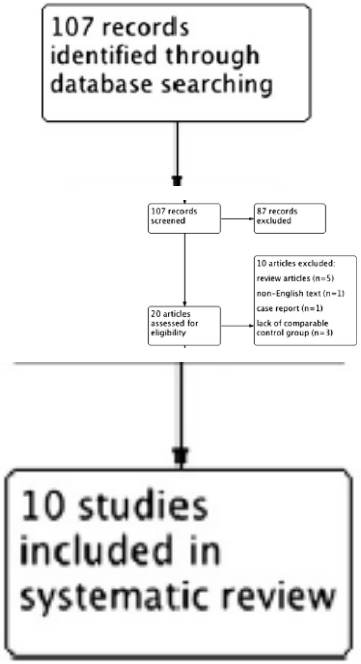
Resistencia a Diuréticos: Salino hipertónico+ Diuréticos

S. Salino hipertónico+furosemida altas dosis	????	????

Review

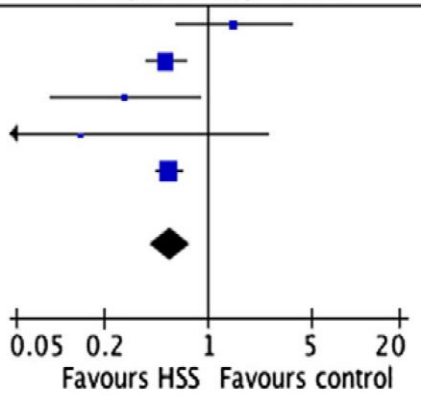
Hypertonic saline with furosemide for the treatment of acute congestive heart failure: A systematic review and meta-analysis☆



Mortalidad

Study or Subgroup	HSS Events	HSS Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Issa 2011	10	20	4	12	9.9%	1.50 [0.60, 3.74]
Licata 2002	24	53	47	54	36.6%	0.52 [0.38, 0.71]
Paterna 2000	3	30	11	30	6.5%	0.27 [0.08, 0.88]
Paterna 2005	0	48	3	46	1.1%	0.14 [0.01, 2.58]
Paterna 2011	114	881	212	890	45.9%	0.54 [0.44, 0.67]
Total (95% CI)		**1032**		**1032**	**100.0%**	**0.56 [0.41, 0.76]**
Total events	151		277			

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 7.01$, df = 4 (P = 0.14); $I^2 = 43\%$
Test for overall effect: Z = 3.63 (P = 0.0003)

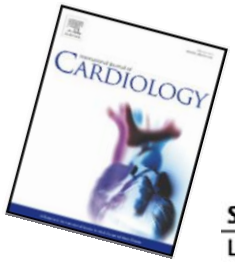


S. Gandhi et al. / International Journal of Cardiology 173 (2014) 139–145

Resistencia a Diuréticos: Salino hipertónico

Review

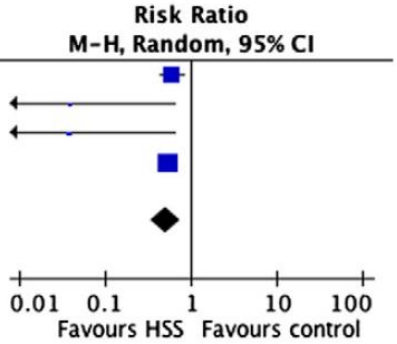
Hypertonic saline with furosemide for the treatment of acute congestive heart failure: A systematic review and meta-analysis ☆



Reingreso por Insuficiencia Cardiaca

Study or Subgroup	HSS Events	HSS Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Licata 2002	25	53	43	54	43.1%	0.59 [0.43, 0.81]
Paterna 2000	0	30	12	30	2.1%	0.04 [0.00, 0.65]
Paterna 2005	0	48	12	46	2.1%	0.04 [0.00, 0.63]
Paterna 2011	163	881	305	890	52.7%	0.54 [0.46, 0.64]
Total (95% CI)		**1012**		**1020**	**100.0%**	**0.50 [0.33, 0.76]**
Total events	188		372			

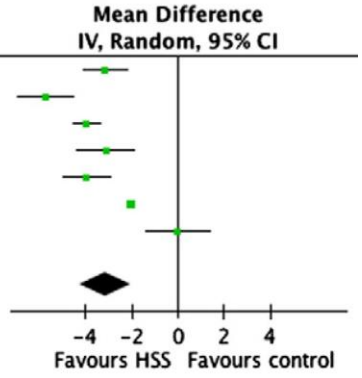
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 7.74$, df = 3 (P = 0.05); $I^2 = 61\%$
Test for overall effect: Z = 3.27 (P = 0.001)



Estancia en el hospital

Study or Subgroup	HSS Mean	HSS SD	HSS Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Licata 2002	8.57	2.3	53	11.7	2.6	54	14.5%	-3.13 [-4.06, -2.20]
Parinello 2011	6.3	3	66	12	4	67	13.5%	-5.70 [-6.90, -4.50]
Parrinello 2012	6.25	2.12	122	10.2	2.54	126	15.4%	-3.95 [-4.53, -3.37]
Paterna 2000	8.57	2.3	30	11.67	2.6	30	13.4%	-3.10 [-4.34, -1.86]
Paterna 2005	6.57	2.3	48	10.5	2.6	46	14.2%	-3.93 [-4.92, -2.94]
Paterna 2011	3.5	1	953	5.5	1	974	16.1%	-2.00 [-2.09, -1.91]
Tuttolomondo 2011	10	5.5	120	10	2.7	30	12.9%	0.00 [-1.38, 1.38]
Total (95% CI)			**1392**			**1327**	**100.0%**	**-3.13 [-4.23, -2.03]**

Heterogeneity: $Tau^2 = 1.95$; $Chi^2 = 107.26$, df = 6 (P < 0.00001); $I^2 = 94\%$
Test for overall effect: Z = 5.58 (P < 0.00001)



S. Gandhi et al. / International Journal of Cardiology 173 (2014) 139–145

MANUAL PRÁCTICO DE MANEJO INTEGRAL DEL PACIENTE CON INSUFICIENCIA CARDÍACA CRÓNICA

Coordinador científico
Luis Manzano Espinosa

Coordinador del Grupo de Insuficiencia Cardiaca y FA de la SEMI

3ª edición

Infusión de altas dosis de furosemida con solución salina hipertónica

Inclusión: Pacientes 55-90 años con IC refractaria y descompensada

* Clase funcional IV, , FEVI <30%,
* Tratados con dosis altas de furosemida (250-500 mg/día) y/o combinaciones de otros diuréticos,
* Tratamiento con IECA a dosis correctas
* Cr < 2mg/dl, diuresis < 500 ml/24h y natriuresis <60 mEq/24 h

Infusión de 150 ml SSH en 30 min/12 h "Y" Furosemida 250-500 mg en 100 de SF en 30 min/ 12 h

S. Salino Hipertónico según natremia

SSH 4.6%:	Na < 125nEq/l	19 amp de ClNa 20% en 1000 de SF
SSH 3.5%	Na 126-135 mEq/l	14 amp de ClNa 20% en 1000 de SF
SSH 2.4%	Na >135 mEq/l	8 amp de ClNa 20% en 1000 de SF
SSH 1.4%	Na >135 mEq/l	3 amp de ClNa 20% en 1000 de SF

Añadir Potasio 40-60 mEq/día

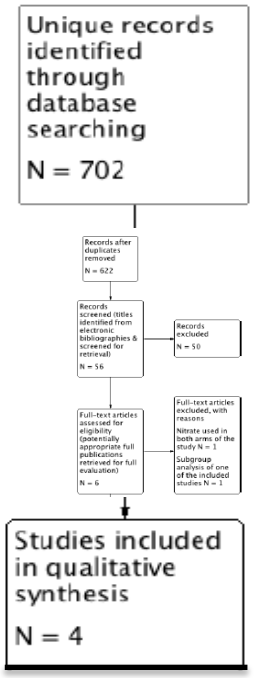
Vasodilatadores en Insuficiencia Cardiaca Aguda

2013 ACCF/AHA Guideline for the Management of Heart Failure

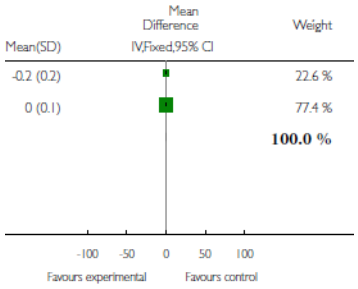
Intravenous nitroglycerin, nitroprusside, or nesiritide may be considered an adjuvant to diuretic therapy for stable patients with HF	IIb	A

Vasodilatadores en Insuficiencia Cardiaca Aguda

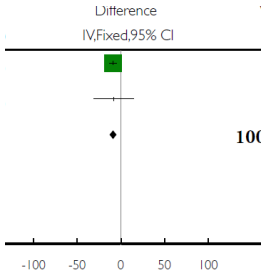
Nitrates for acute heart failure syndromes (Review)



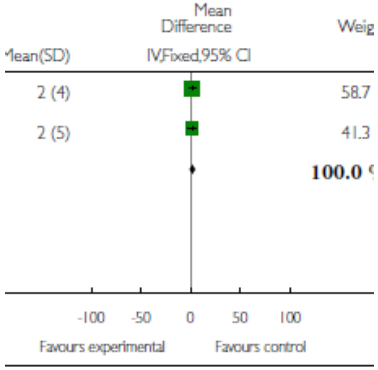
cardiac output, Outcome
(nitrates vs frusemide).



systolic blood pressure,
(nitrates vs frusemide).



heart rate, Outcome
vs frusemide).

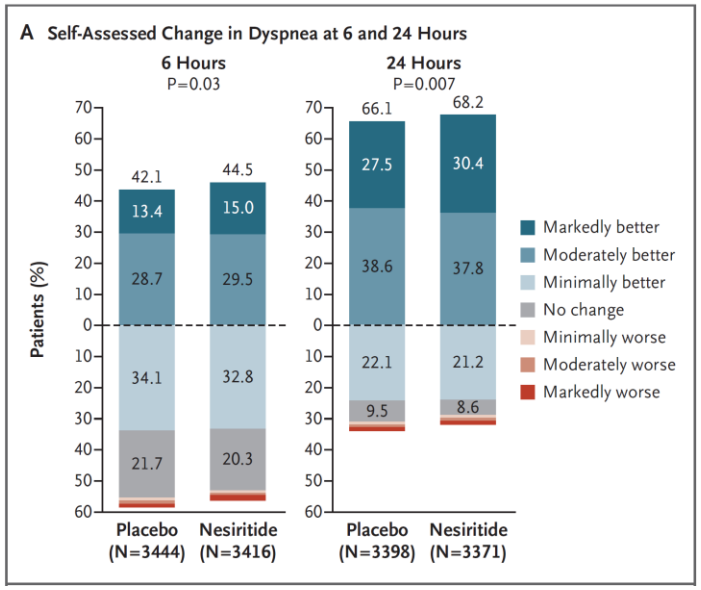


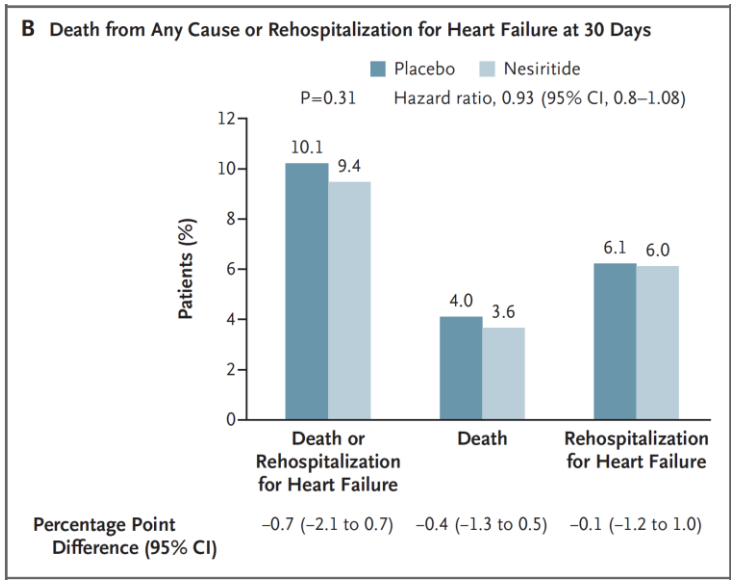
Authors' conclusions

There appears to be no significant difference between nitrate vasodilator therapy and alternative interventions in the treatment of AHFS, with regard to symptom relief and haemodynamic variables. Nitrates may be associated with a lower incidence of adverse effects after three hours compared with placebo. However, there is a lack of data to draw any firm conclusions concerning the use of nitrates in AHFS because current evidence is based on few low-quality studies.

