Síndrome de Eisenmenger

Algo más que hipertensión pulmonar

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I.

Die angeborenen Defecte der Kammerscheidewand des Herzens.

Von

Dr. **Victor Eisenmenger.**

(Hierzu Tafel I.)

I.

Durch die Untersuchungen Rokitansky's[1]) ist der Lehre von der Entstehung angeborener Defecte des Septum ventriculorum eine Basis gegeben, die nicht mehr verlassen werden darf.

Alle vorkommenden Formen entstehen durch Entwickelungshemmung und die überaus grösste Mehrzahl hat ihren Grund in abnormen Theilungsvorgängen des Truncus arteriosus communis.

Trotzdem tauchen immer wider auf's Neue Theorien auf, die in dem mechanischen Moment des strömenden Blutes die Ursache für viele Entwickelungsfehler und — in neuester Zeit — sogar für die normale Evolution des Herzens suchen.

Hunter[2]) und Morgagni[3]) sind die Begründer dieser Theorien.

Hunter lehrt: Wenn beim Fötus ein Hinderniss für den Blutstrom in der Lungenarterie erwächst, so lange die Kammerscheidewand nicht fertig ist, muss zwischen beiden Ventrikeln eine Oeffnung fortbestehen. Der kräftige Widerstand des Blutstroms, der von einer Kammer in die andere fliesst, hindert die Kammerscheidewand sich auszubilden.

Aehnlich Morgagni.

Diese Lehren fanden eifrige Verfechter. Lebert gestattet sich auf Grund derselben sogar den Schluss, dass in zwei von Bouillaux und

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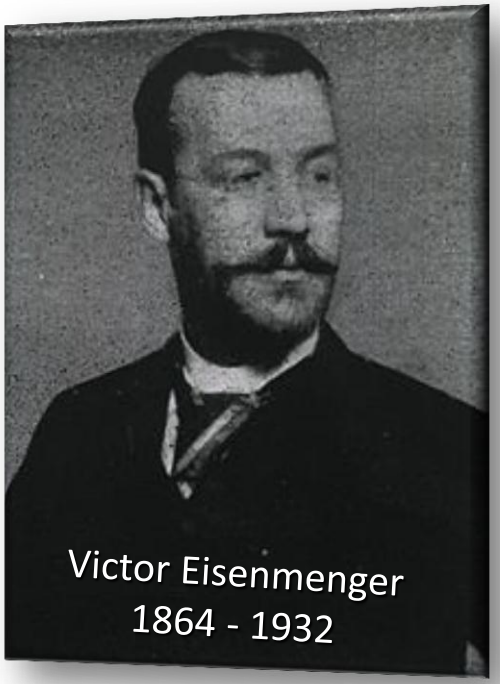
1) Rokitansky, Die Defecte der Scheidewände des Herzens. Wien 1875.
2) Hunter, Med. Observat. and engu. 1783. V. 6. -Cit. bei Kussmaul.
3) Morgagni, Cit. bei Burresi, Sperimentale. Bd. 46.



Victor Eisenmenger
1864 - 1932

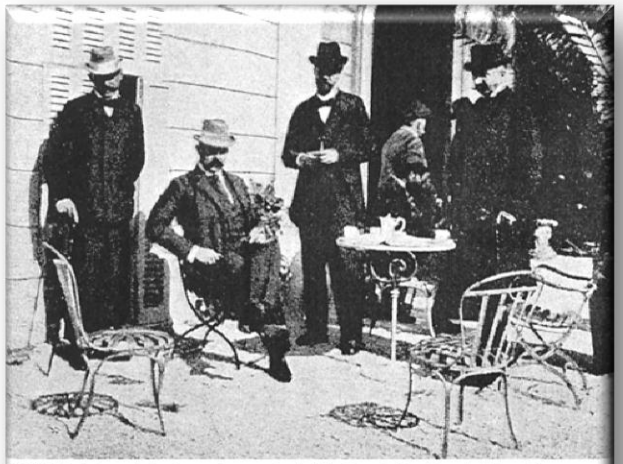


FIGURE 2. *Left to right*: Baron Bronn, Archduke Francis Ferdinand, Victor Eisenmenger, Count Cavriani.

Z. Klin. Med 1897

BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 27 1958

THE EISENMENGER SYNDROME

OR PULMONARY HYPERTENSION WITH REVERSED CENTRAL SHUNT*

BY

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Distinctive Characteristics of Individual Members of the Eisenmenger Group

Patent Ductus.—(1) The catheter passed through the duct more easily than through any other central communication between the two circulations. It did so in 90% of cases, and usually took an anticlockwise course to enter the descending aorta. (2) The shunt was wholly reversed far more frequently (50%) than with other defects. (3) Patent ductus was the only lesion which was occasionally associated with no shunt in either direction. (4) Differential oxygen desaturation between right brachial and femoral samples was pathognomonic of patent ductus, and occurred in all but two cases in which there was no shunt in either direction. The oxygen saturation of samples from the right brachial artery averaged 89.6% (range 81 to 96%), and from the descending aorta or femoral artery 77.1% (range 65 to 88%).

Aorto-pulmonary Septal Defect.—(1) When the catheter passed through the defect it entered the ascending aorta from the pulmonary artery. (2) In other respects the findings were similar to those of patent ductus with bidirectional shunt but no differential desaturation.

Eisenmenger's Complex.—(1) Passage of the catheter via the defect (28%) into the ascending aorta followed a characteristic medial course as in Fallot's tetralogy. (2) An appreciable left-to-right shunt at ventricular level, as described by Bing *et al.* (1947), could be detected in all but two cases, in both of which the diagnosis was subsequently proved at necropsy. (3) Pulmonary artery samples were always between 5 and 20% less saturated than aortic or arterial samples.

Single Ventricle.—In all respects but one these cases resembled Eisenmenger's complex. The increase in oxygen saturation at ventricular level averaged 16%. The one distinctive feature was the similarity of aortic (or arterial), pulmonary artery, and ventricular samples. The arterial oxygen saturation was no lower than in other members of the Eisenmenger group, averaging 82%. Three such cases were proved at necropsy.

Transposition of the Great Vessels.—These cases also resembled Eisenmenger's complex in all major respects but one. The distinctive feature was the higher oxygen saturation of samples from the pulmonary artery compared with those from the aorta and right ventricle. In the three cases studied the difference was 32, 17, and 5%. The rise in oxygen saturation at ventricular level averaged 20%. Three cases in the series resembled Eisenmenger's complex in all respects except that the catheter took a left anterolateral convex course as it entered the ascending aorta (Plate, Fig. 1, *Journal*, September 20, facing p. 709), characteristic of one type of corrected transposition. The pulmonary artery is not readily entered in such cases.

Persistent Truncus.—There were three characteristic features in the two cases studied. (1) The physiological situation was similar to that in aorto-pulmonary septal defect with the addition of a second left-to-right shunt at ventricular level. As the catheter passed from the right atrium, through the right ventricle, into the truncus, the oxygen saturation of respective samples rose first by 10 and 12.5%, and then by a further 10 and 14%. (2) The catheter entered the pulmonary arteries from the "aorta," instead of vice versa as in aorto-pulmonary septal defect. (3) Samples from the "aorta" and pulmonary arteries were identical.

Atrial Septal Defect.—(1) The catheter passed through the defect in two-thirds of 18 proved cases. (2) The pulmonary artery pressure was less than the systemic pressure by an average of 27/34 mm. Hg in 30% of the cases; in 10% it was higher; and in the remainder about the same. When mean pressures were similar the pulse pressure was usually greater in the pulmonary artery, the systolic pressure being higher and the diastolic lower than in the systemic arteries. Agents affecting pulmonary or systemic flow or resistance selectively usually altered the pressure relationship between the two circulations. (3) A direct shunt at atrial level was demonstrated in 84% of the cases, right atrial samples being on the average 13% more saturated than samples from the superior vena cava (range 6 to 21%). (4) The oxygen saturation of left atrial samples averaged 81% in the eight cases in which they were obtained (range 72 to 88). Left ventricular samples were similar when secured, and arterial samples likewise (average 82% saturated; range 70 to 88%).

Persistent Ostium Primum.—The physiological findings in four cases could not be distinguished from a combination of low atrial septal defect and ventricular septal defect, there being bidirectional shunts at both atrial and ventricular levels. The rise in oxygen saturation averaged 10% in the right atrium and 7.5% in the right ventricle. The tip of the catheter when it entered the aorta was similar in both groups to that in Fallot's tetralogy and Eisenmenger's complex.

Common Atrioventricular Canal.—A single proved case that came to necropsy had virtually both a single atrium and a single ventricle. The rise in oxygen saturation resulting from the left-to-right component of the bidirectional shunt occurred at atrial level and measured 23%. Samples from the common ventricle, pulmonary artery, and femoral artery were similar at around 80% saturated.

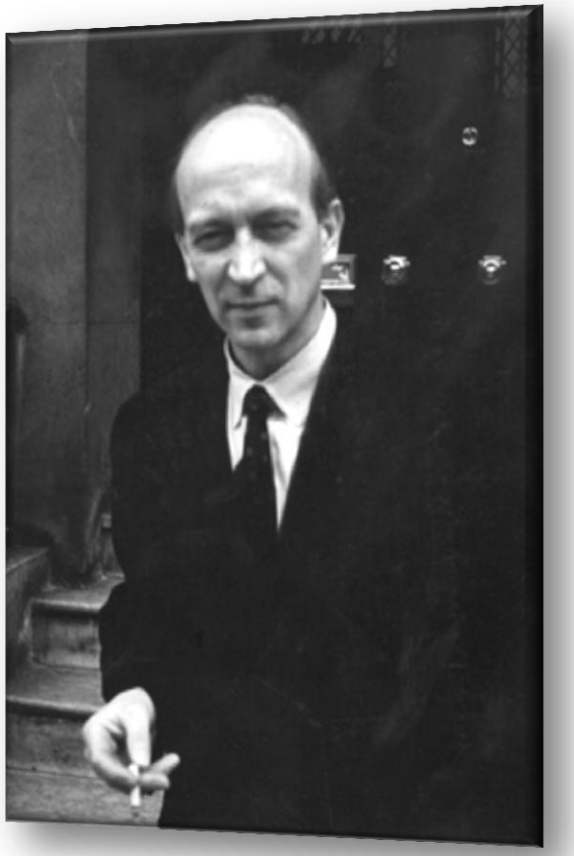
Anomalous Pulmonary Venous Drainage.—As a cause of the Eisenmenger reaction both total and hemianomalous pulmonary venous drainage must be rare, for no case was recognized amongst the 127 studied in this paper. One of

*Croonian Lectures delivered before the Royal College of Physicians of London on May 15, 1958. See last week's *Journal* (p. 701) for first part.

Paul Wood
1907-1962

Wood P, et al. Br Med J 1958:758-62

Síndrome de Eisenmenger



"pulmonary hypertension at systemic level due to high pulmonary vascular resistance with reversed bi-directional shunt" - "...**it matters very little where the shunt happens to be**. The **distinguishing feature** is not anatomy, but the **physiological behaviour of the pulmonary circulation**."

Guidelines for the diagnosis and treatment of pulmonary hypertension

The Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT)

A. Eisenmenger's syndrome

Eisenmenger's syndrome includes all systemic-to-pulmonary shunts due to large defects leading to a severe increase in PVR and resulting in a reversed (pulmonary-to-systemic) or bidirectional shunt. Cyanosis, erythrocytosis, and multiple organ involvement are present.

Galié N, et al. Eur Heart J;2009:2493-2537

Clasificación anatómica-fisiopatológica de los cortocircuitos asociados con hipertensión pulmonar

TIPO DE LESIÓN

- **Cortocircuito pre-tricuspideo simple**
  - CIA
  - Drenaje venoso pulmonar anómalo
- **I Cortocircuito post-tricuspideo simple**
  - CIV
  - Ductus persistente
- **Cortocircuitos combinados**
- **Cardiopatías congénitas complejas**
  - Canal AV completo
  - Truncus arteriosus
  - Ventrículo único sin obstrucción al flujo pulmonar
  - Transposición de grandes vasos + CIV/DAP
  - Otras

DIRECCIÓN DEL CORTOCIRCUITO

- **Sistémico-pulmonar (I-D)**
- **Pulmonar-sistémico (D-I)**
- **Bidireccional**

TAMAÑO

- **Hemodinámico (Qp/Qs)**
  - Restrictivo
  - No restrictivo
- **Anatómico**
  - Pequeño o moderado (CIA ≤ 2cm, CIV ≤ 1 cm)
  - Grande (CIA > 2cm, CIV > 1 cm)

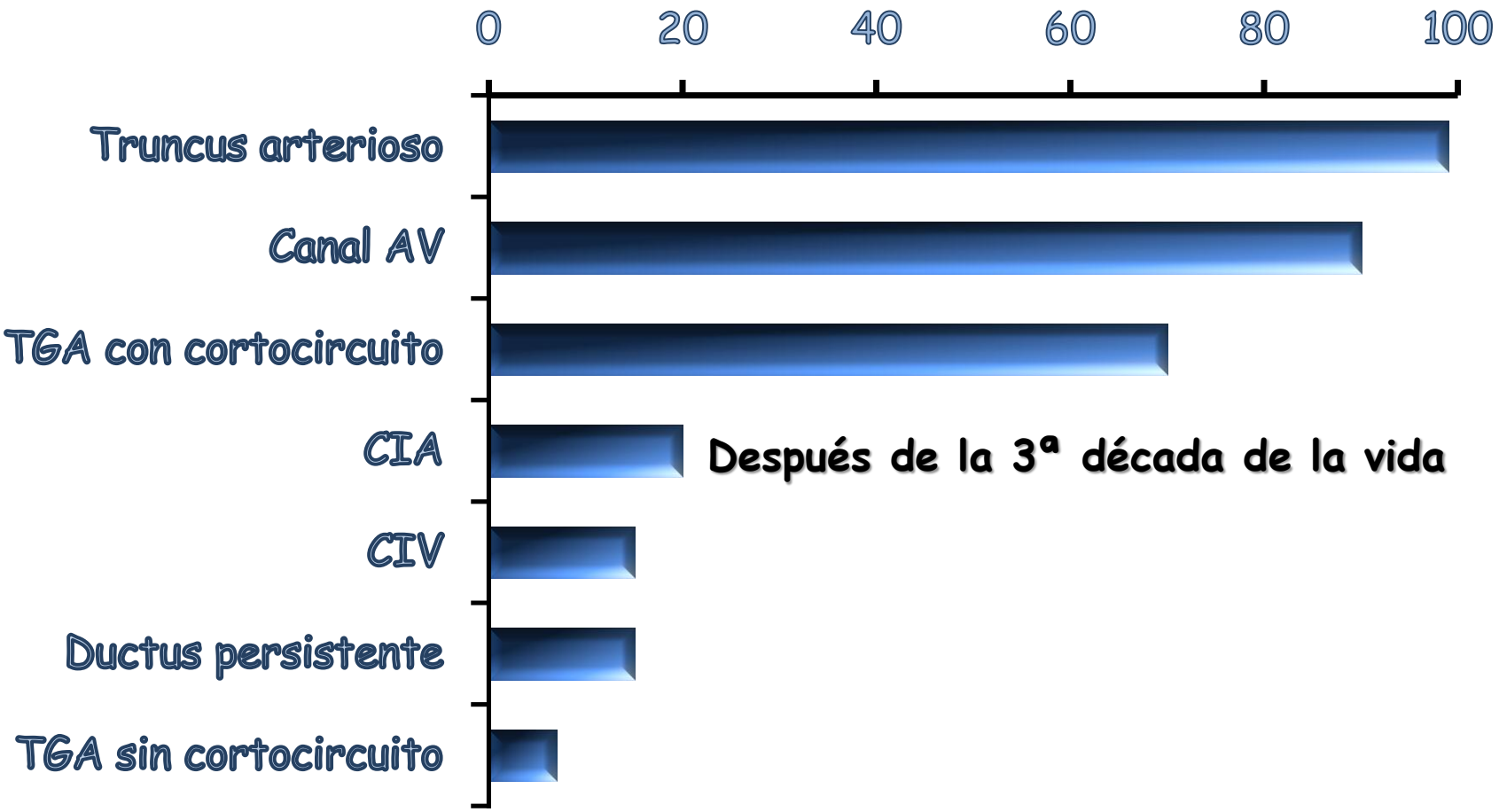
ANOMALÍAS CARDIACAS/EXTRACARDIACAS ASOCIADAS

REPARADO

- **No operado**
- **Cirugía paliativa**
- **Cirugía correctora**

Galie N et al. Eur Heart J 2009;30: 2493-2537

Riesgo de desarrollar HAP en pacientes con cortocircuitos



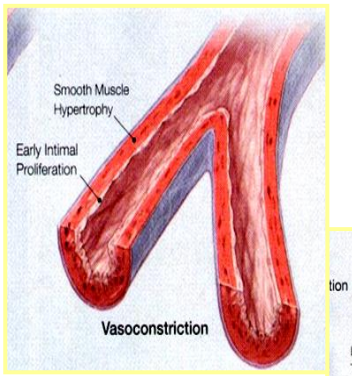
Collins NR, et al. Cardiol Clin 1993,11: 675-687

