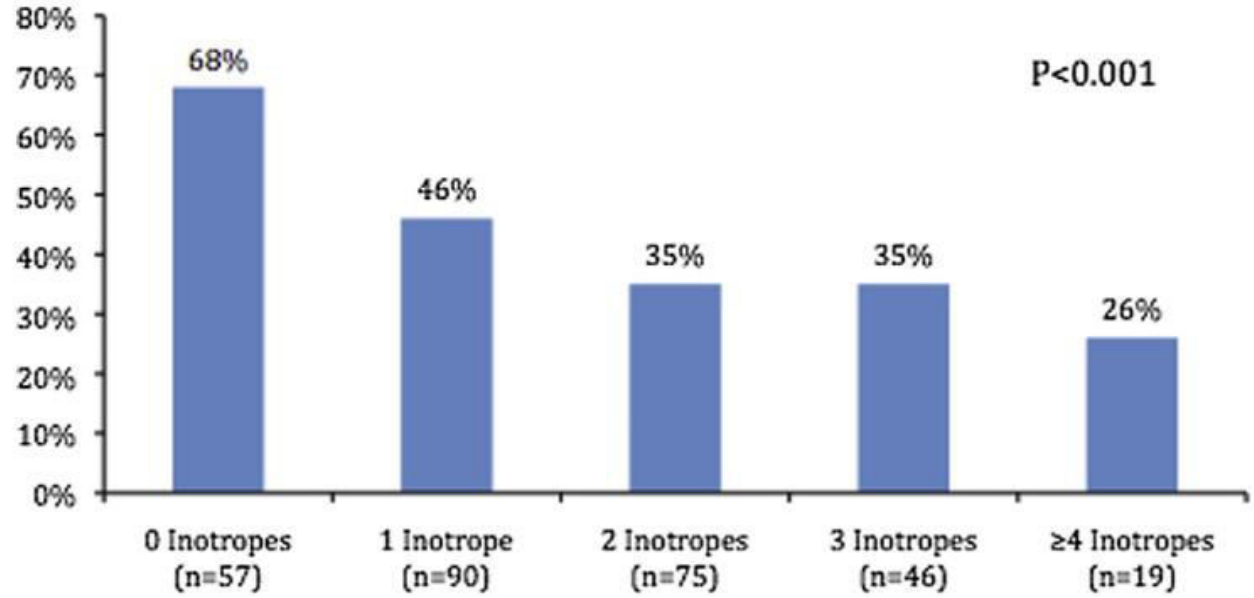
Physiopathologie



Assistance circulatoire et choc

Quand???

Effect of Early Initiation of Mechanical Circulatory Support on Survival in Cardiogenic Shock



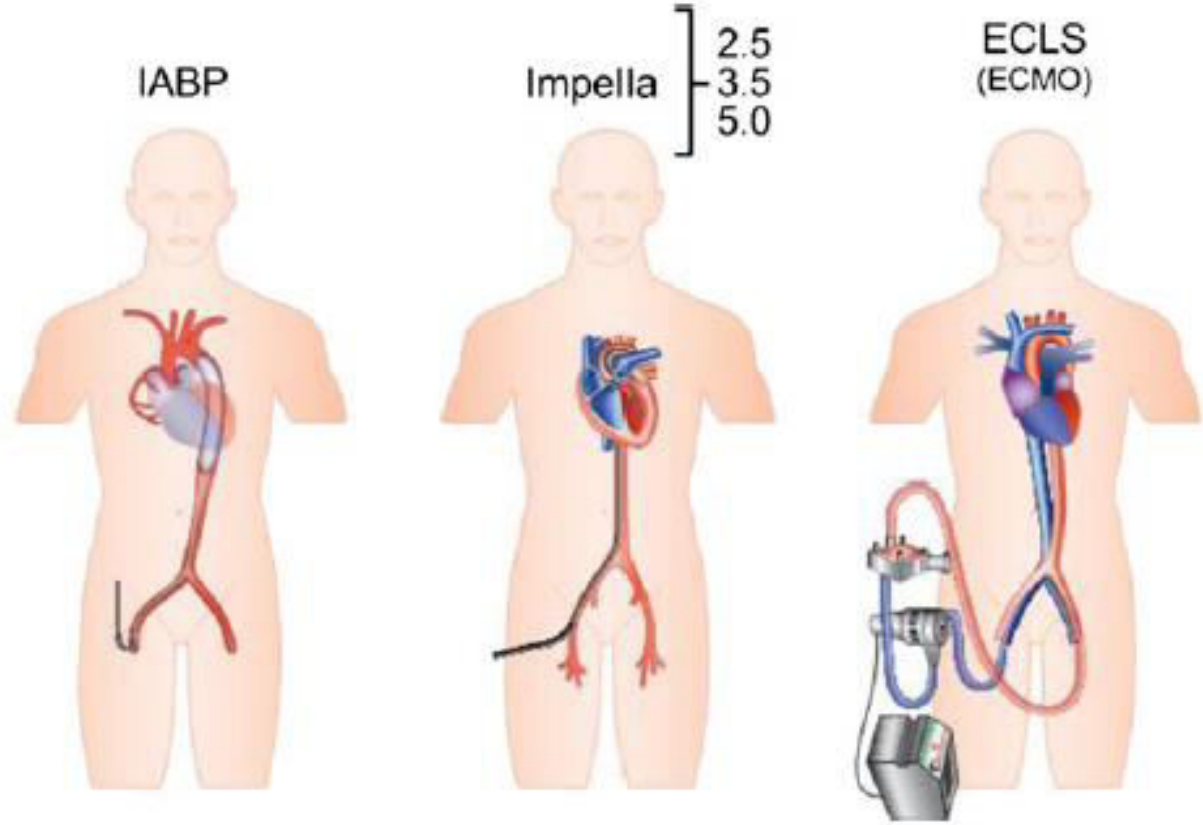
Basir, Am J Cardiol 2017; 119:845-851

Assistance circulatoire et choc

Quand???

Assistance circulatoire et choc.

Quelle machine???



Assistance circulatoire et choc.

Quelle machine???

Advanced Percutaneous Mechanical Circulatory Support Devices for Cardiogenic Shock

P. Elliott Miller, MD[1]; Michael A. Solomon, MD[1,2]; Dorothea McAreavey, MD[1] *Crit Care Med* 2017

DEVICE SELECTION

Once a decision to deploy mechanical support has been made for cardiogenic shock, the device should be inserted without delay to prevent progressive myocardial dysfunction. As discussed, definitive evidence for choice of device is lacking.

