

• Insuficiència aòrtica
severa asimptomàtica.
Controvèrsies.

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Acadèmia de Ciències Mèdiques i de la Salut.

10 de desembre de 2012, Barcelona.



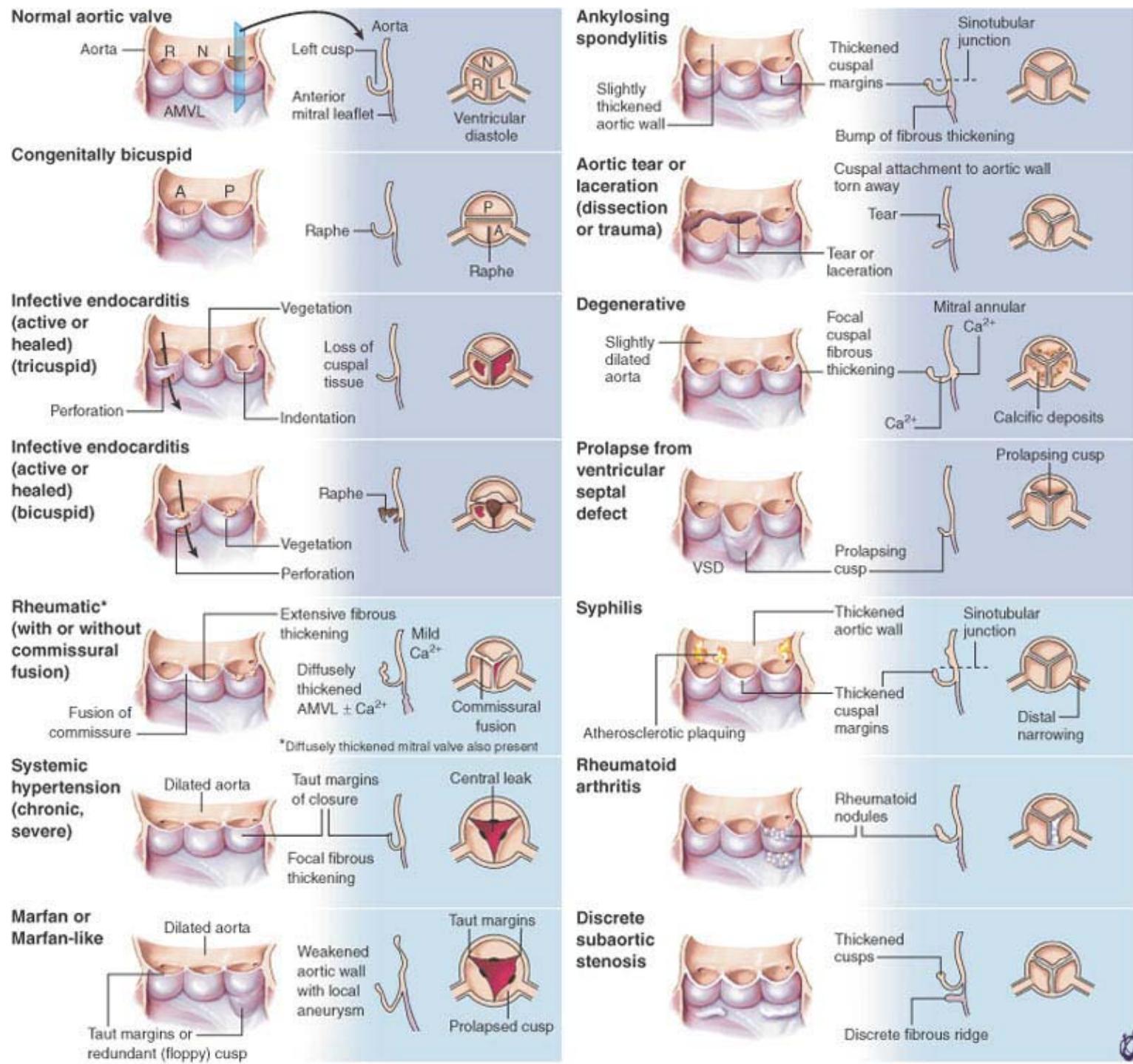
Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

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Índex

- **Freqüència**
- **Diagnosi:**
 - Ecografia.
- **Historia natural.**
- **Tractament:**
 - Mèdic.
 - Quirúrgic.



CLINICAL PRACTICE

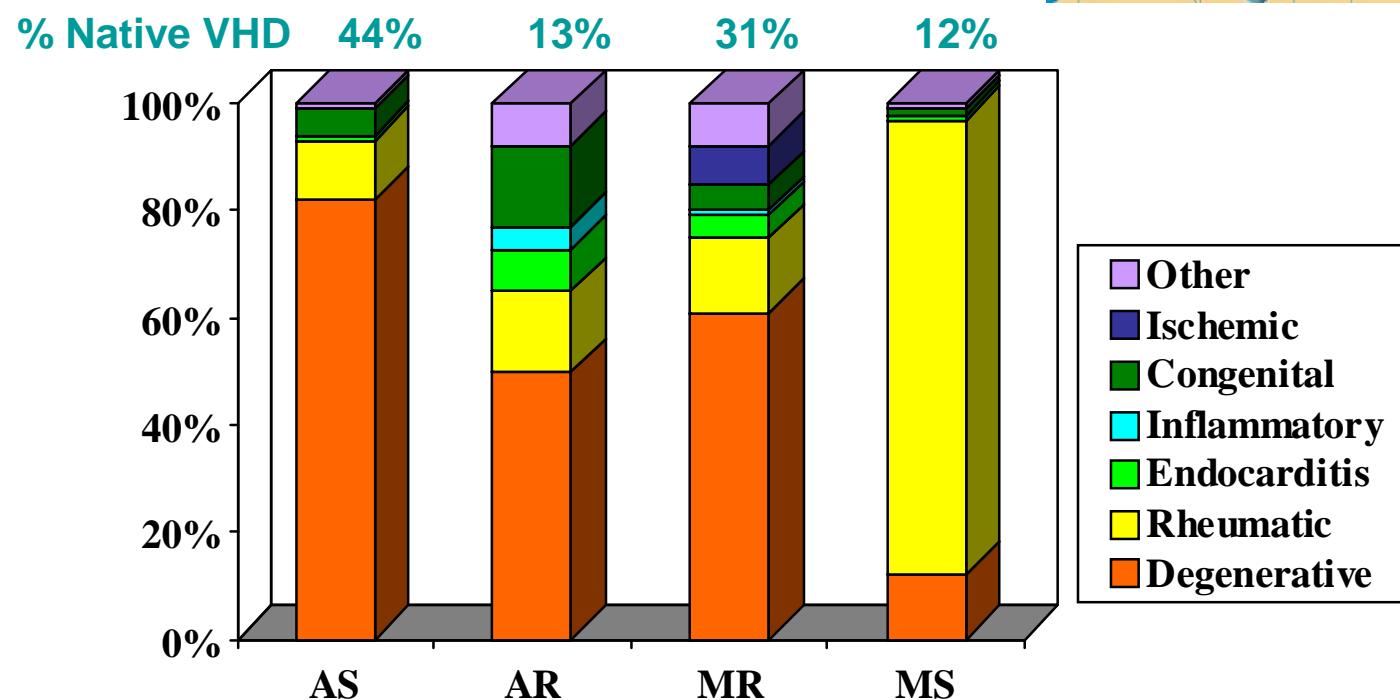
Aortic Regurgitation

Maurice Enriquez-Sarano, M.D., and A. Jamil Tajik, M.D.

THE CLINICAL PROBLEM

The most common cause of aortic regurgitation in developing countries is rheumatic disease, with clinical presentation in the second or third decade of life. In Western countries, rheumatic disease is now rare, and severe aortic regurgitation is most frequently due to diseases that are congenital (in the bicuspid valve) or degenerative (such as annuloaortic ectasia), which typically present in the fourth to sixth decades.¹ In rare cases, aortic regurgitation is acute, caused by endocarditis or aortic dissection.

Freqüència de la IA



lung B, et al. Eur Heart J 2003

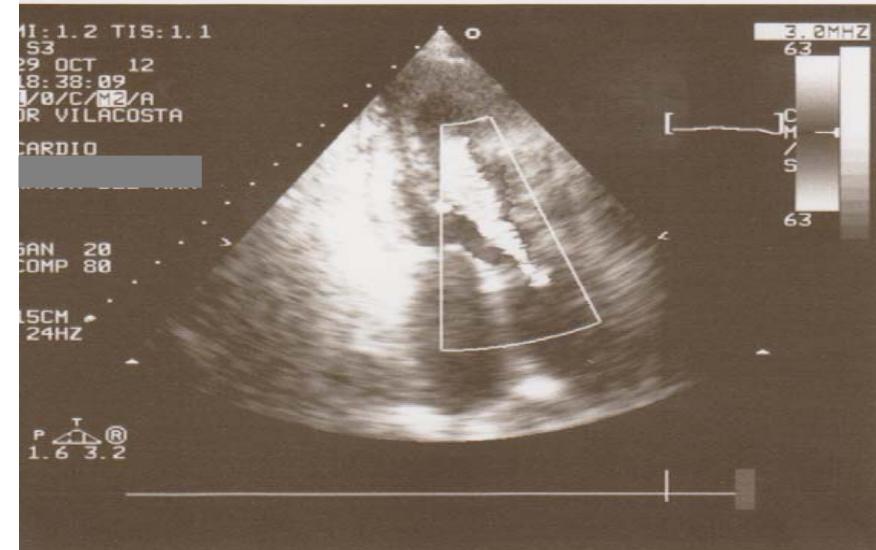
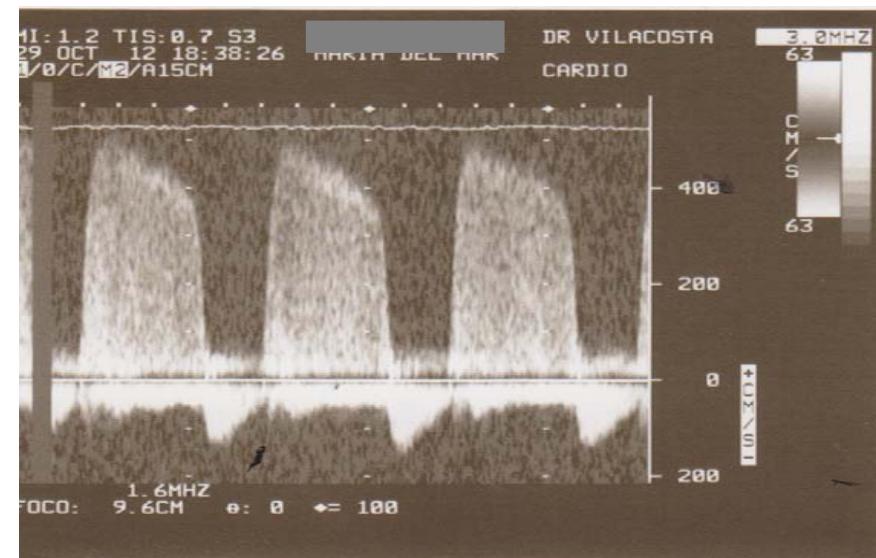
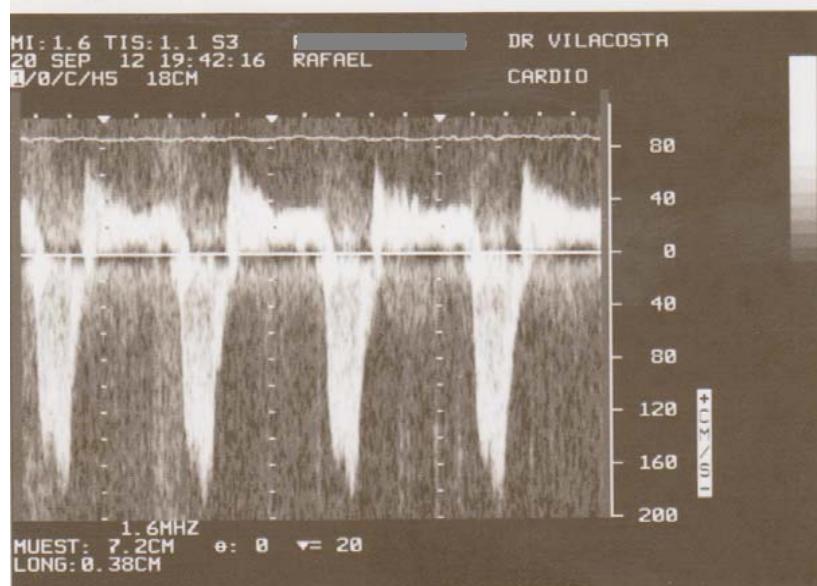
Diagnosi de la malaltia

