Ivabradine and outcomes in chronic heart failure (SHIFT)

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				<0·0001
Mortality endpoints				
All-cause mortality	503 (16%)	552 (17%)	0·90 (0·80–1·02)	0·092
Cardiovascular mortality				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				<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

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

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

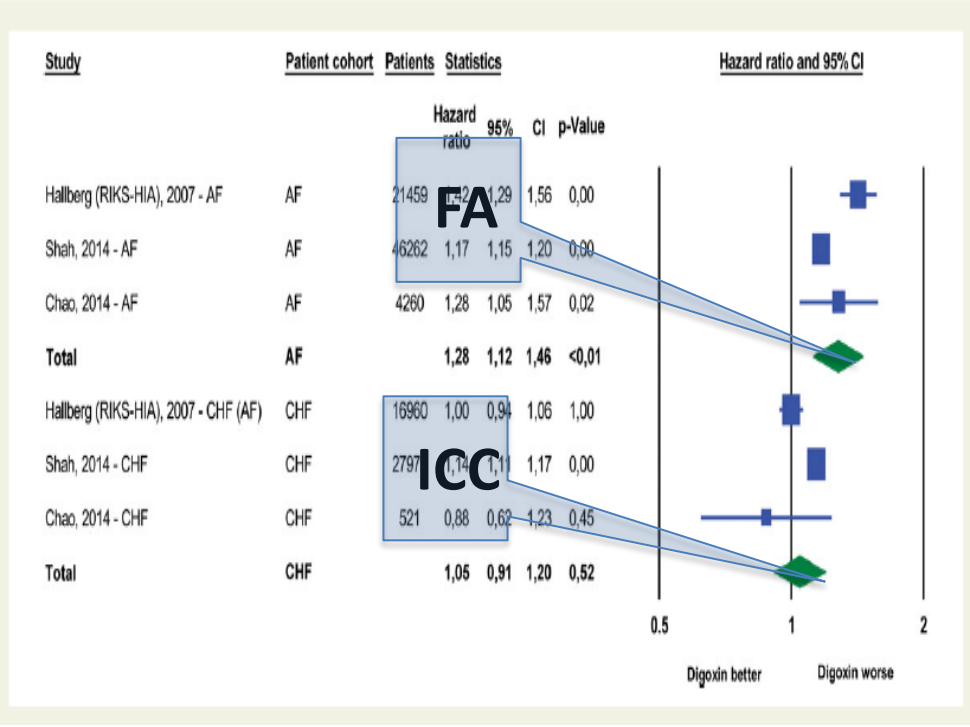
Ivabradine		
Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35%, a heart rate remaining ≥70 b.p.m., and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE 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-associated mortality: a systematic review

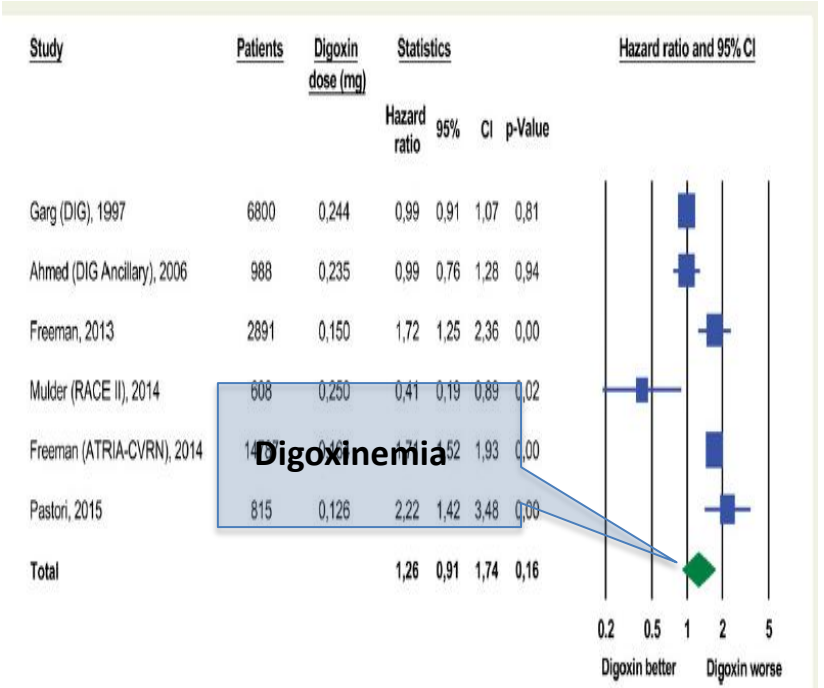
Clinical perspective

This systematic review and meta-analysis of the current literature indicates that digoxin therapy is associated with increased mortality in patients treated for atrial fibrillation or for heart failure. Our data call for randomized trials of dose-adjusted digoxin therapy in these two clinical entities under contemporary conditions.

Mortalidad en FA / IC

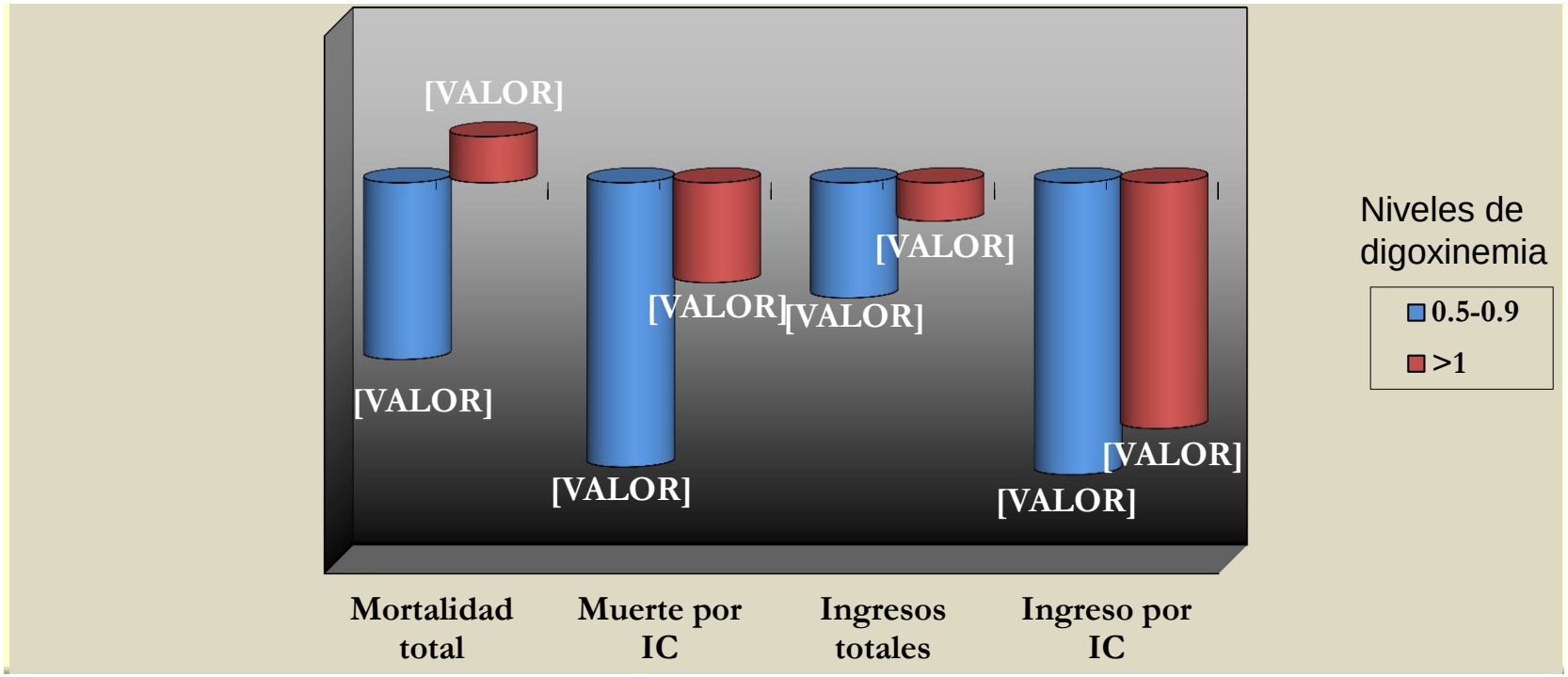


Mortalidad con digoxinemia



European Heart Journal May 4, 2015

Digoxina Insuficiencia Cardiaca
Niveles de digoxinemia.(Subestudio DIG)



Porcentaje de mortalidad y hospitalización en el estudio DIG en pacientes con concentración de 0.5-0.9 ng/ml y > 1 ng/ml

Ahmed A. Eur Heart J 2006;27:178-86

Ahmed A. Eur Heart J 2006;27:178-86

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

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**

Ivabradina

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

Neprilysin Inhibition Potentiates Actions of Endogenous Vasoactive Peptides That Counter Maladaptive Mechanisms in Heart Failure

Endogenous vasoactive peptides

(natriuretic peptides, adrenomedullin, bradykinin, substance P, calcitonin gene-related peptide)

- Neurohormonal activation
- Vascular tone
- Cardiac fibrosis, hypertrophy
- Sodium retention

Neprilysin → Inactive metabolites

Neprilysin inhibition

Inhibidor Nefrilisina+IECA (LCZ696)
efecto potenciador

Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM-HF)

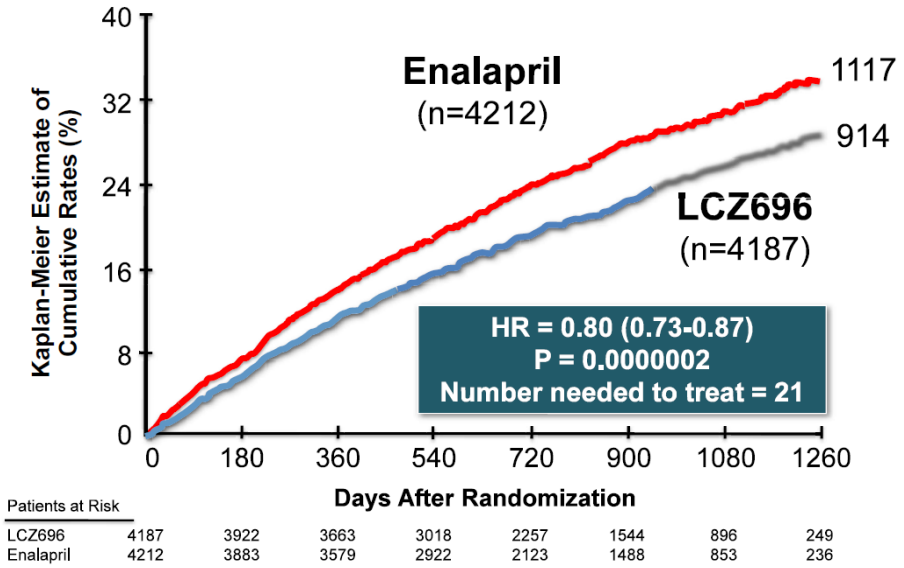
LCZ696 400 mg daily ⟷ **Enalapril 20 mg daily**

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

ın J.V. McMurray, M.D., Milton Packer, M.D., Akshay S. Desai, M.D., M.P.H., Jianjian Gong, Ph.D.,

N= 8399 patients
NYHA II-IV
LVEF < 35-40%

PARADIGM-HF: Cardiovascular Death or Heart Failure Hospitalization (Primary Endpoint)

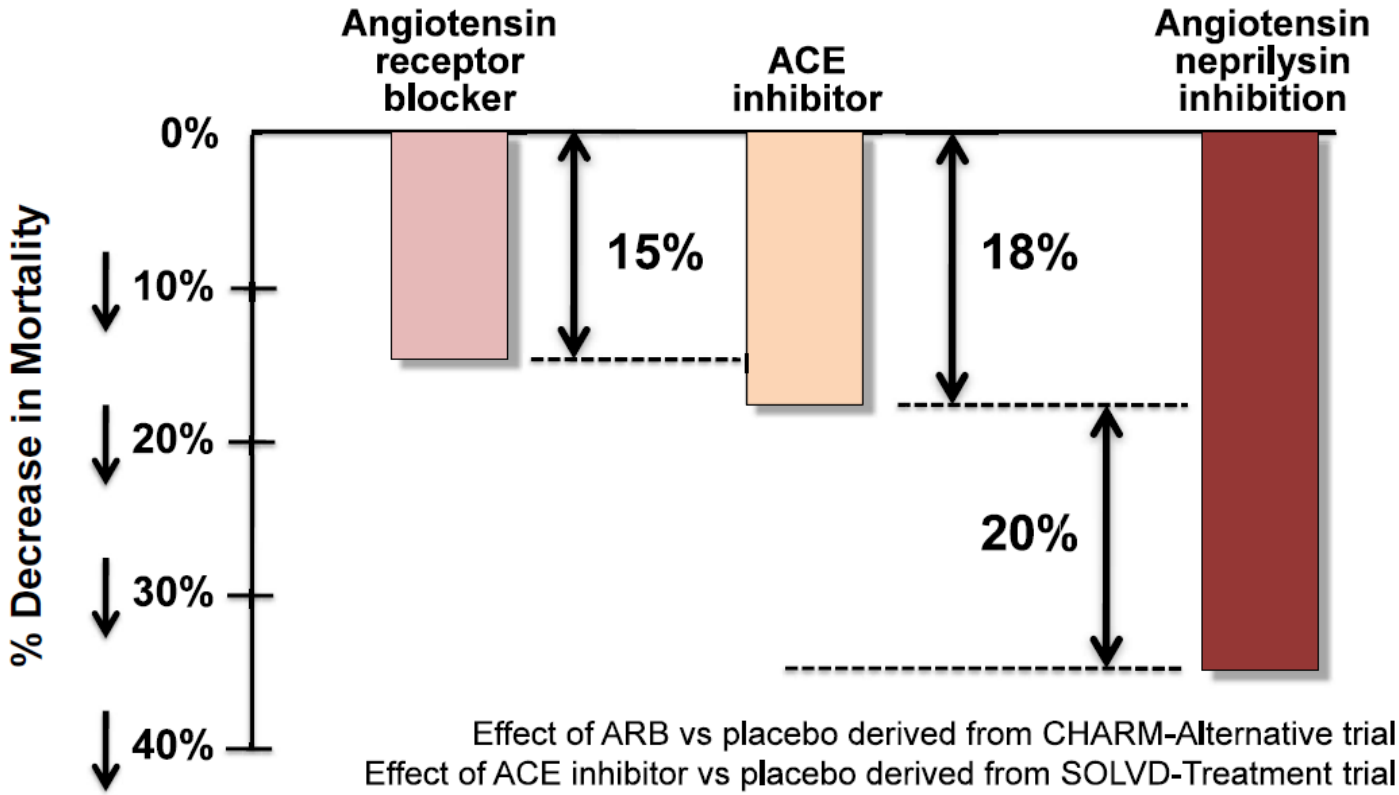


CONCLUSIONS

LCZ696 was superior to enalapril in reducing the risks of death and of hospitalization for heart failure. (Funded by Novartis; PARADIGM-HF ClinicalTrials.gov num-

N Engl J Med 2014;371:993-1004.