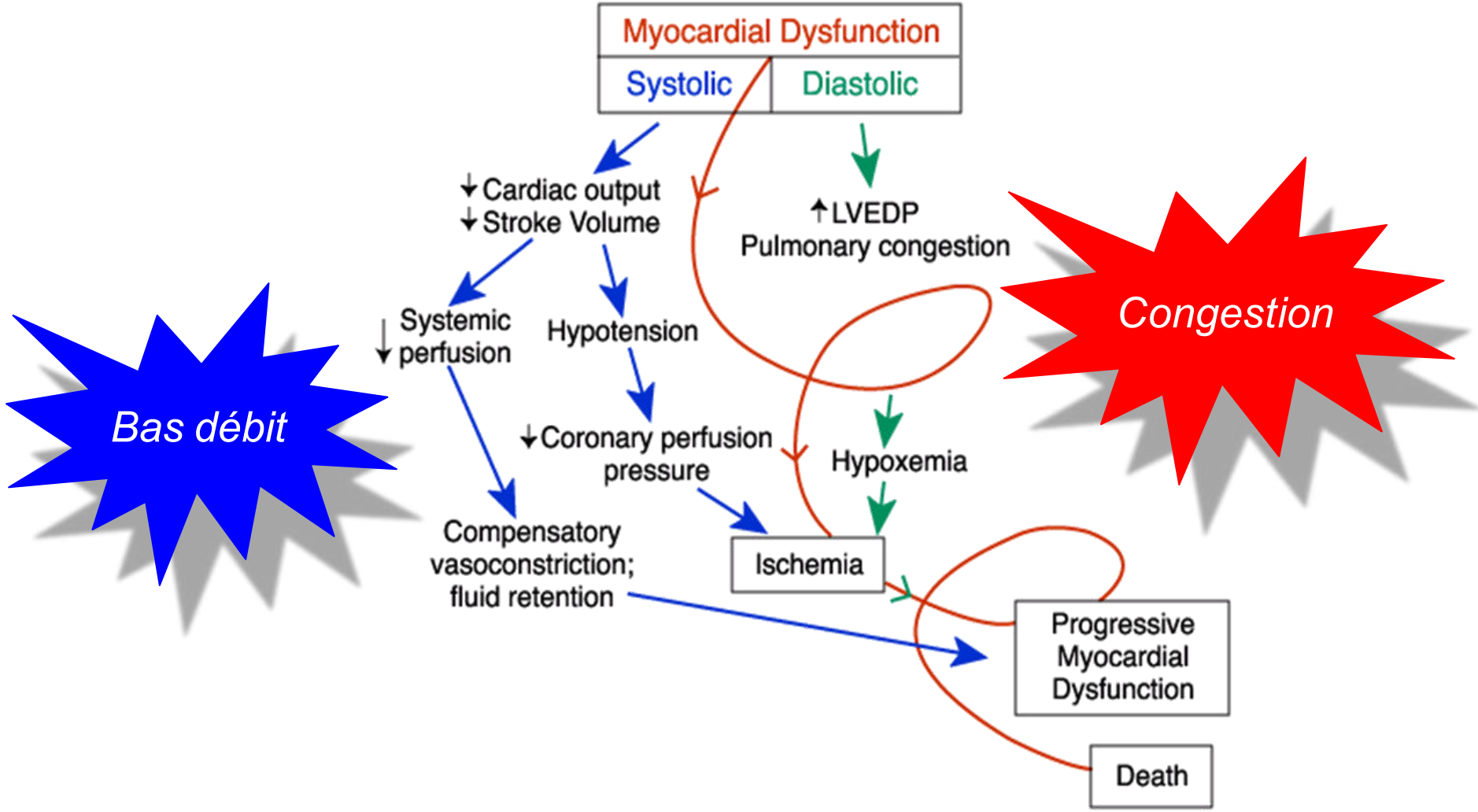
GAPS IN KNOWLEDGE

CONCLUSIONS

The prognosis for patients with cardiogenic shock remains poor despite current therapy. Temporary pMCS offers the opportunity to improve these outcomes but still requires large studies powered to evaluate mortality and continued improvements in technology to decrease complications.

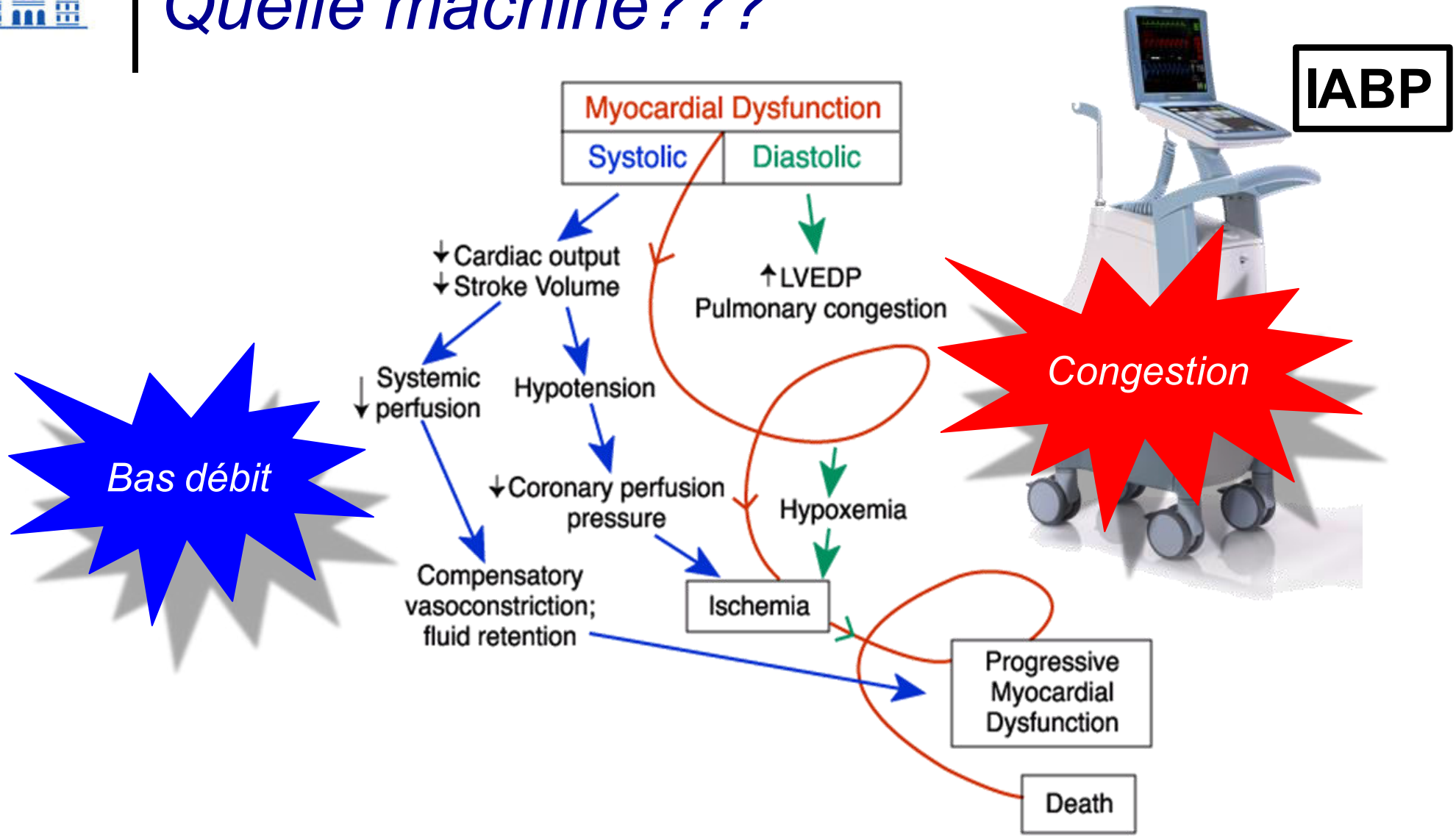
Assistance circulatoire et choc.

Quelle machine???



Assistance circulatoire et choc.

Quelle machine???



Assistance circulatoire et choc.

Quelle machine???

