

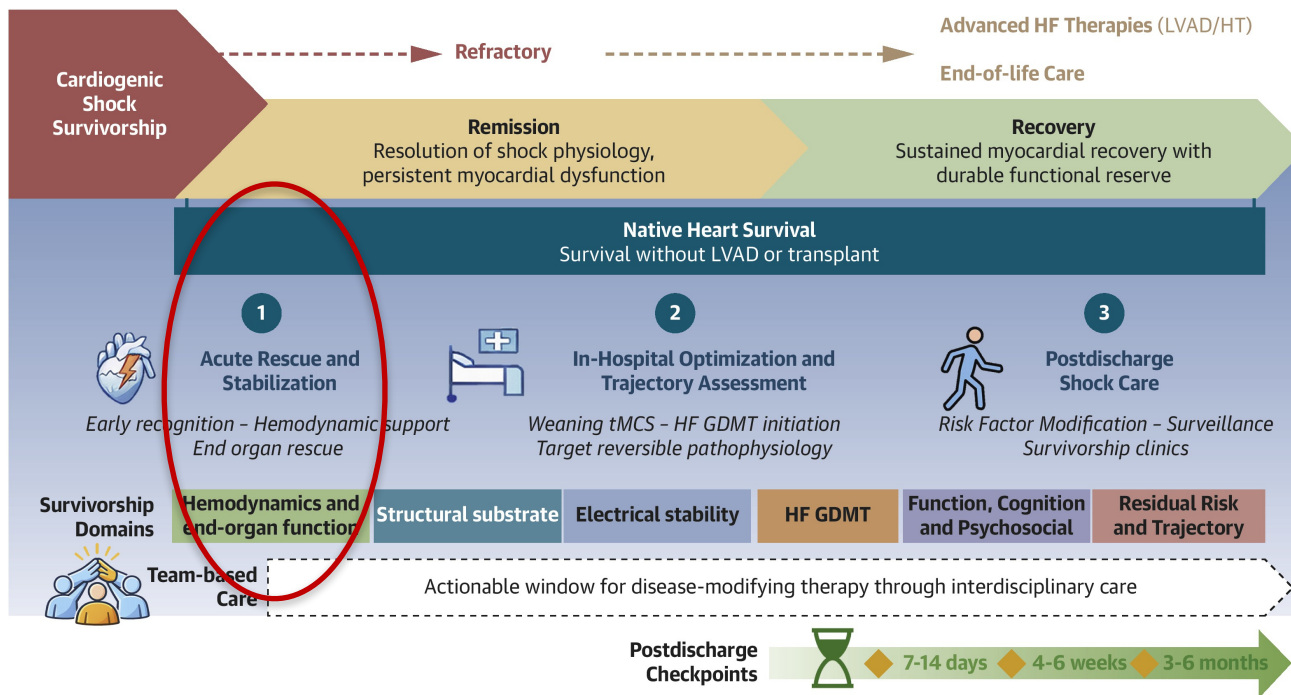
INSUFFICIENZA CARDIACA ACUTA E AVANZATA

L'utilizzo di inotropi e sostanze vasoattive nello scompenso cardiaco avanzato

Roberta Della Bona, MD, PhD
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Genova



CENTRAL ILLUSTRATION: Cardiogenic Shock Survivorship Continuum



Blumer V, et al. JACC. 2026;10.1016/j.jacc.2026.02.5080



CONTEMPORARY REVIEW

State of Shock: Contemporary Vasopressor and Inotrope Use in Cardiogenic Shock

Jason E. Bloom  BSc, MBBS; William Chan  MBBS, PhD; David M. Kaye  MBBS, PhD*; Dion Stub  MBBS, PhD*



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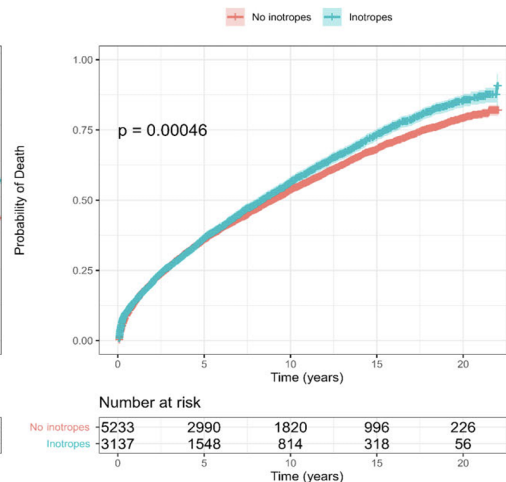
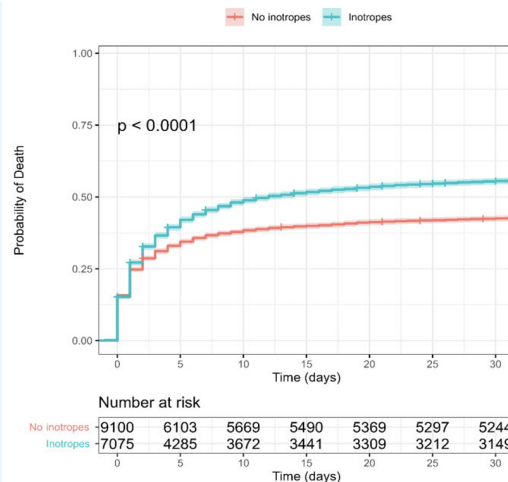
Vasoactive medication and RCTs: an impossible marriage

A review and introduction of the concept "enough"

We provide a brief overview of important physiology and the pharmacology of vasoactive drugs that are currently used in the ICU as well as newer agents, along with a concise review of recent publications comparing these agents. We attempt to answer the question what drug dose should be administered as well as what haemodynamic values to pursue, and how much fluids must be infused by introducing the concept of "enough".

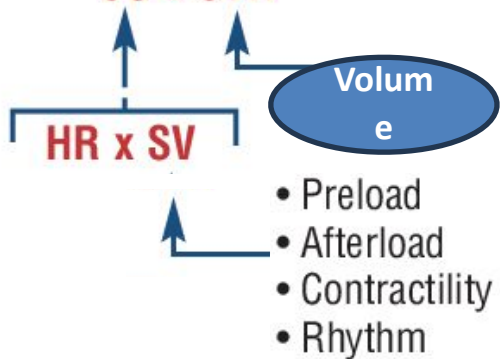
In the intensive care unit (ICU) setting,
≈25% of admitted patients
receive
at least 1 vasoactive medication

increasing to **>90%** in patients with **CS**



Why Do We Need Inotropes and Vasoactive Agents?

$$\text{MAP} = \text{CO} \times \text{SVR}$$

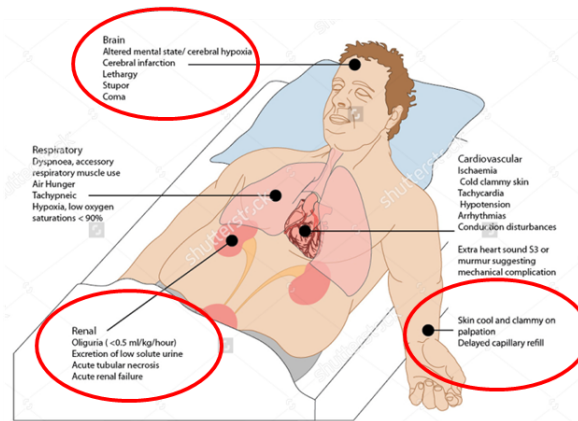


Ventricular arterial coupling

Inotropes / Vasopressors and more



Microcirculation alteration during cardiogenic shock



**Tissue perfusion
(end organ rescue)**

Inotropes and Vasoactive Agents: when?

SCAI Shock Classification

Stage A - At risk

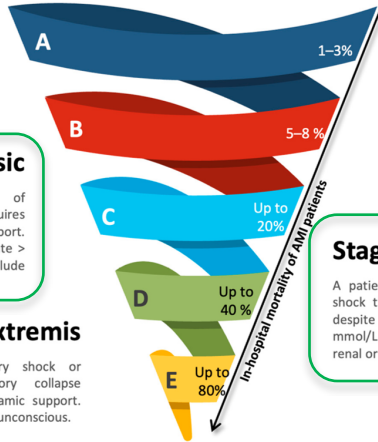
A hemodynamically stable patient who is not experiencing signs or symptoms of CS, but is at risk for its development