Angiotensin Neprilysin Inhibition With LCZ696 Doubles Effect on Cardiovascular Death of Current Inhibitors of the Renin-Angiotensin System



Effect of ARB vs placebo derived from CHARM-Alternative trial
Effect of ACE inhibitor vs placebo derived from SOLVD-Treatment trial
Effect of LCZ696 vs ACE inhibitor derived from PARADIGM-HF trial

DAI/Resincronización

DAI en Insuficiencia cardiaca
Importancia de la "Muerte Súbita"

- **Estimaciones:** 184.000-400.000 muertes anuales en USA.
- **FEVI** : Incremento exponencial con FEVI<30%.
- **NYHA:**
  - IV: 35 % de las muertes son "muerte súbita"
  - II: 64% de las muertes son "muerte súbita"
- **Tratamiento:**
  - La medidas farmacológicas (amiodarona) han dado escasos resultados.
  - DAI se ha desmarcado como la mejor opción.

DAI en IC Prevención Primaria/Secundaria

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

Recommendations for the use of implanted cardioverter defibrillators in patients with heart failure

Recommendations	Class[a]	Level[b]
Secondary prevention An ICD is recommended in a patient with HF (NYHA class II–III) and an EF ≤35% despite ≥3 months of optimal pharmacological therapy who is expected to survive for >1 year with good functional status, to reduce the risk of sudden death.	I	A
Primary prevention An ICD is recommended in a patient with HF (NYHA class II–III) and an EF ≤35% despite ≥3 months of optimal pharmacological therapy who is expected to survive for >1 year with good functional status, to reduce the risk of sudden death. (i) Ischaemic aetiology and >40 days post myocardial infarction	I	A
(ii) Non-ischaemic aetiology	I	B

PREVENCIÓN SECUNDARIA IA
- HF FEVI < 35%
- NYHA II-IV
- Episodio de arritmia ventricular grave
- Buen estado funcional
- Esperanza de vida > 1 año

PREVENCIÓN PRIMARIA IA/B
- HF FEVI < 35%
- NYHA II-IV
- 3 meses de tratamiento correcto (IECA/ARA2, BB, InhAld)
- Buen estado funcional
- Esperanza de vida > 1 año

An expanded indication for cardiac resynchronization therapy (CRT)

Recommendations for the use CRT where the evidence is strong–patients in sinus rhythm with NYHA functional class II heart failure and a persistently reduced ejection fraction [illegible] optimal medical therapy.

RESINCRONIZACIÓN BCRI IA

- HF FEVI ≤ 30%
- NYHA II-IV
- Qrs ≥130 mm
- Sintomáticos a pesar de ttº correcto (IECA/ARA2, BB, Antald)
- Buen estado funcional
- Esperanza de vida > 1 año

Recommendations	Class	Level
LBBB QRS morphology		
CRT, preferably CRT-D is recommended in patients in sinus rhythm with a QRS duration of ≥150 ms and LBBB QRS morphology, and an EF ≤30%, who are expected to survive for a year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death.	I	A

2 trials: MADIT-CRT and RAFT

www.escardio.org/guidelines

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

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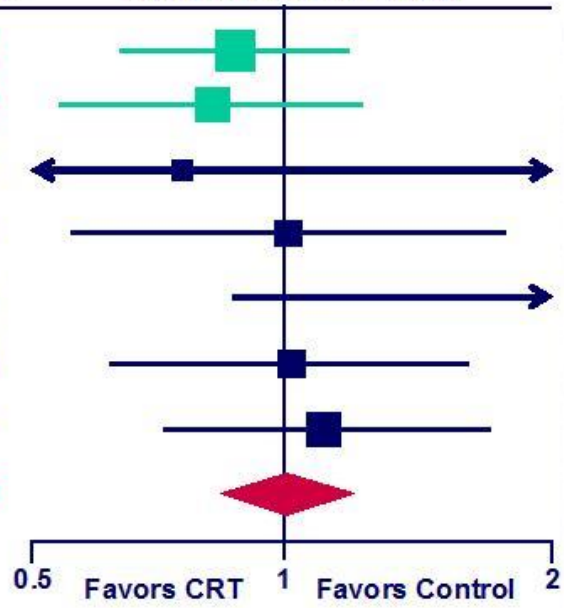
What to do about non-LBBB?

Study name	Risk Ratio	Lower Limit	Upper Limit	Z-Value	P-Value
COMPANION - Non-LBBB	0.86	0.63	1.17	-0.96	0.34
CARE-HF - RBBB	0.81	0.54	1.22	-0.99	0.32
CARE-HF - TVCD	0.75	0.24	2.33	-0.50	0.62
MADIT-CRT – RBBB	0.99	0.55	1.79	-0.03	0.97
MADIT-CRT - IVCD	1.44	0.88	2.36	1.45	0.15
RAFT - RBBB	1.00	0.62	1.62	0.00	1.00
RAFT - IVCD	1.10	0.71	1.69	0.43	0.67
Meta Analysis	0.97	0.82	1.15	-0.32	0.75



Am Heart J 2012;163:260-267.e3.

www.escardio.org/guidelines

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

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QRS morphology, duration and effect of CRT

CRT-D vs. ICD only HR for primary endpoint

Patients		RAFT	MADIT-CRT
All		0.75 (0.64, 0.87)	0.66 (0.52, 0.84)
LBBB	QRS < 150	0.89 (0.60, 1.32)	0.55 (0.35, 0.86)
	QRS ≥ 150	0.51 (0.37, 0.69)	0.41 (0.30. 0.56)
Non-LBBB	QRS < 150	1.24 (0.70, 2.19)	1.41 (0.85, 2.32)
	QRS ≥ 150	**0.83 (0.47, 1.47)**	**0.92 (0.52, 1.64)**

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

An expanded indication for cardiac resynchronization therapy (CRT)

Recommendations for the use CRT where the evidence is strong–patients in sinus rhythm with NYHA functional class II heart failure and a persistently reduced ejection fraction, despite optimal pharmacological therapy.

Recommendations	Class	Level
LBBB QRS morphology		
CRT-P/CRT-D is recommended in patients in sinus rhythm with a QRS duration of ≥ 130 ms, LBBB QRS morphology, and an EF ≤ 30%, who are expected to survive > 1 year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death.	I	A
Non-LBBB QRS morphology		
CRT preferably CRT-D should be considered in patients in sinus rhythm with a QRS duration of ≥ 150 ms, irrespective of QRS morphology, and an EF ≤ 30%, who are expected to survive > 1 year with good functional status to reduce the risk of HF hospitalization and the risk of premature death.	IIa	A

RESINCRONIZACIÓN No-BCRI IIaA

- HF FEVI ≤ 30%
- NYHA II-IV
- Qrs ≥150 mm
- Sintomáticos a pesar de ttº correcto (IECA/ARA2, BB, Antald)
- Buen estado funcional
- Esperanza de vida > 1 año

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

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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

Comorbidity in heart failure. Results of the Spanish RICA

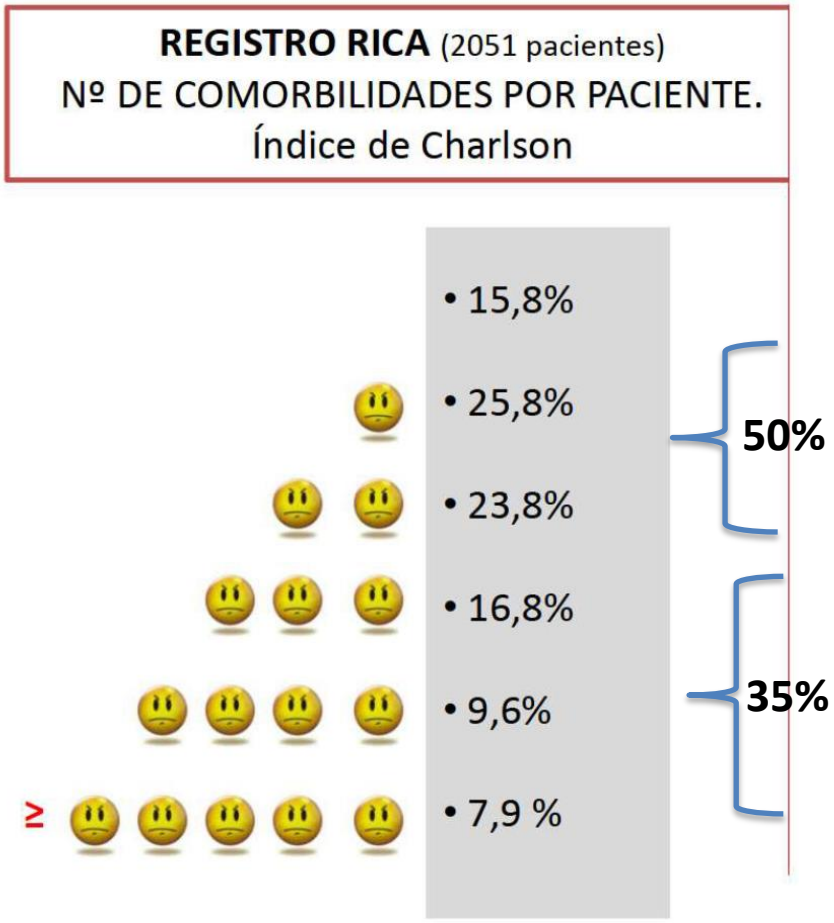
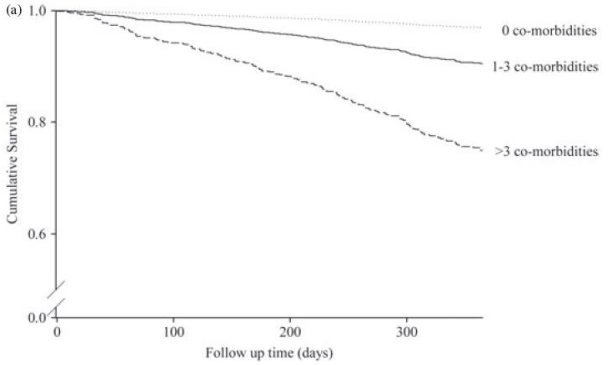


Table 2 Comorbidities frequency

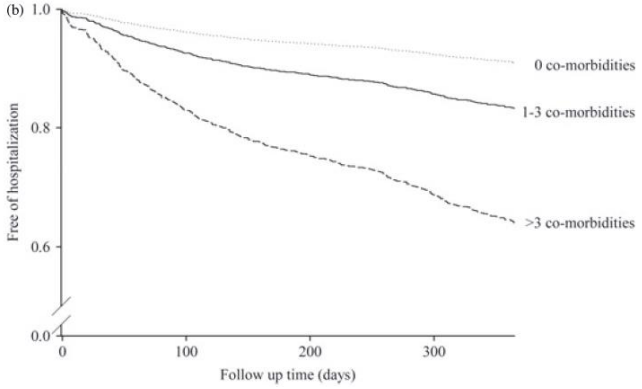
Comorbidities (ChI)	*N*	%
Myocardial infarction	452	22
Peripheral arterial disease	277	13.5
Cerebrovascular disease	276	13.5
Dementia	126	13,5
Chronic obstructive pulmonary disease	562	27.4
Connective tissue diseases	88	4.3
Peptic ulcer	205	10
Mild liver disease	107	5.2
Diabetes	909	44.3
Hemiparesis	36	1.7
Chronic renal impairment	632	30.8
Diabetes with target-organ damage	416	20.3
Any tumor	227	11.1
Leukemia	20	1
Lymphoma,	17	0.8
Severe or moderate chronic liver disease	37	1.8
Metastatic solid tumors	18	0.9
AIDS	11	0.5
Other comorbidities		
Anemia[a]	1091	53.2
Hypertension	1744	85
Obesity[b]	738	36
Dyslipidemia	962	46.9
Atrial fibrillation	1113	54.3

QJM Advance Access published July 2, 2014

Co-morbidities in patients with heart failure: an analysis of the European Heart Failure Pilot Survey



Mortality among groups of multiple co-morbilities



HF hospitalization among groups of multiple co-morbilities

Table 3 Univariate and multivariate associations between co-morbidities and all-cause mortality