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 4, 2012 VOL. 367 NO. 14

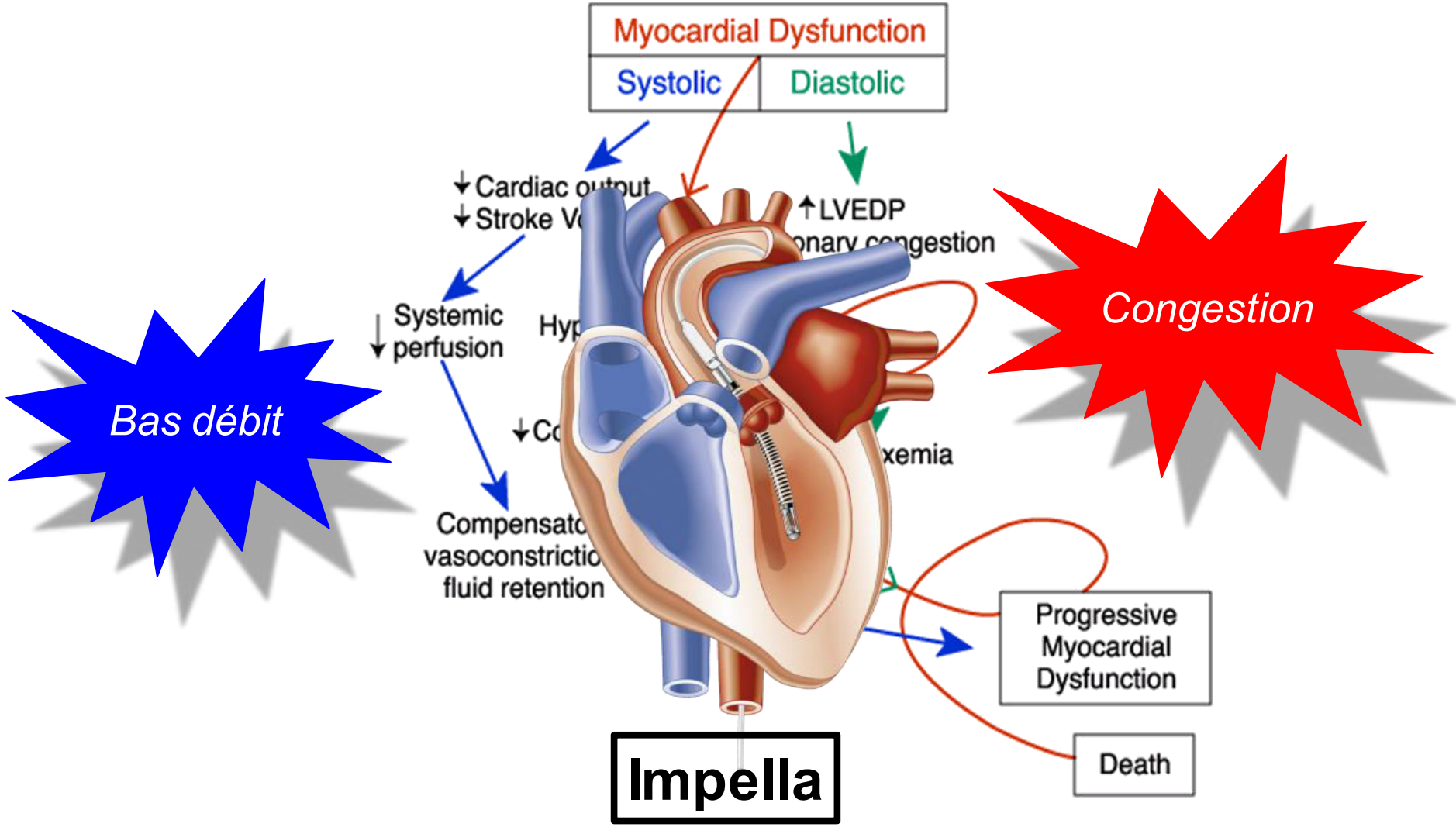
Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock

CONCLUSIONS

The use of intraaortic balloon counterpulsation did not significantly reduce 30-day mortality in patients with cardiogenic shock complicating acute myocardial infarction for whom an early revascularization strategy was planned. (Funded by the

Assistance circulatoire et choc.

Quelle machine???

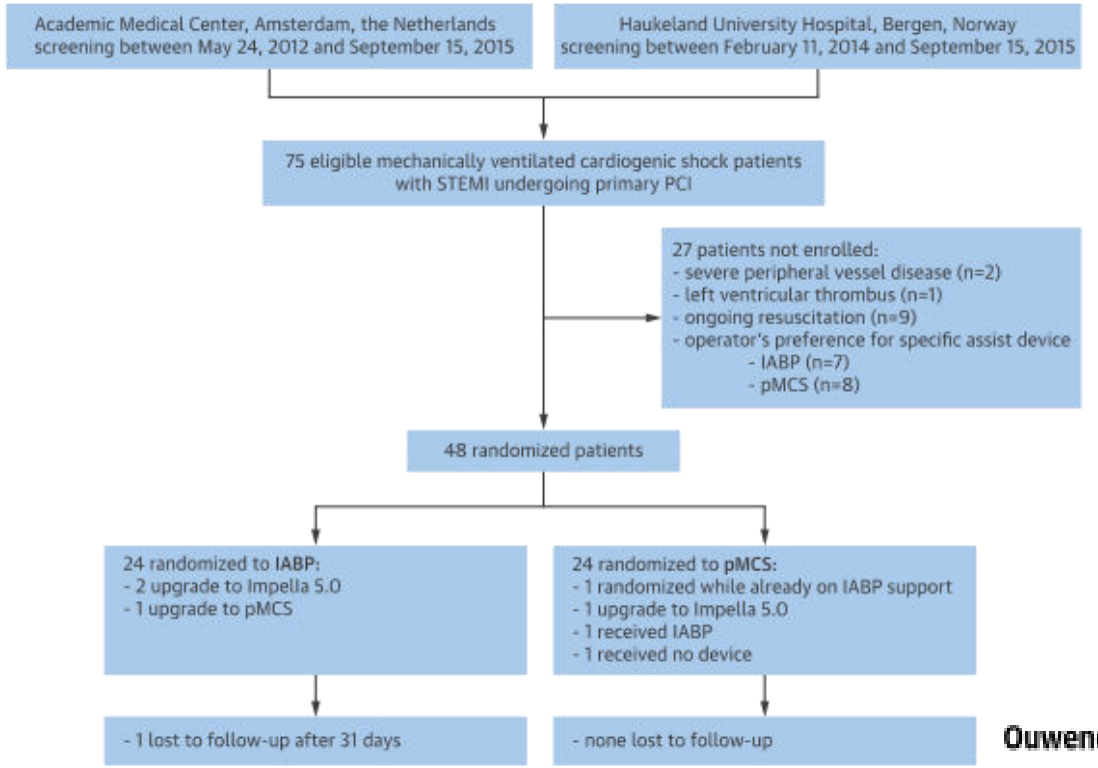


Assistance circulatoire et choc.

Quelle machine???

JACC, 2017

Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction



Ouweneel, D.M. et al. J Am Coll Cardiol. 2017;69(3):278-87.

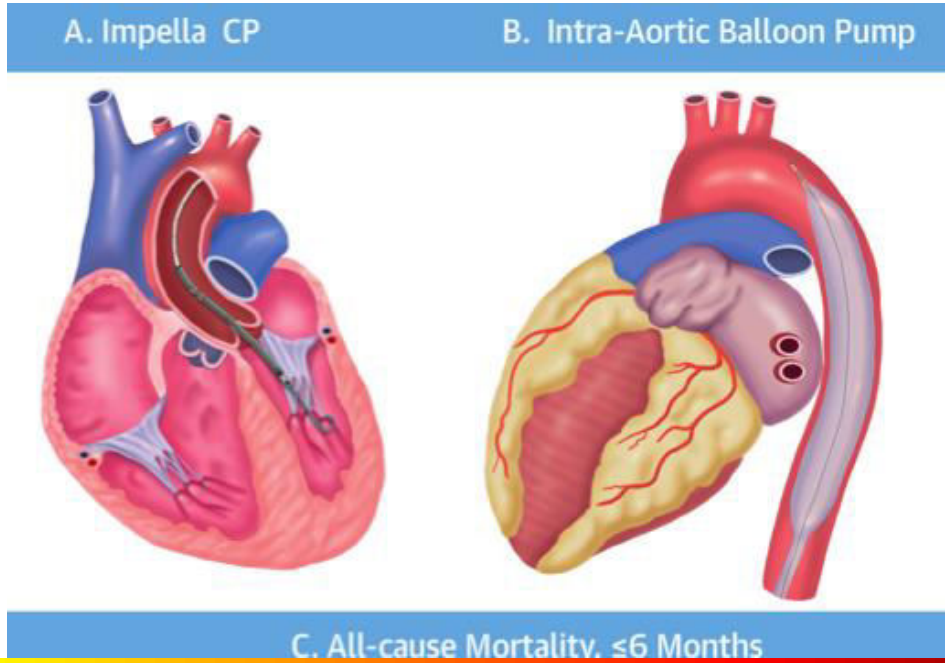
Assistance circulatoire et choc.

