Inotrópicos en el peroperatorio de cirugía cardiovascular , su uso basado en la evidencia

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DEPARTAMENTO DE CARDIOLOGIA

CATEDRA DE FISIOLOGÍA

Universidad Abierta Interamericana

5 preguntas

Algunas reflexiones…

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¿Qué pasa con los Materiales y métodos de la bibliografía publicada?

1

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QUE PARAMETRO TOMA LA EVIDENCIA PUBLICADA

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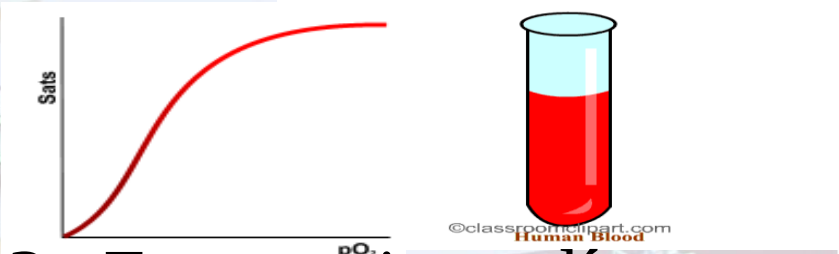
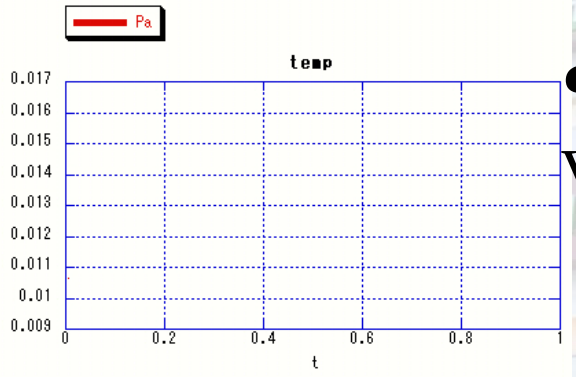
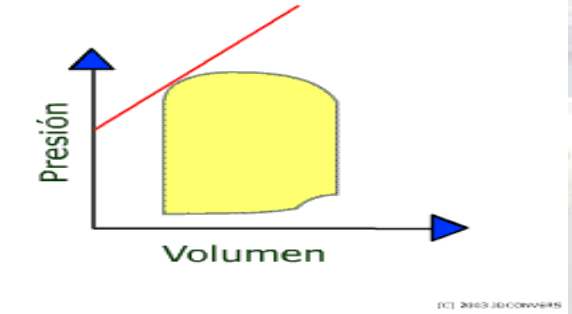
DO2: Gasto cardíaco x (SatO x Hbx 1.34)

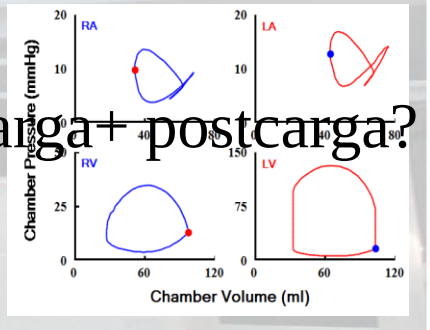




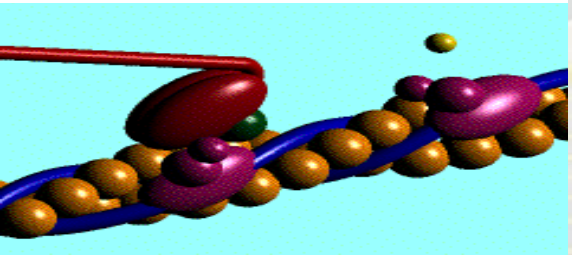
¿Gasto cardíaco? : Frecuencia cardíaca x volumen sistólico



¿Volumen sistólico? → ¿Precarga+ postcarga?



¿Contractilidad o inotropismo?



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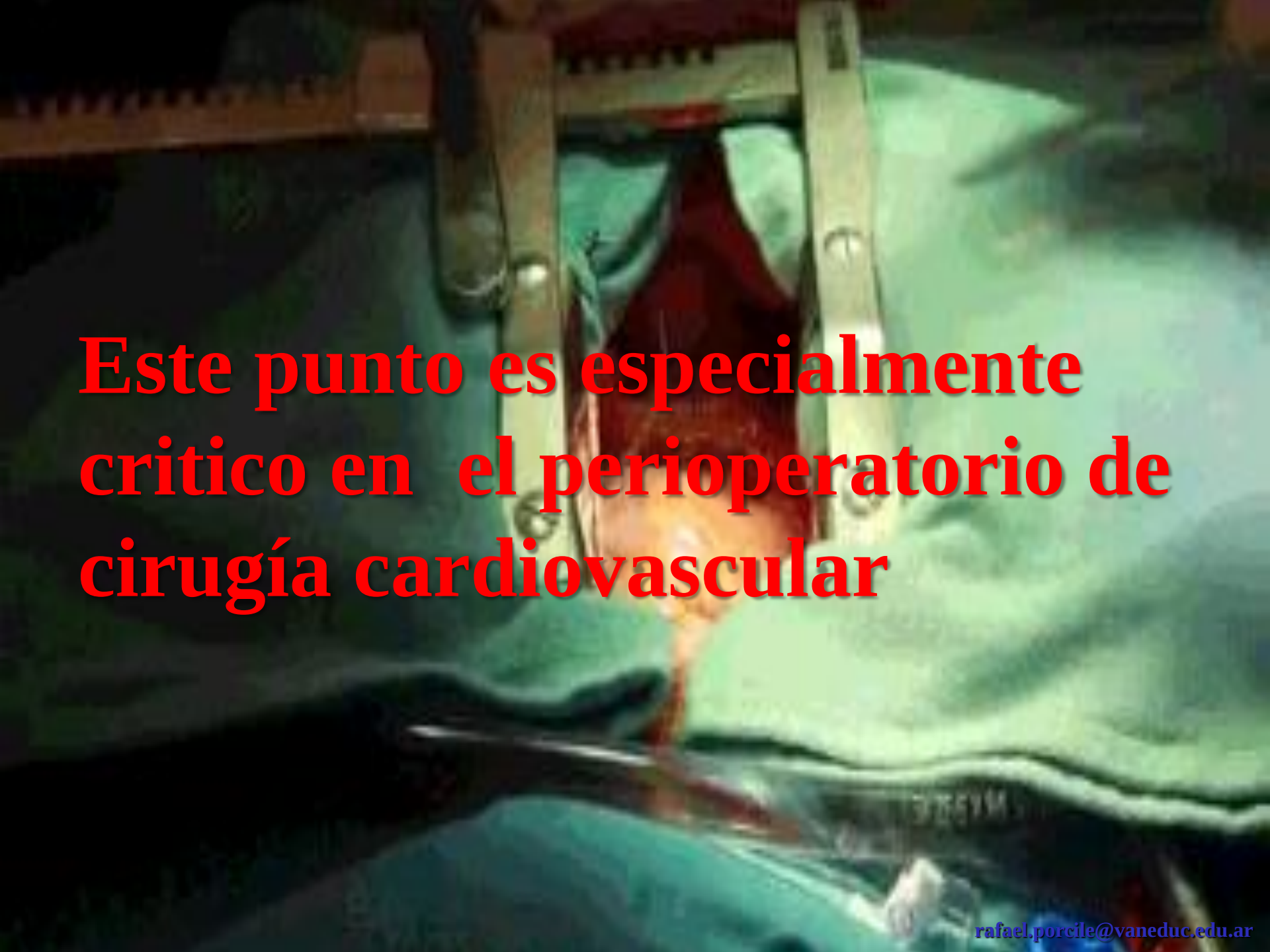

Este punto es especialmente critico en el perioperatorio de cirugía cardiovascular

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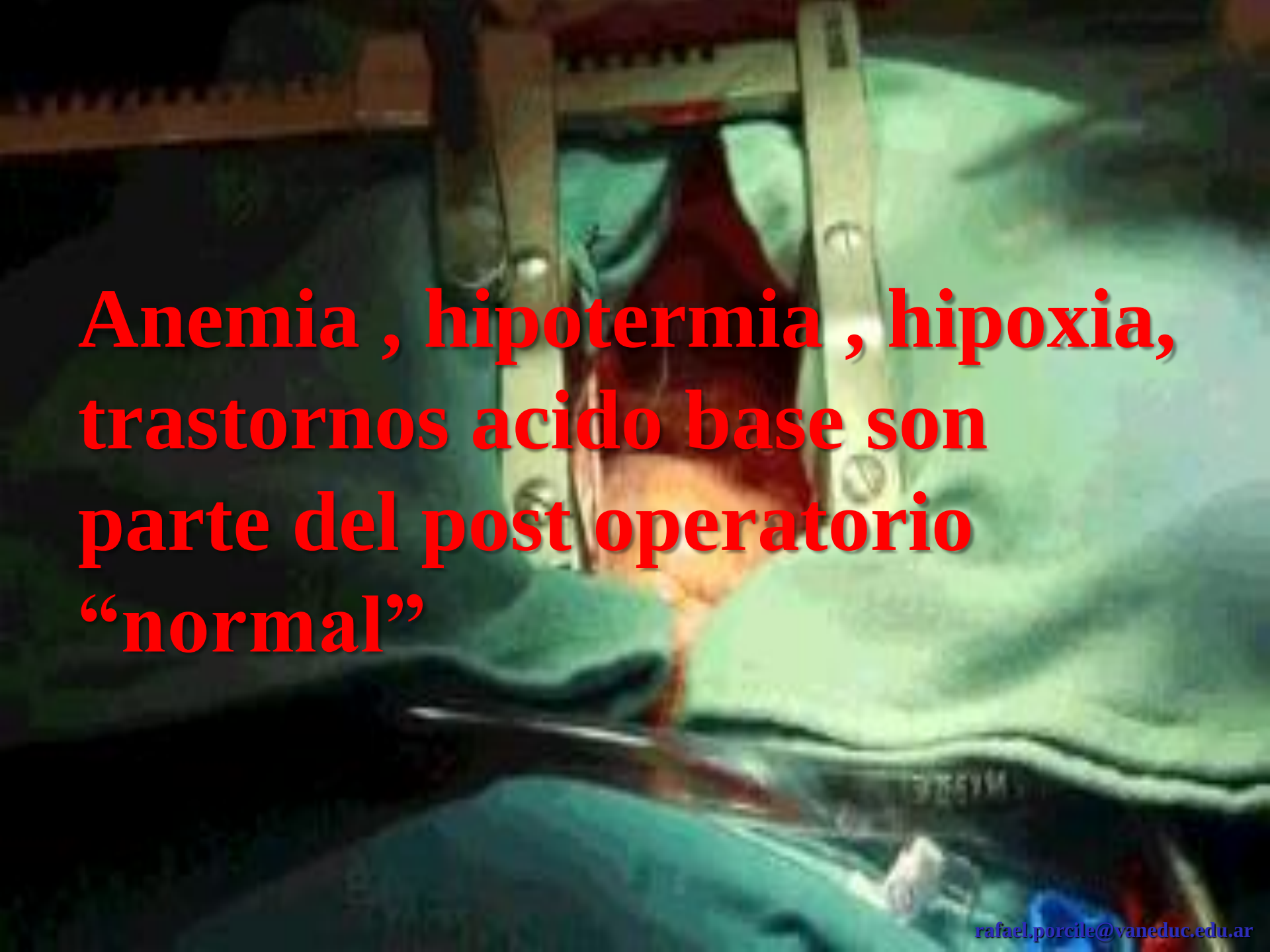

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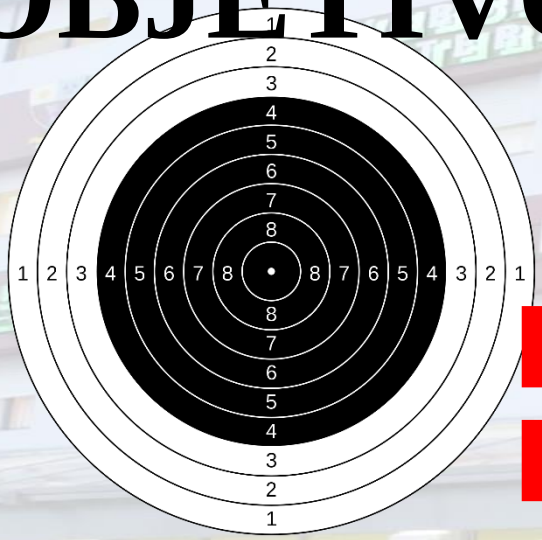
DO2:Gasto cardíaco x (SatO x Hbx 1.34)

Contenido arterial de oxigeno

OBJETIVO



≠

HERRAMIENTA

¿Contractilidad o inotropismo?

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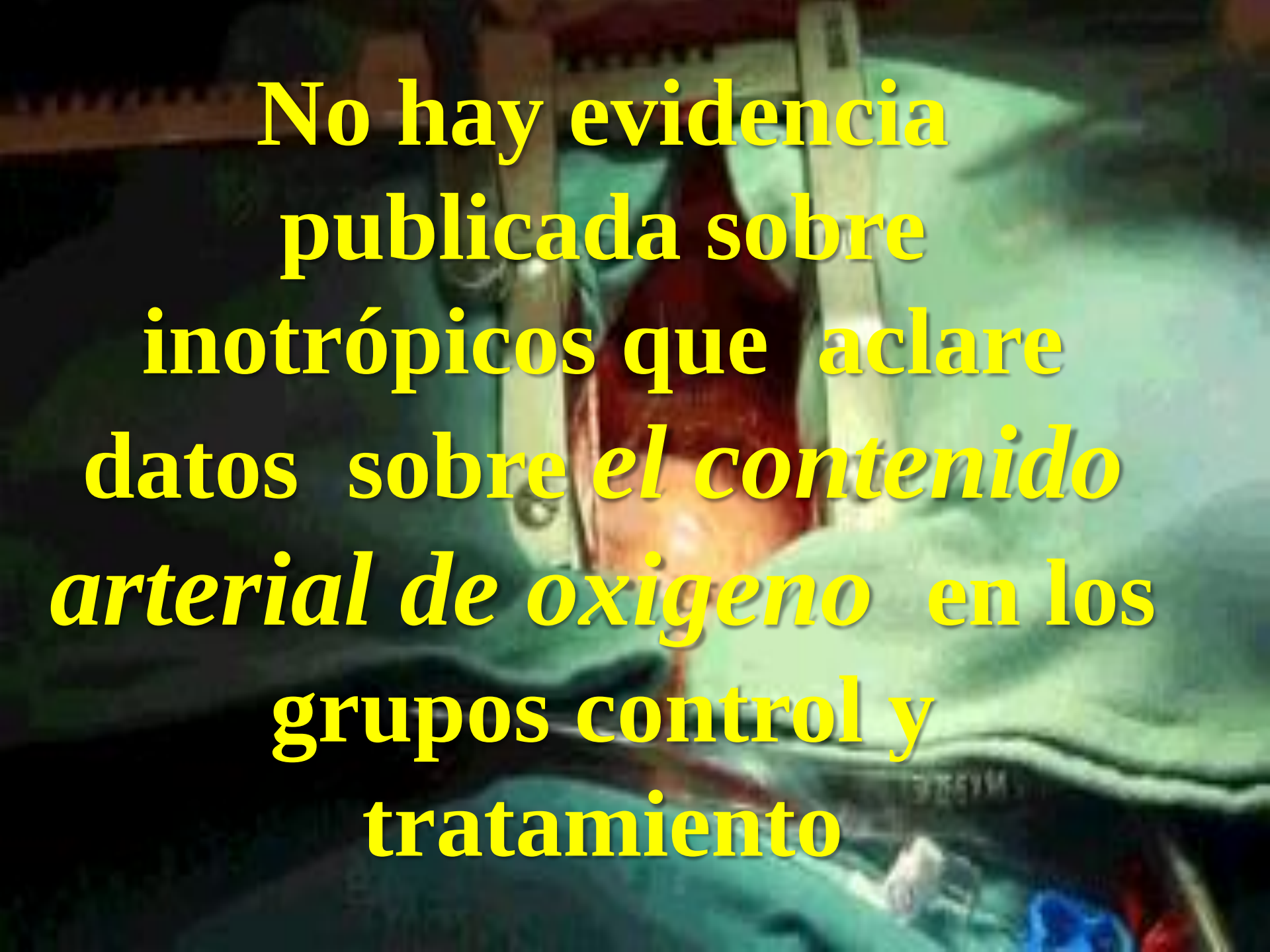
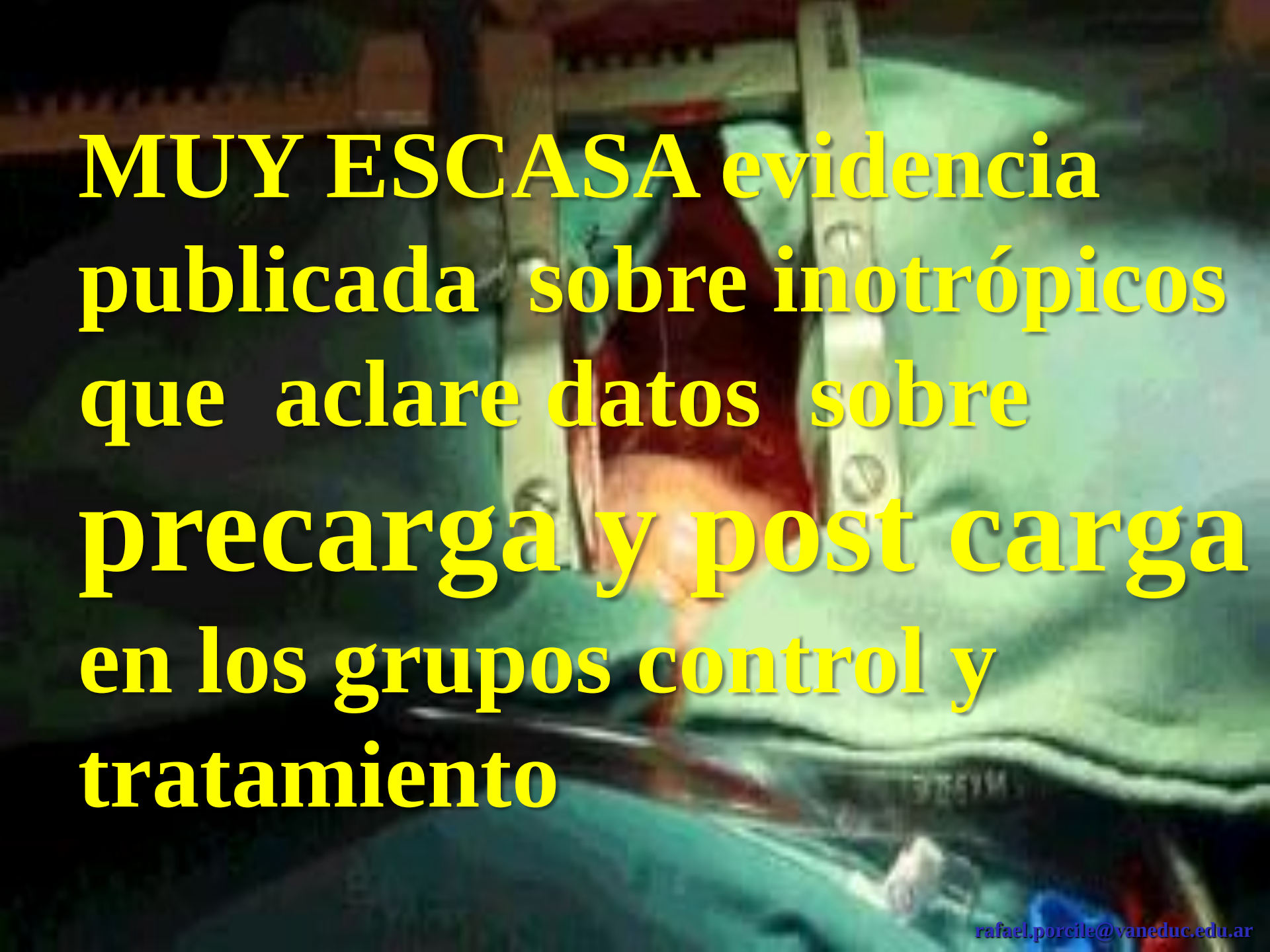

No hay evidencia publicada sobre inotrópicos que aclare datos sobre *el contenido arterial de oxigeno* en los grupos control y tratamiento



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¿Bajo gasto es sinónimo de fármacos inotrópicos?