Remodelado vascular

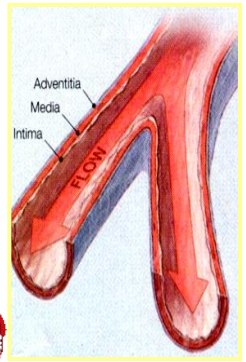
Estrés parietal

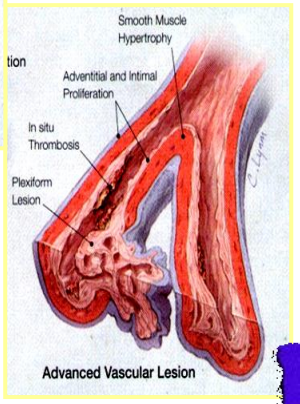
Disfunción endotelial

↑ Flujo pulmonar



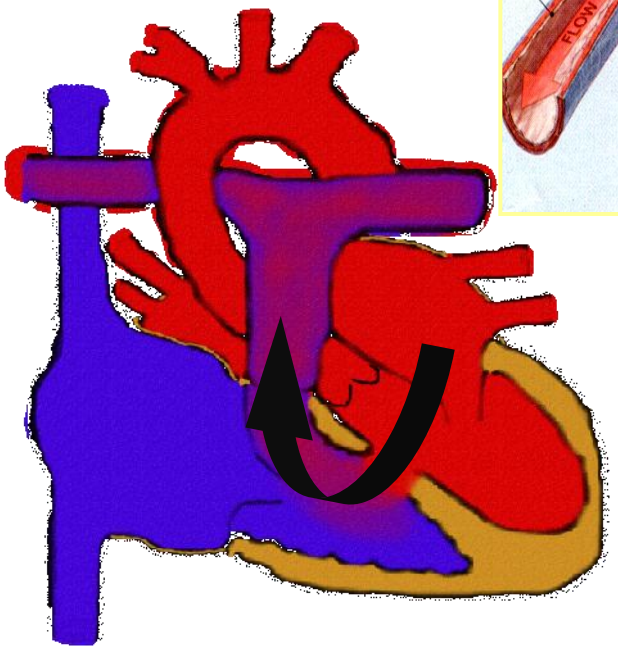
↑ RVP

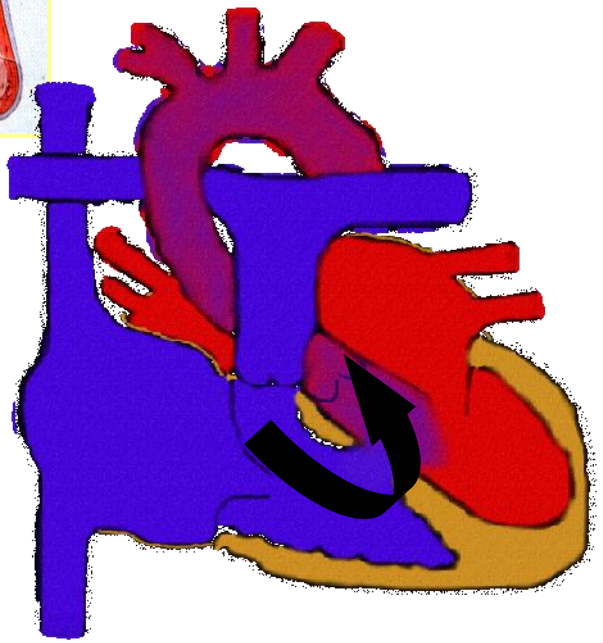




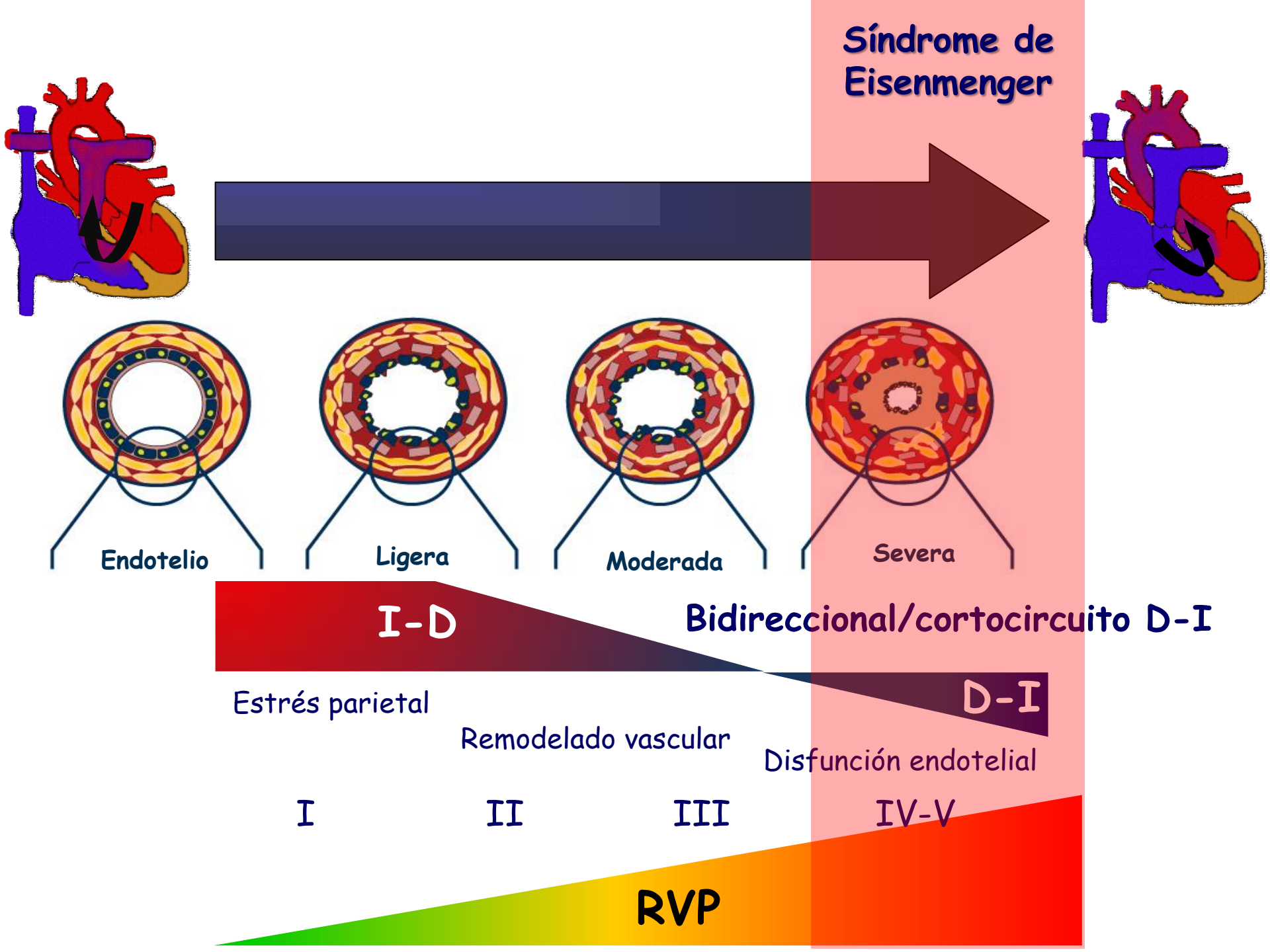
Cortocircuito I-D

Cortocircuito D-I

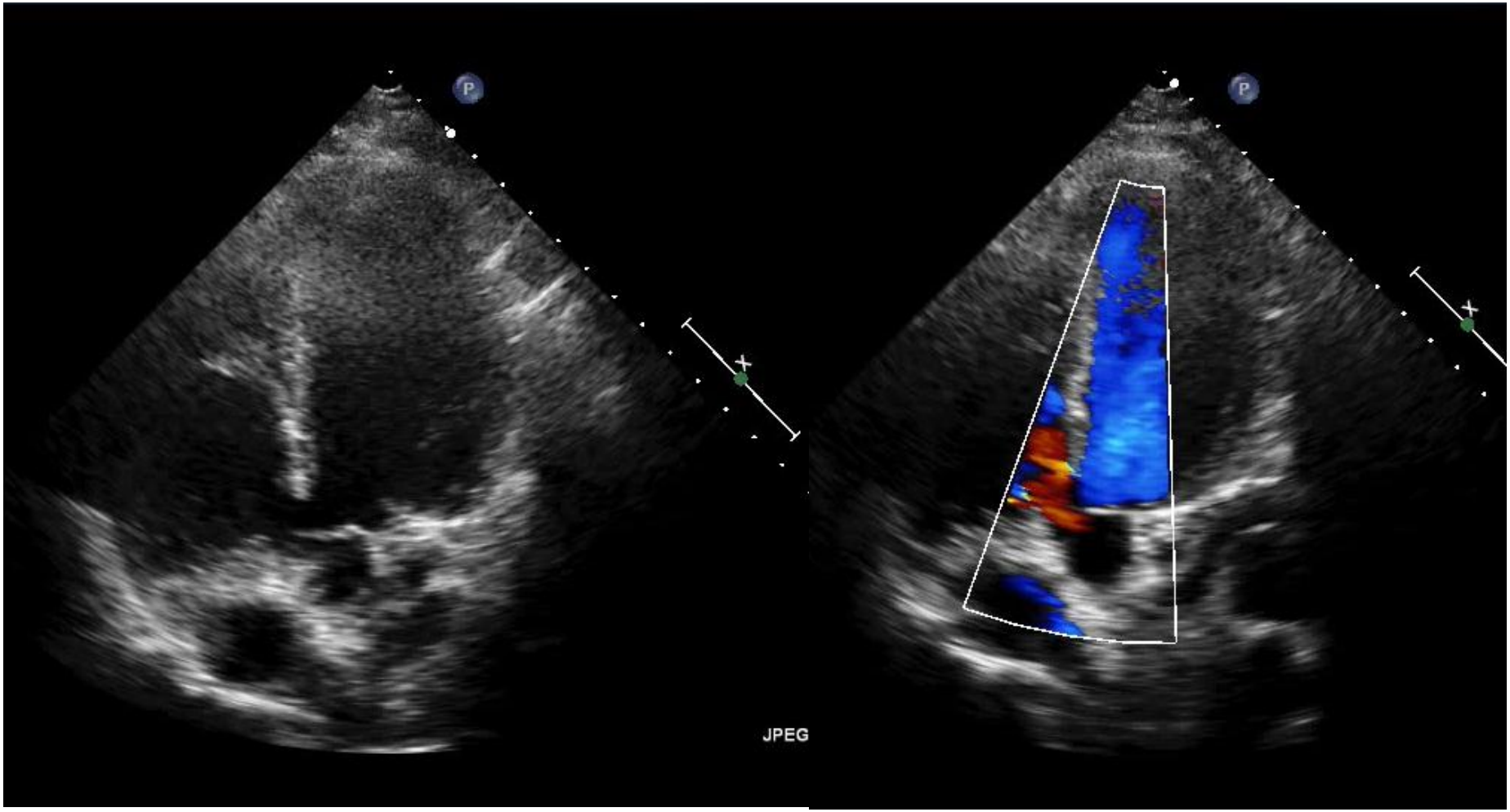


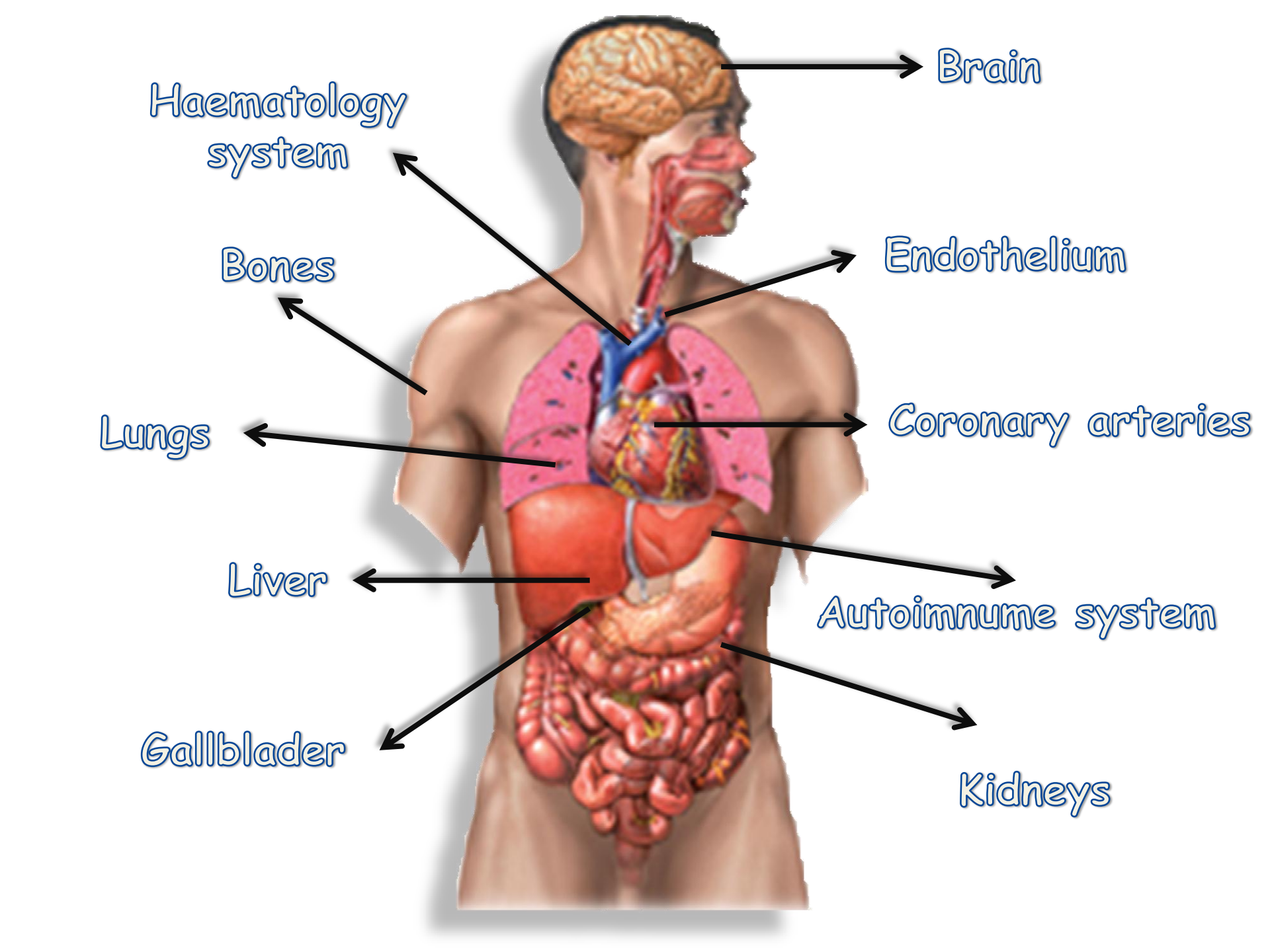


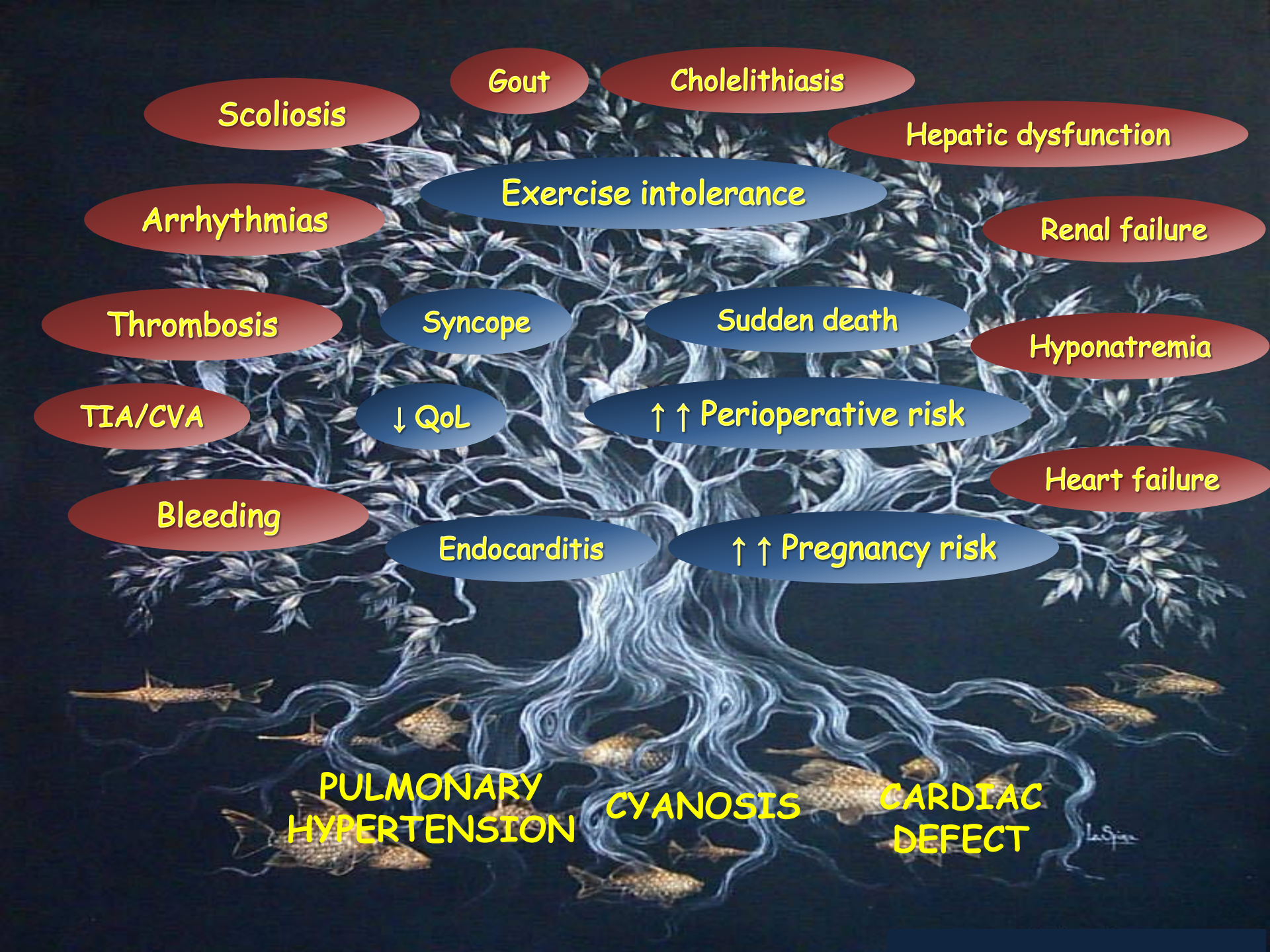
Fisiopatología


Síndrome de Eisenmenger
Endotelio
Ligera
Moderada
Severa
I-D
Bidireccional/cortocircuito D-I
D-I
Estrés parietal
Remodelado vascular
Disfunción endotelial
I
II
III
IV-V
RVP

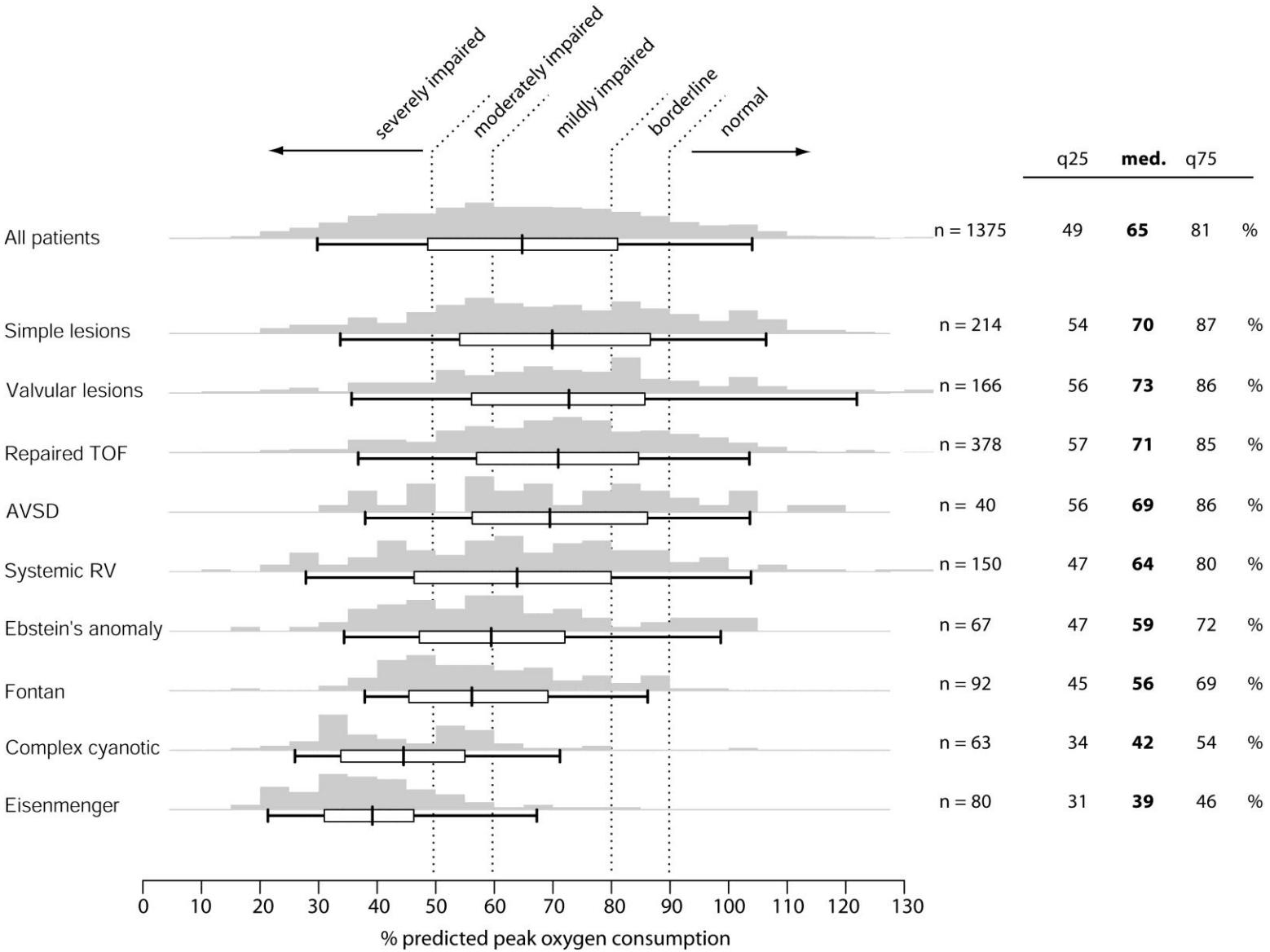
Cortocircuito derecha-izquierda




Brain
Haematology system
Endothelium
Bones
Lungs
Coronary arteries
Liver
Autoimnume system
Gallblader
Kidneys


Gout
Cholelithiasis
Scoliosis
Hepatic dysfunction
Exercise intolerance
Arrhythmias
Renal failure
Thrombosis
Syncope
Sudden death
Hyponatremia
TIA/CVA
↓ QoL
↑ ↑ Perioperative risk
Heart failure
Bleeding
Endocarditis
↑ ↑ Pregnancy risk
PULMONARY HYPERTENSION
CYANOSIS
CARDIAC DEFECT

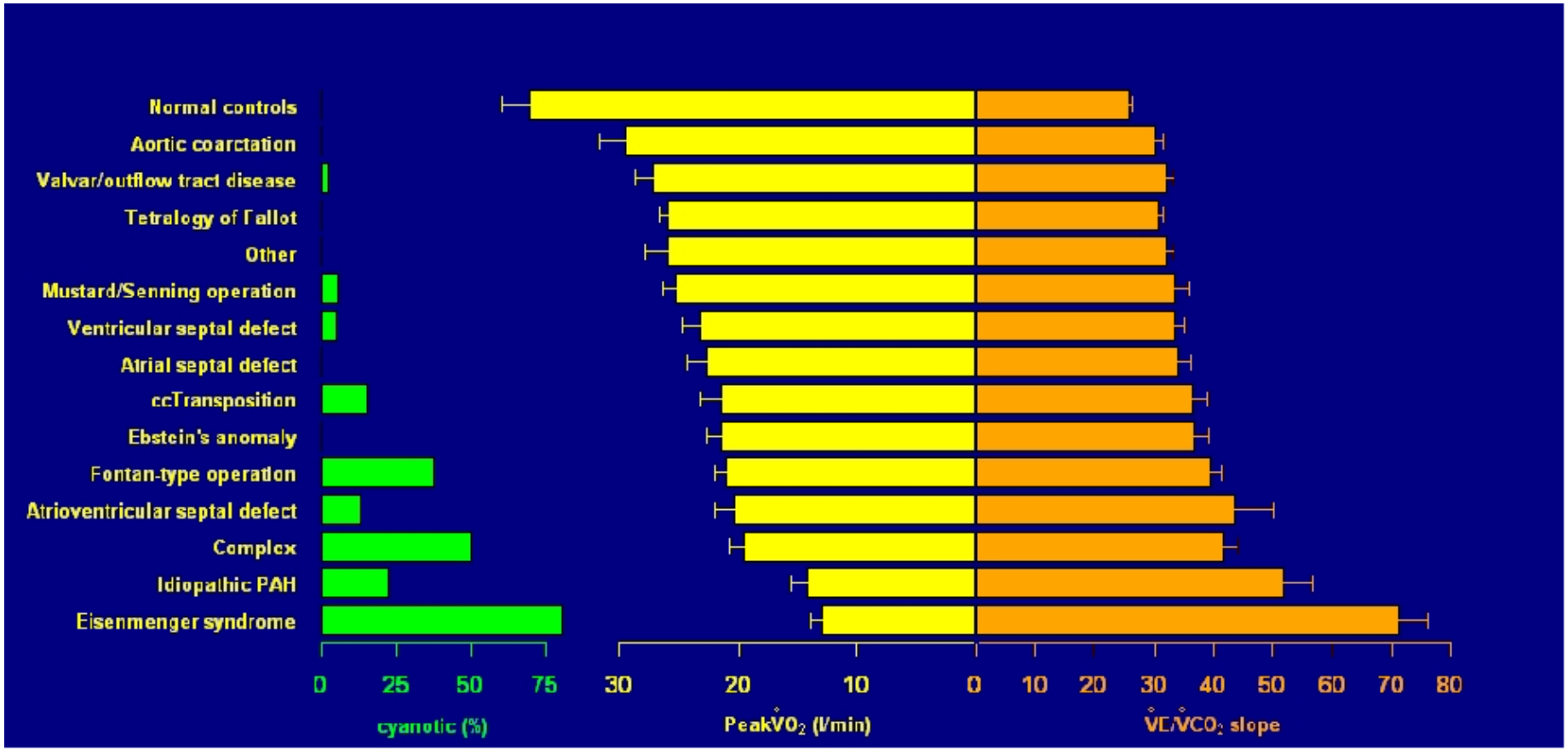
Capacidad de ejercicio



		q25	**med.**	q75	
All patients	n = 1375	49	**65**	81	%
Simple lesions	n = 214	54	**70**	87	%
Valvular lesions	n = 166	56	**73**	86	%
Repaired TOF	n = 378	57	**71**	85	%
AVSD	n = 40	56	**69**	86	%
Systemic RV	n = 150	47	**64**	80	%
Ebstein's anomaly	n = 67	47	**59**	72	%
Fontan	n = 92	45	**56**	69	%
Complex cyanotic	n = 63	34	**42**	54	%
Eisenmenger	n = 80	31	**39**	46	%

Inuzuka R, et al. Circulation 2012, 125:250-259

Capacidad de ejercicio



Diller GP, et al. Circulation 2005,112:828-35
Dimopoulos K, et al Circulation 2006, 113:2796-802


Afectación del sistema hematológico

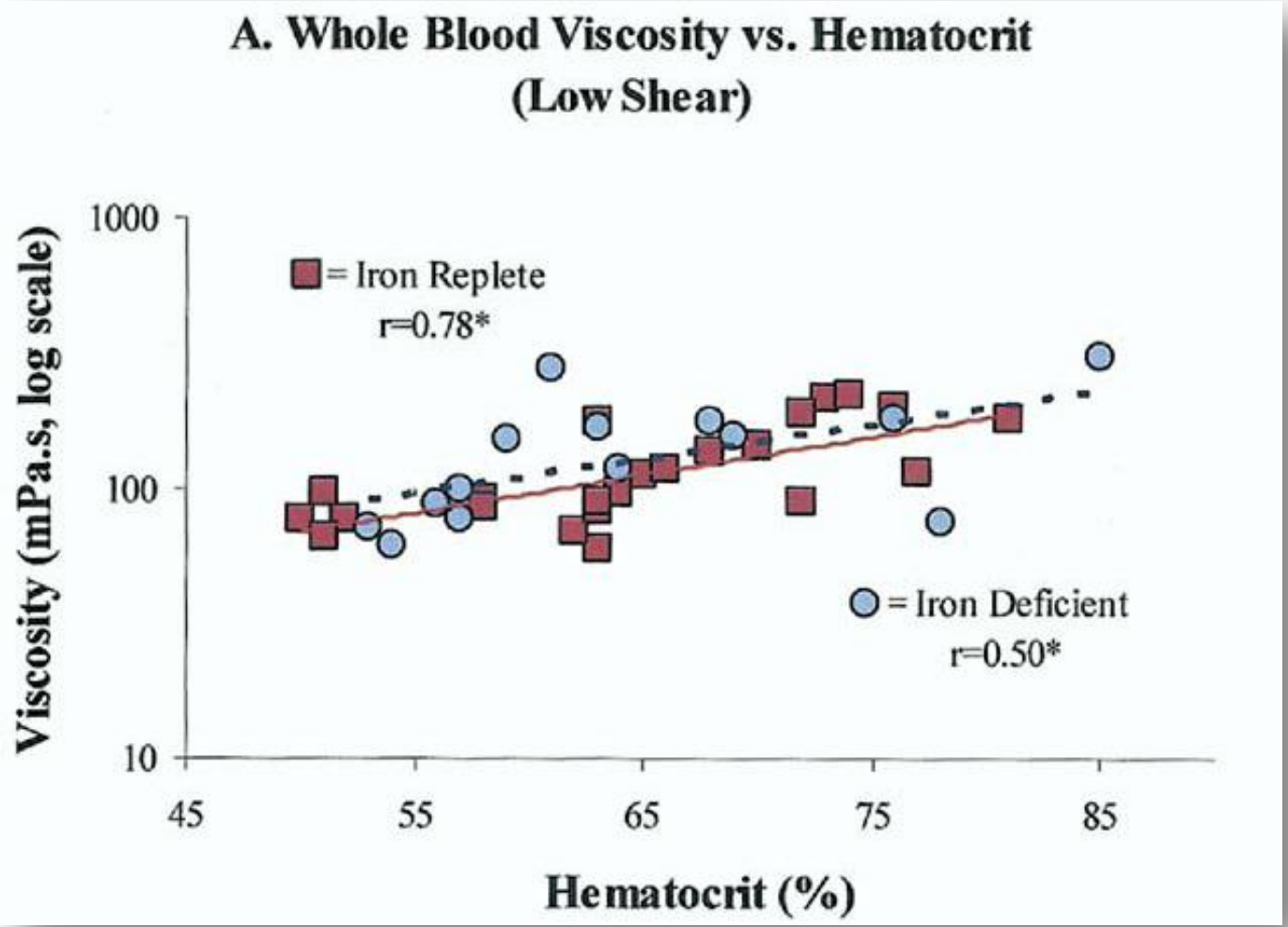
Afectación del sistema hematológico

HAEMOGLOBIN	*19.0	g/dL	11.5 - 15.1
PCV	*0.61		0.34 - 0.45
RBC	*7.35	10^12/L	3.73 - 4.92
MCV	*83	fL	84 - 98
MCH	*25.8	pg	28.3 - 33.3
MCHC	*31.2	g/dL	32.4 - 35.0
PLATELETS	*91	10^9/L	147 - 397
WBC TOTAL	*3.7	10^9/L	5.1 - 11.4
Neutrophils	*2.3	10^9/L	2.6 - 7.9
Lymphocytes	*1.0	10^9/L	1.3 - 3.7
Monocytes	0.3	10^9/L	0.3 - 1.0
Eosinophils	0.1	10^9/L	0.1 - 0.5
Basophils	0.0	10^9/L	0.0 - 0.2

Eritrocitosis secundaria

- Aumento fisiológico del número de eritrocitos como consecuencia de la hipoxemia
- Aumento de la hemoglobina y del hematocrito
  - Aumenta el aporte tisular de oxígeno
  - Aumento de la viscosidad
- Tipos de eritrocitosis secundaria
  - Compensada
  - Descompensada

