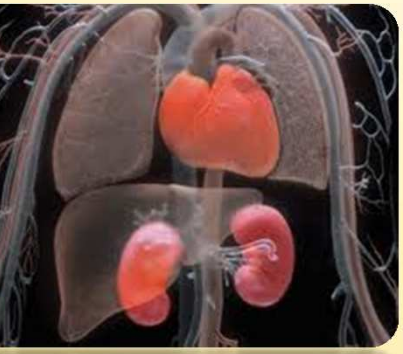
SINDROME DE ANEMIA CARDIO – RENAL
MAS ALLA DE LA CORRECCION DE LA ANEMIA
LA VISION DEL CARDIOLOGO

JULIAN DARIO ÑAÑEZ
RESIDENTE - TERCER AÑO
MEDICINA INTERNA
UNIVERSIDAD DEL CAUCA

OBJETIVOS

ENTENDER LA IMPORTANCIA DE LA ANEMIA ASOCIADA AL SINDROME CARDIO - RENAL

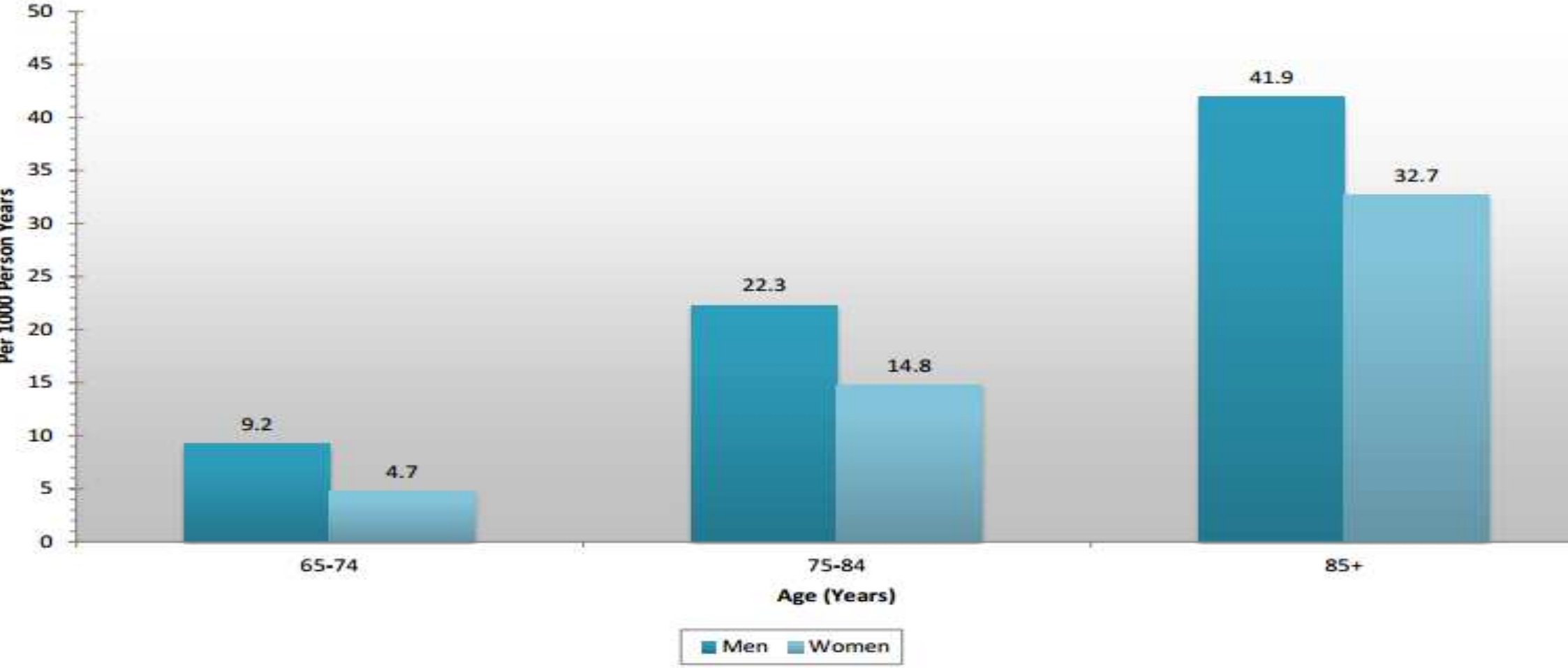
REVISAR LA EVIDENCIA DISPONIBLE CON RELACION AL USO DE LOS FACTORES ESTIMULANTES DE LA ERITROPOYESIS



COMPRENDER LA FISIOPATOLOGIA DE LA ANEMIA EN ESTE GRUPO DE PACIENTES

REALIZAR UN ACERCAMIENTO A LAS PROPUESTAS TERAPEUTICAS DISPONIBLES

Incidence of heart failure (heart failure based on physician review of medical records and strict diagnostic criteria) by age and sex (Framingham Heart Study 1980-2003)



rce: National Heart, Lung, and Blood Institute.

Go, AS et al. *Circulation*. 2013; 127

FALLA CARDIACA Y ANEMIA

20
MILLONES ALREDEDOR DEL MUNDO

10 %
MAYORES 65 AÑOS

1
MILLON
HOSPITALIZACIO-NES AÑO

80 %
NYHA IV

28 %
MORTALIDAD

50 %
CARDIOPATIA ISQUEMICA

F.RIESGO INDEPENDIENTE
MORBIMORTALIDAD

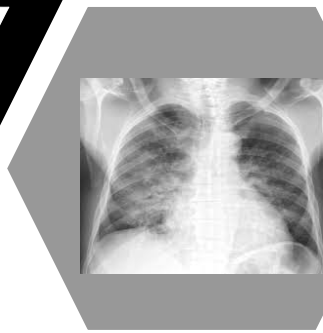
FRAMINGHAM HEART STUDY
A Project of the National Heart, Lung and Blood Institute and Boston University

10 %
POBLACION GENERAL

55 %
PREVALENCIA EN FALLA CARDIACA

20 – 80 %
NYHA IV

OMS
Hb < 13 – H
Hb < 12 - M



ENFERMEDAD RENAL CRONICA Y ANEMIA

TABLE 131-2 -- STAGES OF CHRONIC KIDNEY DISEASE (CKD) WITH PROJECTED NUMBERS OF INDIVIDUALS AND THE FREQUENCY COMPLICATIONS

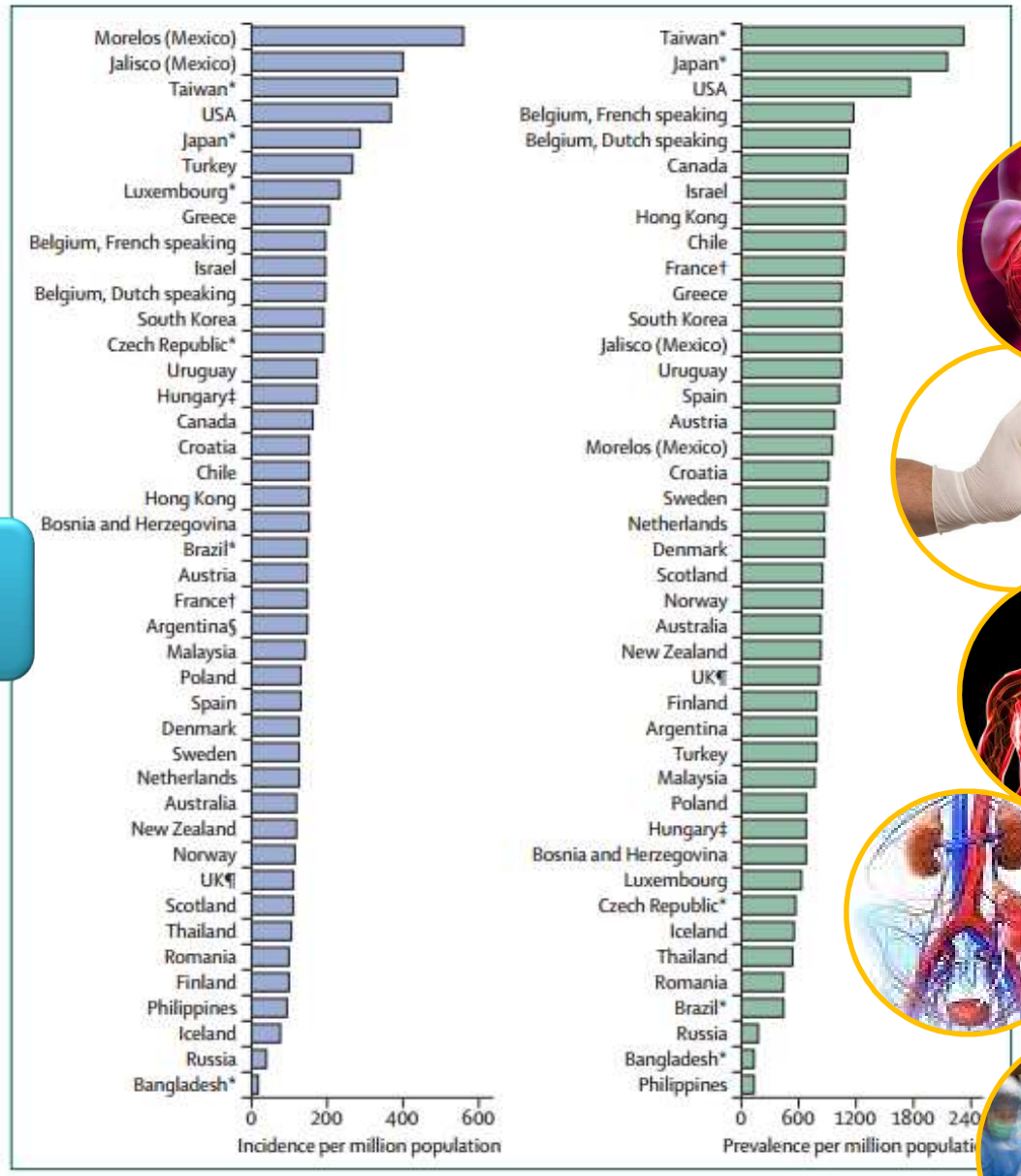
Stage	Description	GFR [*] (mL/min/1.73 m 2)	Projected Number (×1000)	Symptoms or Signs
1	Chronic kidney damage with normal or increased GFR	>90	5900	Anemia 4%
				Hypertension 40%
				5-year mortality 19%
2	Mild GFR loss	60–89	5300	Anemia 4%
				Hypertension 40%
				5-year mortality 19%
3	Moderate GFR loss	30–59	7600	Anemia 7%
				Hypertension 55%
				5-year mortality 24%
4	Severe GFR loss	15–29	400	Hyperphosphatemia 20%
				Anemia 29%
				Hypertension 77%
				5-year mortality 46%
5	Kidney failure	<15 or dialysis	300	Hyperphosphatemia 50%
				Anemia 69%
				Hypertension >75%
				3-year mortality 14%

De Jong PE, Brenner BM: From secondary to primary prevention of progressive renal disease: The case for screening for albumin
Int 2004; 66:2109-2118.*Screening for albuminuria detects patients with early kidney disease*

LANCET

Chronic kidney disease

Andrew S Levey, Josef Coresh



KDOQI 3 – 4
MILLONES - USA

CAUSAS ERC – 2003
44.8 % - DIABETES
27.1 % - HTA

INCIDENCIA
65 AÑOS

38 MIL PERSONAS
2 % POBLACION
5 MIL – KDOQI 5

RIESGO CARDIOVASCULAR

F. RIESGO ENF. CV
PROTEINURIA
↓ TFG

ADHERE
30 % HOSPITALIZACIONES POR ICC
CURSABAN CON ERC (CREA > 2 mg/dl)

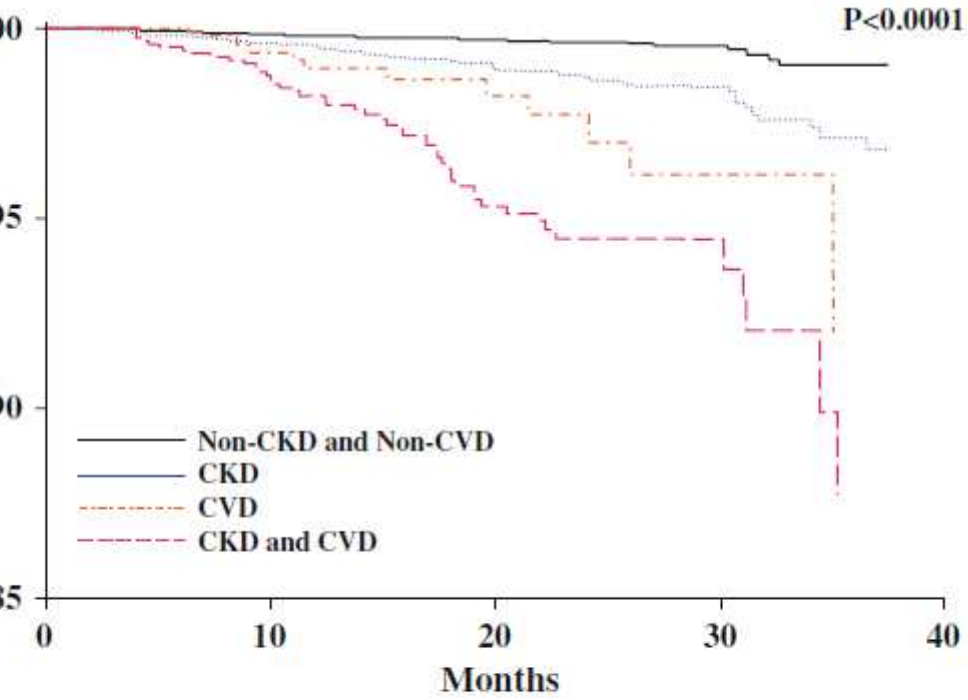
F.RIESGO INDPTES MORTALIDAD
↑ CREATININA / N. UREICO
INGRESO

7 %
↑ MORTALIDAD
↓ TFG = 10 ML / MIN

Sarnak MJ, Levey AS, et al. Kidney disease as a risk factor for development of cardiovascular disease. A statement from the AHA Councils on Kidney in Cardiovascular Dis
Blood Pressure Research, Clinical Cardiology, and Epidemiology Blood Pressure Research, Clinical Cardiology, and Epidemiology

nogenesis and therapeutic implications of cardiorenal drome

u Nitta



Kaplan–Meier curves for all-cause mortality stratified accord-
the presence or absence of chronic kidney disease (*CKD*) and/
liovascular disease (*CVD*). Cited from McCullough et al. [16]

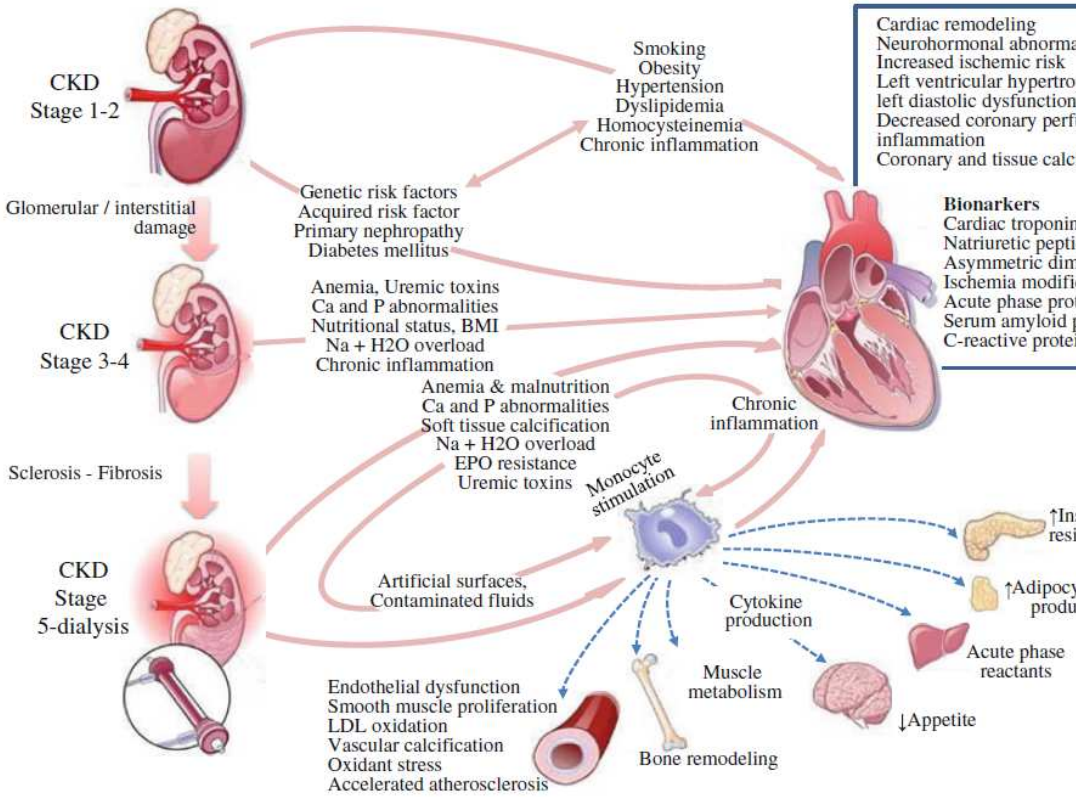
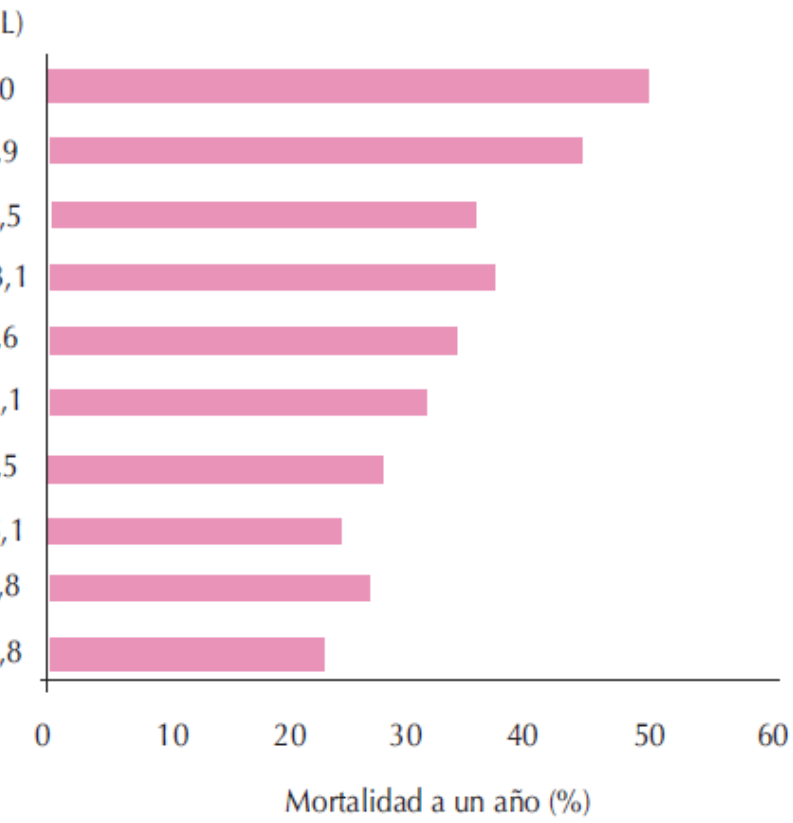


