

Ισχαιμική - λειτουργική ανεπάρκεια της μιτροειδούς βαλβίδος.

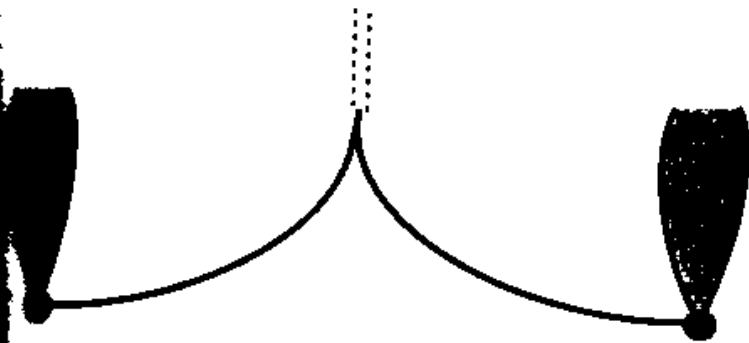
Χαράλαμπος Ι. Καρβούνης.

Η ισχαιμική ανεπάρκεια της
μιτροειδούς αποτελεί ένα σύνθετο
πρόβλημα της σημερινής
καρδιολογίας, τόσο από πλευράς
κατανόησης των μηχανισμών που
την προκαλούν, όσο και από την
πλευρά της κατάλληλης
αντιμετώπισής της.

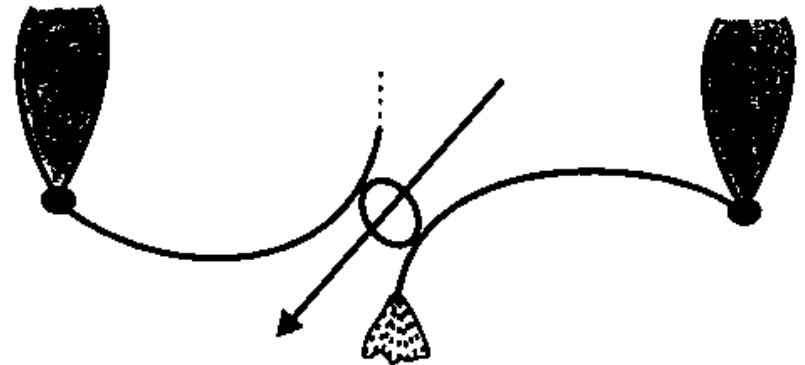
Παραδοσιακά η ισχαιμική ανεπάρκεια της μιτροειδούς αφορά την ανεπάρκεια που προκαλείται από τις συνέπειες της στεφανιαίας νόσου, κυρίως μετά από έμφραγμα μυοκαρδίου, με τις γλωχίνες της μιτροειδούς να έχουν φυσιολογική ανατομία.

Σήμερα χρησιμοποιείται περισσότερο ο όρος λειτουργική (functional) ανεπάρκεια της μιτροειδούς, διότι το φαινόμενο της ανεπάρκειας με ανατομικά φυσιολογικές μιτροειδικές γλωχίνες παρατηρείται και σε άλλες καταστάσεις πλην της στεφανιαίας νόσου.

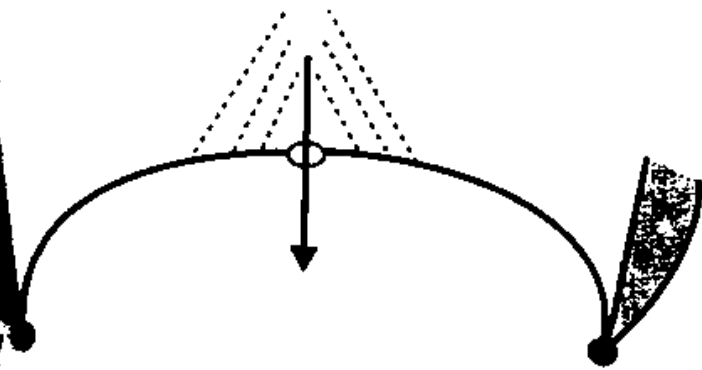
Στην ισχαιμική-λειτουργική ανεπάρκεια της μιτροειδούς, οι κατά τα άλλα φυσιολογικές γλωχίνες της μιτροειδούς, κατά την συστολή μετακινούνται προς την κορυφή της αριστερής κοιλίας, με αποτέλεσμα την ατελή σύγκλιση της μιτροειδούς βαλβίδας.



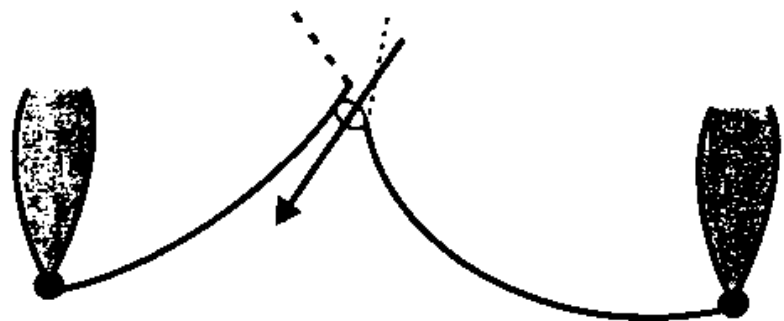
Normal



Flail Leaflet /
Ruptured Papillary Muscle



Functional Mitral
Regurgitation



Restricted
Leaflet Motion

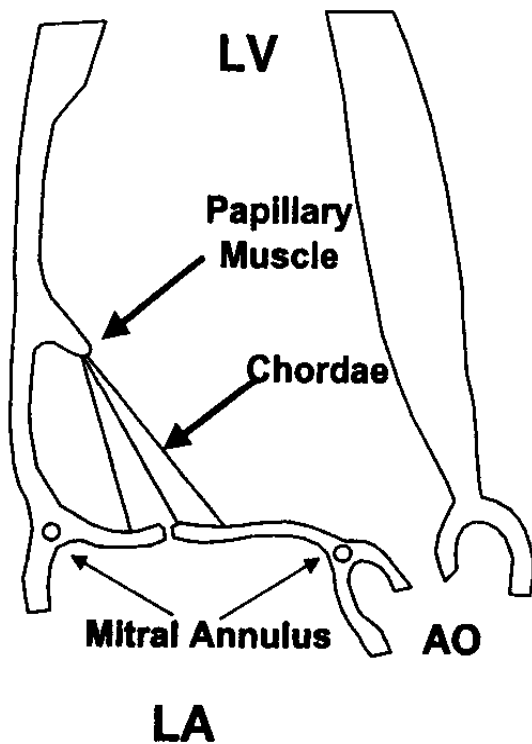
| Cause | Mechanism | | | |
|--------------|--|---|---|---|
| | Organic | | | Functional |
| | Type I | Type II | Type IIIa | Type I/IIIb |
| Nonischaemic | Endocarditis (perforation); degenerative (annular calcification); congenital (cleft leaflet) | Degenerative (mitral valve prolapse, flail leaflet); endocarditis (ruptured chords) | Rheumatic; iatrogenic (radiation/drug); inflammatory (lupus, anticardiolipin); etc. | Cardiomyopathy; myocarditis; left ventricular dysfunction (any cause) |
| Ischaemic | | Ruptured PM | | Functional ischaemic |

MR = mitral regurgitation. PM = papillary muscle. Classification according to Carpentier: Type I: normal leaflet movement; Type II: excessive leaflet movement; Type III: restricted leaflet movement (IIIa in diastole, IIIb in systole).

Θεωρίες πάνω στον μηχανισμό πρόκλησης της ισχαιμικής-λειτουργικής ανεπάρκειας της μιτροειδούς.

- Μεταβολές στην γεωμετρία της αριστερής κοιλίας, λόγω αναδιαμόρφωσης, με μετατόπιση των θηλοειδών μυών που συγκρατούν και εμποδίζουν τις γλωχίνες να έλθουν στο φυσιολογικό σημείο σύγκλισης.
- Ελάττωση της δύναμης που αναγκάζει τις γλωχίνες να κλείσουν, λόγω ελαττωμένης συσταλτικότητας της αριστερής κοιλίας.

Normal Mitral Valve



Functional Mitral Regurgitation

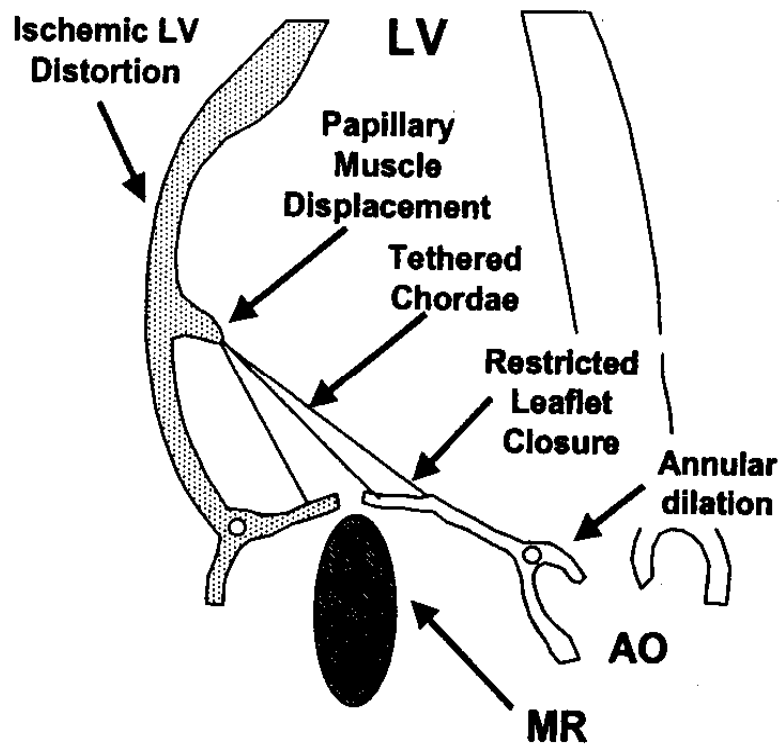
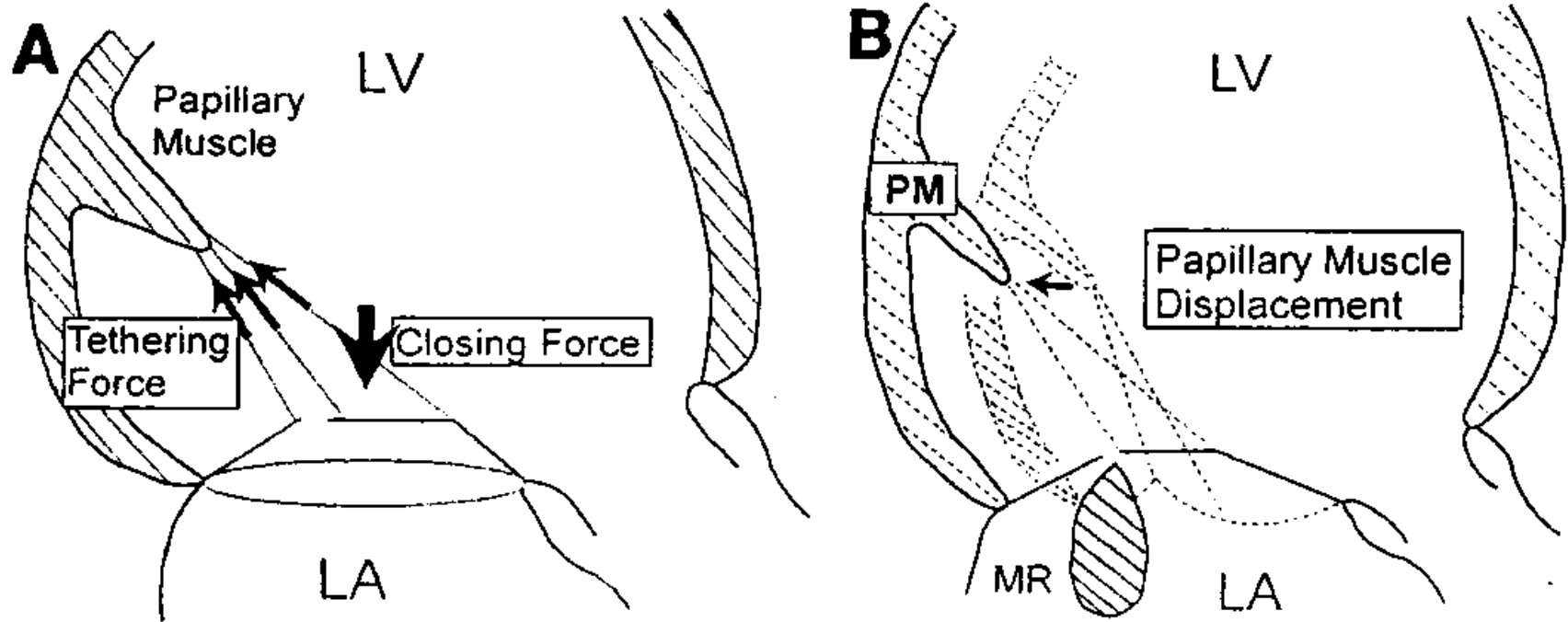
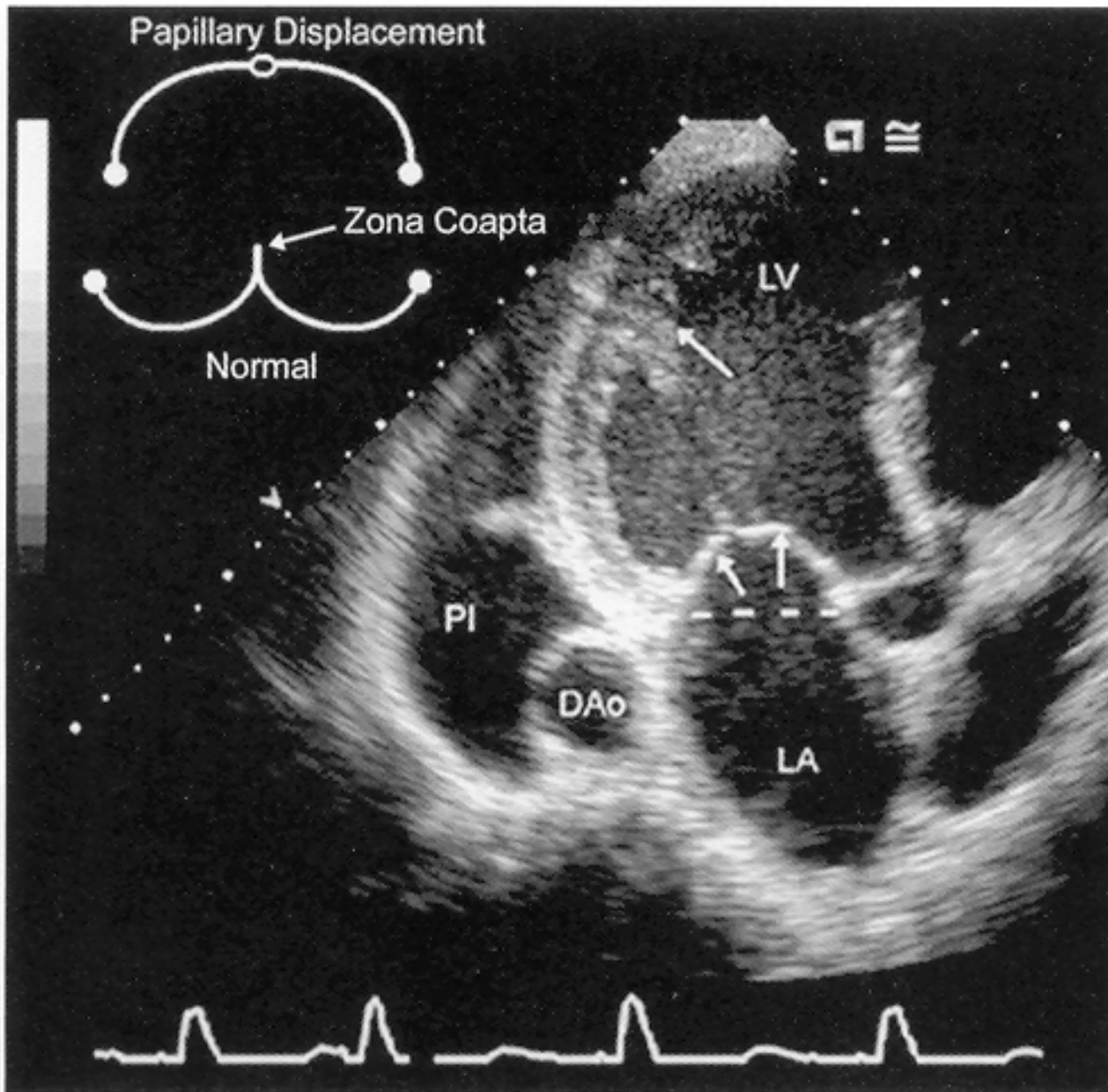