Quelle machine???

Impella

Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction

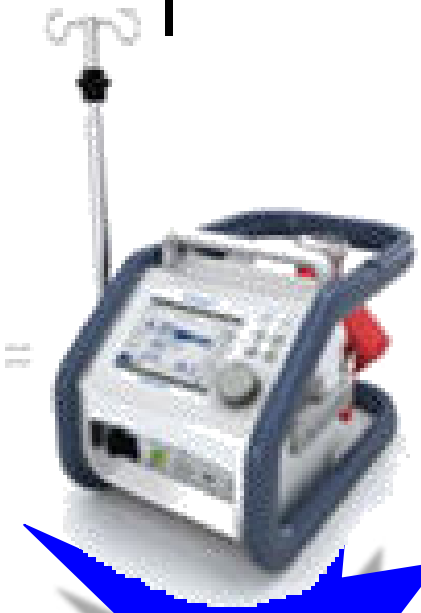
JACC, 2017



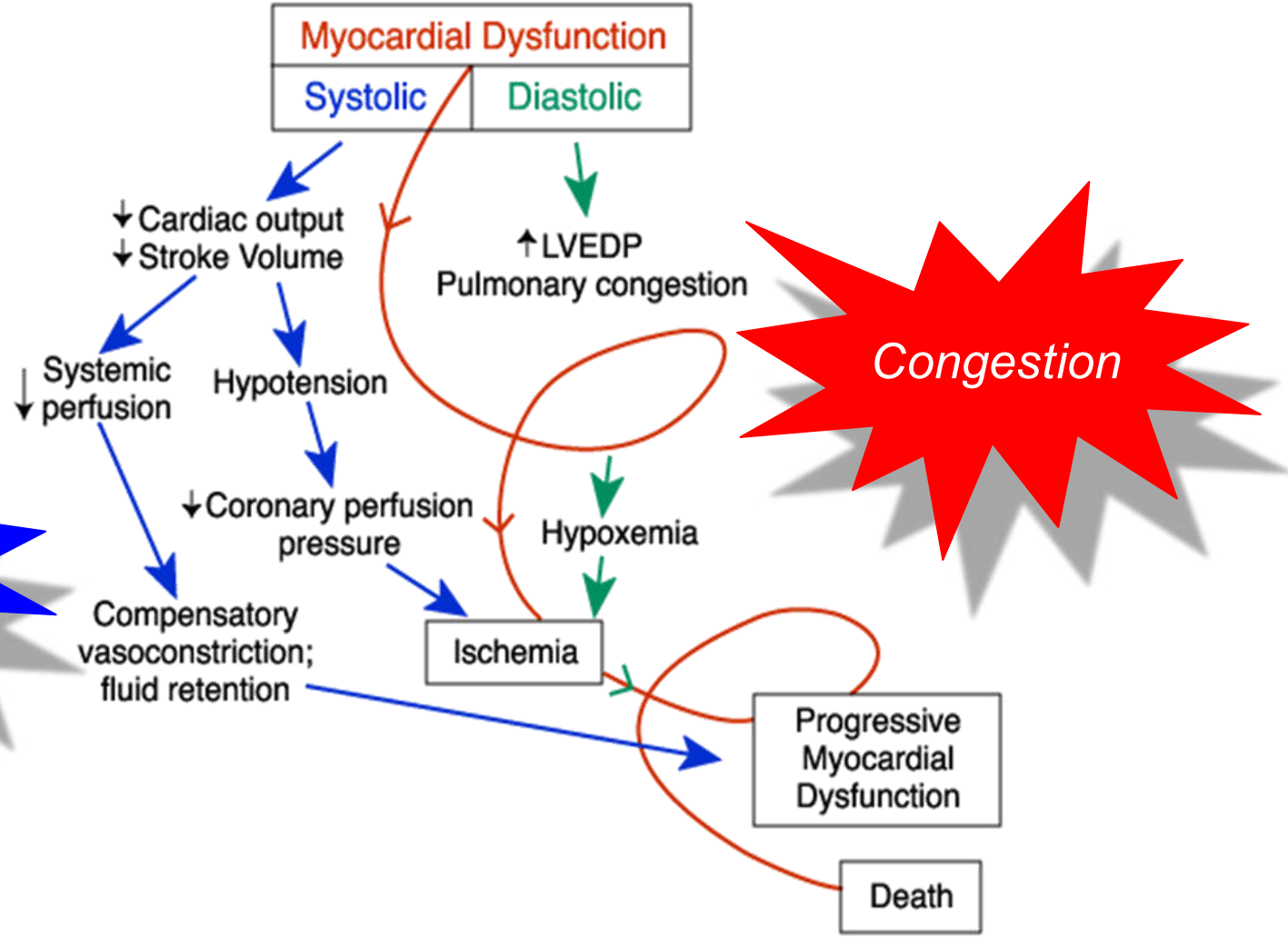
€

Assistance circulatoire et choc.

Quelle machine???