	No. of deaths (%)	Univariate		Multivariate	
		HR (95% CI)	*P*-value	HR (95 % CI)	*P*-value
I. Renal		2.77 (2.08–3.69)	<0.0001	1.50 (1.06–2.11)	0.0212
II. Anemia		3.12 (2.36–4.12)	<0.0001	1.69 (1.22–2.35)	0.0017
III. Diabetes		1.57 (1.21–2.04)	<0.0001	1.74 (1.28–2.37)	0.0004
		1.76 (1.29–2.40)	<0.0001	1.37 (0.96–1.94)	0.0819
		1.35 (0.93–1.97)	0.1109	1.20 (0.79–1.82)	0.3873
		0.85 (0.42–1.72)	0.6509	1.00 (0.48–2.06)	0.9894
Hypothyroidism	27 (1%)	1.47 (0.98–2.19)	0.0617	1.31 (0.83–2.07)	0.2412
Hyperthyroidism	10 (0%)	1.41 (0.75–2.65)	0.2915	1.16 (0.58–2.30)	0.6720

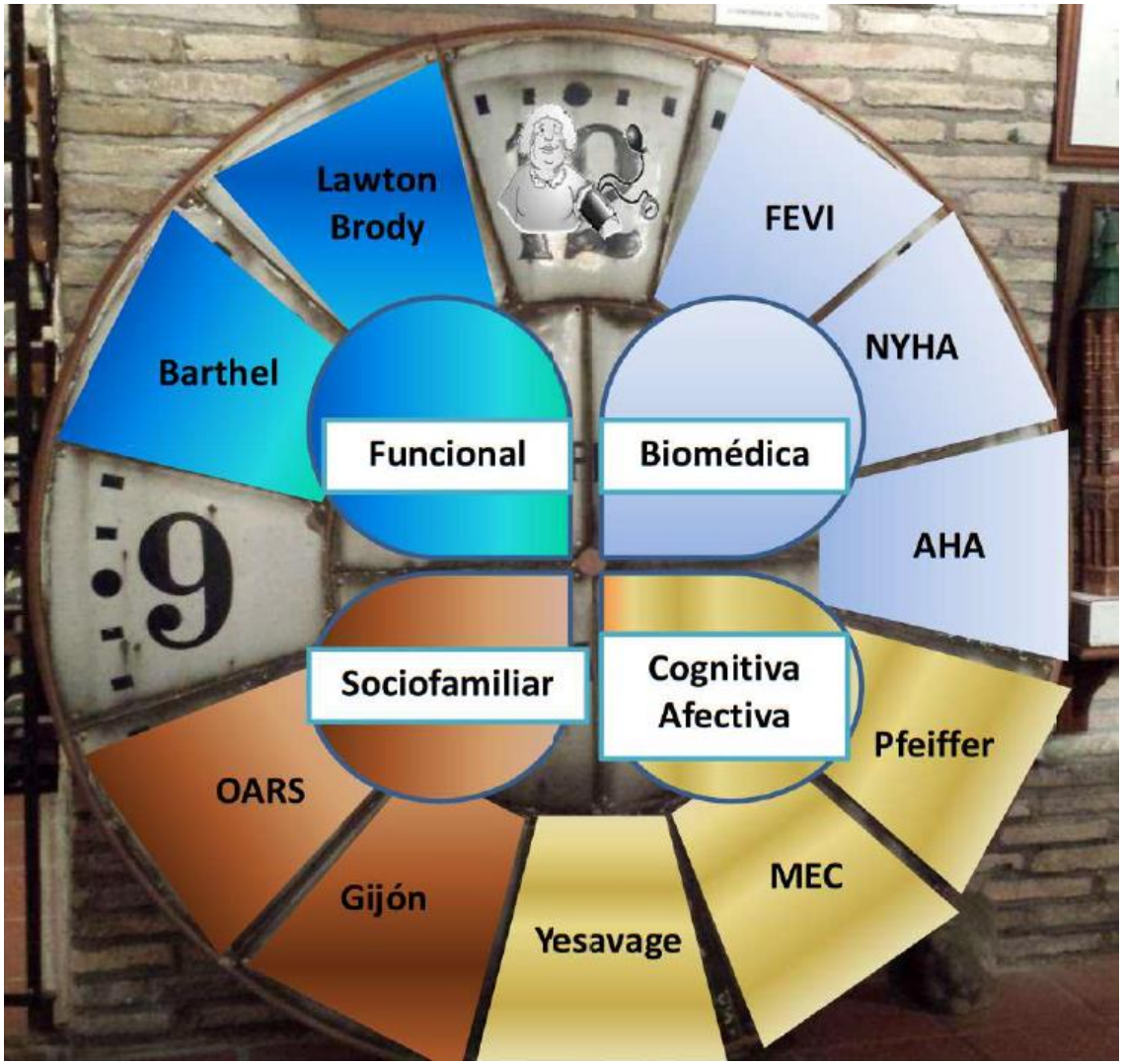
Multivariate hazard ratios (HRs) are corrected for age, sex, aetiology, hypertension, AF, congestion, body surface area, systolic blood pressure, and heart rate per co-morbidity. CI, confidence interval.

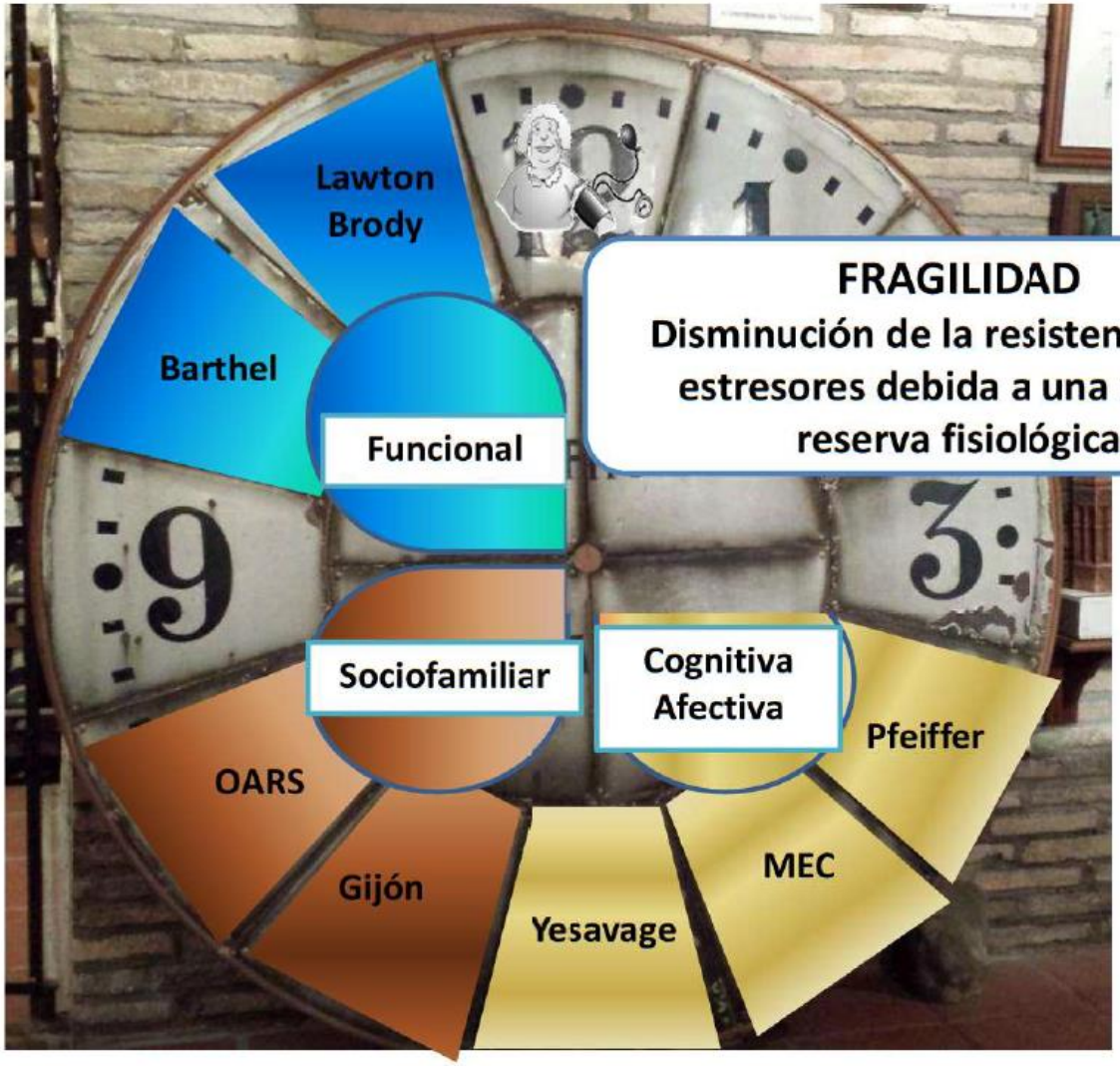
Table 4 Univariate and multivariate associations between co-morbidities and heart failure hospitalization

	Univariate		Multivariate	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
I. Renal	1.75–2.66)	<0.0001	1.59 (1.23–2.06)	0.0005
II. Anemia	1.72–2.61)	<0.0001	1.44 (1.13–1.84)	0.0034
III. Diabetes	1.21–1.79)	<0.0001	1.31 (1.04–1.65)	0.0239
	1.14–1.84)	0.0026	1.09 (0.82–1.44)	0.5745
	0.88–1.57)	0.2844	1.09 (0.79–1.52)	0.5839
	0.78–1.91)	0.3742	0.94 (0.56–1.58)	0.8156
Hypothyroidism	1.66 (1.25–2.21)	<0.0001	1.46 (1.06–2.01)	0.0221
Hyperthyroidism	1.20 (0.73–1.97)	0.4753	1.07 (0.64–1.81)	0.7877

Multivariate hazard ratios (HRs) are corrected for age, sex, aetiology, hypertension, AF, congestion, body surface area, systolic blood pressure, and heart rate per co-morbidity. CI, confidence interval.

European Journal of Heart Failure (2014) **16**, 103–111


Lawton Brody
FEVI
Barthel
NYHA
Funcional
Biomédica
AHA
Sociofamiliar
Cognitiva Afectiva
Pfeiffer
OARS
Gijón
Yesavage
MEC



FRAGILIDAD

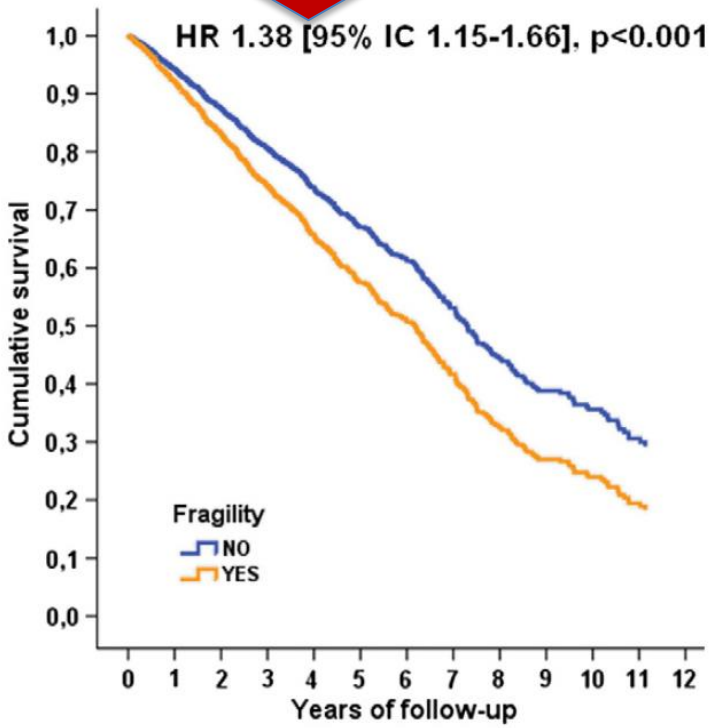
Disminución de la resistencia a los estresores debida a una menor reserva fisiológica

Fragility is a key determinant of survival in heart failure patients ☆

Paloma Gastelurrutia [a], Josep Lupón [b,c], Salvador Altimir [b,c]

La Fragilidad es un factor independiente de mortalidad en Insuficiencia Cardiaca

Fragility: the presence of at least one abnormal evaluation
* **Barthel < 90**
* **OARS <10 in women and 6 in men**
* **Pfeiffer test >3 (±1 depending on edcational grade)**
* **Abreviated GDS ≥1 positive response for depression**



Prevalence of abnormal geriatric scores

Meassurements	Total: 1314	
Abnormal Barthel	268	20.4%
OARS scale	175	13.3%
Pfeiffer test	69	5.3%
Depressive symtoms	412	31.4%
Fragility	581	44.2%

International Journal of Cardiology 175 (2014) 62–66

Valoración del tratamiento en la comorbilidad

Age and Ageing 2013; **42:** 62–69
doi: 10.1093/ageing/afs100
Published electronically 21 August 2012

Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity

Lloyd D. Hughes[1], Marion E. T. McMurdo[2], Bruce Guthrie[3]

Drug-disease and drug-drug interactions: systematic examination of recommendations in 12 UK national clinical guidelines

Siobhan Dumbreck,[1] Angela Flynn,[1] Moray Nairn,[2] Martin Wilson,[3] Shaun Treweek,[4] Stewart W Mercer,[5] Phil Alderson,[6] Alex Thompson,[7] Katherine Payne,[7] Bruce Guthrie[1]

Fortin et al. BMC Family Practice 2011, 12:74
http://www.biomedcentral.com/1471-2296/12/74

BMC Family Pr

RESEARCH ARTICLE Open Ac

Canadian guidelines for clinical practice: an analysis of their quality and relevance to the care of adults with comorbidity

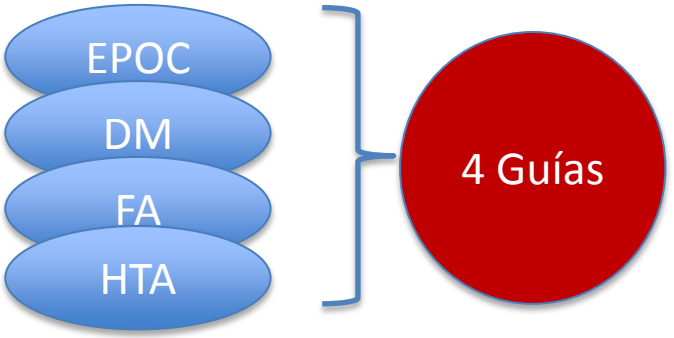
Martin Fortin*, Eric Contant, Catherine Savard, Catherine Hudon, Marie-Eve Poitras and José Almirall

Multi-drug therapy in chronic condition multimorbidity: a systematic review

Lucy Doos[a,*], Eyitope O Roberts[b], Nadia Corp[c] and Umesh T Kadam[d]

Martin Fortin , Eric Contant, Catherine Savard, Catherine Hudon, Marie-Eve Poitras and José Almirall

- Las GPC no ofrecen recomendaciones para pacientes con múltiples comorbilidades
- Las GPC no ofrecen evidencia científica para pacientes > 65 años.
- Raramente dan indicaciones para pacientes con tres o más comorbilidades.
- Su aplicación rígida:
  - Fomenta la polifarmacia
  - Fomenta los errores en la administración.
  - Aumenta los efectos adversos
  - Facilita las interacciones medicamentosas
  - Aumenta las hospitalizaciones
  - Da recomendaciones de vida insostenibles



Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association.

