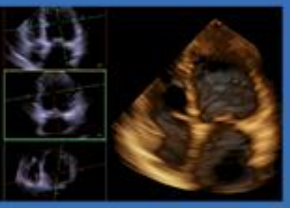


EuroValve

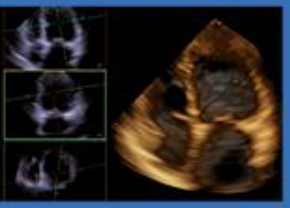
April 26-27, 2018

Secondary MR joint with the mitral academy

What is new in our understanding of this disease?

Luc Pierard

University Hospital, Liège



EuroValve
April 26-27, 2018

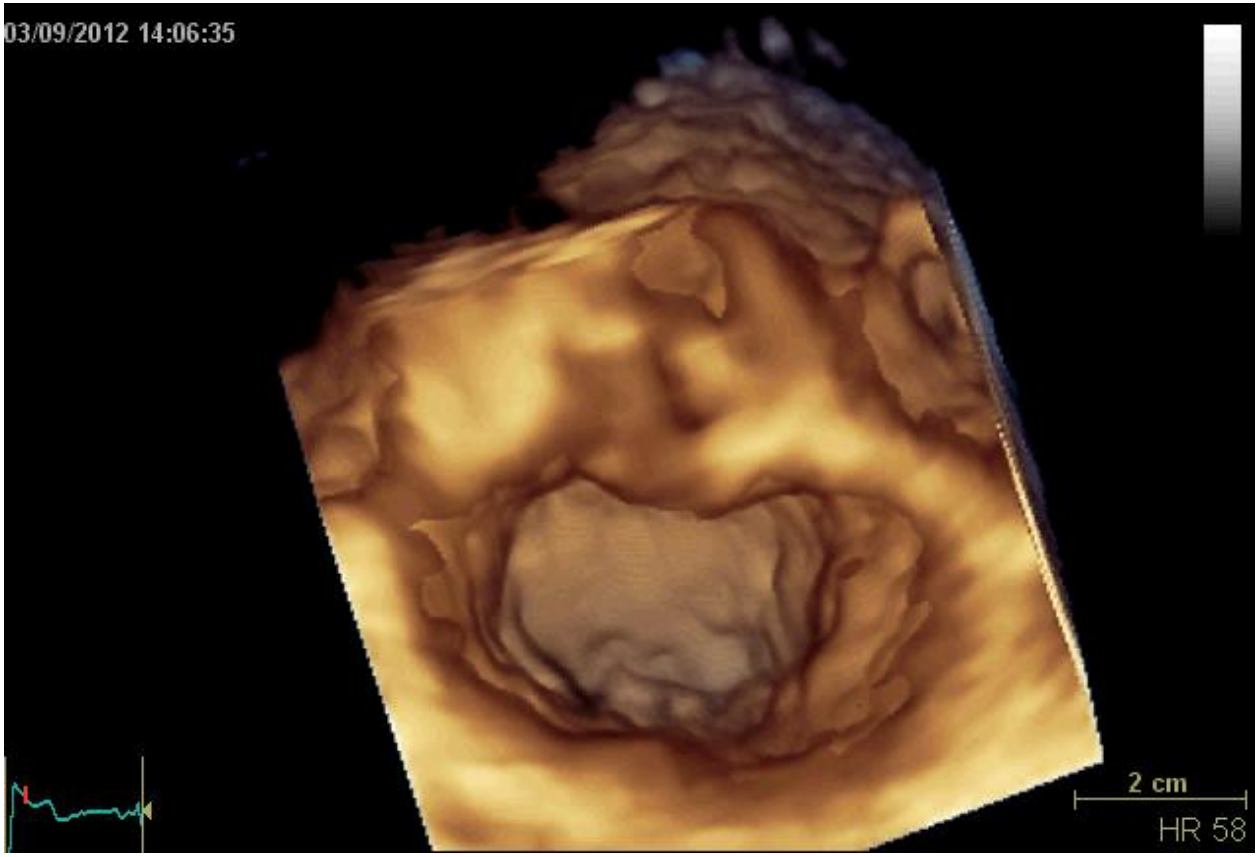
Faculty disclosure

Luc Pierard

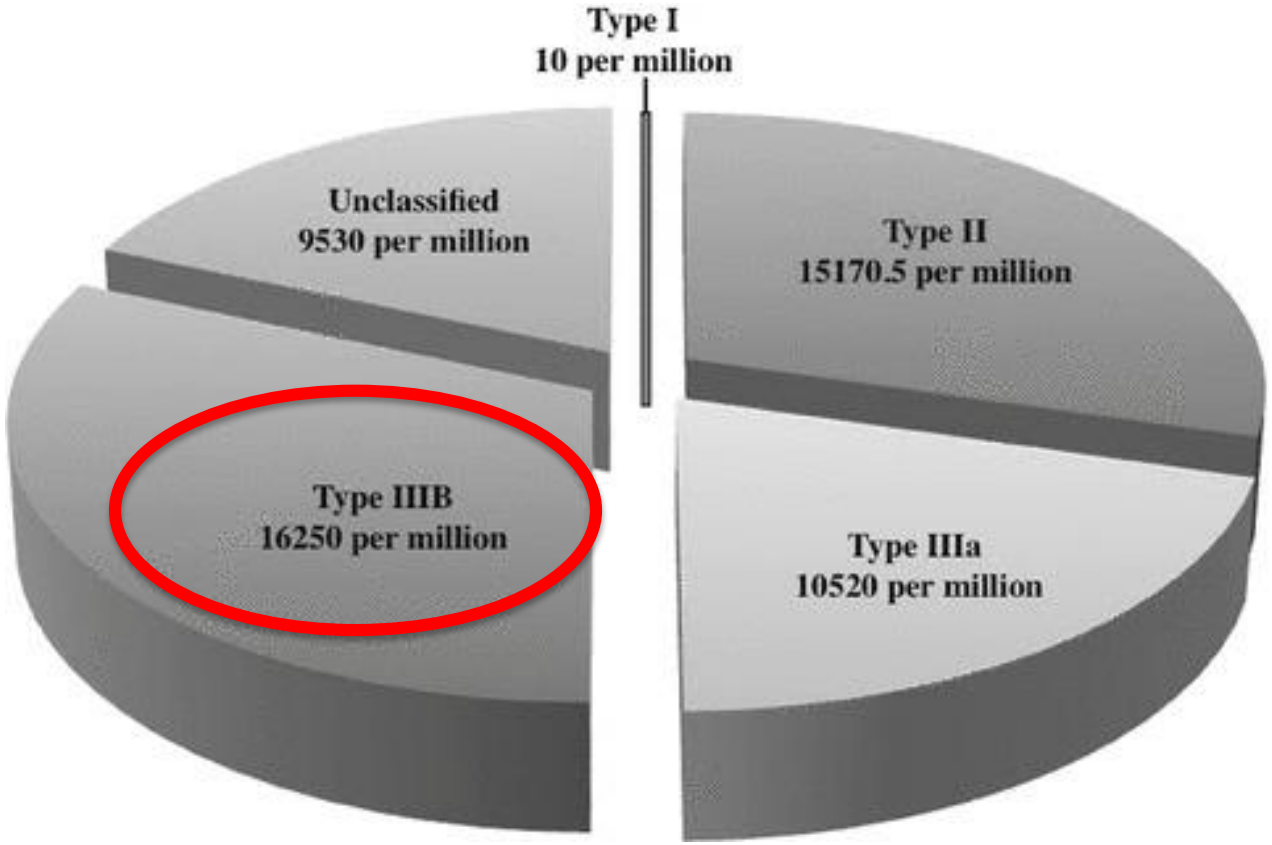
I have **no financial relationships** to disclose.

