

Fármacos inotrópicos

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Universidad Abierta Interamericana

A black and white photograph of a hand in a dark suit sleeve moving a chess king piece on a chessboard. The background is a light blue gradient. The text is overlaid in a large, yellow, serif font.

Mas vale una
estrategia
inotrópica que
un inotropico

Inotropismo

D/P D/T

*Ley de Starling y
Ley de Laplace*

**Volumen
Sistólico**

Lusitropismo

Precarga y post carga

05.03.0006 12.04.14
Osteira
Frequ.: 1.7 MHz @ 5 MHz
FPS: 19.8
Cycle: 16.0 cm



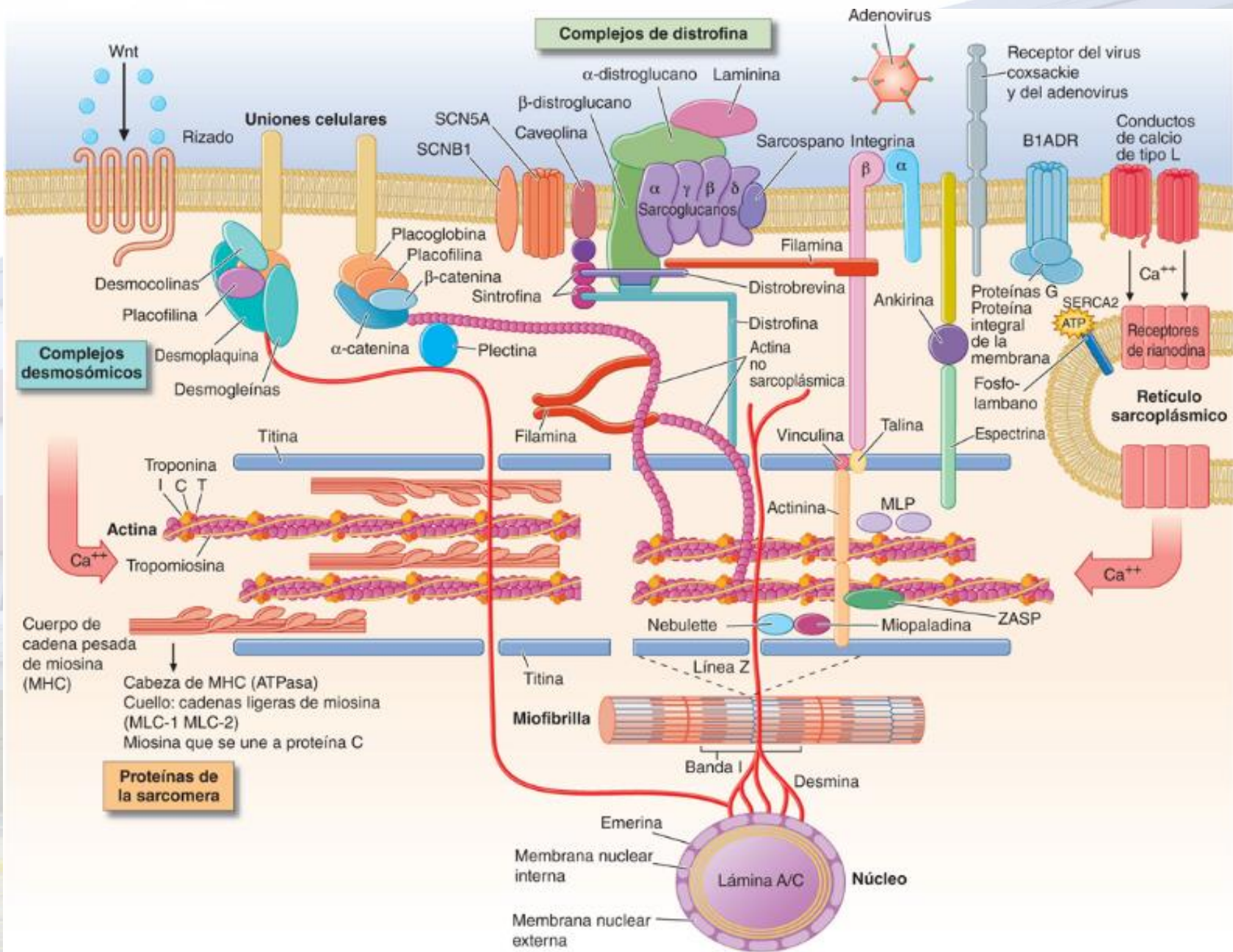
EL INOTROPISMO

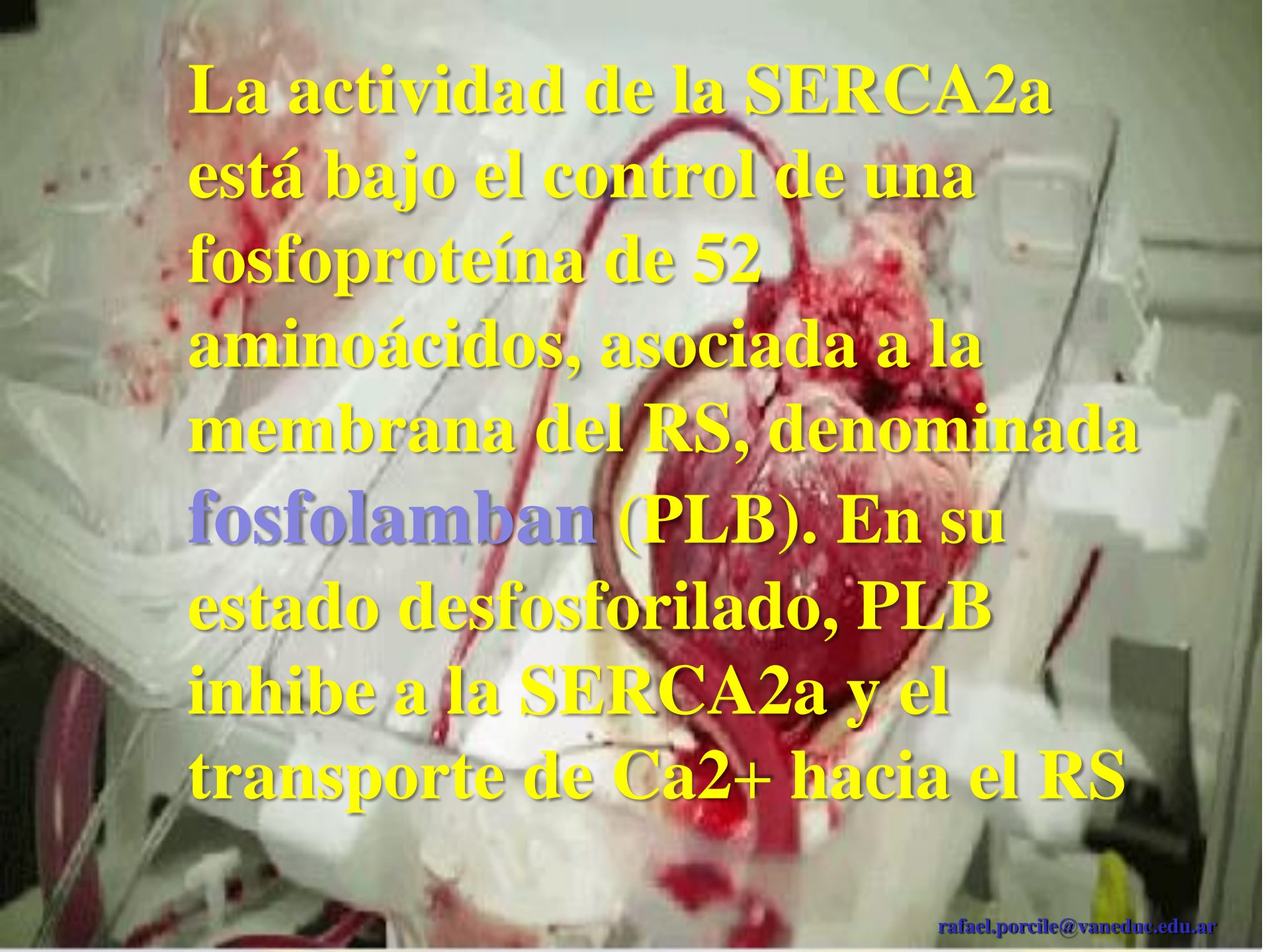


Calcium Signaling and Transcriptional Regulation in Cardiomyocytes

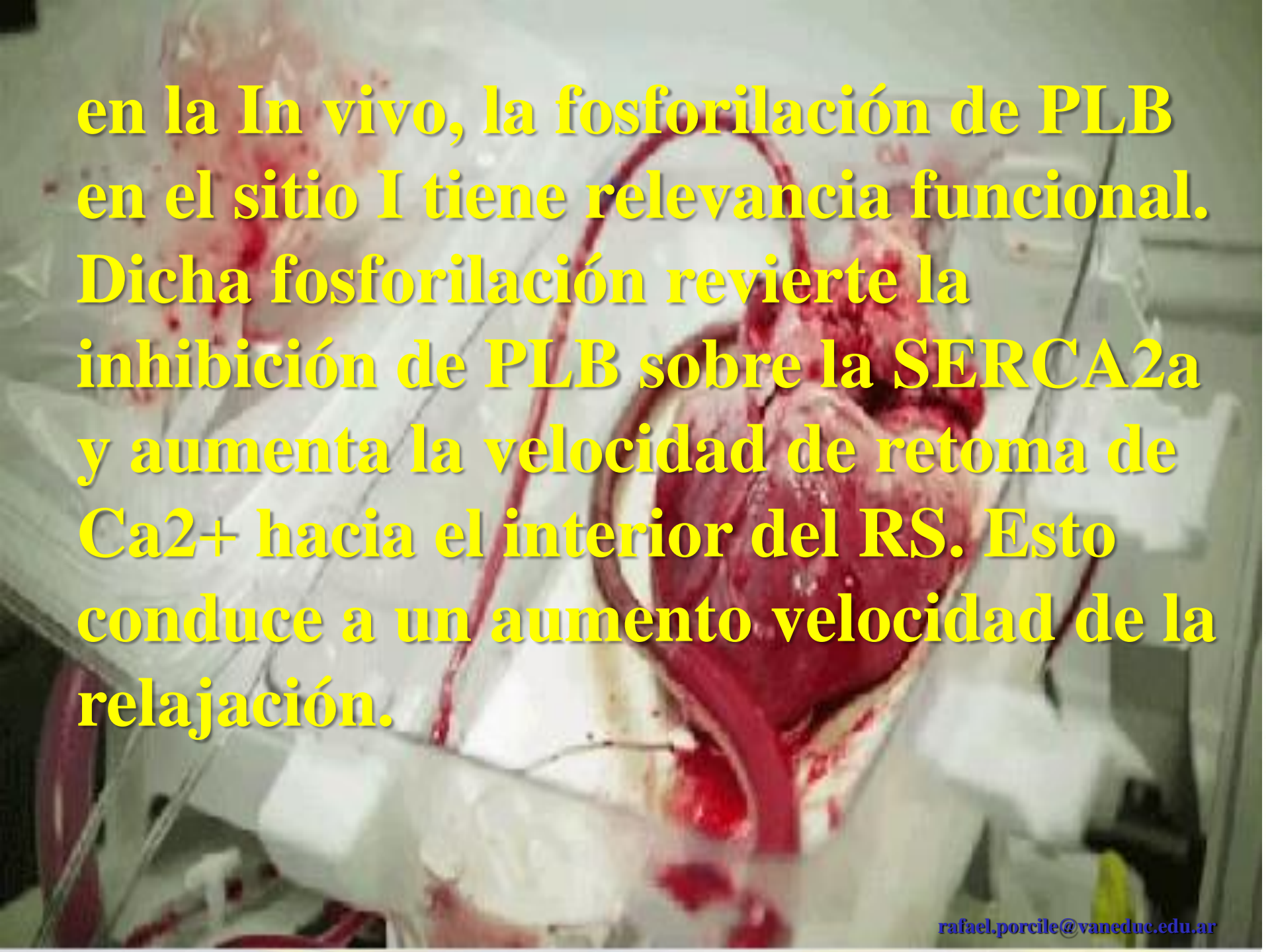
Circulation Research September 29, 2017

Given ***the central role of Ca_{2+} in controlling EC coupling***, a strict regulation of Ca_{2+} -handling is crucial for cardiac function.



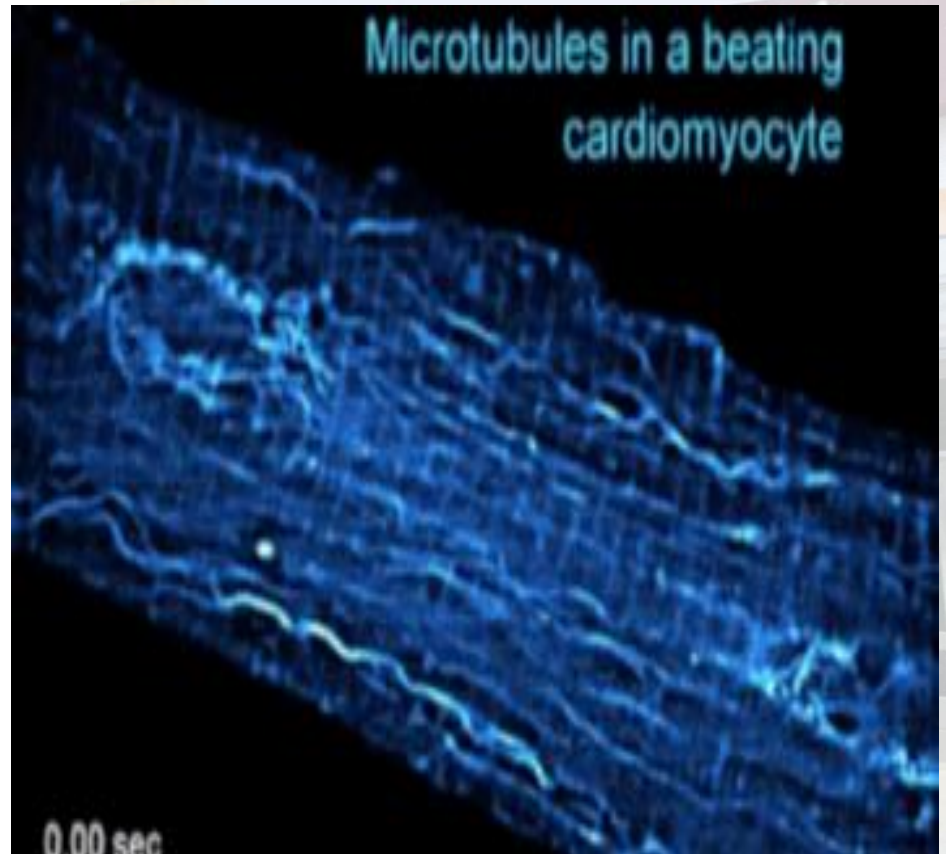
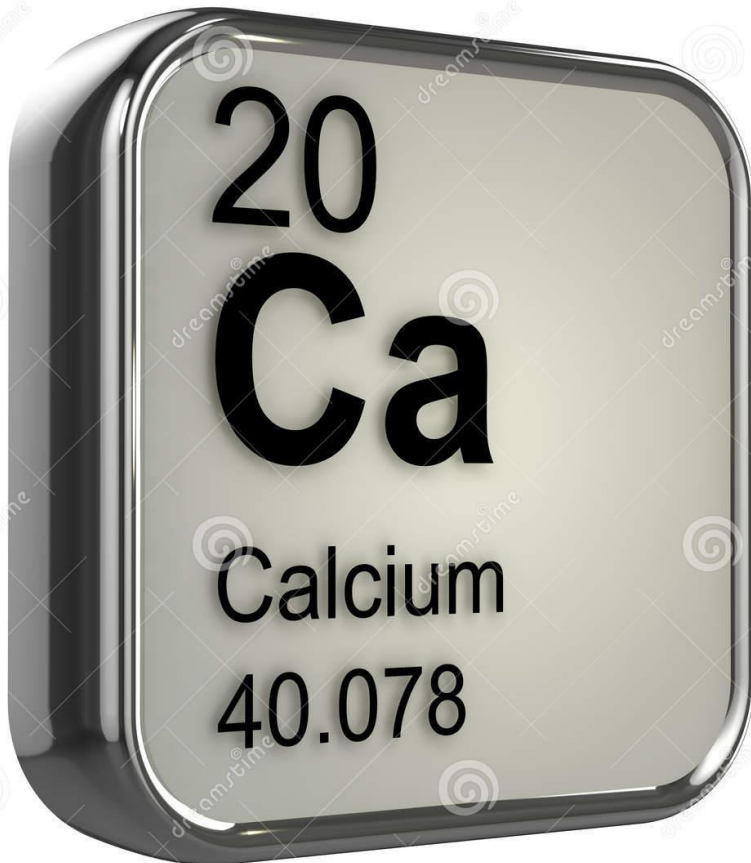


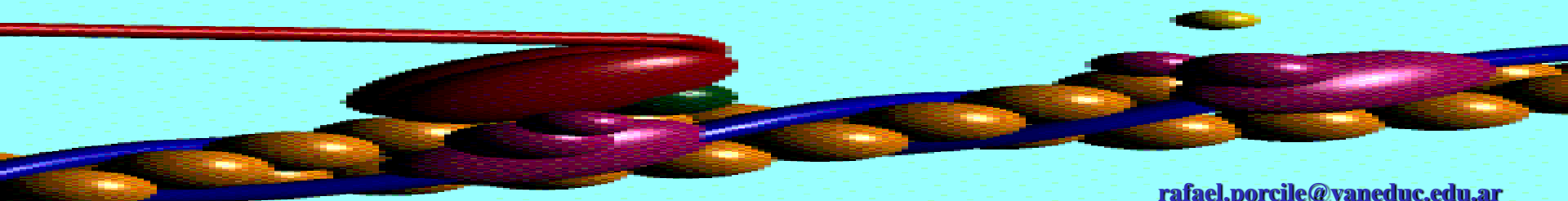
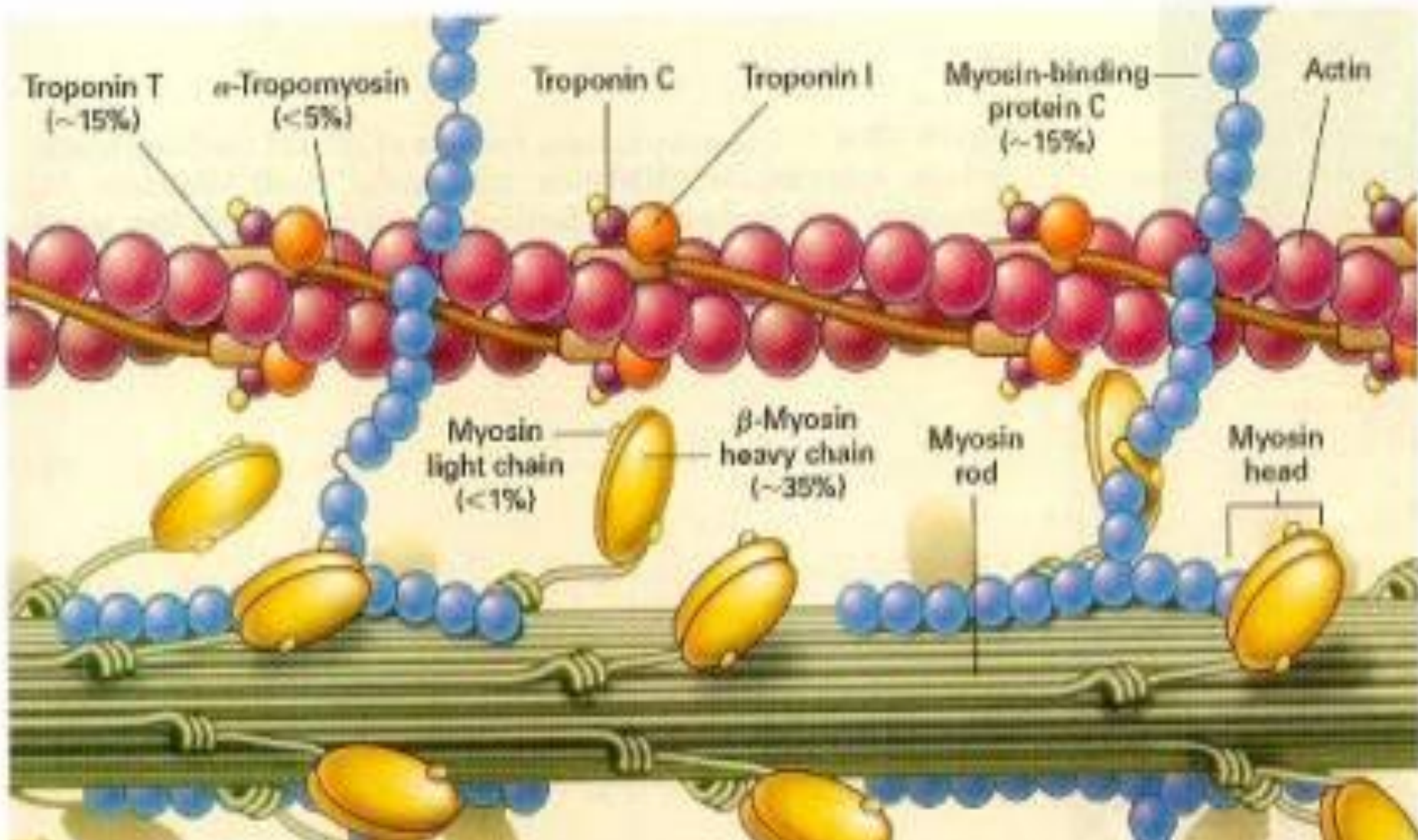
La actividad de la SERCA2a está bajo el control de una fosfoproteína de 52 aminoácidos, asociada a la membrana del RS, denominada **fosfolamban (PLB)**. En su estado desfosforilado, PLB inhibe a la SERCA2a y el transporte de Ca^{2+} hacia el RS

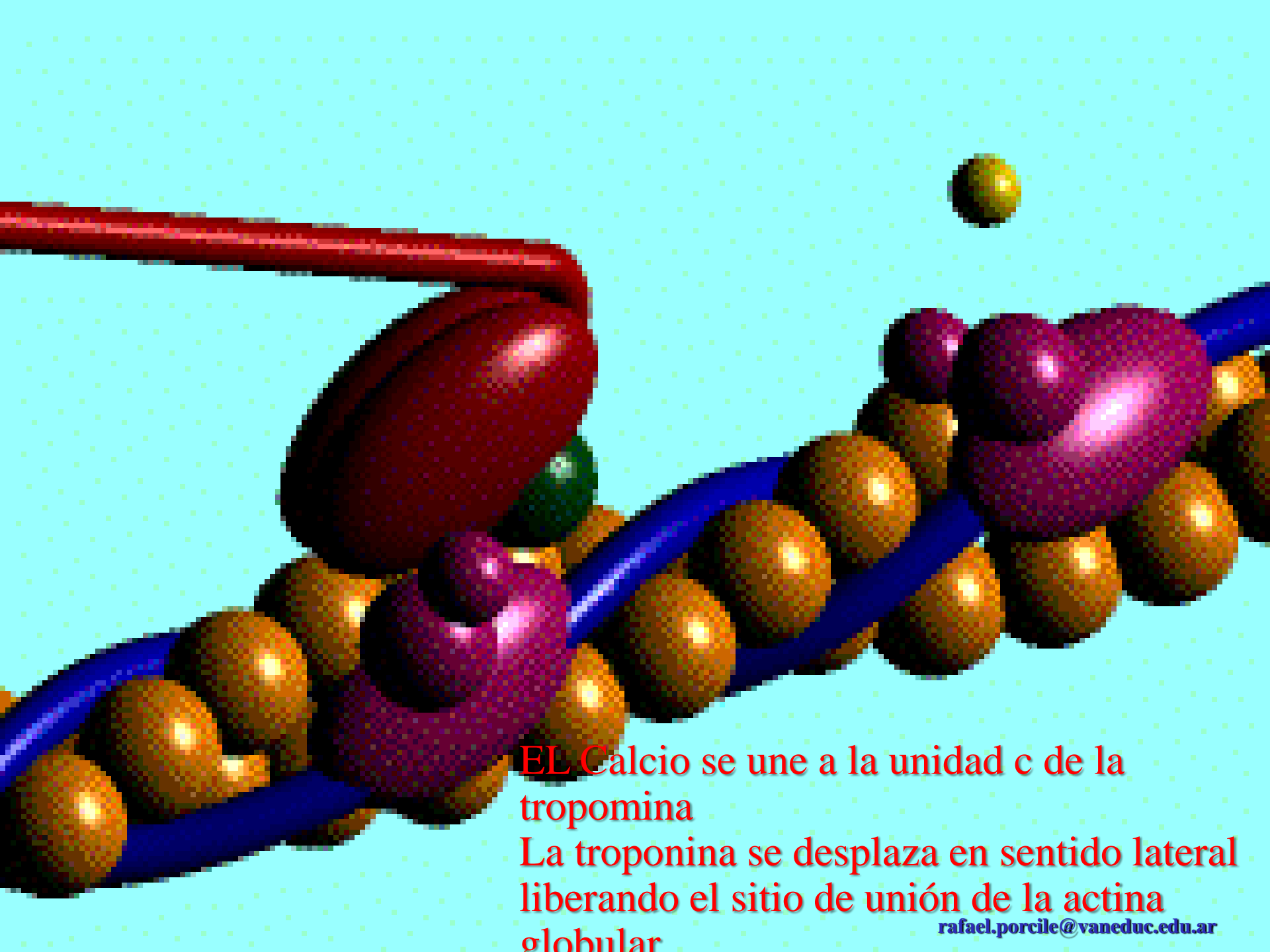


en la In vivo, la fosforilación de PLB en el sitio I tiene relevancia funcional. Dicha fosforilación revierte la inhibición de PLB sobre la SERCA2a y aumenta la velocidad de retoma de Ca^{2+} hacia el interior del RS. Esto conduce a un aumento velocidad de la relajación.

Del Calcio a la contracción






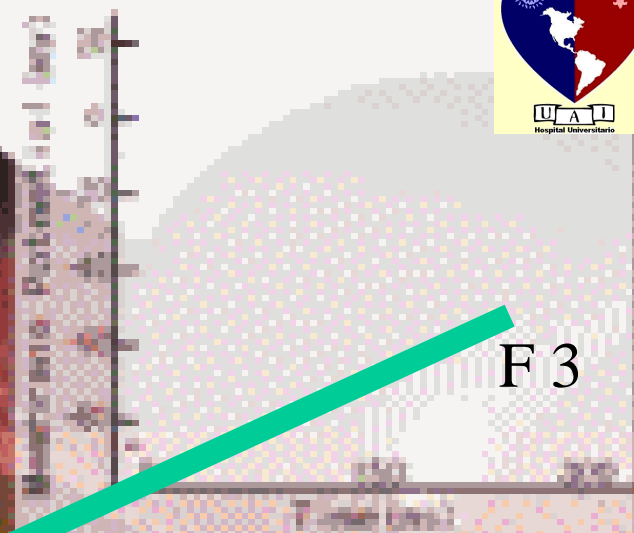
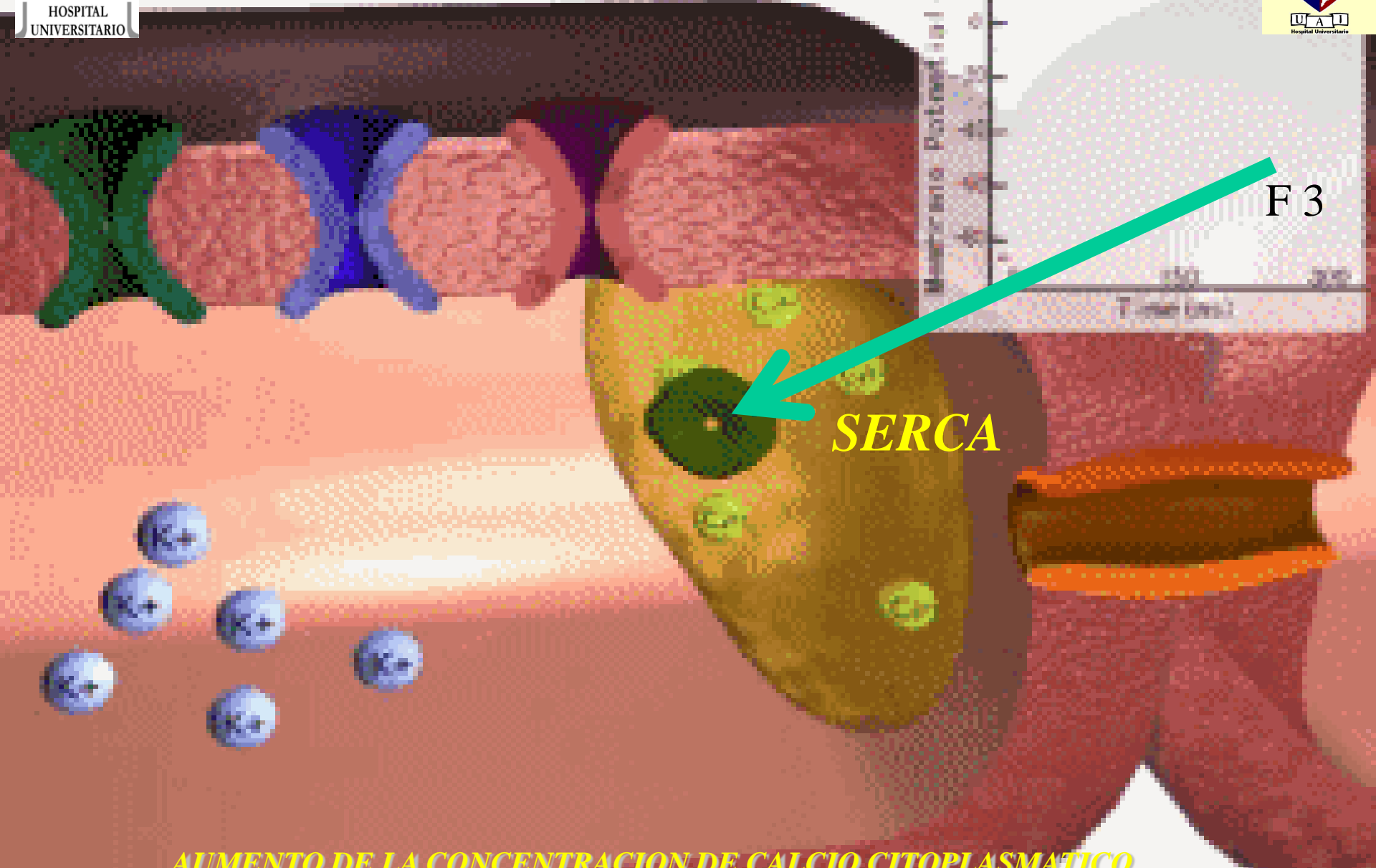


EL Calcio se une a la unidad c de la tropomina


La troponina se desplaza en sentido lateral liberando el sitio de unión de la actina globular



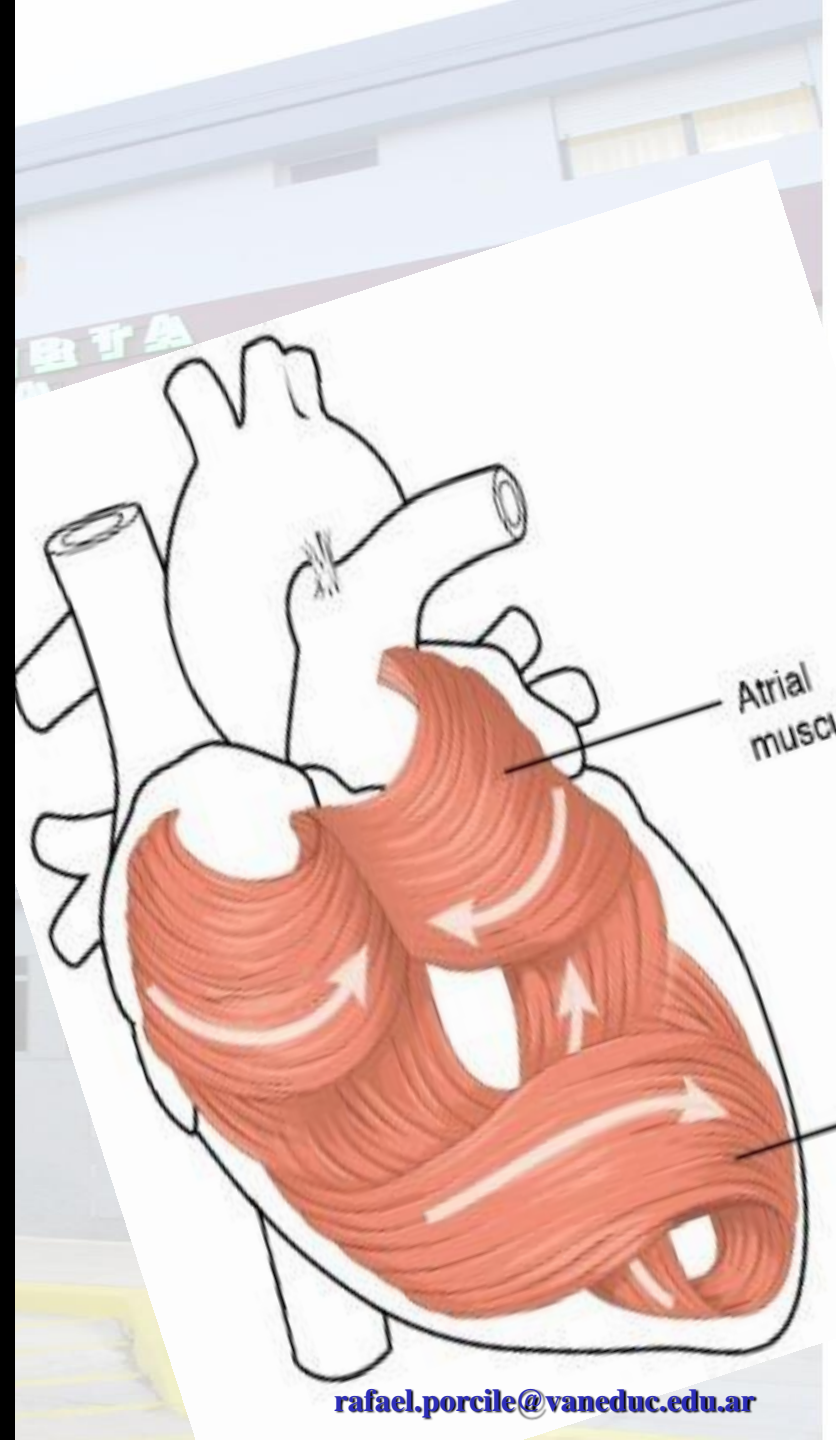
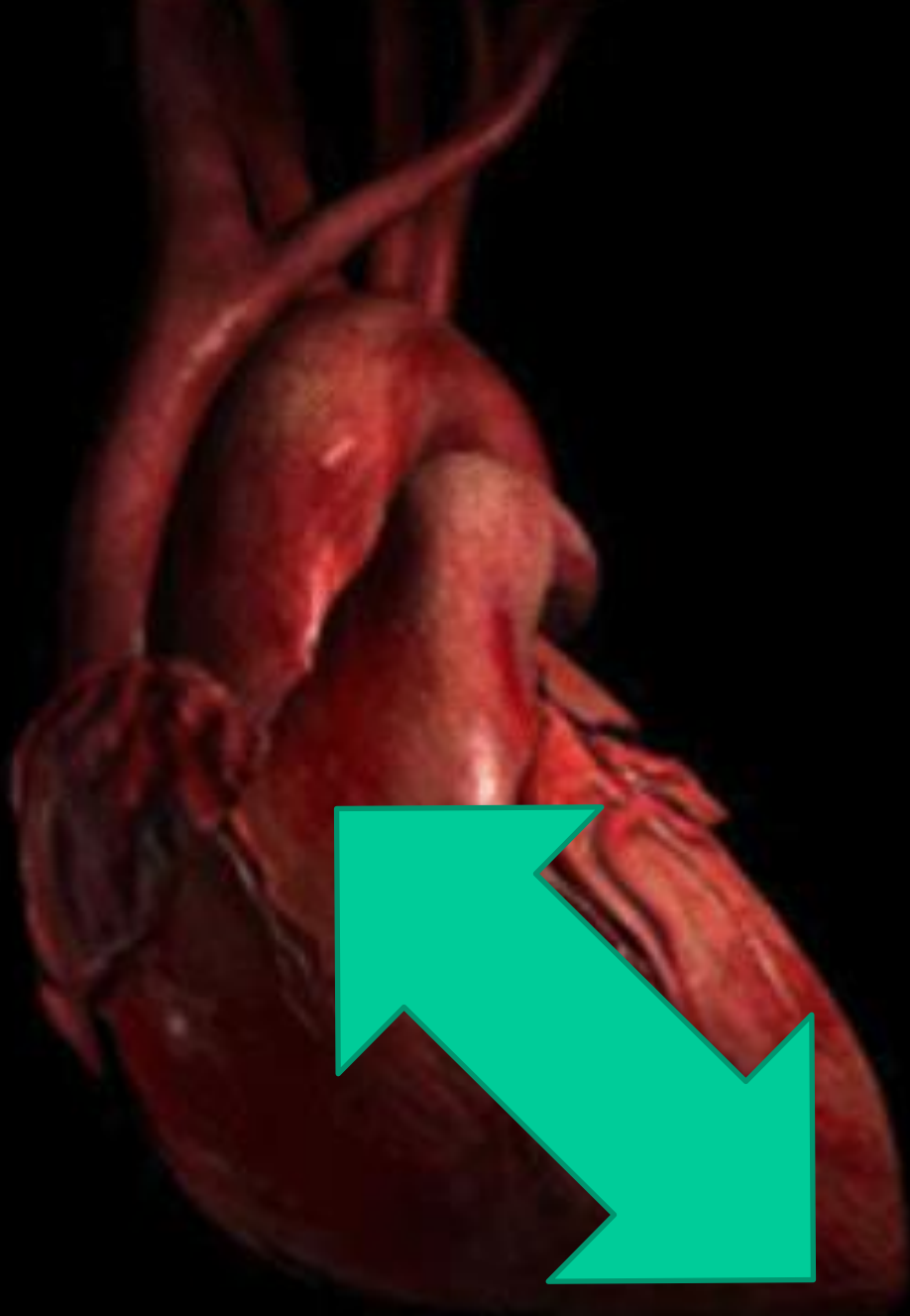
Luego, la relajación es provocada por la disminución del Ca^{2+} citosólico. Esto es llevado a cabo principalmente por la bomba Ca^{2+} -ATPasa (SERCA2a) del RS que retoma el Ca^{2+} hacia el interior de esta organela, y en menor proporción por el intercambiador $\text{Na}^{+}/\text{Ca}^{2+}$ (NCX), que extruye Ca^{2+} hacia el espacio extracelular.