Eritrocitosis secundaria

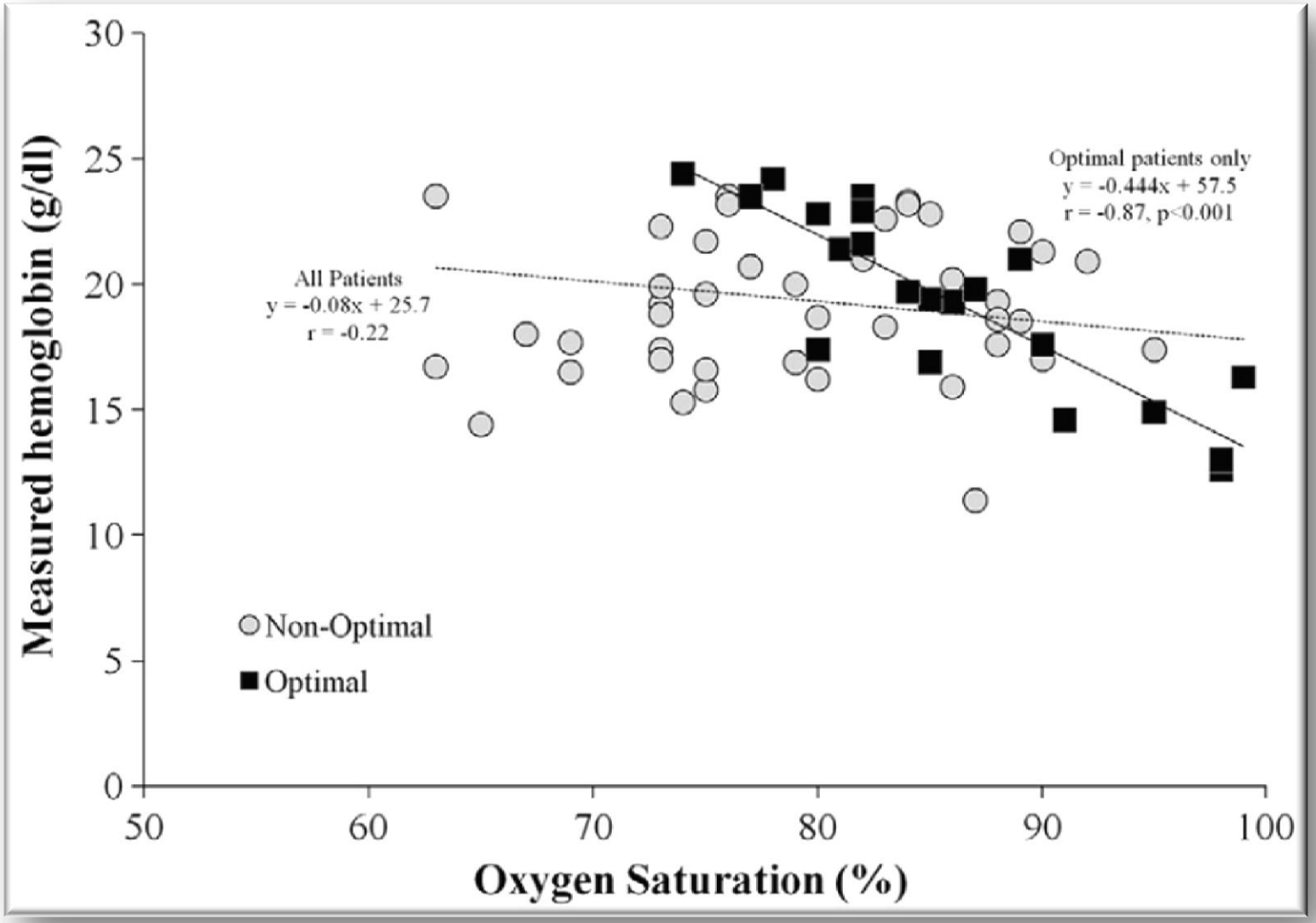


Borberg CS, et al. J Am Coll Cardiol 2006;48:356-65

Síndrome de hiperviscosidad

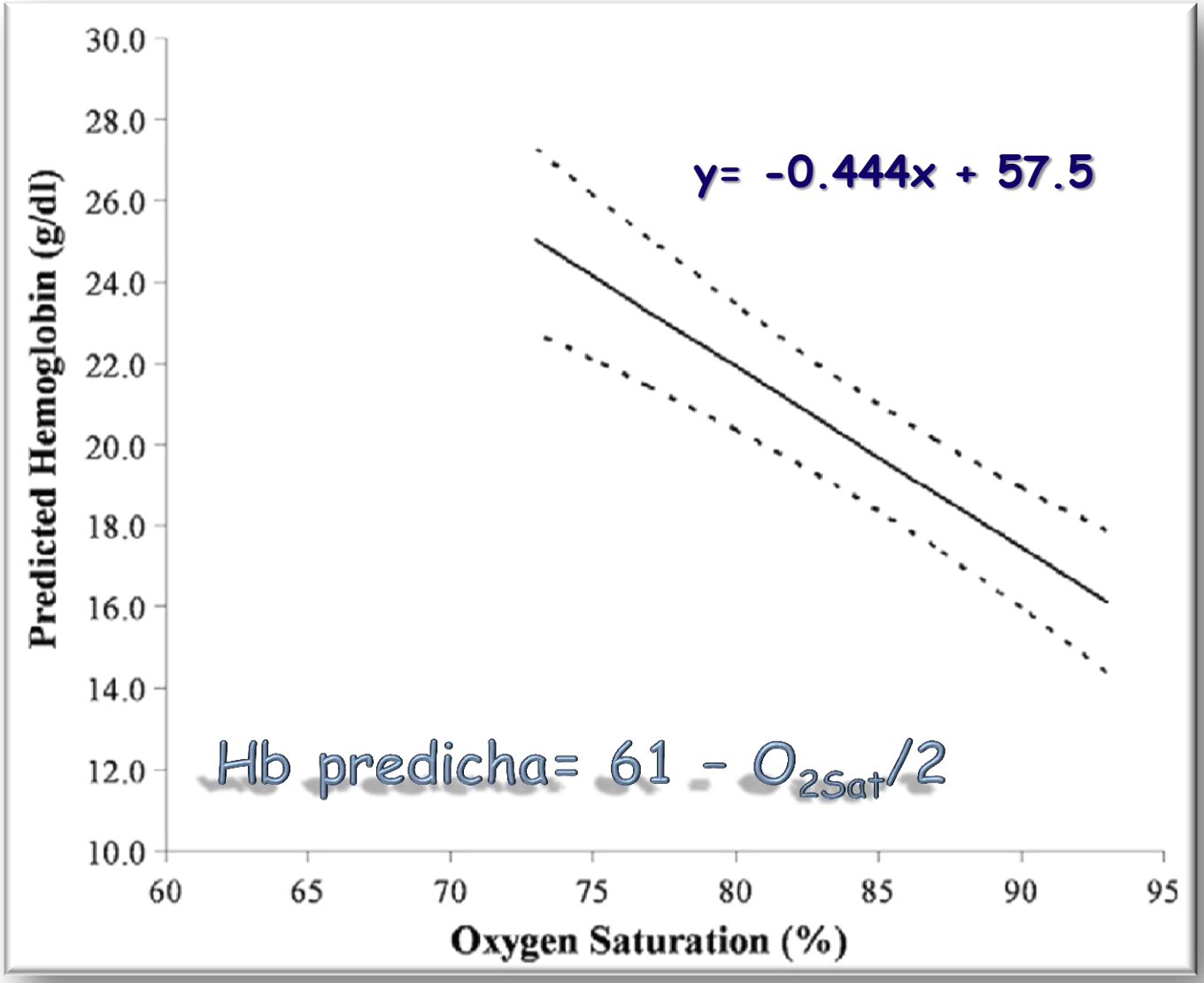
SÍNTOMAS DE HIPERVISCOSIDAD
Dolores de cabeza
Mareo, inestabilidad
Disminución del estado de alerta
Dificultad para la concentración
Alteraciones visuales (visión borrosa, doble)
Parestesias de labios y dedos
Tinnitus
Cansancio, fatiga
Dolores musculares, torácico o abdominal

Relación entre Hb y $SatO_2$



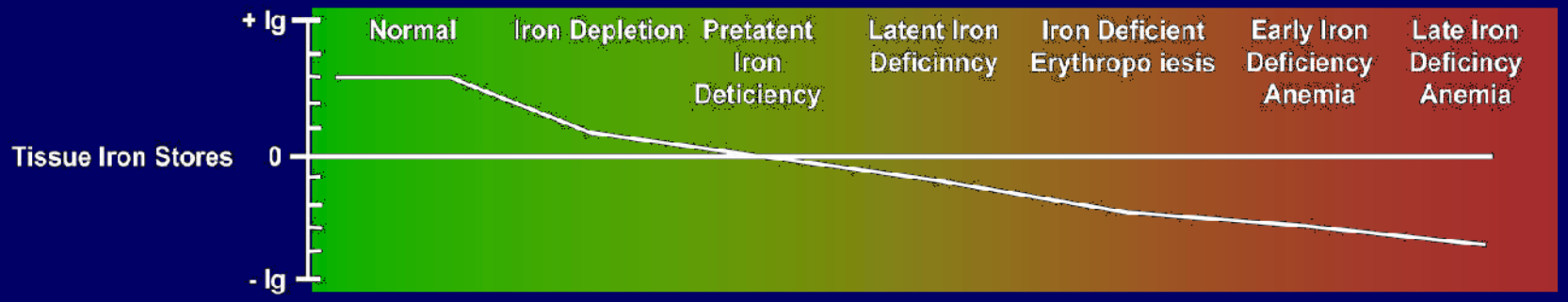
Borberg CS, et al. Am J Cardiol 2011;107:595-99

Relación entre Hb y $SatO_2$



Borberg CS, et al. Am J Cardiol 2011;107:595-99

Déficit de hierro

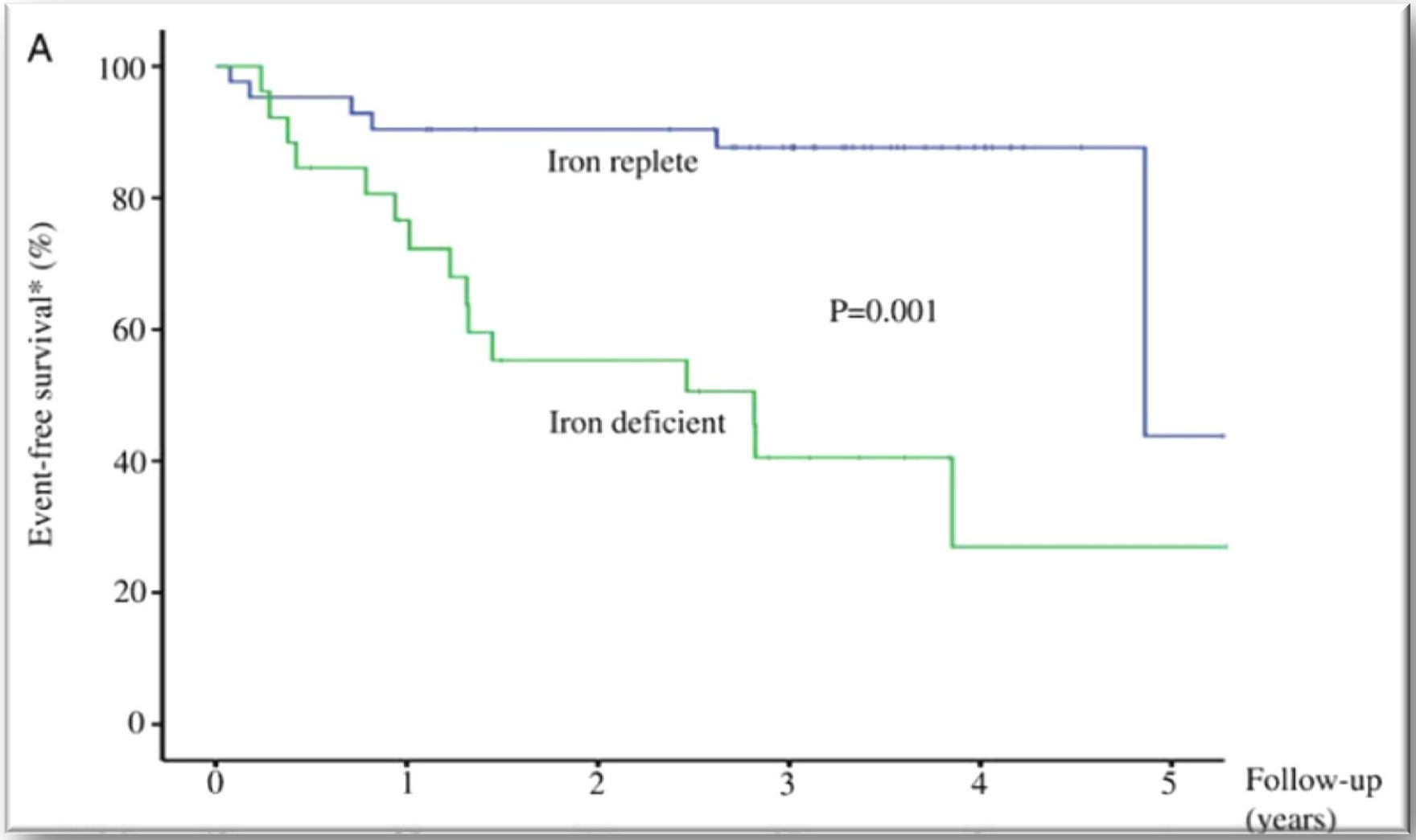


Serum Ferritin (µg/1)	60	20	<12	<12	<12	<12	<12
Stainable Tissue Iron (0-4+)	2+	1+	0	0	0	0	0
Transferrin Saturation (%)	35	35	35	20	<16	<16	<16
Free Erythrocyle Protoporhyrin (µg/dl)	30	30	30	75	>100	>100	>100
Hemoglobin (g/dl)	14	14	14	14	13	<12	<12
Mean Corpuscular Volume (μ^3)	90	90	90	90	88	86	<82
Mean Corpuscular Hemoglobin Concentration (0/0)	33	33	33	33	33	31	<28

Riesgo de ACV aumentado en presencia de:

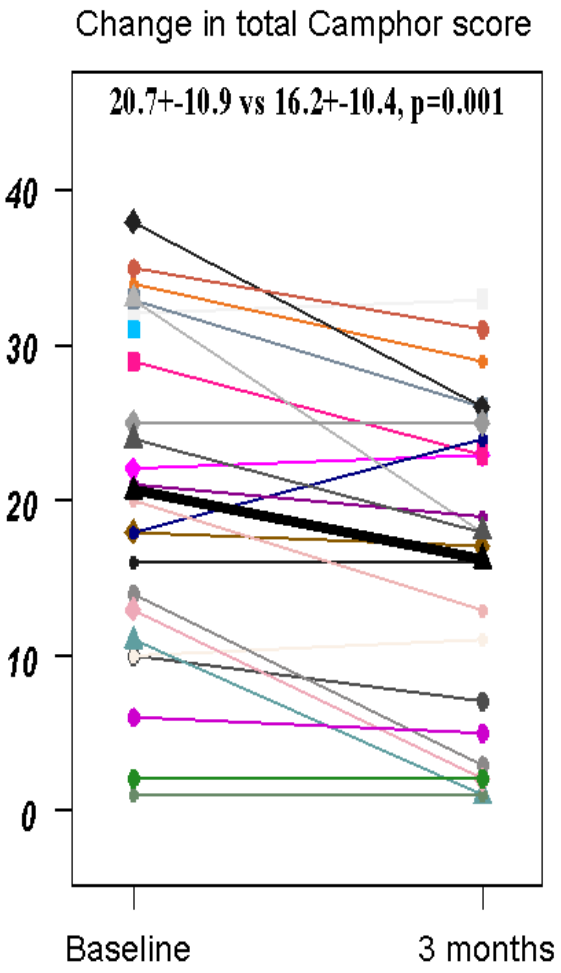
HTA, FA, **historia previa de sangrías** y **microcitosis** (p = 0.005)

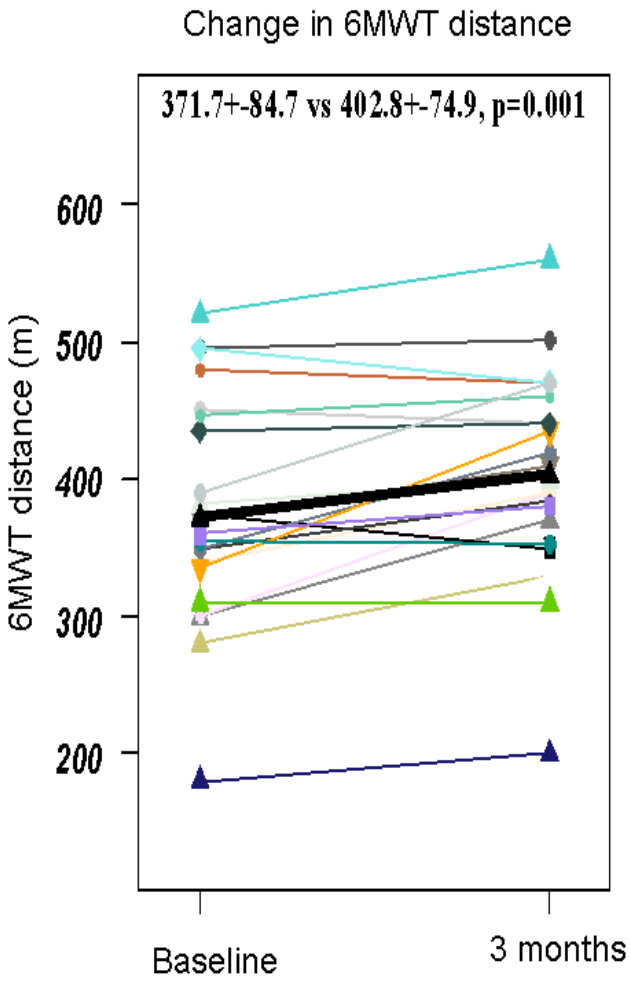
Déficit de hierro



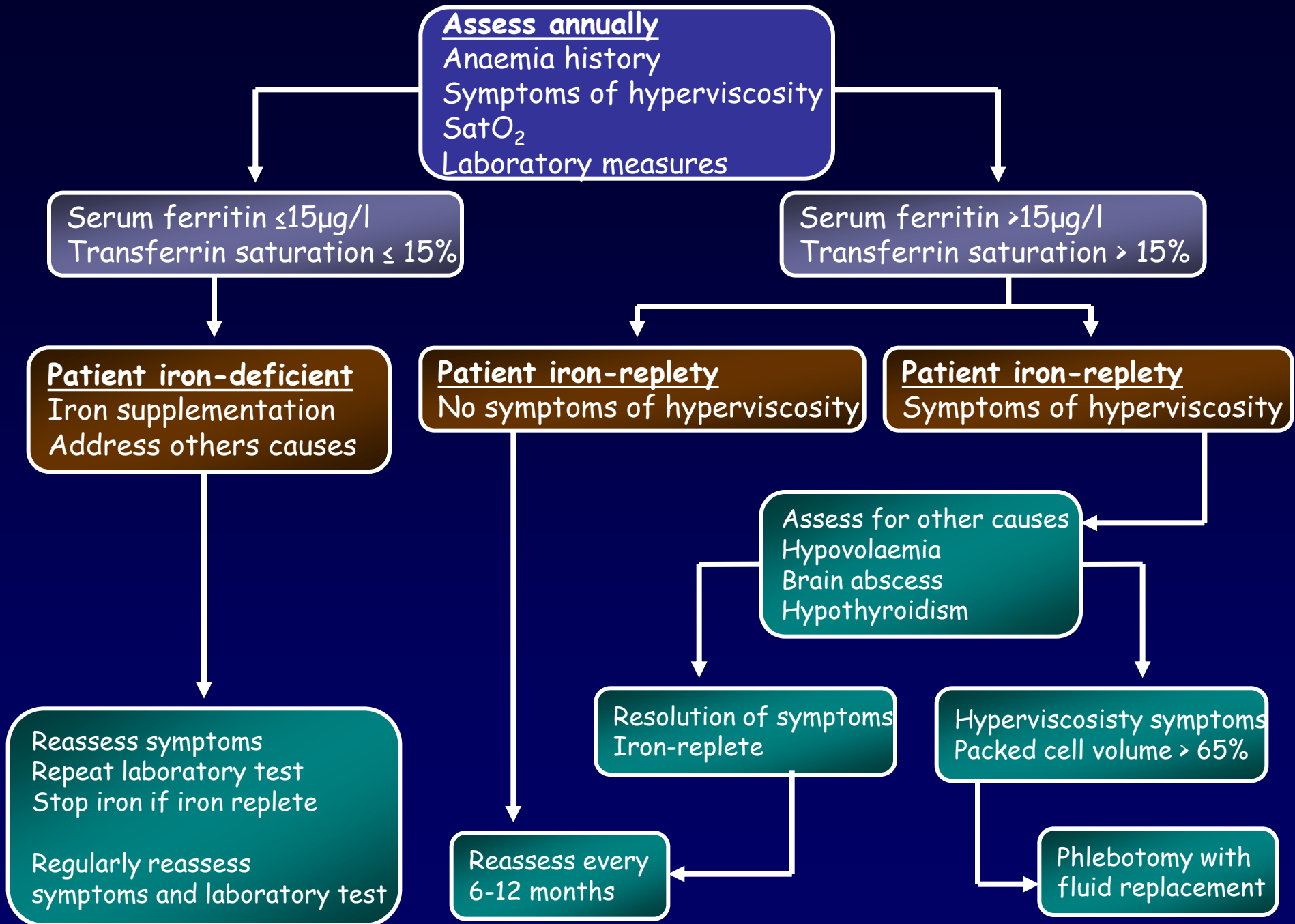
Van de Bruaene, et al. Eur Heart J 2011;32:2790-99

Déficit de hierro





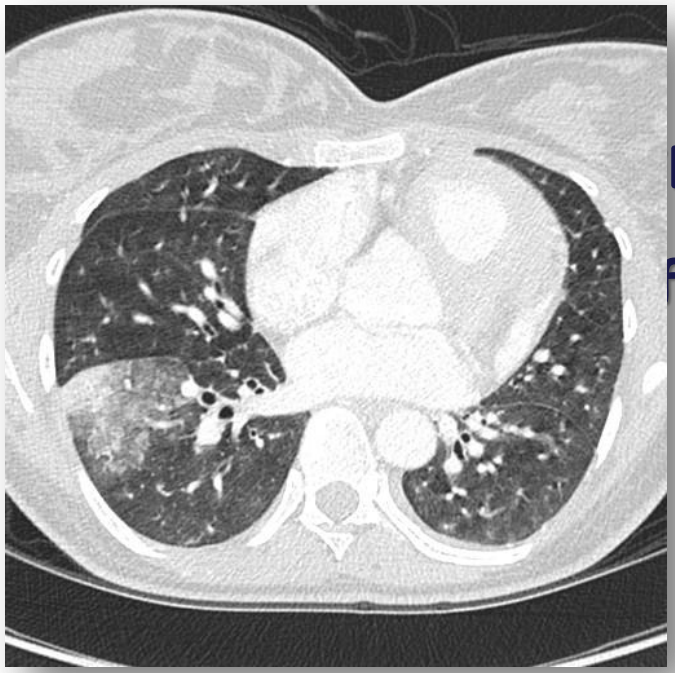
Tay E, et al. Int J Cardiol. 2011;151:307-12