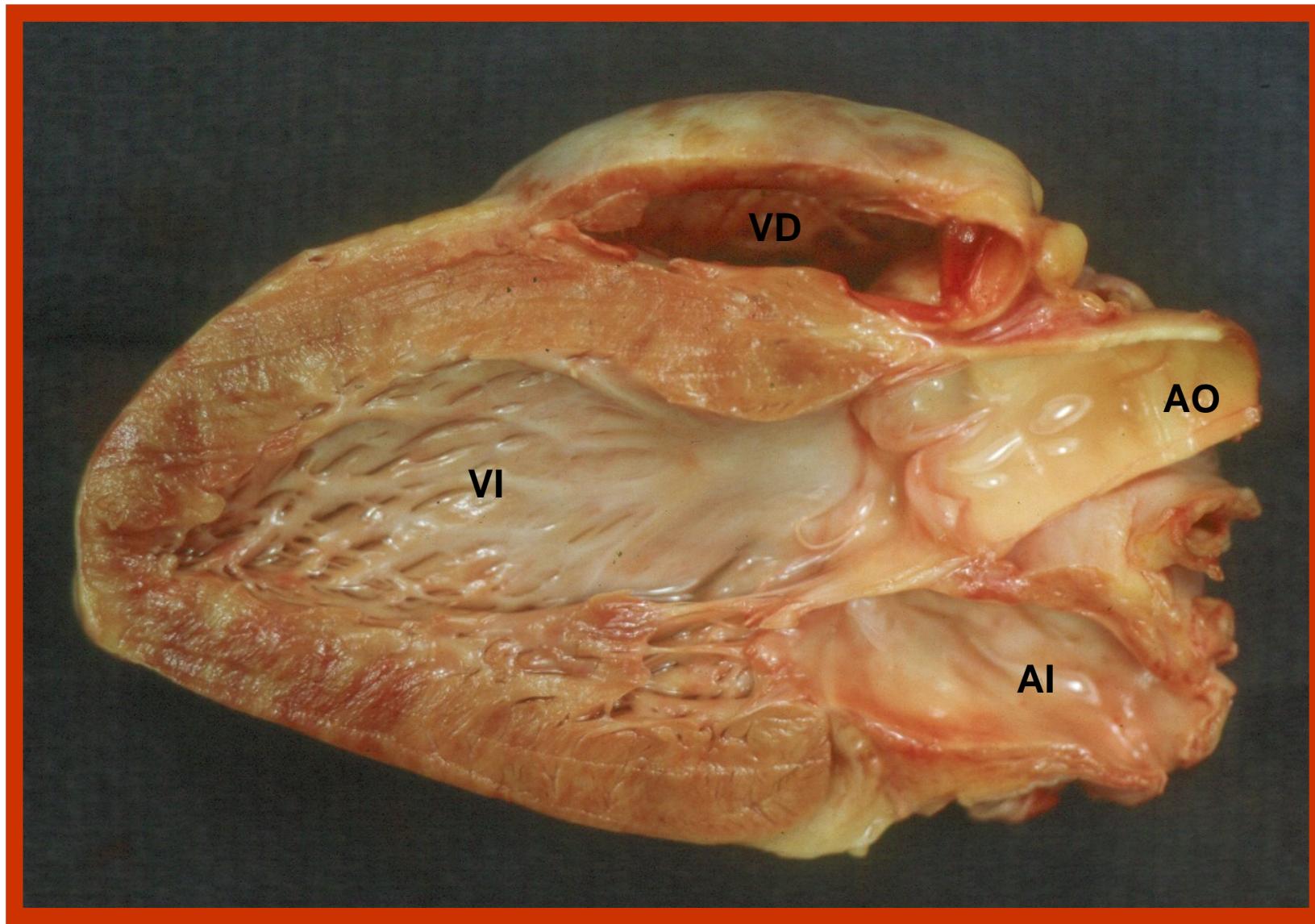
- Ecografia: diagnosi i quantificació de la IA.
- Morfologia valvular i mecanisme de la IA.
- Anatomia de l'arrel aòrtica (4 nivells); indexar per la sc.; ETE si necessari.
- Determinar les dimensions i la funció del VE es essencial. Indexar.
- Es necessari conèixer la anatomia de la aorta ascendent-arc-descendent en malalts de Marfan, VAB,..

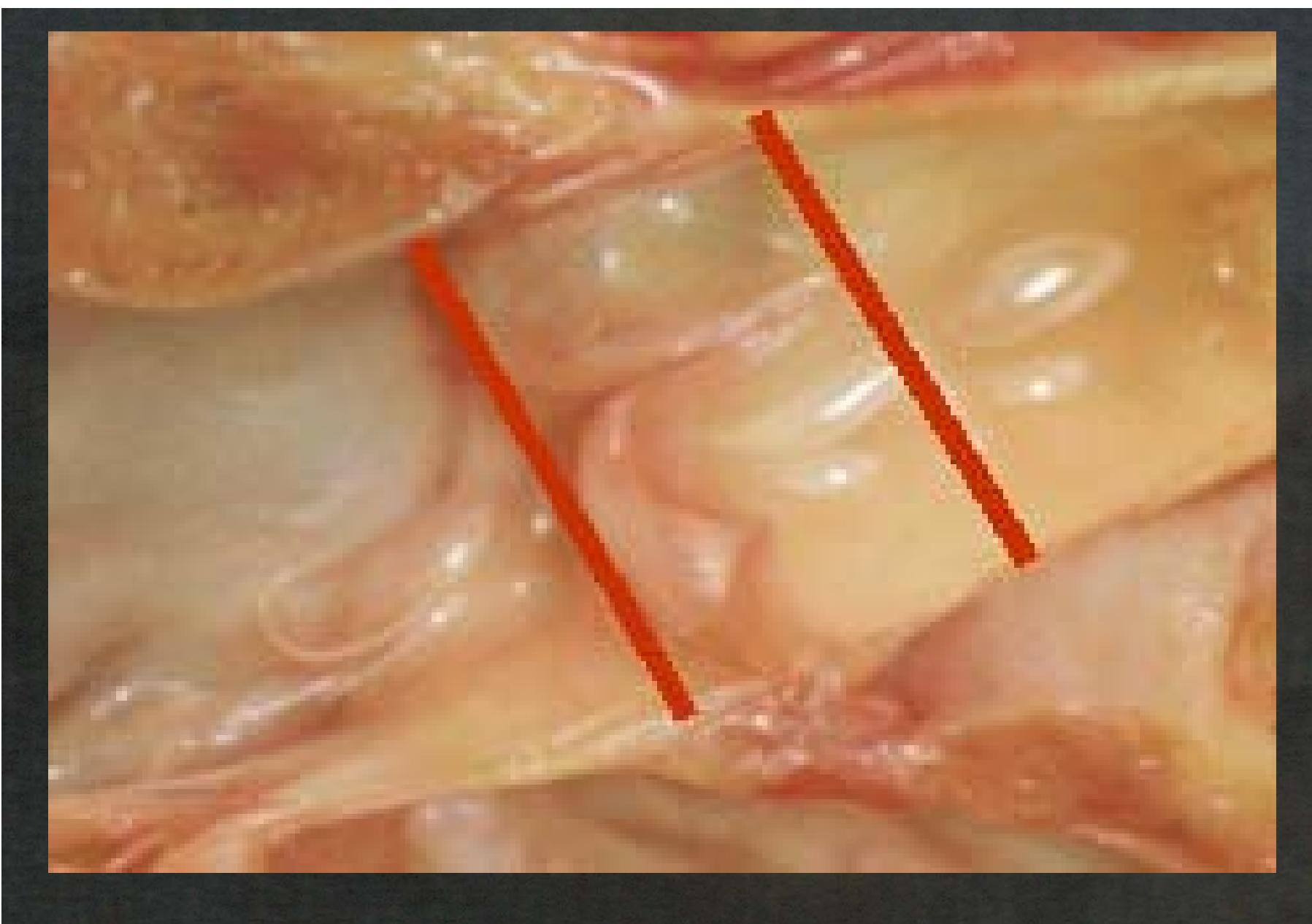
Echocardiographic criteria of severe aortic regurgitation

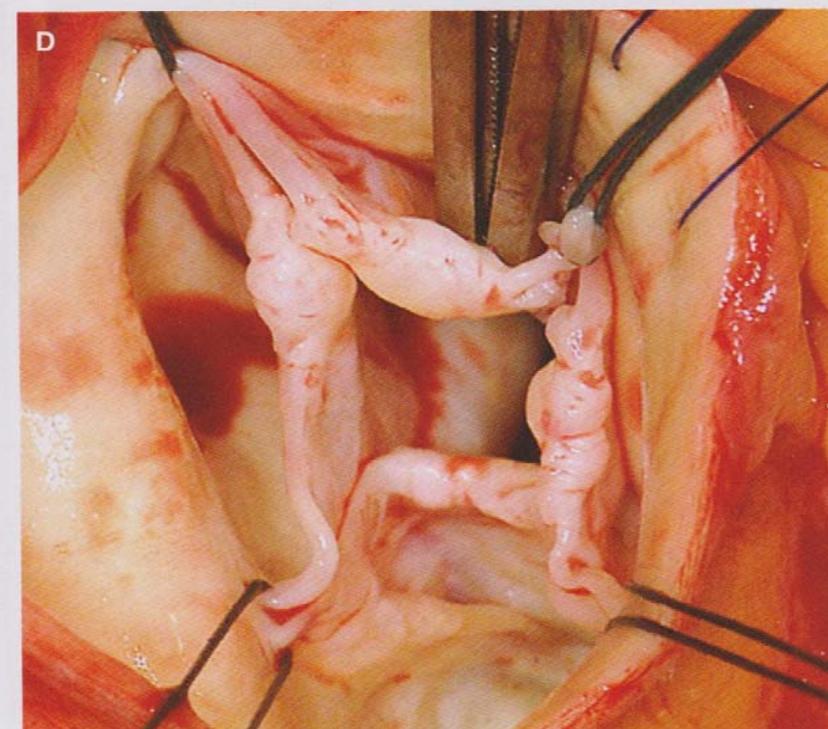
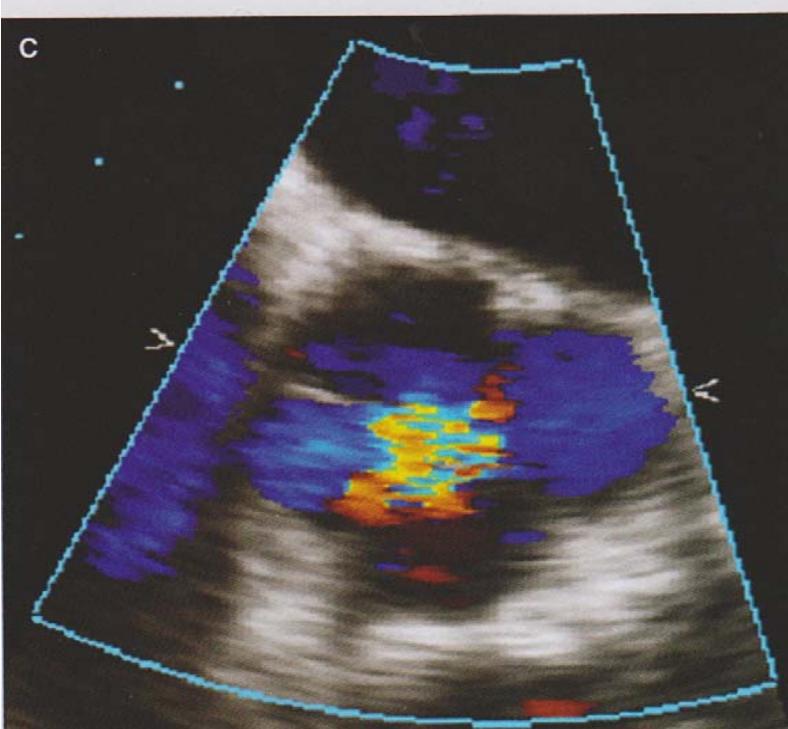
	Aortic regurgitation
Qualitative	
Valve morphology	Abnormal/flail/large coaptation defect
Colour flow regurgitant jet	Large in central jets, variable in eccentric jets*
CW signal of regurgitant jet	Dense
Other	Holodiastolic flow reversal in descending aorta (EDV >20 cm/s)
Semiquantitative	
Vena contracta width (mm)	>6
Upstream vein flow ^a	—
Inflow	—
Other	Pressure half-time <200 ms ^b
Quantitative	
EROA (mm ²)	≥30
R Vol (ml/beat)	≥60
+ enlargement of cardiac chambers/vessels	LV

Echocardiographic assessment of aortic regurgitation

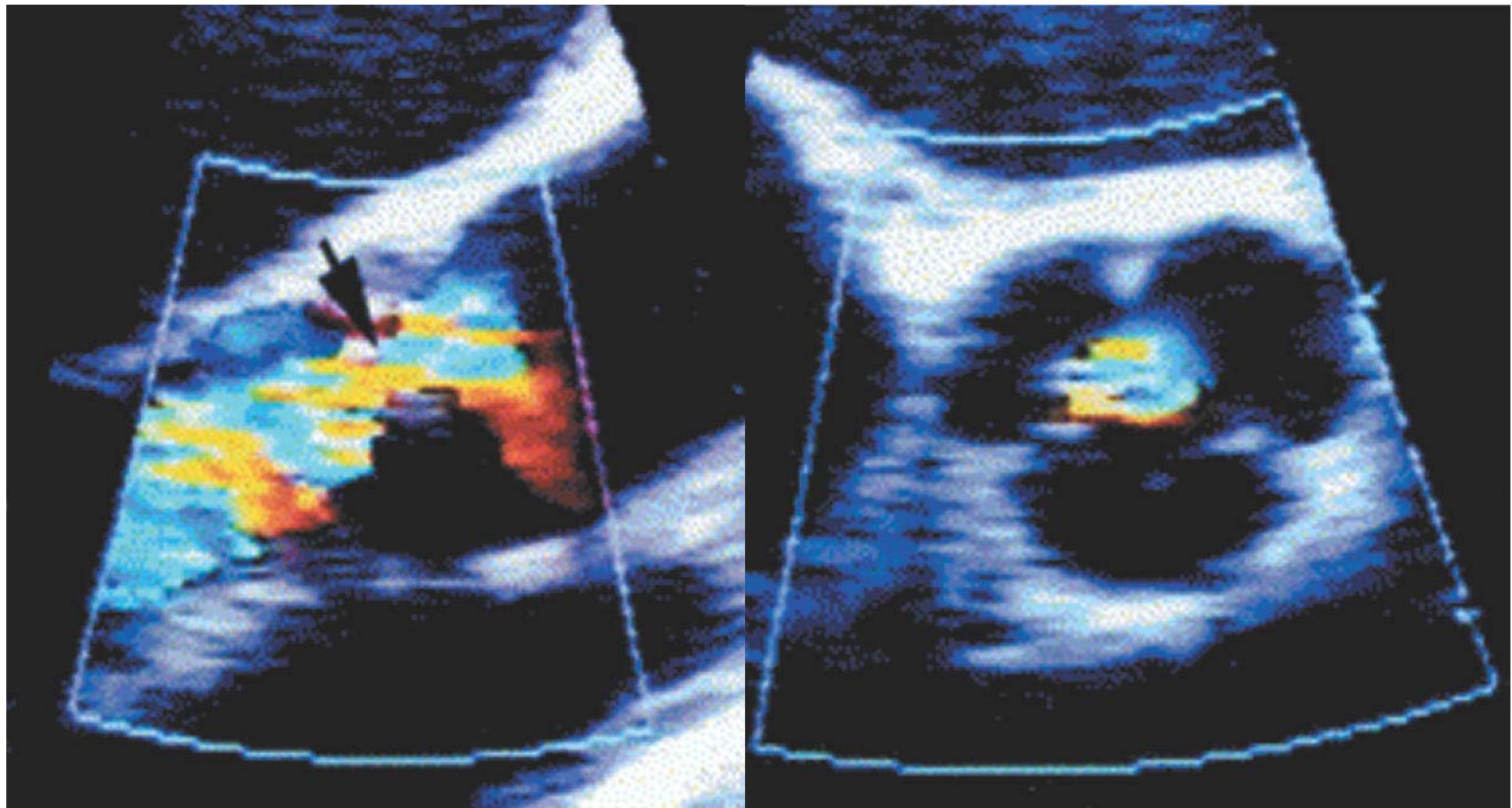








Echocardiographic assessment of aortic regurgitation jet



Criteria for severe aortic regurgitation

Specific signs	Central jet, width $\geq 65\%$ of left ventricular outflow tract Vena contracta > 0.6 cm
Supportive signs	Pressure half-time < 200 ms Holodiastolic aortic flow reversal in descending aorta Moderate or greater left ventricular enlargement
Quantitative parameters	Regurgitant volume ≥ 60 mL/beat Regurgitant fraction $\geq 50\%$ Effective regurgitant orifice area ≥ 0.30 cm 2