AUMENTO DE LA CONCENTRACION DE CALCIO CITOPASMATICO



**El Ca es bombeado de
regreso al retículo
sarcoplasmico
Se libera el Ca de la
troponina c
Cesa la interacción entre
actina y miosina**

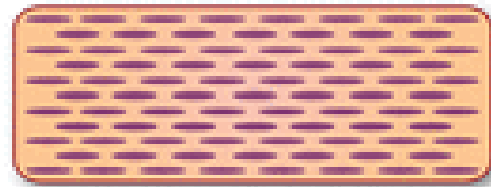
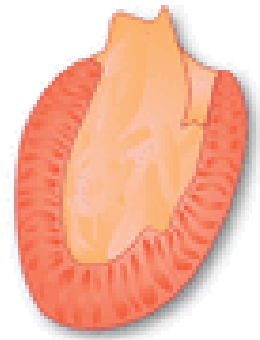
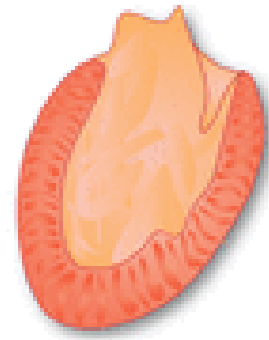


Diastole

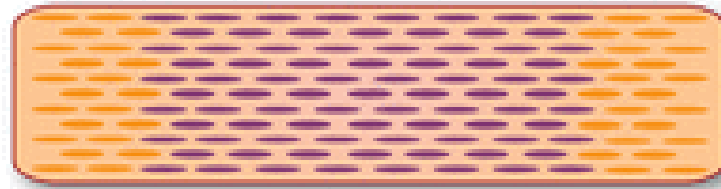
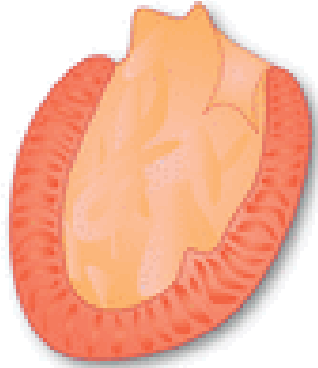
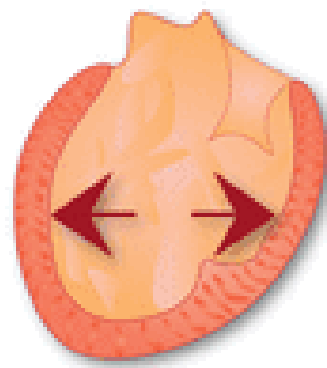
Systole

Myocyte architecture

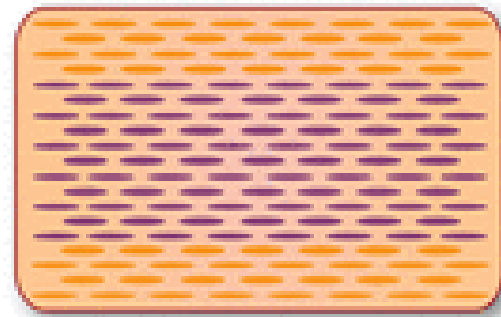
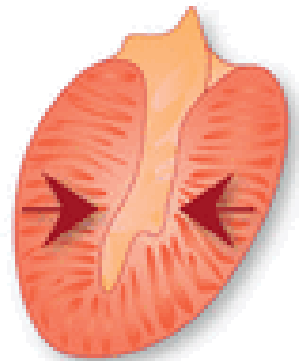
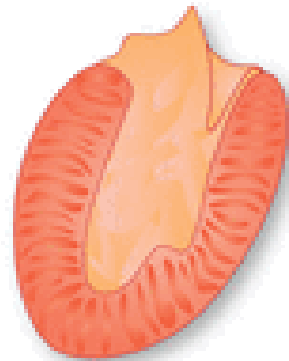
Normal



Dilated



Concentric hypertrophy



INOTROPISMO : V MAX

- **MAXIMA VELOCIDAD DE CONTRACCIÓN CUANDO LA FIBRA NO ESTA EXPUESTA A CARGA (CONTR ISOTONICA)**
 - NO PUEDE SER MEDIDA DIRECTAMENTE
 - SE EVALUA LA dP/dT
- **LONGITUD MUSCULAR DE REPOSO**
 - LEY DE FRANK STARLING
- **MECANISMO BETA ADRENERGICO**
 - AUMENTO POR AUMENTO DEL INFLUJO DE CALCIO

Relación dP/dt

- Velocidad con la cual el ventrículo logra desarrollar cambios de presión
- La máxima dP/dt se logra al final de la CIS antes de la apertura valvular aortica
- Es el mejor indicador de trabajo ventricular
- Se retrasa con el deterioro inotrópico pudiendo producirse aun después de la apertura aortica con gran perdida de la eficiencia contráctil

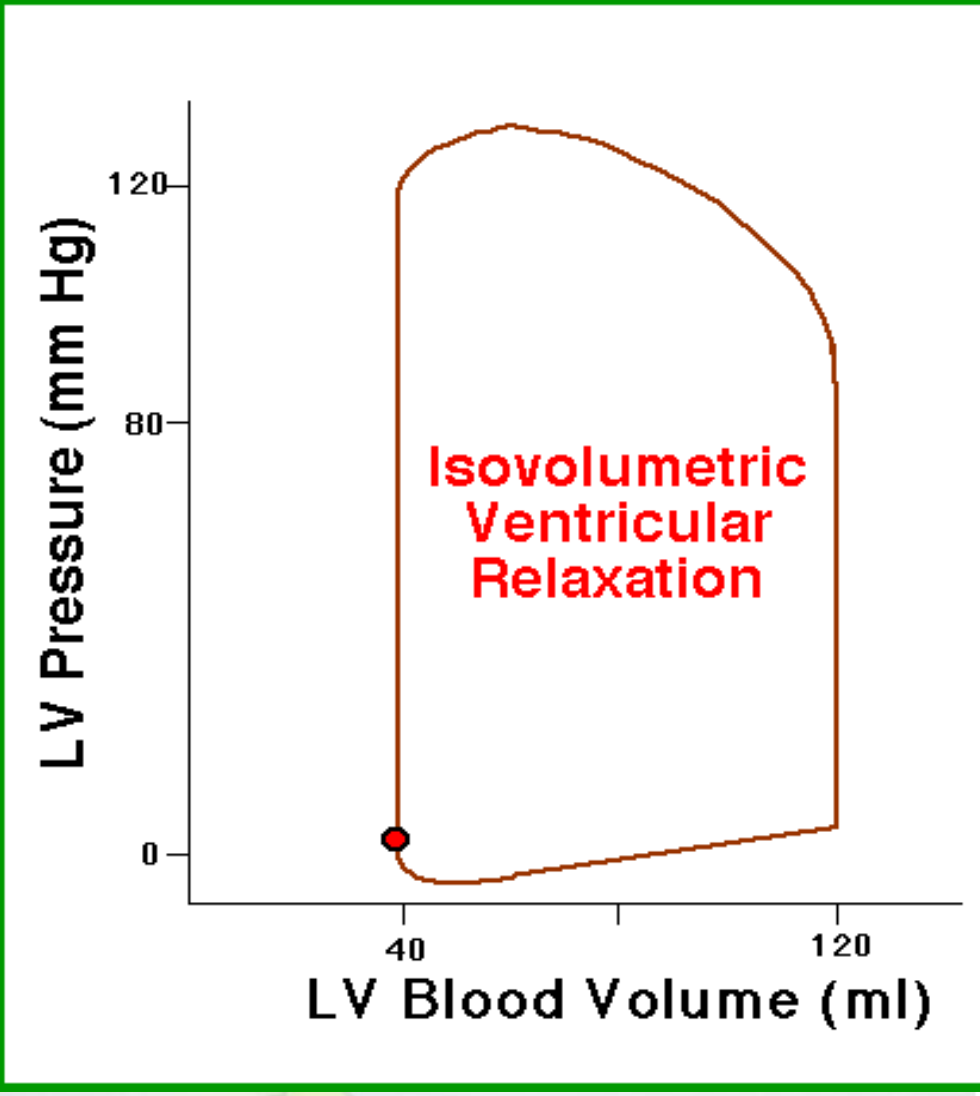
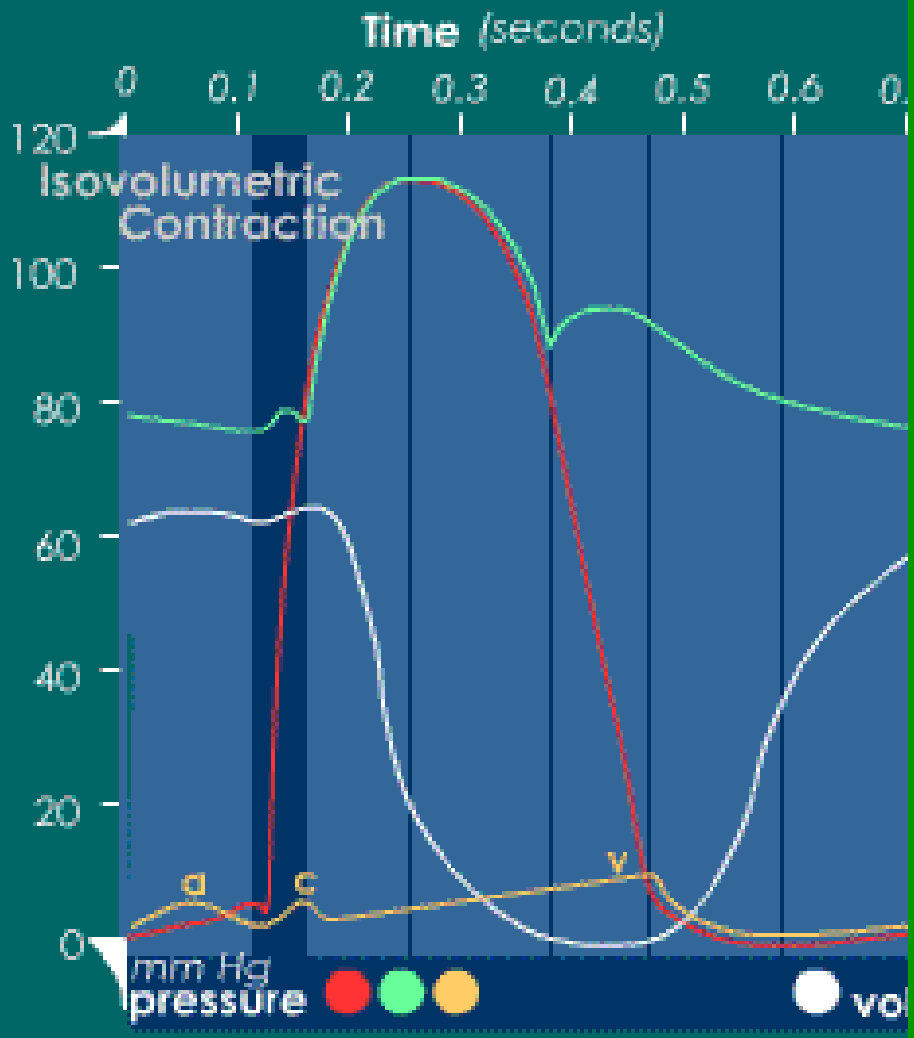
Valoración no invasiva de la función ventricular izquierda

$$dP/dT = 32 \times 1000 / 60 = 533 \text{ mm Hg/seg}$$

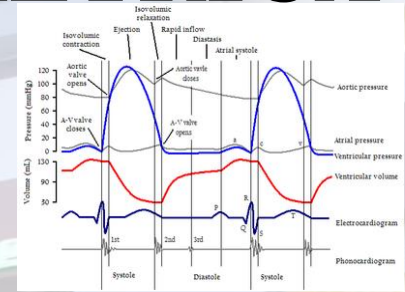
¿Que es esto...?



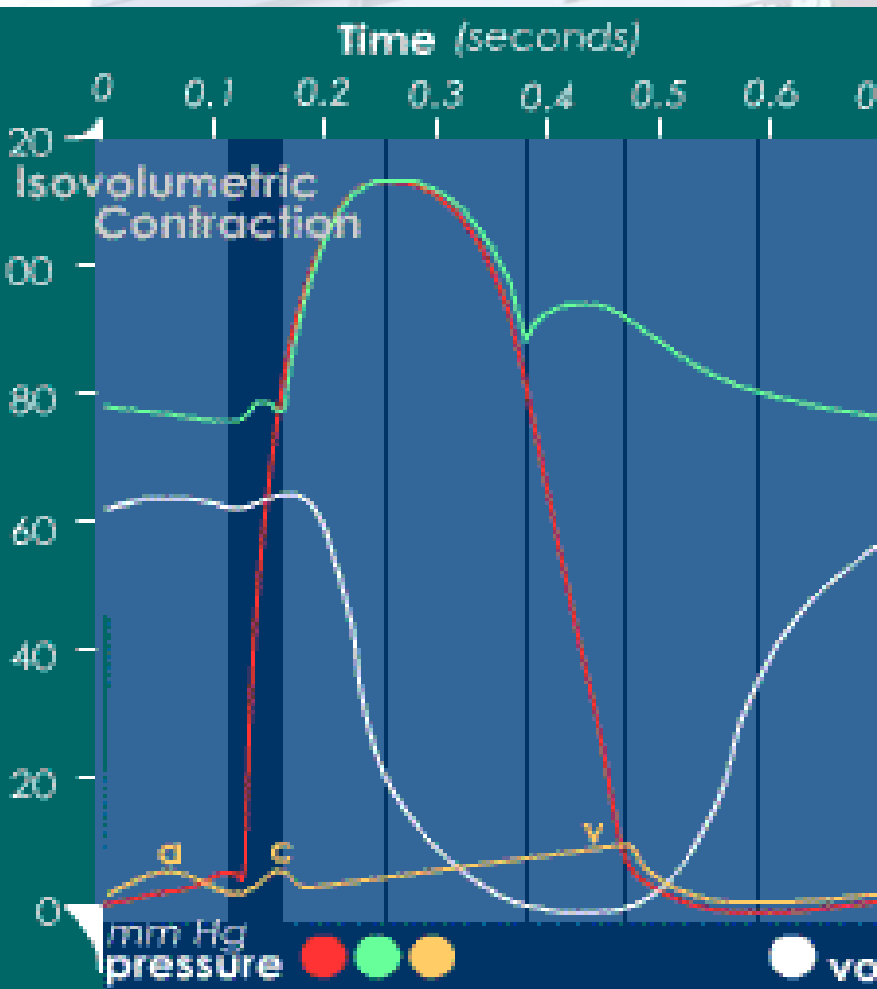
Tiempo Fig 10



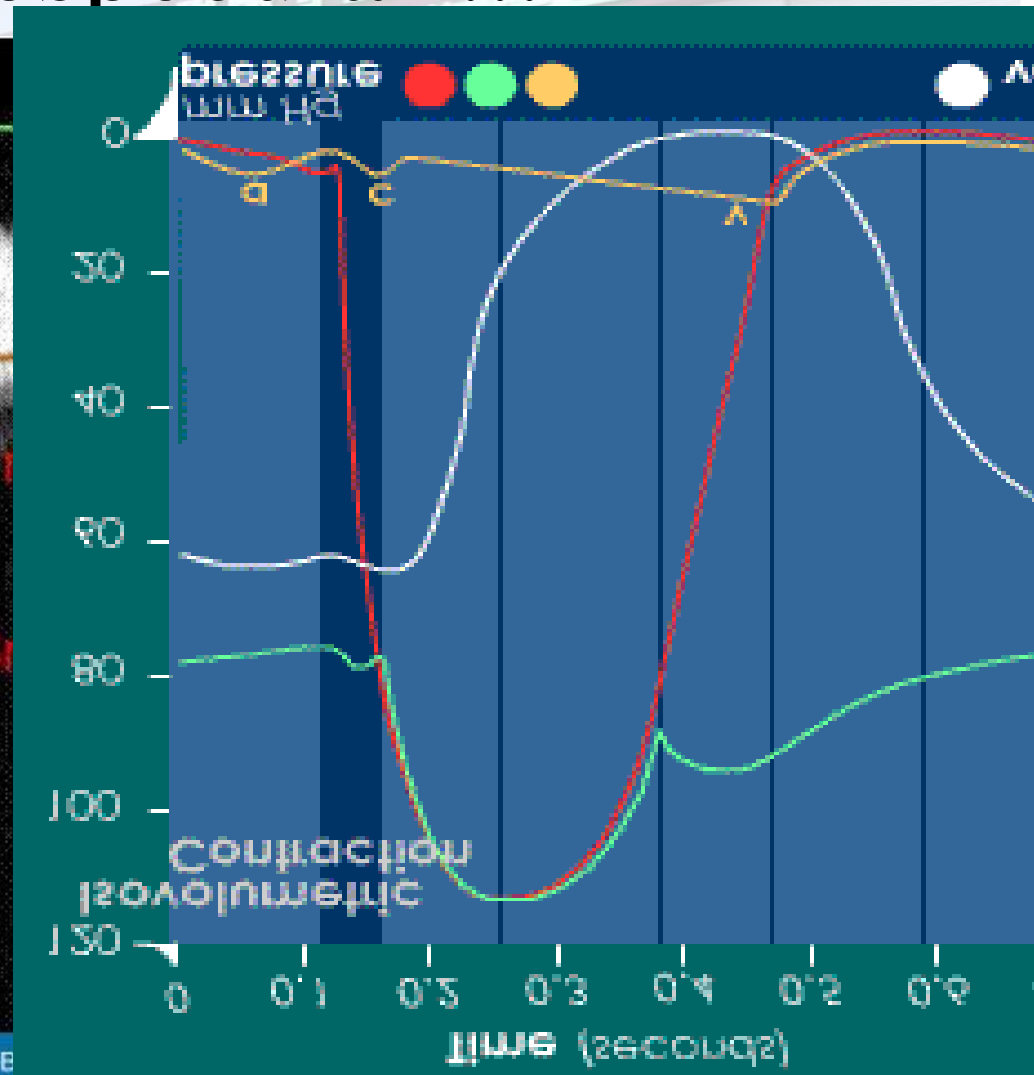
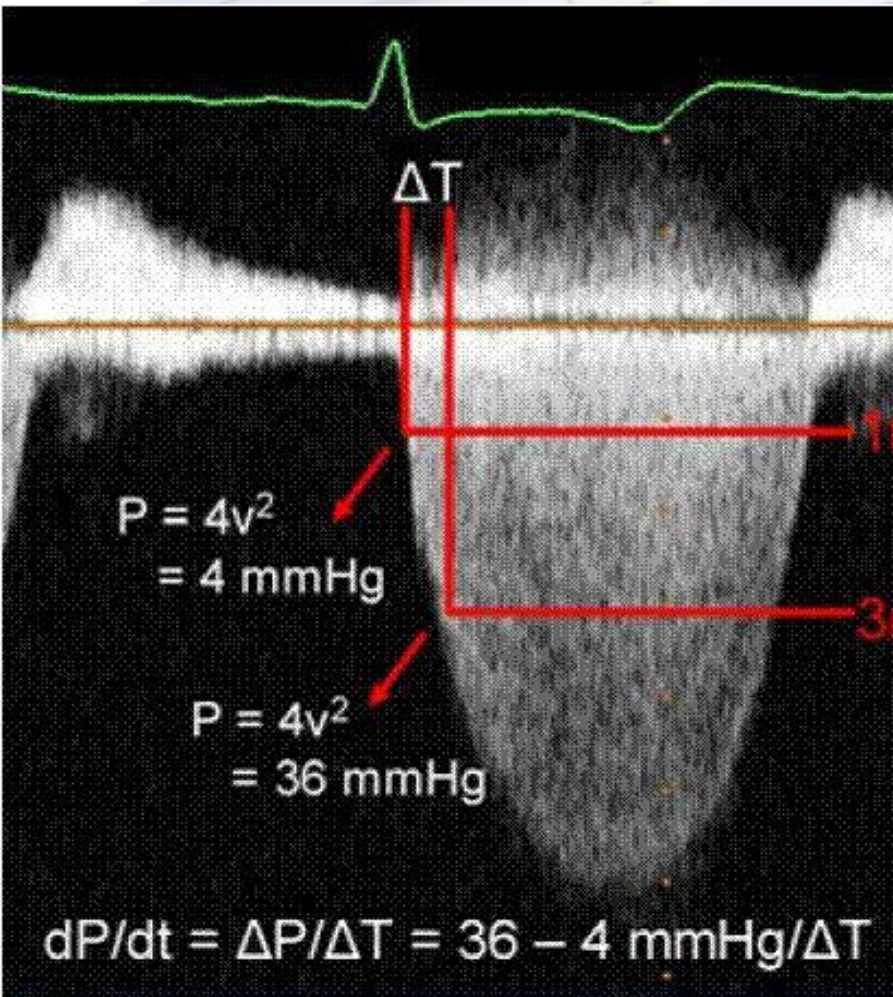
CONTRACCIÓN ISOVOLUMETRICASISTÓLICA

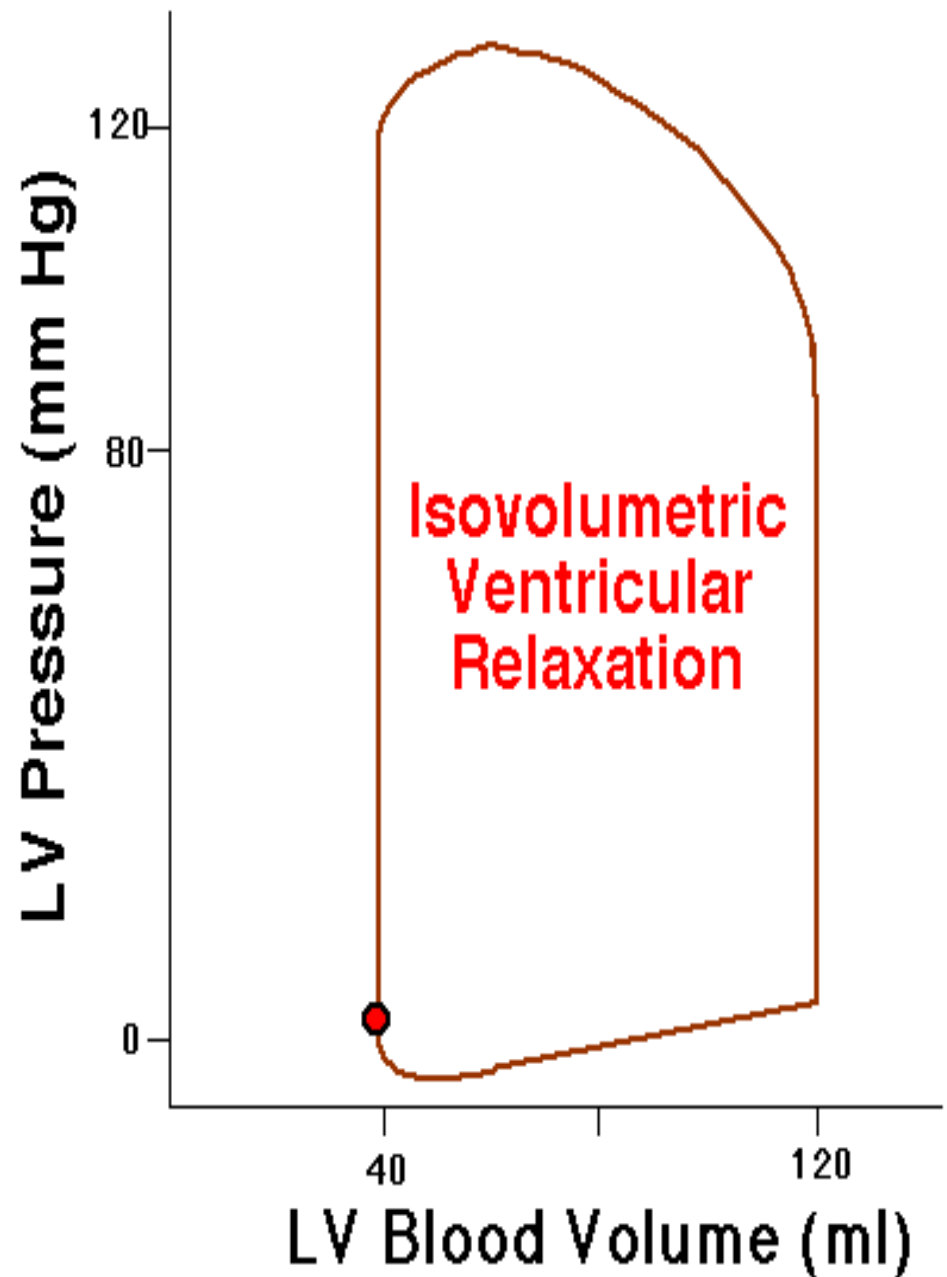
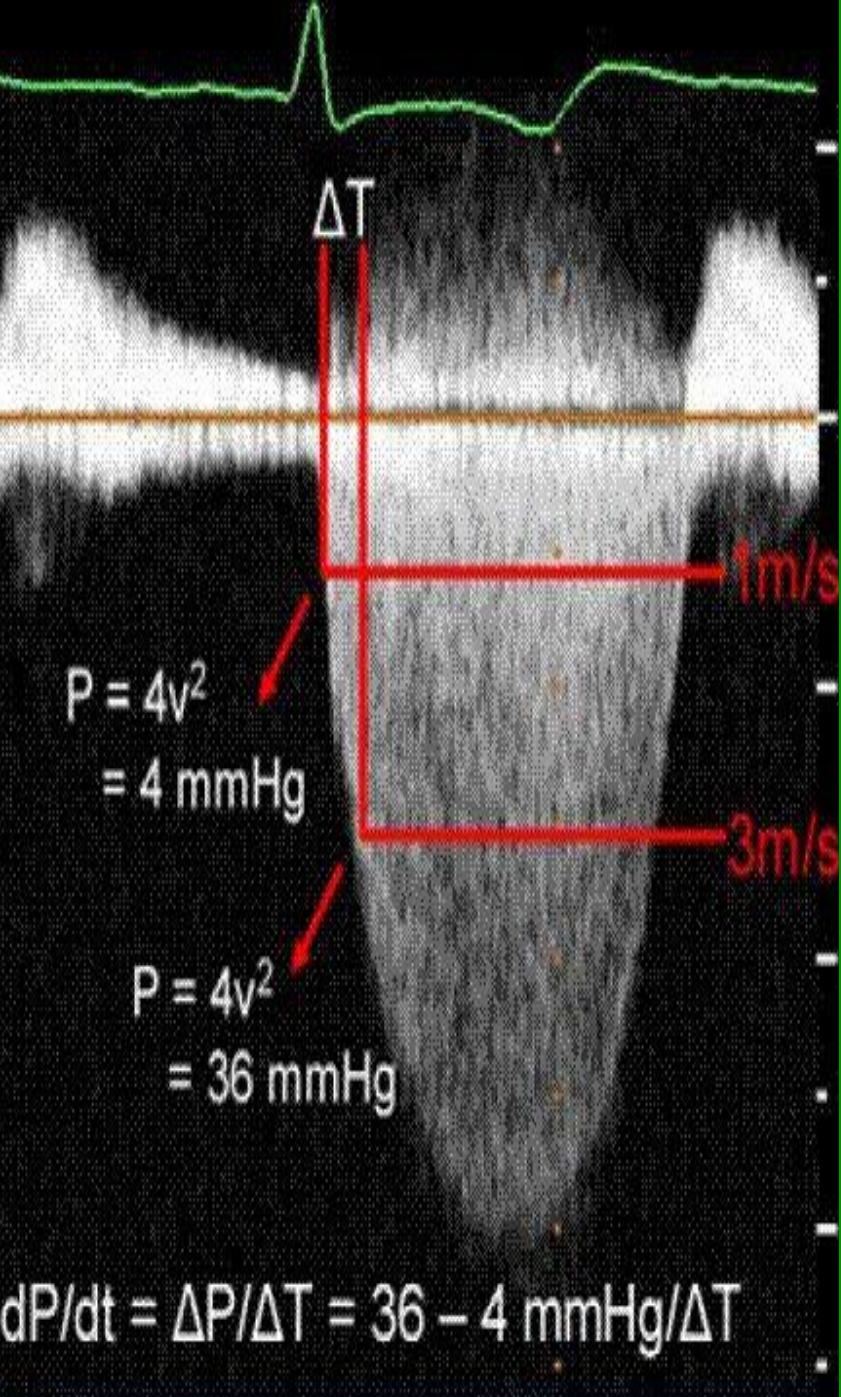


- LAS VALVULAS V/A CIERRAN CUANDO LA PRESIÓN (ROJO) SUPERA LA PRESION EN LA AURICULA (AMARILLO).
- EL VENTRICULO SE CONTRAE SIN CAMBIOS DE VOLUMEN ACERCANDO LA PRESIÓN A LA ARTERIAL (VERDE).

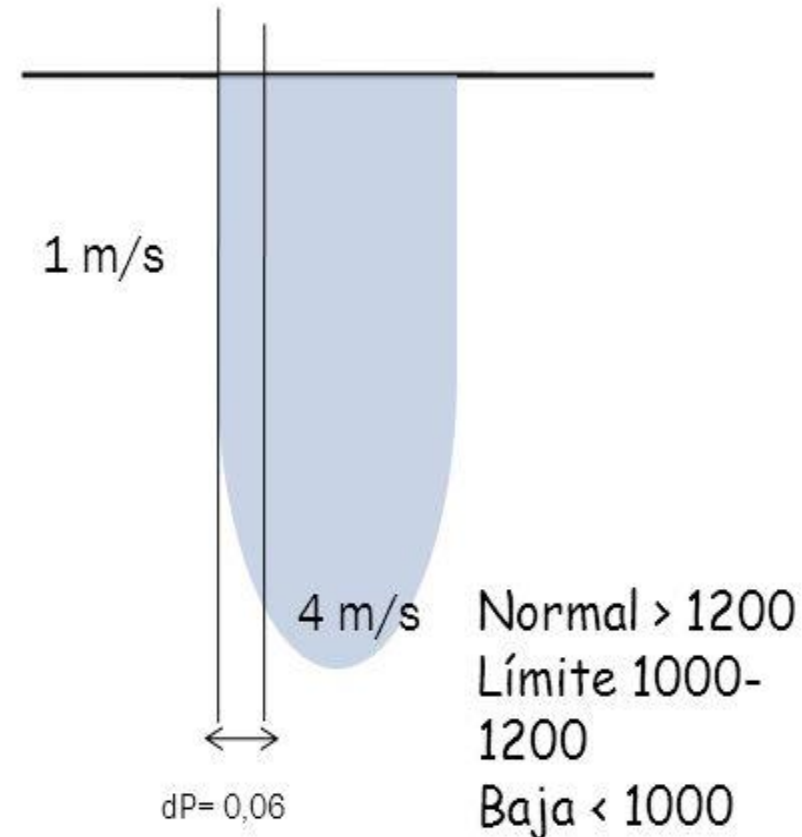


Así lo ve el doppler pulsado... al revés y especular ...





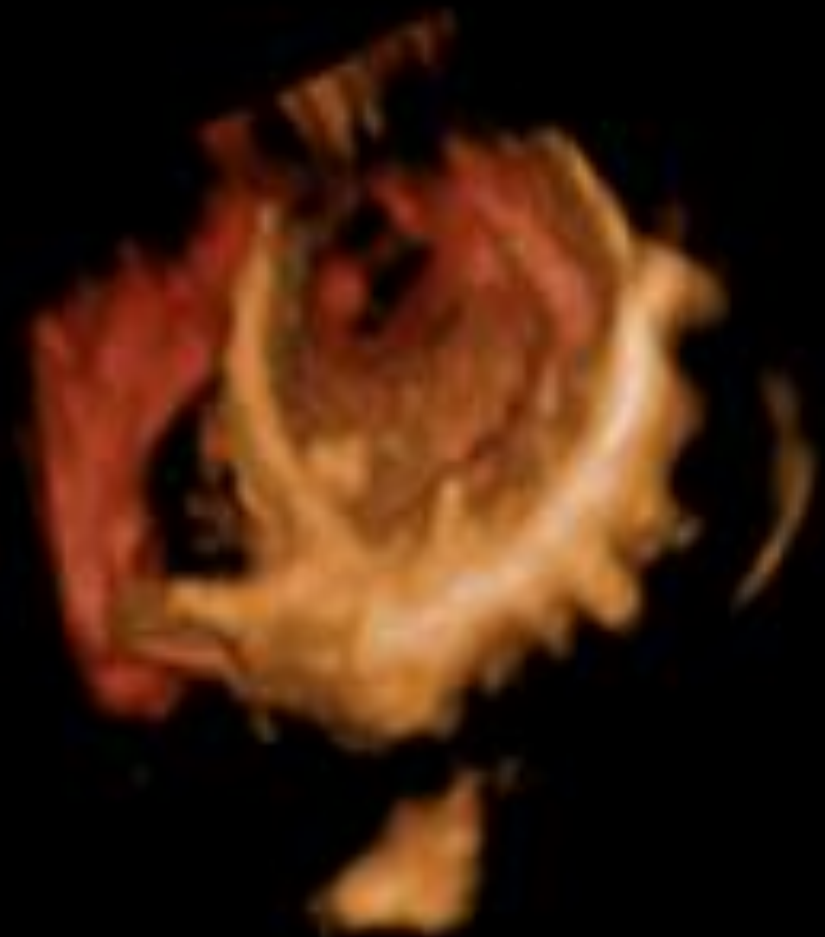
- Índice de contractilidad miocárdica.
- Método de Bargiggia (1 a 3 m/s o 1 a 4 m/s).
- Diferencia de presión.



$$\frac{dP}{Dt} = \frac{64 - 4}{0,06} = \frac{60}{0,06} = 1000$$

05.03.0006 12.04.14
Osteve
Frequ.: 1.7 MHz @ 5 MHz
FPS: 19.8
Cycle: 16.0 cm

V

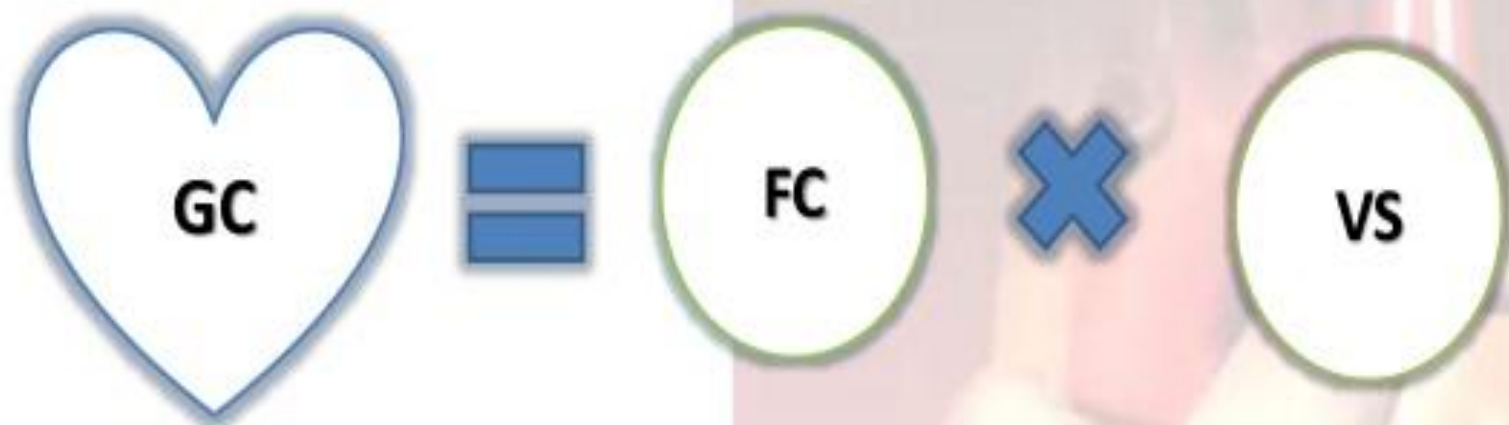


Inotropismo

D/P D/T

**Volumen
Sistólico**

Precarga y post carga



Variables que modifican el volumen sistólico

PRECARGA

POSCARGA

CONTRACTIBILIDAD

PRECARGA

- Volumen telediastólico del ventrículo

POSTCARGA

- Tensión de la pared ventricular durante la sístole

POST CARGA

POSTCARGA

- ◆ Carga ulterior al inicio de la contracción, contra la cual el Ventrículo Izquierdo se contrae durante la expulsión.



