CARDIOGENIC SHOCK

EPIDEMIOLOGY, PATHOPHYSIOLOGY, THERAPY

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CONFLICTS OF INTEREST

ESC European Society of Cardiology

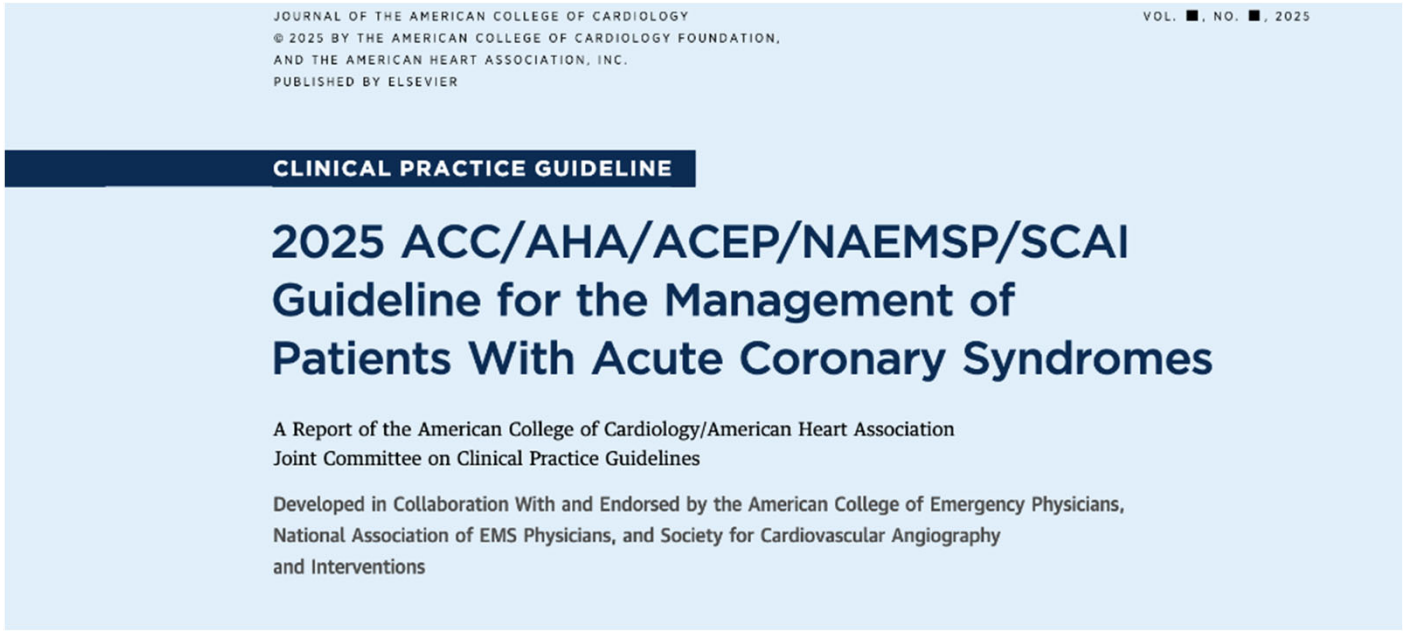
European Heart Journal (2021) **42**, 3599–3726
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC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CLINICAL PRACTICE GUIDELINE

2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes

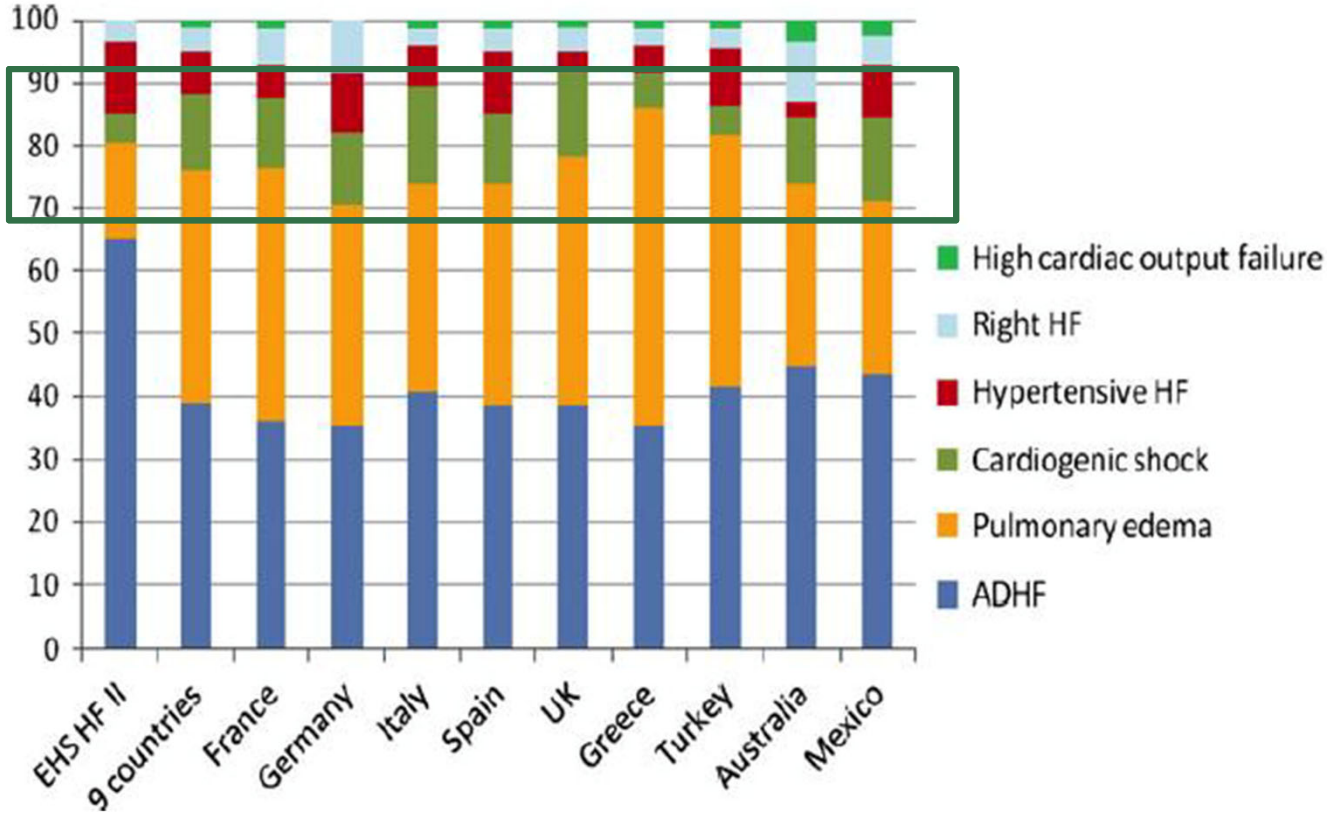
A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Developed in Collaboration With and Endorsed by the American College of Emergency Physicians, National Association of EMS Physicians, and Society for Cardiovascular Angiography and Interventions

CLINICAL DEFINITION

- Life threatening end-organ hypoperfusion and tissular hypoxia from cardiac dysfunction
- Persistent low-cardiac output unresponsive to volume loading (fluid loading challenge+++)
- Both clinical and biochemical manifestation
- Majority of Cardiogenic Shock (≈80%) are caused by Acute Coronary Syndrome (STEMI+++)
- 5-10% of patients hospitalized for AMI (leading cause of mortality in these patients)
- Results from extensive damage to left ventricular myocardium or mechanical complications (**please check by repeating TTE exam!**)

ACUTE HEART FAILURE IS NOT CARDIOGENIC SHOCK...



Follath F et al. Int Care Med 2011

Baseline characteristics and hospital mortality in the Acute Heart Failure Database (AHEAD) Main registry

Jindrich Spinar[1,2], Jiri Parenica[1,2*], Jiri Vitovec[2,3], Petr Widimsky[4], Ales Linhart[5], Marian Fedorco[6], Filip Malek[7], Cestmír Cihalik[6], Lenka Spinarová[2,3], Roman Miklik[1], Marian Felsoci[1], Miroslav Bambuch[8], Ladislav Dusek[9] and Jiri Jarkovsky[9]

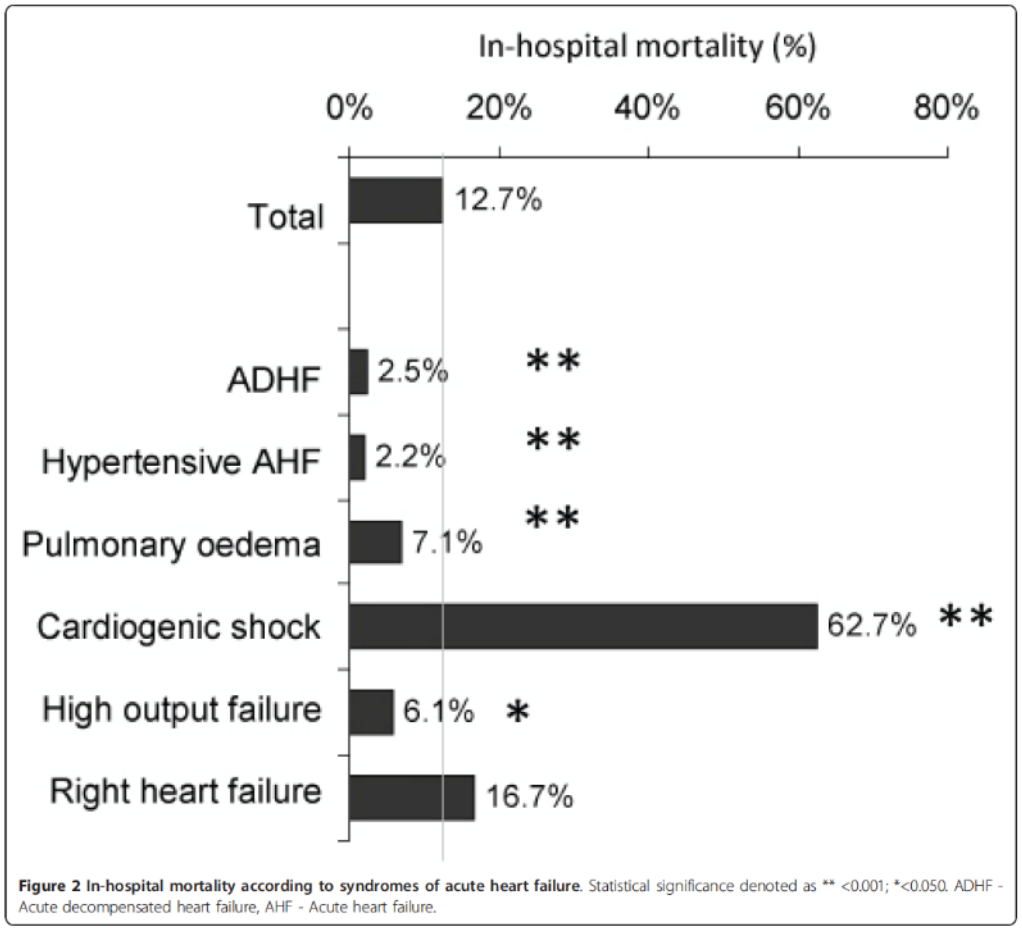


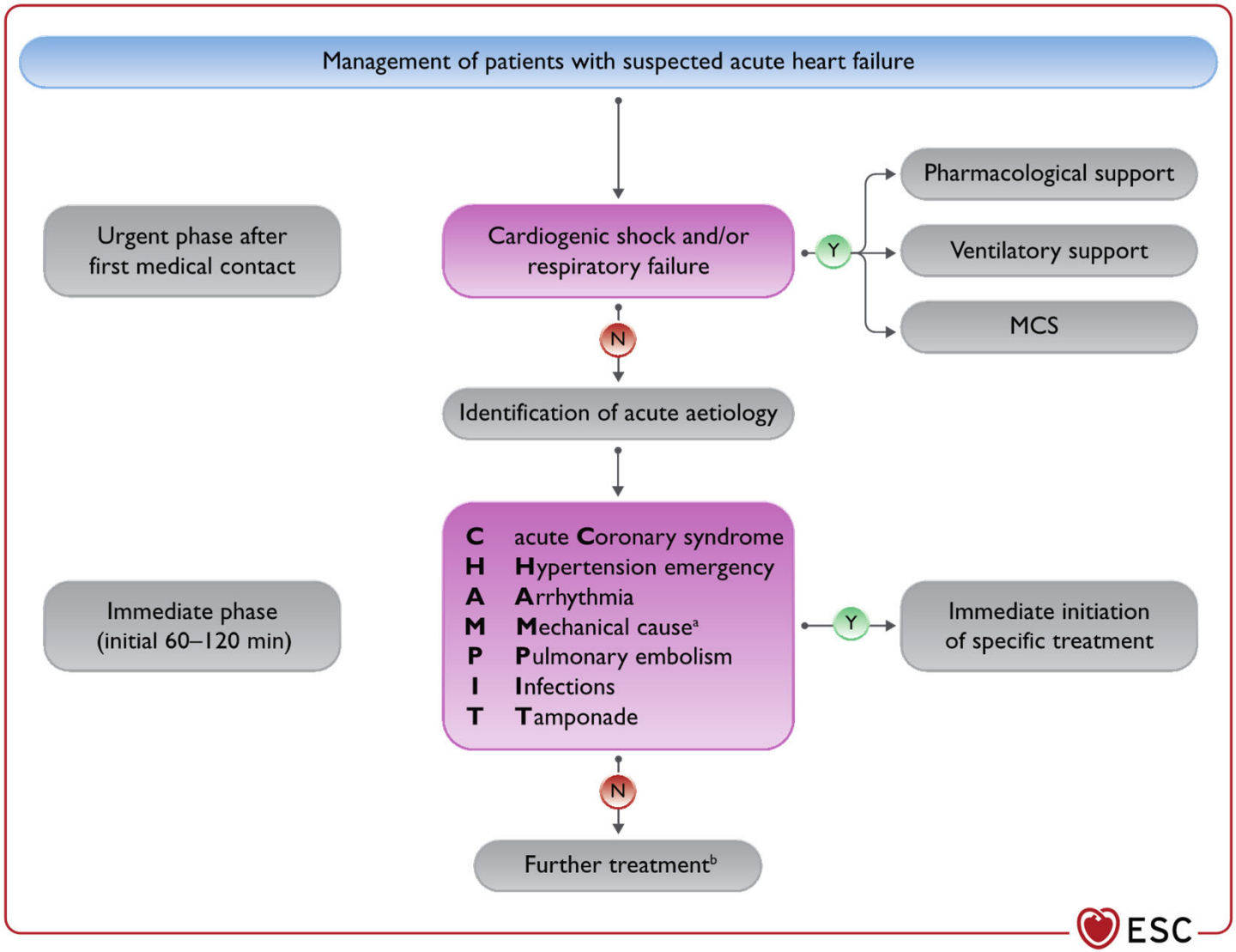
Figure 2 In-hospital mortality according to syndromes of acute heart failure. Statistical significance denoted as ** <0.001; *<0.050. ADHF - Acute decompensated heart failure, AHF - Acute heart failure.

CAUSES OF CARDIOGENIC SHOCK (SPECIFIC PHARMACOLOGICAL AND MECHANICAL THERAPEUTIES)

- Acute myocardial infarction
  - Pump failure
    - Large infarction
    - Smaller infarction with preexisting left ventricular dysfunction
    - Infarction extension
    - Severe recurrent ischemia
    - Infarction expansion
  - Mechanical complications
    - Acute mitral regurgitation caused by papillary muscle rupture
    - Ventricular septal defect
    - Free-wall rupture
    - Pericardial tamponade
  - Right ventricular infarction

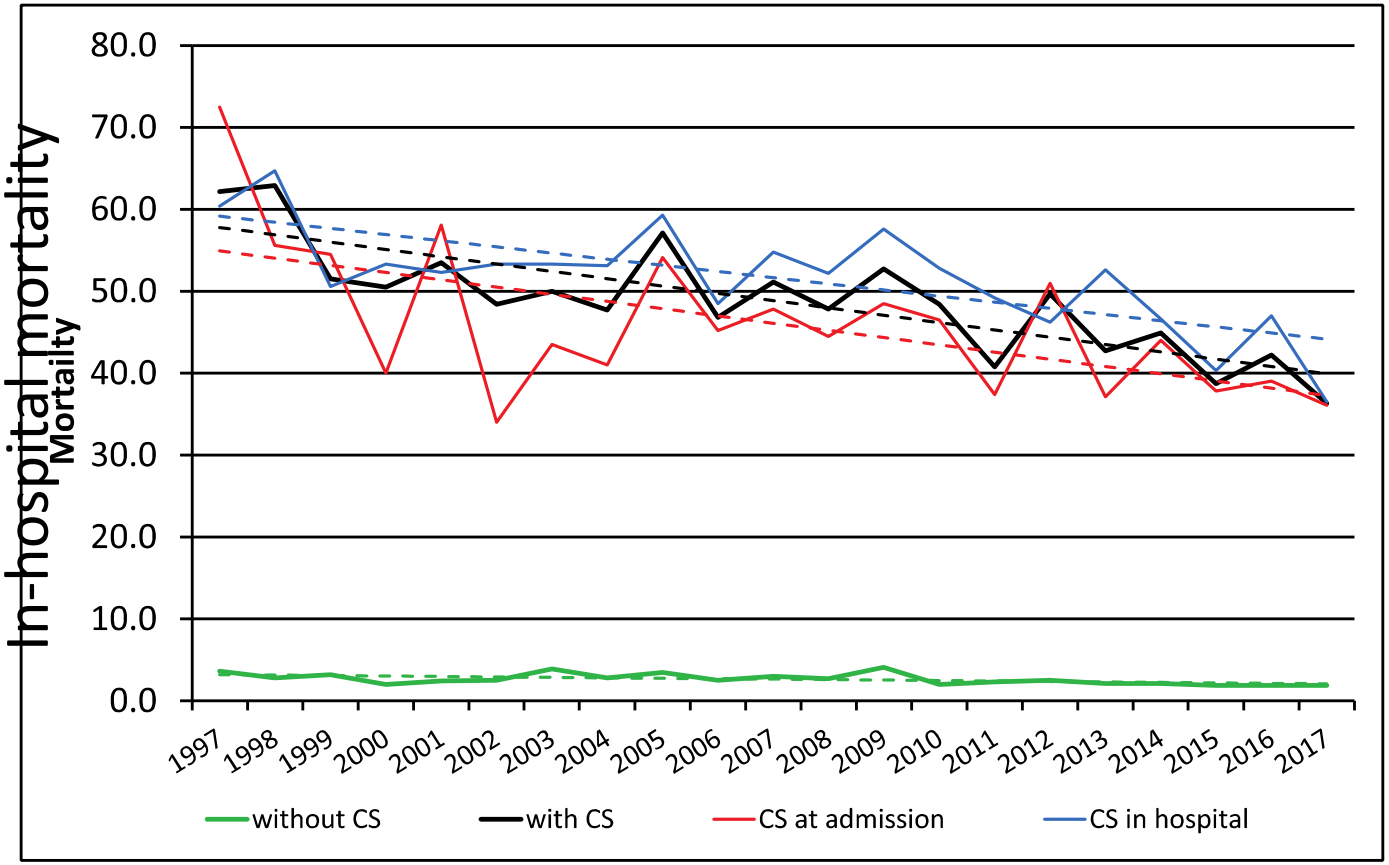
- Other conditions
  - End-stage cardiomyopathy
  - Myocarditis
  - Myocardial contusion
  - Prolonged cardiopulmonary bypass
  - Septic shock with severe myocardial depression
  - Left ventricular outflow tract obstruction
    - Aortic stenosis
    - Hypertropic obstructive cardiomyopathy
  - Obstruction to left ventricular filling
    - Mitral stenosis
    - Left atrial myxoma
  - Acute mitral regurgitation (chordal rupture)
  - Acute aortic insufficiency
  - Acute massive pulmonary embolism
  - Acute stress cardiomyopathy
  - Pheochromocytoma

Reynolds HR et al. Circulation 2008;117:686-97



Mc Donagh TA et al. Eur Heart J 2021; 42:3599-3726

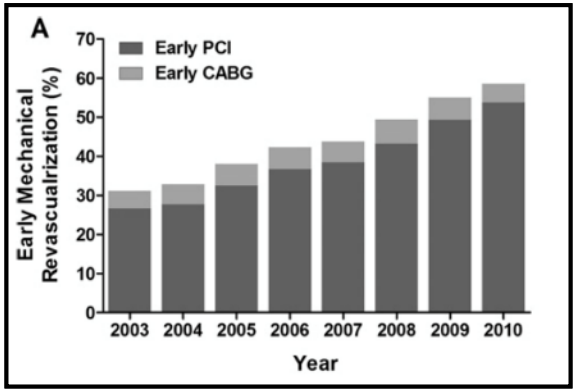
Poor prognosis of cardiogenic shock

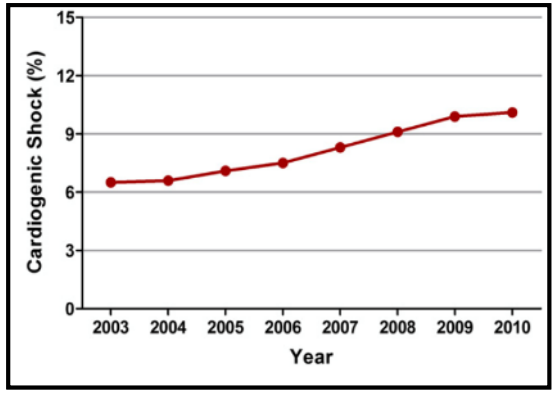


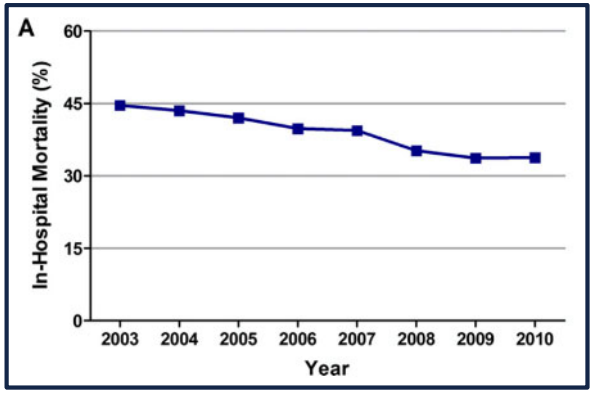
Hunziker L et al. Circ Cardiovasc Interv. 2019;12:e007293

TRENDS IN INCIDENCE AND OUTCOMES OF CARDIOGENIC SHOCK

- From 2003 to 2010, 1 990 486 patients (≥ 40 years) with STEMI
- Early revascularization increased from **30.4% to 50.7%**
- Overall incidence of cardiogenic shock was **7.9% (trends to increase...)**
- Global in-hospital mortality was **39% (trends to decrease...)**







Kolte D et al. J Am Heart Assoc 2014

The FRENSHOCK registry

A Real Life Picture of Cardiogenic Shock in France

48 centers

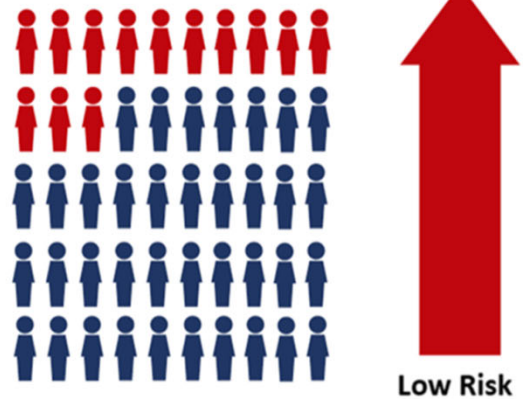
772 patients

FRENSHOCK definition of cardiogenic shock (at least one criterion of each component):

1. *Hemodynamic criteria*
2. *Left and/or right overload criteria*
3. *Organ malperfusion criteria*

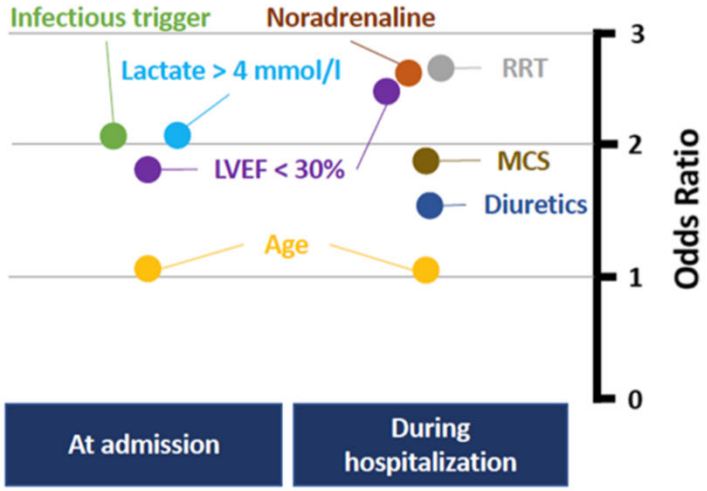
Non-Ischemic CS = 63.7%

30-day mortality 26%



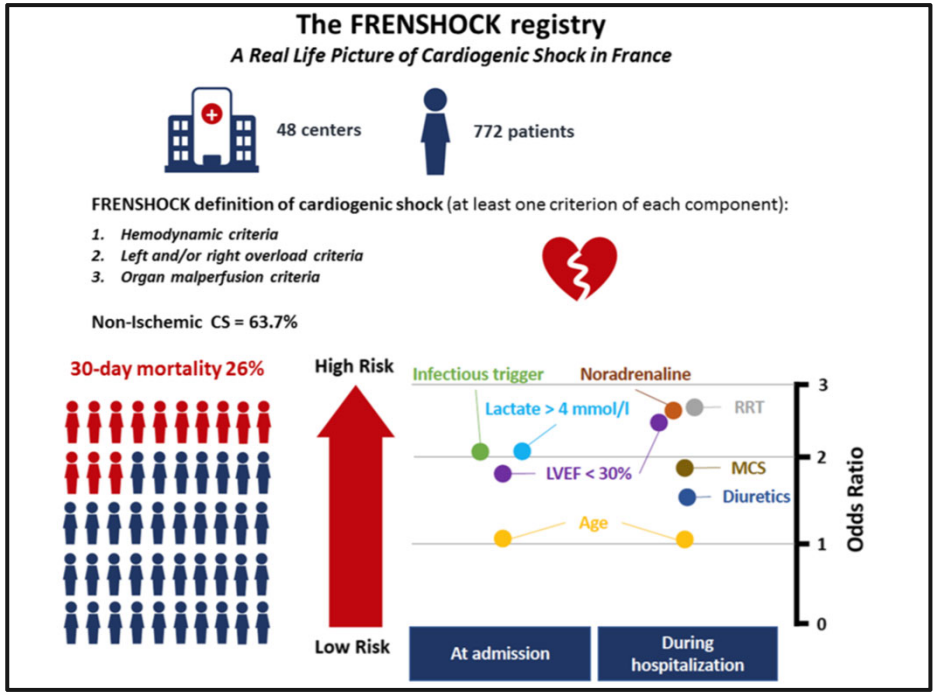
High Risk

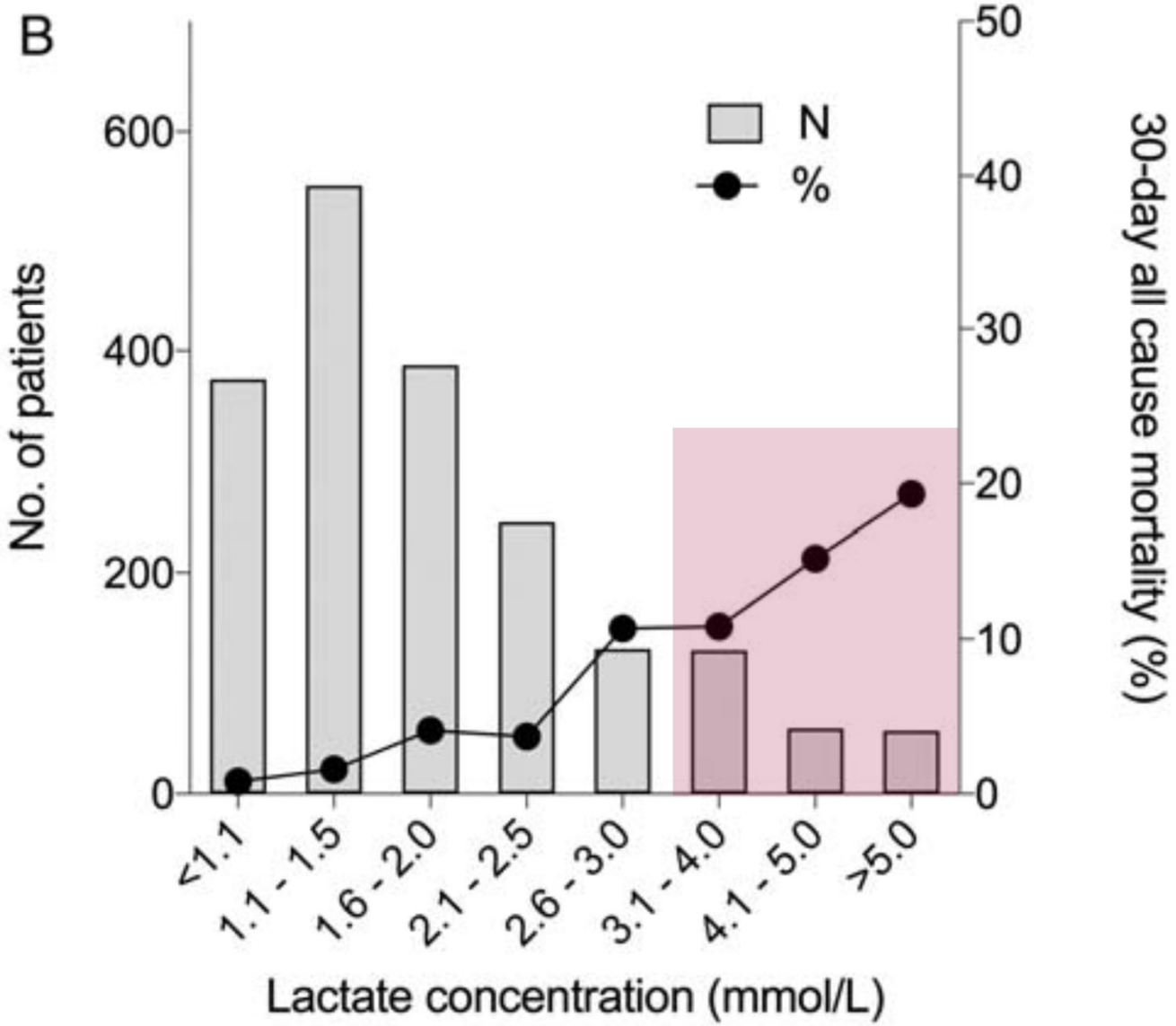
Low Risk



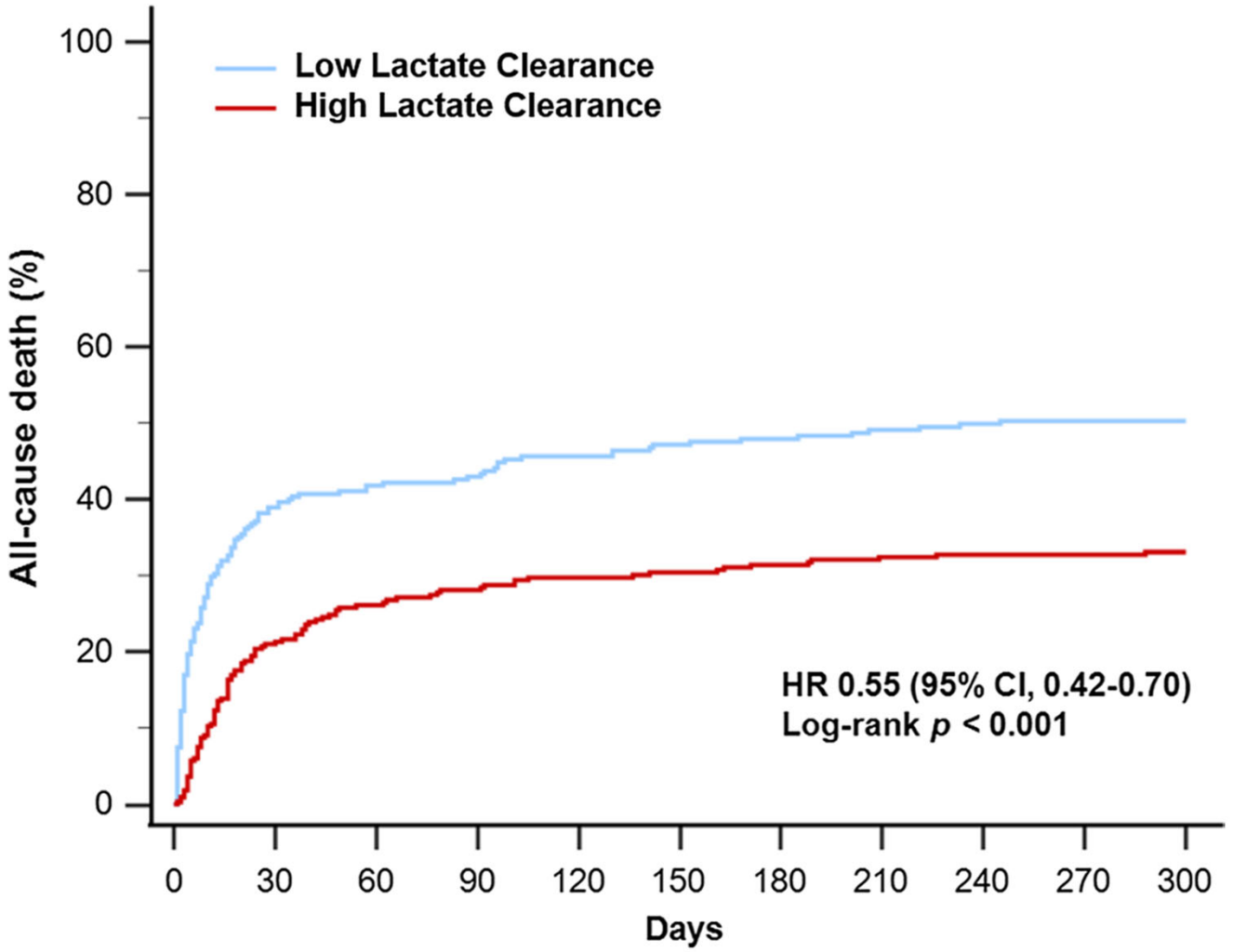
Delmas C et al. ECS Heart Failure 2022; 9:408-19

	Overall population (n = 772)
Medications used, *n* (%)	
Diuretics	633 (82.0)
Volume expander	321 (41.6)
Dobutamine	632 (81.9)
Maximum dose:	
5–10 μg/kg/min	405/632 (52.5)
10–15 μg/kg/min	136/632 (17.6)
>15 μg/kg/min	47/632 (6.1)
Unknown	184/632 (23.8)
Norepinephrine	410 (53.1)
Epinephrine	95 (12.4)
Norepinephrine and dobutamine combination	352 (45.6%)
Levosimendan	57 (7.4)
Dopamine	2 (0.3)
Isoprenaline	32 (4.1)
Antiarrhythmic	298 (38.6)
Transfusion	128 (16.6)
Fibrinolysis	13 (1.7)
Organ replacement therapies, *n* (%)	
Respiratory support	
Invasive	291 (37.9)
Non-invasive	199 (25.9)
Mechanical circulatory support	143 (18.6)
IABP	48/143 (34.3)
Impella	26/143 (18.6)
ECLS	85/143 (60.7)
Renal replacement therapy	122 (15.8)



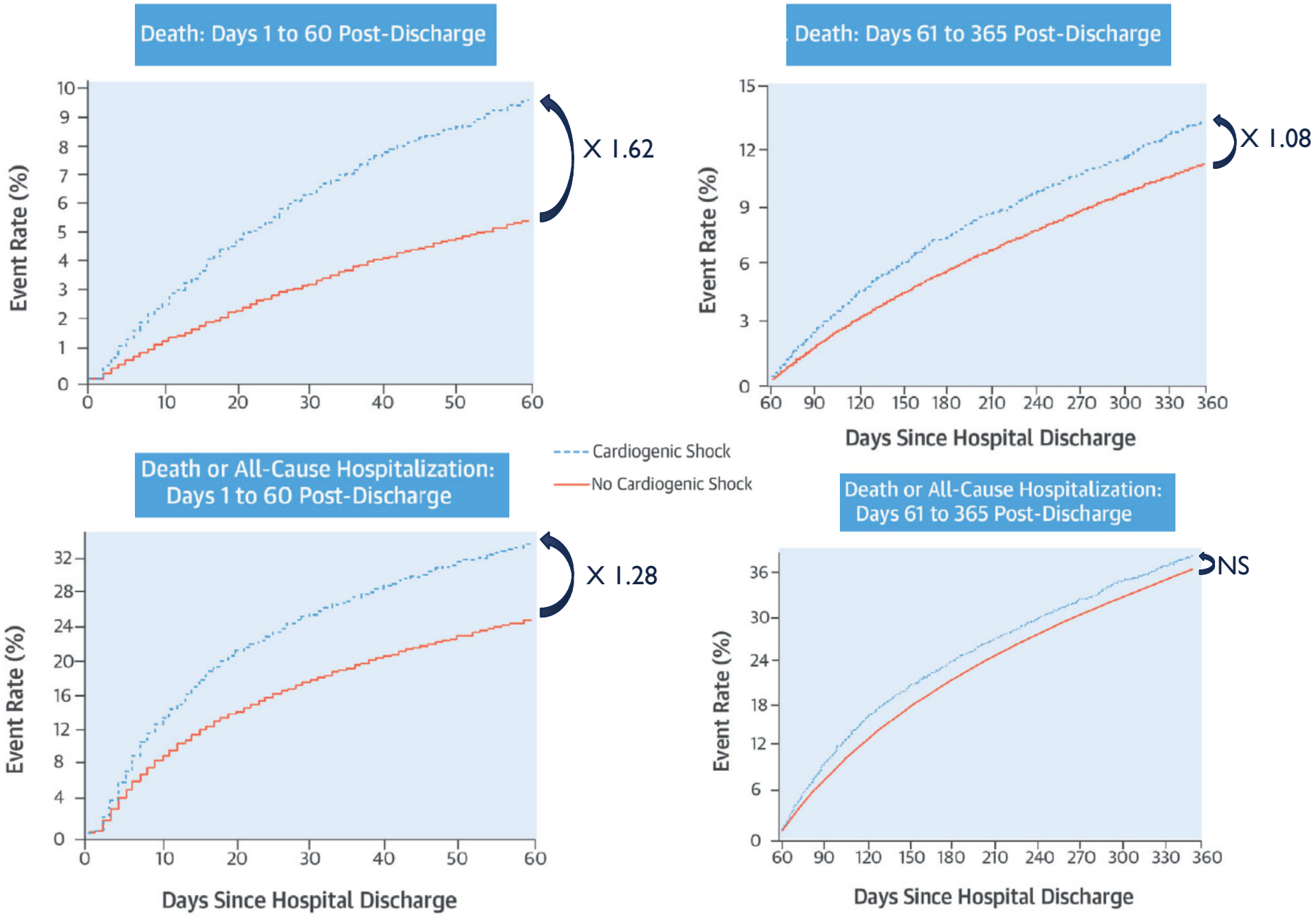

B
No. of patients
600
400
200
0
N
%
50
40
30
20
10
0
30-day all cause mortality (%)
<1.1
1.1 - 1.5
1.6 - 2.0
2.1 - 2.5
2.6 - 3.0
3.1 - 4.0
4.1 - 5.0
>5.0
Lactate concentration (mmol/L)