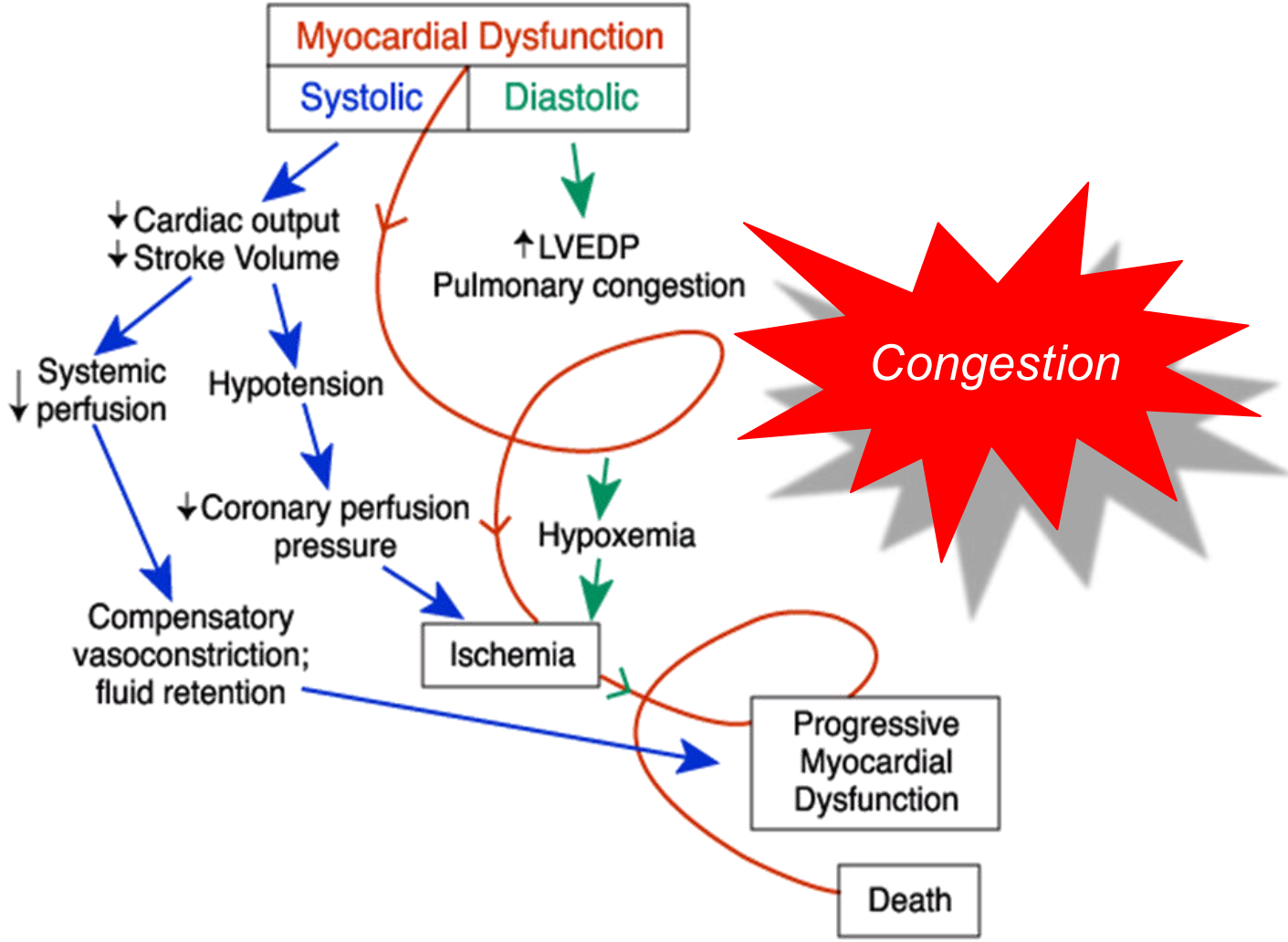


Bas débit



Assistance circulatoire et choc.

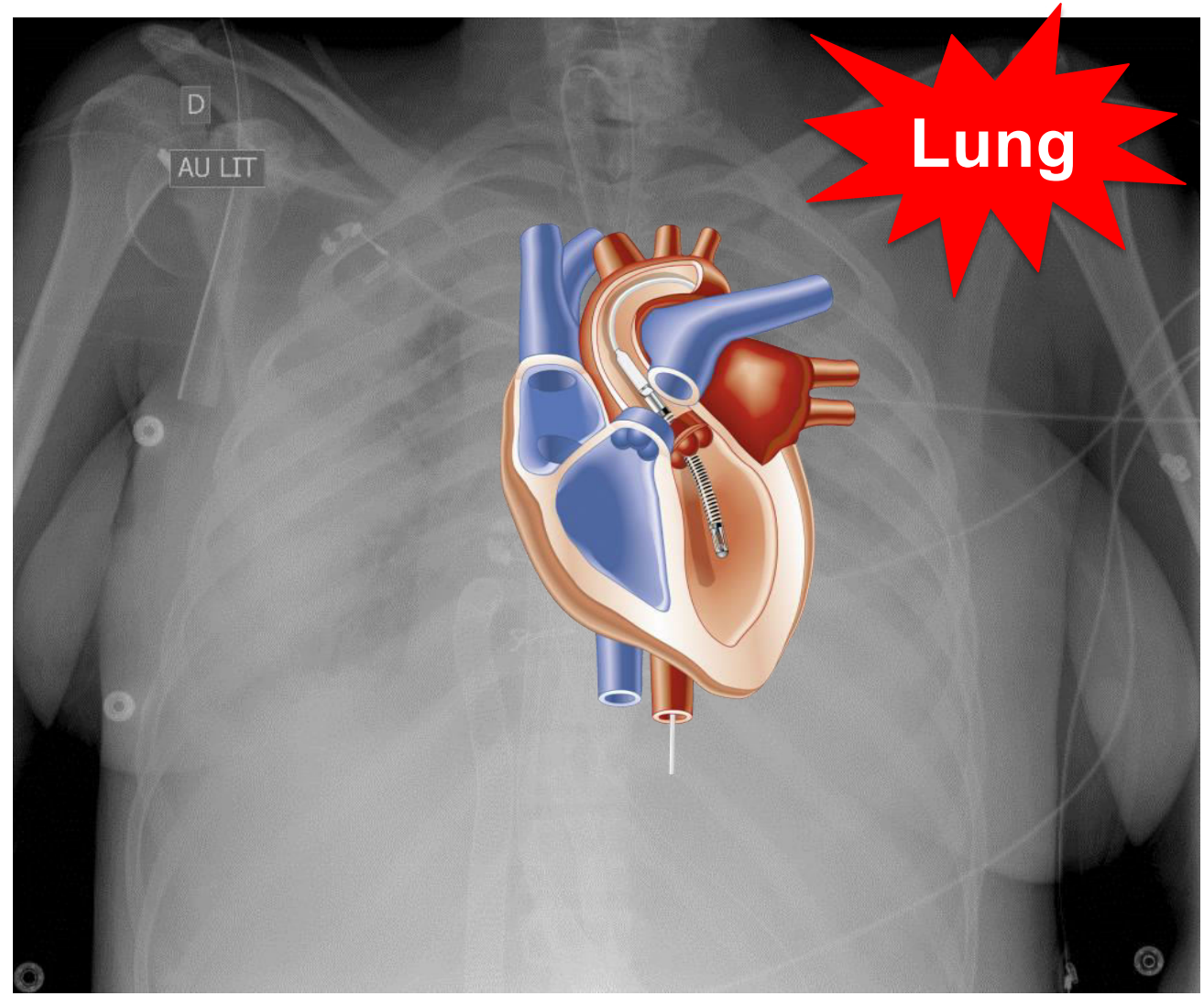
Quelle machine???