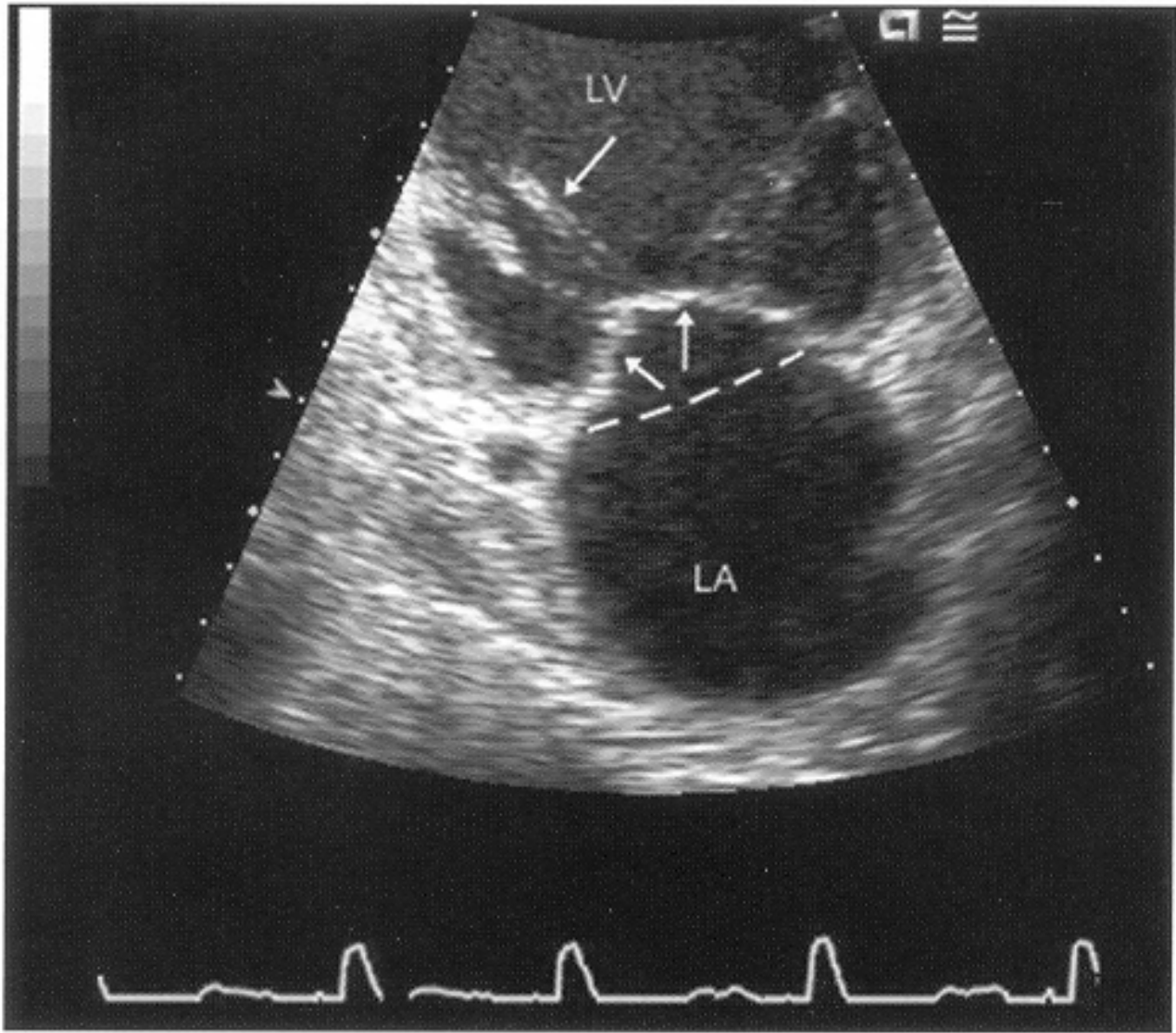
Figure 1. Mechanism of functional mitral regurgitation (MR). AO = aorta; LA = left atrium; LV = left ventricle.

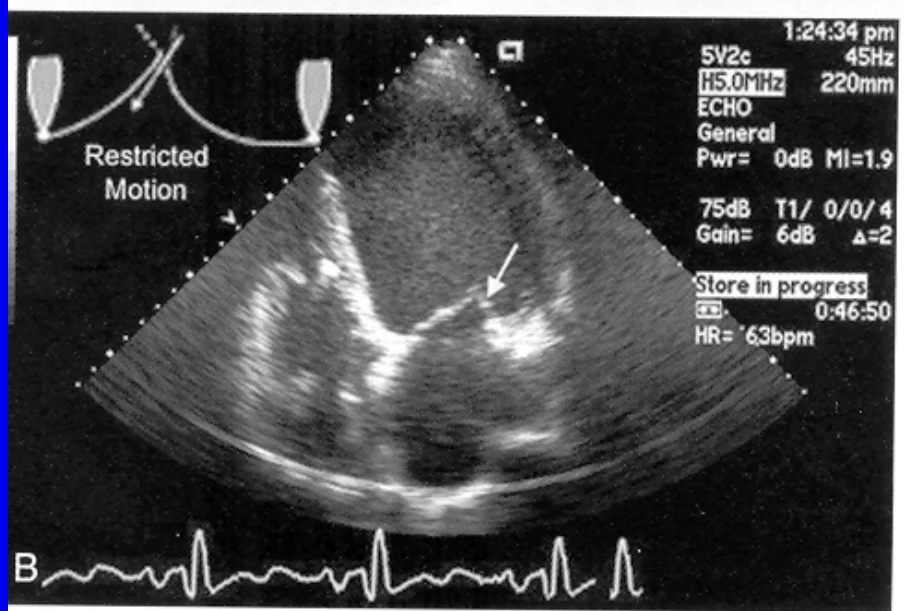
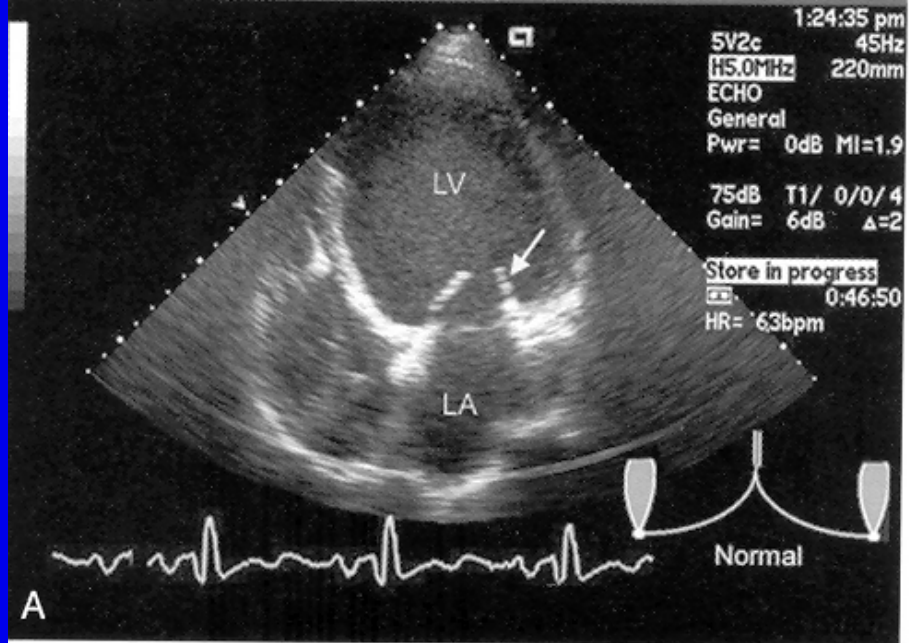


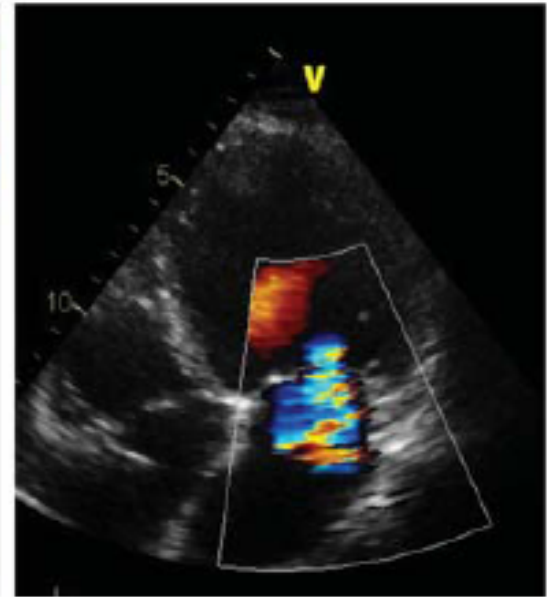
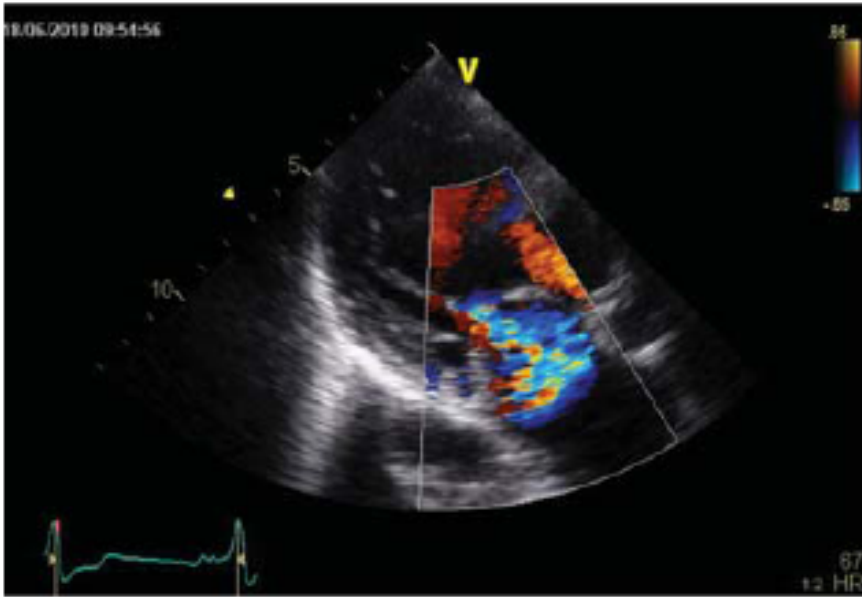
Otsuji Y et al: Circulation 1997;96:1999-2008.

Η ισχαιμική-λειτουργική ανεπάρκεια της μιτροειδούς μπορεί να διαγνωσθεί τόσο ποιοτικά, όσο και ποσοτικά, με εξαιρετική ακρίβεια με το υπερηχοκαρδιογράφημα-Doppler.









MI: 1.6
S3 1.6/3.2

2/8/F/H5
UM HOSPITAL (c)

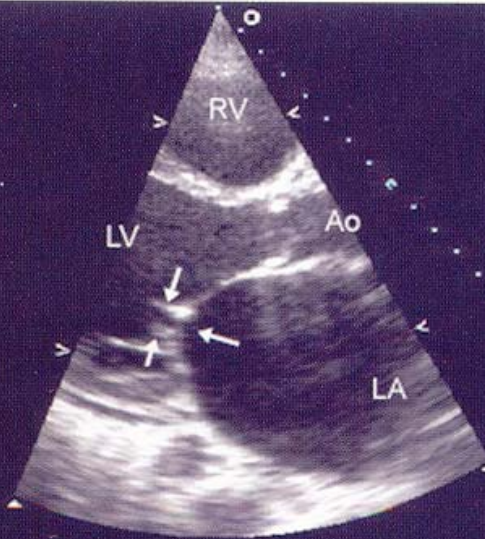
0:42:11.24

GAIN 70
COMP 62
119BPM

17CM
48HZ

P T R
1.6 3.2

A



TIS: 1.0
S3 1.6/3.2

2/1/F/L3/A
UM HOSPITAL (c)