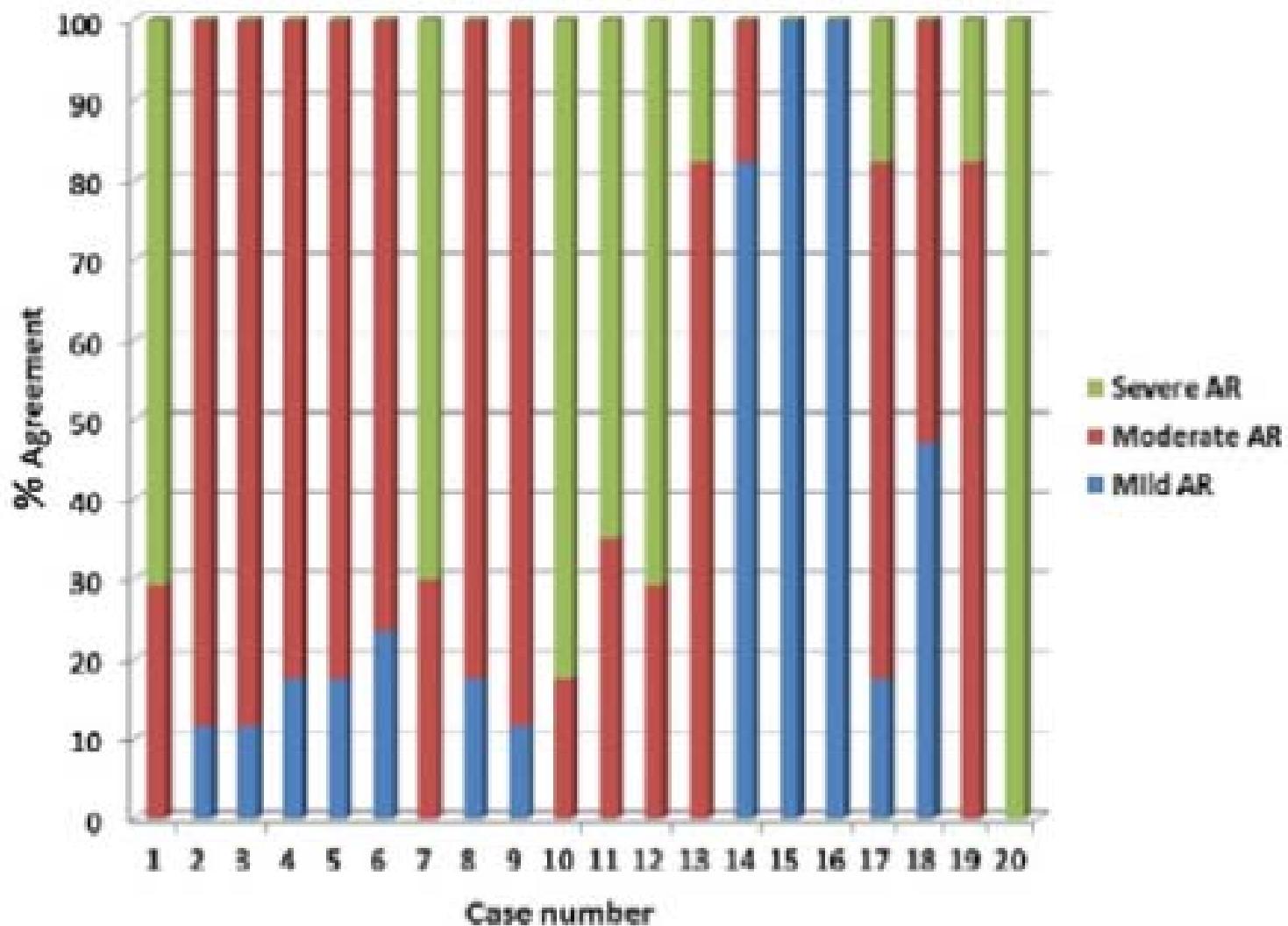
Zoghbi WA, et al. J Am Soc Echocardiogr 2003

Exactitud del diagnòstic

Development of a Consensus Document to Improve Multireader Concordance and Accuracy of Aortic Regurgitation Severity Grading by Echocardiography Versus Cardiac Magnetic Resonance Imaging

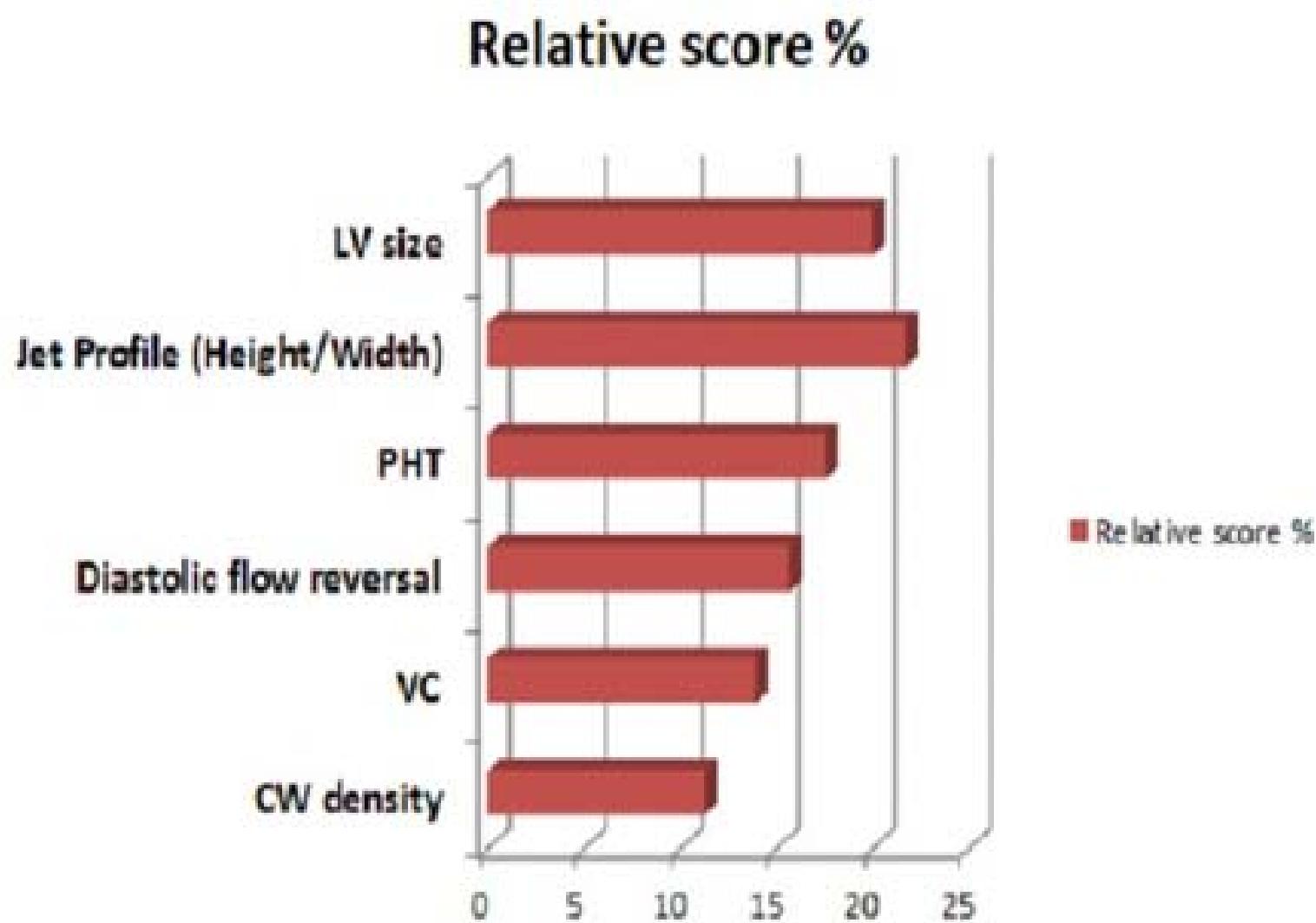
Arun Dahiya, MD, Michael Bolen, MD, Richard A. Grimm, DO, L. Leonardo Rodriguez, MD, James D. Thomas, MD, and Thomas H. Marwick, MD, PhD, MPH*; on Behalf of the AR Concordance Investigators†