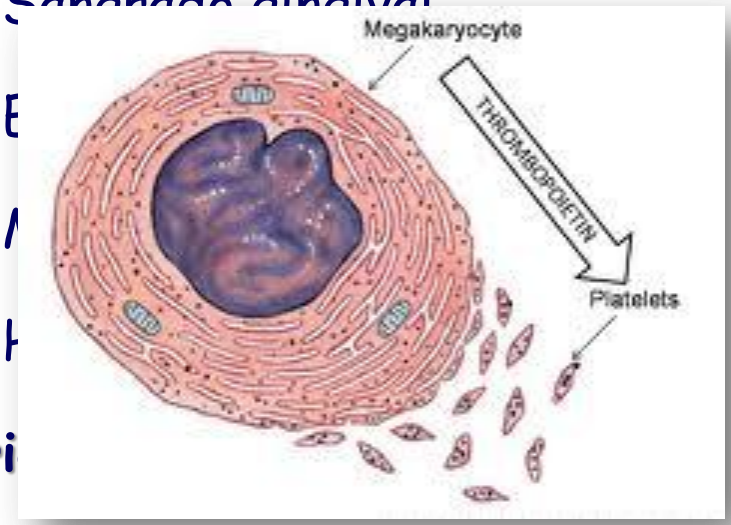


Spencer M. Lancet 2007; 370:1530-32

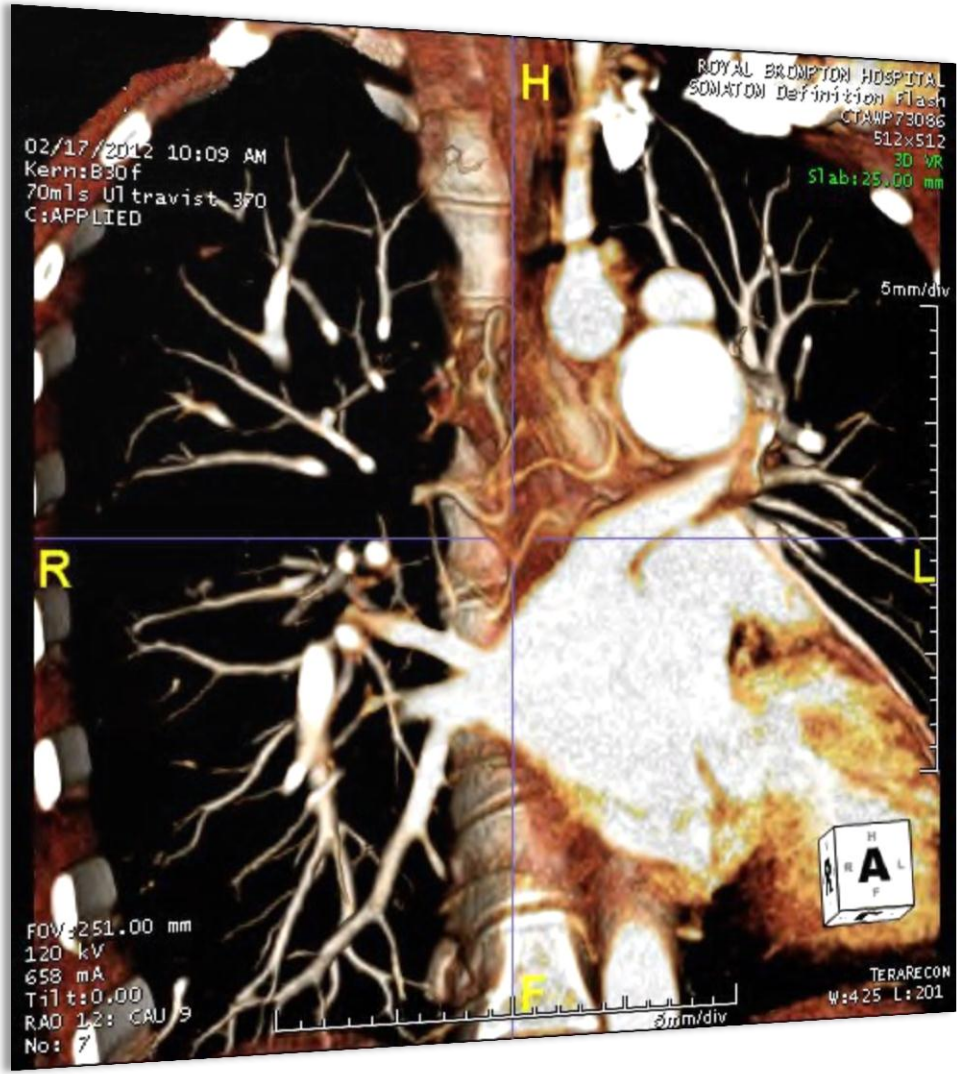
Diátesis hemorrágica

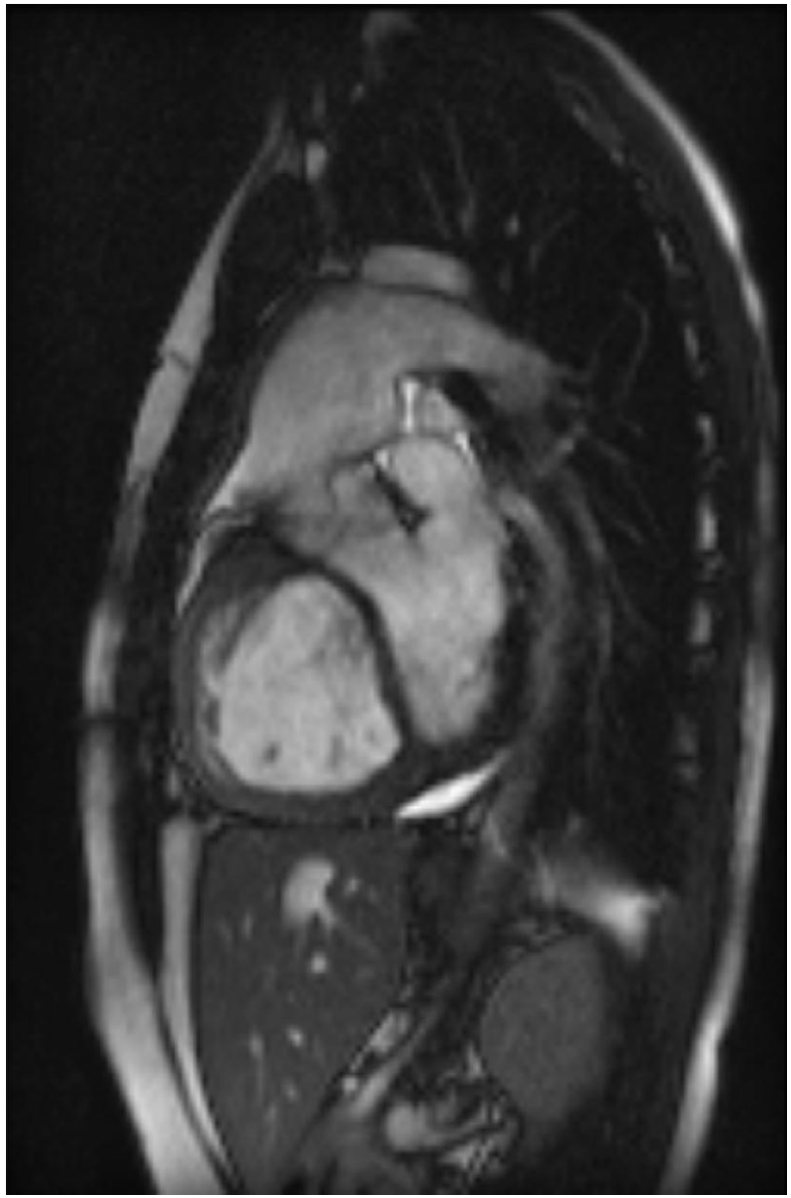
- **Trombocitopenia**
  - <130.000, factor predictor de mortalidad a largo plazo
- **Déficit de factores de la coagulación**
  - Vitamina K dependientes (II, VII, IX y X)
- **Espontáneas**
  - Hematomas espontáneos
  - Sangrado gingival
  - E
  - M
  - H
- **llebrand**
- **fibrinolítica**
- **Peri**



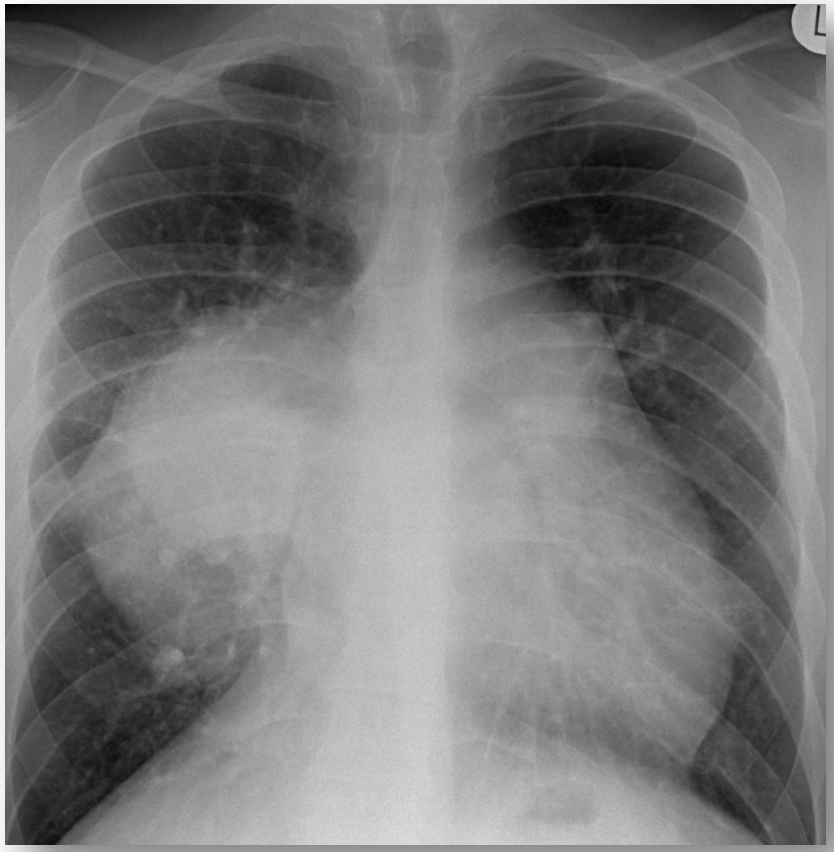


Diátesis hemorrágica





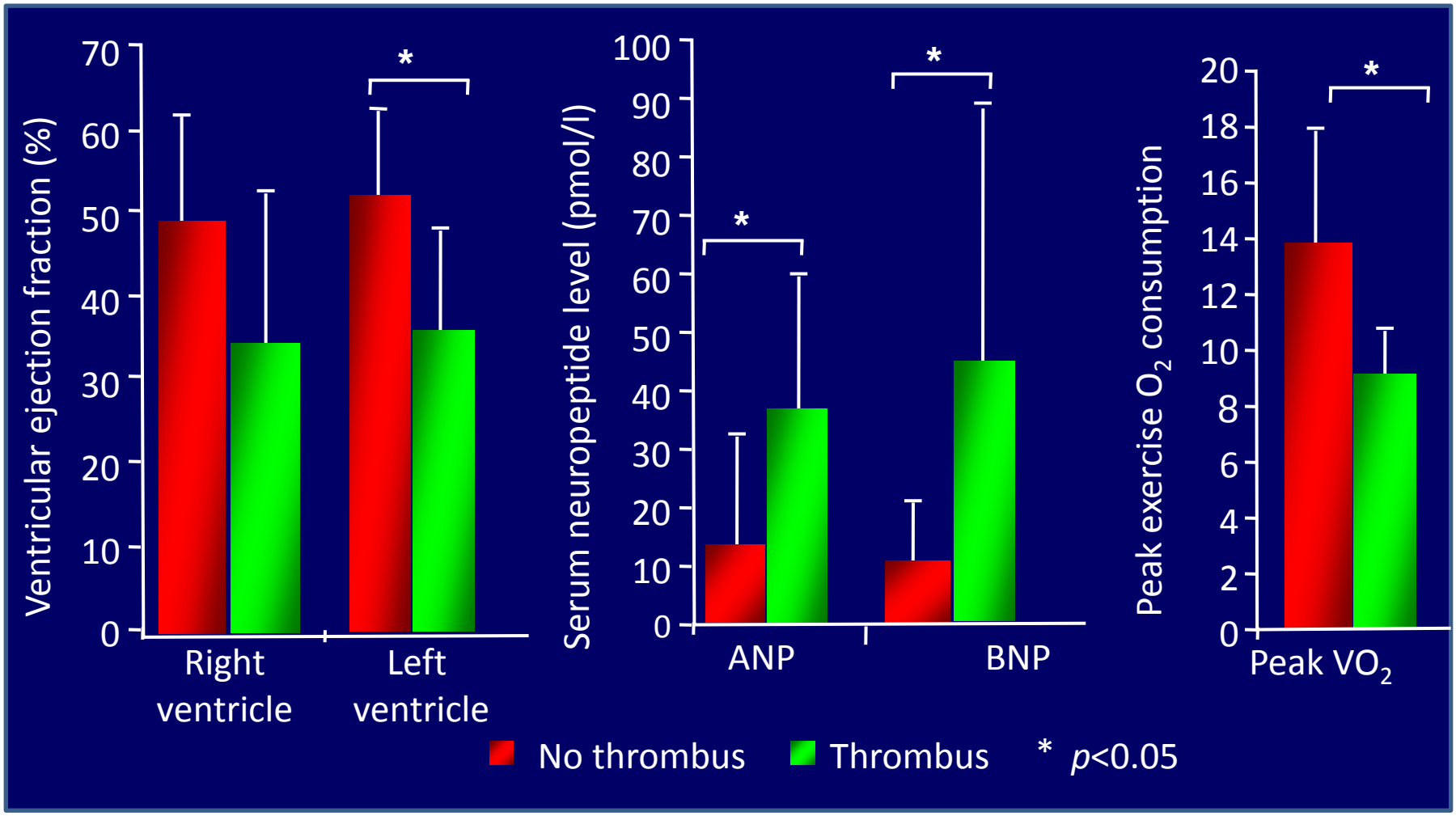
Eventos tromboembólicos



- Incidencia de hemoptisis: 11%
- Incidencia de trombosis: 20%
- Más frecuente:
  - Pacientes mayores
  - Disfunción biventricular
  - Arteria pulmonar dilatada
  - Flujo pulmonar lento

Broberg CS, et al. J Am Coll Cardiol 2007; 50:634-42

Trombosis pulmonar



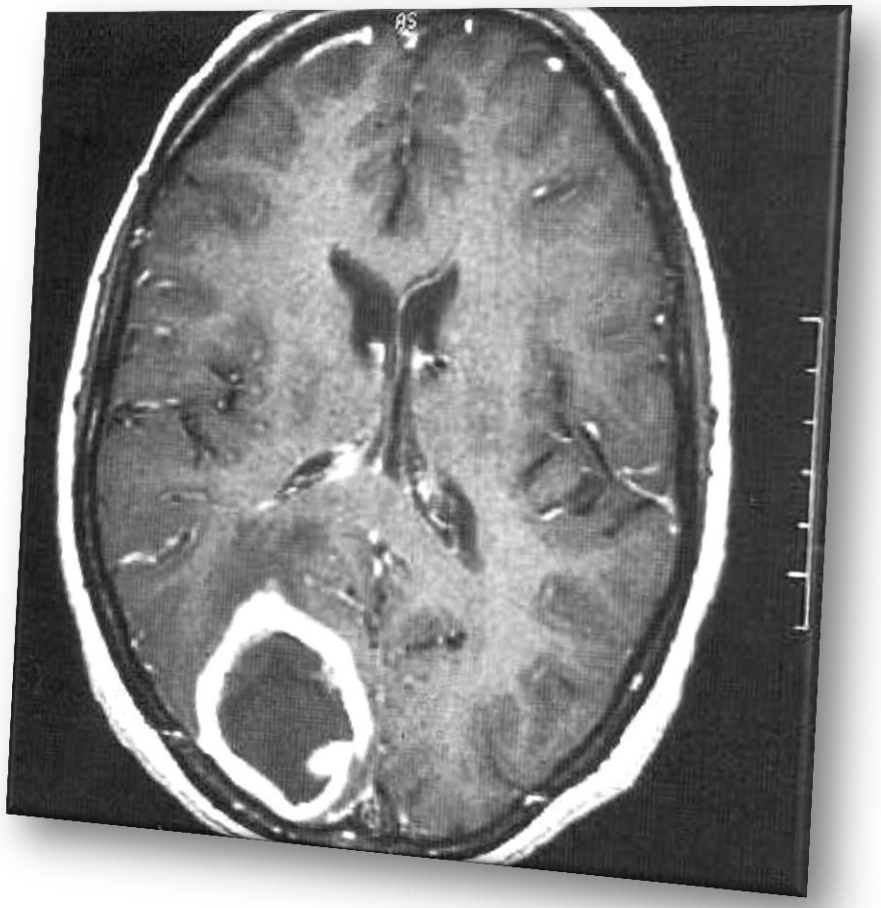
Broberg CS, et al. J Am Coll Cardiol 2007; 50:634-42

Table 25 Recommendations for PAH associated with congenital cardiac shunts

Statement	Class[a]	Level[b]
The ERA bosentan is indicated in WHO-FC III patients with Eisenmenger's syndrome	I	B
Other ERAs, phosphodiesterase type-5 inhibitors, and prostanoids should be considered in	IIa	C
In the absence of significant haemoptysis, oral anticoagulant treatment should be considered in patients with PA thrombosis or signs of heart failure	IIa	C

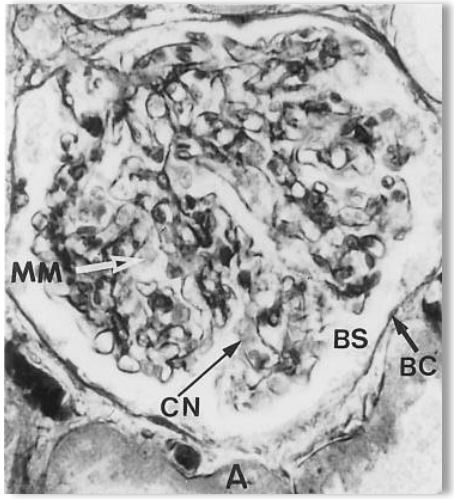
Eventos cerebrovasculares

- 14% de los pacientes
- Factores de riesgo:
  - Vías periféricas
  - Hipertensión
  - Microcitosis
- Abceso cerebral: 3,7%

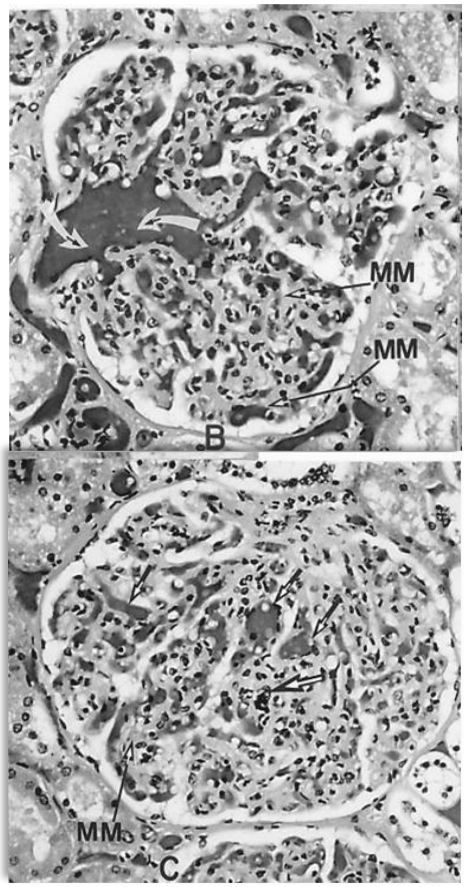


Daliento L, et al. Eur Heart J 1998;19:1845-55

Alteraciones de la función renal



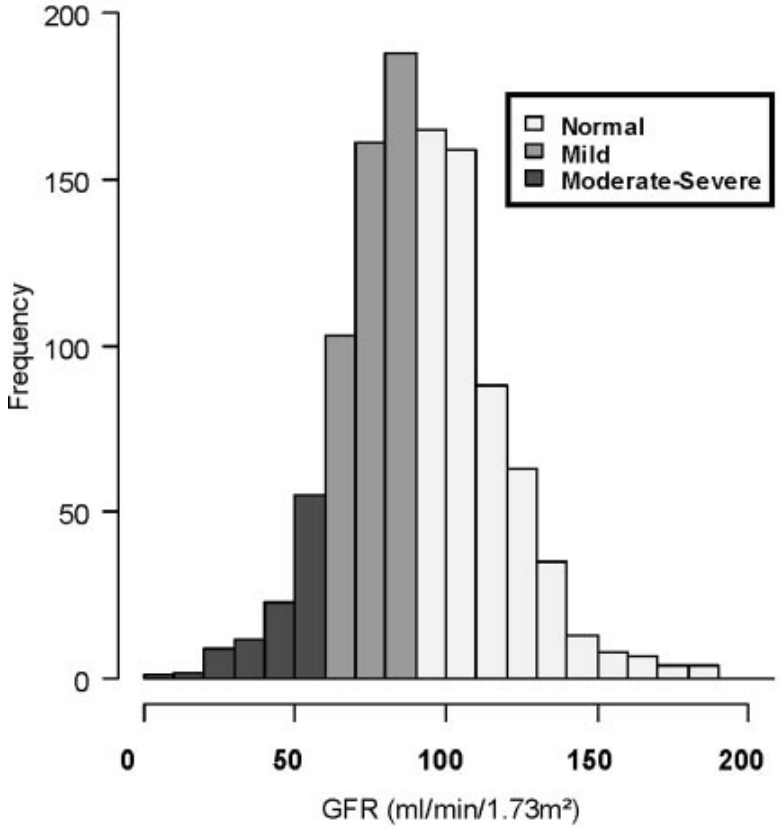
ALTERACIONES ESTRUCTURALES
Engrosamiento de la membrana basal
Aumento de la matriz mesangial
Dilatación de los capilares glomerulares
Esclerosis segmentaria

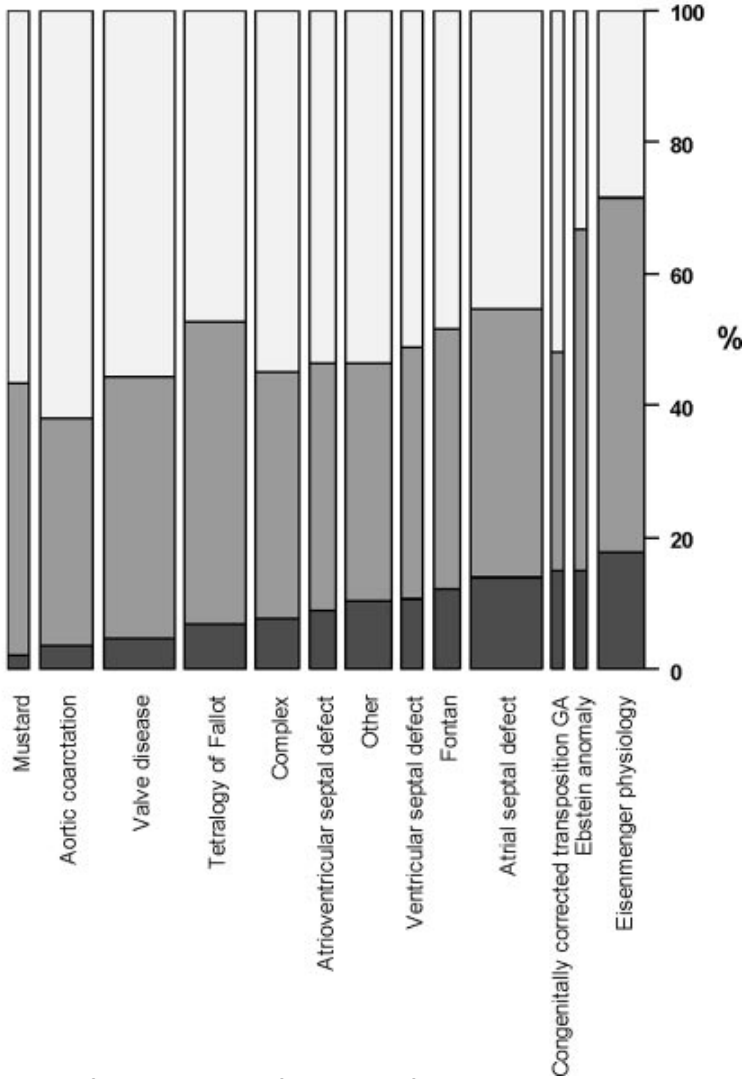


ALTERACIONES FUNCIONALES
Proteinuria
Aumento de las resistencias vasculares
Disminución del flujo plasmático
Disminución de la fracción de filtración
Aumenta la reaabsorción tubular de ácido úrico