2

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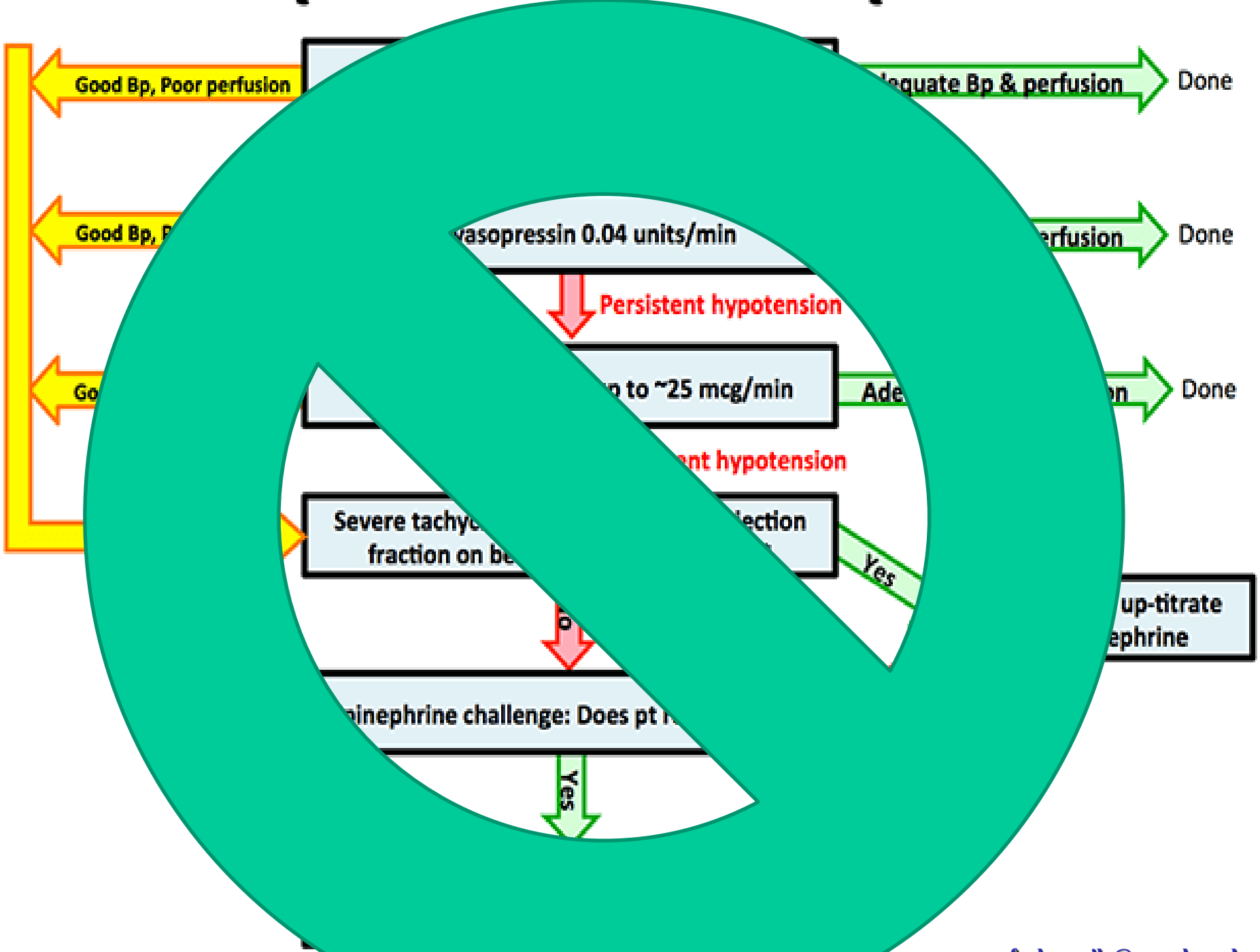

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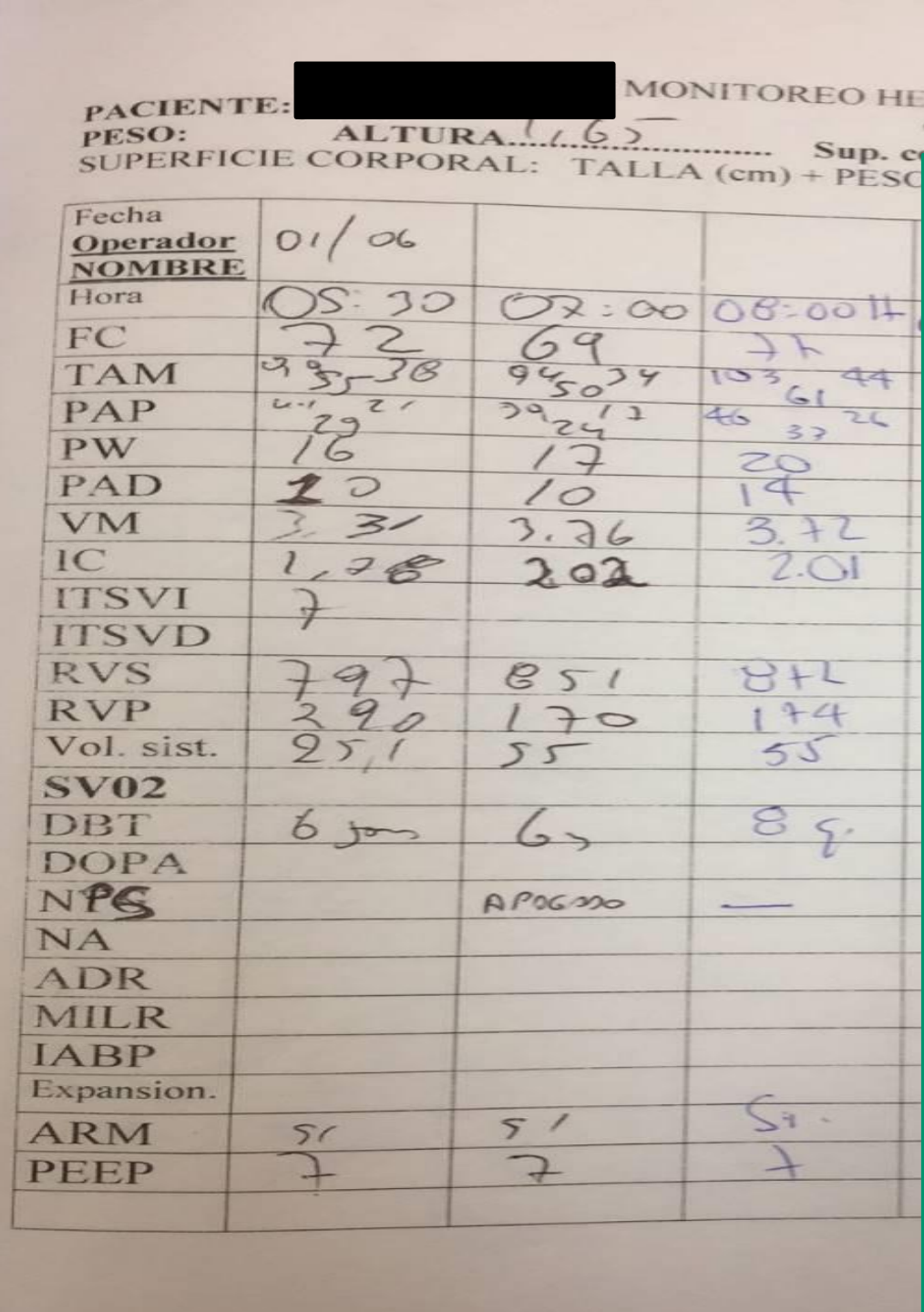

PACIENTE: [redacted] MONITOREO HEMODINAMICO
PESO: ALTURA: 1.63 CAMA:
SUPERFICIE CORPORAL: TALLA (cm) + PESO

75 kg.

Fecha / Operador / NOMBRE	01/06		
Hora	05:30	07:00	08:00
FC	72	69	71
TAM	93 55 38	94 50 34	103 61 44
PAP	41 29 21	39 24 17	46 33 26
PW	16	17	20
PAD	10	10	14
VM	3.31	3.76	3.72
IC	1,78	2.02	2.01
ITSVI	7		
ITSVD			
RVS	797	851	842
RVP	390	170	174
Vol. sist.	25,1	55	55
SV02			
DBT	6	6	8
DOPA			
NPS		APOYO	—
NA			
ADR			
MILR			
IABP			
Expansion.			
ARM	SI	SI	SI
PEEP	7	7	7

Entre las 5:30 y 0800 AM expansión e inotrópicos

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PACIENTE: [redacted] MONITOREO H

PESO: ALTURA 1.63 Sup.

SUPERFICIE CORPORAL: TALLA (cm) + PES

Fecha / Operador / NOMBRE	01/06		
Hora	05:30	07:00	08:00
FC	72	69	71
TAM	93 55 38	94 50 34	103 61 44
PAP	41 29 21	39 24 17	46 33 26
PW	16	17	20
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IC	1,78	2.02	2.01
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RVS	797	851	872
RVP	390	170	174
Vol. sist.	25,1	55	55
SV02			
DBT	6	6	8
DOPA			
NPS		APOGEO	—
NA			
ADR			
MILR			
IABP			
Expansion.			
ARM	SI	SI	SI
PEEP	7	7	7

0830 AM

Insuficiencia aortica severa

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Cambiemos de planes

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75 Kg.

PACIENTE: [redacted] MONITOREO HEMODINAMICO

PESO: ALTURA 1.65 CAMA:

SUPERFICIE CORPORAL: TALLA (cm) + PESO (kg) − 60 = 65 Sup. corporal .....

Fecha / Operador / NOMBRE	01/06						
Hora	05:30	07:00	08:00 Hs	09:25 hs.	10:00 Hs.	11:00 Hs	13:25 Hs
FC	72	69	74	109	83	93	75
TAM	49 35 38	94 50 74	103 61 44	142 48 79	110 60 41	134 68 43	119 56 32
PAP	41 29 21	39 24 17	46 33 26	41 26 31	36 26 20	42 30 24	34 21
PW	16	17	20	16	14	20	16
PAD	10	10	14	7	7	7	8.
VM	3.31	3.76	3.72	6,9	5,4	5,46	6,91
IC	1,78	2.02	2.01	3,86.	2.9	2,77	3.75
ITSVI	7						
ITSVD							
RVS	797	851	872	789	964	882	680
RVP	390	170	174	137	200	207	190
Vol. sist.	25,1	55	55			53	72
SV02							
DBT	6 hs	6 hs	8 hs.	6 hs.	4 hs	4 hs.	4
DOPA							
NPS		APOGEO	—	3ml	3ml	3ml.	4
NA							
ADR							
MILR							
IABP							
Expansion.							
ARM	SI	SI	SI.	SI	SI	SI	SI
PEEP	7	7	7	4.	4	4.	4.

1ml Kg/Hs

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El Dogma :

Deterioro inotrópico = inotrópicos

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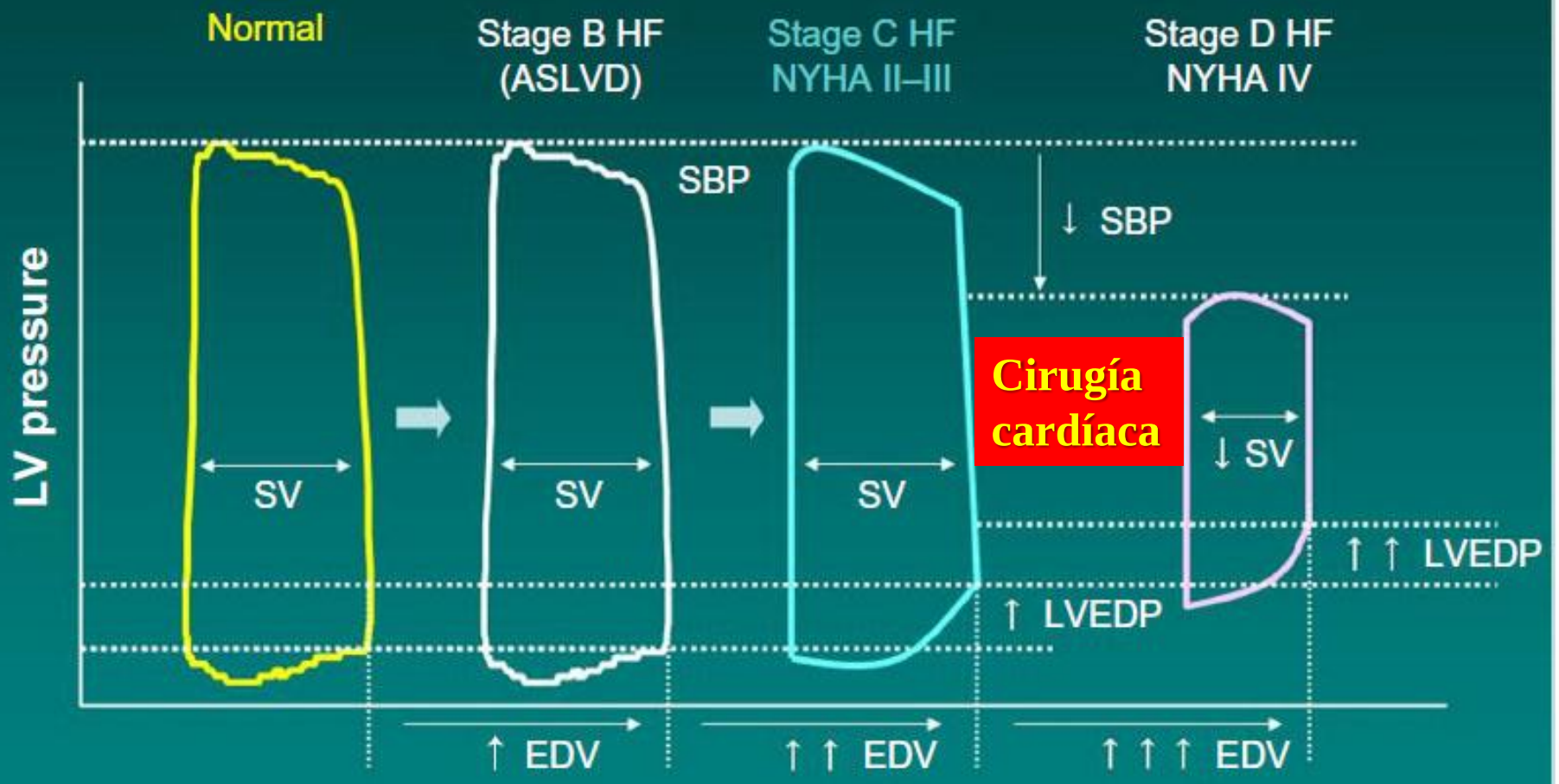
Hemodynamic derangements in HFrEF: a progression



Borlaug BA, unpublished

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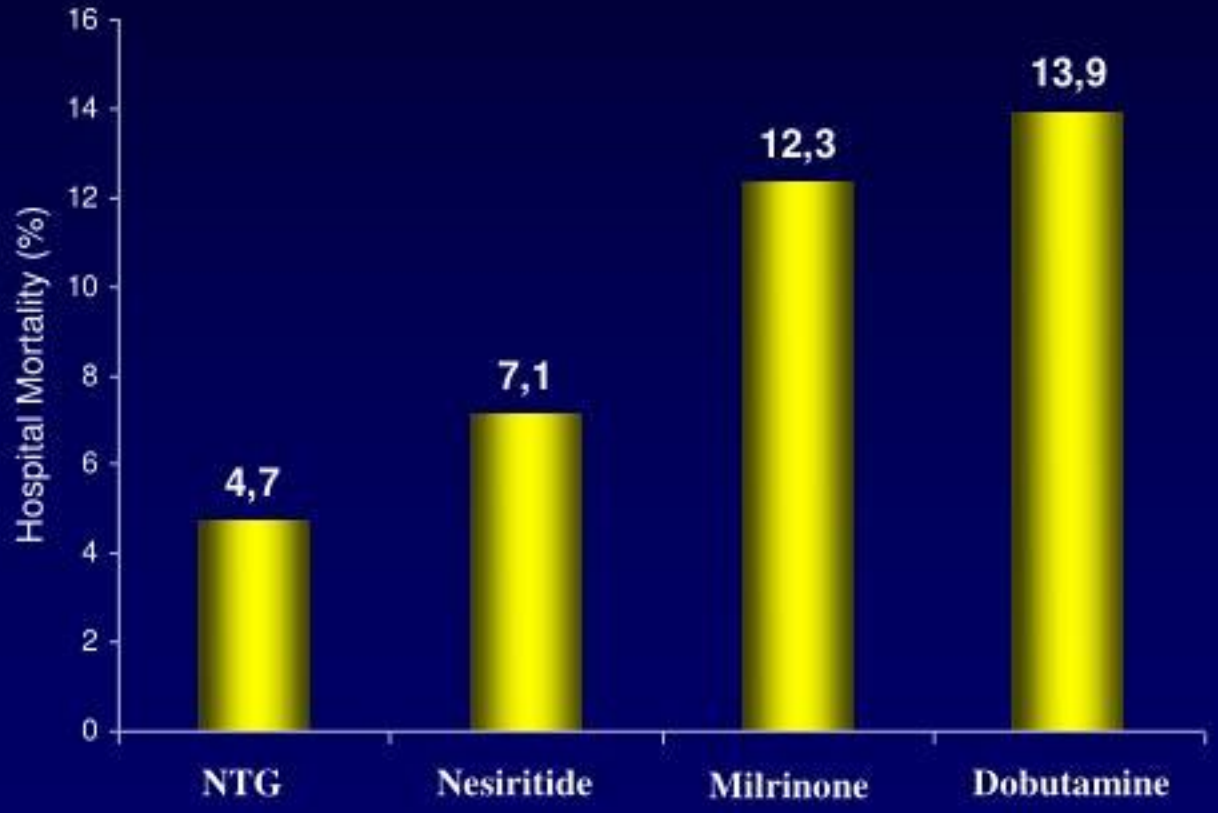
ADHERE registry: Inotropic agents and mortality in acute heart failure

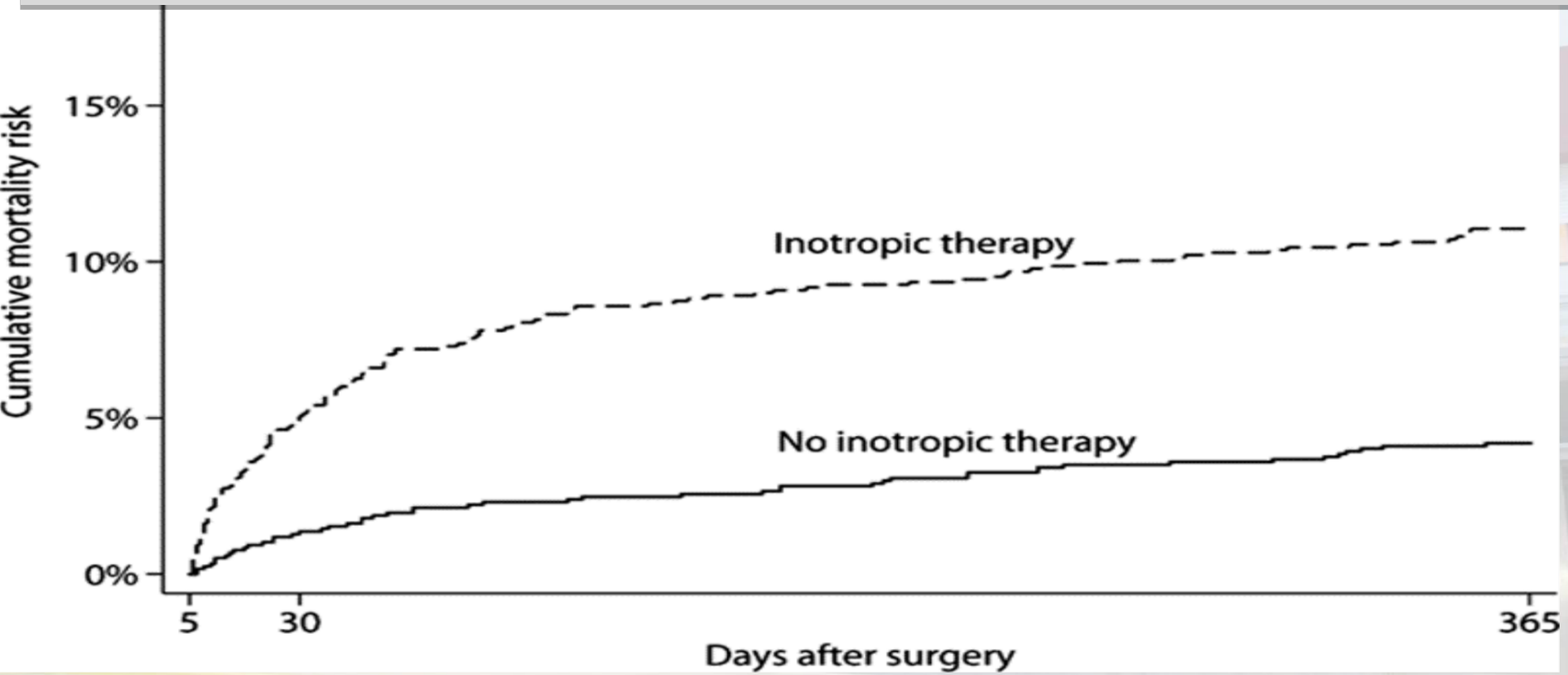


Abraham WT, et al. JACC 2005;46(1):57–64.

ANESTHESIOLOGY
The Journal of the American Society of Anesthesiologists, Inc.

Health Outcomes with and without Use of Inotropic Therapy in Cardiac Surgery:Results of a Propensity Score–matched Analysis

Anesthesiology. 2014;120(5):1098-1108. doi:10.1097/ALN.0000000000000224



Cumulative 1-yr mortality risk by treatment status. Log-rank P value <0.00001.

Figure Legend:

ANESTHESIOLOGY
The Journal of the American Society of Anesthesiologists, Inc.

From: Health Outcomes with and without Use of Inotropic Therapy in Cardiac Surgery:Results of a Propensity Score–matched Analysis

Anesthesiology. 2014;120(5):1098-1108. doi:10.1097/ALN.0000000000000224

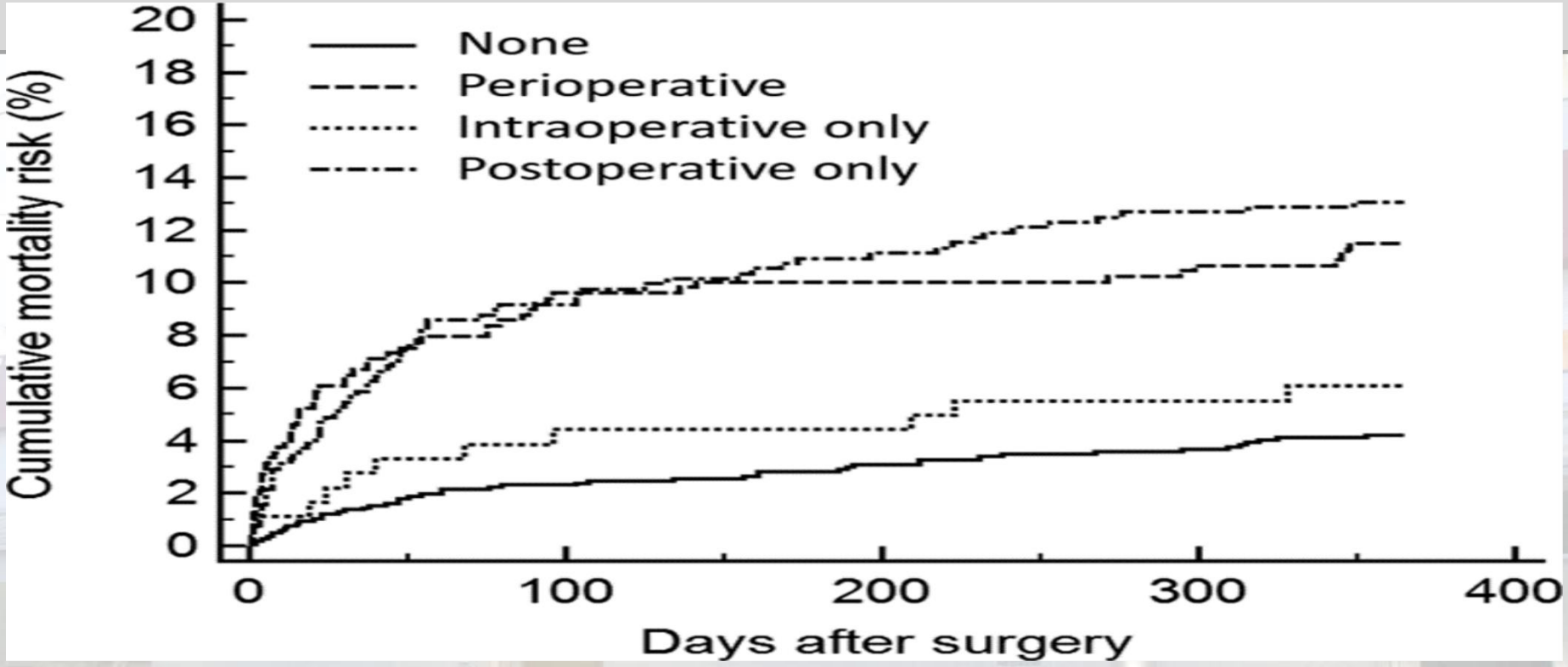
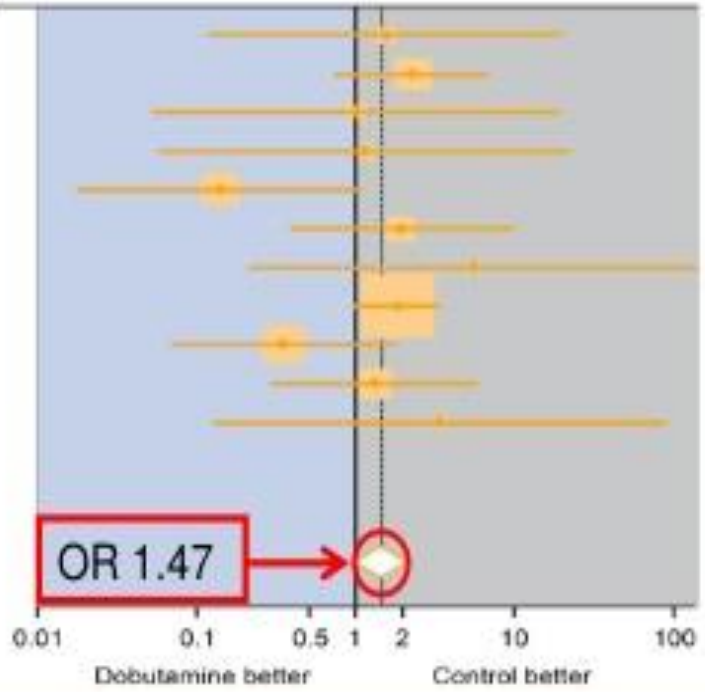


Figure Legend:

Cumultative 1-yr mortality risk stratified by timing of inotropic therapy. Log-rank P value <0.0001.