ECMO VA périphérique

Congestion du VG…

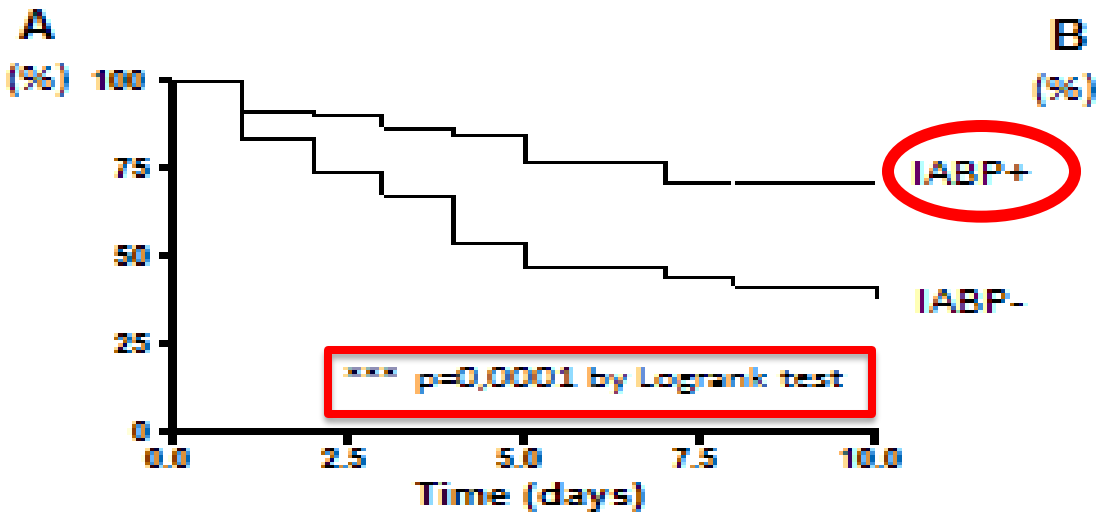
- Centralisation
- BCPIA
- Impella



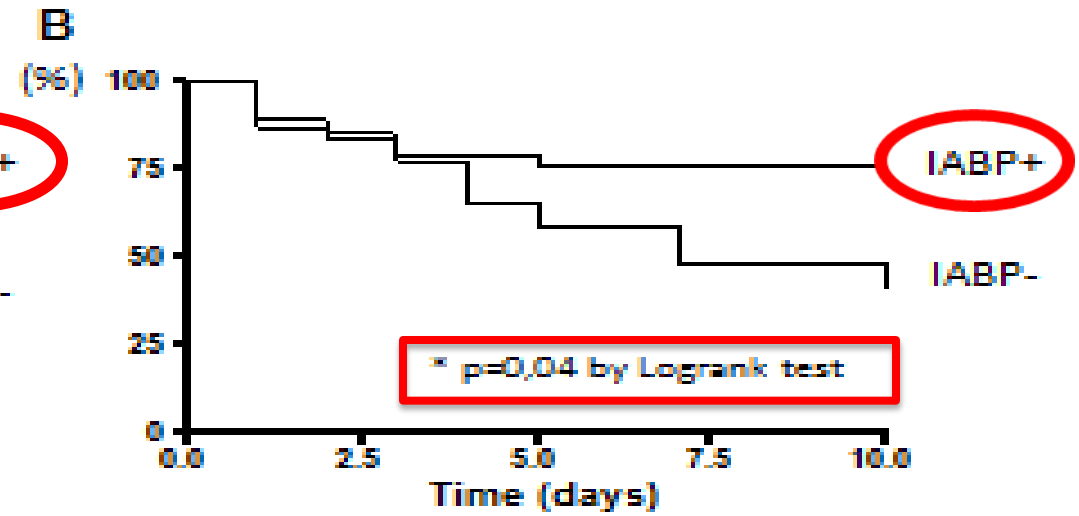
ECMO VA périphérique

Congestion du VG…

Survival without clinical Pulmonary Oedema



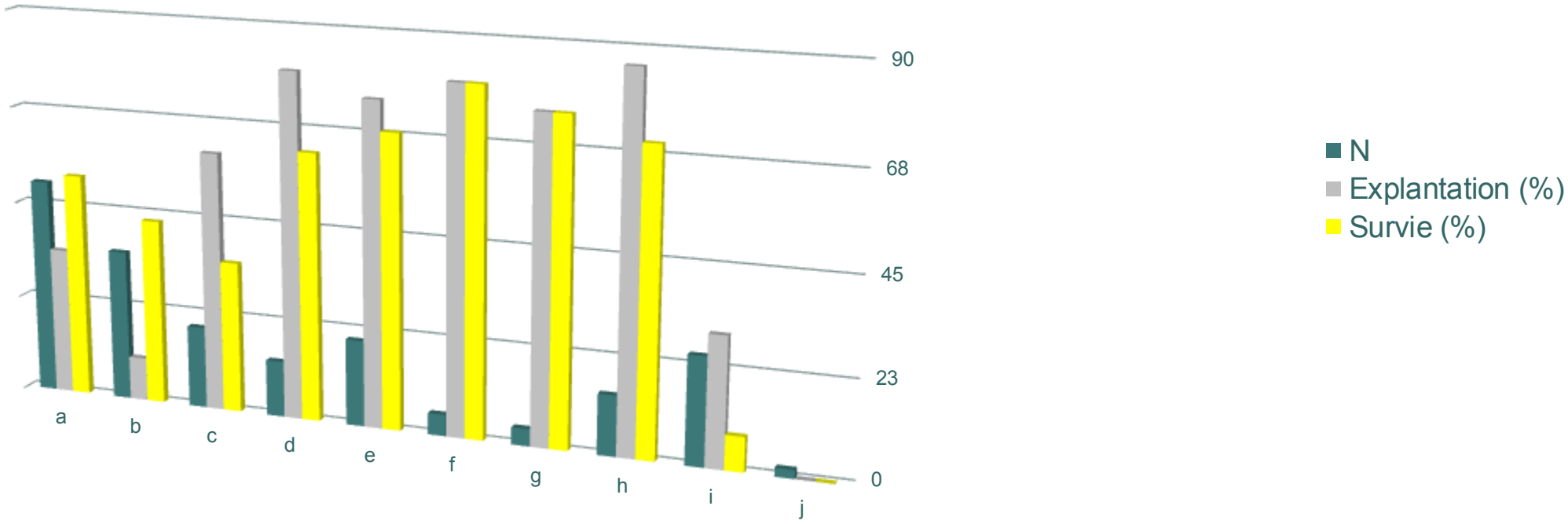
Unmatched patients



Propensity-matched patients

ECMO VA périphérique

Expérience de la Pitié



a. IDM
b. Cardiopathie dilatée
c. Post-cardiotomie
d. Dysfonction primaire du greffon
e. Myocardite
f. Intox médicamenteuse
g. EP
h. Choc septique réfractaire
I. ACR extra hospitalier
j. Dysfonction de greffon tardive

2010-2011
200 ECMO VA périph

La Pitié-Salpêtrière Database

ECMO VA périphérique

Complications

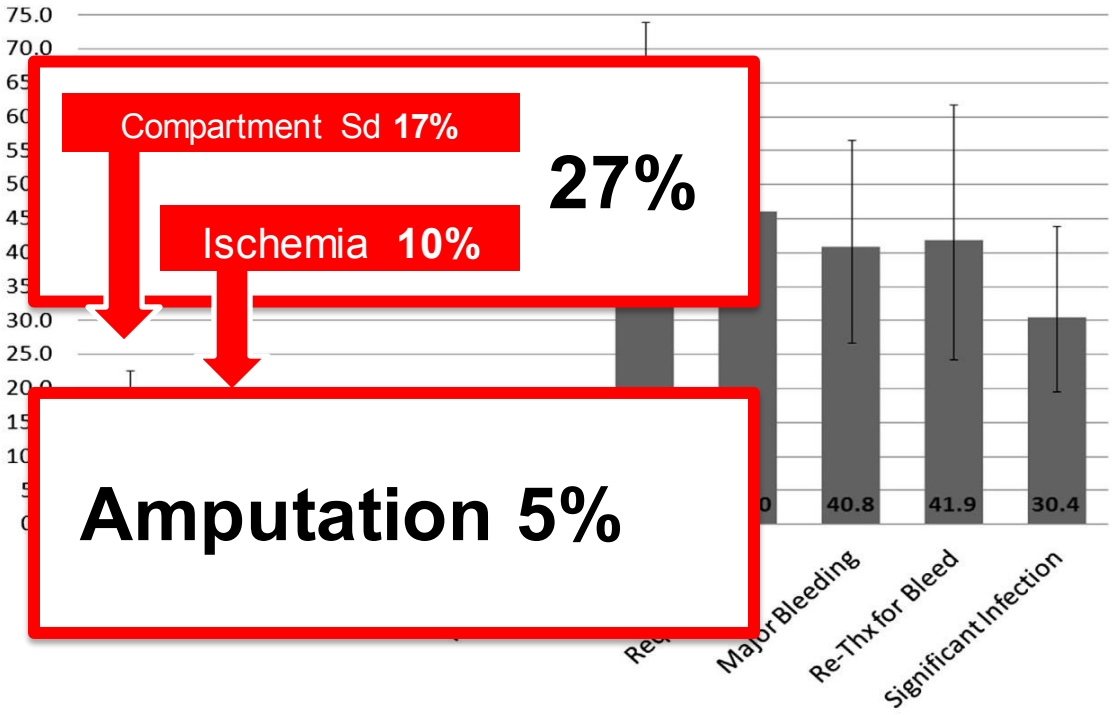
- Mécaniques
  - OAP
  - Ischémiques
- Infectieuses
- Thrombotiques
- Hémorragiques
- Hémolytiques
- … Accident…