www.eurovalvecongress.com

Secondary mitral regurgitation

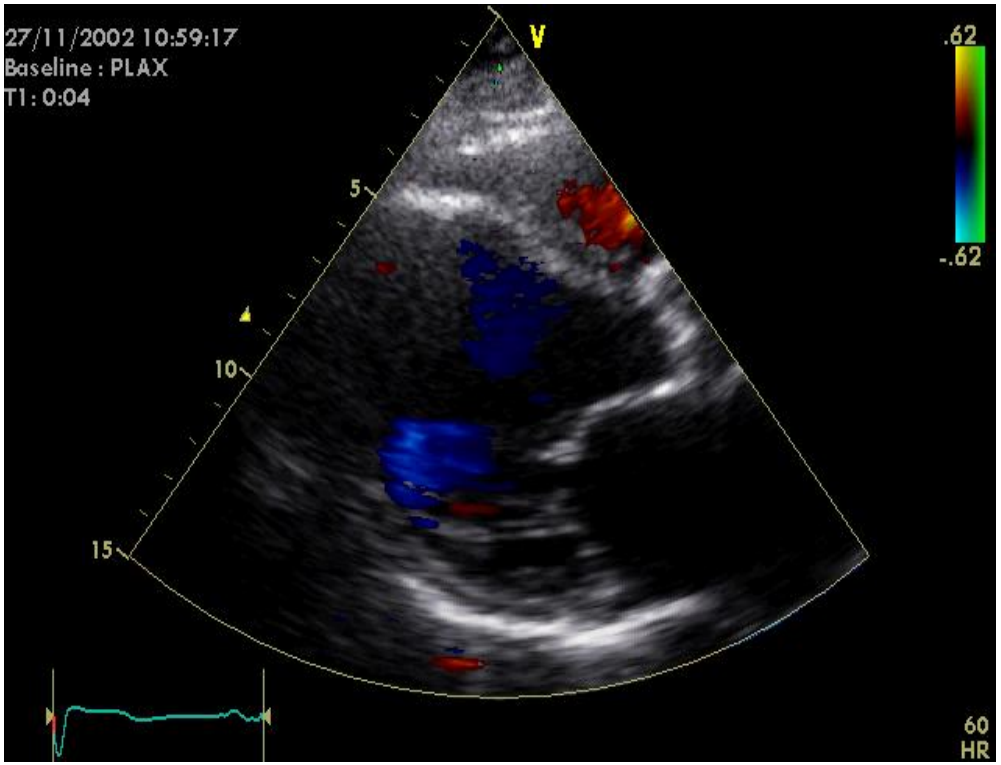


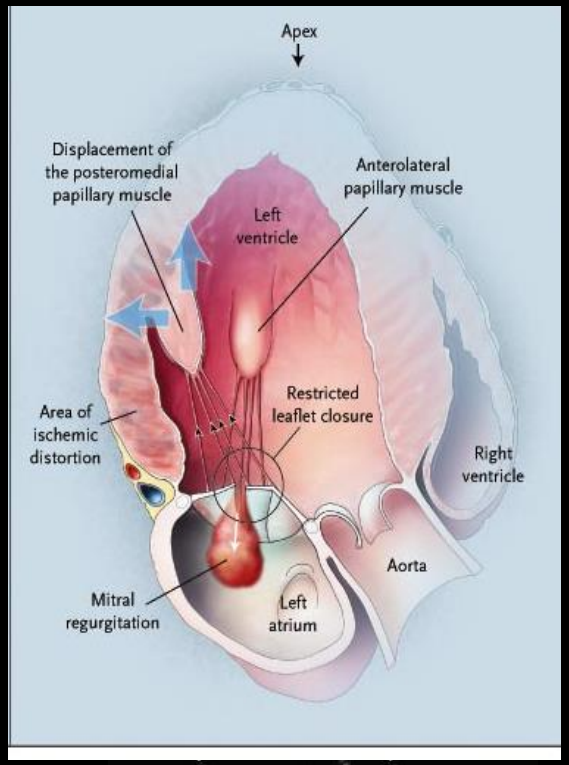
Prevalence of MR according to the Carpentier's functional class

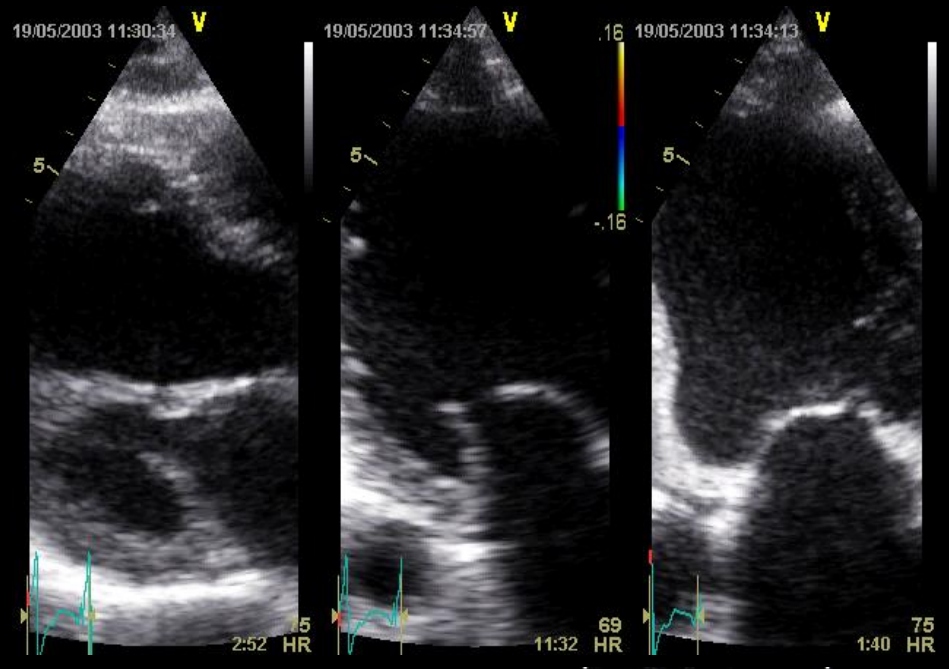


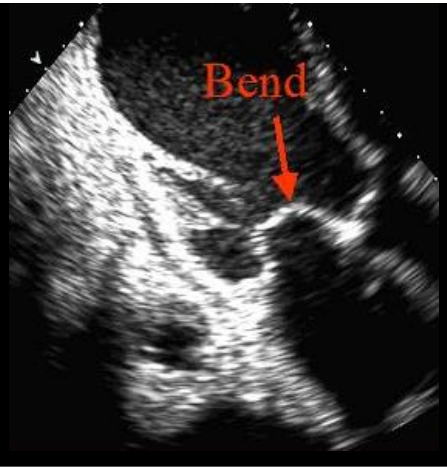
Marchena J Card Surg 2011, 26:385-92

Secondary MR: global LV remodeling and dysfunction

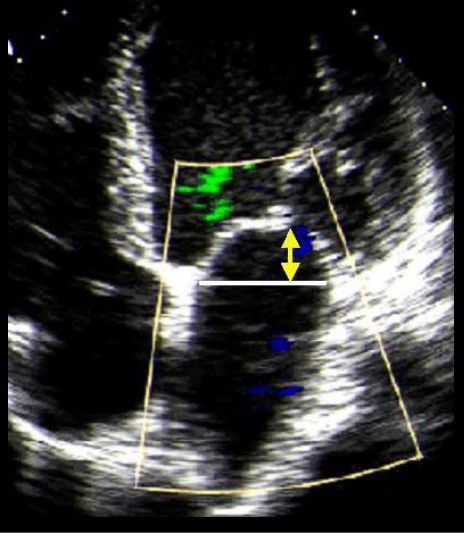



Apex
Displacement of the posteromedial papillary muscle
Anterolateral papillary muscle
Left ventricle
Area of ischemic distortion
Restricted leaflet closure
Right ventricle
Aorta
Mitral regurgitation
Left atrium