TIPOS DE CONTRACCIÓN

- CONTRACCIÓN ISOMETRICA

- CONTRACCIÓN ISOTONICA



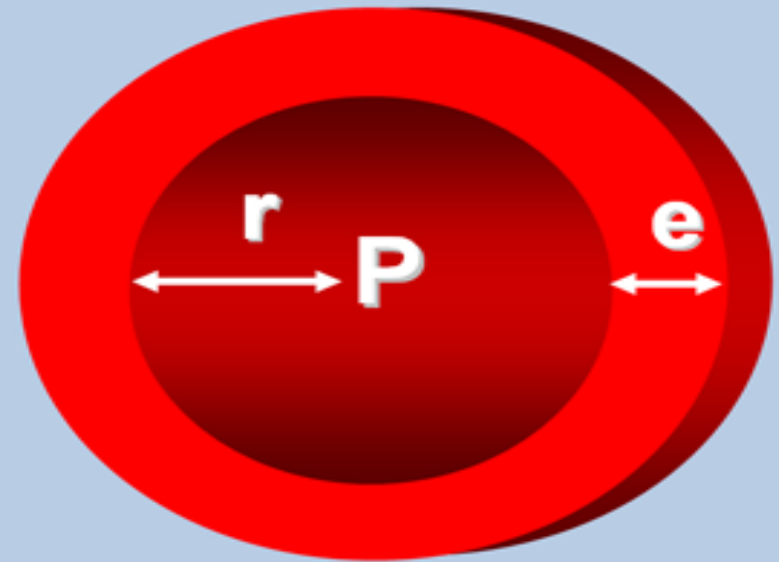
POST CARGA

$$T = \frac{p \times r}{2E}$$



STRESS PARIETAL

$$T_{\text{pared}} = \frac{P \times r}{2e}$$

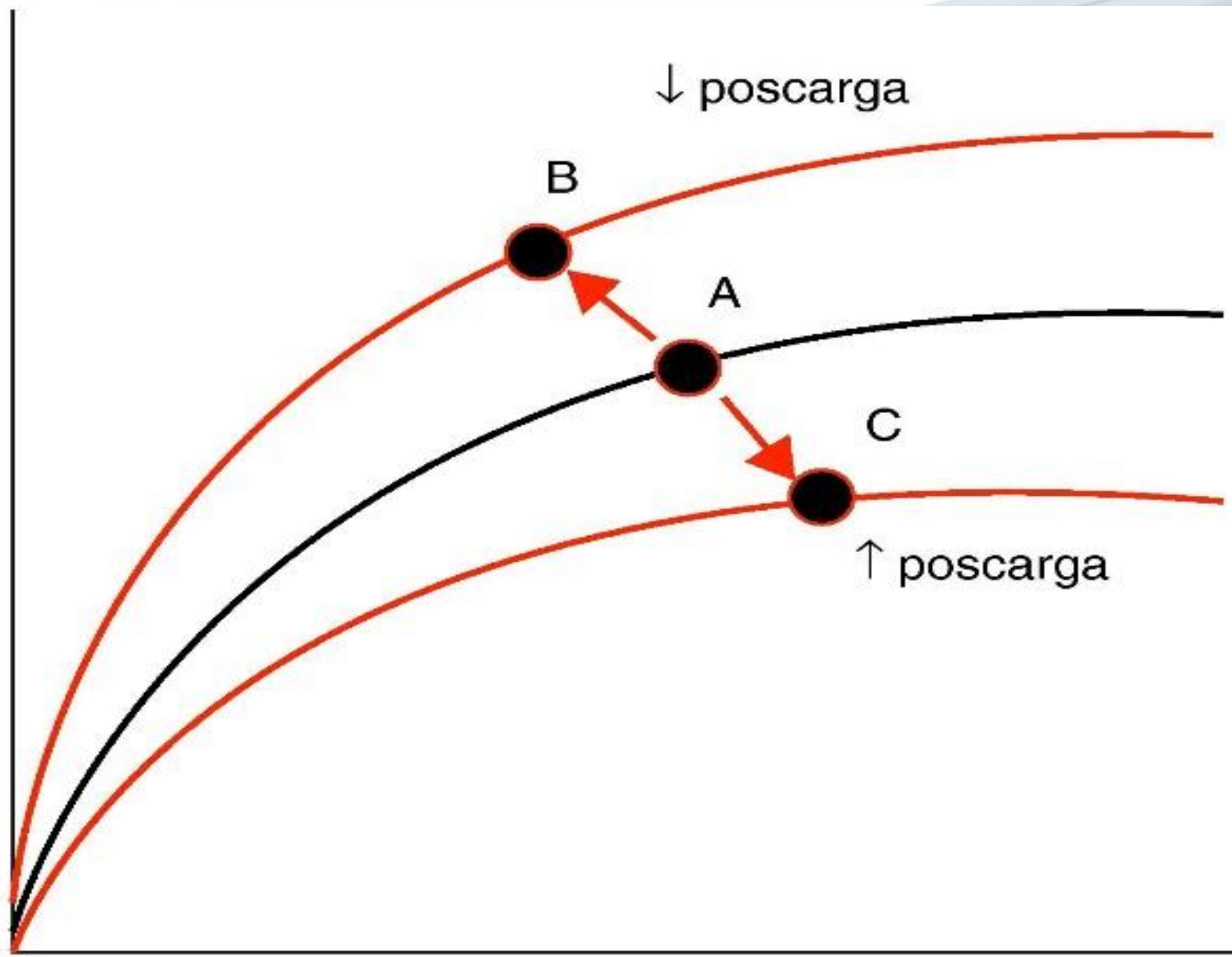


Ley de Laplace

Ley de Laplace

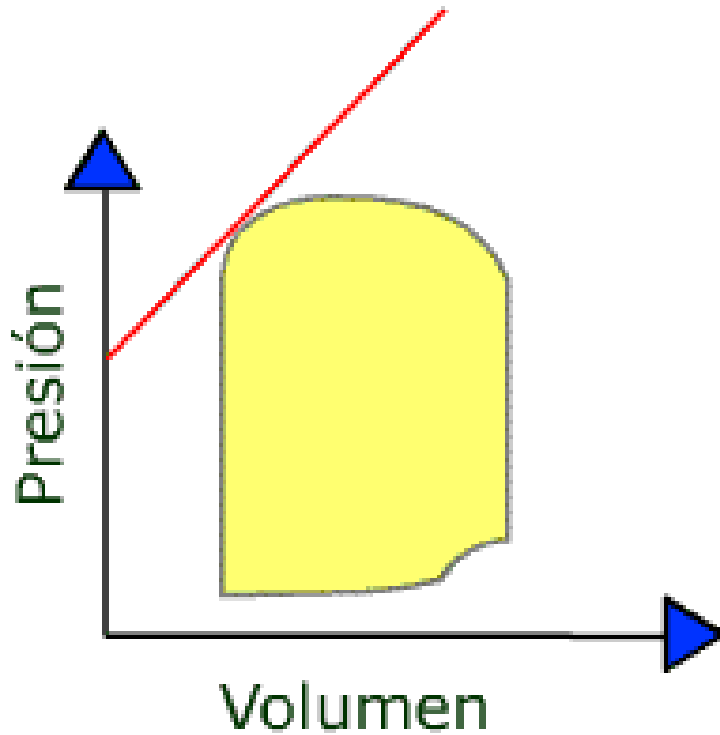
- ◆ La tensión de la pared es uno de los aspectos determinantes principales de la captación miocárdica de O_2 .
- ◆ La reducción de la poscarga y la precarga disminuye la demanda miocárdica de O_2 al disminuir el radio del VI.

Volumen sistólico (ml)

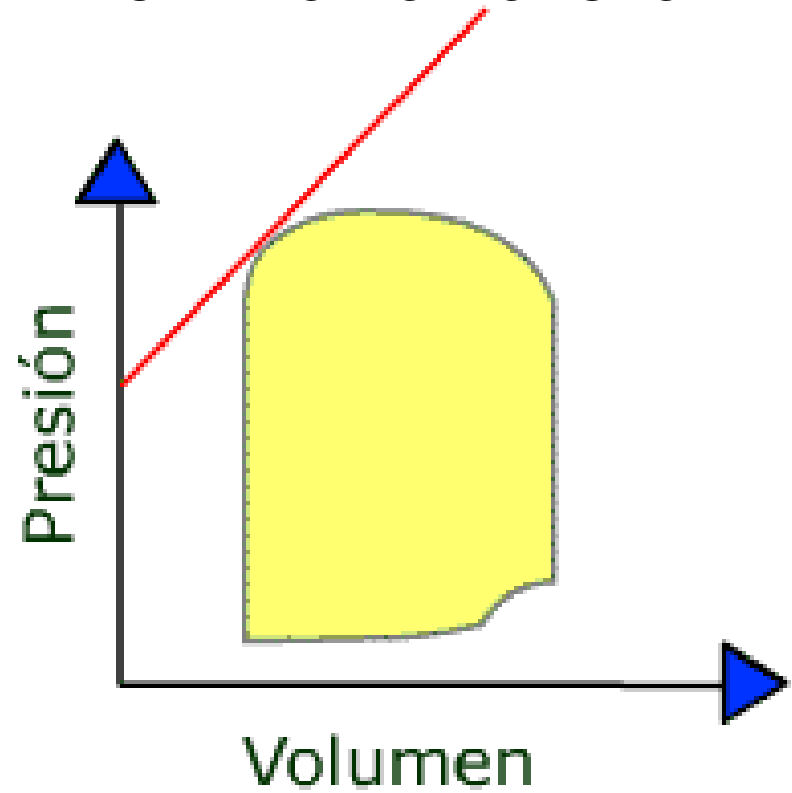


PTDVI (mm Hg)