Vasodilatadores en ICA: Nesiretide

Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF)





Safety end points	Nesiritide (N=3496)	Placebo (N=3511)	Difference or Odds Ratio (95% CI)†	P Value
Hypotension — no./total no. (%)	930/3498 (26.6)	538/3509 (15.3)	11.3 (9.4 to 13.1)	<0.001
Asymptomatic	748/3498 (21.4)	436/3509 (12.4)	9.0 (7.2 to 10.7)	<0.001
Symptomatic	250/3496 (7.2)	141/3509 (4.0)	3.2 (2.1 to 4.2)	<0.001

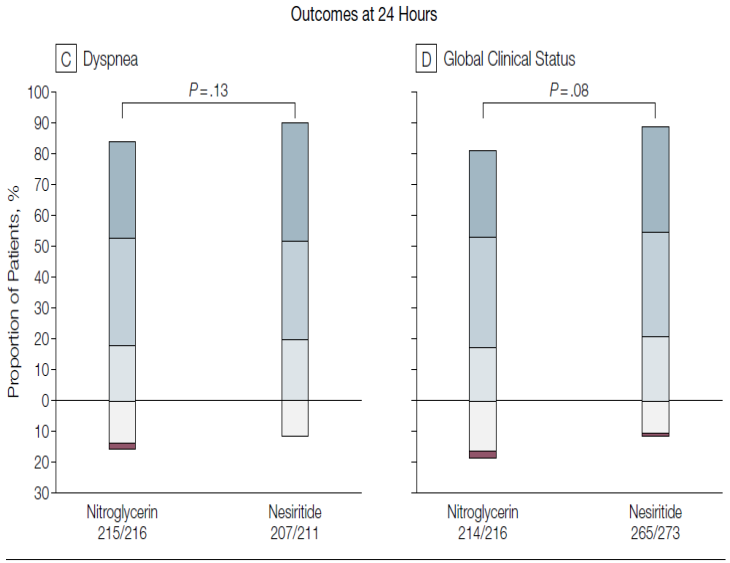
Conclusions: In base of these results, nesiritide cannot be recommended for routine use in the broad population of patients with acute heart failure

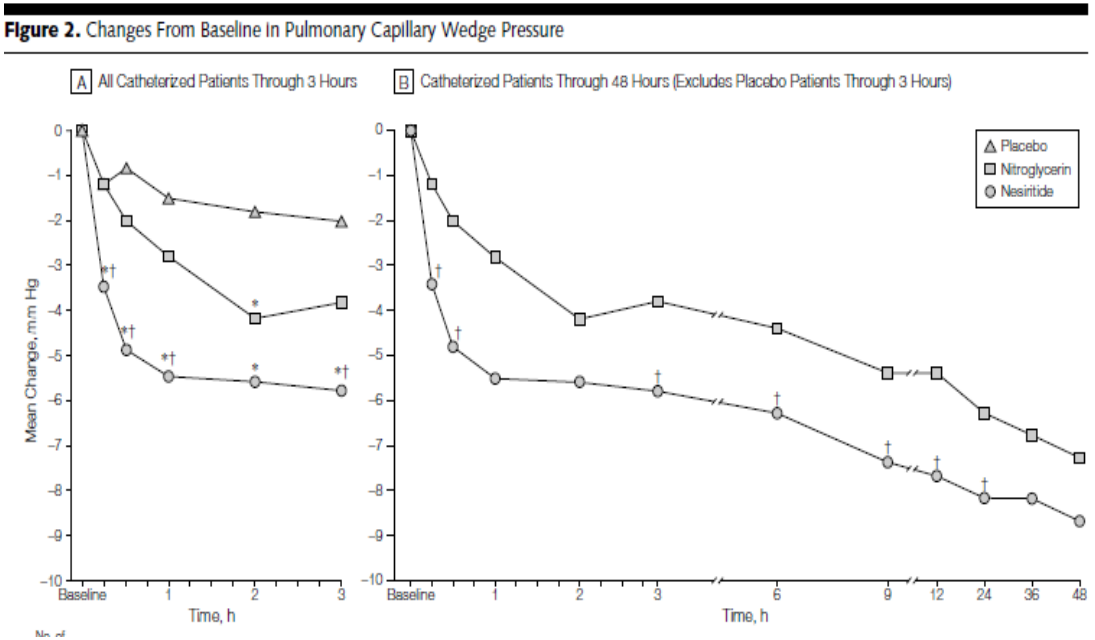
N Engl J Med 2011;365:32-43.

Vasodilatadores en ICA: Nesiretide/NTG

Intravenous Nesiritide vs Nitroglycerin for treatment of descompensanted Congestive Heart Failure (VMAC-trial)

Objective To compare the efficacy and safety of intravenous nesiritide, intravenous nitroglycerin, and placebo.





Conclusiones: Discreta mejoría de los parámentros hemodinámicos (PCP) sin ventajas en la sintomatologia

JAMA 2002; 287:1531-40

Tratamiento de la Insuficiencia Cardiaca Aguda

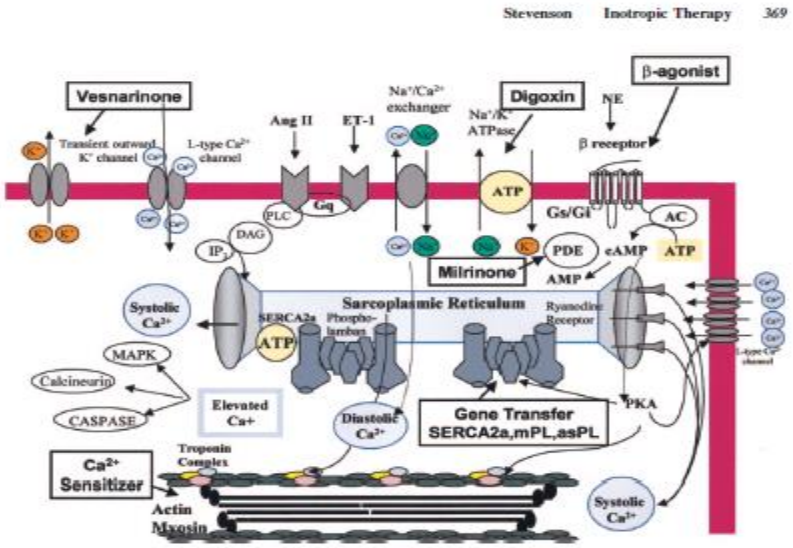
Patients with hypotension, hypoperfusion or shock

Ionotropos

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

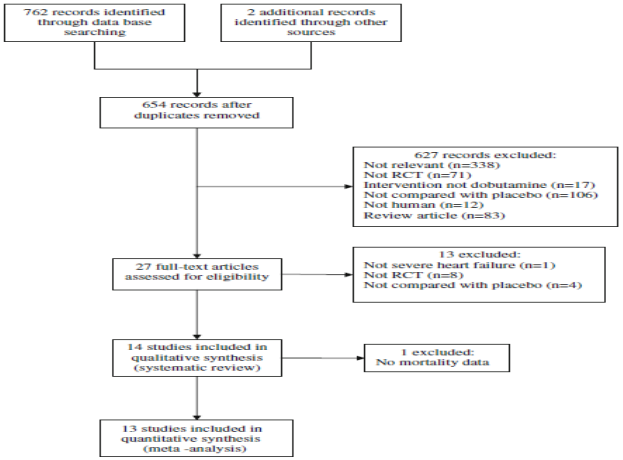
Ionotropos en Insuficiencia Cardiaca Aguda

Dobutamina	Levosimendan
Farmacología: catecolamina sintética que actúa sobre los receptores β1-β2	**Farmacología:** estabilizador de la unión Ca+Troponina C
Efecto: ionotropo y vasodilatador periférico	**Efecto:** ionotropo y vasodilatador periférico (*no mediado por receptores β*)
E. secundarios: hipotensión y taquiarritmias	**E. secundario:** hipotensión, taquiarritmias y cefalea
Metanálisis 2012: no mejora la mortalidad y sugiere que la aumenta	**SURVIVE, Metanálisis 2015**: mejora mortalidad con más hipotensión y arritmias.



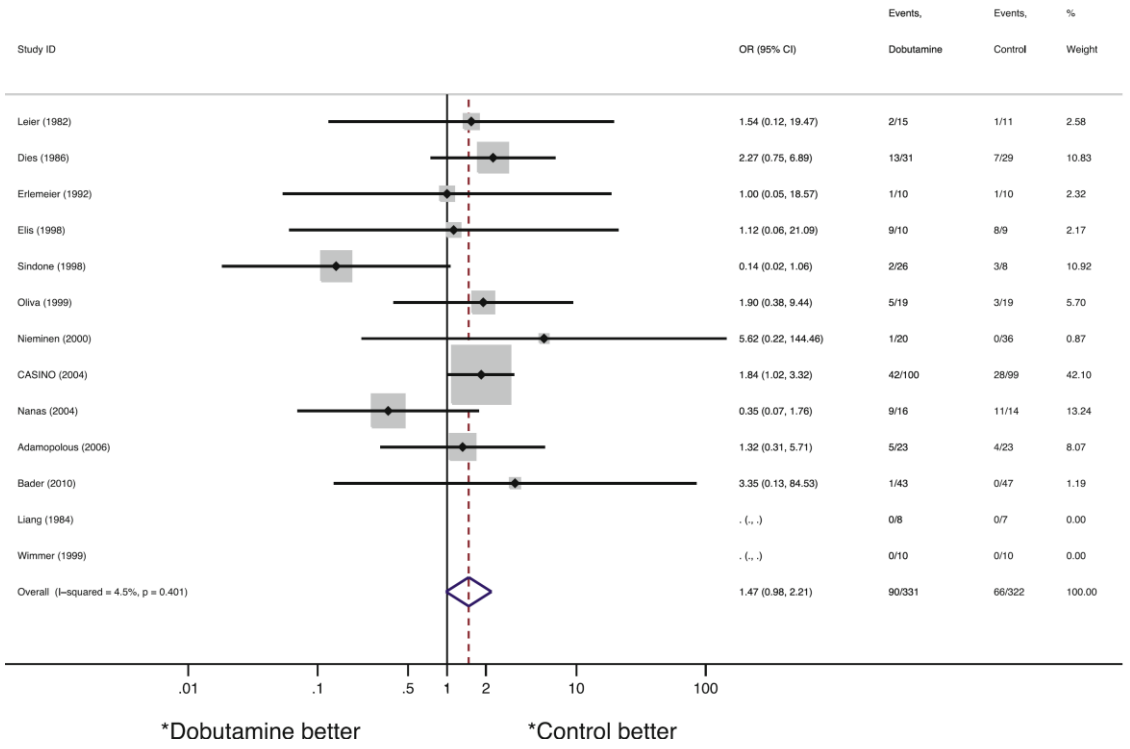
Dobutamine for patients with severe heart failure: a systematic review and meta-analysis of randomised controlled trials

Catherine L. Tacon
John McCaffrey
Anthony Delaney



Conclusions: This meta-analysis showed that dobutamine is not associated with improved mortality in patients with heart failure, and there is a suggestion of increased mortality associated with its use, although this did not reach the conventional level of statistical significance. Further research to define the role of dobutamine in treatment of severe heart failure should be a priority.

Dobutamina/Control: Mortalidad

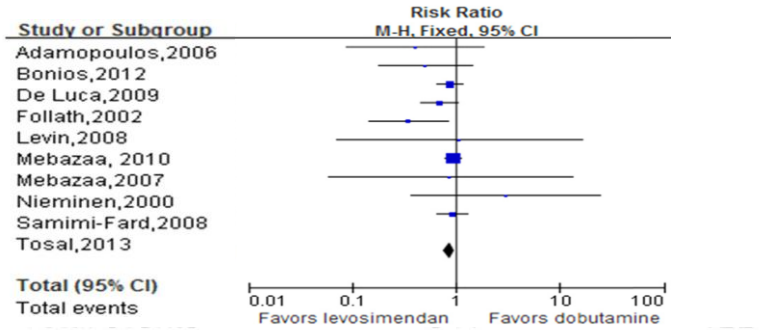


Intensive Care Med (2012) 38:359–367
DOI 10.1007/s00134-011-2435-6

Levosimendan Treatment for Heart Failure: A Systematic Review and Meta-Analysis.

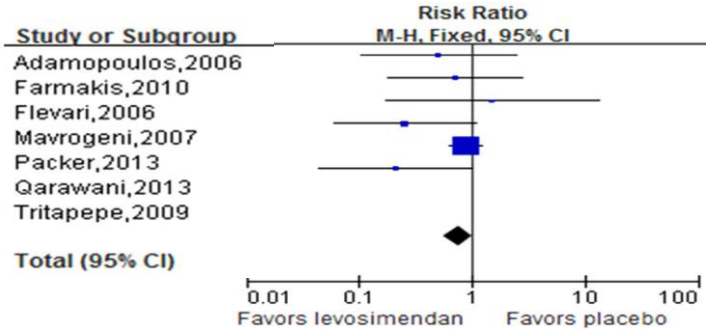
Gong B1, Li Z2, Yat Wong PC2.

Levosimendan/dobutamina: Mortalidad



Heterogeneity: Chi² = 9.68, df = 9 (P = 0.38); I² = 7%
Test for overall effect: Z = 2.36 (P = 0.02)

Levosimendan/Placebo: Mortalidad



Heterogeneity: Chi² = 6.31, df = 5 (P = 0.28); I² = 21%
Test for overall effect: Z = 1.88 (P = 0.06)

Meta-análisis Levosimendan/Placebo: Efectos adversos

Adverse Events	Studies, n	Levosimendan Group, n	Control Group, n	*P* Value
Ventricular tachycardia[11–13,33]	4	1,176	1,170	0.27
Extrasystoles[11–13]	3	1,107	1,102	0.002
Hypotension[11–13,22,25,35]	6	1,206	1,208	0.0001
Constipation[12,13]	2	1,004	1,002	0.91
Diarrhea[12,13]	2	1,004	1,002	0.18
Hypokalemia[12,13,22]	3	1,033	1,033	0.13
Nausea[12,13,22]	3	1,033	1,033	0.36
Vomiting[12,33]	2	1,004	1,002	0.93
Urinary tract infection[12,13,22]	3	1,033	1,033	0.41
Dizziness[11–13]	3	1,107	1,102	0.2
Headache or migraine[11–13,22]	4	1,136	1,133	<0.0000
Angina pectoris,chest pain or myocardial ischaemia	5	1,228	1,220	0.1

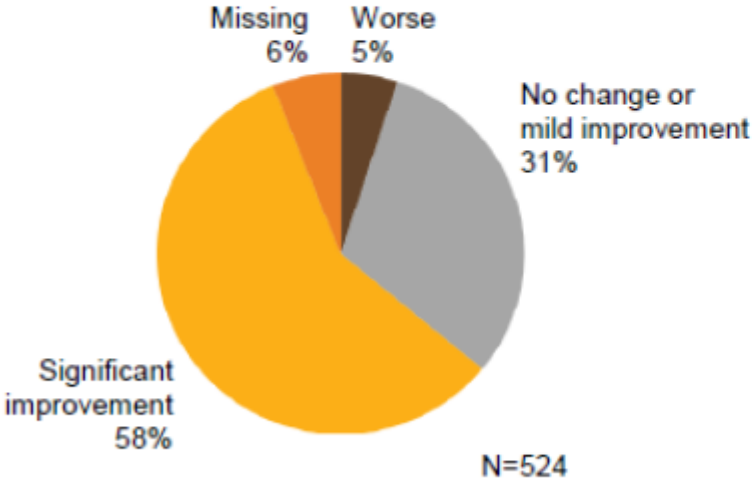
Conclusiones: Levosimendan presenta beneficios en la mortalidad de ICA pero con mayor riesgo de eventos cardiovasculares

J Cardiothorac Vasc Anesth. 2015 Mar 26.