Park IH et al. J Intensive Care 2021;9:63

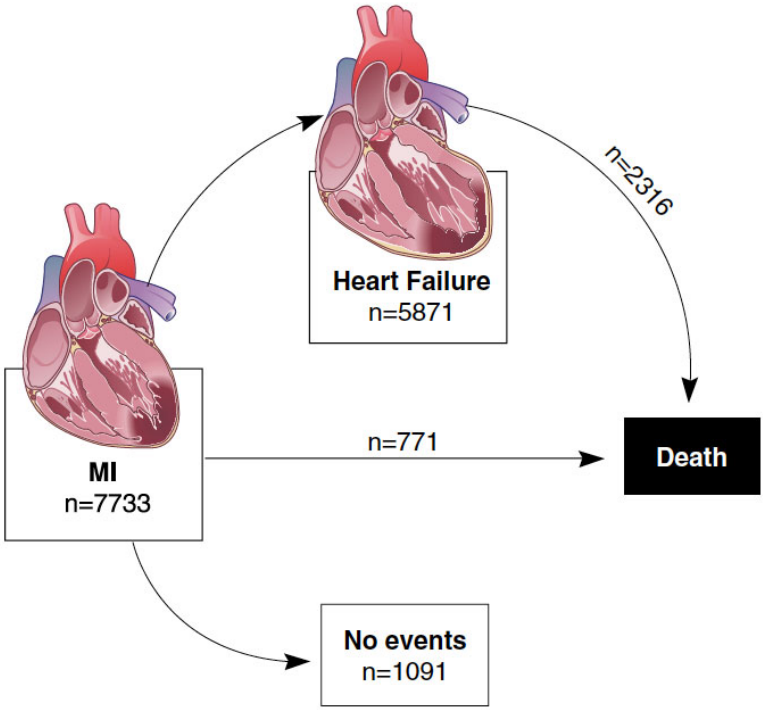


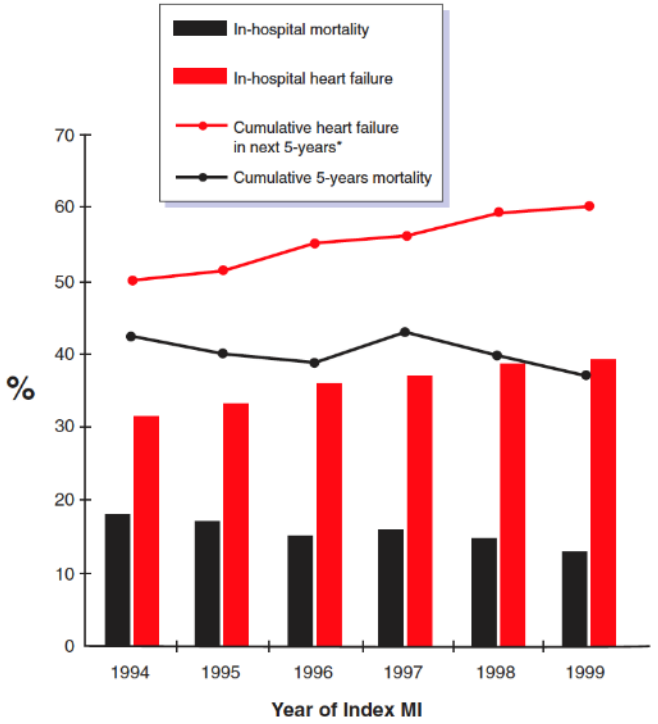
**High lactate clearance was defined as > 66% in 24 hours*

Shah RU et al. JACC 2016;67:739-47



CHRONIC HEART FAILURE ATFER MYOCARDIAL INFARCTION

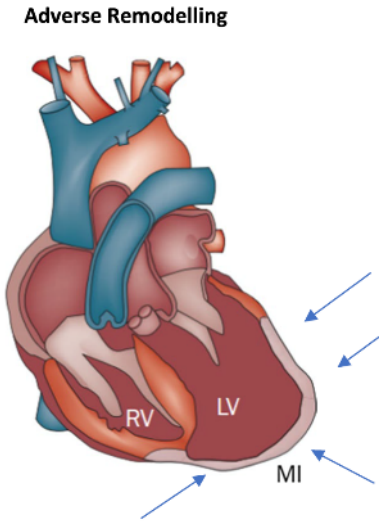




Ezekowitz JA et al. J Am Coll Cardiol 2009;53:13-20

VENTRICULAR REMODELING

- 30% of patients after MI (infarct size is the principal risk factor)
- Main origin of chronic heart failure after MI
- Increased parietal stress (+++) and myocardial work
- Increased myocardial oxygen consumption
- Decreased coronary blood flow (+++)
- Increased compliance of infarcted zone
  - Thinning of myocardial wall
  - Left ventricular dilation



Deja MA et al. Circulation 2012; 125:2639-48

Michler RE et al. J Thorac Cardiovasc Surg 2013;146:1139-45

Jackson BM JACC 2002; 40:1160-7

Van Diepen S et al. Circulation 2017;136:e232-68

SHOCK Trial[9]*	IABP-SHOCK II[1]†	ESC HF Guidelines[15]
Clinical criteria: SBP <90 mm Hg for ≥30 min OR Support to maintain SBP ≥90 mm Hg AND End-organ hypoperfusion (urine output <30 mL/h or cool extremities) Hemodynamic criteria: CI of ≤2.2 L·min^{-1}·m^{-2} AND PCWP ≥15 mm Hg	Clinical criteria: SBP <90 mm Hg for ≥30 min OR Catecholamines to maintain SBP >90 mm Hg AND Clinical pulmonary congestion AND Impaired end-organ perfusion (altered mental status, cold/clammy skin and extremities, urine output <30 mL/h, or lactate >2.0 mmol/L)	SBP <90 mm Hg with adequate volume and clinical or laboratory signs of hypoperfusion Clinical hypoperfusion: Cold extremities, oliguria, mental confusion, dizziness, narrow pulse pressure Laboratory hypoperfusion: Metabolic acidosis, elevated serum lactate, elevated serum creatinine

Peripheral Circulation	Volume Status: Wet	Volume Status: Dry
Cold	Classic Cardiogenic Shock (↓CI; ↑SVRI; ↑PCWP) 64%	Euvolemic Cardiogenic Shock (↓CI; ↑SVRI; ↔PCWP) 28%
Warm	Vasodilatory Cardiogenic Shock or Mixed Shock 5% (↓CI; ↓/↔SVRI; ↑PCWP)	Vasodilatory Shock (Not Cardiogenic Shock) 3% (↑CI; ↓SVRI; ↓PCWP)

5% of patients presented end-organ hypoperfusion while SAP was > 90 mmHg

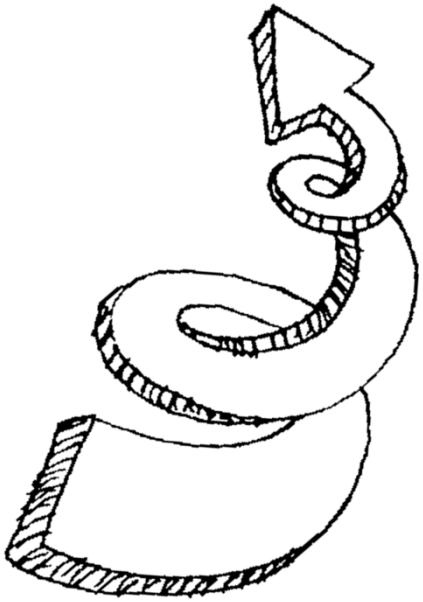
Table 4: INTERMACS Profiles

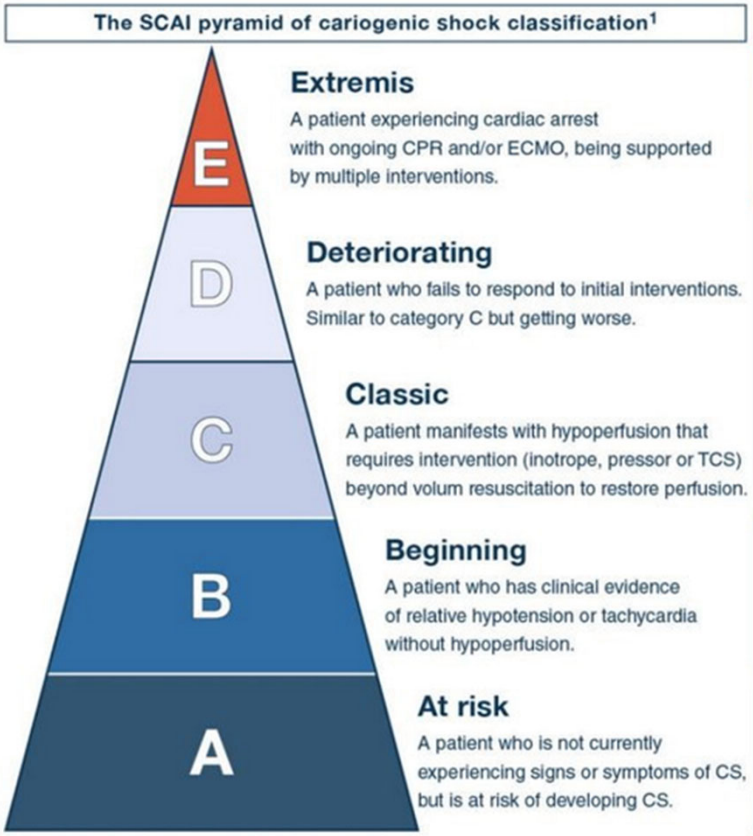
Profiles	Brief Description	Details
INTERMACS 1	Critical cardiogenic shock (Crash and burn)	Life-threatening hypotension despite rapidly escalating inotropic support.
INTERMACS 2	Progressive decline (Sliding fast on inotropes)	Declining function despite intravenous inotropic support.
INTERMACS 3	Stable but inotrope dependent (Dependent stability)	Stable on continuous intravenous inotropic support.
INTERMACS 4	Resting symptoms on oral therapy at home	Patient experiences daily symptoms of congestion at rest or during activities of daily living.
INTERMACS 5	Exertion intolerant	Patient is comfortable at rest and with activities of daily living but unable to engage in any other activity.
INTERMACS 6	Exertion limited (Walking wounded)	Patient has fatigue after the first few minutes of any meaningful activity.
INTERMACS 7	Advanced NYHA class III (Placeholder)	Patients living comfortably with meaningful activity limited to mild physical exertion.

INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support; NYHA = New York Heart Association. Adapted from: Stevenson LW, et al.[25]

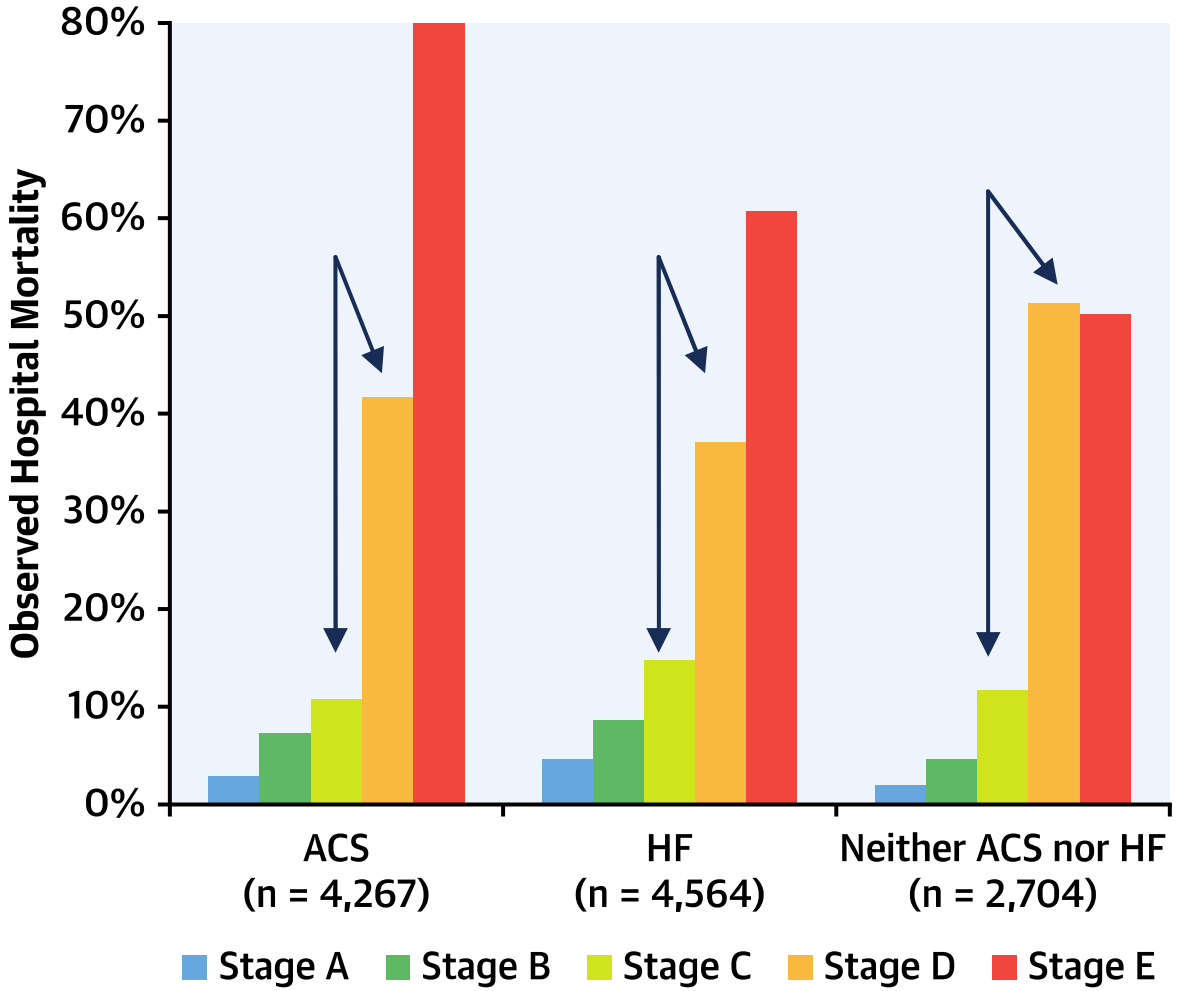
CALSSIFICATION SCAI DU CHOC CARDIOGÉNIQUE

SCAI: Society for Cardiovascular Angiography and Interventions (SCAI)

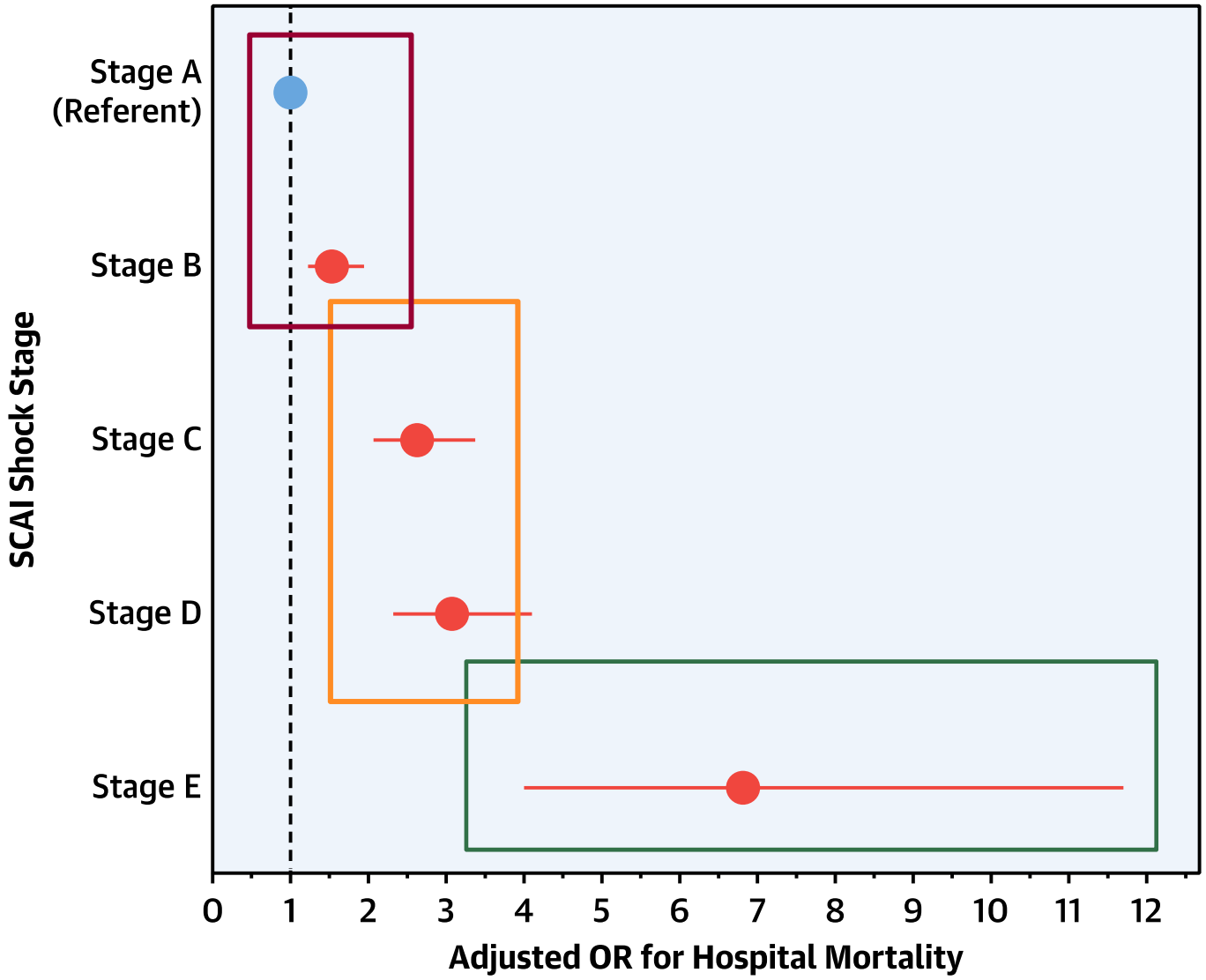




Baran DA, et al. Catheter Cardiovasc Interv. 2019;94: 29–37



Jentzer JC et al. A Am Coll Cardiol 2019; 74:2117-28



Jentzer JC et al. A Am Coll Cardiol 2019; 74:2117-28

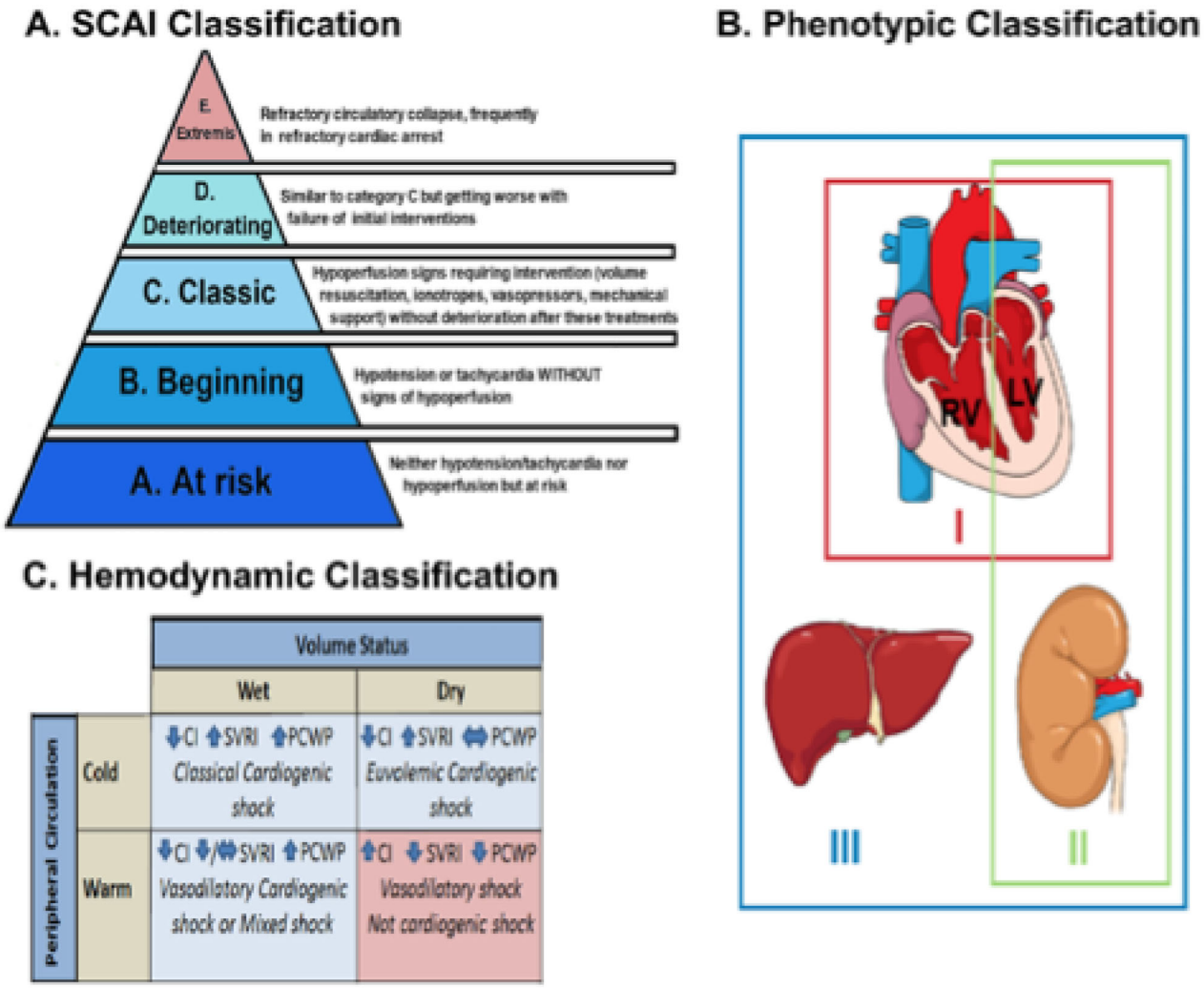


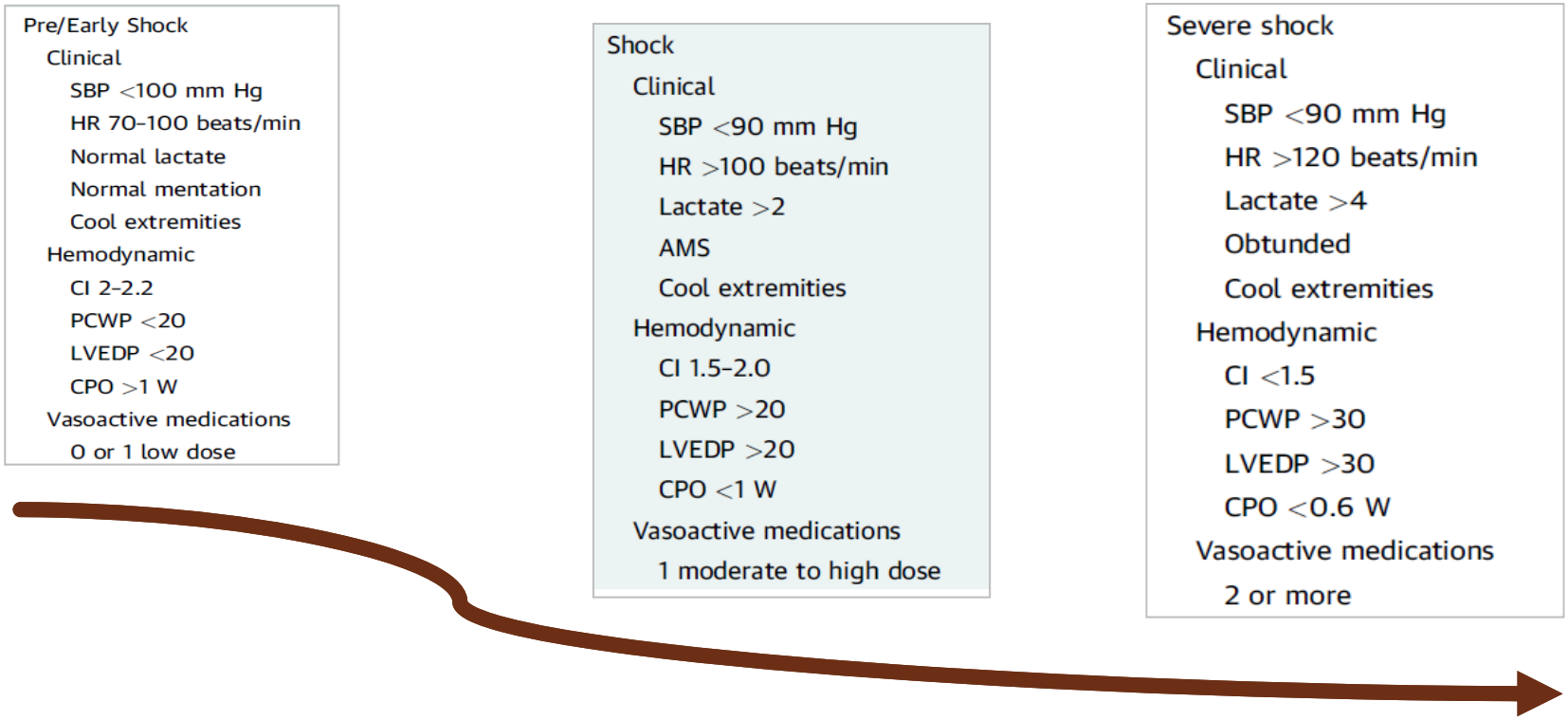
Fig. 1 Classifications of cardiogenic shock. **A** SCAI classification. **B** Phenotypic classification: Three different phenotypes are proposed (I-Not congested, II-cardiorenal, and III-cardiometabolic). **C** Hemodynamic classification: CI, cardiac index; PCWP, pulmonary capillary wedge pressure; and SVRI, systemic vascular resistance index

A Practical Approach to Mechanical Circulatory Support in Patients Undergoing Percutaneous Coronary Intervention

An Interventional Perspective

Atkinson TM et al. J Am Coll Cardiol Interv 2016;9:871–83

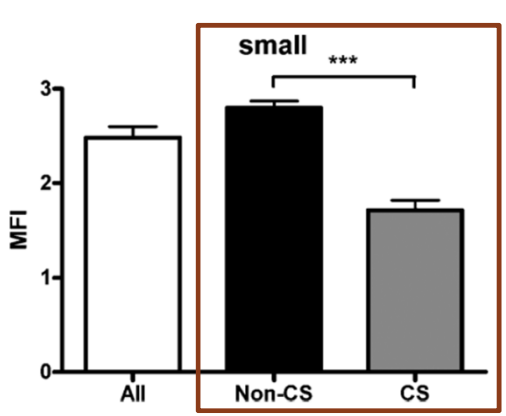
Spectrum of Cardiogenic Shock

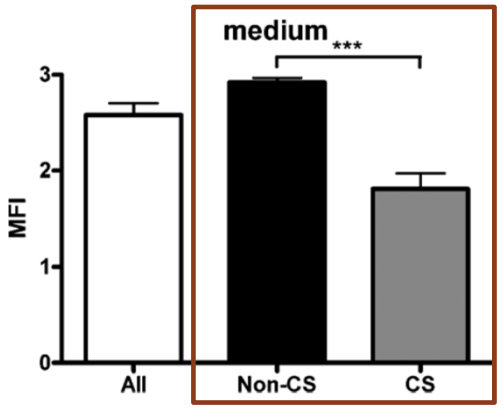


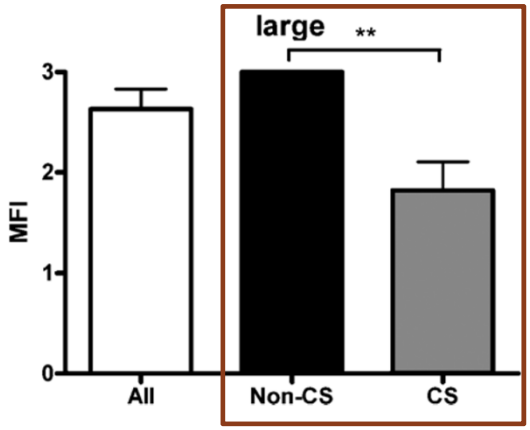
DISEASE OF ENTIRE CIRCULATORY SYSTEM

- Decreased stroke volume and thus reduced cardiac output while compensatory mechanism (tachycardia)
- Reduction myocardial contractility
- Inadequate oxygen delivery: mismatch between oxygen delivery and oxygen consumption
- Disturbances of entire circulatory system (peripheral vasculature)
- Adaptative vasoconstriction through increased afterload (neurohumoral system)
- Pathological vasodilation related to systemic inflammatory response (end organ hypoperfusion and/or ischemia reperfusion phenomenon)

ALTERATION OF MICROCIRCULATORY BLOOD FLOW

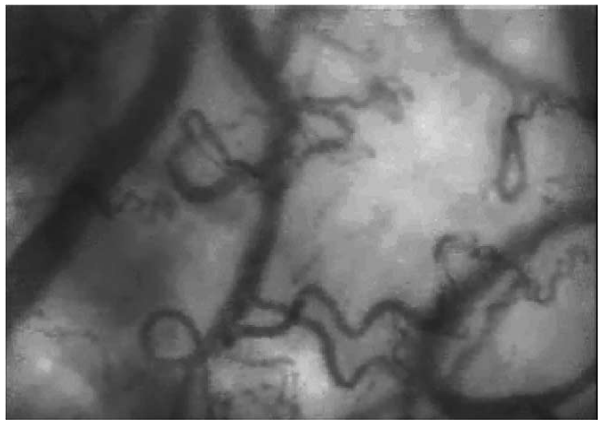






All
Non-CS
CS

Microvascular flow index (MFI)



Jung C et al. Clin Hemorheol Microcirc 2009; 42:141-8

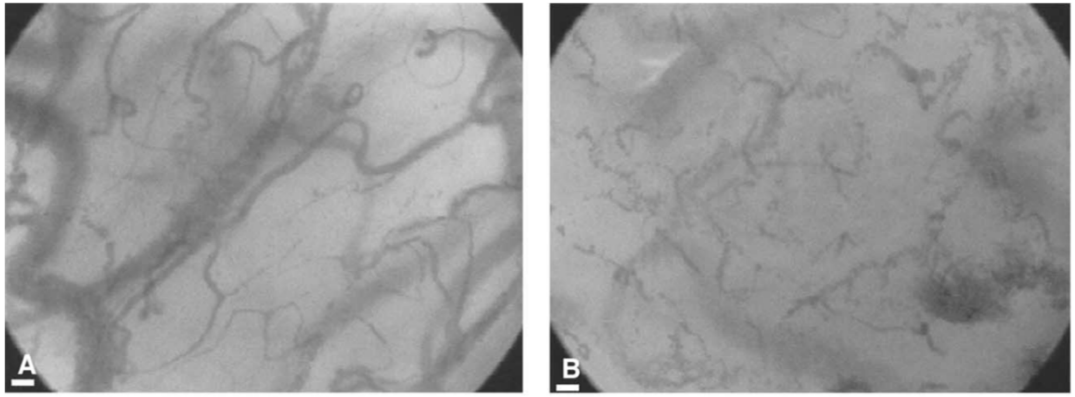


Table III. Vessel density (n/ mm)

	Control patients (n = 15)	Cardiac failure (n = 9)	Cardiogenic shock (n = 31)
Total number of vessels	5.9 [5.4–6.7]	4.8 [4.0–5.2]	5.1 [3.9–6.5]
Perfused vessels	5.8 [5.5–6.3]	4.6 [3.6–4.9]*	4.1 [2.8–5.0]†
Perfused large vessels	2.2 [1.9–2.7]	2.1 [1.8–2.9]	2.0 [1.6–2.8]
Perfused small vessels	4.0 [3.7–4.4]	1.3 [1.1–1.7]†	1.2 [0.7–1.9]†

*$P < .01$ versus control patients.
†$P < .001$ versus control patients.