19/05/2003 11:30:34
19/05/2003 11:34:57
19/05/2003 11:34:13
.16
-.16
5
2:52 HR
11:32 HR
1:40 HR

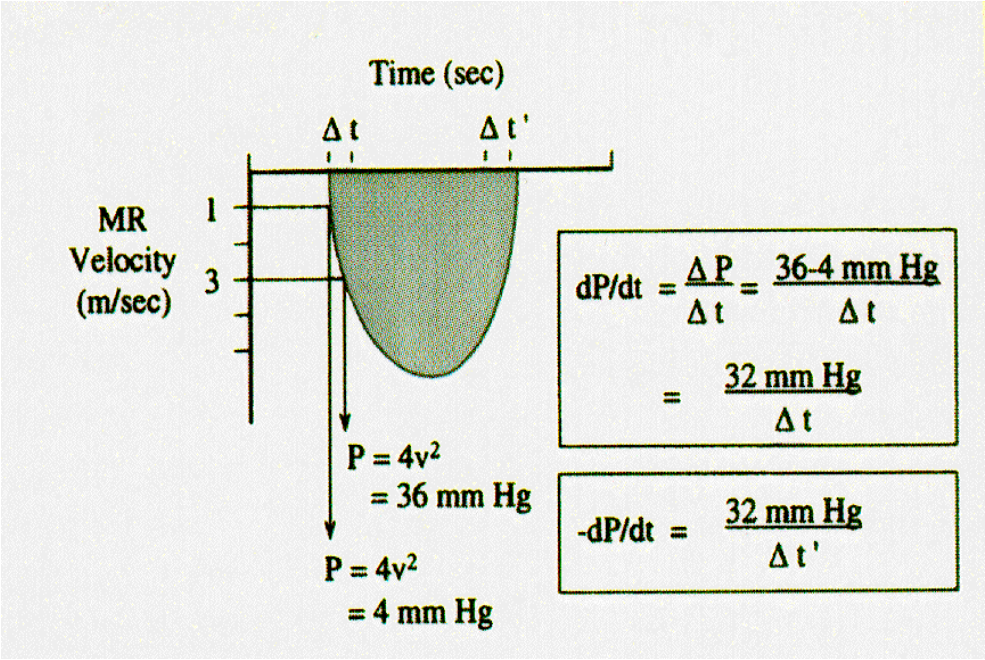

Bend


LV
Ao
LA
T

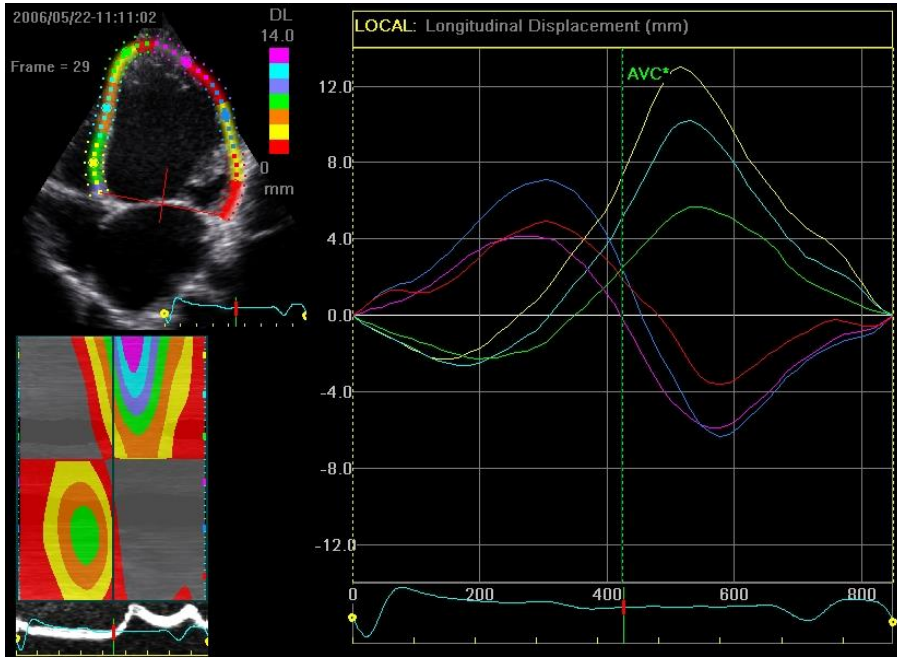


Reduced closing force

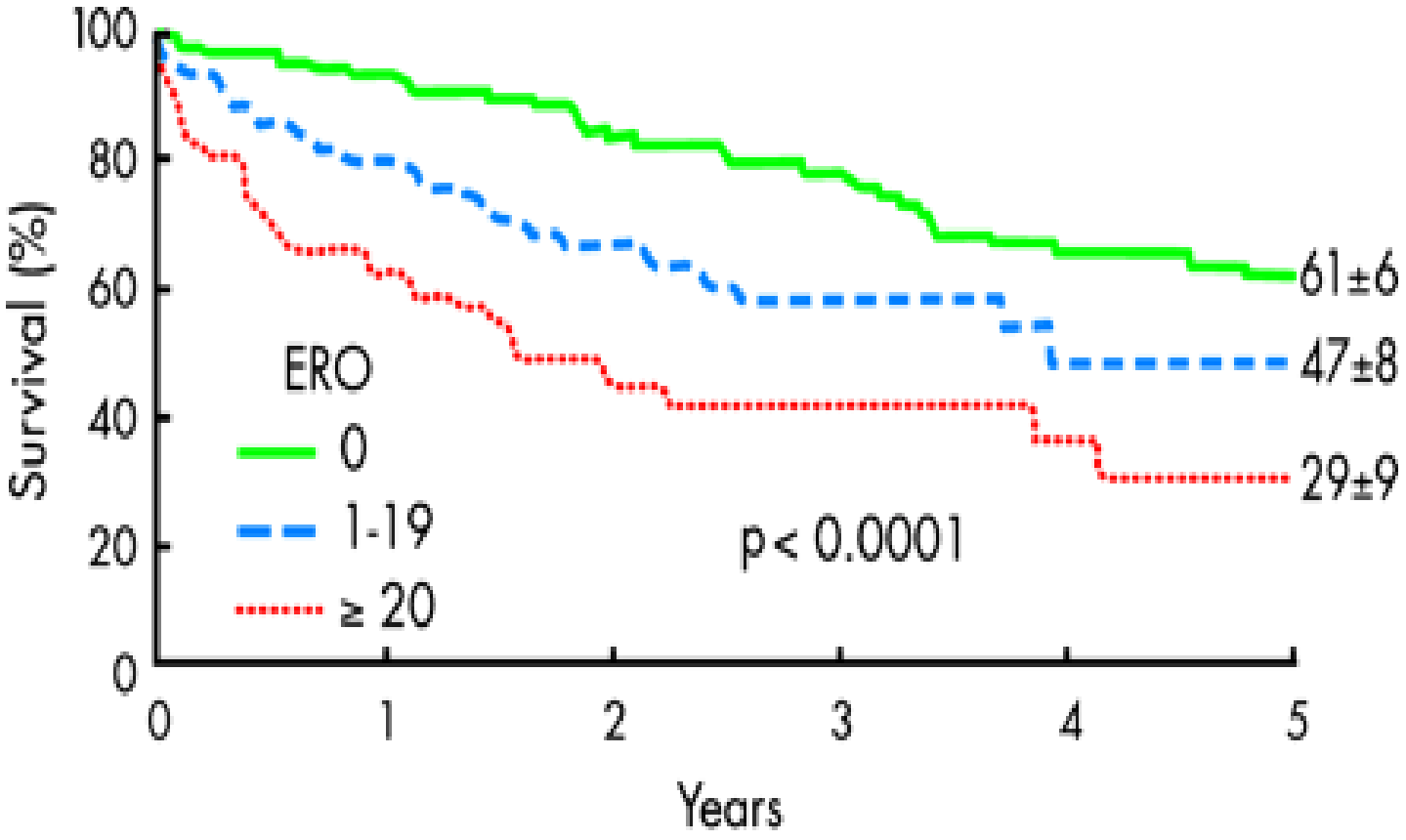
Reduced contractility



LV dyssynchrony



Prognosis of ischaemic MR

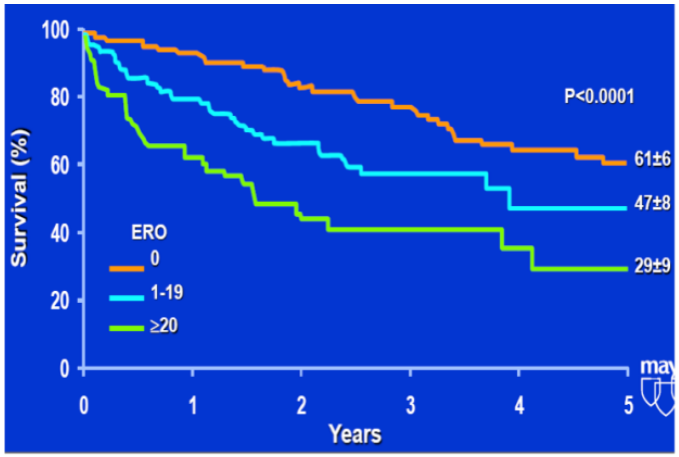


Grigioni et al Circulation 2001; 103:1759-64

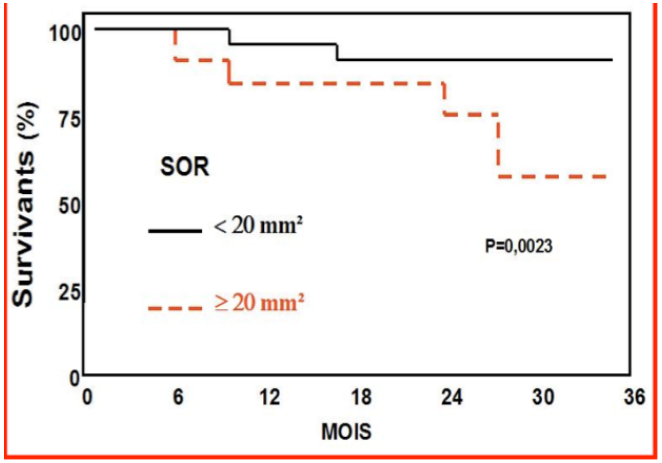
Parameters	Severe
Quantitative	
EROA (mm²)	≥20 **for secondary**
R Vol (ml)	≥ 30 for **secondary**

ACC/AHA New **≥ 40 mm²**

≥ 60 mL



Grigioni, Sarano Circulation 2001 103



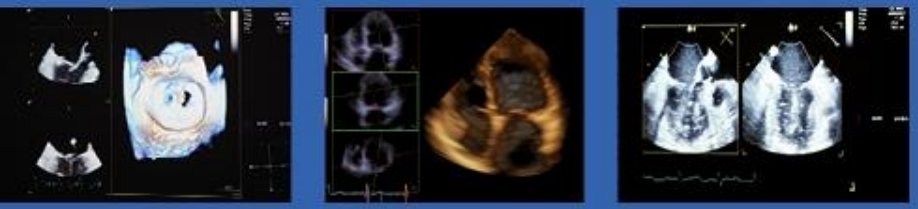
Lancellotti, Pierard Circulation 2003 108

Indications for mitral valve intervention in chronic secondary mitral regurgitation

Recommendations	Class	Level
Surgery is indicated in patients with severe secondary mitral regurgitation **undergoing CABG** and LVEF >30%.	I	C
Surgery should be considered in symptomatic patients with severe secondary mitral regurgitation, LVEF <30% but with **an option for revascularization, and evidence of myocardial viability**.	IIa	C