Perloff JK, et al.Am J Cardiol 2000;86:1198-204

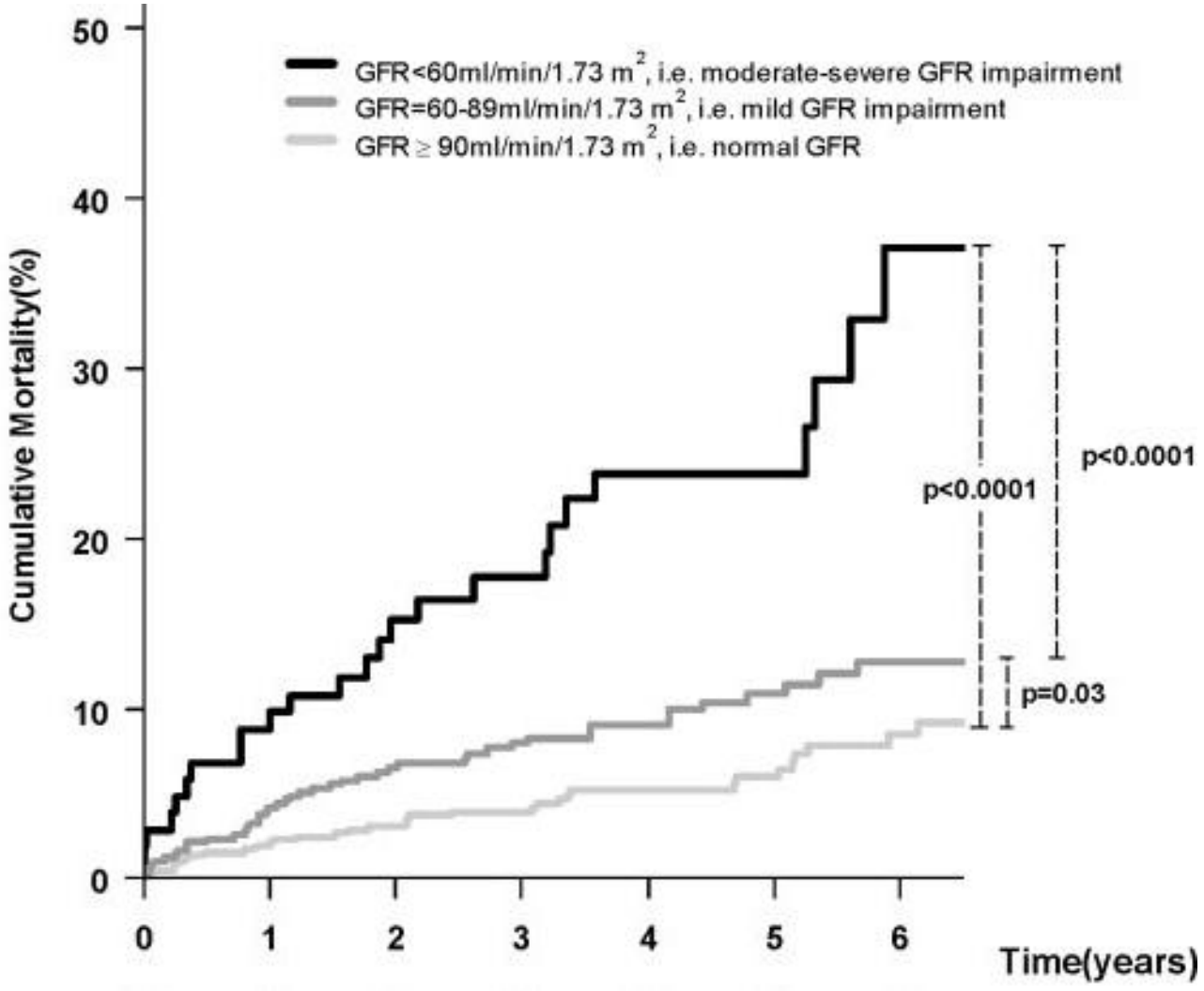
Alteraciones de la función renal





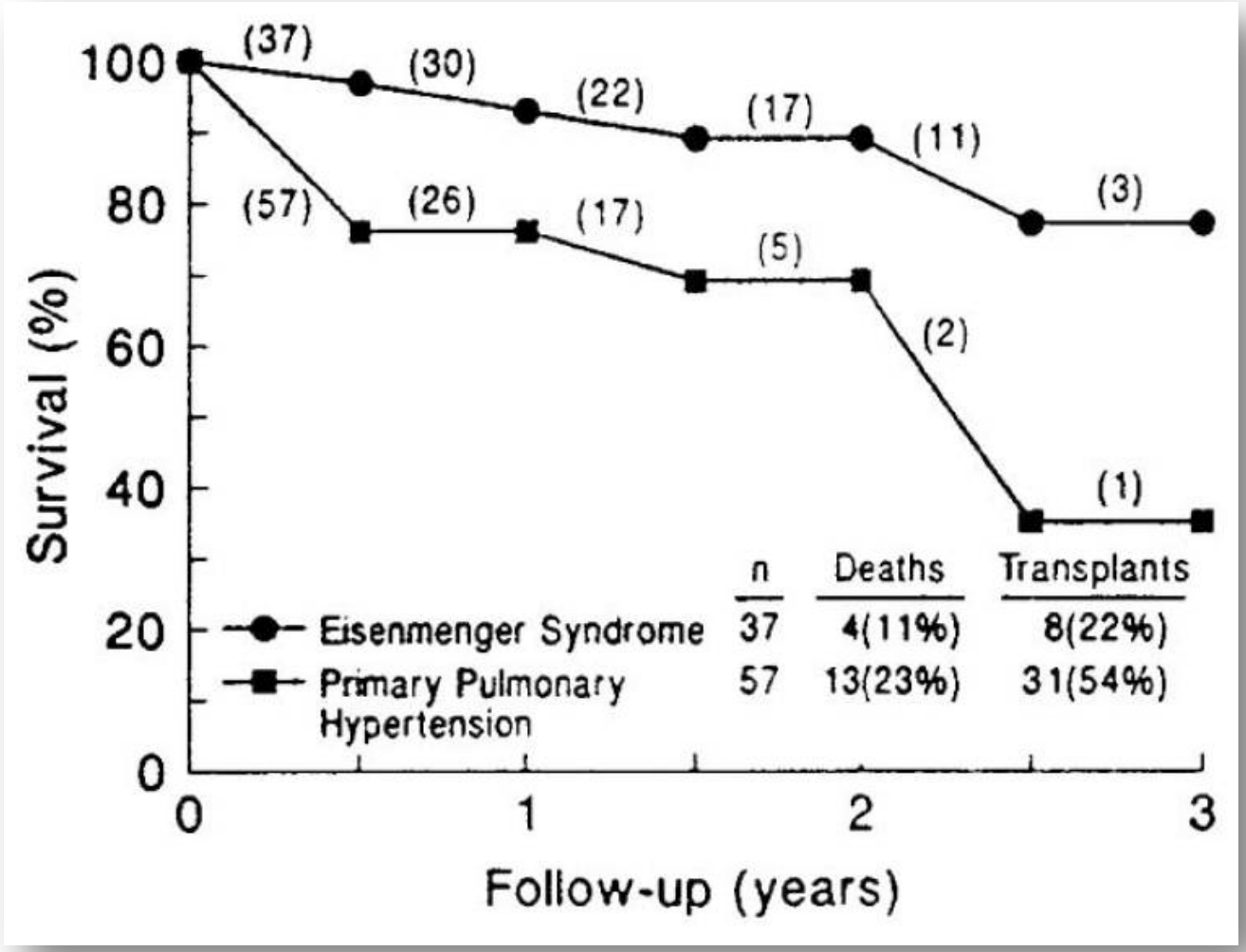
Dimopoulos K, et al. Circulation 2008;117:2320-28

Alteraciones de la función renal



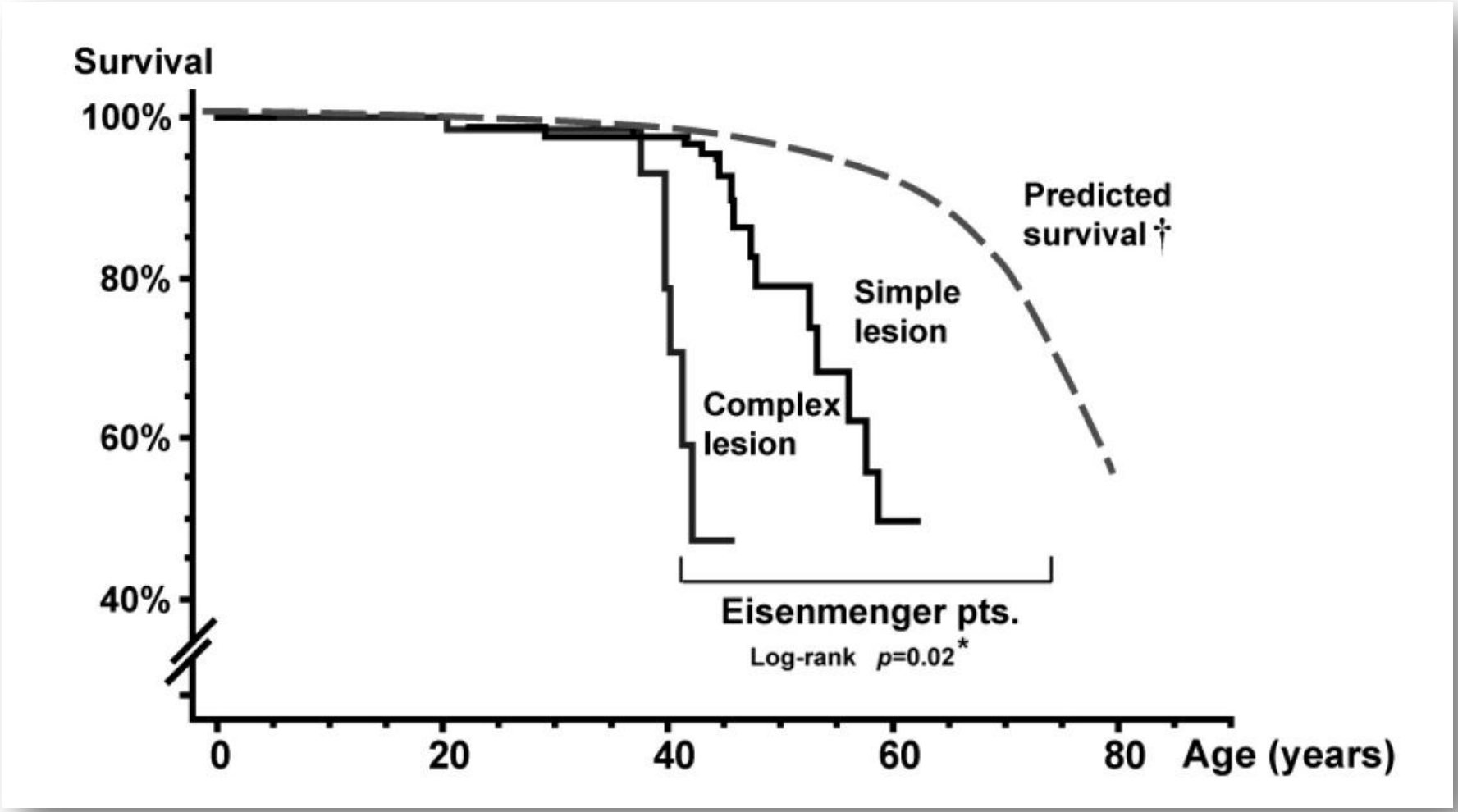
Dimopoulos K, et al. Circulation 2008;117:2320-28

Supervivencia



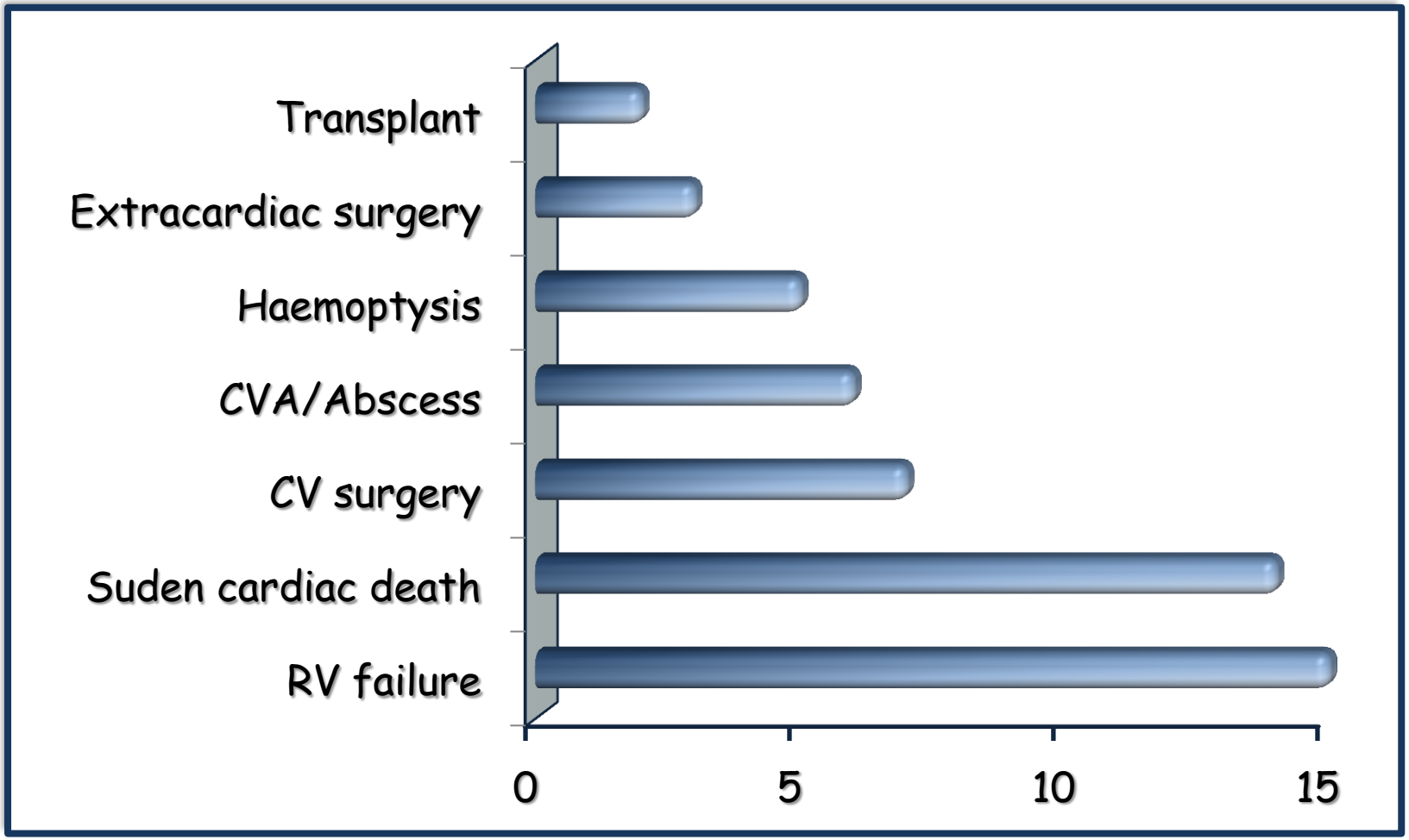
Hopkins et al. Journal of Heart & Lung Transplant, 1996

Supervivencia



Diller GP, et al. Eur Heart J 2006;27:1737-42

Causa de muerte



Somerville J, et al. Int J Cardiol 1998;63:1-8

CLASICAL PREDICTORS OF DEATH
Complex congenital heart disease
Syncope
Younger age at presentation or symptoms
Poor functional class
Signs of heart failure
Presence of right ventricular dysfunction
Supraventricular arrhythmias
RAP>7 mmHg
Renal failure
Serum uric acid
Long QRS
Down syndrome

Daliento et al. Eur Heart J 1998

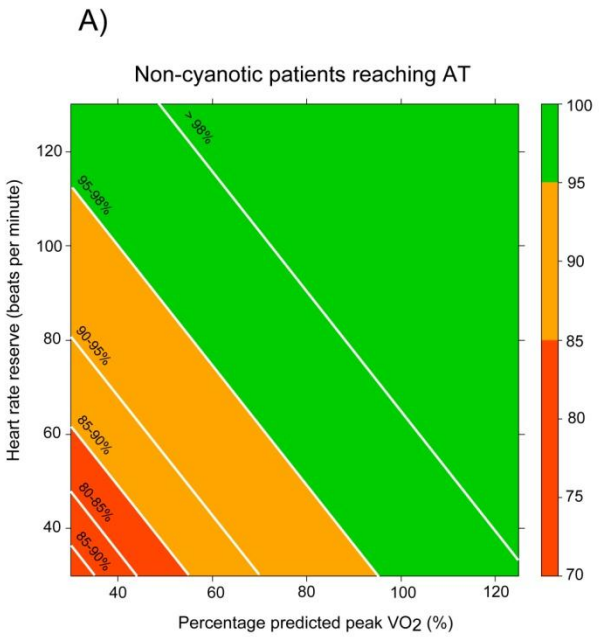
Cantor WJ et al. Am J Cardiol 1999

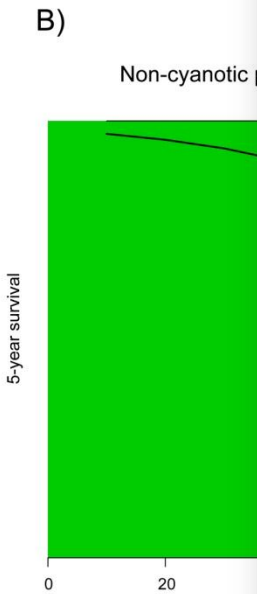
Oya H et al. Heart 2000

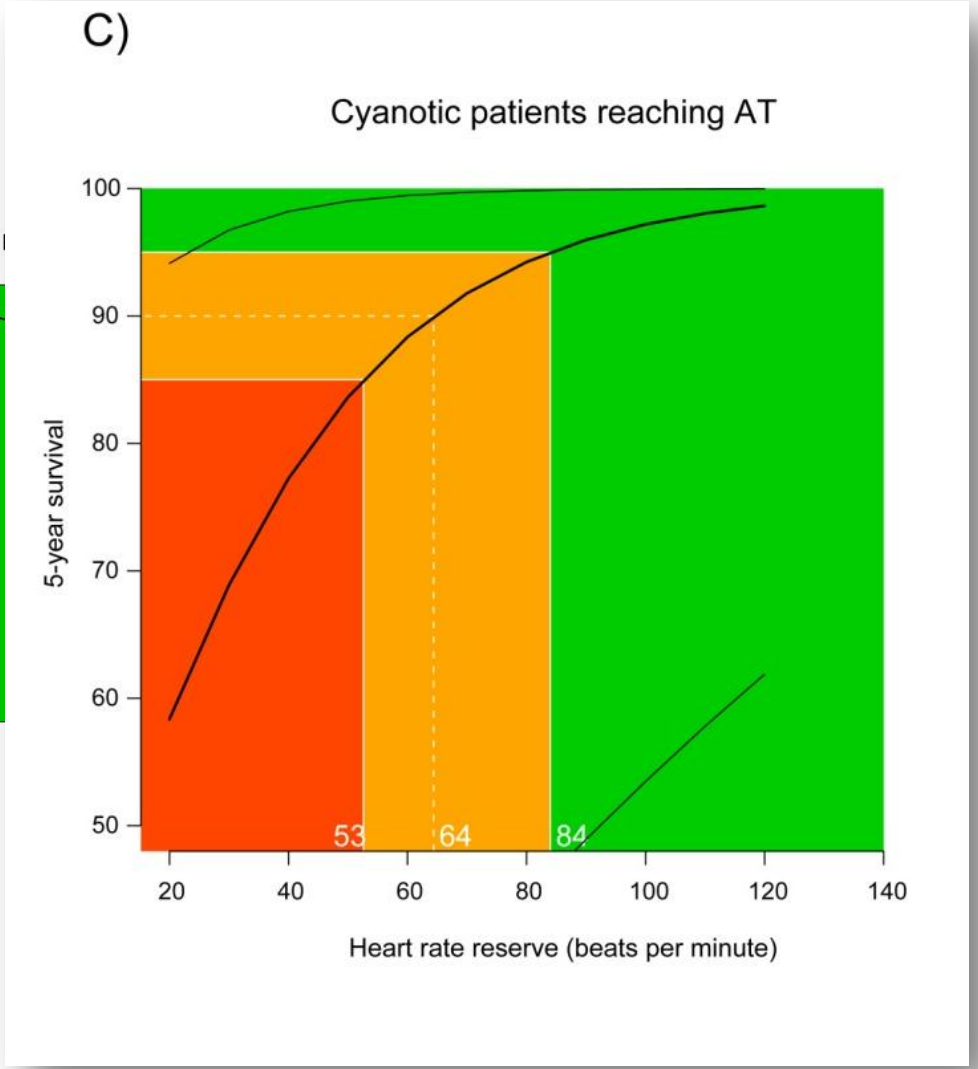
Oya H et al. Am Heart J 2002

Diller GP. Eur Heart J 2006

Pronóstico







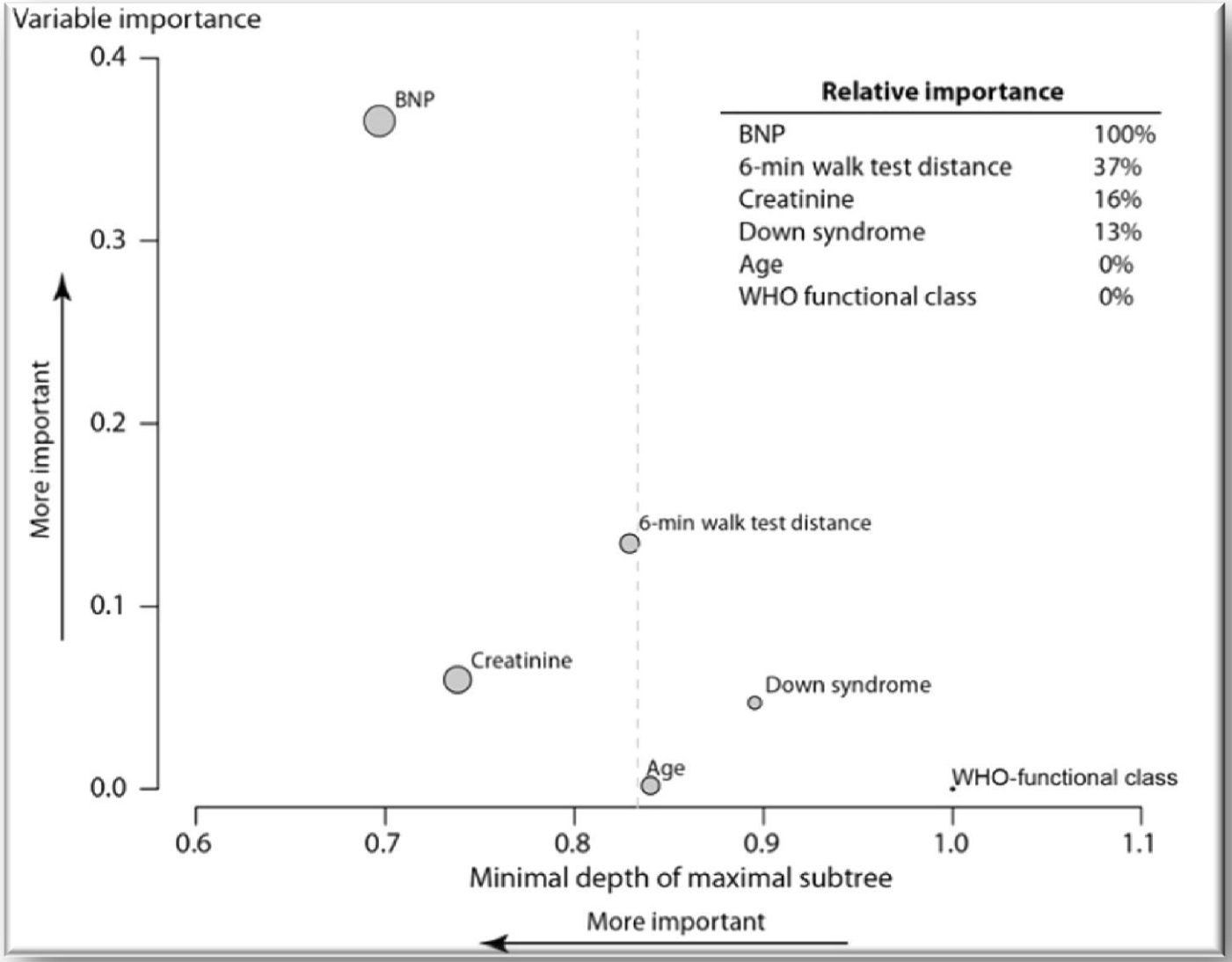
Inuzuka R et al. Circulation 2012;125:250-259

BNP factor pronóstico

Variable	HR (95% CI)	p Value
All patients		
BNP (per 100 pg/ml)	1.68 (1.40 to 2.04)	<0.0001
6 min walk test distance (per 10 m)	0.93 (0.87 to 0.99)	0.02
Resting oxygen saturation (%)	0.87 (0.78 to 0.98)	0.02
Creatinine (per 10 μm/l)	1.15 (1.07 to 1.25)	0.0003
Non-Down patients		
BNP (per 100 pg/ml)	1.63 (1.30 to 2.05)	<0.0001
6 min walk test distance (per 10 m)	0.92 (0.87 to 0.98)	0.006
Resting oxygen saturation (%)	0.83 (0.71 to 0.97)	0.02
Creatinine (per 10 μm/l)	1.49 (1.20 to 1.75)	0.0001
WHO functional class	1.51 (1.04 to 2.20)	0.03
Age	1.06 (1.01 to 1.10)	0.01
Down patients		
BNP (per 100 pg/ml)	3.81 (1.87 to 7.78)	0.0002

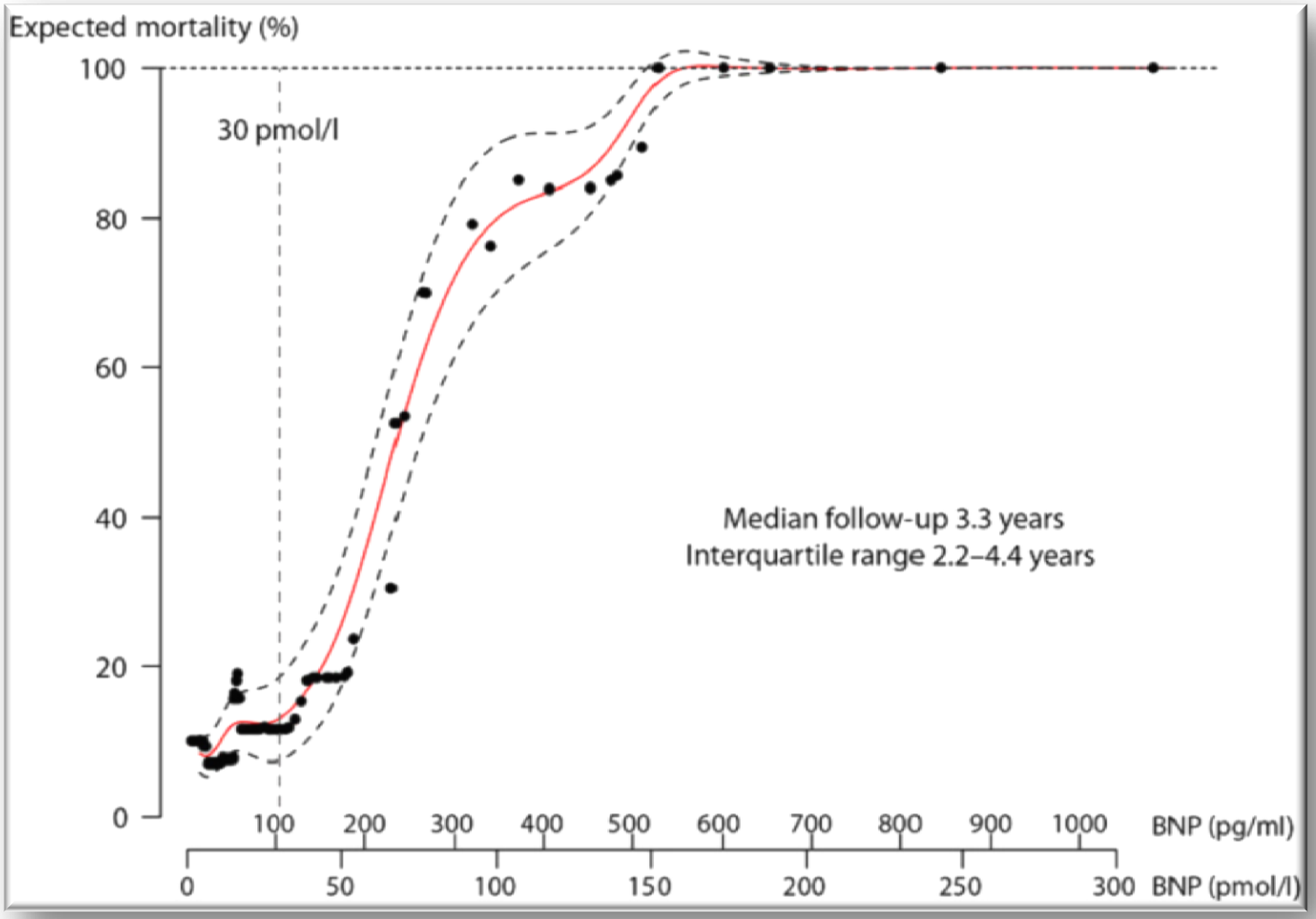
Diller GP, Alonso-Gonzalez R, Kempny A et al. Heart 2012;May 98:736-742