Exactitud del diagnòstic



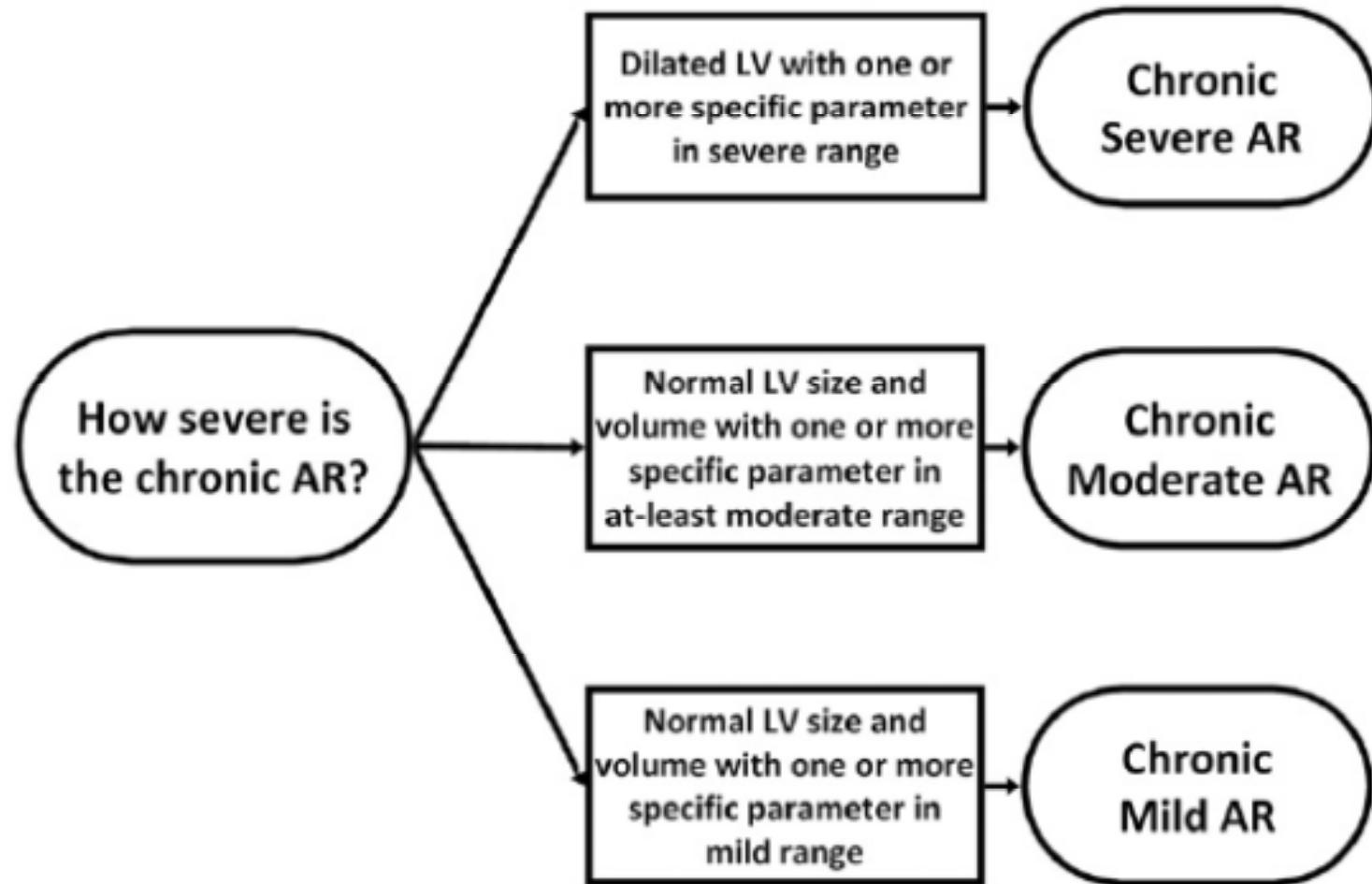
Dahiya A, et al. Am J Cardiol 2012

Exactitud del diagnòstic



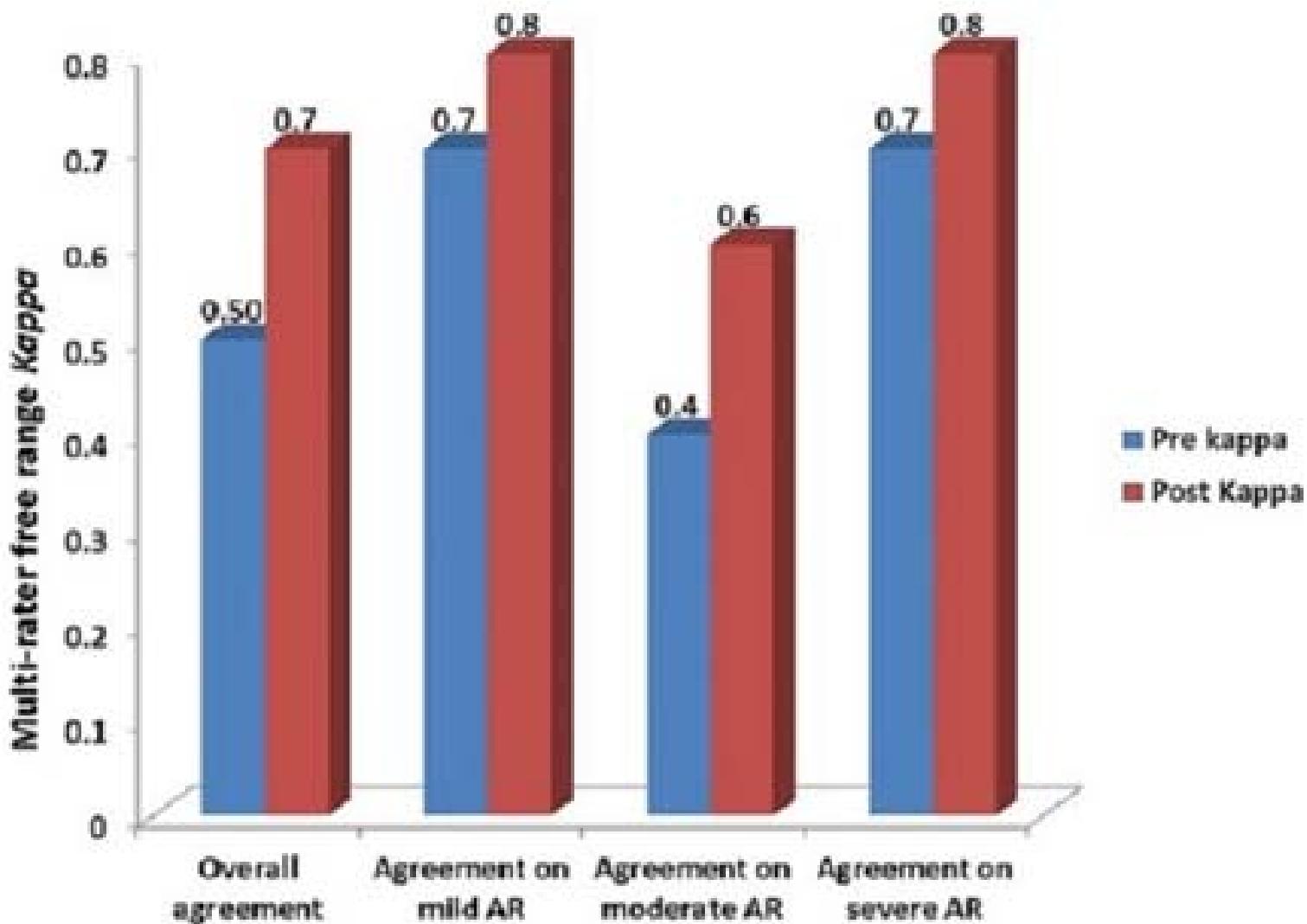
Dahiya A, et al. Am J Cardiol 2012

Exactitud del diagnòstic



Dahiya A, et al. Am J Cardiol 2012

Exactitud del diagnòstic



Dahiya A, et al. Am J Cardiol 2012

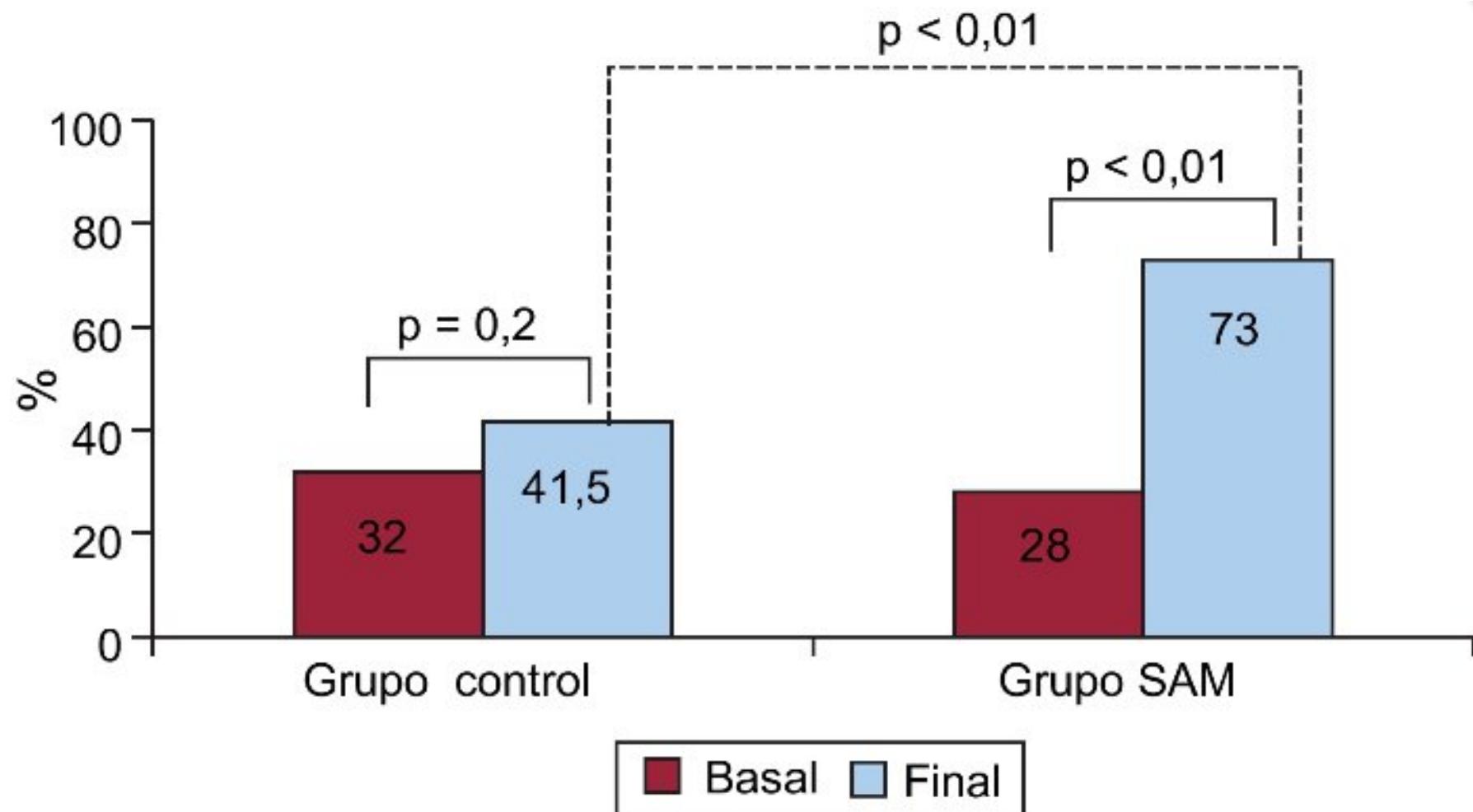
Exploració física

Initial examination should include a detailed clinical evaluation. AR is diagnosed by the presence of a diastolic murmur with the appropriate characteristics. Exaggerated arterial pulsations and low diastolic pressure represent the first and main clinical signs for quantifying AR. In acute AR, peripheral signs are attenuated, which contrasts with a poor clinical status.¹²

Exploració física



Auscultació



Acierto diagnóstico de ruidos cardíacos según entrenamiento (SAM).

Martínez G, et al. Rev Esp Cardiol 2012

Auscultació

TABLE I

Clinical Characteristics of 210 Patients With Valvular Regurgitation

Variable	Subgroups of Patients					
	AR (n = 40)	MR (n = 170)	P Value	MR Org (n = 112)	MR I/F (n = 58)	P Value
Age (y)	58 ± 16	64 ± 13	0.04	63 ± 13	67 ± 13	0.03
Sex (% male)	65	54	0.21	50	62	0.13
Atrial fibrillation (%)	8	21	0.05	17	28	0.12
Blood pressure (mm Hg)						
Systolic	145 ± 24	135 ± 21	0.01	137 ± 21	130 ± 22	0.04
Diastolic	71 ± 20	79 ± 11	0.01	79 ± 11	77 ± 12	0.30
Murmur type	Diastolic	Systolic	0.08*	Systolic	Systolic	0.0001*
Grade 0	13%	10%		5%	19%	
Grade 1	15%	11%		11%	12%	
Grade 2	37%	32%		28%	41%	
Grade 3	35%	34%		37%	28%	
Grade 4	0%	11%		16%	0%	
Grade 5	0%	2%		4%	0%	

*Refers to the comparison of murmur intensity between subgroups.

AR = aortic regurgitation; MR = mitral regurgitation; MR I/F = mitral regurgitation of ischemic or functional cause; MR Org = organic mitral regurgitation.

Desjardins VA, et al. Am J Med 1996

Auscultació

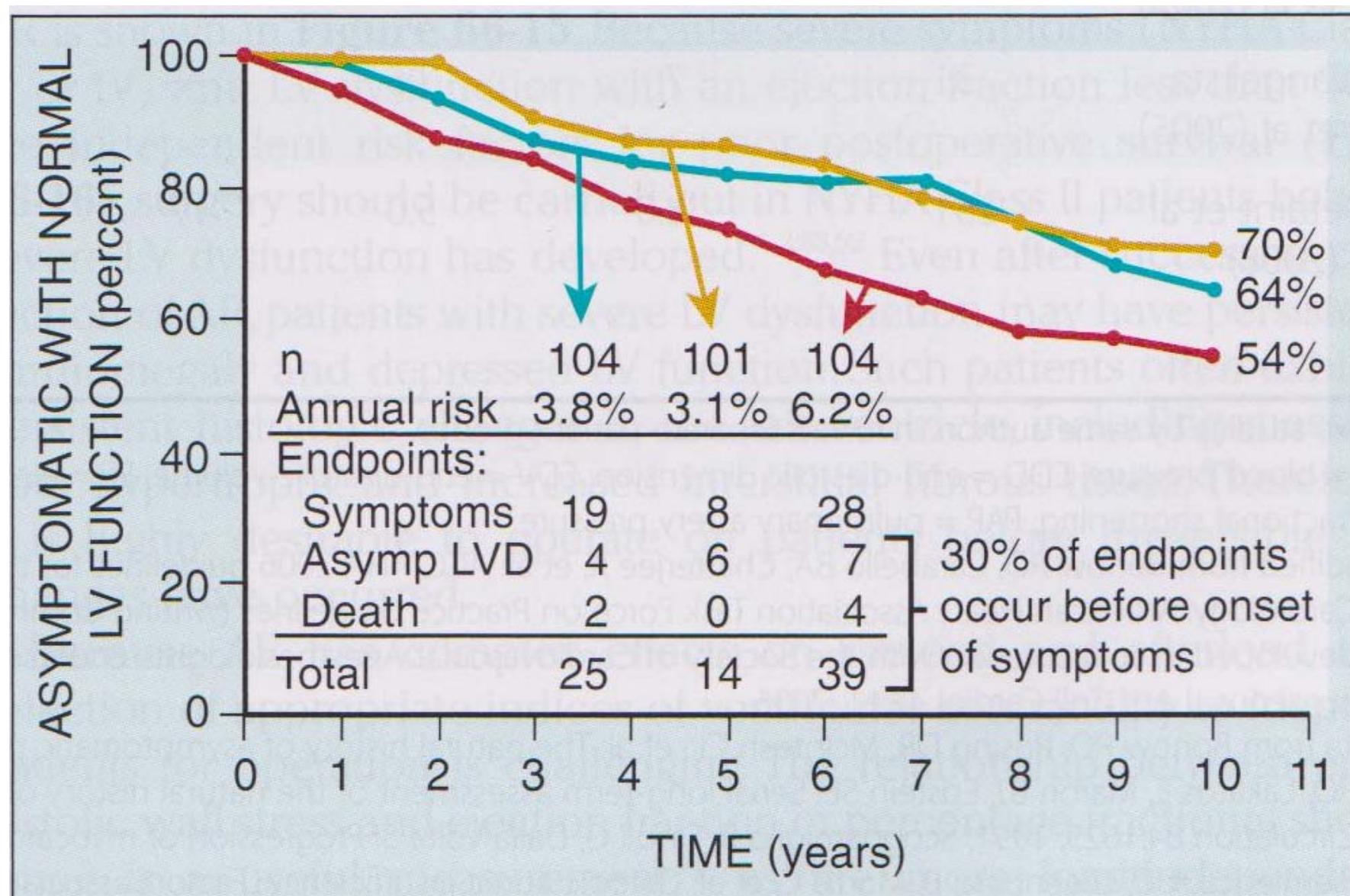
TABLE III

Correlations (r) Between Murmur Intensity
and Degree of Regurgitation

Variable	AR (n = 40)	MR (n = 170)	MR Org (n = 112)	MR I/F (n = 58)
Regurgitant volume				
DE	.60	.64	.67	.47
2DE	.58	.65	.68	.42
Regurgitant fraction				
DE	.67	.67	.73	.45
2DE	.65	.65	.71	.36

AR = aortic regurgitation; DE = Doppler echocardiography; 2DE = two-dimensional echocardiography; MR = mitral regurgitation; MR I/F = mitral regurgitation of ischemic or functional cause; MR Org = organic mitral regurgitation.