Fig. 2 Complex pathogenesis of chronic kidney disease (*CKD*) in cardiovascular disease (*CVD*). Cited from McCullough

VISIÓN DEL CARDIÓLOGO

3. Prevalencia de anemia en falla cardiaca y asociación con resultados adversos



ENSEÑANZAS DEL CHARM
Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity

- FALLA CARDIACA - ANEMIA
- ↑ NUMERO INGRESOS HOSPITALARIOS

- FACTOR PRONOSTICO DE MORTALIDAD
- INDEPENDIENTE DE LA FEVI

- FALLA CARDIACA – ERC
- COMPARTEN FACTORES DE RIESGO
- PARA INICIO – PROGRESION
- ERC – COMORBILIDAD FRECUENTE EN ICC

- MORTALIDAD – 2 AÑOS
- FALLA CARDIACA = 26 %
- ENFERMEDAD RENAL CRONICA = 16 %
- COEXISTENCIA = 38 %
- CONCOMITA – ANEMIA = 45 %

ín Gómez
ia

EVISTA ESPAÑOLA DE
CARDIOLOGIA

RT FAILURE

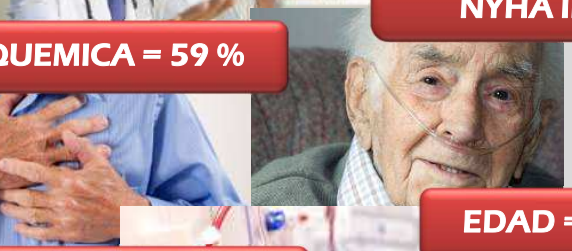
nostic Significance of Hemoglobin Levels in Patients Heart Failure

upón, Agustín Urrutia, Beatriz González, Juan Herreros, Salvador Altimir, Ramon Coll, rat Prats, Celestino Rey-Joly, and Vicente Valle

337 PACIENTES

NYHA II = 46 %
NYHA III = 44 %

QUEMICA = 59 %



EDAD = 65 AÑOS

FEVI = 31 %

CREA > 2.5 mg/dl = 6 %

Hb < 12 gr / dL

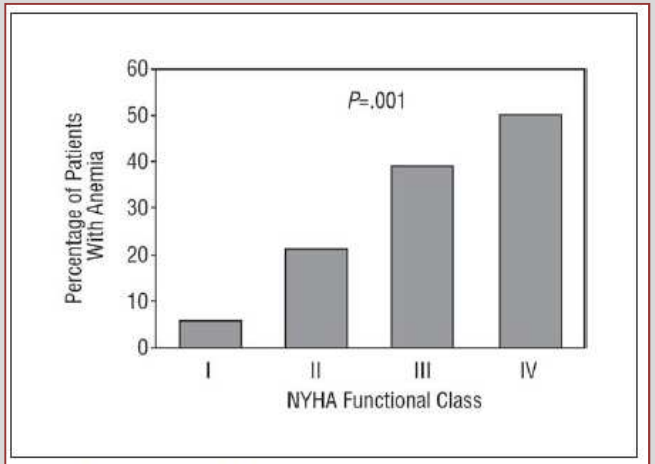


Figure 1. Percentage distribution of patients with anemia by functional class for heart failure (NYHA).

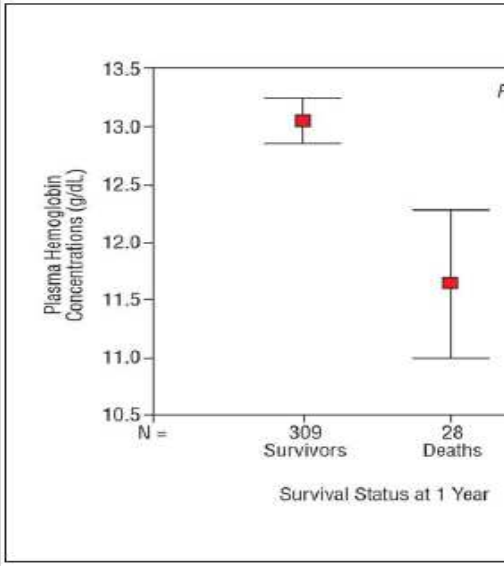


Figure 2. Graph showing means and standard deviation bin levels for survivors and patients who died at 1 year

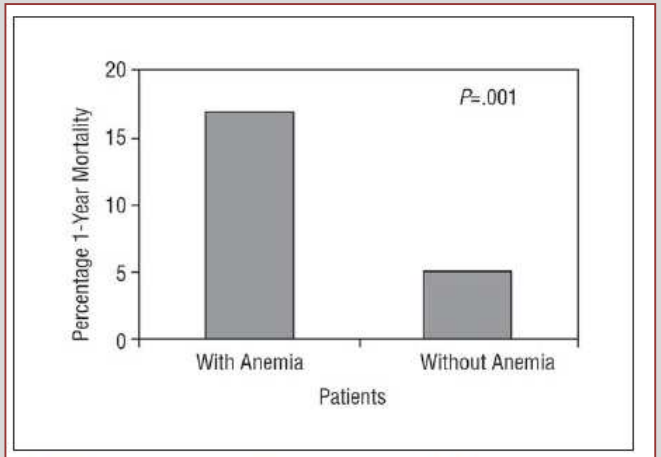


Figure 3. One-year mortality in patients with and without anemia on initial visit.

The
can Journal
of
diology

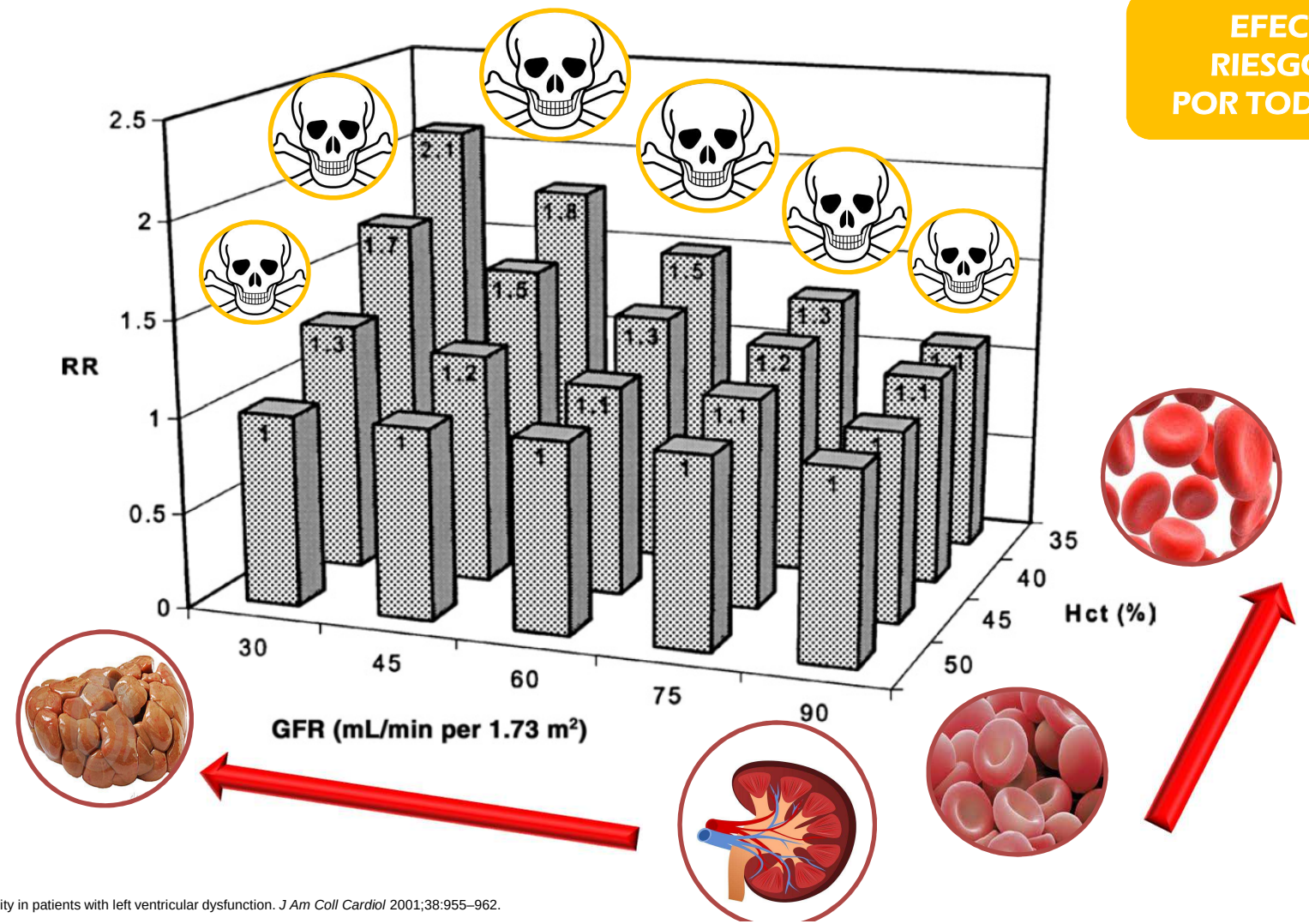
Emerging Role of Anemia in Heart Failure

Judith E. Mitchell, MD

EÑANZAS DEL SOLVD
ies Of LV Dysfunction

RETROSPECTIVO
228 – PREVENCION
69 – TRATAMIENTO
FEVI < 35 %
EA HASTA 2.5 mg/dL

EFECTO ADITIVO
RIESGO DE MUERTE
POR TODAS LAS CAUS



WM. Reduced kidney function and anemia as risk factors for mortality in patients with left ventricular dysfunction. *J Am Coll Cardiol* 2001;38:955–962.

io-renal anemia syndrome

iadis G[1], Konstantinou D[2], Chytas I[3], Vergoulas G[4]

1. Two-year mortality and incidence of ESRD in a 5% le of Medicare patients from the USA

	Two-year mortality(%)	Two-year incidence of ESRD(%)
anemia, CHF or CKI	7,7	0,1
mia	16,6	0,2
F	26,1	0,2
F and anemia	34,6	0,3
	16,4	2,6
and anemia	27,3	5,4
F and CKI	38,4	3,5
,CKI and anemia	45,6	5,9

Congestive Heart Failure, CKI: Chronic Kidney Insufficiency, : End Stage Renal Disease

DKRATIA 2008, 12, 1: 11-16

National Heart, Lung, and Blood Institute

NHLBI Working Group
Cardio-Renal Connections in Heart Failure and Cardiovascular Disease

August 20, 2004

Summary of characteristics of the cardiorenal syndrome

Characteristics of the cardiorenal syndrome
Reduced RBF and GFR
Increased venous congestion
Increased renovascular resistance
Albuminuria
Tubular damage
Worsening renal function
Diuretic resistance
Activation of the TGF
Anemia
Increased mortality

Abbreviations: TGF, tubuloglomerular feedback mechanism.

CRA
Academ

Baliga RR, Young JB. Baliga RR, Young JB. **Staying in the pink of health for patients with cardiorenal anemia requires a multidisciplinary approach.** Heart Fail Cli

ropoietin in cardiovascular diseases

an der Meer[a], Adriaan A. Voors[a], Erik Lipsic[a,b], Wiek H. van Gilst[b]*,
van Veldhuisen[a]

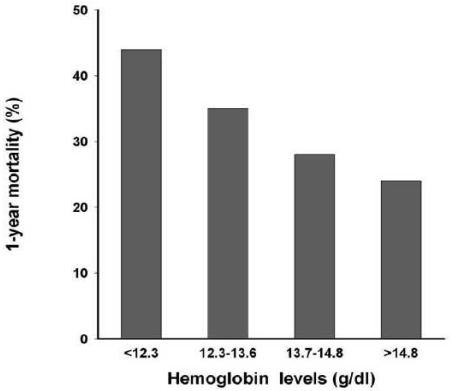
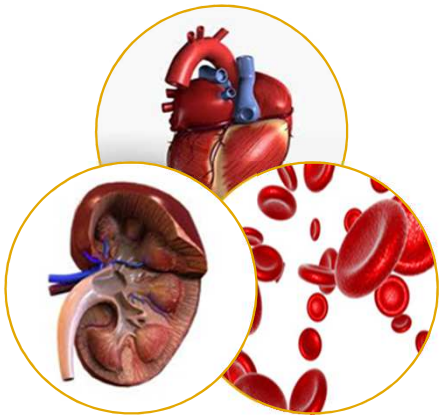
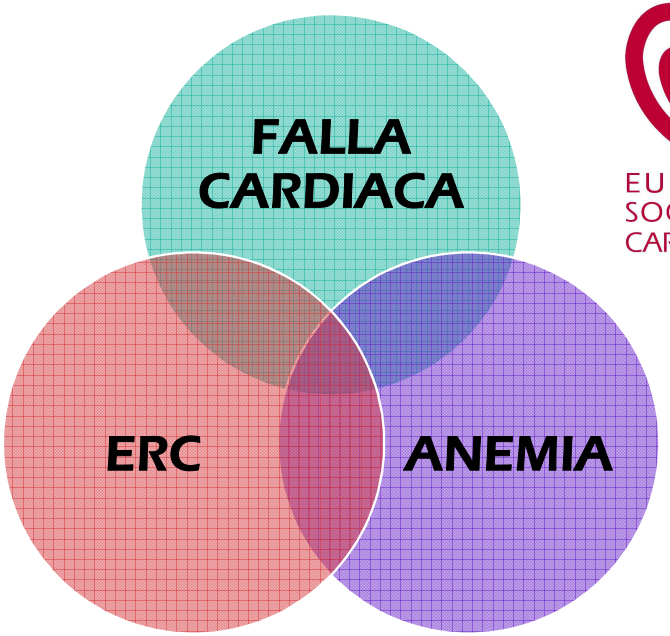
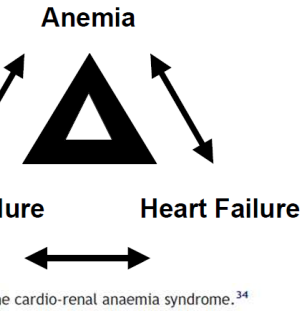


Fig. 1 One-year mortality in NYHA functional class III and IV patients for the different haemoglobin levels.[26]







e cardio-renal anaemia syndrome.[34]

FE + ESA
PROGRESION ERC – ICC - QoL

ASOCIACION ERC / ANEMIA + ICC

50 % ICC TIENEN ANEMIA

CORRECCION DE LA ANEMIA BUENOS RDOS

ANEMIA – FACTOR POBRE PRONOSTICO

SILVERBERG 2002 TERMINO CRAS

PUBLICACIONES ESA + Fe EN ICC / ERC

CRAS 2010 ESTUDIOS AWG

ALES – 1990

2013 .