When **revascularization is not indicated**, surgery may be considered in patients with severe secondary mitral regurgitation and LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have a low surgical risk.	IIb	C

www.escardio.org/guidelines

2017 ESC/EACTS Guidelines for the Management of Valvular Heart Disease
(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx391)
)



EuroValve
April 26-27, 2018

The NEW ENGLAND JOURNAL of MEDICINE

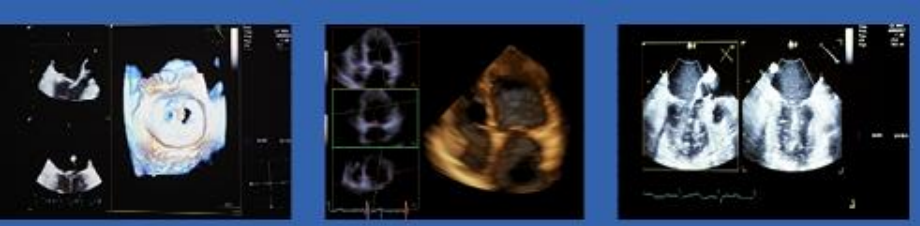
ORIGINAL ARTICLE

Surgical Treatment of Moderat
Mitral Regurgitation

P.K. Smith, J.D. Puskas, D.D. Ascheim, P. Voisine, A.C. Ge
J.W. Hung, M.K. Parides, G. Ailawadi, L.P. Perrault, M.A.
V. Thourani, J.S. Gammie, M.A. Miller, P. Pagé, J.R. Overbey,
E.H. Blackstone, I.L. Kron, D.J., E.A. Rose, E.G. Moquete, N
P.T. O'Gara, J.H. Alexander, and R.E. Michler, for the Car
Trials Network Investigators*

- ❑ No measurements of MV deformation
- ❑ No info on viability
- ❑ High recurrence rate 11% vs. 0-4% in other studies
- ❑ No exercise echo info at follow-up
- ❑ Only ring annuloplasty, no individualized treatment

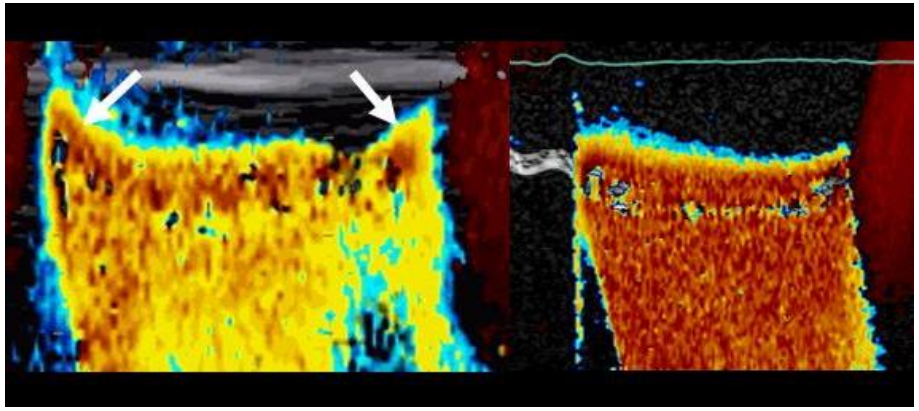
RCT, n =301 pts, moderate SMR, CABG alone vs. CABG+MV plasty
FUP at 1 year, no difference in LVSVi