0:42:22.38

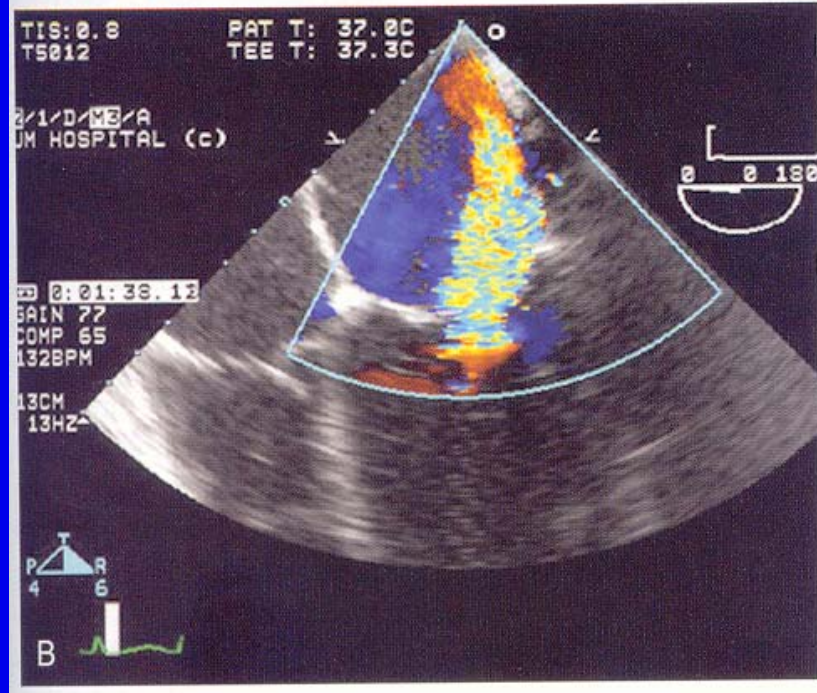
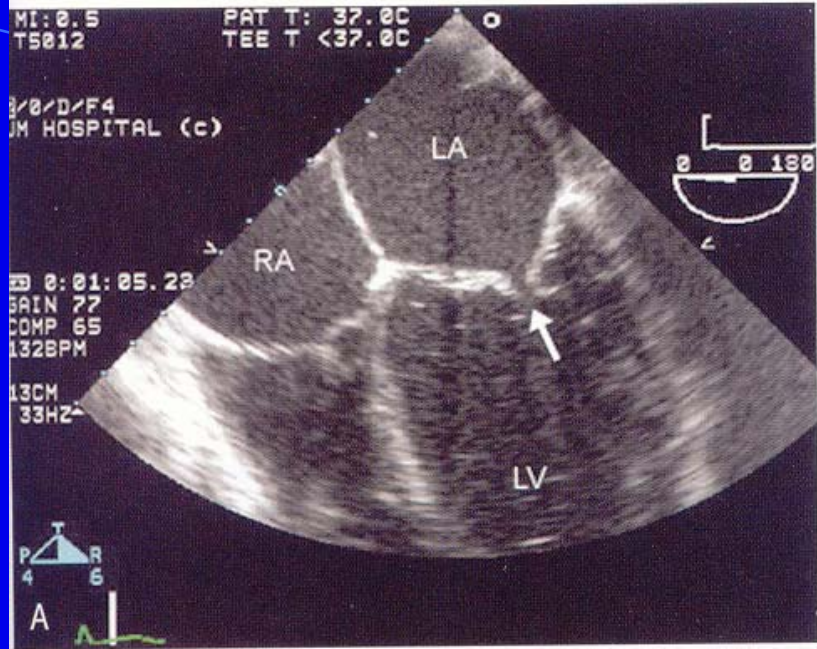
GAIN 70
COMP 62
119BPM

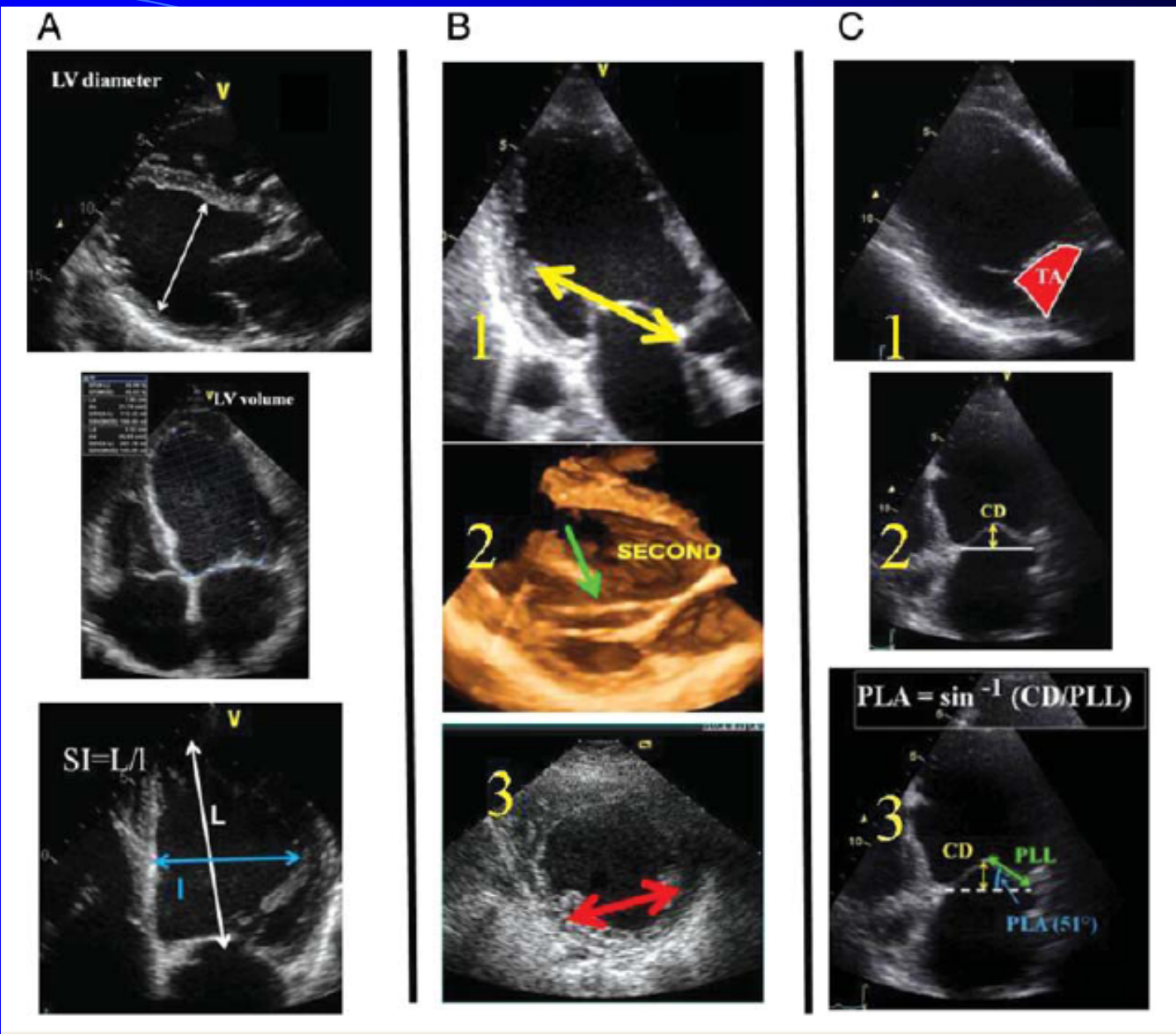
17CM
11HZ

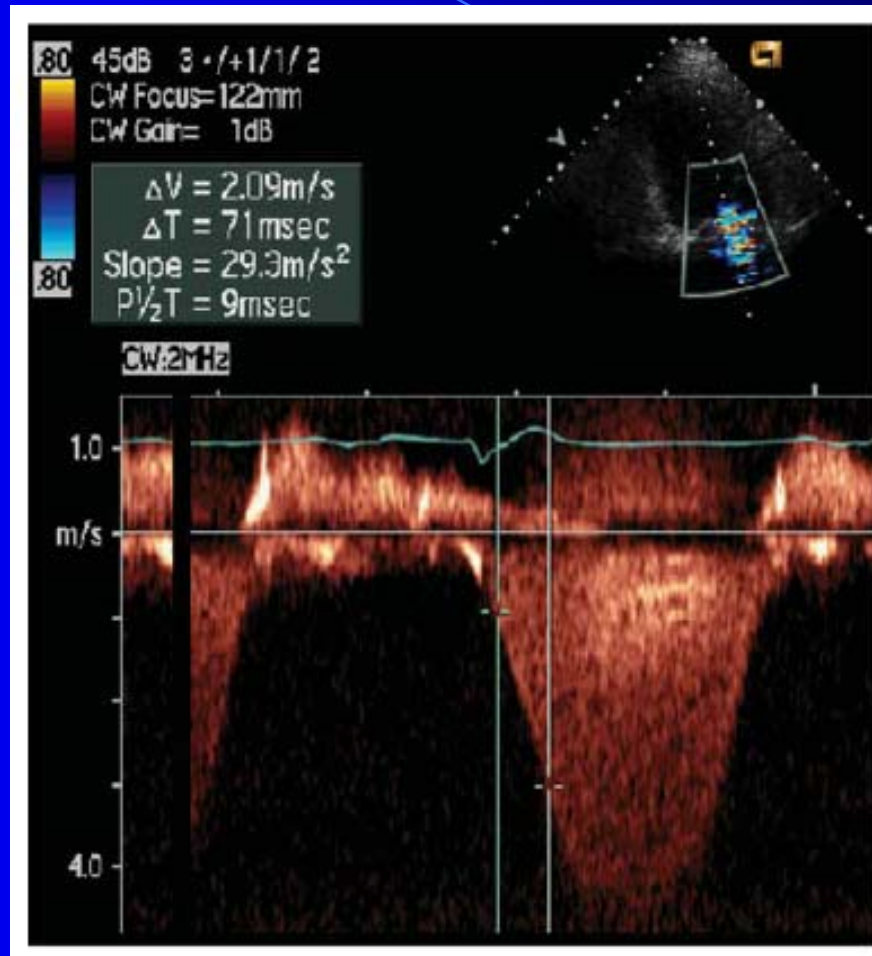
P T R
1.6 3.2

B









Eur Heart J 2010;31:2996-3005.