ACTA MÉDICA COLOMBIANA
ISSN 2248-6054

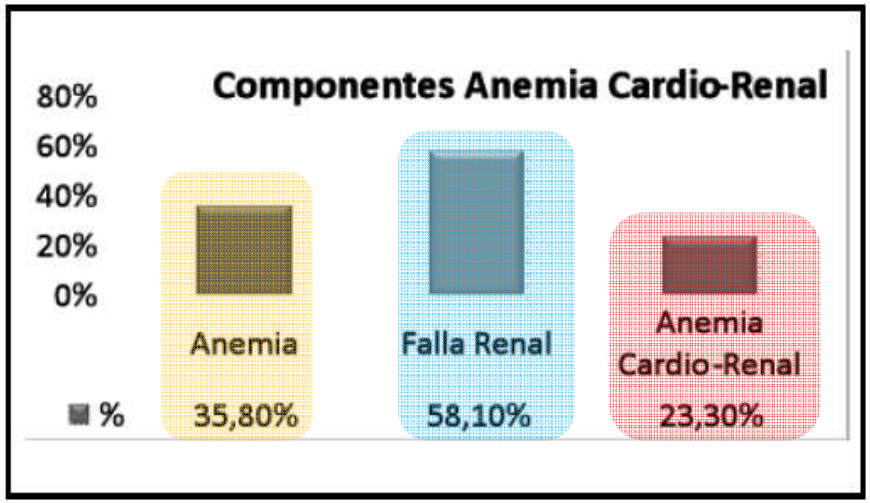


Figura 1. *Componentes anemia cardiorrenal.*

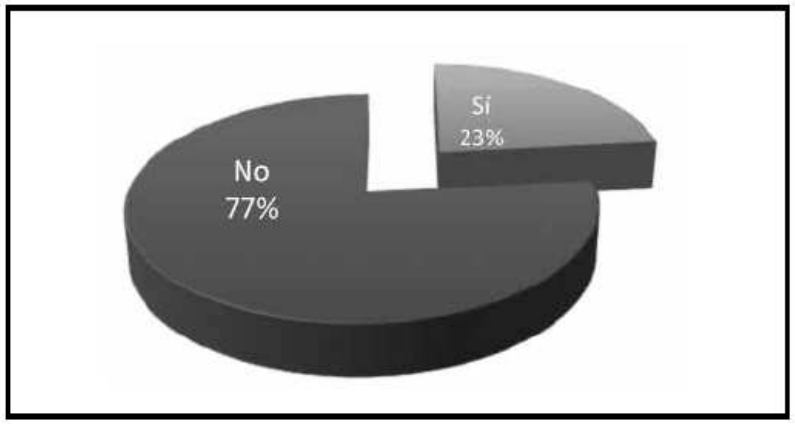


Figura 2. *Anemia cardiorrenal.*

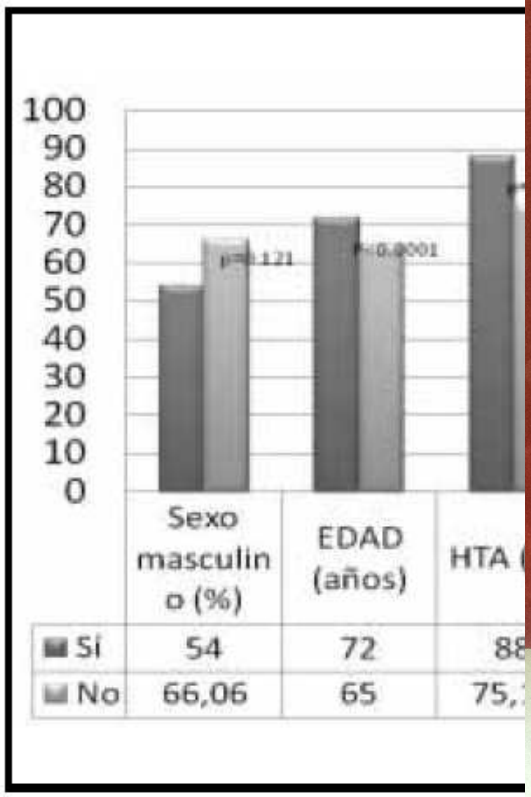
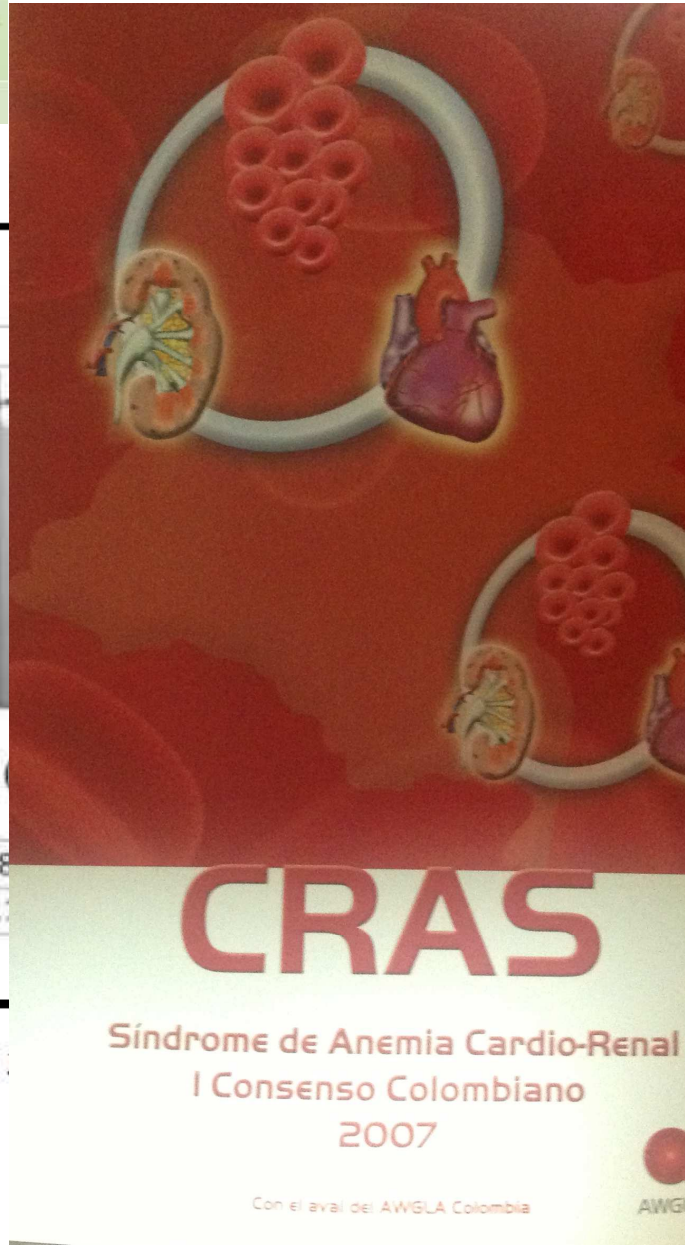
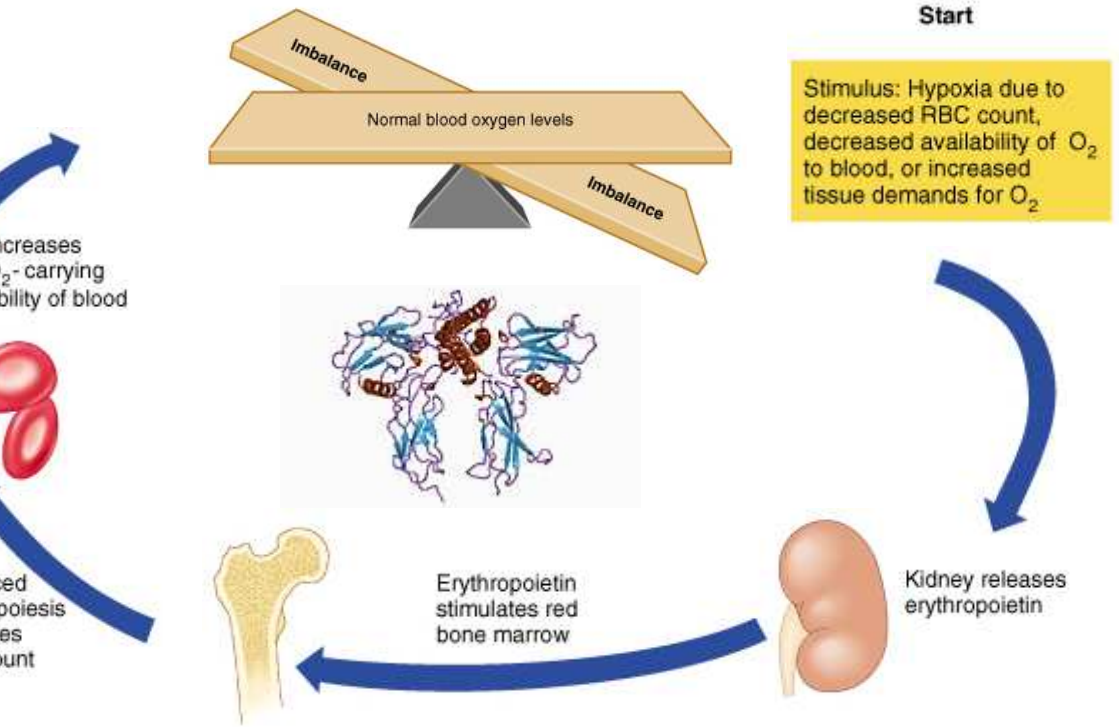
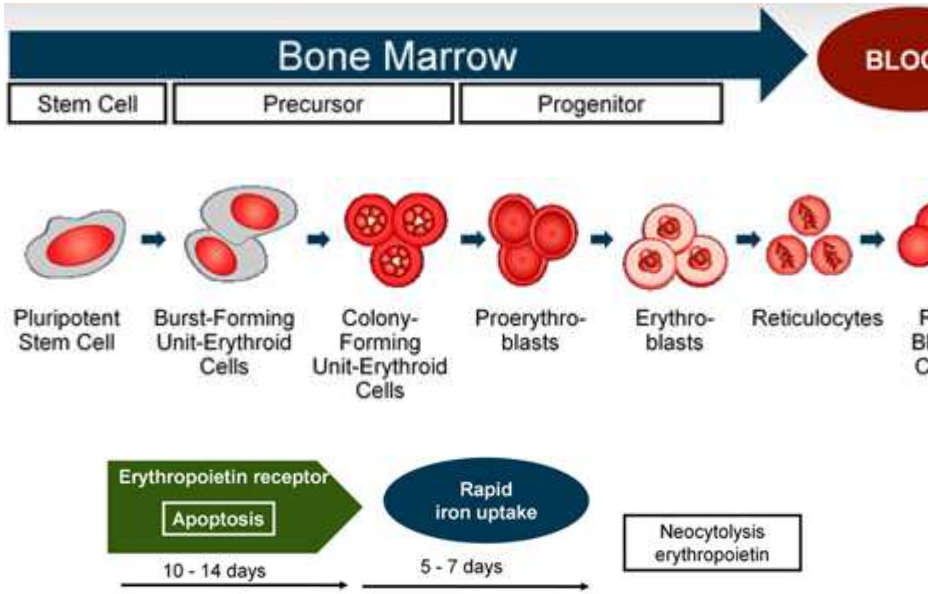


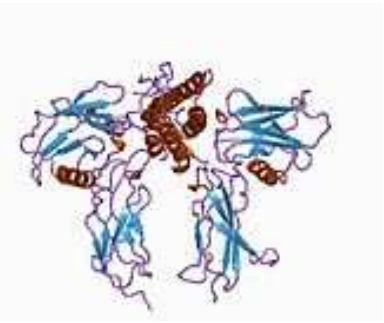
Figura 3. *Porcentaje de pacientes con bilidades*



ERITROPOYETINA - FISIOLOGIA







↑ VIABILIDAD GR

EVITA LA APOPTOSIS DE LOS PROGENITORES ERITROIDES

ESTIMULA LA PROLIFERACION Y DIFERENCIACION DE L PRECURSORES ERITROI

The Story of Erythropoietin By John W. A

ESTIMULANTES DE LA ERITROPOYESIS

1905
CARNOT / DEFLANDRE
CONEJOS
HEMATOPOYETINA
LINK HORMONA -RIÑON

1948
ERITROPOYETINA

A Humoral Mechan
Erythrocytosis.

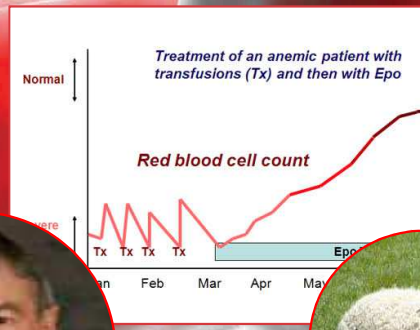
By

EVA BONSDORFF and EEVA JALAVISTO.

Received 1 June 1948.

Jefferson Medical College

1950
REISSMAN / ERLEV
RATONES
HIPOXICOS
ESTIMULACION GR



1968
PURIFICACION EPO
IDENTIFICACION
GENES

AMGEN

1980
PRIMER ENSAYO
FORMA SINTETICA

Correction of the Anemia of End-Stage Renal Disease with Recombinant Human Erythropoietin

Joseph W. Eschbach, M.D., Joan C. Egrie, Ph.D., Michael R. Downing, Ph.D., Jeffrey K. Browne, Ph.D., and John W. Adamson, M.D.

1985
EPO RECOMBINANTE

DEPARTMENT OF HEALTH & HUMAN SERVICES • USA

FD

and expression of the human erythropoietin gene

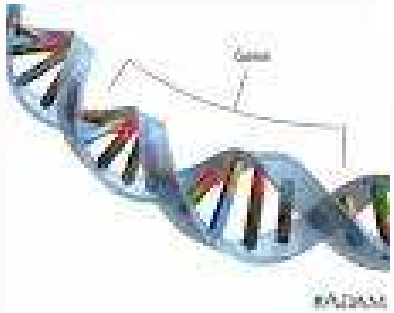
ic factor/glycoprotein hormone/mixed oligonucleotide probes/genomic screening)

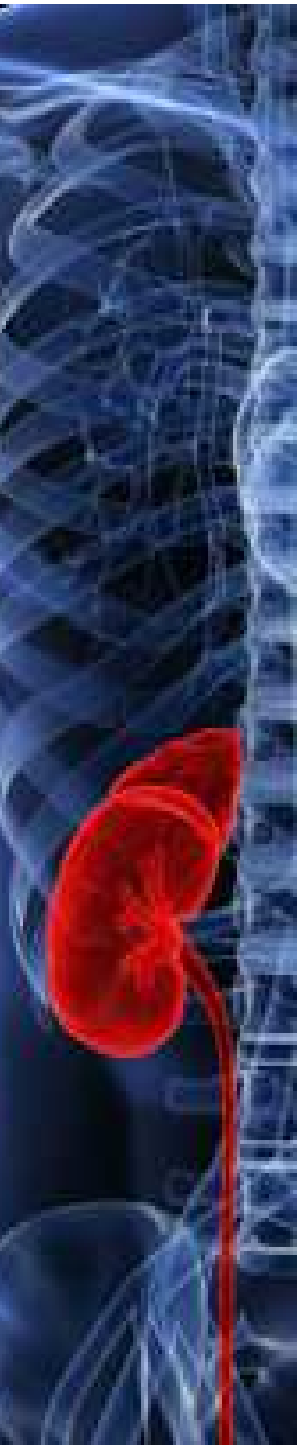
, Sidney Suggs, Chi-Hwei Lin*, Jeffrey K. Browne*, Ralph Smalling*,
e*, Kenneth K. Chen*, Gary M. Fox*, Frank Martin*, Zippora Stabinsky*,
drawi*, Por-Hsiung Lai*, and Eugene Goldwasser†

cation of Human Erythropoietin

ake,‡ Charles K.-H. Kung, and Eugene Goldwasser

The Journal of Biological Chemistry
Vol. 252, No. 15, Issue of August 10, pp. 5558–5564, 1977
Printed in U.S.A.



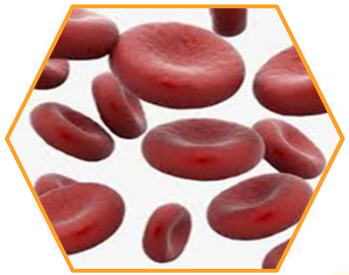


Anemia: The Point of Convergence or Divergence for Kidney Disease and Heart Failure?