AHA/ACC/HHS Strategies to Enhance Application of Clinical Practice Guidelines in Patients With Cardiovascular Disease and Comorbid Conditions: From the American Heart Association, American College of Cardiology, and US Department of Health and Human Services

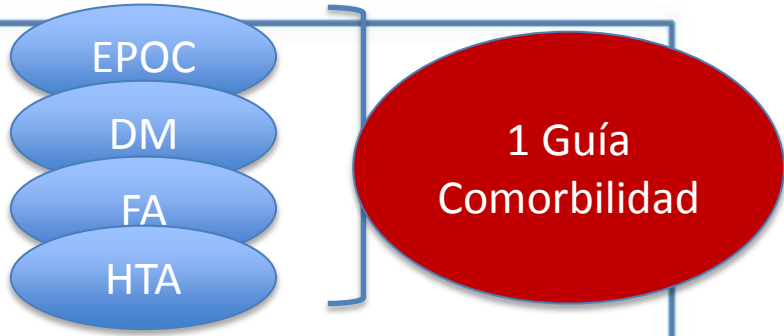
Donna K. Arnett, Richard A. Goodman, Jonathan L. Halperin, Jeffrey L. Anderson, Anand K. Parekh and William A. Zoghbi

Circulation. 2014;130:1662-1667

IOM and DHHS Meeting on Making Clinical Practice Guidelines Appropriate for Patients with Multiple Chronic Conditions

Richard A. Goodman, Ann Fam Med 2014;256-259.

- Integrar la comorbilidad
- Elaboración multidisciplinar
- Evidencia múltiple
- Valorar la aplicabilidad
- Orientadas al paciente
- Fomentando la coordinación entre proveedores de salud



Modelo de recomendaciones de tratamiento orientadas

Table 2: Summary of the literature most relevant to the concurrent management of HF and the ten pre-specified concurrent conditions

Co-morbidity	Prevalence & Impact on heart failure (HF)	Management Options	Clinical Caveats & Considerations
Renal impairment/disease	• Renal dysfunction is present in 35–50% of CHF patients and is often chronic in nature (110) • It is consistently an independent marker of adverse outcome in HF (110, 111) • HF mortality is significantly higher in patients with baseline renal impairment (RI) (112, 113) • Renal impairment can range from reversible ischemic damage to renal failure requiring short- or long-term renal replacement therapy (114)	• Clinical guidelines routinely recommend the use of ACE inhibitors or ARBs to treat patients with comorbid renal and cardiac diseases (115) • The ARB valsartan effectively reduces glomerular filtration rate and morbidity in those with HF and Chronic Kidney Disease (CKD)-The Valsartan in Heart Failure RCT (Val-HeFT) (116) • Beta blockers provide benefits in HF and renal dysfunction with no contraindications (117) • Vasopressin antagonists may improve fluid retention, hyponatremia and renal dysfunction in HF, but further research is needed into long-term benefits and contraindications (118) • There is limited evidence regarding the benefits of Implantable Cardioverter Defibrillator (ICD) therapy for patients with HF and renal dysfunction, but there do not appear to be contraindications (119, 120) • Cardiac resynchronization therapy may provide the largest survival benefit in HF	• ACE inhibitors and ARBs are contraindicated in patients with a history of angioedema (126). • If renal function deteriorates to a significant degree (e.g. 25% increase in serum creatinine or 15% decrease in eGFR), the risk benefit effect of treatment should be reevaluated (127) • Valsartan is safe and well-tolerated in those with stable to moderate HF (116, 128) • Nesiritide should not be used in patients with concurrent renal impairment as it is associated with an increased risk of mortality (129)

ORIGINAL

Pacientes con el diagnóstico de insuficiencia cardiaca en Atención Primaria: envejecimiento, comorbilidad y polifarmacia

Gisela Galindo Ortego[a,b,*] Inés Cruz Esteve[a,b] Jordi Real Gatius[b]
Leonardo Galván Santiago[c] Carmen Monsó Lacruz[d] Plácido Santafé Soler[e]

POLIFARMACIA

ADHERENCIA AL TRATAMIENTO

Tratamiento farmacológico de los pacientes con insuficiencia cardíaca

	Total
N° de principios activos, media	8,69 ± 3,48
Cuartiles 25-50-75	6-8-11
Tratamiento para la insuficiencia cardiaca	
Diuréticos %	73,9
IECA/ARAII %	66,4
Beta-bloqueantes %	29,9
Glucósidos cardíacos %	19,9
IECA/ARAII + BB %	24,9
Otros fármacos	
Antiagregantes/anticoagulantes %	59,9
Anti úlcera péptica %	58,3
Antibióticos %	51,1
Antiasmáticos %	37
Aines %	33,4
Ansiolíticos %	30,6
Hipolipemiantes %	28,7
Analgésicos %	27
Calcio antagonistas %	23,6
Nitritos %	21,9
Antidepresivos %	20,75
AINE tópics %	20,3
Hipoglicemiantes %	19,5
Antigripales/antitusígenos %	18,7
Hipnóticos %	16,7
Neurolépticos %	13,9
Insulina %	8,9
Antiarrítmicos %	7,5
Antirresotivos óseos %	7,4
Alfa bloqueantes %	6,2
Analgésicos narcóticos %	4,6

» Look Inside » Get Access

Original Research Article
Drugs & Aging
July 2014, Volume 31, Issue 7, pp 541-546

First online: 14 May 2014

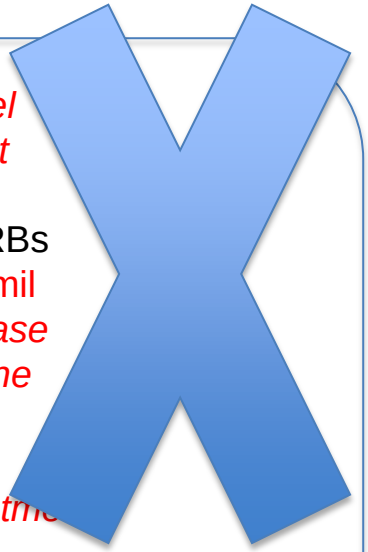
Appropriateness of Medications Prescribed to Elderly Patients with Advanced Heart Failure and Limited Life Expectancy Who Died During Hospitalization

Montserrat Barceló ✉ , Olga Torres, Domingo Ruiz, Jordi Casademont

Pacientes con NYHA III-IV, con pronóstico vital inferior a 6 meses al ingreso y que fallecen durante el mismo.

AAS or clopidogrel
Oral anticoagulant
Statin
ACE inhibitors/ARBs
Diltiazem/Verapamil
Acetylcholinesterase inhibitor/memantine
Iron
Vitamins
Osteoporosis treatme
Loop diuretics
Thiazides
Beta-Blockers
Aldosterone inhibitors
Antidepressants
- SSRIs
- TCAs
- Other

Bezodiazepin
Analgesics
Opiates:
- Tratadol
- Fentanyl
- Morphine



•Barceló M. Drugs Aging 2014; 31: 541-6

Management of co-morbidities

- Anaemia
- Angina
- Asthma/COPD
- Cachexia
- Cancer
- Depression
- Diabetes mellitus
- Erectile dysfunction
- Gout
- Hyperlipidaemia
- Hypertension
- Iron deficiency
- Kidney dysfunction
- Obesity
- Prostatic obstruction
- Sleepdisturbance/ sleep disordered breathing

www.escardio.org/guidelines

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

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Management of co-morbidities

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- /
- ction
- Prostatic obstruction
- Sleepdisturbance/ sleep disordered breathing

ANAEMIA IN HEART FAILURE

www.escardio.org/guidelines

European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

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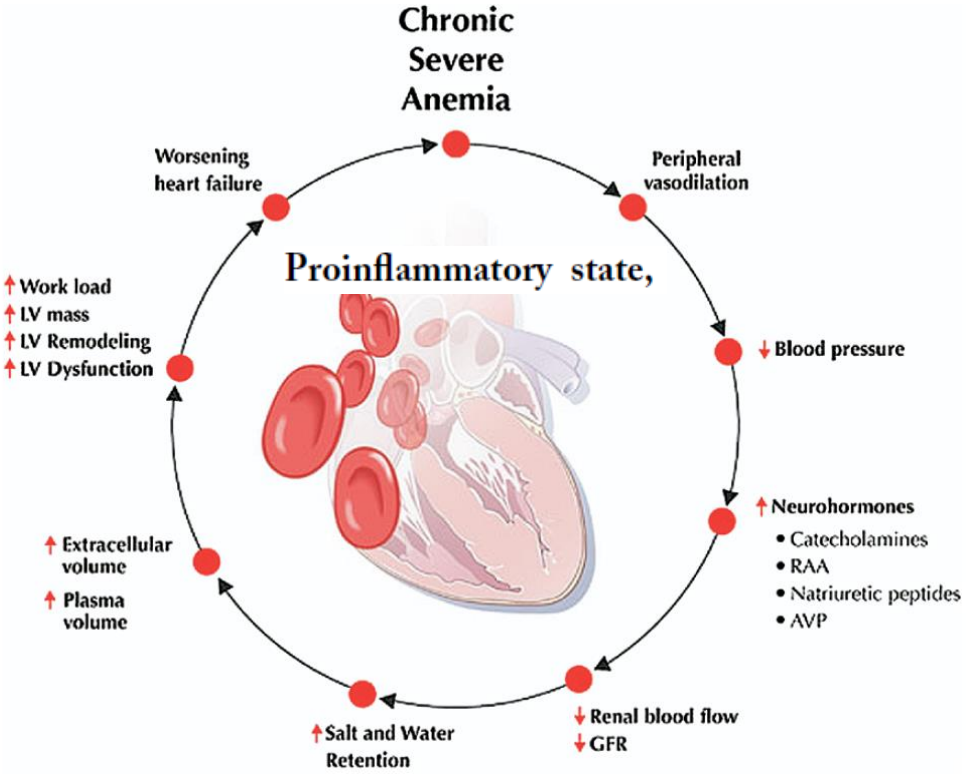
Anemia and Chronic Heart Failure

Implications and Treatment Options

Prevalence of Anemia in HF

The World Health Organization defines anemia as hemoglobin (Hgb) <13.0 g/dl in men and <12.0 g/dl in women

- Comorbilidad más frecuente
- Su incidencia aumenta con la edad, progresión de IC y deterioro de función renal
- Factor independiente de mortalidad, reingreso y deterioro de calidad de vida



(J Am Coll Cardiol 2008;52:501–11)