AUMENTO POST CARGA



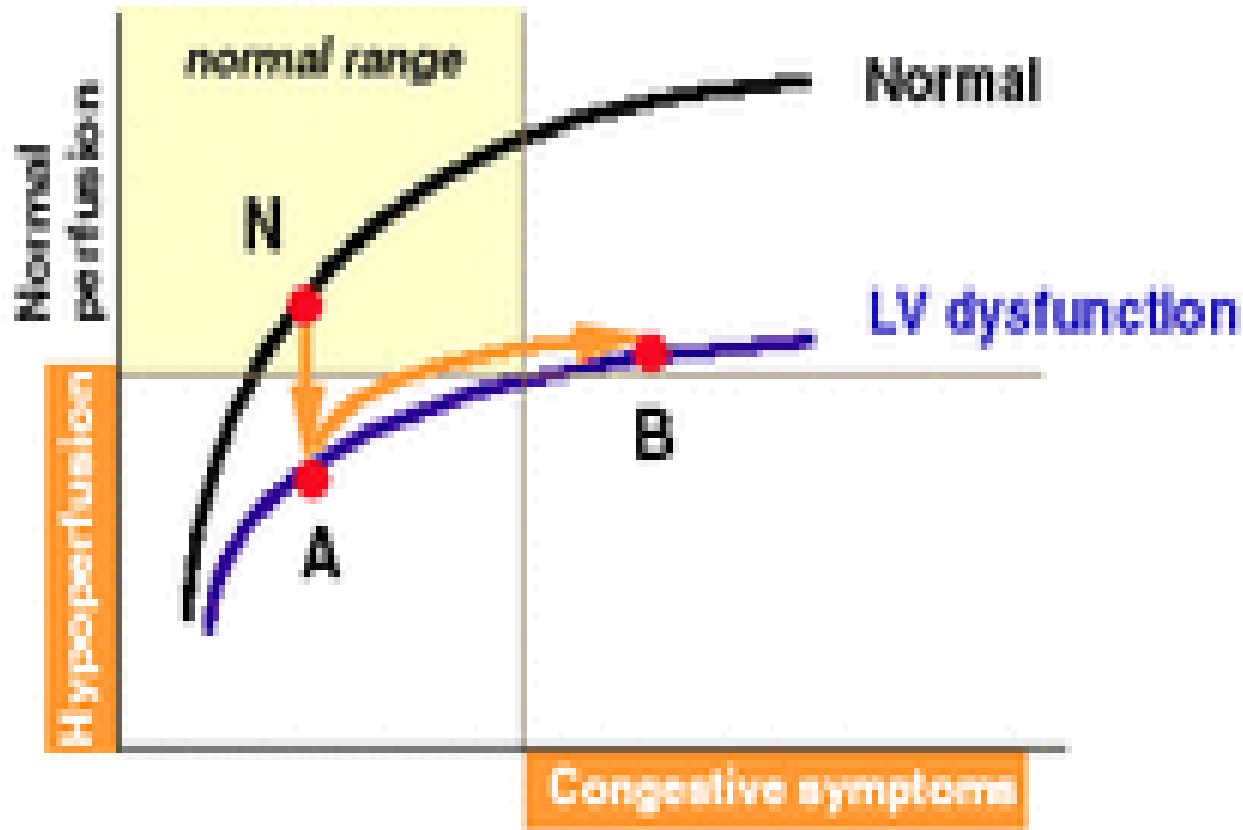
AUMENTO INOTROPISMO



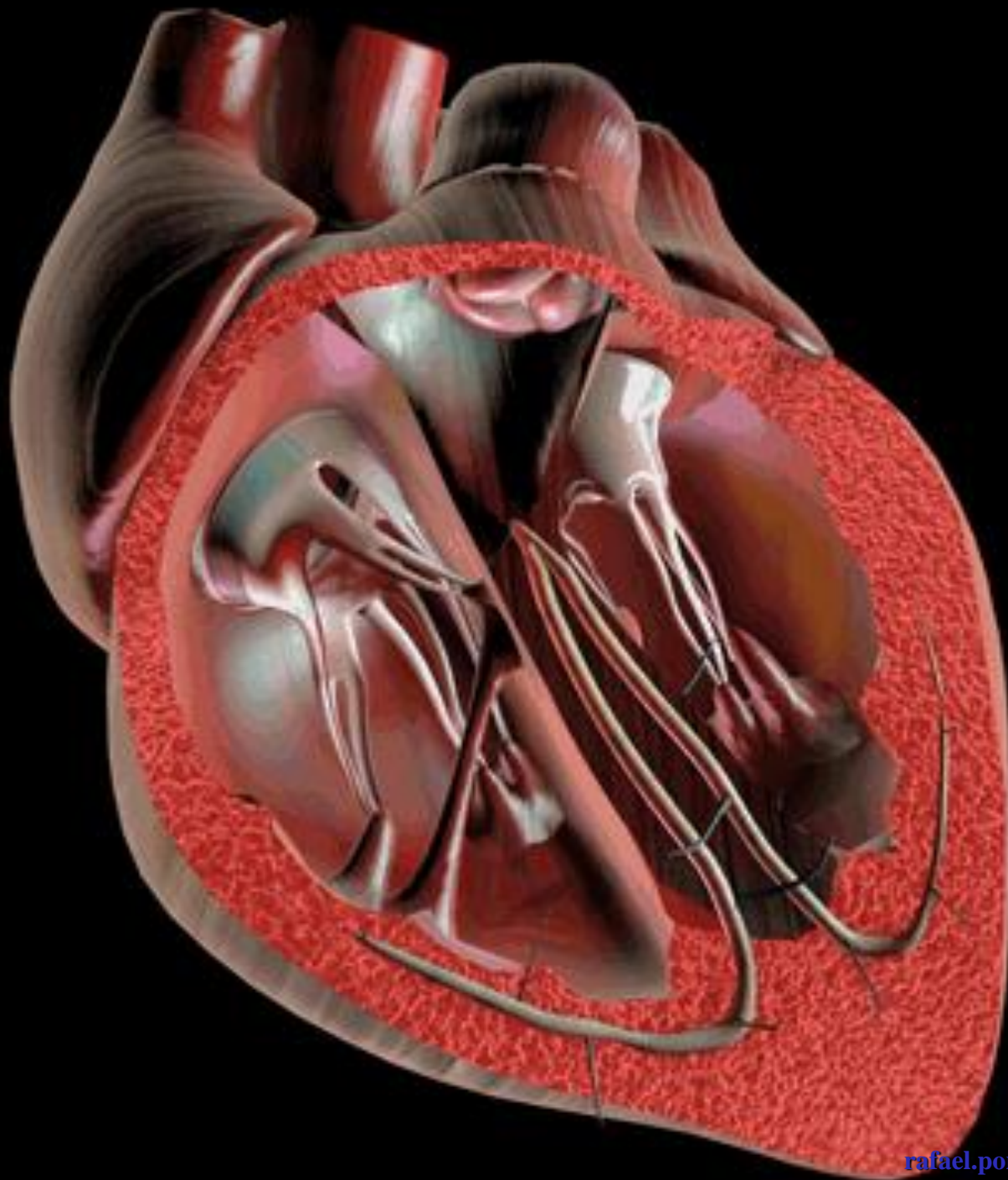
[C] 2013 JDCOMV

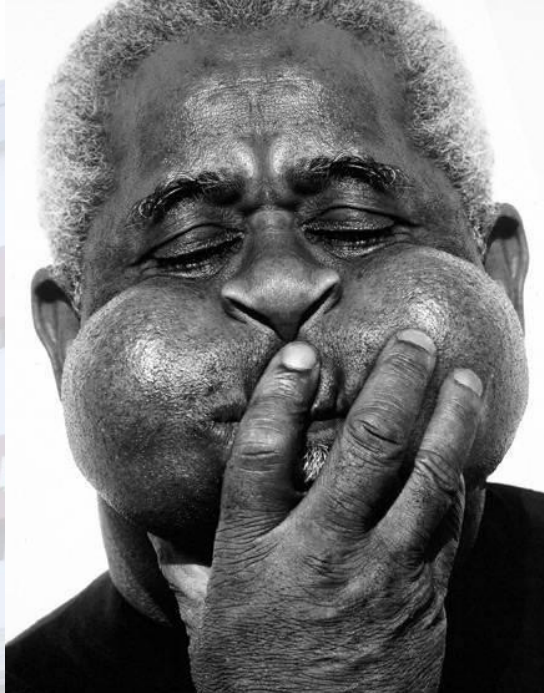
[C] 2013 JDCOMV

Cardiac Output



Left Ventricular End-Diastolic Pressure

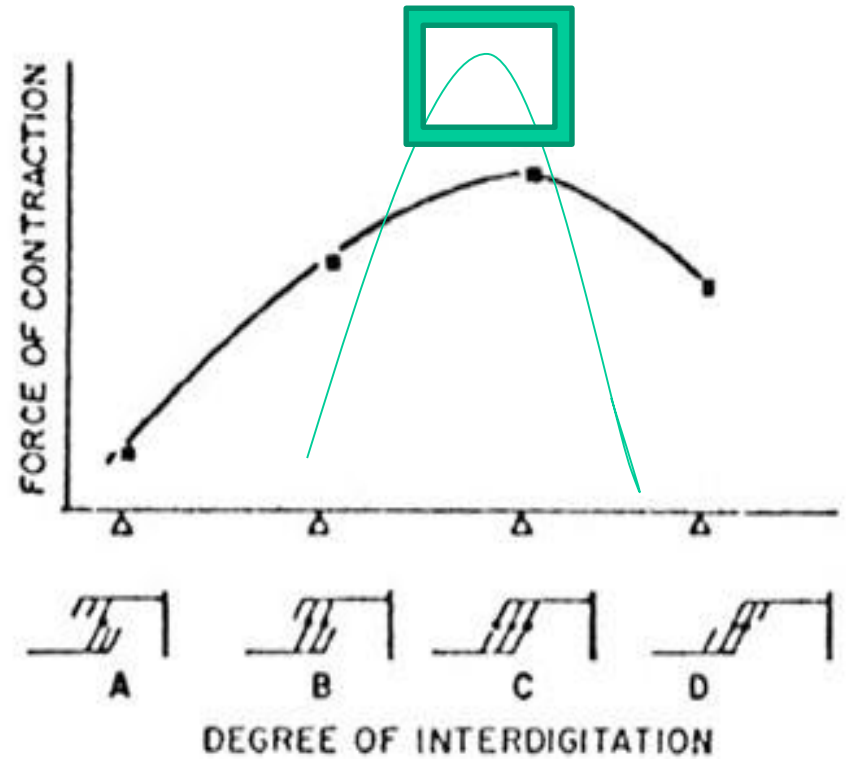




PRECARGA

Explicación ultraestructural de la Ley de Starling

MYOCARDIAL CONTRACTILITY



MYOSIN

ACTIN

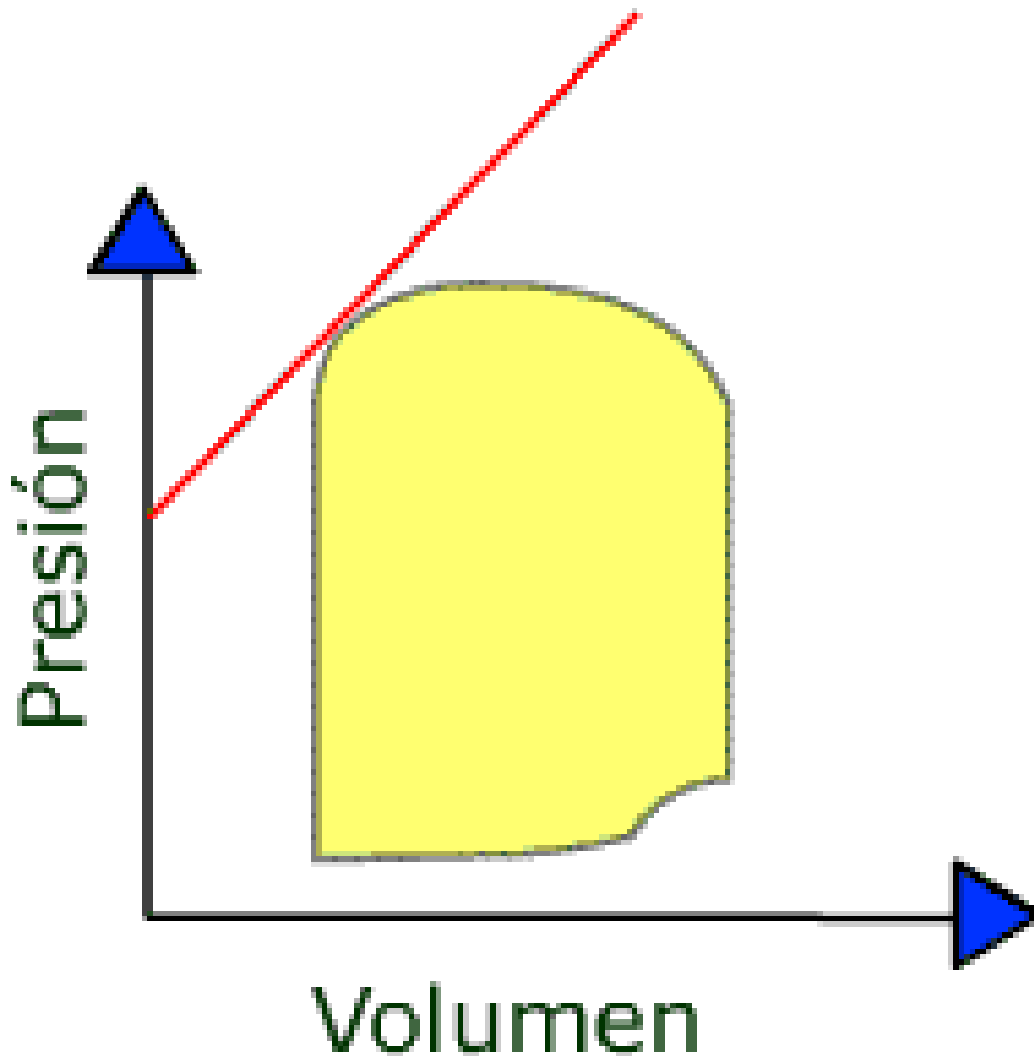


Z + SARCOMERE 1/2

LEY DE FRANK

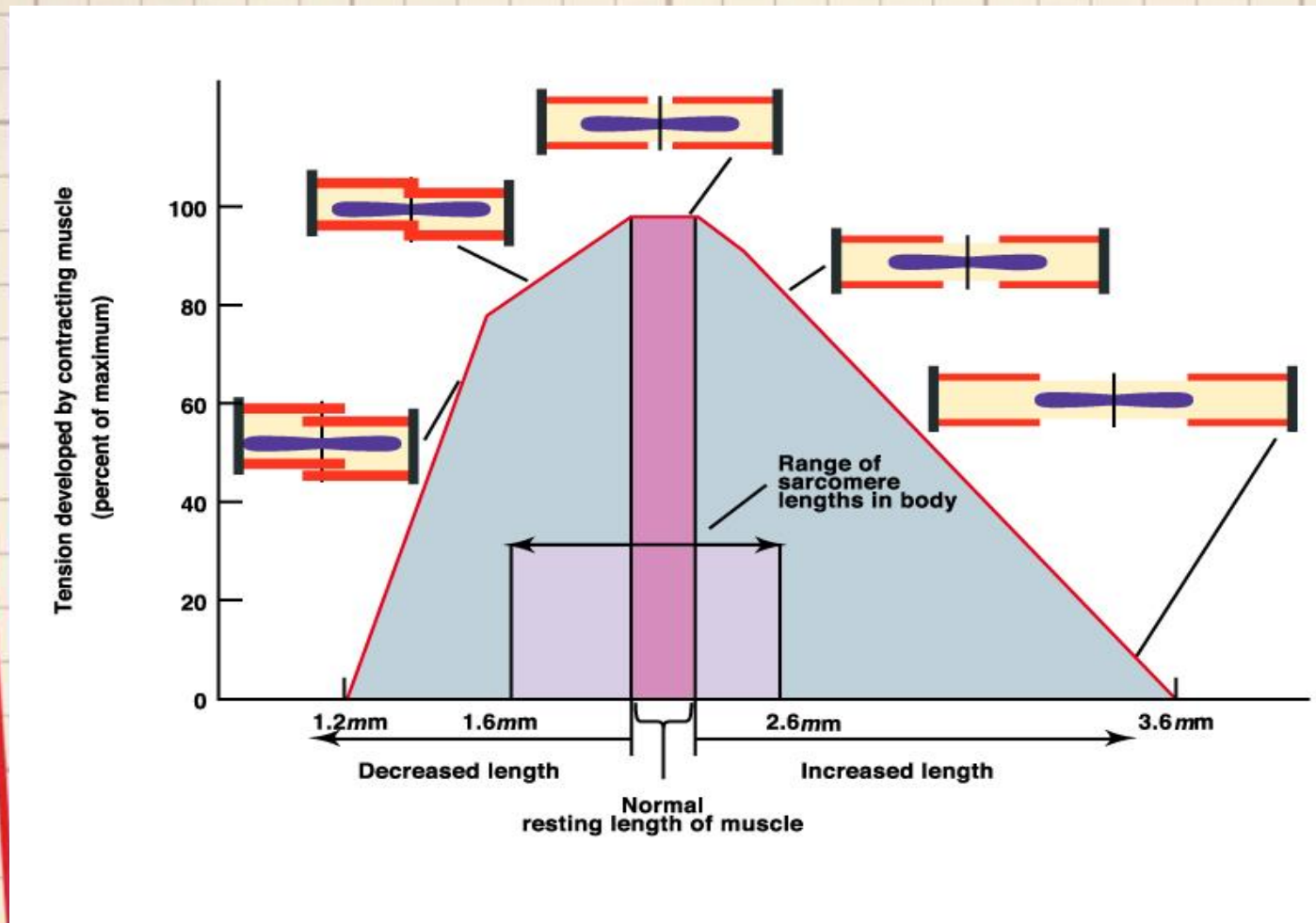
STARLING

PRECARGA



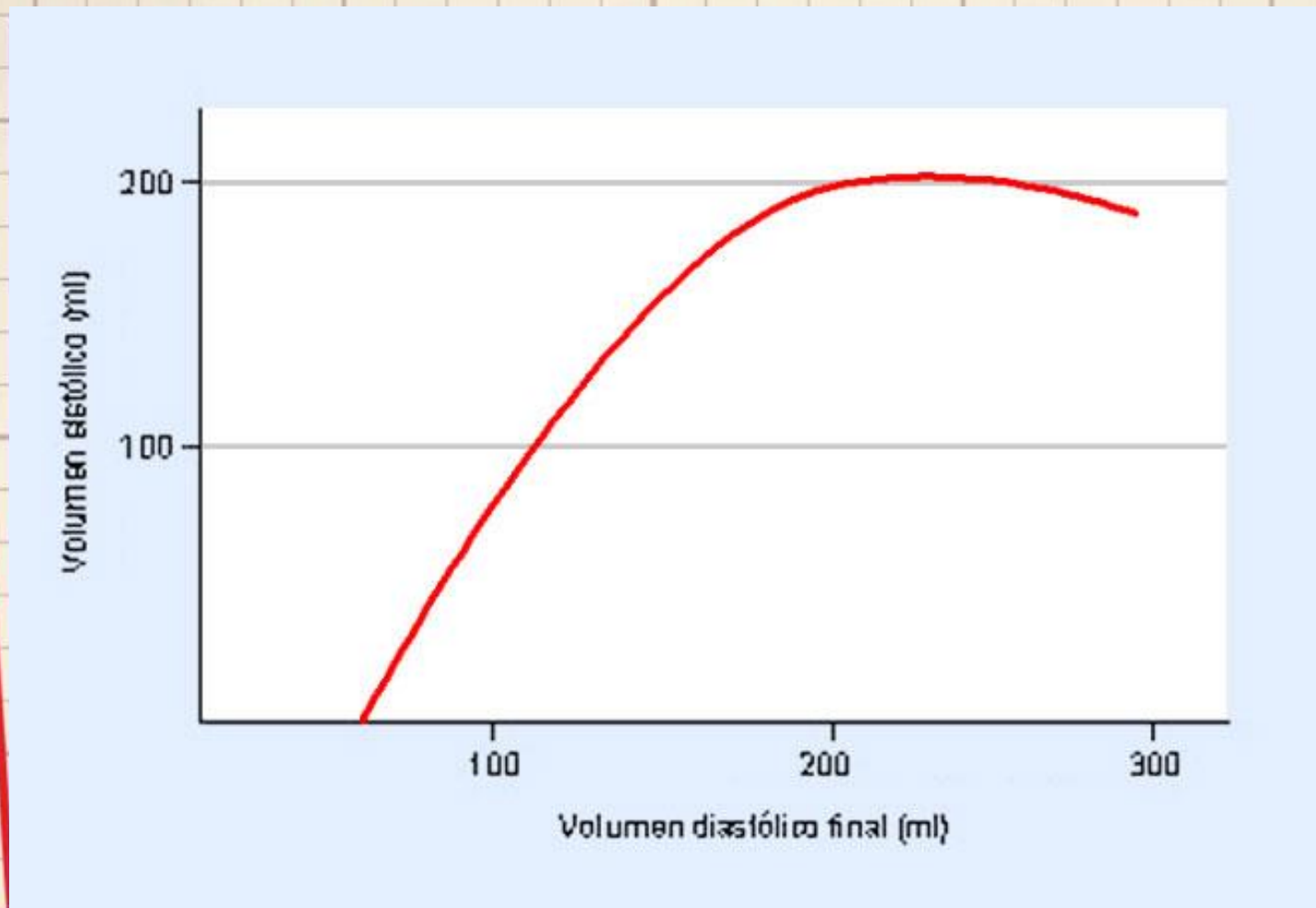
Mecanismos de compensación

1) Mecanismo de Frank-Starling



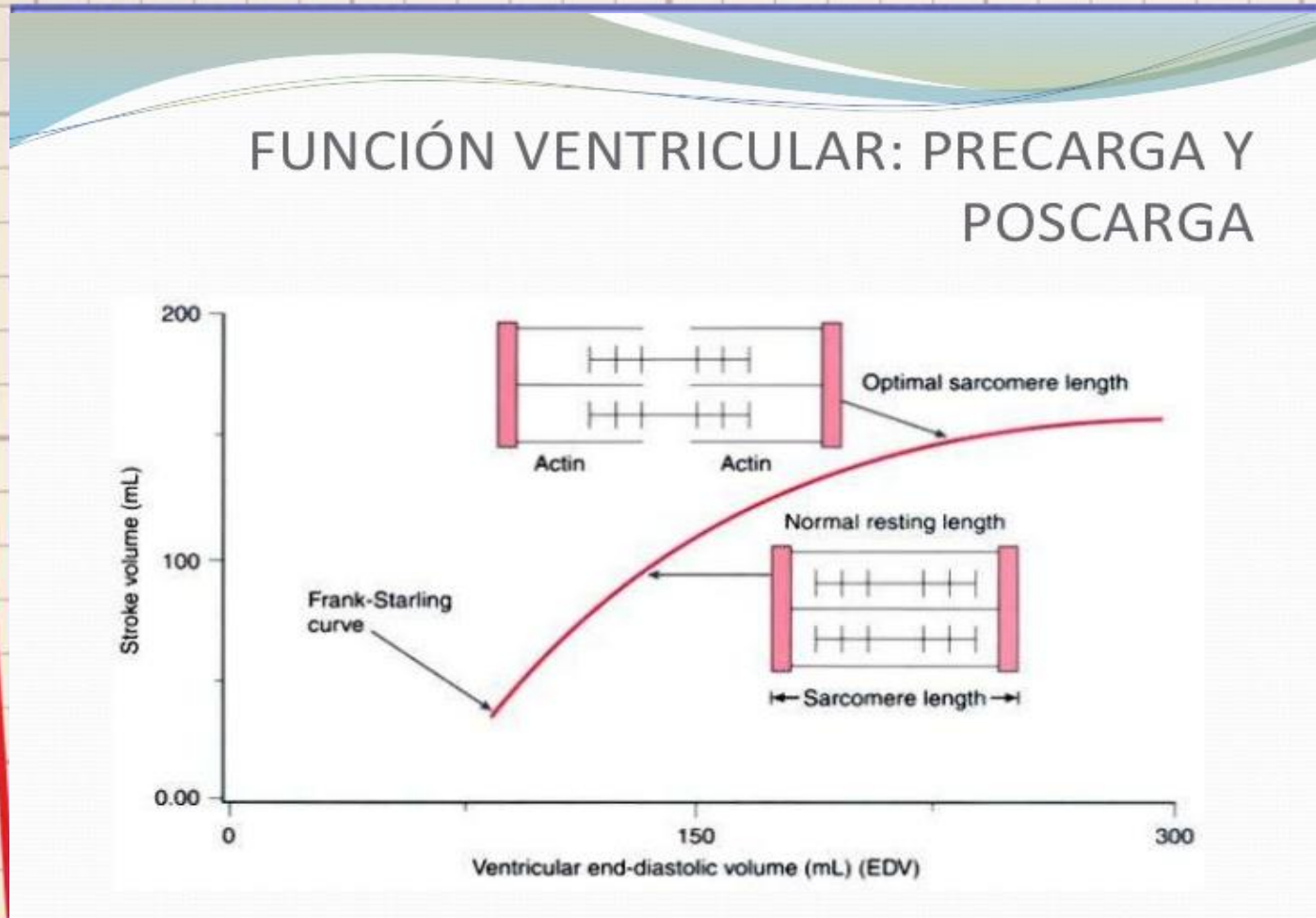
Mecanismos de compensación

1) Mecanismo de Frank-Starling



Mecanismos de compensación

1) Mecanismo de Frank-Starling



Inotropismo

D/P D/T

*Ley de Starling y
Ley de Laplace*

**Volumen
Sistólico**

Lusitropismo

Precarga y post carga

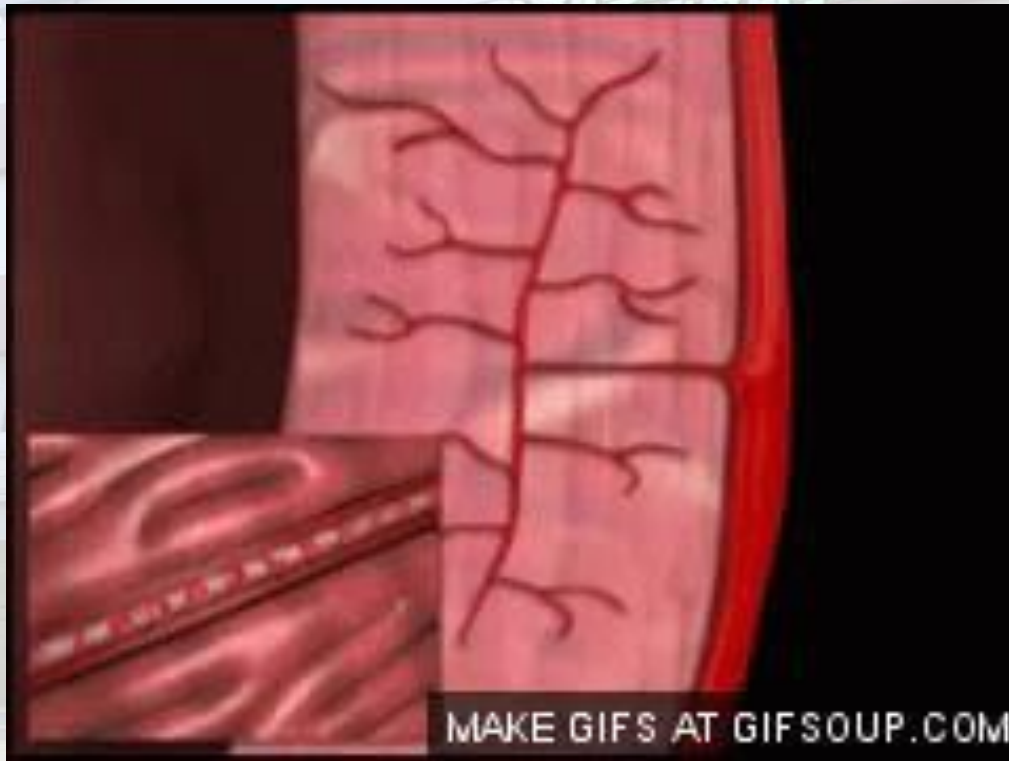


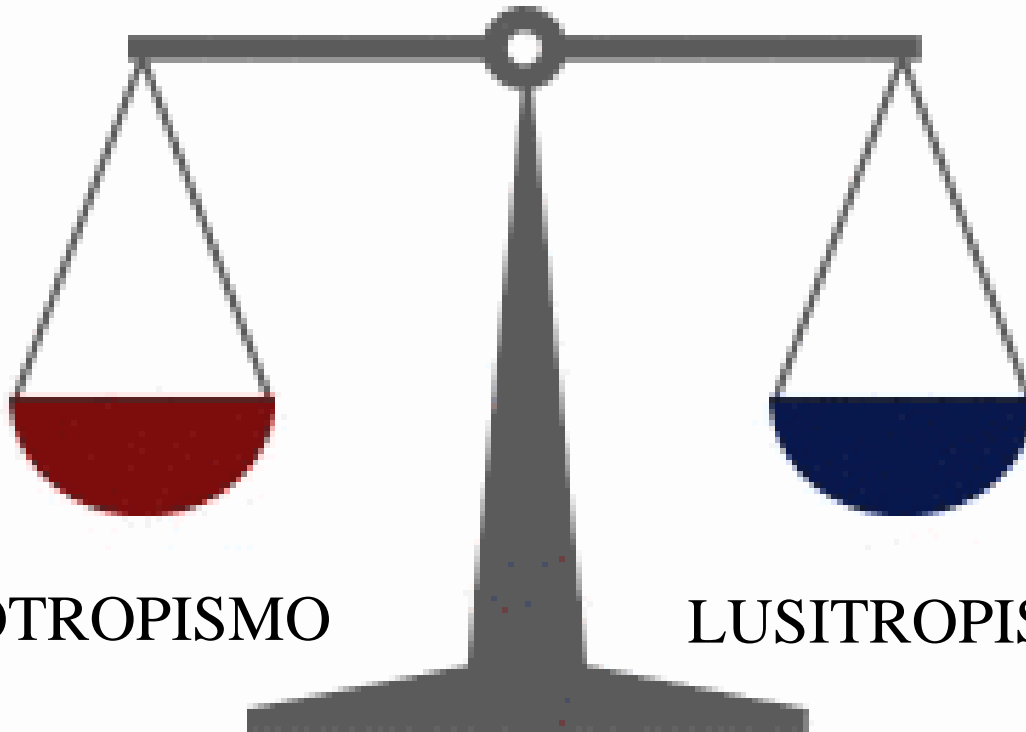
LUSITROPISMO

PRECARGA

DINAMICA DEL CALCIO

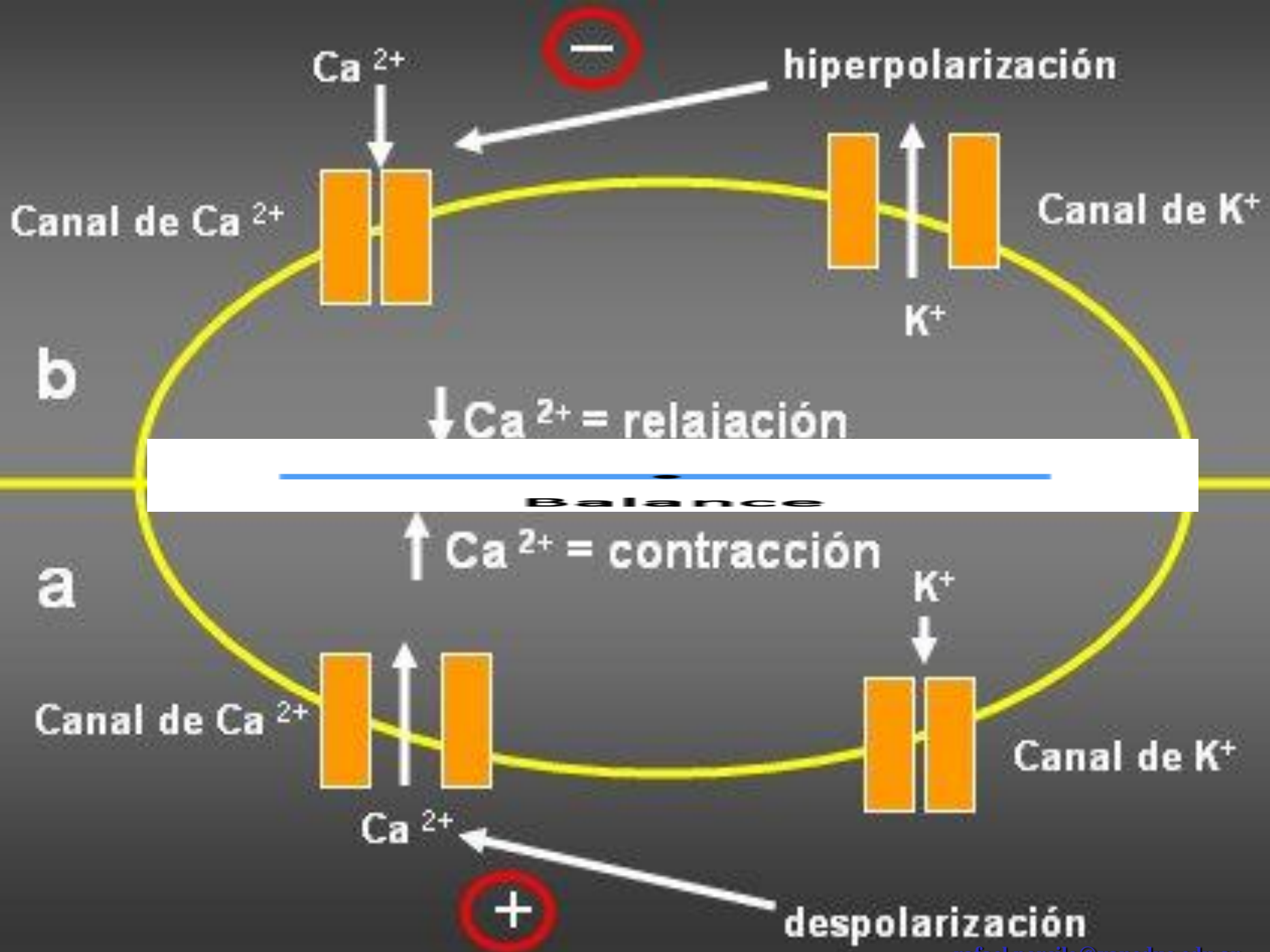
Nutrición miocárdica

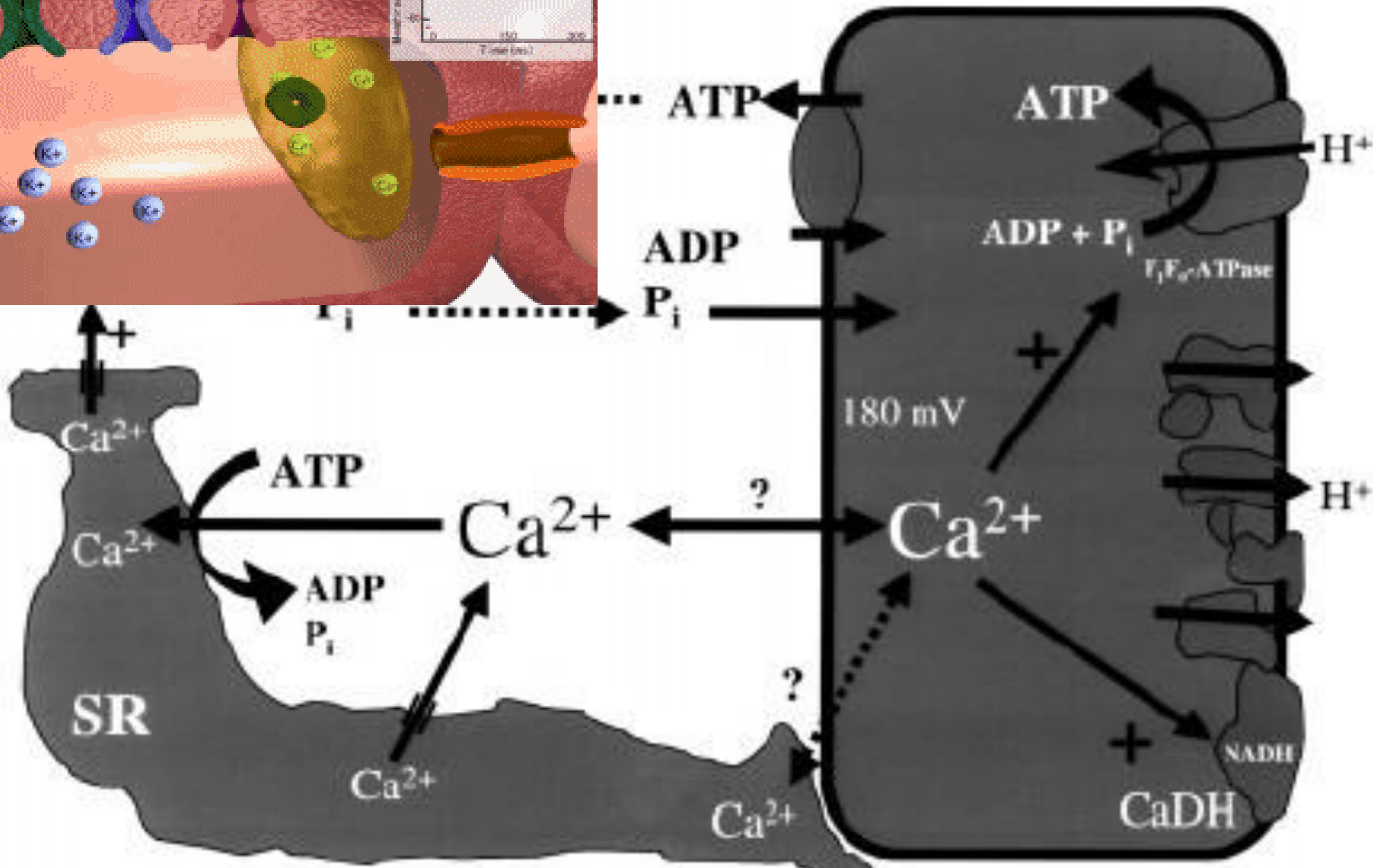
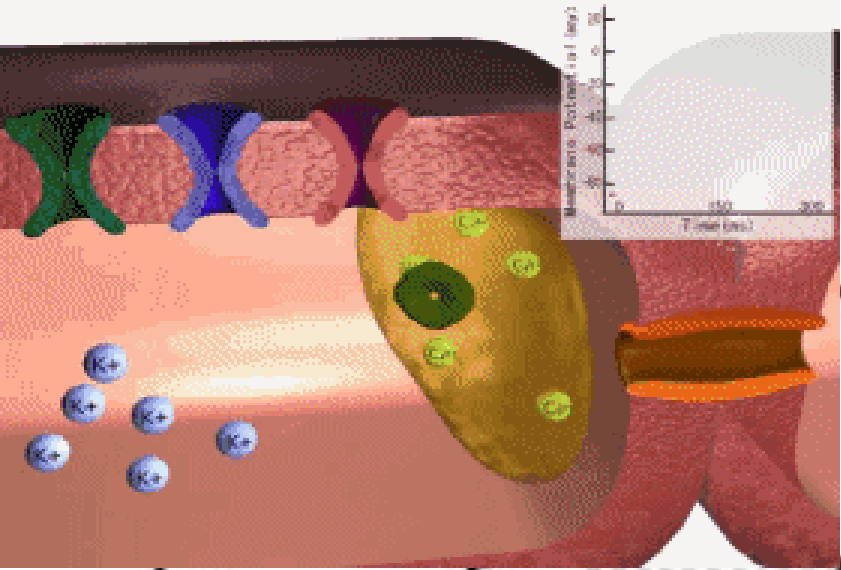




INOTROPISMO

LUSITROPISMO





Mitochondria

Inotropismo

D/P D/T

*Ley de Starling y
Ley de Laplace*

**Volumen
Sistólico**

Lusitropismo

Precarga y post carga

PRESSURE

increased inotropy

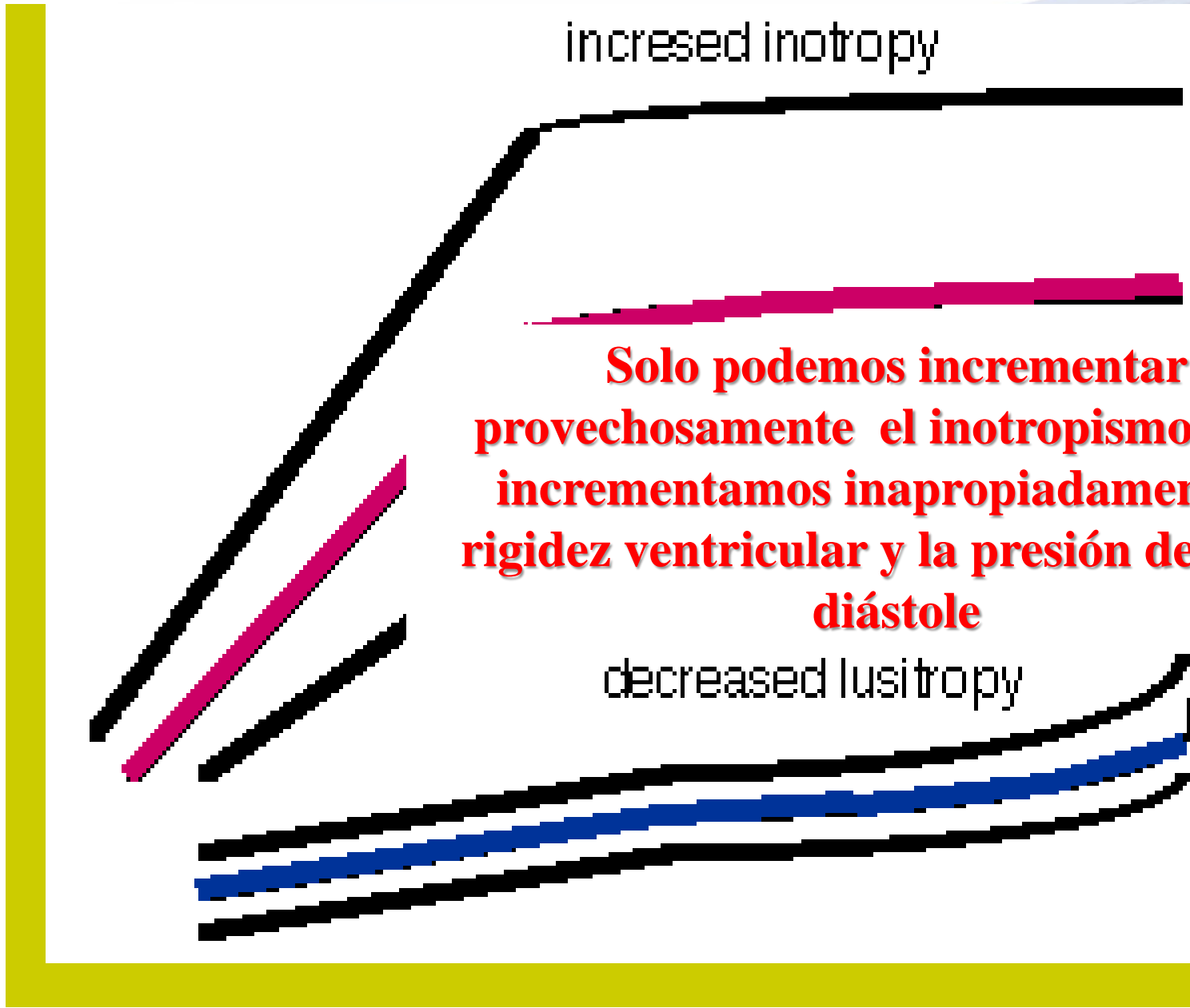
NORMAL

**Solo podemos incrementar
provechosamente el inotropismo si no
incrementamos inapropiadamente la
rigidez ventricular y la presión de fin de
diástole**

decreased lusitropy

NORMAL

VOLUME



PRESSURE

increased inotropy

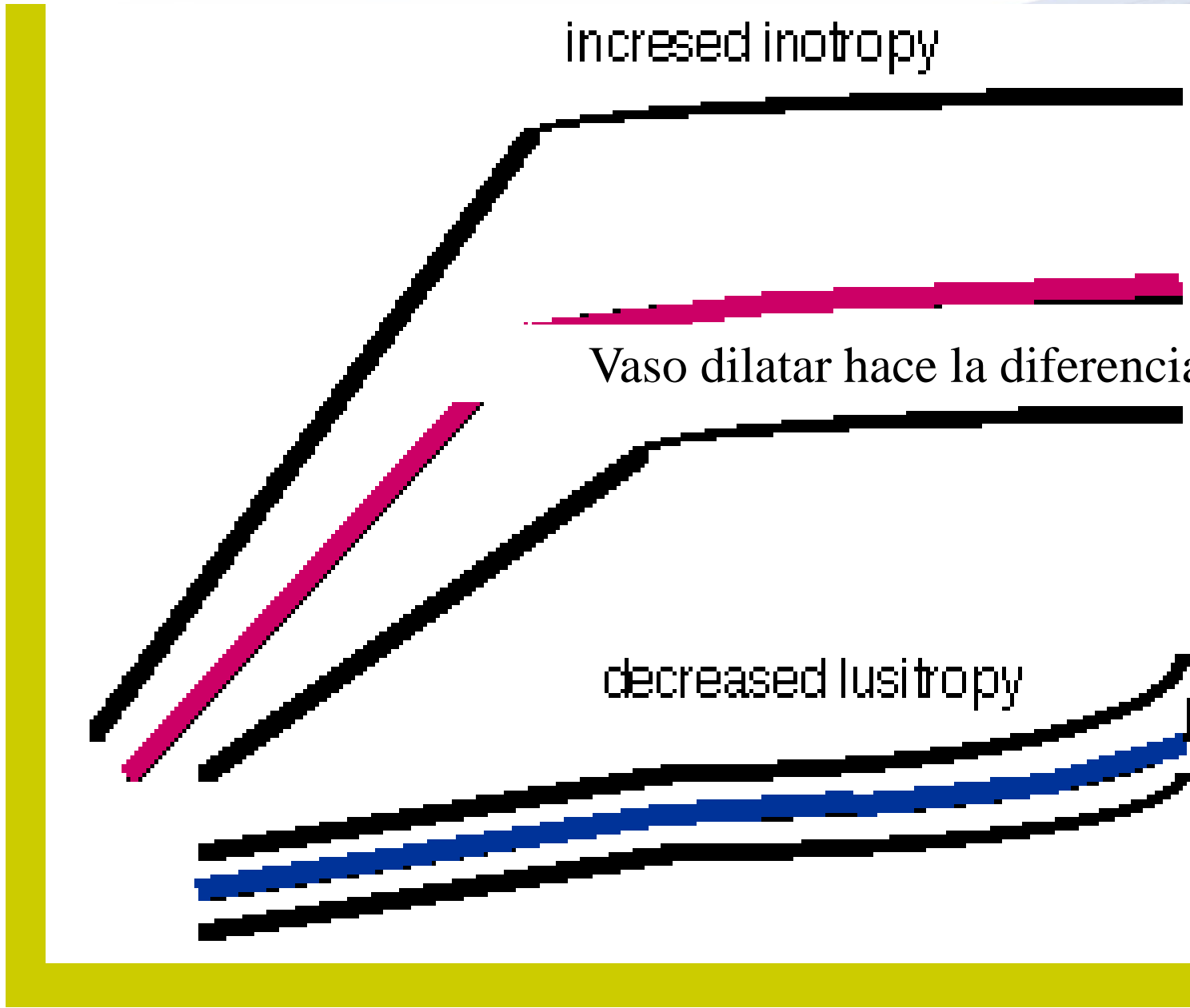
NORMAL

Vaso dilatar hace la diferencia

decreased lusitropy

NORMAL

VOLUME



Resistencia vascular

Es la oposición al flujo de sangre debido a la fricción entre la sangre y las paredes de los vasos sanguíneos

Tamaño de la luz del vaso sanguíneo

La viscosidad de la sangre

El largo total del vaso sanguíneo

Relación entre los glóbulos rojos y el volumen del líquido plasmático (DHT-policitemia)

A mayor longitud mayor resistencia (obesas)



¿Que parámetro fisiológico modificar para incrementar la fuerza de contracción miocárdica?

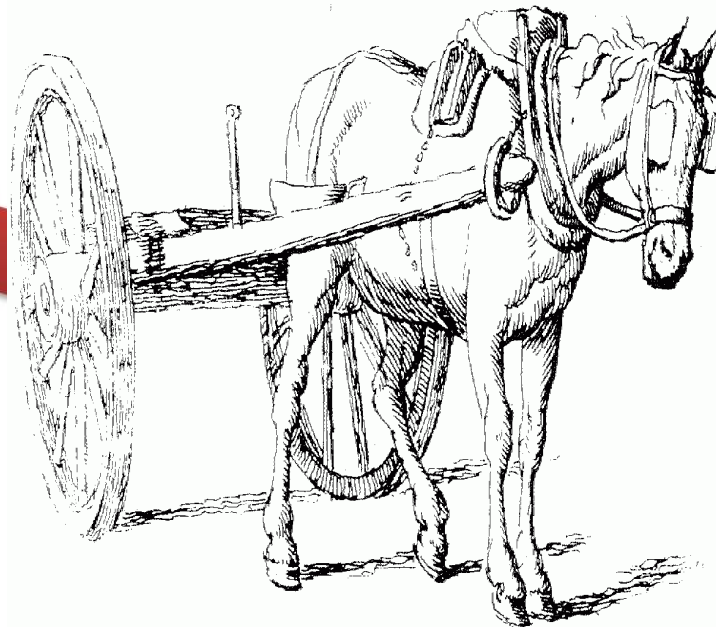
Classification of inotropes

Drugs that facilitates
actin-myosin
binding to Ca^{2+}

Drugs that affects
metabolism and
endocrine functions

Drugs that
increase
intracellular
 Ca^{2+}

Newer drugs
in the
market



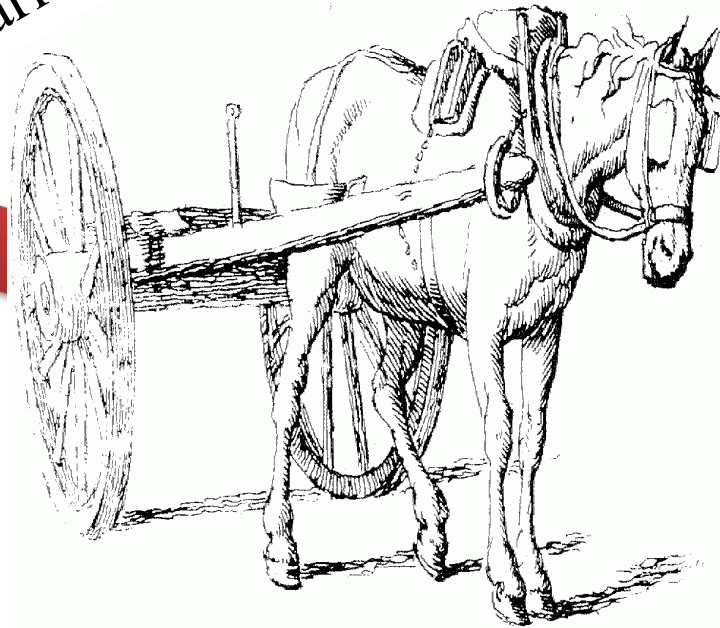
Classification of inotropes

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increase
cellular
 Ca^{2+}

Newer drugs
in the
market



¿Y si en vez de pegarle al caballo intentamos descargar el carro?

Los

inotrópicos

y la

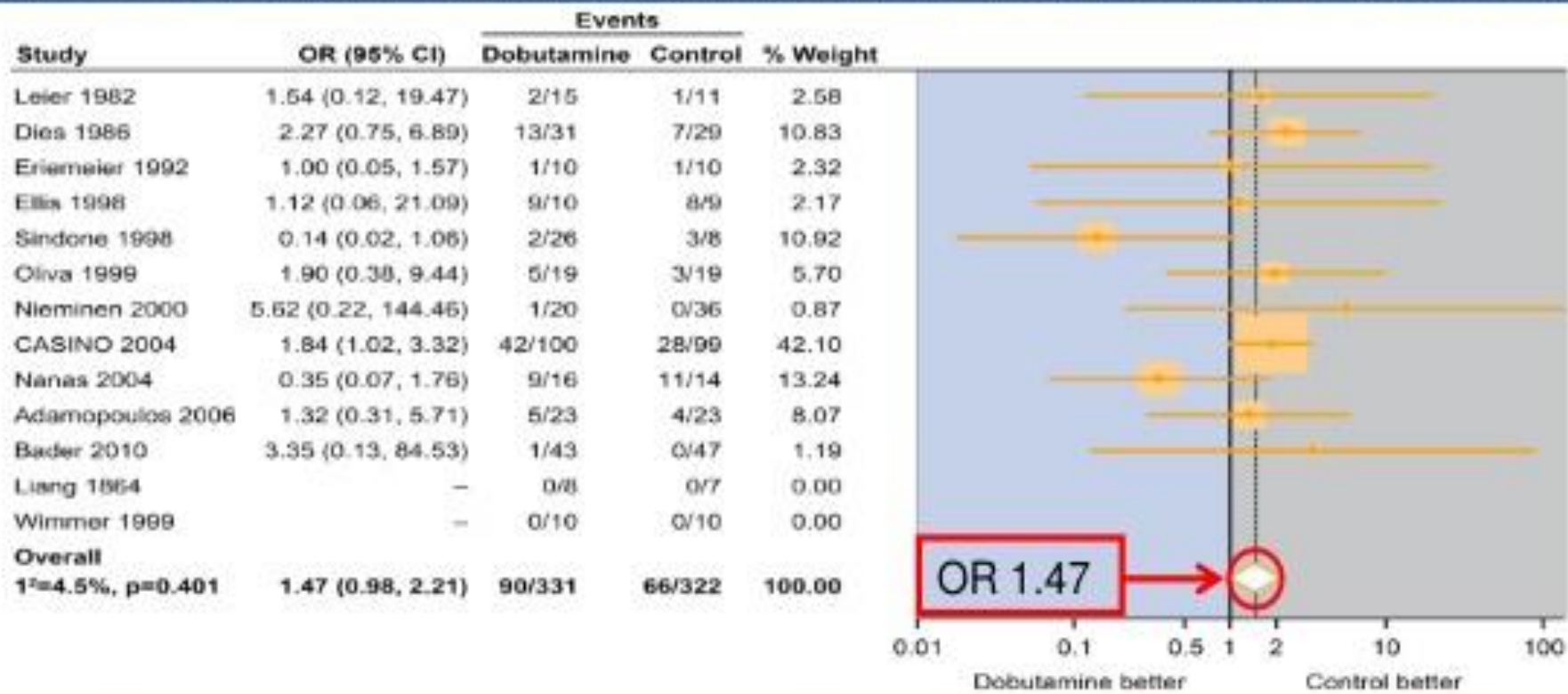
mortalidad

Los

inotrópicos

En pulsos

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



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

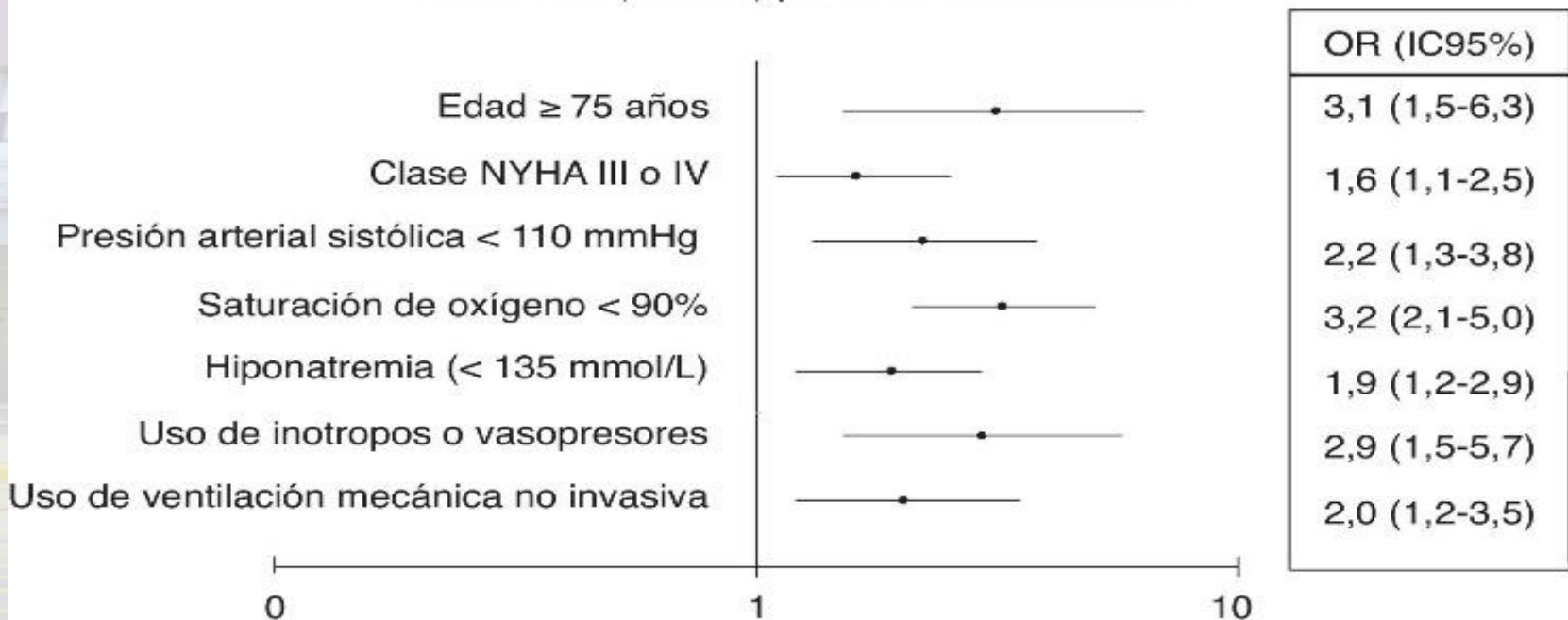


Los inotrópicos En insuficiencia cardiaca crónica

Predicción de la mortalidad a muy corto plazo de los pacientes con insuficiencia cardiaca crónica agudizada: escala EAHFE-3D

<http://dx.doi.org/10.1016/j.medin.2015.07.013>

Odds ratio (CI 95%) para mortalidad a 3 días



Continuous intravenous dobutamine is associated with an increased risk of death in patients with advanced heart failure: insights from the Flolan International Randomized Survival Trial (FIRST).

O'Connor CM¹, Gattis WA, Uretsky BF, Adams KF Jr, McNulty SE, Grossman SH, McKenna WJ, Zannad F, Swedberg K, Gheorghiu M, Califf RM.

Author information


Abstract

OBJECTIVE: To evaluate clinical characteristics and outcomes of patients with advanced heart failure receiving intravenous continuous dobutamine in the FIRST Trial (Flolan International Randomized Survival Trial).

METHODS: Four hundred seventy-one patients with class IIIb to IV heart failure who were enrolled in the FIRST trial were included. Eighty patients treated with dobutamine at FIRST randomization were compared with 391 patients not treated with dobutamine at randomization. The occurrence of worsening heart failure, need for vasoactive medications, resuscitated cardiac arrest, myocardial infarction, and total mortality were compared between the 2 groups.

RESULTS: The dobutamine group had a higher occurrence of first event (85.3% vs 64.5%; $P = .0006$) and a higher mortality rate (70.5% vs 37.1%; $P = .0001$) compared with the no dobutamine group. Intravenous continuous dobutamine was an independent risk factor for death after adjusting for baseline differences.

CONCLUSIONS: Dobutamine use at the time of randomization was associated with a higher 6-month mortality rate. This effect persisted after adjustment for baseline differences. This analysis challenges the concept that continuous intravenous dobutamine is beneficial to advanced heart failure patients with respect to survival.

The background image shows a multi-story building with a light blue facade and a dark red horizontal band. The band contains the text 'UNIVERSIDAD INTERAMERICANA' in green and white, and 'HOSPITAL ESCUELA' in green. There are logos on the building, including a stylized book icon. The text 'Los inotrópicos' is overlaid in large black font, with 'Add on sobre' and 'terapia optima' below it in a smaller black font.