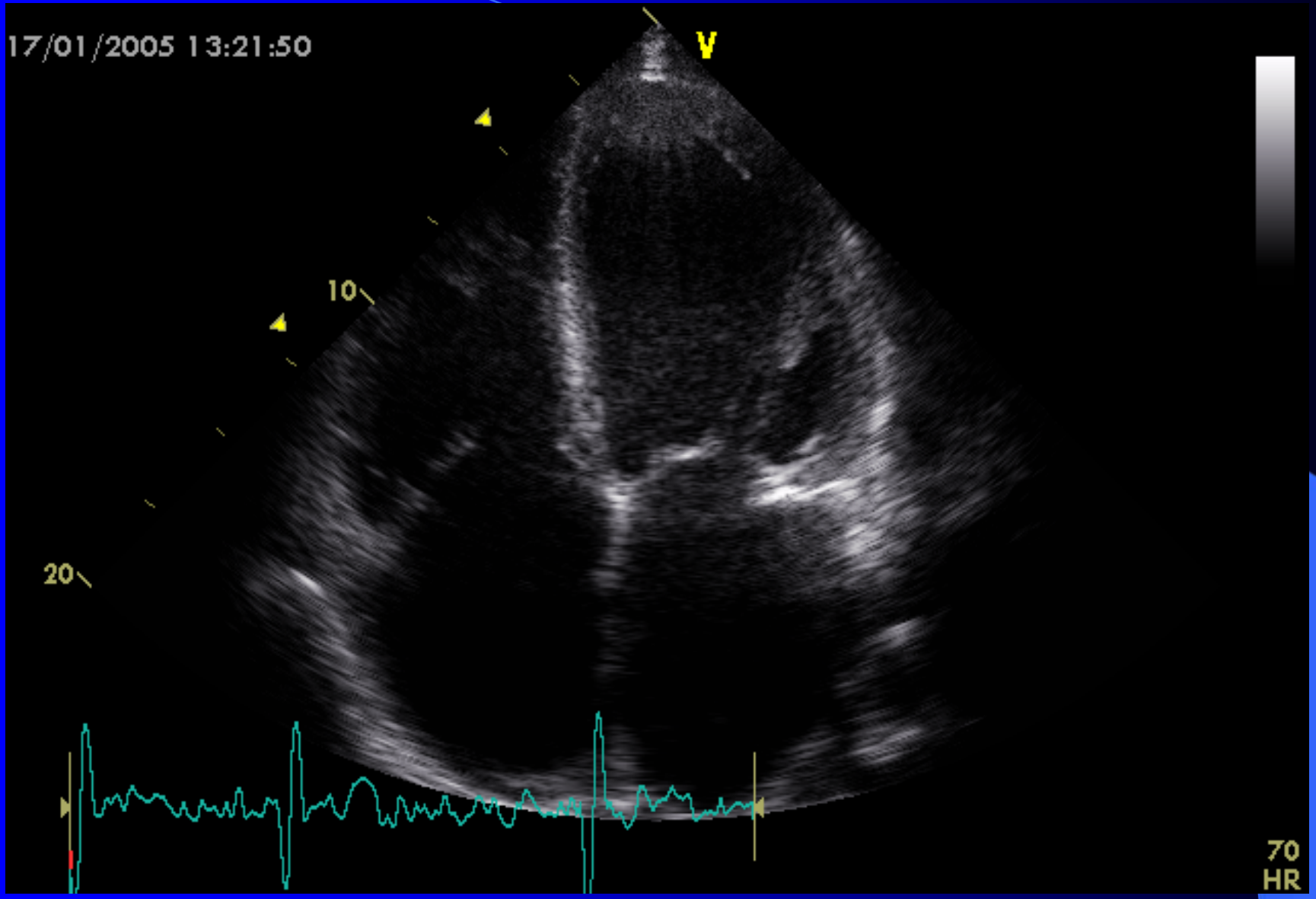
17/01/2005 13:21:50

V

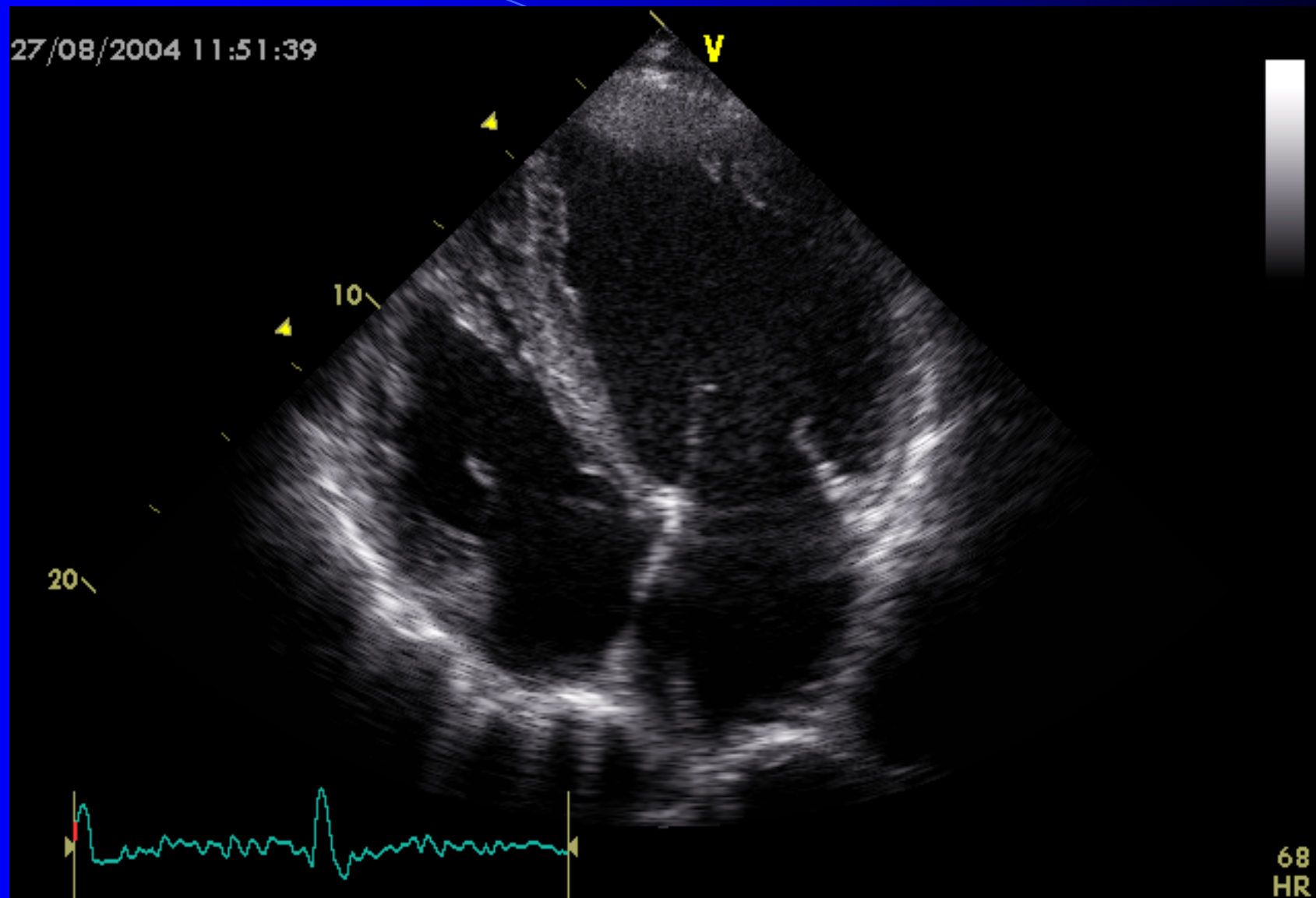
10

20

70
HR



27/08/2004 11:51:39



10

20

68
HR

08/12/2004 14:51:09

V

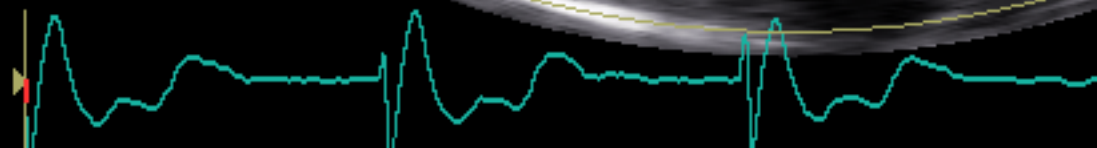
.58

-.58

5

10

15



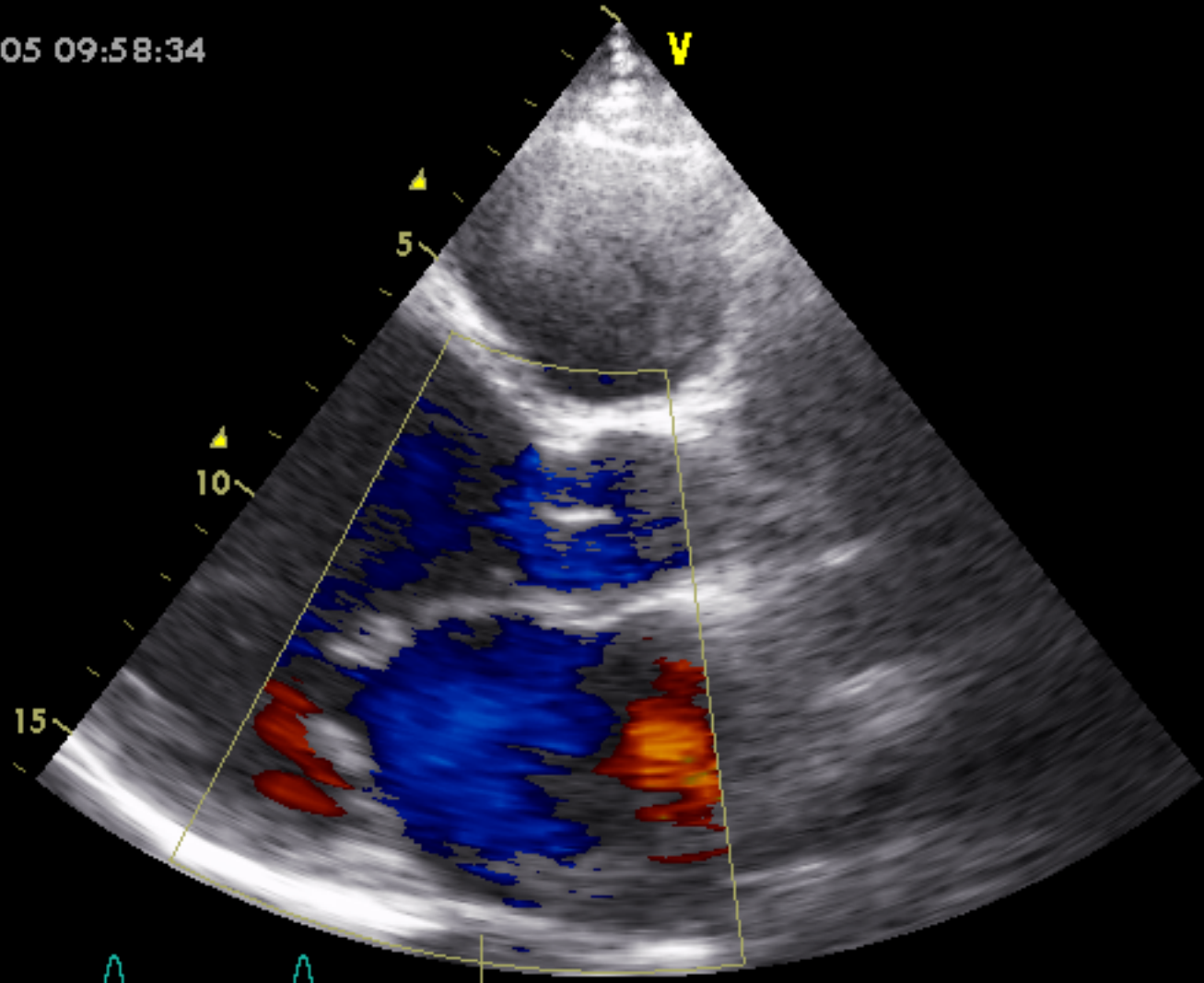
60
HR

10/02/2005 09:58:34

V

.62

-.62



5

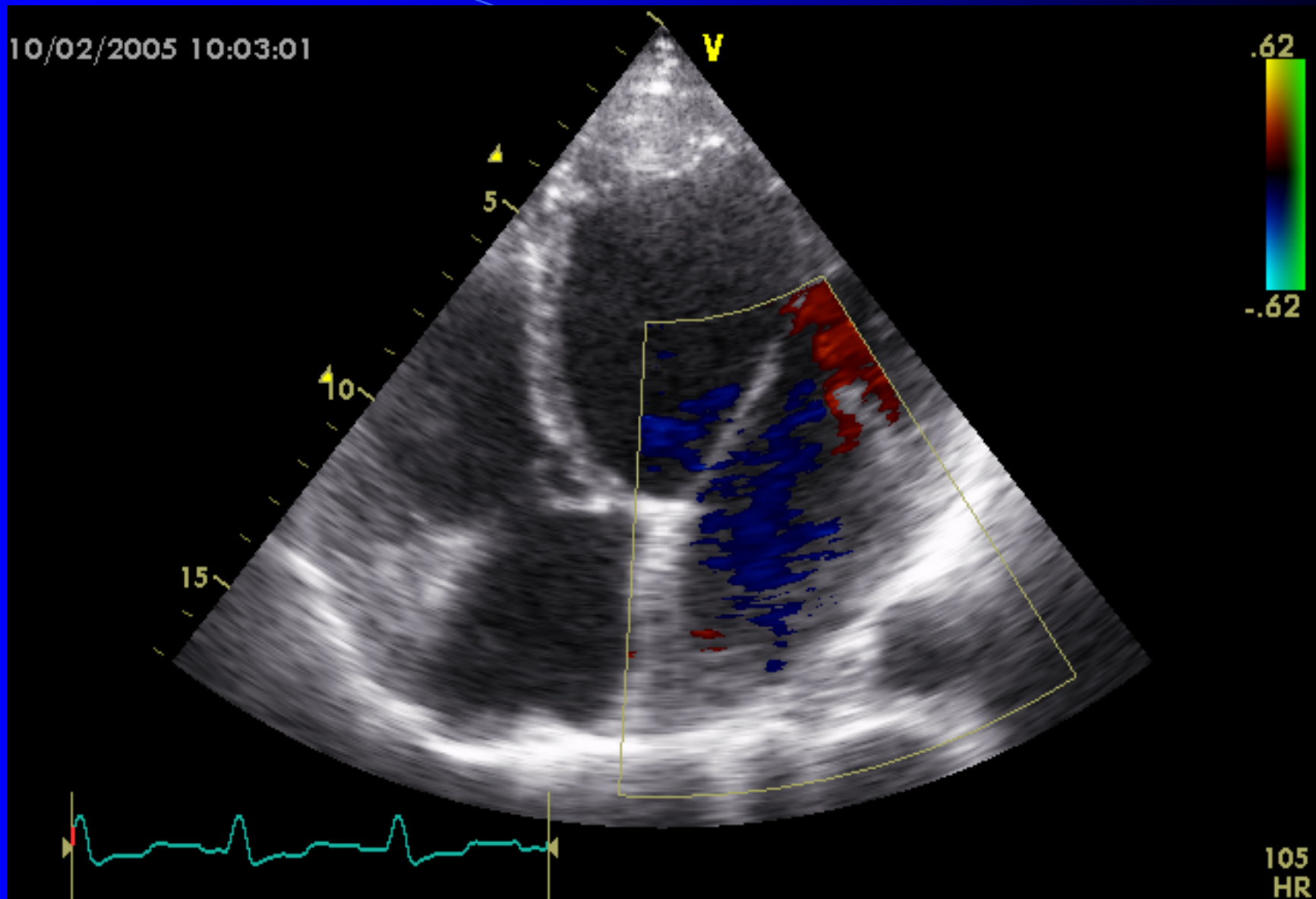
10

15



105
HR

10/02/2005 10:03:01



.62

-.62

105
HR

21/02/2005 13:15:46

V

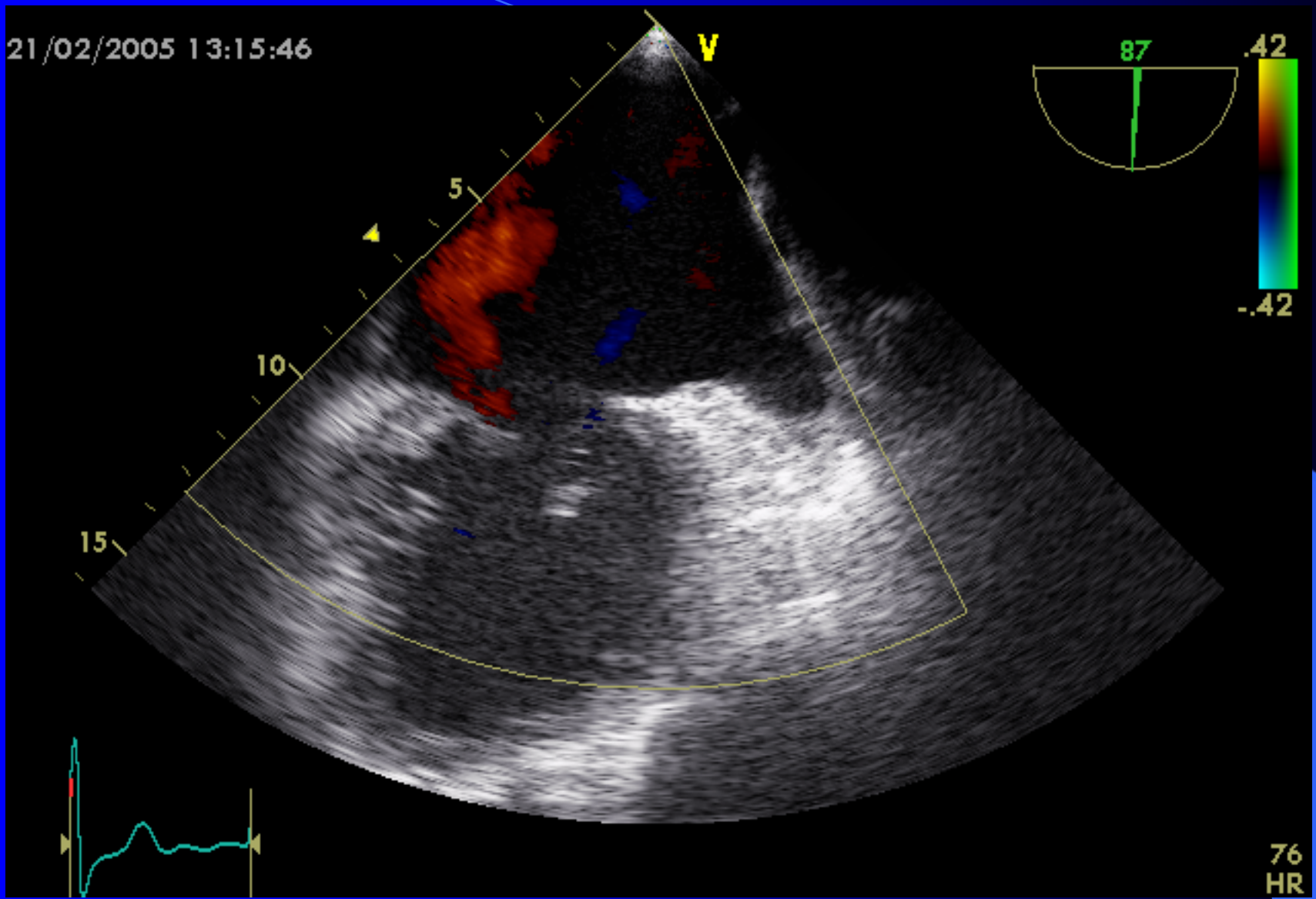
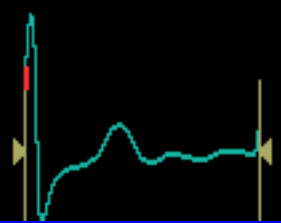
87