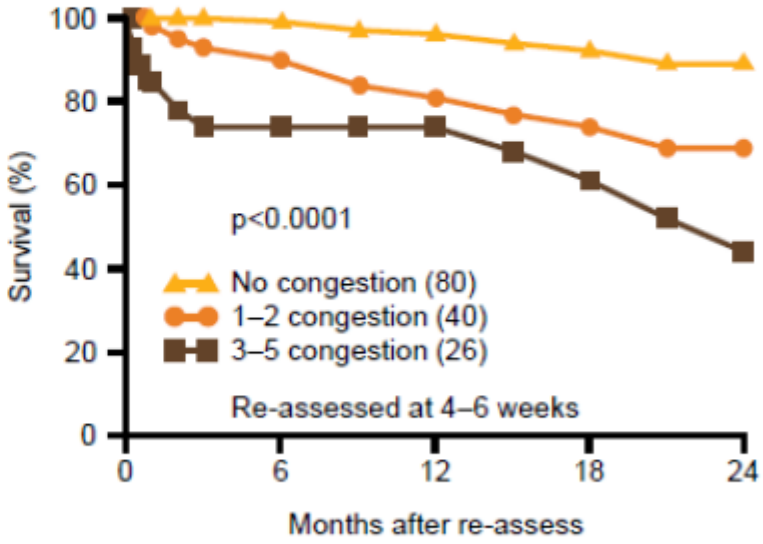
Tratamiento de la Insuficiencia Cardiaca Aguda

Current therapies do not provide optimal relief from acute heart failure signs and symptoms

Only 58% of patients hospitalized for acute HF show good symptom relief with standard therapy at 6 hours[1,2]



Signs and symptoms of congestion after hospitalization predict poor survival‡[3]



- 24% of patients hospitalized for HF in Europe have signs of congestion at discharge[4]

1. Mebazaa et al. Eur Heart J 2010;31:832–41; 2. Hogg & McMurray. Eur Heart J 2010;31:771–2;
3. Lucas et al. Am Heart J 2000;140:840–7; 4. Maggioni et al. Eur J Heart Fail 2010;12:1076–84

Tratamiento de la Insuficiencia Cardiaca Aguda

The evidence base for many commonly used acute heart failure treatments is limited with no proven long-term benefits

Group	Medication	Class of recommendation	Level of evidence† (A–C)
Diuretics	IV loop diuretics	I	B
Vasodilators	IV nitrates	IIa	B
	Sodium nitroprusside	IIb	B
IV opiates	Morphine	IIa	C
Inotropes*		IIa or IIb	C

"The treatment of acute heart failure remains largely opinion-based with little good evidence to guide therapy"

McMurray et al. Eur Heart J 2012;33:1787–847

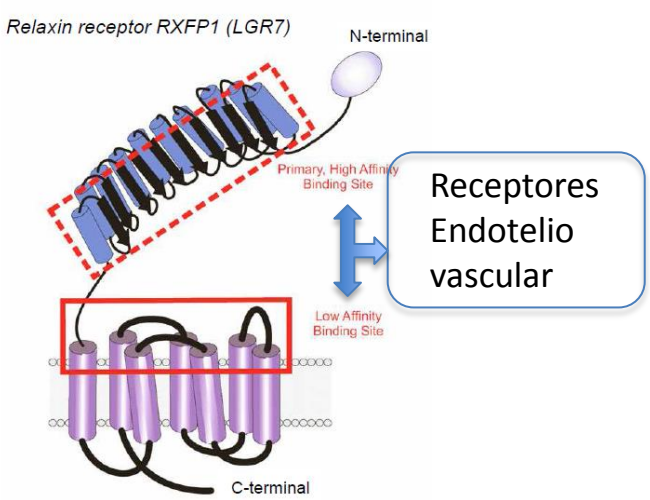
Tratamiento de la Insuficiencia Cardiaca Aguda

Large randomized controlled trials in acute heart failure have failed to demonstrate outcome benefits

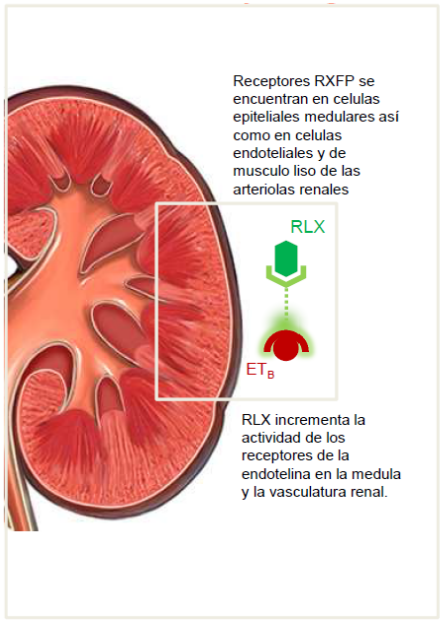
Trial name	Patient population	Intervention	Primary endpoint	Significant effect?
OPTIME-CHF[1]	951 patients admitted with exacerbation of systolic HF	i.v. **milrinone** vs pbo for 48 hours	Length of hospitalization for CV causes	✗
VERITAS[2]	1,448 patients hospitalized with AHF	i.v. **tezosentan** vs pbo for 24–72 hours	Change in dyspnea, incidence of death and worsening HF at 7 days	✗
SURVIVE[3]	1,327 patients hospitalized with AHF	i.v. **levosimendan** vs dobutamine	All-cause mortality at 180 days	✗
EVEREST[4]	4,133 patients hospitalized with AHF	**Tolvaptan** 30 mg once-daily vs pbo for 60 days	All-cause mortality and CV death or hospitalization for HF	✗
ASCEND-HF[5]	7,141 patients hospitalized for AHF	i.v. **nesiritide** vs pbo for 24 hours–7 days	Change in dyspnea and 30-day all-cause mortality or HF hospitalization	✗
PROTECT[6]	2,033 patients hospitalized for AHF	i.v. **rolofylline** vs pbo for up to 3 days	Composite of survival, HF status and renal function	✗

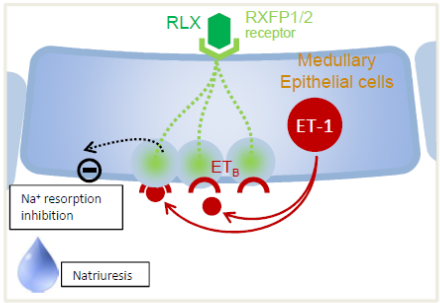
Serelaxina

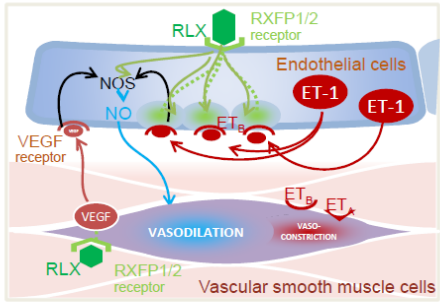
Hormona peptidica que interviene en los cambios sistémicos hemodinámicos y la adaptación renal durante la gestación.



Renal effects: serelaxin increases renal blood flow and stimulates natriuresis/diuresis







1. Teichman et al. Curr Heart Fail Rep 2010;7:75–82
2. Schneider et al. Ann Rev Pharmacol Toxicol 2007;47:731–59

Vascular effects: serelaxin stimulates NO-mediated vasodilation via activation of the endothelial ET_B receptor

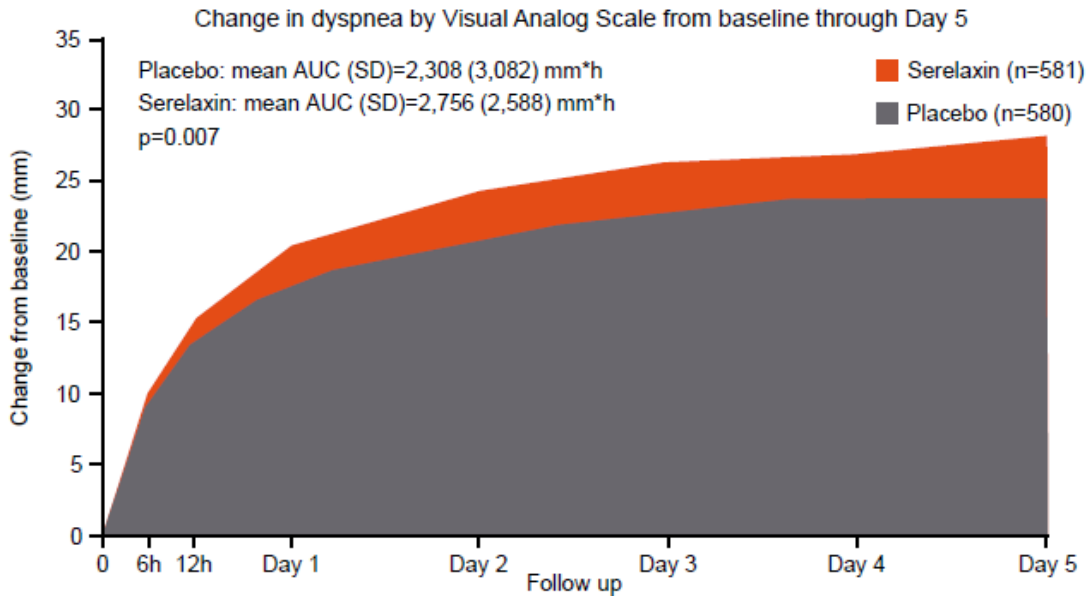
Serelaxina

Serelaxin for treatment of acue heart failure (RELAX-HF): a randomised placebo-controlled trial

Randomized:* 1.161 patients hospitalized with AHF, normal or elevated BP and mild-moderate renal impairment

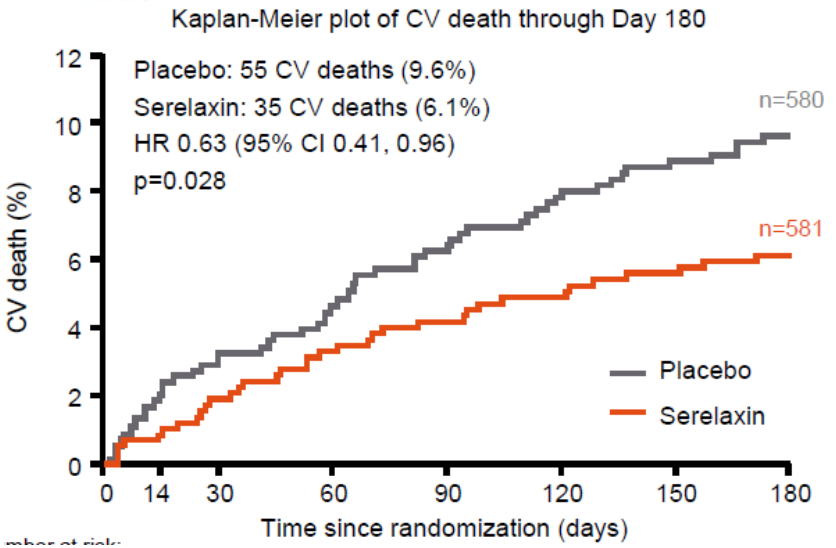
* Serelaxina 48 h/Placebo

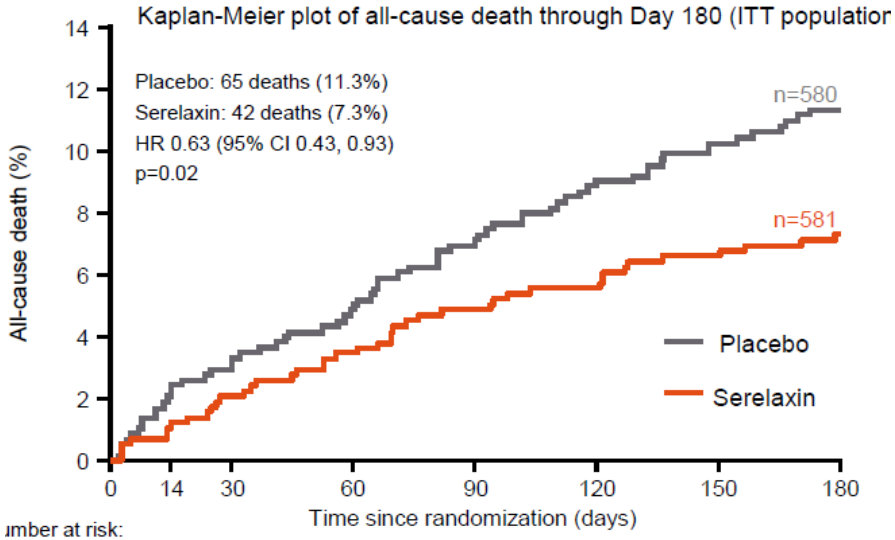
- Serelaxin significantly improved the primary efficacy endpoint of dyspnea relief through Day 5 assessed by the Visual Analog Scale AUC compared with placebo (448 mm*h, 95% CI 120, 775; p=0.007)

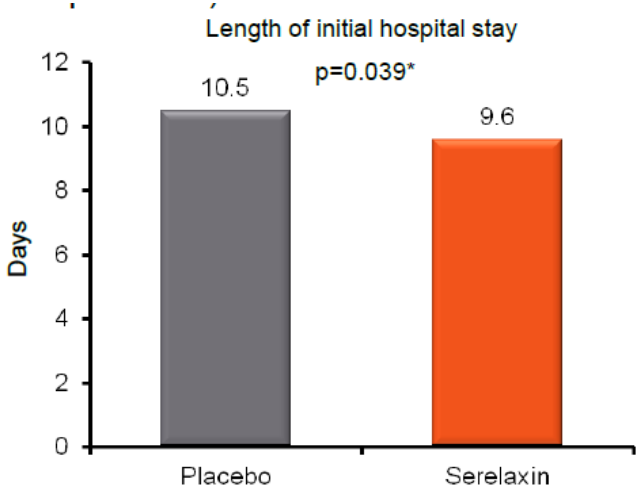


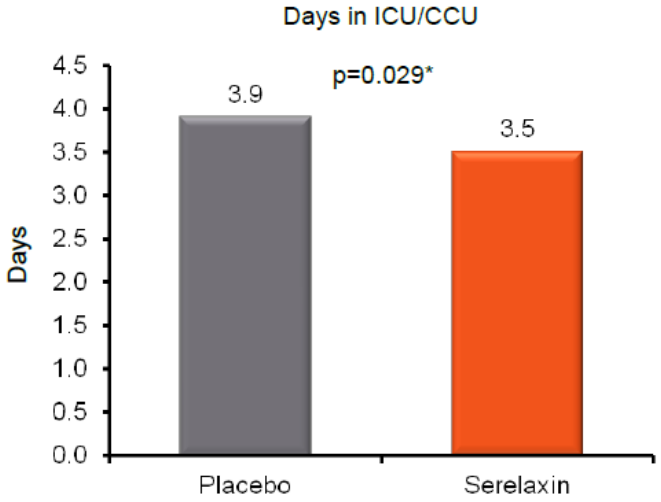
Lancet 2013; 381: 29–39

Serelaxin for treatment of acue heart failure (RELAX-HF: a randomised placebo-controlled trial