Història natural de la IA asimptomàtica



Bonow RO, et al. Circulation 1991; Tornos MP, et al. Am Heart J 1995; Borer JS, et al. Circulation 1998

Vasodilatadores en la IA severa

Study (year)	Patients (n)	Duration of study	Active treatment	Study design
Greenberg <i>et al.</i> (1988)	80	2 years	Hydralazine (at an average dose of 216 ± 64 mg/day)	Randomized, double-blind, placebo-controlled
Scognamiglio <i>et al.</i> (1990)	72	12 months	Nifedipine (40 mg/day)	Randomized, double-blind, placebo-controlled
Scognamiglio <i>et al.</i> (1994)	143	6 years	Nifedipine (40 mg/day) and digoxin (0.25 mg/day)	Randomized, nonblind, active-controlled
Schön <i>et al.</i> (1994)	12	12 months	Quinapril (10–20 mg/day)	Nonrandomized, non-controlled
Wisenbaugh <i>et al.</i> (1994)	23	6 months	Captopril (75 mg/day)	Randomized, double-blind, placebo-controlled
Lin <i>et al.</i> (1994)	76	12 months	Enalapril (mean dose 31 mg/day) and hydralazine (mean dose 177 mg/day)	Randomized, double-blind, active-controlled
Evangelista <i>et al.</i> (2005)	95	7 years	Nifedipine (40 mg/day) and enalapril (20 mg/day)	Randomized, open-label, three arms with no treatment as control

VD therapy in asymptomatic severe aortic regurgitation

The New England Journal of Medicine

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Number 11

NIFEDIPINE IN ASYMPTOMATIC PATIENTS WITH SEVERE AORTIC REGURGITATION AND NORMAL LEFT VENTRICULAR FUNCTION

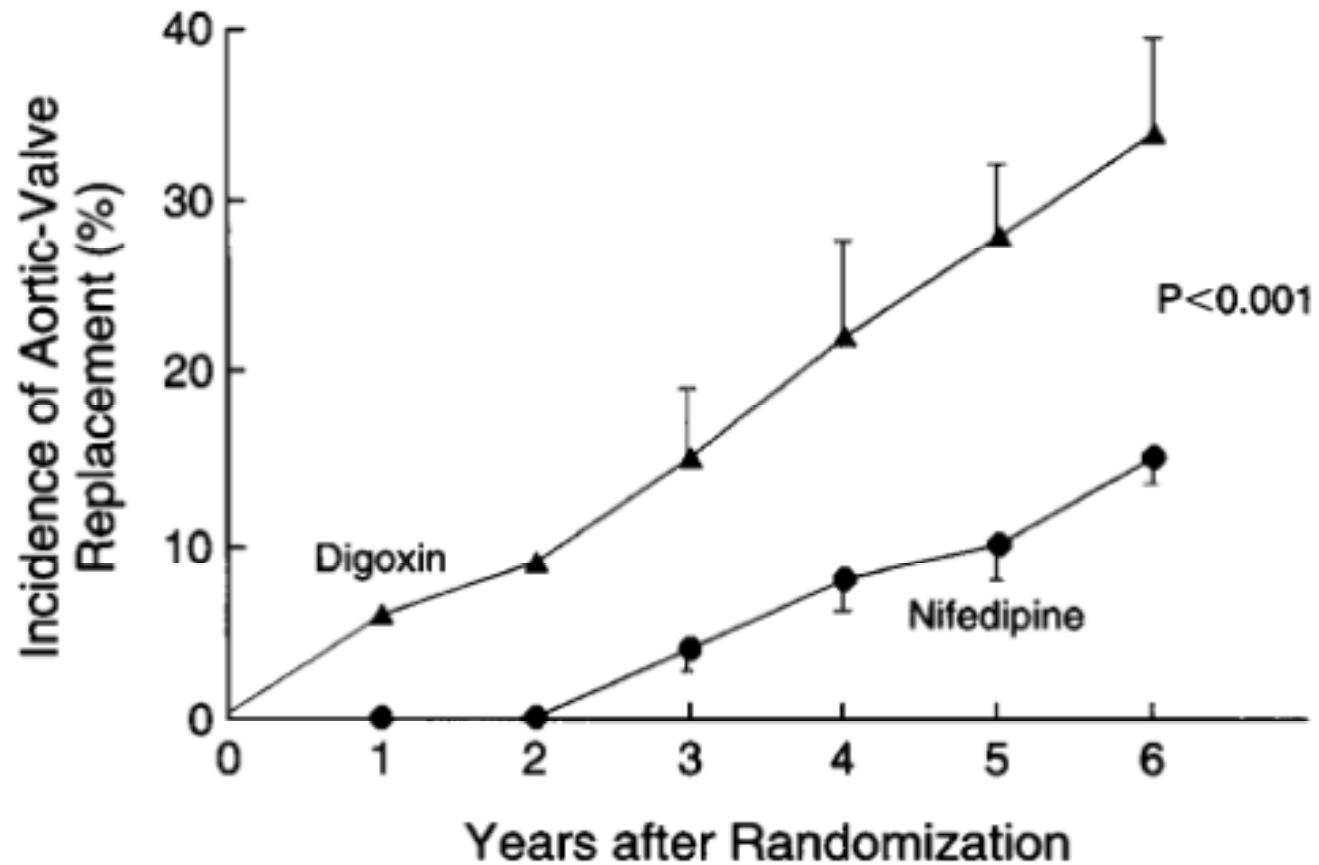
ROLDANO SCOGNAMIGLIO, M.D., SHAHBUDIN H. RAHIMTOOLA, M.B., F.R.C.P., GIUSEPPE FASOLI, M.D.,
STEFANO NISTRI, M.D., AND SERGIO DALLA VOLTA, M.D.

VD therapy in asymptomatic severe aortic regurgitation

- 143 asymptomatic pts. with isolated severe AR and normal LV function (EF > 50%).
 - Nifedipine (20 mg / 12h): 69 pts.
 - Digoxin (0,25 mg / 24h): 74 pts.
- Criteria for Ao. valve replacement:
 - LV dysfunction: EF < 50% (TTEx2).
 - NYHA ≥ II or angina.
 - Progressive LV dilatation (>15% LVEDV index).
- Mean follow-up time: 6 years

Scognamiglio R, et al. N Engl J Med 1994.

VD therapy in asymptomatic severe aortic regurgitation



Scognamiglio R, et al. N Engl J Med 1994.

VD therapy in asymptomatic severe aortic regurgitation

Table 3. Left Ventricular Volume and Ejection Fraction before Randomization and at the End of the Study, According to Treatment Group.*

	EDVI	ESVI	EF	MASS
	<i>ml/m²</i>		%	<i>g/m²</i>
Nifedipine group				
Before randomization	126±16	52±9	64±4	139±16
End of study†	112±28	51±22	62±14	108±34
Digoxin group				
Before randomization	128±22	49±8	62±6	134±18
End of study†	140±25	56±19	58±14	142±22
P value				
Nifedipine vs. digoxin before randomization	NS	NS	NS	NS
Nifedipine vs. digoxin at end of study	0.003	0.004	0.03	0.02

Scognamiglio R, et al. N Engl J Med 1994.

VD therapy in asymptomatic severe aortic regurgitation

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STEFANO NISTRÌ, M.D., AND SERGIO DALLA VOLTA, M.D.

Conclusions. Long-term vasodilator therapy with nifedipine reduces or delays the need for aortic-valve replacement in asymptomatic patients with severe aortic regurgitation and normal left ventricular systolic function. (N Engl J Med 1994;331:689-94.)

ORIGINAL ARTICLE

Long-Term Vasodilator Therapy in Patients with Severe Aortic Regurgitation

Artur Evangelista, M.D., Pilar Tornos, M.D., Antonia Sambola, M.D.,
Gaietà Permanyer-Miralda, M.D., and Jordi Soler-Soler, M.D.

CONCLUSIONS

Long-term vasodilator therapy with nifedipine or enalapril did not reduce or delay the need for aortic-valve replacement in patients with asymptomatic severe aortic regurgitation and normal left ventricular systolic function. Furthermore, such therapy did not reduce the aortic regurgitant volume, decrease the size of the left ventricle, or improve left ventricular function.

N Engl J Med 2005; 353:1342

VD therapy in asymptomatic severe aortic regurgitation

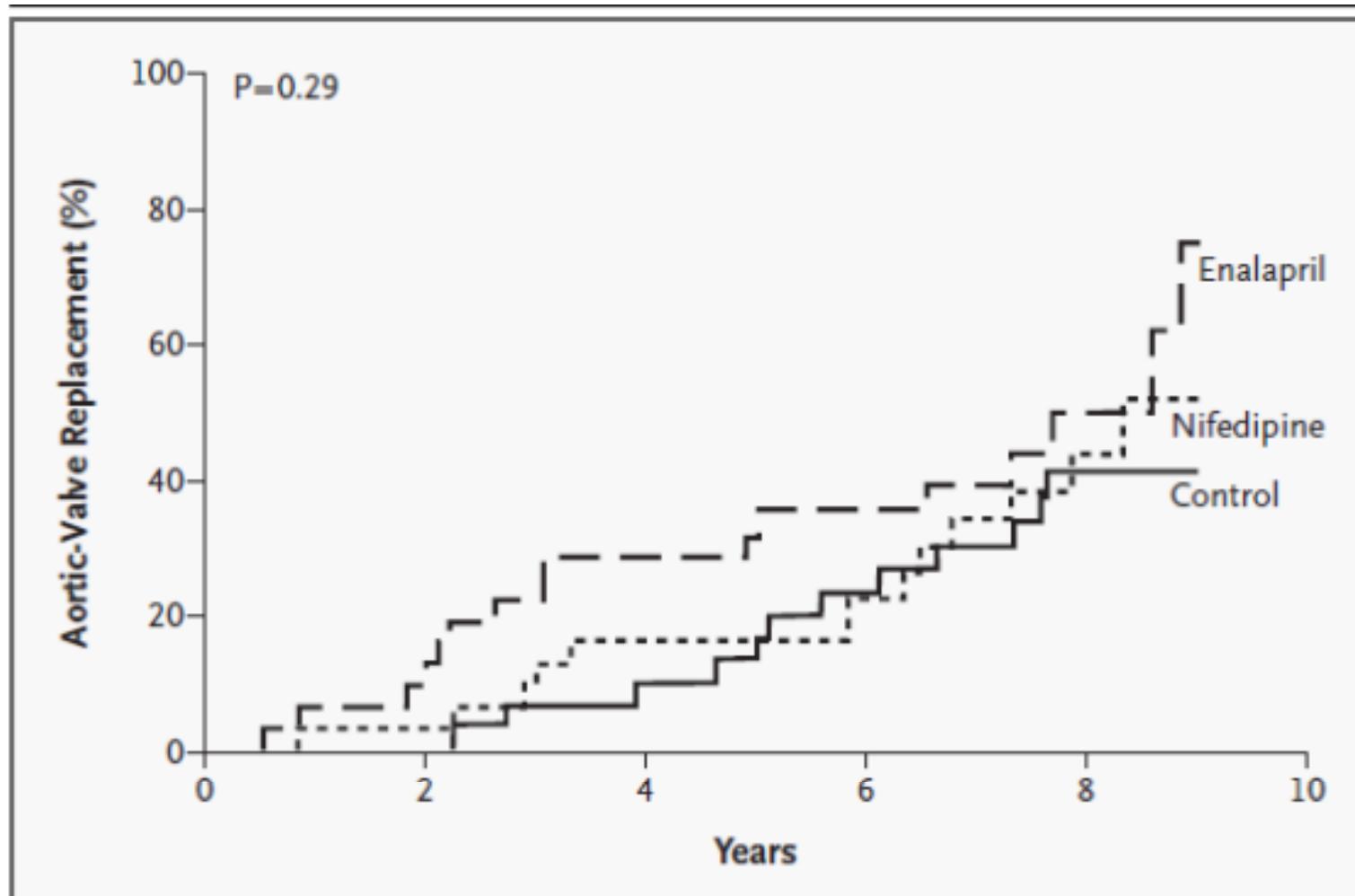
- 95 asymptomatic pts. with isolated severe AR and normal LV function ($EF \geq 50\%$; $LVEDD < 50$ mm).
 - Nifedipine (20 mg / 12h): 32 pts.
 - Enalapril (20 mg / 24h): 32 pts.
 - Control group (no therapy): 31 pts.
- Criteria for Ao. valve replacement:
 - LV dysfunction: $EF < 50\%$ (TTEx2 + Radionuclide V.).
 - NYHA $\geq II$, syncope or angina.
 - Progressive LV dilatation: $LVEDD > 50$ mm (TTEx2).
- Mean follow-up time: 7 ± 2 years

Evangelista A, et al. N Engl J Med 2005

VD therapy in asymptomatic severe aortic regurgitation

- Aortic-valve replacement at follow-up:
 - Nifedipine group: 13 (41%).
 - Enalapril group: 16 (50%).
 - Control group: 12 (39%).
- Surgical indication:
 - Symptoms: 7 pts.
 - Asymptomatic LV dysfunction: 15 pts.
 - Both criteria: 19 pts.
 - (EF < 50%: 18 pts.)