Resistance to erythropoietin

Reduced expression of erythropoietin receptors

Relative erythropoietin deficiency

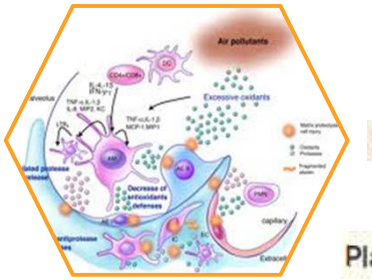


Perturbed erythropoietin signal transduction

Impaired proliferation of erythroid precursor cells

Nutrition deficiencies (e.g., iron, folate, and vitamin B12)

Limited availability of iron for erythropoiesis

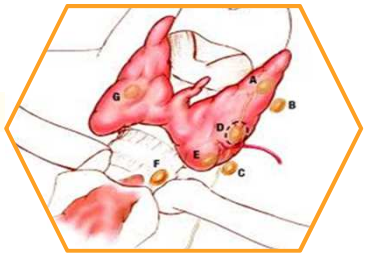


Elevated levels of inflammatory cytokines

Platelet dysfunction resulting in blood loss

Retained blood in extracorporeal circuits for patients with

Drugs (e.g., ACE-I, ARB, and



Hyperparathyroidism

Causes of Anemia in Chronic Kidney Disease

JACC Vol. 53
February 24, 2

DEFICIENCIA RELATIVA y/o RESISTENCIA DE EPO

DEFICIT NUTRICIONAL (Fe-Folato-B12)

MALABSORCION – EDEMA MUCOSA INTESTINAL

DISPONIBILIDAD LIMITADA DE Fe PARA ERITROPOYESIS

↑ CITOQUINAS PROINFLAMATORIAS

HEMODILUCION – MEDICAMENTOS
IECA – ARA II – WARFARINA - ASA

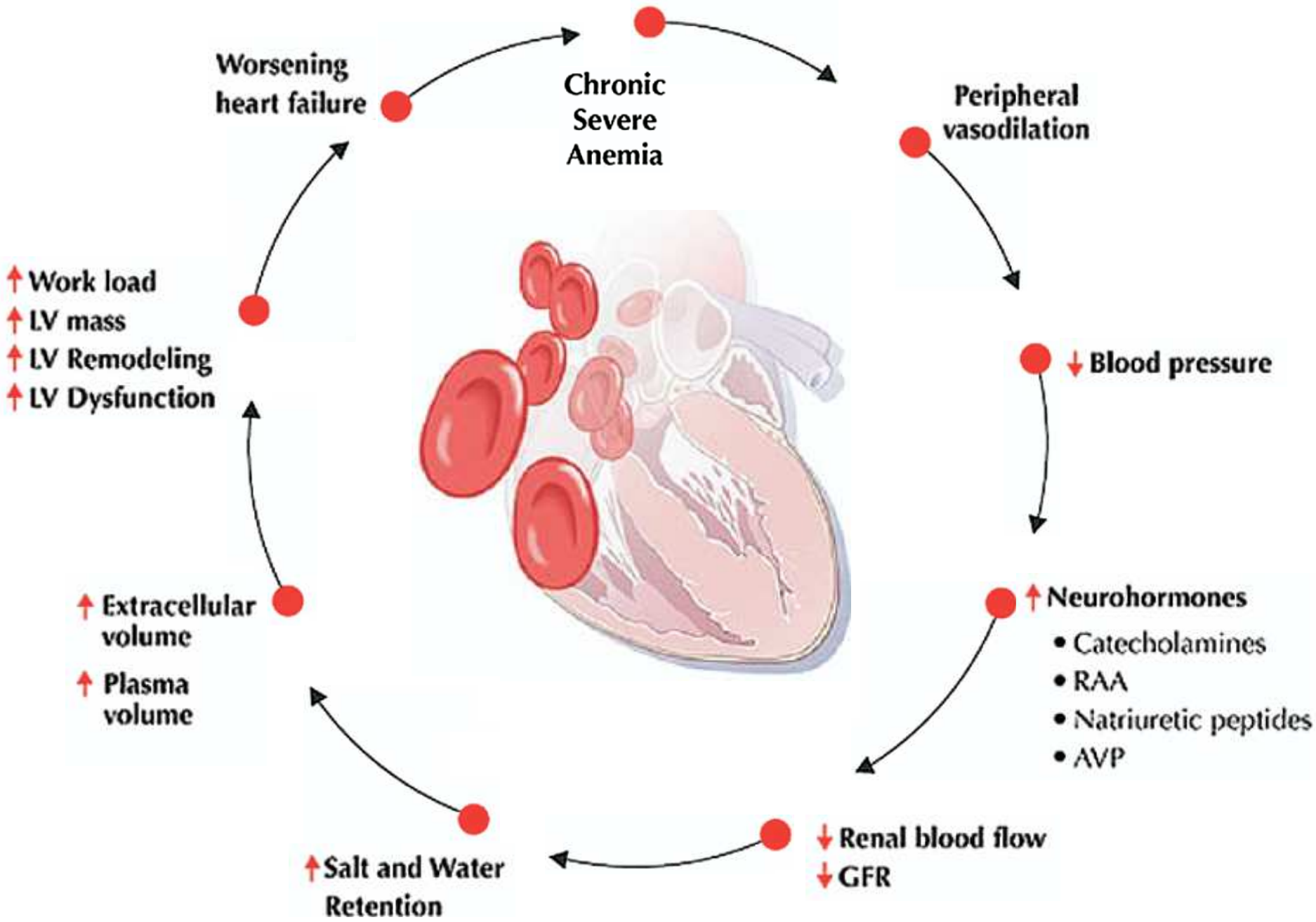
JACC
Journal of the American College of C
JACC Vol. 53, N
February 24, 200

CAUSAS DE ANEMIA EN FALLA CARDIACA

STATE-OF-THE-ART PAPER

Anemia: The Point of Convergence or Divergence for Kidney Disease and Heart Failure?

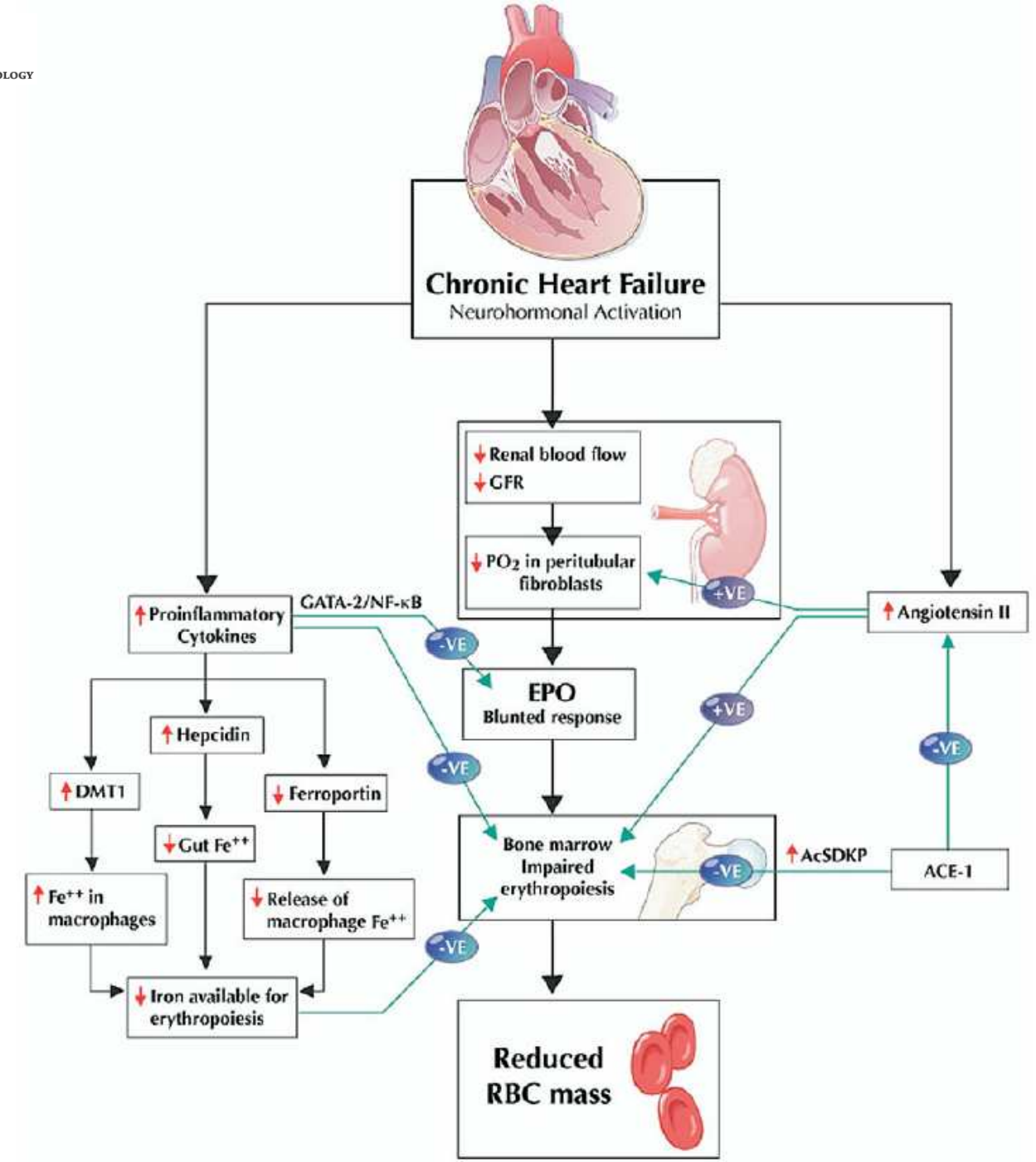
Amir Kazory, MD, Edward A. Ross, MD
Gainesville, Florida



J Am Coll Cardiol 2008;52:5

JACC
Journal of the American College of Cardiology

JOURNAL
CARDIAC FA



J Am Coll Cardiol 2008;52

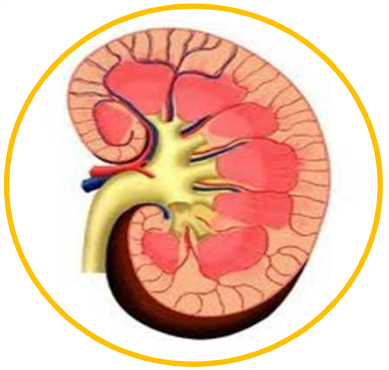
a in Heart Failure: Pathophysiology, Pathogenesis, ent, and Incognitae

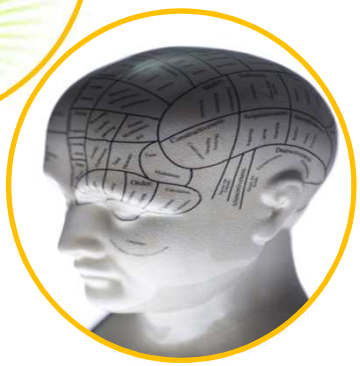
amelo,[a] Soledad Just,[a] and Paloma Gil[b]

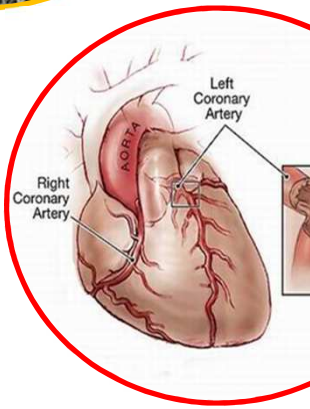
TABLE 1. Consequences of Anemia in Heart Failure*

- Cardiovascular
  - Left ventricular hypertrophy
  - Precipitation of HF
  - Precipitation of CRF
  - Exacerbations of ischemic heart disease
- Reduction
  - Aerobic capacity
  - Exercise tolerance
  - Subjective well-being: quality of life
  - Higher mental functions
  - Possible acceleration of the course of HF and RF

*CRF indicates cardiorenal failure; HF, heart failure; RF, renal failure.







CIRCULO VICIOSO DEL SINDROME DE ANEMIA CARDIO - RENAL

K. Akram, B.L. Pearlman / International Journal of Cardiology 117 (2007) 2

a en la insuficiencia cardiaca: fisiopatología, patogenia, ento e incógnitas

amelo[a], Soledad Justo[a] y Paloma Gil[b]

TABLA 2. Posibles mecanismos proanémicos de los inhibidores de la enzima de conversión de la angiotensina y los antagonistas de la angiotensina I

Renal
- Disminución de la síntesis endógena de EPO

Médula ósea
- Disminución de la respuesta a EPO
- Inhibición del crecimiento de precursores eritroides.
  - Modificación de la respuesta al tratamiento con rHuEPO
  - Disminución de los valores de IGF-1
  - Inhibición del catabolismo de N-acetil-seril-aspartil-prolina, péptido que disminuye la proliferación de precursores de la serie roja

A VISIÓN DEL CARDIÓLOGO

a 6. Cambios en los niveles de depuración de creatinina en terapia con
o, en pacientes con falla cardiaca, anemia y enfermedad renal moderada

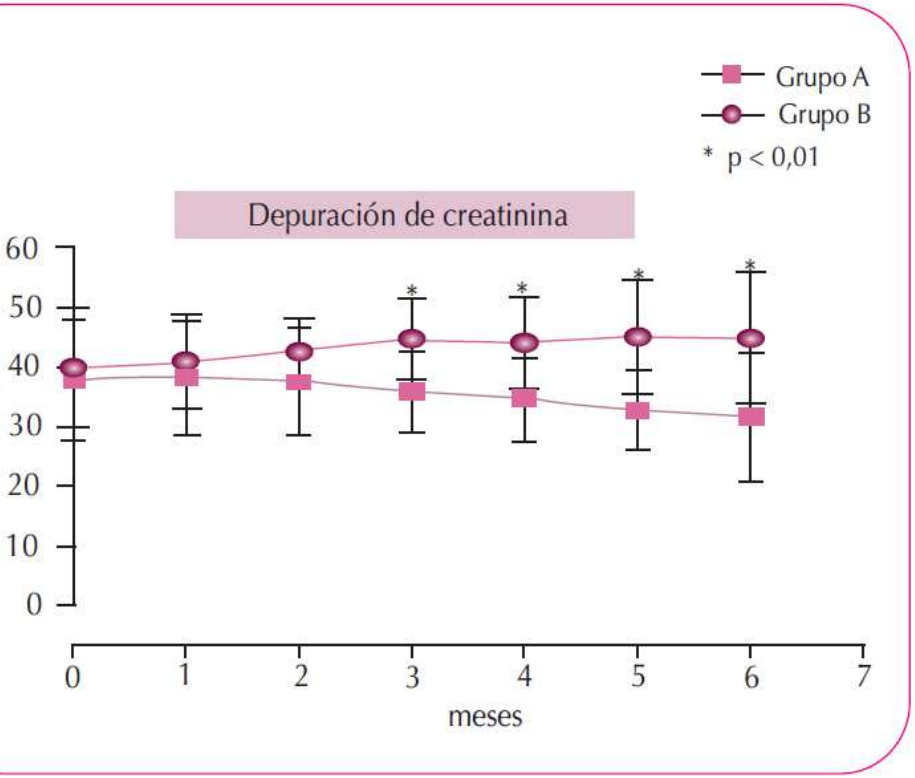
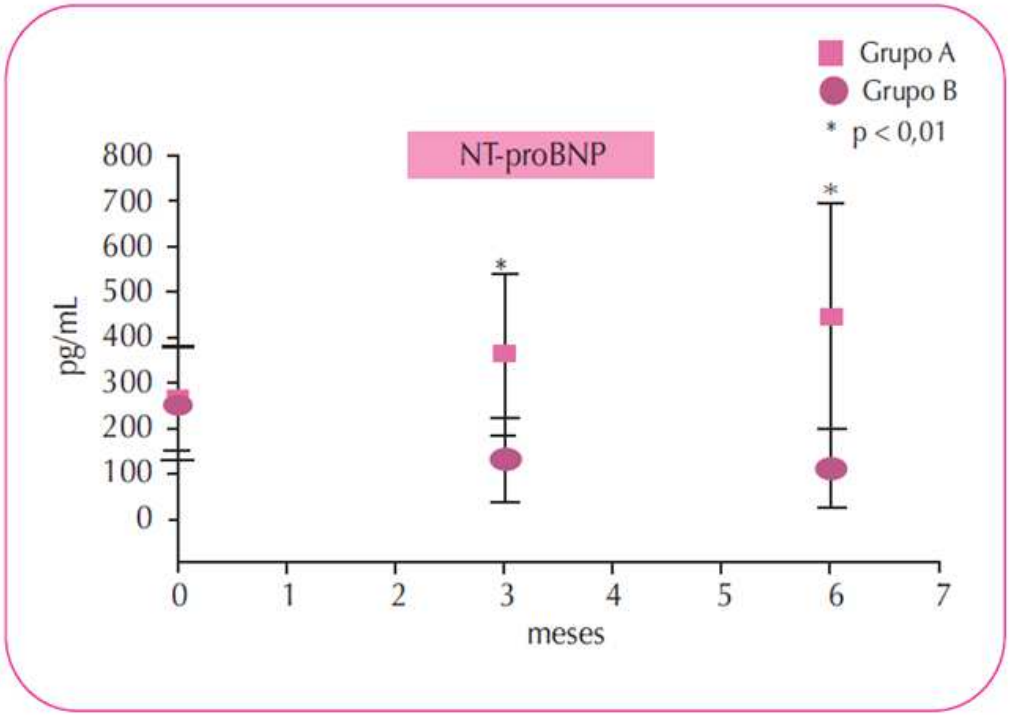


Figura 5. Cambio en los niveles de factor natriurético tipo B (NT-proBNP) en terapia con hierro intravenoso en pacientes con anemia, falla cardiaca e insuficiencia renal.