Stage C - Classic

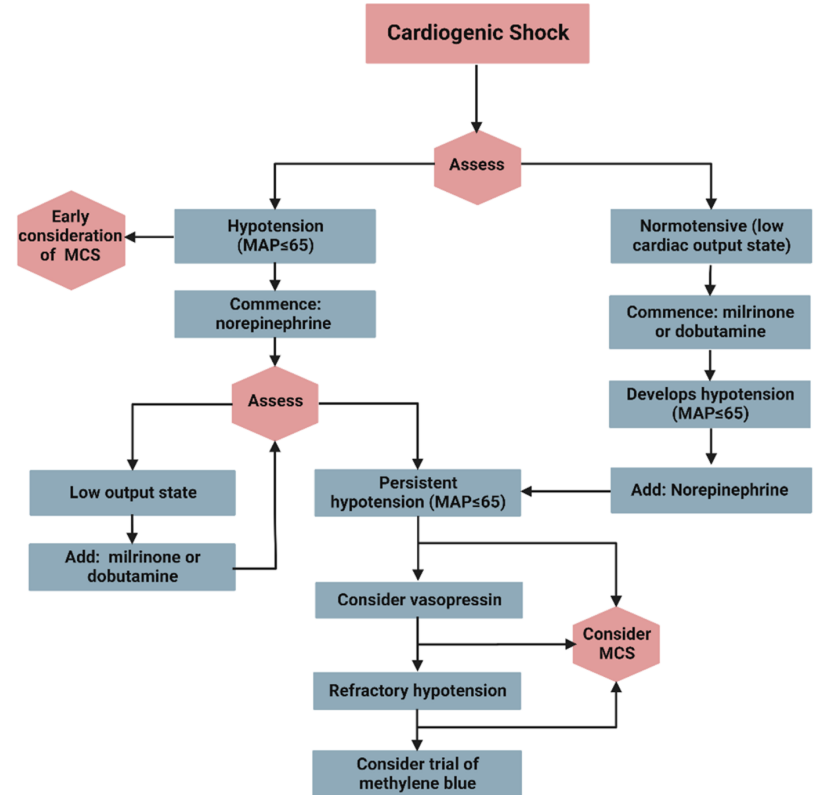
A patient who has clinical of hypoperfusion that initially requires pharmacological or mechanical support. Hypotension is usually present. Lactate > 2 mmol/L. CI < 2.2 L/min/m². May include impairment of renal or liver function.

Stage E - Extremis

A patient with refractory shock or actual/impending circulatory collapse despite maximal hemodynamic support. Lactate > 8 mmol/L. Typical unconscious.



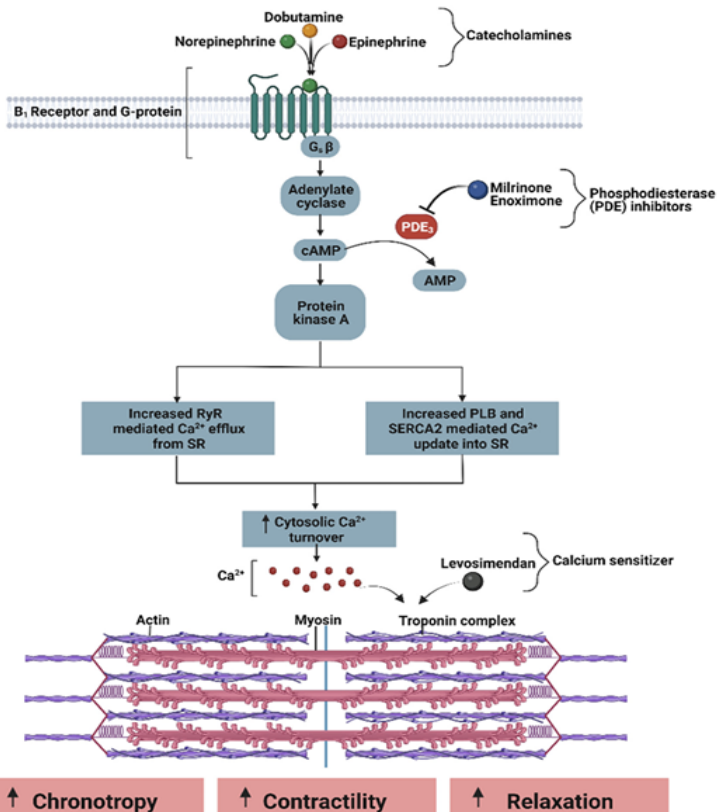
Proposed Vasoactive Treatment Strategy



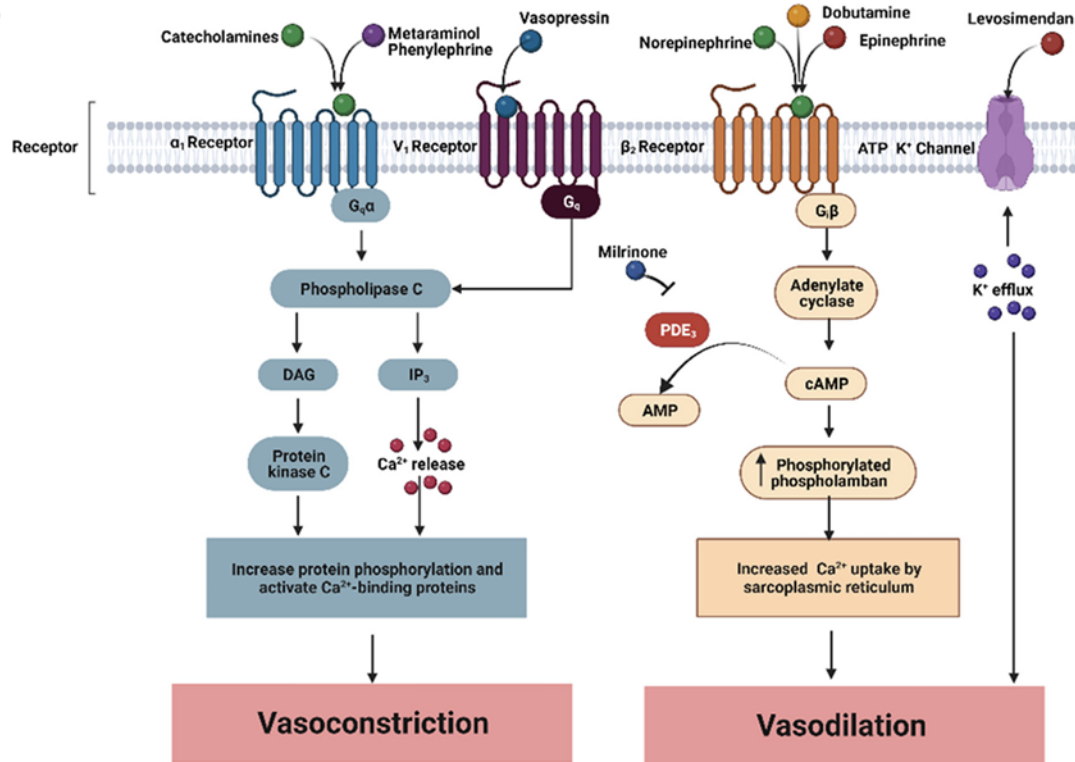
Indication to commence therapy	Hypotension (systolic blood pressure <90 mm Hg) and/or evidence of end-organ hypoperfusion				
Societal guideline	ESC HF	ACC/AHA HF	ESC STEMI	AHA CS	AHA AMI-CS
Recommendation and level of evidence	IIb - B/C	IIa - B	IIb - C	N/A	N/A
First-line agent	Hypotensive: Norepinephrine Low output: No recommendation	Hypotensive: Clinician preference Low output: Clinician preference	Hypotensive: Norepinephrine Low output: Dobutamine	Hypotensive: Norepinephrine or Dopamine Low output: Norepinephrine or Dopamine	Hypotension: Norepinephrine



Cardiac Tissue



Vascular Smooth Muscle



VASOCONSTRICTION

Which Inotropes and Vasoactive Agents?

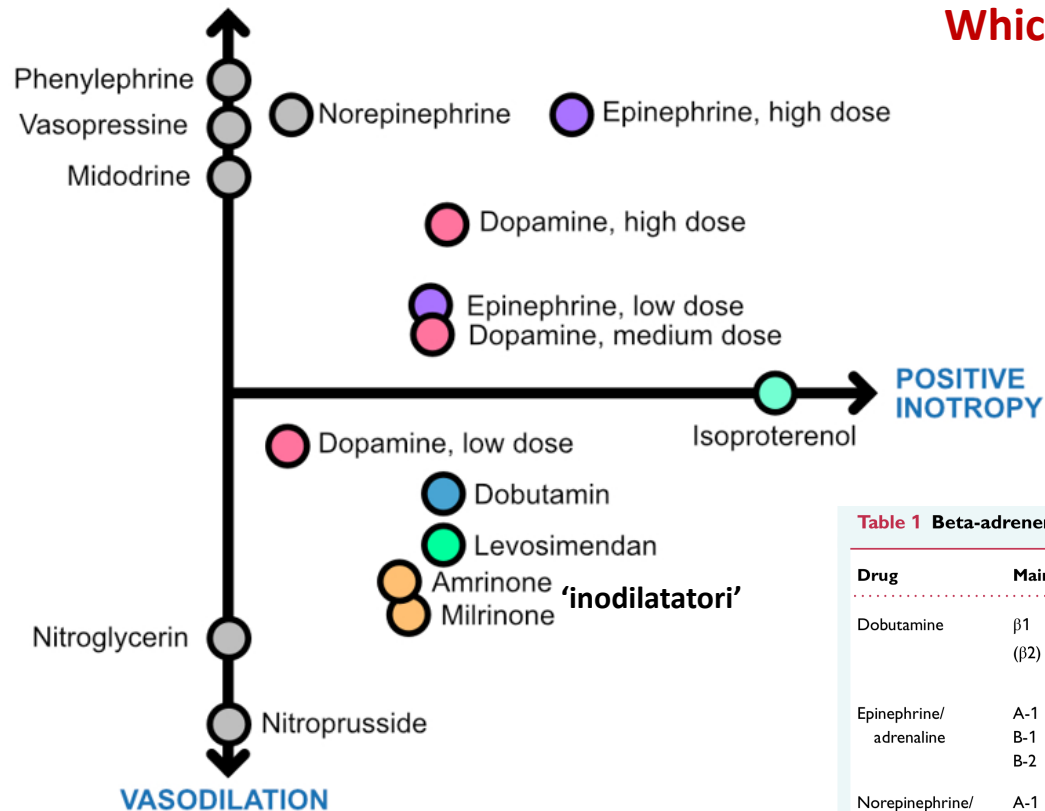
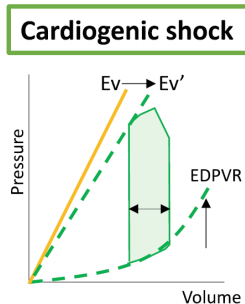
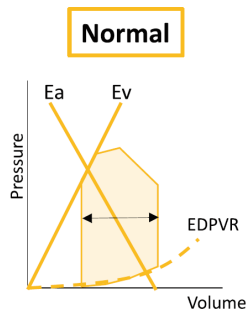