ADULT CARDIAC

Complications of Extracorporeal Membrane Oxygenation for Treatment of Cardiogenic Shock and Cardiac Arrest: A Meta-Analysis of 1,866 Adult Patients

Richard Cheng, MD, Rory Hachamovitch, MD, Michelle Kittleson, MD, PhD, Jignesh Patel, MD, PhD, Francisco Arabia, MD, Jaime Moriguchi, MD, Fardad Esmailian, MD, and Babak Azarbal, MD

Cedars-Sinai Heart Institute, Los Angeles, California, and Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, Ohio



Meta-analysis

- 22 studies
- 1866 patients
- VA ECMO
- Survival 21 to 65 %

Conclusions. Although ECMO can improve survival of patients with advanced heart disease, there is significant associated morbidity with performance of this intervention. These findings should be incorporated in the risk–benefit analysis when initiation of ECMO for cardiogenic shock is being considered.

(Ann Thorac Surg 2014;97:610–6)
© 2014 by The Society of Thoracic Surgeons

ECMO VA périphérique

Expérience de la Pitié

- Jan 2015- Dec 2017, 1017 VA ECMO
  - 72 % ♂, Age : 55 ± 1,7 (18; 84).
  - Lactates pre-ECMO : 5,8 ± 5,7 (0,4;21,5)

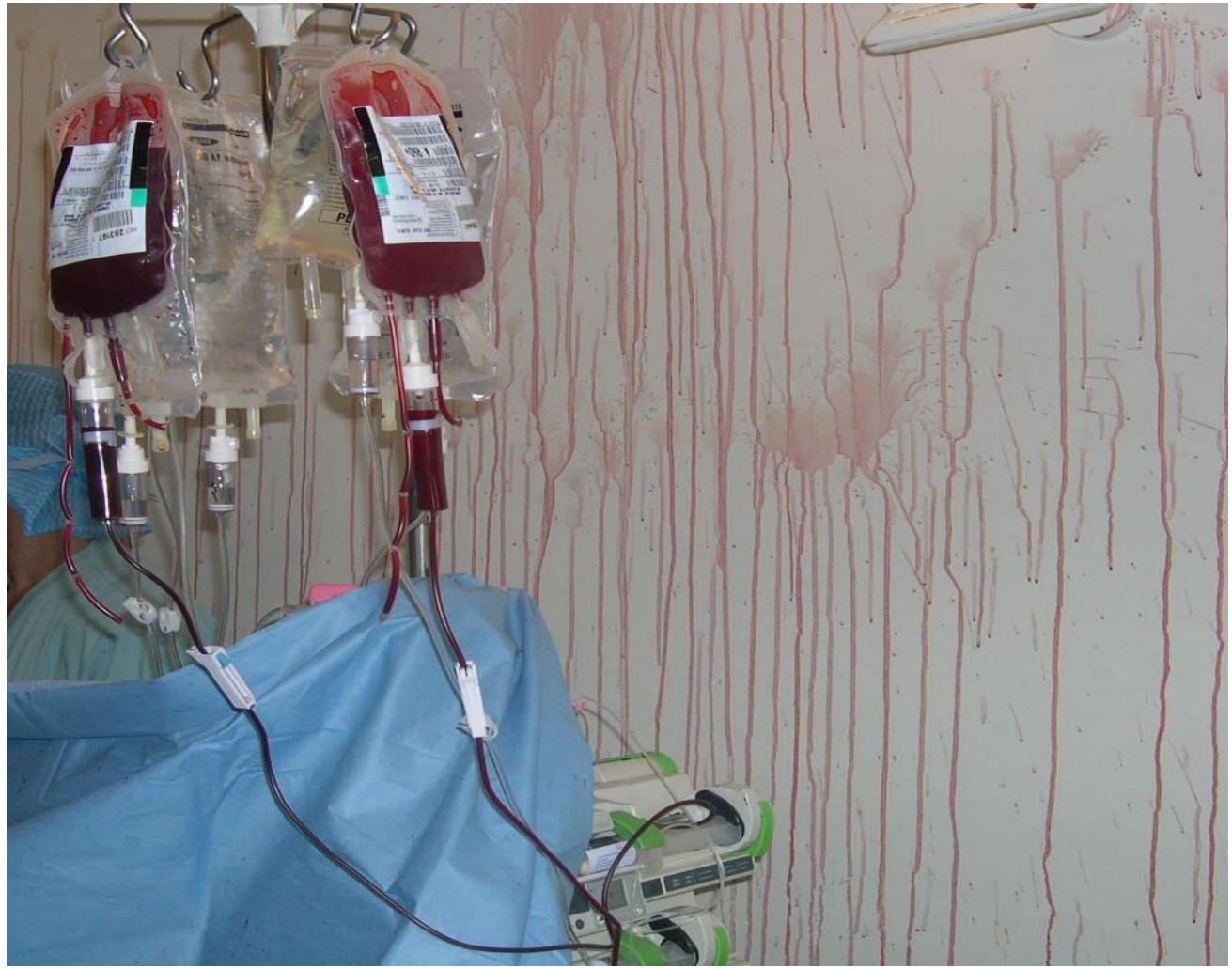
Fémoro-fémorale	*Percut*	*Chirurgicale*	*Total*
Ischémie de membre	10,0%	6,8%	**8,9%**
Amputation	0,9%	0%	**0,6%**
Revascularisation chirurgicale	6,4%	3,34%	**4,1%**
Infection	12,7%	30,5%	**18,9%**
Debridement	4,5%	10,2%	**6,5%**

Durée ECMO = 6,1 jours (0-40)