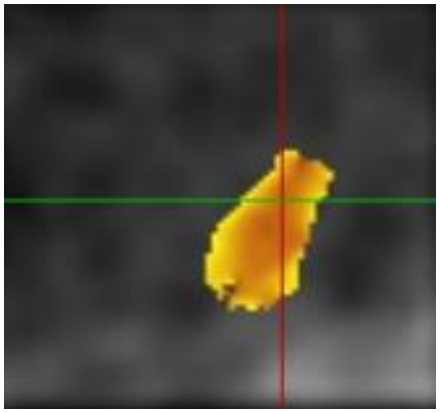
Secondary Mitral Regurgitation

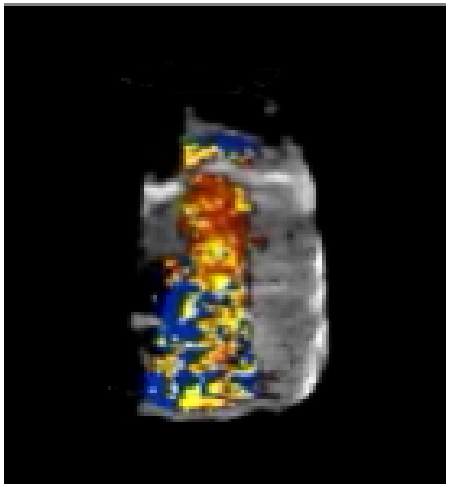
The assessment of MR severity

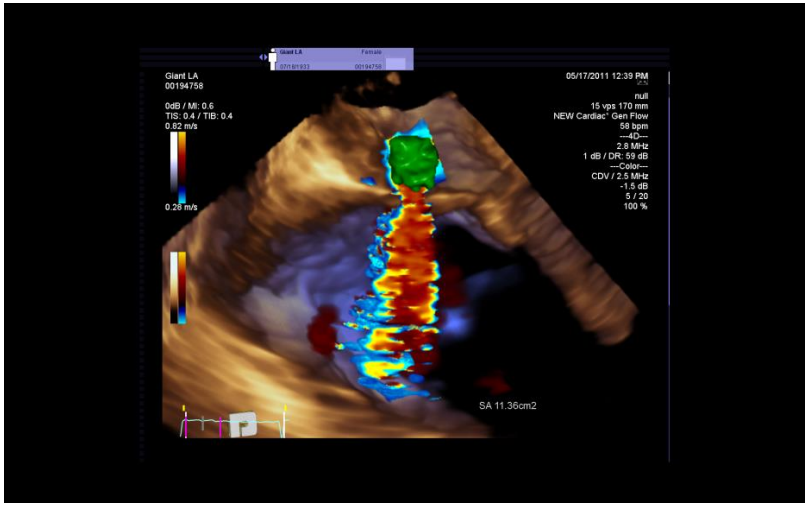
Potential pitfalls



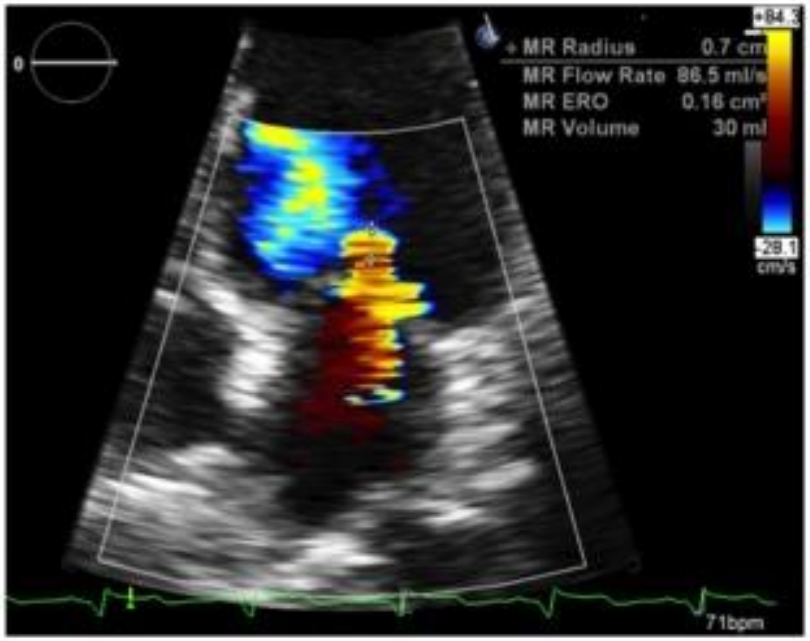
Crescent shape



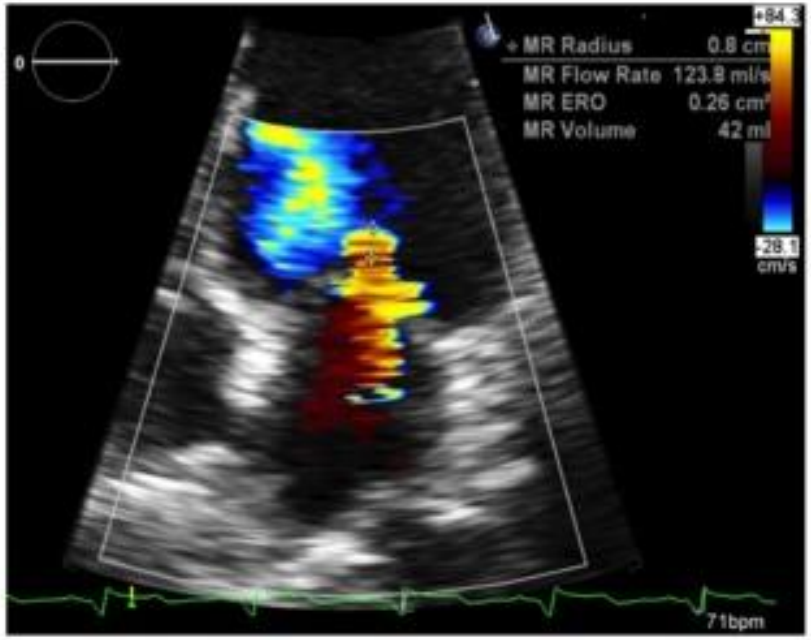




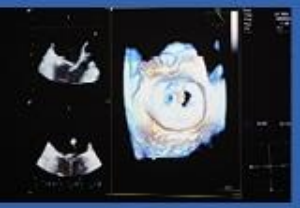
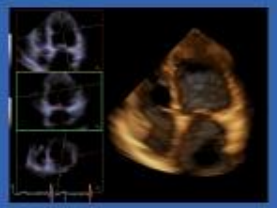
Moderate or Severe Secondary MR ?



PISA radius = 7 mm
EROA = 0.16 cm²
R Vol = 30 mL



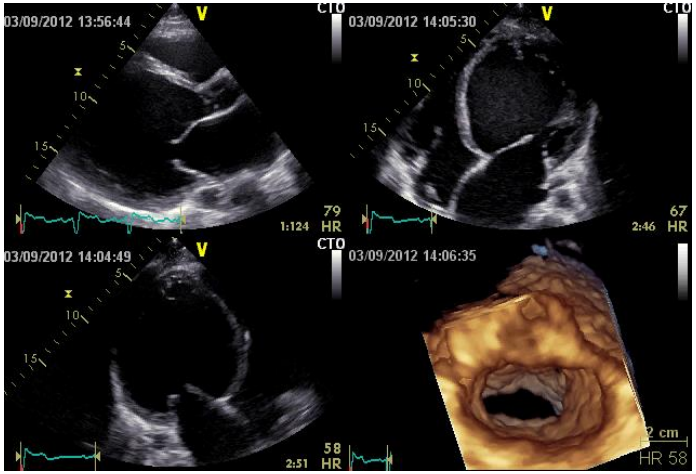
PISA radius = 8 mm
EROA = 0.26 cm²
R Vol = 42 mL

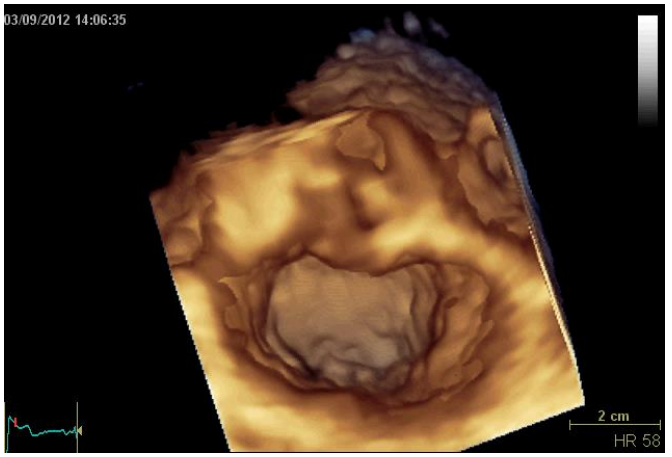



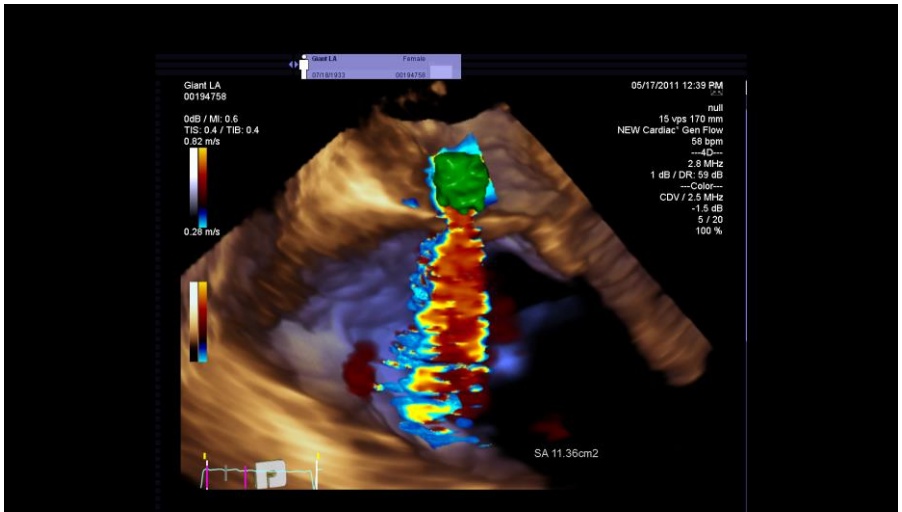

Limitations of the PISA Method

Assumes an hemispheric jet
Regurgitant orifice is usually crescent shape
Flow convergence shape is difficult to judge
Shape affected by aliasing velocity
Errors in measurement are squared
Regurgitation flow changes during systole
Interobserver variability
Not valid for multiple jets