Anemia and Chronic Heart Failure

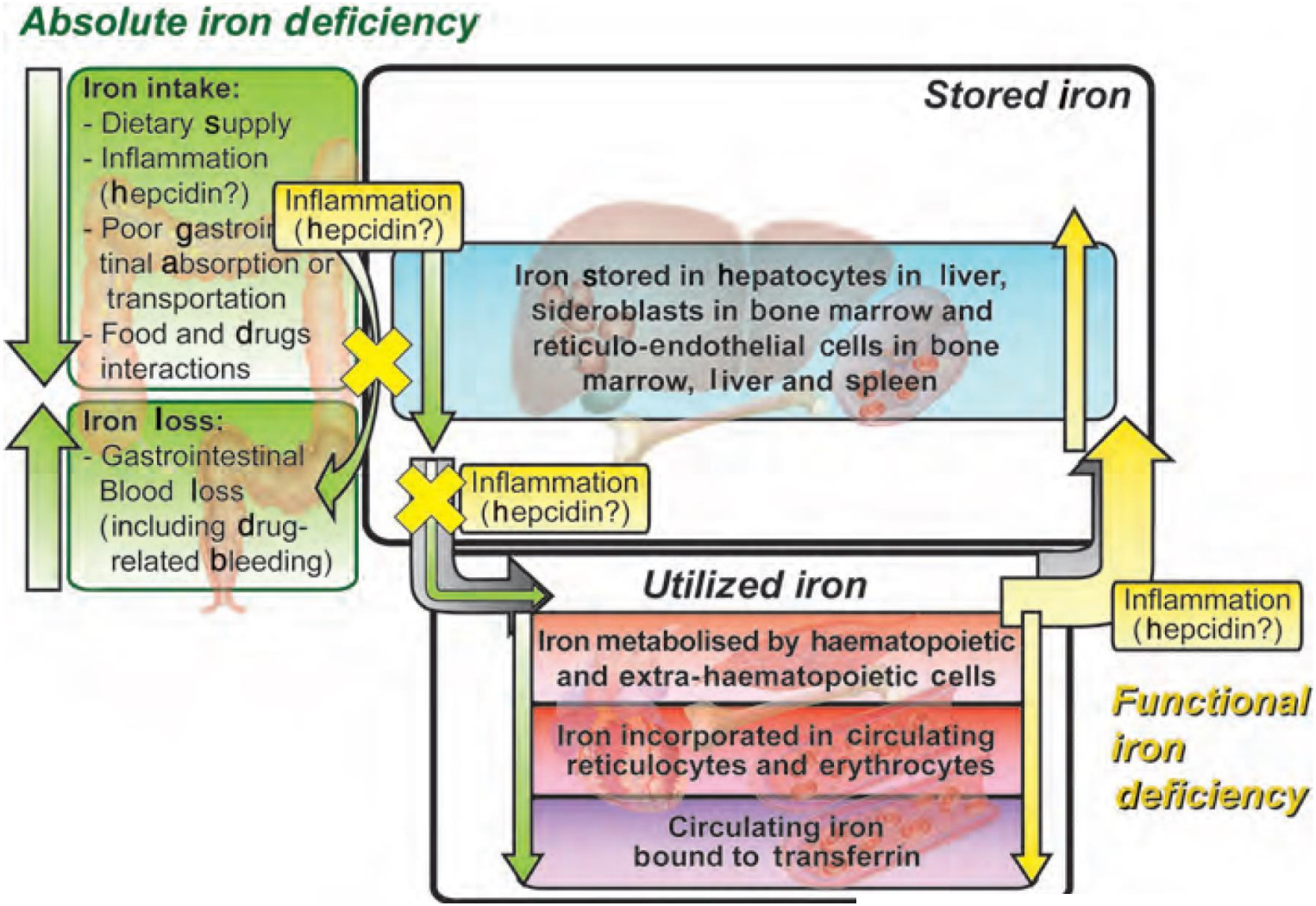
Implications and Treatment Options

ETIOLOGÍA:

- Pseudoanemia por hemodiución
- Ferropenia absoluta: <Fe, Ferritina< 30 ng/ml, Sat Trf<20%
  - Déficit de aporte
  - Malabsorción
  - Pérdidas digestivas
- Ferropenia funcional: *Ferritina < 100 ng/ml ó 100-300 ng/ml+Sat Trf<20%*
  - Déficit de absorción y movilización de los depósitos mediado por fenómenos y mediadores de la inflamación
- Anemia de trastornos crónicos
  - 60% Insuficiencia renal
  - 10% la propia IC
  - 30% comorbilidades
- Déficit de factores madurativos (Vit B12, fólico) ó hipotiroidismo

(J Am Coll Cardiol 2008;52:501–11)

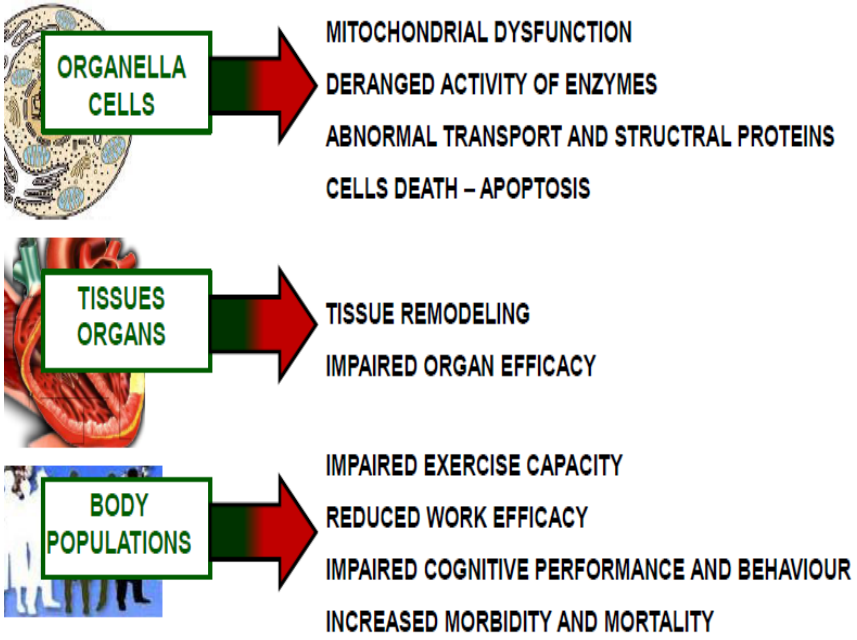
The concept of absolute and functional iron deficiency.



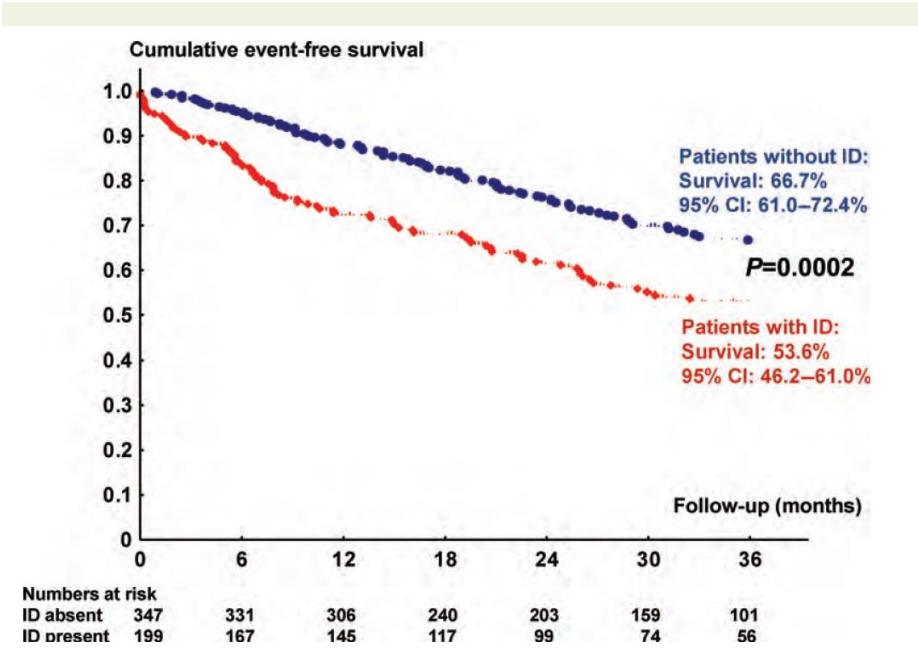
(J Am Coll Cardiol 2008;52:501–11)

Iron deficiency and heart failure: diagnostic dilemmas and therapeutic perspectives

Consequences of iron deficiency



Three year event free survival in 546 patients with sistolic HF with vs without iron deficiency

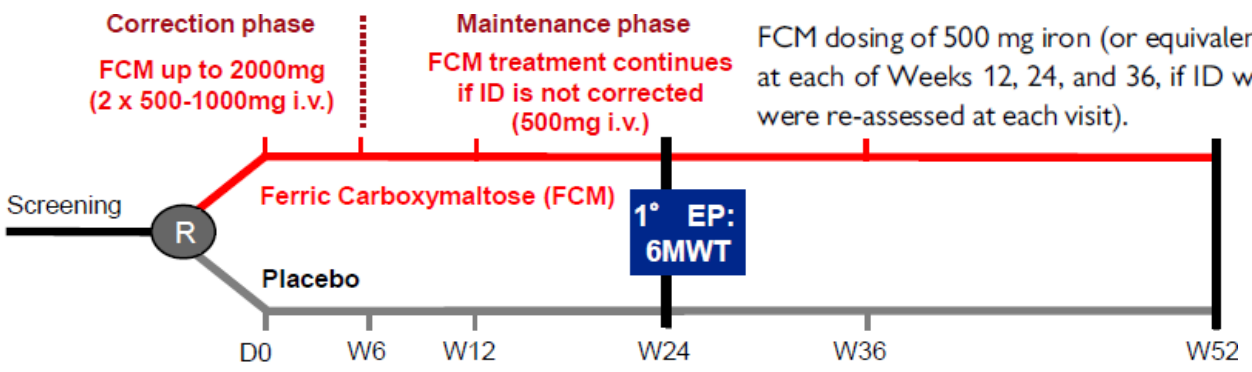


European Heart Journal (2013) **34**, 816–826

Effect of ferric carboxymaltose on functional capacity in patients with heart failure and iron deficiency

CONFIRM-HF

- **Main inclusion criteria:**
  - ✓ NYHA class II / III, LVEF ≤45%
  - ✓ BNP > 100 pg/mL or NT-proBNP > 400 pg/mL
  - ✓ Iron deficiency: serum ferritin <100 ng/mL or 100-300 ng/mL if TSAT <20%
  - ✓ Hb < 15 g/dL



Primary endpoint:
change in 6-minutes walking test distance at Week 24

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European Heart Journal
doi:10.1093/eurheartj/ehu385

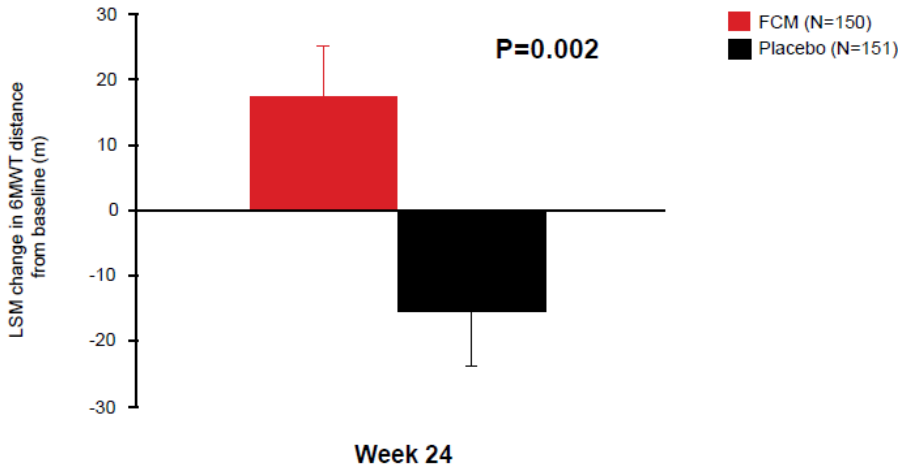
Effect of ferric carboxymaltose on functional capacity in patients with heart failure and iron deficiency

CONFIRM-HF

Primary endpoint: change in 6-minutes walking test distance at Week 24

FCM improved 6MWT at week 24

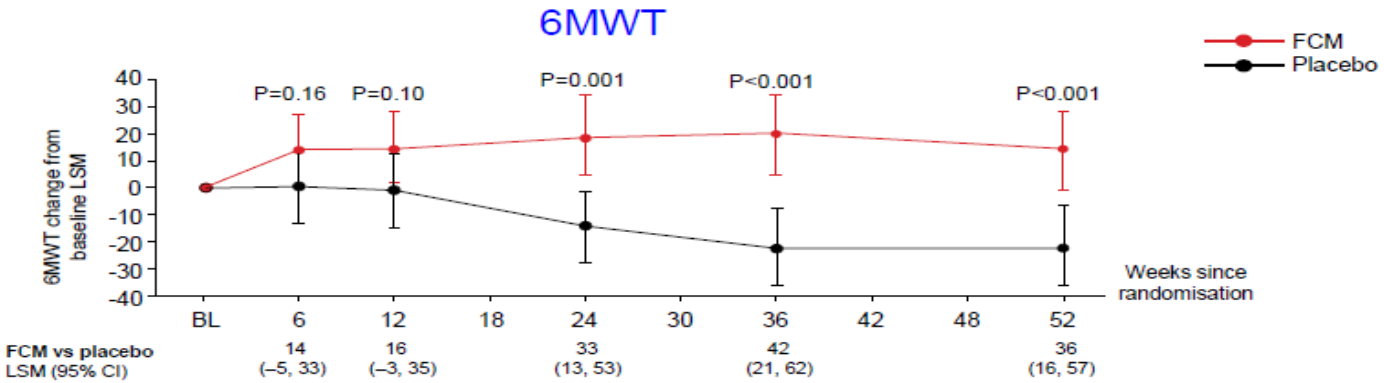
FCM vs placebo: 33 ± 11 m *(least squares mean ± SE)*