VD therapy in asymptomatic severe aortic regurgitation



Evangelista A, et al. N Engl J Med 2005

VD therapy in asymptomatic severe aortic regurgitation

Table 2. Comparison of Baseline and Final Values.*

Study Group and Assessment	Systolic Blood Pressure	Diastolic Blood Pressure	Heart Rate	LVEDD	LVESD	LVMI	LVMWS	LVEDVI	LVESVI	LVEF	Jet Width	Regurgitant Volume
	mm Hg		beats/min	mm		g/m ²	kdyn/cm ²	ml/m ²		%	mm	ml
Control group												
Baseline	143±19	74±10	67±8	64±5	44±5	135±31	307±48	109±35	45±19	60±6	11±3	82±36
Final†	141±18	70±9	68±16	69±7	46±7	168±42	310±38	114±33	49±16	57±8	11±3	85±38
Change‡	-1±8	-4±13	1±13	3.9±5	2.6±5	33±40	3.0±10	15±29	8.5±18	-2.5±8	-0.4±3	3.3±18
Enalapril group												
Baseline	142±15	75±10	68±10	68±6	46±5	141±44	307±38	114±33	49±16	58±6	11±3	89±43
Final†	140±20	69±10	69±10	70±7	48±6	162±50	311±63	124±37	53±17	57±6	11±3	93±51
Change‡	-1±7	-4±13	1±10	2.2±4	2.0±4	21±6	4.0±25	8.2±30	2.6±15	-1.0±9	-0.2±3	4.5±24
Nifedipine group												
Baseline	147±18	78±11	68±8	65±7	44±5	139±44	311±61	94±27	40±14	59±7	11±4	81±33
Final†	141±20	77±11	69±8	68±6	46±6	151±37	310±61	104±36	46±18	58±7	11±4	81±35
Change‡	-6±4	-1±13	1±8	2.9±4	2.1±4	12±7	-1±0	9.8±3	8.2±15	-1.8±9	0.2±3	0.9±20

Evangelista A, et al. N Engl J Med 2005

VD therapy in asymptomatic severe aortic regurgitation

Table 1. Base-Line Characteristics of 143 Patients with Severe Aortic Regurgitation and Normal Left Ventricular Function, According to Treatment Group.*

CHARACTERISTIC	DICLODXIN	NIFEDIPINE
No. of patients	74	69
Age (yr)	36±12	34±14
Sex (no.)		
Male	62	60
Female	12	9
Cardiothoracic ratio	0.52±0.06	0.54±0.04
Blood pressure (mm Hg)		
Systolic	150±22	154±20
Diastolic	58±14	60±8
Left ventricular values		
End-diastolic volume index (ml/m ²)	128±22	126±16
End-systolic volume index (ml/m ²)	49±8	52±9
Ejection fraction (%)	62±6	64±4
Mass (g/m ²)	134±18	139±16

Scognamiglio R, et al. N Engl J Med 1994.

VD therapy in asymptomatic severe aortic regurgitation

Characteristic	Control Group (N=31)	Enalapril Group (N=32)	Nifedipine Group (N=32)
Age (yr)	42±15	44±10	44±14
Sex (no. of patients)			
Male	21	28	25
Female	10	4	7
Blood pressure (mm Hg)			
Systolic	143±19	142±15	147±18
Diastolic	74±10	75±10	78±11
Heart rate (beats/min)	67±8	68±10	68±8
Left ventricular variables			
End-diastolic diameter (mm)	64±5	68±6	65±7
End-systolic diameter (mm)	44±5	45±5	44±5
Mass index (g/m ²)↑	135±3	140±4	141±4
Mean wall stress (kdyn/cm ²)	310±47	308±40	310±61
End-diastolic volume (ml)	196±64	208±61	181±49
End-systolic volume (ml)	81±35	90±33	75±27
Ejection fraction (%)	60±6	58±6	59±7
Severity of aortic regurgitation			
Jet width (mm)	11±3	11±3	11±4
Regurgitant volume (ml)	82±36	89±43	81±33
Morphologic appearance of aortic valve (no. of patients)			
Normal	12	5	7
Bicuspid	10	16	14
Degenerative	6	7	10
Rheumatic	3	4	1

Nifedipine group
(Scognamiglio R, et al.)

Blood pressure (mmHg)

- Systolic: 154 ± 20
- Diastolic: 60 ± 8

Cause of AR:

- Rheumatic: 87 (61%).
- Nonrheumatic:
 - Ao. prolapse: 24
 - Bicuspid: 32

EF: 64 ± 4 %.

ORIGINAL ARTICLE

Long-Term Vasodilator Therapy in Patients with Severe Aortic Regurgitation

Artur Evangelista, M.D., Pilar Tornos, M.D., Antonia Sambola, M.D.,
Gaietà Permanyer-Miralda, M.D., and Jordi Soler-Soler, M.D.

tion. These results, though not ruling out the possibility of a beneficial effect of vasodilators in some subgroups of patients, do at least cast some doubt as to their broad clinical effect in patients with asymptomatic, chronic, severe aortic regurgitation.

VD therapy in asymptomatic AR. El perquè de la discrepància.

- **Malalts:** petit nombre; diferents (TA alta/normal).
- Morfologia **valvular** diferent: (8 reumàtica, 21 normal, 23 degenerativa i 40 VAB / 87reumàtica,32 VAB i 24 prolapse); different grau de severitat (recanvi valvular).
- **Fàrmacs:** dosi inadequada (TA, FC, geometria ventricular, efectes secundaris).

VD-IA; implicació Clínica

- No hi ha consens. Decisió individual (judici clinic).
- Procliu a tractar el malalt amb IAO severa (clínica i ecografia).
- Tractar si té hipertensió, aorta ascendent dilatada.
- Augmentar la dosi fins baixar la pressió.
- No és clar que un VD sigui millor que un altre.

RAAS blockade in AR

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Heart Failure

The Impact of Renin-Angiotensin-Aldosterone System Blockade on Heart Failure Outcomes and Mortality in Patients Identified to Have Aortic Regurgitation

A Large Population Cohort Study

Douglas H. J. Elder,* Li Wei, PhD, MPH,† Benjamin R. Szwejkowski,* Renata Libianto, MBBS,‡
Adnan Nadir,* Maheshwar Pauriah,* Sushma Rekhraj,* Tiong K. Lim, MD,* Jacob George, MD,*
Alex Doney, PhD,* Stuart D. Pringle, MD,* Anna-Maria Choy, MD,* Allan D. Struthers, MD,*
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Dundee, United Kingdom; and Melbourne, Australia

Beta-blockers in chronic AR

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CLINICAL RESEARCH

Valvular Heart Disease

Effect of Beta-Blocker Therapy on Survival in Patients With Severe Aortic Regurgitation

Results From a Cohort of 756 Patients

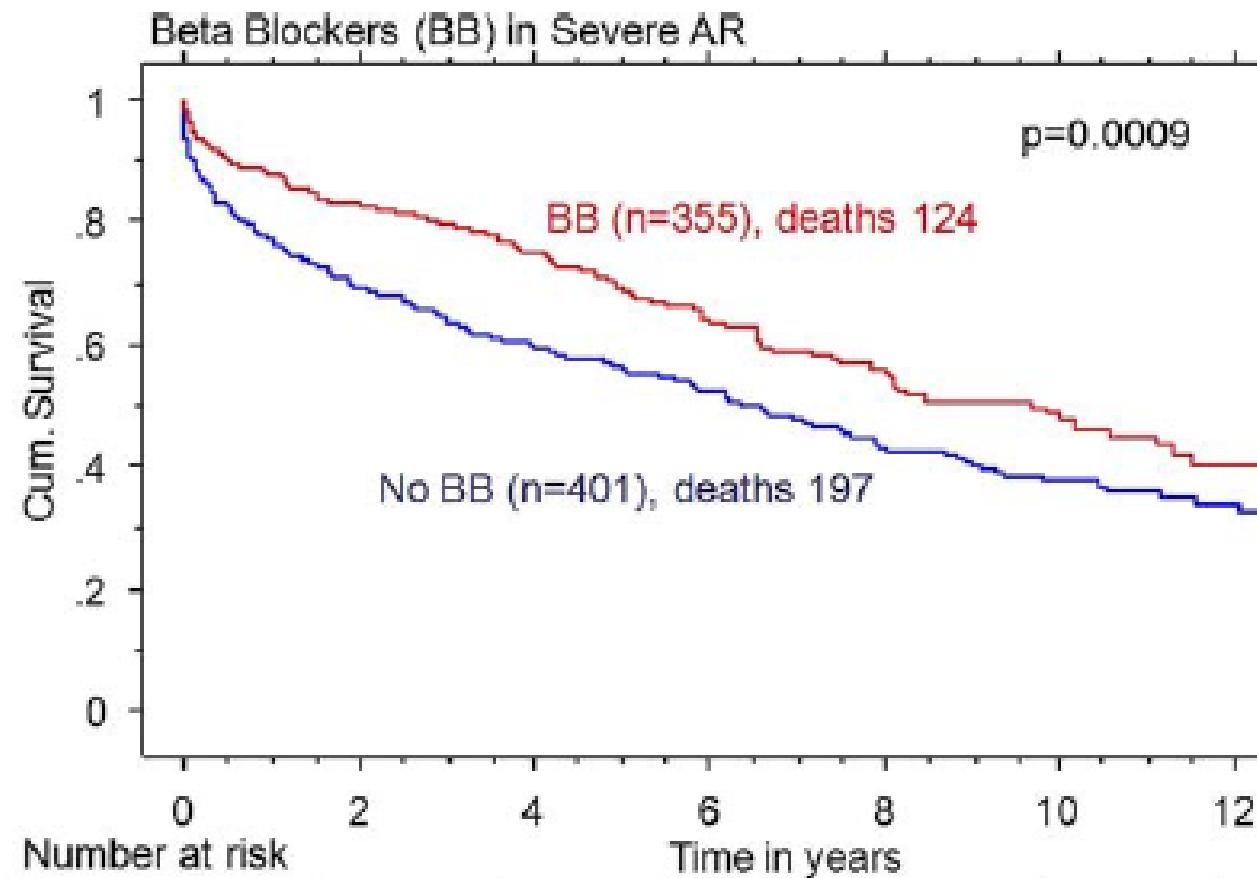
Unnati Sampat, MD, Padmini Varadarajan, MD, Rami Turk, MD, Ashvin Kamath, BA,
Sumit Khandhar, DO, Ramdas G. Pai, MD

Loma Linda, California

Beta-blockers in chronic AR

- **Aim:** impact of BB on survival in severe AR.
- Observational and retrospective study.
- Echo database-National Death Index (SSn^o).
- 756 pts; 61 ± 18 years, LVEF: $54 \pm 19\%$.
- **Causes** of AR based on TTE:
 - BAV:10%, dilated aortic root:10%, degenerative:30%, prior IE: 10%.
 - Mixed or unclear mechanisms: 60%.
- On BB: 355 (47%); 401 without BB.
- Mean follow-up time: $4,4 \pm 4,1$ years.

Beta-blockers in chronic AR



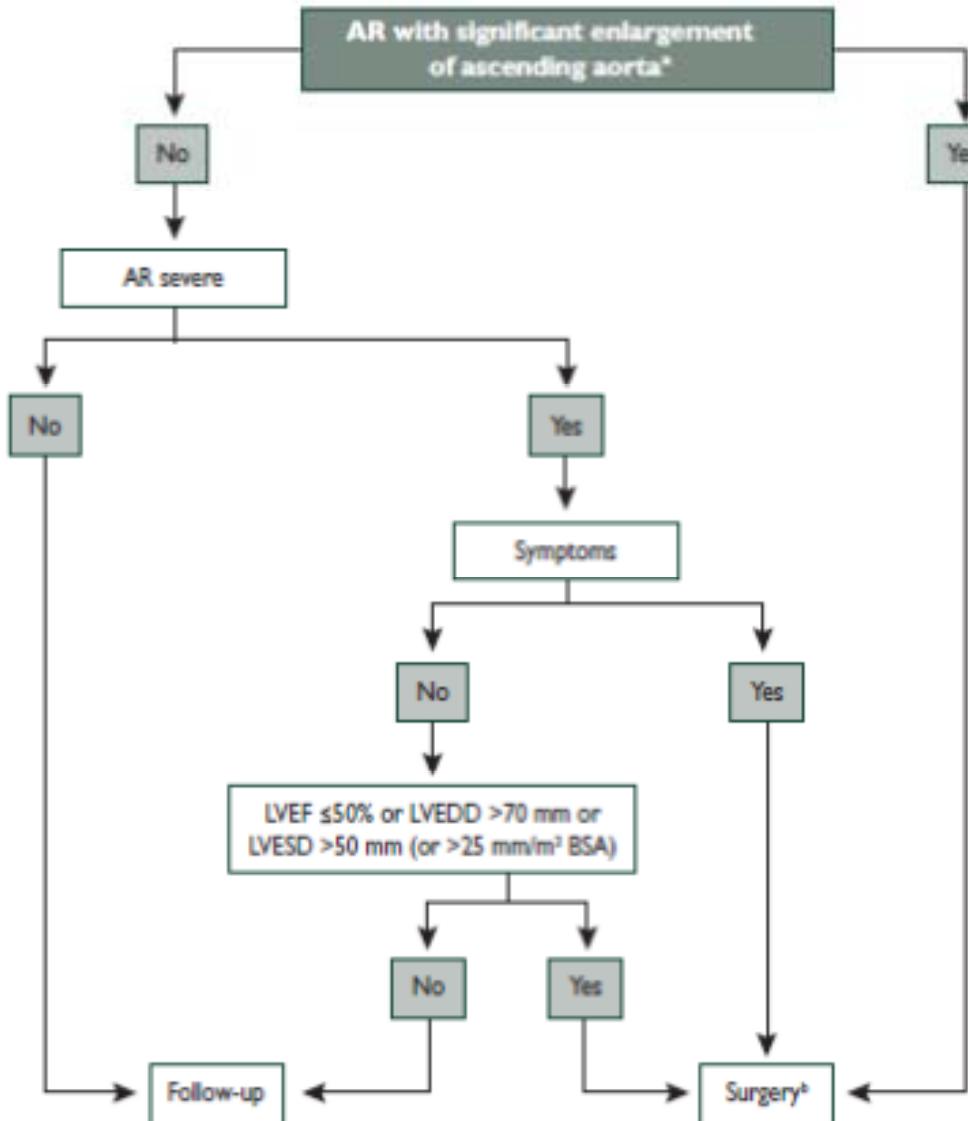
Sampat U, et al. JACC 2009

Variables	No Beta-Blocker (n = 401)	Beta-Blocker (n = 355)	p Value
Age, yrs	63 ± 18	60 ± 17	0.01
Men	56%	63%	0.06
Coronary artery disease	29%	38%	0.007
Hypertension	56%	74%	<0.0001
Diabetes mellitus	13%	15%	0.36
Renal insufficiency	20%	21%	0.67
Heart failure	68%	72%	0.19
Atrial fibrillation	27%	24%	0.27
Heart rate, beats/min	66 ± 38	76 ± 26	<0.0001
Ejection fraction, %	54 ± 19	54 ± 18	0.68
Left ventricular end-diastolic diameter, cm	5.6 ± 1.1	5.8 ± 1.0	0.05
Left ventricular end-systolic diameter, cm	3.9 ± 1.2	4.0 ± 1.2	0.07
Ventricular septum, cm	1.2 ± 0.26	1.3 ± 0.25	0.001
Posterior wall, cm	1.1 ± 0.24	1.2 ± 0.21	0.002
Pulmonary artery systolic pressure >60 mm Hg	18%	16%	0.54
Aspirin use	32%	47%	<0.0001
Angiotensin-converting enzyme inhibitor use	40%	53%	0.0005
Statin use	12%	30%	<0.0001
Dihydropyridine calcium-channel blocker use	16%	22%	0.03
Nondihydropyridine calcium-channel blocker use	14%	13%	0.67
Aortic valve replacement	29%	49%	<0.0001
Coronary artery bypass grafting	13%	20%	0.005