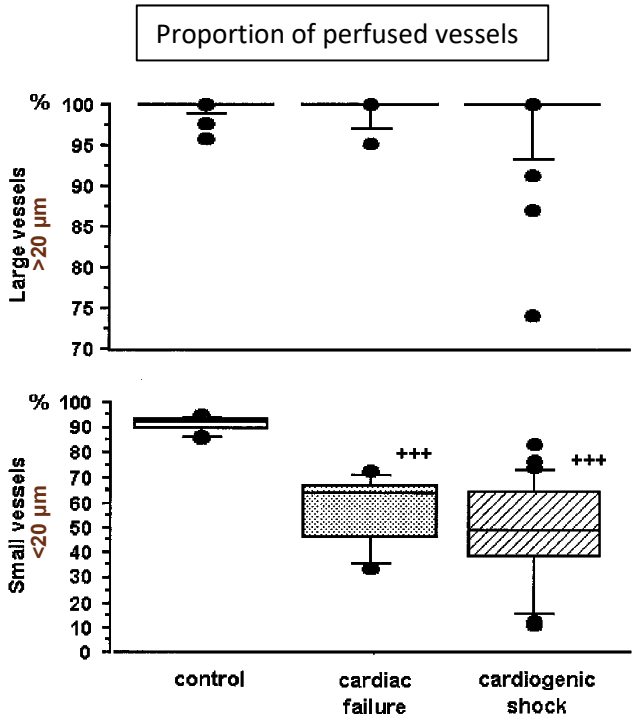
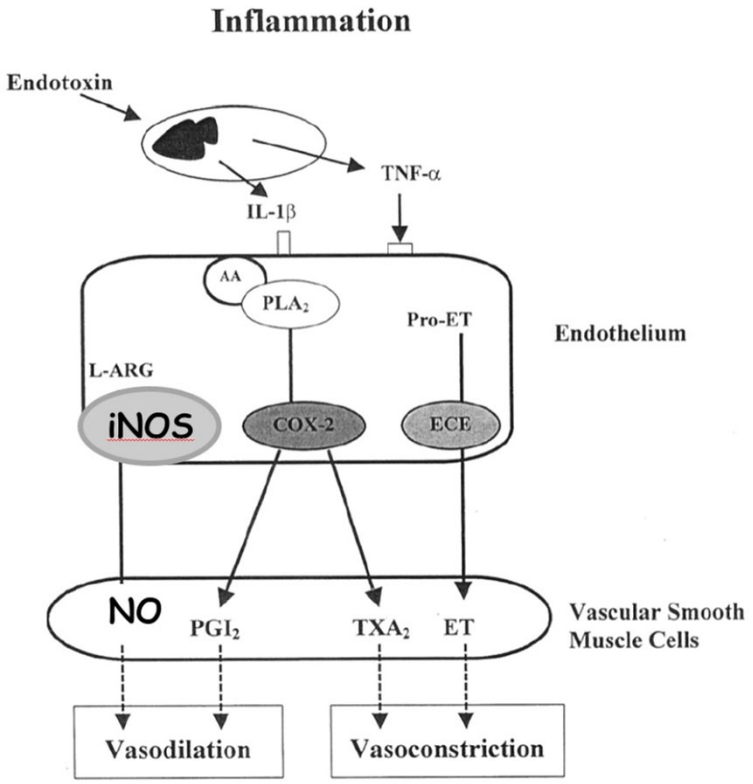


Table IV. Effects of topical acetylcholine (10-2M) application in 10 patients with cardiogenic shock

	Cardiogenic shock (n = 10)	
	Baseline	Acetylcholine 10-2M
Total number of vessels (n/mm)	5.0 [4.8–5.7]	5.8 [4.3–6.2]
Perfused vessels (%)	84 [80–89]‡	98 [97–99]†
Perfused large vessels (%)	100 [96–100]	100 [100–100]
Perfused small vessels (%)	69 [59–73]‡	91 [88–95]†

IMPAIRMENT OF MICROCIRCULATION

- Present early in cardiogenic shock
- Microcirculatory network seems to be initially present and functional
- A decreased in capillary density by reduced blood flow
- Organ dysfunction (liver, kidney…)
- Intestinal barrier (bacterial translocation)
- Lipopolysaccharide (endotoxins) in blood stream (endotoxemia)
- Inflammatory response (cytokine release) and multiorgan failure

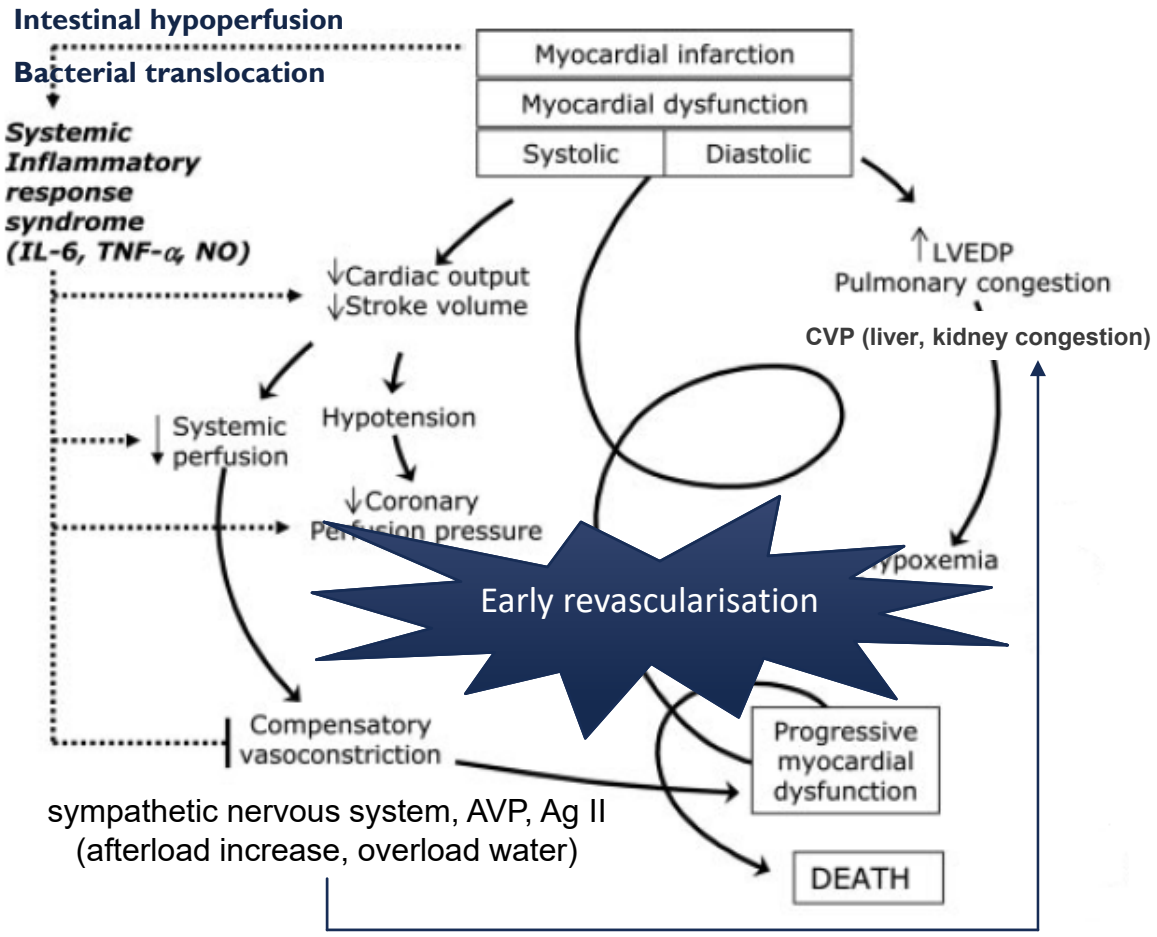


Bertini P et al; Curr Opin Crit Care 2021;27:409-415

SYSTEMIC CARDIOVASCULAR AND INFLAMMATORY DISEASE

Coronary endothelial dysfonction

Myocardial depression



Reynolds HR et al. Circulation 2008; 117:686-97

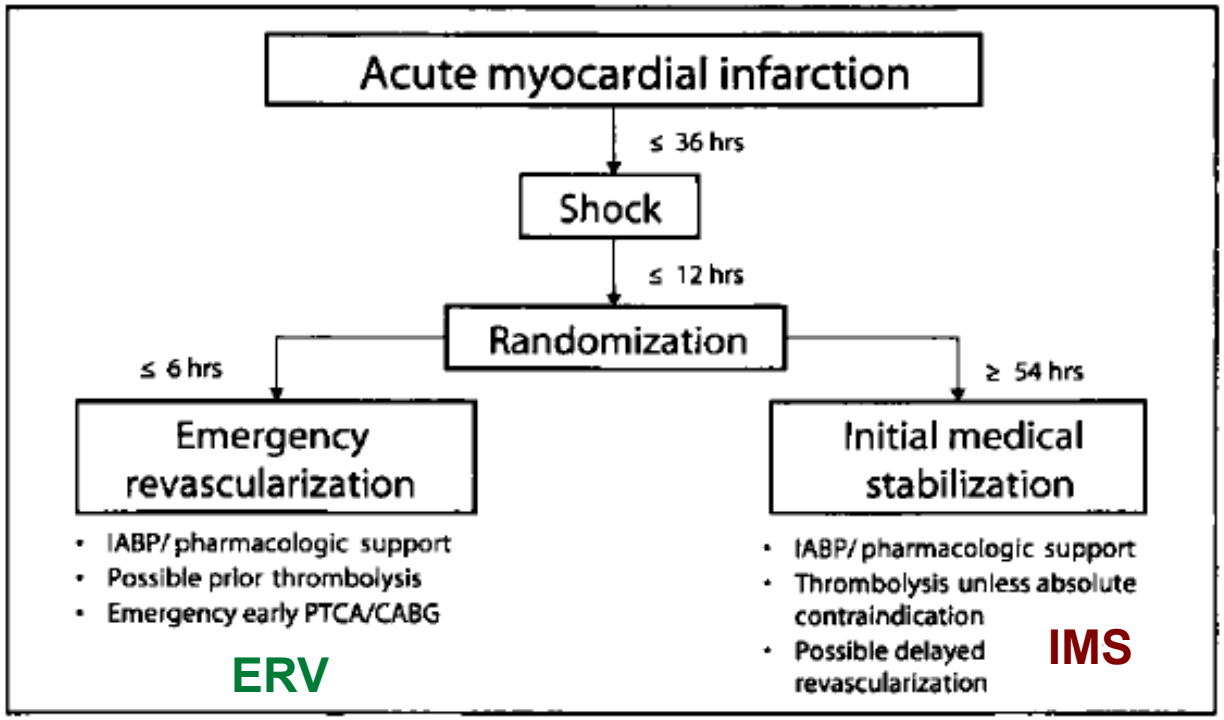
SHOCK TRIAL 1999

The New England
Journal of Medicine

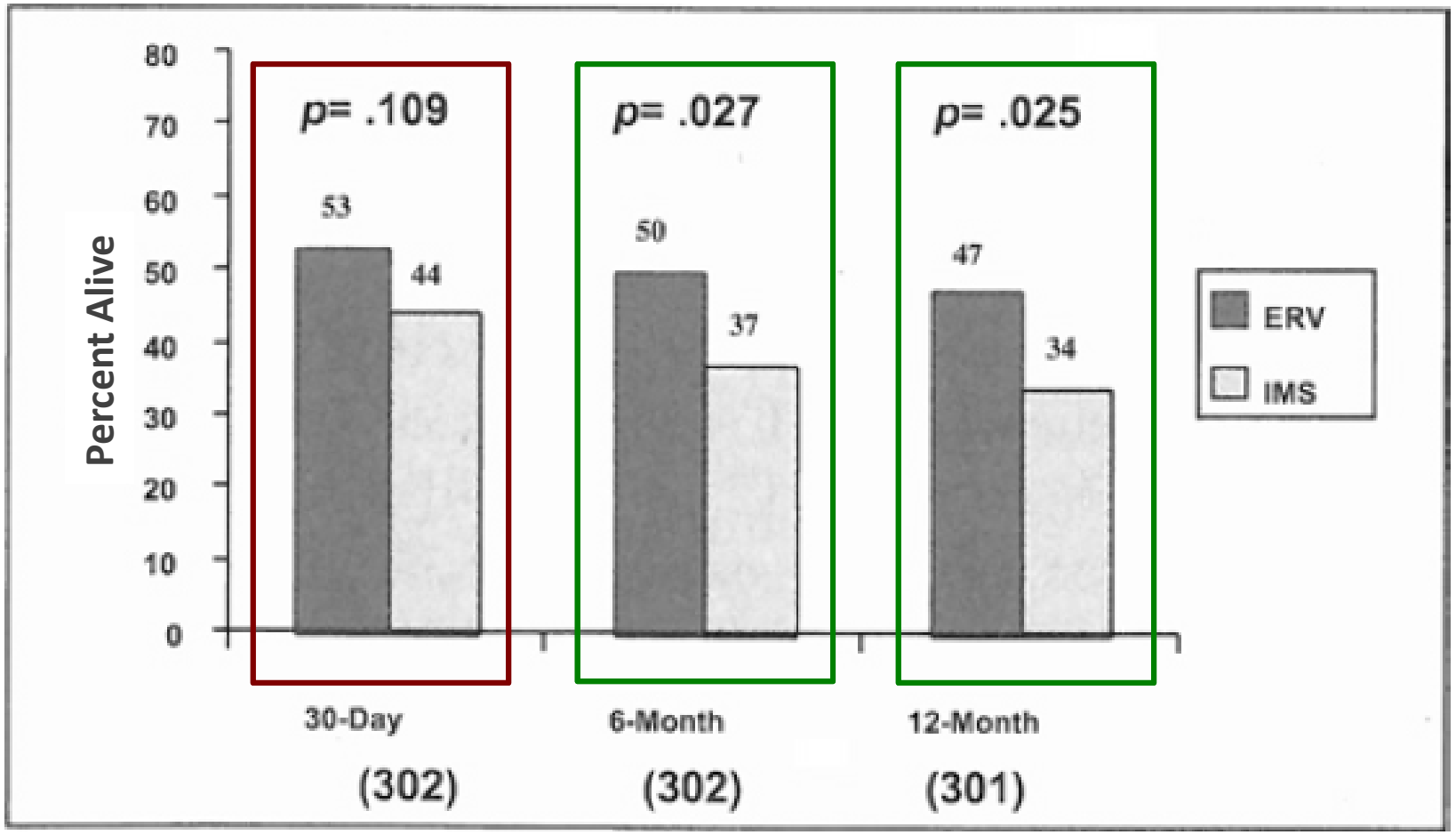
VOLUME 341 AUGUST 26, 1999 NUMBER 9

EARLY REVASCULARIZATION IN ACUTE MYOCARDIAL INFARCTION COMPLICATED BY CARDIOGENIC SHOCK

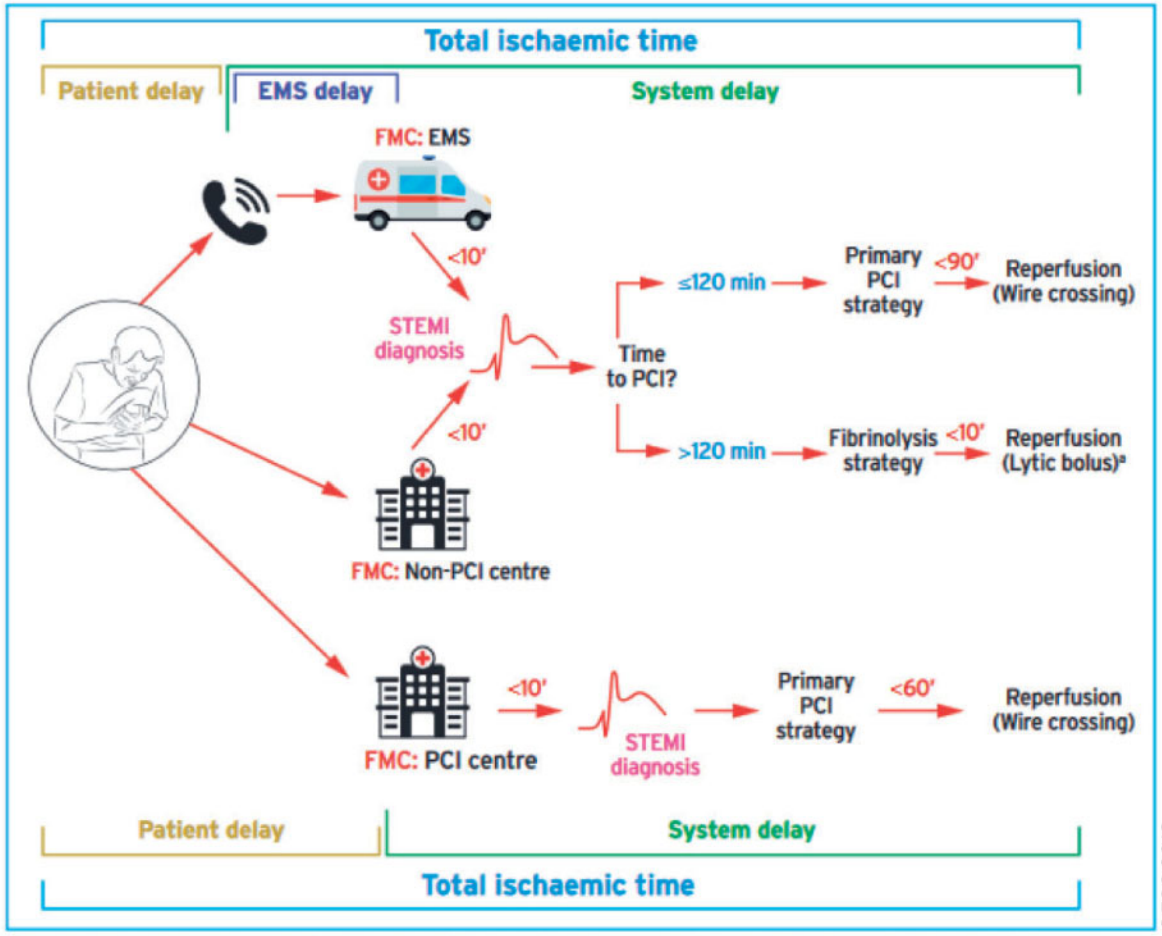
JUDITH S. HOCHMAN, M.D., LYNN A. SLEEPER, SC.D., JOHN G. WEBB, M.D., TIMOTHY A. SANBORN, M.D., HARVEY D. WHITE, D.SC., J. DAVID TALLEY, M.D., CHRISTOPHER E. BULLER, M.D., ALICE K. JACOBS, M.D., JAMES N. SLATER, M.D., JACQUES COL, M.D., SONJA M. MCKINLAY, PH.D., AND THIERRY H. LEJEMTEL, M.D., FOR THE SHOCK INVESTIGATORS*



Early myocardial revascularization (SHOCK Trial)



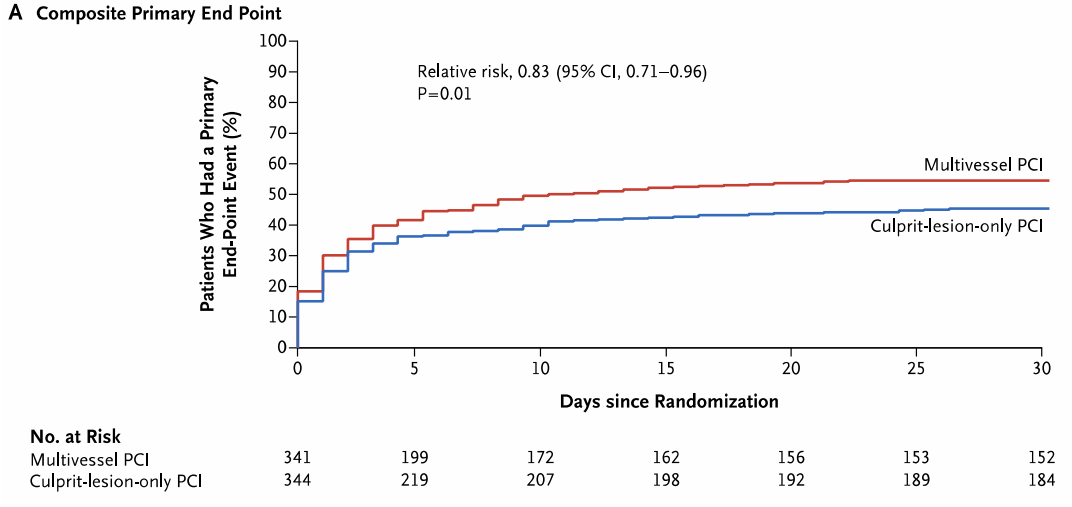
Hochman JS et al. N Engl J Med 1999; 341:625-34

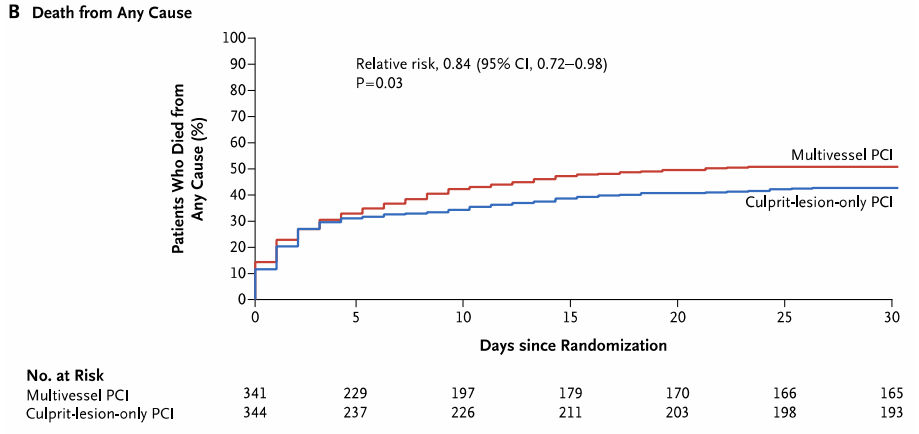


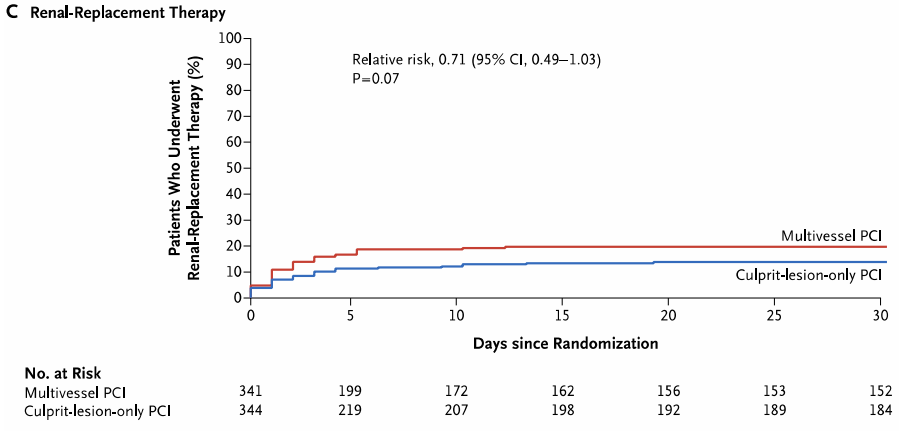
The recommended mode of patient presentation is by alerting the EMS (call national emergency number: 112 or similar number according to region). When STEMI diagnosis is made in the out-of-hospital setting (via EMS) or in a non-PCI centre, the choice of reperfusion strategy is based on the estimated time from STEMI diagnosis to PCI-mediated reperfusion (wire crossing). System delay for patients alerting the EMS starts at the time of phone alert, although FMC occurs when the EMS arrives at the scene. EMS = emergency medical service.
FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction. 'denotes minutes.
[a]Patients receiving fibrinolysis should be transferred to a PCI centre immediately after administration of the lytic bolus.

Neumann FJ et al. Eur Heart J 2019; 40: 87-165

PCI Strategies in Patients with Acute Myocardial Infarction and Cardiogenic Shock

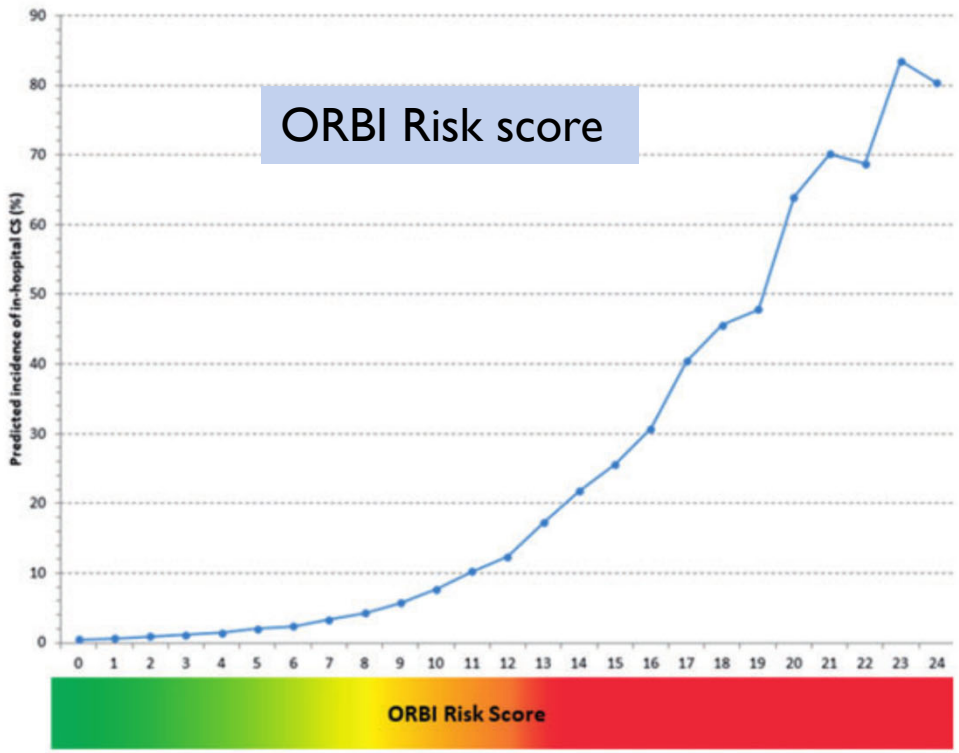






Thiele H et al. New Engl J Med 2017;377: 2419-32

Variable	Points
Age > 70 years old	2
Previous stroke / TIA	2
Presentation as cardiac arrest	3
Anterior myocardial infarction	1
First medical contact-to-pPCI delay > 90 min	2
Killip class II on admission	2
Killip class III on admission	6
Heart rate > 90/min on admission	3
SBP < 125 mmHg and PP < 45 mmHg on admission	4
Glycaemia > 10 mmol/l on admission	3
Culprit lesion of the left main	5
Post-pPCI TIMI flow < 3	5



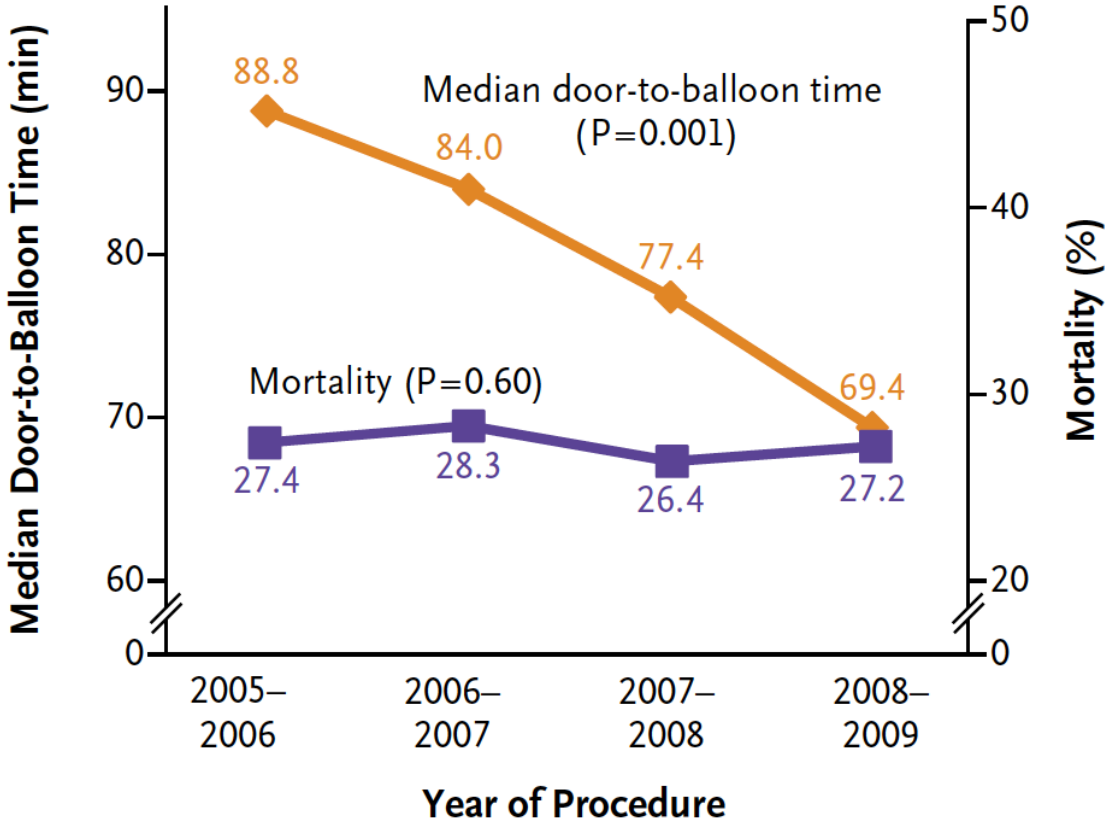
Risk categories

Category	Score	Observed incidence of CS
Low	0-7	1.3
Low-to-intermediate	8-10	6.6
Intermediate-to-high	11-12	11.7
High	≥ 13	31.8

Auffret V et al. Eur Heart J 2018; 379:2090-102

IS « TIME IS MUSCLE » CONCEPT ENOUGH?

Cardiogenic Shock (N=9535)

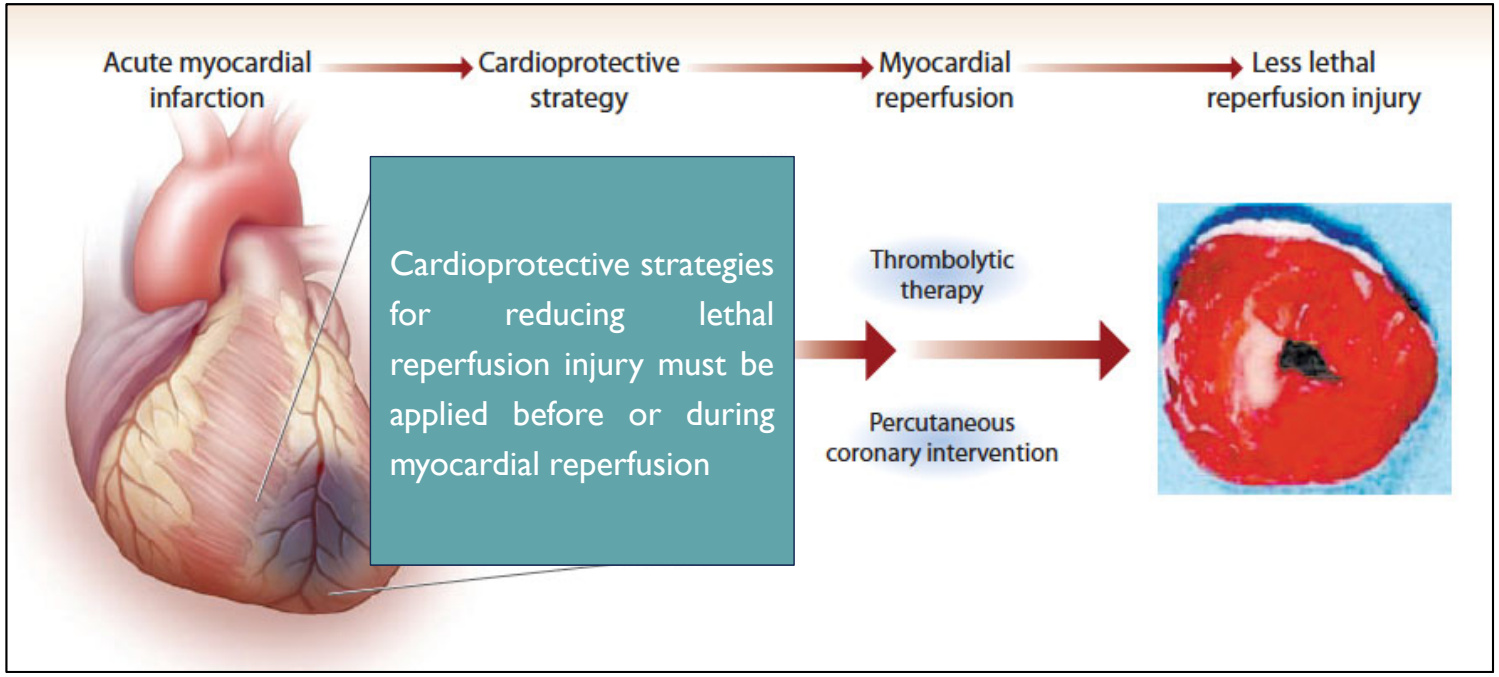


Menees DM. *et al. New Engl J Med 2013; 369:901-9*

From Door-to-Balloon to Door-to-Unload Time

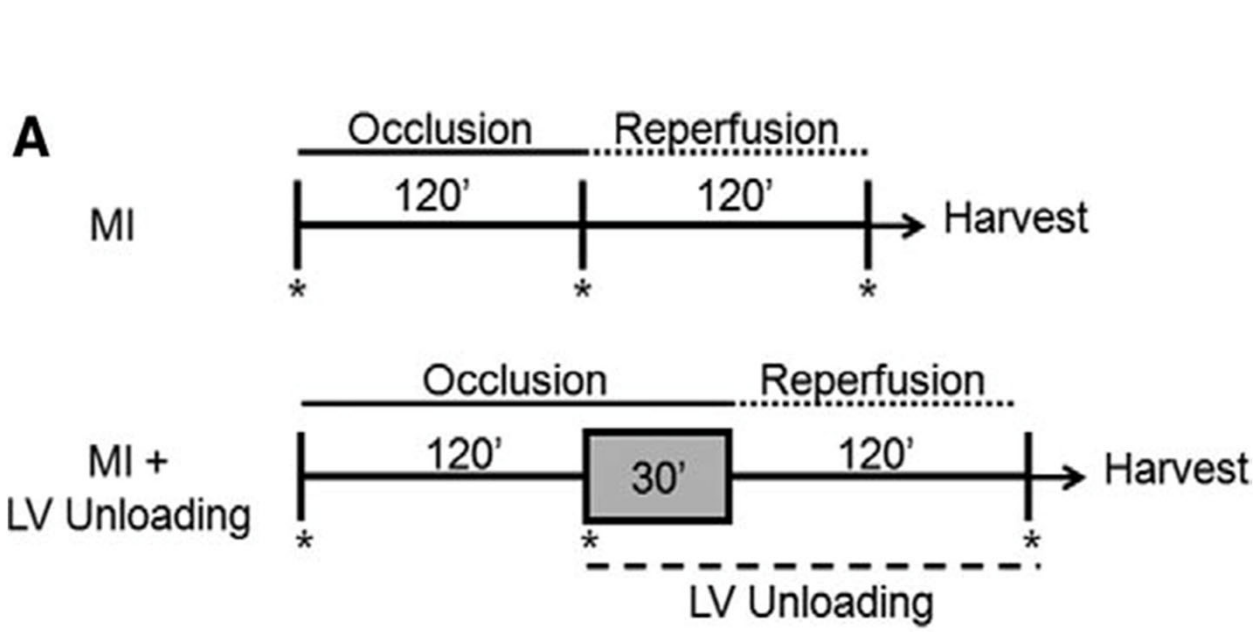
An emerging view on the management of STEMI complicated by cardiogenic shock.

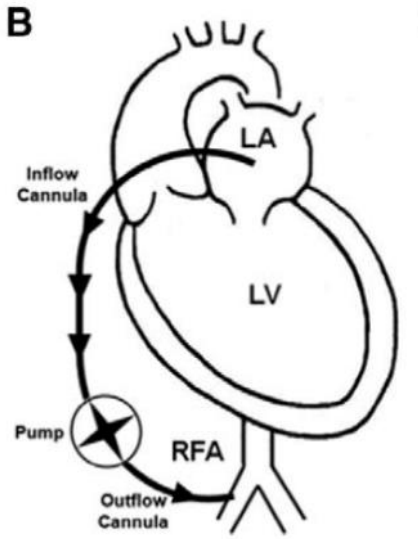
BY NAVIN K. KAPUR, MD



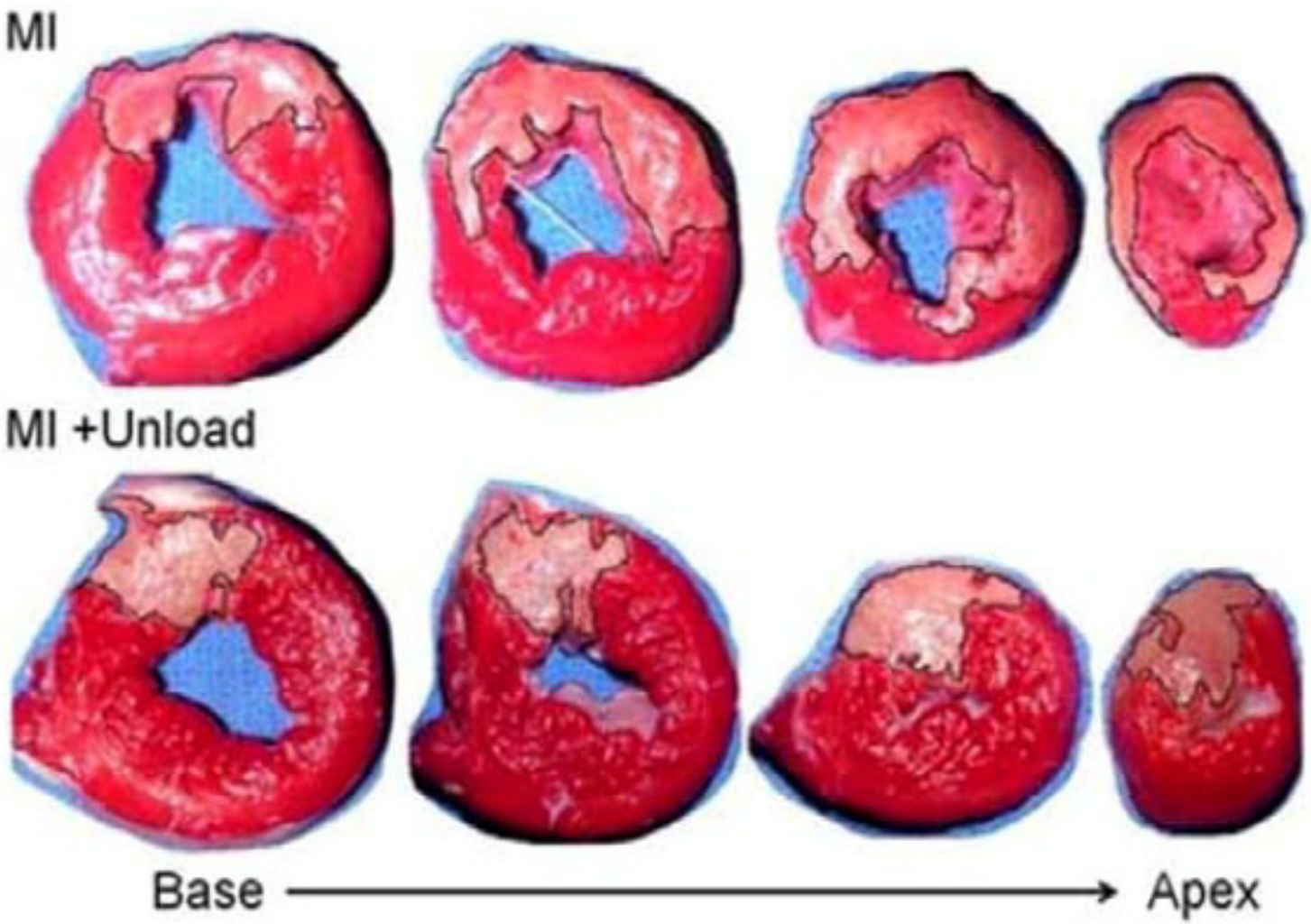
Yellon DM et al. N Engl J Med 2007;357:1121-35

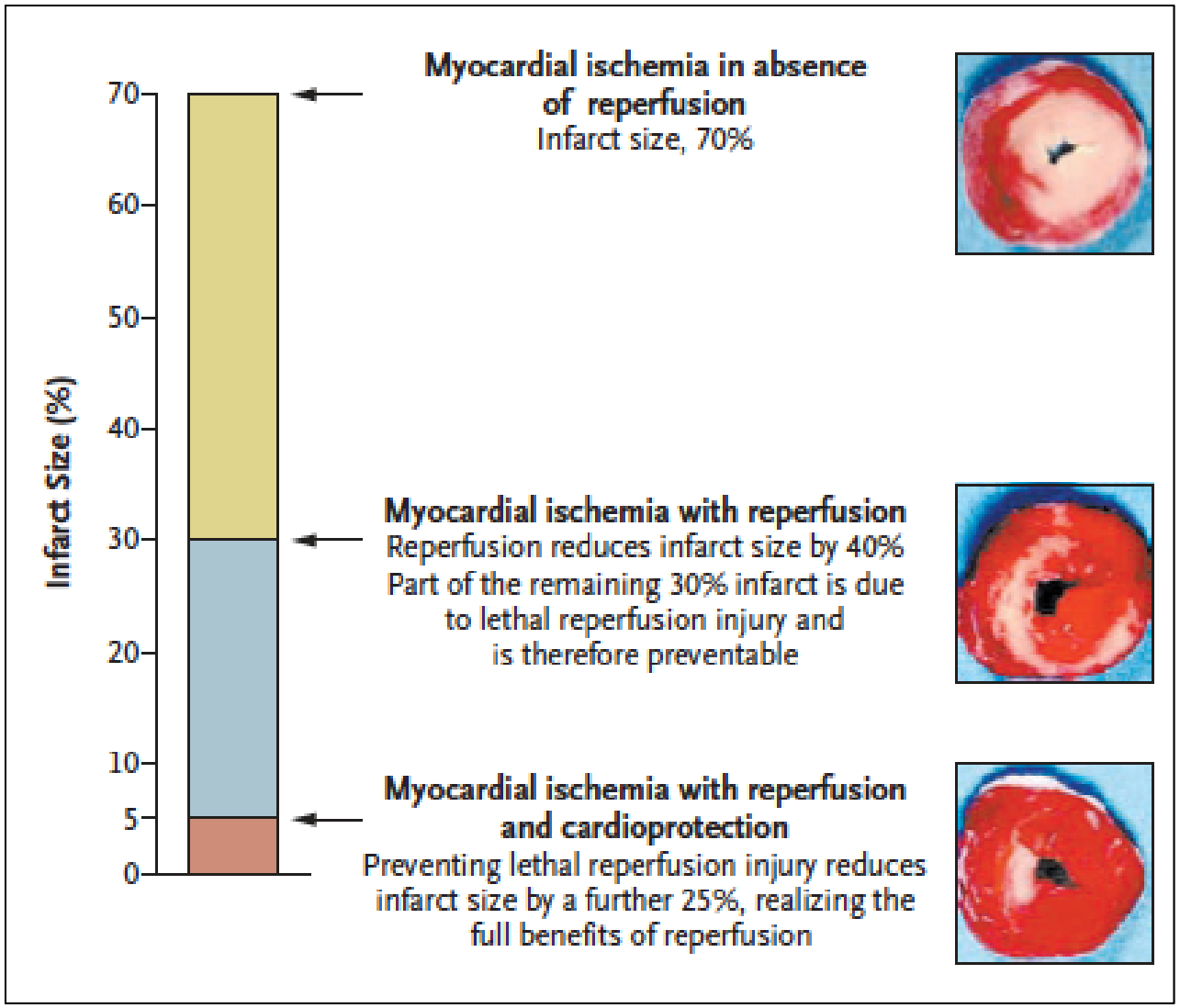
Mechanically Unloading the Left Ventricle Before Coronary Reperfusion Reduces Left Ventricular Wall Stress and Myocardial Infarct Size