BNP factor pronóstico



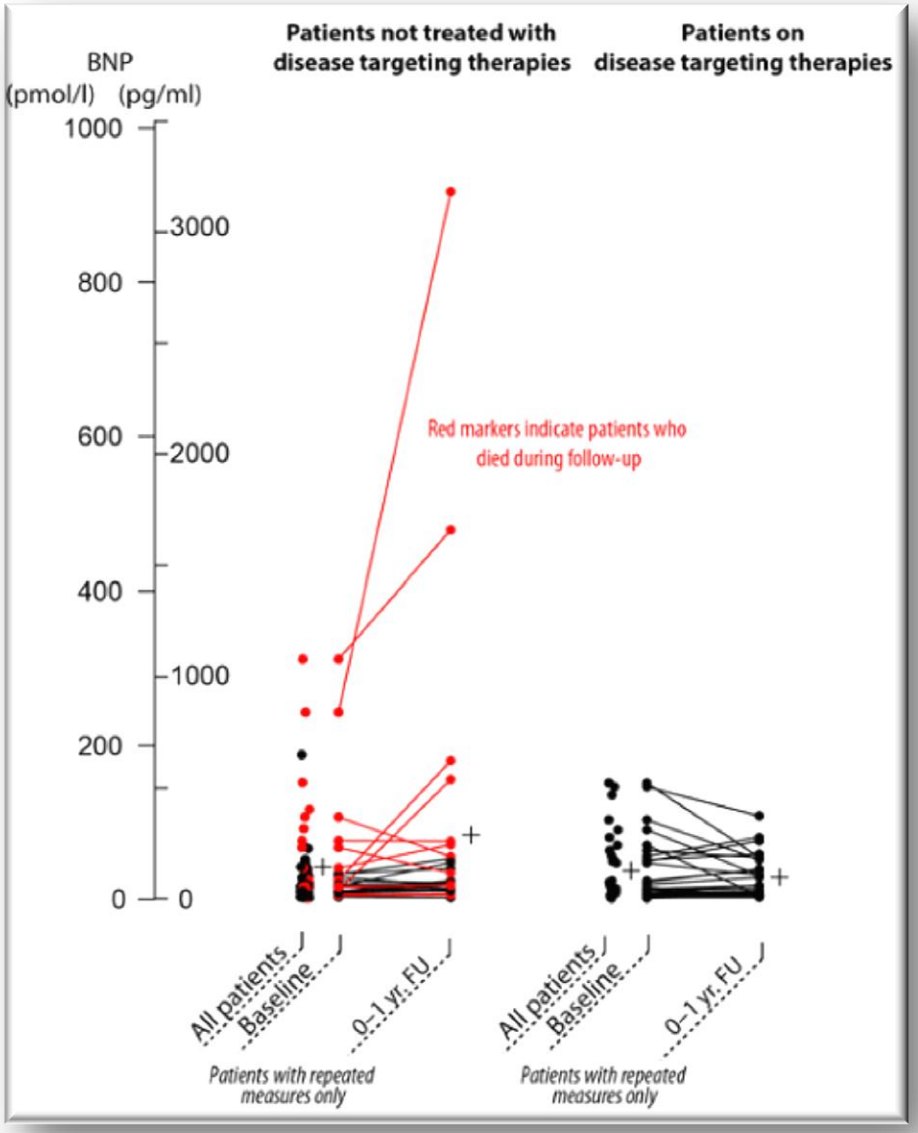
Diller GP, Alonso-Gonzalez R, Kempny A et al. Heart 2012;May 98:736-742

BNP factor pronóstico



Diller GP, Alonso-Gonzalez R, Kempny A et al. Heart 2012;May 98:736-742

BNP factor pronóstico



Diller GP, Alonso-Gonzalez R, Kempny A et al. Heart 2012;May 98:736-742

Anticoagulación oral
Diureticos
Oxígeno
Digoxina
Rehabilitación supervisada

Medidas generales

Evitar ejercicio extenuante
Anticoncepción
Soporte psicosocial
Prevenir infecciones

Referir a un centro de referencia

TEST AGUDO VASODILATADOR

WHO Class I-III

Oral CCB (B)

Sustained response

(WHO I-II)

Yes → Continue CCB

No → WHO Class II

WHO Class II

ERA (A) or PDE-5 I (A)

WHO Class III

ERA (A) o PDE-5 (A)
Iloprost inhalado (A)
Treprostinil SC (B)
Epoprostenol IV (A)
Iloprost IV (C)
Treprostinil IV (C)
Beraprost (C)

WHO Class IV

Epoprostenol IV (A)
Iloprost IV (C)
Treprostinil IV (C)
Iloprost inhalado(B)
Treprostinil SC (B)
ERA (B)
PDE-5 (B)

Inadequate clinical response

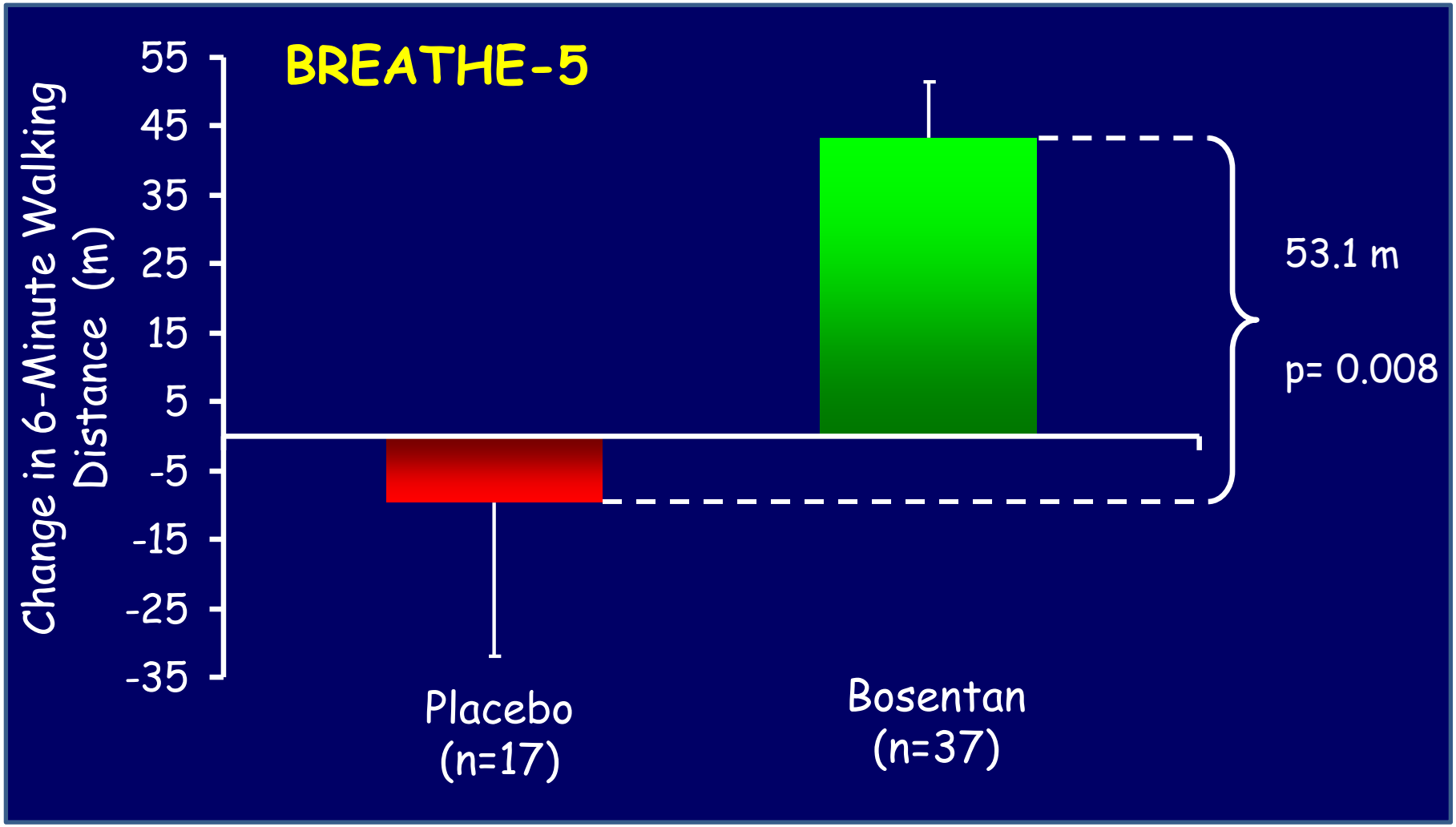
Combination therapy → Inadequate clinical response

+ (B) Prostanoids + (B)
PDE-5 I → +(E/B) ← ERA

BAS (E/B) and/or lung transplant (B)

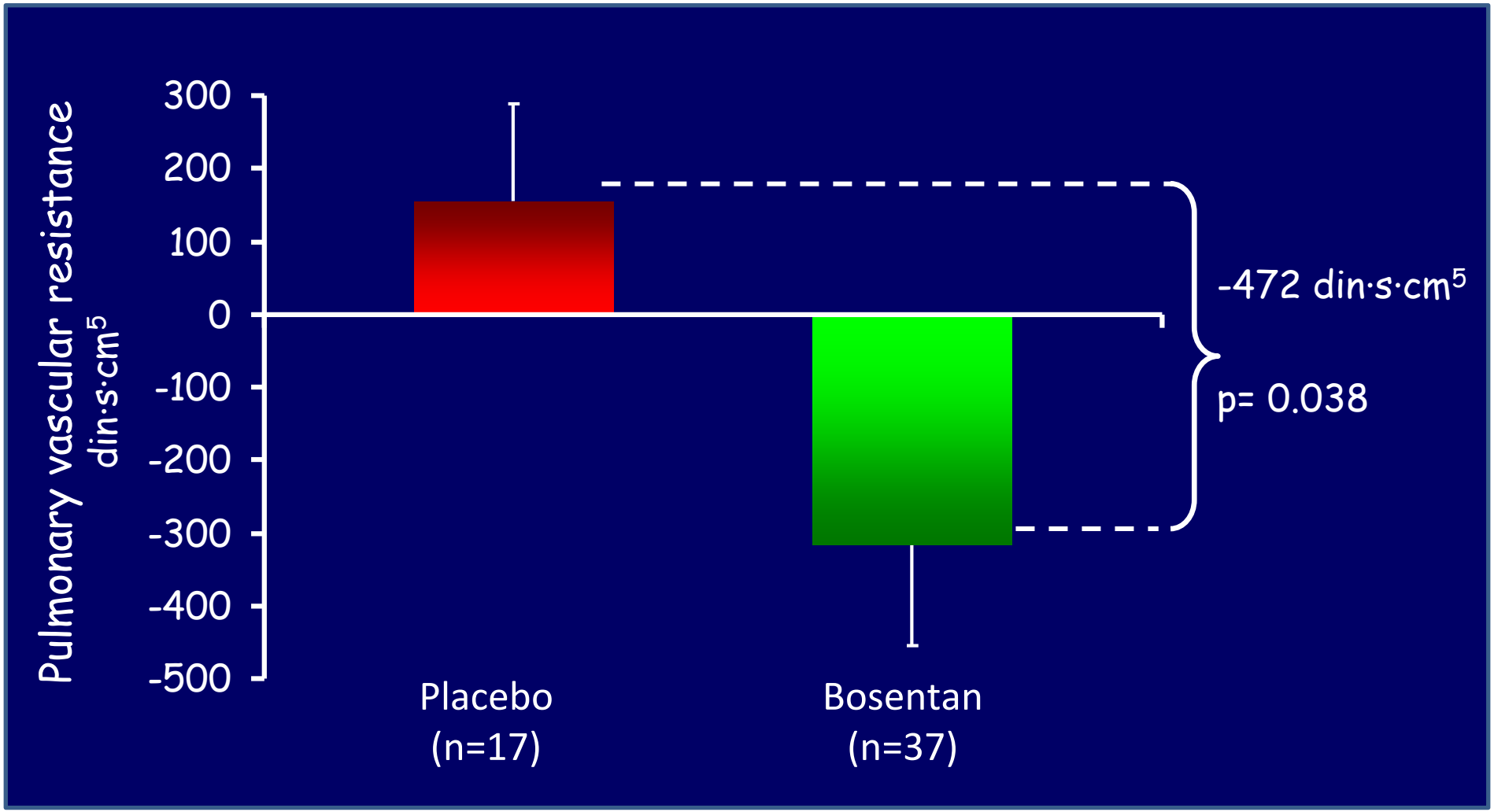
* To maintain 02 at 92%

BREATHE-5



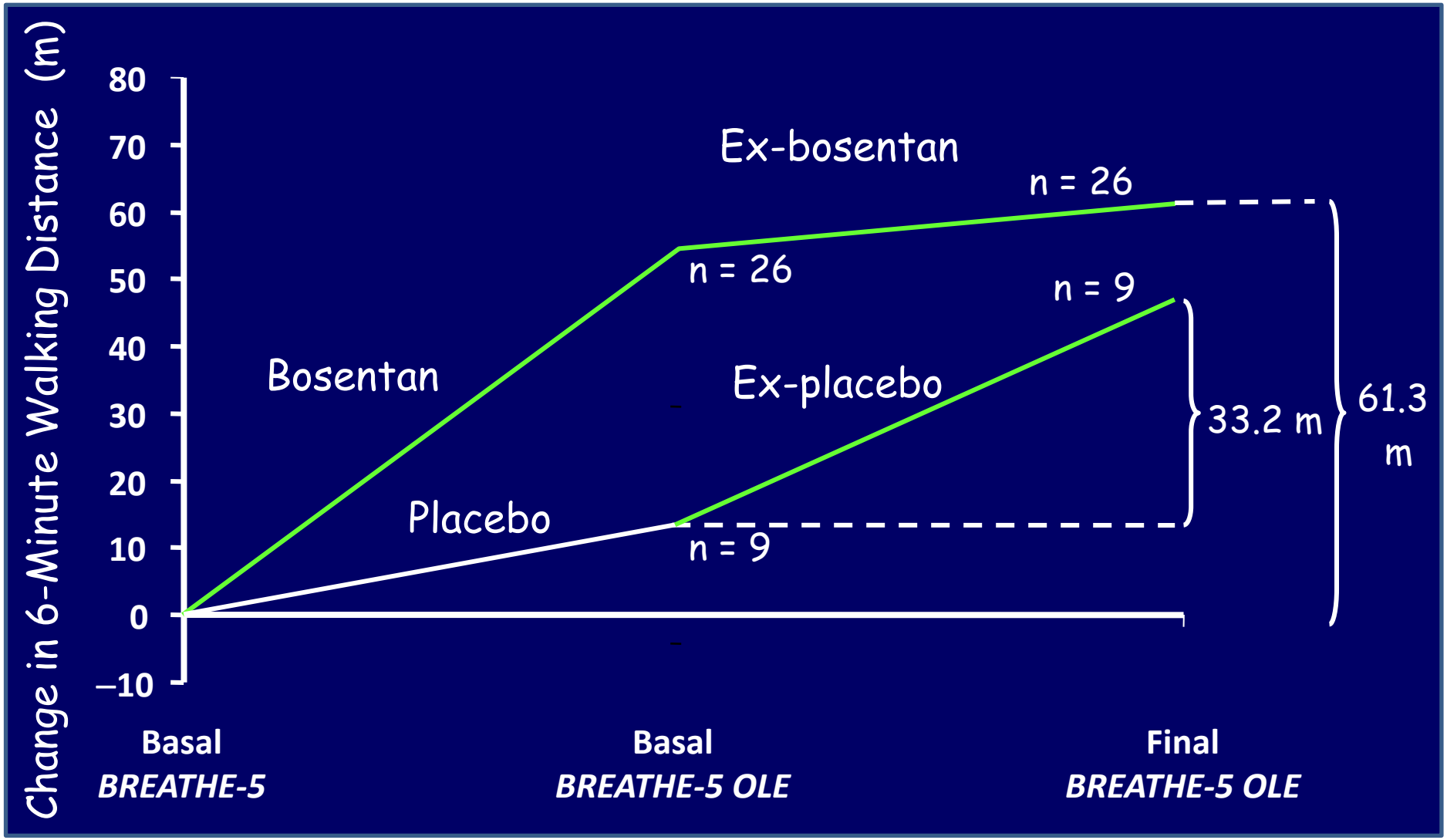
Galie N et al. Circulation 2006;112:48-54

BREATHE-5



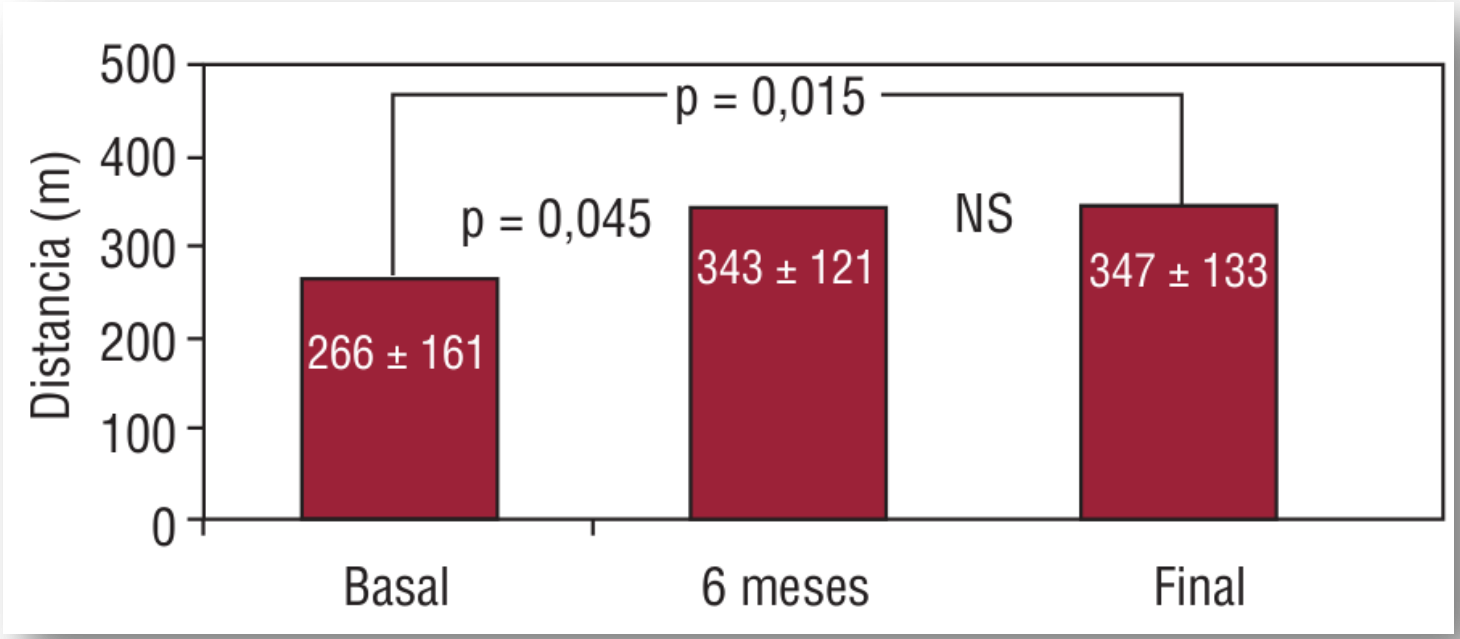
Galie N et al. Circulation 2006;112:48-54

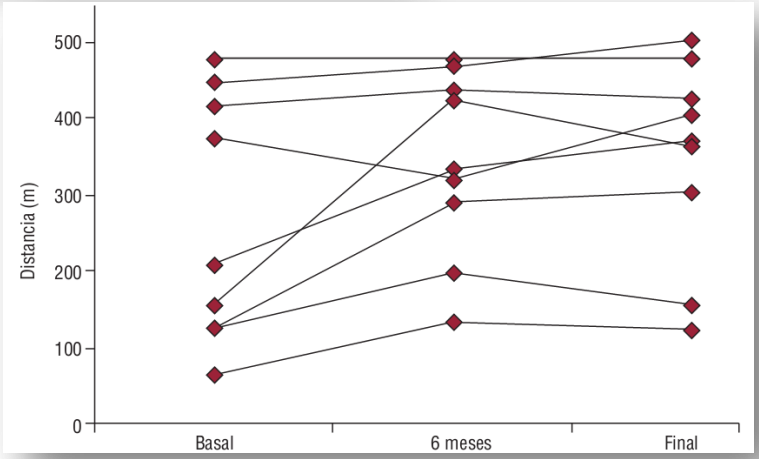
BREATHE-5 OLE



Gatzoulis MA, et al. Int J Cardiol 2008; 127:27-32

Bosentan en CHD-PAH





Diaz-Caravallo E, et al. Rev Esp Cardiol 2009; 1046-9

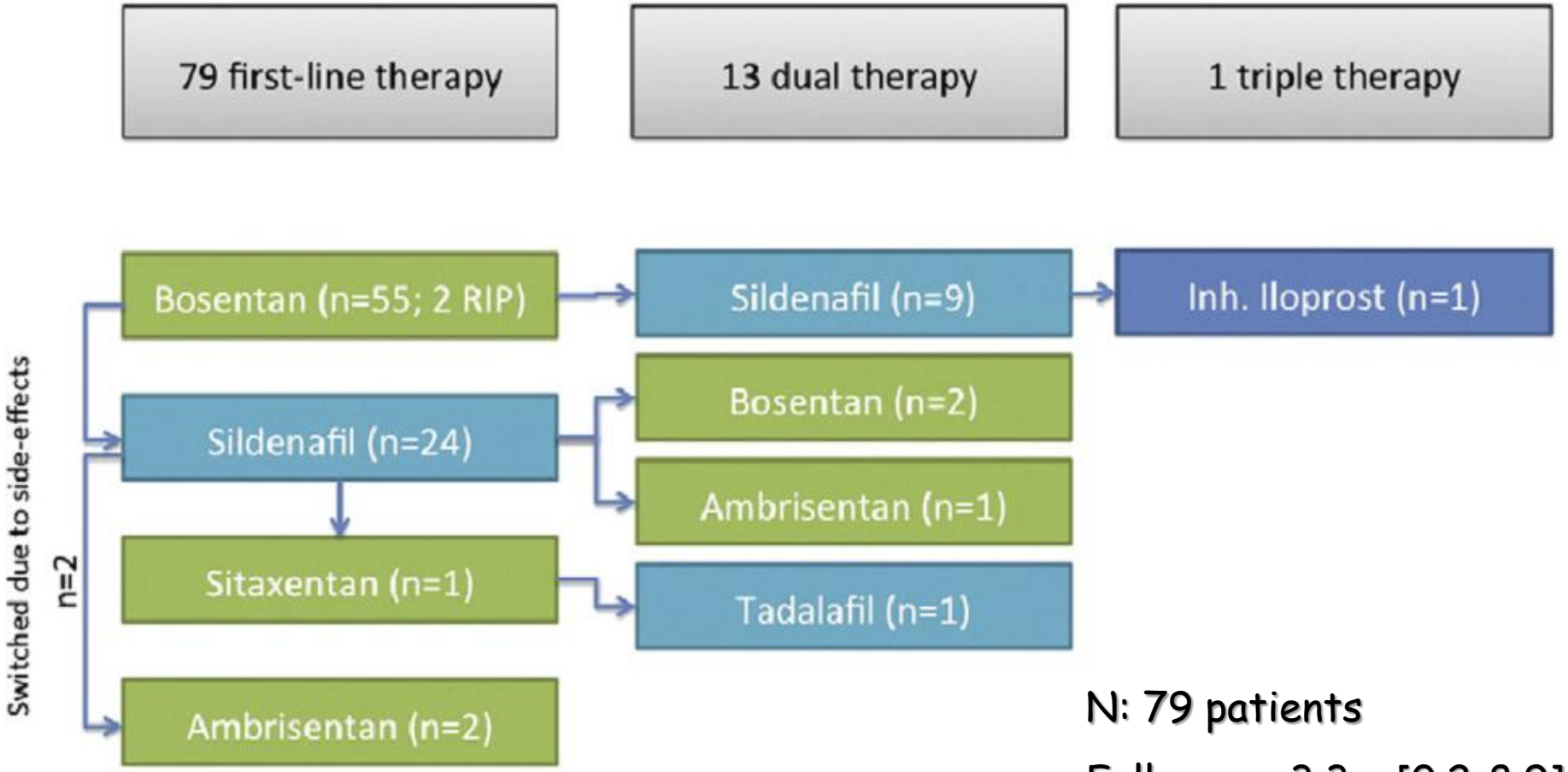
Disease targeting therapies in patients with Eisenmenger syndrome: Response to treatment and long-term efficiency ☆

Gerhard-Paul Diller [a,b,1], Rafael Alonso-Gonzalez [a,1], Konstantinos Dimopoulos [a,b], Maria Alvarez-Barredo [a], Chiehyang Koo [a], Aleksander Kempny [a], Carl Harries [a], Lisa Parfitt [a], Anselm S. Uebing [a], Lorna Swan [a], Philip S. Marino [a,b], Stephen J. Wort [a,b], Michael A. Gatzoulis [a,b,*]

[1] GPD and RAG contributed equally to this work.