. Efraín Gómez
lombia

JACC
Journal of the American College of Ca

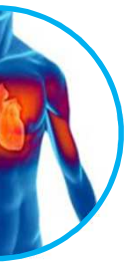
Effect of Correction of Mild Anemia vere, Resistant Congestive Heart Failure Subcutaneous Erythropoietin and enous Iron: A Randomized Controlled Study

Silverberg, MD, Dov Wexler, MD, David Sheps, MD, Miriam Blum, MD, Gad Keren, MD, ch, MD, Doron Schwartz, MD, Tatyana Yachnin, MD, Shoshana Steinbruch, RN, apira, MD, Shlomo Laniado, MD, Adrian Iaina, MD

S DE FUROSEMIDA

Table 3. The Effect of Correction of Anemia by Intravenous Iron and Erythropoietin Therapy on Various Parameters in 16 Patients in the Treatment (A) and 16 in the Control (B) Group

Parameter	Time	Control Mean	Control Std Dev.	Treatment Mean	Treatment Std Dev.	p Value: *t* tests for BL	p Value: Time Effect	p Value: Group Effect	p Value: Interaction Time × Group
IV furosemide mg/wk	Before	49.3	27.6	76.7	36.8	0.03	0.001	NS	<0.0001
	After	63.1	37.1	6.6	28.2				
Oral furosemide mg/d	Before	136.2	86.1	132.2	38.9	NS	NS	0.023	<0.0001
	After	175.0	113.0	64.4	39.1				
Days in hospital	Before	9.9	4.8	13.8	7.2	NS	0.039	0.03	<0.0001
	After	15.6	9.8	2.9	6.6				
Hb, g%	Before	10.9	0.8	10.3	1.2	NS	<0.0001	0.0004	<0.0001
	After	10.8	0.8	12.9	1.1				
Ejection fraction	Before	28.4	7.6	30.8	12.6	NS	NS	<0.013	<0.0001
	After	23.0	6.9	36.3	11.9				
Serum creatine mg%	Before	1.4	0.9	1.7	0.8	NS	0.022	NS	0.006
	After	1.8	0.5	1.7	0.7				

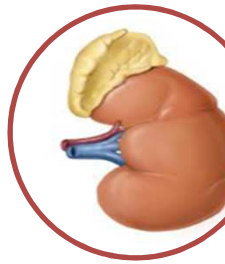


RIA DE LA CLASE FUNCIONAL

PREDICTOR DE HOSPITALIZACION TEMPRANA

REDUCCION EN LOS DIAS DE HOSPITALIZACION

HIERRO → EF ADITIVO



ESTABILIDA DETERIORO

ct of Erythropoietin on Exercise Capacity in Patients With Moderate to Severe Chronic Heart Failure

na M. Mancini, MD; Stuart D. Katz, MD; Chim C. Lang, MD; John LaManca, PhD; Alhakam Hudaihed, MBBS; Ana-Silvia Androne, MD

BLE 1. Clinical Characteristics

	Control (n=8)	EPO (n=15)
Age, y	55±7	60±12
Etiology, n		
CAD	4	8
Cardiomyopathy	4	7
Sex, n		
Male	5	13
Female	3	2
LVEF, %	21±4	24±6
Hemoglobin, g/dL	10.9±1.3	11.0±0.6
Creatinine, mg/dL	1.6±0.5	1.6±0.4
EPO level, mU/L	32±16	24±14
Peak $\dot{V}o_2$, mL · kg^{-1} · min^{-1}	10.0±1.9	11.0±1.8

AD indicates coronary artery disease; LVEF, left ventricular ejection tion.

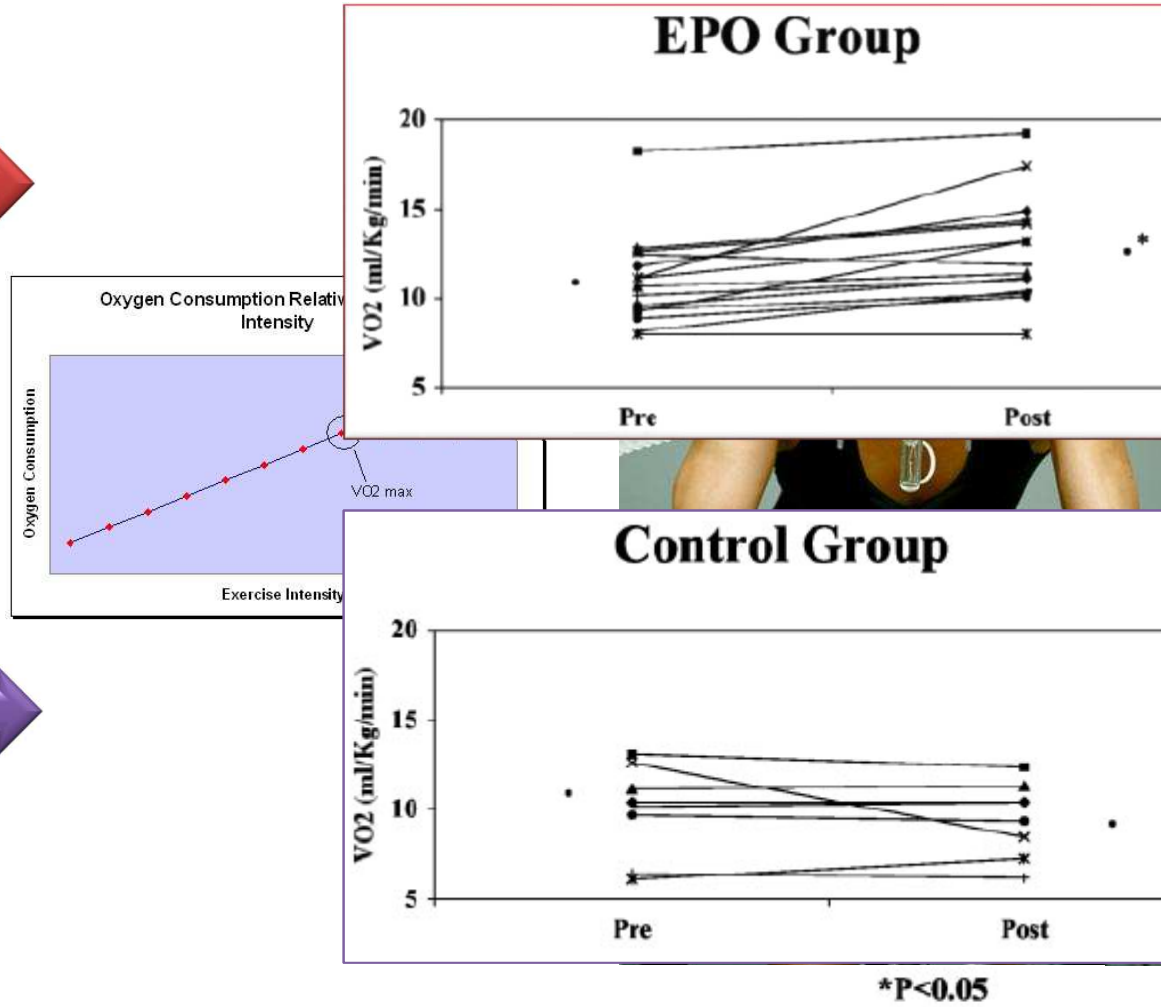


Figure 2. The effect of erythropoietin on peak $\dot{V}o_2$ in the treated and control groups.

rculation

Circulation. 2003;107:

Effect of Erythropoietin on Exercise Capacity in Patients With Moderate to Severe Chronic Heart Failure

Donna M. Mancini, MD; Stuart D. Katz, MD; Chim C. Lang, MD; John LaManca, PhD; Alhakam Hudaihed, MBBS; Ana-Silvia Androne, MD

TABLE 3. Maximal and Submaximal Exercise Capacity at Baseline and End of Study

	Control				EPO			
	Baseline		End		Baseline		End	
	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
Heart rate, bpm	77±9	100±19	81±11	102±22	76±9	106±14	73±7	102±13
Blood pressure, mm Hg	88±8	96±9	81±8	90±10	87±8	94±12	87±8	94±15
Respiratory quotient	0.83±0.04	1.14±0.11	0.88±0.07	1.10±0.11	0.84±0.06	1.13±0.08	0.85±0.07	1.10±0.08
$\dot{V}O_2$		10.0±1.9		9.5±1.6		11.0±1.8		12.7±2.8*
$\dot{V}O_2$ AT		8.2±1.2		7.1±0.8		7.5±1.1		8.7±1.9*
Exercise duration, s		542±115		459±172		590±107		657±119†
6-minute walk distance, ft		929±356		1052±403		1187±279		1328±254*

$\dot{V}O_2$ AT indicates oxygen consumption at anaerobic threshold.
*$P<0.05$ rest vs exercise; †$P<0.004$ rest vs exercise.

↑ DURACION EJERCICIO

↑ DISTANCIA RECORRIDA

American Heart Association.

Circulation. 2003;107:

Currently available erythropoietin stimulating agents

	Biotech company	Main market
ration ESA		
alfa (Epogen)	Amgen	US
alfa (Procrit)	Ortho Biotech	US
alfa (Eprex)	Janssen-Ortho	Worldwide except US
beta ecormon)	Roche	Europe
neration ESA		
oetin (Aranesp)	Amgen	North America, Europe, Canada
eration ESA		
uous poietin receptor r (Mircera)	Roche	Europe

Table 2 Considerations in the use of erythropoietin stimulating agents in chronic kidney disease

1. Etiology of anemia
- Erythropoietin deficiency
- Iron deficiency
- Hyperparathyroidism
- Chronic inflammation
- Angiotensin converting enzyme inhibitors
- Pure red cell aplasia
- Malignancy
- B12 and folate deficiency
- Hemoglobinopathies, eg, sickle cell anemia
- Hemolytic anemia
- Malnutrition

2. Target hemoglobin
- Cardiovascular disease risk

Table 4
Comparative benefits and drawbacks of the use of erythropoietin and red transfusion for the treatment of anemia

Intervention	Advantages	Disadvantages
Erythropoietin	Increased hemoglobin	Delayed hemoglobin improvement
	Improved exercise tolerance	Hypertension
	Improved NYHA functional class	Thrombophilia
	Improved LVEF	Endothelial prolifera
	Decreased diuretic requirement	Unproven cost-effectiveness
	Improved quality of life	
	Decreased hospitalization	
	Decreased apoptosis	
	Regression of LV remodeling	
Red cell transfusion	Rapid hemoglobin improvement	Potential infectious transmission
	Improved hemodynamics	Transfusion reaction
		Immunosuppression
		Proinflammatory sta
		Iron overload with long-term use

Abbreviations: NYHA, New York Heart Association; LVEF, left ventri ejection fraction; LV, left ventricle.

Table 1. Current and Future Erythropoietic Agents for the Treatment of ESRD Anaemia

ESA Class	ESA Type	Marketed as, e.g.	Mol. Weight (KDa)	Serum Half Life (h)/Route of Administ.	Bioavai-lability (%)	Perio-dicity
Unmodified recombinant rhu EPOs ("short-acting")	Epoetin alfa	Procrit (Johnson&Johnson), Epogen (Amgen), Eprex (OrthoBiotech)	32-40	8.8 / i.v. 24.2 / s.c.	30-36	1-3 times/wk
	Epoetin beta	NeoRecormon (Roche)		6.8 / i.v. 19.4 / s.c.	23-42	1-3 times/wk
	Epoetin omega	Epomax (Baxter)				
	Epoetin delta	Dynepo (Shire)				
Long-acting ESAs	Darbepoetin alpha	Aranesp (Amgen)	40	25 / i.v. 49 / s.c.	37	Every 1-2 wk
	C.E.R.A.	Mircera (Roche)	60	133 / i.v. 137 / s.c.	47-52	Every 2-4 wk
EPO analogues (Biosimilar EPOs)	Epoetin alfa	Epoetin alfa Hexal (Hexal Biotech), Binocrit (Sandoz),	32-40	4 / i.v. 24 / s.c.	20	1-3 times/wk
	Epoetin zeta	Silapo (cell pharm), Abseamed (Medice)	30.6	4-5 / i.v. 24 / s.c.	n.a.	1-3 times/wk
Investiga-tional ESAs	Synthetic, peptide-based erythropoietin-receptor agonists	Hematide (Affymax/Takeda)	n.a.	14-60 / p.o.	n.a.	Every 4 wks
	Prolyl hydroxylase inhibitors (HIF stabilizers)	FG-2216*, FG-4592 (FibroGen)	n.a.	7-8 / p.o.	>75	*

Abbreviations: C.E.R.A. Continuous Erythropoietin Receptor Activator, ESA erythropoiesis stimulating agents HIF Hypoxia Inducible Factor, n.a. no information currently available, wk week. Route of administration: p.o. per os, i.v. intravenous, s.c. subcutaneous.

* Note: FDA has for now suspended any further clinical trials with HIF stabilizers, as a female patient developed fatal hepatic necrosis that was temporally related to the introduction of FG-2216.

hropoietin improves anemia exercise tolerance renal function and reduces B-type natriuretic ide and hospitalization in patients with heart re and anemia

alazzuoli, MD, PhD,[a] Donald Silverberg, MD,[b] Francesca Iovine, MD,[a] Stefano Capobianco, MD,[a] Giannotti, MD,[a] Anna Calabrò, PhD,[a] Maria Stella Campagna, PhD,[a] and Ranuccio Nuti, MD[a] *Siena, Italy; wiv, Israel*

Initial status, main etiologies of the cardiac disease, y parameters, and the initial echocardiographic findings groups

	Group A (n = 20)	Group B (n =18)
	72 ± 5	75 ± 6
e ratio	13/7	10/8
s	12 III/8 IV	11 III/7 IV
rtery disease	11	10
diomyopathy	6	3
on	2	3
e disease	1	1
e disease	–	1
ration (g/dL)	10.4 ± 0.6	10.6 ± 0.7
tinine (mg/dL)	2.5 ± 0.4	2.4 ± 0.6
clearance (mL/min)	43 ± 9	45 ± 11
m^2)	108 ± 20	106 ± 12
m^2)	78 ± 17	76 ± 9
	28.3 ± 4	28 ± 6
²)	202 ± 20	197 ± 10

ntricular end-diastolic index; *LVESI*, left ventricular end-systolic index; ntricular mass index.

Table III. Comparison of the initial and final (3-month) heart rate, blood pressure, walking distance with exercise, oxygen consumption exercise, NYHA class, and BNP levels between the 2 groups

	Initial	Final	Initial	F
Heart rate (beat/min)	84 ± 8	80 ± 8	82 ± 8	84
Systolic BP (mm Hg)	134 ± 10	136 ± 10	130 ± 10	128
Diastolic BP (mm Hg)	82 ± 6	85 ± 8	82 ± 5	80
Distance walked (m)	278 ± 55	356 ± 88*	285 ± 68	266
Exercise duration (min)	5.8 ± 2.2	7.8 ± 2.5	5.8 ± 2.4	6.0
$V \cdot O_2$ (mL/kg per min)	12.8 ± 2.8	15.1 ± 2.8†	12.5 ± 3.1	12.0
$V \cdot O_2$ AT (mL/kg per min)	9.2 ± 2.0	13.2 ± 3.6*	9.0 ± 2.5	8.7
Respiratory rate (breath/min)	21.2 ± 4.8	31.1 ± 6.3†	20.8 ± 4.5	21.5
RER ($V \cdot CO_2/V \cdot O_2$)	0.96 ± 0.20	1.15 ± 0.18	0.99 ± 0.18	1.0
NYHA class	3.5 ± 0.6	2.8 ± 0.5†	3.4 ± 0.6	3.6
BNP pg/mL	568 ± 320	271 ± 120*	585 ± 342	496

$V \cdot O_2$, Oxygen consumption during maximal exercise; $V \cdot O_2$ *AT*, is oxygen consumption at anaerobic threshold; *BP*, blood pressure; *RER*, respiratory exchange rat
*$P < .01$ (intergroup and intragroup).
†$P < .05$ (intragroup and intergroup).

rt J 2006;152:1096.e9-1096.e15.

oietin improves anemia exercise tolerance
l function and reduces B-type natriuretic
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ti, MD,[a] Anna Calabrò, PhD,[a] Maria Stella Campagna, PhD,[a] and Ranuccio Nuti, MD[a] *Siena, Italy;*
el

V. Comparison of renal function and red cell parame-
veen the 2 groups at the start and after the 3-month
d study

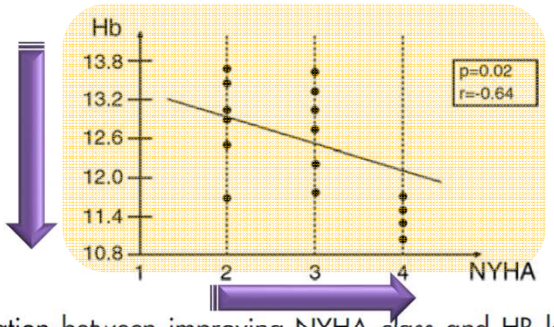
	Group A (n = 20)		Group B (n = 18)	
	Initial	Final	Initial	Final
	2.5 ± 0.3	1.8 ± 0.4*	2.4 ± 0.6	2.2 ± 0.5
	43 ± 9	50 ± 14†	45 ± 11	47 ± 8
	10.4 ± 0.6	12.4 ± 0.8*	10.6 ± 0.7	10.5 ± 0.6
	30 ± 3	36.4 ± 4*	32 ± 4	31 ± 5
	3.3 ± 0.4	4.2 ± 0.6†	3.4 ± 0.5	3.2 ± 0.5

ergroup and intragroup).
ragroup and intergroup).

EJORIA DE LA FUNCION RENAL

rt J 2006;152:1096.e9-1096.e15.