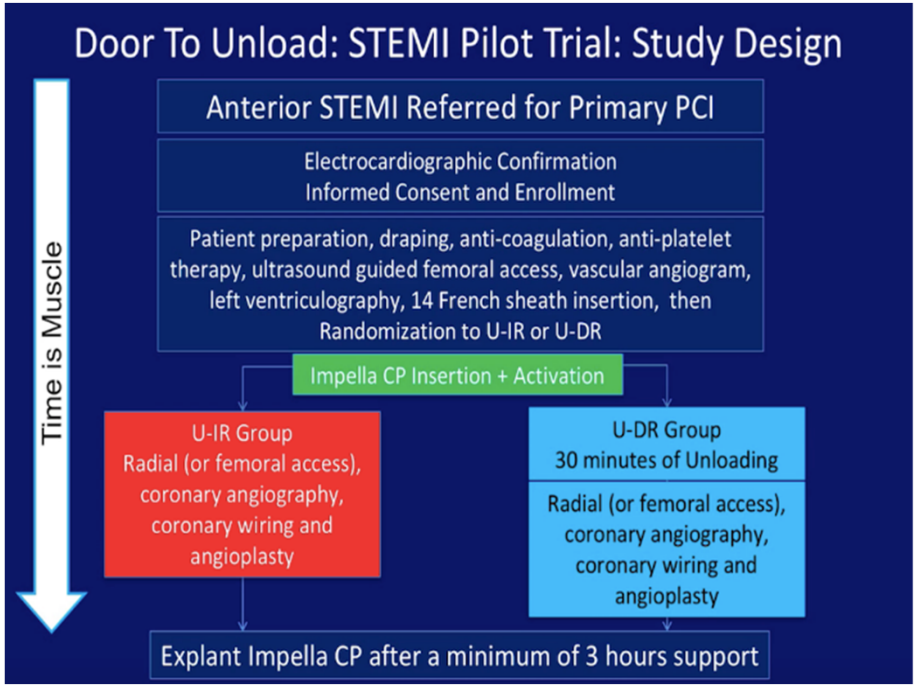
Kapur et al. Circulation 2013; 128:328-36

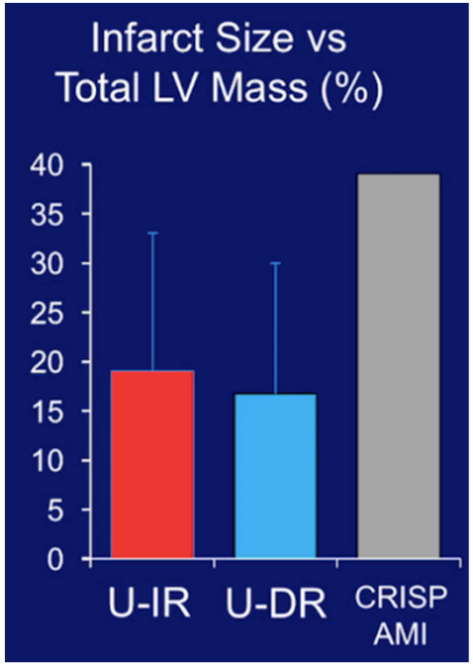

MI
MI +Unload
Base
Apex



Yellon DM et al. N Engl J Med 2007;357:1121-35

CLINICAL FAISABILITY



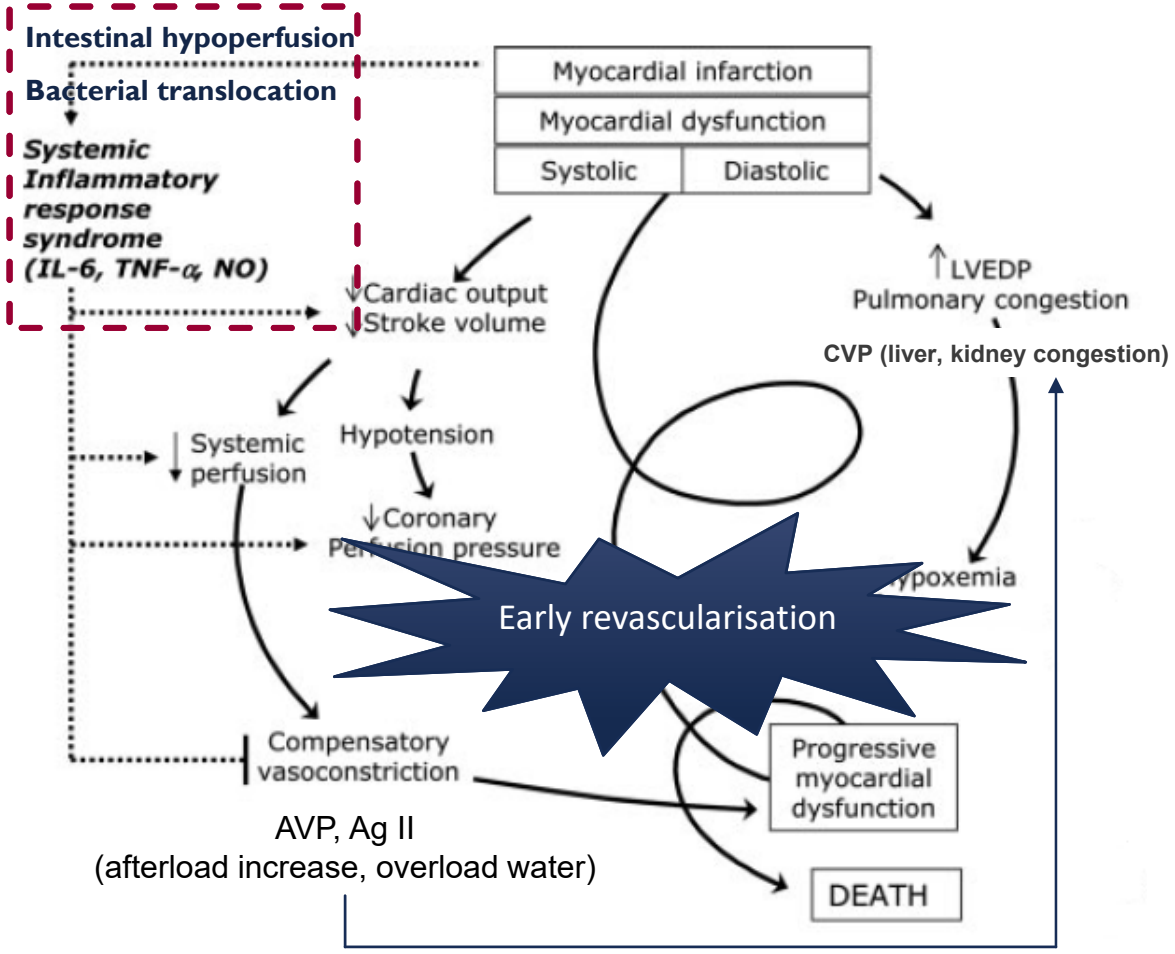


Clinical Variable	U-IR (n=25)	U-DR (n=25)*	p-value
Symptom to Unload Time, Min (mean_SD)	200±152	176±73	NS
Unload to First PTCA Time, Min (mean_SD)	11±7	34±3	<0.01

SYSTEMIC CARDIOVASCULAR AND INFLAMMATORY DISEASE

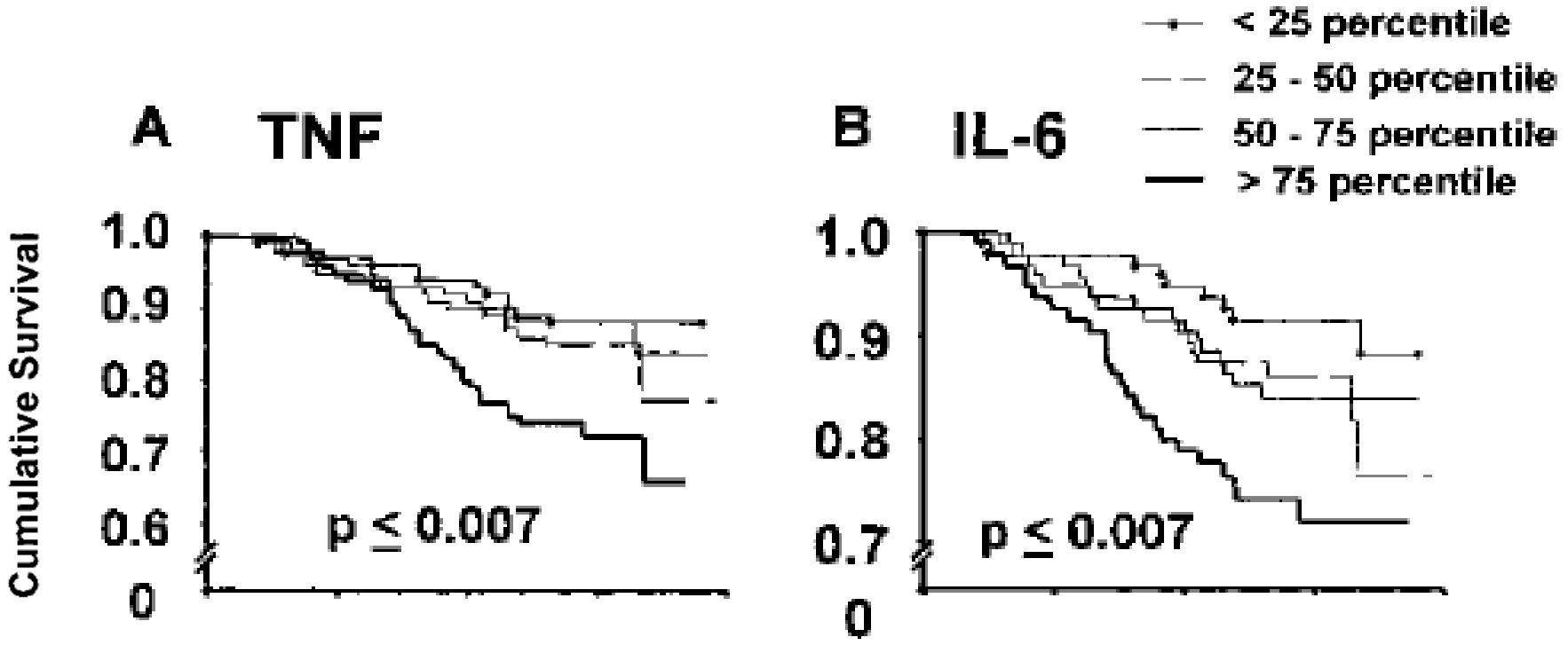
Coronary endothelial dysfonction

Myocardial depression



Reynolds HR et al. Circulation 2008; 117:686-97

SYSTEMIC INFLAMMATORY RESPONSE

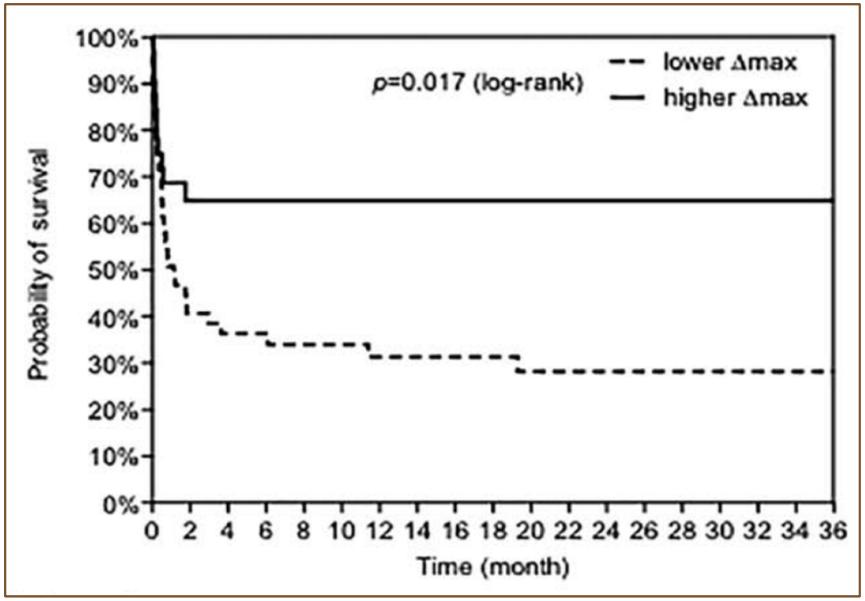


Deswal et al. Circulation 2001

PROGNOSTIC VALUE OF RELATIVE ADRENAL INSUFFICIENCY DURING CARDIOGENIC SHOCK: A PROSPECTIVE COHORT STUDY WITH LONG-TERM FOLLOW-UP

Bagate F et al. Shock 2017; 47:86-92

Plasma cortisol concentration, nmol/L	Survivors (n = 43)	Nonsurvivors (n = 49)	*P*
T0	666 (497–1,191)	819 (527–1,041)	0.34*
T30	949 (603–1,588)	913 (690–1,212)	0.64*
T60	1,332 (635–2,094)	1,155 (899–1,614)	0.89*
Tmax	1,254 (713–1,652)	1,126 (856–1,451)	0.81*
Δmax	369 (122–687)	232 (56–457)	0.04*



Low Dose of Hydrocortisone and Fludrocortisone in Adult Cardiogenic Shock. (COCCA)

ClinicalTrials.gov Identifier: NCT03773822

Recruitment Status : Recruiting
First Posted : December 12, 2018
Last Update Posted : May 15, 2019

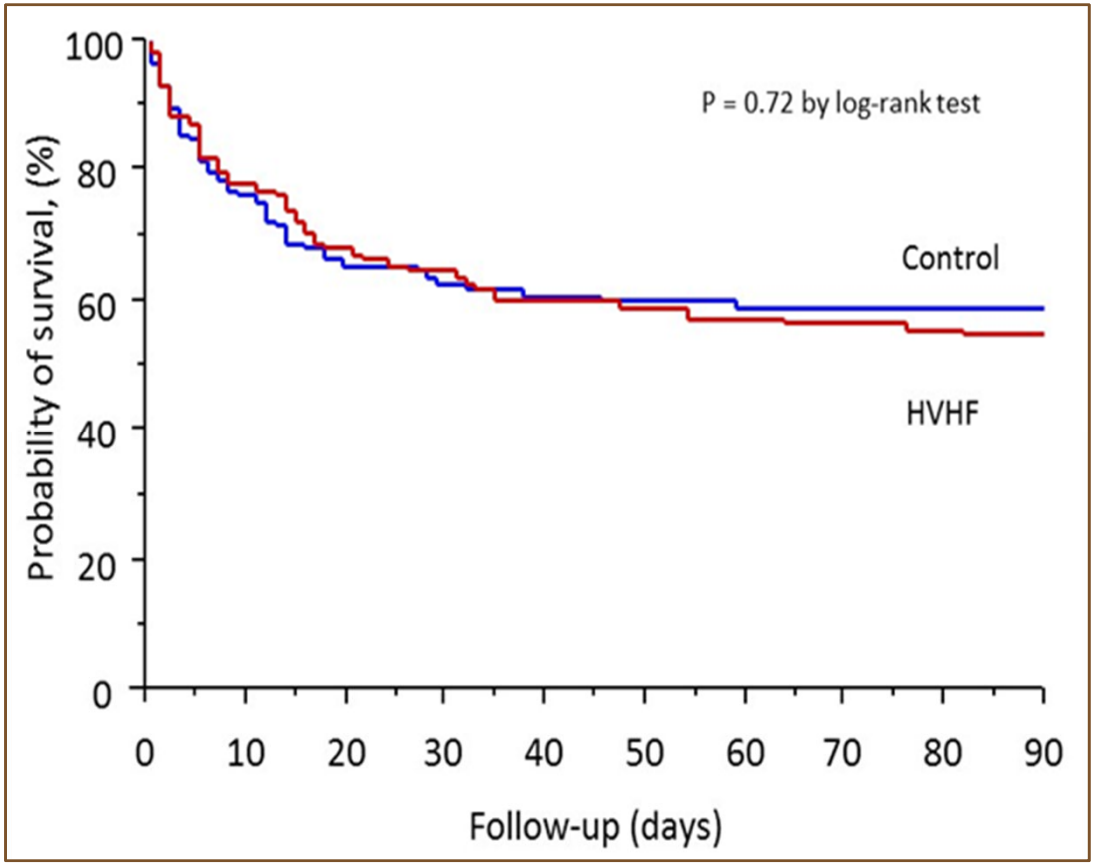
See Contacts and Locations

Sponsor:
CMC Ambroise Paré

Information provided by (Responsible Party):
CMC Ambroise Paré

Early High-Volume Hemofiltration versus Standard Care for Post–Cardiac Surgery Shock

The HEROICS Study



Combes A et al. Am J Respir Crit Care Med 2015;192: 1179-90

2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

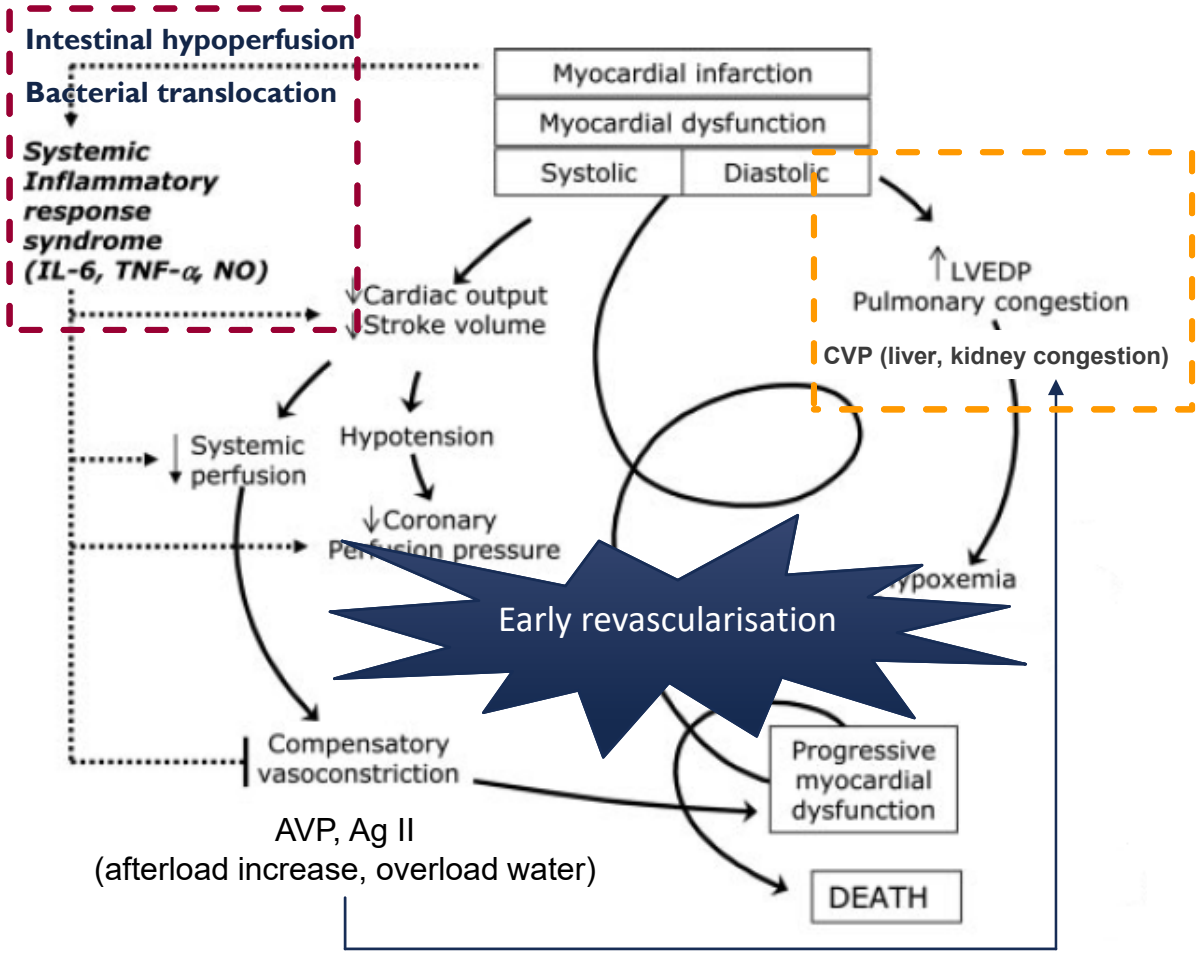
indicated according to blood gases.		
Fibrinolysis should be considered in patients		
Recommendations	**Class**[a]	**Level**[b]
Immediate PCI is indicated for patients with cardiogenic shock if coronary anatomy is suitable. If coronary anatomy is not suitable for PCI, or PCI has failed, emergency CABG is recommended.[248]	I	B
Invasive blood pressure monitoring with an arterial line is recommended.	I	C
Immediate Doppler echocardiography is indicated to assess ventricular and valvular functions, loading conditions, and to detect	I	C

Ibanez B et al. Eur Heart J 2017

SYSTEMIC CARDIOVASCULAR AND INFLAMMATORY DISEASE

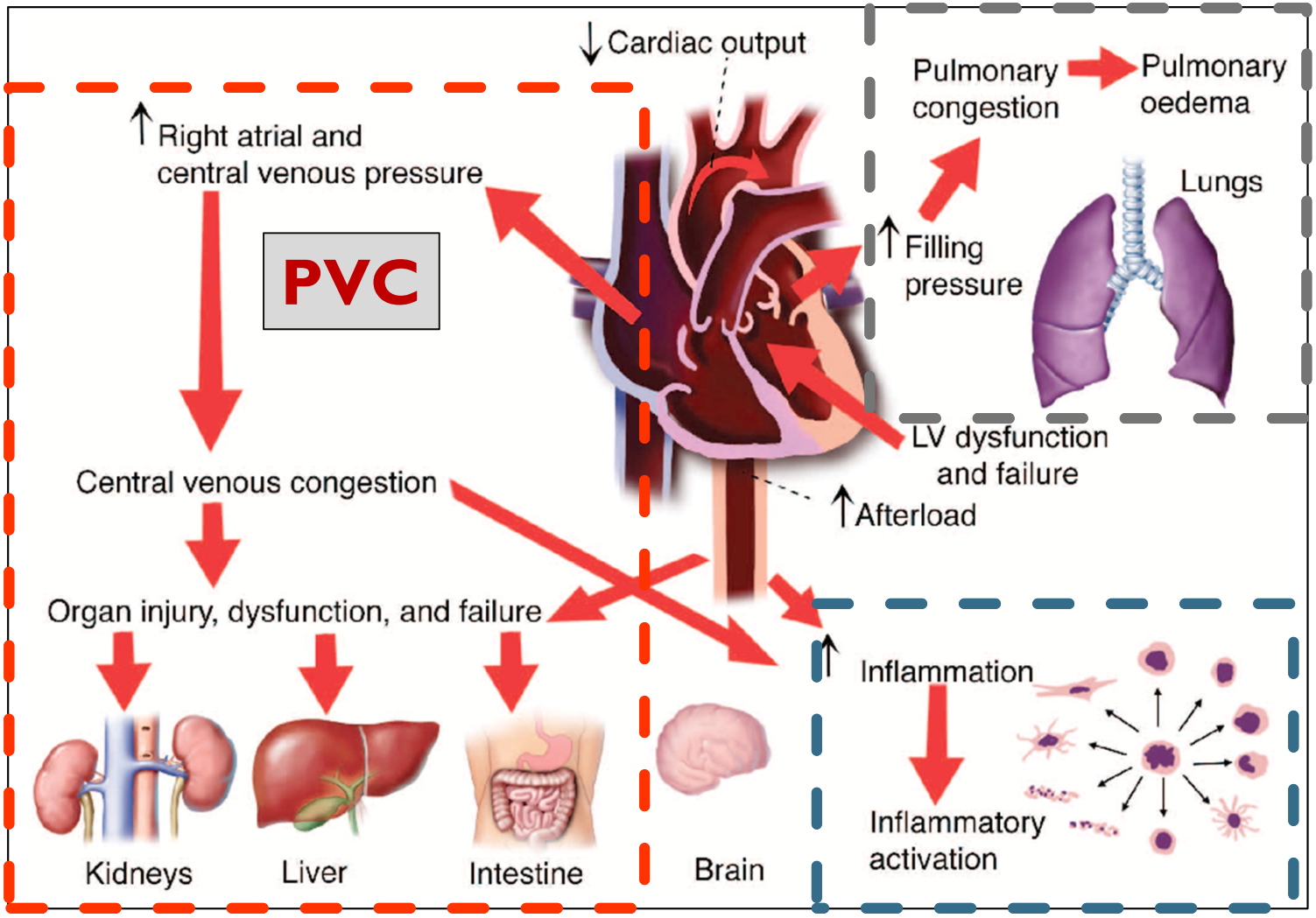
Coronary endothelial dysfonction

Myocardial depression



Reynolds HR et al. Circulation 2008; 117:686-97

Short term consequences of LV congestion



Harjola VP et al. Eur J heart Failure 2017;19:821-36

Risk indicators for acute kidney injury in cardiogenic shock

Johannes P.C. van den Akker [a,*], Jan Bakker [a,b,c,d], A.B.J Groeneveld [a,1], C.A. den Uil [a,e]

[a] Department of Intensive Care Adults, Erasmus University Medical Center, Dr. Molewaterplein 40, 3015GD, Rotterdam, the Netherlands
[b] Division of Pulmonary, Allergy and Critical Care, Columbia University Medical Center, New York, NY, USA
[c] Division of Pulmonary, Critical Care and Sleep Medicine, New York University Langone-Bellevue Hospital, New York, NY, USA
[d] Department of Intensive Care, Pontificia Universidad Católica de Chile, Santiago, Chile
[e] Department of Cardiology, Erasmus MC, University Medical Center, s-Gravendijkwal 230, Rotterdam 3015, the Netherlands

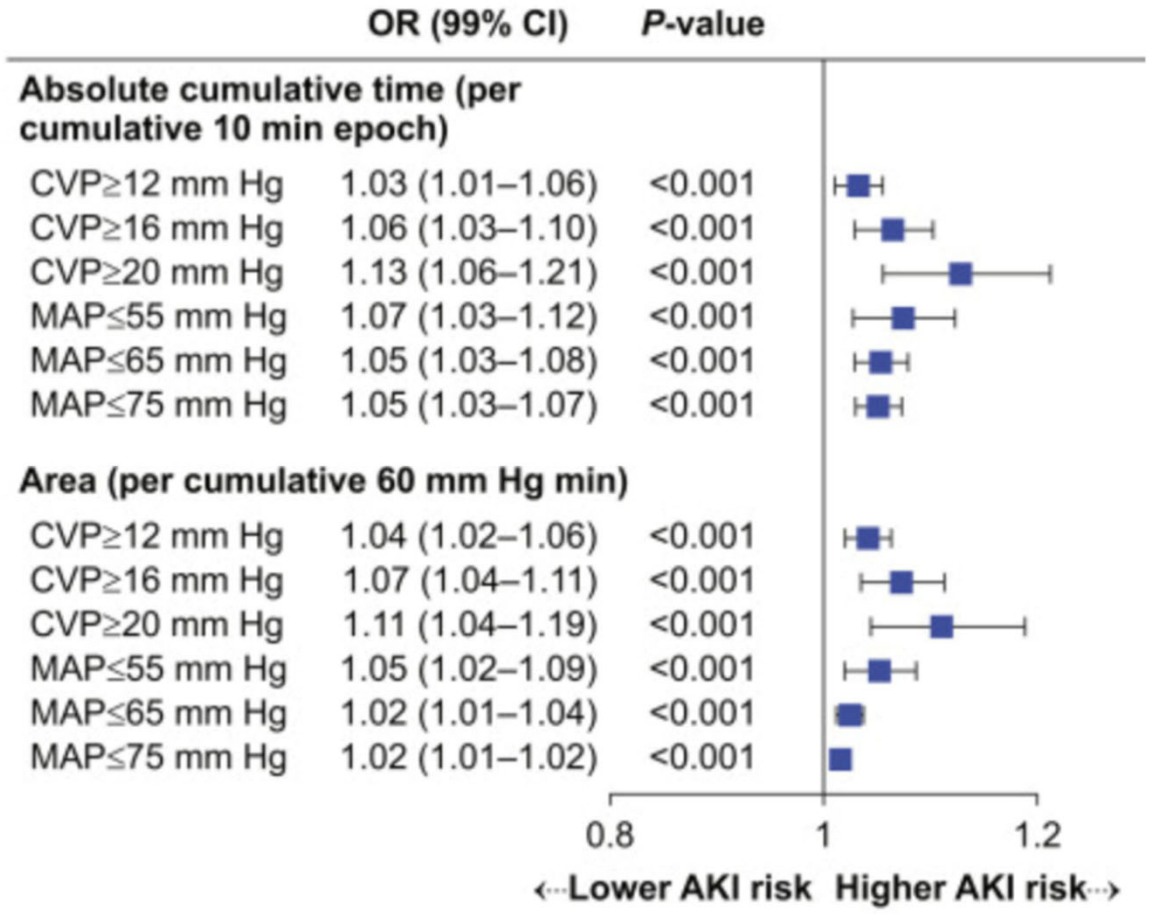
Univariate and multivariate regression analysis ($n = 62$).

	Univariate			Multivariate		
	Odds ratio	95%CI	*P*	Odds ratio	95%CI	*P*
Central Venous Pressure, mmHg (n = 38)	1.199	1.007–1.428	0.041	1.241	1.030–1.495	0.023
Diastolic arterial blood pressure, mmHg	0.950	0.902–1.000	0.049	0.952	0.897–1.010	0.105
PEEP, cm H_2O[a]	1.180	1.017–1.369	0.029	–		
Dobutamine, μg kg^{-1} min^{-1}	1.239	0.985–1.559	0.067	1.264	0.976–1.639	0.076

CI: confidence interval. PEEP: positive end expiratory pressure.
[a] For non-ventilated patients we assumed a pressure of 0 cm H_2O.

Intraoperative venous congestion rather than hypotension is associated with acute adverse kidney events after cardiac surgery: a retrospective cohort study

BJA

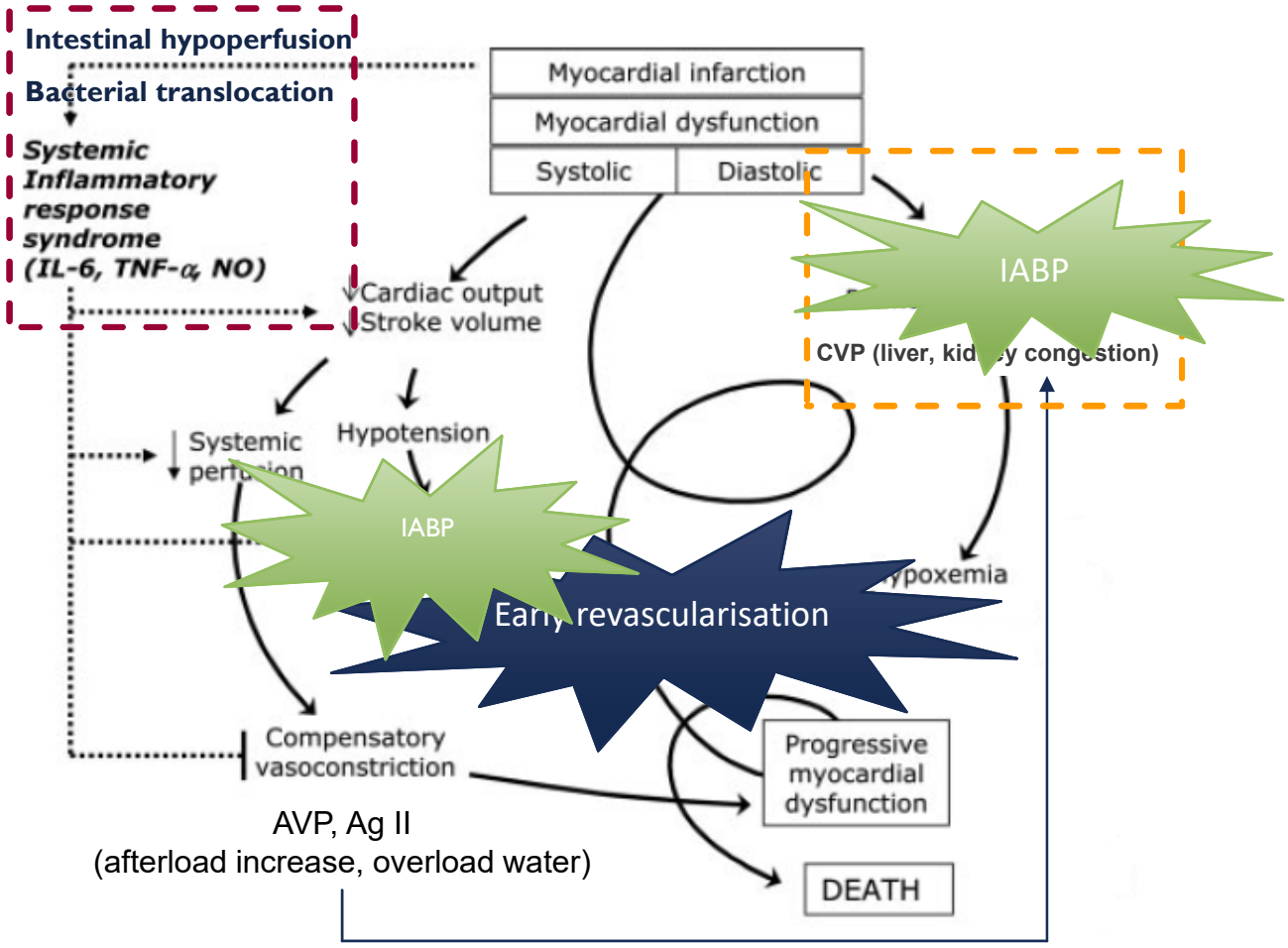


Chen L et al. Br J Anaesth 2022; 128:785-95

SYSTEMIC CARDIOVASCULAR AND INFLAMMATORY DISEASE

Coronary endothelial dysfonction

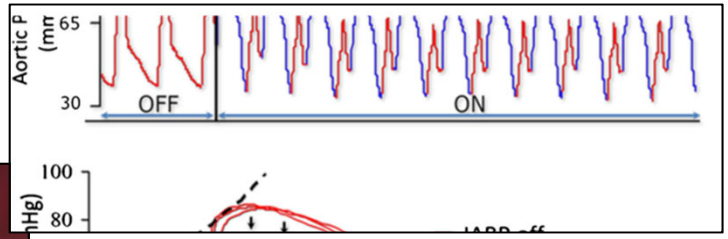
Myocardial depression

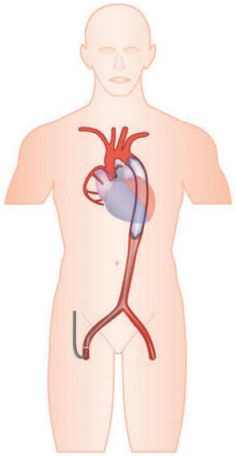


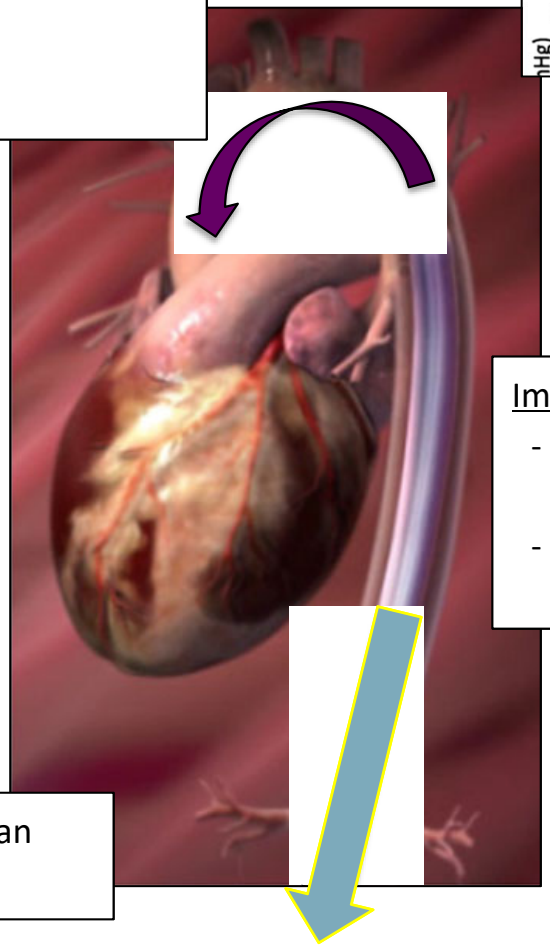
Reynolds HR et al. Circulation 2008; 117:686-97

Intra-aortic balloon pump (IABP)

- Increase diastolic aortic pressure from 30 to 70% (rapid inflation)
- Decrease systolic aortic pressure from 5 to 15% (rapid defletion)
- Decrease LV afterload
- Decrease LV preload
- Decrease HR (10%)
- **Increase SV and CO (5-10%).**







Improvement energetic balance of myocardium

- Increase myocardial oxygen supply (increase coronary perfusion)
- Decrease Myocardial oxygen demand (decrease loading conditions)