Los inotrópicos

Add on sobre terapia optima

OPTIME CHF

A prospective, multicenter, double-blind, placebo-controlled trial of IV milrinone *in addition to best medical therapy*

Patient with Exacerbation of Known Systolic Heart Failure

- No loading dose
- 0.5 mcg/kg/min
- Goal 24–72 hour infusion

RANDOMIZED
within 48 hours of admission

48-hour Milrinone Infusion

48-hour Placebo Infusion

60-day Follow-up

IV Milrinone During Hospitalization for Decompensated HF—Not Low Output

OPTIME-CHF: In-hospital Adverse Events

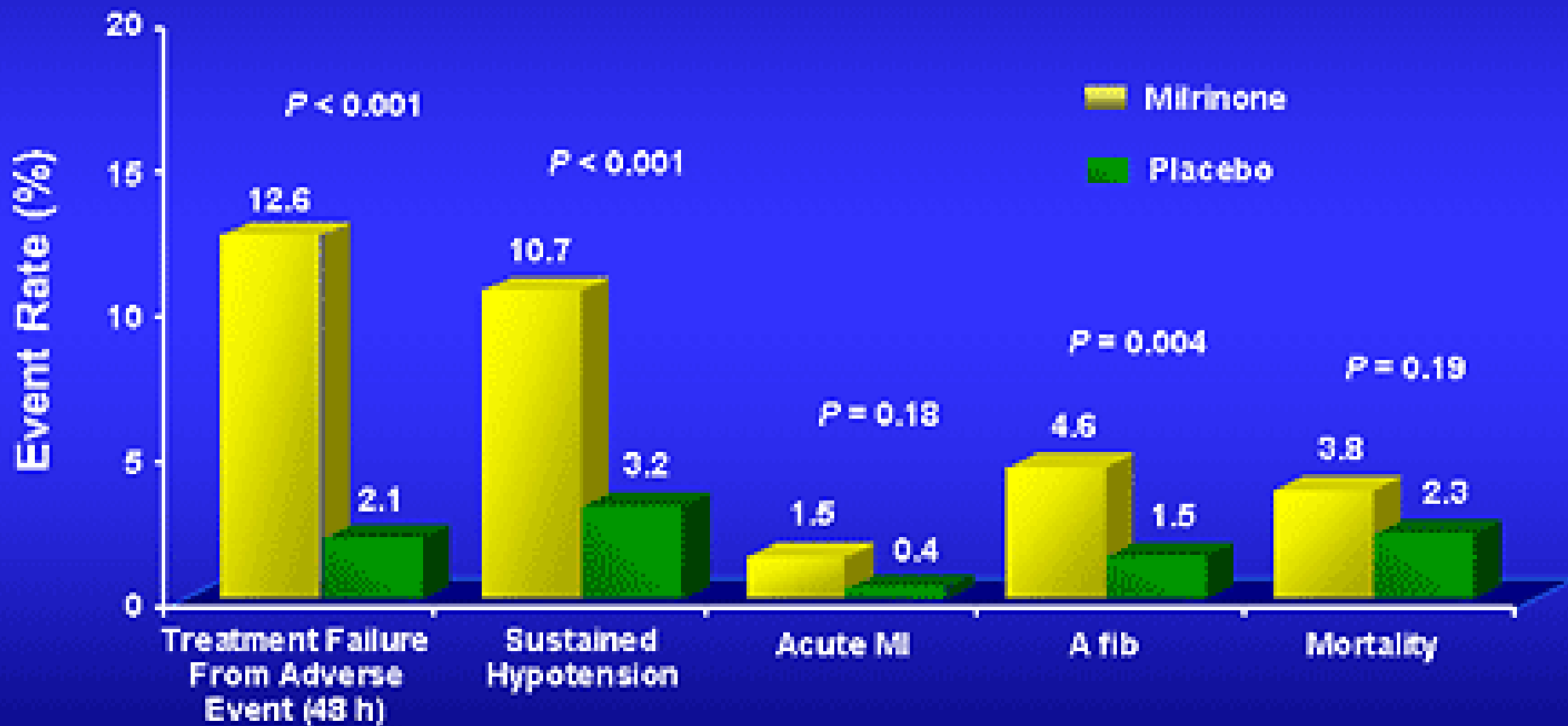


TABLA 3

Resultados del estudio OPTIME⁴⁸

Ítem	Placebo (n = 472)	Milrinona (n = 477)	p
Hospitalización CV postinfusión (días)	12,5 ± 14	12,3 ± 14	0,714
Muerte CV intrahospitalaria (%)	2,3	3,8	0,194
Muerte CV al día 60 (%)	8,9	10,3	0,441
Muerte u hospitalización al día 60 (%)	35,3	35,0	0,915
IAM (%)	0,4	1,5	0,178
Nueva FA aguda (%)	1,5	4,6	0,004
Taquicardia ventricular (%)	1,3	2,7	0,107
Fibrilación ventricular (%)	0,6	1,7	0,127
Hipotensión mantenida (%)	3,2	10,7	< 0,001

CV: por causas cardiovasculares; FA: fibrilación auricular.

Asociación con mortalidad

OPTIME CHF Short-term Intravenous Milrinone for Acute Exacerbation of Chronic Heart Failure
A Randomized Controlled Trial

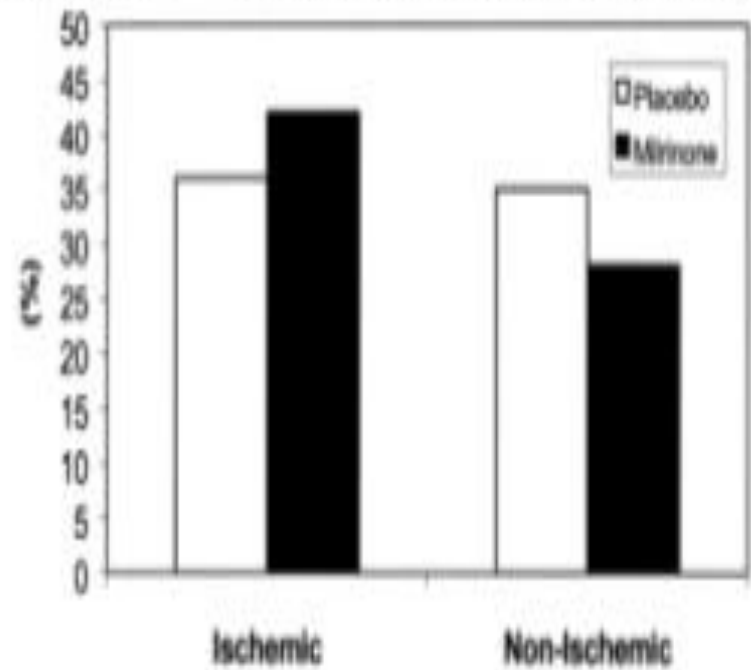
Eventos adversos:
Hipotensión, arritmia

JAMA 2002;287:1541-1547

Sub análisis

Heart Failure Etiology and Response to Milrinone in Decompensated Heart Failure

J Am Coll Cardiol 2003;41:997-1003



949 pacientes
Milrinone vs placebo 48-72h
Mayor mortalidad, rehospitalización o días hospitalizado etiología

ISQUÉMICA

The relationship between inotrope exposure, six-hour postoperative physiological variables, hospital mortality and renal dysfunction in patients undergoing cardiac surgery

Critical Care 2011, 15:R162

- Cohorte 1314 pacientes
- Retrospectivo
- 2 Hospitales Universitarios
- Análisis multivariado, emparejamiento
- 123 pacientes: persistieron desenlaces

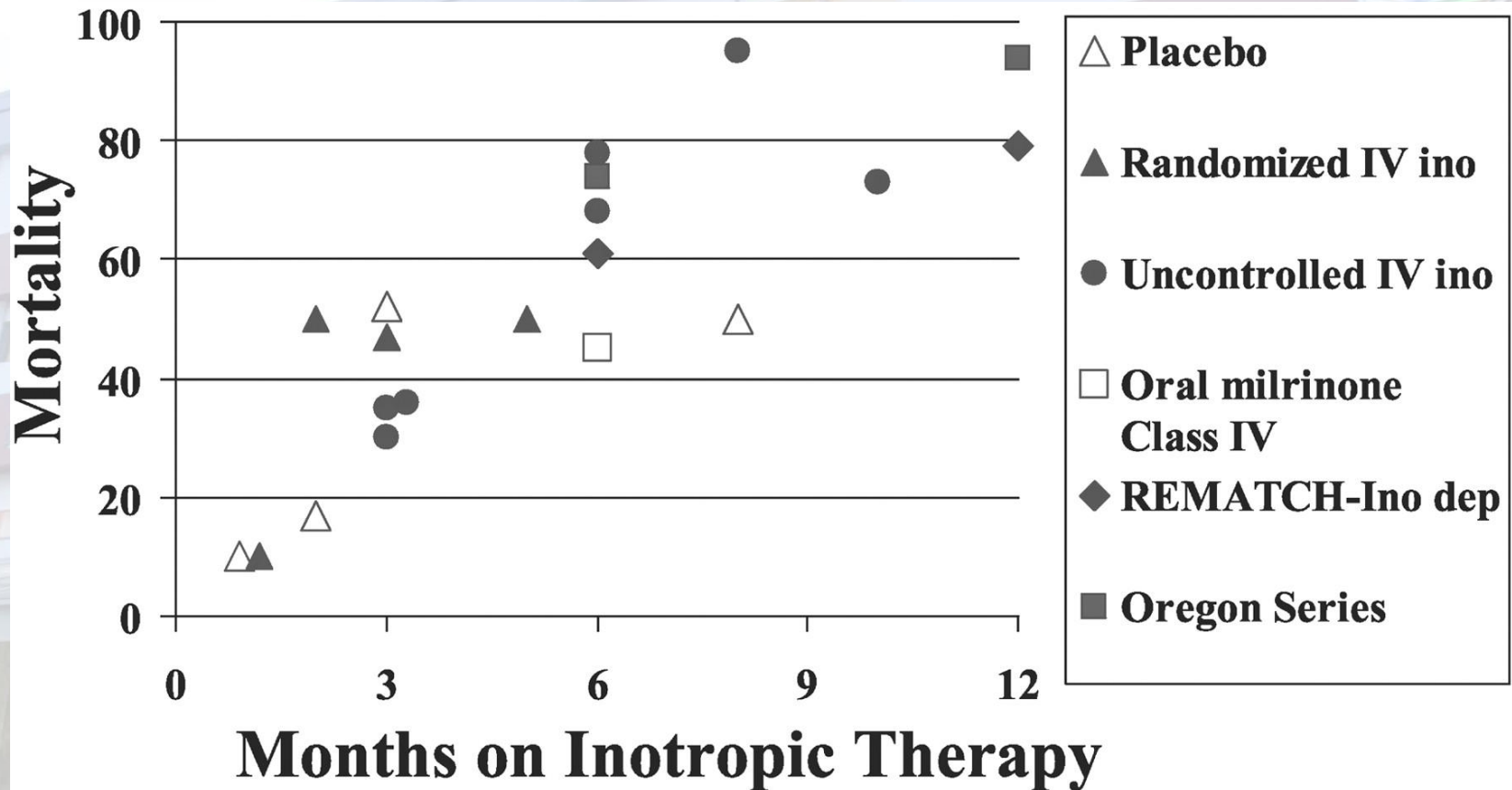
	Cohorte (n = 1,314)	No expuestos a inotrópicos (n = 783)	Expuestos a inotrópicos (n = 531)
Inotrópico usado (%)			
Dobutamina	75 (5.7)	0	75 (14.1)
Milrinone	332 (25.3)	0	332 (62.5)
Desenlaces			
Mortalidad, n (%)	103 (7.8)	15 (1.9)	76 (14.3)
Falla renal, n (%)	105 (8.3)	25 (3.2)	87 (16.8)
Estancia en UCI (días)	1.1 (1.8)	1.0 (0.9, 1.6)	2.1 (1.0, 4.7)
Estancia hospitalaria promedio	8 (6)	7.0 (5.0, 9.0)	10.0 (6.0, 18.0)



Clinical Use of Inotropic Therapy for Heart Failure: Looking Backward or Forward?

Circulation. 2003;108:492-497

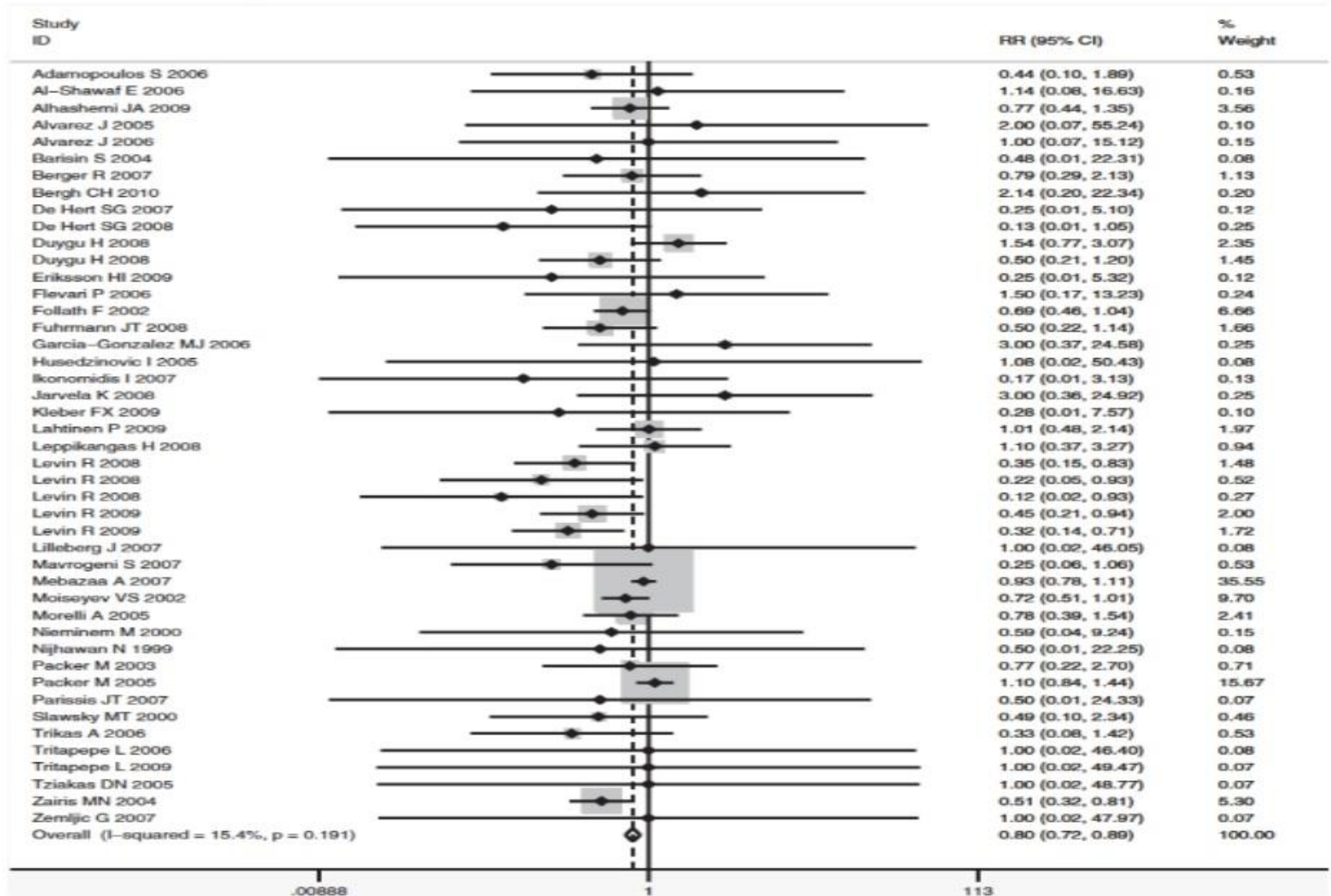
Figure 1. Mortality estimated from selection of experiences with intravenous inotropic (ino) therapy.



Lynne Warner Stevenson *Circulation*. 2003;108:492-497

inotropic infusions in end-stage heart failure with 61% mortality at 6 months and 79% mortality by 1 year

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



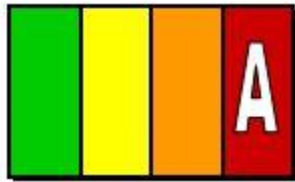
Positive Inotropic agents

- The largest database demonstrating increased mortality with inotropes is the *ADHERE (Acute Decompensated Heart Failure National Registry)*, where short-term inotropic therapy was associated with increased in-hospital mortality
- Despite clear evidence that inotropic therapy increases mortality, there are clinical settings where inotropic support with dopamine, dobutamine, milrinone, or norepinephrine may be life-saving measures.
- short-term use of intravenous positive inotropic drugs may have a clear therapeutic role in patients hospitalized with acute systolic heart failure, where hypoperfusion of vital organs is obvious and the need for improved perfusion is immediate.

Infusion of Positive Inotropic Drugs

OPTIME-CHF, etc.

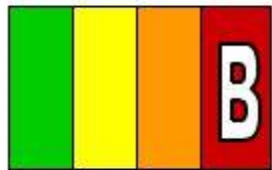
I IIa IIb III



Routine intermittent infusions of vasoactive and positive inotropic agents are not recommended for patients with refractory end-stage HF.



I IIa IIb III



Use of parenteral inotropes in normotensive patients with acute decompensated HF without evidence of decreased organ perfusion is not recommended.



OPTIME-CHF (RCT n = 951)
ADHF not requiring inotrope
Milrinone (500 mcg/kg/min) vs. Placebo

Table 4. Primary Outcome and Hospitalization

Outcome	Placebo (n = 472)	Milrinone (n = 477)	P Value
Days of hospitalization for cardiovascular causes within 60 days			
Median (IQR)*	7 (4, 14)	6 (4, 13)	.71
Mean (SD)	12.5 (14.0)	12.3 (14.1)	
Days of hospitalization from infusion to initial discharge			
Median (IQR)	5 (4, 8)	5 (4, 7)	.99
Mean (SD)	7.0 (6.6)	7.0 (6.2)	
Days of hospitalization for cardiovascular causes from discharge to 60 days			
Median (IQR)	0 (0, 5)	0 (0, 5)	.59
Mean (SD)	5.9 (12.5)	5.7 (12.6)	
Days of hospitalization for any cause within 60 days			
Median (IQR)	8 (4, 16)	7 (4, 15)	.83
Mean (SD)	13.5 (14.4)	13.4 (14.7)	
Death or readmission within 60 days, No./Total (%)	164/464 (35.3)	166/474 (35.0)	.92

*IQR indicates interquartile range.

Table 6. Adverse Events and Mortality*

Adverse Event, No. (%)	Placebo (n = 472)	Milrinone (n = 477)	P Value
Treatment failure cause at 48 hours	43/466 (9.2)	97/470 (20.6)	<.001
Progression of heart failure	6.8	7.9	.54
Adverse event	2.1	12.6	<.001
Events during index hospitalization			
Myocardial infarction	2 (0.4)	7 (1.5)	.18
New atrial fibrillation or flutter	7 (1.5)	22 (4.6)	.004
Ventricular tachycardia or fibrillation†	7 (1.5)	16 (3.4)	.06
Sustained hypotension‡	15 (3.2)	51 (10.7)	<.001
Death	11 (2.3)	18 (3.8)	.19
Events within 60 days			
Myocardial infarction	5/448 (1.1)	10/462 (2.2)	.21
New atrial fibrillation or flutter	16/446 (3.6)	26/462 (5.6)	.14
Ventricular tachycardia or fibrillation	20/446 (4.5)	23/461 (5.0)	.72
Death	41/463 (8.9)	49/474 (10.3)	.41

*Total number of patients listed only when it varies from number randomized as shown.
†Reported by the investigator.
‡Defined as a systolic blood pressure below 80 mm Hg for more than 30 minutes, requiring intervention.





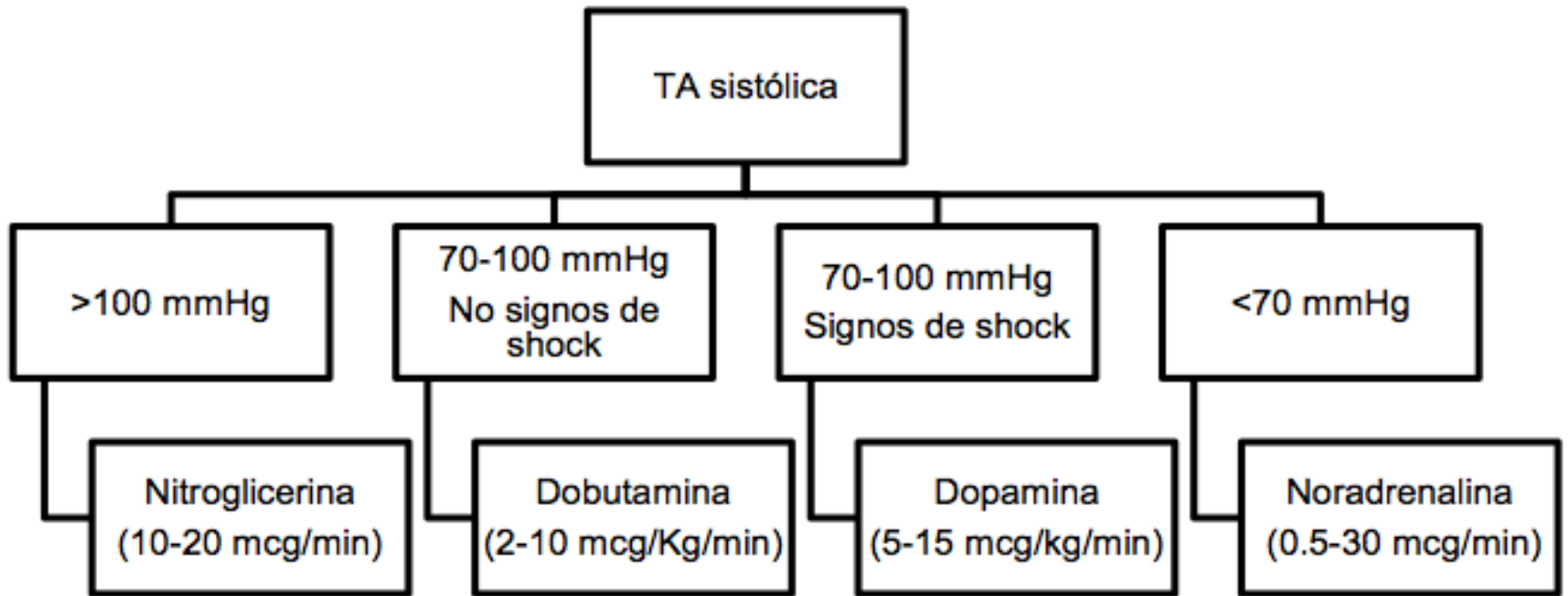
La indicación extemporánea de
inotrópicos aumenta la
mortalidad

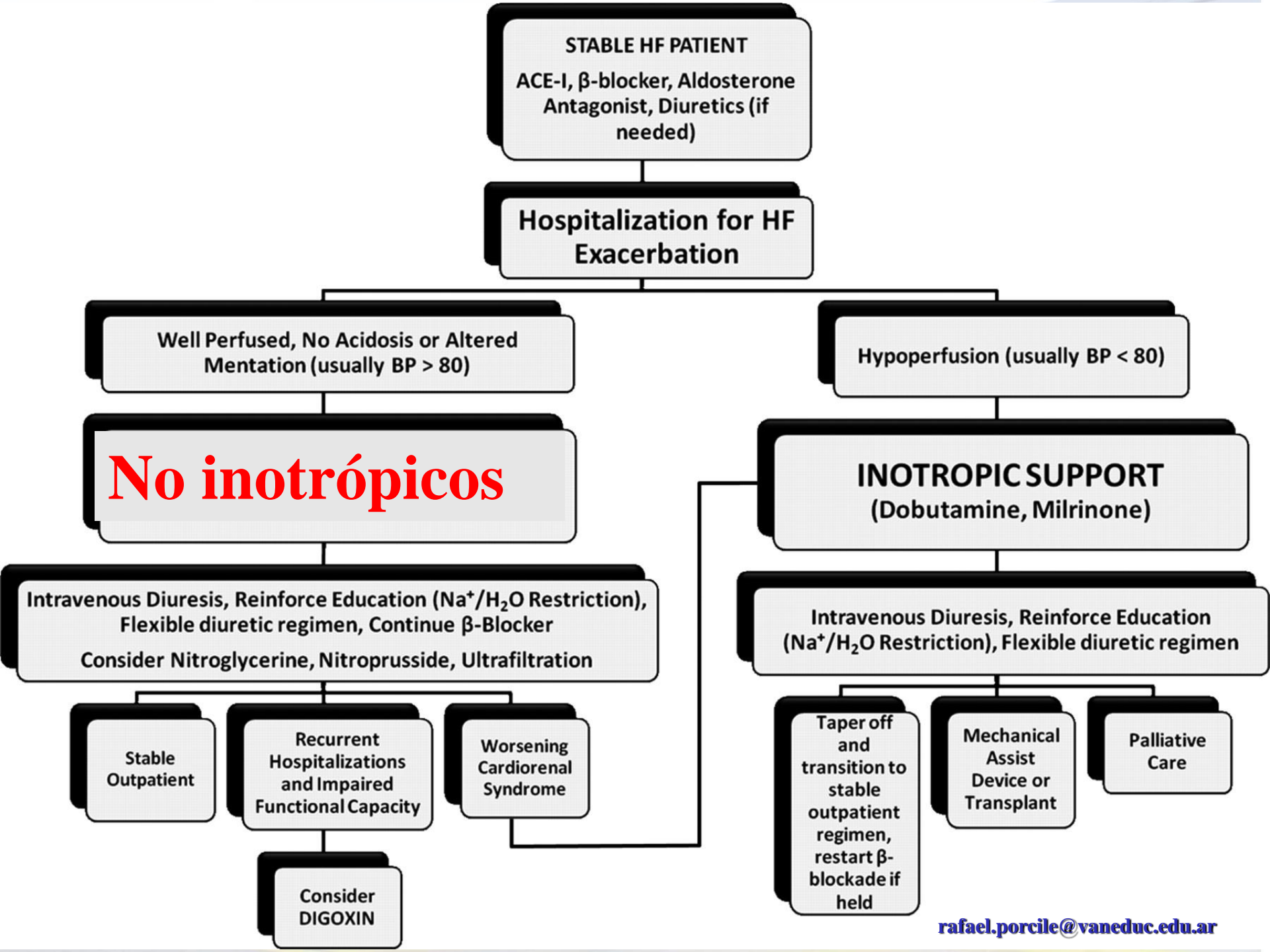
Entonces deberíamos
intentar inicialmente
condicionar precarga y post
carga



Mas vale una
estrategia
inotrópica que
un inotropico

Cuando **NO** inotrópicos





Contraindicaciones

- Disección aórtica.
- I Ao mod a sev.
- Daño cerebral irreversible.
- Insuficiencia Hepática (coagulopatías).
- Infecciones Graves no Controladas.
- Problemas Quirúrgicos no resueltos.

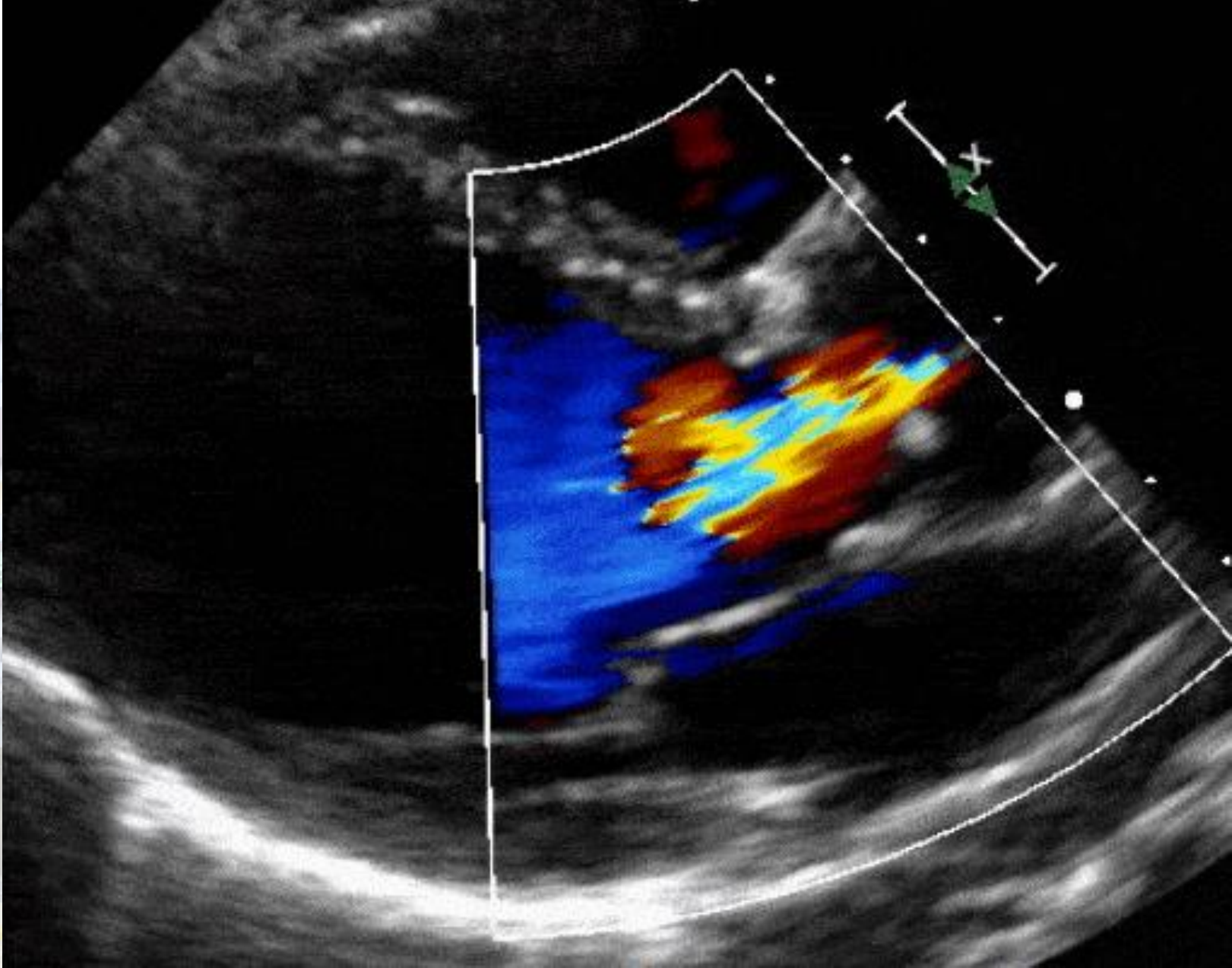


A 2 P 2

S 1

S 2

S 1



75 kg.

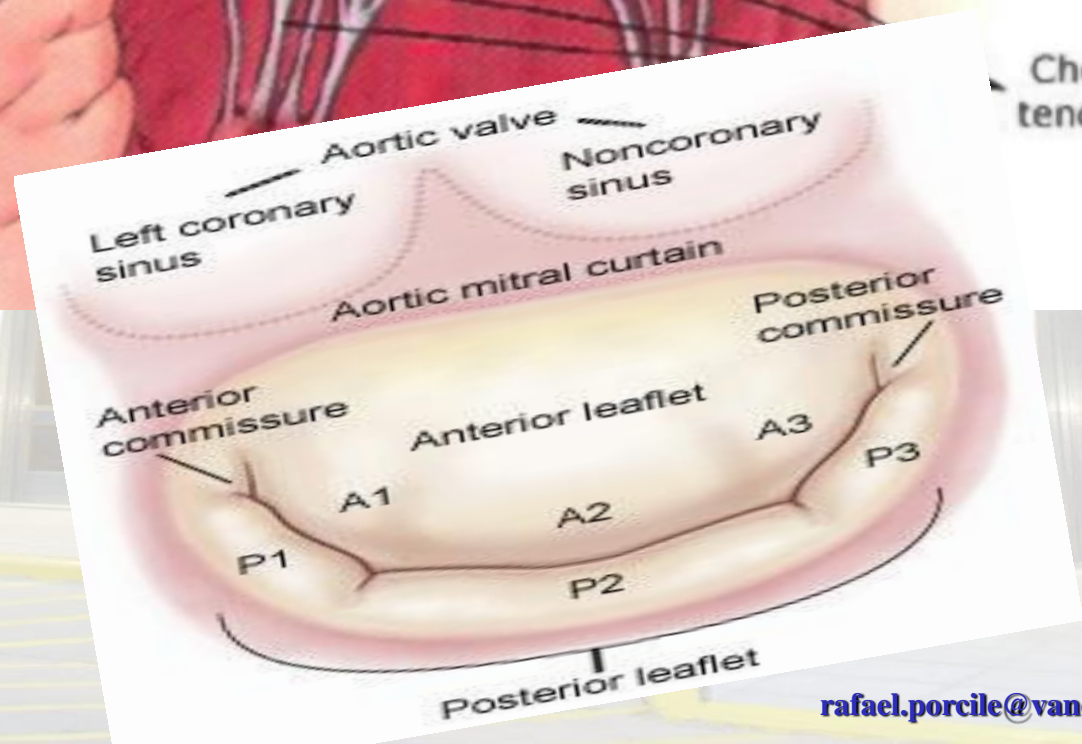
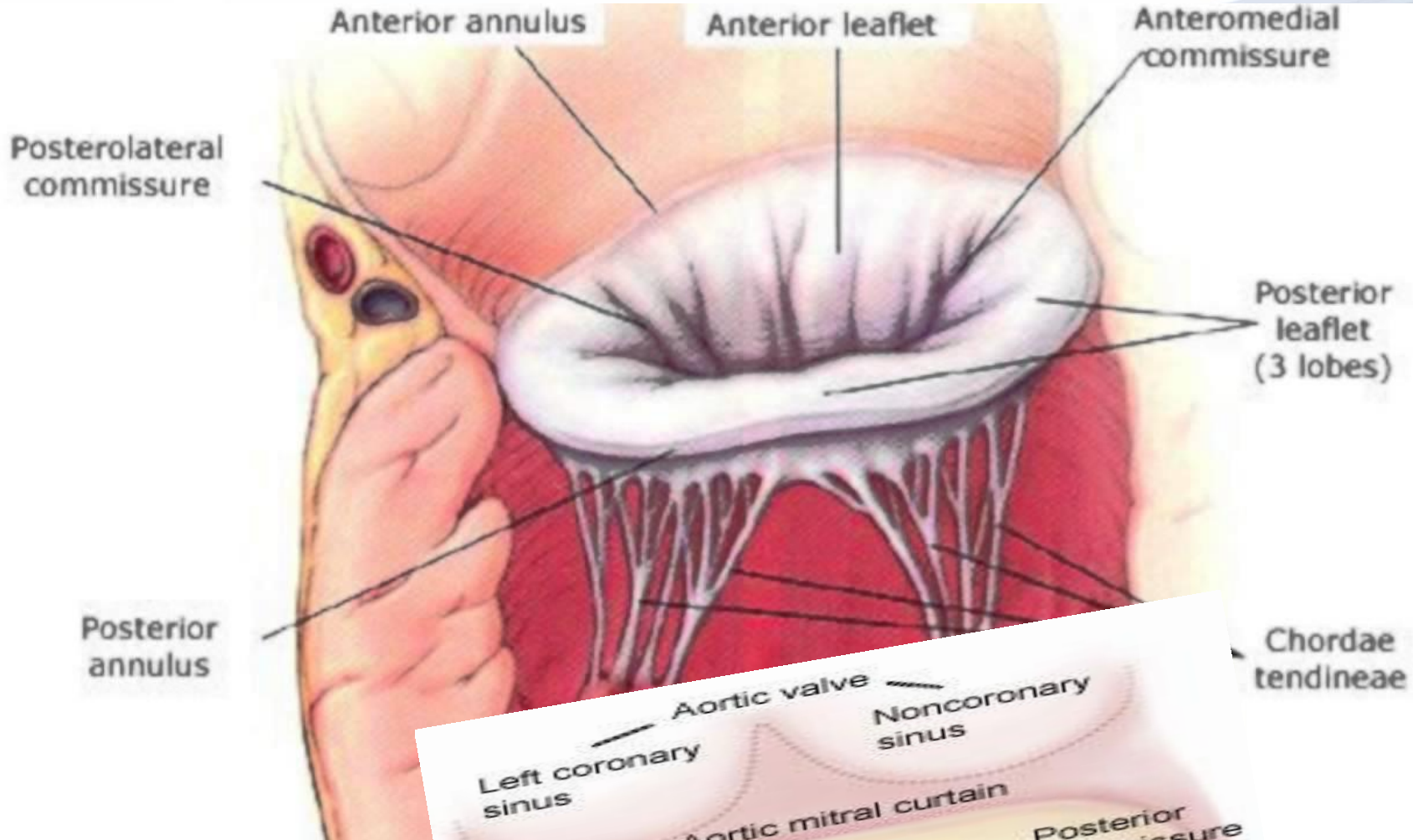
HOJA DE MONITOREO HEMODINAMICO
 PACIENTE: Maria José
 PESO: ALTURA 1,65 CAMA:
 SUPERFICIE CORPORAL: TALLA (cm) + PESO (kg) - 60 = 6.5 Sup. corporal

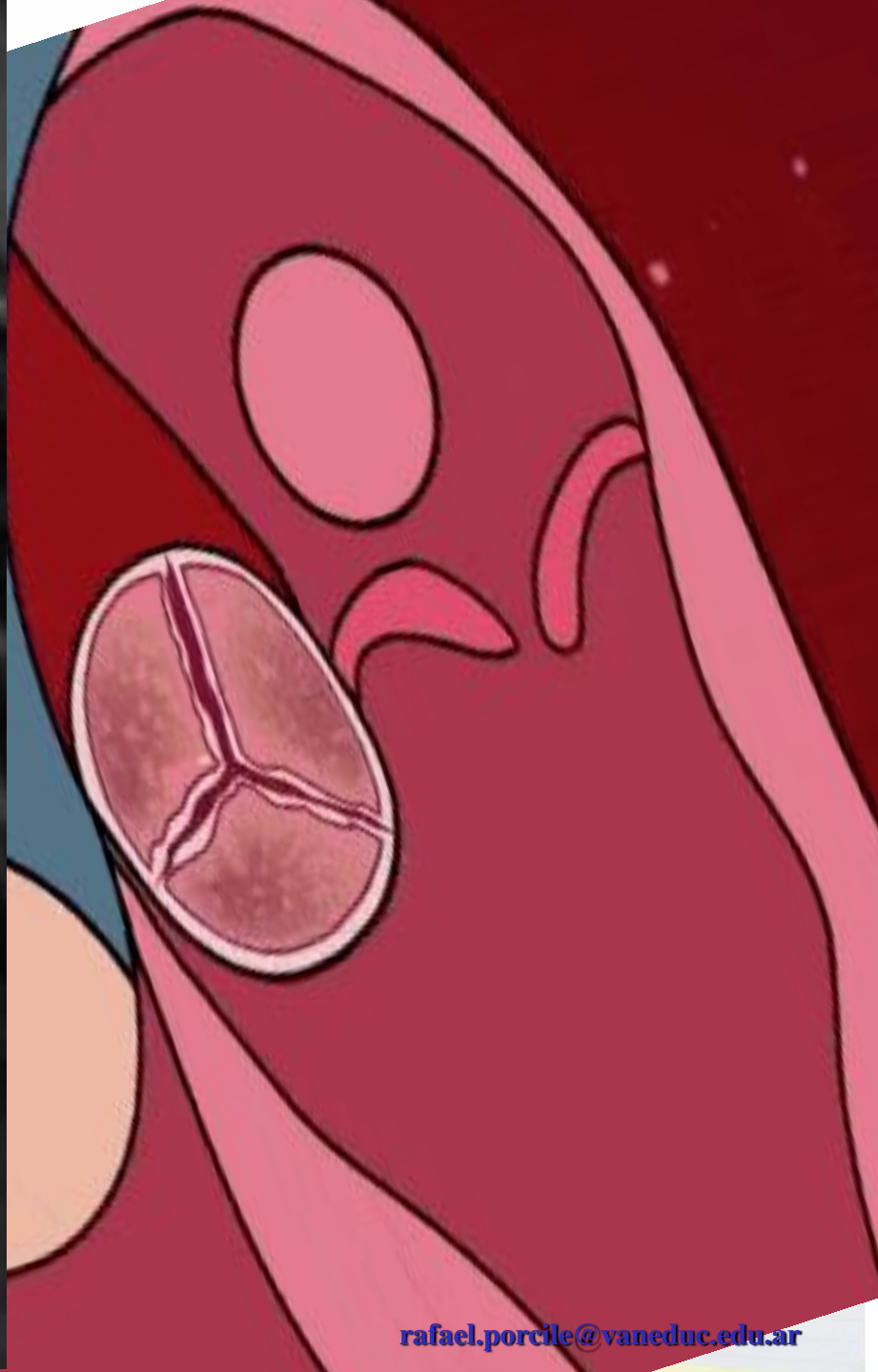
Fecha	01/06						
Operador							
NOMBRE							
Hora	05:30	07:00	08:00H	09:25h.	10:00H.	11:00H	13:25H
FC	72	69	71	109	83	93	75
TAM	35-38	94-50-34	103-61-44	142/48-39	110-60-41	137-68-45	119-56-32
PAP	29-21	29-24-12	46-33-26	41/28-31	36-26-20	42-30-24	31-21-21
PW	16	17	20	18	17	20	16
PAD	20	10	14	7	7	7	8
VM	3.31	3.26	3.72	6.29	5.4	5.46	6.04
IC	1.28	2.02	2.01	3.86	2.9	2.77	3.75
ITSVI	7						
ITSVD							
RVS	797	851	872	789	964	882	680
RVP	290	170	174	137	200	207	190
Vol. sist.	25.1	55	55			53	42
SV02							
DBT	6 mm	6	8 g.	6 g.	4 mm	4 g.	4
DOPA							
NPS		APOG 300	—	3ml	3ml	3ml.	4
NA							
ADR							
MILR							
IABP							
Expansion.							
ARM	S1	S1	S1.	S1	S1	S1	S1
PEEP	7	7	7	4.	4	4.	4.