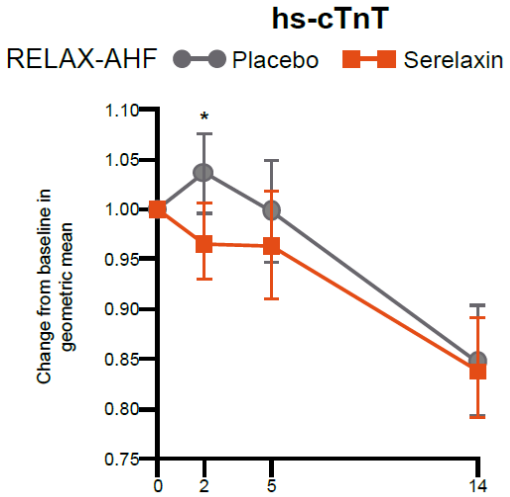


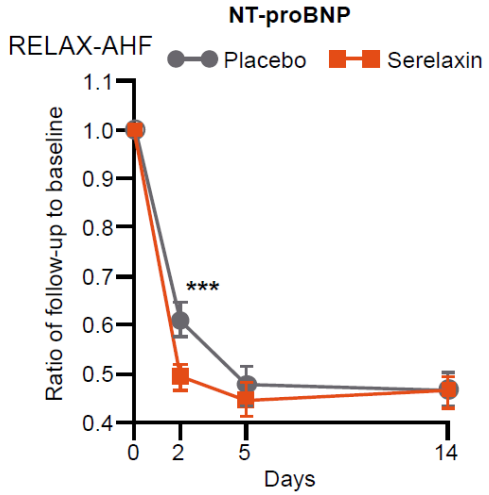


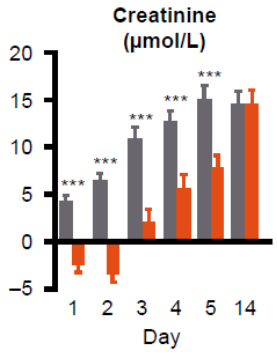
Lancet 2013; 381: 29–39

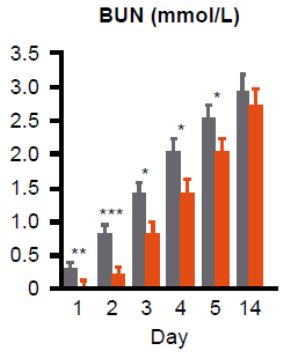
EXPEDITED PUBLICATION

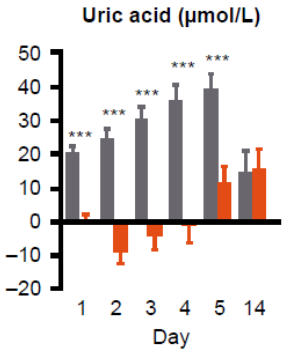
Effect of Serelaxin on Cardiac, Renal, and Hepatic Biomarkers in the Relaxin in Acute Heart Failure (RELAX-AHF) Development Program

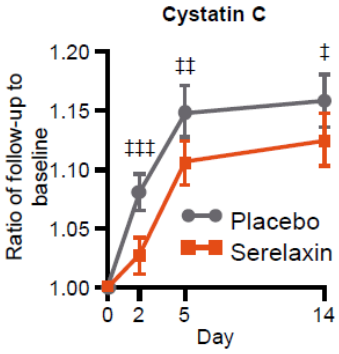












Placebo Serelaxin

Tratamiento de la Insuficiencia Cardiaca Aguda: Tratamientos previos

Management of evidence-based oral therapies

- In case of decompensation of CHF, every attempt should be made to continue evidence-based, disease-modifying, oral therapies in patients with AHF (*Table 3*).
- In the case of *de novo* HF, every attempt should be made to initiate these therapies after hemodynamic stabilization.

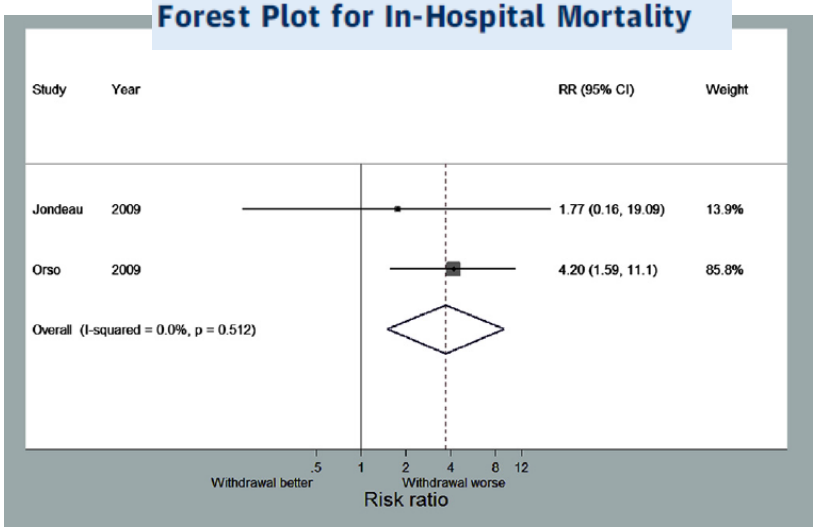
EUROPEAN SOCIETY OF CARDIOLOGY®
European Heart Journal
doi:10.1093/eurheartj/ehv066

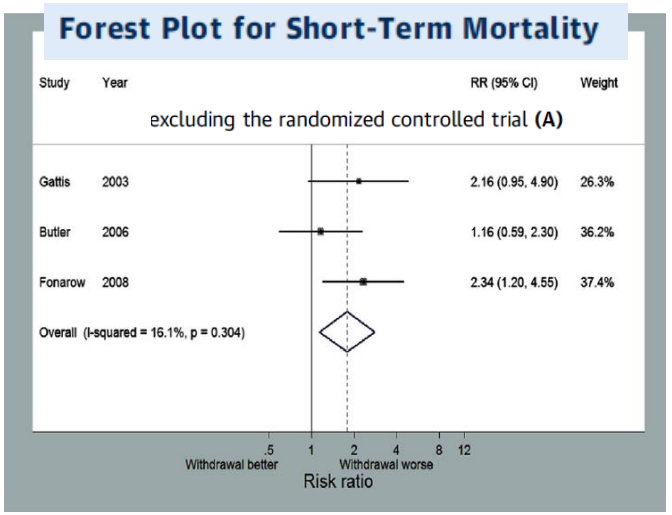
	NTA/HTA	HipoTAs mmHg		FC ppm		K mEq/l		F Renal mg/dl/AclarCr	
		<100->85	<85	<60->50	<50	<3.5	>5.5	<2.5 >30	>2.5 <30
ACE/ARA2	Rev./↑	↓/Stop	Stop	=	=	Rev/↑	Stop	Rev	Stop
BB	=	↓/Stop	Stop	↓	Stop	=	=	=	=
MRA	=	=	Stop	=	=	Rev/↑	↓/Stop	↓	Stop
Diureticos	↑	↓	Stop	=	=	Rev/=	=	=	Rev
Ivabradina	Rev	↓/Stop	Stop	↓/Stop	↓/Stop	↓/Stop	=	=	=

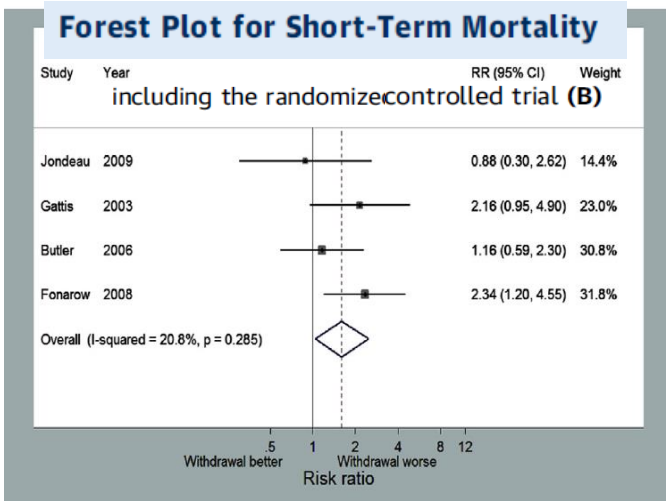
Tratamiento de la Insuficiencia Cardiaca Aguda: Tratamientos previos. BETABLOQUEANTES

Effects of Beta-Blocker Withdrawal in Acute Decompensated Heart Failure

A Systematic Review and Meta-Analysis







CONCLUSIONS

Our meta-analysis showed that continuation of beta-blockers in ADHF was associated with significant reductions in risk of in-hospital mortality, short-term mortality, and short-term combined rehospitalization or death. These data suggest that beta-blockers should be continued in ADHF if the clinical situation allows in an attempt to reduce adverse outcomes.

(J Am Coll Cardiol HF 2015;3:647-53)

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Management of cardiogenic shock

Holger Thiele[1]*, E. Magnus Ohman[2], Steffen Desch[1], Ingo Eitel[1], and Suzanne de Waha[1]

Definición:

- Hipotensión (TAs<90 mmHg)
- Signos de hipoperfusión (oligoanuria, diaforesis, disminución de conciencia)
- Lactato > 2mmol/L
- Acidosis metabólica
- SvO2 < 65%

Precisa atención Urgente:

- Cateter arterial
- Swan-Ganz ??

Valoración UCI

Principios de tratamiento

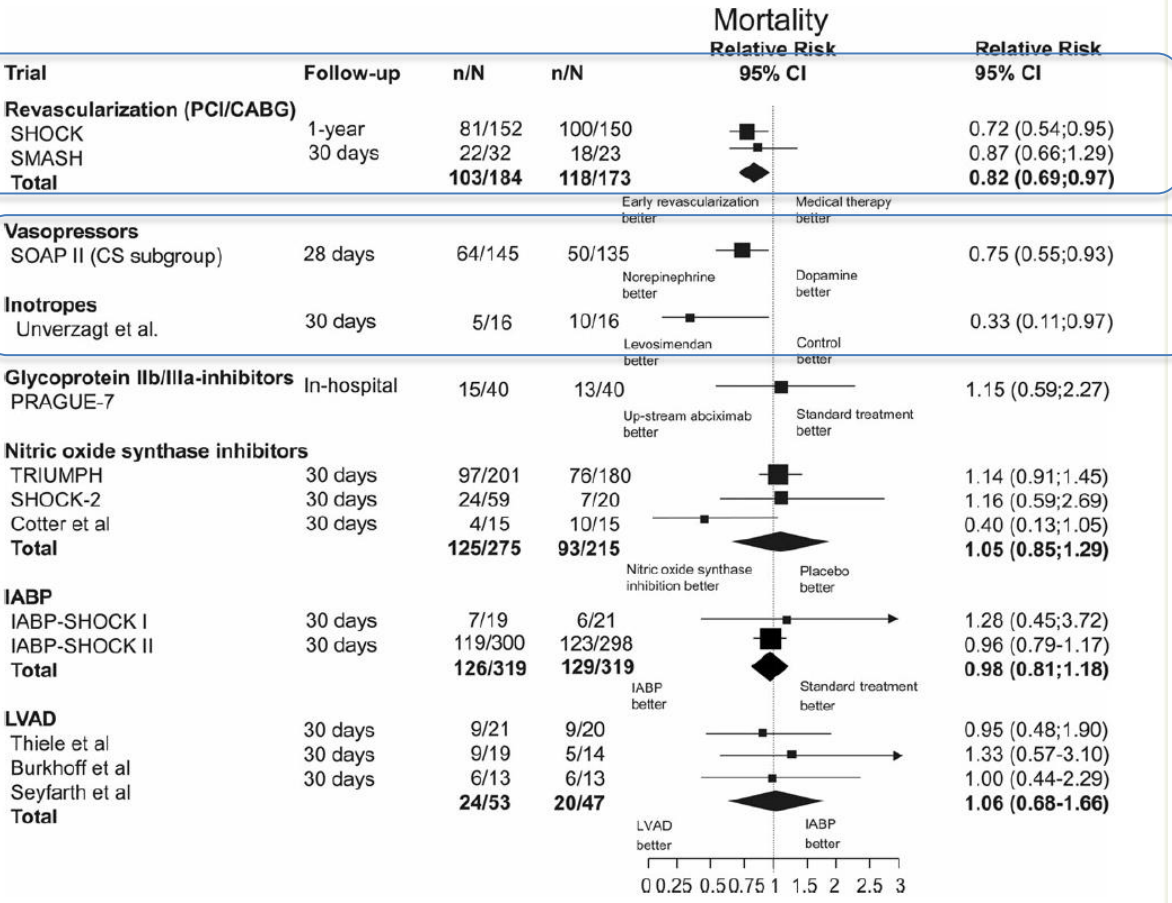
- Fluid challenge (saline or ringer lactate, >200 mL/15–30 min) is recommended as the first line treatment if there is no sign of overt fluid overload — Líquidos
- Dobutamine may be used to increase cardiac output; levosimendan may be considered, especially in CHF patients on oral beta-blockade — Ionotropos
- Vasopressors should only be used if there is a strict need to maintain systolic BP in the presence of persistent hypoperfusion; if needed, norepinephrine is recommended over dopamine — Vasopresores
- All CS should be rapidly transferred to a tertiary care centre which has a 24/7 service of cardiac catheterization, and a dedicated ICU with availability of short-term mechanical circulatory support — Dispositivos de asistencia circulatoria
- Intraaortic ballon pump is not routinely recommended in CS
- Short-term mechanical circulatory support may be considered in refractory CS depending on patient age, comorbidities and neurological function
- Based on current evidence, we do not recommend one mode of short-term circulatory support over another

European Heart Journal (2015) **36**, 1223–1230

Management of cardiogenic shock

Holger Thiele[1]*, E. Magnus Ohman[2], Steffen Desch[1], Ingo Eitel[1], and Suzanne de Waha[1]

Valoración de los diferentes tratamientos del shock cardiogénico



European Heart Journal (2015) **36**, 1223–1230

Comparison of Dopamine and Norepinephrine in the Treatment of Shock

Daniel De Backer, M.D., Ph.D., Patrick Biston, M.D., Jacques Devriendt, M.D., Christian Madl, M.D.,

N = 1679 pacientes con shock

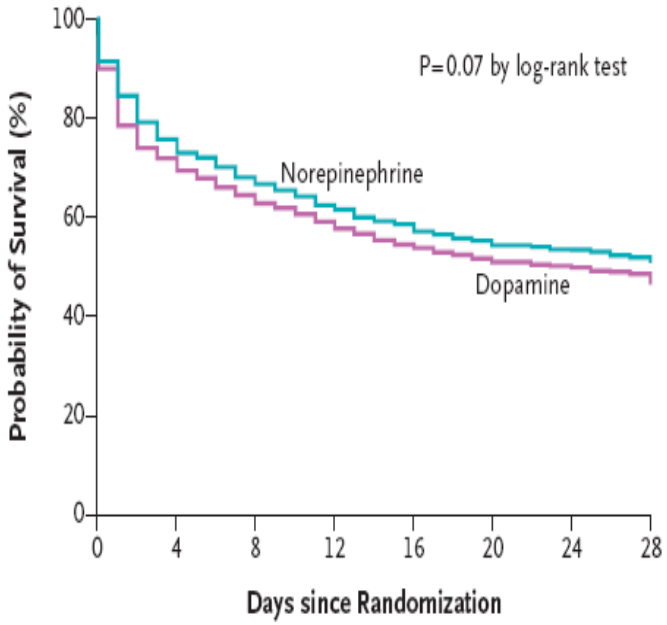


Table 3. Secondary Outcomes and Adverse Events.*

Variable	Dopamine (N=858)	Norepinephrine (N=821)	P Value
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)	

CONCLUSIONS

Although there was no significant difference in the rate of death between patients with shock who were treated with dopamine as the first-line vasopressor agent and those who were treated with norepinephrine, the use of dopamine was associated with a greater number of adverse events. (ClinicalTrials.gov number, NCT00314704.)