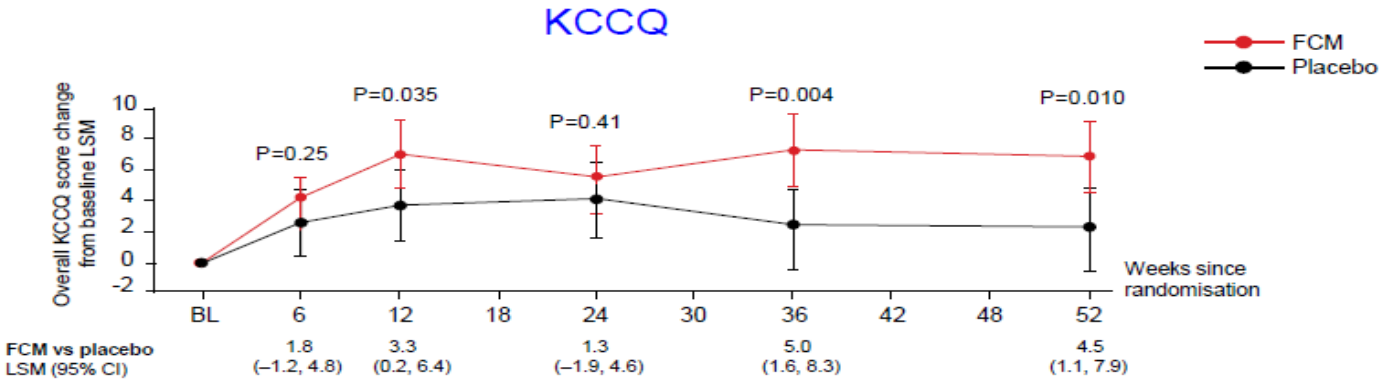


Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency†

Secondary endpoints: Changes in 6MWT distance and QoL over time

CONFIRM-HF



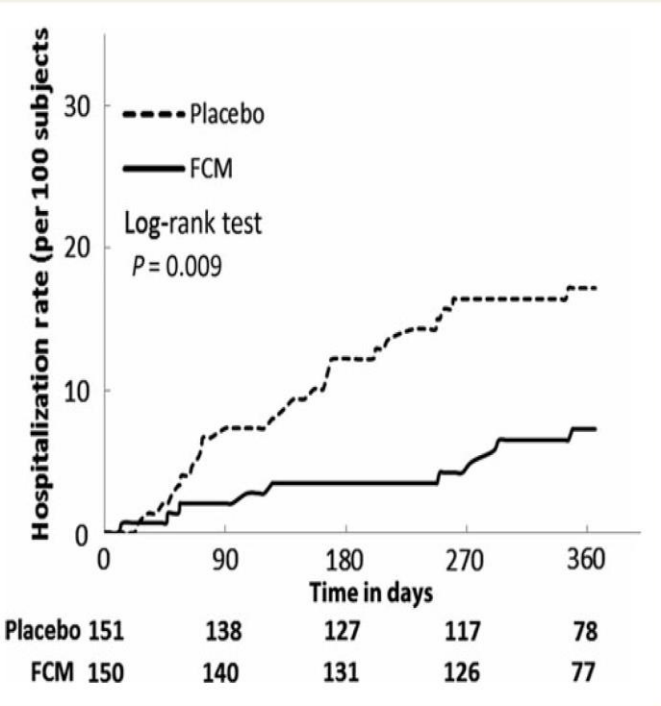


Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency†

Secondary endpoints: Outcome events

CONFIRM-HF

	FCM (N=150)		Placebo (N=151)			
End-point or event	**Total events (n)**	**Incidence/ (100 patient risk-year)**	**Total events (n)**	**Incidence/ (100 patient risk-year**	**Time to first event Hazard ratio 95% CI**	**P-value**
Death	12	12 (8.9)	14	14 (9.9)	0.89 (0.41 – 1.93)	0.77
Death for any CV reason	11	11 (8.1)	12	12 (8.5)	0.96 (0.42 – 2.16)	0.91
Hospitalisation	46	32 (26.3)	69	44 (37.0)	0.71 (0.45 – 1.12)	0.14
Hospitalisation for any CV reason	26	21 (16.6)	51	33 (26.3)	0.63 (0.37 – 1.09)	0.097
Hospitalisation due to worsening HF	**10**	**10 (7.6)**	**32**	**25 (19.4)**	**0.39 (0.19 – 0.82)**	**0.009**



Conclusion Treatment of symptomatic, iron-deficient HF patients with FCM over a 1-year period resulted in sustainable improvement in functional capacity, symptoms, and QoL and may be associated with risk reduction of hospitalization for worsening HF (ClinicalTrials.gov number NCT01453608).

EUROPEAN SOCIETY OF CARDIOLOGY®
European Heart Journal
doi:10.1093/eurheartj/ehu385

Tratamiento de la anemia asociada a Insuficiencia Cardiaca

Ferropenia absoluta **Objetivo Hb> 13 g/dl**	Fe oral Fe iv si no tolerancia o falta respuesta
Ferropenia funcional **Objetivo Hb >13 g/dl**	Eritopoyetina (RED-HF suspendido mayor mortalidad) Fe iv (Fe carboximaltosa) (FAIR-HF, CONFIRM-HF) Fe oral (IRON-HF 18 pacientes)
An. asociada I. Renal	Eritropoyetina+/-Fe oral

Hierro i.v.	Dosis inicial	Dosis máxima
C. Ferrico dextrano (Cosmofer®)	200 mg/sem	600 mg/sem
Hierro sacarosa (Venofer®)	200 mg/sem	600 mg/sem
Hierro carboximaltosa (Ferinject®)	500-1000 mg/dosis	1000 mg/dosis

*Cálculo déficit Fe (Ganzoni) peso (kg) x (Hb deseada (g/dl)-Hb real (g/dl)] x 2.4 + 500mg

¿Tratar la anemia o la ferropenia?

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

Management of co-morbidities

- Anaemia
- Angina
- Asthma/C
- Cachexia
- Cancer
- Depression
- Diabetes mellitus
- Erectile dysfunction
- Gout
- Hyperlipidaemia
- Hypertension
- Prostatic obstruction
- Sleepdisturbance/ sleep disordered breathing

KIDNEY DIFUNCION IN HEART FAILURE

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European Heart Journal (2012) 33, 1787–1847
European Journal of Heart Failure (2012) 14, 803–869

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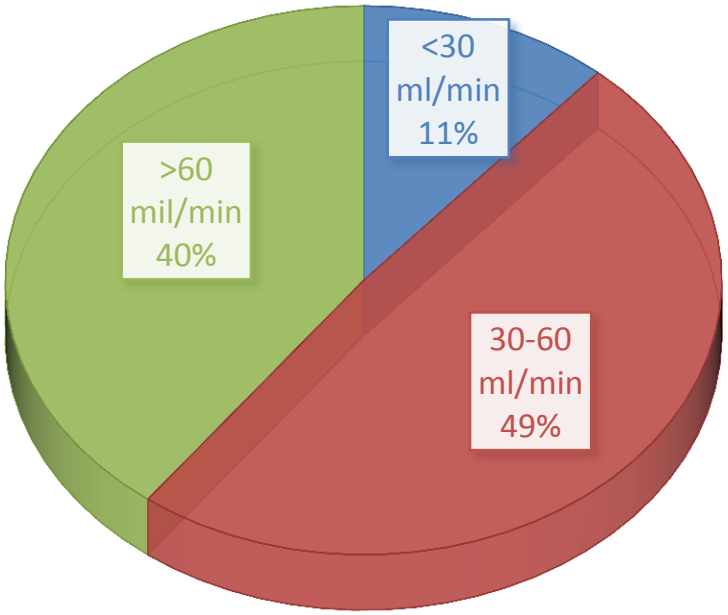
ORIGINAL

Función renal en pacientes con insuficiencia cardiaca: valor pronóstico

J. Casado[a,*], M. Montero[b], F. Formiga[c], M. Camafort[d], C. Sánchez[e], A. Muela[f], J. Díez[g], J.I. Pérez[h] y Grupo RICA[◊]



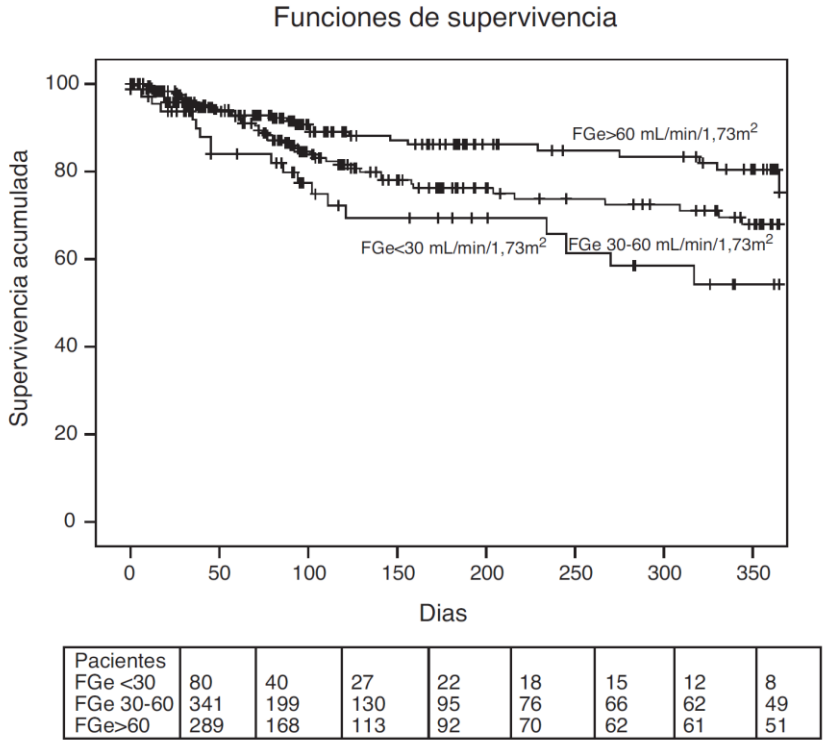


Figura 1 Supervivencia en función del filtrado glomerular

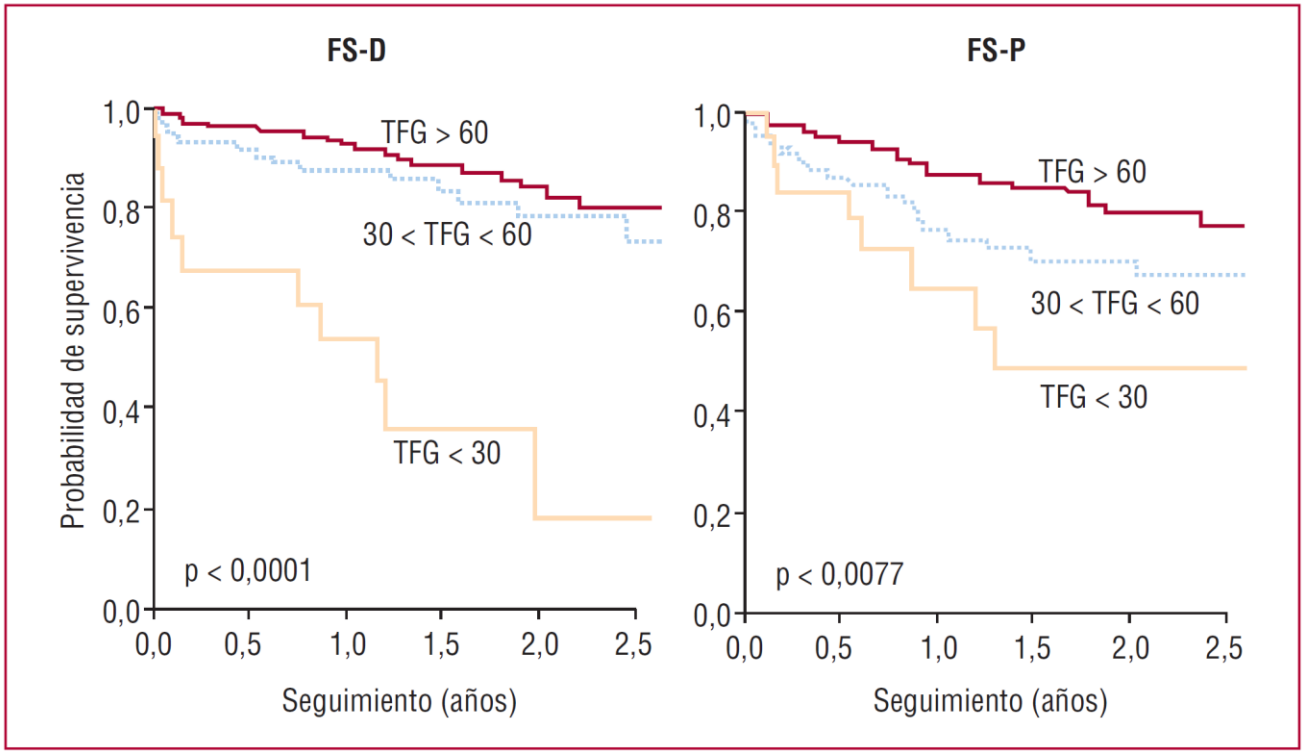
Conclusiones: Cerca del 60% de los enfermos que ingresan en Medicina Interna con IC presentan insuficiencia renal. Esta comorbilidad se asocia a un incremento medio del doble en la mortalidad global.