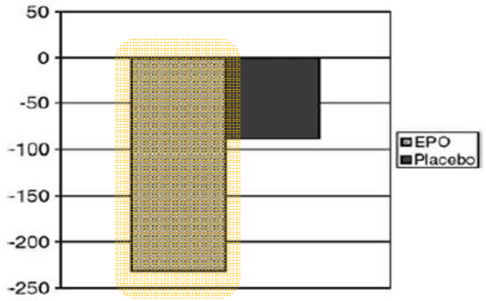
Figure 2



Correlation between improving NYHA class and HB levels in EPO group: increased NYHA classes appear related to lower HB levels.

ANEMIA – EMPEORAMIENTO CLASE FUNCIONAL

Figure 3



Mean ΔBNP reduction values after three months in EPO and placebo groups.

↓ DISMINUCION BNP

American
Asso

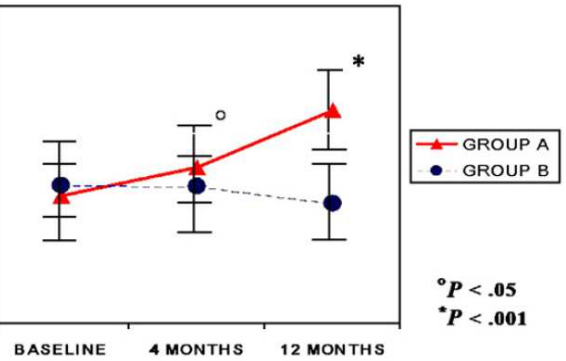
↓ HOSPITALIZACION

Table V. Hematological and BNP values, mortality an
hospitalizations at the end of the one year follow-up

Parameter	Group A	Group B
Hb (g/dL)	11.6 ± 0.4	9.8 ± 0.5
Hct (%)	35.2 ± 3	30.4 ± 2.3
RBC	3.8 ± 0.5	3.2 ± 0.5
BNP	322 ± 187	538 ± 24
Deaths	1	2
Frequency hospitalization per patient per year	0.8	1.7
No. (%) of patients hospitalized over the year	4/20 (20)	8/18 (44.4

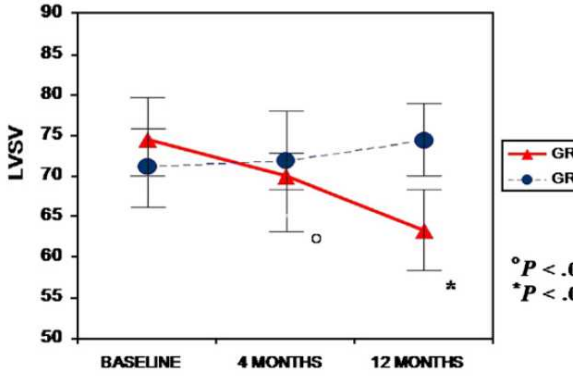
Effects of β-erythropoietin treatment on left ventricular remodeling, systolic function, and B-type natriuretic peptide levels in patients with the cardiorenal anemia syndrome

Alberto Palazzuoli, MD, PhD,[a] Donald S. Silverberg, MD,[b] Francesca Iovine, MD,[a] Anna Calabrò, PhD,[a] Maria S. Campagna, PhD,[a] Maddalena Gallotta, MD,[a] and Ranuccio Nuti, MD[a]



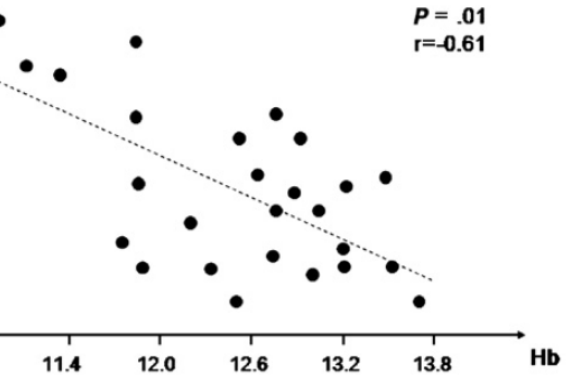
VEF values at start, 4 months, and 12 months of follow-up n group A (EPO) and group B (placebo). Erythropoietin improved LVEF after 12 months.

EDAD = 74 AÑOS
FEVI = 30 %
D. CREA = 43 ml/min
NYHA III – IV
C.ISQUEMICA = 60 %
HB = 10.4 gr/dL

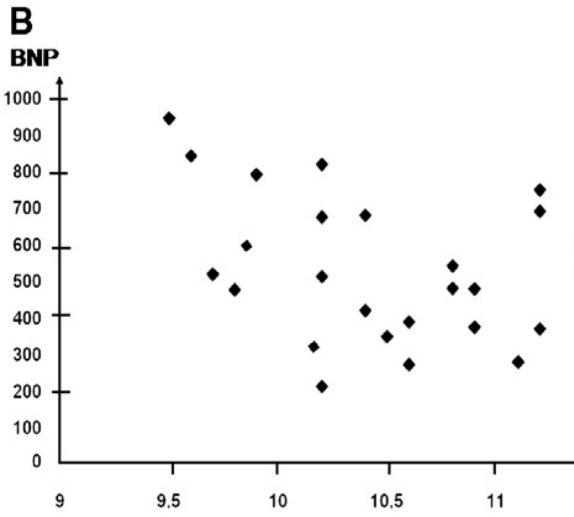


Mean LVSV at start, 4 months, and 12 months of follow-up p group A (EPO) and group B (placebo). Erythropoietin reduced LVSV after 4 and 12 months.

Relationship between BNP and Hb levels after 12 months in 2 groups: in EPO-treated patients, BNP decreased together with Hb increase.

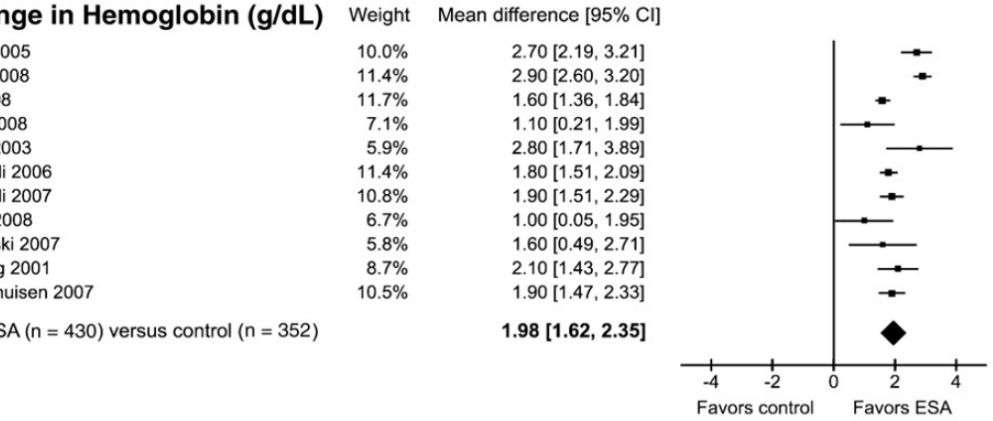


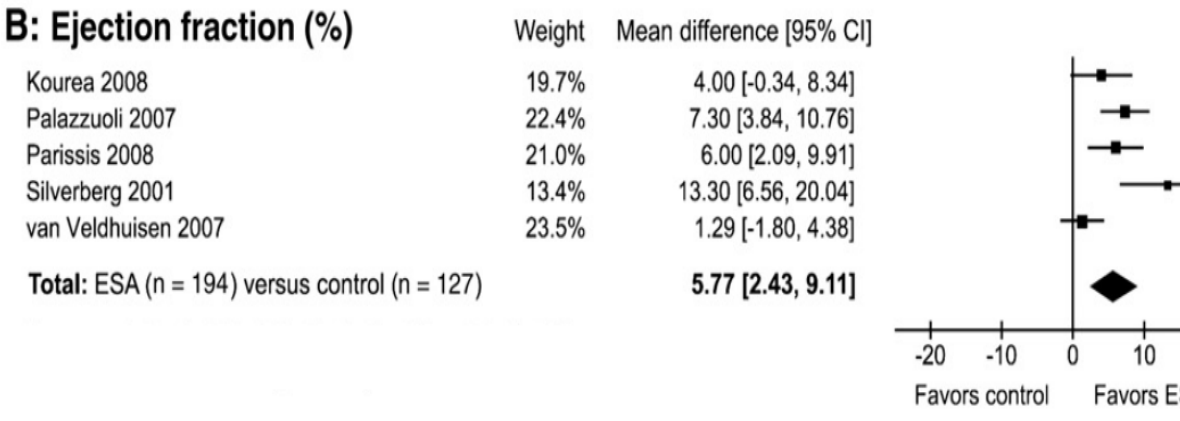
MEJORIA
- ✓ **FEVI**
- ✓ **LVSV**
- ✓ **PSAP**
- ✓ **BNP**

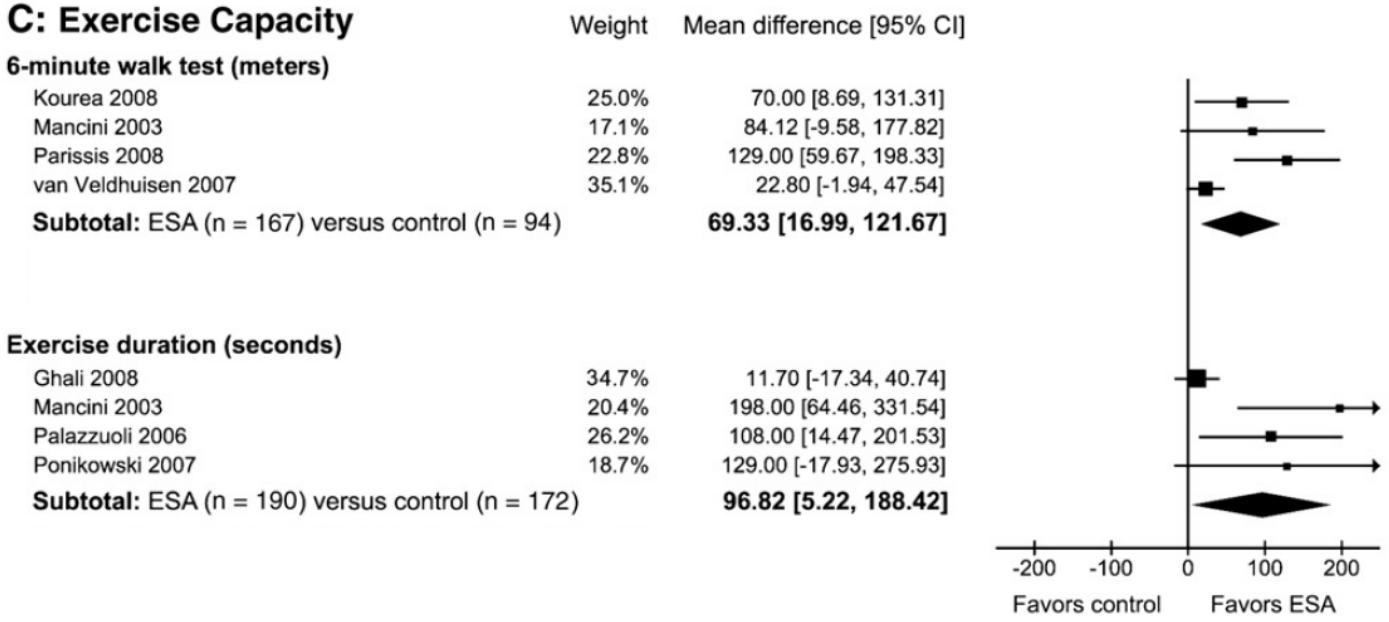


Am Heart J 2007;154:645.e9-645.e15.

ropoietin as a treatment of anemia in heart failure: ematic review of randomized trials





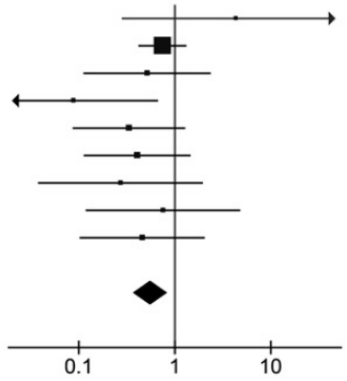


Kotecha D, Ngo K, Walters JA. Erythropoietin as a treatment of anemia in heart failure: systematic review of randomized trials. Am Heart J. 2011 May; 161(5):

t Failure Hospitalizations

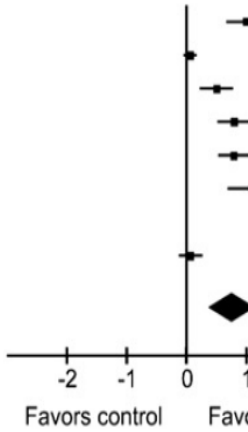
	ESA Events	ESA Total	Control Events	Control Total	Weight	Peto Odds Ratio [95% CI]
05	3	18	0	6	2.2%	4.31 [0.28, 66.37]
	25	162	31	157	50.5%	0.74 [0.42, 1.32]
8	3	21	5	20	7.2%	0.51 [0.11, 2.36]
03	1	15	4	8	4.1%	0.09 [0.01, 0.67]
2006	4	20	8	18	9.2%	0.33 [0.09, 1.28]
2007	4	26	8	25	10.2%	0.40 [0.11, 1.46]
08	2	21	3	11	4.3%	0.27 [0.04, 1.96]
2007	2	19	3	22	4.9%	0.75 [0.12, 4.80]
sen 2007	4	110	4	55	7.4%	0.46 [0.10, 2.05]
SA (48/412) versus control (66/322)						**0.56 [0.37, 0.84]**

ity: Chi² = 7.78, df = 8 (*P* = .46); I² = 0%
erall effect: Z = 2.80 (*P* = .005)



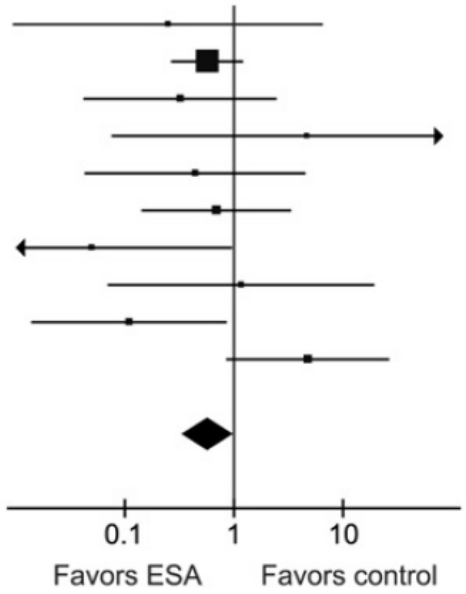
D: NYHA Class

	Weight	Mean difference [95% CI]
Cosyns 2008	12.2%	-1.00 [-1.34, -0.66]
Ghali 2008	13.4%	-0.06 [-0.17, 0.05]
Kourea 2008	12.6%	-0.50 [-0.78, -0.22]
Palazzuoli 2006	12.5%	-0.80 [-1.09, -0.51]
Palazzuoli 2007	12.6%	-0.80 [-1.07, -0.53]
Parissis 2008	11.6%	-1.10 [-1.51, -0.69]
Silverberg 2001	11.9%	-1.70 [-2.07, -1.33]
van Veldhuisen 2007	13.1%	-0.07 [-0.27, 0.13]
Total: ESA (n = 370) versus control (n = 287)		**-0.73 [-1.11, -0.36]**



B: All-Cause Mortality

	ESA Events	ESA Total	Control Events	Control Total	Weight	Peto Odds Ratio [95% CI]
Cleland 2005	1	18	1	6	2.7%	0.25 [0.01, 6.54]
Ghali 2008	11	162	18	157	49.0%	0.57 [0.27, 1.22]
Kourea 2008	1	21	3	20	6.9%	0.32 [0.04, 2.47]
Mancini 2003	1	15	0	8	1.7%	4.63 [0.08, 283.86]
Palazzuoli 2006	1	20	2	18	5.2%	0.44 [0.04, 4.54]
Palazzuoli 2007	3	26	4	25	11.4%	0.69 [0.14, 3.35]
Parissis 2008	0	21	2	11	3.2%	0.05 [0.00, 0.96]
Ponikowski 2007	1	19	1	22	3.6%	1.16 [0.07, 19.41]
Silverberg 2001	0	16	4	16	6.7%	0.11 [0.01, 0.86]
van Veldhuisen 2007	6	108	0	55	9.6%	4.75 [0.85, 26.48]
Total: ESA (25/426) versus control (35/338)						**0.58 [0.34, 0.99]**



Kotecha D, Ngo K, Walters JA. Erythropoietin as a treatment of anemia in heart failure: systematic review of randomized trials. Am Heart J. 2011 May; 161(5):

# of darbepoetin α on right and left ventricular c and diastolic function in anemic patients with c heart failure secondary to ischemic or idiopathic l cardiomyopathy

sis, MD,[a] Kallirrhoe Kourea, MD,[a] Fotios Panou, MD, Dimitrios Farmakis, MD, kevaidis, MD, Ignatios Ikonomidis, MD, Gerasimos Filippatos, MD, and Kremastinos, MD *Athens, Greece*