N Engl J Med 2010;362:779-89.

Management of cardiogenic shock

Holger Thiele[1]*, E. Magnus Ohman[2], Steffen Desch[1], Ingo Eitel[1], and Suzanne de Waha[1]

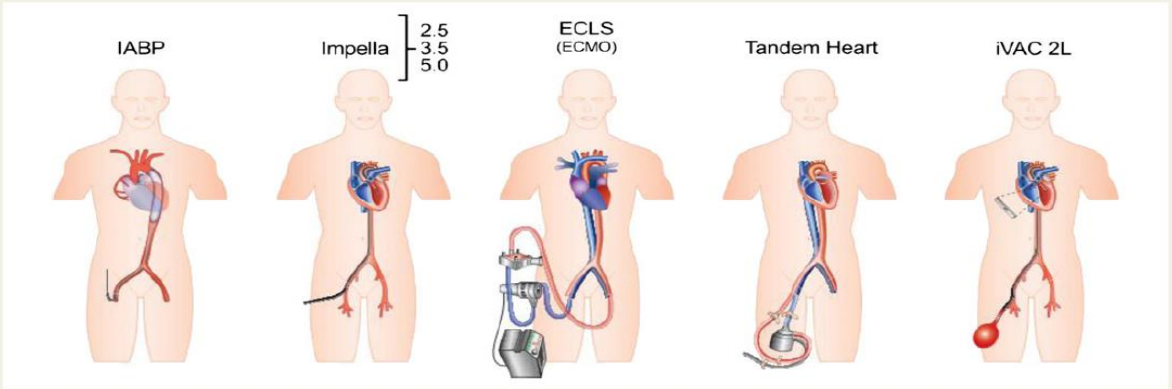


Figure 2 Schematic drawings of current percutaneous mechanical support devices for CS: intraaortic balloon pump (*A*), Impella® (*B*), TandemHeart™, (*C*) extracorporeal life support, (*D*) iVAC 2L®.

Table 2 Technical features of currently available percutaneous support devices

	iVAC 2L®	TandemHeart™	Impella® 5.0	Impella® 2.5	Impella® CP	ECLS (multiple systems)
Catheter size (F)	11 (expandable)	—	9	9	9	
Cannula size (F)	17	21 venous 12–19 arterial	21	12		17–21 venous 16–19 arterial
Flow (L/min)	Max 2.8	Max. 4.0	Max. 5.0	Max. 2.5	3.7–4.0	Max. 7.0
Pump speed (rpm)	Pulsatile, 40 mL/beat	Max. 7500	Max. 33 000	Max. 51 000	Max. 51 000	Max. 5000
Insertion/ Placement	Percutaneous (femoral artery)	Percutaneous (femoral artery + vein for left atrium)	Peripheral surgical (femoral artery)	Percutaneous (femoral artery)	Percutaneous (femoral artery)	Percutaneous (femoral artery + vein)
LV unloading	+	++	++	+	+	−
Anticoagulation	+	+	+	+	+	+
Recommended duration of use	−21 days	−14 days	10 days	10 days	10 days	−7 days
CE-certification	+	+	+	+	+	+
FDA	−	+	+	+	+	+
Relative costs	++	+++++	++++	+++	++++	+(+)

IABP, intraaortic balloon pumping; ECLS, extracorporeal life support system; LV, left ventricular; CE, conformité européenne; FDA, Food and Drug Administration.

European Heart Journal (2015) **36**, 1223–1230

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Criterios para pasar a planta

Discharge from emergency department

- Clinical condition can change dramatically within a few hours of ED arrival. Hence, clinical response to initial treatment is an important indicator of likely disposition.
- Indicators of good response to initial therapy that might be considered in discharge include:
  - Patient-reported subjective improvement
  - Resting HR $<$ 100 bpm
  - No hypotension when standing up
  - Adequate urine output
  - Oxygen saturation $>$ 95% in room air

Tratamiento de la Insuficiencia Cardiaca Aguda: Derivación a hospitalización

Servicios de Cardiología (SC)	**Servicio asistencial especializado en las enfermedades del corazón.**
	Pacientes que cursan el primer episodio de ICA menores de 75 años.
	Pacientes controlados en las unidades de IC y en seguimiento estrecho por Cardiología.
	Pacientes que puedan requerir procedimientos invasivos (intervencionismo coronario, valvular o electrofisiológico; terapia de resincronización cardiaca; desfibrilador implantable, etc).
	Pacientes con afectación valvular responsable de la ICA.
	Pacientes con una alta probabilidad de presentar eventos clínicos adversos relacionados con enfermedad coronaria.
	Pacientes con intervencionismo coronario previo (reciente).
	Pacientes que han presentado hipoperfusión sistémica leve o arritmias cardíacas que requieran monitorización ECG (telemetría).
Servicios de Medicina Interna (SMI)	**Servicio asistencial especializado.** ***(Los criterios de atención a pacientes en Cardiología o Medicina Interna deberán siempre adaptarse a las realidades locales de la organización asistencial concreta. En hospitales sin Servicio de Cardiología los pacientes son atendidos por los SMI).***
	Pacientes de edad avanzada no susceptibles de intervencionismo.
	Pacientes con ICA de origen no coronario con evidencia de comorbilidad significativa que pueda interferir con el tratamiento.
	Pacientes con fragilidad, limitación funcional y comorbilidades o con problemas importantes sociales, así como pacientes en fase terminal.

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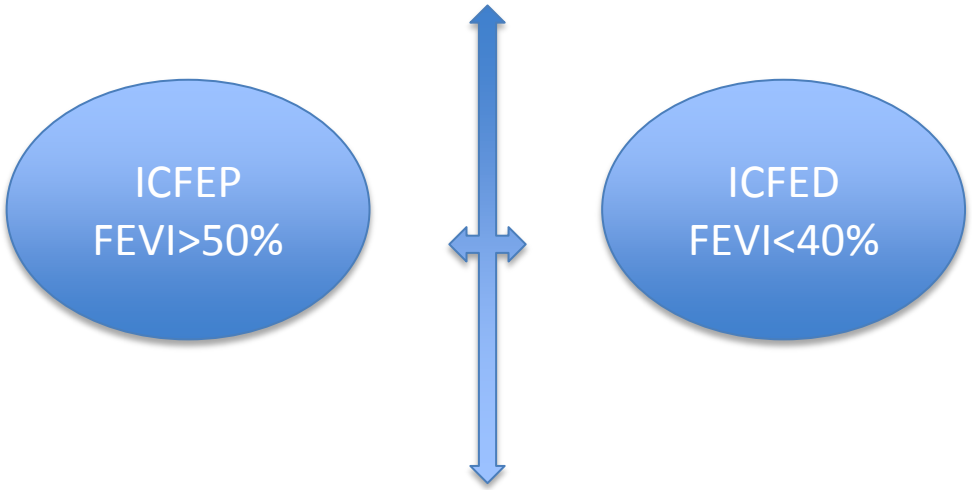
Manejo de la Insuficiencia Cardiaca Crónica

European Heart Journal (2012) 33, 1787–1847
doi:10.1093/eurheartj/ehs104

ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC



ACCF/AHA Practice Guideline

2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American College of Chest Physicians, Heart Rhythm Society and International Society for Heart and Lung Transplantation

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation

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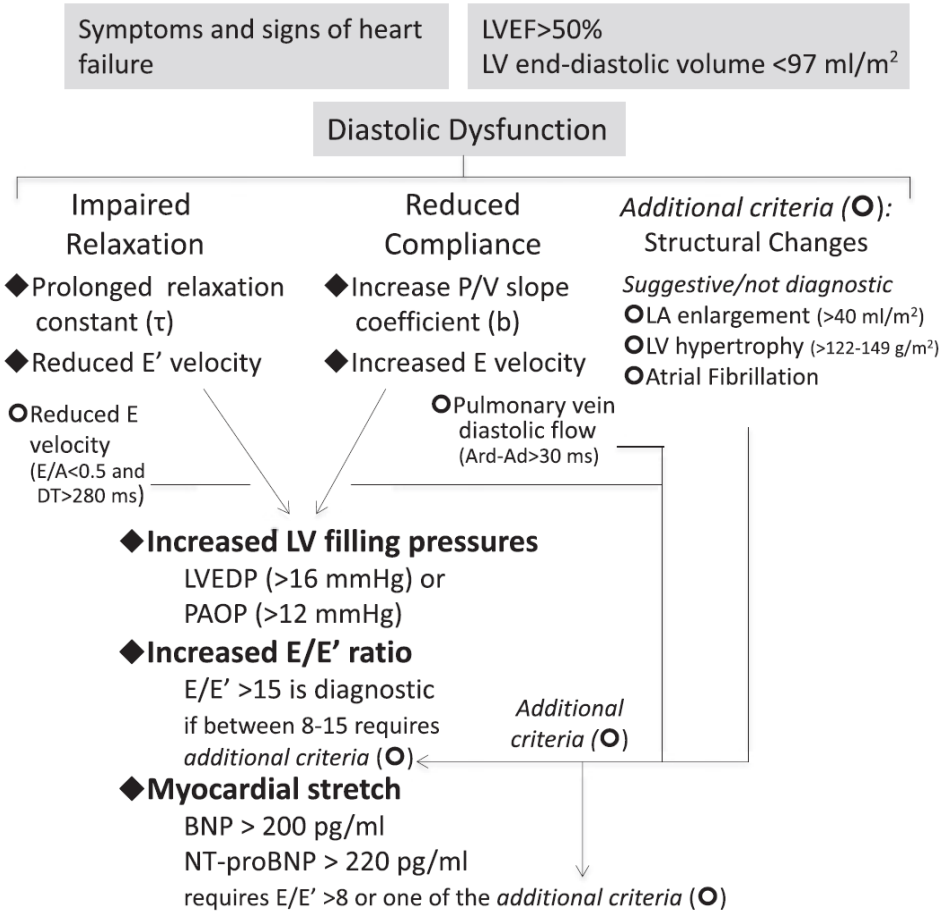
Criterios diagnósticos de ICFEP de la ESC

Heart failure with preserved ejection fraction: Refocusing on diastole

HFpEF



International Journal of Cardiology 179 (2015) 430–440

Outcome of Heart Failure with Preserved Ejection Fraction in a Population-Based Study

Comorbilidades en ICFED y ICFEP

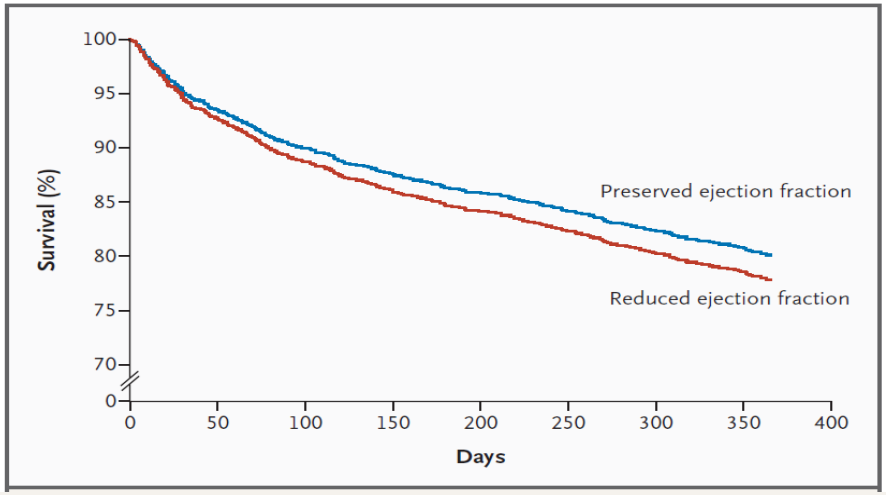
Table 1. Characteristics of Patients.*

Characteristic	Reduced Ejection Fraction (<40%) (N=1570)	Preserved Ejection Fraction (>50%) (N=880)	P Value
Mean LVEF — %	25.9	62.4	<0.001
Age — yr	71.8 ± 12	75.4 ± 11.51	<0.001
Male sex — no. (%)	983 (62.6)	302 (34.3)	<0.001
Coronary artery disease or ischemia — no. (%)	764 (48.7)	312 (35.5)	<0.001
Hypertension — no. (%)	772 (49.2)	485 (55.1)	0.005
Hyperlipidemia — no. (%)	350 (22.3)	136 (15.5)	<0.001
Diabetes — no. (%)	611 (38.9)	279 (31.7)	<0.001
Cerebrovascular accident or transient ischemic attack — no. (%)	229 (14.6)	133 (15.1)	0.72
Angina — no. (%)	440 (28.0)	201 (22.8)	0.005
Ever smoked — no. (%)	754 (48.0)	322 (36.6)	<0.001
Currently smoking — no. (%)	271 (17.3)	106 (12.0)	<0.001
Peripheral vascular disease — no. (%)	236 (15.0)	92 (10.5)	<0.001
Atrial fibrillation — no. (%)	370 (23.6)	280 (31.8)	<0.001
Cancer — no. (%)	182 (11.6)	105 (11.9)	0.80
COPD — no. (%)	207 (13.2)	156 (17.7)	0.002
Prior myocardial infarction — no. (%)	612 (39.0)	146 (16.6)	<0.001
Prior CABG — no. (%)	203 (12.9)	51 (5.8)	<0.001
Prior PCI — no. (%)	48 (3.1)	16 (1.8)	0.07
Peptic ulcer disease — no. (%)	94 (6.0)	74 (8.4)	0.02
Hepatitis or cirrhosis — no. (%)	20 (1.3)	16 (1.8)	0.28
Dementia — no. (%)	76 (4.8)	49 (5.6)	0.43

ICFEP	ICFED
Mayor edad	
Sexo femenino	
Mayor número de Comorbilidades CHARLSON HTA EPOC Demencia Diabetes A. Periférica	Mayor índice de complicaciones isquémicas IAM Angor Hemodinámica
FA	

N ENGL J MED 355;3 WWW.NEJM.ORG JULY 20, 2006

Outcome of Heart Failure with Preserved Ejection Fraction in a Population-Based Study