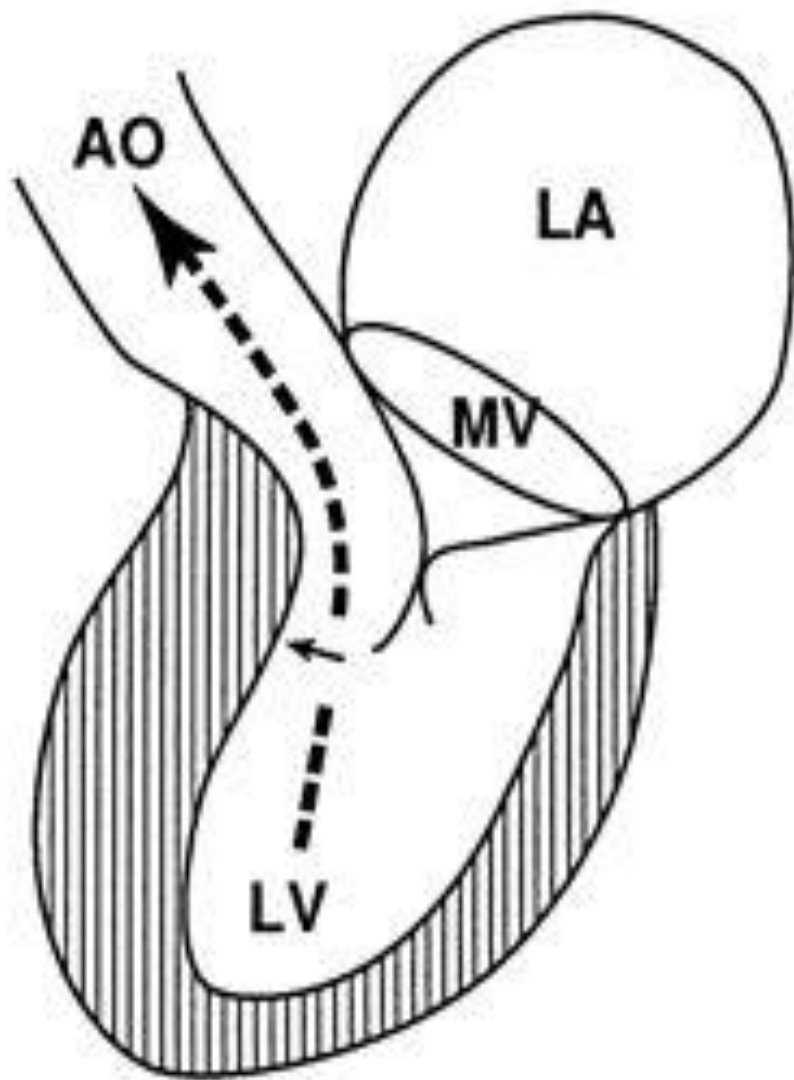
1ml Kg/hora

The background image shows a multi-story building with a light blue facade and a dark red horizontal band. The band contains the text 'UNIVERSIDAD INTERAMERICANA' in white and green, and 'HOSPITAL ESCUELA' in white and green. There are logos on the building, including a stylized book icon. The foreground shows a paved area with yellow markings.

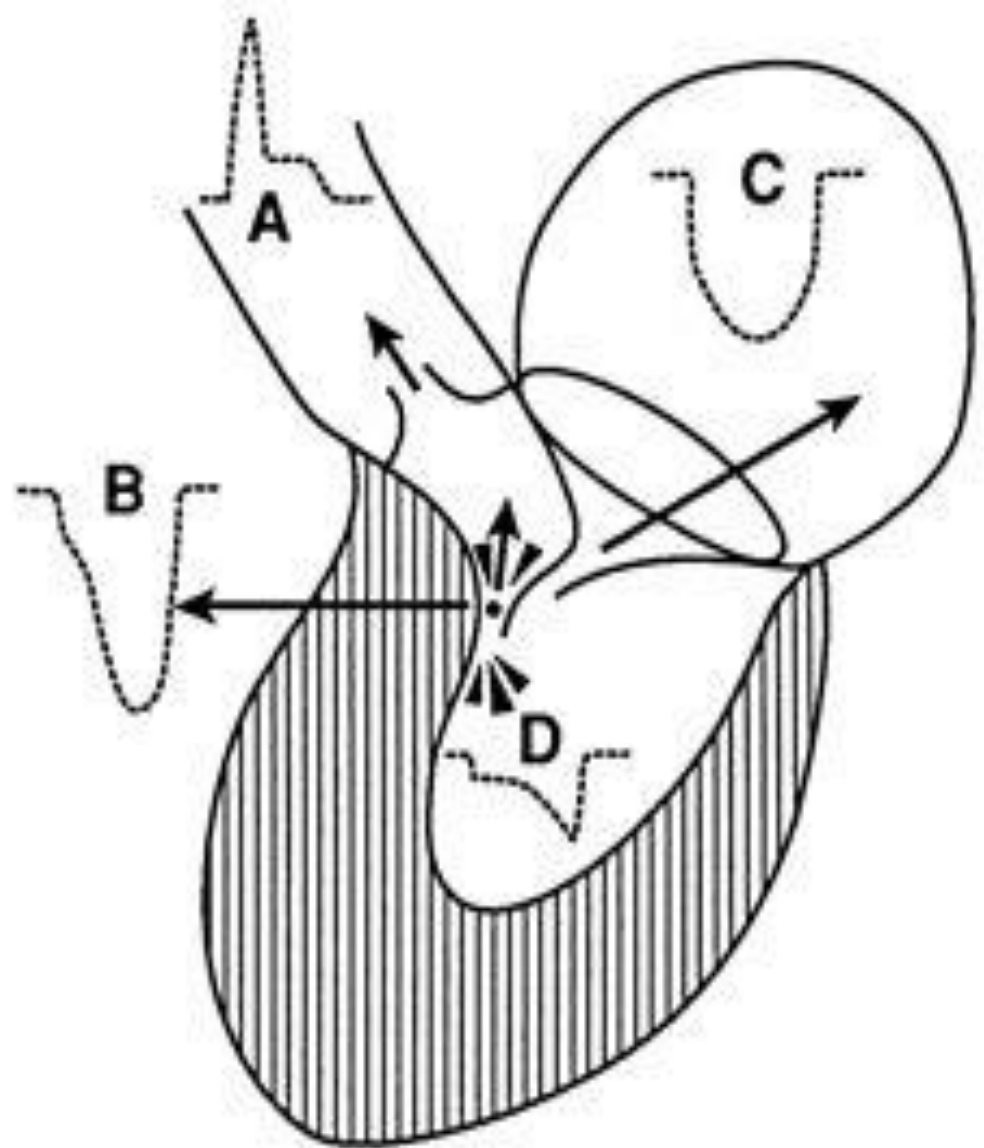
- Miocardiopatía
Hipertrofica y falla
diastólica







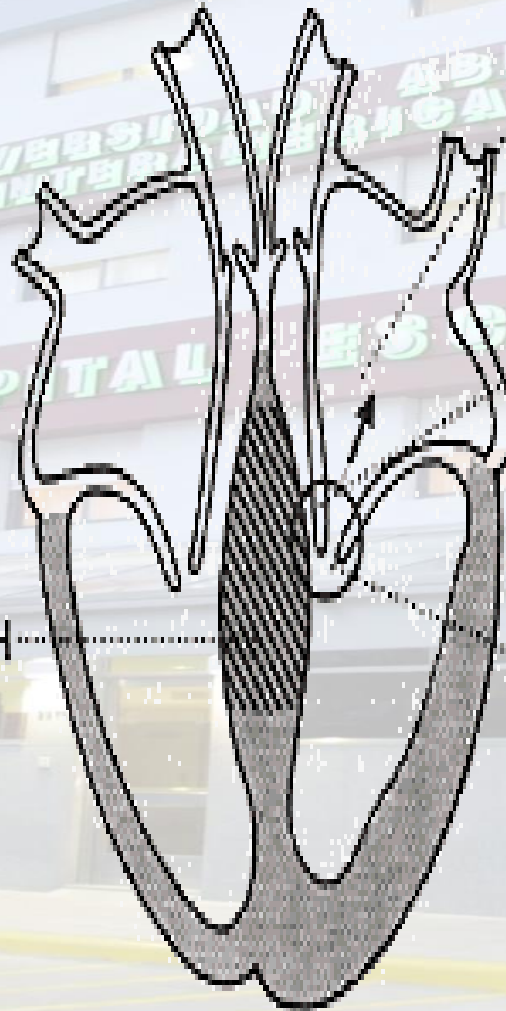
**EARLY
SYSTOLE**



**MITRAL LEAFLET-
SEPTAL CONTACT**

Hypertrophic Cardiomyopathy

Asymmetric septal hypertrophy with obstruction

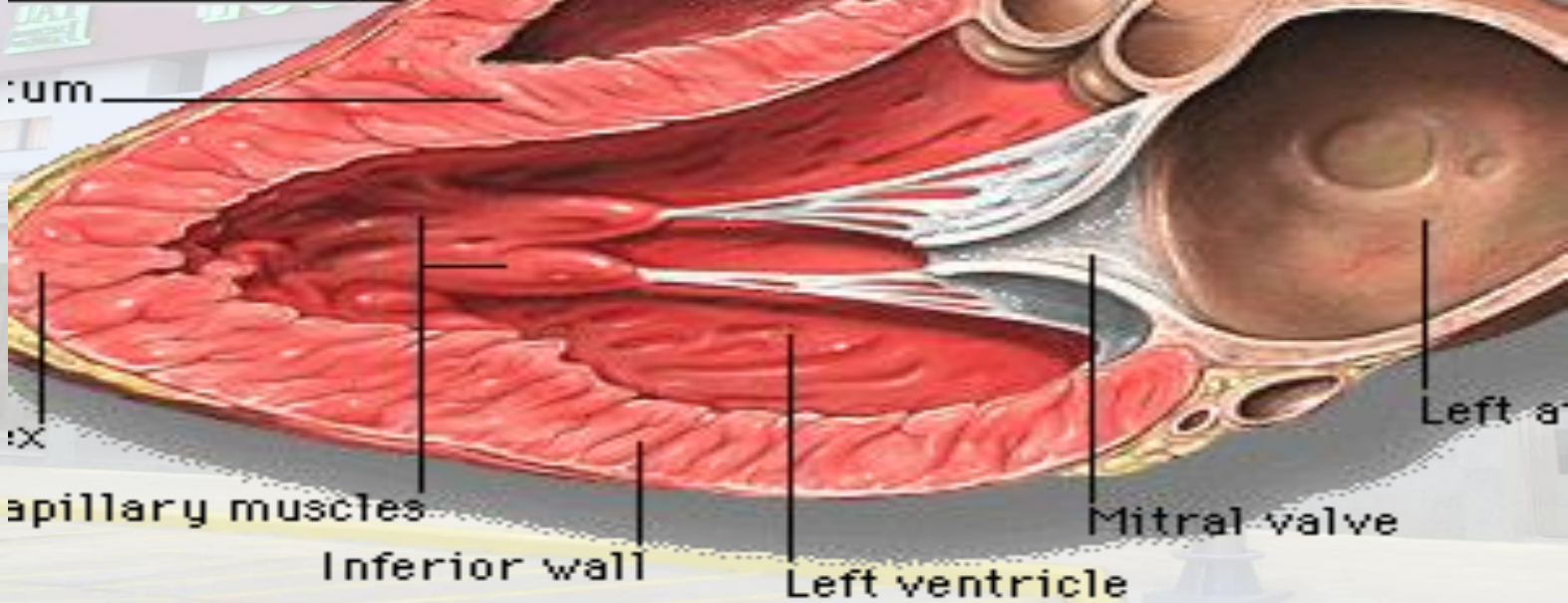


Blood leaks back through mitral valve
■ mitral regurgitation

Mitral valve presses against septum causing obstruction to blood flow

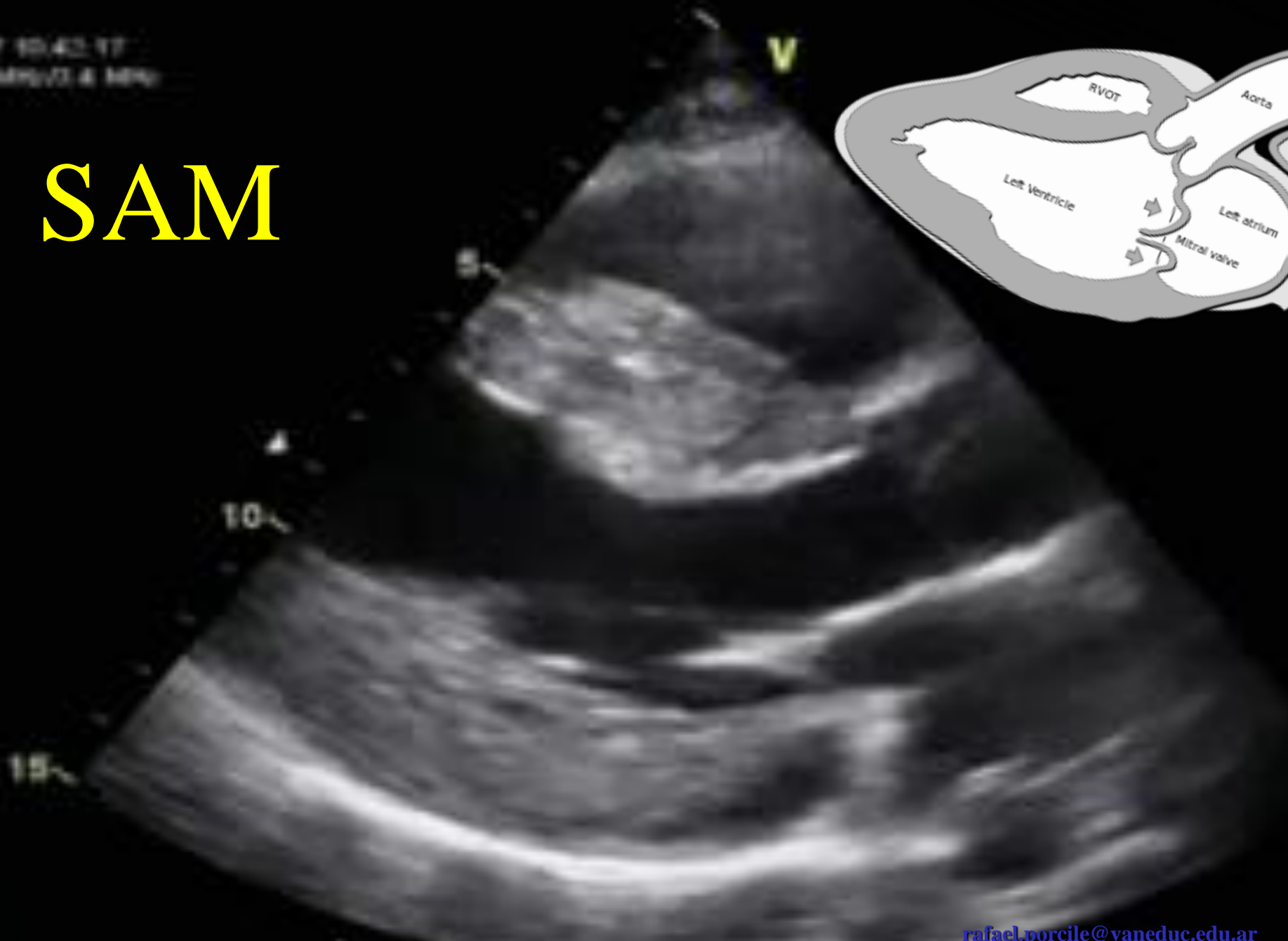
ASH

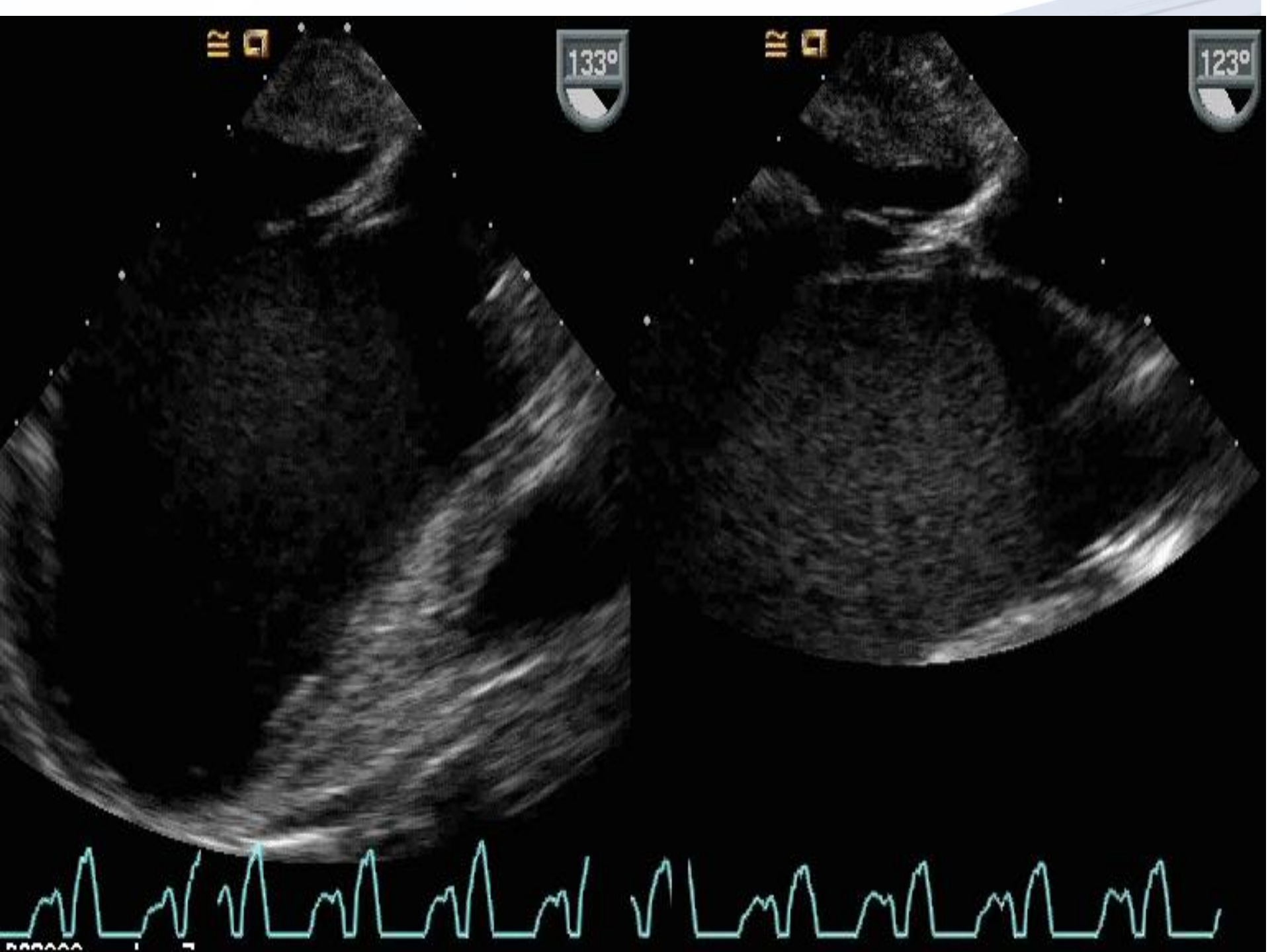
Systolic anterior motion of the mitral valve (SAM)



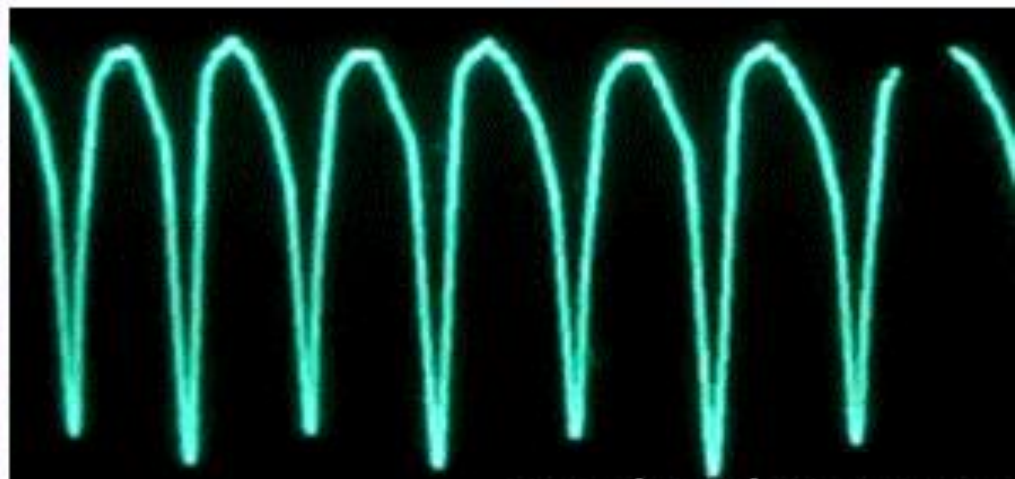
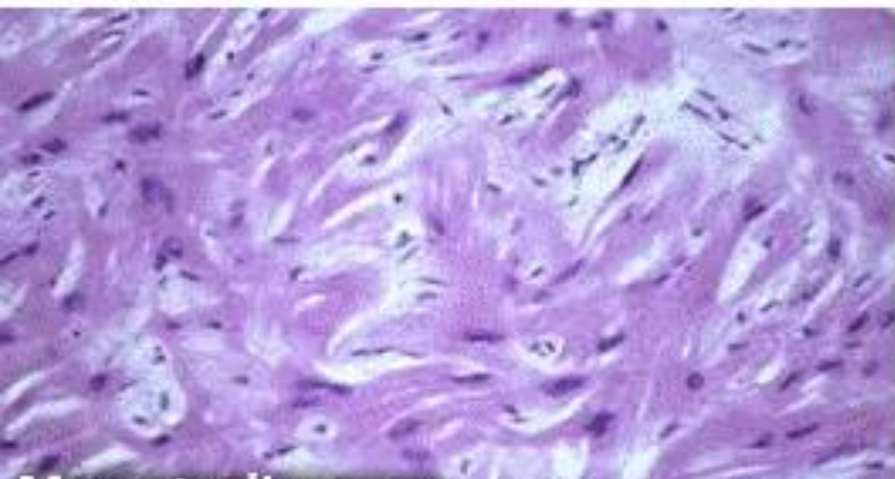
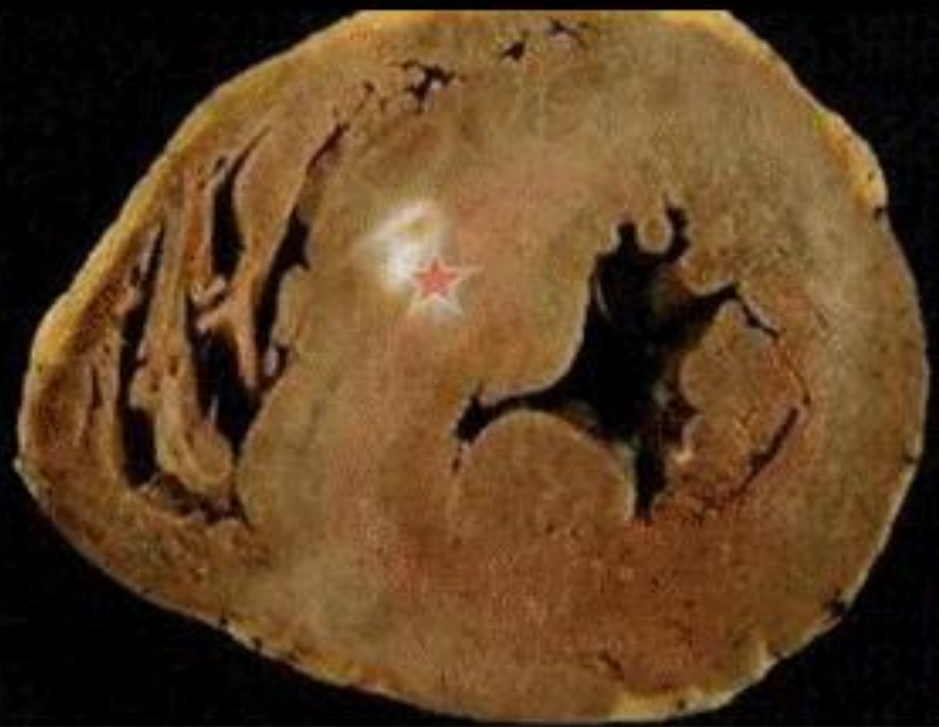
07 10:42:17
7 MHz/3.4 MHz

SAM

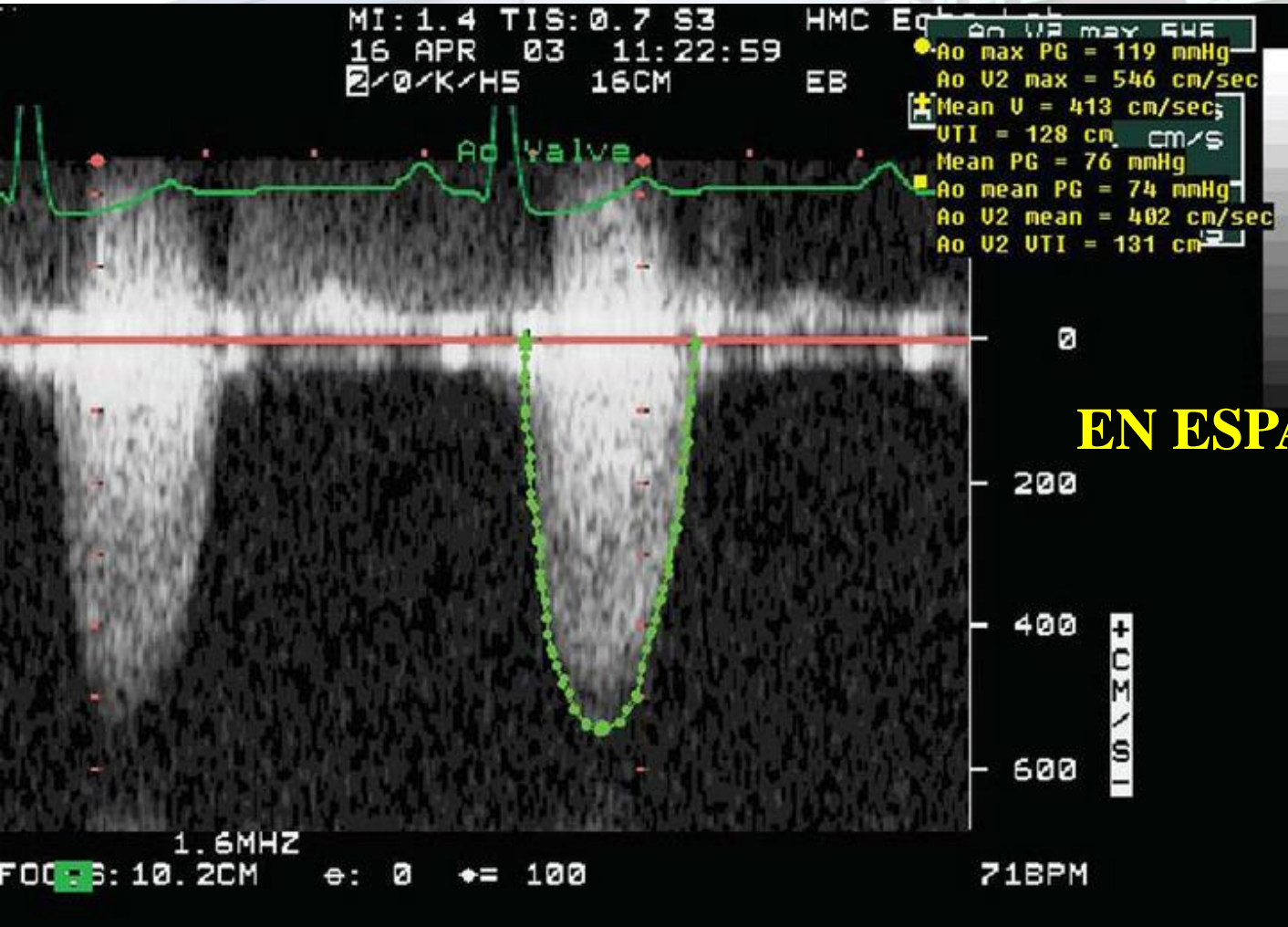




How often LVOT is the arrhythmic focus in ventricular tachycardia of HOCM?