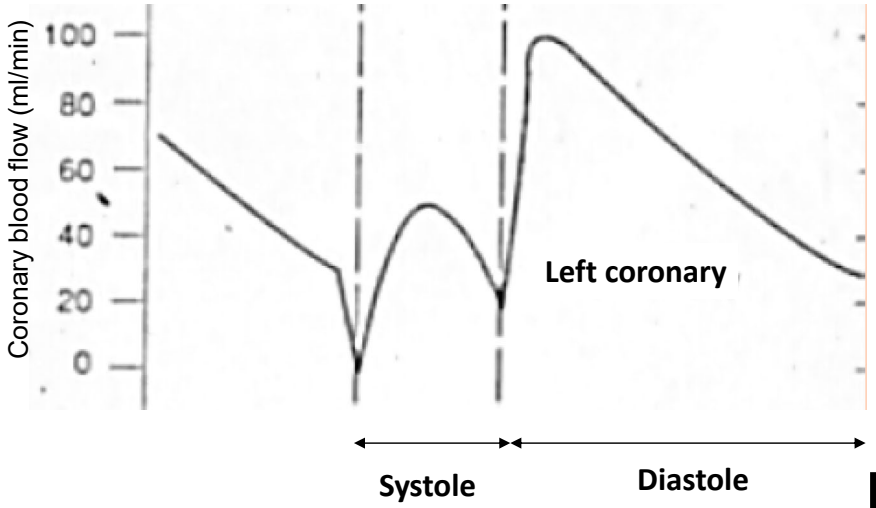
- Improvement of end-organ perfusion (Pulsatility)

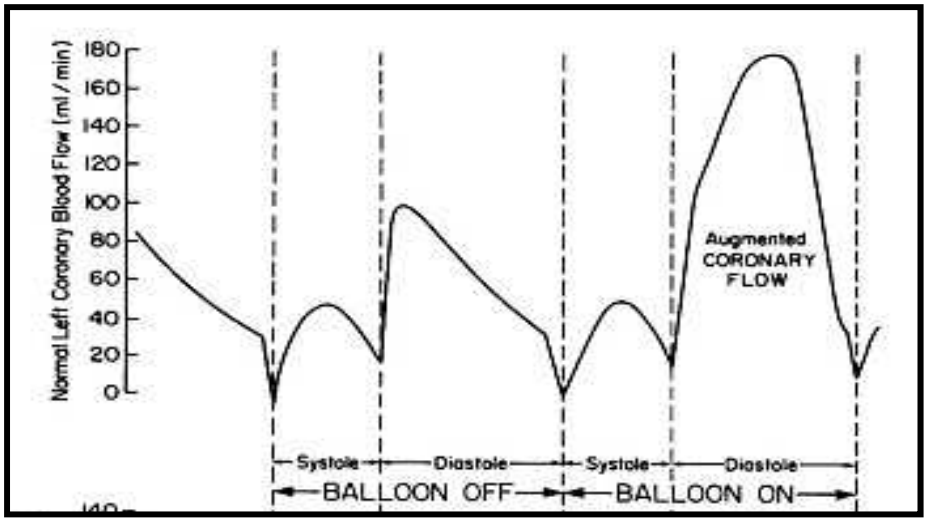
deWaha S et al.Vascular Pharmacology 2014;61:30-34

Ro SK et al. Eur J Cardiothorac Surg 2014; 46:186-92

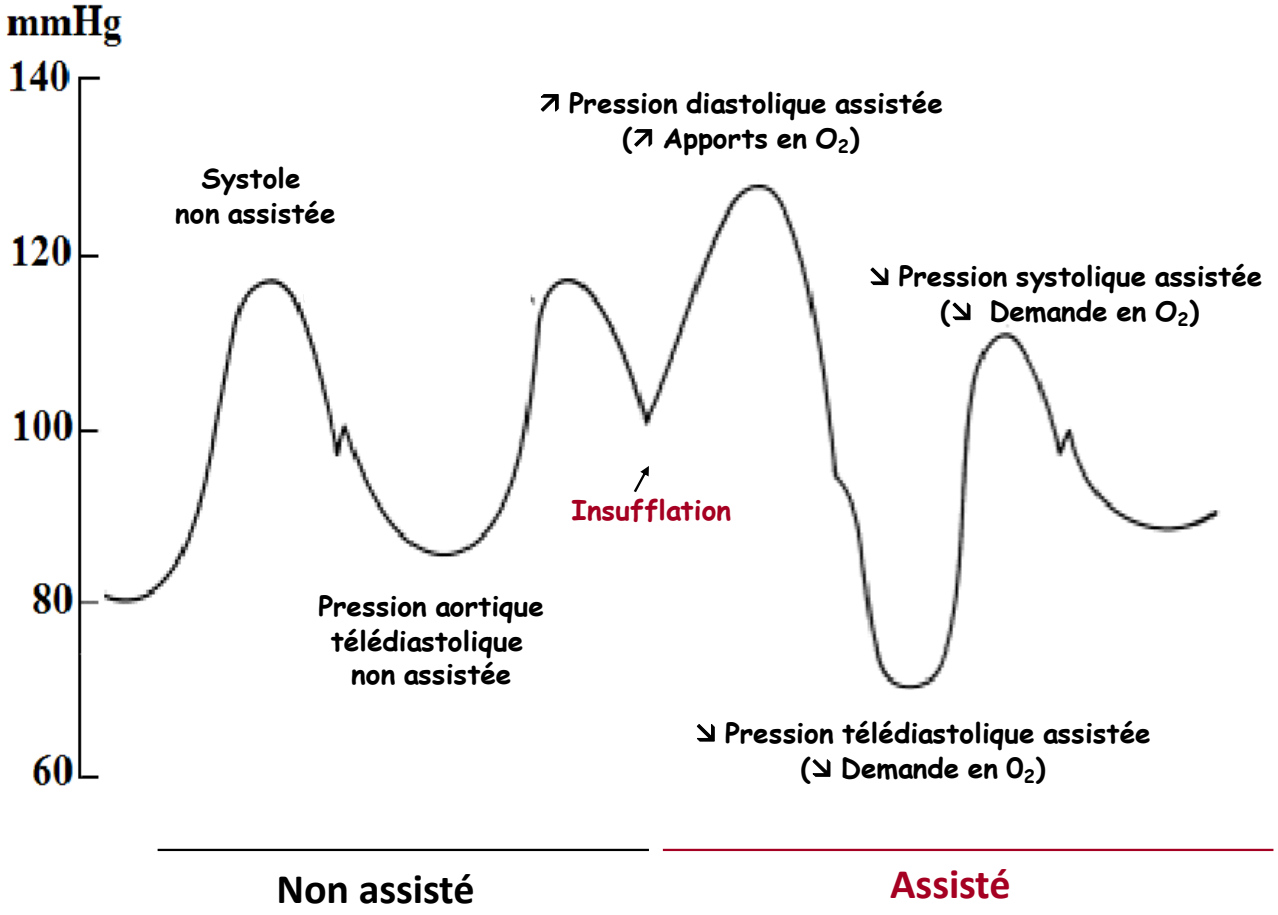
Aso S et al. Crit Care Med 2016; 44:1974-9

Amélioration perfusion coronaire…





COURBES DE PRESSION ARTÉRIELLE

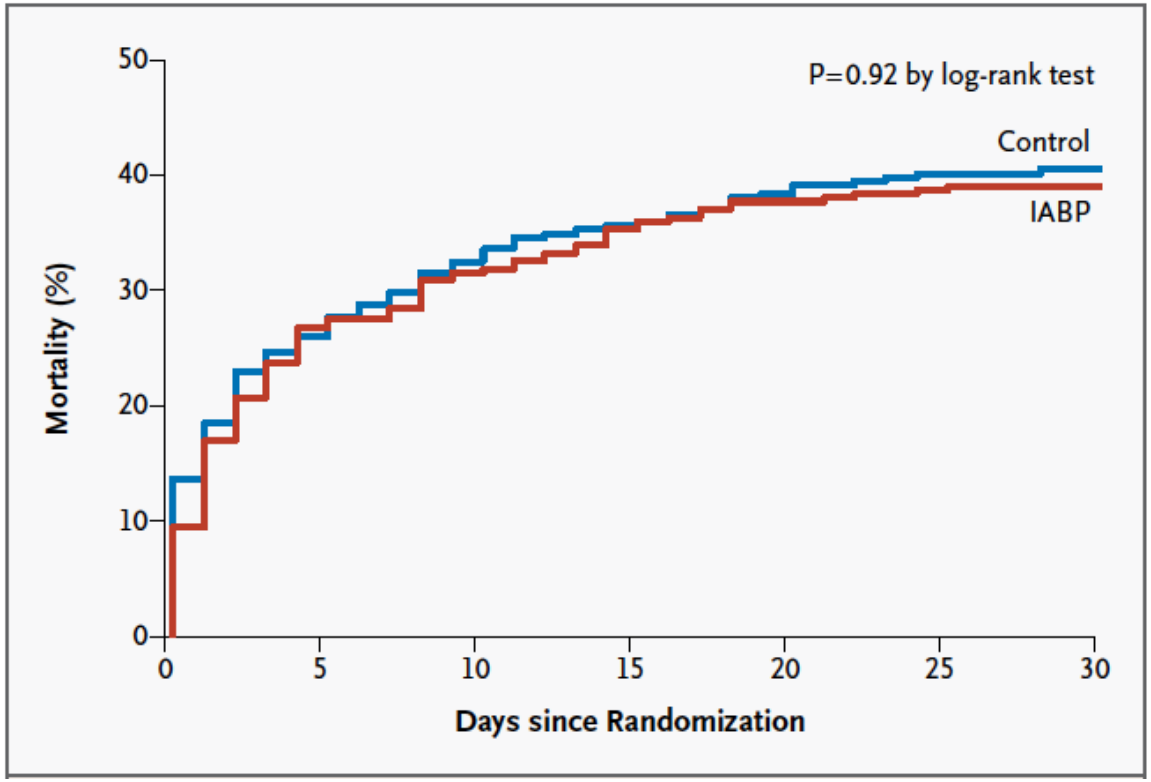


IABP Shock II trial

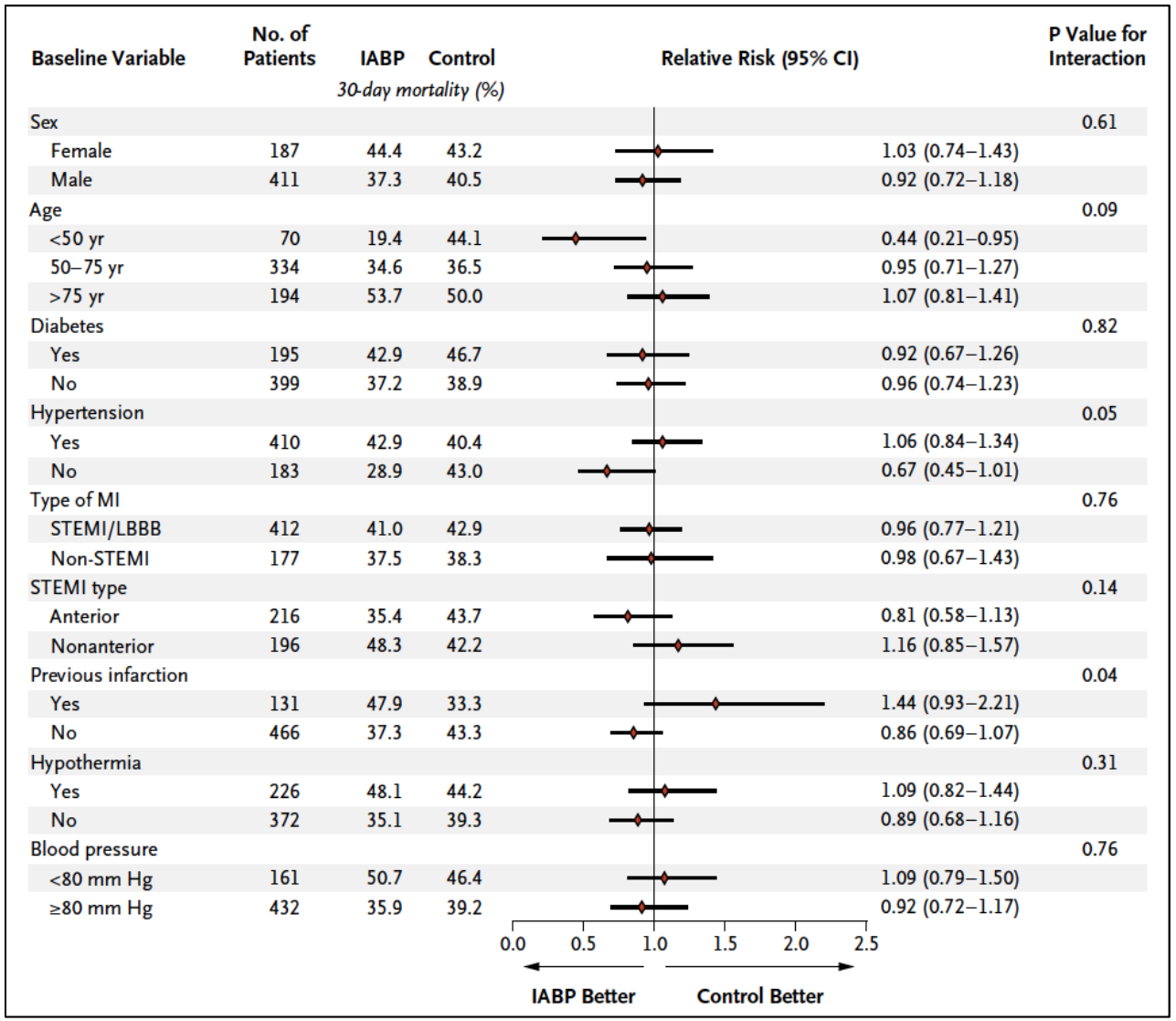
The NEW ENGLAND JOURNAL of MEDICINE

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

Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock

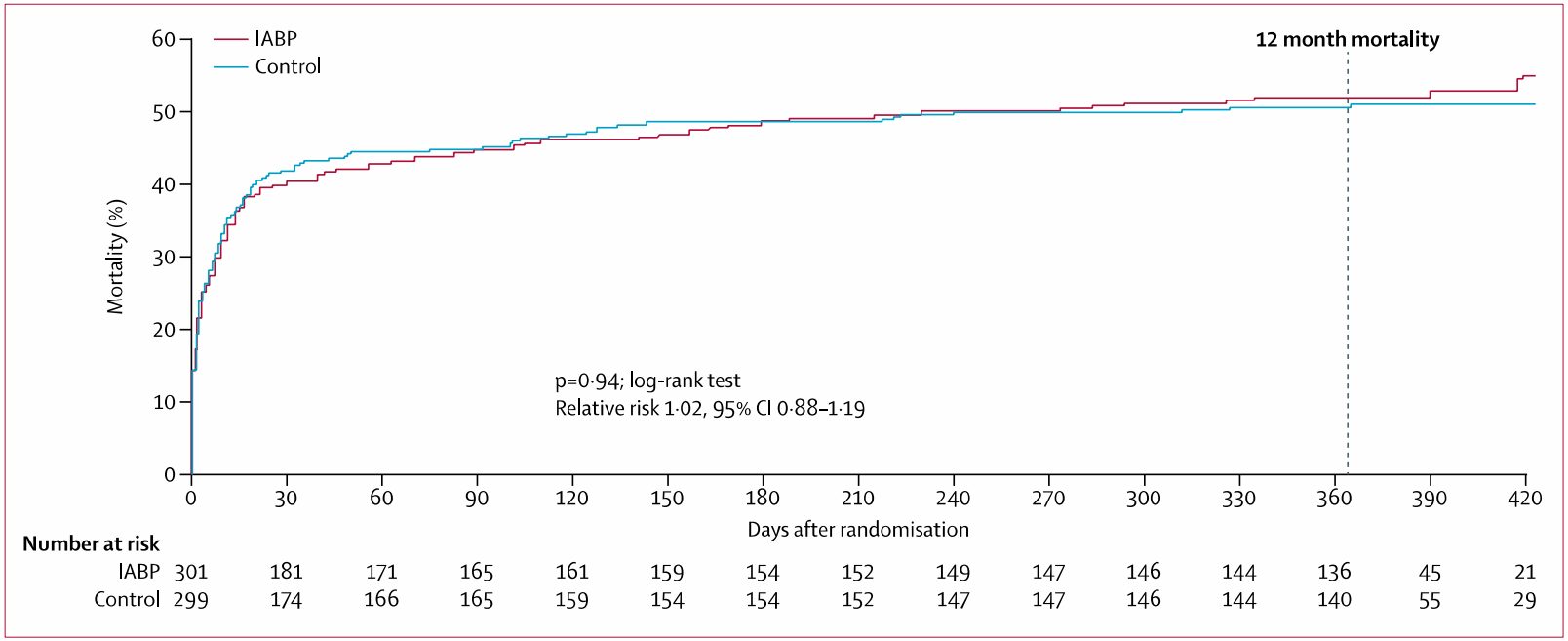


Thiele H et al. N Engl J Med 2012;367:1287-96



Thiele H et al. N Engl J Med 2012;367:1287-96

Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial



Thiele H et al. Lancet 2013; 382:1638-45

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Recommendations	Class[a]	Level[b]
Short-term MCS should be considered in patients with cardiogenic shock as a BTR, BTD, BTB. Further indications include treatment of the cause of cardiogenic shock or long-term MCS or transplantation.	IIa	C
IABP may be considered in patients with cardiogenic shock as a BTR, BTD, BTB, including treatment of the cause of cardiogenic shock (i.e. mechanical complication of acute MI) or long-term MCS or transplantation.[450]	IIb	C
IABP is not routinely recommended in post-MI cardiogenic shock.[500–502]	III	B

McDonagh TA et al. Eur Heart J 2021; 42:3599-3726

Patients were not eligible for the study if they had undergone resuscitation for more than 30 minutes, had no intrinsic heart action, were in coma with fixed dilation of pupils that was not induced by drugs, had a mechanical cause of cardiogenic shock (e.g., ventricular septal defect or papillary muscle rupture);…

Intra-Aortic Balloon Pumping in Acute Decompensated Heart Failure With Hypoperfusion: From Pathophysiology to Clinical Practice

Luca Baldetti, MD; Matteo Pagnesi, MD; Mario Gramegna, MD; Alessandro Belletti, MD; Alessandro Beneduce, MD; Vittorio Pazzanese, MD; Francesco Calvo, MD; Stefania Sacchi, MD; Nicolas M. Van Mieghem, MD, PhD; Corstiaan A. den Uil, MD; Marco Metra, MD; Alberto Maria Cappelletti, MD

ABSTRACT: Trials on intra-aortic balloon pump (IABP) use in cardiogenic shock related to acute myocardial infarction have shown disappointing results. The role of IABP in cardiogenic shock treatment remains unclear, and new (potentially more potent) mechanical circulatory supports with arguably larger device profile are emerging. A reappraisal of the physiological premises of intra-aortic counterpulsation may underpin the rationale to maintain IABP as a valuable therapeutic option for patients with acute decompensated heart failure and tissue hypoperfusion. Several pathophysiological features differ between myocardial infarction- and acute decompensated heart failure–related hypoperfusion, encompassing cardiogenic shock severity, filling status, systemic vascular resistances rise, and adaptation to chronic (if preexisting) left ventricular dysfunction. IABP combines a more substantial effect on left ventricular afterload with a modest increase in cardiac output and would therefore be most suitable in clinical scenarios characterized by a disproportionate increase in afterload without profound hemodynamic compromise. The acute decompensated heart failure syndrome is characterized by exquisite afterload-sensitivity of cardiac output and may be an ideal setting for counterpulsation. Several hemodynamic variables have been shown to predict response to IABP within this scenario, potentially guiding appropriate patient selection. Finally, acute decompensated heart failure with hypoperfusion may frequently represent an end stage in the heart failure history: IABP may provide sufficient hemodynamic support and prompt end-organ function recovery in view of more definitive heart replacement therapies while preserving ambulation when used with a transaxillary approach.

Key Words: cardiac output ■ cardiac output, low ■ heart failure ■ intra-aortic balloon pumping ■ patient selection ■ shock, cardiogenic ■ vascular resistance

Baldetti L. Circ Heart Fail. 2021;14:e008527

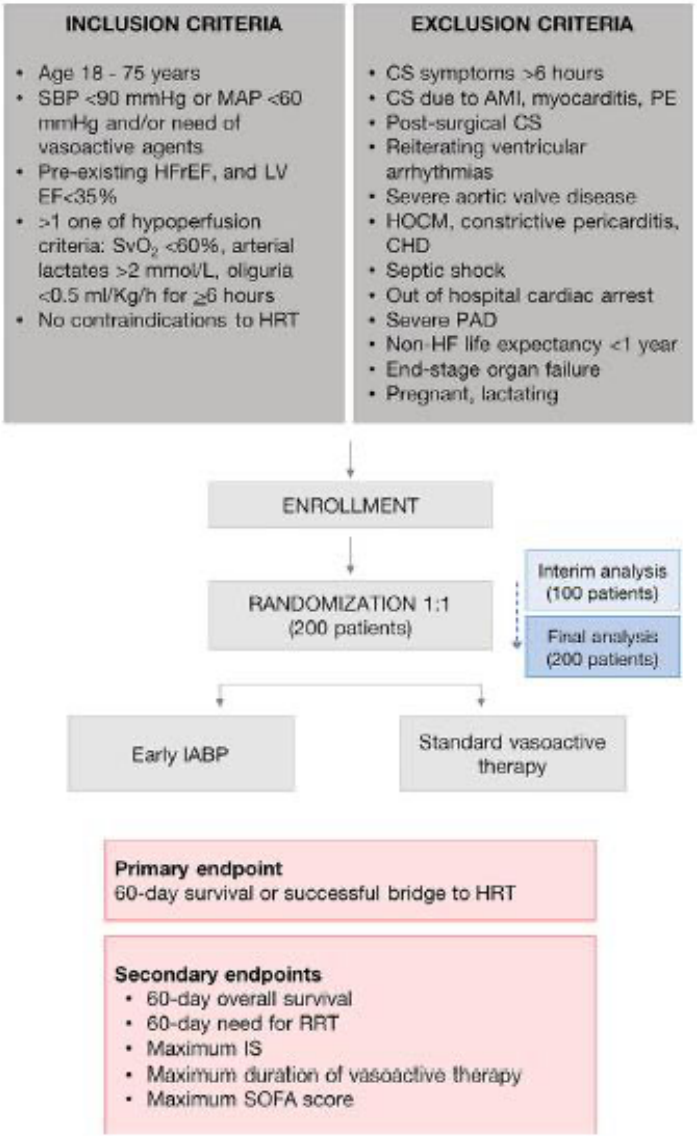
Early intra-aortic balloon pump in acute decompensated heart failure complicated by cardiogenic shock: Rationale and design of the randomized Altshock-2 trial

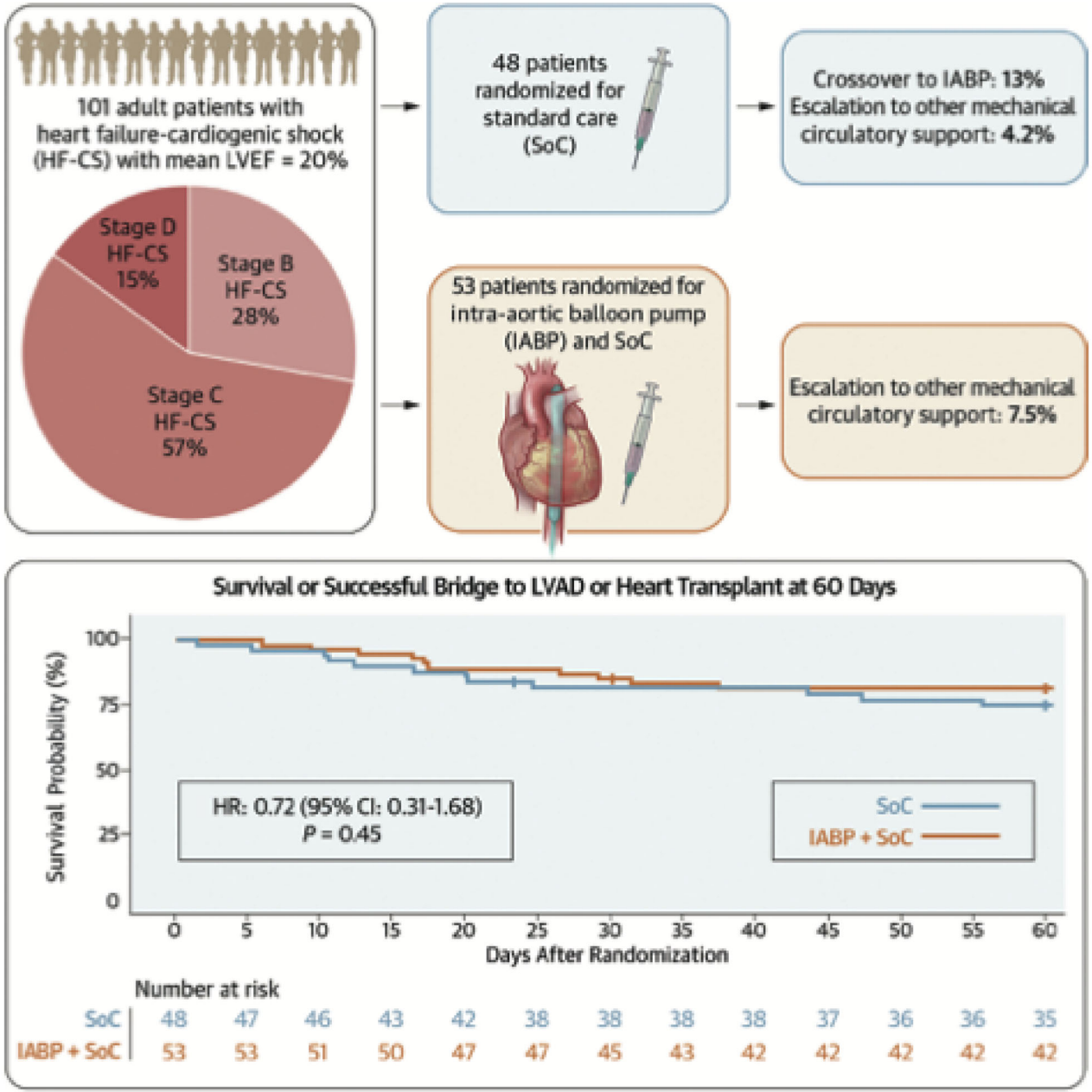
Nuccia Morici, MD[a], Claudia Marini, MD[a], Alice Sacco, MD[a], Guido Tavazzi, MD[b], Manlio Cipriani, MD[c], Fabrizio Oliva, MD[a], Matteo Rota, MD[d], Gaetano Maria De Ferrari, MD[e], Jonica Campolo, MD[f], Gianfranco Frigerio, MD[g], Serafina Valente, MD[h], Sergio Leonardi, MD[i], Elena Corrada, MD[j], Maurizio Bottiroli, MD[k], Daniele Grosseto, MD[l], Luisa Cacciavillani, MD[m], Maria Frigerio, MD[c], and Federico Pappalardo, MD[n], for the Altshock-2 Group *Milan, Italy; Pavia, Italy; Brescia, Italy; Torino, Italy; Siena, Italy; Rozzano, Italy; Rimini, Italy; Padova, Italy; Palermo, Italy*

Background Cardiogenic shock (CS) is a systemic disorder associated with dismal short-term prognosis. Given its time-dependent nature, mechanical circulatory support may improve survival. Intra-aortic balloon pump (IABP) had gained widespread use because of the easiness to implant and the low rate of complications; however, a randomized trial failed to demonstrate benefit on mortality in the setting of acute myocardial infarction. Acute decompensated heart failure with cardiogenic shock (ADHF-CS) represents a growing resource-intensive scenario with scant data and indications on the best management. However, a few data suggest a potential benefit of IABP in this setting. We present the design of a study aimed at addressing this research gap.

Methods and design The Altshock-2 trial is a prospective, randomized, multicenter, open-label study with blinded adjudicated evaluation of outcomes. Patients with ADHF-CS will be randomized to early IABP implantation or to vasoactive treatments. The primary end point will be 60 days patients' survival or successful bridge to heart replacement therapy. The key secondary end point will be 60-day overall survival; 60-day need for renal replacement therapy; in-hospital maximum inotropic score, maximum duration of inotropic/vasopressor therapy, and maximum sequential organ failure assessment score. Safety end points will be in-hospital occurrence of bleeding events (Bleeding Academic Research Consortium >3), vascular access complications and systemic (noncerebral) embolism. The sample size for the study is 200 patients.

Implications The Altshock-2 trial will provide evidence on whether IABP should be implanted early in ADHF-CS patients to improve their clinical outcomes. (Am Heart J 2021;233:39–47.)





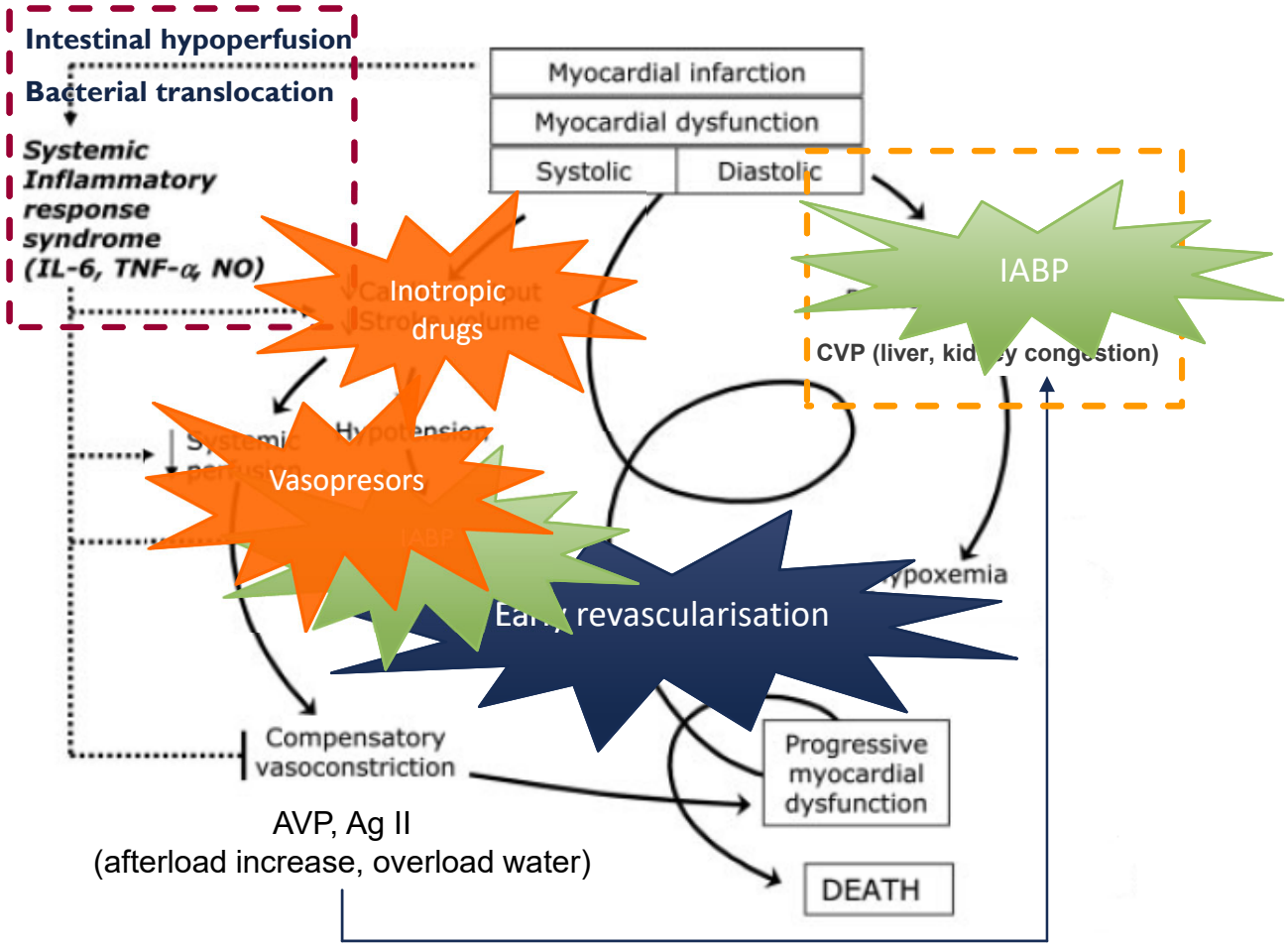
The routine early use of IABP plus standard care, compared to standard care alone, did not result in significantly better survival or successful bridge to LVAD or heart transplantation in patients with HF-CS.

J Am Coll Cardiol. 2025

SYSTEMIC CARDIOVASCULAR AND INFLAMMATORY DISEASE

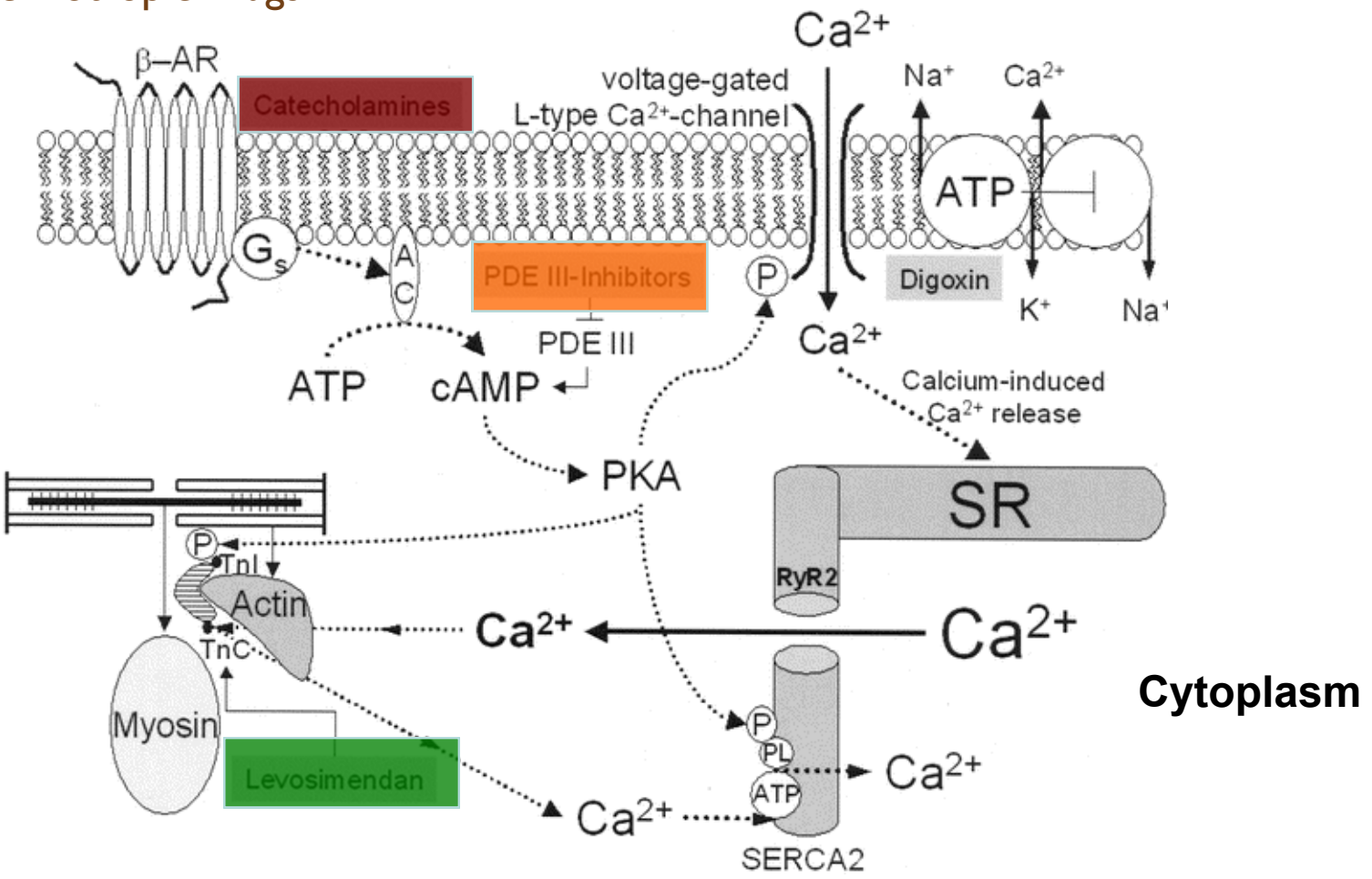
Coronary endothelial dysfonction

Myocardial depression

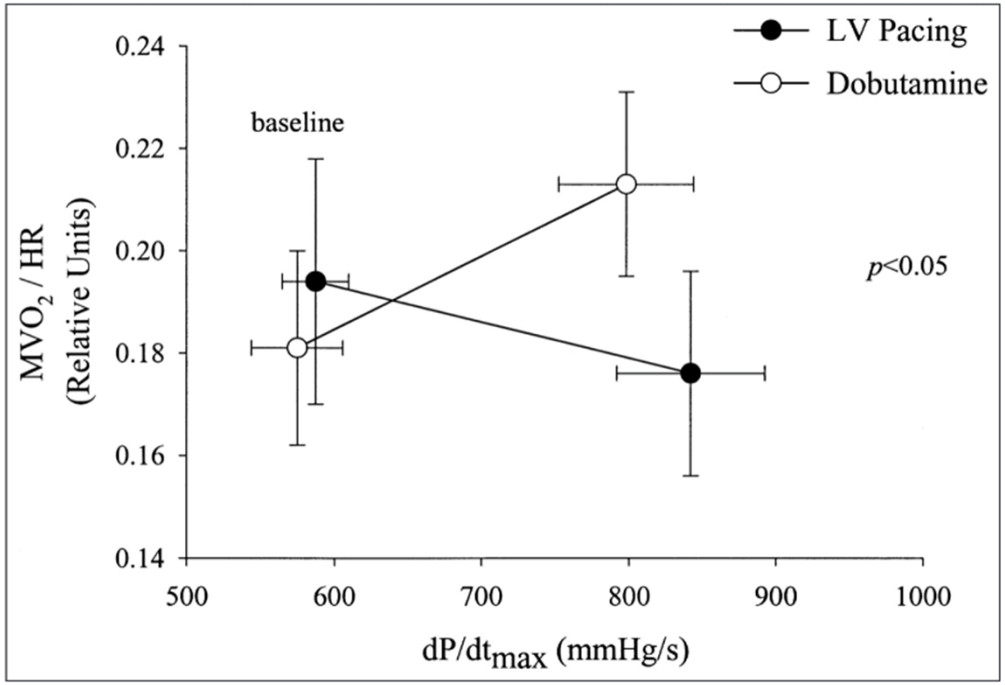


Reynolds HR et al. Circulation 2008; 117:686-97

Positive inotropic drugs



Toller WG. et al. Anesthesiology 2006



Dobutamine

- Increased myocardial oxygen consumption
- High incidence of arrhythmia
- Tolerance (receptor internalisation, decoupling….)
- Profound vasodilation

Nelson GS et al. Circulation 2000; 102: 3053-9

INOTROPES COULD BE HARMFUL
IN DECOMPENSATED HEART FAILURE FROM OPTIME-CHF STUDY?