Variable	Reduced Ejection Fraction (<40%) (N=1570)	Preserved Ejection Fraction (>50%) (N=880)	P Value
	no. (%)		
Outcomes			
30-Day mortality	112 (7.1)	47 (5.3)	0.08
1-Yr mortality	400 (25.5)	195 (22.2)	0.07
30-Day readmission for heart failure*	73 (4.9)	38 (4.5)	0.66
1-Yr readmission for heart failure*	240 (16.1)	114 (13.5)	0.09
30-Day mortality or readmission for heart failure	182 (11.6)	83 (9.4)	0.10
1-Yr mortality or readmission for heart failure	566 (36.0)	274 (31.1)	0.01

Tratamiento de la Insuficiencia Cardíaca con FE preservada

Meta-Analysis of Therapy in HFpEF

CHARM-P 2003 Candesartan	PEP-CHF 2006 Perindopril	I-PRESERVE 2008 Irbersartan	SUB-SENIOR 2009 Nevibolol	J-DHF 2013 Carvedilol	TOP-CAT 2014 Espironolactona

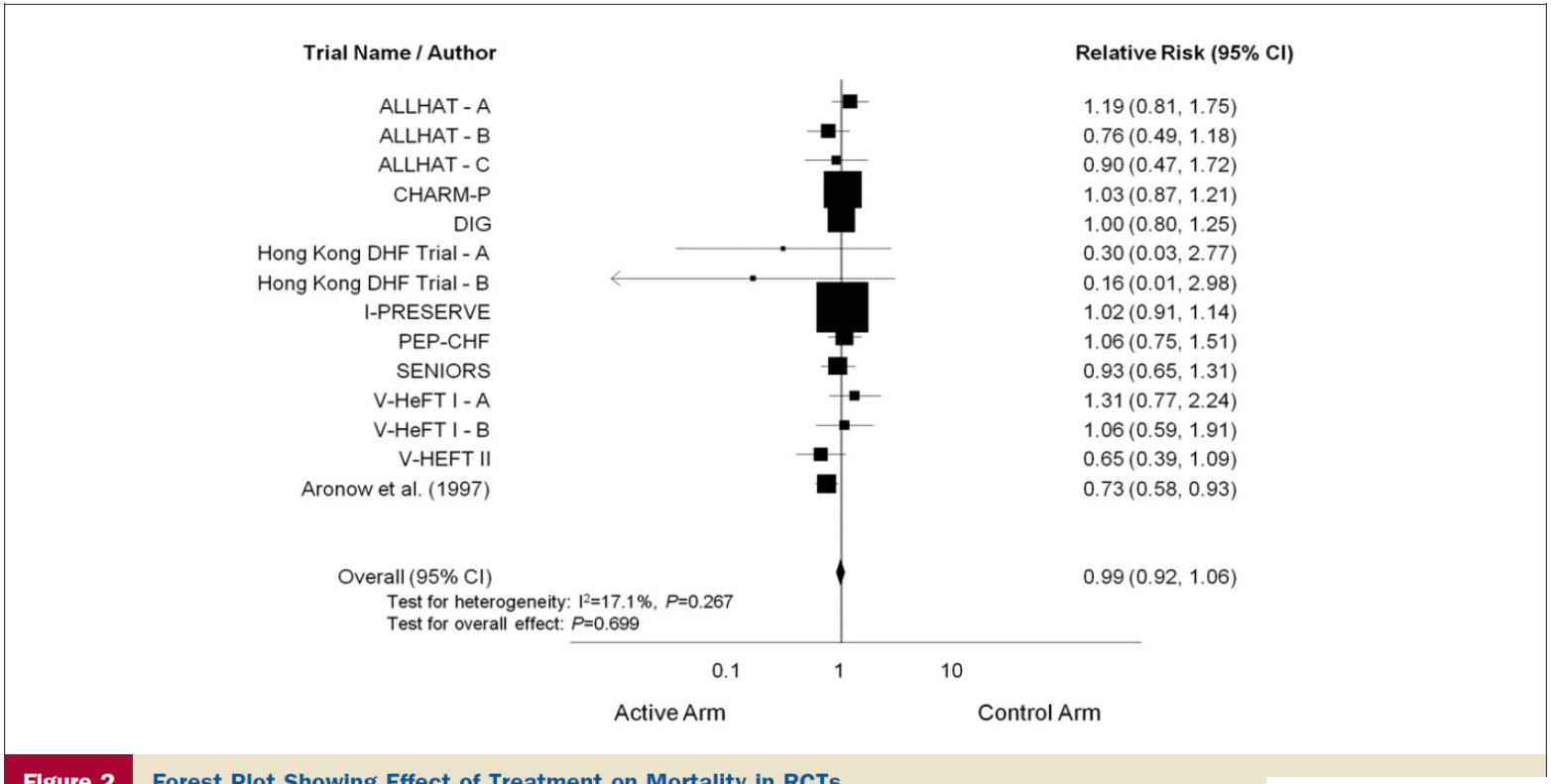


Figure 2 Forest Plot Showing Effect of Treatment on Mortality in RCTs

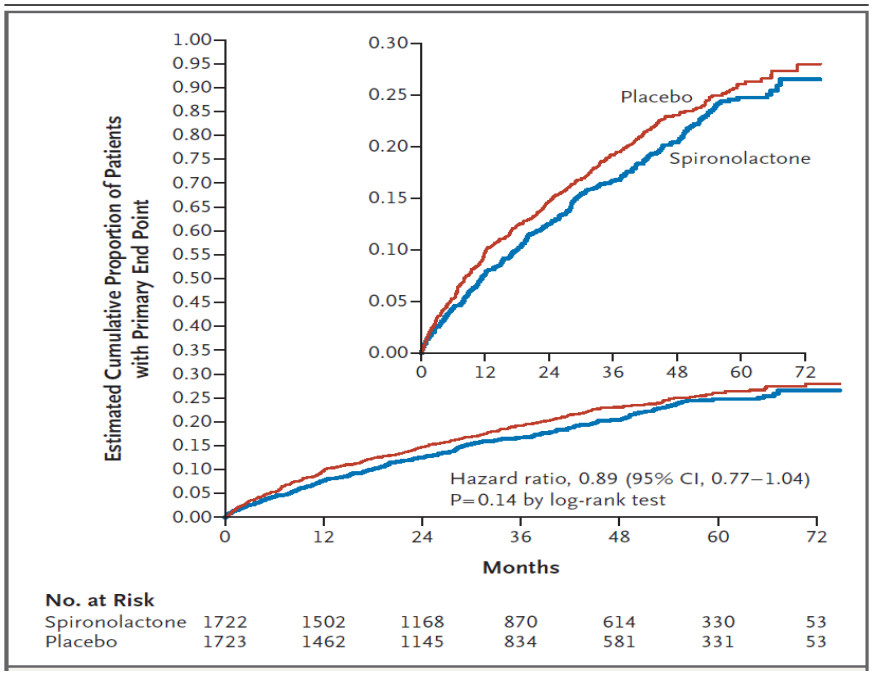
JACC Vol. 57, No. 16, 2011

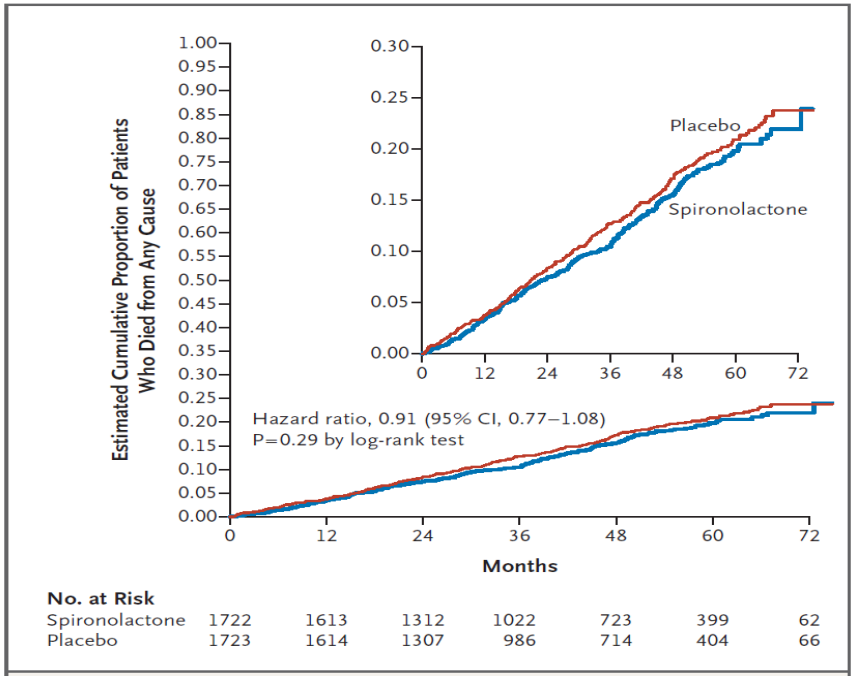
Spironolactone for Heart Failure with Preserved Ejection Fraction

NEJM

3445 patients with symptomatic HF+FEVI>45%
Spironolactone 15-45 mg vs Placebo

TOP-CAT





Composite primary out come: time CV death, aborted cardiac arrest, or hospitalization for management of HF

Estimated Cumulative Proportion of Patients Who Died from Any Cause

Heart Failure

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Regional Variation in Patients and Outcomes in the Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist (TOPCAT) Trial (*Circulation*. 2015;131:34-42.

Backgrond: In a post hoc analysis, an ≈4 fold differences was identified in the composite event rate between the 1678 patients rendomized fron Russia and Georgia compared with the 1767 enrolled the USA, Canada, Brazil and Argentina (America)

Table 1. Baseline Characteristics by Region*

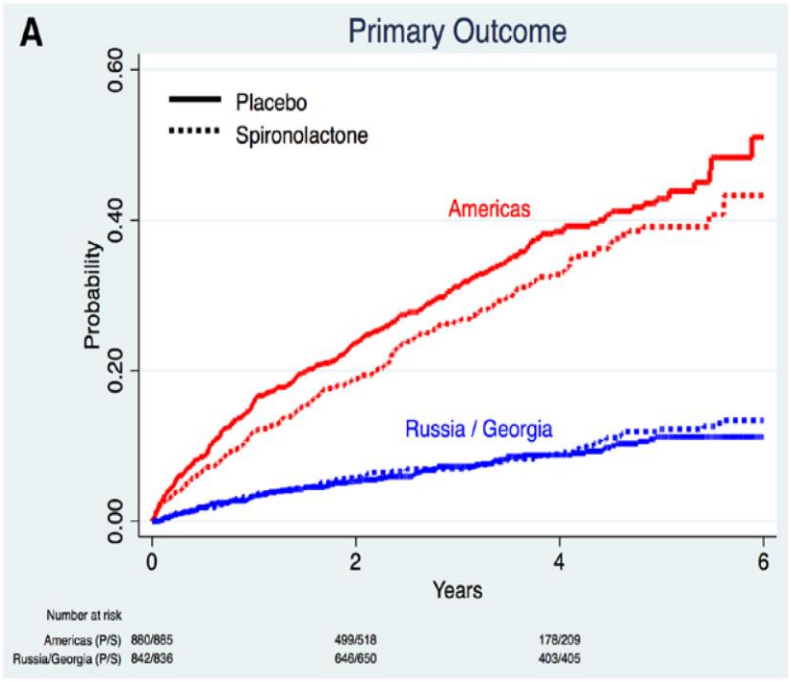
	Americas (n=1767)	Russia/Georgia (n=1678)	*P* Value
Age, y	72 (64, 79)	66 (59, 71)	<0.001
Age ≥75 y, n (%)	720 (41)	228 (14)	<0.001
Female, n (%)	882 (50)	893 (53)	0.05
White race, n (%)	1384 (78)	1678 (100)	<0.001
Ejection fraction, %	58 (53, 64)	55 (50, 60)	<0.001
NYHA class, n (%)			
1	99 (6)	10 (1)	
2	1043 (59)	1151 (69)	
3	610 (35)	511 (30)	0.006†
4	10 (1)	5 (<1)	
Stratum, n (%)			
Hospitalization	976 (55)	1488 (89)	<0.001
BNP	791 (45)	190 (11)	
Current smoker, n (%)	117 (7)	243 (14)	<0.001
Systolic blood pressure, mm Hg	129 (118, 138)	130 (120, 140)	<0.001
Diastolic blood pressure, mm Hg	70 (62, 80)	80 (80, 85)	<0.001
Heart rate, bpm	68 (61, 76)	68 (62, 75)	0.49
Body mass index, kg/m²	32.9 (28.0, 38.4)	29.4 (26.7, 33.2)	<0.001
Any cardiovascular disease history, n (%)	815 (46)	1208 (72)	<0.001
Atrial fibrillation, n (%)	743 (42)	471 (28)	<0.001
Diabetes mellitus, n (%)	788 (45)	330 (20)	<0.001
Insulin-treated	379 (21)	48 (3)	<0.001
Chronic kidney disease, n (%)	855 (48)	477 (28)	<0.001
Myocardial infarction, n (%)	359 (20)	534 (32)	<0.001
Percutaneous coronary intervention or coronary artery bypass graft surgery, n (%)	567 (32)	246 (15)	<0.001
Angina, n (%)	486 (28)	1127 (67)	<0.001
Dyslipidemia, n (%)	1250 (71)	823 (49)	<0.001
Chronic obstructive pulmonary disease, n (%)	291 (16)	112 (7)	<0.001
Stroke, n (%)	158 (9)	107 (6)	0.005
Sodium	140 (138, 142)	143 (140, 146)	<0.001
Potassium, mmol/L	4.2 (3.9, 4.5)	4.4 (4.1, 4.7)	<0.001
Creatinine, mg/dL	1.1 (0.9, 1.4)	1.0 (0.9, 1.1)	<0.001
Estimated glomerular filtration rate, mL/min per 1.73 m²	61 (49, 77)	69 (58, 81)	<0.001
BNP, pg/mL‡	234 (145, 391) (n=430)	376 (175, 702) (n=38)	0.016
NT-proBNP, pg/mL‡	900 (557, 1920) (n=257)	1045 (585, 1885) (n=143)	0.24
Hemoglobin, g/dL	12.8 (11.7, 14.0)	13.7 (12.6, 14.8)	<0.001
Medications, n (%)			
Diuretic	1573 (89)	1244 (74)	<0.001
Angiotensin-converting enzyme or angiotensin receptor blocker	1395 (79)	1505 (90)	<0.001
β-Blocker	1387 (79)	1289 (77)	0.23
Calcium channel blocker	682 (39)	612 (36)	0.19
Aspirin	1027 (58)	1223 (73)	<0.001