Effect of dobutamine on mortality in heart failure (vs. placebo or standard care)

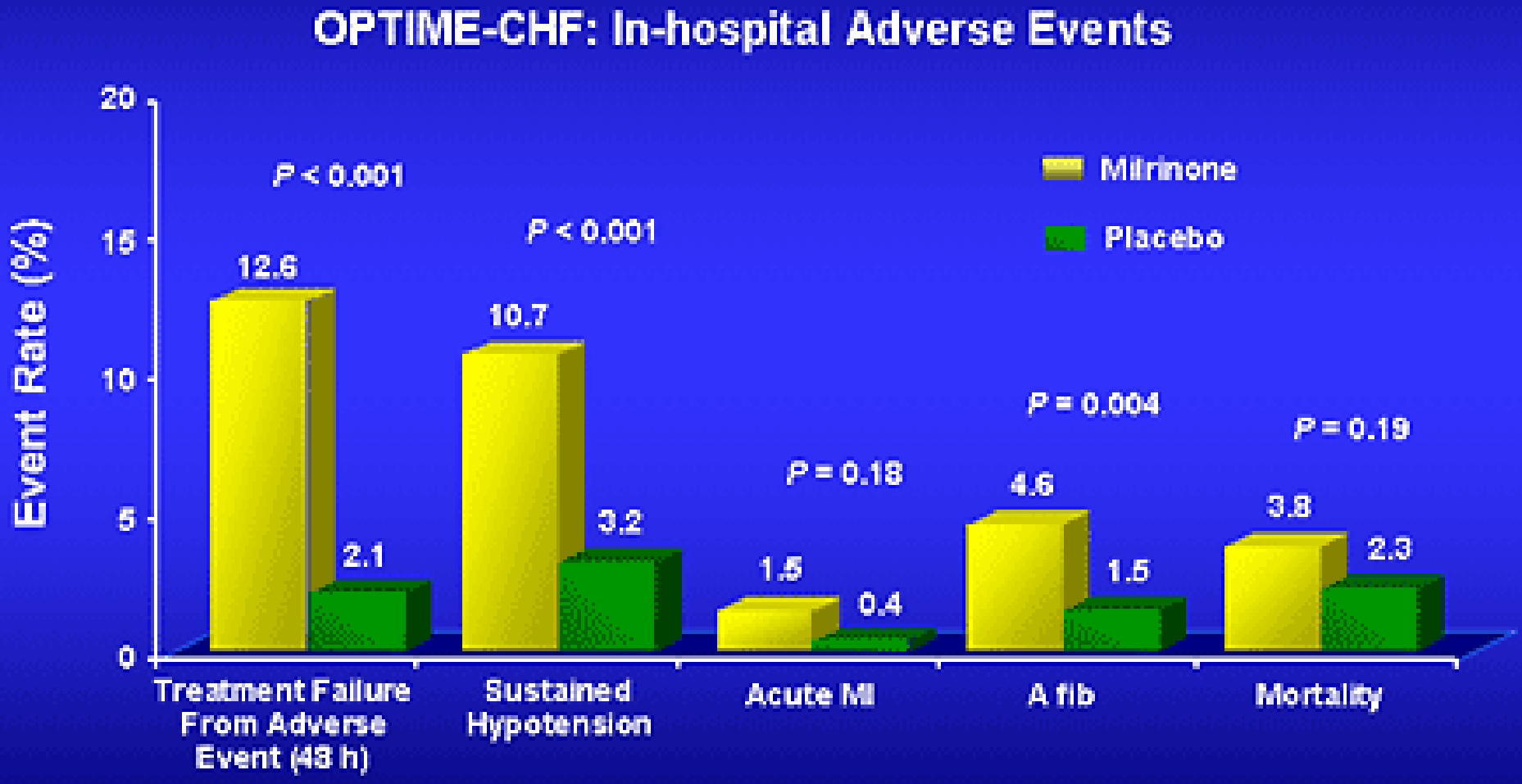
Study	OR (95% CI)	Events: Dobutamine	Events: Control	% Weight
Leier 1982	1.54 (0.12, 19.47)	2/15	1/11	2.58
Dies 1986	2.27 (0.75, 6.89)	13/31	7/29	10.83
Eriemeier 1992	1.00 (0.05, 1.57)	1/10	1/10	2.32
Ellis 1998	1.12 (0.06, 21.09)	9/10	8/9	2.17
Sindone 1998	0.14 (0.02, 1.06)	2/26	3/8	10.92
Oliva 1999	1.90 (0.38, 9.44)	5/19	3/19	5.70
Nieminen 2000	5.62 (0.22, 144.46)	1/20	0/36	0.87
CASINO 2004	1.84 (1.02, 3.32)	42/100	28/99	42.10
Nanas 2004	0.35 (0.07, 1.76)	9/16	11/14	13.24
Adamopoulos 2006	1.32 (0.31, 5.71)	5/23	4/23	8.07
Bader 2010	3.35 (0.13, 84.53)	1/43	0/47	1.19
Liang 1864	–	0/8	0/7	0.00
Wimmer 1999	–	0/10	0/10	0.00
Overall I^2=4.5%, p=0.401	**1.47 (0.98, 2.21)**	**90/331**	**66/322**	**100.00**



There are strong indications from this meta-analysis that dobutamine worsens outcomes in patients with severe heart failure

Tacon et al. (2011) *Intensive Care Med.* **38:***359-367*

IV Milrinone During Hospitalization for Decompensated HF—Not Low Output

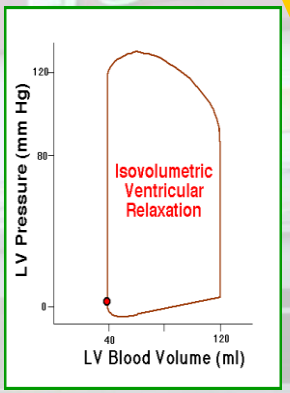


Cuffe MS et al. *JAMA*.2002;287:1541

Inotropismo

D/P D/T

Ley de starling y
Ley de Laplace



Lusitropismo

Precarga y post carga

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Reflexión

Mas vale una estrategia inotrópica que un inotrópico…

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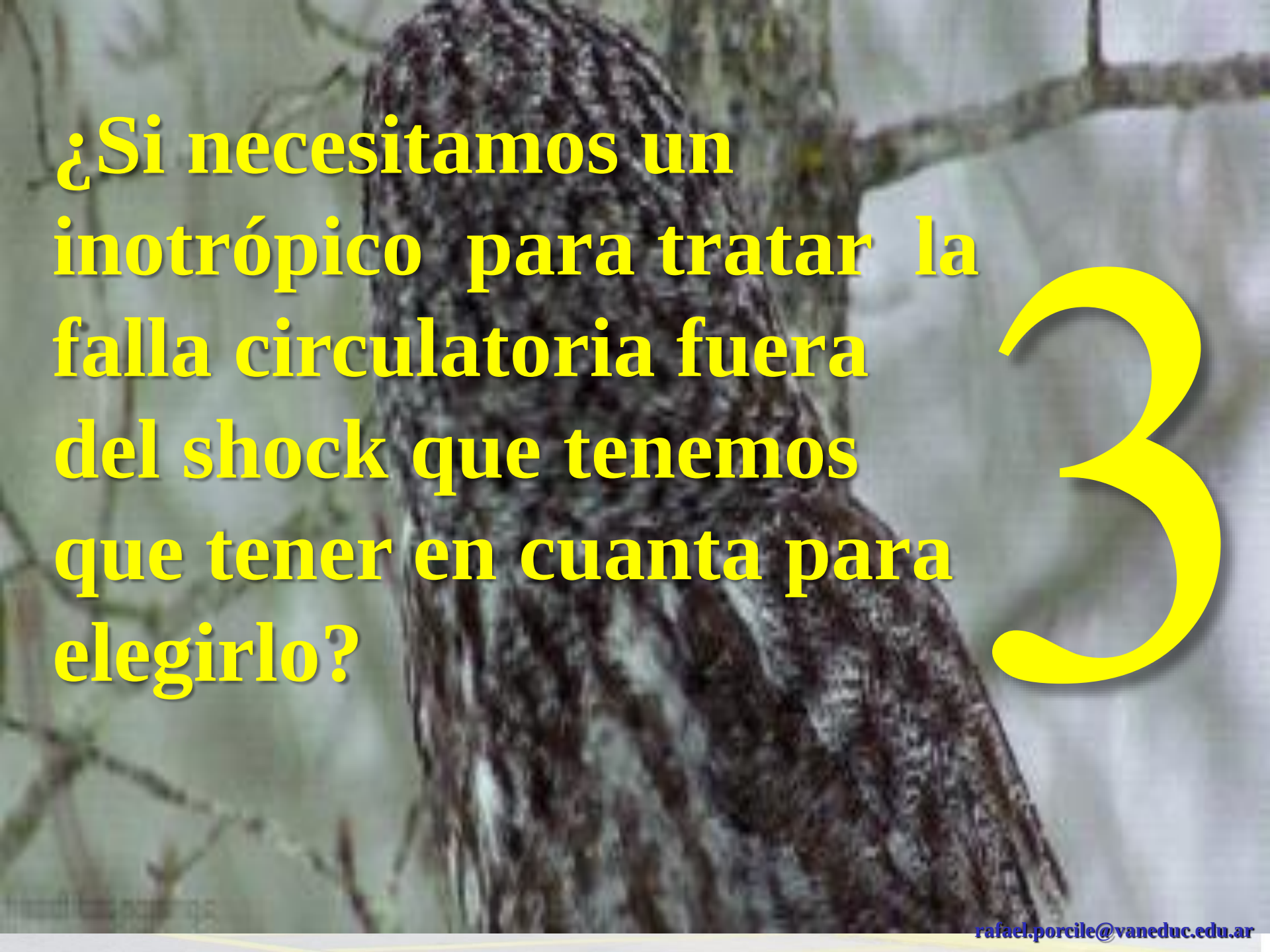

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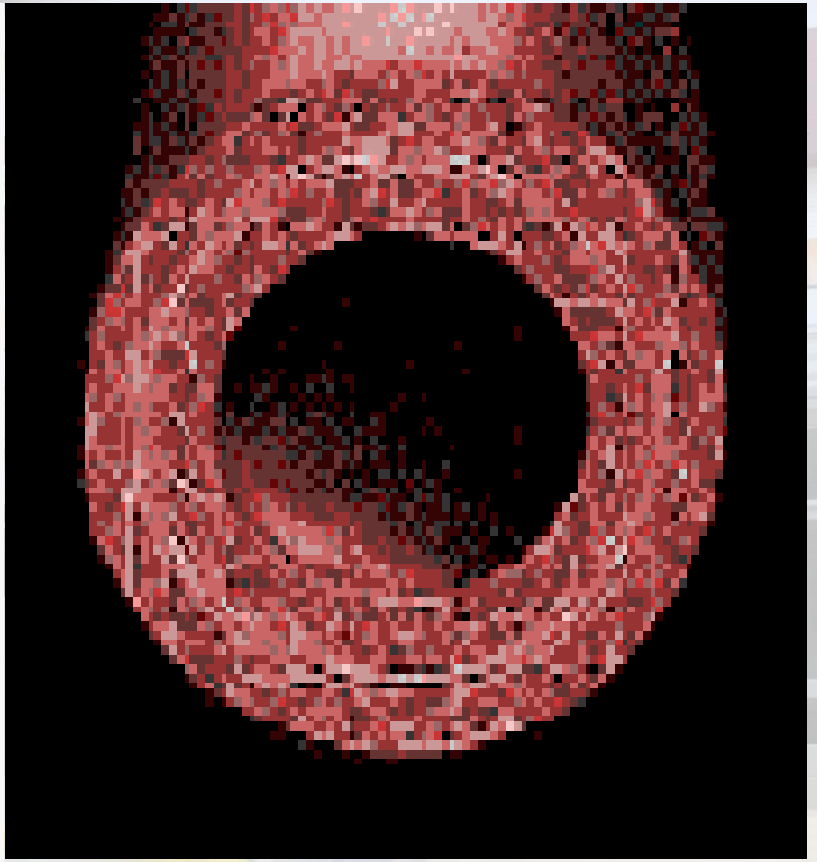
Hay dos universos con los cuales tenemos que negociar



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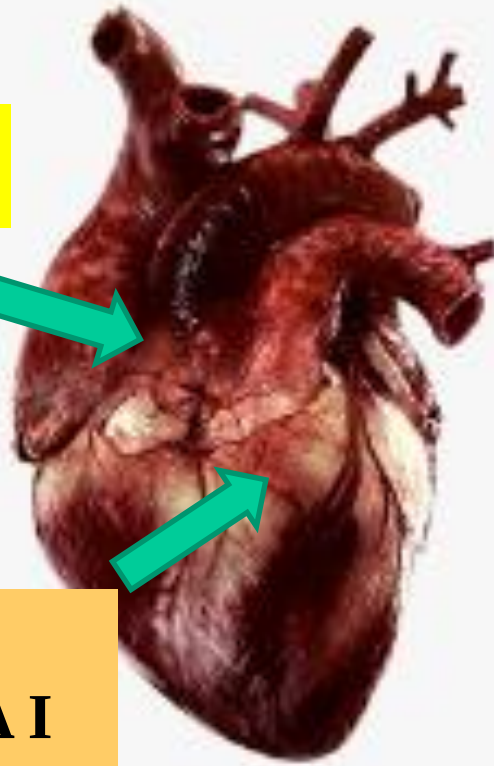
Fosfodiesterasa

Calcio



α

β_1

AMP c

Fosforilación TROPONINA I CARDÍACA

PROTEIN KINASA **A**

RhoKinasa

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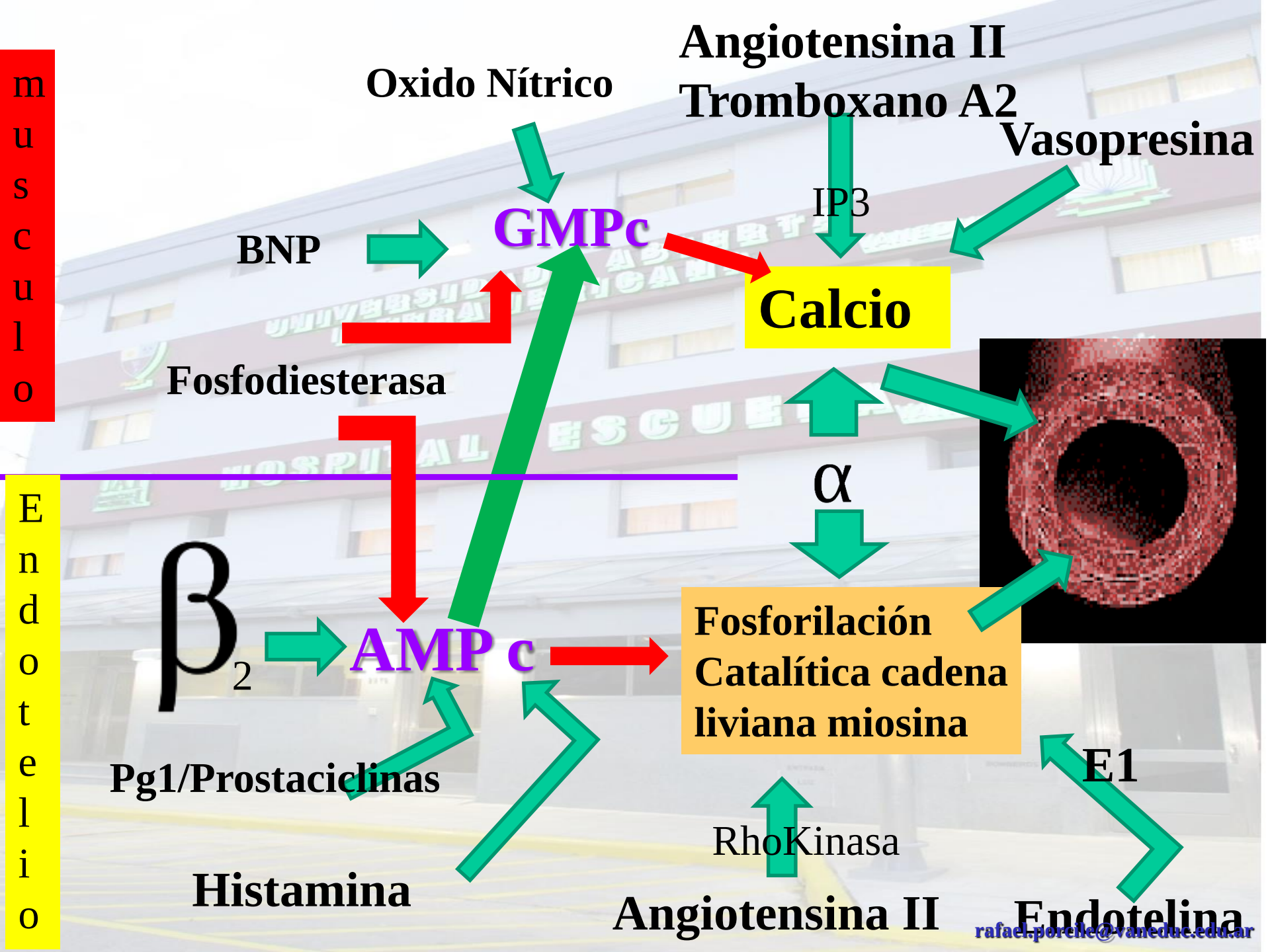
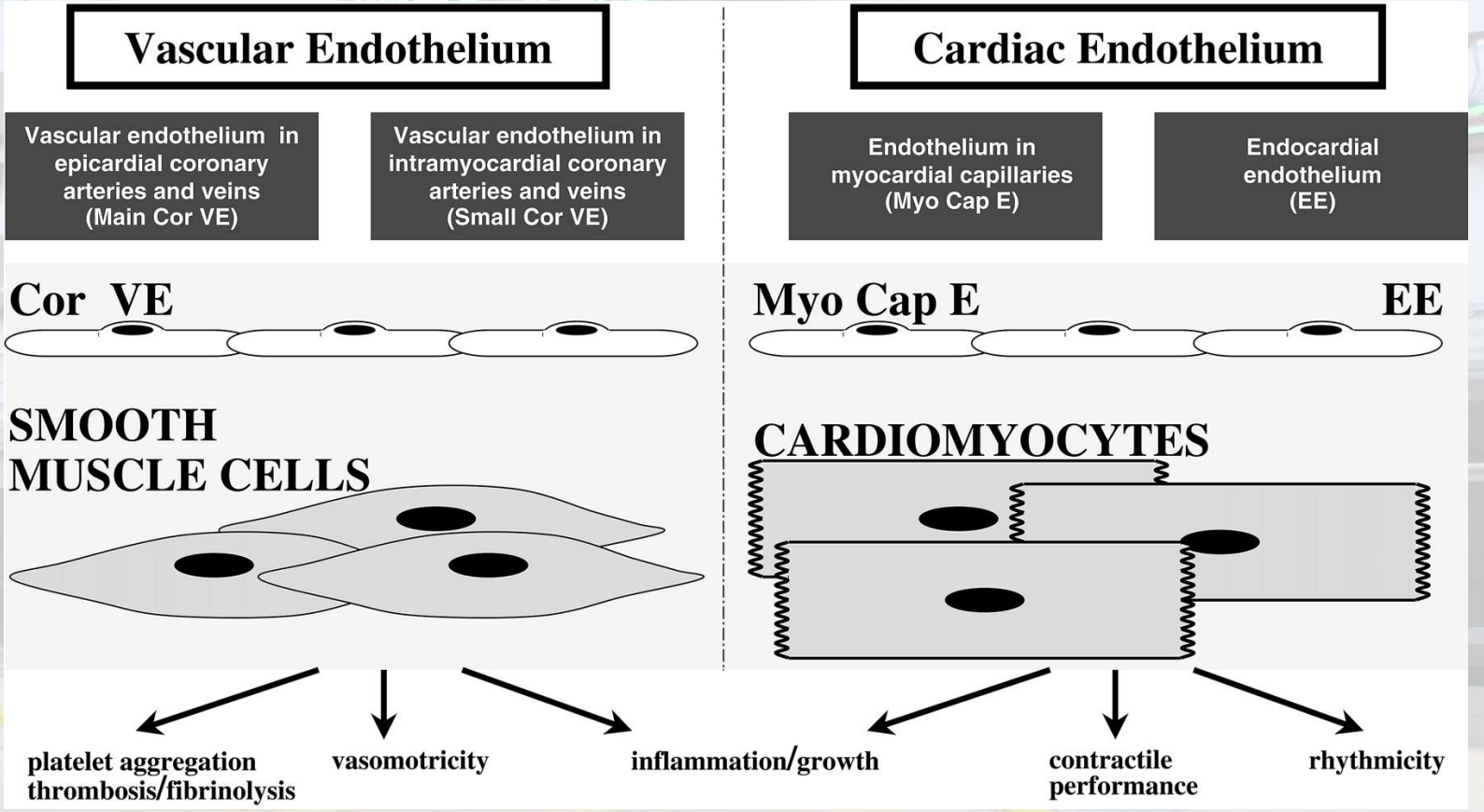


LOS MISMOS MENSAJEROS PUEDEN TENER EFECTOS DIFERENTES EN AMBOS CASOS



El inotrópico ideal

- No incrementa la post carga
- No es batmotropico positivo al incrementar los cationes intracelulares
- Mantiene una relación equilibrada consumo de oxigeno /inotropismo

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•Drogas Inotrópicas y vaso activas

- **Inodilatadores**
  - –Dobutamina
  - –Isoproterenol
  - –Inhibidores de la fosfodiesterasa
  - –Levosimendan