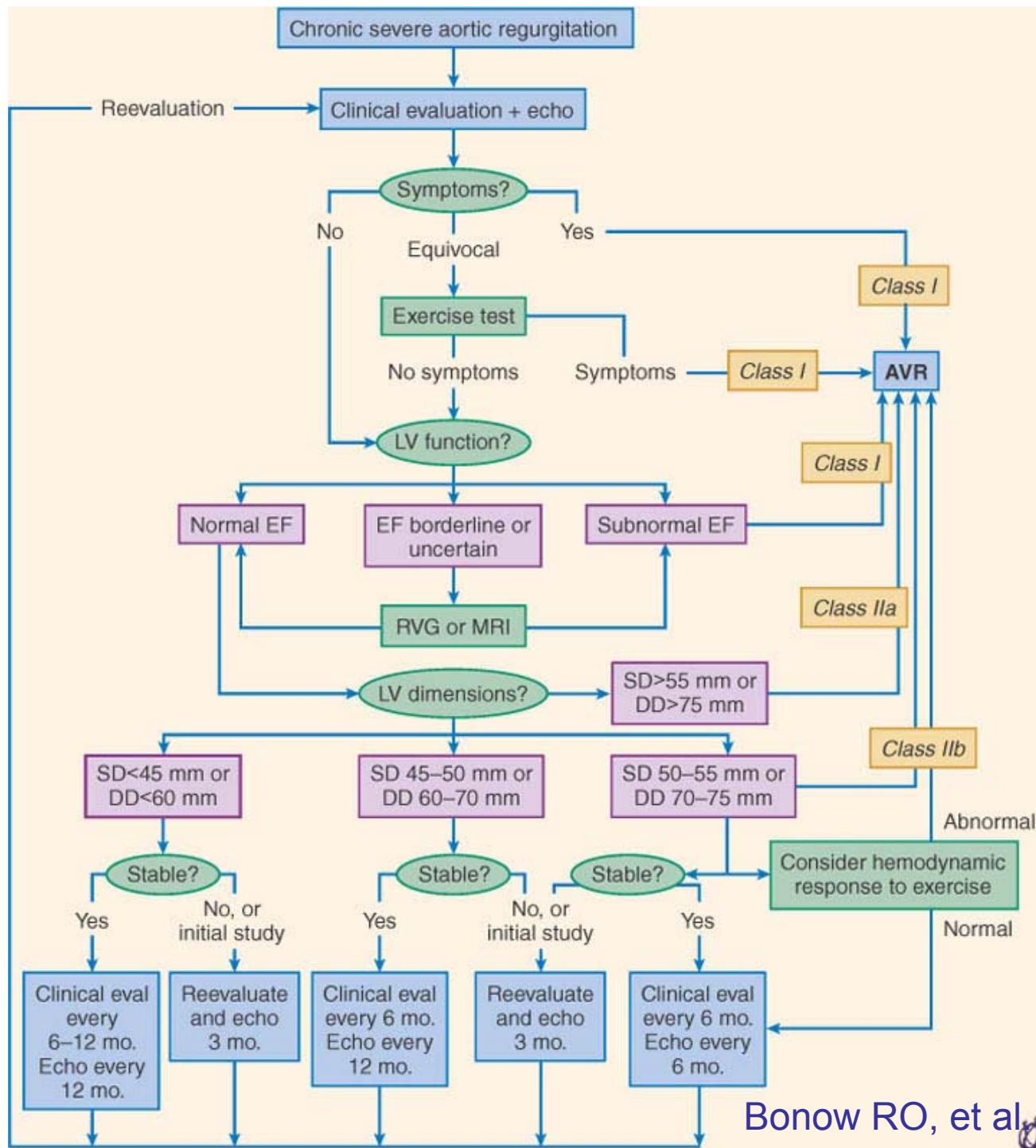
Implicació Clínica

- **Limitacions:**
 - Població molt heterogènia.
 - Dosi i tipus de BB (retrospectiu).
 - Biaix de selecció.
 - No hi ha informació sobre la simptomatologia.
 - Valoració no quantitativa de la severitat de la IAo.
- **Aquells malalts amb IAo. i altres condicions** com hipertensió, trastorns del ritme, isquèmia..sobretot si tenen una freqüència cardíaca > 70 bpm.

Cirurgia. Indications.



Vahanian A, et al. Eur Heart J 2012.

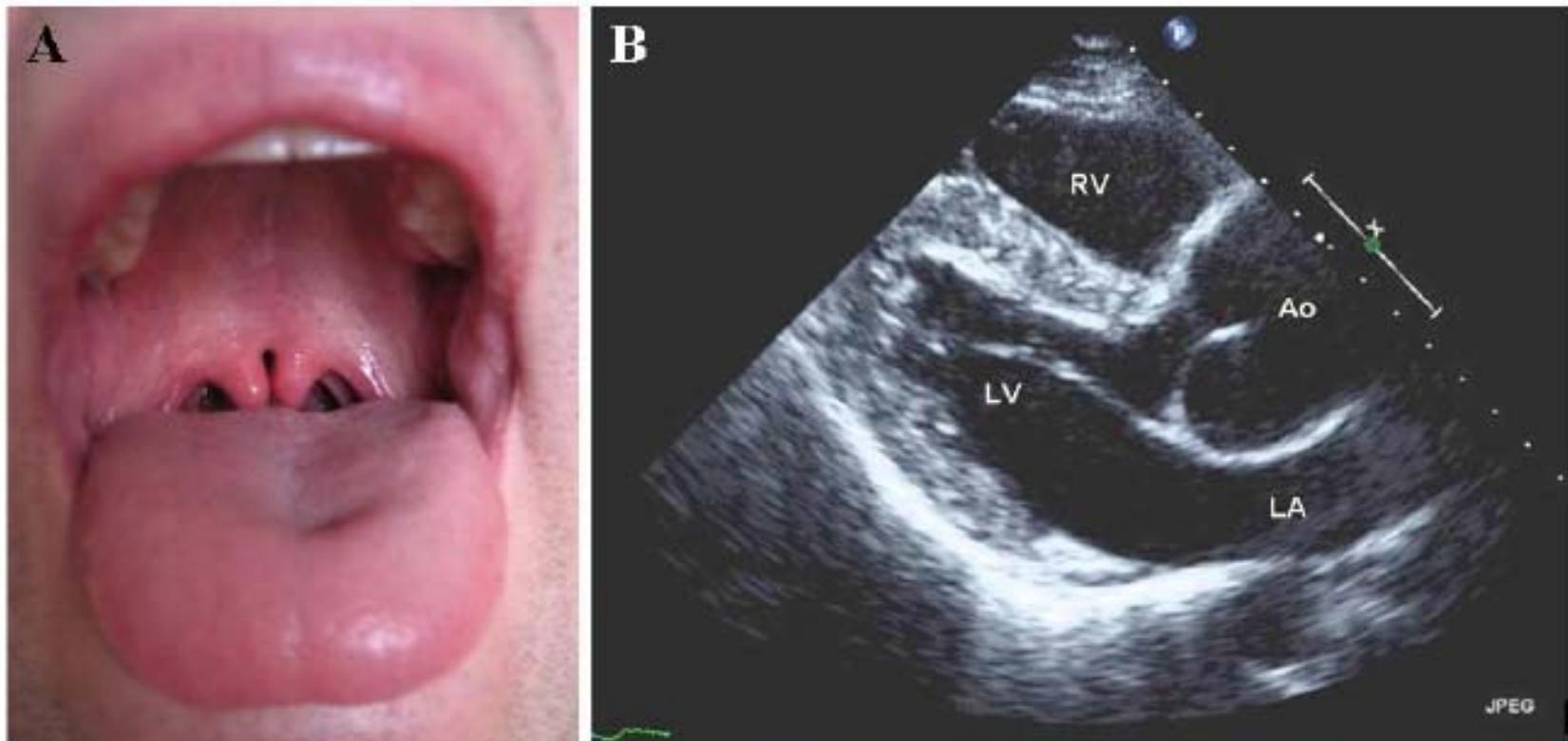


Bonow RO, et al. Circulation 2006

Cirurgia. Indicaciones.

	Class ^a	Level ^b	Ref ^c
A. Indications for surgery in severe aortic regurgitation			
Surgery is indicated in symptomatic patients.	I	B	59
Surgery is indicated in asymptomatic patients with resting LVEF ≤50%.	I	B	71
Surgery is indicated in patients undergoing CABG or surgery of ascending aorta, or on another valve.	I	C	
Surgery should be considered in asymptomatic patients with resting EF >50% with severe LV dilatation: LVEDD >70 mm, or LVESD >50 mm or LVESD >25 mm/m ² BSA. ^d	IIa	C	
B. Indications for surgery in aortic root disease (whatever the severity of AR)			
Surgery is indicated in patients who have aortic root disease with maximal ascending aortic diameter* ≥50 mm for patients with Marfan syndrome.	I	C	
Surgery should be considered in patients who have aortic root disease with maximal ascending aortic diameter: ≥45 mm for patients with Marfan syndrome with risk factors ^e ≥50 mm for patients with bicuspid valve with risk factors ^f ≥55 mm for other patients	IIa	C	

Vahanian A, et al. Eur Heart J 2012.



Vilacosta I, Cañadas V. N Engl J Med 2008.

Prendre une décision

- Is valvular heart disease severe?
- Does the patient have symptoms?
- Are symptoms related to valvular disease?
- What are patient life expectancy^a and expected quality of life?
- Do the expected benefits of intervention (vs. spontaneous outcome) outweigh its risks?
- What are the patient's wishes?
- Are local resources optimal for planned intervention?

Conclusions

- L'història natural de la IA actual no és ben coneguda.
- Elevada variabilitat interobservador en la valoració de la IA per ecografia.
- Recuperar la competència en la exploració física.
- No hi ha consens en el tractament, però no són pocs els malalts que tenen quelcom que pot justificar tractarlos.
- Si es decideix tractar, s'ha de notar.
- No podem oblidarnos de l'aorta.

VD therapy in asymptomatic severe aortic regurgitation

Left Ventricular Variable	Control Group (N=11)	Enalapril Group (N=16)	Nifedipine Group (N=12)
End-diastolic diameter (mm)			
Preoperative	73±6†	75±5†	71±8†
Postoperative	51±4	54±4	53±5
End-systolic diameter (mm)			
Preoperative	51±3†	53±3†	51±3†
Postoperative	35±4	36±5	38±5
Ejection fraction (%)			
Preoperative	48±4‡	53±6§	51±5
Postoperative	56±6	61±8	56±6

Evangelista A, et al. N Engl J Med 2005

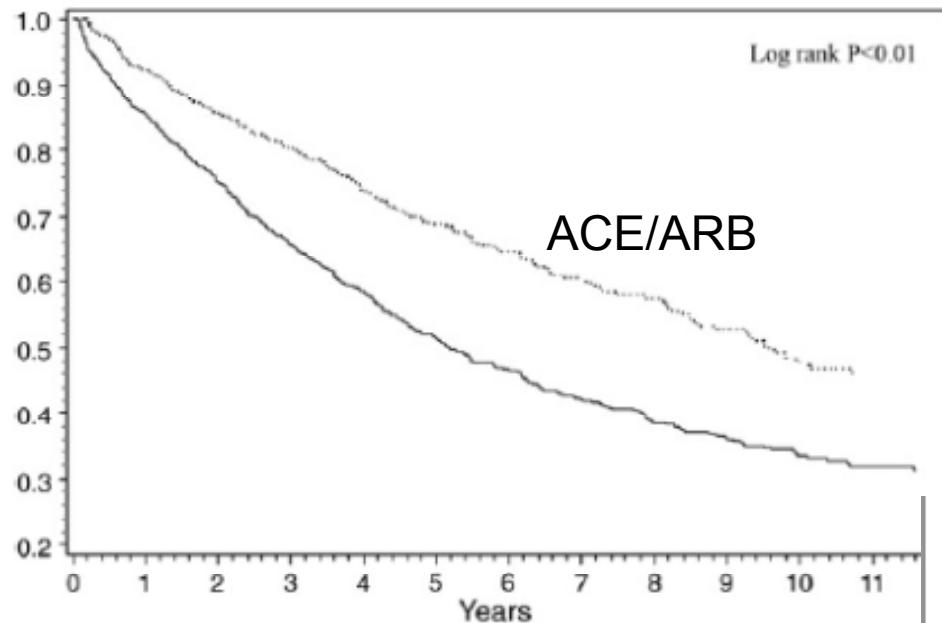
RAAS blockade in AR

- **Aim:** Investigate the effect of RAS blockade on outcomes in pts. with AR.
- Database of Tayside (Scotland). TTE.
- **2266 subjects (mean age: 74 years) with at least moderate AR.**
- Retrospective, observational study.
- Mean follow-up time: $4,4 \pm 3,7$ years.
- 705 pts (31%) with ACEI or ARB therapy.