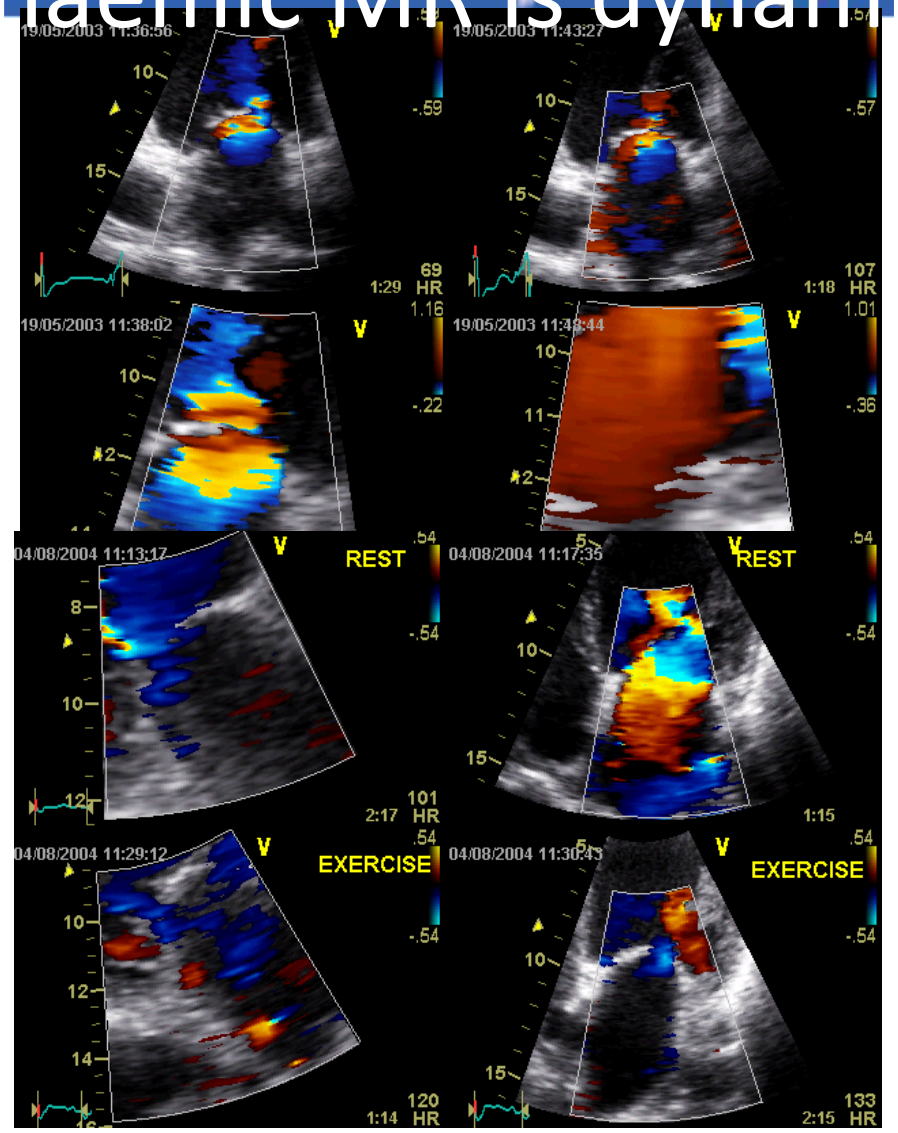
3D parameters are better, but which cut-offs?