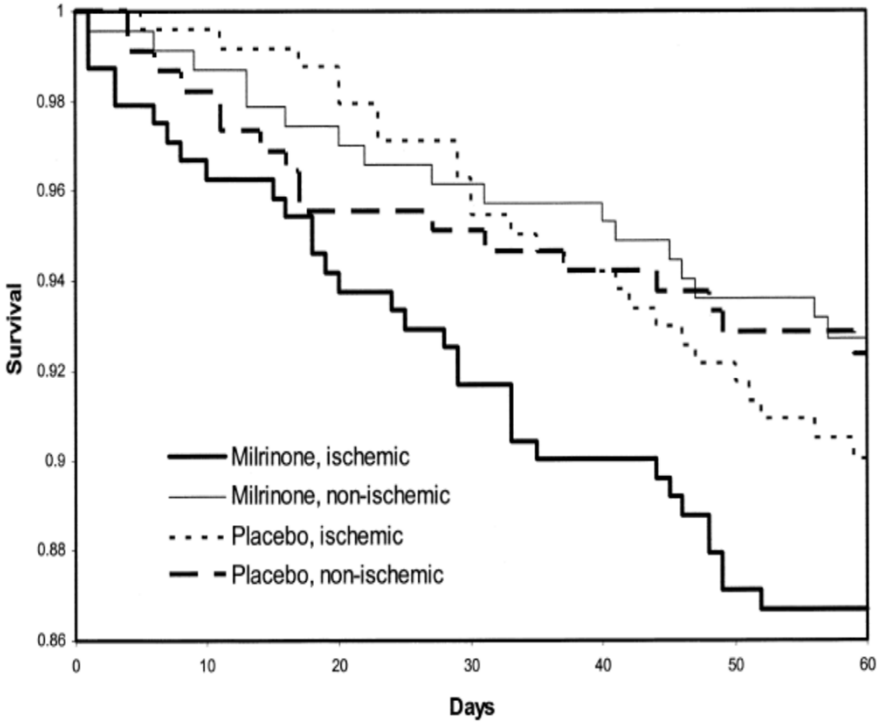
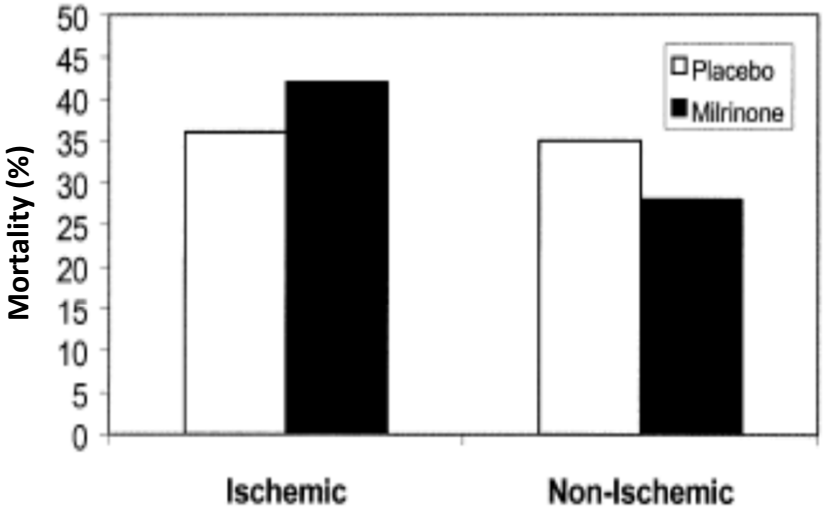


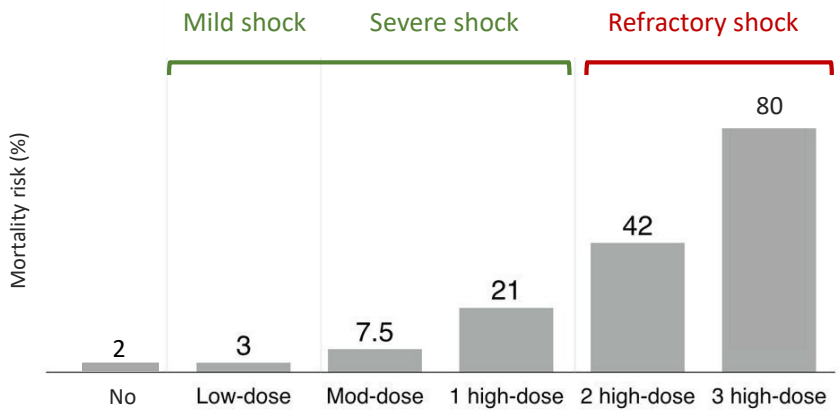
Figure 1. Kaplan-Meier survival curves to 60 days by heart failure etiology and treatment assignment.



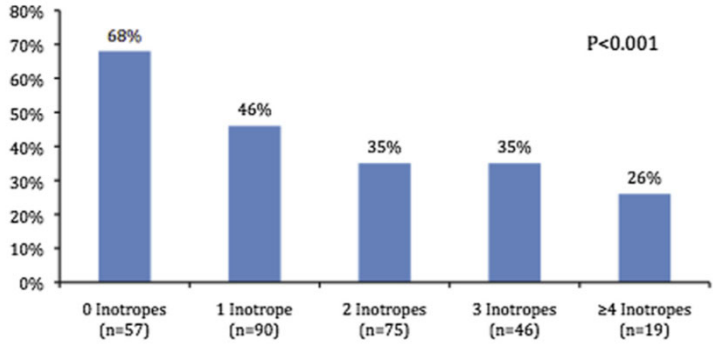
Felker GM et al. J Am Coll Cardiol 2003;41:997-1003

Refractory cardiogenic shock

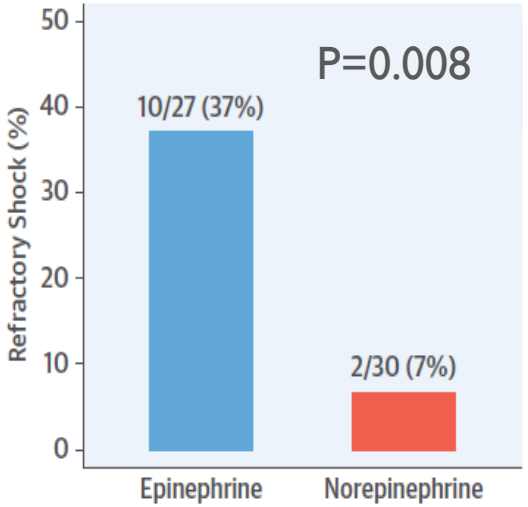
(from <1% to more than 15%...)



Samuels LE et al. J Card Surg 1999; 14:288-93



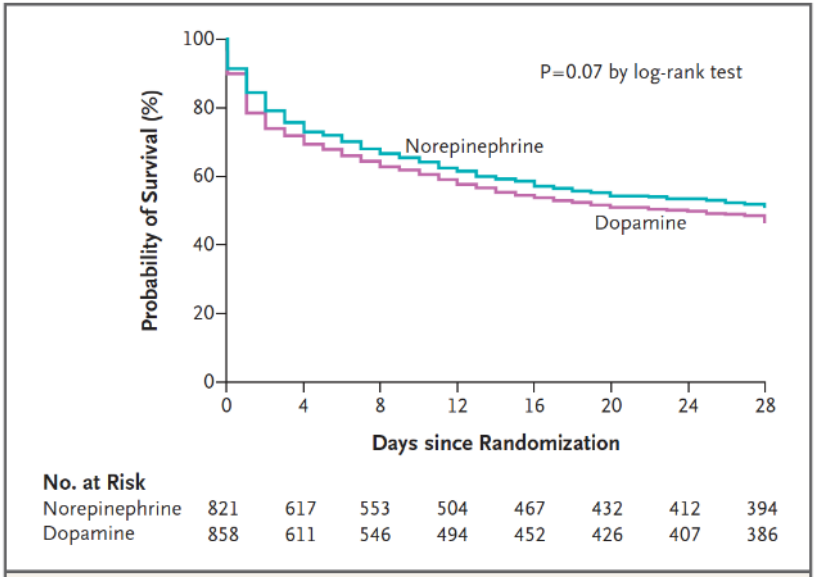
Basir MB et al. Am J Cardiol 2017;119:845-51

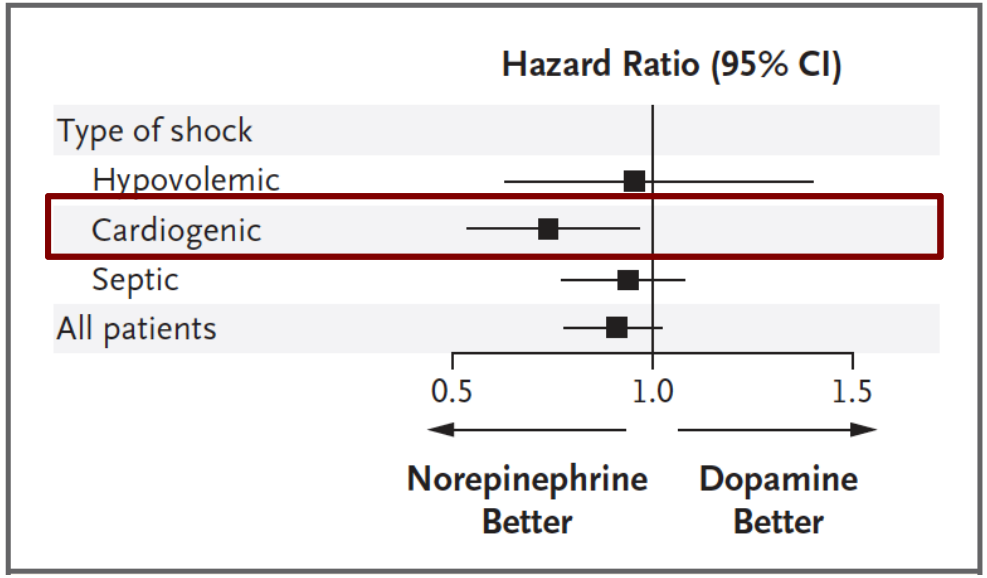


Levy B et al. J Am Coll Cardiol 2018; 72:173-81

The NEW ENGLAND JOURNAL of MEDICINE

Comparison of Dopamine and Norepinephrine in the Treatment of Shock





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)	

De Backer D et al. N Engl J Med 2010;362:779-89

Perioperative Use of Dobutamine in Cardiac Surgery and Adverse Cardiac Outcome

Propensity-adjusted Analyses

Jean-Luc Fellahi, M.D., Jean-Jacques Parienti, M.D.,† Jean-Luc Hanouz, M.D., Ph.D.,‡ Benoît Plaud, M.D., Ph.D.,§ Bruno Riou, M.D., Ph.D.,‖ Alexandre Ouattara, M.D., Ph.D.#*

Table 4. Catecholamines: Crude and Adjusted Effects for Major Cardiac Morbidity and Global In-hospital Mortality Endpoints

Method	Odds Ratio	95% Confidence Interval	*P* Value
Major cardiac morbidity			
Crude	4.2	[2.5–7.3]	<0.001
Stratifying on PS quartiles*	2.1	[1.0–4.4]	<0.05
Covariate adjustment using PS†	2.3	[1.0–5.0]	<0.05
Marginal structural models‡	1.8	[1.3–2.5]	<0.001
PS matching	3.0	[1.2–7.3]	<0.02
In-hospital mortality			
Crude	12.9	[3.7–45.2]	<0.001
Stratifying on PS quartiles	—	—	—
Covariate adjustment using PS§	2.7	[0.4–20.5]	0.33
Marginal structural models	—	—	—
PS matching	2.0	[0.1–32.0]	0.63

* Model adjusted for higher cardiac troponin I level 24 h after surgery ($P < 0.001$) and longer cardiopulmonary bypass time ($P < 0.001$). † Model adjusted for higher cardiac troponin I level 24 h after surgery ($P < 0.001$), combined surgery ($P < 0.04$) and higher propensity score (PS) ($P < 0.15$). ‡ Model adjusted for higher cardiac troponin I level 24 h after surgery ($P < 0.001$), combined surgery ($P < 0.001$), longer aortic cross clamping time ($P < 0.009$), and lower left ventricular ejection fraction ($P < 0.001$). § Model adjusted for higher PS ($P < 0.01$).

Anesthesiology 2008; 108:979-87

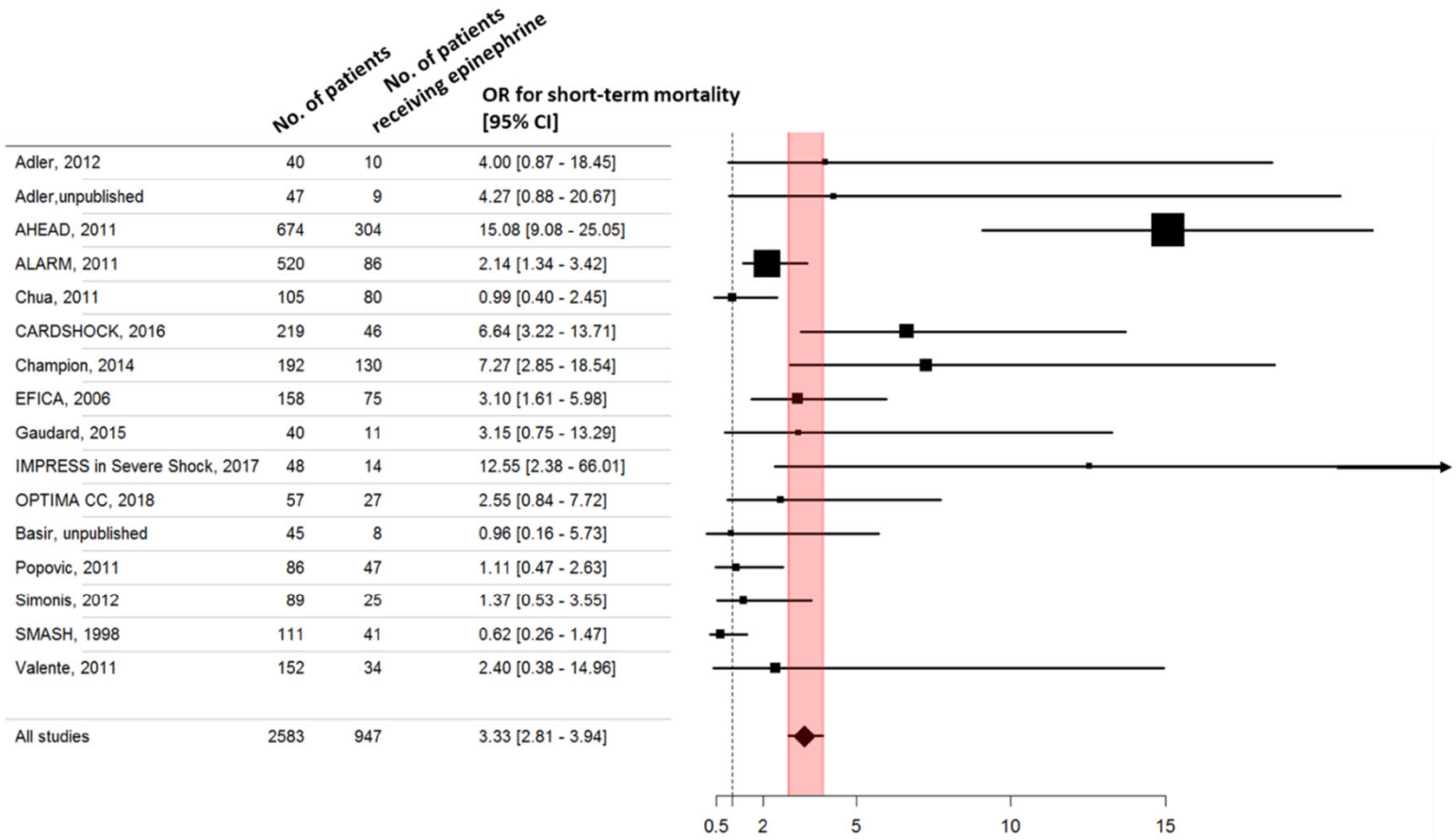


Fig. 3 Forest plot of the meta-analysis of short-term mortality

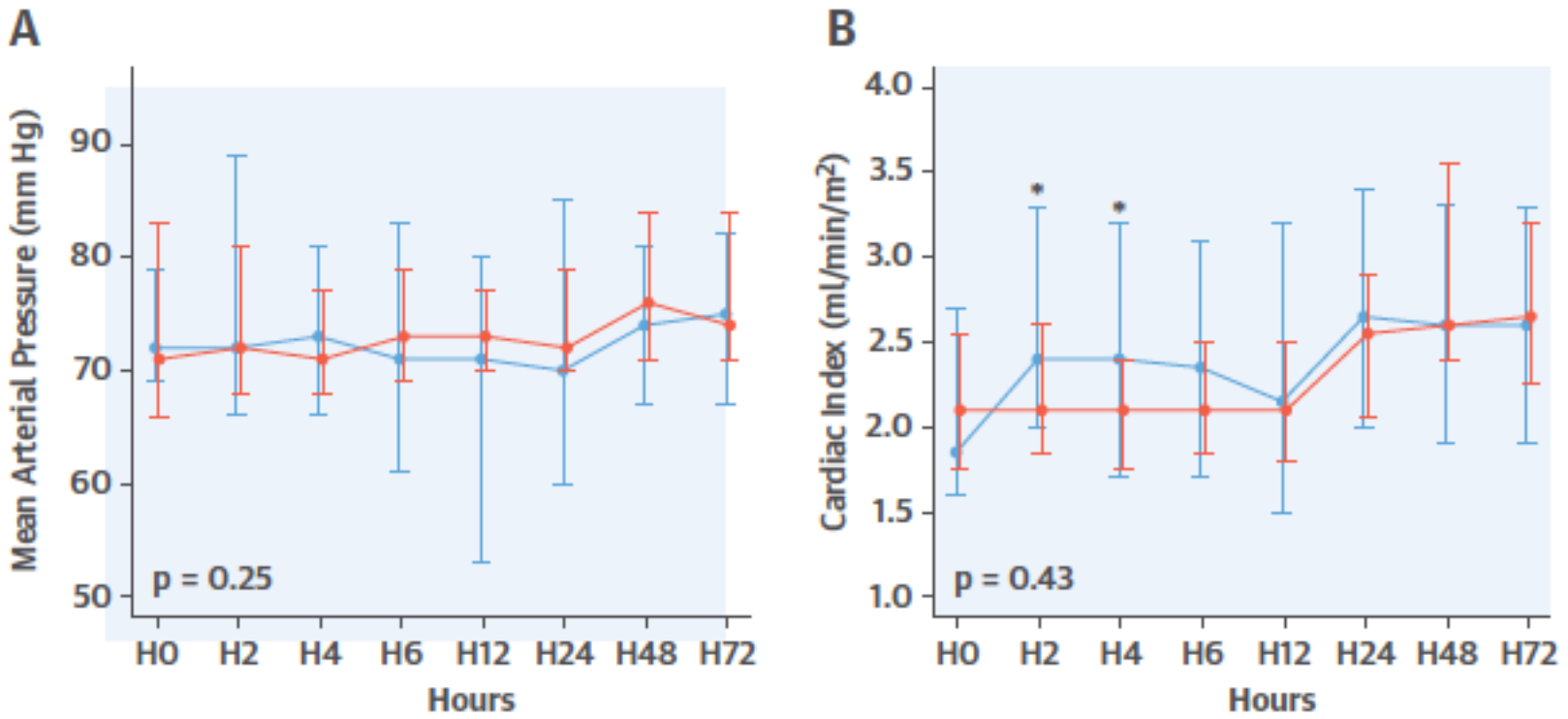
Léopold V et al. Intensive Care Med 2018;44:847-56

Epinephrine Versus Norepinephrine for Cardiogenic Shock After Acute Myocardial Infarction

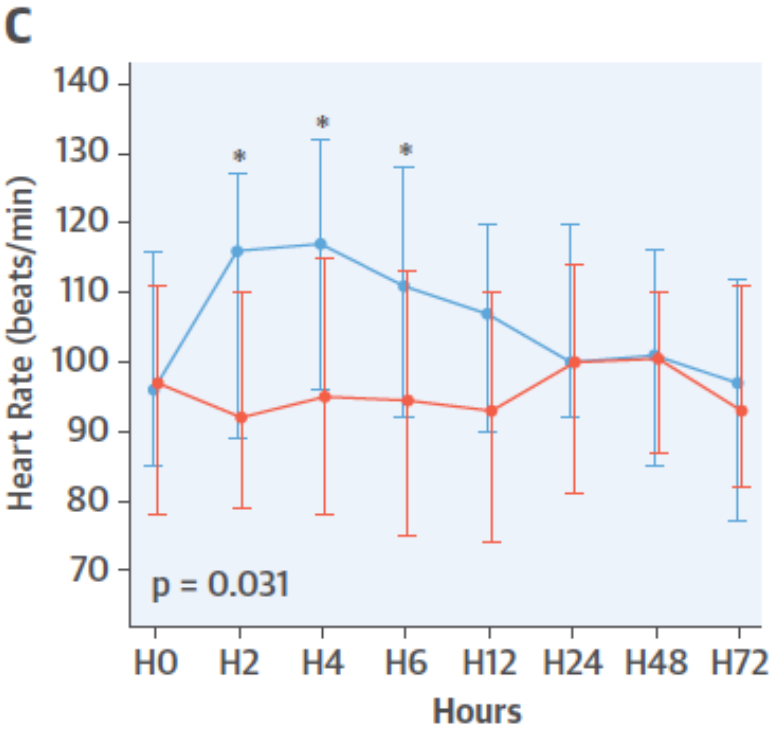
Levy B et al. J Am Coll Cardiol 2018; 72:173-81

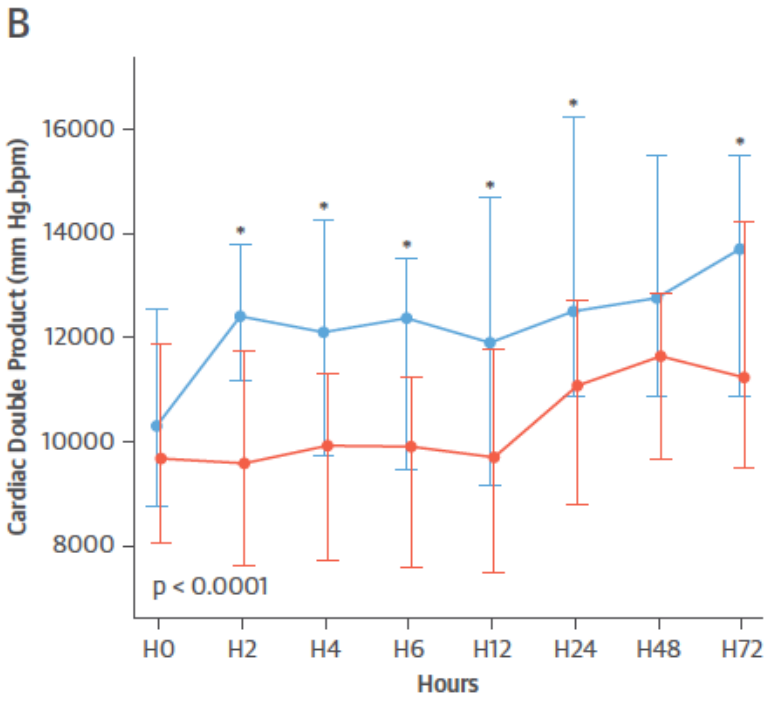
OptimaCC

- Prospective, double-blinded, multicenter RCT
- Haemodynamic efficacy and tolerance of Epinephrine (n=27) and norepinephrine (n=30) in patients with CS due to MI successfully revascularized
- Tested drugs were increased by 0.02 µg/kg/min
- Primary efficacy endpoint was increase in CO
- Primary safety endpoint was the incidence of refractory CS (major cardiac dysfunction according to echocardiography, lactates levels, acute deterioration organ function despite 1 µg/kg/min Epinephrine or 10 µg/kg/min of dobutamine)
- Dobutamine was used in 67% of patients in both groups

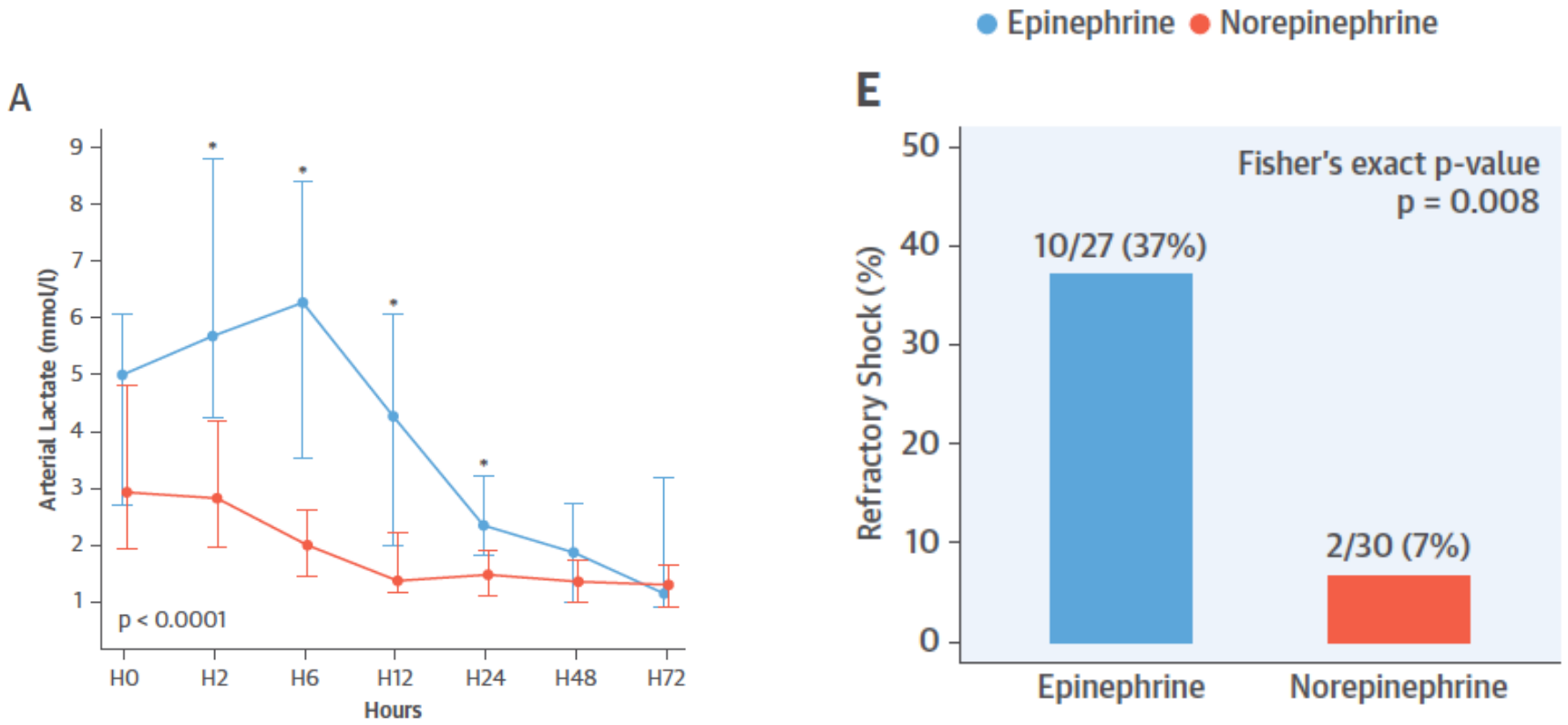


Levy B et al. J Am Coll Cardil 2018; 72:173-81





Levy B et al. J Am Coll Cardil 2018; 72:173-81



Levy B et al. J Am Coll Cardil 2018; 72:173-81

ADVERSE EFFECTS OF CARDIOVASO ACTIVE DRUGS

Increased myocardial oxygen demand

Myocardial ischemia

Tachycardia

Malignant arrhythmia

Increase left ventricular afterload

Pro-apoptotic effect

Valente S et al. Int J Cardiol 2007;114:176-82
Singh K et al. Cardiovasc Res 2000;45: 713–9

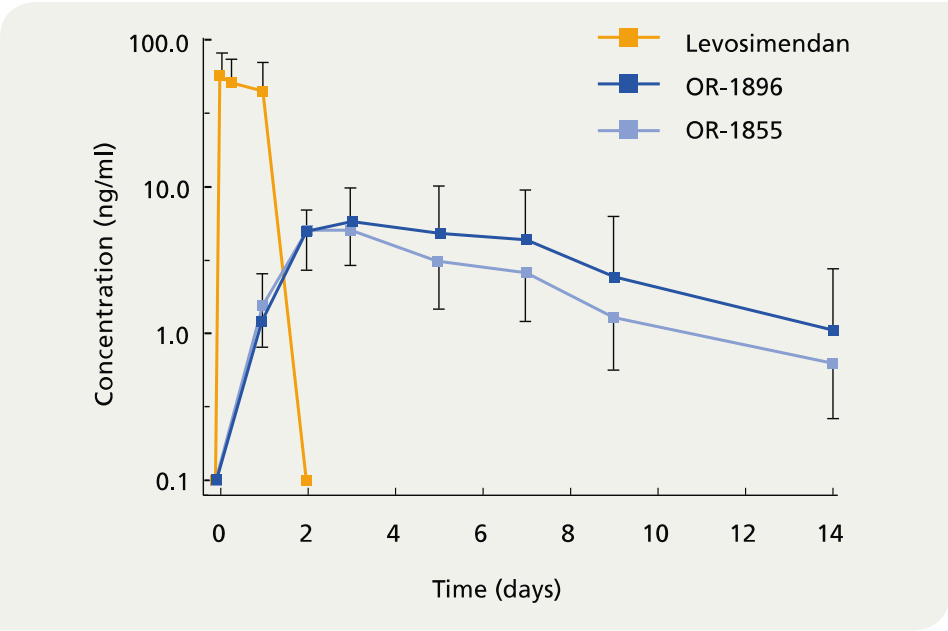
Levosimendan: Attracting properties...

- Inotropic effects:
  - Calcium sensitizer of myocardial contractile proteins
  - Improve cardiac contractility without increasing intracellular calcium concentration
  - Myocardial oxygen consumption unchanged
  - Diastolic function preserved
- Vasodilatory effects (openers K-ATP channels)
  - Coronary, pulmonary and systemic vasodilation
- Organ protective properties (myocardium, liver, kidney, digestive tractus…)
- Anti-apoptotic properties
- Anti-inflammatory effects

Rognoni et al. Recent Pat Cardiovascular Drug Discov 2011; 6:9-15

PHARMACOKINETICS

- Levosimendan: 0.2 µg/kg/min during 24h without initial bolus
- Active metabolites between 7 and 14 days



Levosimendan vs Dobutamine for Patients With Acute Decompensated Heart Failure

The SURVIVE Randomized Trial

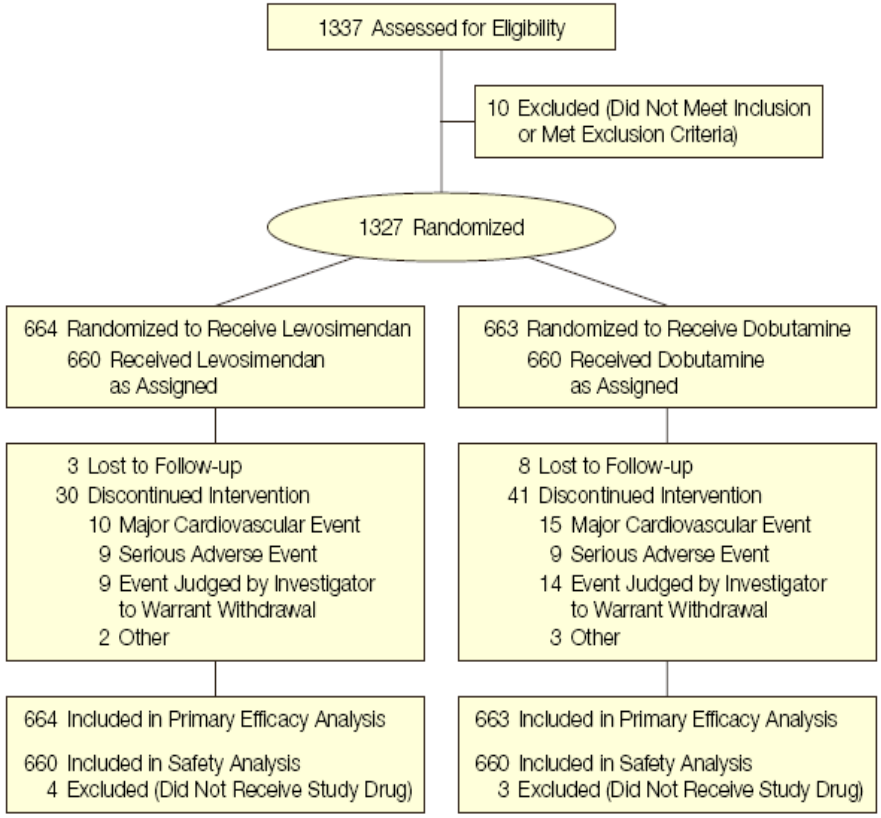
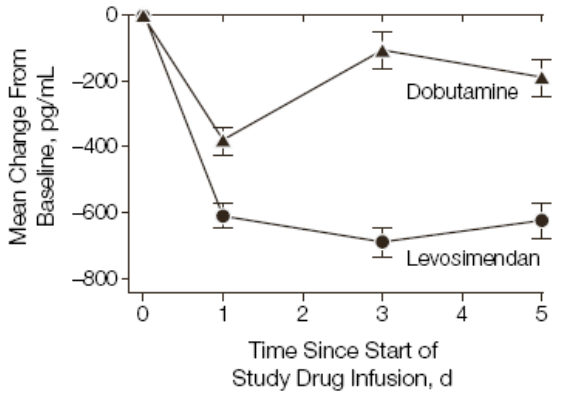
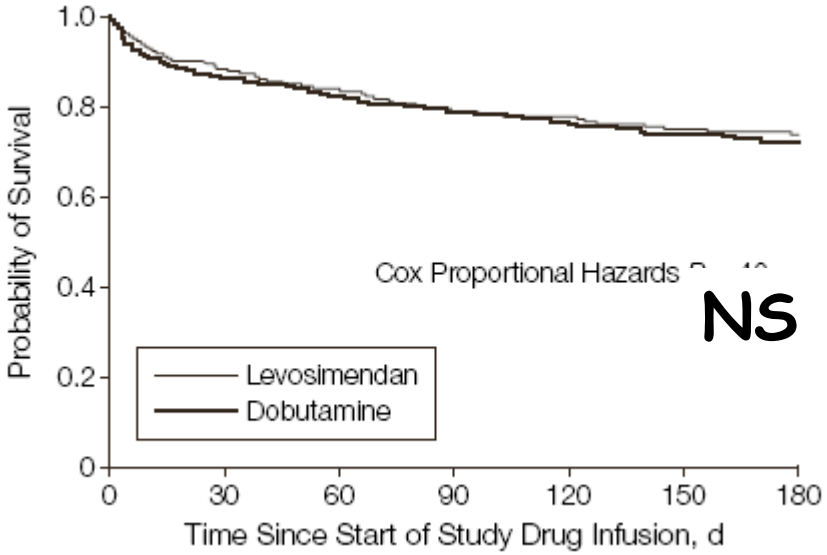


Figure 3. Mean Change From Baseline in B-Type Natriuretic Peptide Levels at 1, 3, and 5 Days by Treatment Group





Mebazaa A et al. JAMA 2007; 297:1883-91

ORIGINAL ARTICLE

Levosimendan in Patients with Left Ventricular Dysfunction Undergoing Cardiac Surgery

R.H. Mehta, J.D. Leimberger, S. van Diepen, J. Meza, A. Wang, R. Jankowich, R.W. Harrison, D. Hay, S. Fremes, A. Duncan, E.G. Soltesz, J. Luber, S. Park, M. Argenziano, E. Murphy, R. Marcel, D. Kalavrouziotis, D. Nagpal, J. Bozinovski, W. Toller, M. Heringlake, S.G. Goodman, J.H. Levy, R.A. Harrington, K.J. Anstrom, and J.H. Alexander, for the LEVO-CTS Investigators*

ABSTRACT

BACKGROUND

Levosimendan is an inotropic agent that has been shown in sma… vent or treat the low cardiac output syndrome after cardiac …

METHODS

In a multicenter, randomized, placebo-controlled … efficacy and safety of levosimendan in patien… tion of 35% or less who were undergoing … monary bypass. Patients were random… simendan (at a dose of 0.2 μg p… followed by a dose of 0.1 μg… the infusion started bef… ponent composite … 30, perioperati… diac assist … day 30 … …ndomization, 849 of whom received levosi- …luded in the modified intention-to-treat popula- …rimary end point occurred in 105 of 428 patients …ive levosimendan and in 103 of 421 (24.5%) assigned to …justed odds ratio, 1.00; 99% confidence interval [CI], 0.66 to …he two-component primary end point occurred in 56 patients …igned to receive levosimendan and in 48 (11.4%) assigned to receive … (adjusted odds ratio, 1.18; 96% CI, 0.76 to 1.82; P=0.45). The rate of ad- …se events did not differ significantly between the two groups.