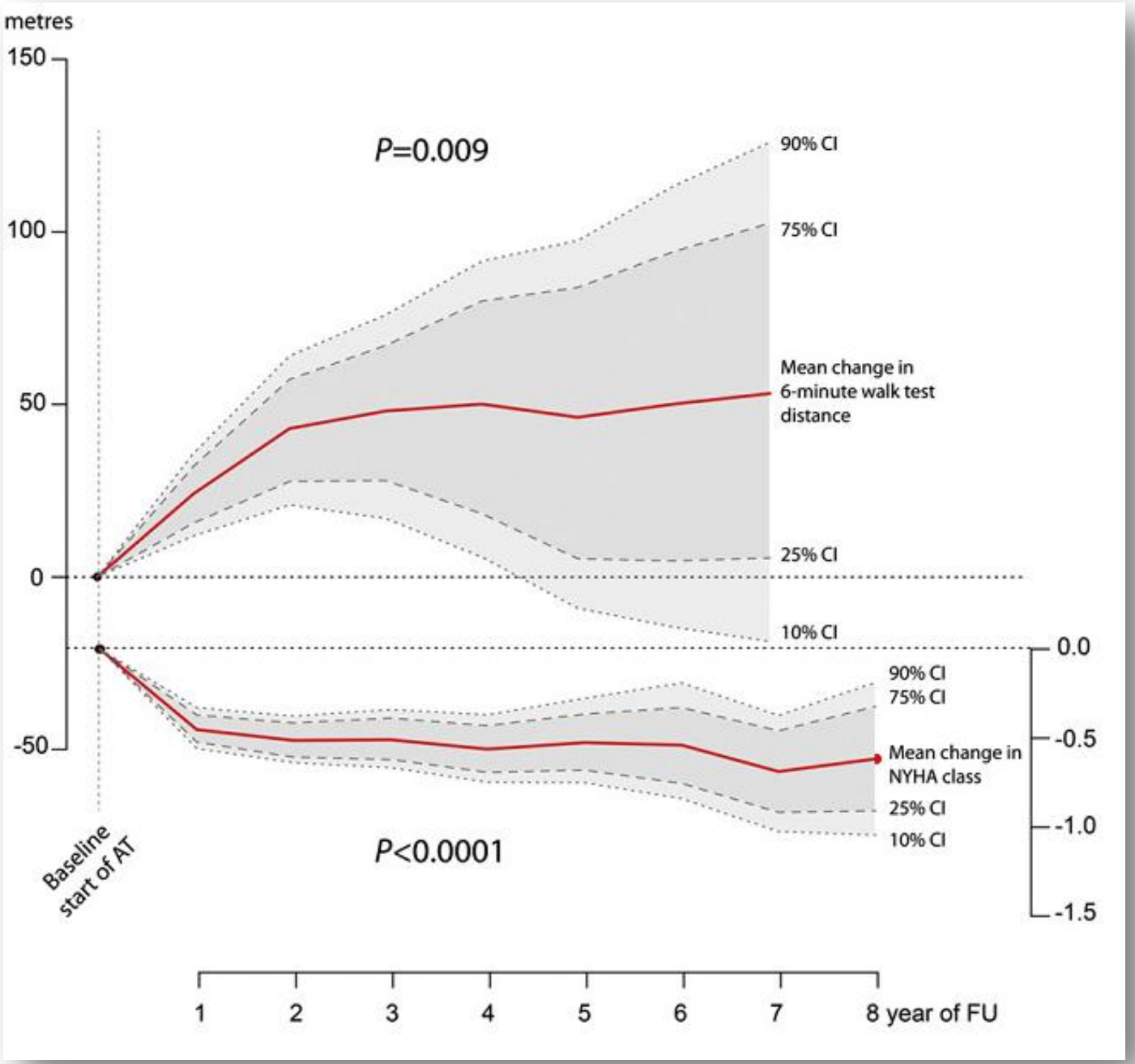
[a] *Adult Congenital Heart Disease Centre and Centre for Pulmonary Hypertension, Royal Brompton Hospital, London, UK*

[b] *National Heart and Lung Institute, Imperial College School of Medicine, London, UK*



N: 79 patients

Follow-up: 3.3 y [0.2-8.9]



Diller GP, Alonso-Gonzalez R et al. Int J Cardiol 2012, Mar 3; [Epub ahead of print]

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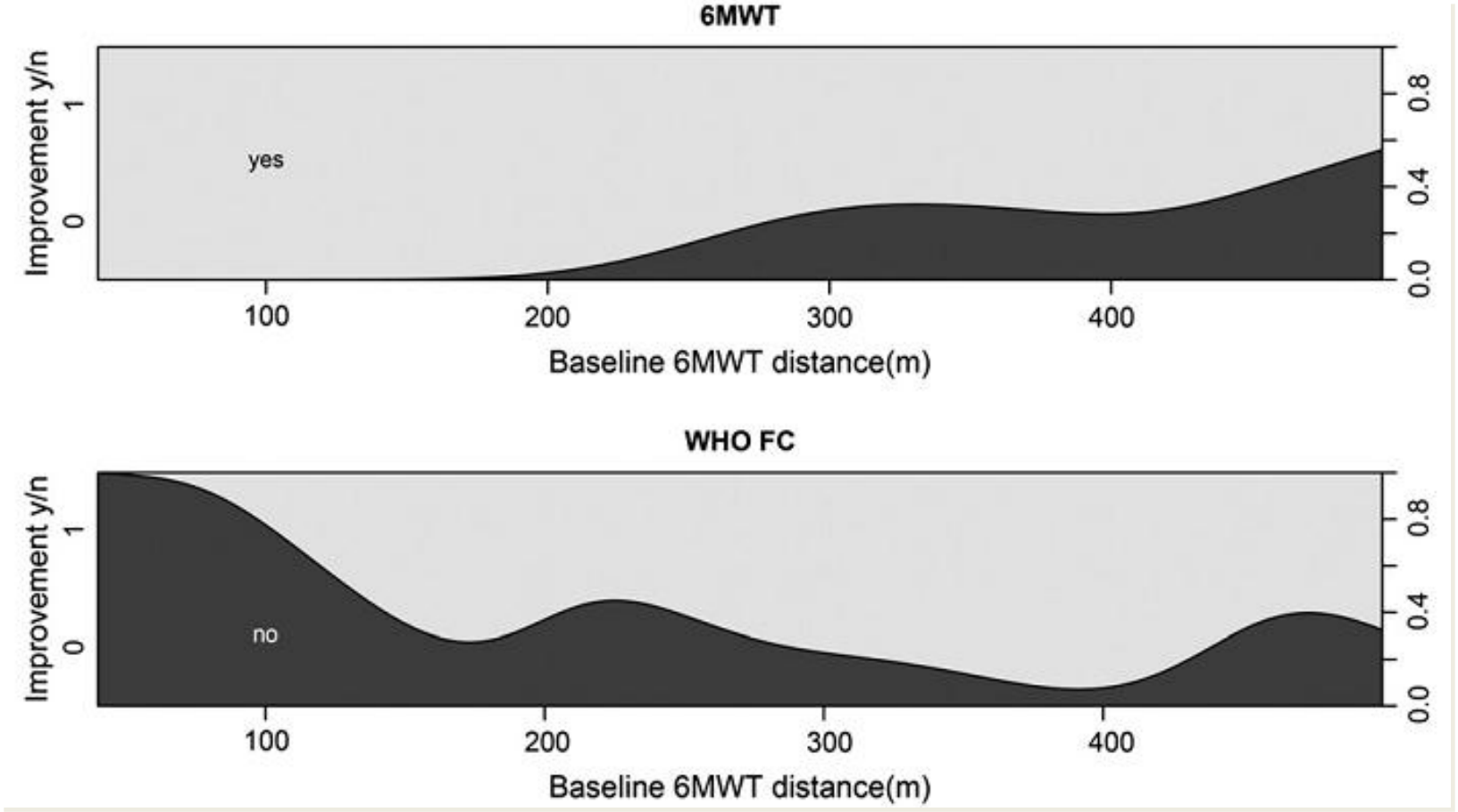
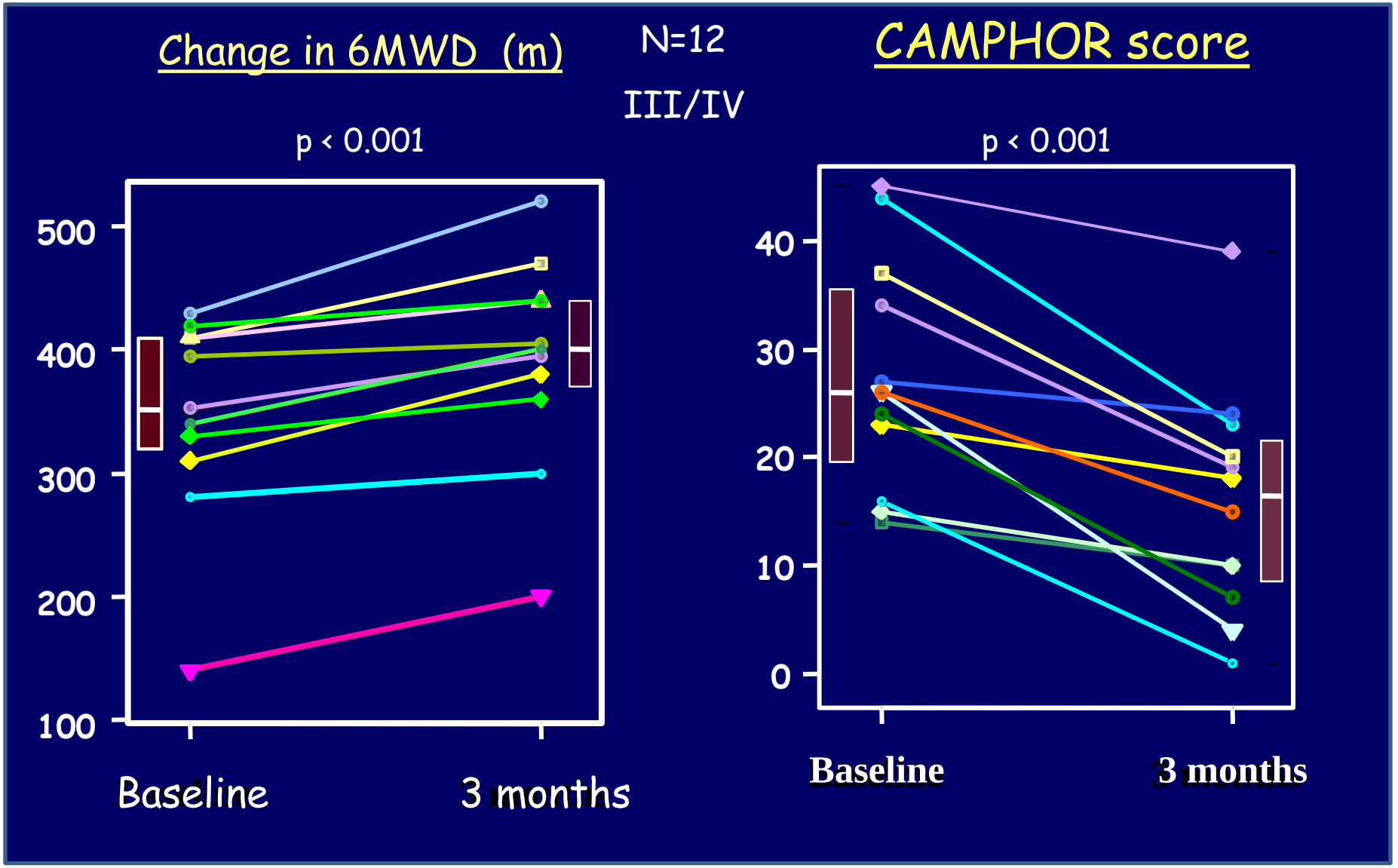


Inhibidores de la PDE-5



Tay EL et al. Int J Cardiol Int J Cardiol 2011;149:372-76]

Oral sildenafil treatment for Eisenmenger syndrome: a prospective, open-label, multicentre study

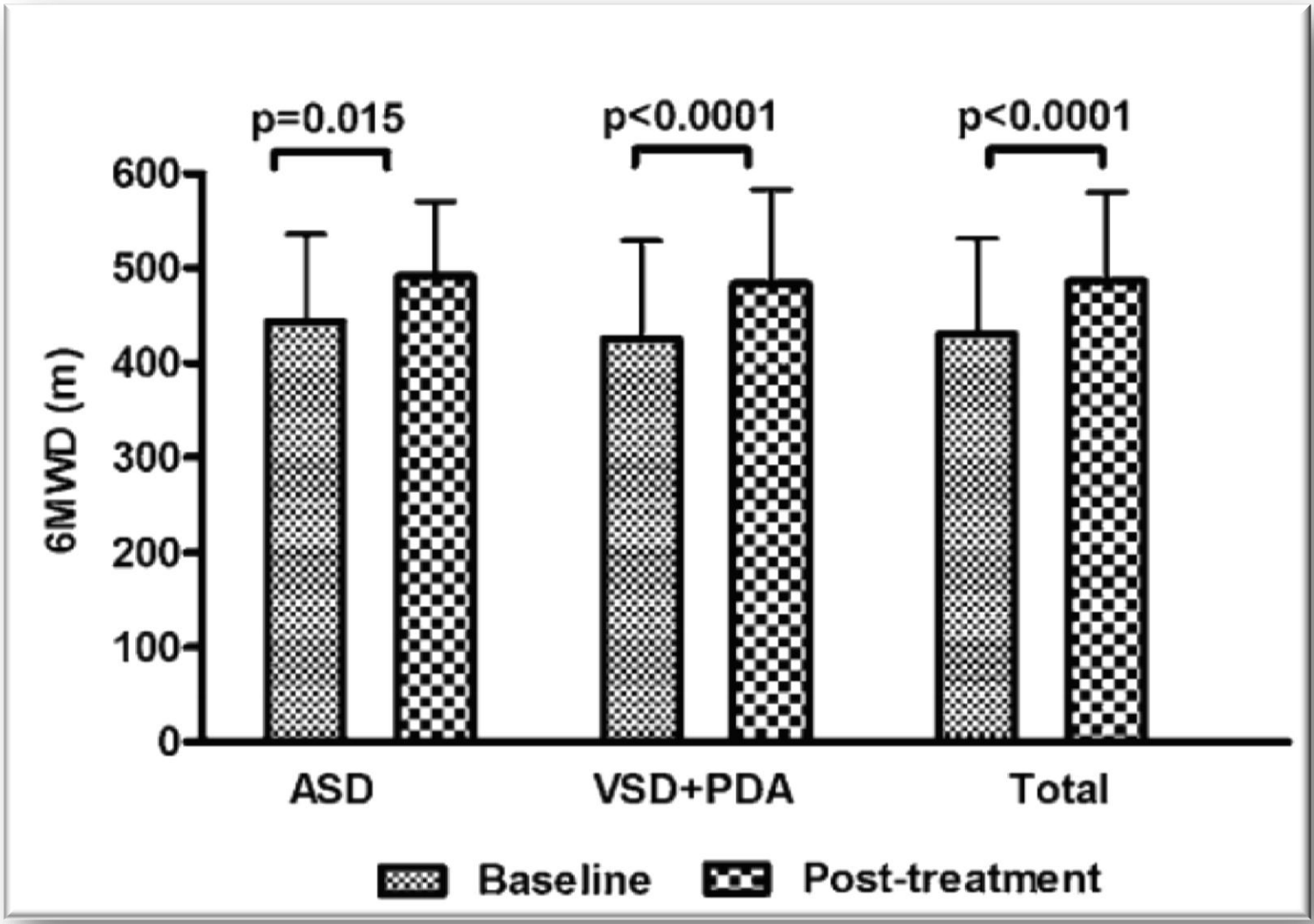
Zhen-Ning Zhang,[1,2] Xin Jiang,[1] Rui Zhang,[1] Xin-Li Li,[3] Bing-Xiang Wu,[4] Qin-Hua Zhao,[1] Yong Wang,[2] Li-Zhi Dai,[1] Lei Pan,[2] Mardi Gomberg-Maitland,[5] Zhi-Cheng Jing[1]

Table 1 Baseline clinical characteristics (n=84)

Characteristics*	ASD (n=25)	VSD and/or PDA (n=59)	Total (n=84)
Functional class			
II, n (%)	12 (48)	32 (54)	44 (52)
III, n (%)	13 (52)	20 (34)	33 (39)
IV, n (%)	0 (0)	7 (12)	7 (8)
6MWD, m	443±92	425±104	430±101
Borg dyspnoea score	3.4±2.2	3.1±2.0	3.2±1.9
Hgb, g/l	161±31	172±31	169±32
UA, μmol/l	372±88	393±109	387±103
Haemodynamic variables			
HR, bpm	81±11	82±12	82±12
mRAP, mm Hg	6±4	5±5	5±5
mPCWP, mm Hg	5±5	5±5	5±5
mSAP, mm Hg	81±11	82±10	82±10
mPAP, mm Hg	70±19	83±18†	79±19
Qpi, l/min/m^2	2.4±0.6	2.6±0.8	2.5±0.8
Qsi, l/min/m^2	2.5±0.7	3.1±1.0†	2.9±1.0
PVRi, dyn×s×cm^{-5}×m^2	2271±879	2711±1267	2580±1177
SVRi, dyn×s×cm^{-5}×m^2	2639±870	2220±784	2344±828
PVRi/F SVRi ratio	0.93±0.48	1.27±0.57	1.17±0.56
Resting SaO_2 in room air, %	89.0±3.5	85.0±5.5†	85.9±5.5

Zhang ZN et al. Heart 2011;97:1876-81

Inhibidores de la PDE-5



Zhang ZN et al. Heart 2011;97:1876-81

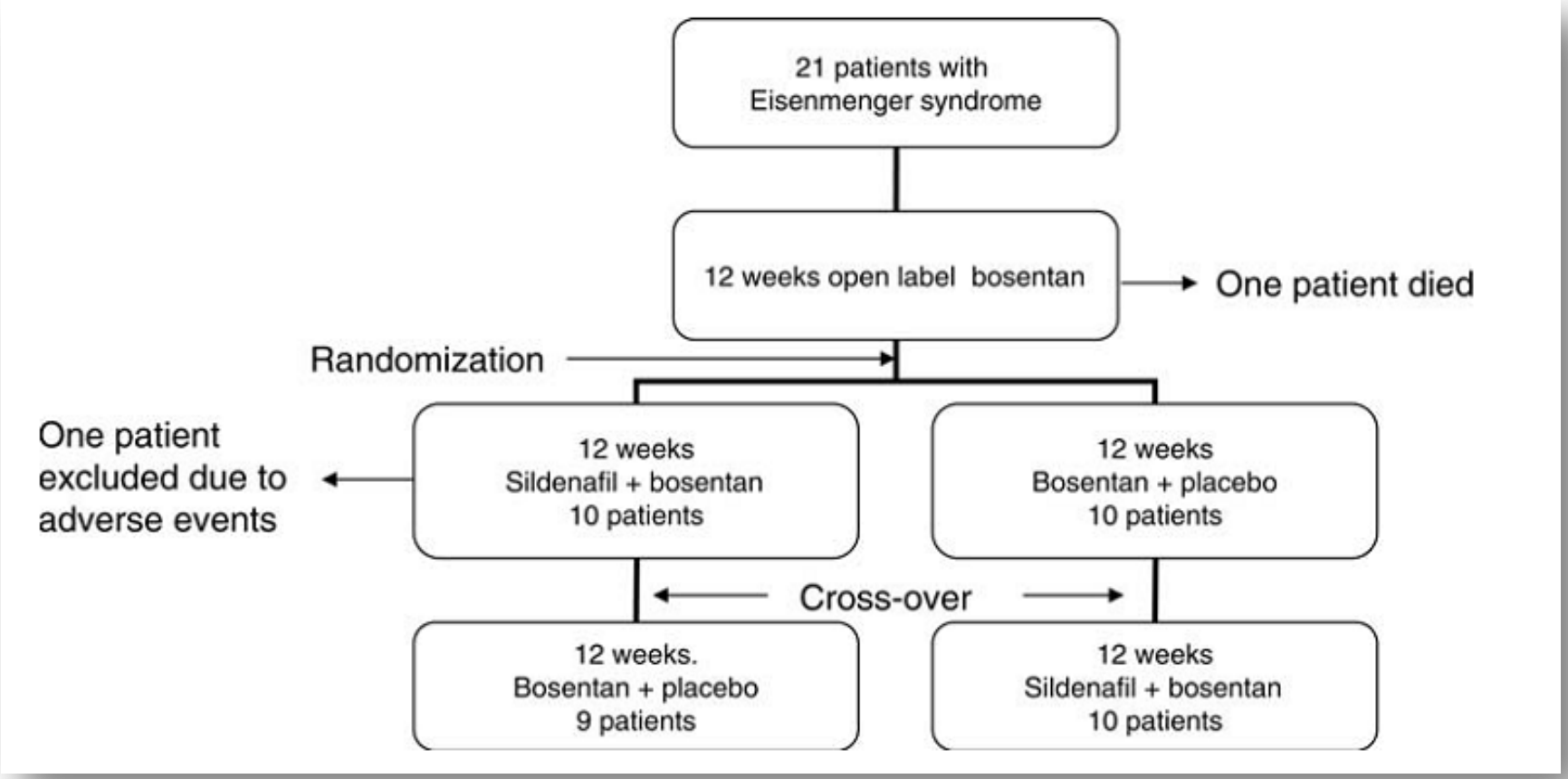
Inhibidores de la PDE-5

Table 2 Percentage changes in clinical and haemodynamic variables at 12 months compared with baseline*

Parameter	ASD (n=25) Treatment effect	p Value	VSD and/or PDA (n=59) Treatment effect	p Value	Total (n=84) Treatment effect	p Value
Clinical variables						
SaO2, %	1.3 (0.3 to 2.3)	0.015	2.8 (2.2 to 3.4)	<0.0001	2.4 (1.8 to 2.9)	<0.0001
6MWD, m	48 (22 to 74)	0.001	59 (42 to 75)	<0.0	56 (42 to 69)	0.0001
	−1.2 (−1.9 to −0.5)	0.002	−0.9 (−1.4 to −0.4)	0.0		0.0001
	−7.3 (−12.2 to −2.4)	0.005	−7.0 (−12.6 to 1.1)	0.02		0.002
UA, µmol/l	−33 (−66 to −1)	0.105	−8 (−34 to 18)	0.556	−15 (−36 to 5)	0.139
Haemodynamic variables†						
HR, bpm	−2.8 (0−7.4 to 1.8)	0.212	−2.2 (−5.5 to 1.1)	0.1	−1.4 (−4.2 to 1.4)	0.323
mSAP, mm Hg	−1.0 (−6.1 to 4.1)	0.692	−1.4 (−3.9 to 1.0)	0.244	−1.3 (−3.5 to 0.9)	0.248
mRAP, mm Hg	0.6 (−1.1 to 2.2)	0.492	0.8 (−0.5 to 2.2)	0.222	−0.8 (−0.3 to 1.8)	0.159
mPCWP, mm Hg	0.1 (−1.8 to 1.9)	0.929	−0.4 (−1.7 to 1.0)	0.608	−0.2 (−1.3 to 0.9)	0.682
mPAP, mm Hg	−5.4 (−10.0 to 0.9)	0.022	−4.4 (−8.0 to −0.9)	0.016	−4.7 (−7.5 to −1.9)	0.001
Qpi, l/min/m²	0.4 (0.1 to 0.8)	0.011	0.7 (0.2 to 1.1)	0.009	0.6 (0.2 to 0.9)	0.001
	0.1 (0.1 to 0.2)	0.270	0.2 (0.1 to 0.3)			
PVRi, m²	−466 (−744 to 189)	0.002	−477 (−677 to −27		−474 (−634 to −314)	
m²	−282 (−629 to 64)	0.452	−70 (−247 to −107			
PVRi/FSVRi ratio	−0.07 (−0.31 to 0.17)	0.539	−0.14 (−0.25 to −0.02)	0.027	−0.12 (−0.22 to −0.01)	0.033