.42

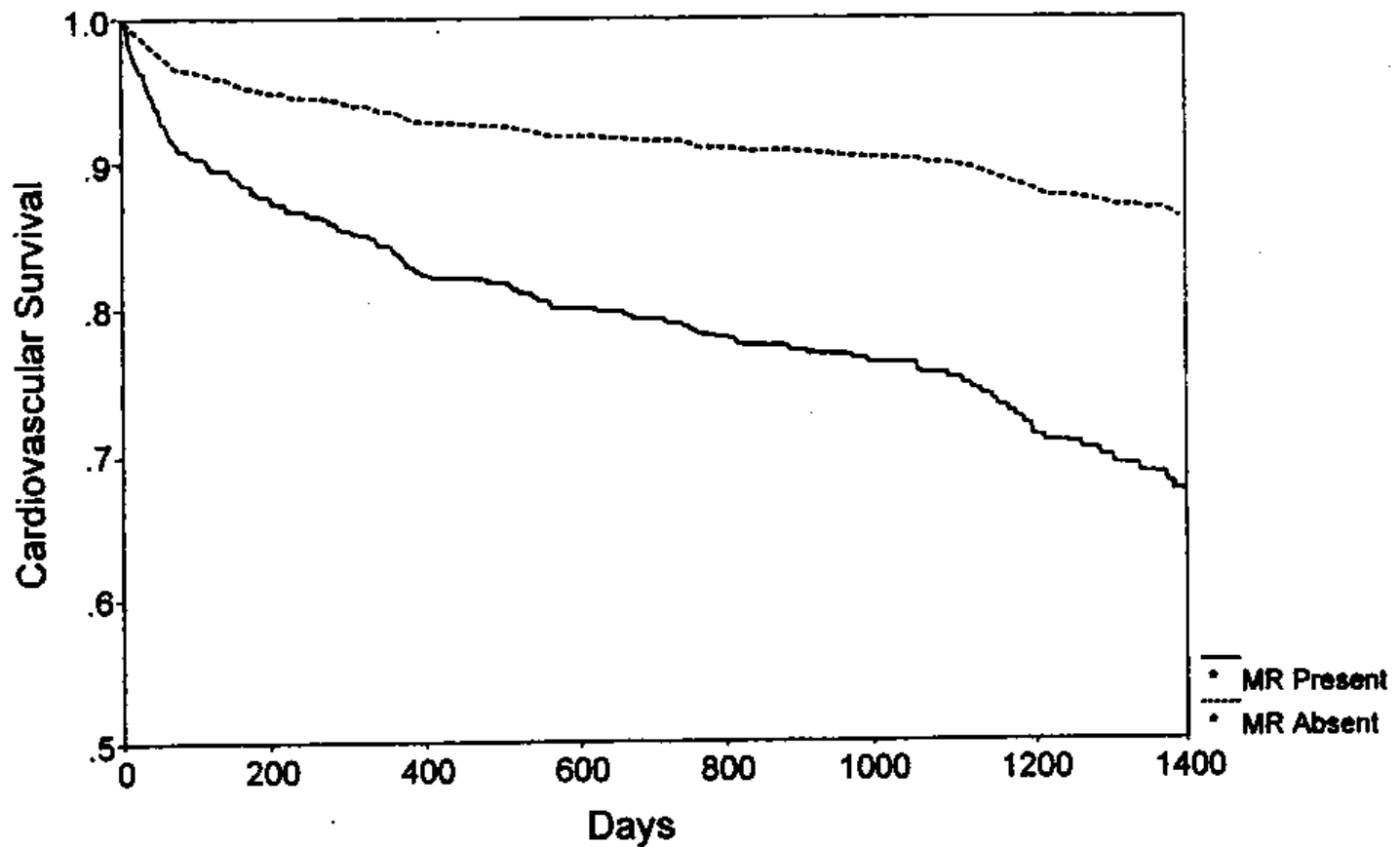
-.42

5
10
15

76
HR



Σοβαρού βαθμού ισχαιμική-
λειτουργική ανεπάρκεια της
μιτροειδούς εμφανίζεται σε υψηλό
ποσοστό χρόνιας συστολικής
καρδιακής ανεπάρκειας και σχετίζεται
με πολύ μειωμένη πενταετή
επιβίωση.



Kaplan-Meier curves of cardiovascular survival in patients with (n=141) and without (n=586) MR (multivariate $P=.0022$).

Lamas GA et al: Circulation 1997;96:827-833.

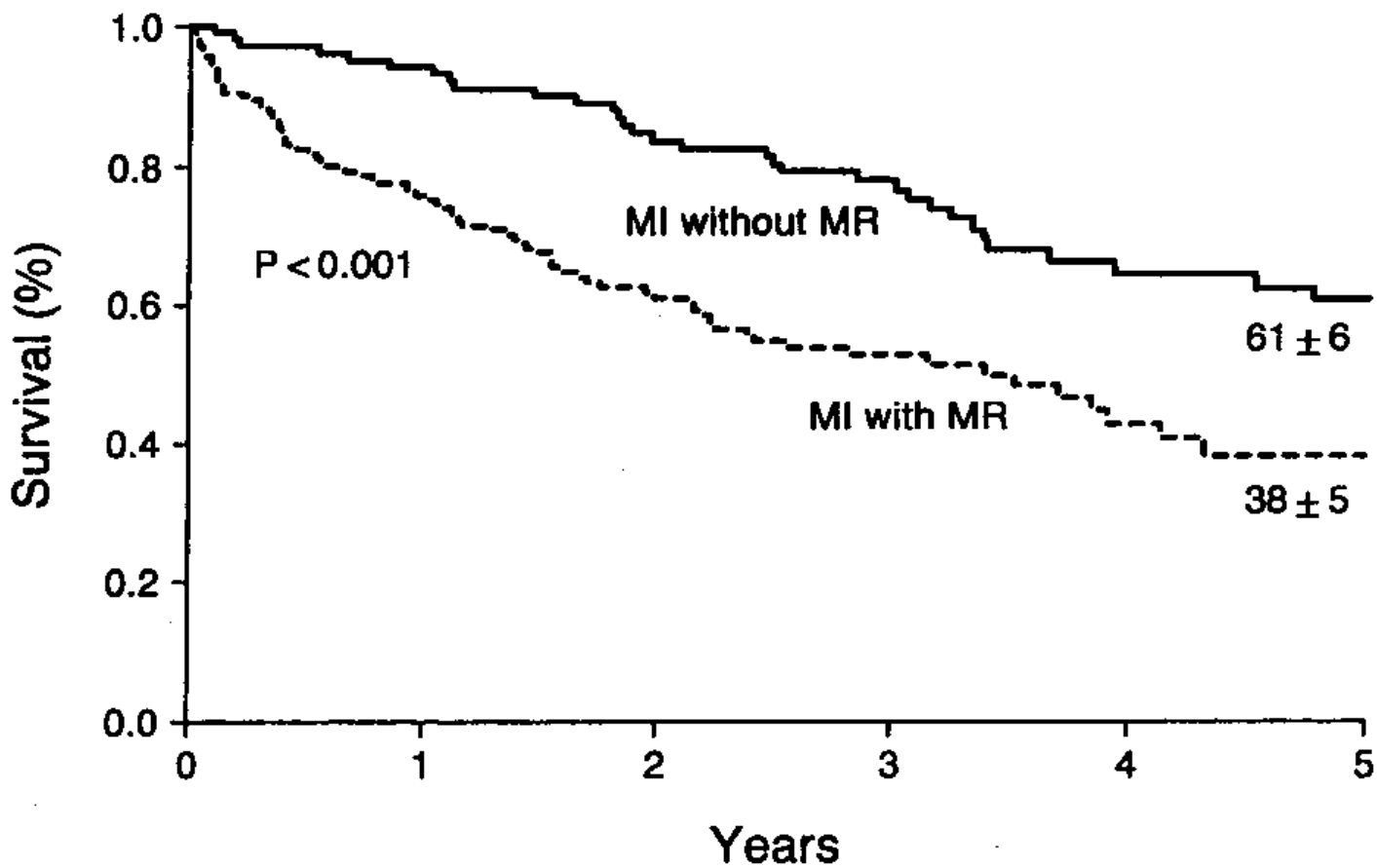
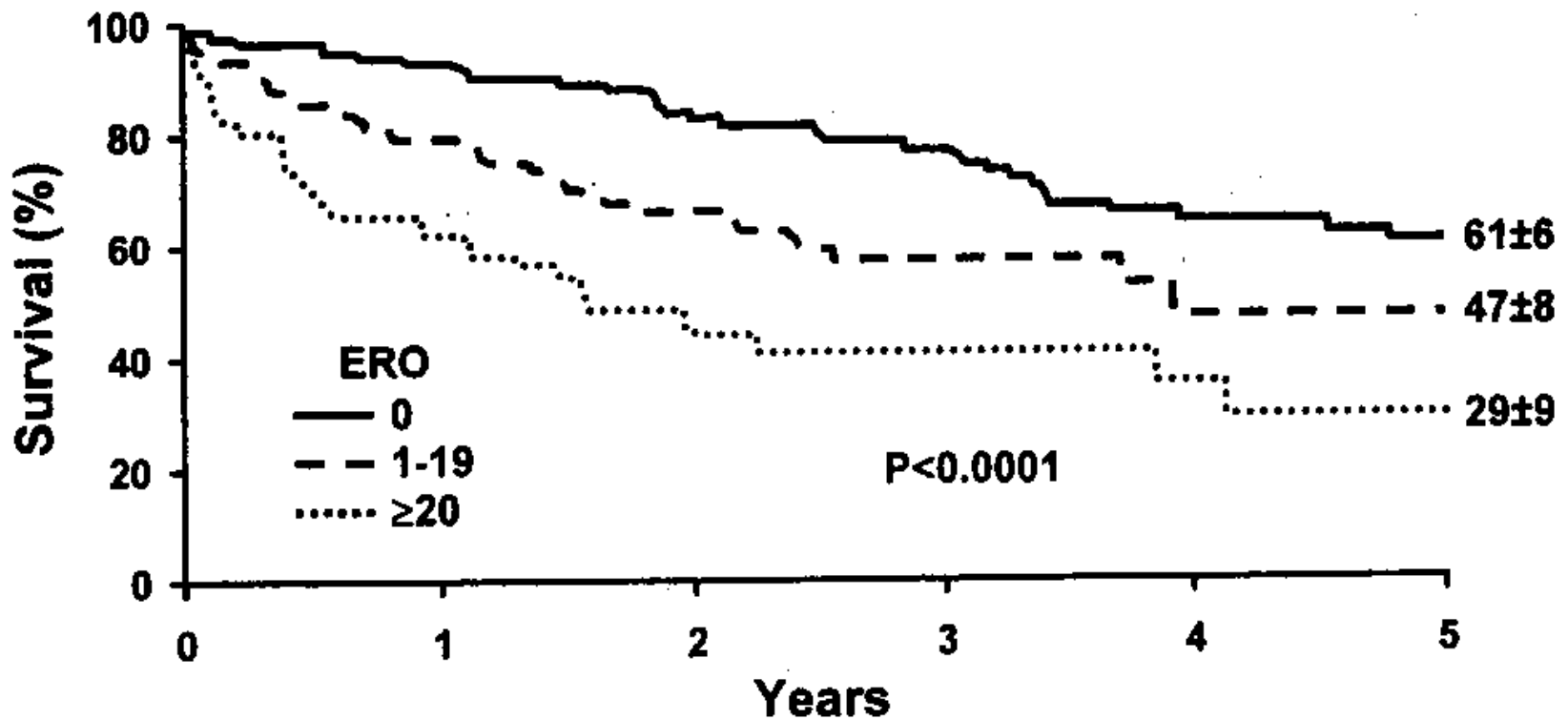


Figure 1. Survival (\pm SE) after diagnosis according to presence of IMR.

Grigioni F et al: Circulation 2001;103:1759-1764.

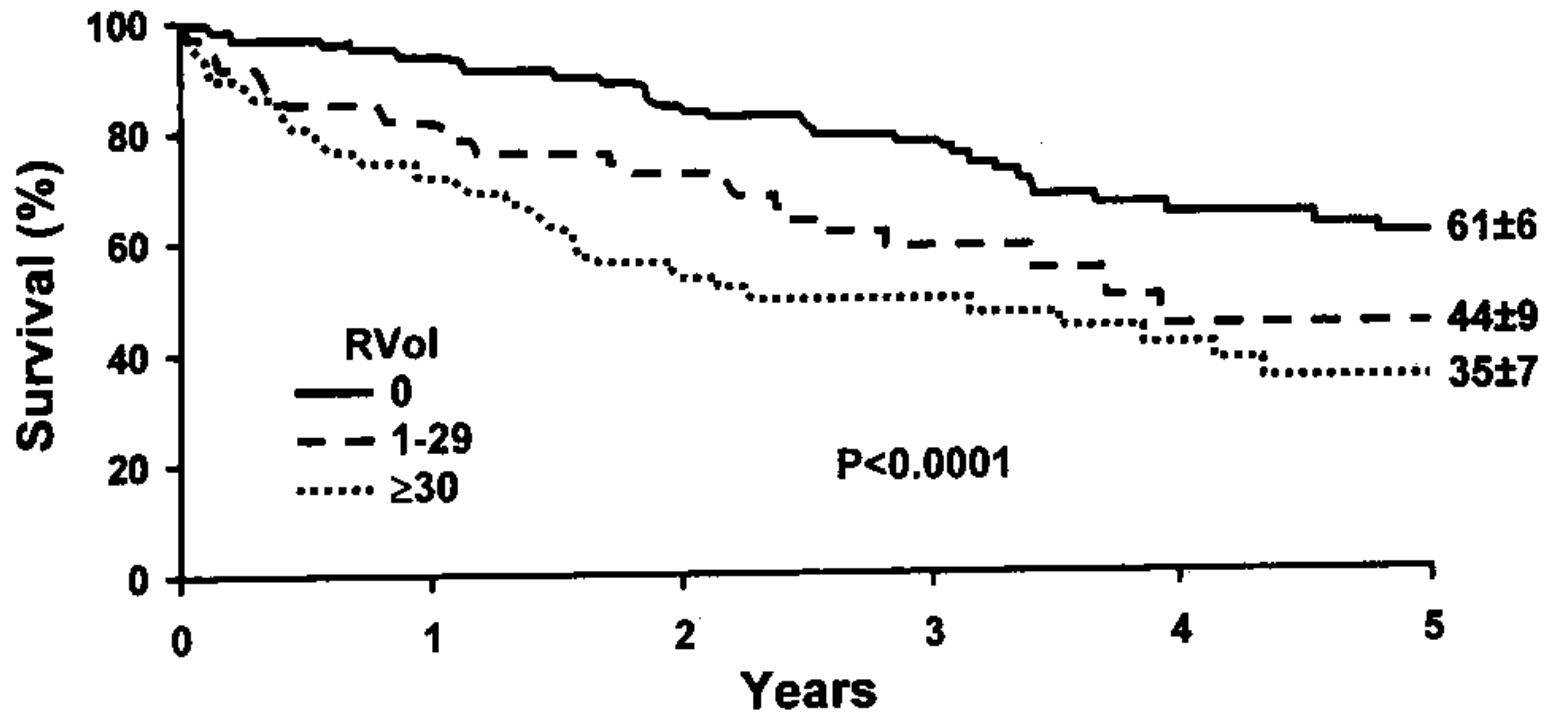
Ο υπολογισμός του δραστικού στομίου της ανεπάρκειας (ERO) με τη μέθοδο PISA, είναι η πιο χρήσιμη μέθοδος για την ποσοτική εκτίμηση της ισχαιμικής-λειτουργικής ανεπάρκειας της μιτροειδούς.