↓ INJURIA ISQUEMIA - REPERFUSION

↓ TAMAÑO INFARTO

↑ ENTREGA O2

EFECTO ANGIOGENICO

↓ REMODELACION

ROL ANTIAPOPTOTICO

↓ STRESS PARED

↑ CITOQUINAS CARDIOPROTECTORAS

↑ CONTRACTILIDAD

↑ FEVD

↓ PSAP

PREVIENE LA HIPERTROFIA COMPENSATORIA

MEJORIA DE LOS PARAMETROS HEMODINAMICO

↓ VOLUMENES INTRACARDIACOS

↑ TOLERANCIA AL EJERCICIO

↓ NEUROHORMONAL

PRESERVA LA RESERV CARDIOVASCULAR

OPTIMIZA LA FUNCION VENTRICULAR DERECHA

	Darbepoetin α (n = 2	
	Baseline	Fir
LV end-diastolic diameter (mm)	67.6 ± 9	65.8
LV end-systolic volume (mL)	172 ± 73	154
LVEF (%)	26 ± 6	
RVEF (%)	45 ± 9	
RV systolic pressure (mm Hg)	51 ± 15	4

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Volume 46, Number 2,

Once-Monthly Administration of Darbepoetin Alfa for the Treatment of Patients with Chronic Heart Failure and Anemia

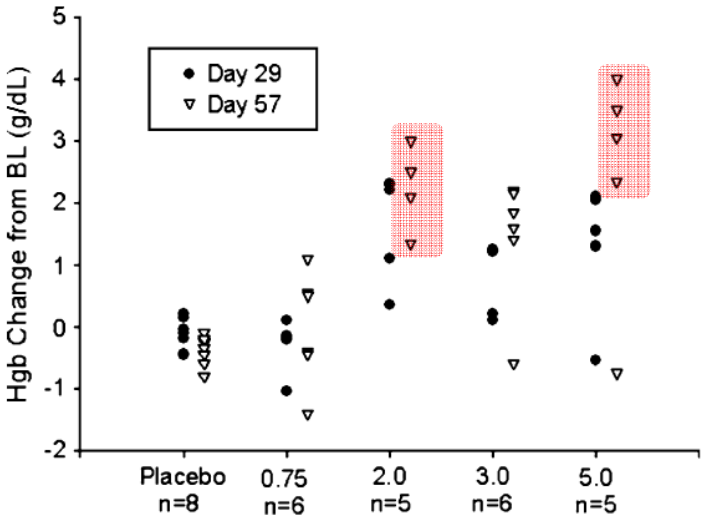
A Pharmacokinetic and Pharmacodynamic Investigation

TABLE 1. Baseline Demographics of Study Population

	Placebo*		Darbepoetin Alfa 0.75 µg/kg SC/IV		Darbepoetin Alfa 2.0 µg/kg SC		Darbepoetin Alfa 3.0 µg/kg SC		Darbepoetin Alfa 5.0 µg/kg SC	
	CHF (n = 9)	HS (n = 8)	CHF (n = 6)	HS (n = 4)	CHF (n = 6)	HS (n = 6)	CHF (n = 6)	HS (n = 6)	CHF (n = 6)	HS (n = 6)
Mean age (y)	74 (9)	74 (9)	69 (14)	64 (13)	72 (8)	69 (7)	64 (19)	64 (17)	67 (8)	65 (8)
NYHA Class III/IV (n)	6		5		2		3		5†	
LVEF (%)	28 (7)†		34 (6)		36 (4)†		32 (6)		35 (9)	
Hgb (g/dL)	11.5 (0.5)	13.8 (1.1)	11.8 (0.6)	14.3 (0.4)	11.0 (1.0)	14.0 (0.7)	12.1 (0.6)	14.4 (0.6)	11.2 (1.1)	14.0 (0.3)
CrCl (mL/min)	41 (14)	54 (12)	39 (19)	100 (36)	43 (24)	61 (18)	68 (48)	62 (18)	43 (13)	66 (13)

30 PACIENTES SANOS
3 PACIENTES F. CARDIACA

FEVI < 40 %
CREATININA < 46 ML / MIN
HB < 12 gr/dL
64% NYHA III – IV
CLUYERON OTRAS CAUSAS ANEMIA



↑ SOSTENIDO HB
SIN CAMBIOS BNP – FEVI –

MUERTES
1 PACIENTE SANO
3 PACIENTES ICC

Effect of Darbepoetin Alfa on Exercise Tolerance in Anemic Patients With Symptomatic Chronic Heart Failure

A Randomized, Double-Blind, Placebo-Controlled Trial

OBJETIVO PRIMARIO.
MBIOS TOLERANCIA EJERCICIO
SAL – SEMANA 27
O VO2

OBJETIVO SECUNDARIO.
URACION EJERCICIO
AMBIOS HEMOGLOBINA
ASE FUNCIONAL
VELES BNP

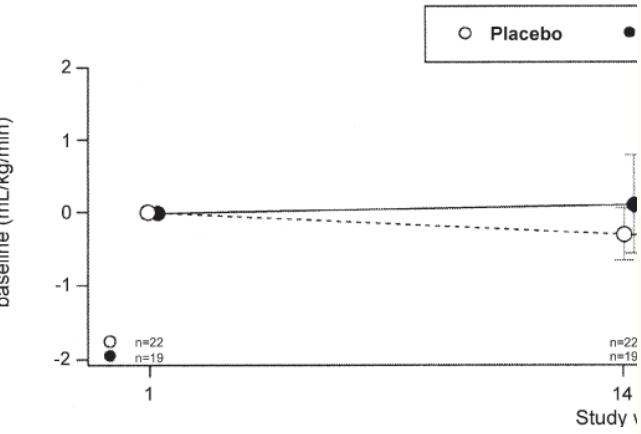
Table 5 Adverse Events

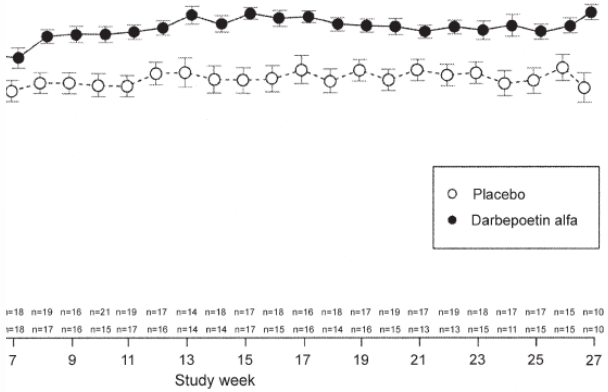
	Placebo (n = 22)	Darbepoetin Alfa (n = 19)
All adverse events, n (%)	13 (59)	15 (79)
Serious adverse events	5 (23)	4 (21)
Life-threatening adverse events	2 (9)	1 (5)
Deaths	1 (5)	1 (5)
Events with a >5% difference in incidence between treatment groups, n (%)		
Neurologic signs and symptoms NEC	1 (5)	4 (21)
Upper respiratory tract infections	0 (0)	3 (16)
Coughing and associated symptoms	4 (18)	2 (11)
Joint-related signs and symptoms	0 (0)	2 (11)
Musculoskeletal and connective tissue signs and symptoms NEC	4 (18)	2 (11)
Appetite disorders	2 (9)	0 (0)
Breathing abnormalities	4 (18)	0 (0)
Gastrointestinal atonic and hypomotility disorders NEC	2 (9)	0 (0)
Ischemic coronary artery disorders	2 (9)	0 (0)
Nausea and vomiting symptoms	5 (23)	0 (0)
Physical examination procedures	2 (9)	0 (0)
Adverse events of special interest, n (%)	3 (14)	3 (16)
Hypertension	0 (0)	1 (5)
Deep vein thrombosis	0 (0)	0 (0)
Pulmonary emboli	0 (0)	0 (0)
Congestive heart failure	2 (9)	1 (5)
Cerebrovascular disorder	0 (0)	1 (5)
Myocardial infarction	1 (5)	0 (0)
Seizure	0 (0)	0 (0)

NEC = not elsewhere classifiable.

MEJORIA
✓ NIVELES HEMOGLOBINA
✓ PGA – CALIDAD DE VIDA

RESULTADOS
✓ PICO VO2 SIN CAMBIOS
✓ SIN CAMBIOS – C. FUNCIONAL
HOSPITALIZACION
DARBO. - n = 4
PLACEBO – n = 9





al.
Alfa in Heart Failure

JACC Vol. 49
February 20,

pean Heart Journal

EUROPEAN SOCIETY OF CARDIOLOGY

Randomized, double-blind, placebo-controlled to evaluate the effect of two dosing regimens of darbepoetin alfa in patients with heart failure and anaemia

Dirk J. van Veldhuisen[1]*, Kenneth Dickstein[2], Alain Cohen-Solal[3], Dirk J.A. Lok[4], Scott M. Wasserman[5], Nigel Baker[6], Dylan Rosser[6], John G.F. Cleland[7], and Piotr

44 CENTROS

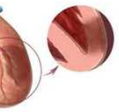
USA / EUROPA

15 PAISES

165 PACIENTES

EDAD – 71 AÑOS

NYHA II - III



FEVI = 29 %

70 % - C. ISQUEMICA

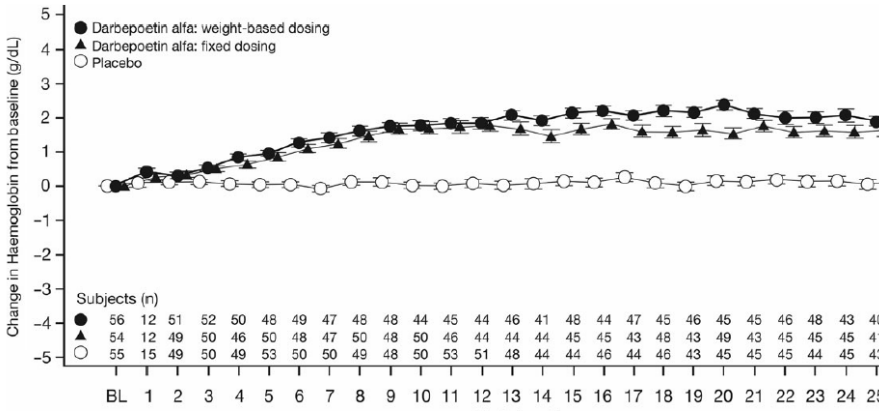
Hb = 11 .2 gr / dL

D.C= 54 ml / min

METODOLOGIA
2 REGIMENES
BASADO PESO vs DOSIS FIJA
B. PESO – n = 56
D. FIJA – n = 54
PLACEBO – n = 55
26 SEMANAS

RESULTADOS
↑ NIVELES HEMOGLOBINA
↑ D. CREATININA
↓ NIVELES CREATININA

SN CAMBIOS
6MWT
NYHA
PGA - KCCQ



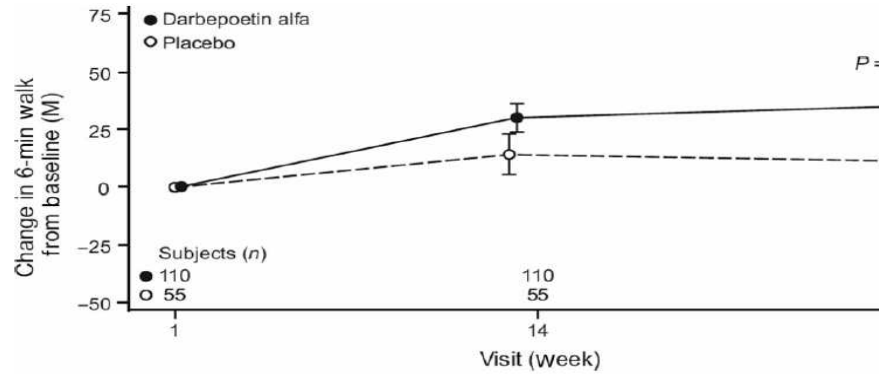


Figure 3 Change from baseline at week 27 in 6 min walk distance. Values are mean ± standard err

Table 3 Summary of adverse events

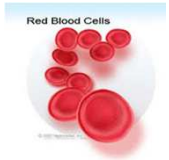
Adverse event (*n*, %)	Placebo (*n* = 55) *n* (%)	Darbepoetin alfa		
		Weight-based dosing (*n* = 55) *n* (%)	Fixed dosing (*n* = 53) *n* (%)	All (*n* = 108) *n* (%)
Any adverse event	42 (76)	45 (82)	41 (77)	86 (80)
Serious adverse events	15 (27)	13 (24)	12 (23)	25 (23)
Treatment-related adverse events	4 (7)	5 (9)	7 (13)	12 (11)
Related serious adverse events	0 (0)	0 (0)	1 (2)	1 (1)
Related fatal adverse events	0 (0)	0 (0)	0 (0)	0 (0)
Adverse events of specific interest				
Congestive heart failure	9 (16)	9 (16)	3 (6)	12 (11)
Hypertension	2 (4)	2 (4)	0 (0)	2 (2)
Myocardial infarction	0 (0)	1 (2)	1 (2)	2 (2)
Cerebrovascular disorder	0 (0)	0 (0)	0 (0)	0 (0)
Deep vein thrombosis	0 (0)	0 (0)	0 (0)	0 (0)
Pulmonary emboli	1 (2)	0 (0)	0 (0)	0 (0)
Seizure	0 (0)	0 (0)	0 (0)	0 (0)
Discontinuation due to adverse events	1 (2)	0 (0)	0 (0)	0 (0)
Deaths on study[a]	0 (0)	5 (9)	1 (2)	6 (6)

[a]Includes deaths occurring within 30 days of study drug administration, or until end of study, whichever is later.

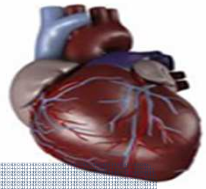
Randomized Double-Blind Trial of Darbepoetin Alfa in Patients With Symptomatic Heart Failure and Anemia

Jalal K. Ghali, Inder S. Anand, William T. Abraham, Gregg C. Fonarow, Barry Greenberg, Henry Krum, Barry M. Massie, Scott M. Wasserman, Marie-Louise Trotman, Yan Sun, Beat Knusel and Paul Armstrong

	Placebo (N=157)	Darbepoetin alfa (N=162)
Medical history, n (%)		
Ischemic heart disease	124 (79)	
Hypertension	104 (66)	
Myocardial infarction	97 (62)	
Diabetes	79 (50)	
assification, n (%)		
ng	1 (1)	0 (0)
I	3 (2)	1 (1)
II	51 (32)	62 (38)
III	97 (62)	96 (59)
IV	5 (3)	3 (2)



Age, mean (SD), y	69 (10)	
n, g/dL	11.3 (10.7, 11.9)	11.5 (11.0, 12.0)

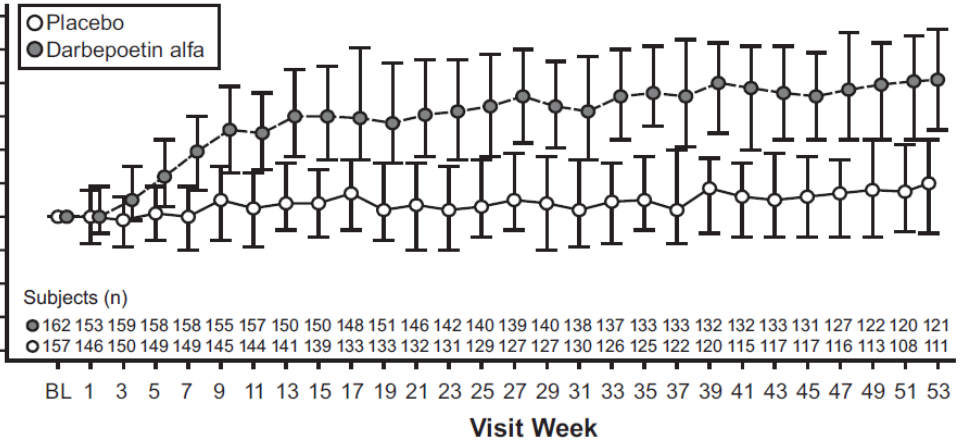


Left ventricular ejection fraction, mean (SD), %	36 (9)	35 (10)
Creatinine, mg/dL	1.4 (1.2, 1.8)	1.5 (1.1, 1.9)
eGFR, mL · min^{-1} · 1.73 m^{-2}*	47.5 (37.4, 62.3)	47.2 (36.3, 64.6)

rculation
OF THE AMERICAN HEART ASSOCIATION

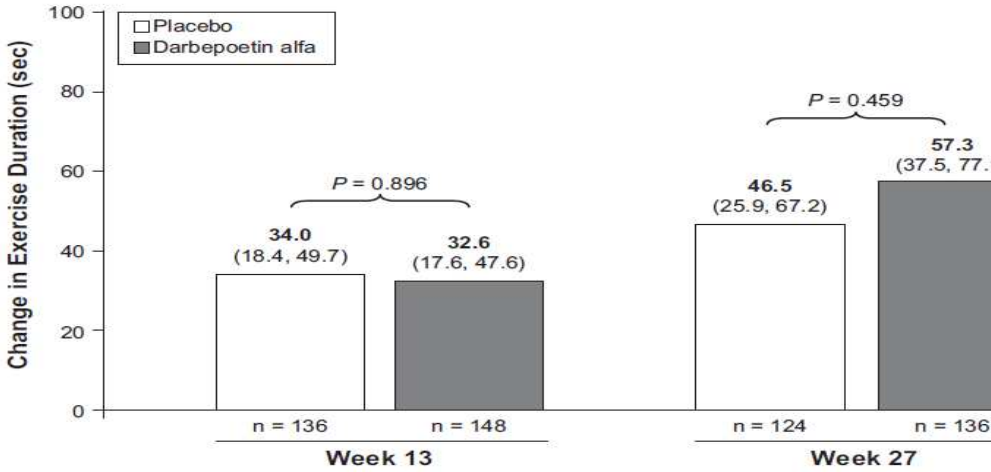
Circulation. 2008;117:5

Randomized Double-Blind Trial of Darbepoetin Alfa in Patients With Symptomatic Heart Failure and Anemia

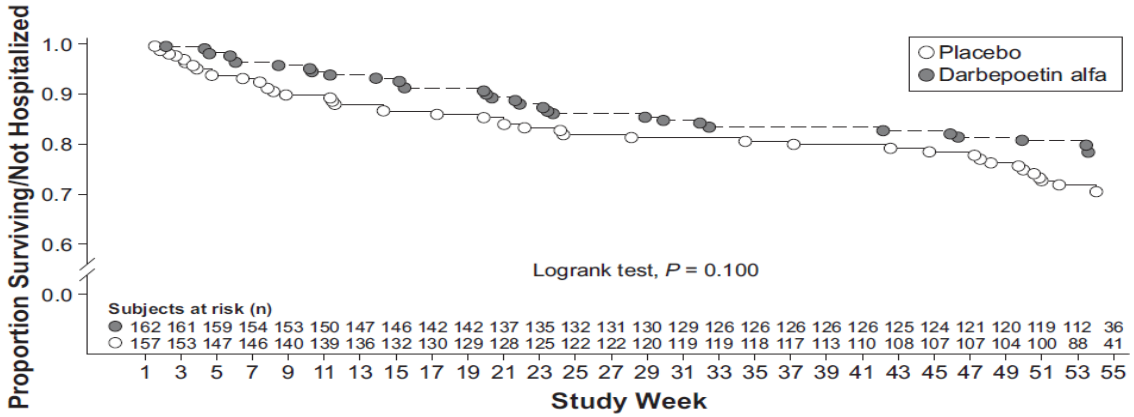


. Median change from baseline in hemoglobin over time (safety analysis set). Vertical lines represent IQR.