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DOBUTAMINA

Calcio

β_1

AMP c

PROTEIN KINASA A

Fosforilación TROPONINA I CARDÍACA

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Isoproterenol

Dopexamine

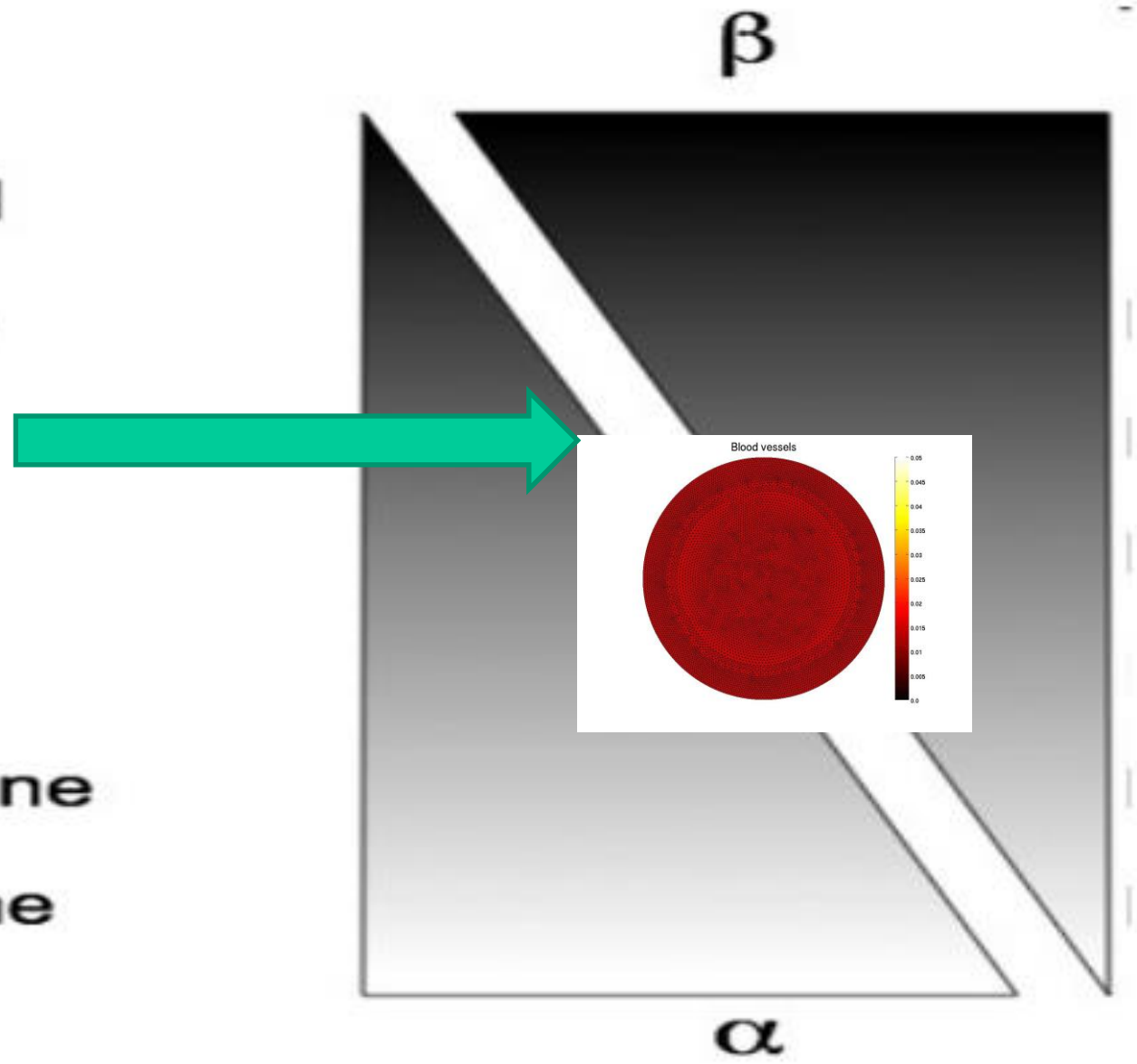
Dobutamine

Dopamine

Epinephrine

Norepinephrine

Phenylephrine



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Milrinone

Calcio

β 1

AMP c

PROTEIN KINASA **A**

Fosforilación TROPONINA I CARDÍACA

RhoKinasa

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BNP

GMPc

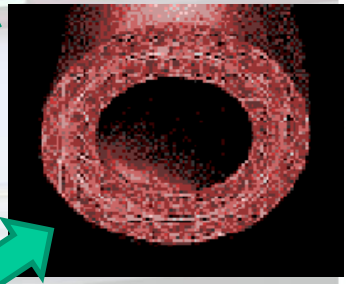
Calcio

Fosfodiesterasa

Milrinone

Fosfodiesterasa

α



AMP c

Fosforilación Catalítica cadena liviana miosina

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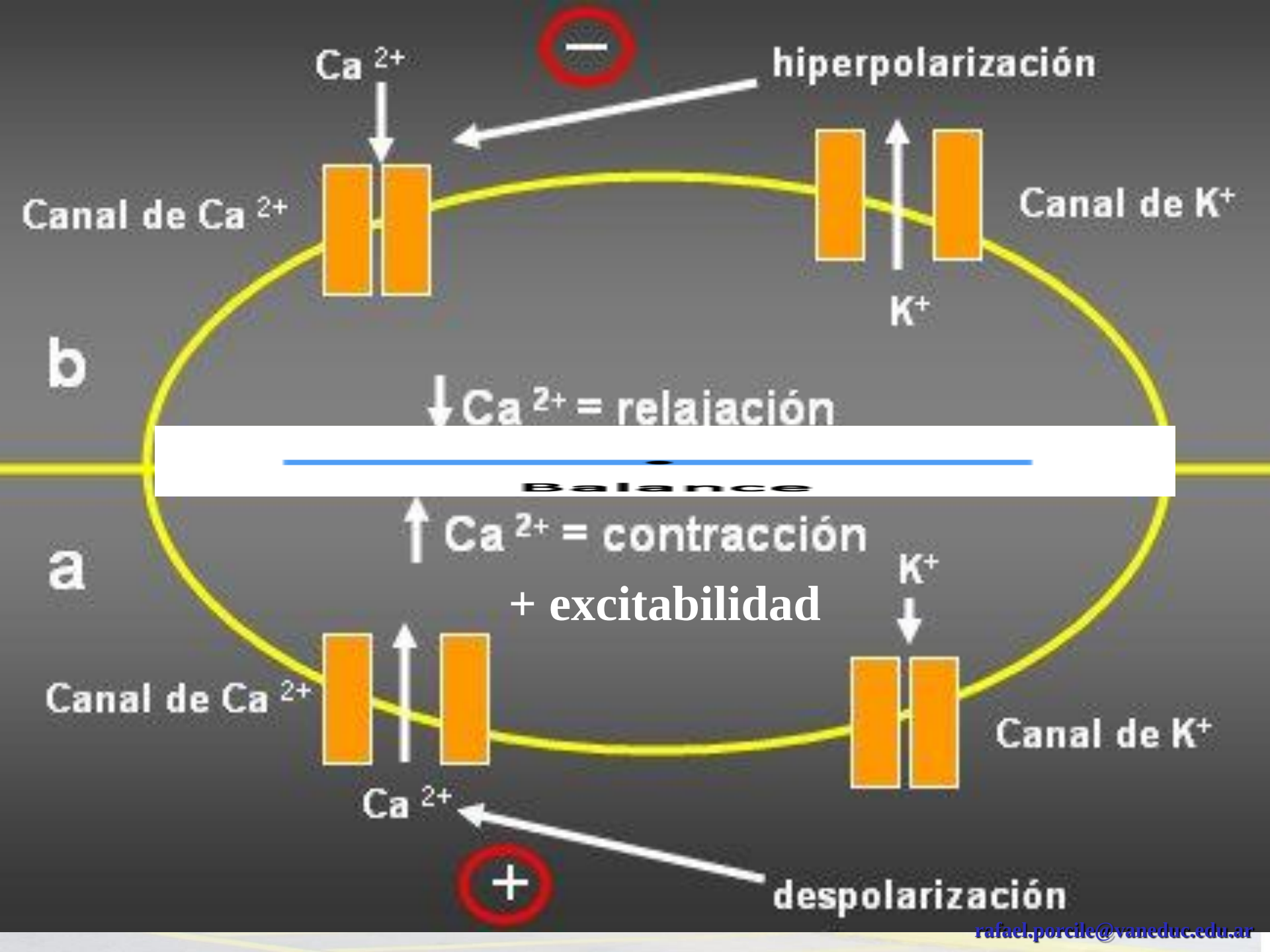

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•Drogas Inotrópicas y vaso activas

- **Inodilatadores**
  - –Dobutamina
  - –Isoproterenol
  - –Inhibidores de la fosfodiesterasa
  - –Dopexamina
  - –Levosimendan

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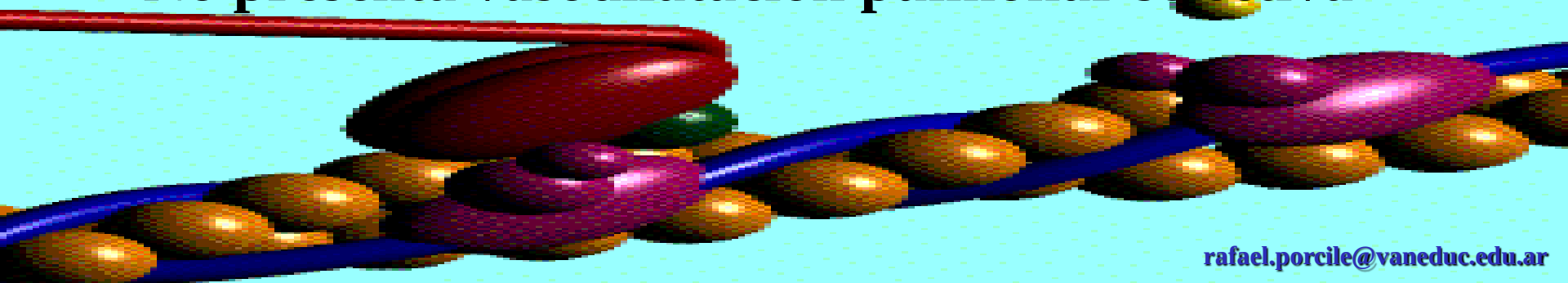
Inotrópicos-Calcio sensibilizantes

- **Levosimendan**
  - **Cambio conformacional en troponina C que aumenta la sensibilidad de la miofibrilla al Calcio circulante**
  - **Acción adicional sobre canales de potasio ATP dependientes en musculo liso**
  - **Inodilatador**
  - **No arritmogénico**
  - **Efecto prolongado por sus metabolitos activos (OR 1896) con vida media de 80 hs y actividad hasta por 2 semanas**
  - **No presenta vasodilatación pulmonar selectiva**



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¿Cómo nos fue con casi 10 años de levosimendan ?

4

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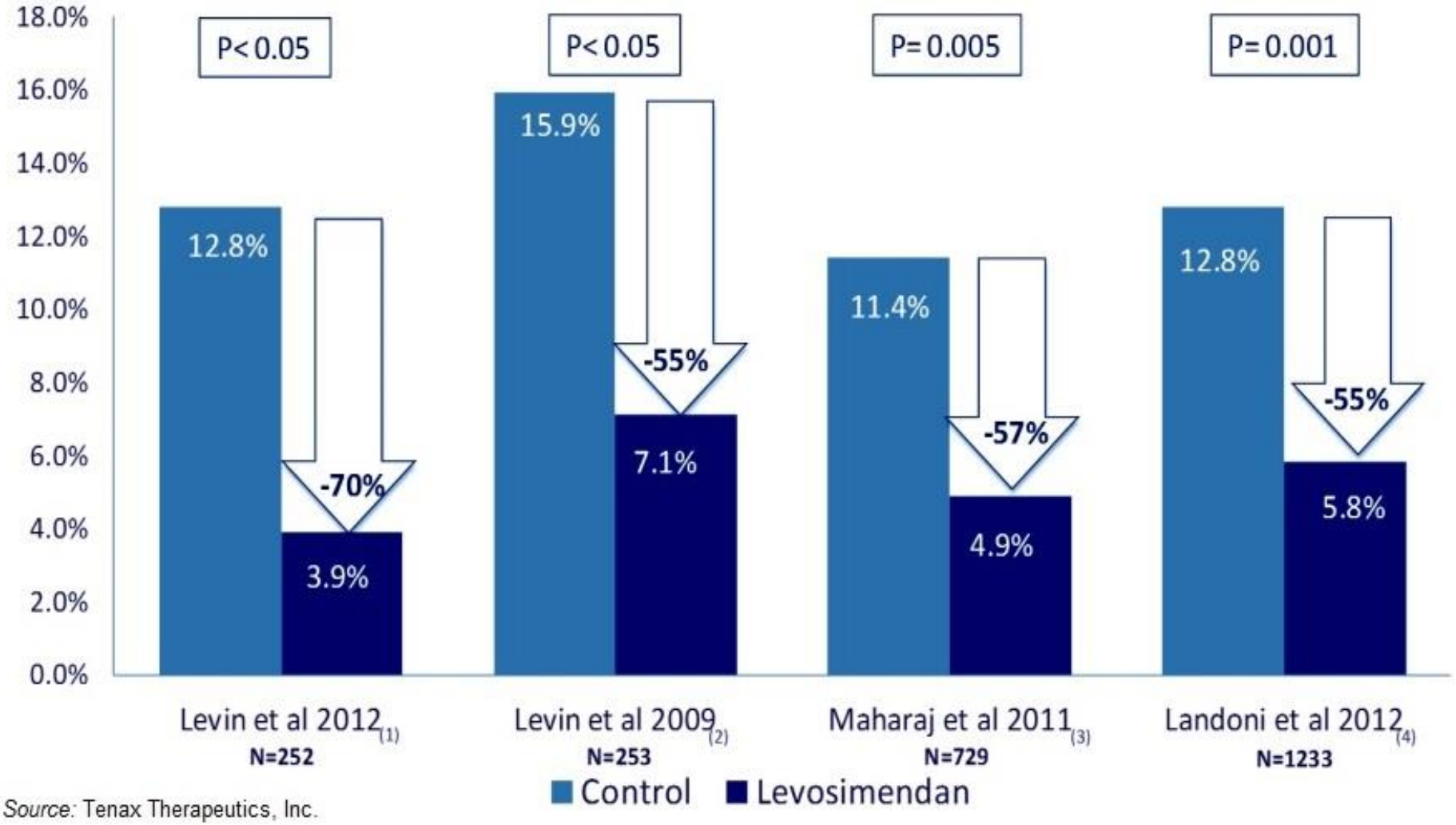
POTENTIAL MORTALITY REDUCTION



Source: Tenax Therapeutics, Inc.

1) Levin et al - Pending Exp and Clinical Cardiology 2012
2) Levin et al Circulation. 2009;120:S987-S988
3) Maharaj et al Critical Care 2011, 15:R140 June 2011
4) Landoni et al Crit Care Med 2012 Vol. 40, No. 2(CV Surgery Pts only)

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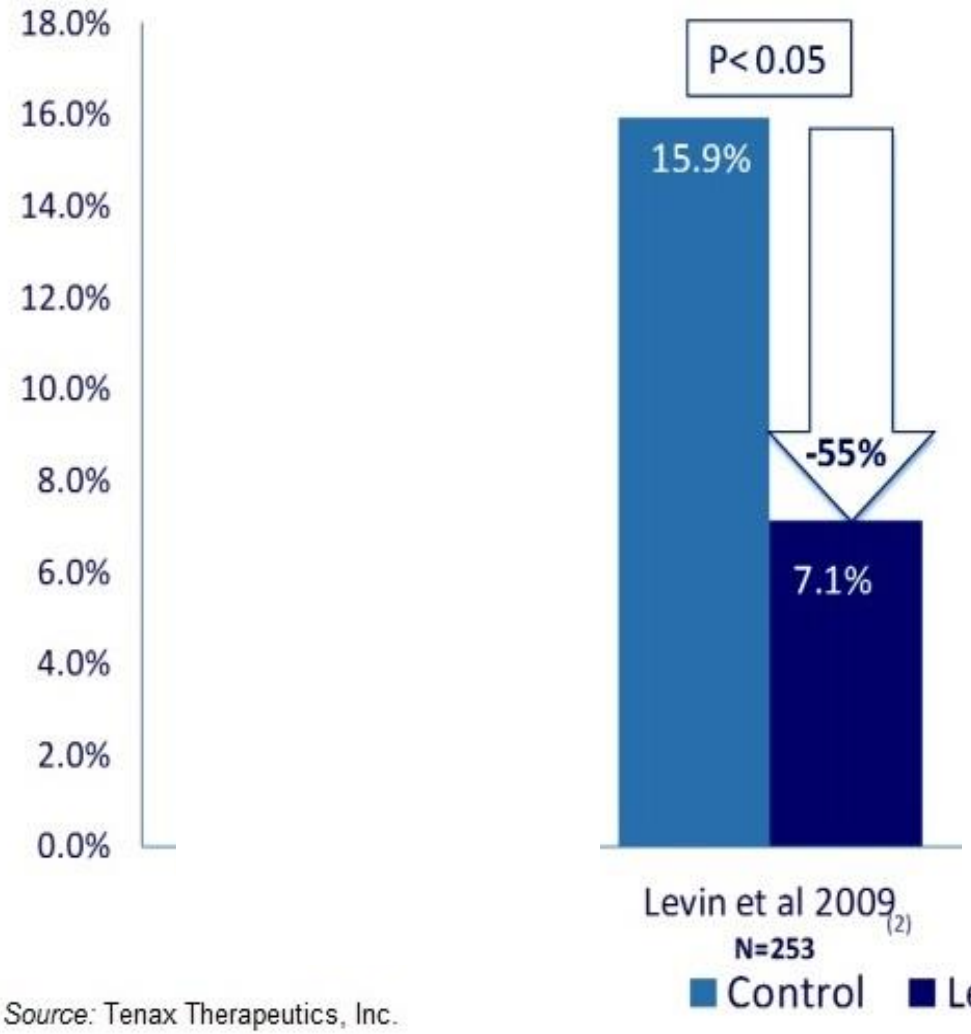
POTENTIAL MORTALITY REDUCTION



Source: Tenax Therapeutics, Inc.

Levin RL, Degrange M, Porcile R, et al.

Preoperative use of calcium sensitizer levosimendan reduces mortality and low cardiacoutput syndrome in patients with aortic stenosisand left ventricular dysfunction. ***Circulation 2008; 118:E217***

1) Levin et al - Pending Exp and Clinical Cardiology 2012
2) Levin et al Circulation. 2009;120:S987-S988
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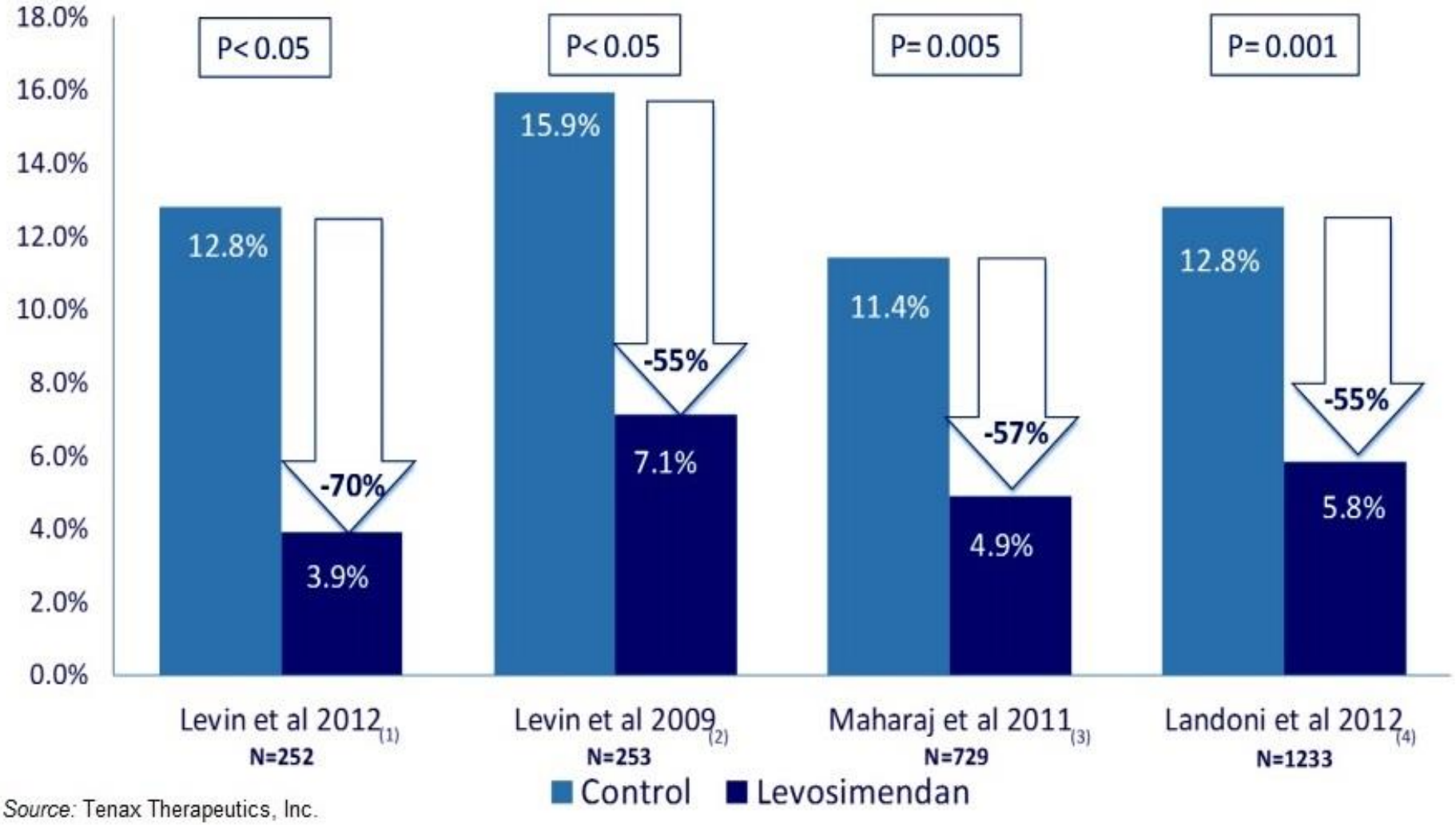

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POTENTIAL MORTALITY REDUCTION

Source: Tenax Therapeutics, Inc.