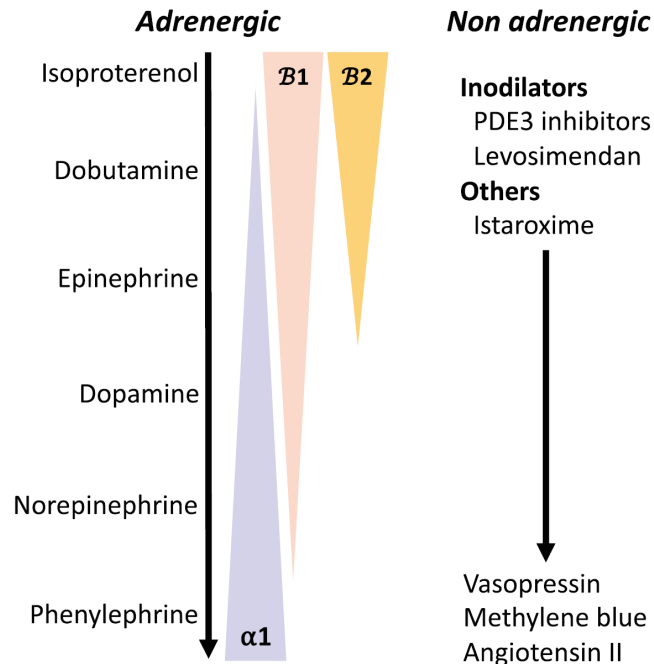
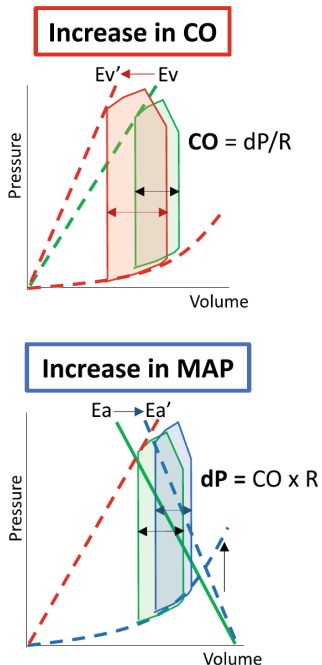
Table 1 Beta-adrenergic drugs: pharmacology and clinical effects

Drug	Main mode of action	Main clinical effect	Bolus	Infusion rate	Elimination $t_{1/2}$
Dobutamine	β_1 (β_2)	Inotropy Chronotropy Vasodilatation	–	2–20 $\mu\text{g/kg/min}$	± 2 min
Epinephrine/ adrenaline	A-1 B-1 B-2	Inotropy Chronotropy Vasoconstriction	+	0.05–0.5 $\mu\text{g/kg/min}$	± 2.5 min
Norepinephrine/ noradrenaline	A-1 (B-1)	Vasoconstriction	–	0.2–1.0 $\mu\text{g/kg/min}$	± 1 –2 min
Dopamine	Low dose: Dopamine receptors High dose: B-1 and A-1	Low dose: selective vasodilatation High dose: vasoconstriction and inotropy	–	Low dose: <3 $\mu\text{g/kg/min}$ High dose: >5 $\mu\text{g/kg/min}$	± 2 min

Pathophysiology



Inotropes



Vasopressors



Contents lists available at ScienceDirect
International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard



Sodium nitroprusside in acute heart failure: A multicenter historic cohort study

Laura Garatti^a, Simone Frea^b, Pier Paolo Bocchino^b, Filippo Angelini^b, Marco Cingolani^b, Alice Sacco^a, Giulia Maria Rondinara^a, Vincenzo Bagnardi^c, Isabella Maria Sala^c, Navin K. Kapur^d, Paolo C. Colombo^e, Gaetano Maria De Ferrari^b, Nuccia Morici^{f,*}

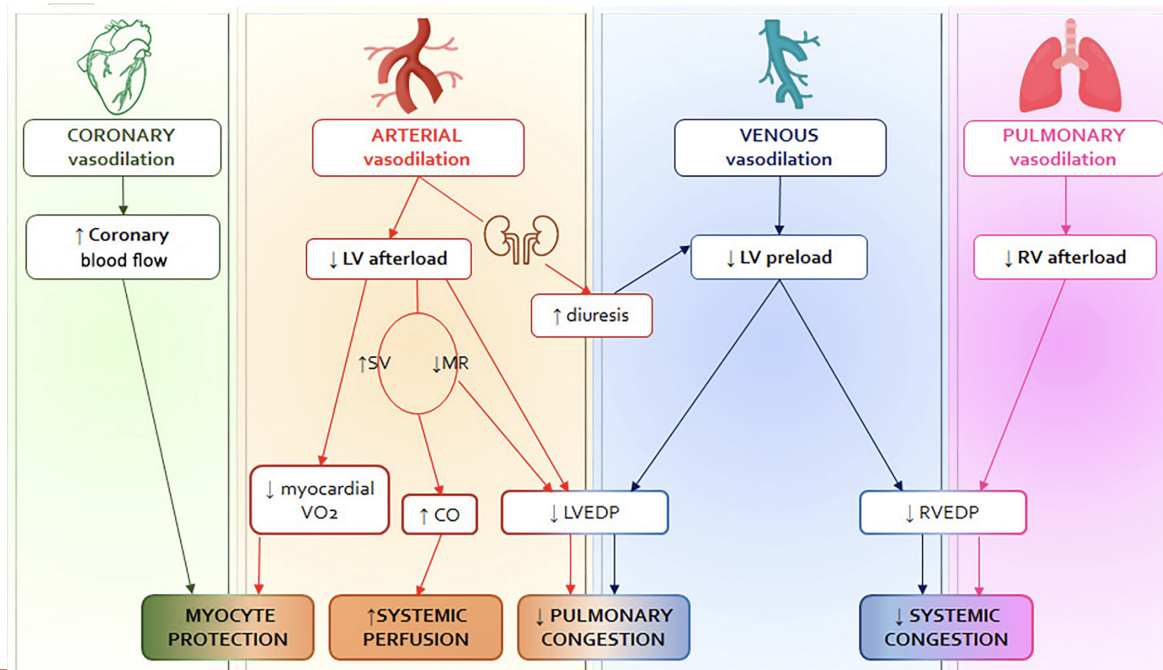
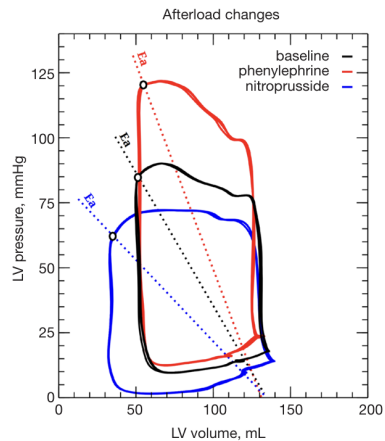




Table 2 Randomized controlled trials on the use of inotropes/vasopressors in cardiogenic shock