Rev Clin Esp. 2012;212(3):119–126

ARTÍCULO ORIGINAL

La insuficiencia renal es un predictor independiente de la mortalidad en pacientes hospitalizados por insuficiencia cardíaca y se asocia con un peor perfil de riesgo cardiovascular

IC con FEVI deprimida **IC con FEVI conservada**



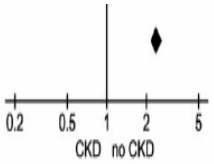
Rev Esp Cardiol. 2006;59(2):99-108

Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis

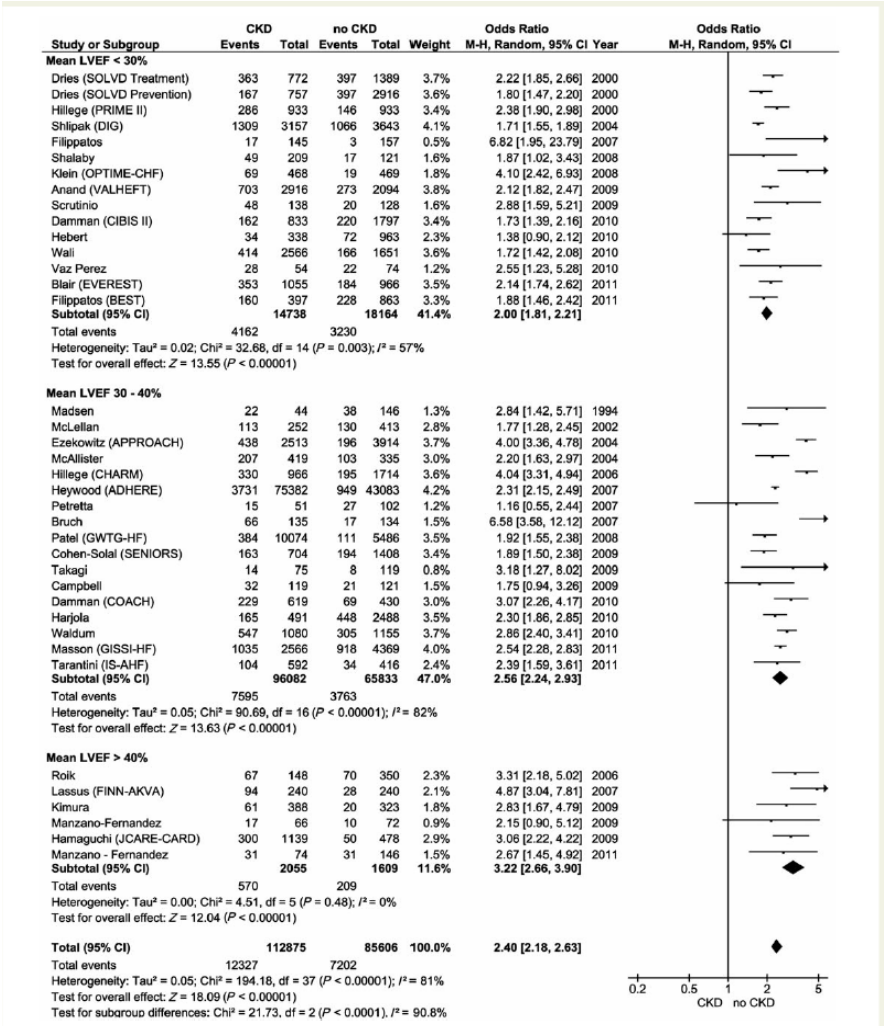
Meta-análisis de 85 estudios IC/IR

Total (95% CI)	**112875**	**85606**	**100.0%**	**2.40 [2.18, 2.63]**
Total events	12327	7202		

Heterogeneity: Tau² = 0.05; Chi² = 194.18, df = 37 (P < 0.00001); I^2 = 81%
Test for overall effect: Z = 18.09 (P < 0.00001)
Test for subgroup differences: Chi² = 21.73, df = 2 (P < 0.0001), I^2 = 90.8%



Conclusiones: En todos los grupos de pacientes con Insuficiencia cardiaca, la Insuficiencia renal es prevalente y está asociada con un incremento importante de la mortalidad, especialmente la IR crónica.



Study or Subgroup	CKD Events	CKD Total	no CKD Events	no CKD Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Mean LVEF < 30%							
Dries (SOLVD Treatment)	363	772	397	1389	3.7%	2.22 [1.85, 2.66]	2000
Dries (SOLVD Prevention)	167	757	397	2916	3.6%	1.80 [1.47, 2.20]	2000
Hillege (PRIME II)	286	933	146	933	3.4%	2.38 [1.90, 2.98]	2000
Shlipak (DIG)	1309	3157	1066	3643	4.1%	1.71 [1.55, 1.89]	2004
Filippatos	17	145	3	157	0.5%	6.82 [1.95, 23.79]	2007
Shalaby	49	209	17	121	1.6%	1.87 [1.02, 3.43]	2008
Klein (OPTIME-CHF)	69	468	19	469	1.8%	4.10 [2.42, 6.93]	2008
Anand (VALHEFT)	703	2916	273	2094	3.8%	2.12 [1.82, 2.47]	2009
Scrutinio	48	138	20	128	1.6%	2.88 [1.59, 5.21]	2009
Damman (CIBIS II)	162	833	220	1797	3.4%	1.73 [1.39, 2.16]	2010
Hebert	34	338	72	963	2.3%	1.38 [0.90, 2.12]	2010
Wali	414	2566	166	1651	3.6%	1.72 [1.42, 2.08]	2010
Vaz Perez	28	54	22	74	1.2%	2.55 [1.23, 5.28]	2010
Blair (EVEREST)	353	1055	184	966	3.5%	2.14 [1.74, 2.62]	2011
Filippatos (BEST)	160	397	228	863	3.3%	1.88 [1.46, 2.42]	2011
Subtotal (95% CI)		**14738**		**18164**	**41.4%**	**2.00 [1.81, 2.21]**	
Total events	4162		3230				
Heterogeneity: Tau² = 0.02; Chi² = 32.68, df = 14 (P = 0.003); I^2 = 57%							
Test for overall effect: Z = 13.55 (P < 0.00001)							
Mean LVEF 30 - 40%							
Madsen	22	44	38	146	1.3%	2.84 [1.42, 5.71]	1994
McLellan	113	252	130	413	2.8%	1.77 [1.28, 2.45]	2002
Ezekowitz (APPROACH)	438	2513	196	3914	3.7%	4.00 [3.36, 4.78]	2004
McAllister	207	419	103	335	3.0%	2.20 [1.63, 2.97]	2004
Hillege (CHARM)	330	966	195	1714	3.6%	4.04 [3.31, 4.94]	2006
Heywood (ADHERE)	3731	75382	949	43083	4.2%	2.31 [2.15, 2.49]	2007
Petretta	15	51	27	102	1.2%	1.16 [0.55, 2.44]	2007
Bruch	66	135	17	134	1.5%	6.58 [3.58, 12.12]	2007
Patel (GWTG-HF)	384	10074	111	5486	3.5%	1.92 [1.55, 2.38]	2008
Cohen-Solal (SENIORS)	163	704	194	1408	3.4%	1.89 [1.50, 2.38]	2009
Takagi	14	75	8	119	0.8%	3.18 [1.27, 8.02]	2009
Campbell	32	119	21	121	1.5%	1.75 [0.94, 3.26]	2009
Damman (COACH)	229	619	69	430	3.0%	3.07 [2.26, 4.17]	2010
Harjola	165	491	448	2488	3.5%	2.30 [1.86, 2.85]	2010
Waldum	547	1080	305	1155	3.7%	2.86 [2.40, 3.41]	2010
Masson (GISSI-HF)	1035	2566	918	4369	4.0%	2.54 [2.28, 2.83]	2011
Tarantini (IS-AHF)	104	592	34	416	2.4%	2.39 [1.59, 3.61]	2011
Subtotal (95% CI)		**96082**		**65833**	**47.0%**	**2.56 [2.24, 2.93]**	
Total events	7595		3763				
Heterogeneity: Tau² = 0.05; Chi² = 90.69, df = 16 (P < 0.00001); I^2 = 82%							
Test for overall effect: Z = 13.63 (P < 0.00001)							
Mean LVEF > 40%							
Roik	67	148	70	350	2.3%	3.31 [2.18, 5.02]	2006
Lassus (FINN-AKVA)	94	240	28	240	2.1%	4.87 [3.04, 7.81]	2007
Kimura	61	388	20	323	1.8%	2.83 [1.67, 4.79]	2009
Manzano-Fernandez	17	66	10	72	0.9%	2.15 [0.90, 5.12]	2009
Hamaguchi (JCARE-CARD)	300	1139	50	478	2.9%	3.06 [2.22, 4.22]	2009
Manzano - Fernandez	31	74	31	146	1.5%	2.67 [1.45, 4.92]	2011
Subtotal (95% CI)		**2055**		**1609**	**11.6%**	**3.22 [2.66, 3.90]**	
Total events	570		209				
Heterogeneity: Tau² = 0.00; Chi² = 4.51, df = 5 (P = 0.48); I^2 = 0%							
Test for overall effect: Z = 12.04 (P < 0.00001)							
Total (95% CI)		**112875**		**85606**	**100.0%**	**2.40 [2.18, 2.63]**	
Total events	12327		7202				
Heterogeneity: Tau² = 0.05; Chi² = 194.18, df = 37 (P < 0.00001); I^2 = 81%							
Test for overall effect: Z = 18.09 (P < 0.00001)							
Test for subgroup differences: Chi² = 21.73, df = 2 (P < 0.0001), I^2 = 90.8%							

Figure 4 Forest plot of combined all-cause mortality for CKD vs. no CKD, stratified by mean LVEF of included studies. CKD, chronic kidney disease; LVEF, left-ventricular ejection fraction.

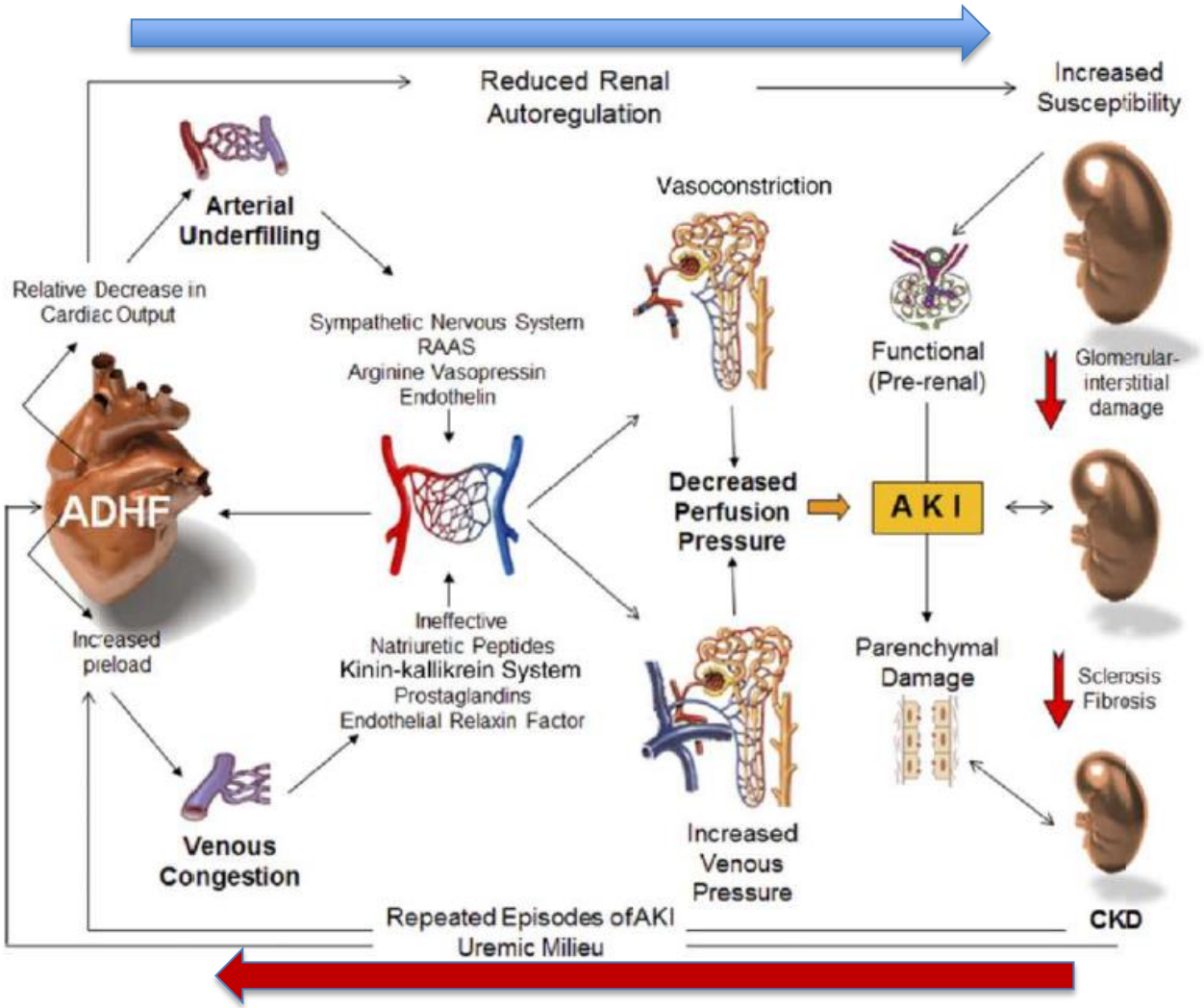
European Heart Journal (2014) **35**, 455–469

SÍNDROME CARDIORRENAL

Type	Definition
SCR1  AGUDO	Abrupt worsening of cardiac function (e.g. acute cardiogenic shock or acute decompensated HF) leading to kidney injury
SCR2  CRÓNICO	Chronic abnormalities in cardiac function (e.g. chronic HF) causing progressive chronic kidney disease
SCR3  AGUDO	Abrupt worsening of renal function (e.g. acute kidney failure or glomerulonephritis) causing acute cardiac disorder (e.g. HF, arrhythmia, pulmonary edema)
SCR4  CRÓNICO	Chronic kidney disease (e.g. chronic glomerular disease) contributing to decreased cardiac function, cardiac hypertrophy and/or increased risk of cardiovascular events
SCR5 alteración sistémica 	Systemic condition (e.g. diabetes mellitus, sepsis) causing both cardiac and renal dysfunction

Ronco C, et al. JACC 2012; 60: 1031-1042.