Preoperative levosimendan decreases mortality and the development of low cardiac output in high-risk patients with severe left ventricular dysfunction undergoing coronary artery bypass grafting with cardiopulmonary bypass

Ricardo Levin MD1, Marcela Degrange MD2, Carlos Del Mazo MD3, Rafael Porcile MD4

Exp Clin Cardiol Vol 17 No 3 2012

1) Levin et al - Pending Exp and Clinical Cardiology 2012
2) Levin et al Circulation. 2009;120:S987-S988
3) Maharaj et al Critical Care 2011, 15:R140 June 2011
4) Landoni et al Crit Care Med 2012 Vol. 40, No. 2(CV Surgery Pts only)

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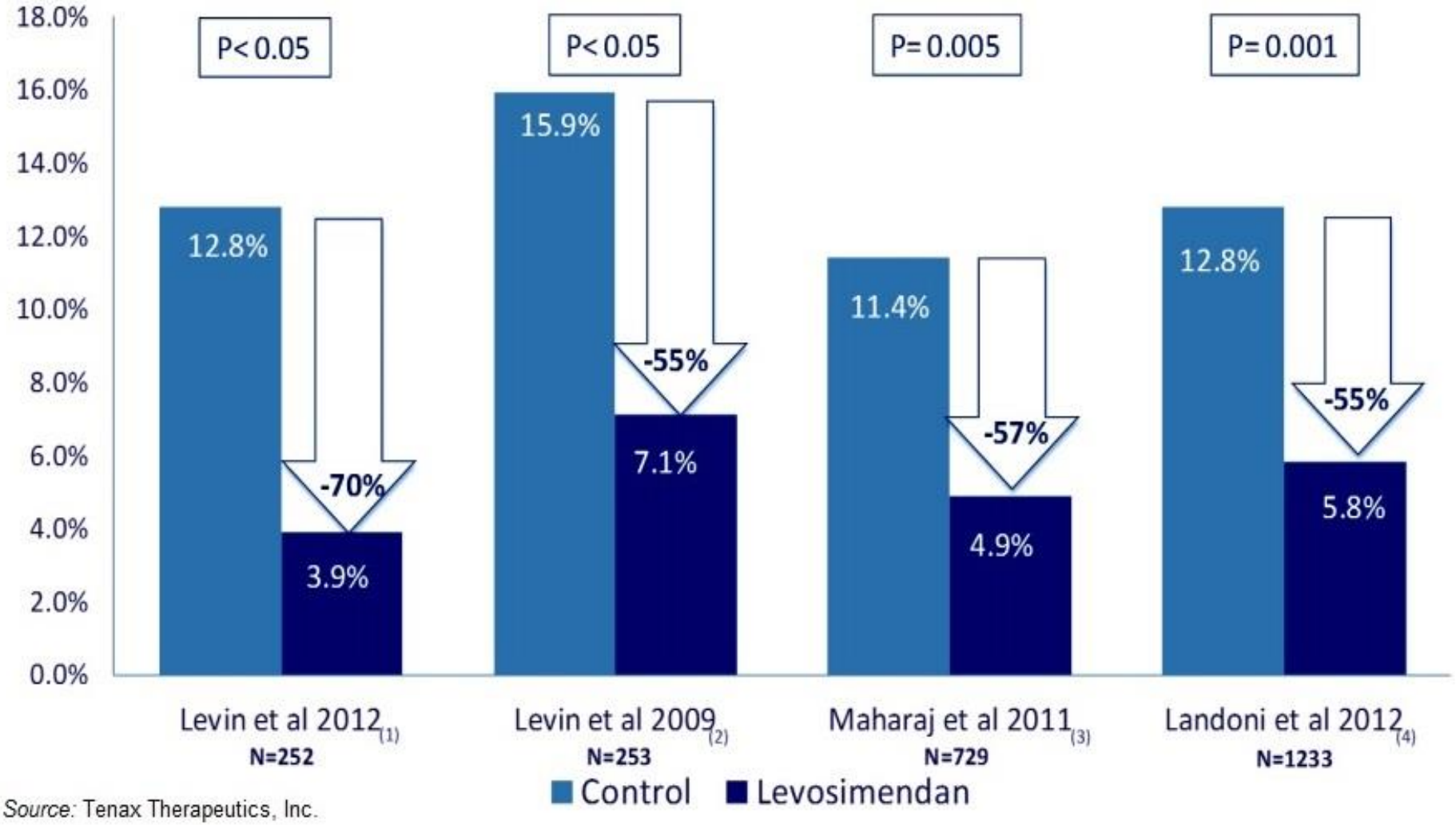
POTENTIAL MORTALITY REDUCTION



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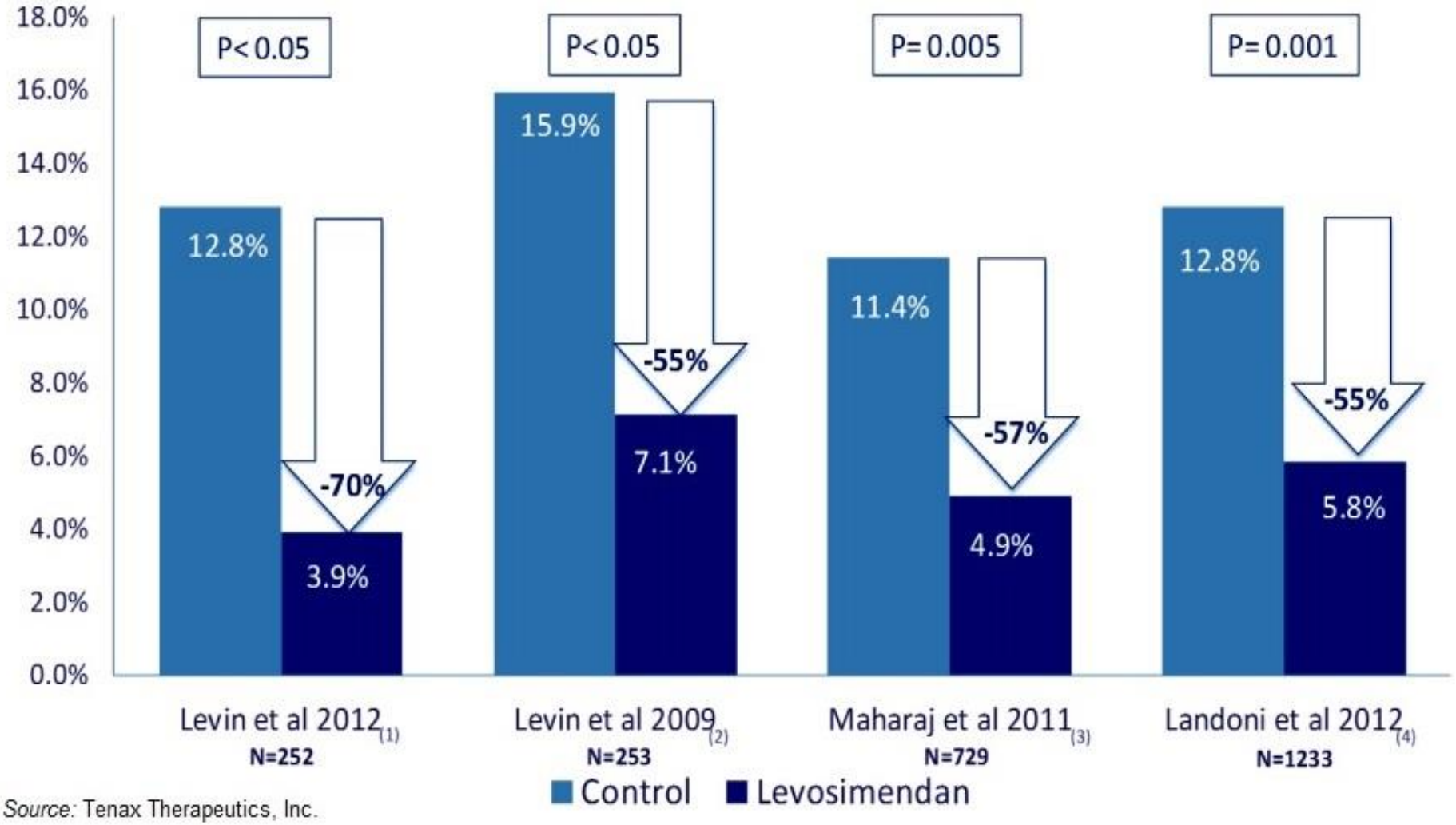

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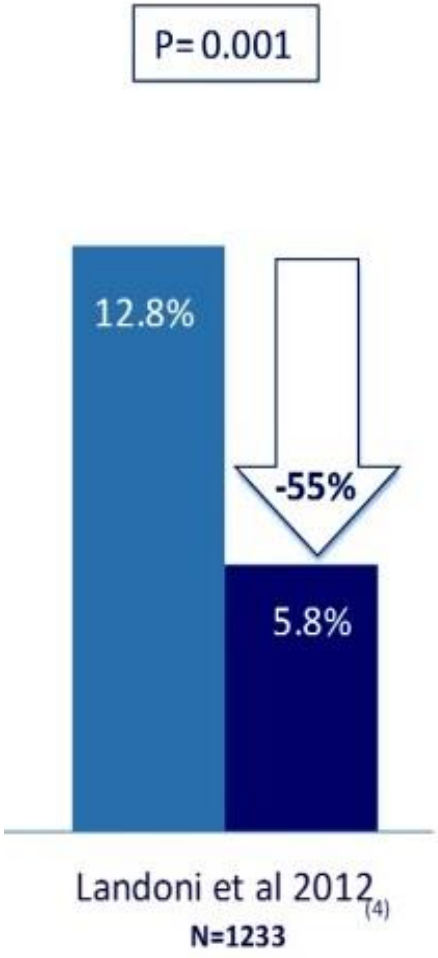
POTENTIAL MORTALITY REDUCTION

Crit Care Med. 2012 Feb;40(2):634-46..

Effects of levosimendan on mortality and hospitalization. A meta-analysis of randomized controlled studies.

Landoni G[1], Biondi-Zoccai G, Greco M, Greco T,



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3) Maharaj et al Critical Care 2011, 15:R140 June 2011
4) Landoni et al Crit Care Med 2012 Vol. 40, No. 2(CV Surgery Pts only)

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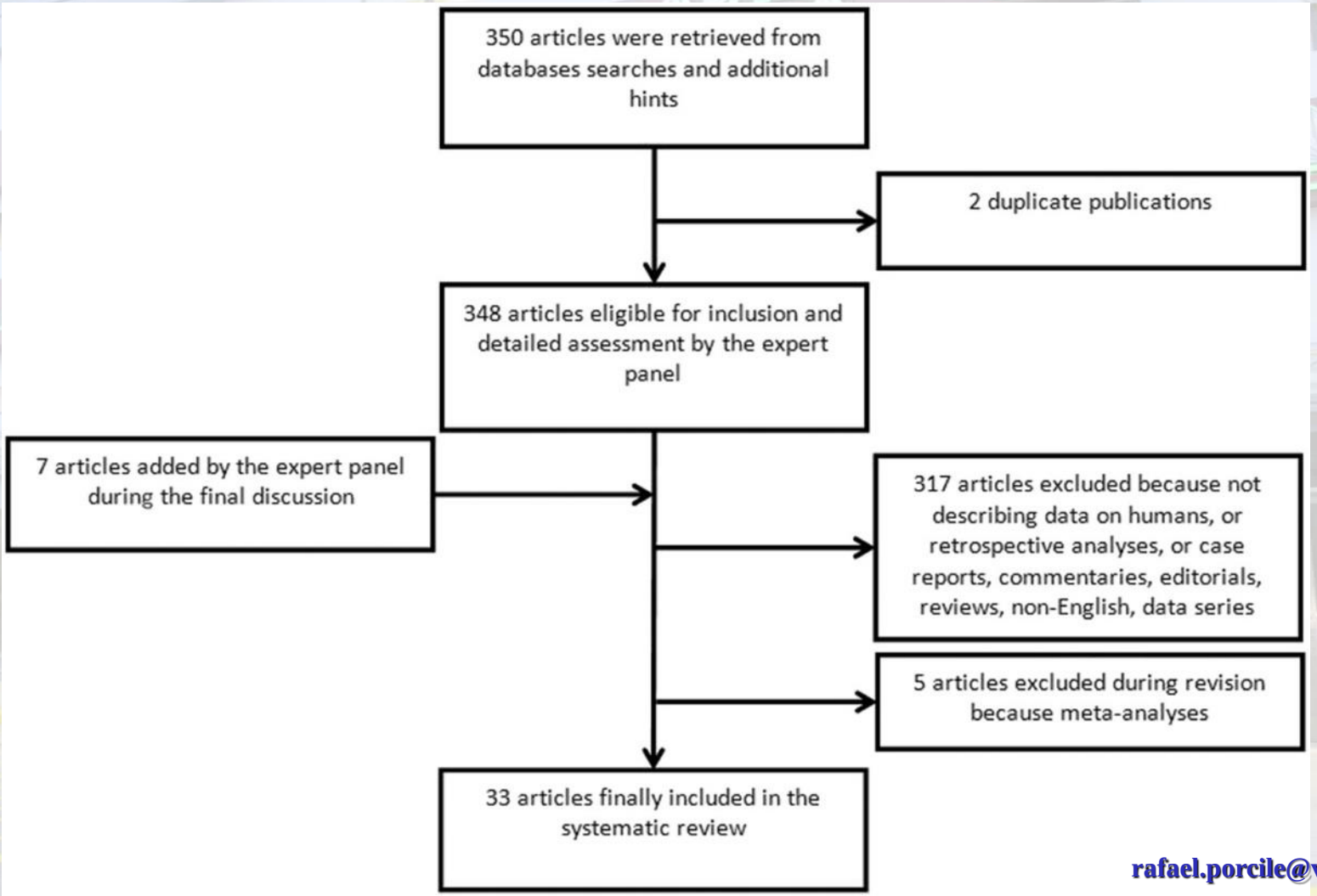
Effects of levosimendan on mortality and hospitalization. A meta-analysis of randomized controlled studies.



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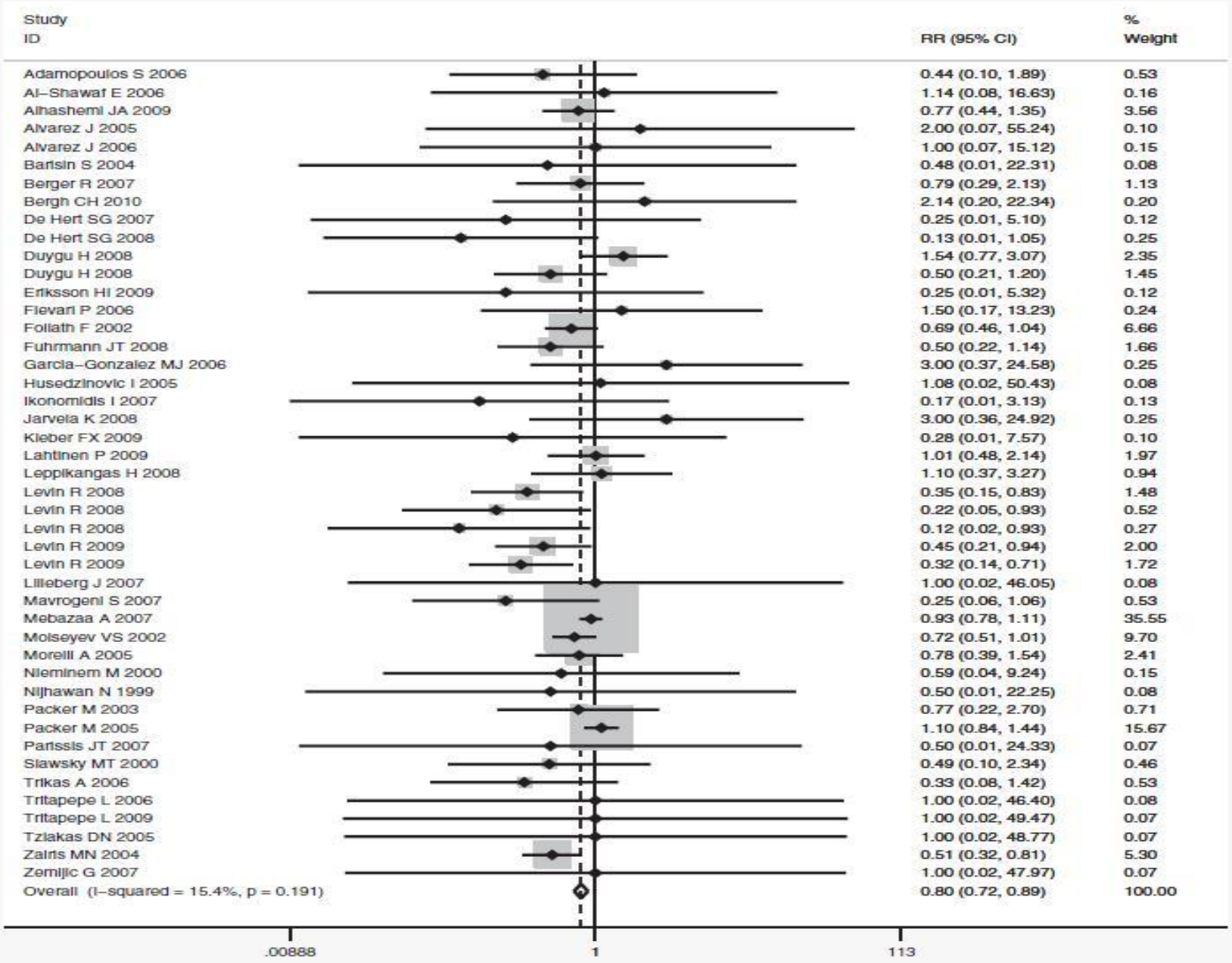
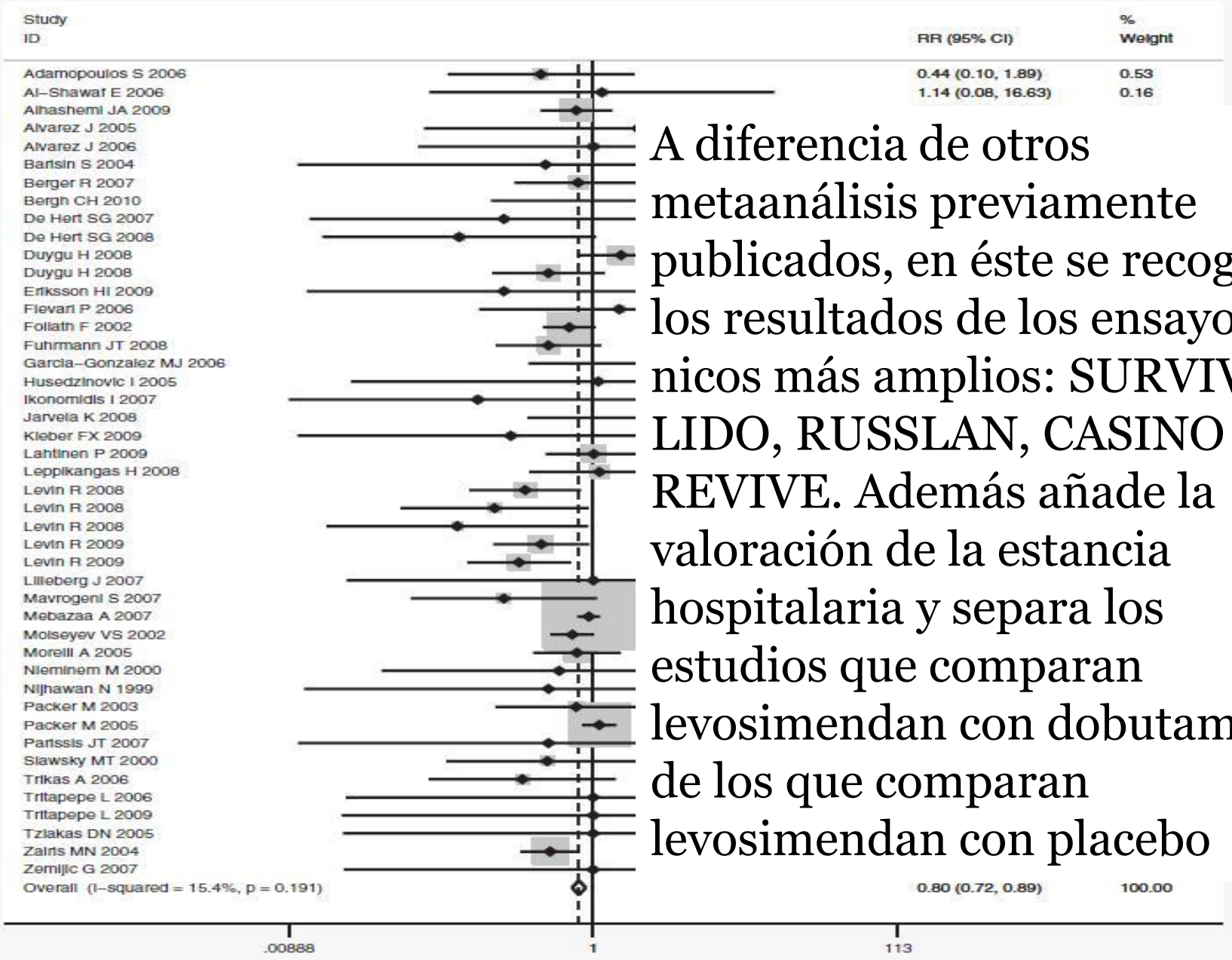
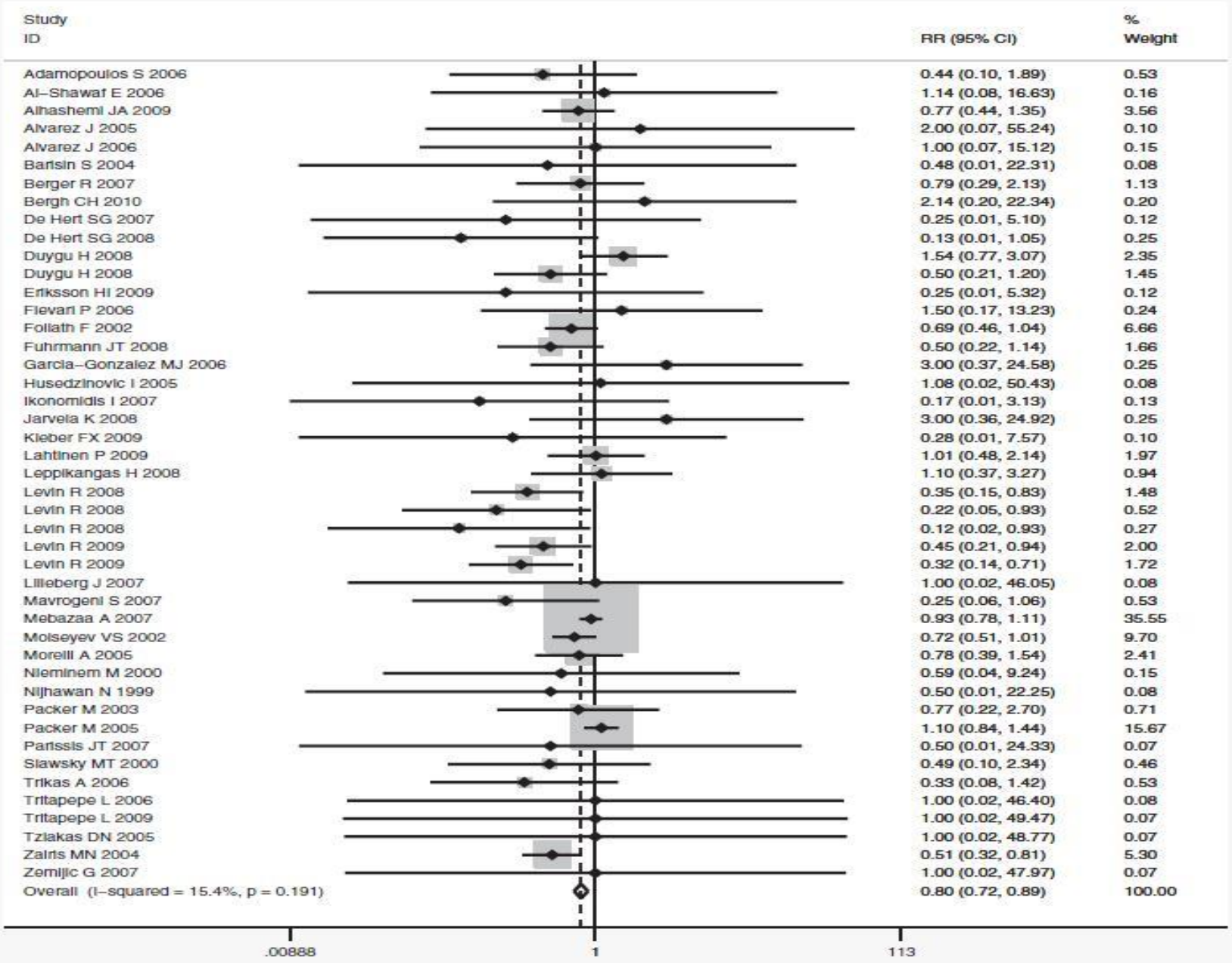


igure 2. Forest plot for the risk of mortality. The use of levosimendan was associated with a significant reduction in mortality at the longest follow-up vailable (507 of 2915 [17.4%] in the levosimendan group vs. 598 of 2565 [23.3%] in the control arm, risk ratio [*RR*]: 0.80 [0.72; 0.89], *p* for effect < .001, = 51.98, *p* for heterogeneity = .191, I^2 = 15.4%, NNT = 17 with 5,480 patients and 45 studies included). *CI*, confidence interval.