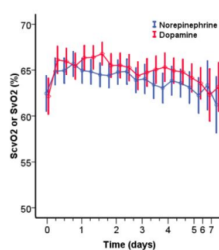
Trial, year	Drugs	No. of patients	Main inclusion criteria	Primary endpoint	Results	Safety
SOAP-II, 2010 ¹⁴	Dopamine vs. norepinephrine	1679 (dopamine $n=858$; norepinephrine $n=821$); among these patients, 280 had CS (135 in the dopamine group and 145 in the norepinephrine group)	Shock (defined as MAP <70 mmHg or SBP <100 mmHg with signs of hypoperfusion) with need for vasopressor agent	Death at 28 days	Increased rate of death among the 280 patients with CS treated with dopamine ($p=0.03$)	More arrhythmic events in the dopamine group (24.1%) vs. norepinephrine group (12.4%) ($p<0.001$)
CAT, 2008 ¹⁵	Epinephrine vs. norepinephrine	280 ($n=140$ in each treatment arm); among these, 128 had CS (64 in each treatment arm)	Need for infusion of epinephrine or norepinephrine for any cause	Time taken to achieve a MAP ≥ 70 mmHg for >24 h without vasopressors	No difference in the time to achieve MAP both in the whole population and in CS setting (RR 0.89, 95% CI 0.62–1.27, $p=0.49$)	Development of significant tachycardia and lactic acidosis with epinephrine, in addition to increased insulin requirements
OptimaCC, 2018 ¹⁶	Epinephrine vs. norepinephrine	57 (epinephrine $n=27$; norepinephrine $n=30$)	AMI-CS successfully revascularized, SBP <90 mmHg or MAP <65 mmHg, cardiac index <2.2 L/min/m ² , PCWP >15 mmHg, LVEF <40% and evidence of tissue hypoperfusion	Change in cardiac index (primary efficacy endpoint); occurrence of refractory CS (primary safety endpoint)	Cardiac index evolution was similar between groups ($p=0.43$). Higher incidence of refractory shock in the epinephrine group (37% vs. 7%, $p=0.008$)	HR increased significantly with epinephrine ($p<0.0001$); increase in cardiac double product ($p=0.0002$) and lactic acidosis ($p<0.0001$) with epinephrine
Levy et al., 2011 ¹⁷	Norepinephrine-dobutamine vs. epinephrine	30 ($n=15$ in each treatment arm)	Non-AMI-CS (defined as LVEF <30% and cardiac index <2.2 L/min/m ² , absence of hypovolaemia, lactate >2 mmol/L, MAP <60 mmHg or SBP <90 mmHg, urine output <0.5 mL/kg/h, signs of hypoperfusion, no signs of acute cardiac ischaemia)	Haemodynamic effects using the drugs to obtain a MAP of 65–70 mmHg	Both regimes increased cardiac index and oxygen-derived parameters in a similar manner	HR, lactate levels and PCO ₂ gap, a surrogate for splanchnic perfusion adequacy, increased in the epinephrine group ($p<0.05$, $p<0.01$ and $p<0.01$, respectively)
DOREMI, 2021 ¹⁸	Dobutamine vs. milrinone	192 ($n=96$ in each treatment arm)	CS SCAI B-D	Composite of in-hospital death from any cause, resuscitated cardiac arrest, cardiac transplant or MCS, non-fatal MI, TIA/stroke or RRT	Primary endpoint was 49% in the milrinone group vs. 54% in the dobutamine group (RR 0.90, 95% CI 0.69–1.19, $p=0.47$)	No significant differences in HR, MAP, serum lactate level, serum creatinine level, or hourly urine output between the treatment groups
Fuhrmann et al., 2008 ¹⁹	Enoximone vs. levosimendan	32 ($n=16$ in each group)	Refractory CS patients requiring additional therapy	Survival at 30 days	Survival rate at 30 days was higher in the levosimendan group (69% vs. 37%, $p=0.023$)	N/A
LIDO, 2002 ²⁰	Dobutamine vs. levosimendan	203 (levosimendan $n=103$; dobutamine $n=100$)	Low-output HF (including ADHF)	Proportion of patients with haemodynamic improvement at the end of the 24-h infusion period	Primary endpoint met in 28% of patients in the levosimendan group vs. 15% in the dobutamine group (hazard ratio 1.9, 95% CI 1.1–3.3, $p=0.022$)	Angina pectoris, chest pain, or myocardial ischaemia more frequent in the dobutamine group, in addition to a higher proportion of patients with rate and rhythm disorders; trend towards a higher frequency of headache or migraine in the levosimendan group
SURVIVE, 2007 ²¹	Dobutamine vs. levosimendan	1327 (levosimendan $n=664$; dobutamine $n=663$)	ADHF $\pm$ low cardiac output	All-cause mortality at 180 days	No significant difference in 180-day death (26% in the levosimendan group vs. 28% in the dobutamine group; hazard ratio 0.91, 95% CI 0.74–1.13, $p=0.40$)	Higher incidence of cardiac failure in the dobutamine group; higher incidence of AF, hypokalaemia and headache in the levosimendan group
Samimi-Fard et al., 2008 ²¹	Dobutamine vs. levosimendan	22 ($n=11$ in each group)	AMI-CS	Cardiac death at 12 months	No significant difference in 1-year cardiac death ($p=0.24$)	N/A
LEAF, 2013 ²²	Levosimendan vs. placebo	61 (levosimendan $n=30$; placebo $n=31$); among these, 9 had CS (levosimendan $n=4$; placebo $n=5$)	STEMI with signs of decreased wall motion in at least 3 of 16 segments of the LV with clinical HF	Wall motion score index at 5 days	Larger improvement from baseline to day 5 in the levosimendan group (from 1.94 ± 0.20 to 1.66 ± 0.31 vs. 1.99 ± 0.22 to 1.83 ± 0.26 , $p=0.031$)	Significantly more episodes of hypotension during study drug infusion in the levosimendan group (67% vs. 36%, $p=0.029$); in CS subgroup, NSVT was observed in 3 patients in the placebo group and in 1 in the levosimendan group

Comparison of Dopamine and Norepinephrine in the Treatment of Shock

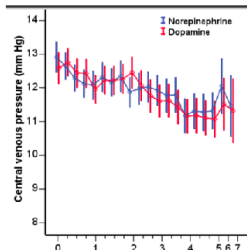
SOAP II Trial

De Backer D, Biston P, Devriendt J, et al. Comparison of dopamine and norepinephrine in the treatment of shock. N Engl J Med 2010;362:779-89.

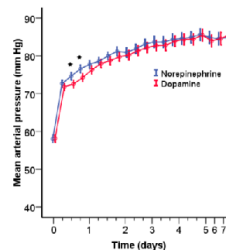
- Multicenter RCT, 1679 patients
- Blinded solutions of Dopamine vs Norepi
- Open label norepi to achieve desired BP as second agent followed by vasopressin as 3rd
- Predominantly septic shock



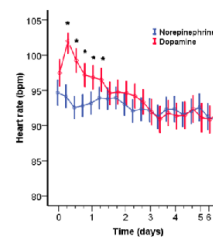
SvO2



CVP



MAP



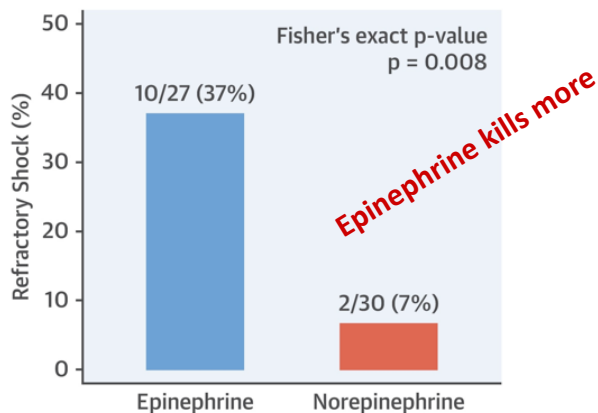
HR

More arrhythmias w/
dopamine



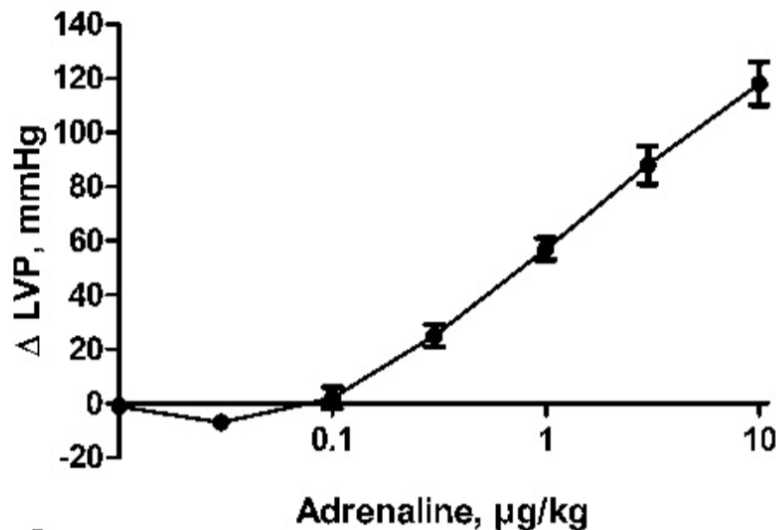
Epinephrine Versus Norepinephrine for Cardiogenic Shock After Acute Myocardial Infarction

57 patients
Randomized 1:1



Dosage? MAP target strategy

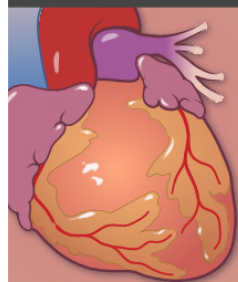
**Epinephrine up to 3 gamma
to obtain a MAP of 70 mmHg**



The NEW ENGLAND JOURNAL of MEDICINE

Milrinone vs. Dobutamine in Cardiogenic Shock

DOUBLE-BLIND, RANDOMIZED TRIAL



192

Patients admitted to the cardiac ICU with cardiogenic shock

Milrinone

N=96



Dobutamine

N=96



In-hospital death from any cause, TIA, stroke, or cardiovascular or renal events

49%

47 patients

54%

52 patients

Relative risk, 0.90; 95% CI, 0.69–1.19; P=0.47

No between-group difference was observed in the primary composite outcome or in important secondary outcomes.