Τιμές ERO $> 20\text{mm}^2$, σημαίνουν
σημαντική ισχαιμική-λειτουργική
ανεπάρκεια μιτροειδούς και
σχετίζονται με αυξημένη
θνητότητα.



| | | | | | | |
|-------|-----|----|----|----|----|----|
| — | 109 | 94 | 77 | 60 | 35 | 30 |
| - - | 102 | 71 | 39 | 20 | 8 | 2 |
| | 63 | 33 | 19 | 10 | 6 | 1 |

Figure 3. Survival (\pm SE) after diagnosis according to degree of MR as graded by ERO ≥ 20 mm² or < 20 mm². Numbers at bottom indicate patients at risk for each interval.



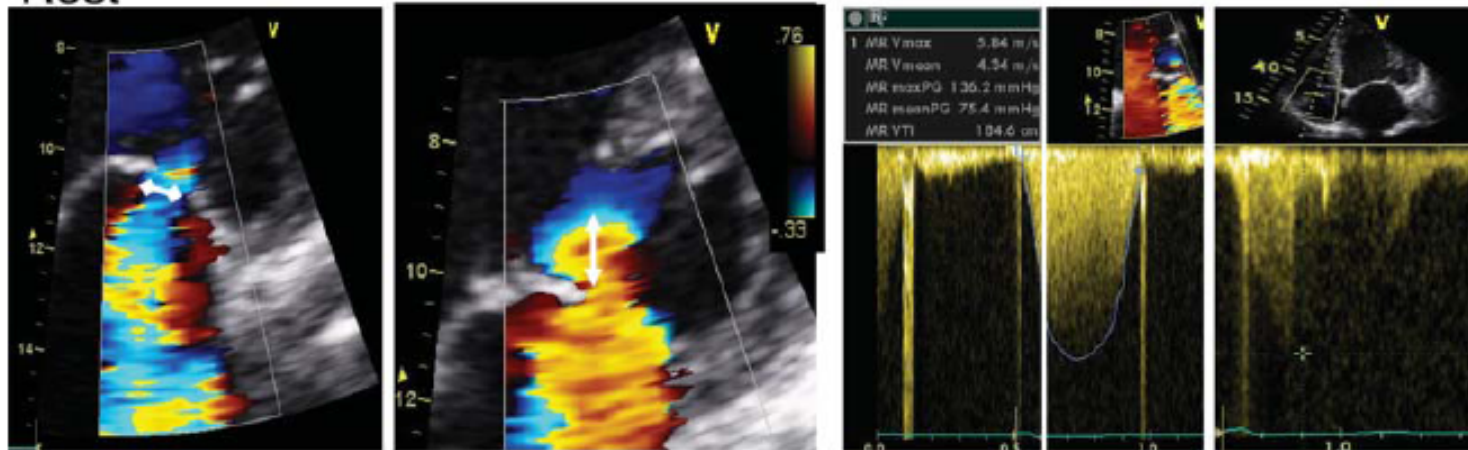
| | | | | | | |
|-------|-----|----|----|----|----|----|
| — | 109 | 94 | 77 | 60 | 35 | 30 |
| - - | 83 | 56 | 35 | 19 | 8 | 3 |
| | 111 | 69 | 39 | 23 | 14 | 5 |

Figure 2. Survival (\pm SE) after diagnosis according to degree of MR as graded by RVol ≥ 30 mL/beat or < 30 mL/beat. Numbers at bottom indicate patients at risk for each interval.

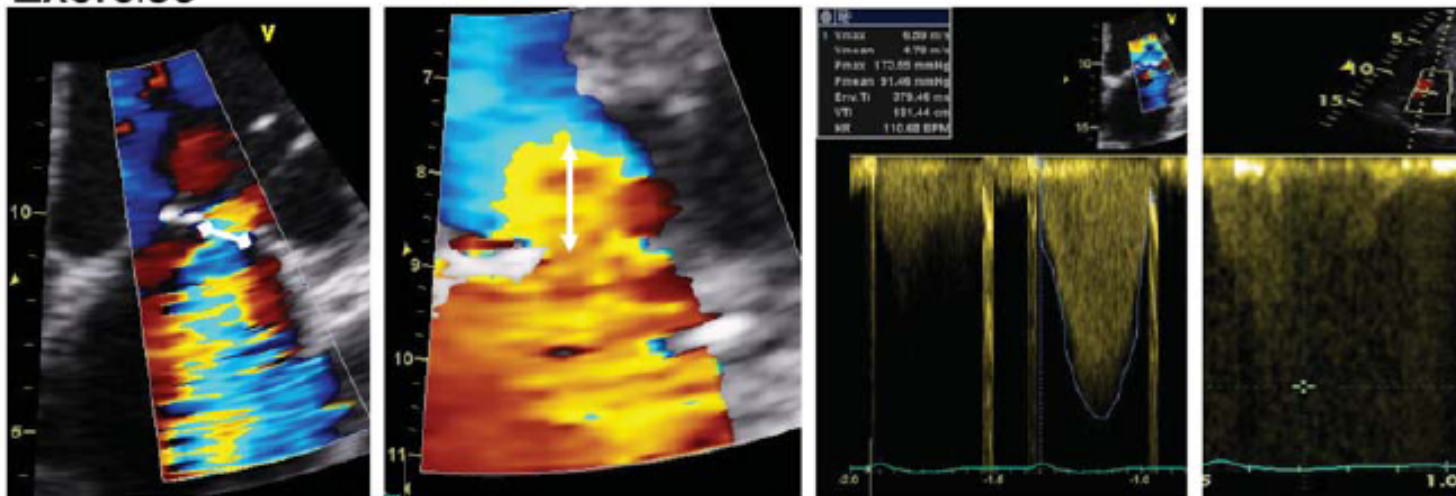
Σύμφωνα με τις μελέτες των Lancellotti και Pierard, υπάρχει δυναμικό στοιχείο στην λειτουργική-ισχαιμική ανεπάρκεια της μιτροειδούς, η οποία μπορεί να αυξάνεται σημαντικά κατά την άσκηση, χωρίς ταυτόχρονες ισχαιμικές διαταραχές της τοιχωματικής κινητικότητας.

Στους ασθενείς με λειτουργική-ισχαιμική ανεπάρκεια της μιτροειδούς βαλβίδας μπορεί να εμφανισθεί οξύ πνευμονικό οίδημα, λόγω δυναμικών μεταβολών της μιτροειδικής ανεπάρκειας, με παράλληλη αύξηση των πνευμονικών αγγειακών πιέσεων.

Rest



Exercise



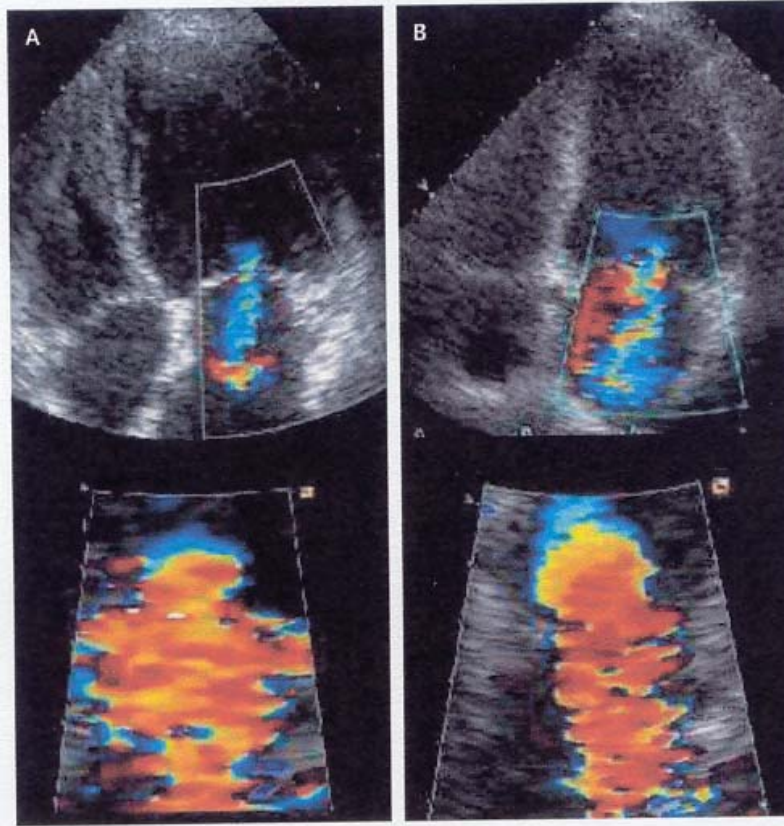


Figure 2. Mid-Systolic Apical Four-Chamber View Obtained at Rest and during Exercise in a Patient Who Presented with Acute Pulmonary Edema. Panel A shows a color-flow Doppler echocardiogram and the flow convergence proximal to the effective regurgitant orifice while the patient is at rest (effective regurgitant orifice area, 24 mm²), and Panel B while the patient is exercising (effective regurgitant orifice area, 48 mm²). The patient presented with acute pulmonary edema four days before the exercise test. A large exercise-induced increase in mitral regurgitation was observed.

Table 3. Multivariate Predictors of Recent Pulmonary Edema.*

| Variable* | Odds Ratio (95% CI) | P Value |
|------------------------------------|----------------------------|----------------|
| Effective regurgitant orifice area | 1.15 (1.05–1.25) | <0.001 |
| Transtricuspid pressure gradient | 1.13 (1.05–1.21) | 0.001 |
| Left ventricular ejection fraction | 0.86 (0.77–0.96) | 0.02 |

* The odds ratios indicate the association of recent pulmonary edema with exercise-induced changes in the variables shown. CI denotes confidence interval.

Pierard LA et al : N Engl J Med 2004;351:1627-1634.

Η αύξηση της δραστηκής επιφάνειας του στομίου της ανεπάρκειας (ERO) πάνω από 13mm^2 στην άσκηση, συσχετίζεται με αυξημένη θνητότητα, τόσο βραχυπρόθεσμα, όσο και μακροπρόθεσμα.

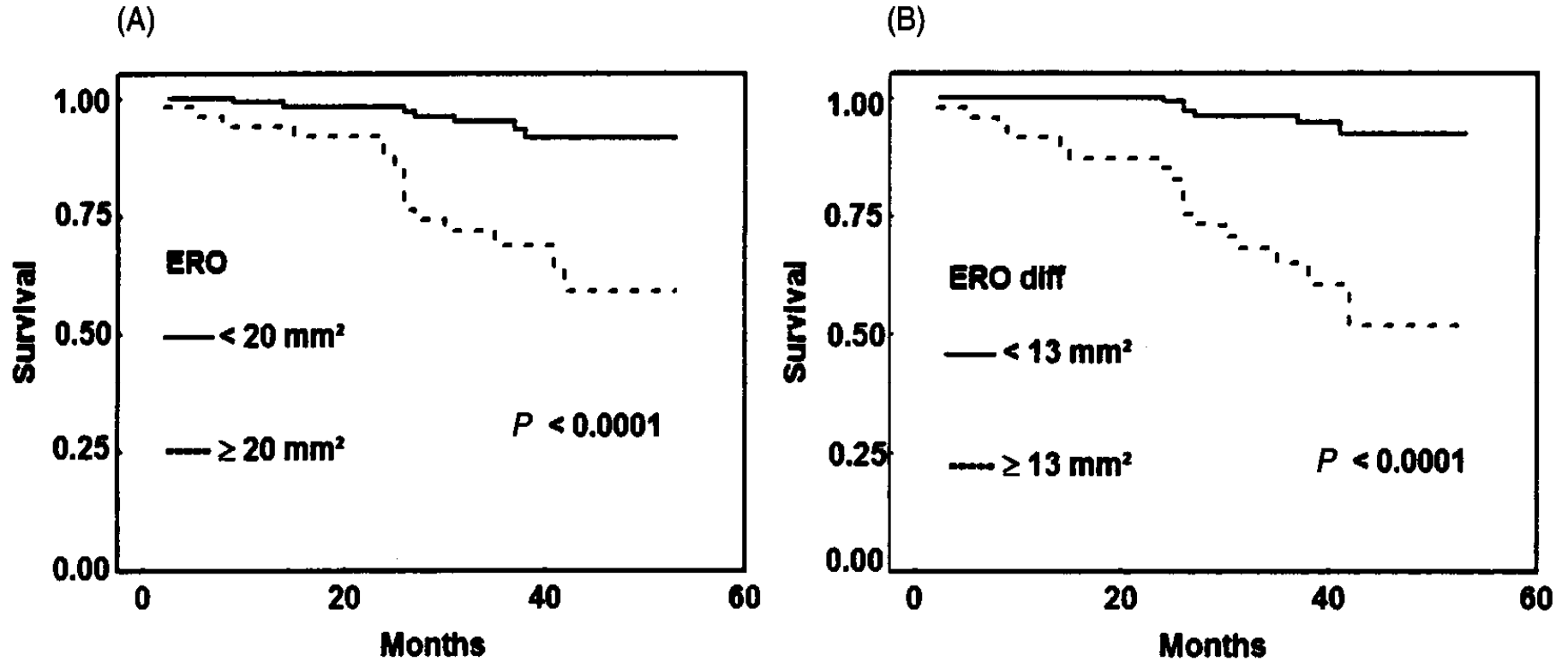


Figure 1 Survival curves according to the severity of MR. (A) at rest and (B) during exercise.

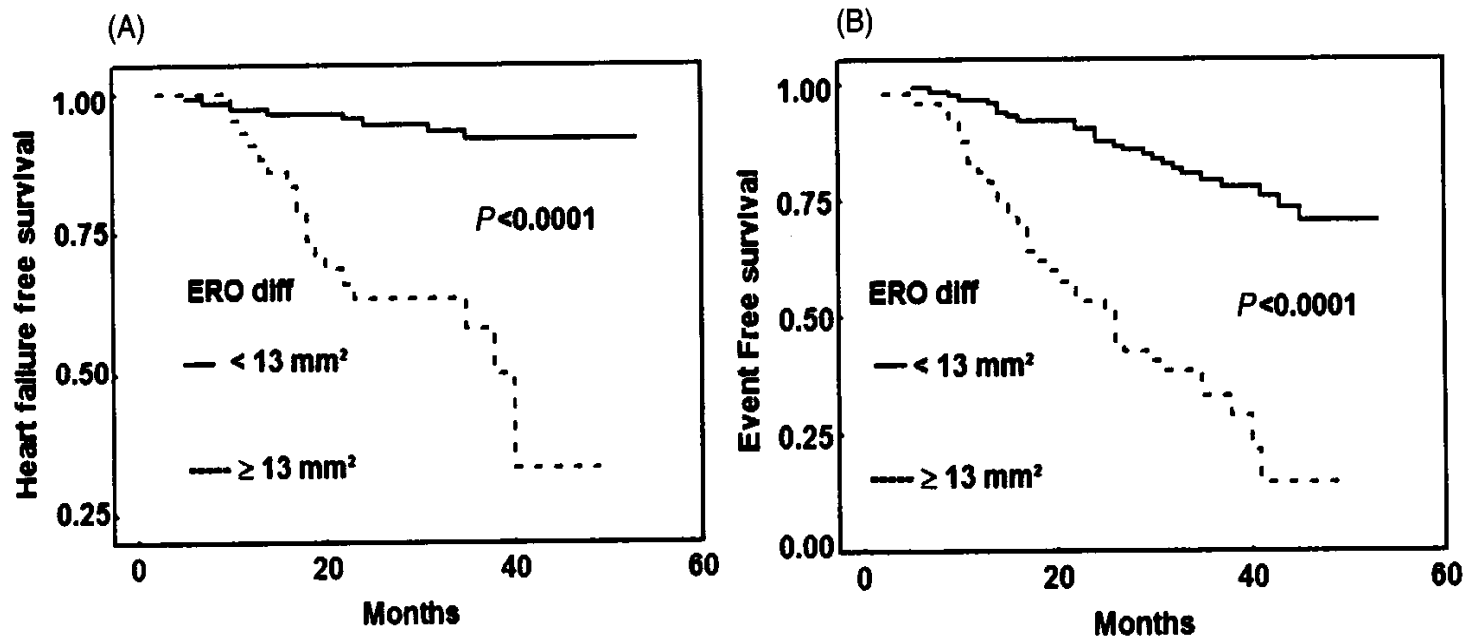


Figure 2 (A) Proportion of patients without admission for heart failure and (B) without major adverse cardiac events, according to exercise-induced differences in effective regurgitant orifice area of mitral regurgitation.