CONCLUSIONS

Prophylactic levosimendan did not result in a rate of the short-term composite end point of death, renal-replacement therapy, perioperative myocardial infarction, or use of a mechanical cardiac assist device that was lower than the rate with placebo among patients with a reduced left ventricular ejection fraction who were undergoing cardiac surgery with the use of cardiopulmonary bypass. (Funded by Tenax Therapeutics; LEVO-CTS ClinicalTrials.gov number, NCT02025621.)

…complete … the Levosim… Ventricular … going Card… diopulmona… is provided … pendix, avai…

This article w… 2017, at NEJM…

DOI: 10.1056/…

The study population was patients with low preoperative LVEF (< 35%) undergoing scheduled or urgent cardiac surgery . Patients received 0.2 μg/kg/min for 60 min followed by 0.1 μg/kg/min for 23 hours or placebo was started at the induction of anesthesia. Primary end point of death, perioperative myocardial infarction, and need for renal replacement therapy or a mechanical ventricular assist device.

ORIGINAL ARTICLE

Levosimendan for Hemodynamic Support after Cardiac Surgery

G. Landoni, V.V. Lomivorotov, G. Alvaro, R. Lobreglio, A. Pisano, F. Guarracino, M.G. Calabrò, E.V. Grigoryev, V.V. Likhvantsev, M.F. Salgado-Filho, A. Bianchi, V.V. Pasyuga, M. Baiocchi, F. Pappalardo, F. Monaco, V.A. Boboshko, M.N. Abubakirov, B. Amantea, R. Lembo, L. Brazzi, L. Verniero, P. Bertini, A.M. Scandroglio, T. Bove, A. Belletti, M.G. Michienzi, D.L. Shukevich, T.S. Zabelina, R. Bellomo, and A. Zangrillo, for the CHEETAH Study Group*

ABSTRACT

BACKGROUND

Acute left ventricular dysfunction is a major complicatio… associated with increased mortality. Meta-analyses o… simendan may result in a higher rate of survival … surgery.

METHODS

We conducted a multicenter, ra… volving patients in whom … cardiac surgery, accord… to receive levosim… kilogram of b… from the … was … …patients were enrolled. A total of 248 pa- …ndan and 258 to receive placebo. There was no …mortality between the levosimendan group and …s [12.9%] and 33 patients [12.8%], respectively; abso- …ercentage points; 95% confidence interval [CI], −5.7 to 5.9; …e no significant differences between the levosimendan group …group in the durations of mechanical ventilation (median, 19 hours …rs, respectively; median difference, −2 hours; 95% CI, −5 to 1; P=0.48), …y (median, 72 hours and 84 hours, respectively; median difference, −12 hours; …% CI, −21 to 2; P=0.09), and hospital stay (median, 14 days and 14 days, respectively; median difference, 0 days; 95% CI, −1 to 2; P=0.39). There was no significant difference between the levosimendan group and the placebo group in rates of hypotension or cardiac arrhythmias.

CONCLUSIONS

In patients who required perioperative hemodynamic support after cardiac surgery, low-dose levosimendan in addition to standard care did not result in lower 30-day mortality than placebo. (Funded by the Italian Ministry of Health; CHEETAH ClinicalTrials.gov number, NCT00994825.)

Most patients underwent randomization in the operating room because high doses of inotropes were indicated for weaning from cardiopulmonary bypass or in the ICU. The mean infusion rate and duration of levosimendan were 0.07μg/kg/min for 33 hours, and the median EF was 50% in both groups, with 11% of patients having an EF of 25%. There was no significant difference in 30-day mortality between the levosimendan and placebo groups: 32 patients (12.9%) versus 33 (12.8%)

JAMA | Original Investigation

Effect of Levosimendan on Low Cardiac Output Syndrome in Patients With Low Ejection Fraction Undergoing Coronary Artery Bypass Grafting With Cardiopulmonary Bypass

The LICORN Randomized Clinical Trial

Bernard Cholley, MD, PhD; Thibaut Caruba, PharmD, PhD; Sandrine Grosjean, MD; Julien Amour, MD, PhD; Alexandre Ouattara, MD, PhD; Judith Villacorta, MD; Bertrand Miguet, MD; Patrick Guinet, MD; François Lévy, MD; Pierre Squara, MD; Nora Aït Hamou, MD; Aude Carillon, MD; Julie Boyer, MD; Marie-Fazia Boughenou, MD; Sebastien Rosier, MD; Emmanuel Robin, MD; Mihail Radutoiu, MD; Michel Durand, MD; Catherine Guidon, MD, PhD; Olivier Desebbe, MD; Anaïs Charles-Nelson, MSc; Philippe Menasché, MD, PhD; Bertrand Rozec, MD, PhD; Claude Girard, MD, PhD; Jean-Luc Fellahi, MD, PhD; Romain Pirracchio, MD, PhD; Gilles Chatellier, MD, PhD

IMPORTANCE Low cardiac output syndrome after cardiac surgery is associated with high morbidity and mortality in patients with impaired left ventricular function.

OBJECTIVE To assess the ability of preoperative levosimendan to prevent postoperative low cardiac output syndrome.

DESIGN, SETTING, AND PARTICIPANTS Randomized, double-blind, placebo-controlled trial conducted in 13 French cardiac surgical centers. Patients with a left ventricular ejection fraction less than or equal to 40% and scheduled for isolated or combined coronary bypass grafting with cardiopulmonary bypass were enrolled from June 201 and followed during 6 months (last follow-up, November 30, 2015).

INTERVENTIONS Patients were assigned to a 24-hour infusi (n = 167) or placebo (n = 168) initiated after anesthetic

MAIN OUTCOMES AND MEASURES Composit syndrome with need for a catecholami on, need for a left ventricular mechanical a ours after study drug initiation when the de renal replacement therapy at any time po imendan would reduce the incidence of t on with placebo.

RESULT ge, 68 years; 16% women), 333 c curred in 87 patients (52%) in the levosimendan ebo group (absolute risk difference taking into l, −17% to 3%]; *P* = .15). Predefined subgroup analyses ction fraction less than 30%, type of surgery, and preoperative ortic balloon pump, or catecholamines. The prevalence of s 48%), atrial fibrillation (50% vs 40%), and other adverse events did not iffer between levosimendan and placebo.

CONCLUSIONS AND RELEVANCE Among patients with low ejection fraction who were undergoing coronary artery bypass grafting with cardiopulmonary bypass, levosimendan compared with placebo did not result in a significant difference in the composite end point of prolonged catecholamine infusion, use of left ventricular mechanical assist device, or renal replacement therapy. These findings do not support the use of levosimendan for this indication.

TRIAL REGISTRATION EudraCT Number: 2012-000232-25; clinicaltrials.gov Identifier: NCT02184819

JAMA. 2017;318(6):548-556. doi:10.1001/jama.2017.9973

Primary endpoint: (1) need for inotropic agents beyond 48 hours after initiation of the study drug; (2) need for postoperative mechanical assist devices or failure to wean from these devices when inserted preoperatively; and (3) need for renal replacement therapy.

Supplemental content

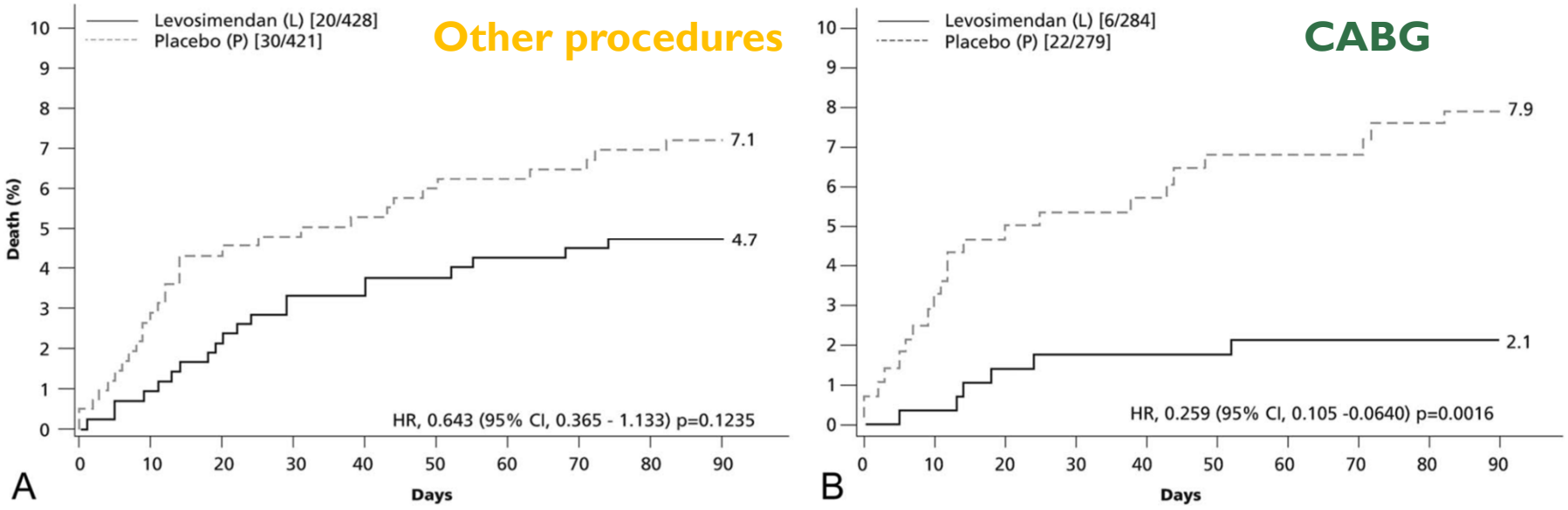
CME Quiz at jamanetwork.com/learning

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Bernard Cholley, MD, PhD, Department of Anesthesiology and Critical Care Medicine, Hôpital Européen Georges Pompidou, AP-HP, 20 rue Leblanc, 75908 Paris Cedex 15, France (bernard.cholley@aphp.fr).

Use of Levosimendan in Cardiac Surgery: An Update After the LEVO-CTS, CHEETAH, and LICORN Trials in the Light of Clinical Practice

Fabio Guarracino, MD, PhD, Matthias Heringlake, MD, PhD,† Bernard Cholley, MD, PhD,‡§ Dominique Bettex, MD, PhD,¶ Stefaan Bouchez, MD, PhD,|| Vladimir V. Lomivorotov, MD, PhD,** Angela Rajek, MD,†† Matti Kivikko, MD, PhD,‡‡§§ and Piero Pollesello, PhD‡‡*



J Cardiovasc Pharmacol 2018; 71:1-9

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 should be included**

Inotropic agents		
Inotropic agents may be considered in patients with SBP <90 mmHg and evidence of hypoperfusion who do not respond to standard treatment, including fluid challenge, to improve peripheral perfusion and maintain end-organ function.[387]	IIb	C
Inotropic agents are not recommended routinely, due to safety concerns, unless the patient has symptomatic hypotension and evidence of hypoperfusion.[387,467,478]	III	C

Vasopressors		
A vasopressor, preferably norepinephrine, may be considered in patients with cardiogenic shock to increase blood pressure and vital organ perfusion.[485–487]	IIb	B

Mc Donagh TA et al. Eur Heart J 2021; 42:3599-3726

Involvement of RV dysfunction or failure

Incidence of CS 33%

Primary predominant 3-5%

Higher intra-hospital mortality

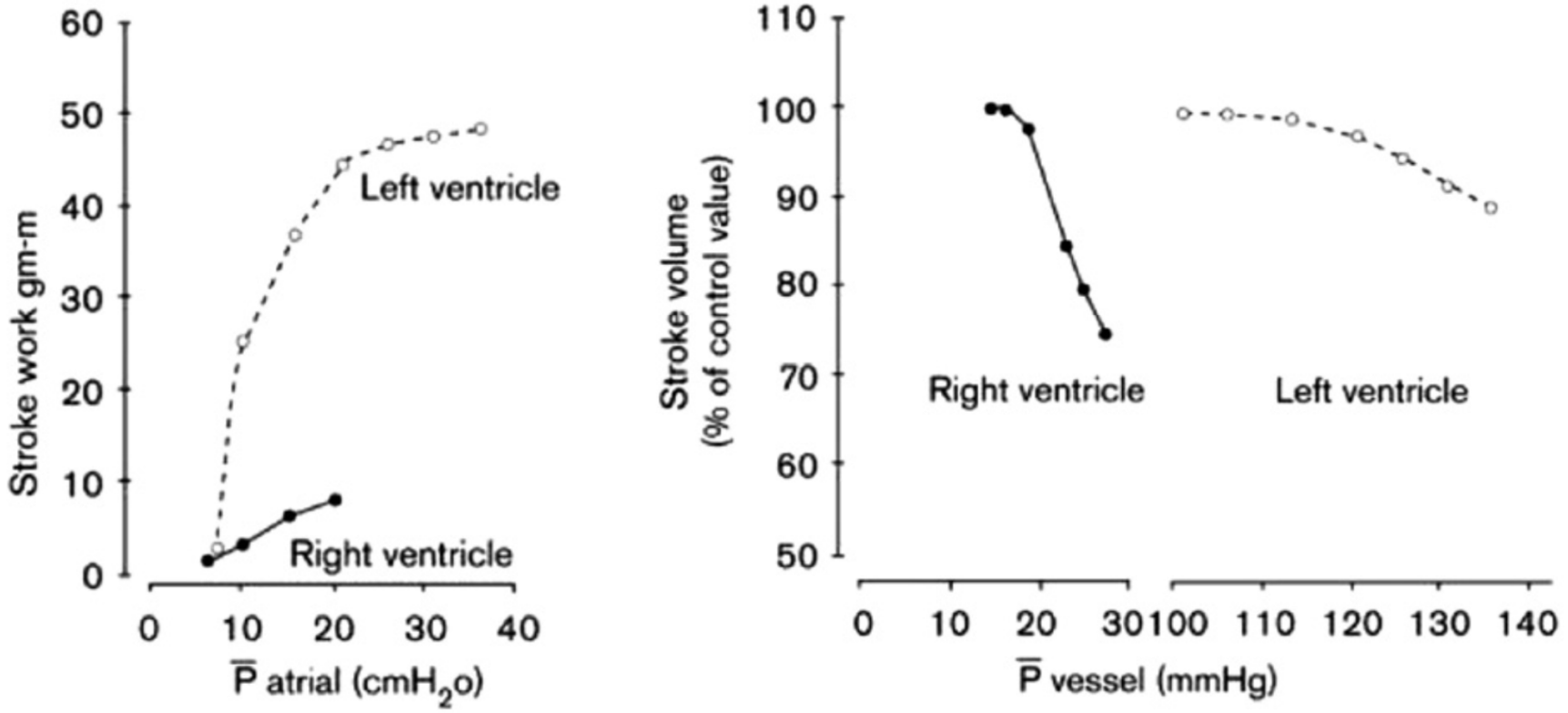
9.4% versus 3.0%

More difficult management

Cardiac index <2.2 L/min/m^2 despite continuous high dose inotropes or >1 inotrope or vasopressor medication + any of the following criteria:	
	CVP >10 mm Hg CVP/PCWP ratio >0.63 PAPi <2 RVSWI <450 mm Hg*mL/m^2 RV dysfunction and/or dilation on echocardiography: TAPSE <17 mm RV systolic TDI S′ velocity <10 cm/sec RVFAC $<35\%$ RV free wall longitudinal strain $<-20\%$ RV basilar diameter >42 mm RV short axis (or mid cavity) diameter >35 mm
Severe RV dysfunction	CVP >15 mm Hg CVP/PCWP ratio >0.8 PAPi <1.5 RVSWI <300 mm Hg*mL/m^2
Clinical	Ascites Edema Bilirubin elevation Creatinine elevation

Kapur NK et al. Circulation 2017; 136:314-26

Different adaptative response to changes in loading conditions



Ventetuolo CE et al. Ann Am Thorac Soc 2014; 11:811-22

RIGHT VENTRICULAR DYSFUNCTION

Pulmonary artery pulsatility index= (sPAP-dPAP)/RAP < 1.0

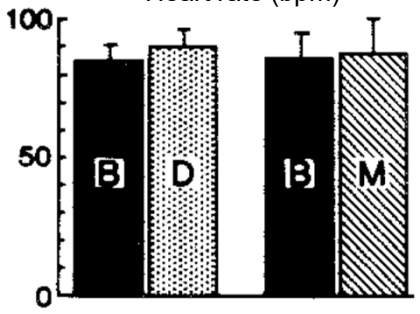
RAP/PCWP > 0.6

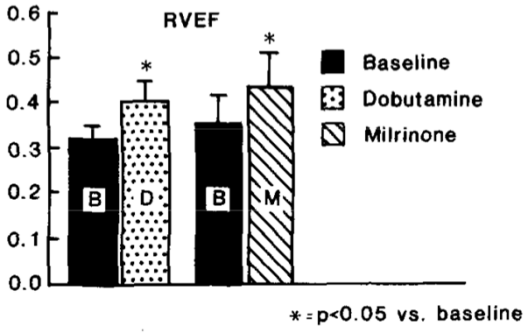
Korabathina R et al. Catheter Cardiovasc Interv 2012; 80:593-600

Tehrani BN et al. J Am Coll Cardiol 2019; 73:1659-69

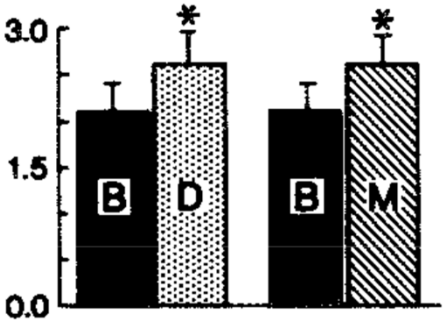
Eichhorn EJ et al. Am J Cardiol 1987;60:1329-33

Heart rate (bpm)

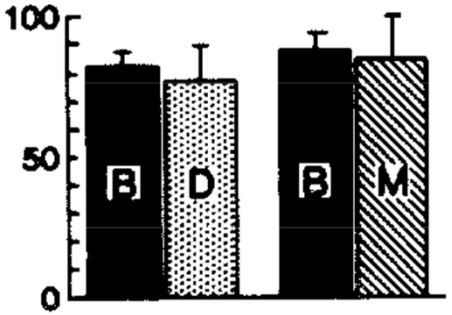


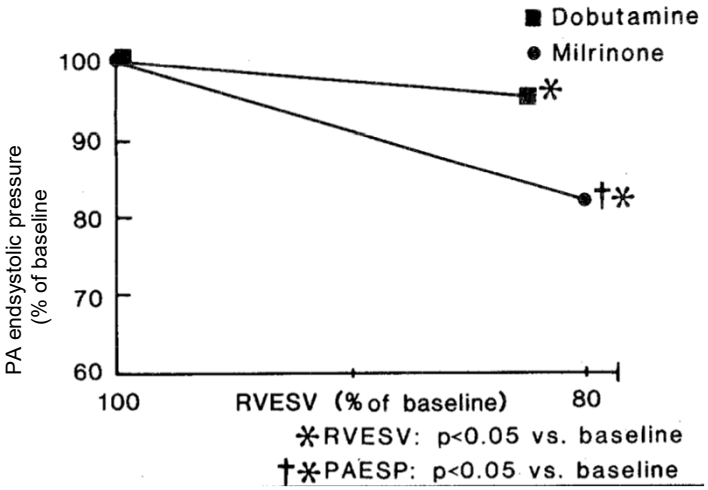


Cardiac index (L.min^{-1}.m^{-2})

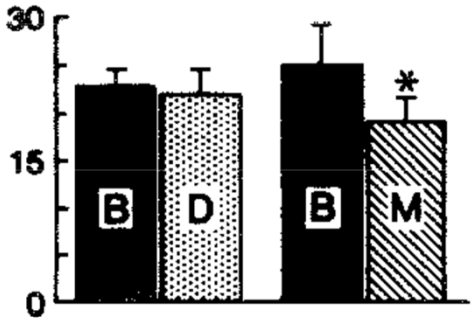


MAP (mmHg)

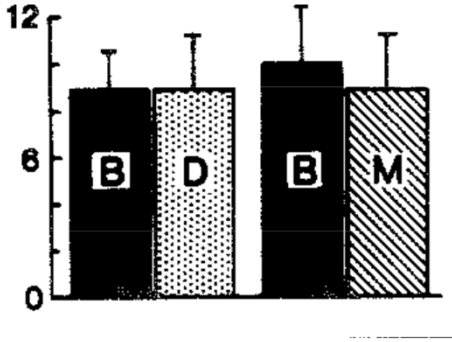


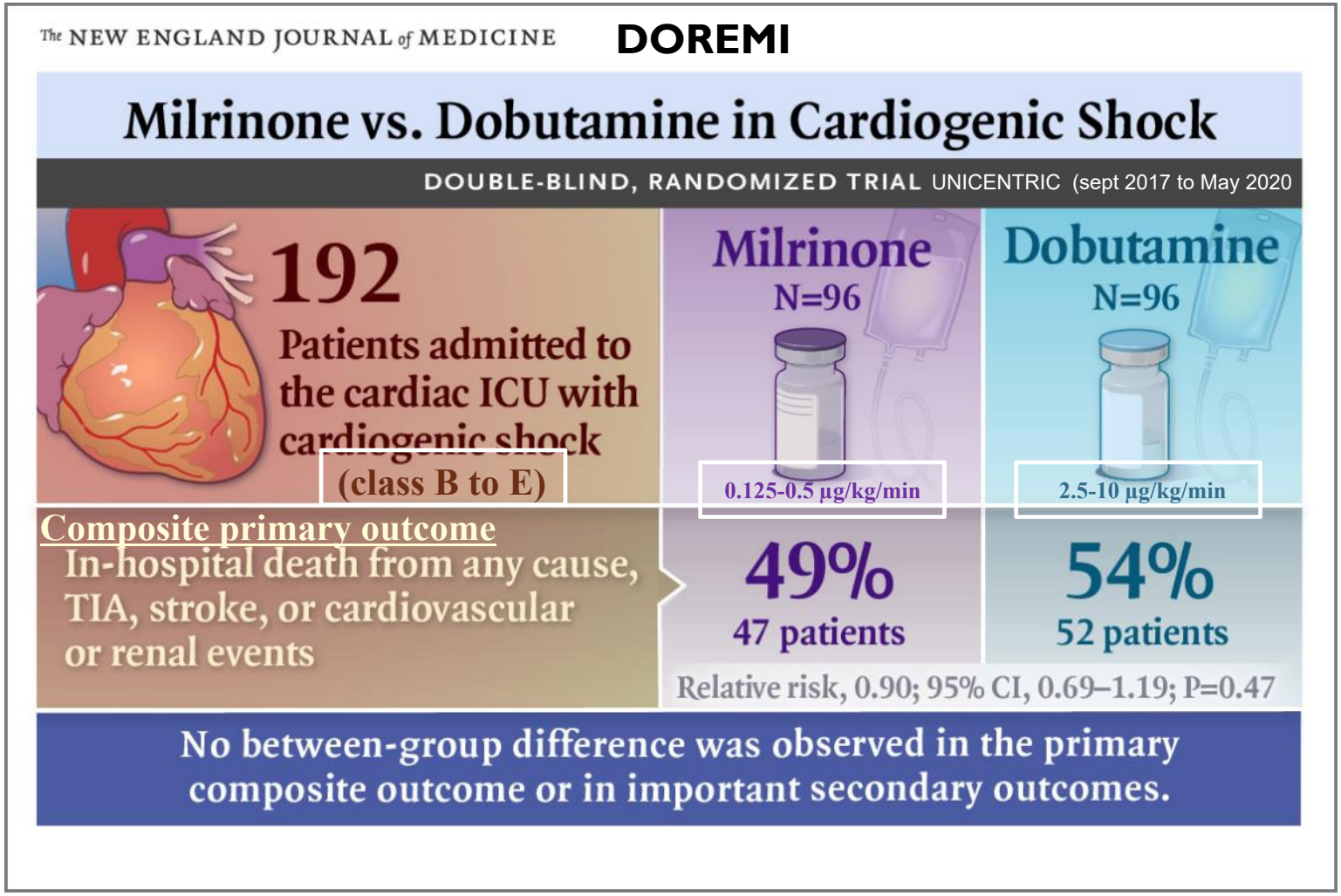


PCWP (mmHg)



CVP (mmHg)





Mathew R et al. New Engl Med 2021 385; 516-25

PLEASE, USE VASOACTIVE

AND INOTROPICS AT THE

LOWEST DOSE AND DURING

THE SHORTEST TIME

POSSIBLE ...

Recruiting

CAPITAL DOREMI 2: Inotrope Versus Placebo Therapy for Cardiogenic Shock (DOREMI-2)

ClinicalTrials.gov ID NCT05267886

Sponsor Ottawa Heart Institute Research Corporation

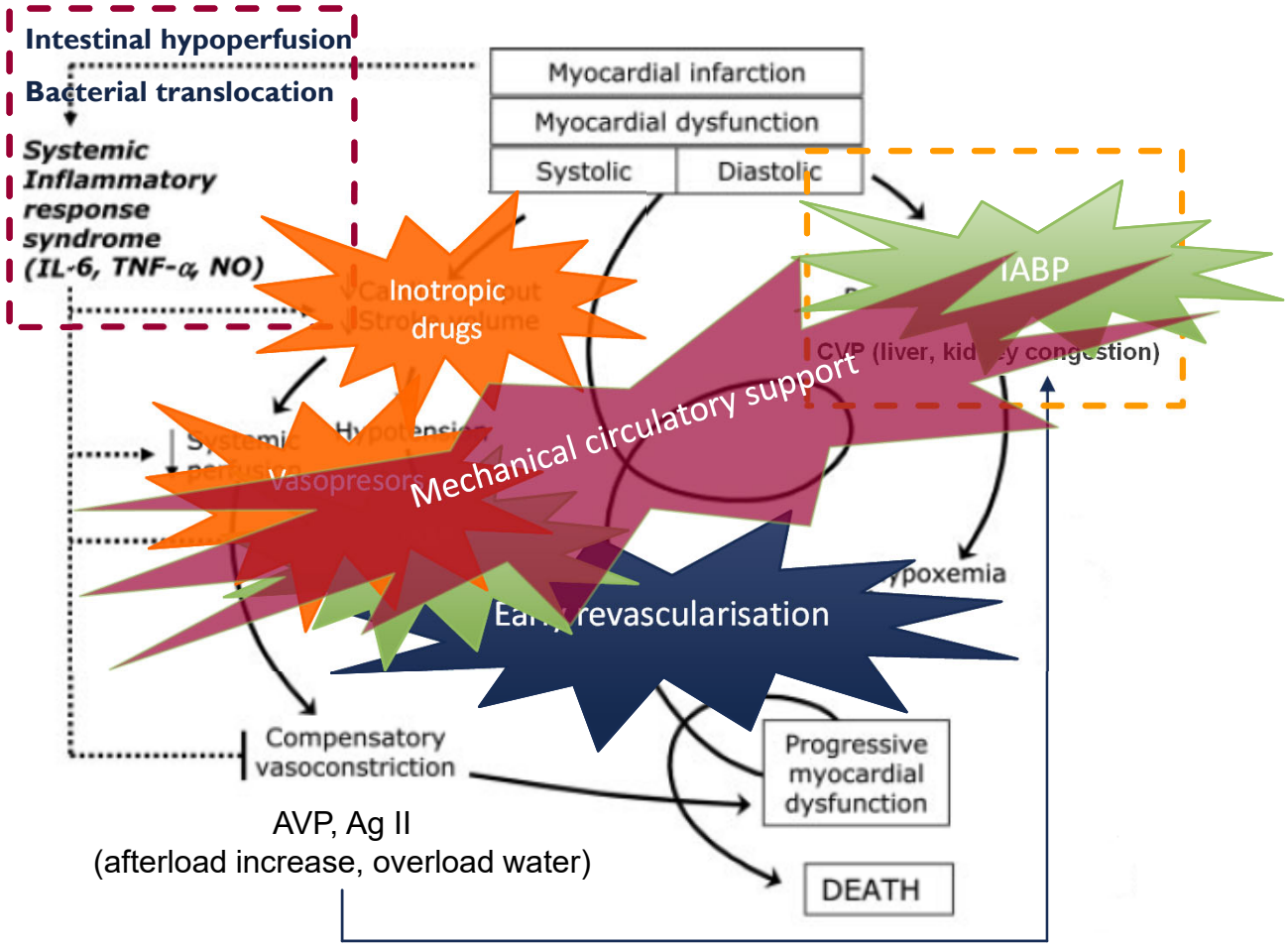
Information provided by Ottawa Heart Institute Research Corporation (Responsible Party)

Last Update Posted 2024-04-08

SYSTEMIC CARDIOVASCULAR AND INFLAMMATORY DISEASE

Coronary endothelial dysfonction

Myocardial depression



Reynolds HR et al. Circulation 2008; 117:686-97

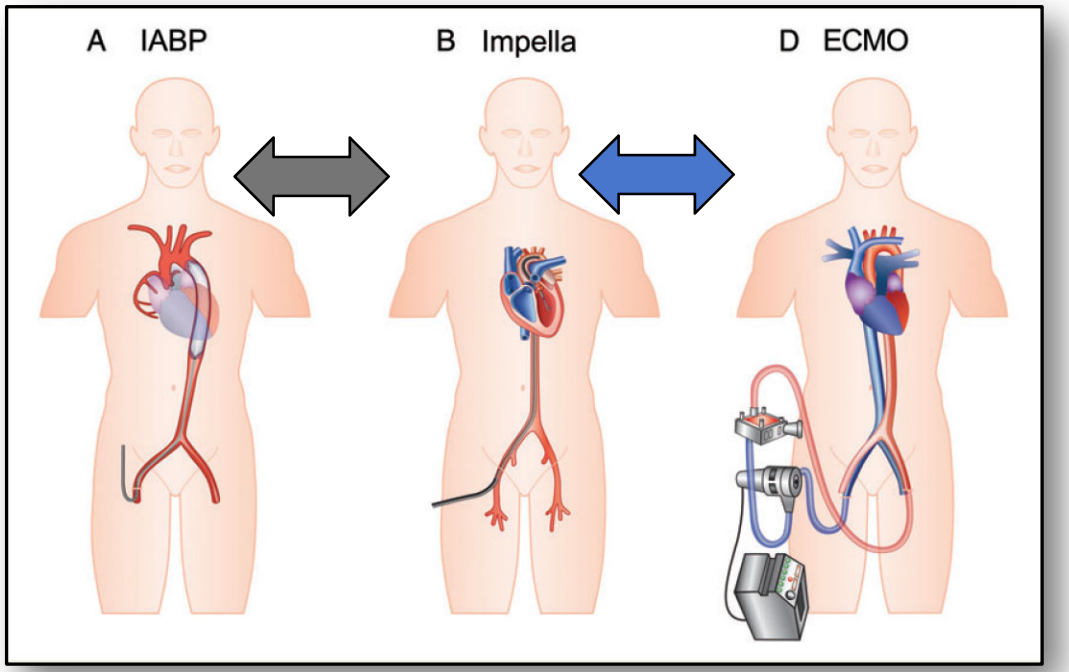
REVIEW Open Access

Experts' recommendations for the management of adult patients with cardiogenic shock

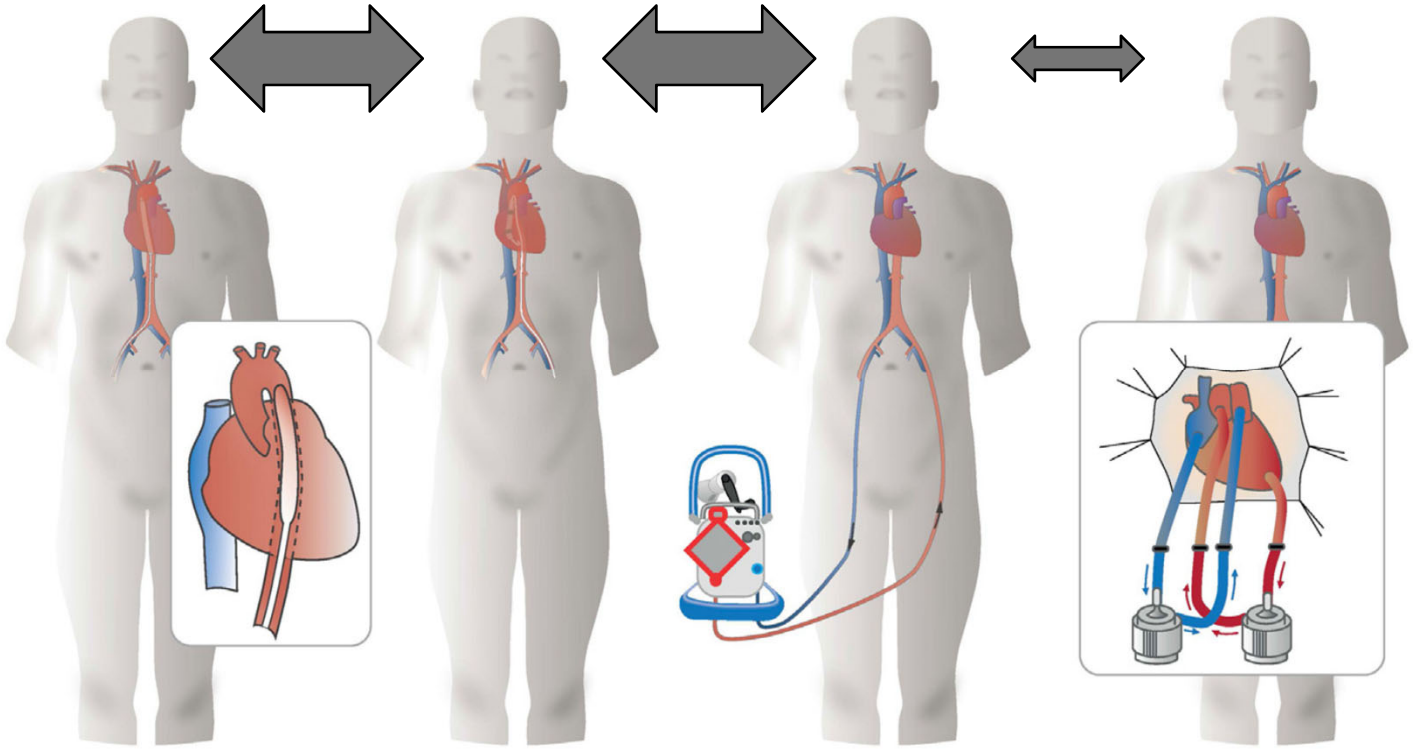
Annals of Intensive Care
a SpringerOpen Journal

Ann Intensive Care 2015; 5:17

Bruno Levy[1*], Olivier Bastien[2], Karim Benjelid[3], Alain Cariou[4], Tahar Chouihed[5], Alain Combes[6], Alexandre Mebazaa[7], Bruno Megarbane[8], Patrick Plaisance[9], Alexandre Ouattara[10], Christian Splaulding[11], Jean-Louis Teboul[12], Fabrice Vanhuyse[13], Thierry Boulain[14] and Kaldoun Kuteifan[15]



SHORT TERM MECHANICAL CIRCULATORY SUPPPORT (STMCS)



IABP IMPELLA ECMO pVAD

BY WHO? CARDIOGENIC SHOCK TEAM

Patient with suspected cardiogenic shock (CS)

Clinical criteria to rapidly identify shock state:

Systolic blood pressure (SBP) <90 mm Hg for >30 minutes
(or use of inotropes/vasopressors to maintain SBP)

Evidence of end-organ hypoperfusion

Lactate level >2 mmol/l

Activate Shock Team through a one-call line for multidisciplinary discussion:
Interventional Cardiology; Cardiac Surgery; Advanced Heart Failure; Critical Care

Transfer patient to cardiac catheterization lab or cardiac intensive care unit (CICU) for evaluation

If acute decompensated heart failure cardiogenic shock (ADHF-CS) suspected:

Right heart catheterization

Echo

If acute myocardial infarction cardiogenic shock (AMI-CS) suspected:

Right heart catheterization

Coronary angiography + revascularization

Assessment of peripheral vascular anatomy

Hemodynamic Criteria for Cardiogenic Shock:

Fick cardiac index <1.8 l/min/m^2 without inotropes/vasopressors
(or <2.2 l/min/m^2 with inotropes/vasopressors)

Pulmonary capillary wedge pressure >15 mm Hg

Cardiac power output (CPO) <0.6 W

PAPi <1.0

If Hemodynamic Criteria are met, consider Percutaneous Mechanical Circulatory Support (PMCS)

Admit Patient to CICU

Daily bedside echocardiograms for patients with PMCS

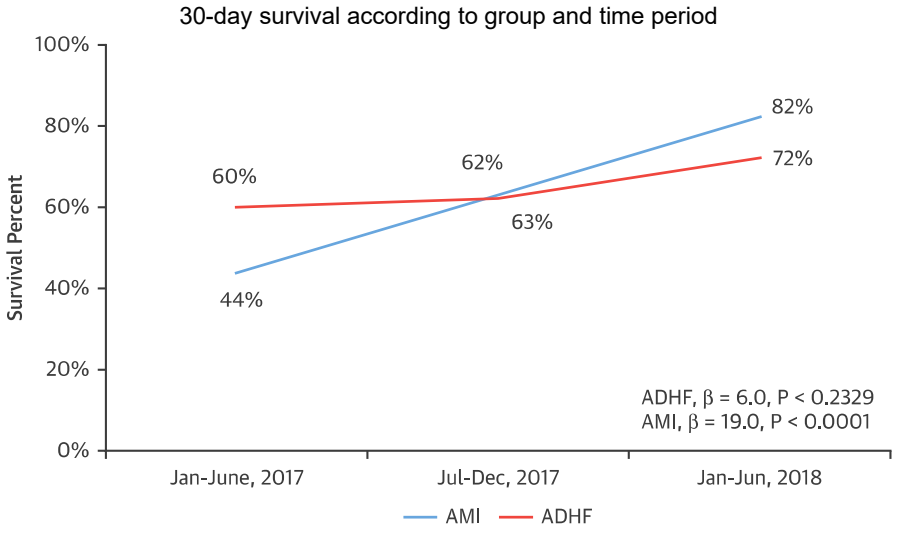
Frequent neurovascular assessments for patients with PMCS

Serial assessment of end-organ perfusion and hemodynamics: CPO, PAPi and lactate

Evaluation for weaning vs. escalation of support

Multidisciplinary “Shock team” :