DOREMI Trial

CS SCAI B-D

Only 8 patients with right dysfunction



Levosimendan vs. dobutamine: outcomes for acute heart failure patients on β -blockers in SURVIVE[†]

Alexandre Mebazaa^{1*}, Markku S. Nieminen², Gerasimos S. Filippatos³, John G. Cleland⁴, Jeffrey E. Salton⁵, Roopal Thakkar⁵, Robert J. Padley⁵, Bidan Huang⁵, and Alain Cohen-Solal⁶

[†]Department of Anaesthesiology and Critical Care Medicine, Hôpital Lariboisière, APHP; Université Paris 7 Paris Diderot; U 942 INSERM, 2 rue Ambroise-Paré, Paris Cedex 10 75475, France; ²Division of Cardiology, Helsinki University Central Hospital, Helsinki, Finland; ³Department of Cardiology, Athens University Hospital, Athens, Greece; ⁴Department of Cardiology, University of Hull, Kingston-Upon-Hull, UK; ⁵Abbott Laboratories, Abbott Park, IL, USA; and ⁶Department of Cardiology, Hôpital Lariboisière, APHP; Université Paris 7 Paris Diderot; U 942 INSERM, Paris, France

Received 2 June 2008; revised 9 October 2008; accepted 15 December 2008; online publish-ahead-of-print 21 January 2009

Aims Many chronic heart failure (CHF) patients take β -blockers. When such patients are hospitalized for decompensation, it remains unclear how ongoing β -blocker treatment will affect outcomes of acute inotrope therapy. We aimed to assess outcomes of SURVIVE patients who were on β -blocker therapy before receiving a single intravenous infusion of levosimendan or dobutamine.

Methods and results Cox proportional hazard regression revealed all-cause mortality benefits of levosimendan treatment over dobutamine when the SURVIVE population was stratified according to baseline presence/absence of CHF history and use/non-use of β -blocker treatment at baseline. All-cause mortality was lower in the CHF/levosimendan group than in the CHF/dobutamine group, showing treatment differences by hazard ratio (HR) at days 5 (3.4 vs. 5.8%; HR, 0.58, CI 0.33–1.01, $P = 0.05$) and 14 (7.0 vs. 10.3%; HR, 0.67, CI 0.45–0.99, $P = 0.045$). For patients who used β -blockers ($n = 669$), mortality was significantly lower for levosimendan than dobutamine at day 5 (1.5 vs. 5.1% deaths; HR, 0.29; CI 0.11–0.78, $P = 0.01$).

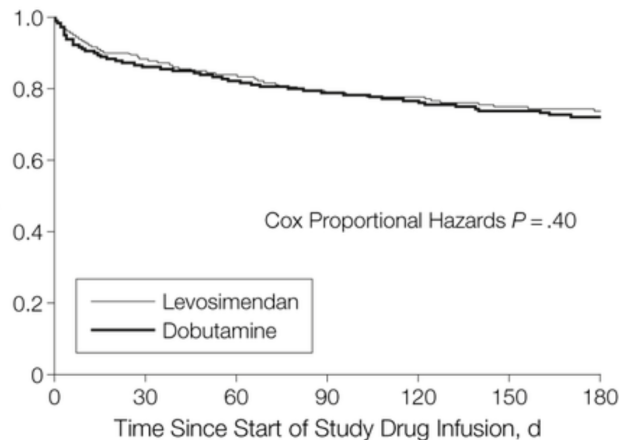
Conclusion Levosimendan may be better than dobutamine for treating patients with a history of CHF or those on β -blocker therapy when they are hospitalized with acute decompensations. These findings are preliminary but important for planning future studies.

Keywords Levosimendan • Dobutamine • Heart failure, congestive • Cardiac output, low • β -blockers, adrenergic

ents With Acute

r, MD; et al

† Levosimendan Treatment on All-Cause Mortality During 180 Days Following



664	608	586	525	462
663	596	568	519	454

Inotropic agents and vasodilator strategies for the treatment of cardiogenic shock or low cardiac output syndrome (Review)



Cochrane
Library

Cochrane Database of Systematic Reviews

Authors' conclusions

(Beta-blocker therapy)

Apart from low quality of evidence data suggesting a short-term mortality benefit of levosimendan compared with dobutamine, at present there are no robust and convincing data to support a distinct inotropic or vasodilator drug-based therapy as a superior solution to reduce mortality in haemodynamically unstable people with cardiogenic shock or LCOS.

Considering the limited evidence derived from the present data due to a generally high risk of bias and imprecision, it should be emphasised that there remains a great need for large, well-designed randomised trials on this topic to close the gap between daily practice in critical care medicine and the available evidence. It seems to be useful to apply the concept of 'early goal-directed therapy' in cardiogenic shock and LCOS with early haemodynamic stabilisation within predefined timelines. Future clinical trials should therefore investigate whether such a therapeutic concept would influence survival rates much more than looking for the 'best' drug for haemodynamic support.



Medical therapy of cardiogenic shock: Contemporary use of inotropes and vasopressors



CARDIOGENIC SHOCK

Inadequate cardiac output
PLUS
Clinical signs of hypoperfusion
AND/OR
Biochemical manifestations of
hypoperfusion



Few evidence-
based data

AMI-CS:
Lower SVR and trend towards higher CI
vs

ADHF-CS:
Higher SVR and lower CI

AMI-CS

First-line therapy:

- ☞ Norepinephrine (if hypotension prevails)
- ☞ Dobutamine OR Milrinone OR Levosimendan (if CS «normotensive»)

Second-line therapy:

- ☞ Norepinephrine + Dobutamine/Levosimendan

ADHF-CS

First-line therapy:

- ☞ Norepinephrine (if hypotension prevails)
- ☞ Dobutamine OR Milrinone OR Epinephrine + Sodium Nitroprusside OR Levosimendan (if CS «normotensive»)

Second-line therapy:

- ☞ Norepinephrine + Dobutamine/Levosimendan

RV-predominant CS

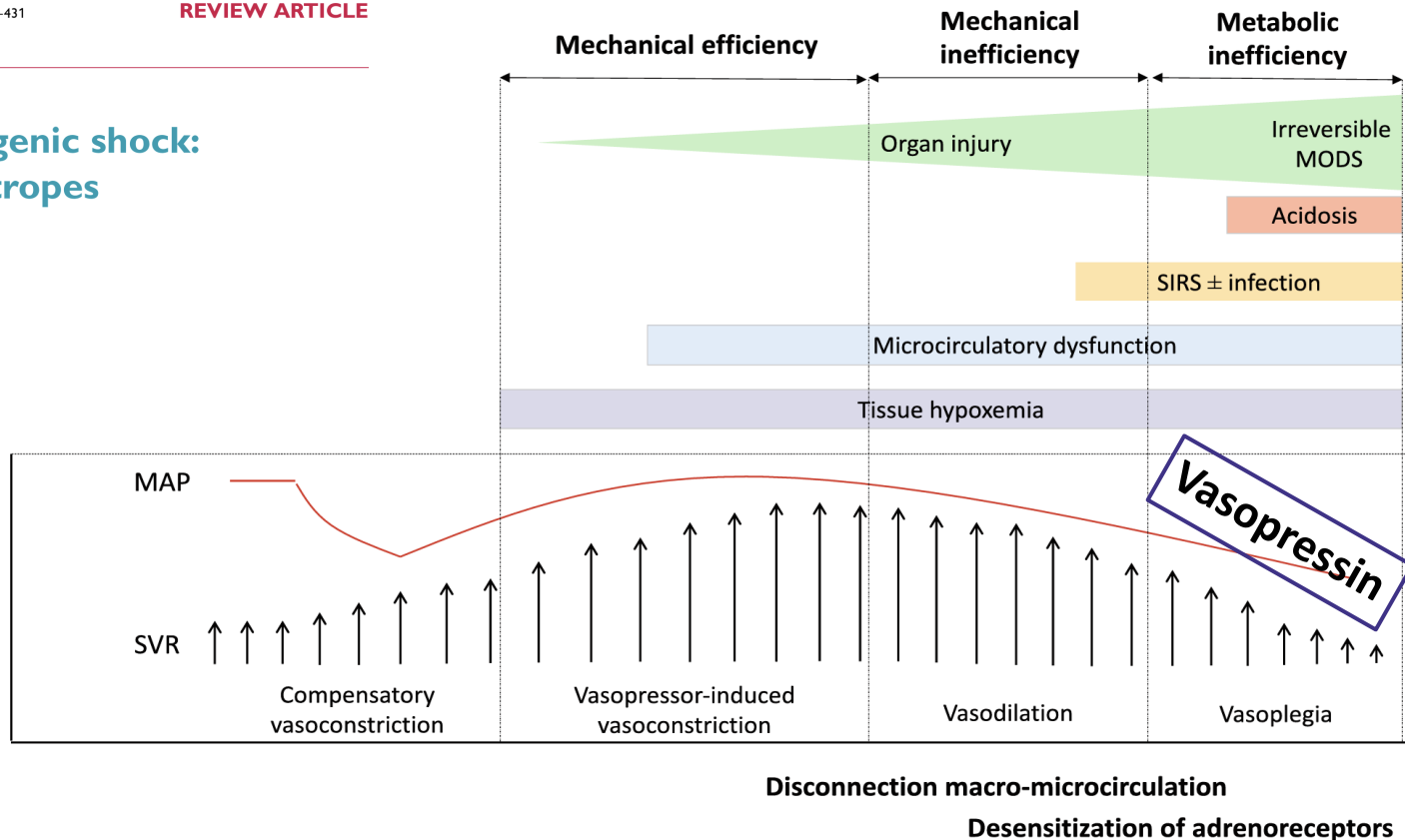
First-line therapy:

- ☞ Norepinephrine (if hypotension prevails)
- ☞ Milrinone OR Levosimendan (if CS «normotensive»)

Second-line therapy:

- ☞ Norepinephrine + Milrinone/Levosimendan/Dobutamine

Medical therapy of cardiogenic shock: Contemporary use of inotropes and vasopressors



CS pts who received vasopressors during the first 24 hours between 2007 and 2015

Maximum doses of each vasopressor were converted to norepinephrine equivalents (NEE).