A diferencia de otros metaanálisis previamente publicados, en éste se recogen los resultados de los ensayos clínicos más amplios: SURVIVE, LIDO, RUSSLAN, CASINO Y REVIVE. Además añade la valoración de la estancia hospitalaria y separa los estudios que comparan levosimendan con dobutamina de los que comparan levosimendan con placebo

igure 2. Forest plot for the risk of mortality. The use of levosimendan was associated with a significant reduction in mortality at the longest follow-up vailable (507 of 2915 [17.4%] in the levosimendan group vs. 598 of 2565 [23.3%] in the control arm, risk ratio [*RR*]: 0.80 [0.72; 0.89], *p* for effect< .001, = 51.98, *p* for heterogeneity = .191, I^2 = 15.4%, NNT = 17 with 5,480 patients and 45 studies included). *CI*, confidence interval.



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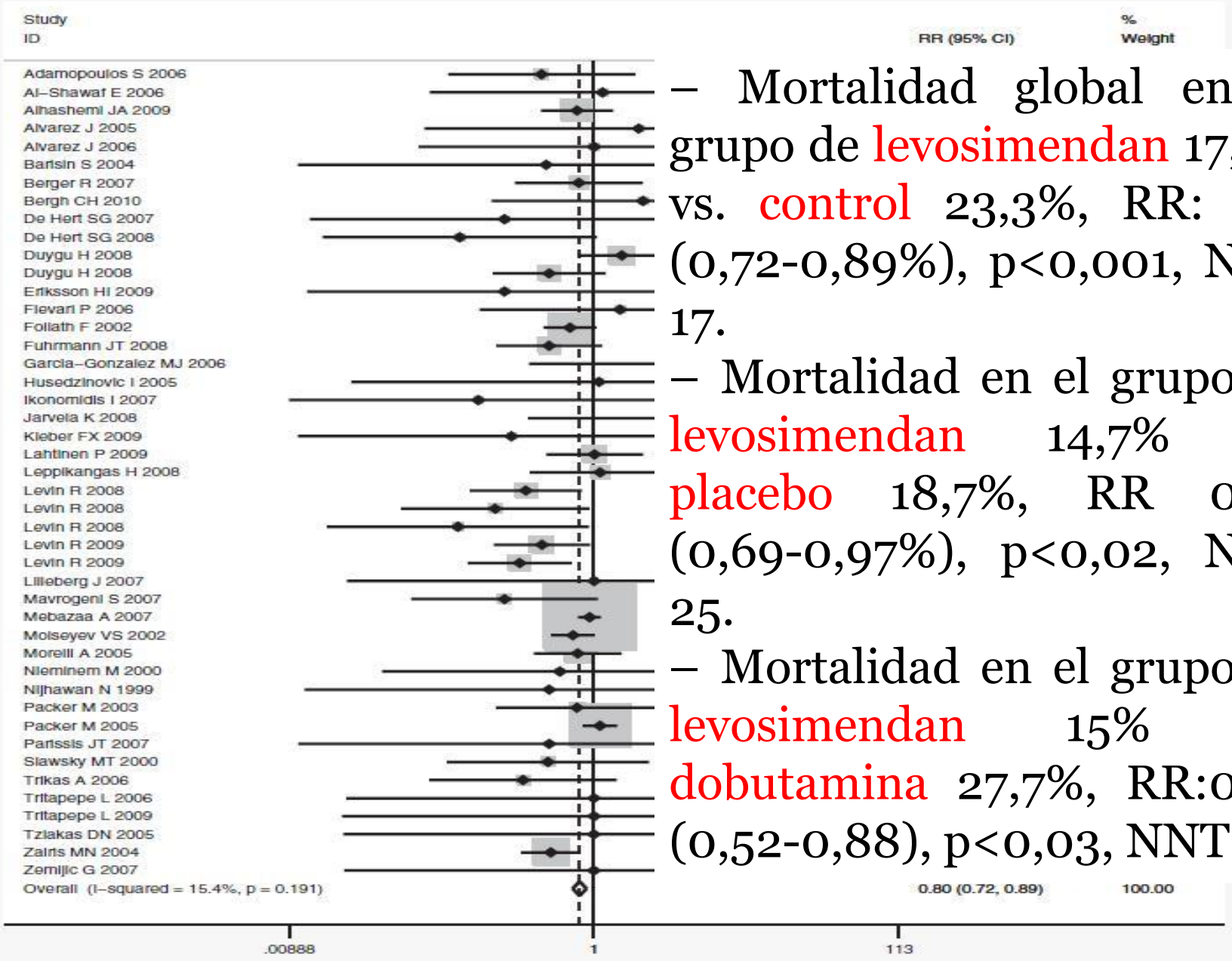

– Mortalidad global en el grupo de levosimendan 17,4% vs. control 23,3%, RR: 0,8 (0,72-0,89%), p<0,001, NNT 17.

– Mortalidad en el grupo de levosimendan 14,7% vs. placebo 18,7%, RR 0,82 (0,69-0,97%), p<0,02, NNT 25.

– Mortalidad en el grupo de levosimendan 15% vs. dobutamina 27,7%, RR:0,68 (0,52-0,88), p<0,03, NNT 13.

igure 2. Forest plot for the risk of mortality. The use of levosimendan was associated with a significant reduction in mortality at the longest follow-up vailable (507 of 2915 [17.4%] in the levosimendan group vs. 598 of 2565 [23.3%] in the control arm, risk ratio [*RR*]: 0.80 [0.72; 0.89], *p* for effect < .001, = 51.98, *p* for heterogeneity = .191, I^2 = 15.4%, NNT = 17 with 5,480 patients and 45 studies included). *CI*, confidence interval.

¿Levosimendan o dobutamina?

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Revista Española de Cardiología
Volume 61, Issue 5, May 2008, Pages 471-479

Superioridad del sensibilizante al calcio levosimendán comparado con dobutamina en el síndrome de bajo gasto cardiaco postoperatorio

Ricardo L. Levin. Marcela A. Degrange. Rafael Porcile

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DO2:Gasto cardíaco x (SatO x Hbx 1.34)

Contenido arterial de oxigeno

OBJETIVO

≠

HERRAMIENTA

¿Contractilidad o inotropismo?

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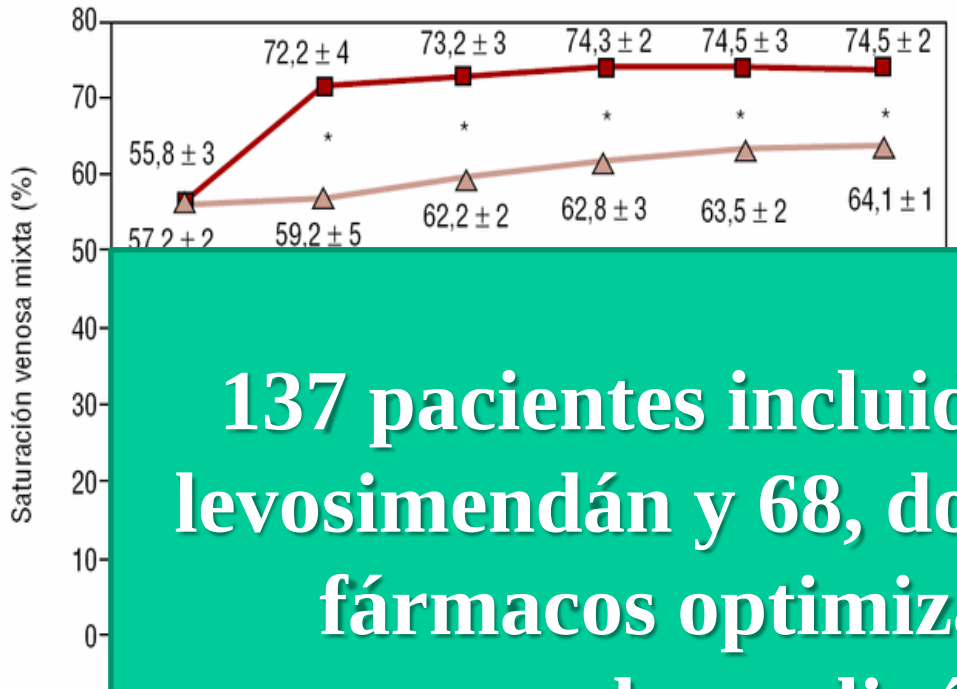
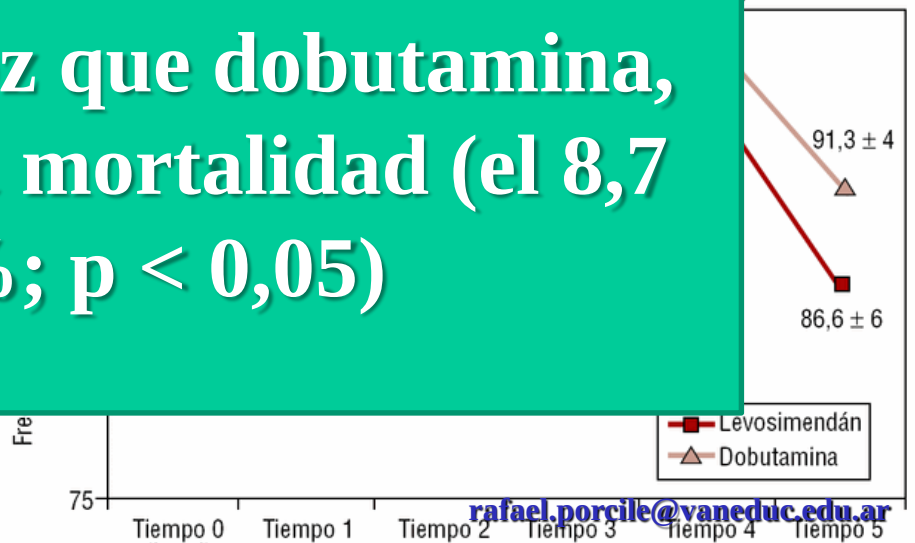


137 pacientes incluidos, 69 recibieron levosimendán y 68, dobutamina. Ambos fármacos optimizaron variables hemodinámicas

El efecto del levosimendán resultó superior y más precoz que dobutamina, además de reducir la mortalidad (el 8,7 frente al 25%; p < 0,05)



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SURVIVE-W: Design

1327 patients with acute decompensated heart failure, left ventricular ejection fraction ≤ 30%, clinical need for inotropic therapy after intravenous diuretics and/or vasodilators

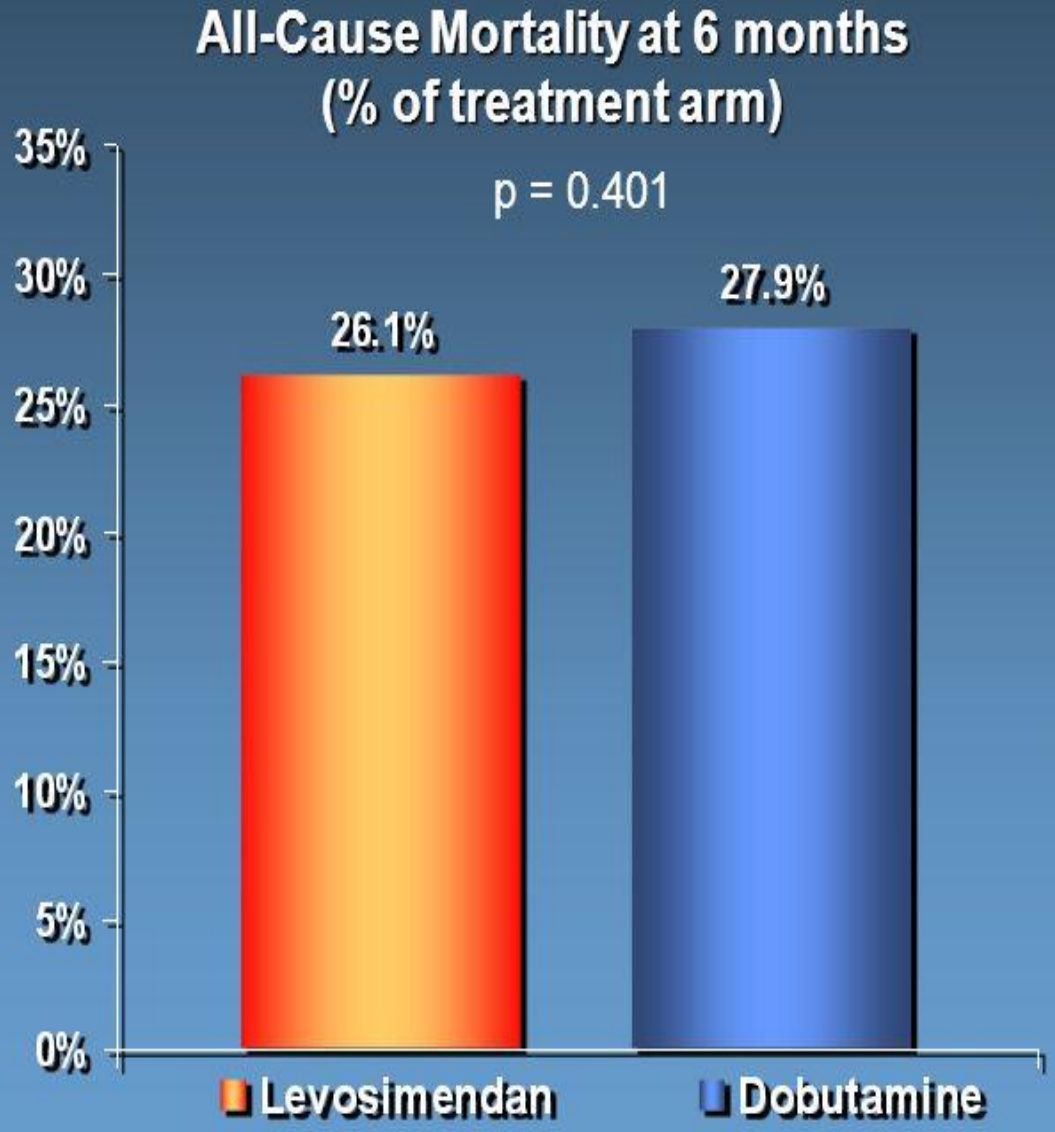
Levosimendan
(12 µg/kg bolus plus 0.1-0.2 µg/kg/min infusion for 24 hours)
n=663

Dobutamine
(≥5 µg/kg/min infusion for ≥ 24 hours)
n=664

Endpoints:

- Primary – All cause mortality at 6 months
- Secondary – All-cause mortality at 31 days, BNP at 24 hours, days alive out of hospital, change in patient dyspnea assessment, change in patient global assessment

SURVIVE-W: Primary endpoint



- There was no significant difference in the primary endpoint of all-cause mortality between the levosimendan and dobutamine groups

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¿Levosimendan o Milrinone?

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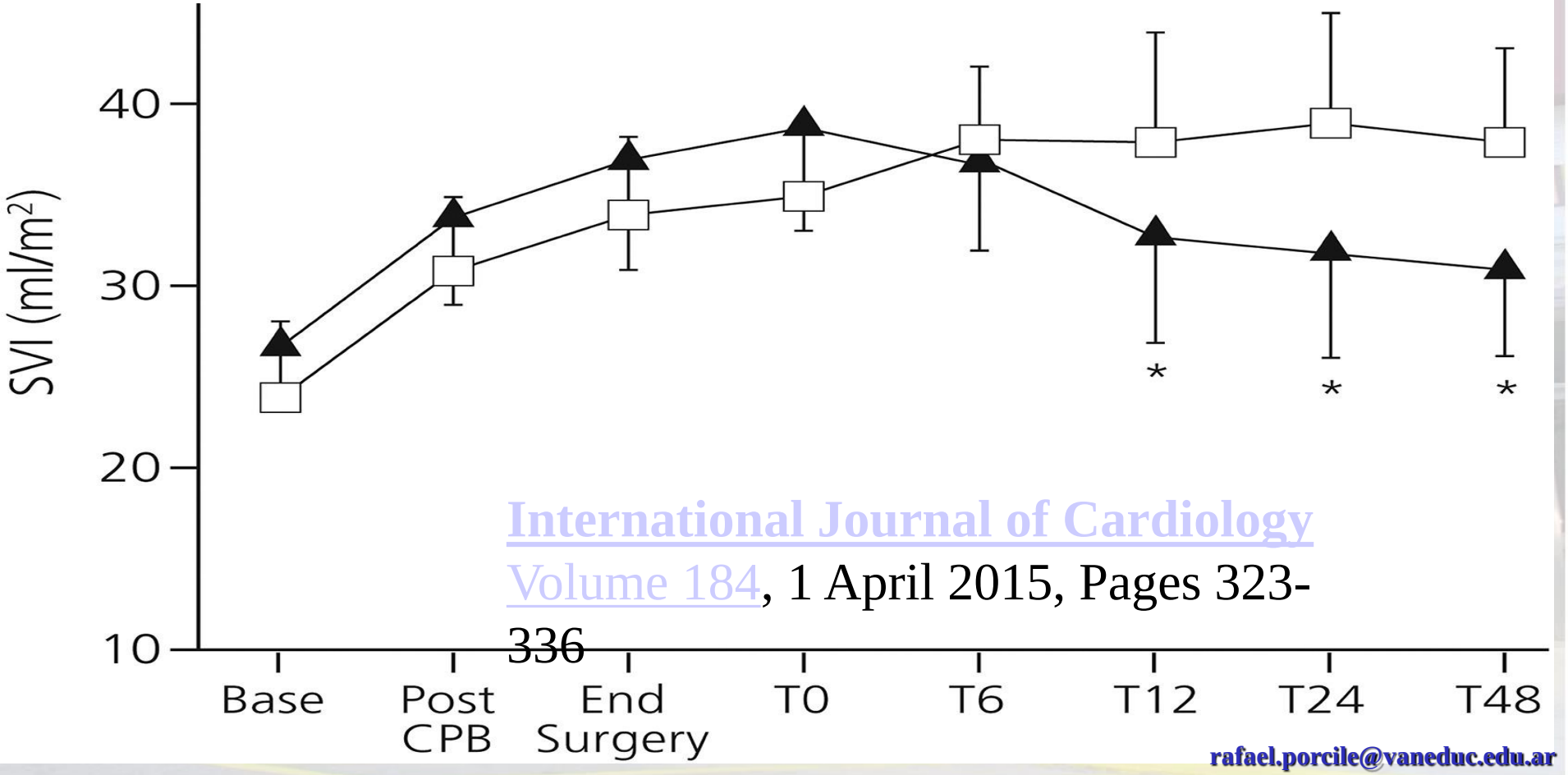
1. Stroke volume (SVI) at the start of surgery (base), 15 min after the end of cardiopulmonary bypass (post-CPB), at the end of the operation (end surgery), at arrival in the intensive care unit (T0), and 6 (T6), 12 (T12), 24 (T24), and 48 (T48) h later. Levosimendan (□) and Milrinone (▲). Data are mean ± standard deviation. *, statistically significant difference between groups for $P < 0.05$.



International Journal of Cardiology
Volume 184, 1 April 2015, Pages 323-336

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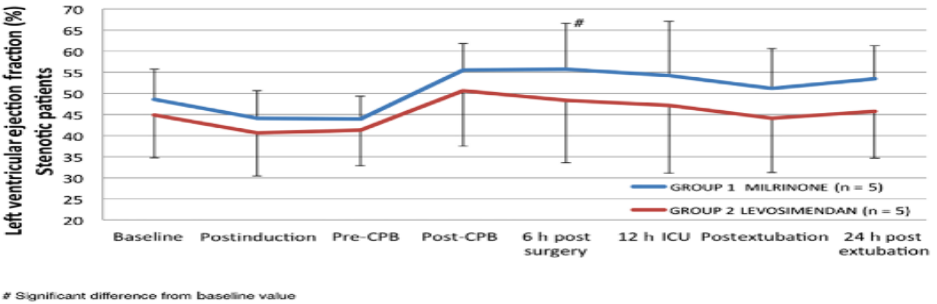
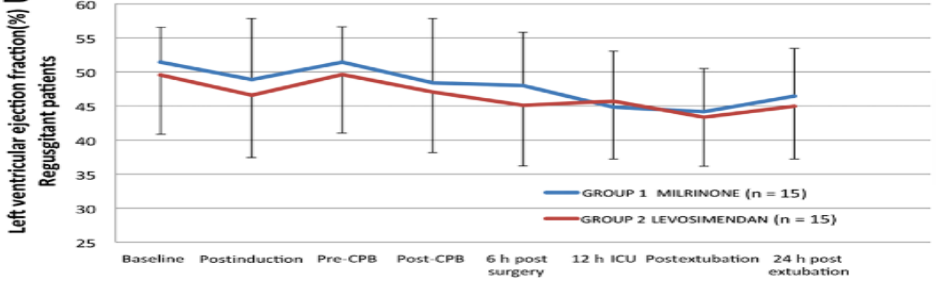
LEVOSIMENDAN VS MILRINONE

A



Significant difference from baseline value

B



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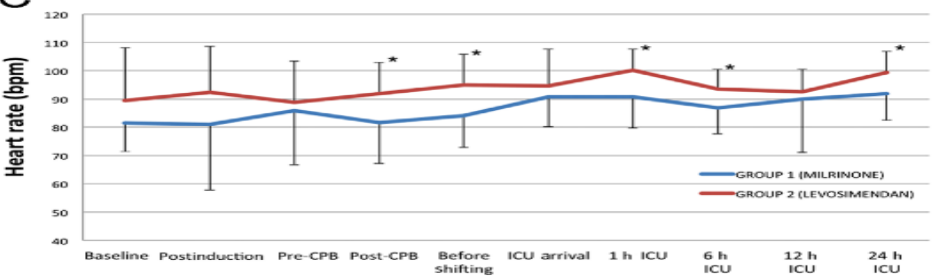
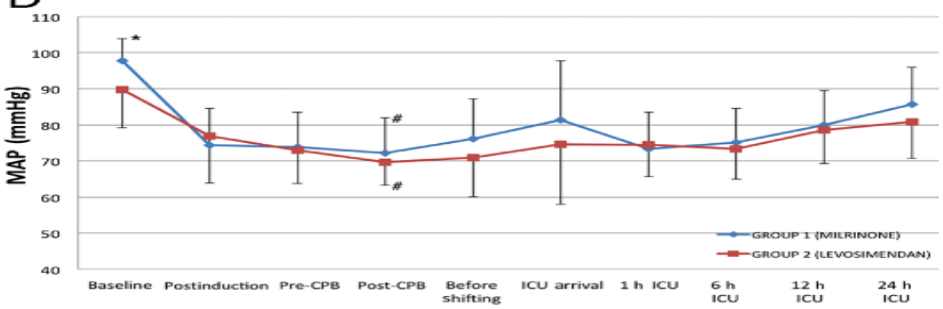


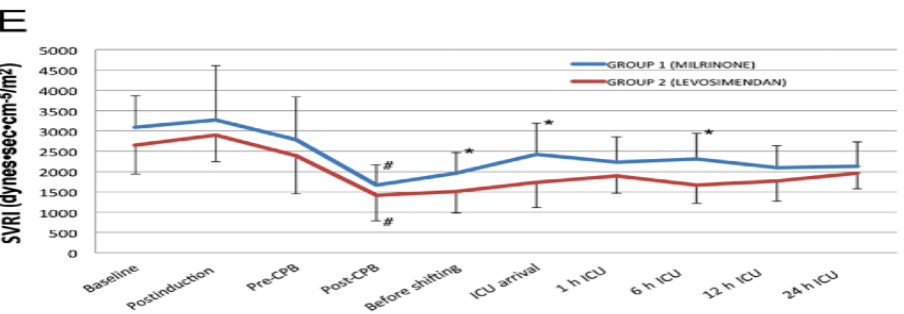
* Significant difference between the groups