INCREMENTO EN LAS CIFRAS DE HEMOGLOBINA



DURACION DEL EJERCICIO SIN CAMBIOS



MENOR RIESGO DE MUERT Y/O HOSPITALIZACION

Hazard ratio (95% CI) darbepoetin alfa (N = 162) vs placebo (N = 157)	
All-cause mortality or first HF-related hospitalization	0.68 (0.43, 1.08)
All-cause mortality	0.56 (0.27, 1.19)
HF-related hospitalization	0.74 (0.44, 1.26)

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Circulation. 2008;117

Treatment of Anemia with Darbepoetin Alfa in Systolic Heart Failure

The NEW ENGLAND JOURNAL of MEDICI

CRITERIOS DE INCLUSION
NYHA > II
FEVI < 40 %
Hb 9.0 – 12.0 gr/Dl
MANEJO PARA FALLA CARDIACA.

DARBOPOYETINA
n = 1136

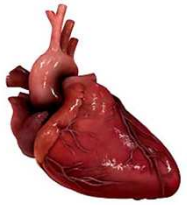
PLACEBO
n = 1142

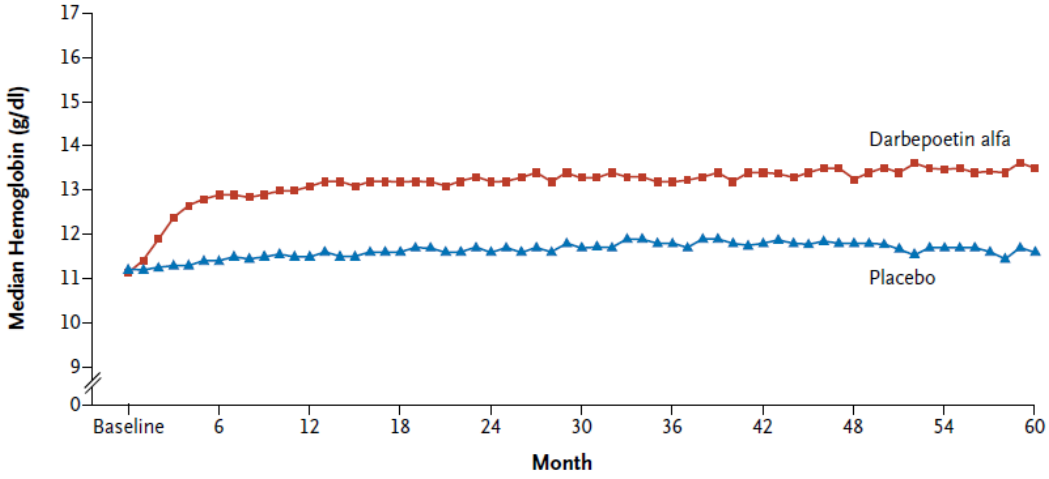
JUN 13, 2006 – 16 MAY,2012

OBJETIVO PRIMARIO.
MUERTE POR CUALQUIER CAUSA o 1ra HOSPITALIZACION POR ICC

OBJETIVO SECUNDARIO.
MUERTE POR CAUSA CV
CAMBIOS SCORE KCCQ
CAMBIOS EN NIVELES Hb

EDAD = 72 AÑOS
NYHA III / IV = 65 %
FEVI = 31 %
D. CREA = 45.6 ml/min



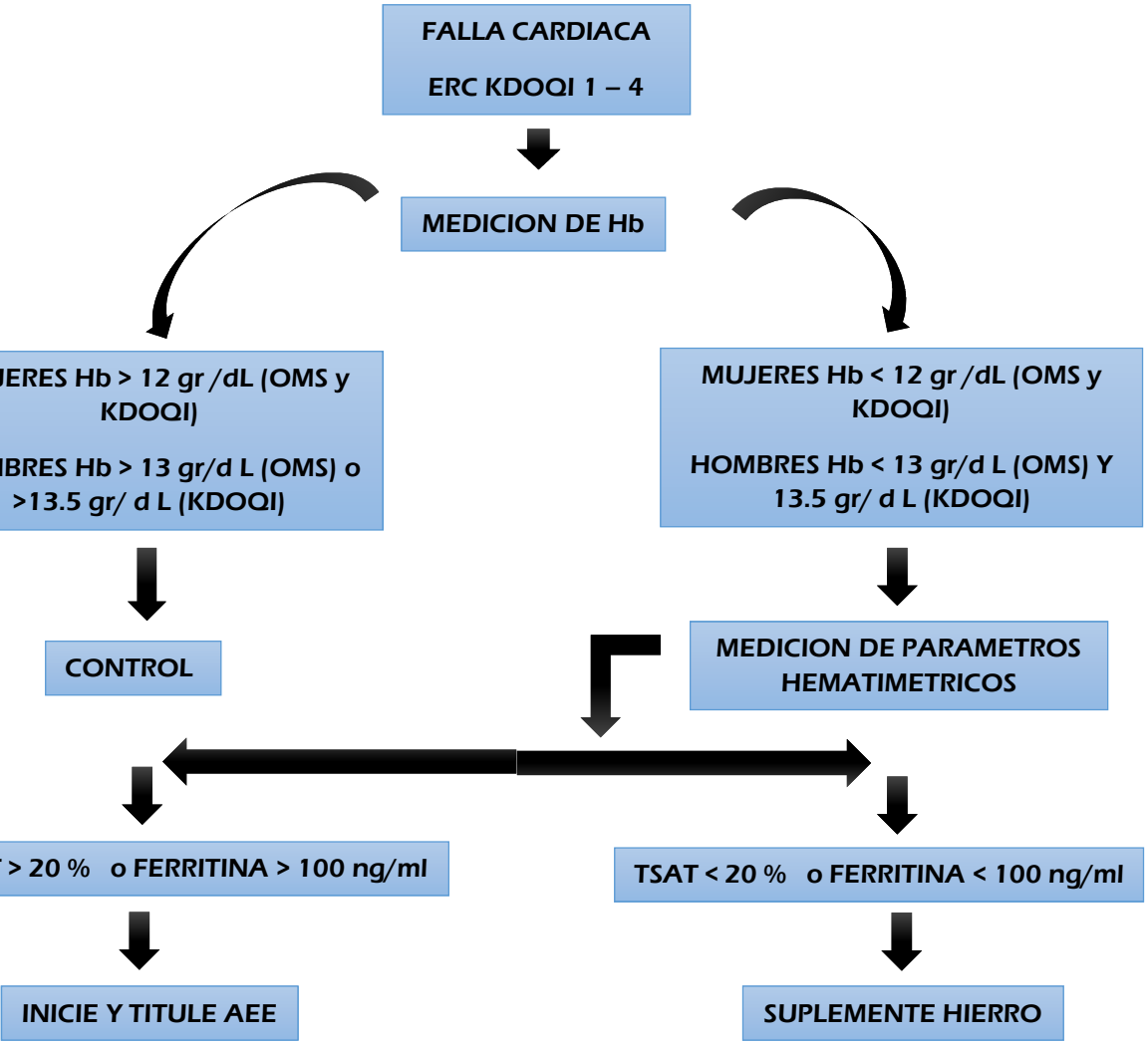


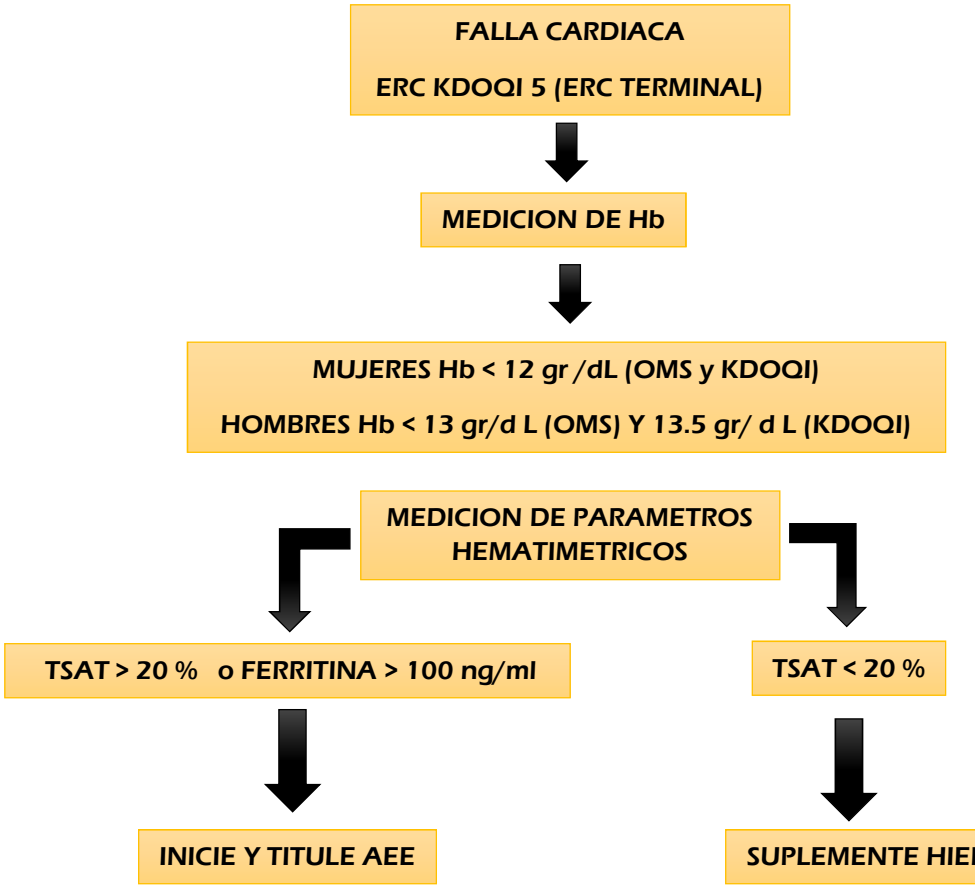
MUERTE POR CUALQUIER CAUSA o HOSPITALIZACION POR ICC
DARBOPOYETINA = 50.7 %
PLACEBO = 49.5 %

MUERTE POR CAUSA CV
DARBOPOYETINA = 45.2 %
PLACEBO = 44.3 %

EVENTOS ADVERSOS
DARBOPOYETINA / PLACEBO
FALLA CARDIACA = 58 vs 58.1
C. ISQUEMICA = 13.7 vs 14.4
ECV = 5.4 vs 3.9 %
E. EMBOLICOS = 13.5 vs 10 %
HTA = 7.1 vs 6.1 %

Swedberg K, Young JB, Anand IS. Treatment of anemia with darbepoetin Alfa in systolic heart failure. N Engl J Med. 2013 Mar 28; 368(1





*ERC = ENFERMEDAD RENAL CRONICA

*KDOQI = KIDNEY DISEASE OUTCOMES QUIALITY INITIA

*CRAS = CARDIO – RENAL ANEMIA SYNDROME

*Hb = HEMOGLOBINA

*TSAT = SATURACION DE TRANSFERRINA

*AEE = AGENTES ESTIMULANTES DE LA ERITROPOYESIS

53, No. 8, 2009
4, 2009:639–47

Anemia: The Point of Convergence or Divergence for Kidney Disease and Heart Failure?

ALGORITMO DE TRATAMIENTO CON AEE

CRAS

ALGORITMO DE TRATAMIENTO CON AEE*

* AGENTES ESTIMULANTES DE LA ERITROPOYESIS

SI HAY DEFICIENCIA ABSOLUTA O FUNCIONAL DE HIERRO, ESTA DEBERIA SER CORREGIDA ANTES DE DECIDIR SI LA TERAPIA CON AGENTES ESTIMULANTES DE LA ERITROPOYESIS (AEE) ES NESCESARIA

DOSIS INICIAL DE CORRECCION

(EL HIERRO IV TIENE EFECTO SINERGICO)

EPO (ALFA O BETA)

EPO (Alfa – Beta) = 50 – 150 UI / Kg / Semana

DARBOPOYETINA ALFA = 0.45 – 0.75 ug/Kg/Semana

SELECCIÓN DEL AGENTE Y VIA DE ADMINISTRACION

VIA INTRAVENOSA (IV)

UTILIZAR EN SITUACIONES ESPECIALES

PACIENTE ANTICOAGULADO, DOLOR INTOLERABLE POR APLICACIÓN SC

EPO ALFA = EPREX

USO EXCLUSIVO IV

VIA SUBCUTANEA (SC) DA LUGAR A RESPUESTA SIMILAR A LA VIA IV, PERO ES MAS FACIL DE APLICAR

DOSIS ES MENOR 50 % A LA IV

FRECUENCIA:

EPO – Alfa o Beta: 1 – 3 Veces / Semana

50 – 150 UI / Kg / Semana

DARBOPOYETINA CADA 1 – 2 SEMANAS

ETAPA DE CORRECCION

CONTROL DE Hb CADA 4 SEMANAS

AEE + HIERRO IV HASTA ALCANZAR Hb NO MAYOR DE 13 gr / dL

FERRITINA 400 – 500 ug/L

TSAT 40 – 50 %

SI Hb AUMENTA < 1 gr/MES, AUMENTAR DOSIS DE EPO 25 %

SI Hb AUMENTA > 2 gr/MES, DISMINUIR DOSIS DE EPO 25 %

MANTENIMIENTO

CONTROL DE Hb CADA 1 – 2 MESES

Hb No > 13 gr/dl

FERRITINA 400 – 500 ug/L

TSAT 40 – 50 %

PASAR A UNA FASE DE CONTROL CADA 4 MESES

EN CASO DE AUMENTO Hb > 2 gr / MES ENTONCES REDUCIR DOSIS D ERITROPOYETINA UN 25 %, TAMBIEN REDUCIR LA FRECUENCIA DE L APLICACIÓN DE LA EPO O AUMENTAR EL INTERVALO DE TIEMPO

horquez Ricardo, et al. CRAS – Sindrome de Anemia Cardio – Renal. I Consenso Colombiano. AWGLA Colombia. 2007. Vol 1. p 22 – 23.

CONCLUSIONES.

La anemia constituye un importante factor de riesgo para morbi mortalidad en pacientes con falla cardiaca y disfunción renal asociada.

l Síndrome de Anemia Cardio – Renal (CRAS) describe este circu icioso donde la anemia acelera el deterioro de ambas condicion empeorando su pronostico.

Actualmente se disponen de pocos consensos para el manejo d este tipo de pacientes.

El empleo de hierro parenteral constituye una terapia adyuvant en los casos donde esta se encuentre indicada.

CONCLUSIONES.

a corrección de la anemia asociada al Síndrome Cardio – Renal co
el empleo de eritropoyetina tiene un impacto positivo en la
reducción de hospitalizaciones y mortalidad.

La darbopoyetina hasta el momento no ha demostrado tener un
impacto sobre la tolerancia al ejercicio, la clase funcional, la
fracción de eyección o la morbi – mortalidad.

altan mas estudios acerca de la seguridad de este tipo de terapia
y el desarrollo de nuevos fármacos que puedan impactar sobre e
Síndrome de Anemia Cardio – Renal.

GRACIAS POR SU ATENCION

"LAS PREGUNTAS ABREN PUERTAS. LAS RESPUESTAS LA CIERRAN".