High dose vasopressor (HDV) use was defined as peak 24-hour NEE ≥ 0.3 mcg/kg/min.

The primary outcome was in-hospital mortality.

VASOPRESSIN ADMINISTRATION IN PATIENTS WITH CARDIOGENIC SHOCK

Moderated Poster Contributions
Moderated Poster Theater 09
Monday, April 8, 2024, 10:00 a.m.-10:10 a.m.

Session Title: Critical Care Cardiology Perspectives on Shock: Our Hats Are in the Ring
Abstract Category: 61. Spotlight on Special Topics: Critical Care Cardiology
Presentation Number: 1105-11

Authors: Dhruv Sarma, Mitchell Padkins, Kianoush Kashani, Benjamin M. Hibbert, Jacob Colin Jentzer, Mayo Clinic, Rochester, MN, USA

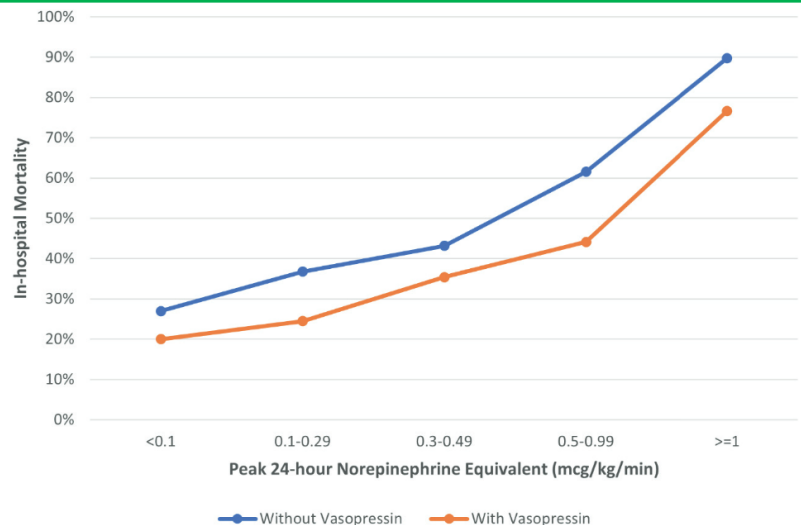
Background: A catecholamine-sparing vasopressor strategy has been proposed for septic shock but has not been examined in cardiogenic shock (CS). We investigated the association between vasopressin use and in-hospital mortality in patients with CS.

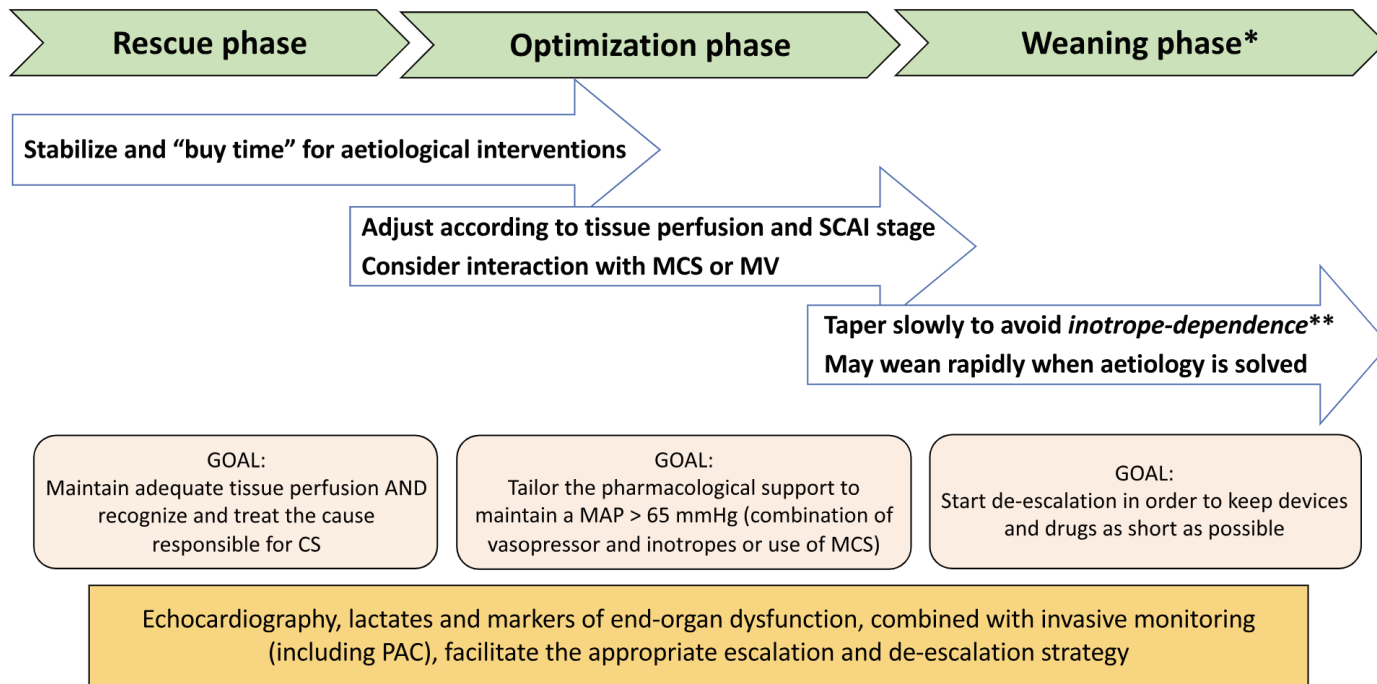
Methods: We included cardiac intensive care unit (CICU) patients with CS who received vasopressors during the first 24 hours between 2007 and 2015. Maximum doses of each vasopressor during the first 24 hours were converted to norepinephrine equivalents (NEE). High-dose vasopressor (HDV) use was defined as peak 24-hour NEE ≥ 0.3 mcg/kg/min. The primary outcome was in-hospital mortality.

Results: Of 721 patients (median age 69, 36% female, 61% with myocardial infarction), 207 (29%) received vasopressin in the first 24 hours. Patients receiving vasopressin had higher median lactate (3.1 vs 2.7, $p=0.02$) and peak NEE (0.32 vs 0.10, $p<0.001$). Rates of STEMI and mechanical circulatory support were similar. At any given NEE, vasopressin use was associated with lower mortality (Fig. 1). Among patients requiring HDV ($n=234$), vasopressin use was associated with significantly lower mortality (49.1% vs 63.9%, $p=0.02$). After multivariable adjustment, vasopressin was associated with lower in-hospital mortality (adjusted OR 0.59, 95% CI 0.37-0.94, $p=0.03$).

Conclusion: Vasopressin use was associated with lower in-hospital mortality in patients with CS, particularly those receiving HDV, justifying prospective evaluation as a catecholamine-sparing therapy.

Prospective evaluation as a catecholamine-sparing therapy



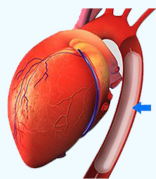


*Dopa, Dob: 1 µg/kg/min per hour; NE: 0.1 µg/kg/min per hour

**Worsening end-organ function, deteriorating hemodynamics, exacerbation of HF symptoms, or significant hypotension on attempted inotrope wean



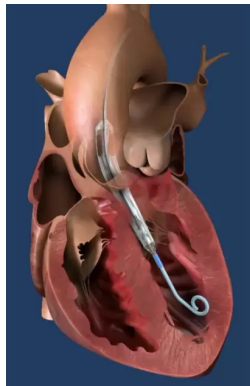
Concomitant mechanical circulatory support treatment



**Intra-Aortic
Balloon Pump
(IABP) Therapy**

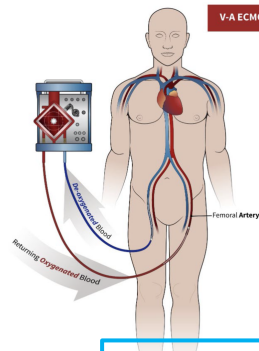
**Increases only modestly CO (0.5 L/min),
but significantly reduces LV afterload**

**Concomitant inotropic/vasopressor therapy
remains frequently needed**



**Relevant support in terms of CO
(peak flows up to 4.3 L/min with Imp CP,
Up to 6 L/min with Imp 5.5)**

**Concomitant inotropic/vasopressor therapy
not frequently needed
Persistent inotropic support is
frequently needed in case of *concomitant RV
dysfunction***



**Provide both circulatory and respiratory support,
generating a circulatory support up to 6 L/min.**

**Concomitant epinephrine use was independently
associated with **higher mortality**
Levosimendan for LV unloading (weak impact)**



JAMA[®]

QUESTION In patients with severe but potentially reversible cardiogenic shock who are receiving venoarterial extracorporeal membrane oxygenation (VA-ECMO), does early administration of levosimendan improve time to successful ECMO weaning?