Fisiopatología del Síndrome Cardiorrenal I



Ronco C, et al. JACC 2012; 60: 1031-1042.

Management of the Cardiorenal Syndrome in Decompensated Heart Failure

Frederik Hendrik Verbrugge[a, b] Lars Grieten[a, c] Wilfried Mullens[a, c]

CONGESTION (increased cardiac filling pressures)

VOLUME OVERLOAD

⊕ edema, weight increase, ascites

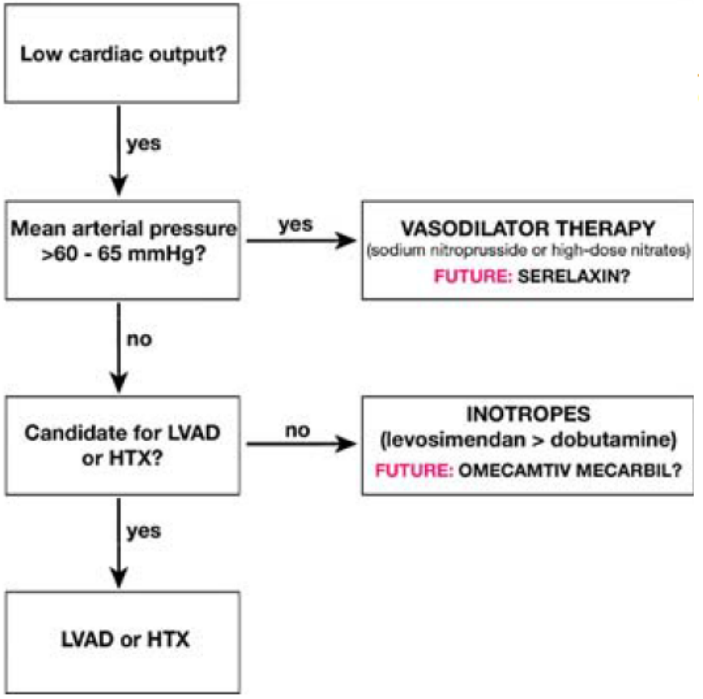
INTRAVASCULAR VOLUME OVERLOAD → INDUCE NEGATIVE SODIUM BALANCE

1. **LOOP DIURETICS:**
   - Intravenous bolus
   - Adequately dosed
   - Monotherapy in diuretic naïve patients
2. **THIAZIDE-TYPE DIURETICS**
   - Maximize fractional sodium excretion in case of low glomerular filtration
   - Counteract distal nephron hypertrophy due to chronic loop diurectic use
3. **MINERALOCORTICOID RECEPTOR ANTAGONISTS**
   - Improve natriuresis if potassium < 5 mmol/L
4. **ACETAZOLAMIDE**
   - Counteract increase proximal reabsorption in case of poor renal perfusion
5. **ULTRAFILTRATION**
   → Break diuretic resistance

FLUID ACCUMULATION IN THIRD SPACES

- **Ascites:** PARACENTESIS
- **Non-recruitable edema:** COMPRESSION THERAPY

NO VOLUME OVERLOAD



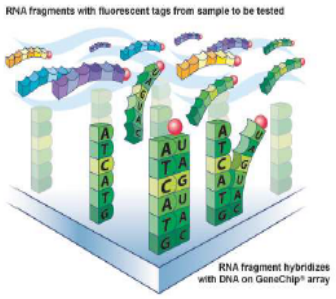
Cardiorenal Med 2014;4:176–188

Novel Markers and Therapies for Patients with Acute Heart Failure and Renal Dysfunction

Peter A. McCullough, MD, MPH,[a,b] John L. Jefferies, MD, MPH[c]

BIOMARCADORES RENALES

1. CLÁSICOS (*filtrado*)
   - A. CREATININA
   - B. UREA/BUN
   - C. CISTATINA
2. NUEVOS (*daño*)
   - A. NGAL
   - B. KIM-1
   - C. IL-18
   - D. L-FABP
   - E. N Acetil Glucosaminidasa (NAG)
   - F. Proteína B traza
   - G. Glutation-S-Transferasa
   - H. Glutamil transferasa
   - I. Thioredoxin-1
   - J. etc.



The American Journal of Medicine (2015) 128, 312.e1-312.e22

Daño orgánico y síndrome cardiorrenal en la insuficiencia cardíaca aguda

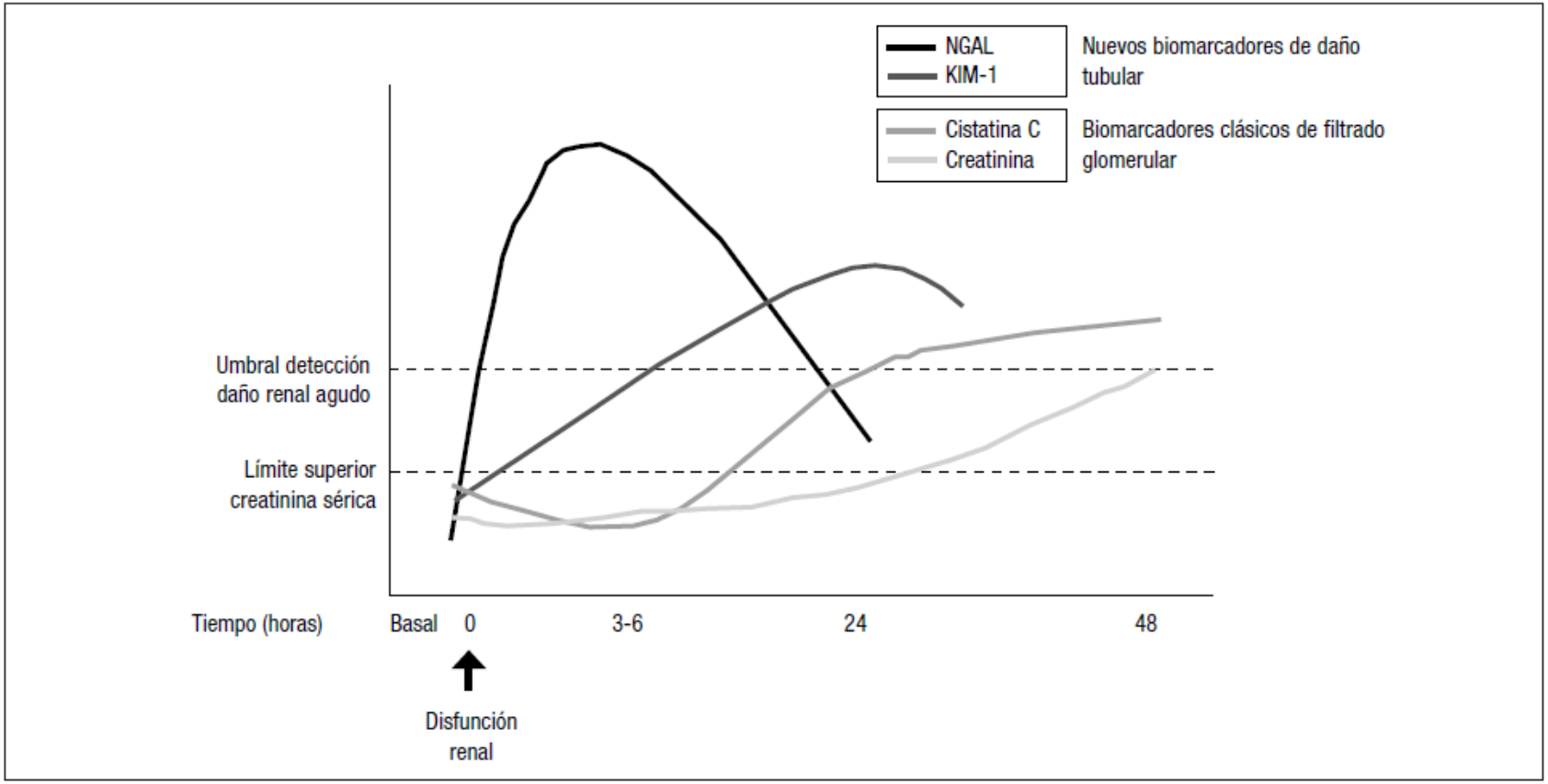
Jesús Casado Cerrada[a,*] y Juan Ignacio Pérez Calvo[b]

NGAL

Neutrophil Gelatinase-Associated Lipocalin

KIM-1

Kidney Injury Molecule 1

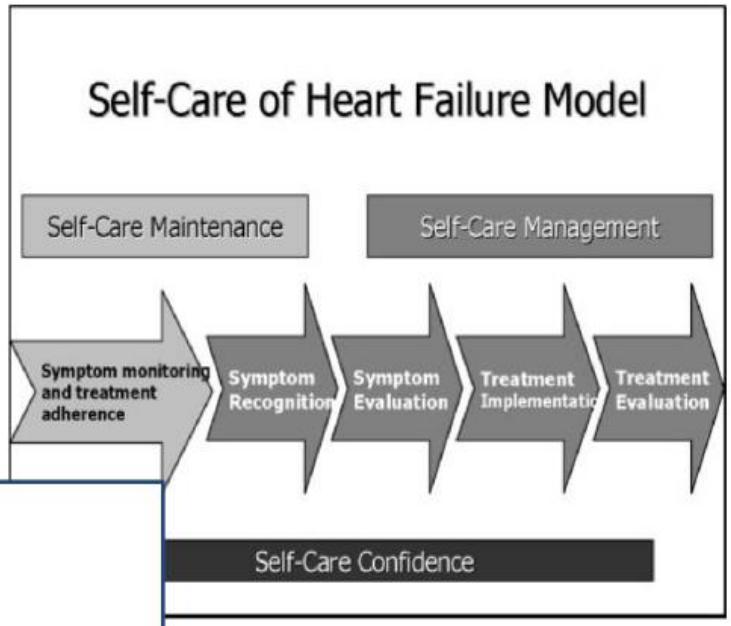


*J. Casado Cerrada et al / Med Clin (Barc). 2014;**142(Supl 1)**:26-31*

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

Educación sanitaria y autocuidado



El paciente:
- Adopta medidas preventivas
- Monitoriza síntomas
- Cumple el tratamiento
- Identifica las reagudizaciones
- Modifica el tratamiento según síntomas

- Adherencia a la medicación
- Monitorización de los síntomas
- Adherencia a la dieta
- Restricción de líquidos
- Restricción de alcohol
- Pérdida de peso
- Ejercicio
- Dejar de fumar
- Prevención
- No automedicación

Impact of a Multidisciplinary Heart Failure Post-hospitalization Program on Heart Failure Readmission Rates

Annals of Pharmacotherapy
1–8

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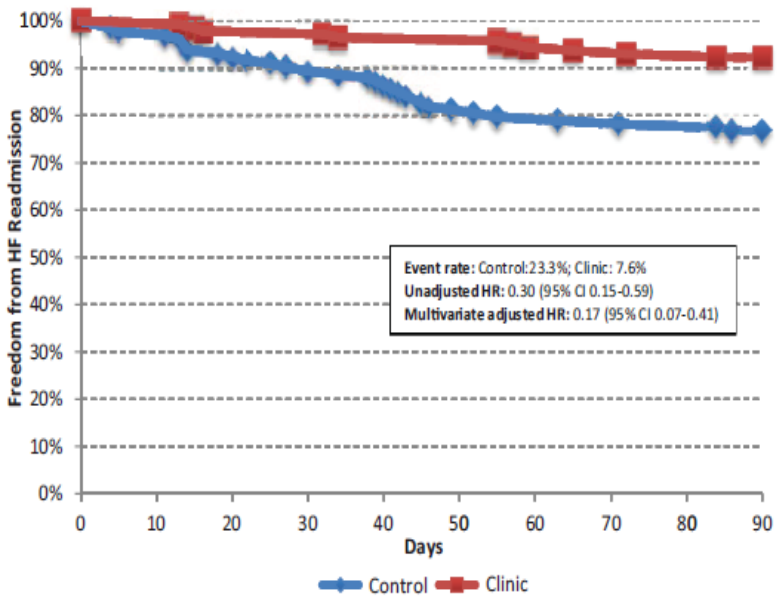
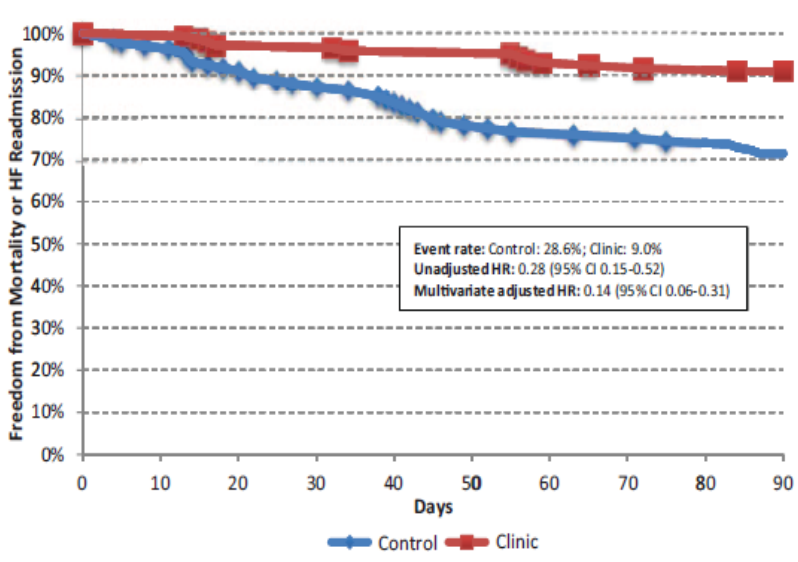
A



heart failure readmission at 90 days

B



heart failure readmission or all-cause mortality at 90 days.