Zhang ZN et al. Heart 2011;97:1876-81

Combination therapy with bosentan and sildenafil in Eisenmenger syndrome: a randomized, placebo-controlled, double-blinded trial†



Iversen K et al. Eur Heart J 2010;31:1124-31

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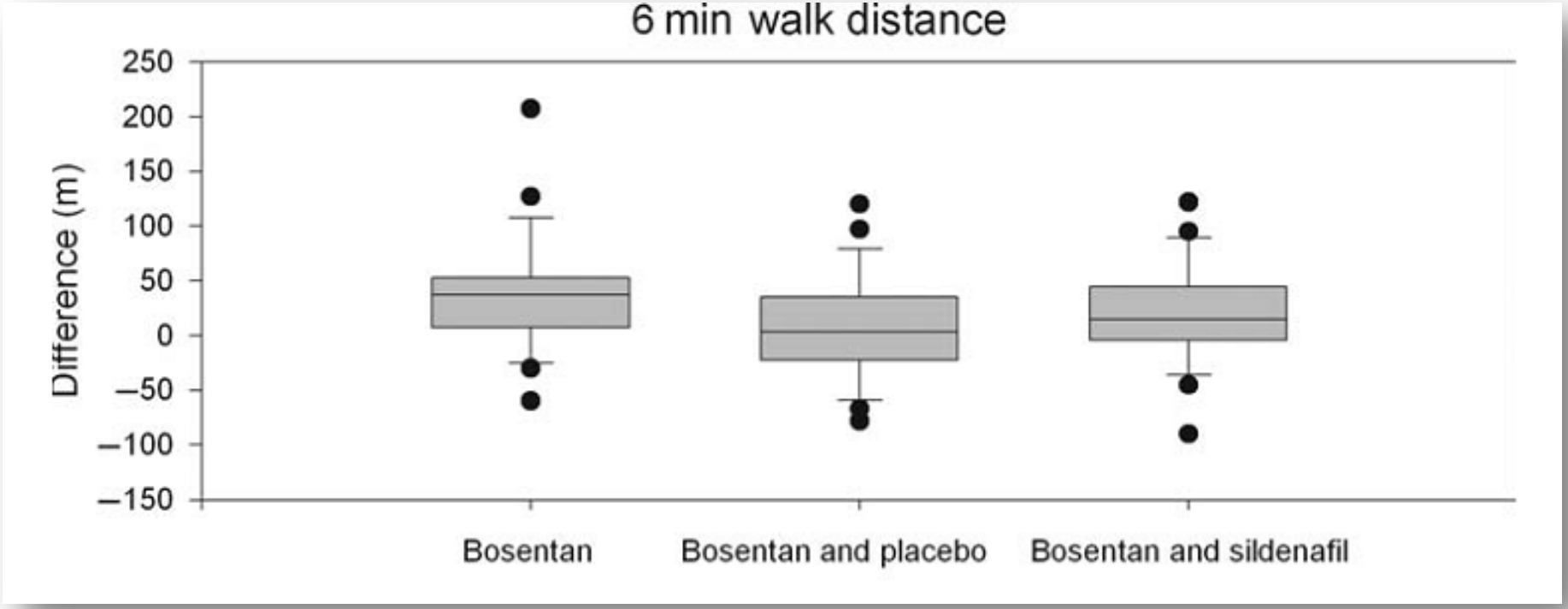

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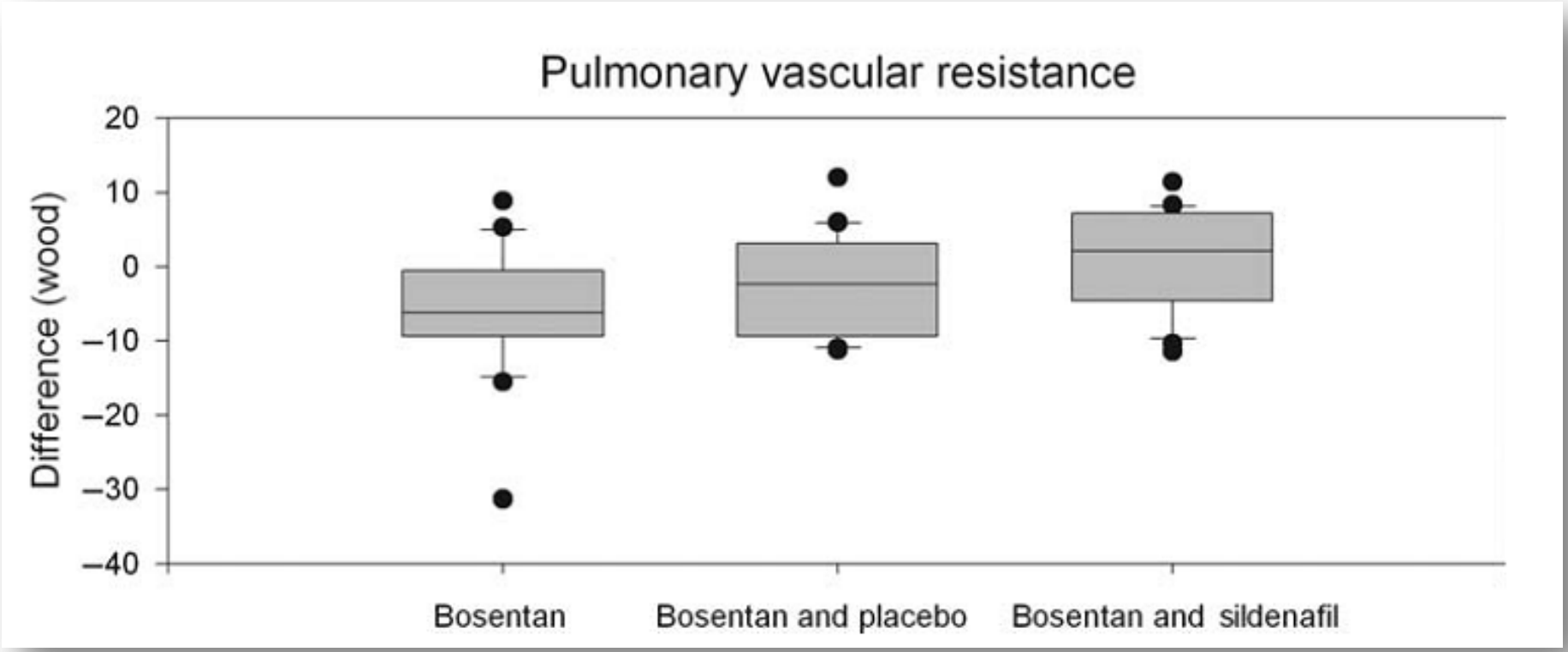

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Gerhard-Paul Diller [a,b,1], Rafael Alonso-Gonzalez [a,1], Konstantinos Dimopoulos [a,b], Maria Alvarez-Barredo [a], Chiehyang Koo [a], Aleksander Kempny [a], Carl Harries [a], Lisa Parfitt [a], Anselm S. Uebing [a], Lorna Swan [a], Philip S. Marino [a,b], Stephen J. Wort [a,b], Michael A. Gatzoulis [a,b,*]

[1] GPD and RAG contributed equally to this work.

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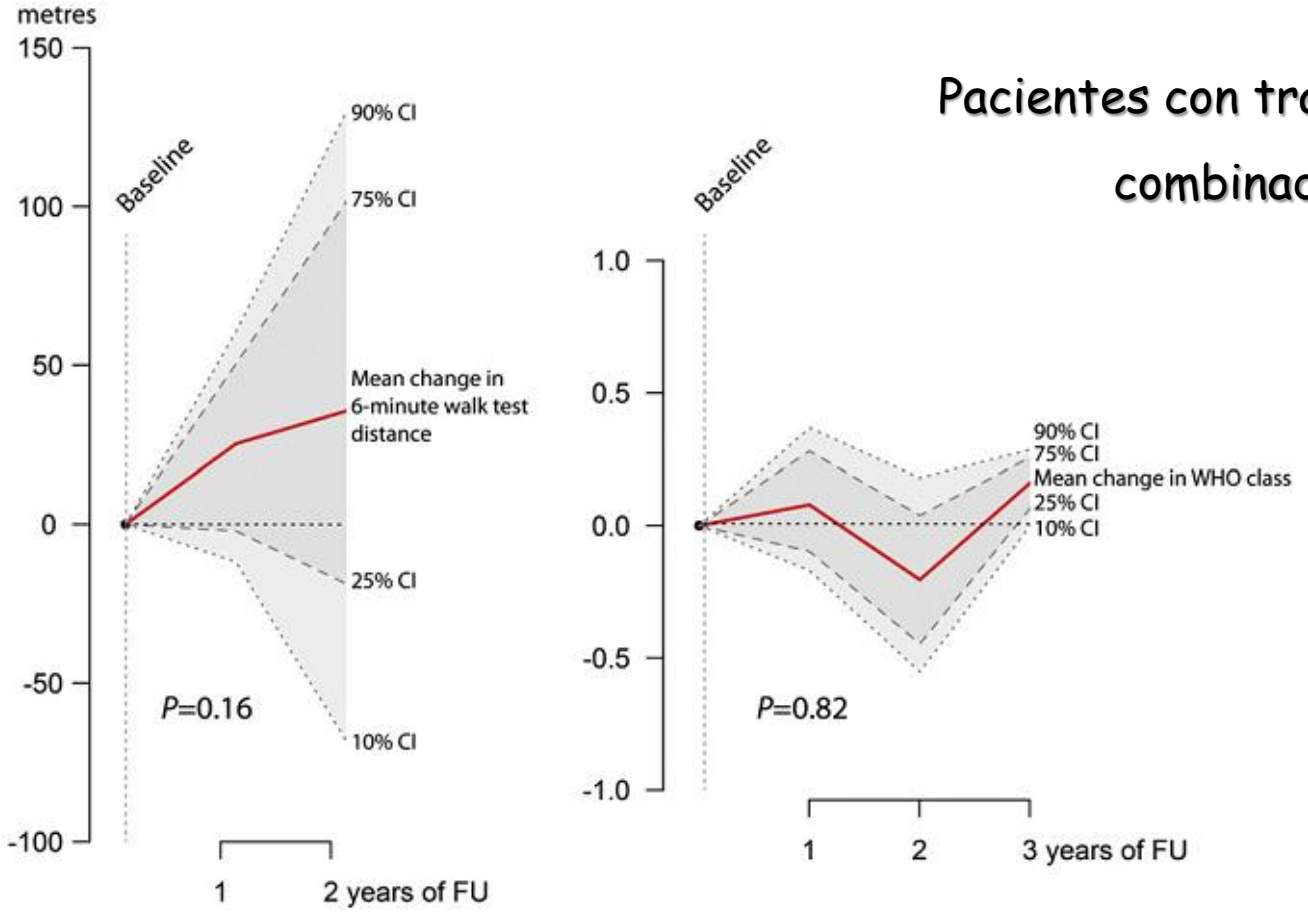
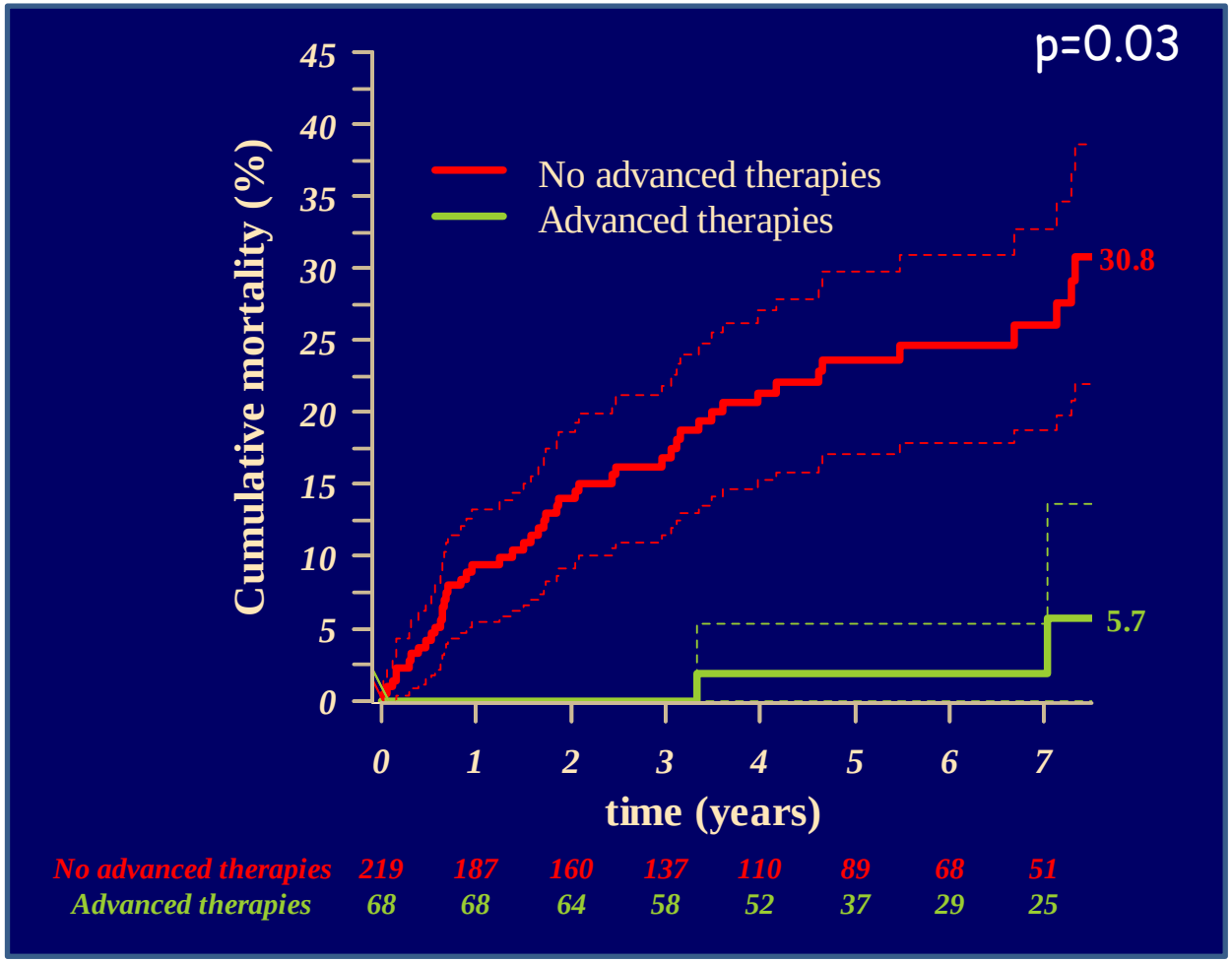


Pacientes con tratamiento combinado

Tratamiento de HAP-CHD y supervivencia



Dimopoulos et al. Circulation 2010;120:20-25

Cuándo empezar a tratar?

Table 25 **Recommendations for PAH associated with congenital cardiac shunts**

Statement	Class[a]	Level[b]
The ERA bosentan is indicated in WHO-FC III patients with Eisenmenger's syndrome	I	B
Other ERAs, phosphodiesterase type-5 inhibitors, and prostanoids should be considered in patients with Eisenmenger's syndrome	IIa	C
consistent increase in arterial oxygen saturation and reduces symptoms		
If symptoms of hyperviscosity are present, phlebotomy with isovolumic replacement should be considered usually when the haematocrit is > 65%	IIa	C
Combination therapy may be considered in patients with Eisenmenger's syndrome	IIb	C
The use of CCBs is not recommended in patients with Eisenmenger's syndrome	III	C

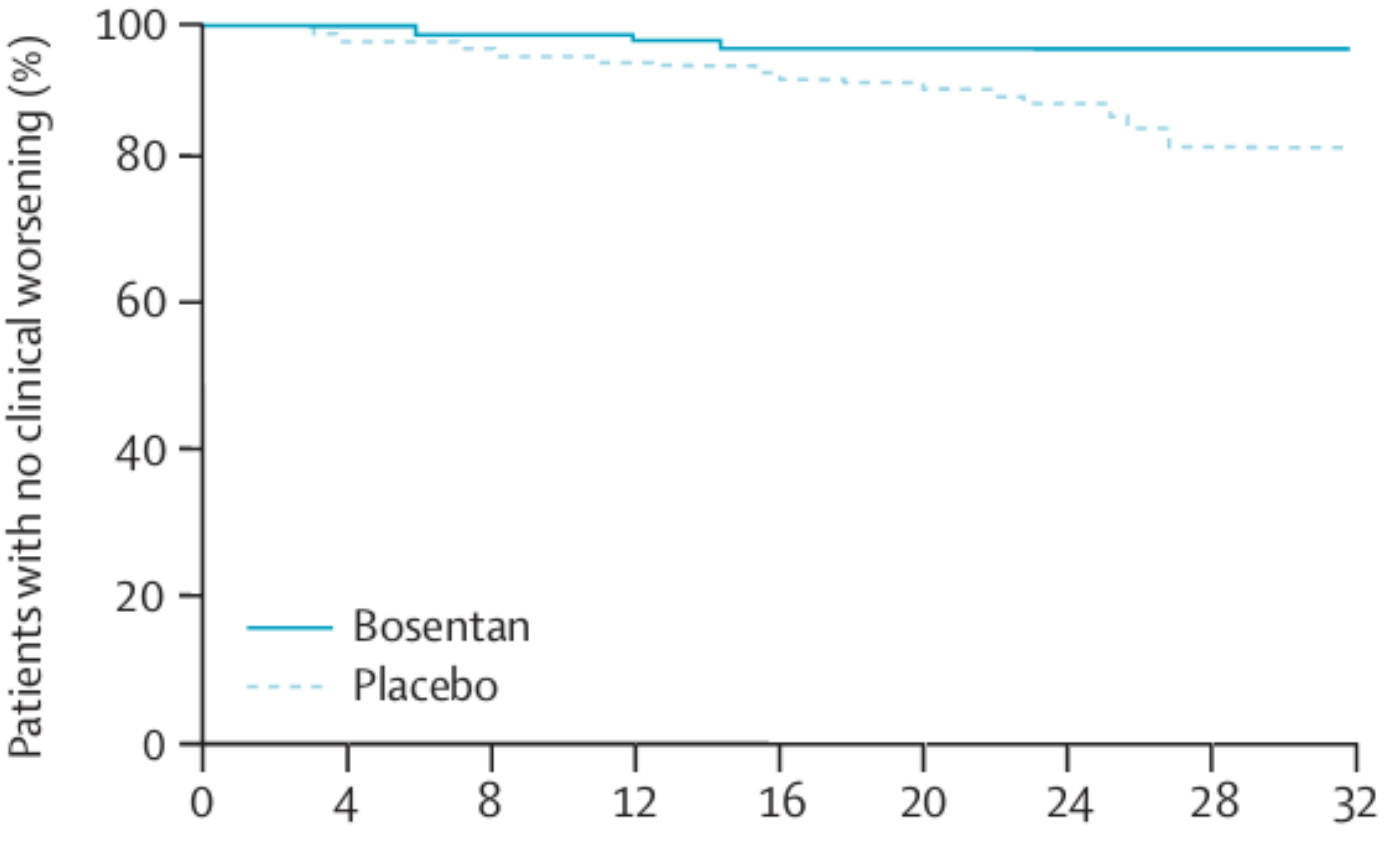
Cuándo empezar a tratar?

Table 1 Baseline clinical characteristics (n=84)

Characteristics*	ASD (n=25)	VSD and/or PDA (n=59)	Total (n=84)
Age, years	28±9	27±9	28±9
Gender (female/male; n, %)	20/5 (80)	38/21 (64)	58/26 (69)
Body surface area, m^2	1.5±0.1	1.5±0.2	1.5±0.2
Functional class			
II, n (%)	12 (48)	32 (54)	44 (52)
III, n (%)	13 (52)	20 (34)	33 (39)
IV, n (%)	0 (0)	7 (12)	7 (8)
6MWD, m	443±92	425±104	430±101
Borg dyspnoea score	3.4±2.2	3.1±2.0	3.2±1.9
Hgb, g/l	161±31	172±31	169±32
UA, μmol/l	372±88	393±109	387±103
Haemodynamic variables			
HR, bpm	81±11	82±12	82±12
mRAP, mm Hg	6±4	5±5	5±5
mPCWP, mm Hg	5±5	5±5	5±5
mSAP, mm Hg	81±11	82±10	82±10
mPAP, mm Hg	70±19	83±18†	79±19
Qpi, l/min/m^2	2.4±0.6	2.6±0.8	2.5±0.8
Qsi, l/min/m^2	2.5±0.7	3.1±1.0†	2.9±1.0
PVRi, dyn×s×cm^{-5}×m^2	2271±879	2711±1267	2580±1177
SVRi, dyn×s×cm^{-5}×m^2	2639±870	2220±784	2344±828
PVRi/F SVRi ratio	0.93±0.48	1.27±0.57	1.17±0.56
Resting SaO_2 in room air, %	89.0±3.5	85.0±5.5†	85.9±5.5

Zhang ZN et al. Heart 2011;97:1876-81

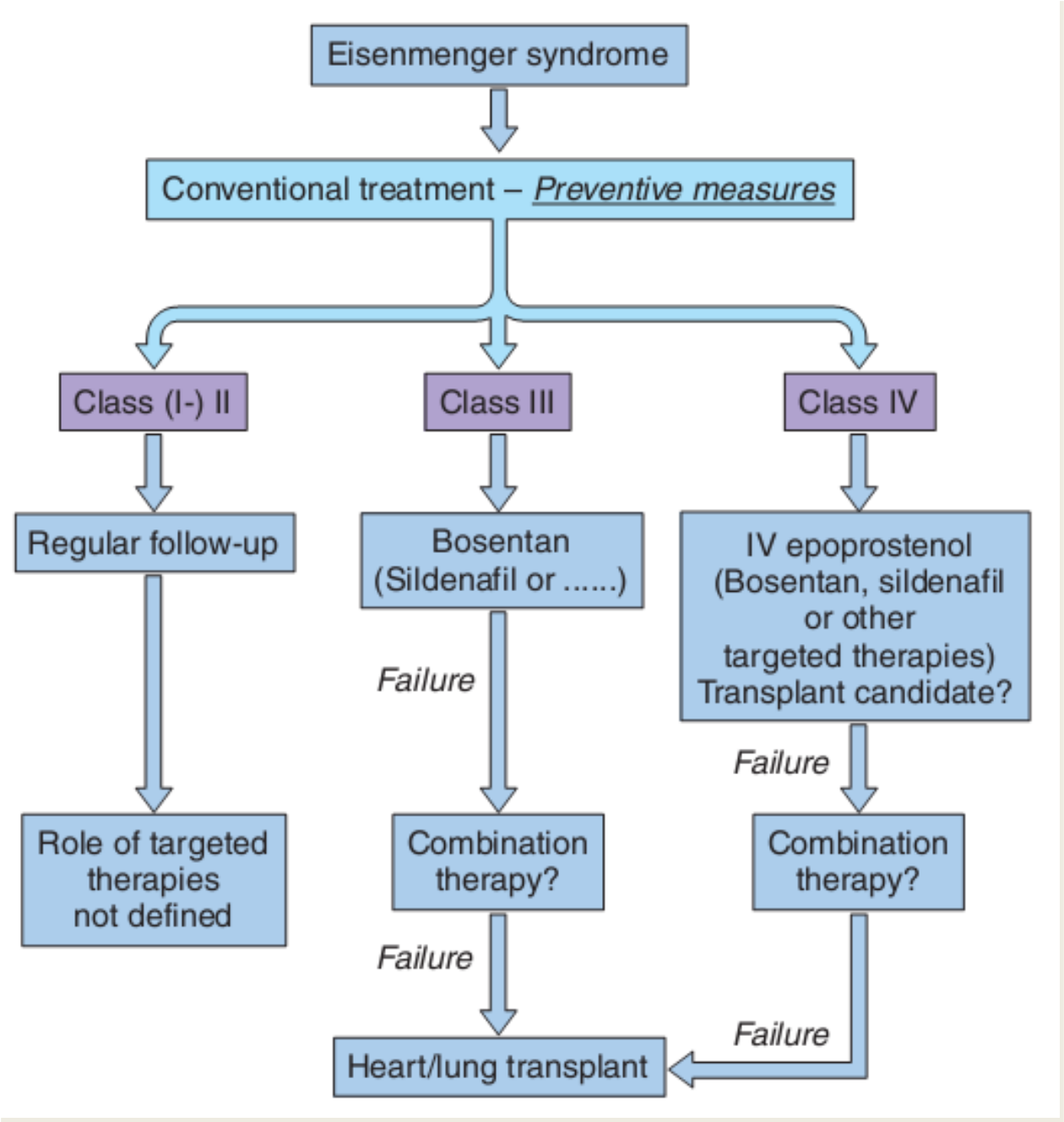
EARLY-study



Number at risk

Placebo	92	90	89	86	84	83	77	18	9
Bosentan	93	92	87	85	84	83	80	27	15

Galié et al. Lancet 2008; 371: 2093-100



Erwin Oechslin, 48. Eisenmenger Syndrome. *Diagnosis and Management of Adult Congenital Heart Disease* 2011, 358-370


GRACIAS