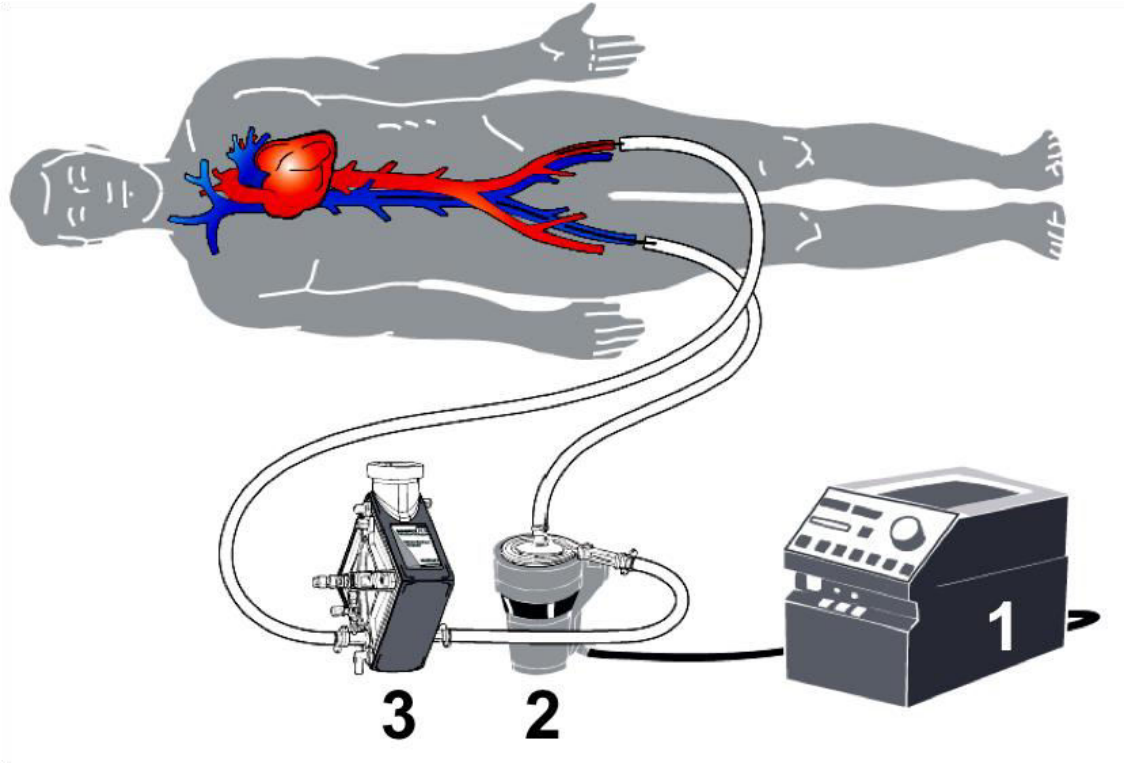
Survie = 60,5%

La Pitié-Salpêtrière Database

Accidents



L'ECMO… *"Gold standard"?*



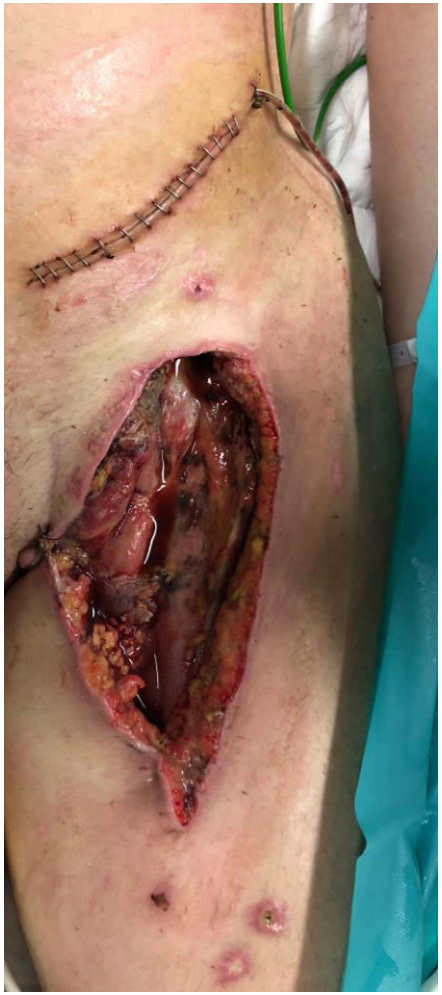
Assistance circulatoire (5-6L/min)

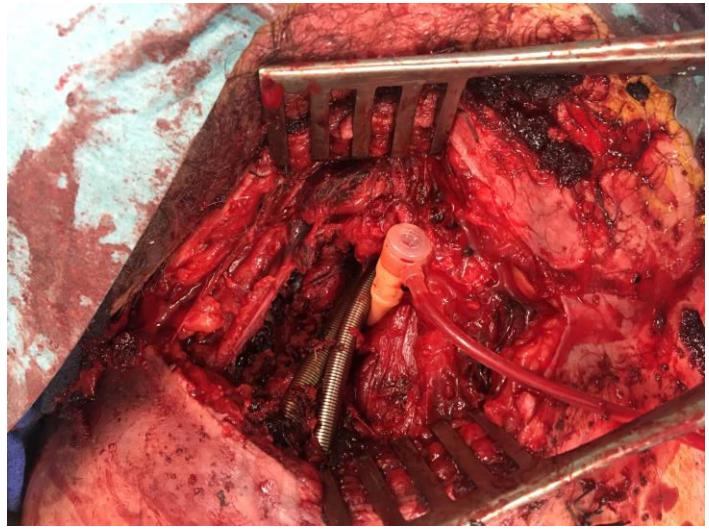
- Oxygénation
- Rapport coût efficacité
- Simple et rapide (lit)

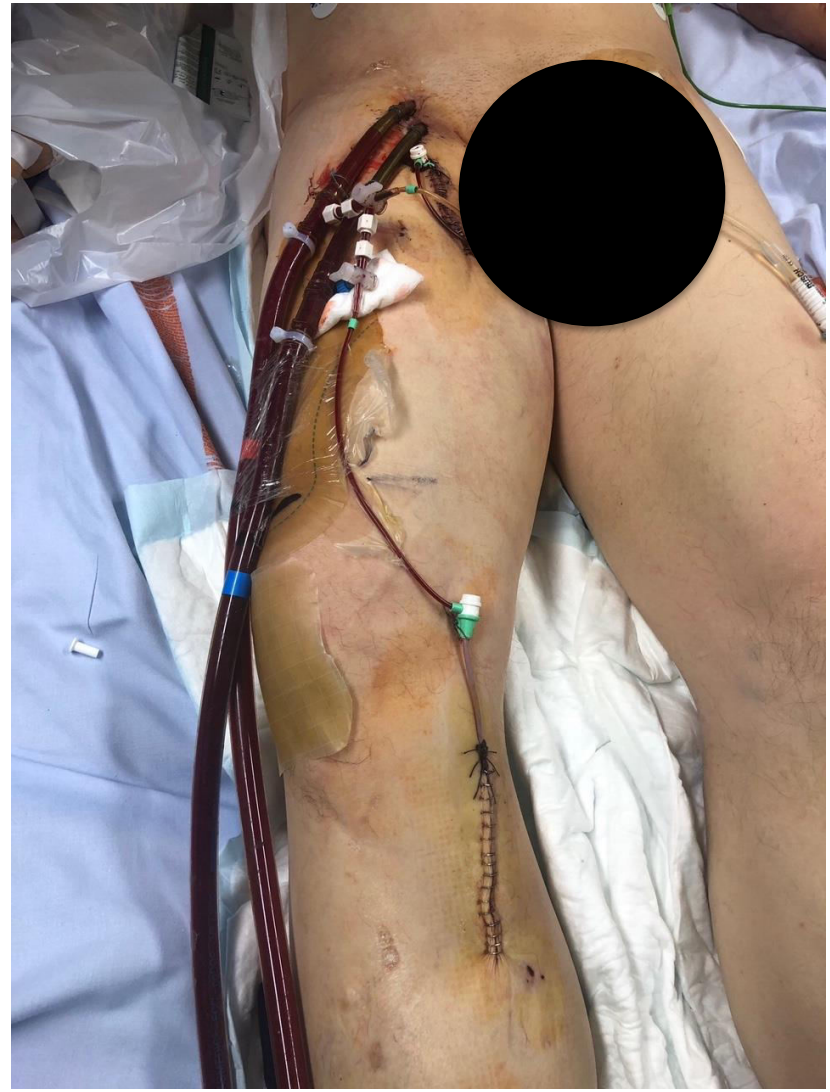
Limitations:

- augmentation Post-Charge
- complications.
- équipe spécialisée

L’ECMO…équipe spécialisée +++







Assistance circulatoire et choc cardiogénique

Choc cardiogénique & ***Choc cardiogénique***

Réponse appropriée

Inotropes
IABP

Impella

ECLS

Death

Merci pour votre attention

docmarinaclement@gmail.com

CoSAC
Le congrès des Sociétés Africaines de Cardiologie

STCCCV
Société Tunisienne de Cardiologie & de Chirurgie Cardio-Vasculaire