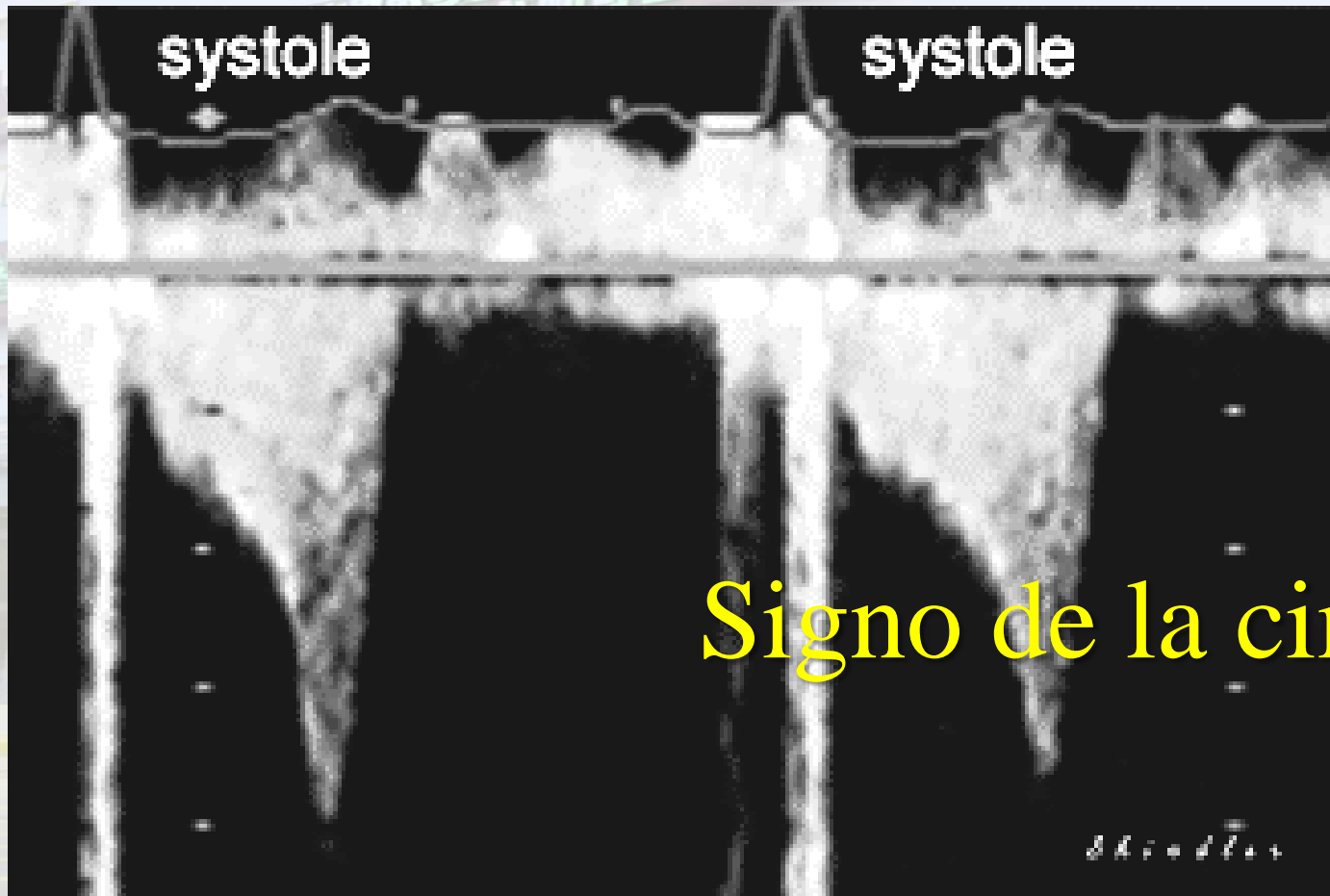
DOPLER EN ESTENOSIS VALVULAR AORTICA





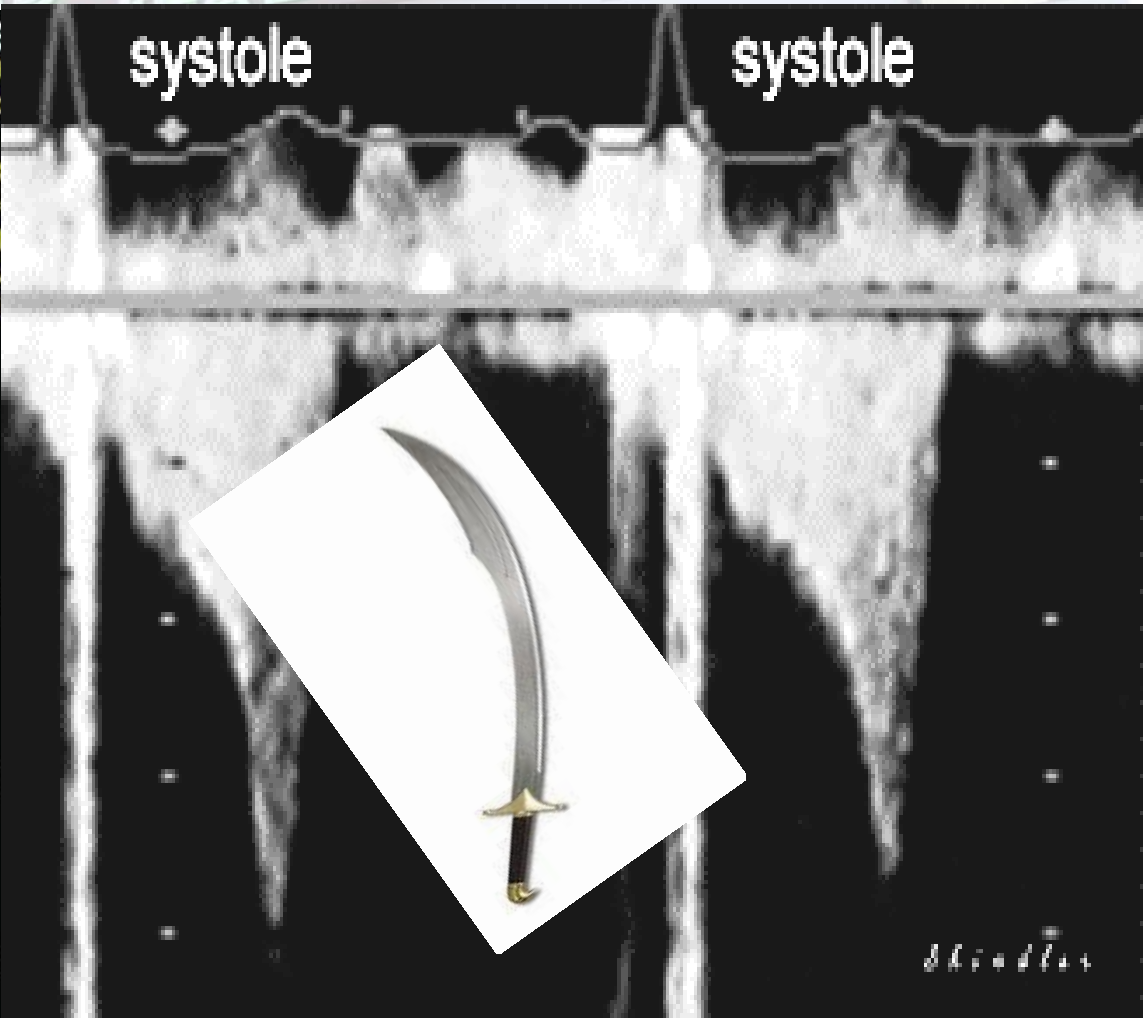
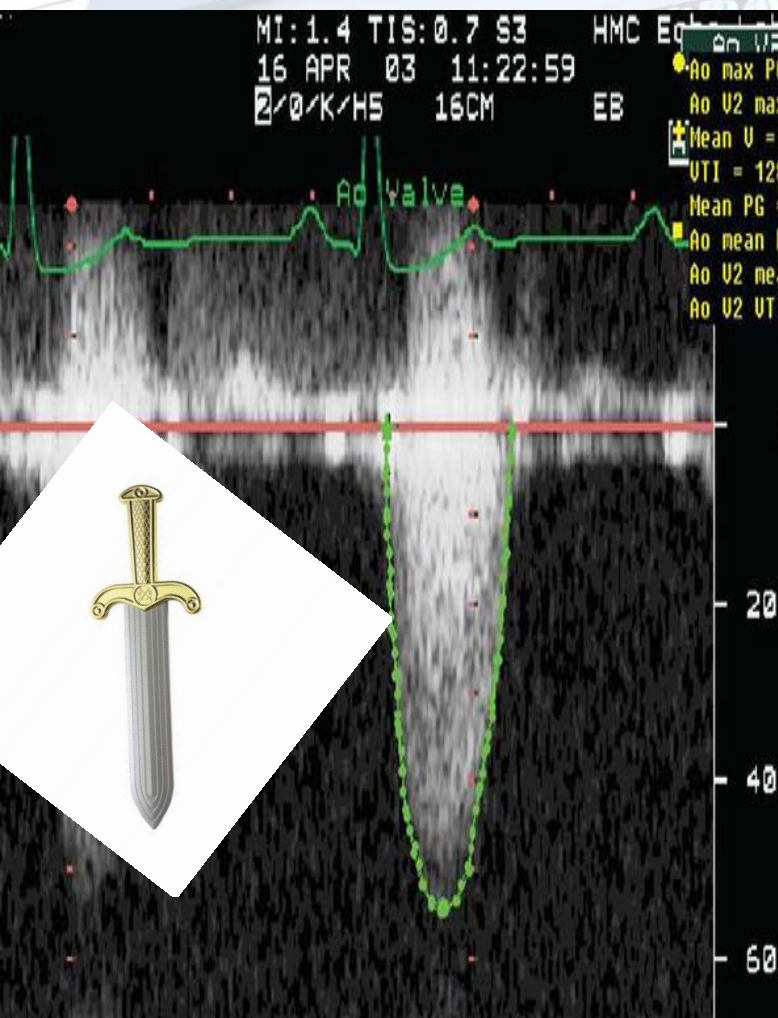
BionicBlonde.com

DOPLER EN OBSTRUCCIÓN DINAMICA TSVIS

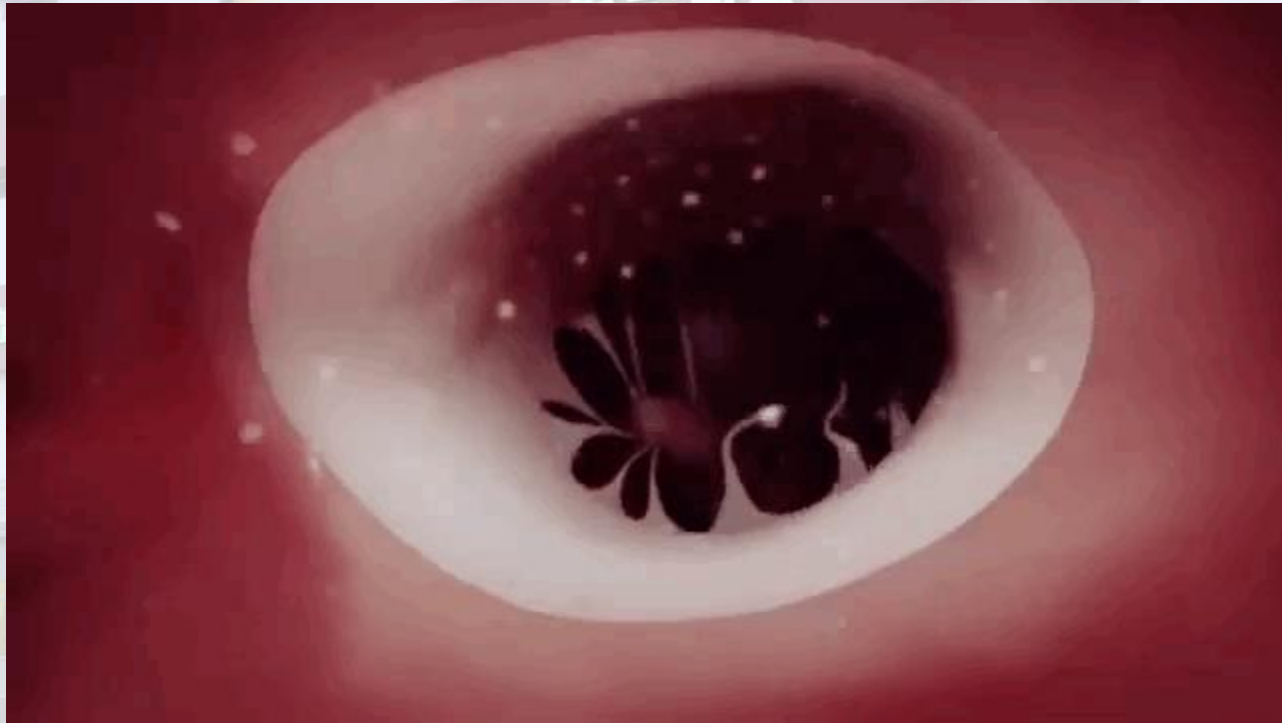




DIFERENCIA DINAMICA



IM



Glucósidos cardiacos: Digitalicos



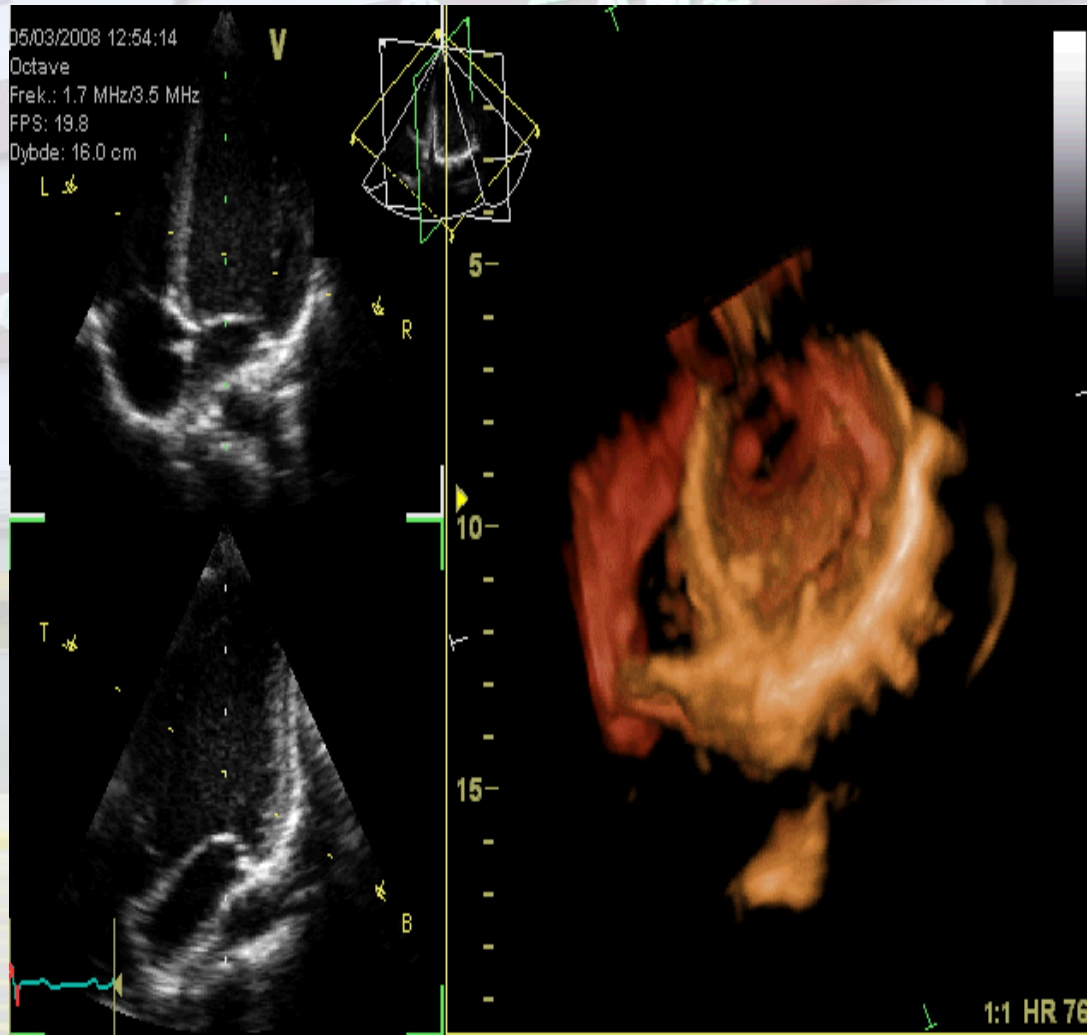
William Withering 1785
:Diuréticos



En 1920 se descubre su
acción inotrópica



DIGOXINA



Digitalicos

Digoxina

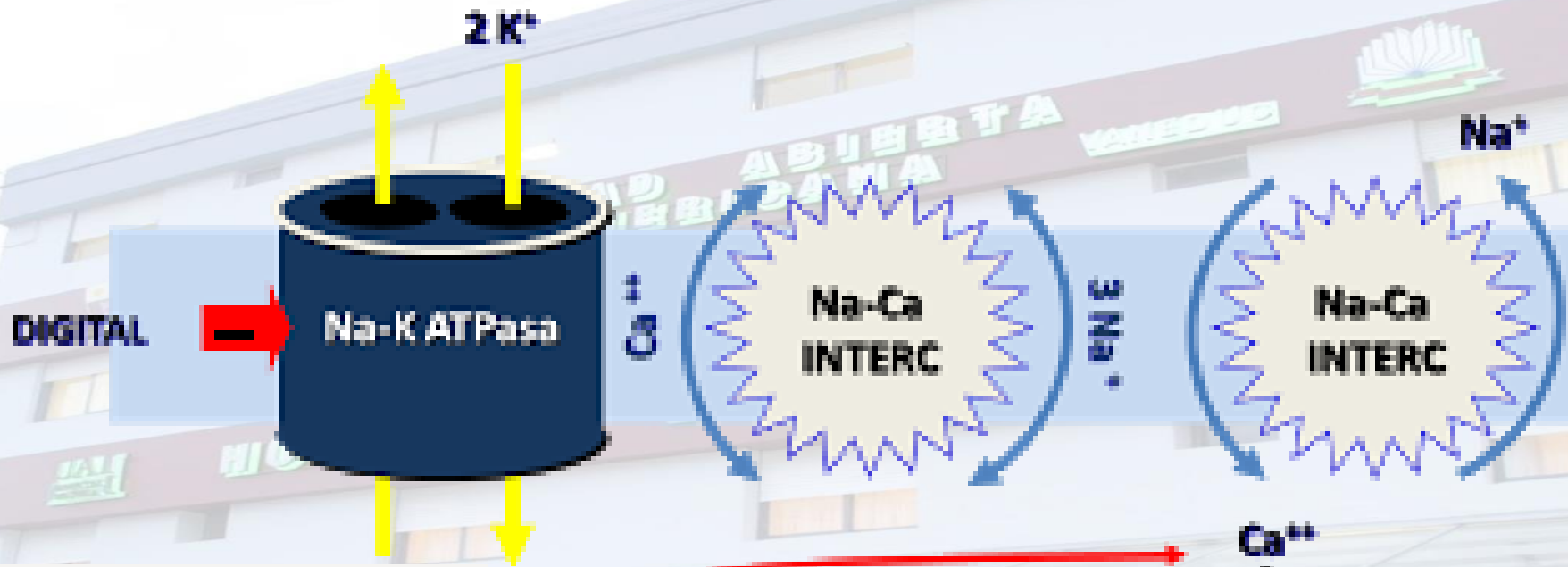
Metildigoxina

Bloquean la bomba ATPasa Na-K

Se incrementa la concentración de sodio intracelular

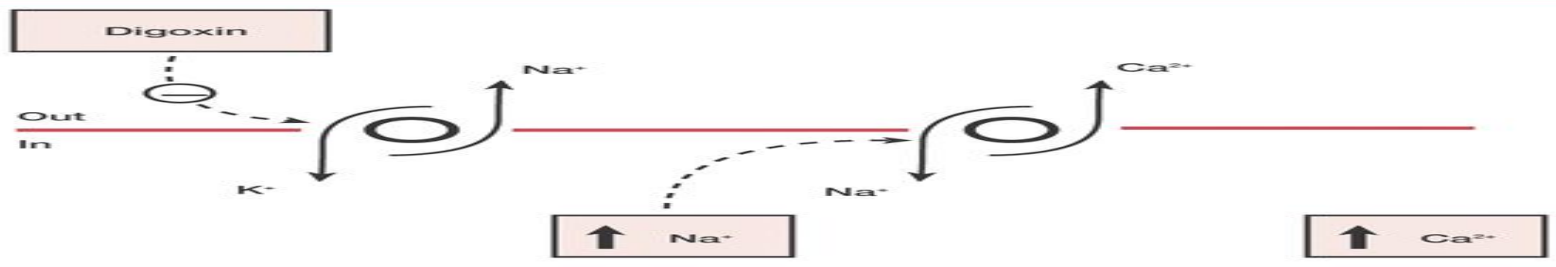
Se activa el intercambiador $\text{Na}^+/\text{Ca}^{++}$ de la membrana

Incrementa la concentración de calcio intracelular

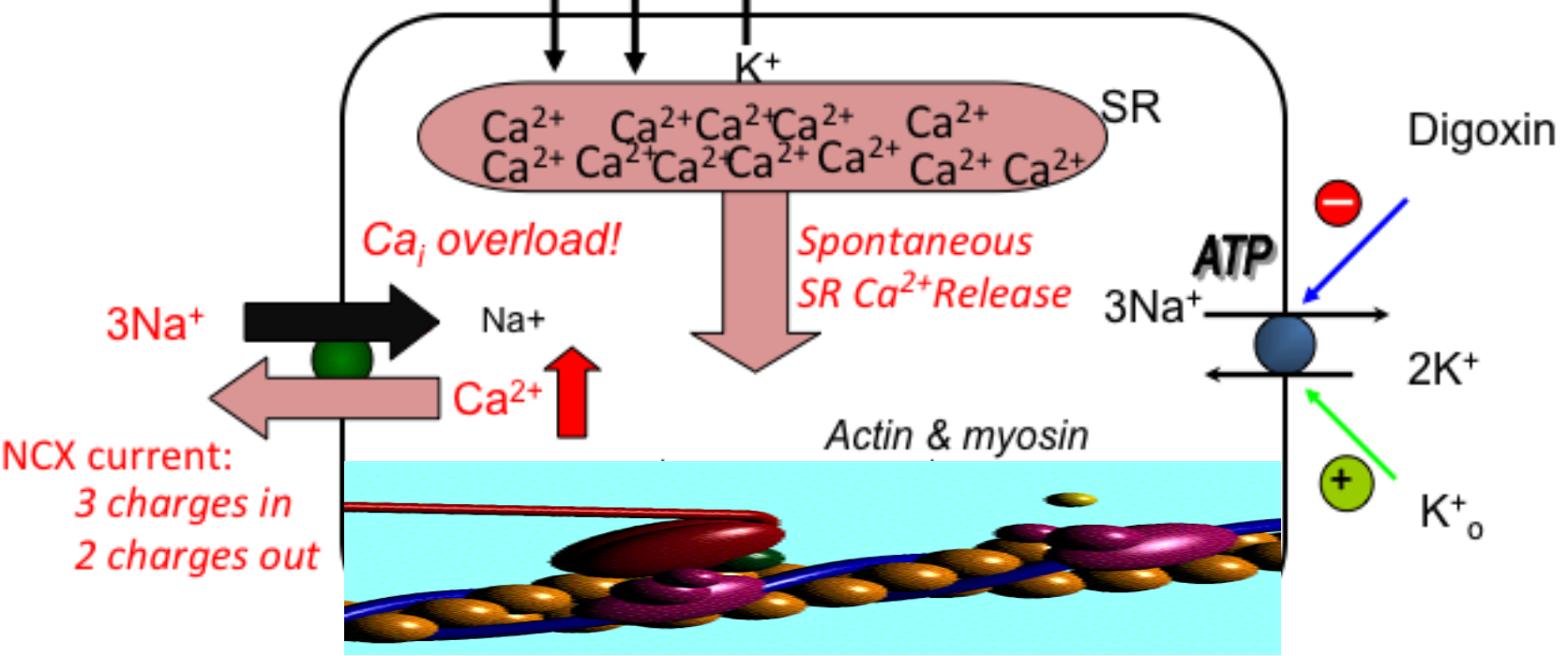


Al aumentar cargas positivas intracelulares reduce la polarización diastólica

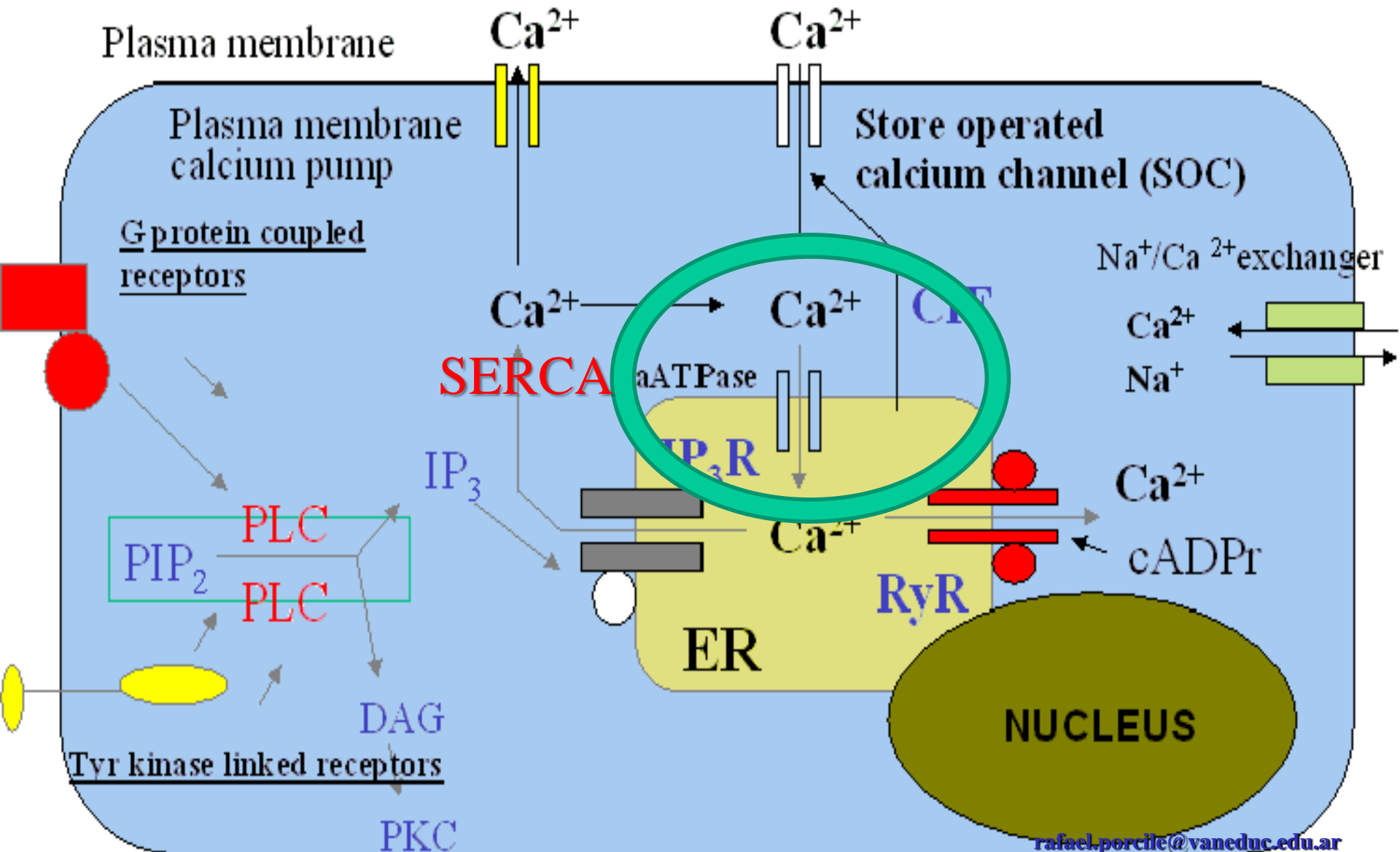


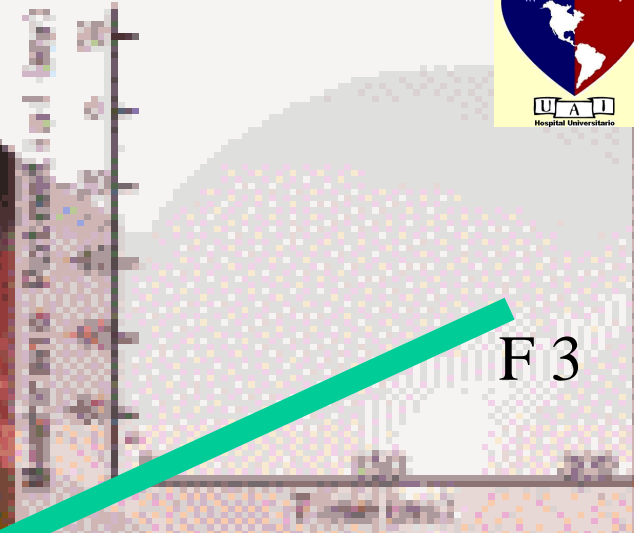


Na_o^+ : 140 mM	Na_i^+ : 7 mM
Ca_o^{2+} : 2 mM	Ca_i^{2+} : ~100 nM
K_o^+ : 4 mM	K_i^+ : 145 mM



Calcium homeostasis





SERCA

SARCOPLASMIC
ENDO
RETUCULUM CALCIUM
ATPASE PUMP

AUMENTO DE LA CONCENTRACION DE CALCIO CITOPLASMATICO

F 3



SERCA

**SARCOPLASMIC
ENDO
RETUCULUM CALCIUM
ATPASE PUMP**

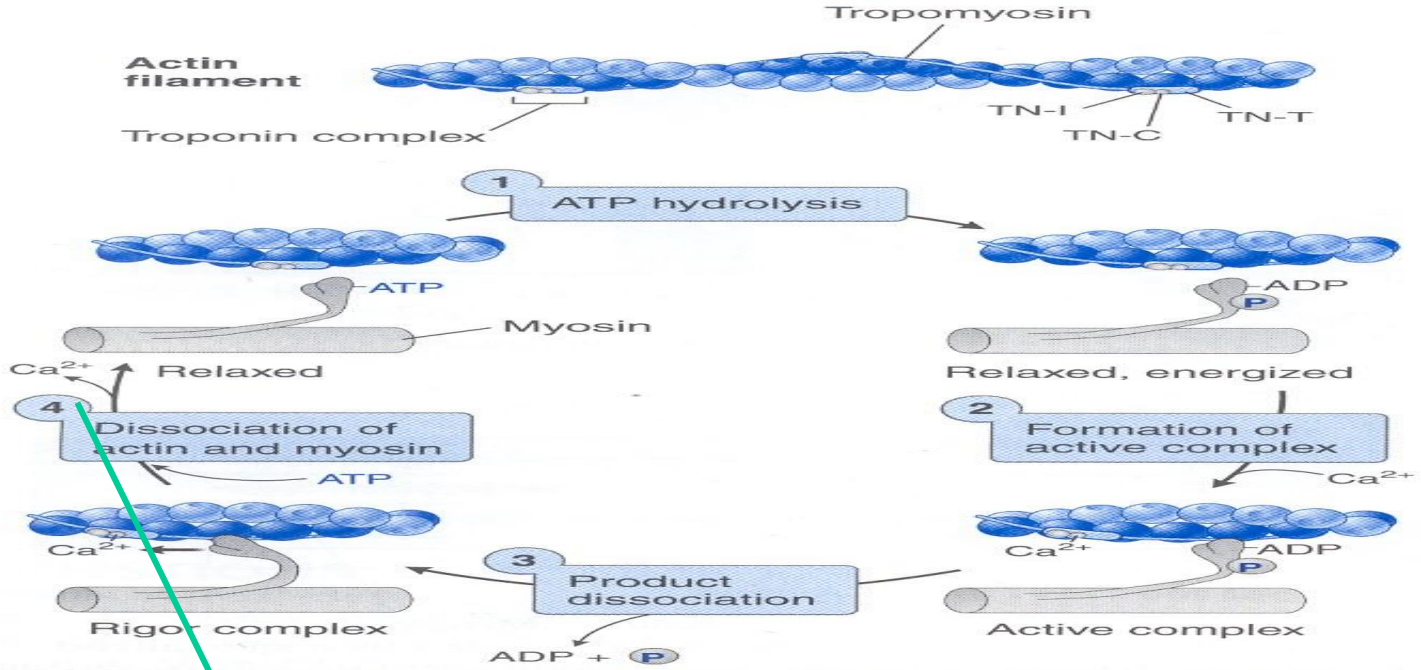
AUMENTO DE LA CONCENTRACION DE CALCIO CITOPLASMATICO



***DEUDA DE
OXIGENO***



O₂



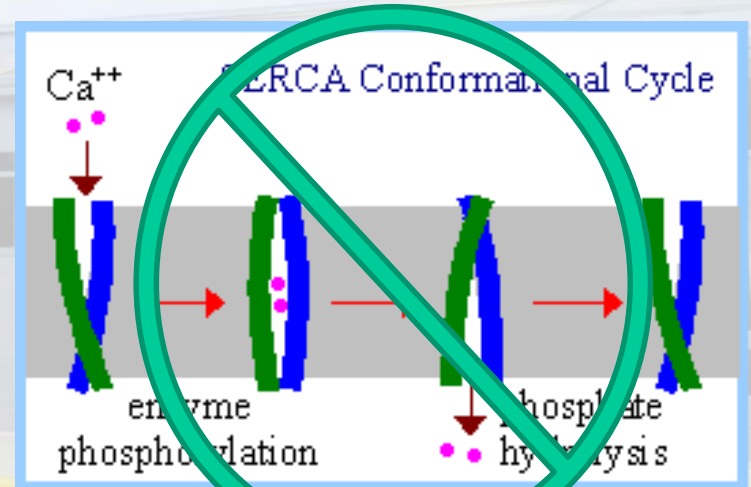
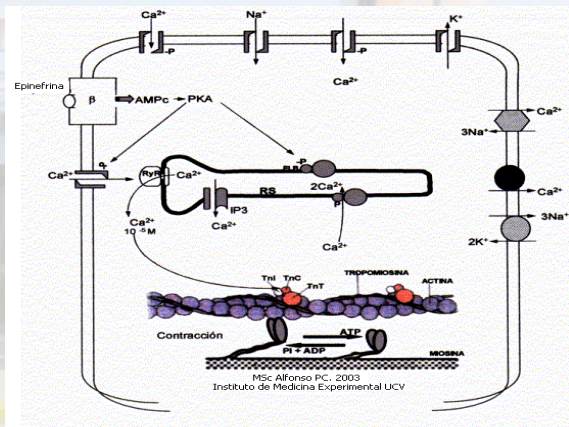
CONTRACCIÓN

**Gradiente de Calcio
DEPENDIENTE**

RELAJACIÓN

Digitalicos Aumentan el Calcio citoplasmático

- Aumentan de su ingreso extra celular
- Reducen su bombeo al circuito sarcoplasmico

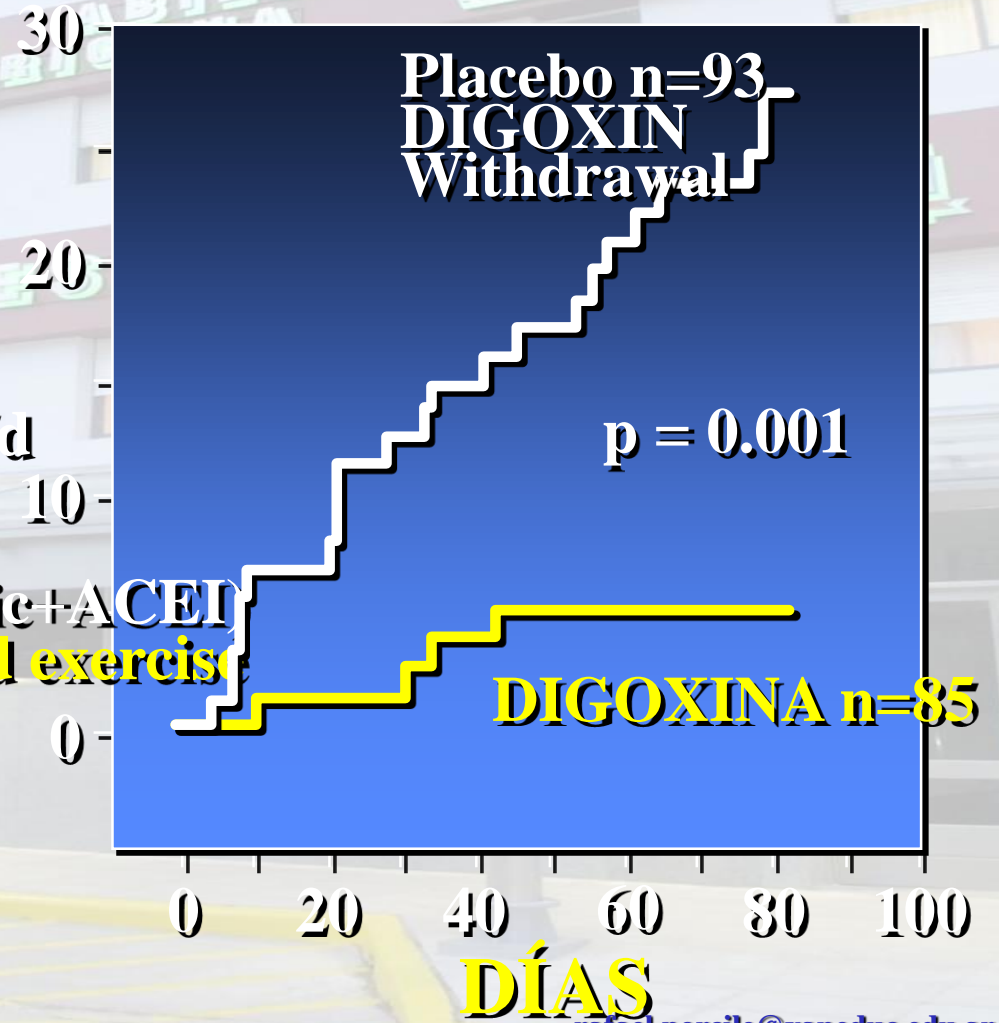


DIGOXINA

EFFECTO SOBRE EVOLUCIÓN DE LA ICC

**%
PROGRESIÓN**

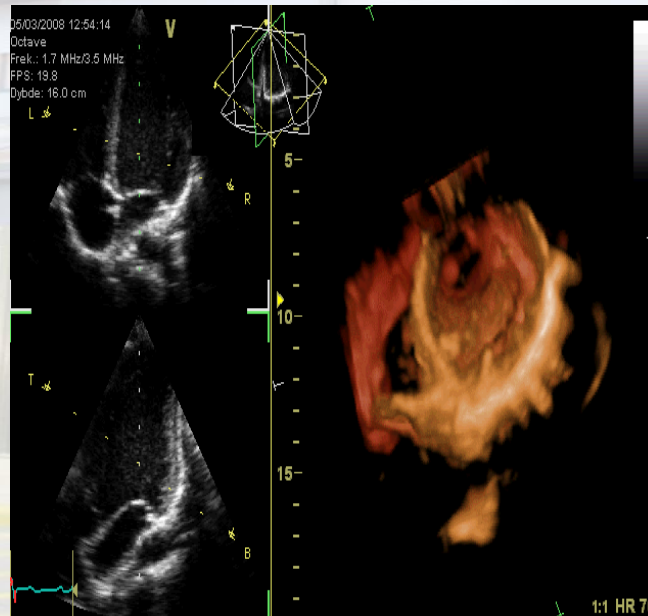
DIGOXIN: 0.125 - 0.5 mg /d
(0.7 - 2.0 ng/ml)
EF < 35%
Class I-III (digoxin+diuretic+ACEI)
**Also significantly decreased exercise
time and LVEF.**