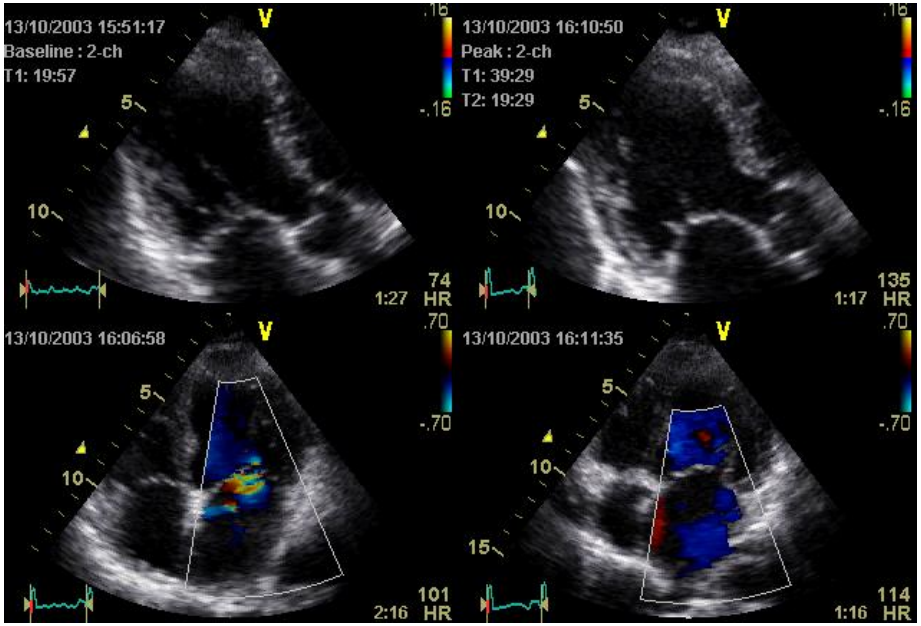


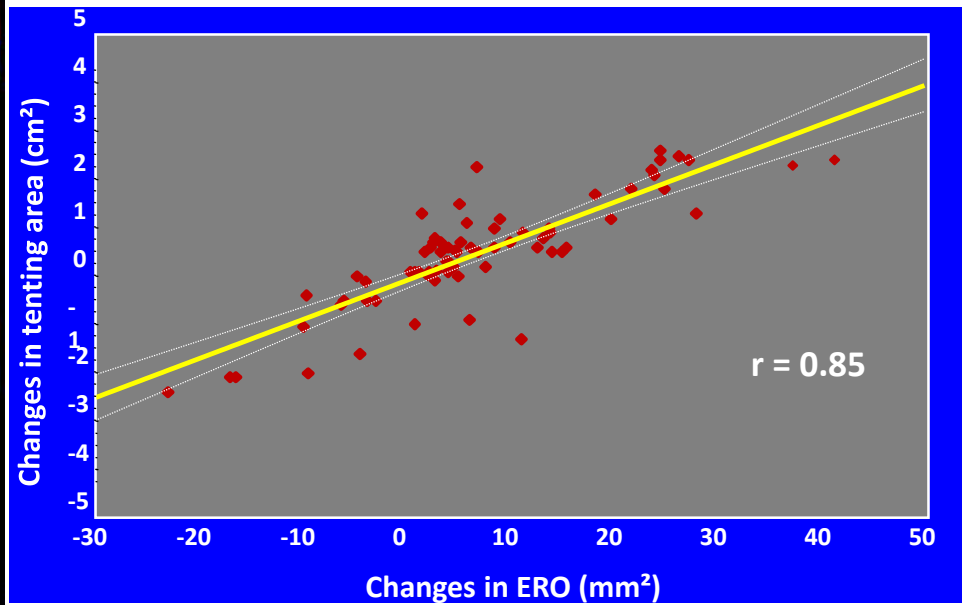


Ischaemic MR is dynamic



Exercise-induced changes in tethering force



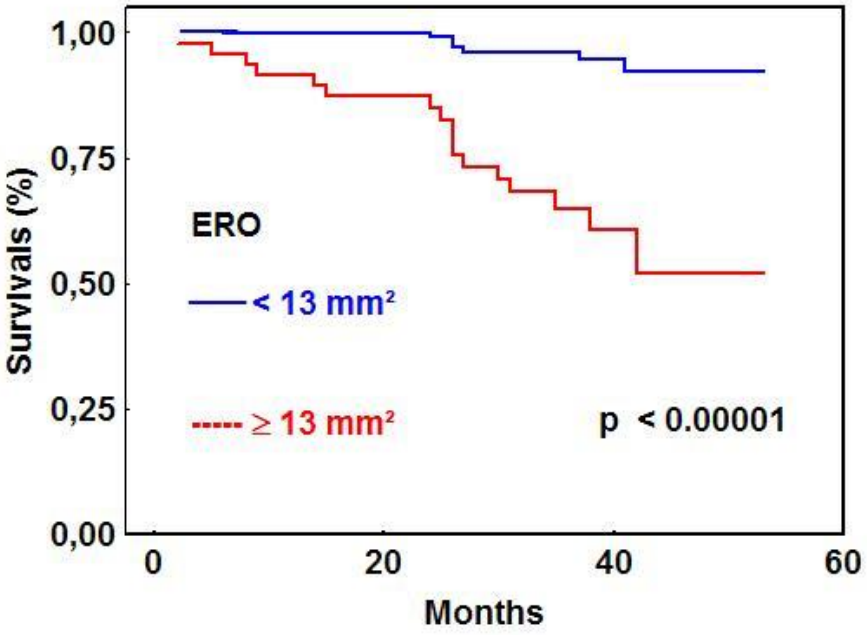


Lancellotti, Lebrun, Piérard JACC 2003, 42,1921-28

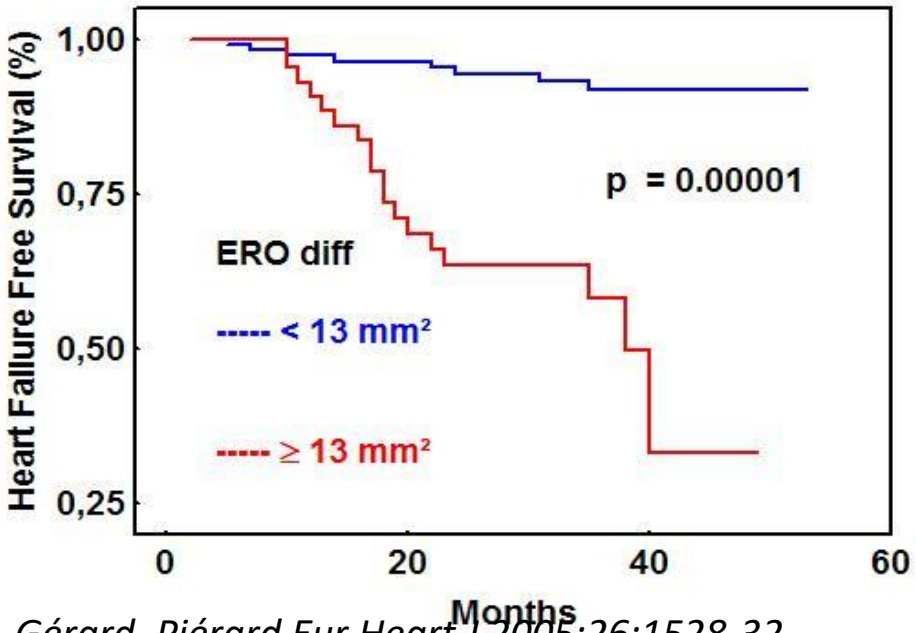
Giga et al Eur Heart J 2005;26:1860-65

Prognosis of dynamic ischaemic MR

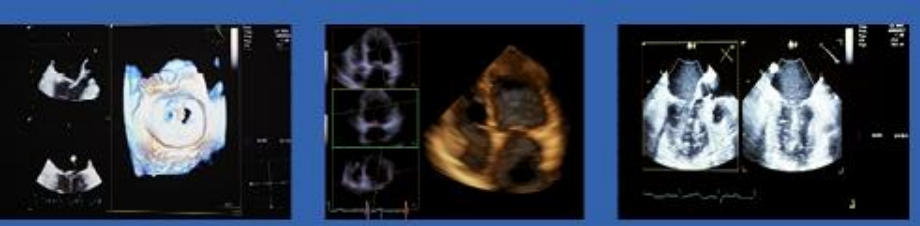
Survival



Acute Heart Failure



Lancellotti, Gérard, Piérard Eur Heart J 2005;26:1528-32



Secondary Mitral Regurgitation: what is new?

Secondary MR is not purely functional

Valve adaptation to stretch

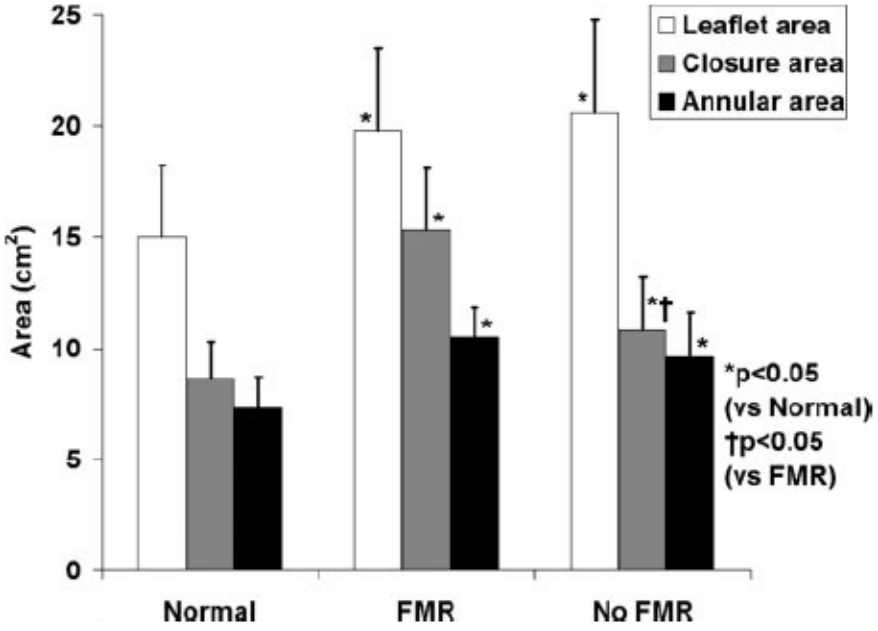
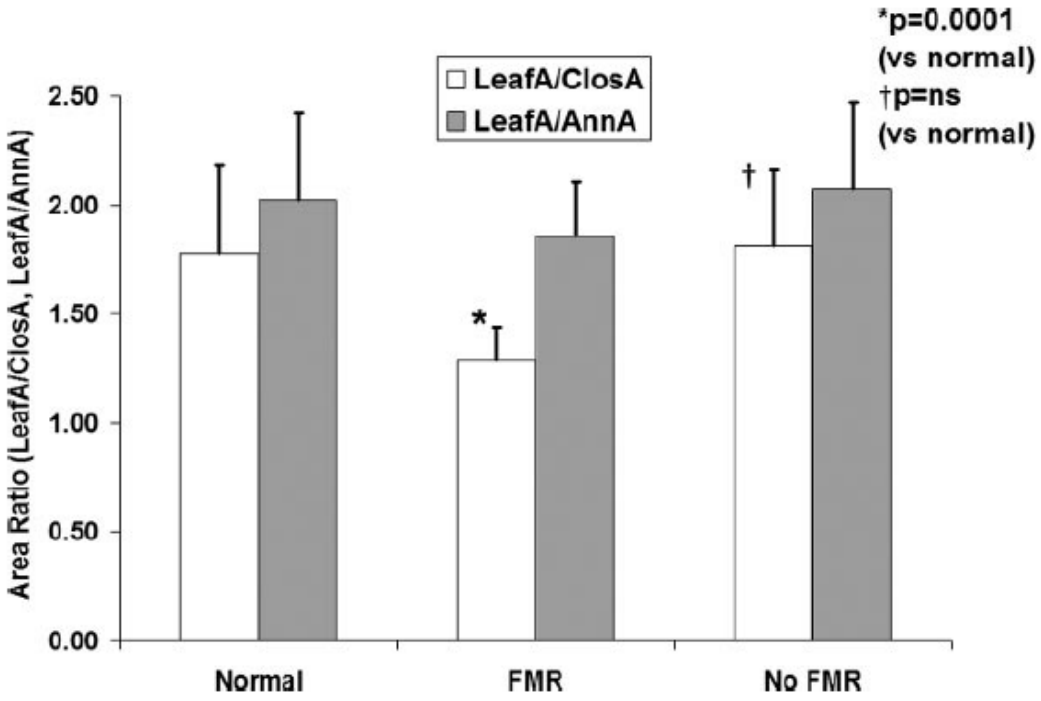


Figure 4. Annular and leaflet areas in different patient groups.