CONCLUSION In patients with potentially reversible cardiogenic shock supported by VA-ECMO, levosimendan did not reduce the time to successful weaning from ECMO compared with placebo.

© AMA

POPULATION

149 Men
56 Women



Adult patients with acute cardiogenic shock who started VA-ECMO in the preceding 48 hours

Median age: 58 years

LOCATIONS

11
Intensive care
units in France



INTERVENTION



205 Patients randomized

101

Levosimendan

Infusion of levosimendan starting at 0.15 µg/kg per minute and increased to 0.20 µg/kg per minute after 2 hours



104

Placebo

Infusion of identical-appearing placebo

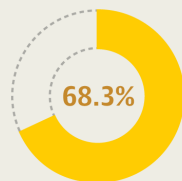
PRIMARY OUTCOME

Successful ECMO weaning within 30 days following randomization

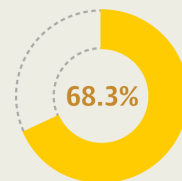
FINDINGS

Patients with ECMO weaning

Levosimendan
69 of 101 patients



Placebo
71 of 104 patients



Levosimendan did not improve ECMO weaning:

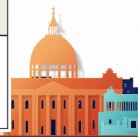
Risk difference, **0.0%**

(95% CI, -12.8% to 12.7%)

Subdistribution hazard ratio, **1.02**

(95% CI, 0.74-1.39); *P* = .92

Combes A, Saura O, Nessler N, et al; LEVOECMO Trial Group; International ECMO Network (ECMONet). Levosimendan to facilitate weaning from ECMO in patients with severe cardiogenic shock: the LEVOECMO randomized clinical trial. *JAMA*. Published online December 1, 2025. doi:10.1001/jama.2025.19843

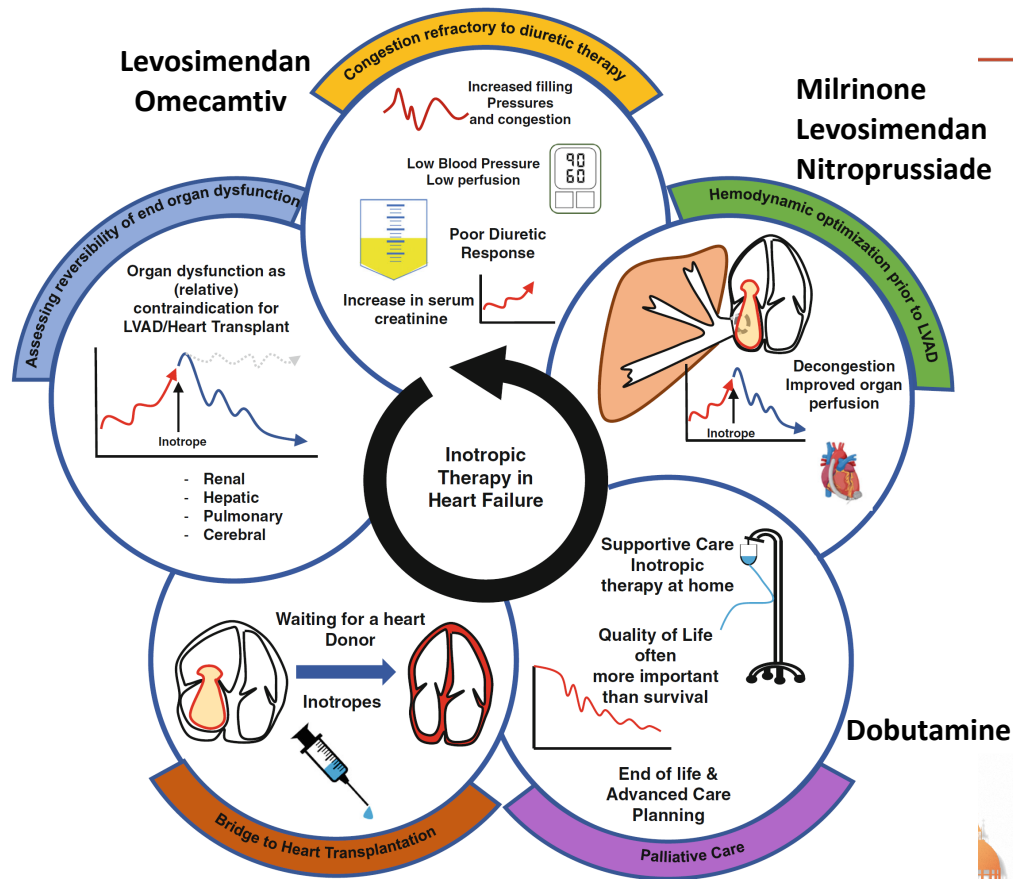


Guideline-recommended indications for the use of inotropes in advanced heart failure, acute heart failure and cardiogenic shock

	Recommendation	AHA	ESC
Advanced HF	Inotropes and vasopressors as a bridge to MCS or heart transplantation	IIA	IIA
	Inotropes and vasopressors as a palliative therapy in ineligible patients for MCS or heart transplantation	IIB	Consensus statement
	Continuous or intermittent long-term use of inotropes, for reasons other than palliative care or as a bridge to advanced therapies, is potentially harmful	III	-
Acute HF	Inotropic agents for patients with SBP <90 mmHg and evidence of hypoperfusion, when refractory to fluid challenge	-	IIB
	Inotropic agents should not be used routinely unless symptomatic hypotension is present	-	III
Cardiogenic Shock	Inotropic agents for patients with signs of cardiogenic shock	I	IIB



Inotropic therapy in patients with advanced heart failure. A clinical consensus statement from the Heart Failure Association of the European Society of Cardiology

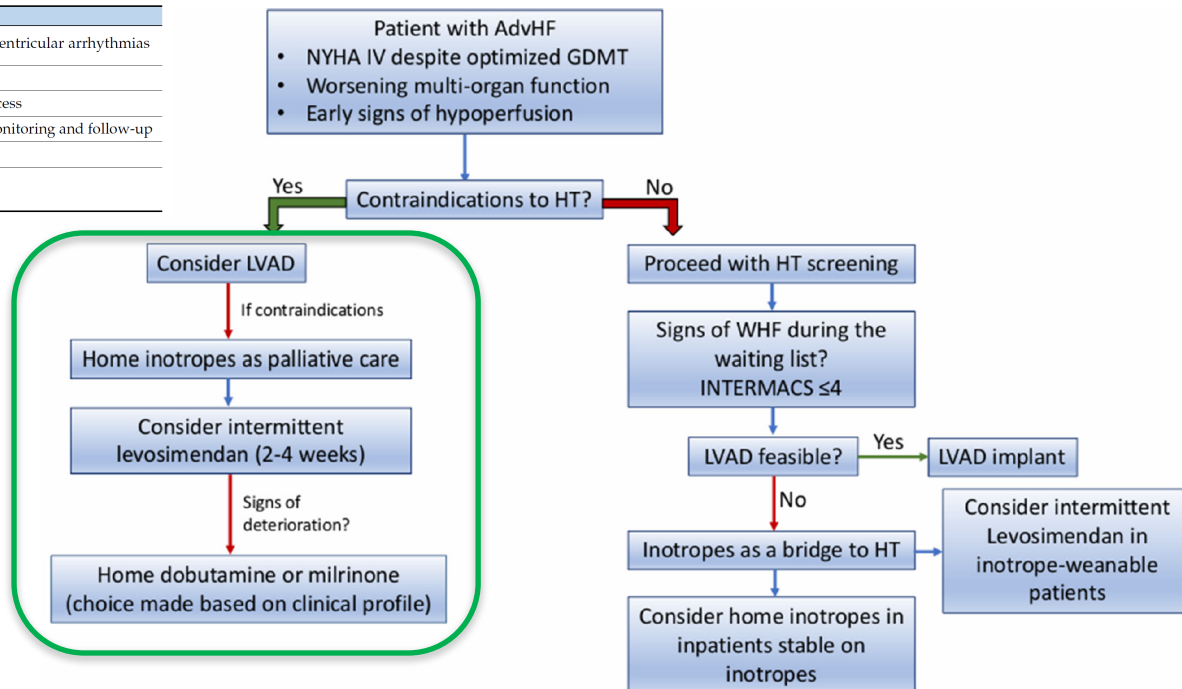


Home Inotropes in Advanced Heart Failure: A Practical Review

Paolo Manca^{1,2}, Maria Vittoria Matassini^{2,3} , Luca Fazzini⁴ , Matteo Bianco^{2,5} , Concetta Di Nora^{2,6} , Vittoria Rizzello^{2,7}, Samuela Carigi^{2,8} , Luisa De Gennaro^{2,9}, Maria Denitza Tinti^{2,10}, Renata De Maria^{2,11} , Furio Colivicchi¹² , Massimo Grimaldi¹³ , Fabrizio Oliva¹⁴ and Mauro Gori^{2,4,*} 

Table 2. Indications and contraindications for Home Inotropes in Advanced Heart Failure.