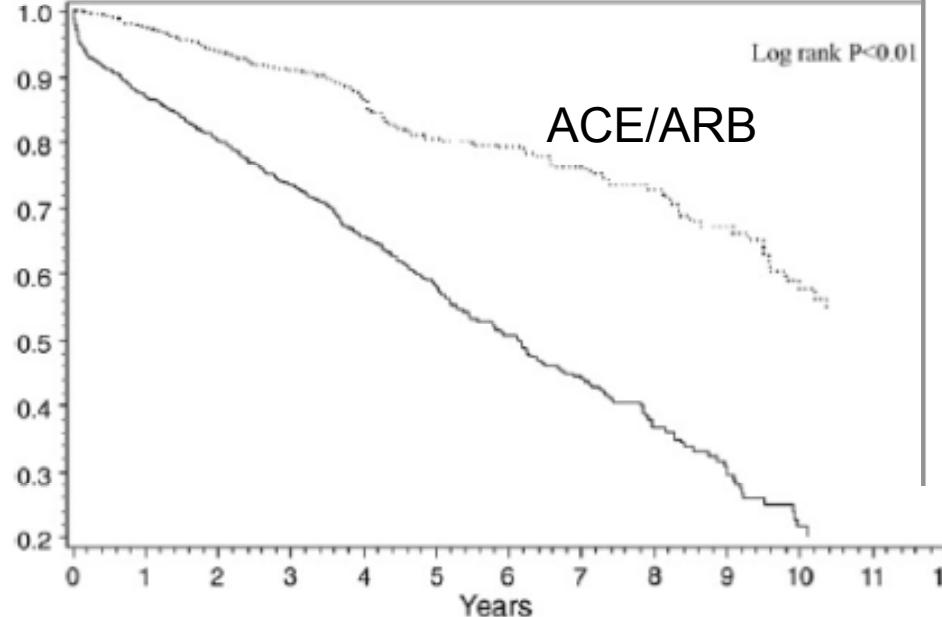
RAAS blockade in AR

- Deaths: 582 (26%).
- CV events (CV death or hospitalization): 1069 (47%).
- Aortic R. events: (HF hospitalization, HD death or AVR): 354 (16%).
- Aortic v. replacement: 65 (2,7%).

A Cardiovascular events



B All cause mortality



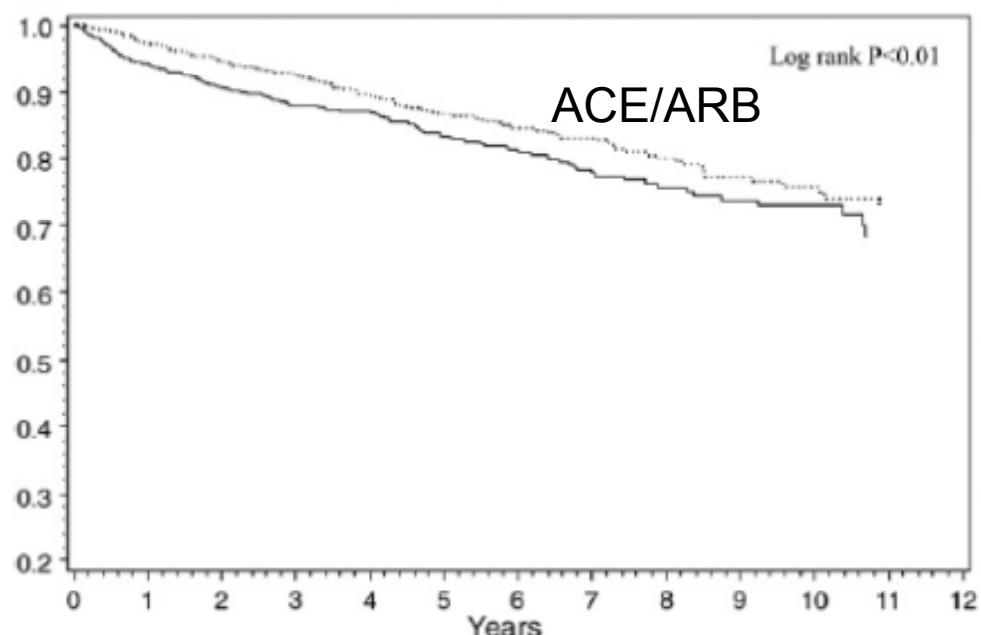
Survival benefits:

A: CV hospitalization or death.

B: All-cause mortality.

C: AVR, HF hospitalization, or HF death.

C Aortic regurgitation events



Elder DHJ, et al. JACC 2011

RAAS blockade in AR

Variable	All	No ACE Inhibitors	ACE Inhibitors	p Value (ACE Inhibitors vs. No ACE Inhibitors)
n	2,266	1,390 (61.34%)	876 (38.66%)	
Age (yrs)	74 (64-81)	75 (66-82)	72 (63-79)	<0.001
Men	902 (40%)	526 (37.84%)	376 (42.9%)	0.02
BMI (kg/m ²)	25 (23-29)	25.4 (23-29)	26 (23-29)	0.87
SBP (mm Hg)	142 (130-160)	140 (130-157)	140 (130-160)	0.68
DBP (mm Hg)	73 (65-82)	75 (64-81)	75 (65-82)	0.71
Hemoglobin (mg/dl)	12.7 (11.6-14)	12.8 (11.4-13.9)	13 (11.8-13.9)	<0.001
Cholesterol (mmol/l)	4.90 (4.13-5.74)	4.88 (4.17-5.74)	4.9 (4.1-5.75)	0.73
Creatinine (mmol/l)	98 (84-120)	97 (83-121)	99 (85-117)	0.98
LVISD (cm)	3.03 ± 2.58	2.88 ± 2.54	3.28 ± 2.62	<0.001
Diabetes	298 (13%)	154 (11.07%)	144 (16.44%)	<0.001
Renal admission	60 (3%)	35 (2.52%)	25 (2.85%)	0.63
COPD	79 (3%)	50 (3.6%)	29 (3.31%)	0.72
Previous event	625 (28%)	313 (22.52%)	312 (35.62%)	<0.001
Aspirin	1,154 (51%)	594 (51.47%)	560 (63.93%)	<0.001
Diuretic agents	545 (24%)	301 (21.6%)	244 (27.90%)	<0.001
Beta-blockers	789 (35%)	389 (27.98%)	400 (45.66%)	<0.001
Calcium antagonists	774 (34%)	407 (29.28%)	367 (40.96%)	<0.001
Digoxin	528 (23%)	283 (20.40%)	245 (27.97%)	<0.001
Nitrates	705 (31%)	331 (23.81%)	374 (42.69%)	<0.001
Statins	870 (38%)	369 (26.55%)	501 (57.19%)	<0.001
LV impairment	1,030 (45%)	642 (46.18%)	388 (44.29%)	0.38

Elder DHJ, et al. JACC 2011

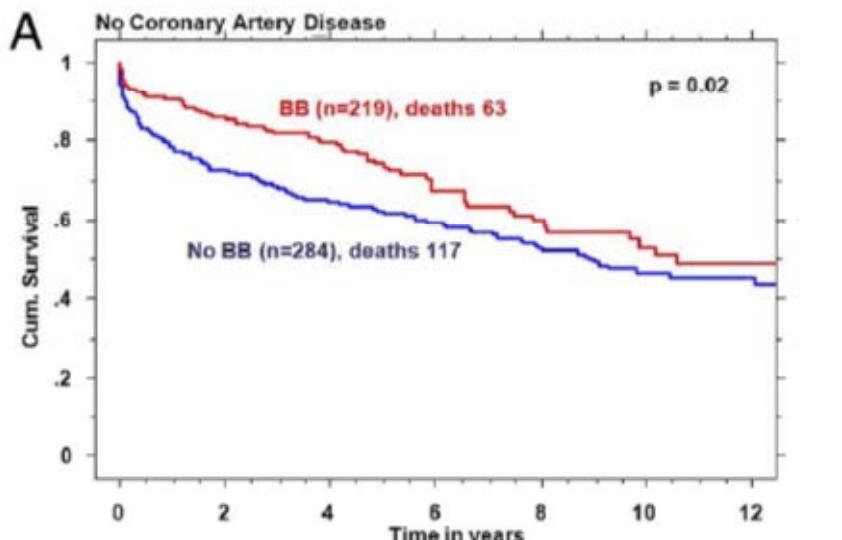
RAAS blockade in AR

- Limitations:
 - No information regarding symptomatology.
 - Mixed valvular disease are not excluded.
 - Retrospective, nonrandomized, observational.
 - Assessment of AR severity was semiquantitative (mild, moderate, severe).
 - Selection bias: BB and other CV therapy were more frequent in the ACEI or ARB group.
 - Small number of AVR vs large number of HF?.

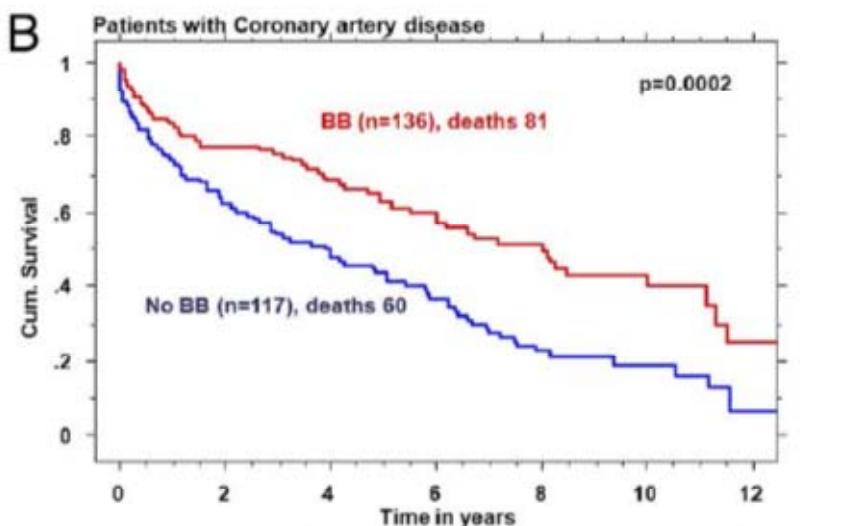
Beta-blockers in chronic AR

- Evaluation of BB effect (**stratification**):
 - stratified by CAD status.
 - stratified based on HTA.
 - stratified based on heart rate.
- **Cox regression models:**
 - RR: 0,74, 95% CI: 0,57-0,97, p= 0,03.
 - RR: 0,74, 95% CI: 0,58-0,93, p=0,01.
- **Propensity score analysis:**
 - BB therapy was an independent predictor of survival after adjusting for the propensity score using the Cox regression model (p=0,01).

BBs and CAD status

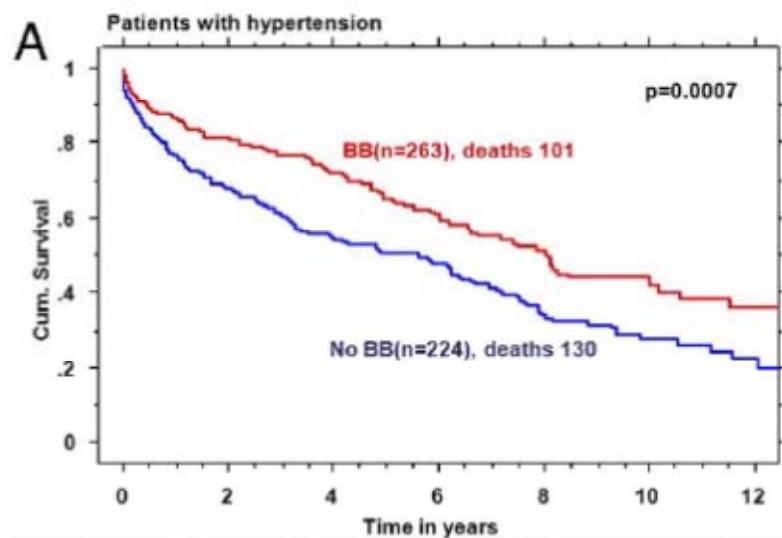


	0	2	4	6	8	10	12
BB	219	140	108	69	43	27	12
No BB	284	156	133	111	77	50	16

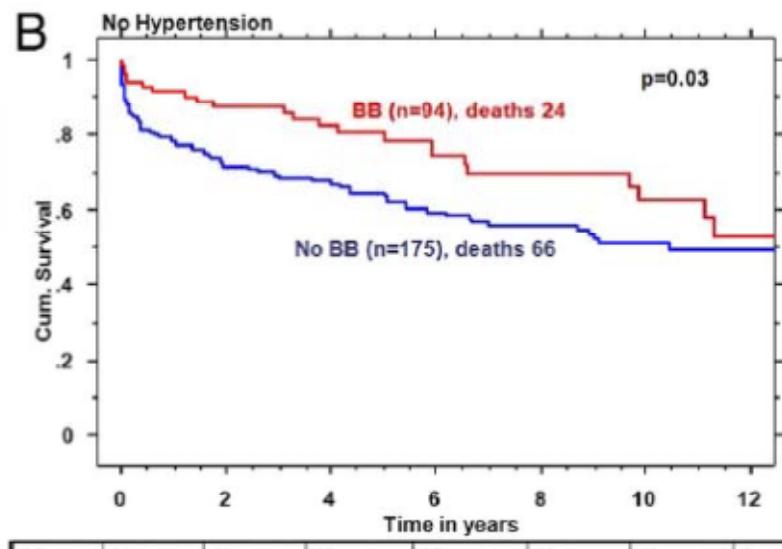


	0	2	4	6	8	10	12
BB	136	87	65	41	31	13	8
No BB	117	62	46	33	17	10	6

BBs and HTA status



	0	2	4	6	8	10	12
BB	263	170	126	76	48	24	15
No BB	224	130	96	74	43	24	14



	0	2	4	6	8	10	12
BB	94	58	47	35	26	16	8
No BB	175	98	83	70	51	36	18

Sampat U, et al. JACC 2009