- Tertiary expert center
- Standardized protocol (clear objectives)
- Advanced hemodynamic monitoring modal)



Tehrani B et al. JACC 2019; 73:1659-69

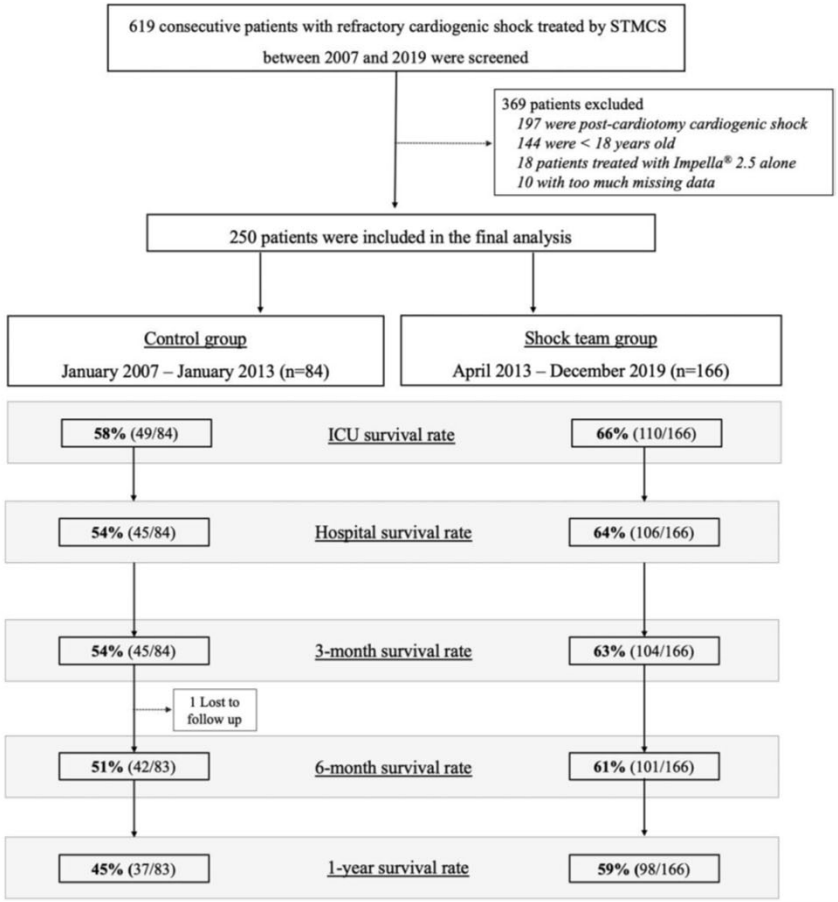
Auteur	Type d'étude	Population	Composition de la team	Déclenchement	Modalité de réunion	Outcome
Garan et al, 2016	Lettre scientifique	Choc Cardiogénique	Chirurgien cardiaque Spécialiste de l'IC avancée Cardiologue interventionnel Réanimateur	Non rapporté	Réunion virtuelle Application smartphone	Non rapporté
Taleb et al, 2019	Monocentrique prospectif, contrôlé contre cohorte historique rétrospective	Choc Cardiogénique n= 123 (Shock team) n= 121 (control)	Chirurgien cardiaque Spécialiste de l'IC avancée Cardiologue interventionnel Réanimateur	Suspicion clinique de CC	Réunion virtuelle Appel téléphonique	Mortalité hospitalière 52% vs 39% (control vs Shock Team)
Tehrani et al, 2019	Monocentrique prospectif	Choc Cardiogénique n= 204 (Shock team)	Chirurgien cardiaque Spécialiste de l'IC avancée Cardiologue interventionnel Réanimateur	Suspicion clinique de CC	Réunion virtuelle Appel téléphonique	Mortalité à 30 jours 53% vs 39% (control vs Shock Team)
Lee et al, 2020	Monocentrique prospectif, contrôlé contre cohorte historique rétrospective	Choc Cardiogénique n= 64 (Shock team), n=36 (control)	Chirurgien cardiaque Spécialiste de l'IC avancée Cardiologue interventionnel Réanimateur	Cas validé par le Spécialiste de l'IC avancée	Réunion virtuelle Application smartphone	Mortalité à 8 mois 67% vs 43% (control vs Shock Team)
Gibbs et al, 2020	Etude qualitative	Choc Cardiogénique	Chirurgien cardiaque Spécialiste de l'IC avancée Cardiologue interventionnel ACT/ECMO spécialiste	Non rapporté	Réunion virtuelle Appel téléphonique	Non rapporté
Hernandez-Perez et al, 2021	Monocentrique rétrospectif	Choc Cardiogénique réfractaire n= 130 (Shock team)	Chirurgien cardiaque Spécialiste de l'IC avancée Cardiologue interventionnel Réanimateur	Choc cardiogénique réfractaire	Réunion virtuelle Appel téléphonique	Mortalité hospitalière 43%
Mannino et al, 2021	Communication, non revue par les pairs Monocentrique rétrospectif	Choc Cardiogénique ischémique Impella® seule n= 154 (Shock team) n= 37 (control)	Cardiologue interventionnel Réanimateur Spécialiste de l'IC avancée si besoin	Suspicion clinique de CC ischémique	Non rapporté	Mortalité hospitalière 56% vs 29% (control vs Shock Team)

Multidisciplinary cardiogenic shock team approach improves the long-term outcomes of patients suffering from refractory cardiogenic shock treated with short-term mechanical circulatory support

François-Xavier Hérion[1,2†], Antoine Beurton[1,2*†], Claire Oddos[1], Karine Nubret[3], Clément Aguerreche[1], Astrid Quessard[1], Maxime Faure[3], Edouard Gerbaud[4,5], Mathieu Pernot[2,6], Julien Imbault[1,2], and Alexandre Ouattara[1,2]

ESC European Society of Cardiology

European Heart Journal: Acute Cardiovascular Care (2023)
https://doi.org/10.1093/ehjacc/zuad108



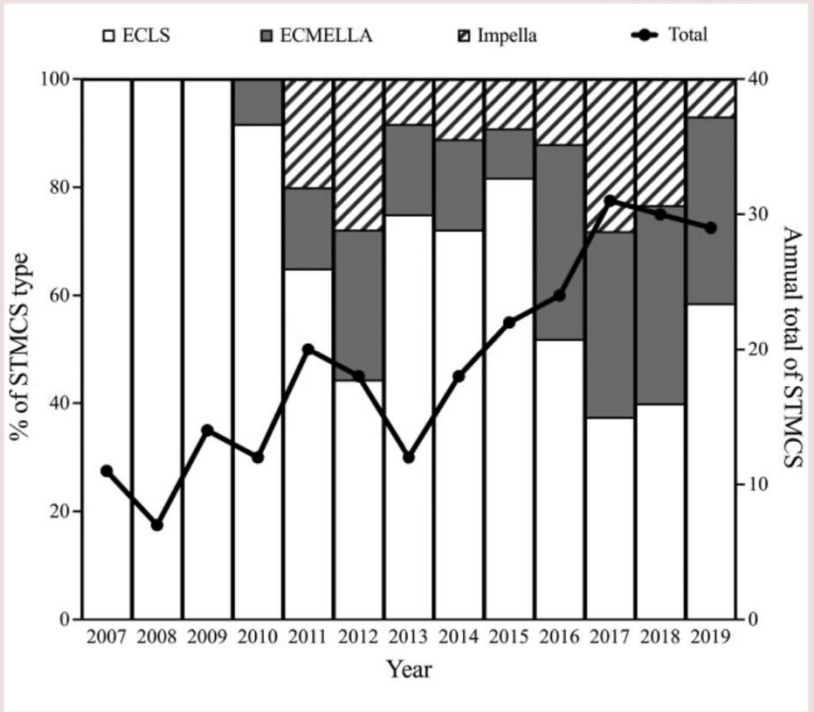


Figure 3 Trends in STMCS over the years. ECLS, extracorporeal life support; ECMELLA, Association of ECLS and Impella® 2.5, CP or 5.0; IABP, intra-aortic balloon pump; STMCS, short-term mechanical circulatory support. The 'Impella®' category includes only CP and 5.0 used alone.

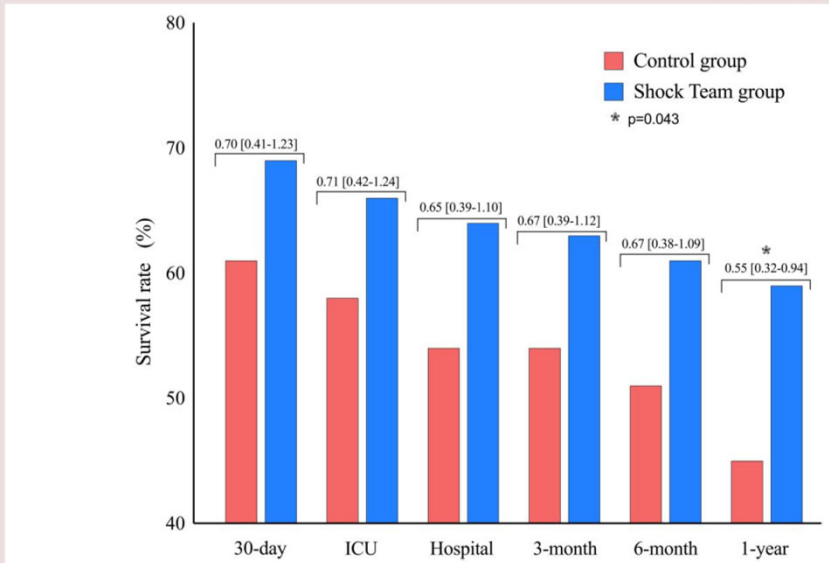


Figure 4 Survival rate evolution. Survival rate evolution for the control group and shock team group after short-term mechanical circulatory support (STMCS) device implantation. Odds ratio including 95% confidence bands was calculated.

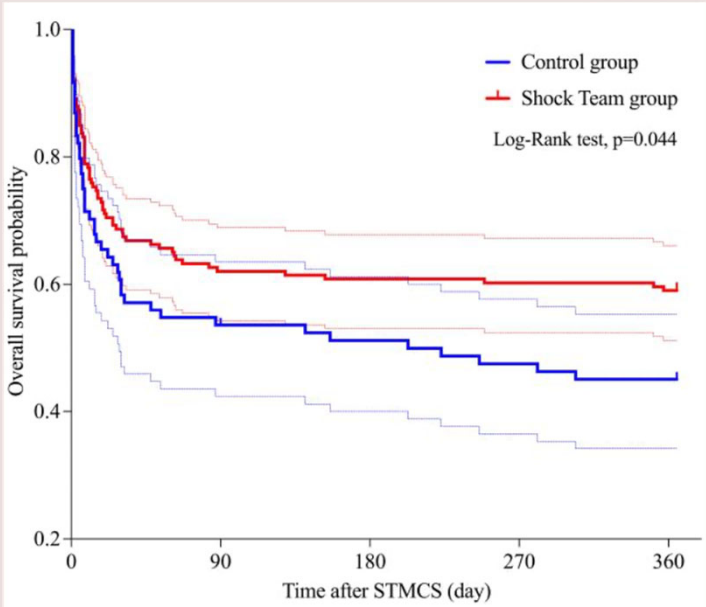


Figure 5 Kaplan–Meier survival. Survival function estimated by the Kaplan–Meier method, including 95% confidence bands, for the control group and shock team group after short-term mechanical circulatory support (STMCS) device implantation. Each vertical step in the curve indicates deaths, and right-censored patients are indicated by a vertical mark in the curve at the censoring time. A visual inspection suggests that survival seems to be more favourable in the shock team group, compared with the control group. The log-rank test indicates a significant difference between the survival curves.

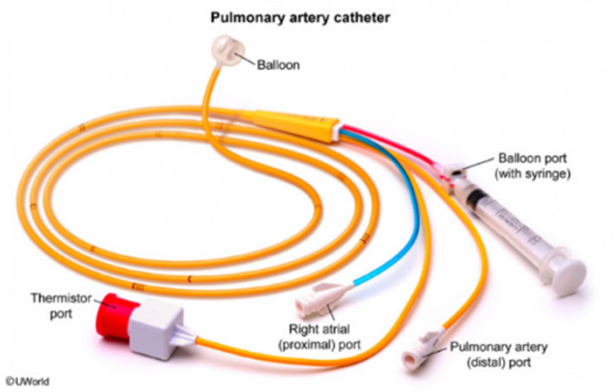
Use of pulmonary artery catheter?

Randomized studies and several meta-analyses have failed to confirm a clinical benefit of the PAC in a wide range of critically ill patient pathologies

Current recommendations of the European Society of Intensive Care Medicine still consider PAC as a useful tool in some patients with severe CS

Especially in case of right ventricular dysfunction or CS unresponsive to initial therapies, reflecting standard practice in expert centers in the management of this condition.

Mebazaa A et al. Intensive Care Med. 2018;44:760-73



Summary of clinical studies of PAC use

Ref.	Year	Number of cases	Study design	Clinical settings	Significant findings
[29]	1995	762 (252/253/257)	RCT (control versus supranormal DO_2 versus minimal SvO_2)	Multicenter, high-risk surgical patients with hemorrhagic, septic ARDS and trauma	No difference in mortality, organ dysfunction, or length of stay
[39]	1995	630 PAC placements in 118 patients	Retrospective analysis	Patients with aneurysmal subarachnoid hemorrhage	13% catheter related sepsis, 2% CHF, 1.2% DVT, 1% pneumothorax, no PA rupture
[45]	1995	32442	Retrospective chart review	OR and ICU	0.03% PA rupture with 70% mortality rate
[5]	1996	2016 (1008/1008)	Prospective cohort, case matching analysis	Critically ill patients	Increased mortality, cost of care and length of ICU stay in PAC group
[21]	1998	120 (60/60)	RCT (PAC versus no PAC)	Surgical low-risk AAA repair	No benefit, possibly with higher intraoperative complications
[6]	2000	10,217	Retrospective database study	Nonoperative patients in medical and surgical ICU	Direct association of PAC use with admission in surgical ICU, white race, care given by noninternists, and having private insurance
[8]	2001	4059 (2213/3839)	Prospective, observational cohort	Elective major noncardiac surgery	Increase in cardiac and noncardiac events with PAC
[18]	2003	1994 (997/997)	RCT (PAC versus no PAC)	High risk, >/= 1-year-old surgical patients	No benefit in PAC group, higher PE in catheter group, survival rate favored non-PAC group
[20]	2003	676 (335/341)	RCT (PAC versus no PAC)	Multicenter, shock and ARDS patients	No impact of PAC on mortality or morbidity
[23]	2005	1041 (519/522)	RCT (PAC versus no PAC)	Multi-center, all adult ICUs	No evidence of benefit or hospital mortality, 10% complications but not fatal
[24]	2005	433 (215/218)	RCT (PAC versus no PAC)	Multicenter, severely symptomatic CHF patients	No evidence of benefit or overall mortality, 5% complications but more fatal

NEJM
JAMA
Ann Surg
JAMA
JAMA
NEJM
JAMA
Lancet

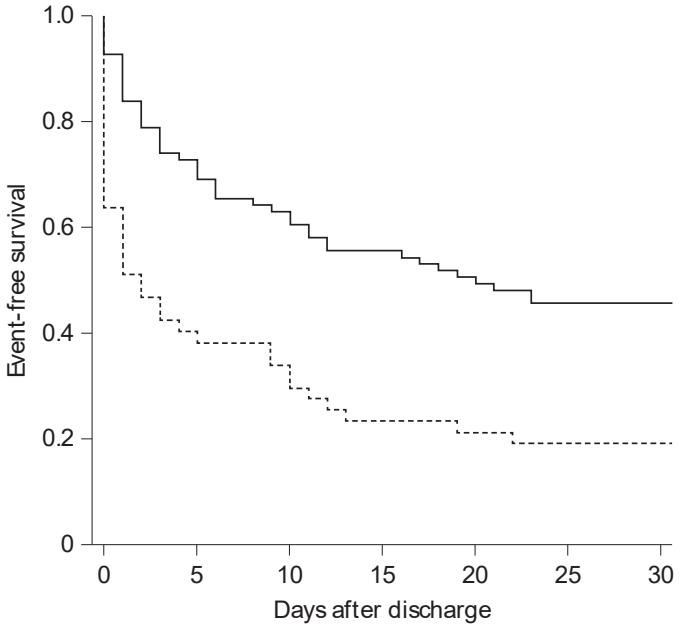
No study conducted in patients suffering from cardiogenic shock treated or not by mechanical circulatory support

Impact of Pulmonary Artery Catheter Use on Short- and Long-Term Mortality in Patients with Cardiogenic Shock

Original Research

Rossello X et al. Cardiology 2017;136:61-9

- Prospective cohort (2005-2009) of patients suffering from CS (n=129) divided in two groups PAC + versus PAC –
- Logistic regression identifying risk factors of 30-day mortality
- 30-day mortality rate was 64%



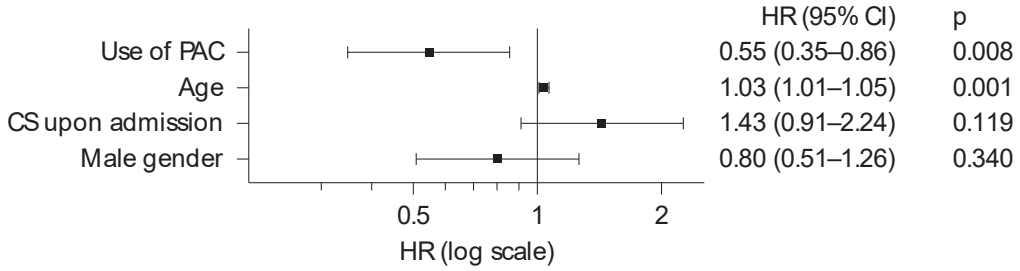


Table 3. In-Hospital Outcomes After Propensity Score Matching

	Cardiogenic Shock				Heart Failure			
Outcome	PAC (n = 11,139)	No PAC (n = 11,139)	OR (95% CI)*	*P* Value	PAC (n = 11,640)	No PAC (n = 11,640)	OR (95% CI)*	*P* Value
Mortality	34.9%	37.0%	0.91 (0.87–0.97)	.001	6.7%	2.4%	2.95 (2.56–3.39)	<.001
MCS use	39.0%	25.8%	1.84 (1.73–1.94)	<.001	3.0%	0.3%	11.18 (7.78- 16.07)	<.001
AKI requiring hemodialysis	9.8%	6.1%	1.66 (1.51–1.84)	<.001	1.0%	3.6%	3.62 (2.95–4.45)	<.001
Acute kidney injury	56.4%	48.6%	1.37 (1.30–1.44)	<.001	32.0%	18.1%	2.13 (2.00–2.26)	<.001
Transfusion	27.9%	22.8%	1.31 (1.23–1.39)	<.001	13.3%	5.6%	2.57 (2.34–2.83)	<.001
Intubation	56.9%	50.8%	1.28 (1.21–1.35)	<.001	10.0%	2.1%	5.14 (4.47–5.91)	<.001
Vascular complications	19.6%	17.6%	1.14 (1.07–1.22)	<.001	5.9%	1.6%	3.84 (3.26–4.52)	<.001
Acute respiratory failure	45.9%	43.4%	1.11 (1.05–1.17)	<.001	13.4%	6.9%	2.07 (1.90–2.27)	<.001
Major Bleeding	7.8%	7.7%	1.03 (0.93–1.13)	.616	3.5%	2.2%	1.60 (1.37–1.87)	<.001
LOS ≥5 d	81.0%	67.7%	2.04 (1.92–2.17)	<.001	75.6%	43.0%	4.10 (3.88–4.34)	<.001
PCI	19.0%	22.4%	0.81 (0.76–0.87)	<.001	2.8%	1.5%	1.92 (1.60–2.31)	<.001
Cardiac arrest	15.1%	18.9%	0.76 (0.71–0.81)	<.001	1.5%	0.6%	2.67 (2.01–3.56)	<.001
Median LOS, d (IQR)	12 (6- 20)	8 (3–15)	–	<.001	8 (5–14)	4 (2–7)	-	<.001
Median hospital costs	$50,911	$31,734	–	<.001	$20,168	$7,869	-	<.001
CABG	15.0%	13.2%	1.16 (1.08–1.25)	<.001	3.5%	0.4%	9.41 (6.91–12.81)	<.001
LVAD placement	4.5%	1.4%	3.27 (2.73–3.91)	<.001	2.2%	0.3%	7.19 (5.09–10.16)	<.001
Heart transplantation	2.0%	0.8%	2.45 (1.91–3.14)	<.001	2.1%	0.3%	8.54 (5.80–12.56)	<.001
Nursing home discharge	10.8%	9.5%	1.17 (1.03–1.33)	.013	15.0%	12.6%	1.90 (1.64–2.20)	<.001

AKI, acute kidney injury; CABG, coronary artery bypass graft; IQR, interquartile range; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention; LVAD, left ventricular assist device; LOS, length of stay.

ESC European Society of Cardiology

European Journal of Heart Failure (2020) **22**, 1315–1341
doi:10.1002/ejhf.1922

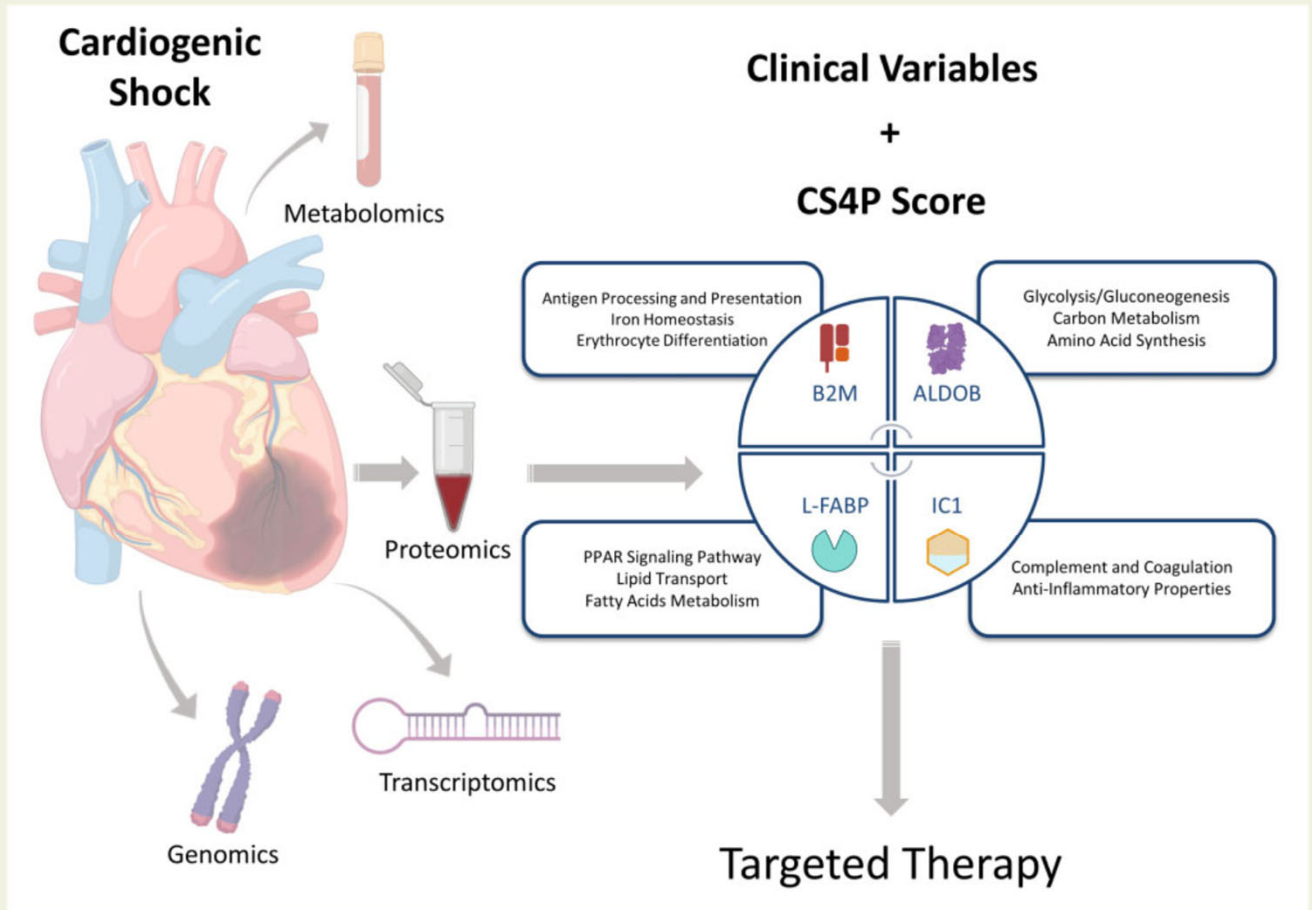
POSITION PAPER

Epidemiology, pathophysiology and contemporary management of cardiogenic shock – a position statement from the Heart Failure Association of the European Society of Cardiology

Ovidiu Chioncel[1,2*], John Parissis[3,4], Alexandre Mebazaa[5], Holger Thiele[6,7], Steffen Desch[6,7], Johann Bauersachs[8], Veli-Pekka Harjola[9], Elena-Laura Antohi[1,2], Mattia Arrigo[10], Tuvia B. Gal[11,12], Jelena Celutkiene[13], Sean P. Collins[14], Daniel DeBacker[15], Vlad A. Iliescu[1,2], Ewa Jankowska[16], Tiny Jaarsma[17,18], Kalliopi Keramida[4,19], Mitja Lainscak[20,21], Lars H Lund[22,23], Alexander R. Lyon[24,25], Josep Masip[26,27], Marco Metra[28], Oscar Miro[29,30], Andrea Mortara[31], Christian Mueller[32], Wilfried Mullens[33,34], Maria Nikolaou[3], Massimo Piepoli[35], Susana Price[36], Giuseppe Rosano[37], Antoine Vieillard-Baron[38,39], Jean M. Weinstein[40], Stefan D. Anker[41,42], Gerasimos Filippatos[43,44], Frank Ruschitzka[10], Andrew JS. Coats[45], and Petar Seferovic[46,47]

"Based on expert opinion, PAC is currently recommended in selected patients who failed to respond to initial therapeutic interventions (persistence of hypotension and hypoperfusion)…"

Molecular signature of cardiogenic shock



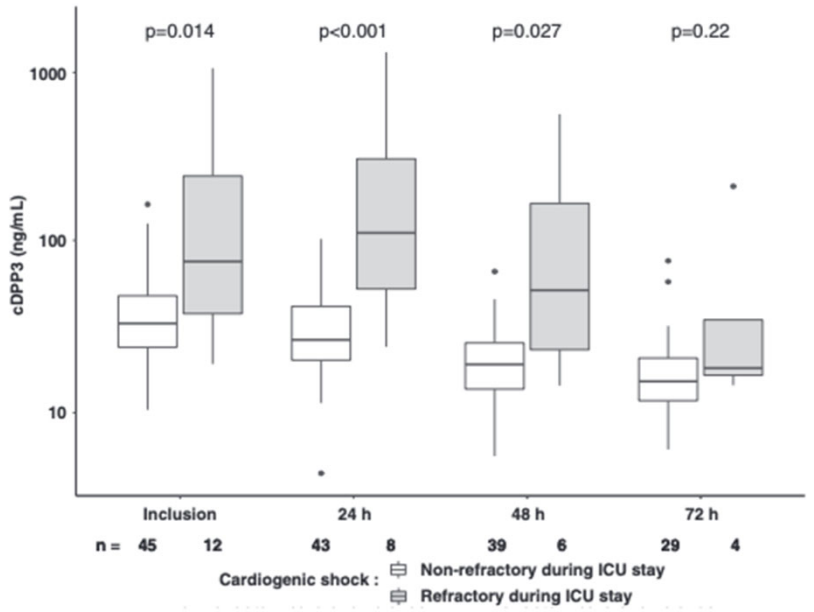
Take home figure In this review, we have studied the current landscape of biomarker utilization in cardiogenic shock. We have investigated the -omics research fields to assess the current use and future possibilities of each discipline in cardiogenic shock and summarized the latest advances in targeted diagnosis/prognosis. Here, we have deepened in the knowledge of four new biomarkers (the CS4P) recently described to strongly predict cardiogenic shock mortality at 90 days. ALDOB, fructose-bisphosphate aldolase B; B2M, beta-2-microglobulin; CS, cardiogenic shock; IC1, plasma protease C1 inhibitor; L-FABP, liver fatty acid-binding protein.

Iborra-Egea O et al. Eur heart J 2020;41:3839-48

ESC European Society of Cardiology
European Journal of Heart Failure (2020) **22**, 279–286
doi:10.1002/ejhf.1600

RESEARCH ARTICLE

Circulating dipeptidyl peptidase 3 and alteration in haemodynamics in cardiogenic shock: results from the OptimaCC trial



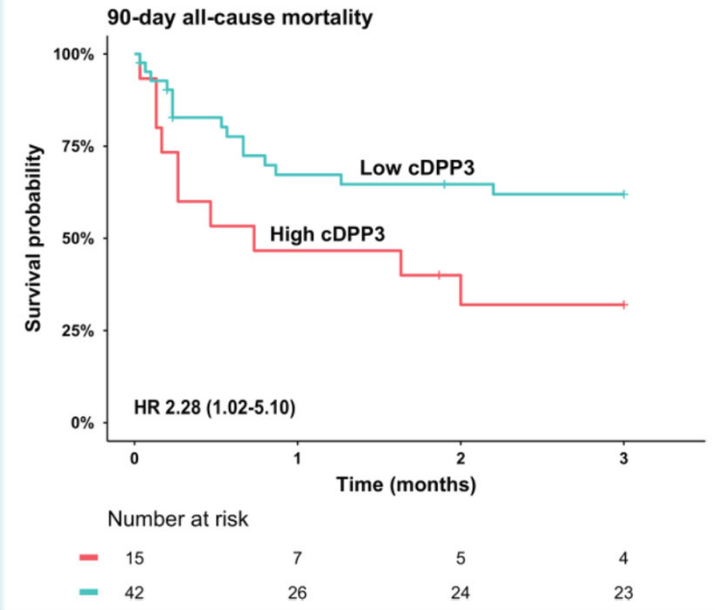
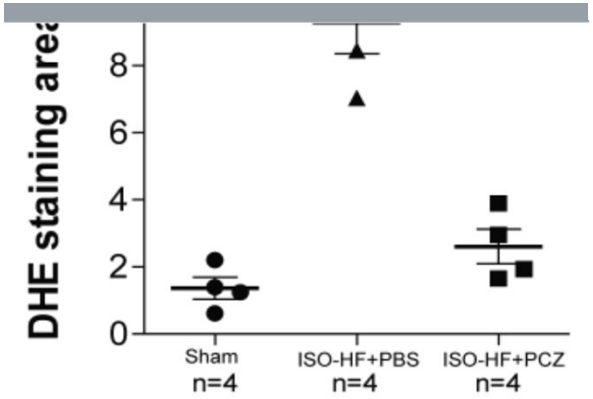
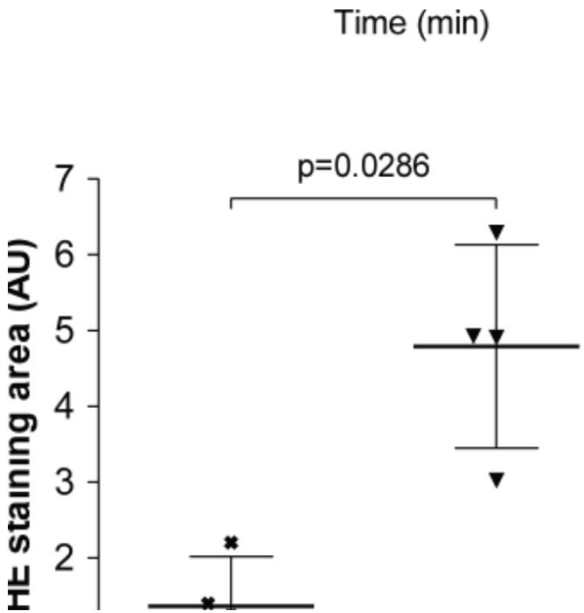
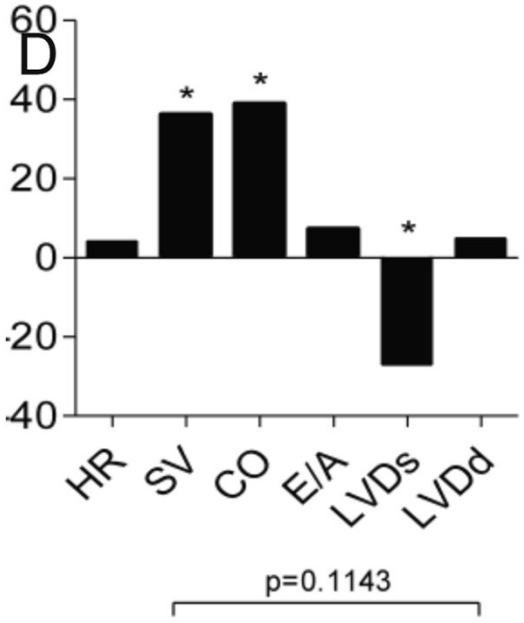


Figure 2 Kaplan–Meier analysis of 90-day all-cause mortality in cardiogenic shock patients with, at inclusion, high (circulating dipeptidyl peptidase 3 [cDPP3] ≥59.1 ng/mL, third quartile) vs. low cDPP3 values (cDPP3 <59.1 ng/mL). HR, hazard ratio.

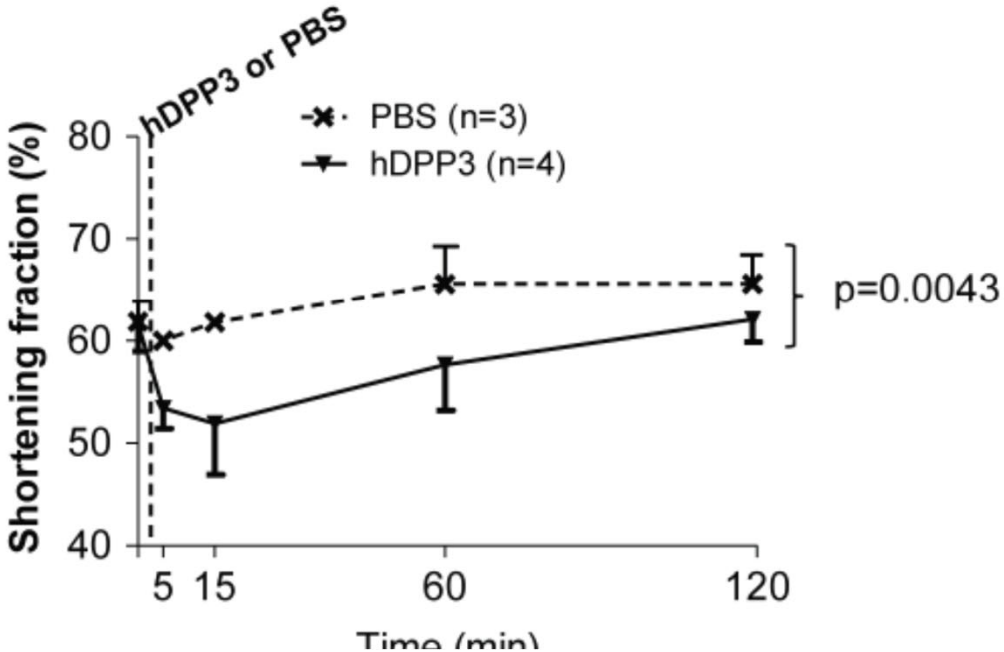
Takagi K et al. Eur heart J 2020; 22: 279-86

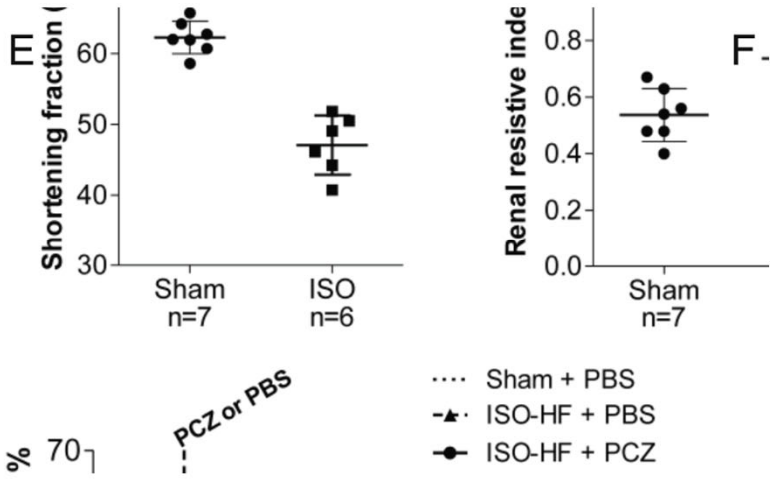






Deniau B et al. Eur heart J 2019; 22:290-9





Deniau B et al. Eur heart J 2019; 22:290-9

Refractory cardiogenic shock

Cardiogenic shock

- SAP < 90 mmHg
- CI < 2-2.2 $L.min^{-1}.m^{-2}$
- PCWP > 25 mmHg (congestion...)
- EF < 25 %
- End-organ hypoperfusion (cold extremities, oliguria…)

In despite of optimal therapy

- Infusion of inotropes and vaso active drugs: epinephrine >0.5 $\mu g.kg^{-1}min^{-1}$ and/or dobutamine > 10 $\mu g.kg^{-1}min^{-1}$

- At least two high dose drugs with IABP

Pagani FD et al. Ann Thorac Surg. mars 2001;71(3 Suppl):S77-81

Combes A, et al. Crit Care Med. 2008;36:1404-11

Bréchot N et al. Crit Care Med. 2013;41:1616-26

CONCLUSION

- Pathophysiology of CS is complex and incompletely known (cardiovascular and inflammatory disease)
- High in-hospital mortality rate 30-40%
- Early myocardial revascularization improve outcomes but does not seem sufficient
- Steroids may have therapeutic place (???)
- Haemodynamic management of CS requires end-organ perfusion supply (organ hypoperfusion) as well as cardiac assist (LV and RV congestion)
- Use of inotropic agents did not demonstrate any outcome improvement but remain useful therapy for restoring haemodynamic
- Further randomized trials still required to define the optimal therapeutic approach

Many thanks…