RADIANCE
N Engl J Med 1993;329:1

DIGOXINA

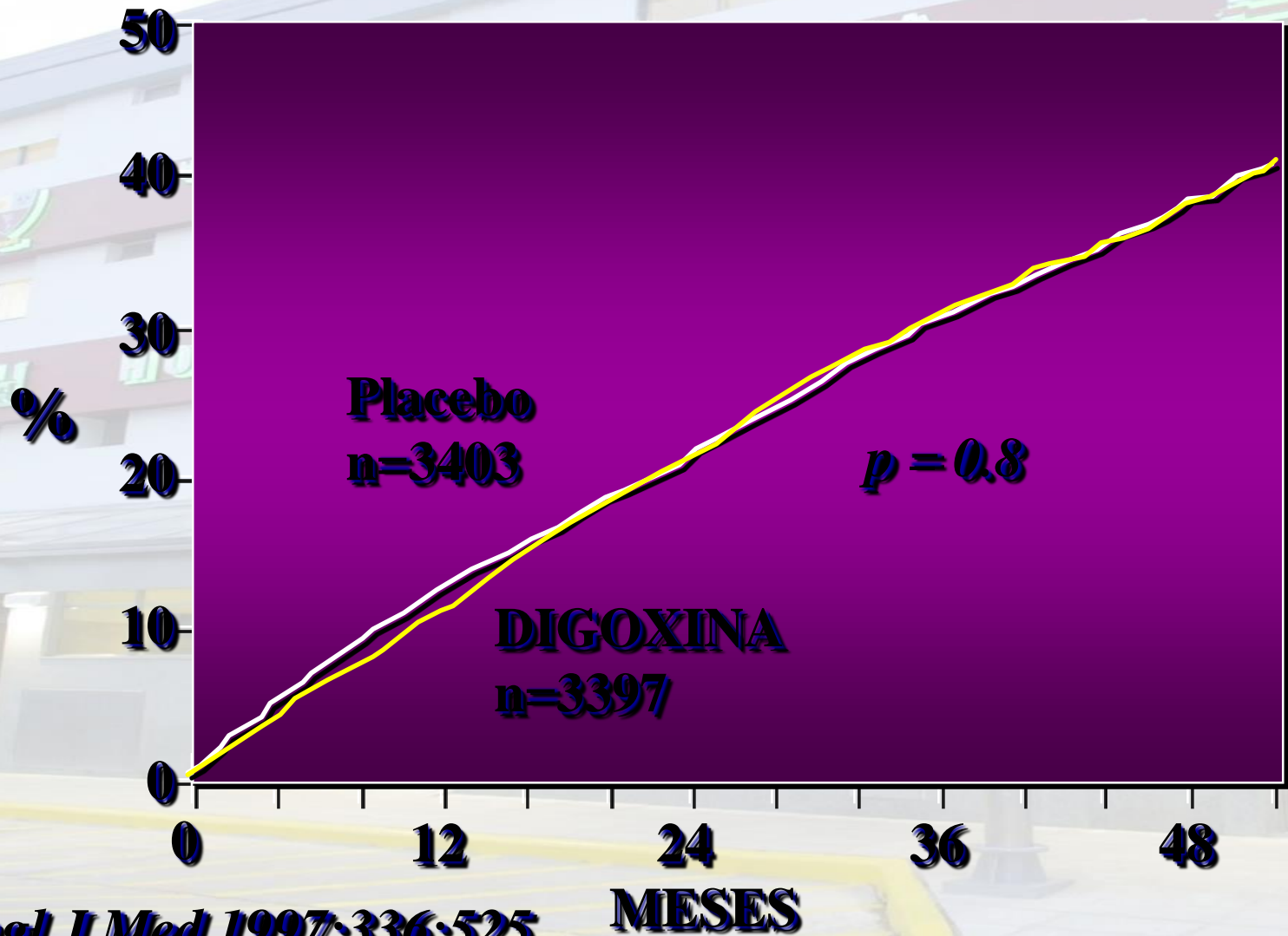
**AUMENTA LA CONCENTRACIÓN DE CALCIO
INTRACELULAR**



ISQUEMIA



DIGOXINA Y MORTALIDAD EN ICC



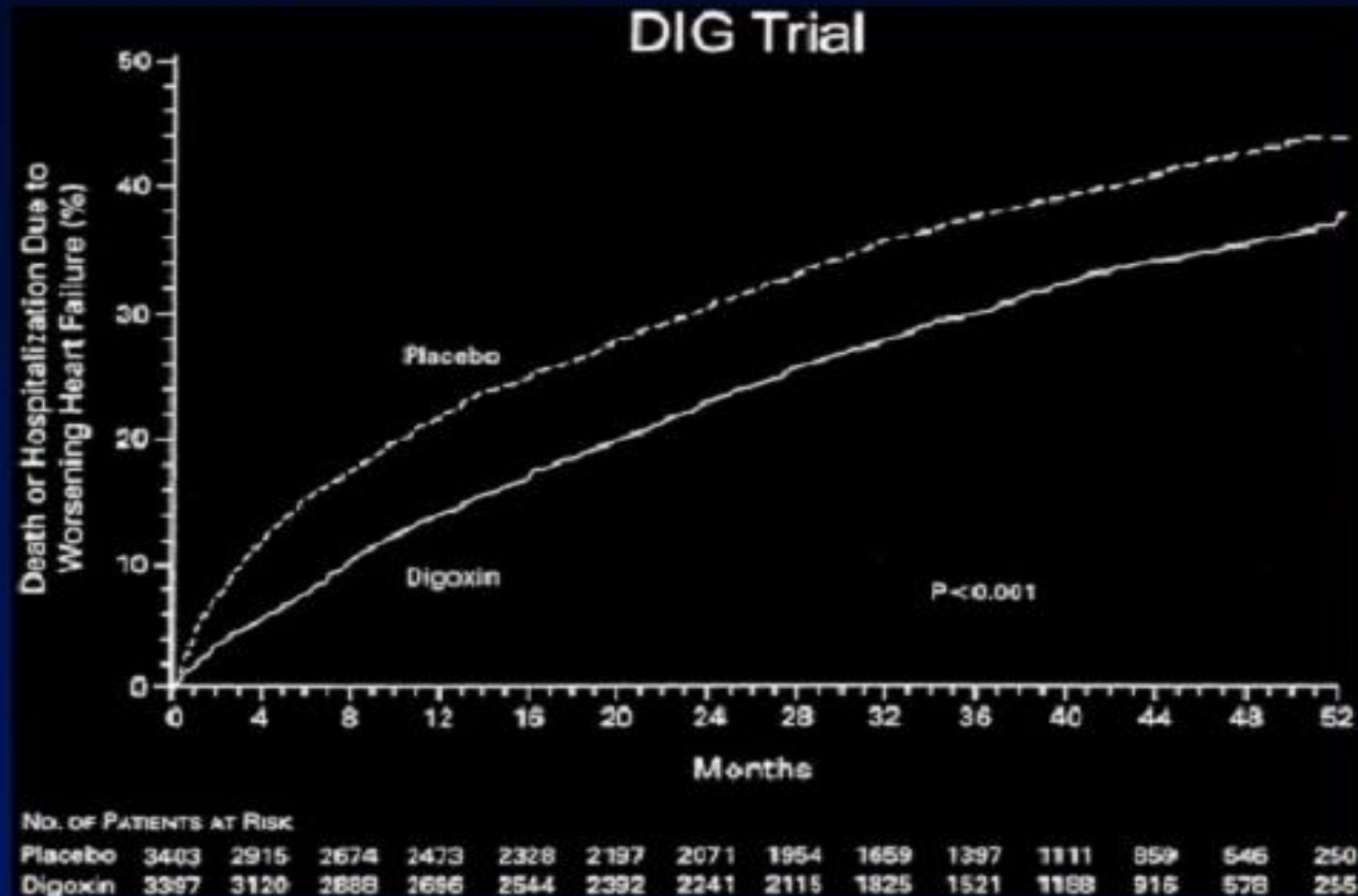
DIG

N Engl J Med 1997;336:525

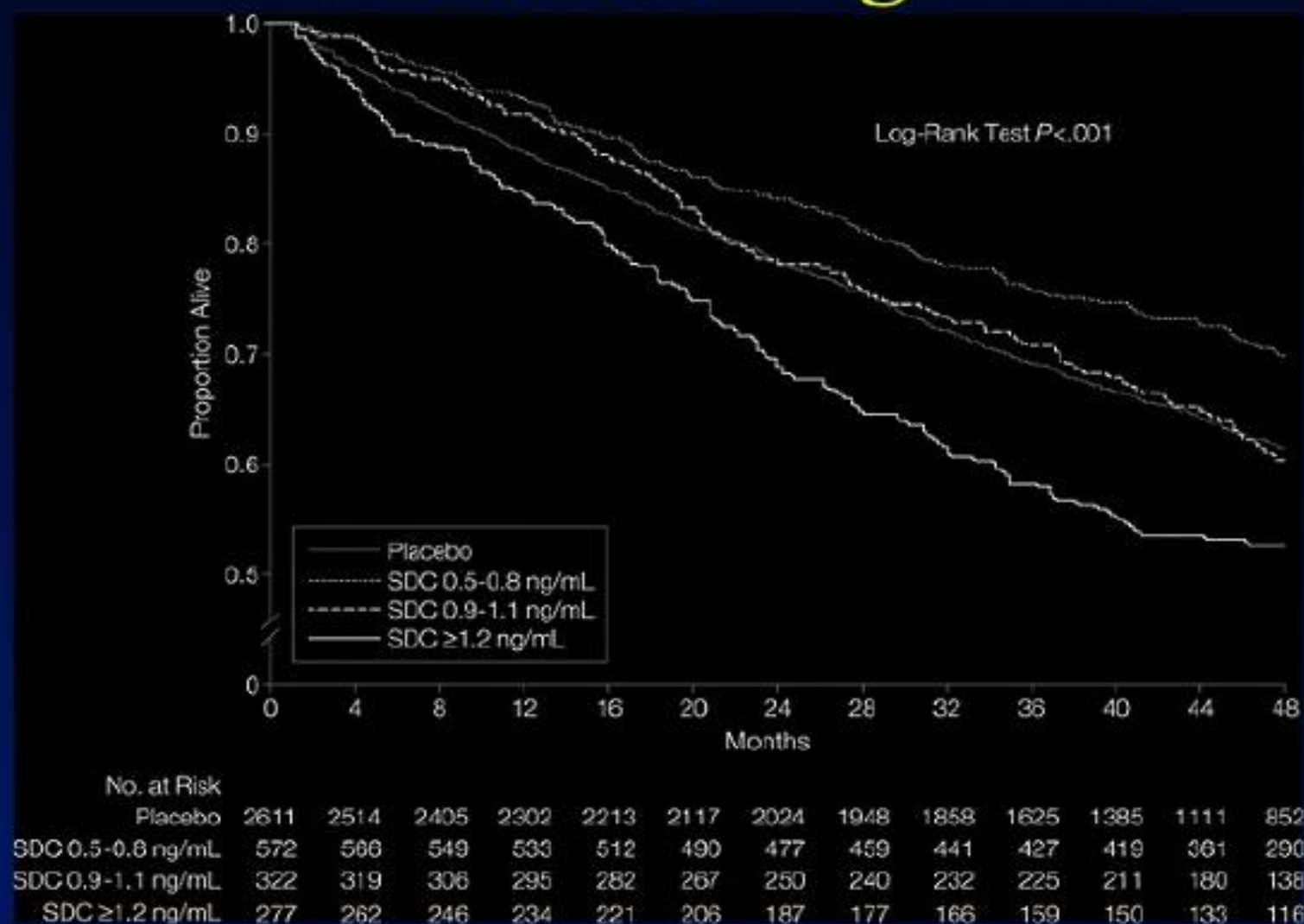
MESES

Pero Disminuye los Internamientos y Síntomas

Mortalidad y hospitalizaciones

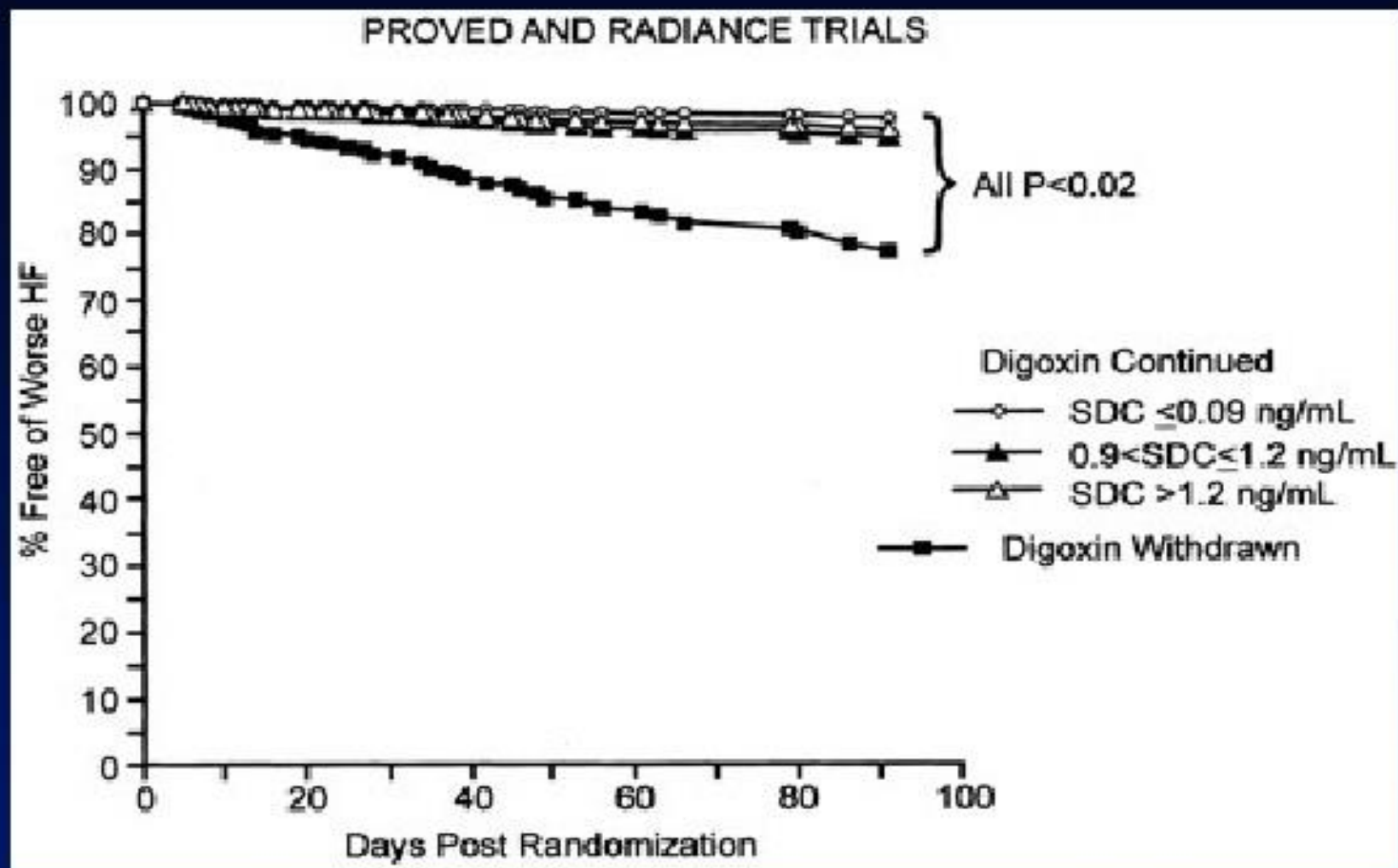


Mortalidad Depende de los Niveles de Digoxina



S S Rathore. *JAMA*. 2003;289:871-878

Digoxin Withdrawal Worsens HF, Independent of Dig Level

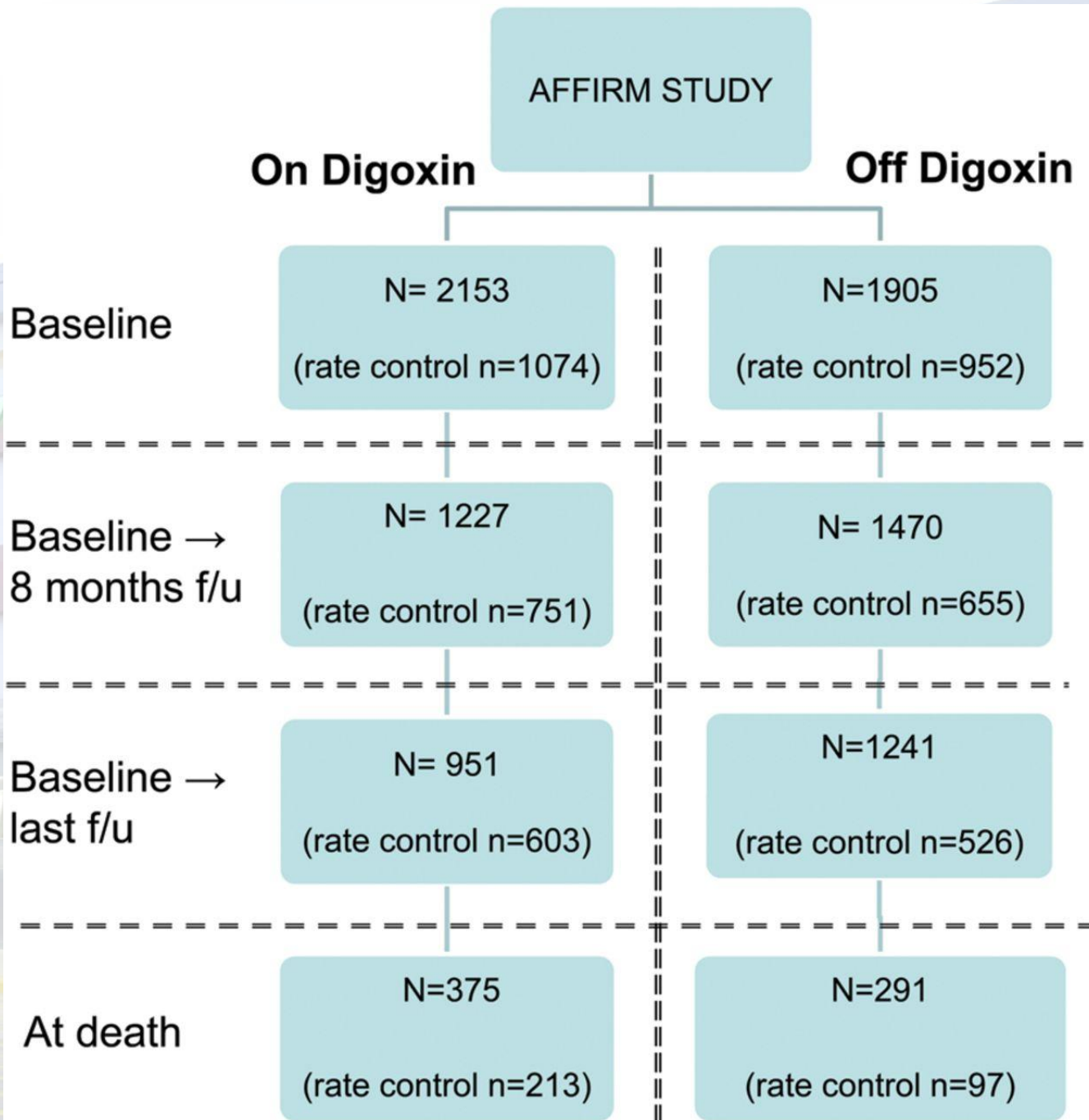


Increased mortality among patients taking digoxin—analysis from the AFFIRM study

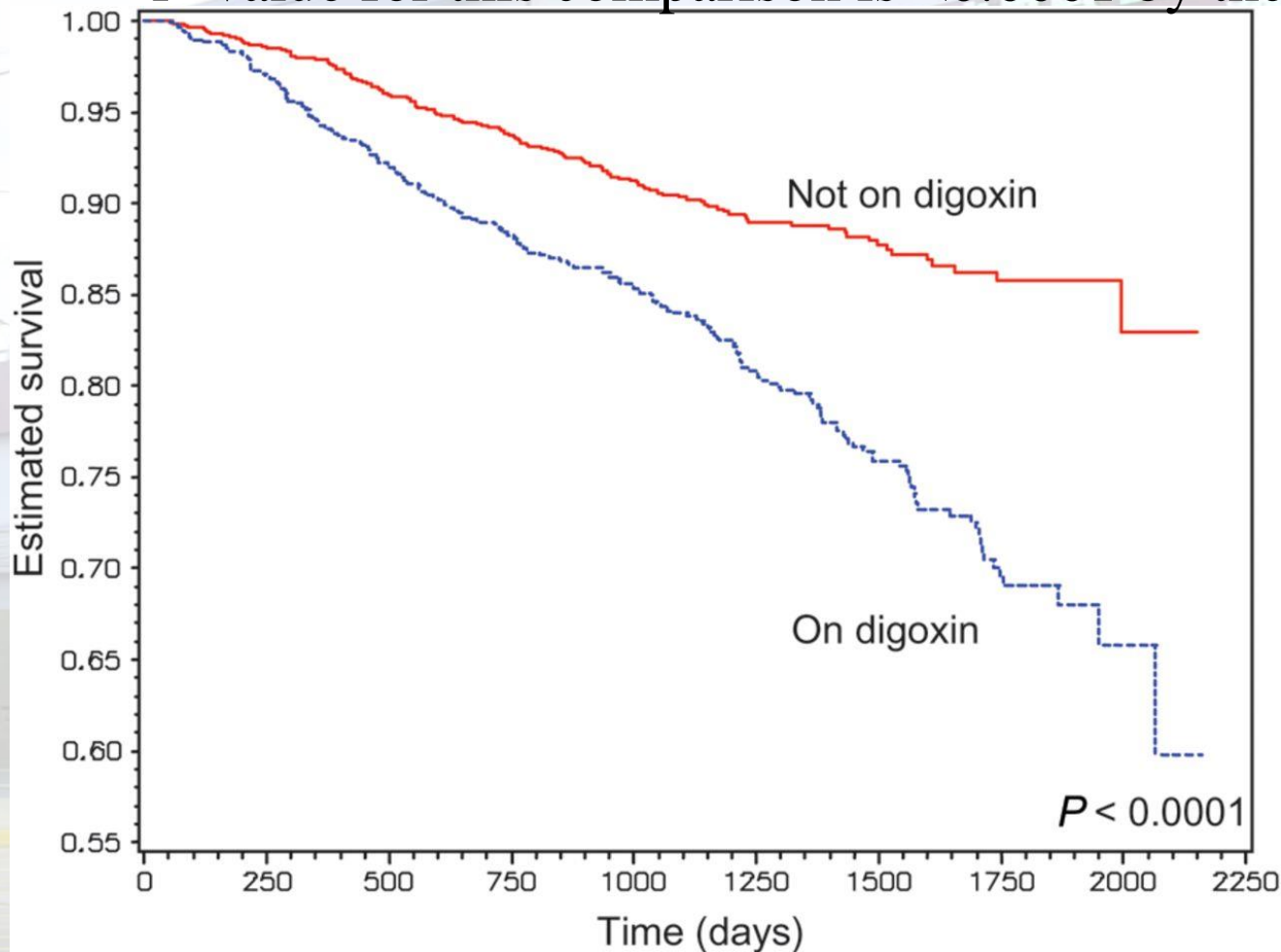
European Heart Journal (2013) 34, 1481–1488
doi:10.1093/eurheartj/ehs348

The AFFIRM trial randomized 4060 patients to rhythm control (2033 patients) vs. rate control (2027 patients).

The study included 1594 females representing 39.3% of the study cohort. Overall, 2816 patients (69.4%) received digoxin within 6 months of randomization and/or during the study.



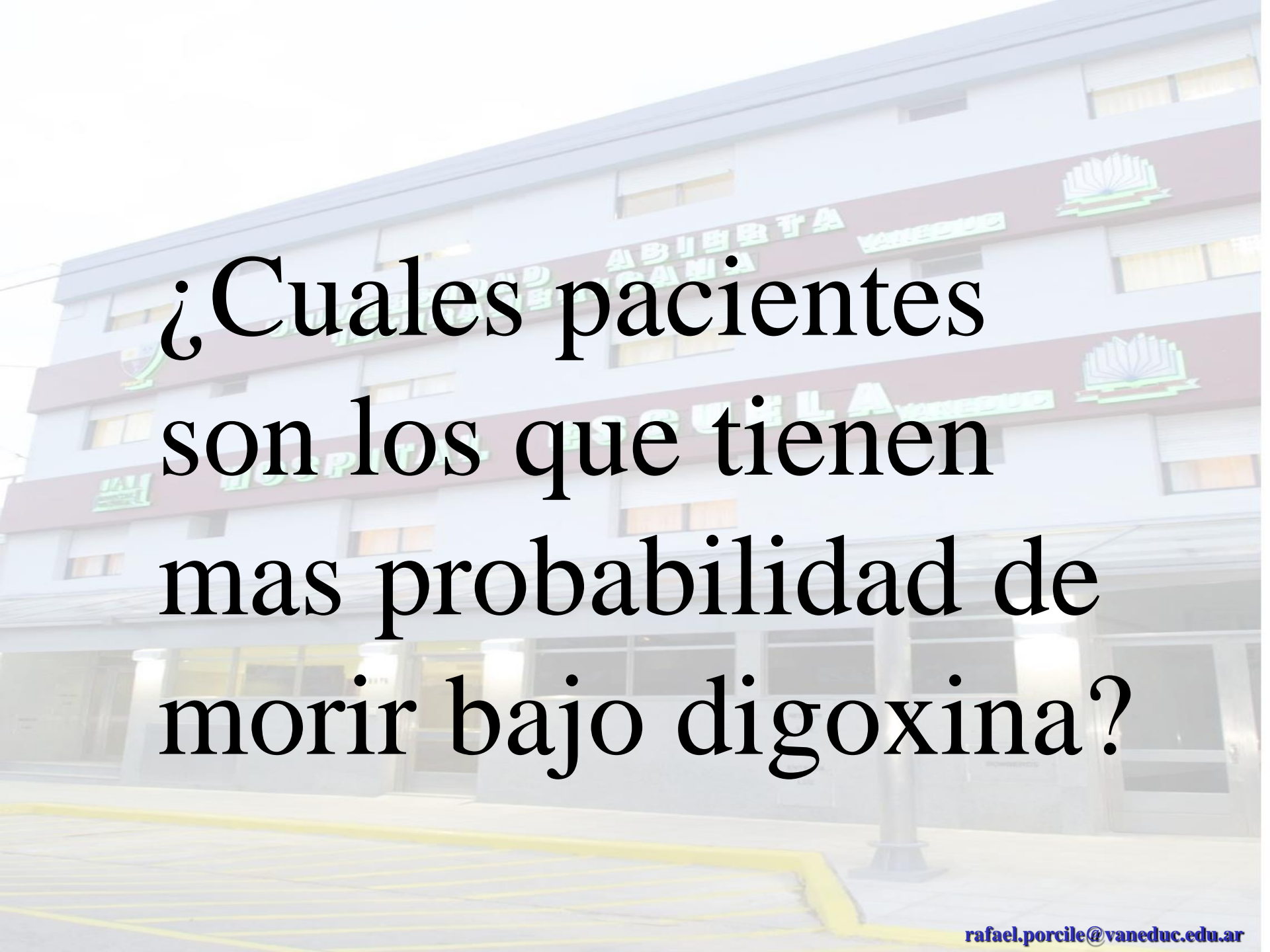
Kaplan–Meier curves for all-cause mortality based on digoxin use during the study. Shown are Kaplan–Meier curves for all-cause mortality in patients always or never on digoxin during the study. *P*-value for this comparison is <0.0001 by the likelihood ratio test.



Increased mortality among patients taking digoxin—analysis from the AFFIRM study

European Heart Journal (2013) 34, 1481–1488
doi:10.1093/eurheartj/ehs348

Digoxin was associated with a significant increase in all-cause mortality in patients with AF after correcting for clinical characteristics and comorbidities, regardless of gender or of the presence or absence of HF. These findings call into question the widespread use of digoxin in patients with AF



¿Cuales pacientes
son los que tienen
mas probabilidad de
morir bajo digoxina?

Patients with no congestive heart failure and ejection fraction $\geq 40\%$

In patients with AF and no HF, digoxin was associated with a 37% increase in mortality.

This group represented more than half of all patients enrolled in AFFIRM.

These findings are consistent with previously published results from the **Registry of Information and Knowledge about Swedish Heart Intensive care Admissions (RIKS-HIA) study.**¹²

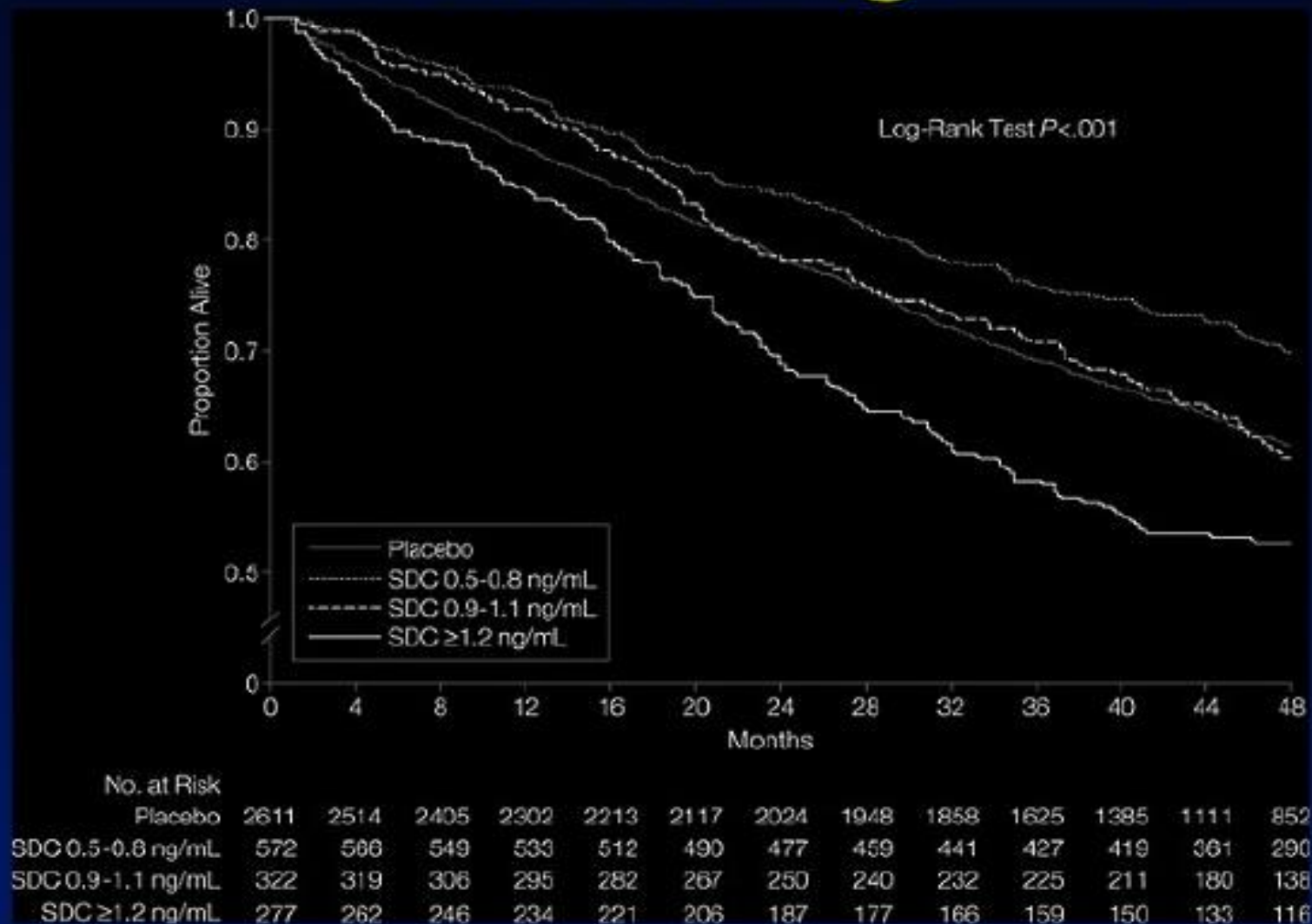
The RIKS-HIA study examined 1-year outcomes of patients with AF, CHF, or both on digoxin by comparing them to a matched group of patients not receiving digoxin.

The 4426 patients with AF and no history of CHF taking digoxin had a significant increase in overall mortality (estimated relative risk 1.42, 95% CI 1.29–1.56) compared with 16 587 controls at discharge.

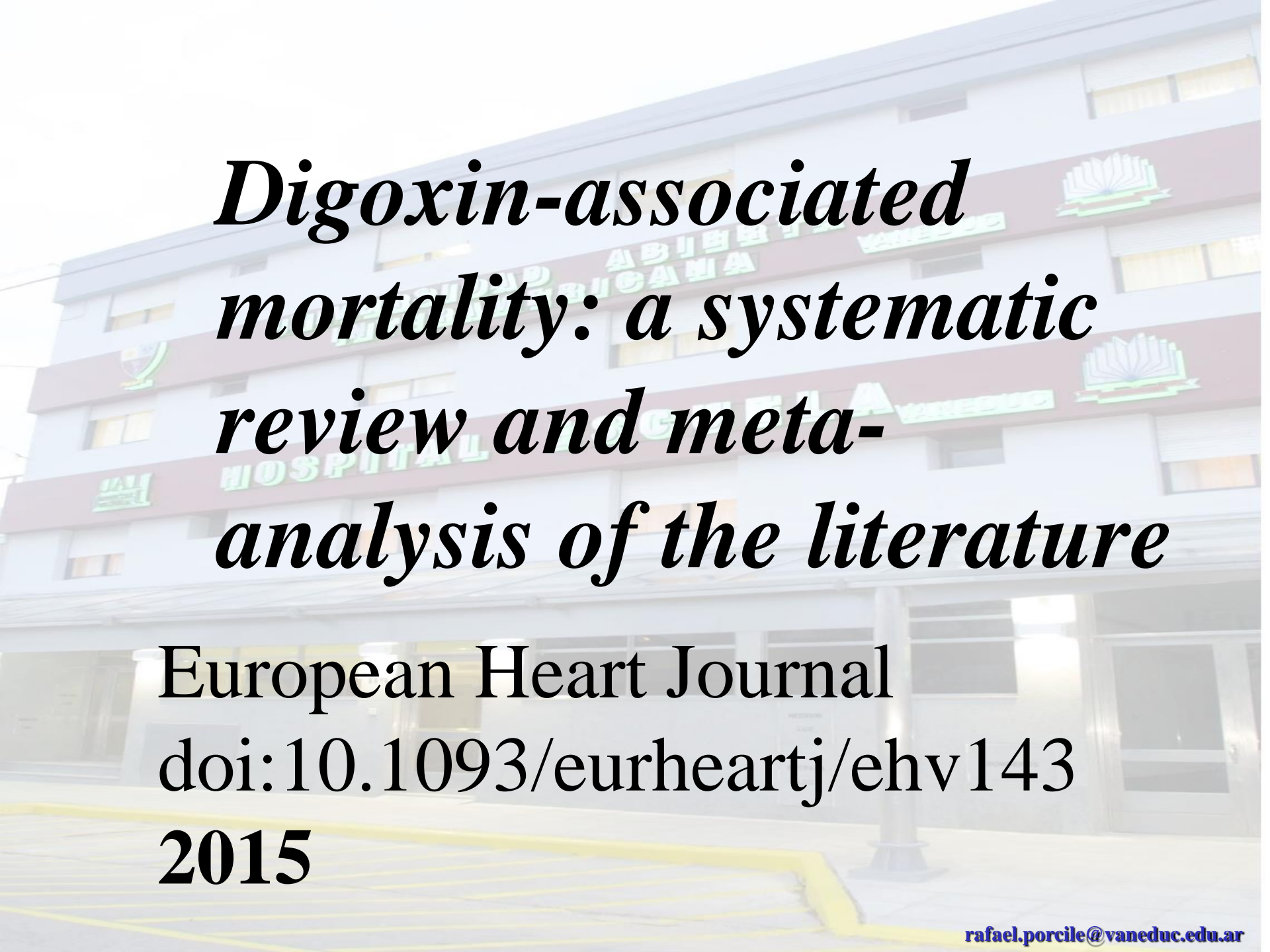
Among the 666 patients who died during the study, 375 (56.3%) received digoxin and 291 (43.7%) had no digoxin at the last follow-up visit before death.

When comparing those two groups, **cardiac death with no evidence of ischaemia was a significantly more frequent cause of death among patients on digoxin** at the last follow-up visit ($n = 139, 37.1\%$ vs. $n = 79, 27.1\%$, $P = 0.007$). There were no statistical differences for the following causes of death: cancer; pulmonary; and non-cardiovascular

Mortalidad Depende de los Niveles de Digoxina



S S Rathore. *JAMA*. 2003;289:871-878



***Digoxin-associated
mortality: a systematic
review and meta-
analysis of the literature***

European Heart Journal

doi:10.1093/eurheartj/ehv143

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Class IIa **Digoxin can be beneficial in patients with HFrEF, *unless contraindicated, to decrease hospitalizations for HF (484-491).***
(Level of Evidence: B)

May be used only in patients who remain symptomatic despite therapy with the neurohormonal antagonists.

2013 ACCF/AHA Guideline for the Management of Heart Failure

CRONOTROPICOS NEGATIVOS

DROGA	DIGITAL	Bloqueantes Cálcicos	BETA Bloqueantes	IVABRADINA
FRECUENCIA CARDIACA	-	-	-- -	- -
CALCIO CITOPLASMATICO	++	- - -	-	0
INOTROPISMO	+	-	-	+
DURACIÓN DIASTOLE	-	+	++	+++
EXITABILIDAD	++	0	--	0

CRONOTROPICOS NEGATIVOS

DROGA	DIGITAL	Bloqueantes Cálcicos	BETA Bloqueantes	IVABRADINA
FRECUENCIA CARDIACA	-	-	-- -	- -
CALCIO CITOPLASMATICO	++	- - -	-	0
INOTROPISMO	+	-	-	+
DURACIÓN DIASTOLE	-	+	++	+++
EXITABILIDAD	++	0	--	0



**MUCHAS
GRACIAS**