Παρεμβάσεις για την διόρθωση
της λειτουργικής – ισχαιμικής
ανεπάρκειας της μιτροειδούς
βαλβίδας.

Table 1. Effects of Various Treatments on Mitral Regurgitation in Chronic Heart Failure

| Intervention | Specific Therapy | Reverse Remodeling | Functional Improvement | Mortality Reduction | Reduction in MR |
|--|-----------------------------------|--------------------|------------------------|---------------------|-----------------|
| “Global” therapy (directed at the primary disease process) | ACE inhibitors | No | Yes | Yes | No |
| | Beta-blockers | Yes | Yes | Yes | Yes |
| “Focused” therapy (directed at the mitral valve) | | | | | |
| Percutaneous | CRT | Yes | Yes | Trend | Yes |
| Surgical | MVA | Yes | Yes | No | Yes |
| Experimental | CS annular constraint device | ? | ? | ? | Yes |
| | Cardiac passive restraint devices | Yes | ? | ? | Yes |

ACE = angiotensin-converting enzyme; CRT = cardiac resynchronization therapy; MR = mitral regurgitation; MVA = mitral valve annuloplasty.

Mehra MR et al: J Am Coll Cardiol 2005;45:388-390.

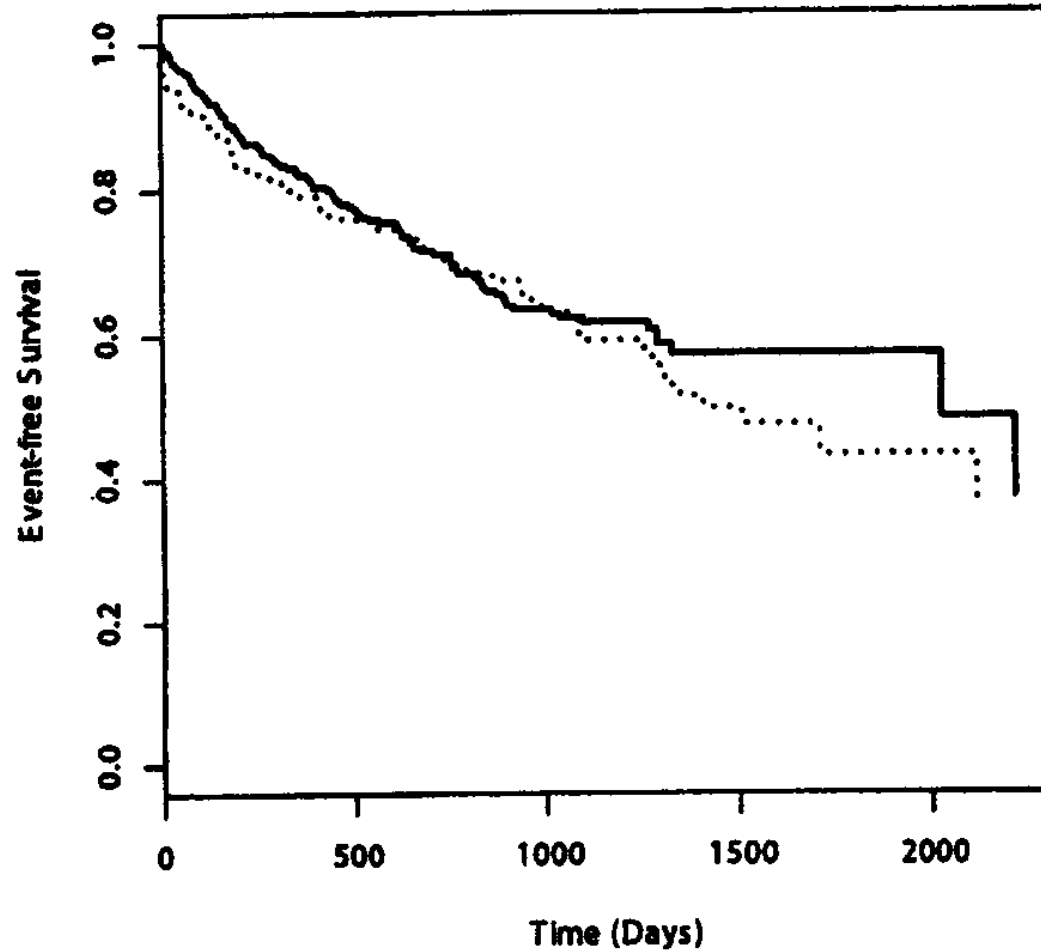


Figure 1. Event-free survival for non-mitral-valve annuloplasty (MVA) group (solid line) and MVA group (dotted line).

Wu AH et al: J Am Coll Cardiol 2005;45:381-387.

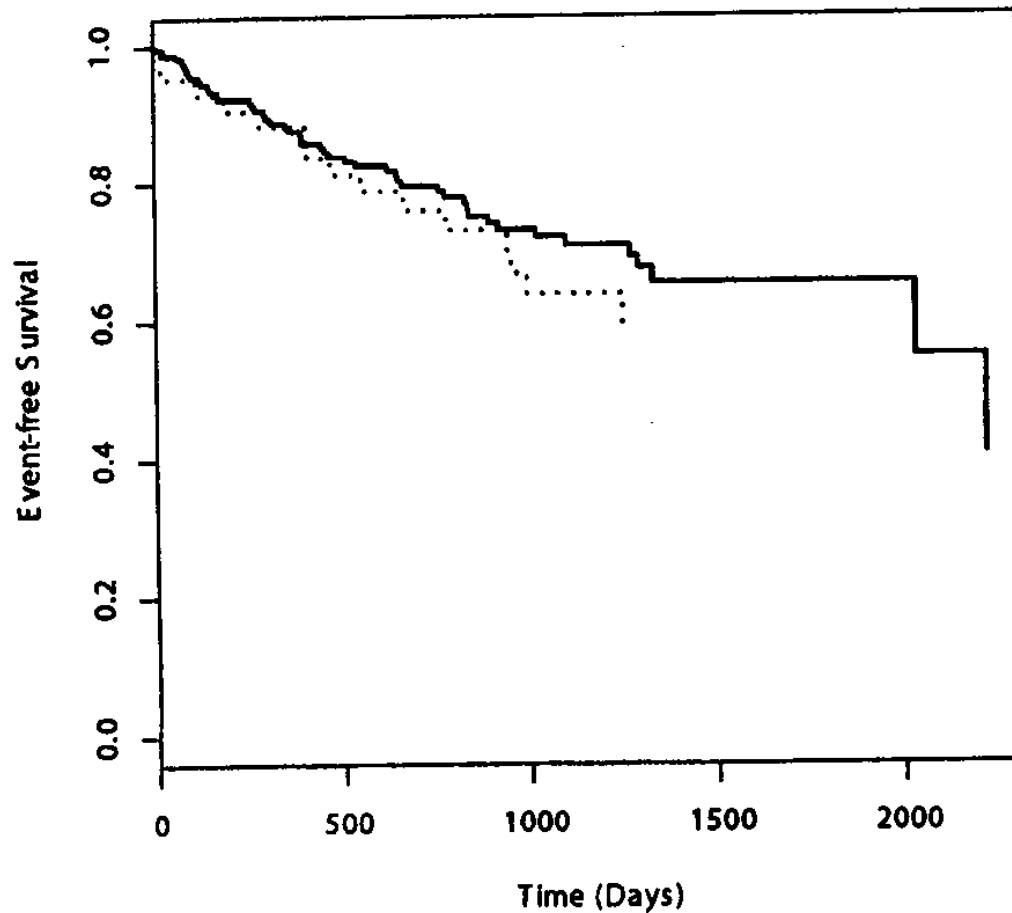


Figure 2. Event-free survival for patients without coronary artery disease in non-mitral-valve annuloplasty (MVA) group (solid line) and MVA group (dotted line).

Wu AH et al: J Am Coll Cardiol 2005;45:381-387.

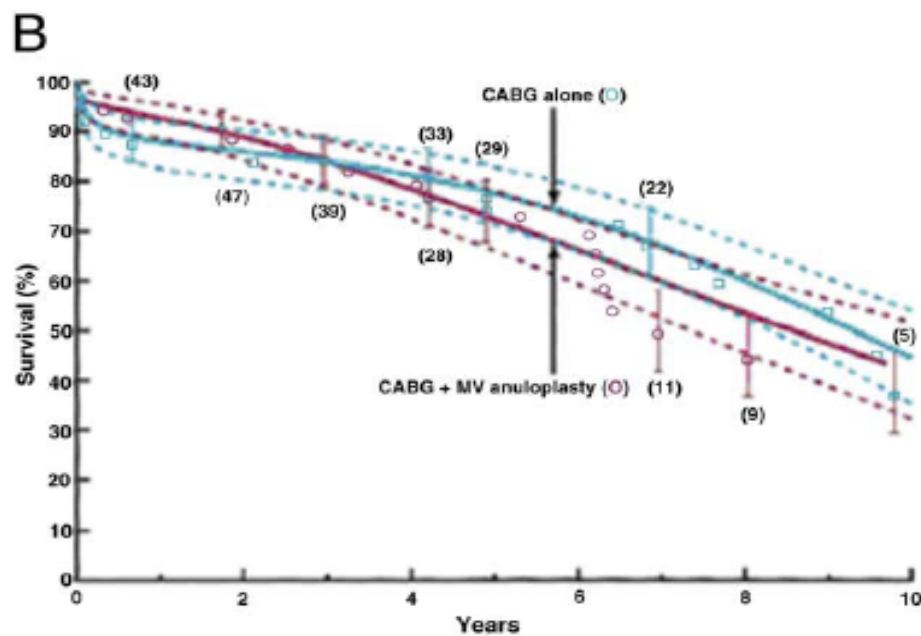
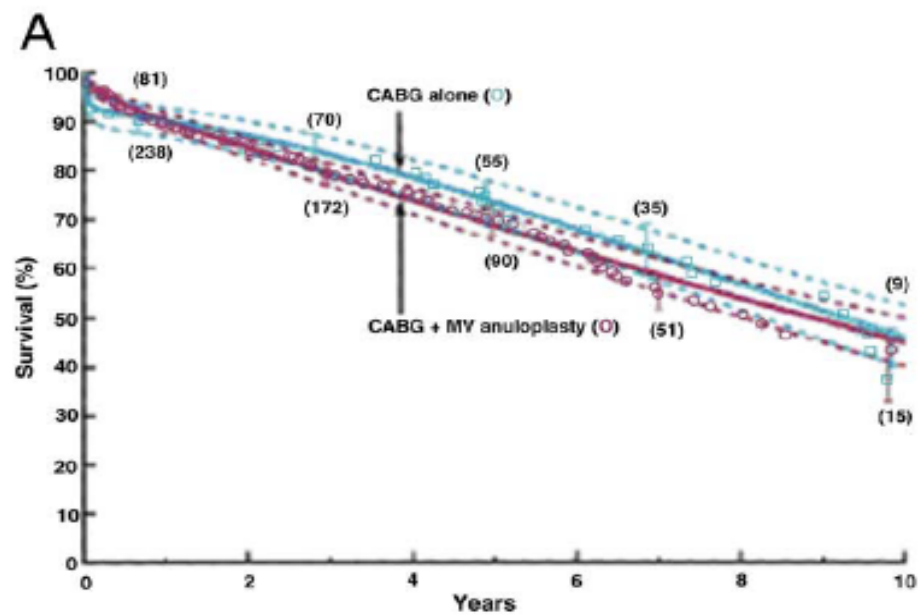


Figure 4 Survival After CABG Plus MV Annuloplasty Versus CABG Alone

J Am Coll Cardiol 2007;49:2191-2201.

Λόγω της πολύπλοκης ανατομικής ανωμαλίας στην ισχαιμική-λειτουργική ανεπάρκεια της μιτροειδούς, φαίνεται ότι η βαλβιδοπλαστική με τοποθέτηση δακτυλίου δεν είναι η κατάλληλη θεραπεία, καθότι στο 30% των ασθενών επανεμφανίζεται ανεπάρκεια μιτροειδούς μέχρι 3⁺- 4⁺.

Η θεραπεία του καρδιακού επανασυχρονισμού ελαττώνει την ισχαιμική-λειτουργική ανεπάρκεια της μιτροειδούς, κυρίως μέσω της αύξησης της δύναμης για την σύγκλιση των γλωχίνων.

Improved Papillary Muscle Function Attenuates Functional Mitral Regurgitation in Patients with Dilated Cardiomyopathy After Cardiac Resynchronization Therapy

Haralambos I. Karvounis, MD, Emmanuela G. Dalamaga, MD, Christodoulos E. Papadopoulos, MD, Theodore D. Karamitsos, MD, Vassilios Vassilikos, MD, Stelios Paraskevaïdis, MD, Ioannis H. Styliadis, MD, Georgios E. Parharidis, MD, and Georgios E. Louridas, MD, *Thessaloniki, Greece*

Background: Functional mitral valve regurgitation attenuation after cardiac resynchronization therapy (CRT) in patients with severe heart failure has been attributed to both the increased rate of left ventricular systolic pressure increase and to papillary muscle (PM) re-coordinated contraction. We hypothesized that an increase in systolic deformation of the PMs or the adjacent myocardial wall may in part account for this effect, by preventing their outward displacement during systole.

Methods: We studied by echocardiography 22 patients with moderate/severe functional mitral valve regurgitation and a mean ejection fraction of $18 \pm 4\%$ at baseline and after implantation of a CRT system.

Results: CRT induced a significant reduction of the effective regurgitant orifice area (0.18 ± 0.11 vs 0.35 ± 0.17 mm², $P < .001$). Strain improved in both PMs and their adjacent walls, although this improvement was significant only in anterolateral PM (-16 ± 4.7 vs $-11 \pm 4.3\%$, $P = .02$) and posteromedial PM adjacent wall (-16 ± 10 vs $-8 \pm 4.6\%$, $P = .01$).

Conclusions: CRT acutely reduces the severity of functional mitral valve regurgitation in patients with heart failure and this effect may be in part attributed to improved strain of PM or adjacent wall. (J Am Soc Echocardiogr 2006;19:1150-1157.)