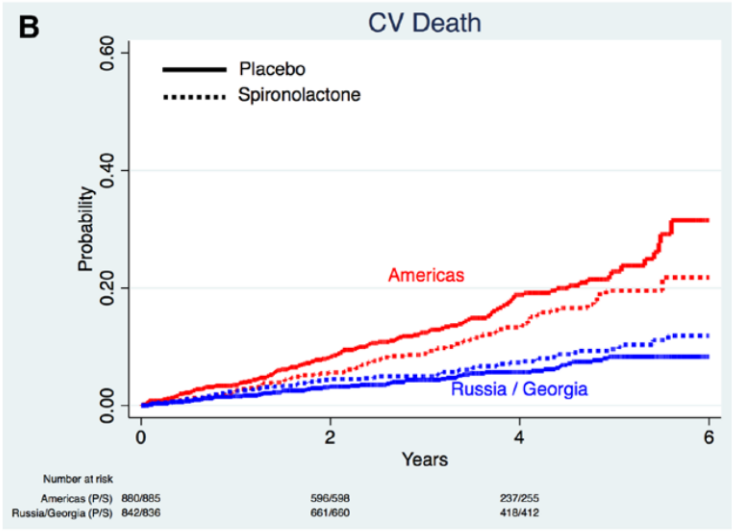
Heart Failure

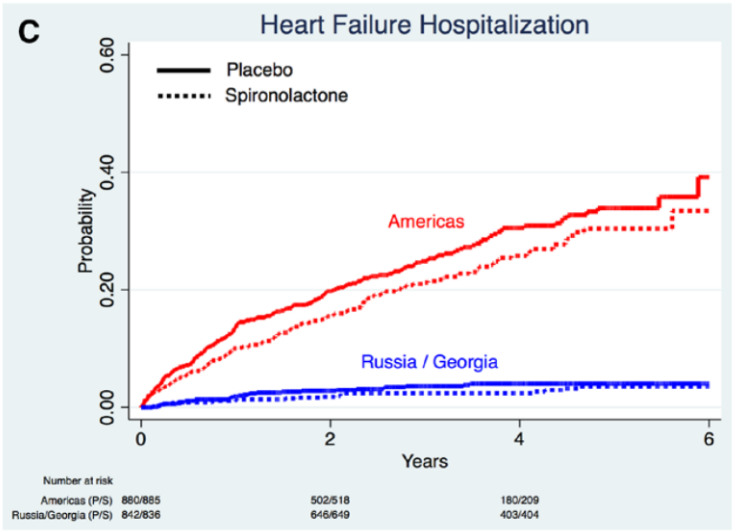
Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Regional Variation in Patients and Outcomes in the Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist (TOPCAT) Trial

Composite primary out come: time CV death, aborted cardiac arrest, or hospitalization for management of HF







(*Circulation*. 2015;131:34-42.

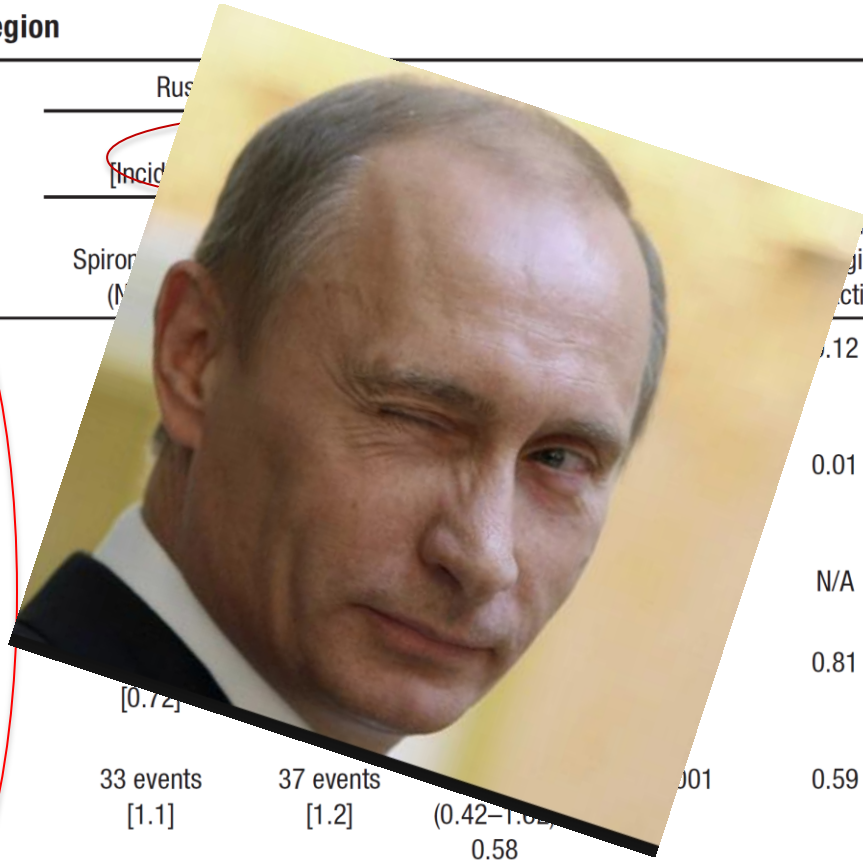
Heart Failure

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Regional Variation in Patients and Outcomes in the Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist (TOPCAT) Trial

Table 4. Summary of Trial Outcomes by Treatment Arm and Region

				Rus			
	[nt-y]			[Incid			
		HR (95% CI) *P* Value		Spiron (N			ent gion ction
		0.82 (69–0.98) .026					.12
Car		74 (-0.97) 97					0.01
Aborte							N/A
Hospital heart fail		0.82 (0.67–0.99) 0.042		[0.72]			0.81
Recurrent	361 events [13.7]	438 events [17.0]	IRR=0.75 (0.58–0.96) 0.024	33 events [1.1]	37 events [1.2]	(0.42–1.0 0.58	001 0.59



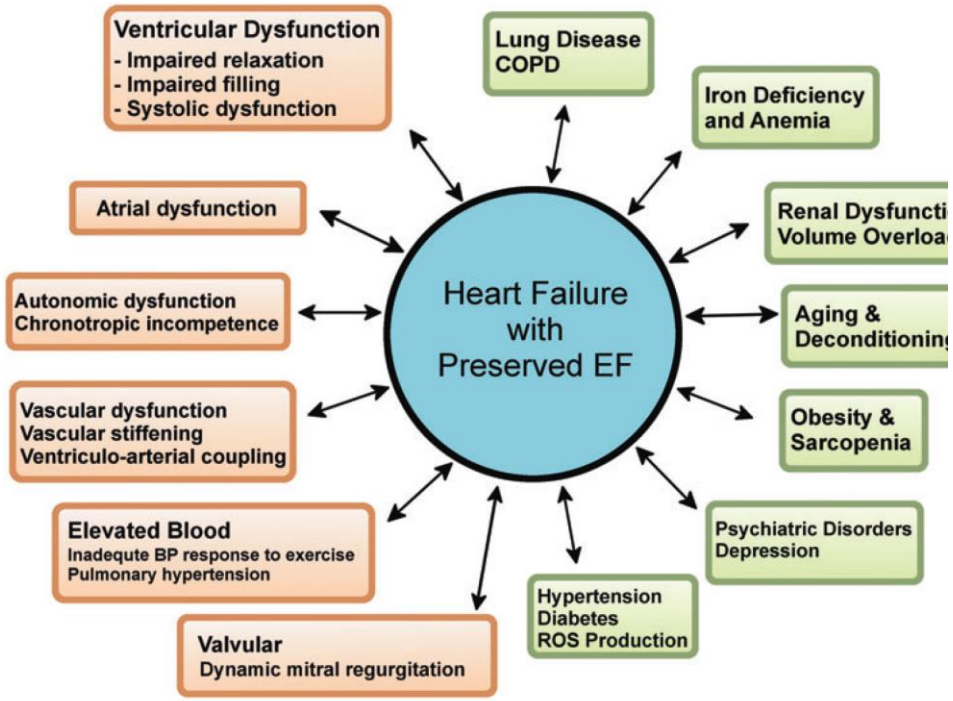
(*Circulation*. 2015;131:34-42.

New strategies for heart failure with preserved ejection fraction: the importance of targeted therapies for heart failure phenotypes

European Heart Journal (2012) **33**, 1787–1847
doi:10.1093/eurheartj/ehs104

8. Pharmacological treatment of heart failure with 'preserved' ejection fraction (diastolic heart failure)

No treatment has yet been shown, convincingly, to reduce morbidity and mortality in patients with HF-PEF. Diuretics are used to

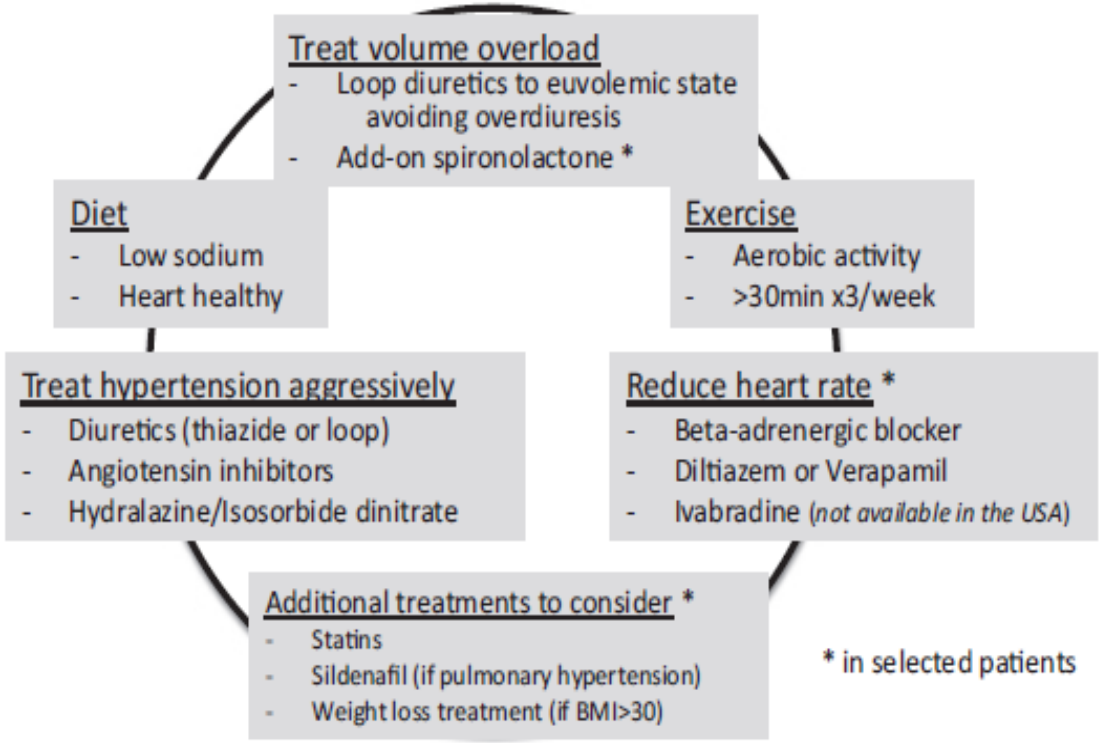


European Heart Journal (2014) **35**, 2797–2811

Tratamiento en ICFEP

Heart failure with preserved ejection fraction: Refocusing on diastole

Therapeutic approach to HFpEF



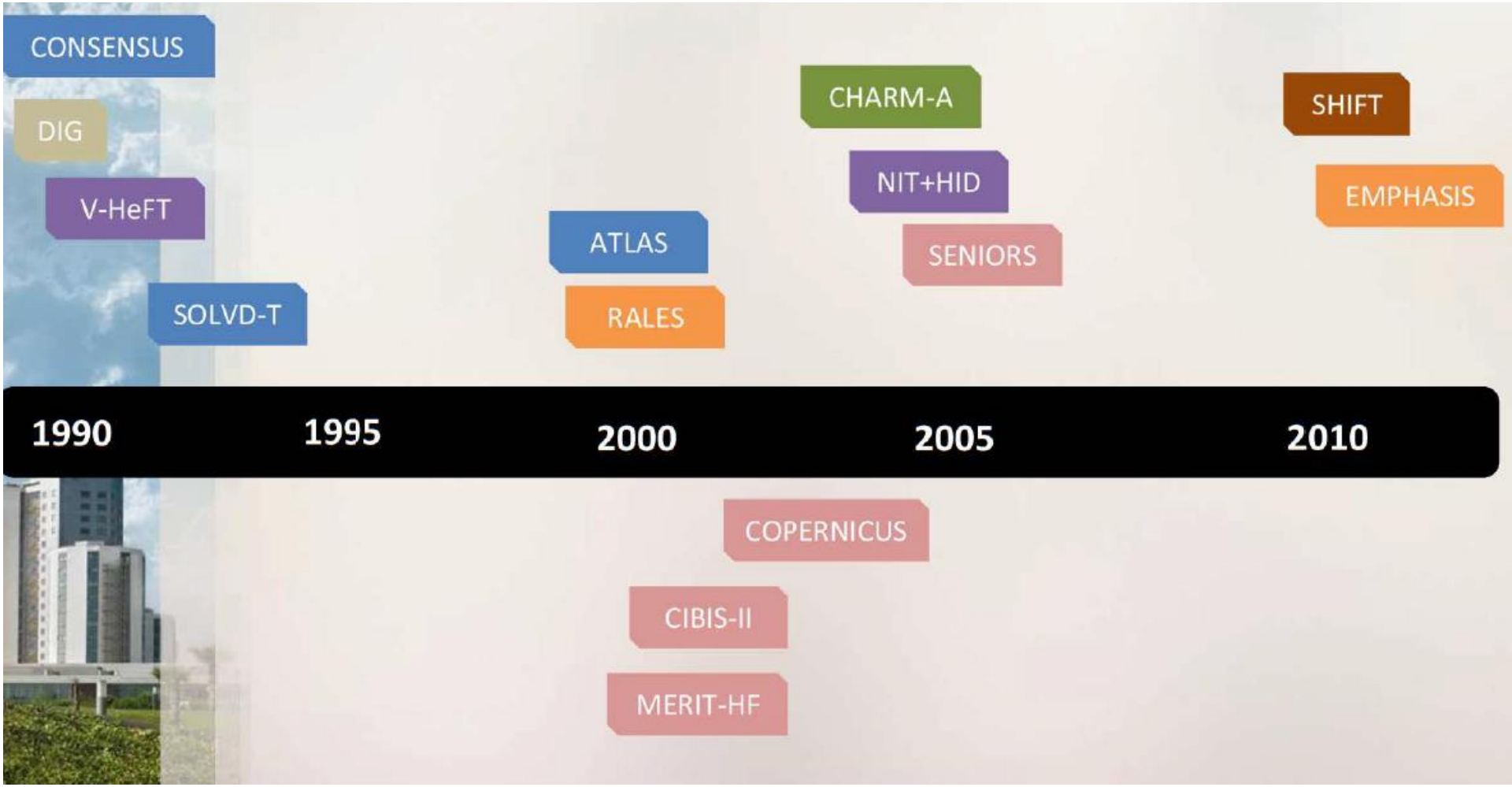
International Journal of Cardiology 179 (2015) 430–440

GUIÓN:

- Introducción y datos epidemiológicos
- Insuficiencia Cardiaca aguda
  - Fase inicial/prehospitalaria
  - Valoración inicial y datos pronósticos
  - Tratamiento farmacológico
- Derivación a Hospitalización
- Insuficiencia cardiaca crónica
  - IC con FEVI Preservada (ICFEP)
  - IC con FE VI Deprimida (ICFED)
- Valoración de Comorbilidades
- Cuidados Paliativos
- Unidades/Programas de valoración multidisciplinar

Tratamiento de la Insuficiencia Cardíaca con FE deprimida

IC con FE deprimida 1990-2013: sólo éxitos??