Indications	Contraindications
Persistently highly symptomatic (NYHA IV) despite optimized medical/device therapy	Uncontrolled or life-threatening ventricular arrhythmias
Refractory congestion not responsive to diuretics	Severe uncontrolled hypertension
Signs of systemic hypoperfusion	Inability to ensure safe venous access
Multiorgan dysfunction	Inability to guarantee adequate monitoring and follow-up
Bridge to advanced therapies (LVAD or HT)	
Palliative option when advanced therapies are not feasible	



There are **no written laws**



Inotropes and vasopressors as a bridge to interventions and strategies that improve outcomes

Thoughtful choice: Take in mind the **pathophysiology** (according to **phenotype**)



Use the **drugs** looking for their **dose-effect** (right dosage for the **shortest time**)

Base your choices on your **knowledge** and **experience**



Hopes for new drugs and new evidence

Grazie per l'attenzione!



roberta.dellabona@gmail.com



Efficacy and safety of intermittent intravenous outpatient administration of levosimendan in patients with advanced heart failure: the LION-HEART multicentre randomised trial

Sixty-nine patients randomised at a 2:1 ratio to levosimendan or placebo groups, receiving treatment by a 6-hour intravenous infusion (0.2 µg/kg/min) every 2 weeks for 12 weeks.

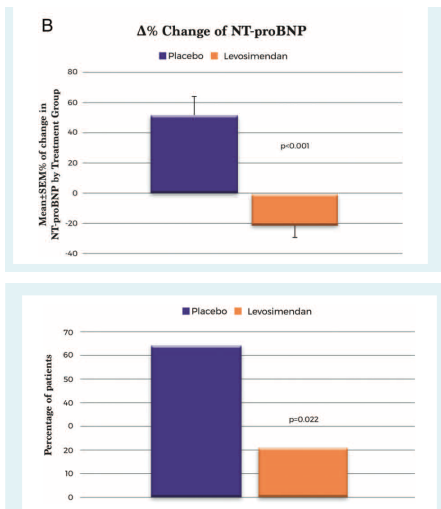


Figure 4 Proportion of patients reporting a clinically significant decline in their self-reported quality of life at 6 months of follow-up, according to treatment group. A clinically significant decline was considered a reduction of 5 points (minimal clinically important difference) on the EQ-5D visual analogue scale between the baseline and visit 10 (6 months).

Efficacy and safety of intermittent repeated levosimendan infusions in advanced heart failure patients: the LAICA study

Martin J. García-González^{1*}, Ana Aldea Perona², Antonio Lara Padron¹, José Luis Morales Rull³, Manuel Martínez-Sellés⁴, Manuel de Mora Martín⁵, Javier López Díaz⁶, Silvia López Fernández⁷, Pilar Ortiz Oficialdegui⁸ and Alejandro Jiménez Sosa⁹

¹Acute Cardiac Care Unit, Department of Cardiology, Hospital Universitario de Canarias, Ctra. La Cuesta—Taco, Ofra s/n, 38320 San Cristóbal de La Laguna, Tenerife, Spain; ²Institut Municipal d'Investigacions Mèdiques (IMIM), Barcelona, Spain; ³Heart Failure Unit, Department of Internal Medicine, Hospital Arnau de Vilanova, Institut de Recerca Biomèdica de Lleida (IRBLleida), Lleida, Spain; ⁴Department of Cardiology, Hospital Universitario Gregorio Marañón, CIBERCV, Universidad Europea, Universidad Complutense, Madrid, Spain; ⁵Department of Cardiology, Hospital Universitario Regional Carlos Haya, Málaga, Spain; ⁶Department of Cardiology, Hospital Clínico Universitario de Valladolid, CIBERCV, Valladolid, Spain; ⁷Heart Failure Unit, Department of Cardiology, Hospital Universitario Virgen de las Nieves, Granada, Spain; ⁸Department of Cardiology, Hospital Sierrallana, Torrelavega, Spain; and ⁹Clinical Research Unit, Hospital Universitario de Canarias, Tenerife, Spain

Abstract

Aims The aim of the LAICA study was to evaluate the long-term effectiveness and safety of intermittent levosimendan infusion in patients with advanced heart failure (AdHF).

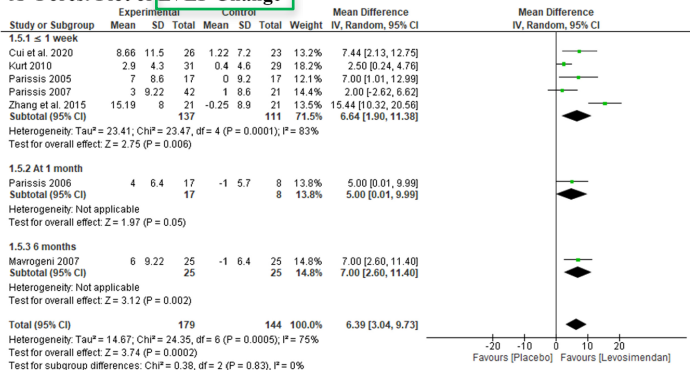
Methods and results This was a multicentre, randomized, double-blind, placebo-controlled clinical trial of intermittent levosimendan 0.1 µg/kg/min as a continuous 24-h intravenous infusion administered once monthly for 1 year in patients with AdHF. The primary endpoint [incidence of rehospitalization (admission to the emergency department or hospital ward for >12 h) for acute decompensated HF or clinical deterioration of the underlying HF] occurred in 23/70 (33%) of the levosimendan group (Group I) and 12/27 (44%) of the placebo group (Group II) ($P = 0.286$). The incidence of hospital readmissions for acute decompensated HF (Group I vs. Group II) at 1, 3, 6, and 12 months was 4.2% vs. 18.2% ($P = 0.036$); 12.8% vs. 33.3% ($P = 0.02$); 25.7% vs. 40.7% ($P = 0.147$); 32.8% vs. 44.4% ($P = 0.28$), respectively. In a secondary pre-specified time-to-event analysis no differences were observed in admission for acute decompensated HF between patients treated with levosimendan compared with placebo (hazard ratio 0.66; 95% CI, 0.32–1.32; $P = 0.24$). Cumulative incidence for the aggregated endpoint of acute decompensation of HF and/or death at 1 and 3 months were significantly lower in the levosimendan group than in placebo group [5.7% vs. 25.9% ($P = 0.004$) and 17.1% vs. 48.1% ($P = 0.001$), respectively], but not at 6 and 12 months [34.2% vs. 59.2% ($P = 0.025$); 41.4% vs. 66.6% ($P = 0.022$), respectively]. Survival probability was significantly higher in patients who received levosimendan compared with those who received placebo (log rank: 4.06; $P = 0.044$). There were no clinically relevant differences in tolerability between levosimendan and placebo and no new safety signals were observed.

Conclusions In our study, intermittent levosimendan in patients with AdHF produced a statistically non-significant reduction in the incidence of hospital readmissions for acute decompensated HF, a significantly lower cumulative incidence of acute decompensation of HF and/or death at 1 and 3 month of treatment and a significant improvement in survival during 12 months of treatment.

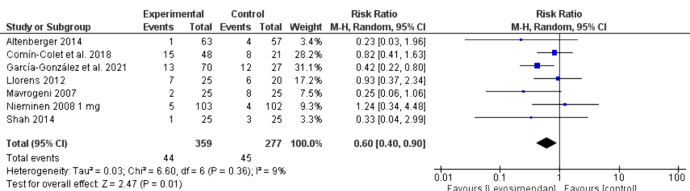


The Efficacy and Safety of Levosimendan in Patients with Advanced Heart Failure: An Updated Meta-Analysis of Randomized Controlled Trials

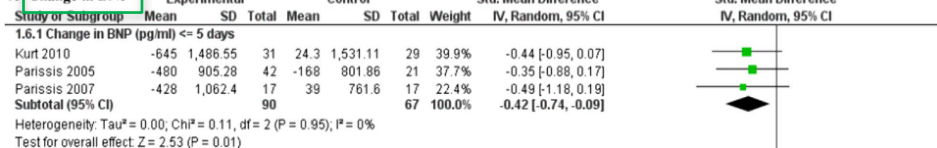
A- Forest Plot of LVEF Change



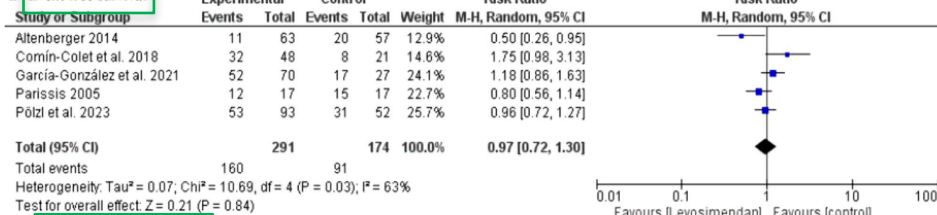
All-cause mortality



A- Change in BNP



B- Event free survival



C- All cause rehospitalization