D



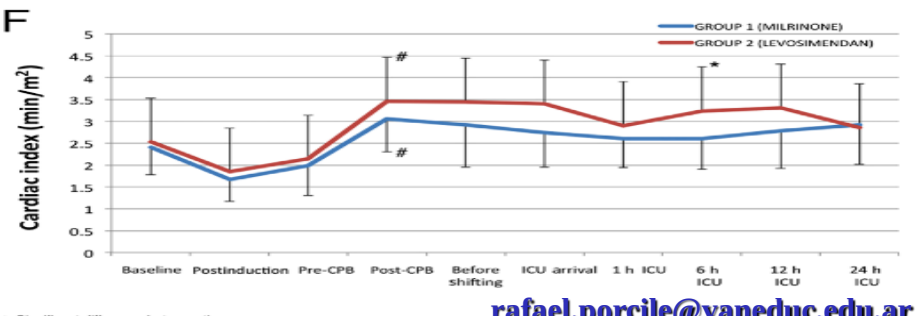
*Significant difference between the groups
#Significant difference from baseline

E



* Significant difference between the groups
# Significant difference from baseline

F



* Significant difference between the groups
# Significant difference from baseline

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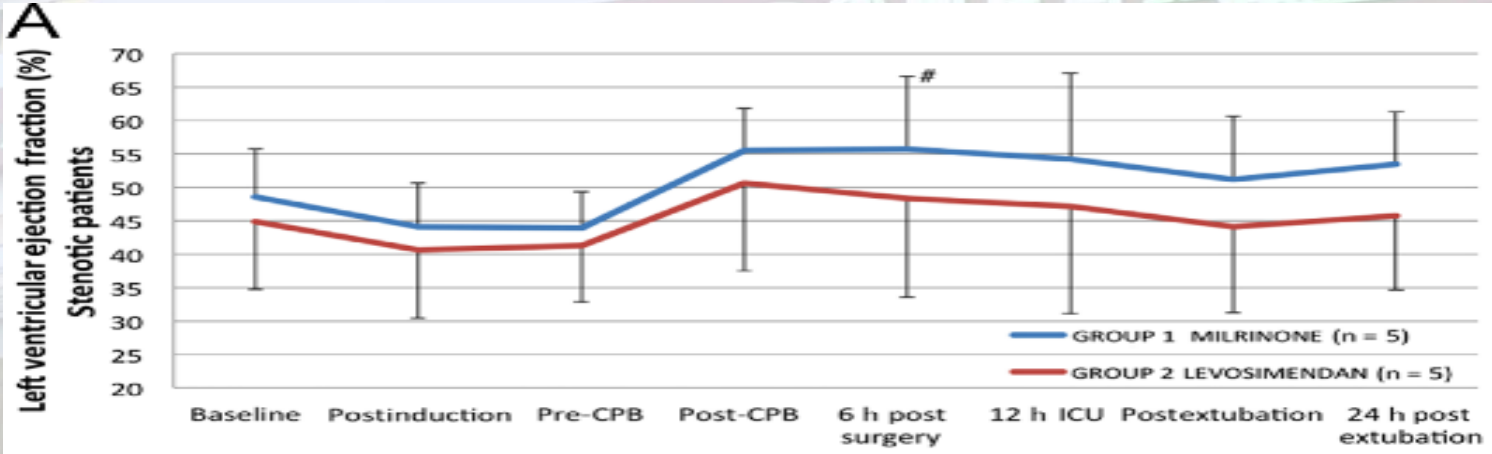
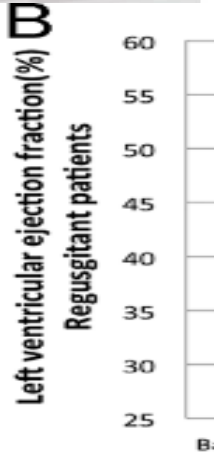
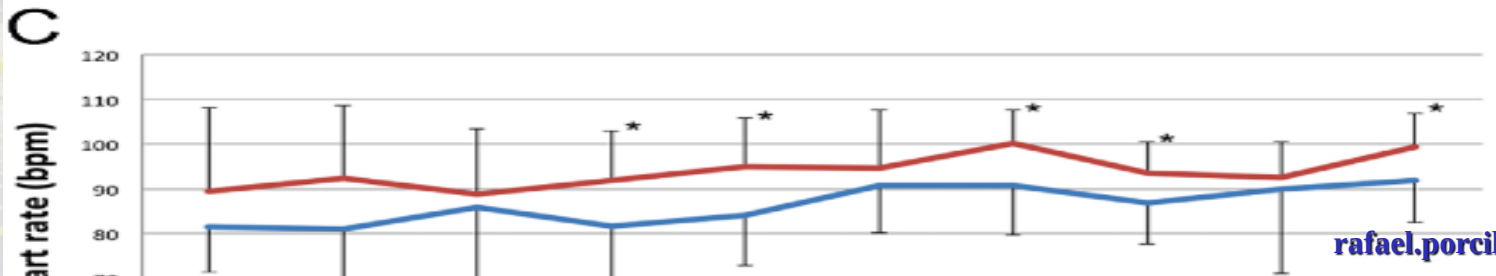
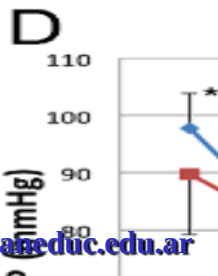
LEVOSIMENDAN VS MILRINONE





Significant difference from baseline value





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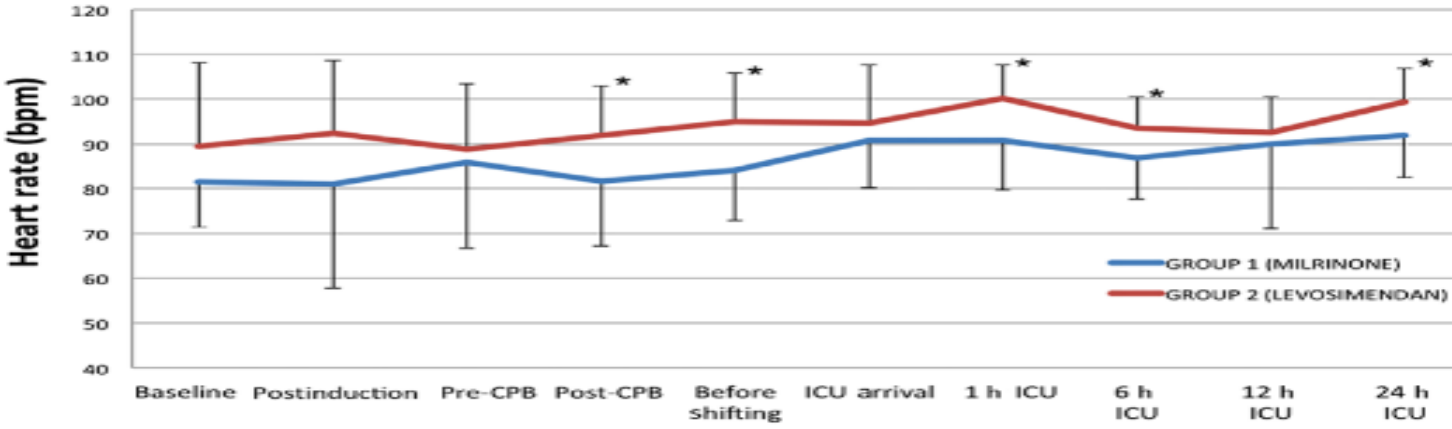
L

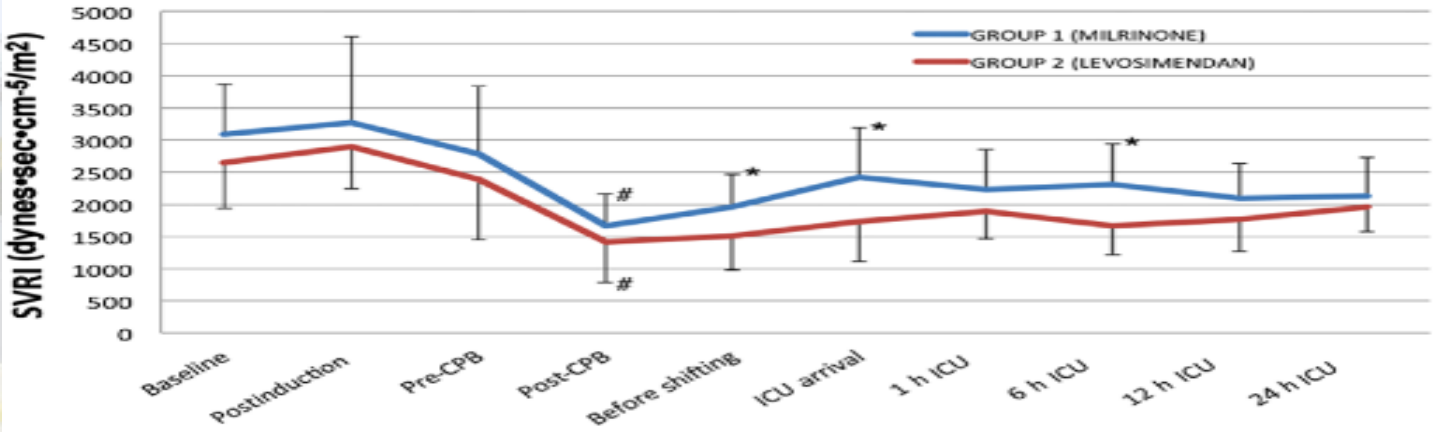
C

Significant difference from baseline value



★ Significant difference between the groups

Π



★ Significant difference between the groups

Significant difference from baseline

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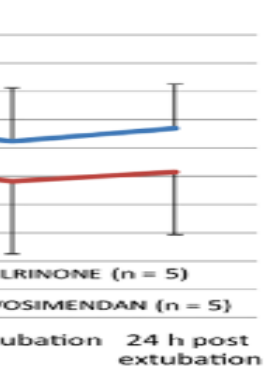

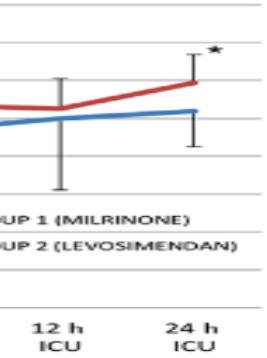

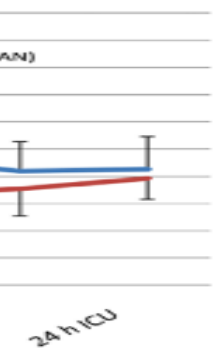

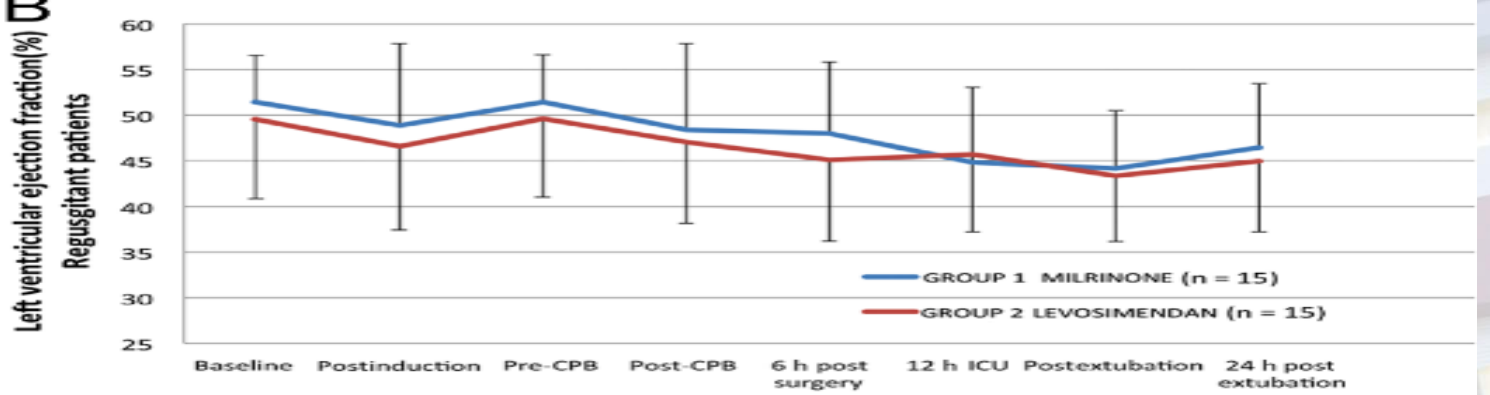

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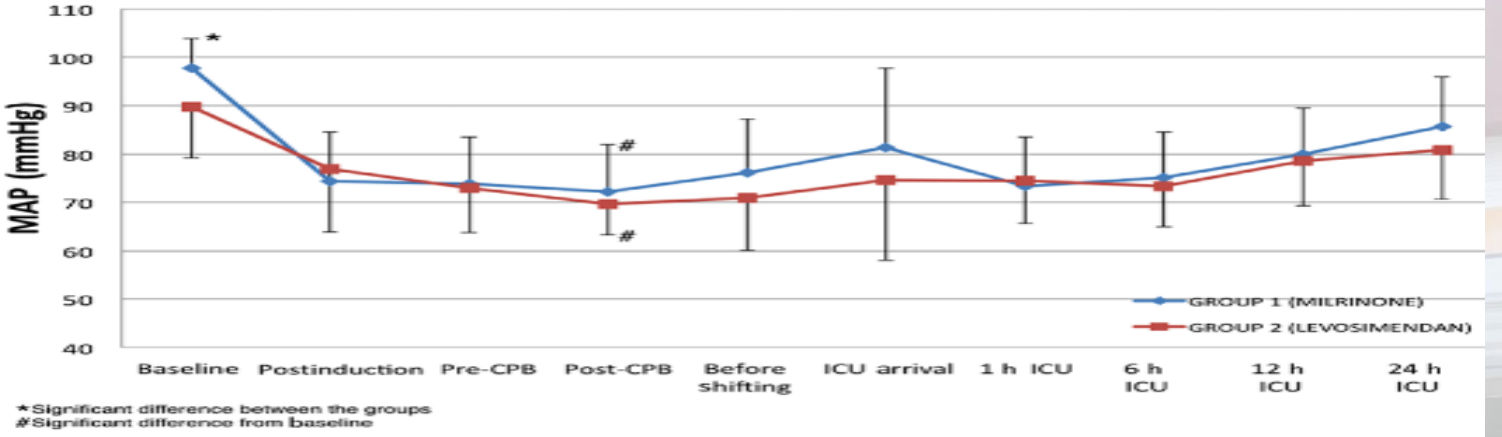
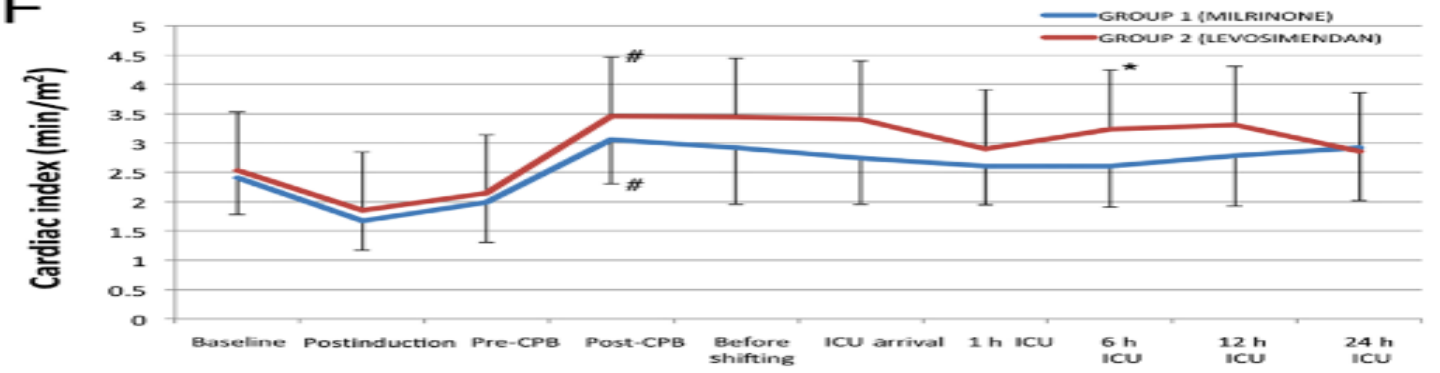


*Significant difference between the groups
#Significant difference from baseline

T



* Significant difference between the groups
# Significant difference from baseline

LEVO-CTS & LeoPARDS trials

Levosimendan	Low Cardiac Output Syndrome	I	II	III

LEVO-CTS trial

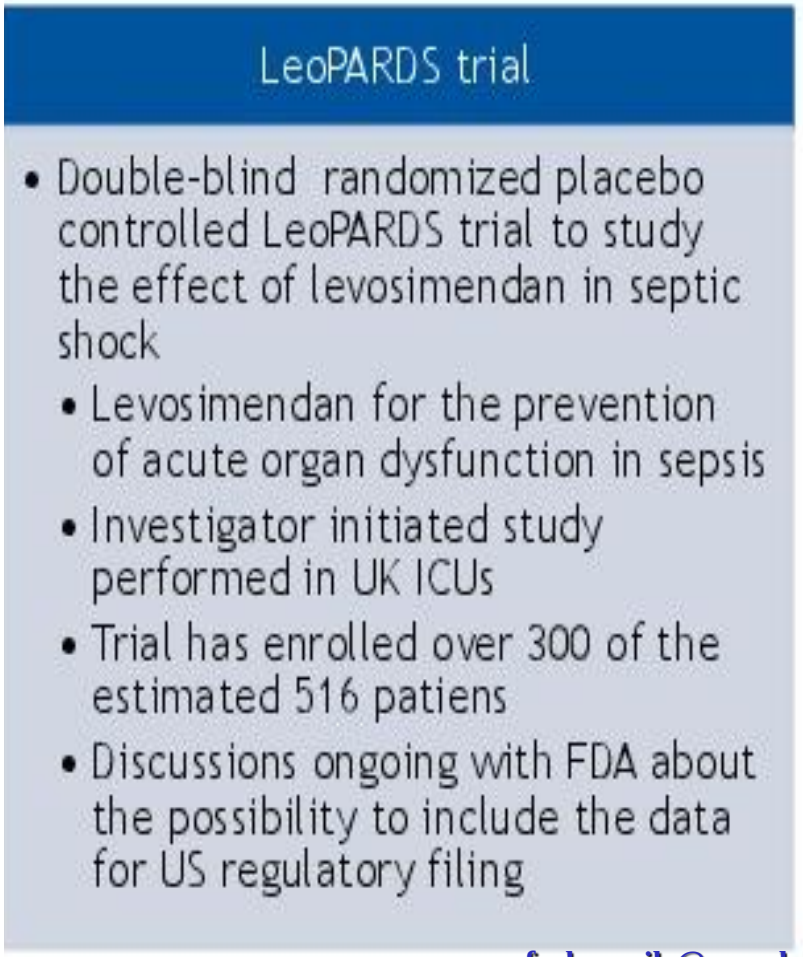
- A Double-Blind, Randomized, Placebo-Controlled Study of Levosimendan in Patients with Left Ventricular Systolic Dysfunction Undergoing Cardiac Surgery Requiring Cardiopulmonary Bypass
- 760 patients, approximately 60 centers
- ClinicalTrials.gov identifier: NCT02025621

LeoPARDS trial

- Double-blind randomized placebo controlled LeoPARDS trial to study the effect of levosimendan in septic shock
  - Levosimendan for the prevention of acute organ dysfunction in sepsis
  - Investigator initiated study performed in UK ICUs
  - Trial has enrolled over 300 of the estimated 516 patiens
  - Discussions ongoing with FDA about the possibility to include the data for US regulatory filing

The addition of levosimendan to standard treatment in adults with sepsis was not associated with less severe organ dysfunction or lower mortality. Levosimendan was associated with a lower likelihood of successful weaning from mechanical ventilation and a higher risk of supraventricular tachyarrhythmia.

October 27, 2016
N Engl J Med 2016; 375:1638-1648
DOI: 10.1056/NEJMoa1609409



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¿Hay nuevas evidencias a analizar?