Tratamiento de la Insuficiencia Cardíaca con FE deprimida

Table 1: Reductions in mortality observed in randomized, controlled trials evaluating drug or device therapies in patients with chronic heart failure that were powered for all-cause mortality and resulted in Level of Evidence A recommendations in clinical guidelines.

Treatment	Target population	Mortality relative risk reduction	Trials
ACE inhibitor*	HF with LVEF ≤40%	16–27%	CONSENSUS [65], SOLVD-T [52]
Beta blocker	HF with LVEF ≤40%	34-35%	CIBIS II [61], MERIT-HF [60], COPERNICUS [59]
Mineralocorticoid receptor antagonist	HF with LVEF ≤35%	24–30%	RALES [64], EMPHASIS HF [62]
Implantable cardioverter defibrillator	HF with LVEF ≤30–35% despite optimal drug therapy	23–31%	MADIT-II [79], SCD-HeFT [78]
Cardiac resynchronization therapy ± implantable cardioverter defibrillator	HF with LVEF ≤30–35% with prolonged QRS duration ≥120–130 ms (especially LBBB) despite optimal drug therapy	24–36%	COMPANION [94], CARE-HF [95], RAFT [92]

Scientifica
Volume 2012, Article ID 279731, 16 pages
http://dx.doi.org/10.6064/2012/279731

Tratamiento de la Insuficiencia Cardíaca con FE deprimida

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

Pharmacological treatments indicated in potentially all patients with symptomatic (NYHA functional class II–IV) systolic heart failure

Recommendations	Class[a]	Level[b]
An ACE inhibitor is recommended, in addition to a beta-blocker, for all patients with an EF ≤40% to reduce the risk of HF hospitalization and the risk of premature death.	I	A
A beta-blocker is recommended, in addition to an ACE inhibitor (or ARB if ACE inhibitor not tolerated), for all patients with an EF ≤40% to reduce the risk of HF hospitalization and the risk of premature death.	I	A
An MRA is recommended for all patients with persisting symptoms (NYHA class II–IV) and an EF ≤35%, despite treatment with an ACE inhibitor (or an ARB if an ACE inhibitor is not tolerated) and a beta-blocker, to reduce the risk of HF hospitalization and the risk of premature death.	I	A

Treatments (or combinations of treatments) that may cause harm in patients with symptomatic (NYHA class II–IV) systolic heart failure

Recommendations	Class[a]	Level[b]
Thiazolidinediones (glitazones) should not be used as they cause worsening HF and increase the risk of HF hospitalization.	III	A
Most CCBs (with the exception of amlodipine and felodipine) should not be used as they have a negative inotropic effect and can cause worsening HF.	III	B
NSAIDs and COX-2 inhibitors should be avoided if possible as they may cause sodium and water retention, worsening renal function and worsening HF.	III	B
The addition of an ARB (or renin inhibitor) to the combination of an ACE inhibitor AND a mineralocorticoid antagonist is NOT recommended because of the risk of renal dysfunction and hyperkalaemia.	III	C

Beta-bloqueantes en Insuficiencia Cardiaca
Principales estudios publicados

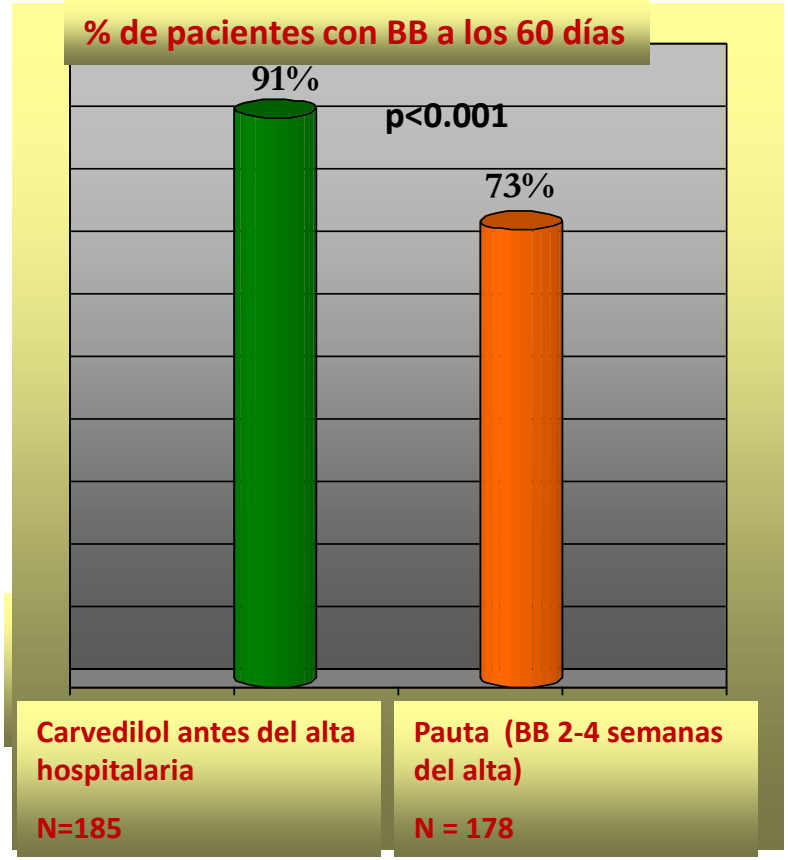
Estudio	Disminución de RR anual de mortalidad total	% Mortalidad anual		Disminución de todas las causas de hospitalización
		B-bloq	Placebo	
CIBIS H (Bisoprolol)	34% (P<0.001)	11.8%	17.3%	20% (p<0006)
MERIT-HF (Metoprolol CR/XL)	34% (p<0.001)	7.2%	11%	18% (p<0.004)
BEST (Buccinolol)	10% (p<0.13)	15%	17%	8% (p<0.08)
US CARVEDILOL (Carvedilol)	65% (p<0.001)	3.2%	7.8%	27% (p<0.0036)
COPERNICUS (Carvedilol)	35% (p<0.001)	11.4%	18.5%	20% (p<0.002)
CAPRICORN (Carvedilol)	23% (p<0.031)	12%	15%	ND
SENIOR (Nebivolol)	12.5% (p<0.21)*	9.1%*	10.4%*	5.1% (p<0.47)*

*no incluido e “primary end point”)

Tratamiento de la Insuficiencia Cardiaca Aguda: Tratamientos previos. BETABLOQUEANTES

Betabloqueantes en Insuficiencia Cardiaca
Pautas de inicio precoz (IMPACT-HF)*

- **Pacientes:**
  - **Ingresados con FEVI <40%.**
  - **Seguimiento 60 días.**
- **Tratamientos:**
  - **Carvedilol al alta, 3.125 mg bid,**
  - **Pauta habitual (cualquier BB 2-4 semanas del alta según criterio).**
- **Conclusión: El inicio previo al alta de carvedilol en pacientes con IC estable puede mejorar la prescripción de betabloqueantes.**



J Am Coll Card. 2004; 43:1534-41

Guía de uso de Inhibidores Aldosterona

Web Table 13: Practical guidance on the use of mineralocorticoid receptor antagonists in patients with systolic heart failure[a]

WHY?

To improve symptoms, reduce the risk of HF hospitalization, and increase survival

IN WHOM AND WHEN?

Indications

- Potentially all patients with persisting symptoms (NYHA Class II-IV) and an EF ≤35% despite treatment with an ACE inhibitor (or ARB) and beta-blocker

Cautions/seek specialist advice

- Significant hyperkalaemia (K^+ >5.0 mmol/L)[b]
- Significant renal dysfunction (creatinine >221 µmol/L [>2.5 mg/dL] or eGFR <30 mL/min/1.73 m^2)[b]

Drug interactions to look out for

- K^+ supplements/ K^+-sparing diuretics (e.g. amiloride and triamterene; beware combination preparations with furosemide)
- ACE inhibitors/ARBs/renin inhibitors[c]
- NSAIDs[d]
- Trimethoprim/trimethoprim-sulfamethoxazole
- 'Low-salt' substitutes with a high K^+ content

Contraindication

- Eplerenone–strong CYP3A4 inhibitors, e.g. ketoconazole, itraconazole, nefazodone, telithromycin, clarithromycin, ritonavir, and nelfinavir

HOW TO USE?

- Check renal function and electrolytes (particularly K^+)
- Start with a low dose (see above)
- Consider dose up-titration after 4–8 weeks
- Check blood chemistry at 1 and 4 weeks after starting/increasing dose and at 8 and 12 weeks; 6, 9, and 12 months; 4-monthly thereafter
- If K^+ rises above 5.5 mmol/L or creatinine rises to 221 µmol/L (2.5 mg/dL)/eGFR <30 mL/min/1.73 m^2, halve dose and monitor blood chemistry closely
- If K^+ rises to >6.0 mmol/L or creatinine to >310 µmol (3.5 mg/dL) eGFR <20 mL/min/1.73 m^2, stop MRA immediately and seek specialist advice
- A specialist HF nurse may assist with education of the patient, follow-up (in person or by telephone), biochemical monitoring, and dose up-titration

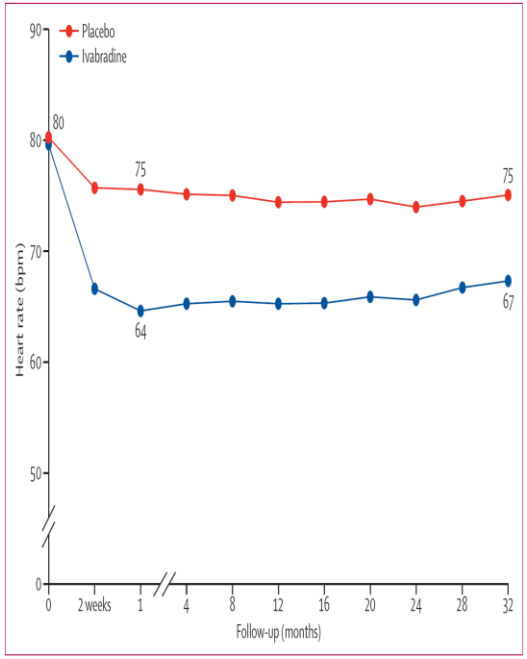
Other treatments with less-certain benefits in patients with symptomatic (NYHA class II–IV) systolic heart failure

Recommendations	Class[a]	Level[b]
ARB		
Recommended to reduce the risk of HF hospitalization and the risk of premature death in patients with an EF ≤40% and unable to tolerate an ACE inhibitor because of cough (patients should also receive a beta-blocker and an MRA).	I	A
Recommended to reduce the risk of HF hospitalization in patients with an EF ≤40% and persisting symptoms (NYHA class II–IV) despite treatment with an ACE inhibitor and a beta-blocker who are unable to tolerate an MRA.[d]	I	A
Ivabradine		
Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35%, a heart rate remaining ≥70 b.p.m., and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB).[e]	IIa	B
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35% and a heart rate ≥70 b.p.m. who are unable to tolerate a beta-blocker. Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).[e]	IIb	C
Digoxin		
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤45% who are unable to tolerate a beta-blocker (ivabradine is an alternative in patients with a heart rate ≥70 b.p.m.). Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).	IIb	B
May be considered to reduce the risk of HF hospitalization in patients with an EF ≤45% and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB).	IIb	B
H-ISDN		
May be considered as an alternative to an ACE inhibitor or ARB, if neither is tolerated, to reduce the risk of HF hospitalization and risk of premature death in patients with an EF ≤45% and dilated LV (or EF ≤35%). Patients should also receive a beta-blocker and an MRA.	IIb	B
May be considered to reduce the risk of HF hospitalization and risk of premature death in patients in patients with an EF ≤45% and dilated LV (or EF ≤35%) and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB).	IIb	B
An *n*-3 PUFA[f] preparation may be considered to reduce the risk of death and the risk of cardiovascular hospitalization in patients treated with an ACE inhibitor (or ARB), beta-blocker, and an MRA (or ARB).	IIb	B

Ivabradine and outcomes in chronic heart failure (SHIFT)

Patients

n=6558, NYHA II-IV HF, LVEF ≤35%
Sinus ryhthm >70 bpm
Admitted to hospital for HF within the previous year
Stable background treatment included BB if tolerares



Effects on primary and major secondary endpoints

	Ivabradine group (n=3241)	Placebo group (n=3264)	HR (95% CI)	p value
Primary endpoint				
Cardiovascular death or hospital admission for worsening heart failure	793 (24%)	937 (29%)	0·82 (0·75–0·90)	<0·0001
Mortality endpoints				
All-cause mortality	503 (16%)	552 (17%)	0·90 (0·80–1·02)	0·092
Cardiovascular mortality	449 (14%)	491 (15%)	0·91 (0·80–1·03)	0·128
Death from heart failure	113 (3%)	151 (5%)	0·74 (0·58–0·94)	0·014
Other endpoints				
All-cause hospital admission	1231 (38%)	1356 (42%)	0·89 (0·82–0·96)	0·003
Hospital admission for worsening heart failure	514 (16%)	672 (21%)	0·74 (0·66–0·83)	<0·0001
Any cardiovascular hospital admission	977 (30%)	1122 (34%)	0·85 (0·78–0·92)	0·0002
Cardiovascular death, or hospital admission for worsening heart failure, or hospital admission for non-fatal myocardial infarction	825 (25%)	979 (30%)	0·82 (0·74–0·89)	<0·0001

Data are number of first events (%), hazard ratio (HR; 95% CI), and p values.

Interpretation Our results support the importance of heart-rate reduction with ivabradine for improvement of clinical outcomes in heart failure and confirm the important role of heart rate in the pathophysiology of this disorder.

Lancet 2010; 376: 875–85