Table 2 Effects of cardiac resynchronization therapy on echocardiographic variables

| | Baseline | CRT | P value |
|---------------------------------------|-------------|-------------|---------|
| LVEF, % | 18 ± 4 | 26 ± 4 | <.001 |
| LVESV, mL | 238 ± 97 | 209 ± 82 | .024 |
| LVEDV, mL | 293 ± 111 | 286 ± 114 | NS |
| Sphericity index | 1.33 ± 0.12 | 1.46 ± 0.14 | .001 |
| EROA, mm ² | 0.35 ± 0.17 | 0.18 ± 0.11 | <.001 |
| Reg Vol, mL | 35 ± 15 | 26 ± 12 | .005 |
| MVR duration, ms | 407 ± 76 | 393 ± 47 | .005 |
| Max transmitral PG, mm Hg | 91 ± 34 | 107 ± 34 | .004 |
| LV +dP/dt _{max} , mm Hg/s | 606 ± 284 | 837 ± 199 | .012 |
| RVSP, mm Hg | 49 ± 18 | 43 ± 15 | .034 |
| HR, beats/min | 75 ± 15 | 79 ± 12 | NS |
| ε _{max} basal, % | -19 ± 8 | -24 ± 11 | .039 |
| ε _{max} mid, % | -17 ± 7 | -14 ± 5 | NS |

CRT, Cardiac resynchronization therapy; EROA, effective regurgitant orifice area; HR, heart rate; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LV +dP/dt_{max}, maximal rate of left ventricular systolic pressure increase; Max transmitral PG, maximal transmitral valve pressure gradient; MVR, mitral valve regurgitation; NS, not significant; Reg Vol, regurgitant volume; RVSP, peak systolic right ventricular pressure; ε_{max} basal, mean peak negative strain of the basal segments; ε_{max} mid, mean peak negative strain of the mid segment.

Table 3 Effects of cardiac resynchronization therapy on mitral valve apparatus deformation

| | Baseline | CRT | <i>P</i> value |
|--|-------------|-------------|----------------|
| MA diameter, cm | 3.1 ± 0.49 | 3.1 ± 0.36 | NS |
| MV tenting area, cm ² | 4 ± 1.23 | 2.7 ± 0.97 | <.001 |
| MV coaptation height, cm | 1.55 ± 0.31 | 1.27 ± 0.32 | .02 |
| ϵ_{\max} Anterolateral PM, % | -11 ± 4.3 | -16 ± 4.7 | .02 |
| ϵ_{\max} Posteromedial PM, % | -13 ± 5.2 | -15 ± 7.1 | NS |
| ϵ_{\max} Midlateral, % | -12 ± 7.5 | -14 ± 6.9 | NS |
| ϵ_{\max} Midinferior, % | -8 ± 4.6 | -16 ± 10 | .01 |
| Δt - ϵ_{\max} PM, ms | 132 ± 116 | 106 ± 83 | NS |
| t - ϵ_{\max} Anterolateral PM, ms | 442 ± 109 | 430 ± 102 | NS |
| t - ϵ_{\max} Posteromedial PM, ms | 362 ± 151 | 378 ± 99 | NS |

MA, Mitral annulus; *MV*, mitral valve; *NS*, not significant; *PM*, papillary muscle; ϵ_{\max} , peak negative strain; t - ϵ_{\max} , time to peak negative strain; Δt - ϵ_{\max} *PM*, interpapillary muscle time delay to peak negative strain.

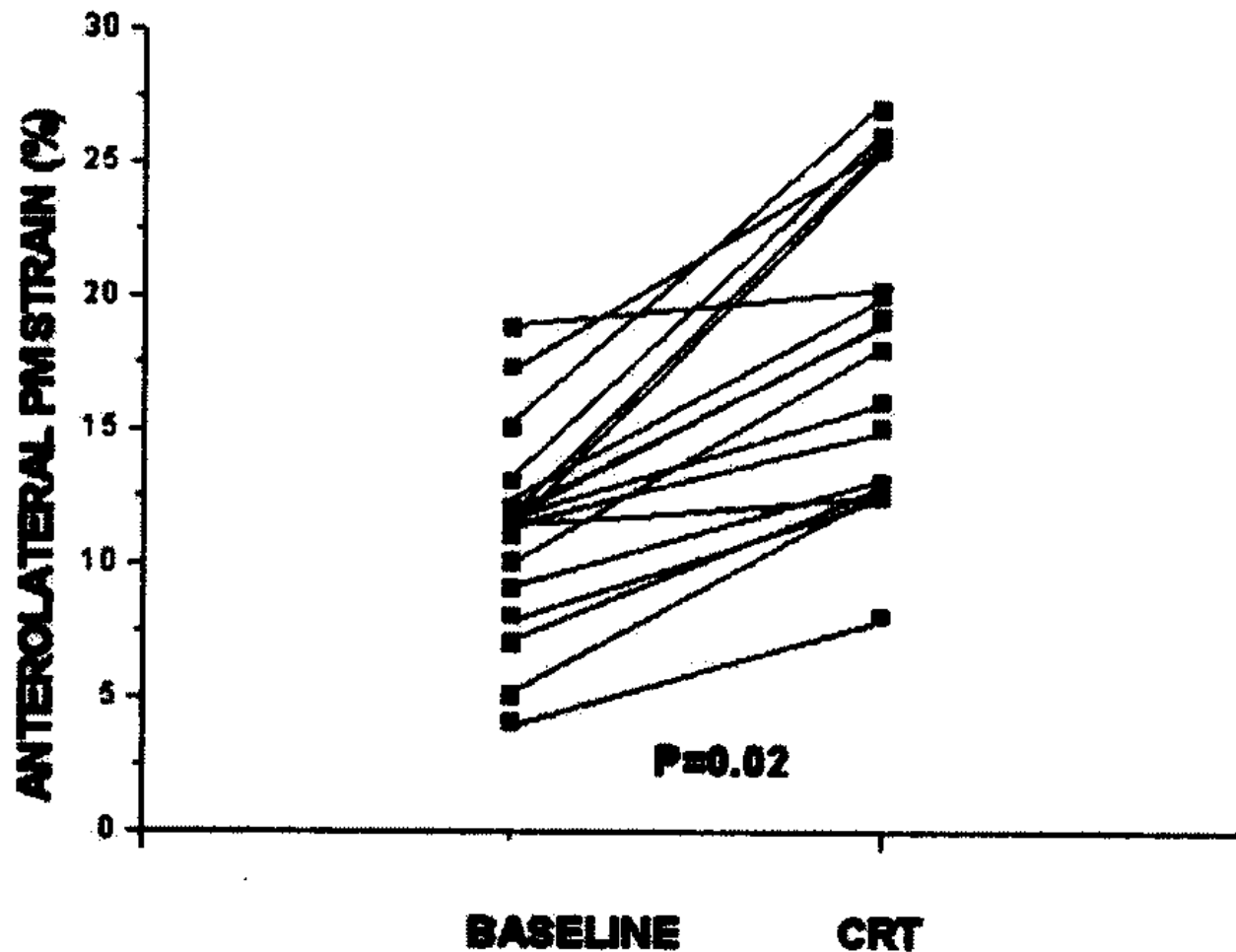


Figure 1 Anterolateral papillary muscle (*PM*) peak negative strain at baseline and after cardiac resynchronization therapy (*CRT*) initiation.

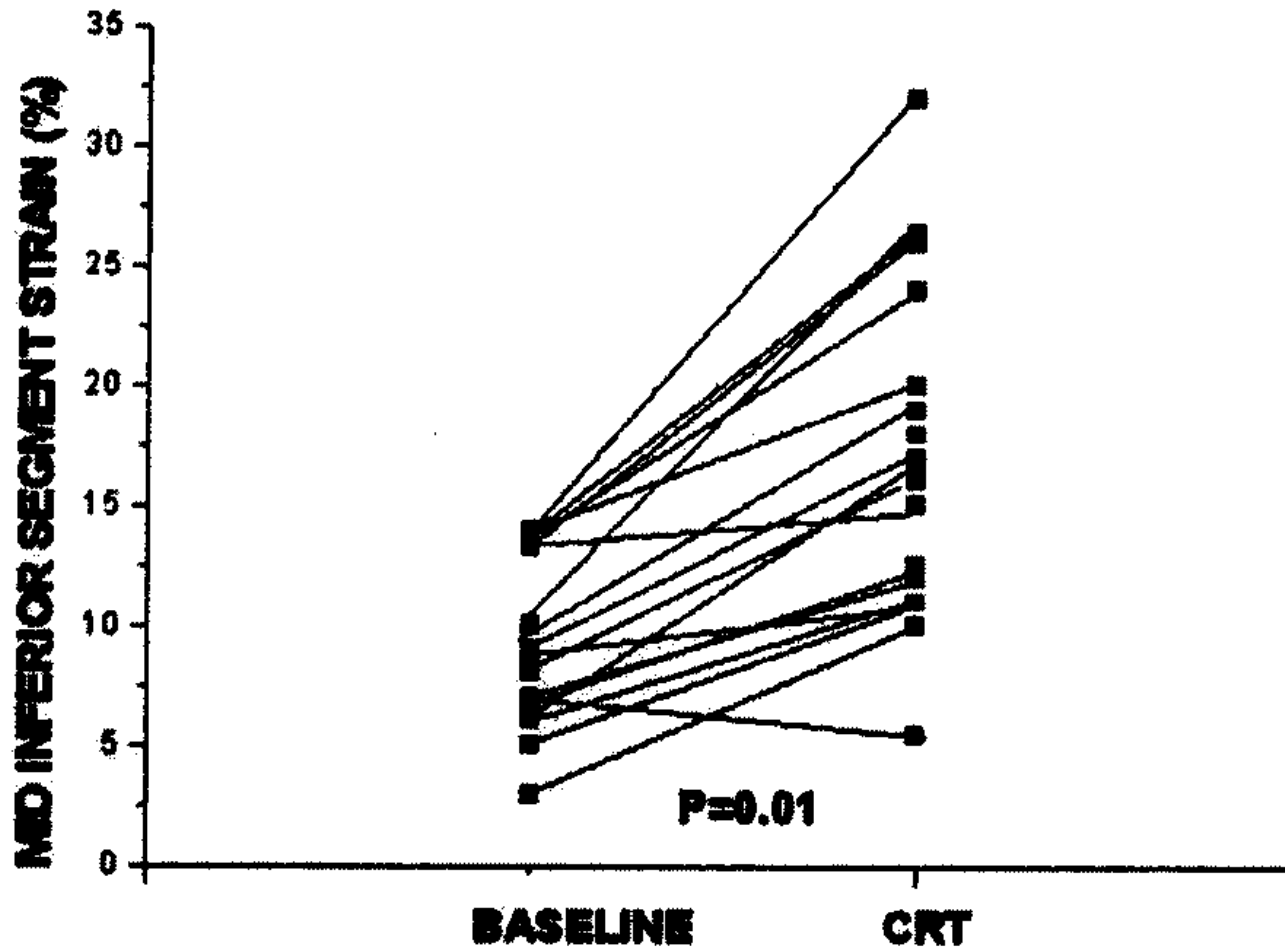


Table 3**Abbreviated Criteria for Selection of Appropriate Operative Candidates****Favorable surgical considerations**

- Coronary artery disease and concurrent revascularization
- Ventricular reconstruction (e.g., Dor)
- Reversible pulmonary hypertension
- No prior operations

Favorable medical considerations

- NSR (or likelihood of restoration)
- “Tolerance” of reasonable doses of vasodilators and beta-blockers
- Preservation of renal function
- Absence of hyponatremia
- Absence of refractory right heart failure
- Absence of cachexia

Favorable LV reverse remodeling viability

- Absence of severe ventricular dilation (LVEDD >80 mm)
- Lower sphericity index
- Preservation of LV torsion
- Presence of contractile reserve
- Beneficial response to cardiac resynchronization

LV = left ventricle; LVEDD = left ventricular end-diastolic diameter; NSR = normal sinus rhythm.

Table 5**Current and Evolving Options for Mitral Valve Surgery in Advanced Heart Failure****1. Mitral repair**

Annulus (annuloplasty)

Ring (rigid, flexible; undersized)

Asymmetrical

Percutaneous techniques

Leaflets

Edge-to-edge leaflet (Alfieri)

Leaflet lengthening

Chordae

Basal chordae resection

Papillary muscle

Scar excision with papillary muscle "reimplantation"

Internal slings

Surgical "buckles"

External bands

Mesh patches

Ventricular "reshaping" (with annuloplasty)

Infarct plication

Infarct excision and patching (e.g., Dor)

Localized infarct patch with epicardial balloon

External restraint (e.g., Acorn CorCap)

2. Mitral replacement with chordal sparing

J Am Coll Cardiol
2010;55:271-282.

Table 4 Suggested Approach to the Management of Severe MR in Advanced Heart Failure

1. Optimize medical therapy

Angiotensin-converting enzyme inhibitor/angiotensin receptor-blocker, beta-blockers, aldosterone antagonists, flexible sliding-scale diuretic program, hydralazine-isosorbide dinitrate

Define adequacy of medical therapy by cardiac catheterization in selected instances

Ensure compliance with medical therapy and lifestyle accommodations

2. Evaluate for revascularization in patients with coronary artery disease

3. Provide CRT

Indications: LV ejection fraction <35%, QRS interval >120 ms, New York Heart Association functional class III to IV

Reassess clinical response and MR severity

4. Reconfirm the severity of MR

“Definitive” imaging modality after optimizing medical therapy, revascularization, and CRT with cardiac magnetic resonance imaging or echocardiography

5. For patients who remain intolerably symptomatic, define perioperative risk and surgical options

Ideally, perioperative risk should be $\leq 2\%$ on the basis of composite medical and surgical factors

Ideal candidates will have heart failure duration <5 years, resting heart rate <100 beats/min, systolic blood pressure >80 mm Hg with normal proportional pulse pressure, serum sodium >135 mmol/dl, blood urea nitrogen >100 mg/dl, creatinine >2.5 mg/dl, normal total bilirubin, LV end-diastolic diameter <80 mm, peak $\text{VO}_2 >14 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, 6-min walk test >350 m, no cachexia, no prior cardiac surgery, reversible pulmonary hypertension, no refractory right heart failure

6. Estimate LV reverse remodeling viability on the basis of aggregate clinical data

7. Discuss mitral valve surgery frankly with the patient and family

Issues to discuss: 1) perioperative risk; 2) durability of planned correction; and 3) clinical outcomes on the basis of available data: functional capacity, long-term LV remodeling and function, and mortality.

CRT = cardiac resynchronization therapy; LV = left ventricular; MR = mitral regurgitation.

Παρά τις μεγάλες προόδους που έχουν γίνει τόσο στην διάγνωση, όσο και στην κατανόηση των μηχανισμών που προκαλούν την ισχαιμική-λειτουργική ανεπάρκεια της μιτροειδούς, πολλά φαίνεται ότι πρέπει να γίνουν ακόμα για την θεραπευτική αντιμετώπιση αυτής της πάθησης.