5

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LEVO CTS
levosimendan in cardio thoracic surgery

ACC.17
66th Annual Scientific Session & Expo

Levosimendan In Patients With Left Ventricular Systolic Dysfunction Undergoing Cardiac Surgery With Cardiopulmonary Bypass

PRIMARY RESULTS OF THE LEVO-CTS TRIAL

John H. Alexander, MD, MHS, FACC

Rajendra H. Mehta, Jeffrey D. Leimberger, Stephen Fremes, John Luber, Wolfgang Toller, Matthias Heringlake, Jerrold H. Levy, Robert A. Harrington, Kevin J. Anstrom

on behalf of the LEVO-CTS Investigators

Duke Clinical Research Institute | FROM THOUGHT LEADERSHIP TO CLINICAL PRACTICE

TENAX THERAPEUTICS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Levosimendan in Patients with Left Ventricular Dysfunction Undergoing Cardiac Surgery

R.H. Mehta, J.D. Leimberger, S. van Diepen, J. Meza, A. Wang, R. Jankowich, R.W. Harrison, D. Hay, S. Fremes, A. Duncan, E.G. Soltesz, J. Luber, S. Park, M. Argenziano, E. Murphy, R. Marcel, D. Kalavrouziotis, D. Nagpal, J. Bozinovski, W. Toller, M. Heringlake, S.G. Goodman, J.H. Levy, R.A. Harrington, K.J. Anstrom, and J.H. Alexander, for the LEVO-CTS Investigators*

Levosimendan, given prophylactically prior to cardiac surgery to patients with reduced left ventricular function**, had no effect** on the co-primary outcomes of…

- death, dialysis, MI, or mechanical assist device use
- death or mechanical assist device use
- Levosimendan was effective and safe as an inotrope to increase cardiac output in patients at risk for perioperative low cardiac output syndrome

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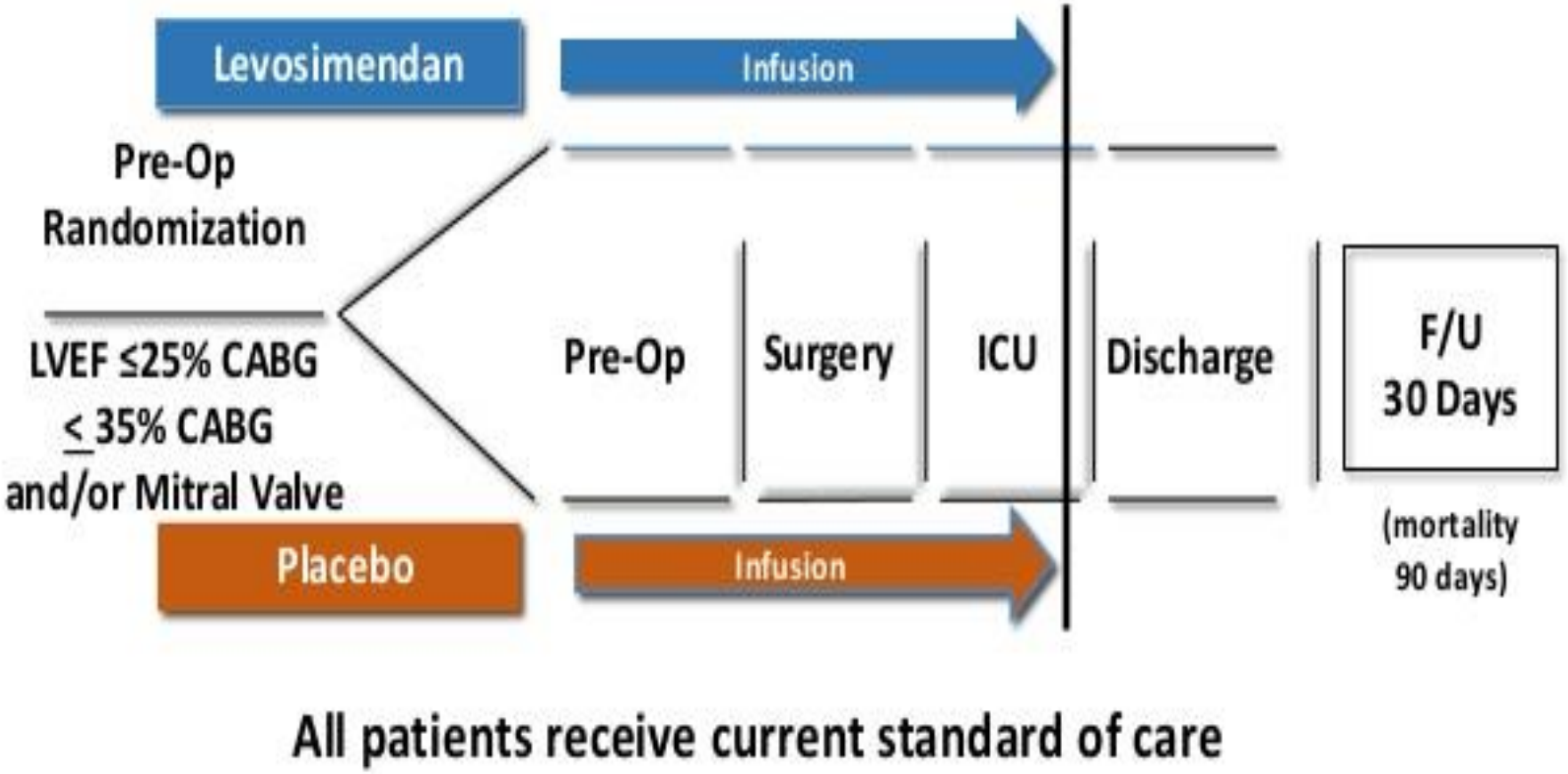
Los pacientes fueron asignados aleatoriamente a recibir levosimendan EV (0,2 ug/kg/min por 1 hora y 0,1 ug/kg/min por 23 horas) o placebo, con la infusión comenzada antes de la incisión quirúrgica



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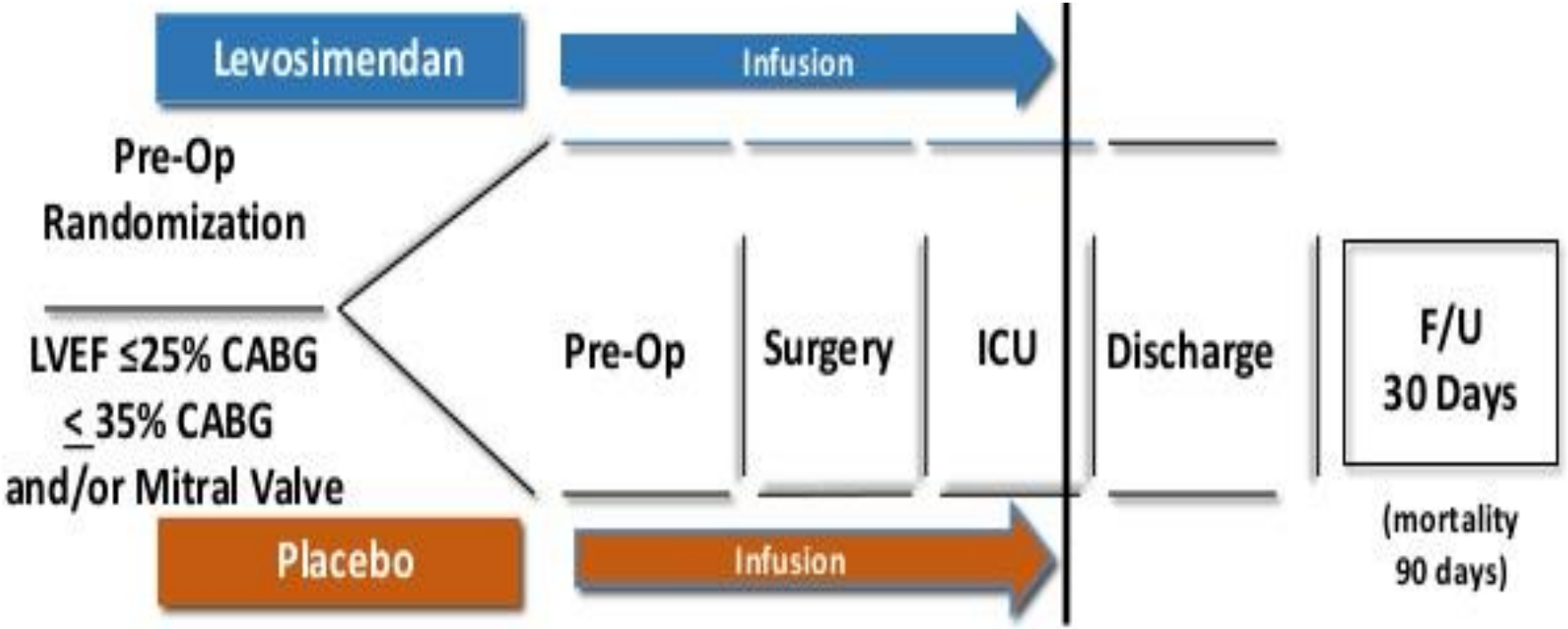
… pero la carga descripta es de 6 A12 ug/Kg Y ALGUNOS SUGIEREN 20….



All patients receive current standard of care

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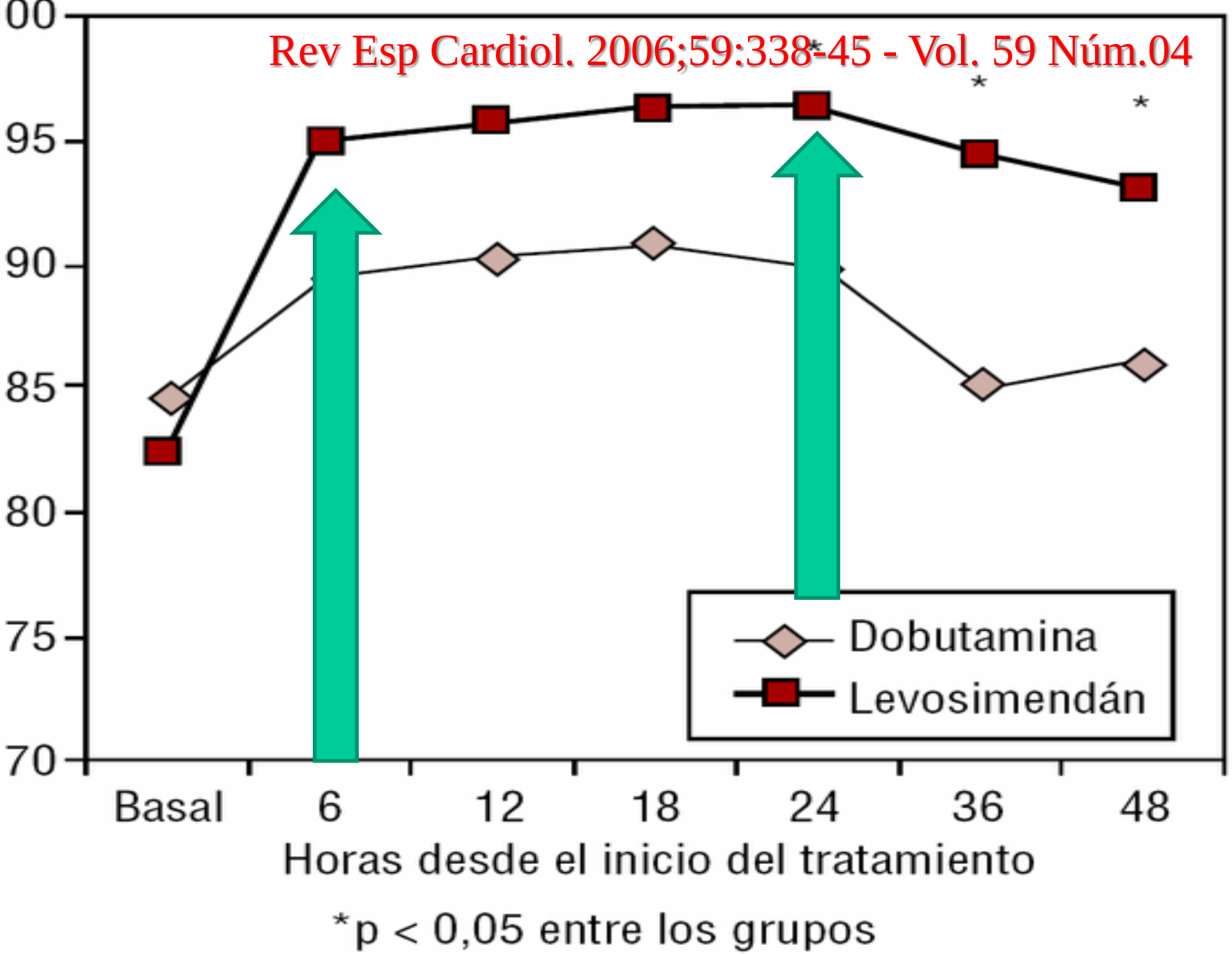
Rev Esp Cardiol. 2006;59:338-45 - Vol. 59 Núm.04



*p < 0,05 entre los grupos

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Estudio randomizado SURVIVE *(The Survival of Patients With Acute Heart Failure in Need of Intravenous Inotropic Support)*

En el grupo del levosimendan, los niveles de BNP fueron significativamente menores a las 24 horas y persistieron así durante 5 días

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Table 4. End Points.*

End Point	Levosimendan (N=428)	Placebo (N=421)	Odds Ratio (95% CI)†	P Value
Primary end points — no. (%)				
Four-component end point‡	105 (24.5)	103 (24.5)	1.00 (0.66–1.54)	0.98
Two-component end point§	56 (13.1)	48 (11.4)	1.18 (0.76–1.82)	0.45
Components of primary end points — no. (%)				
Death at 30 days	15 (3.5)	19 (4.5)	0.77 (0.38–1.53)	0.45
Renal-replacement therapy at 30 days	9 (2.1)	16 (3.8)	0.54 (0.24–1.24)	0.15
Myocardial infarction at 5 days	67 (15.7)	63 (15.0)	1.06 (0.73–1.53)	0.78
Use of mechanical cardiac assist device at 5 days	47 (11.0)	38 (9.0)	1.24 (0.79–1.95)	0.34
Secondary end points¶				
Duration of stay in ICU — days‖				
Median	2.8	2.9	—	0.25
Interquartile range	1.6–4.8	1.8–4.9		
Low cardiac output syndrome — no. (%)‖	78 (18.2)	108 (25.7)	0.62 (0.44–0.88)	0.007
Use of inotrope at or beyond 24 hr after infusion initiation — no. (%)‖	235 (54.9)	264 (62.7)	0.71 (0.53–0.94)	0.02

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Table 4. End Points.*

End Point	Levosimendan (N=428)	Placebo (N=421)	Odds Ratio (95% CI)†	P Value
Primary end points — no. (%)				
Four-component end point‡	105 (24.5)		66–1.54)	0.98
Two-component end point§			.18 (0.76–1.82)	0.45
Components of primary end points — no. (%)				
Death at 30 days		19 (4.5)	0.77 (0.38–1.53)	0.45
Renal-replacement ther	(2.1)	16 (3.8)	0.54 (0.24–1.24)	0.15
Myocardial	67 (15.7)	63 (15.0)	1.06 (0.73–1.53)	0.78
Use of	47 (11.0)	38 (9.0)	1.24 (0.79–1.95)	0.34
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Use of inotrope at or beyond 24 hr after infusion initiation — no. (%)	235 (54.9)	264 (62.7)	0.71 (0.53–0.94)	0.02

Durante las primeras 24 horas….
Ramdomizaron levosimendan contra Placebo o
Placebo contra Placebo

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Table 4. End Points.*

End Point	Levosimendan (N=428)	Placebo (N=421)	Odds Ratio (95% CI)†	P Value
Primary end points — no. (%)				
Four-component end point‡	105 (24.5)	103 (24.5)	1.00 (0.66–1.54)	0.98
T				
Comp				
D				
R				
M				
U				
Secon				
D				
Interquartile range	1.6–4.8	1.8–4.9		
Low cardiac output syndrome — no. (%)	78 (18.2)	108 (25.7)	0.62 (0.44–0.88)	0.007
Use of inotrope at or beyond 24 hr after infusion initiation — no. (%)	235 (54.9)	264 (62.7)	0.71 (0.53–0.94)	0.02

Y si es así… Que pasó a las 24 horas

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Four-component end point‡	103 (24.3)	109 (27.1)	1.00 (0.80–1.24)	0.98
Two-component end point§	56 (13.1)	48 (11.4)	1.18 (0.76–1.82)	0.45
Components of primary end points — no. (%)				
Death at 30 days	15 (3.5)	19 (4.5)	0.77 (0.38–1.53)	0.45
R				5
M				8
U				4
Secon				
D				
				6
Interquartile range	1.6–4.8	1.8–4.9		
Low cardiac output syndrome — no. (%)	78 (18.2)	108 (25.7)	0.62 (0.44–0.88)	0.007
Use of inotrope at or beyond 24 hr after infusion initiation — no. (%)	235 (54.9)	264 (62.7)	0.71 (0.53–0.94)	0.02

Y si es así… Que pasó a las 24 horas

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Lo que viene…

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Sub análisis del levo cts

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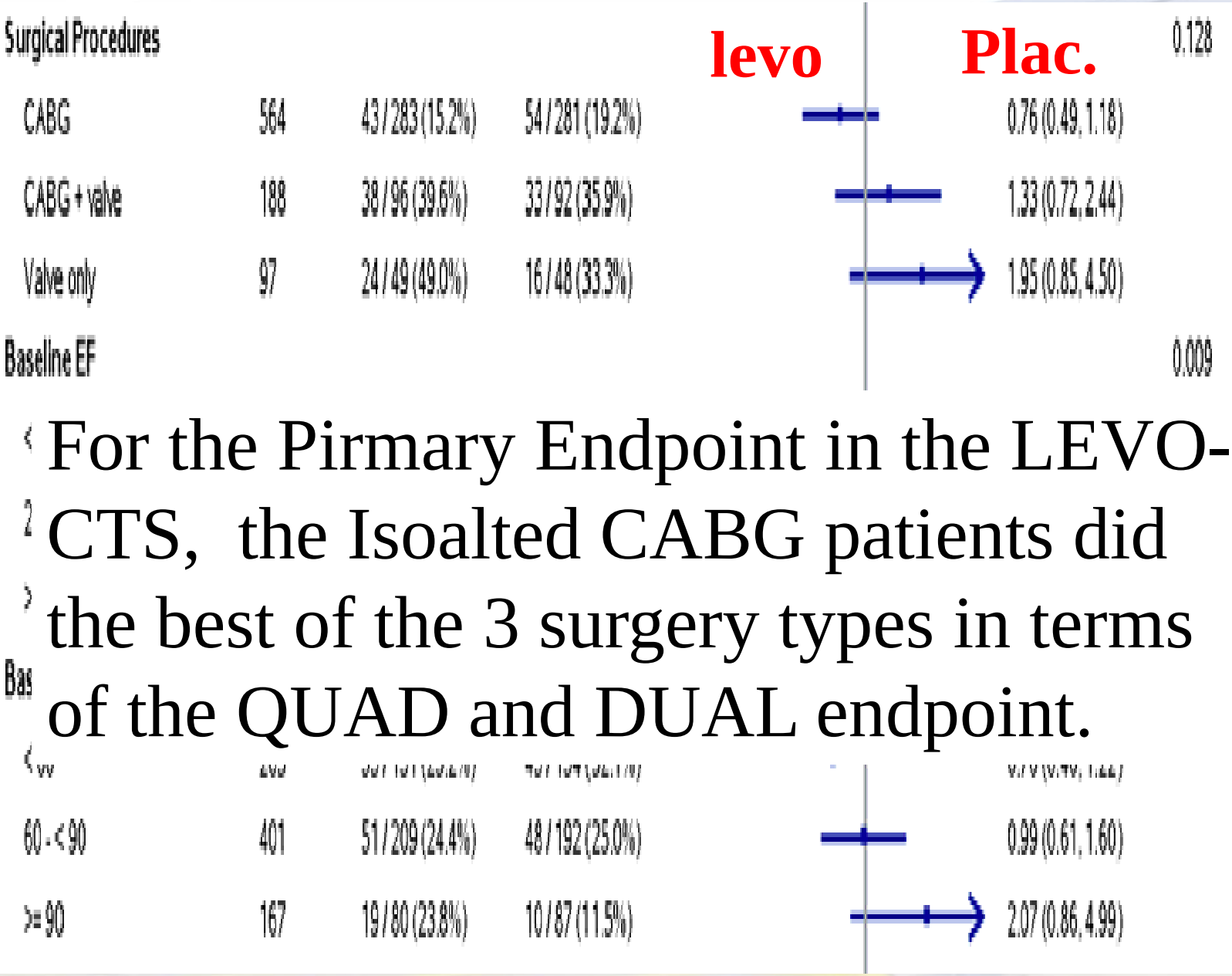

For the Pirmary Endpoint in the LEVO-CTS, the Isoalted CABG patients did the best of the 3 surgery types in terms of the QUAD and DUAL endpoint.

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The mortality trend for 288 Valve patients went in the **other/wrong direction**.This is one of the reasons why we did not meet the primary endpoints for the overall trial.

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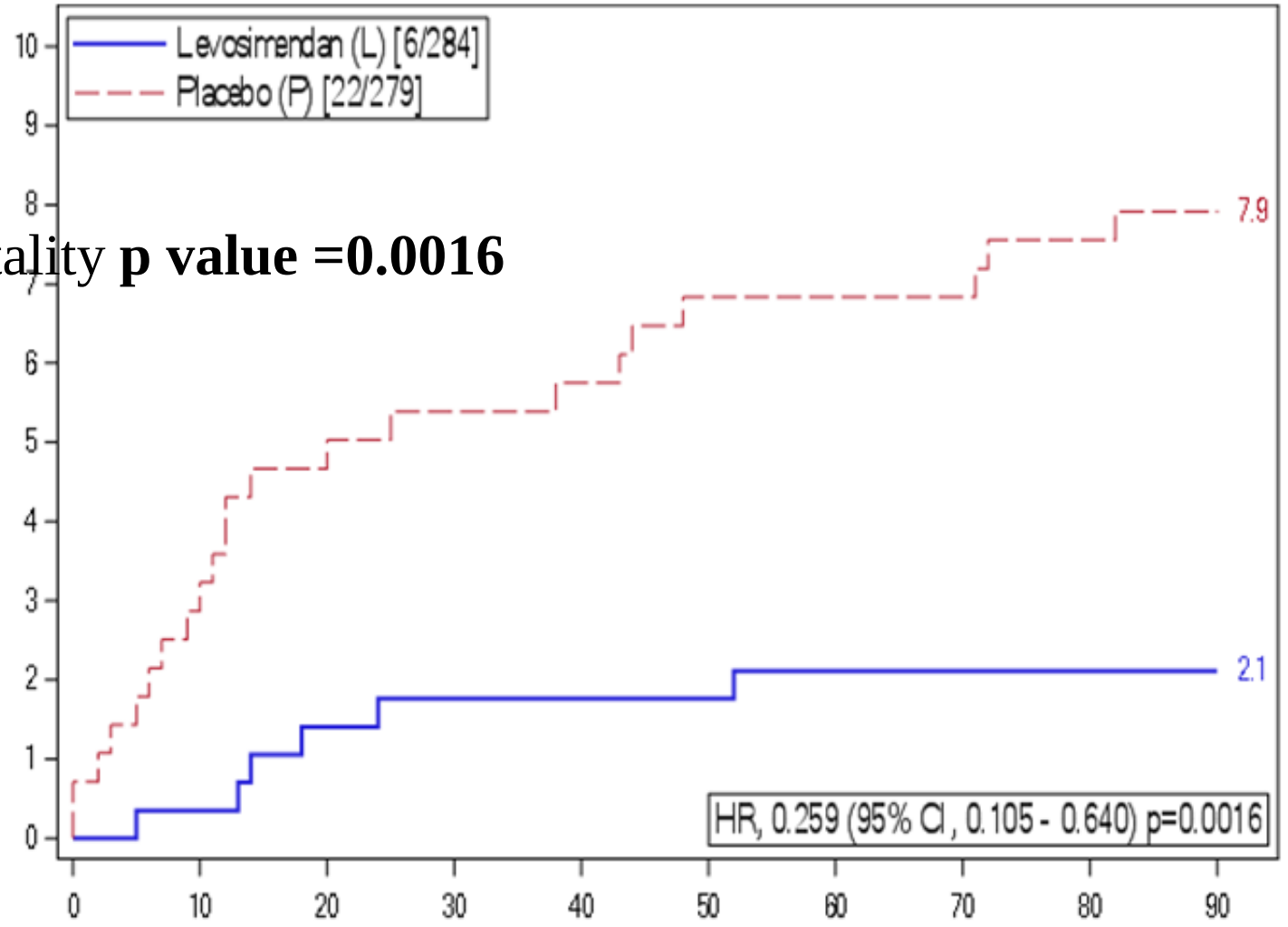
LEVO-CTS
90-Day Mortality in Isolated CABG Patients

The 90-day Mortality **p value =0.0016**



Kaplan-Meier plot of mortality to day 90 (Safety Population, As Treated)
for patients with Isolated CABG

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Levosimendan en coronarios

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Ann Card Anaesth. **2018** Apr-Jun;21(2):123-128. doi: 10.4103/aca.ACA_178_17.

Prophylactic preoperative levosimendan for off-pump coronary artery bypass grafting in patients with left ventricular dysfunction: Single-centered randomized prospective study.

Conclusion:

Preoperative levosimendan helps in successful conduct of OPCAB and reduces the incidence of Low Cardiac OùputS, POAFibril, conversion to CPB, and requirement of intra-aortic balloon pump.

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Int J Cardiol. **2018** Jun 1;260:53. doi: 10.1016/j.ijcard.2018.03.006.

Perioperative levosimendan in cardiac surgery: Positive, neutral, or detrimental effects?

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Clinical studies show that levosimendan effectively improves general and pulmonary haemodynamics in patients undergoing cardiac surgery, thereby reducing the need for inotropic agents and mechanical circulatory support, and additionally optimising renal and hepatic function. In general, the length of stay on the ICU and in the hospital is shortened. Overall, levosimendan treatment is considered as a kind of “safety net” in the surgical setting

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MUCHAS GRACIAS POR SU ATENCIÓN

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