Diastolic MV area increases as a result of stresses imposed by the dilated LV (35% greater)

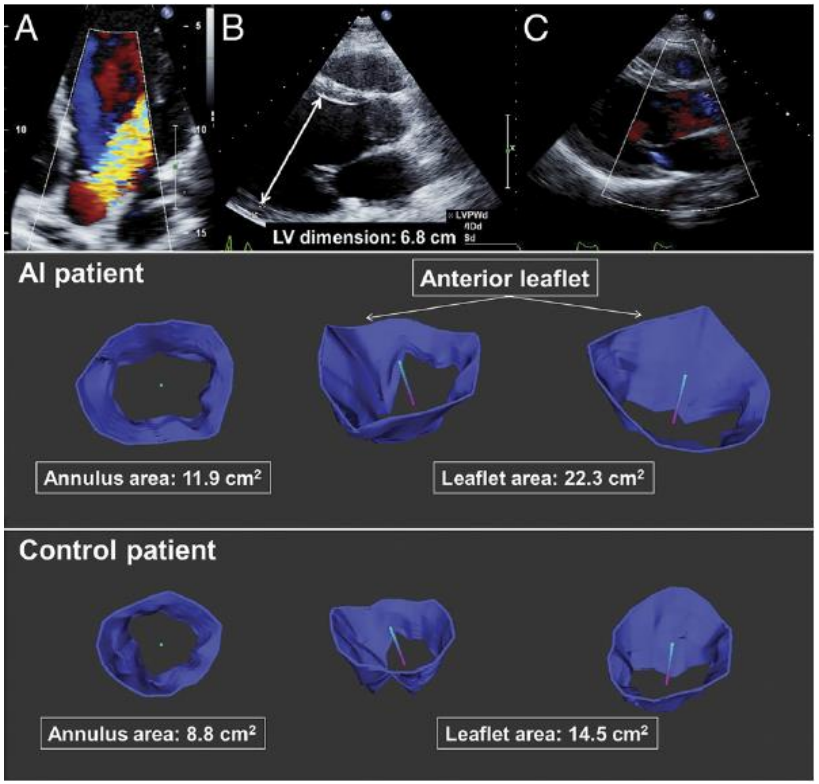
Chaput M, Circulation 2008; 118: 845-52

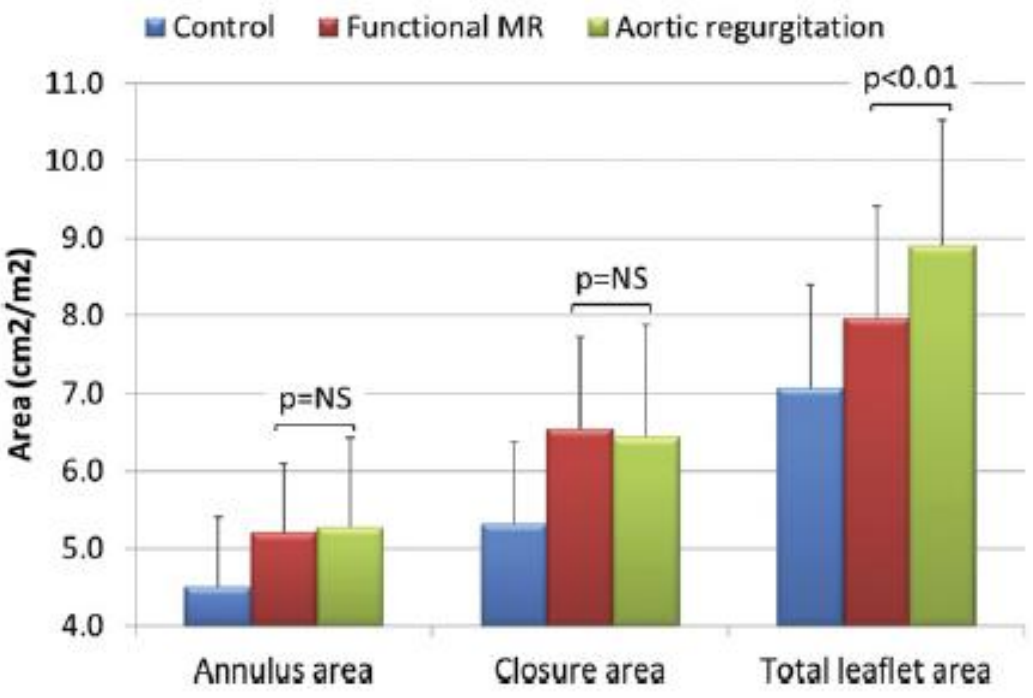


Significant MR: reduced leaflet-to-closure area ratio
Incomplete adaptation in pts who develop MR

Chaput M, Circulation 2008; 118: 845-52

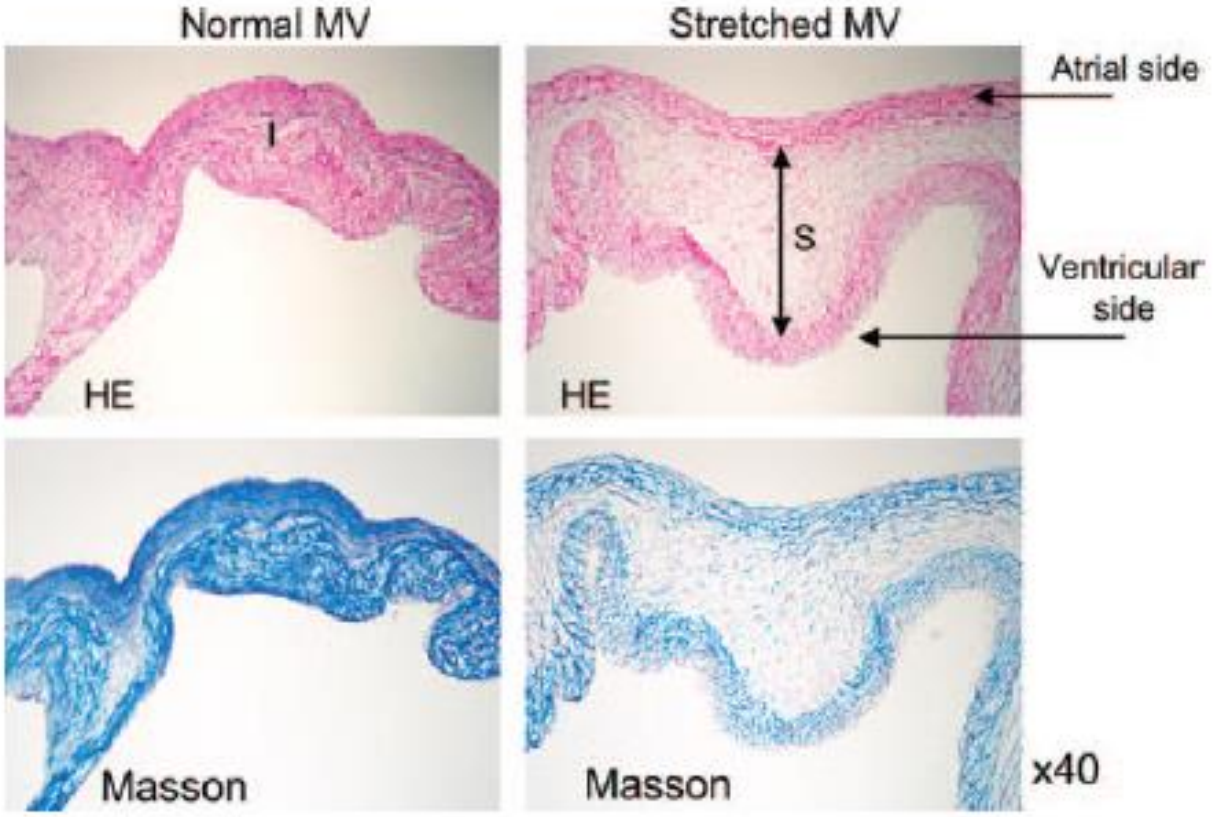
MV enlargment in AR prevents secondary MR





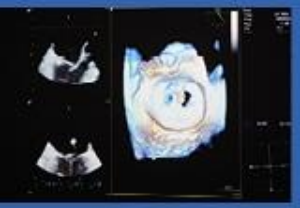
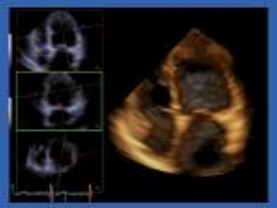
Baudoin F et al JACC 2013; 61: 1809-16

Biologically active adaptative mechanism



Increased spongiosa layer : 2.8 times thicker

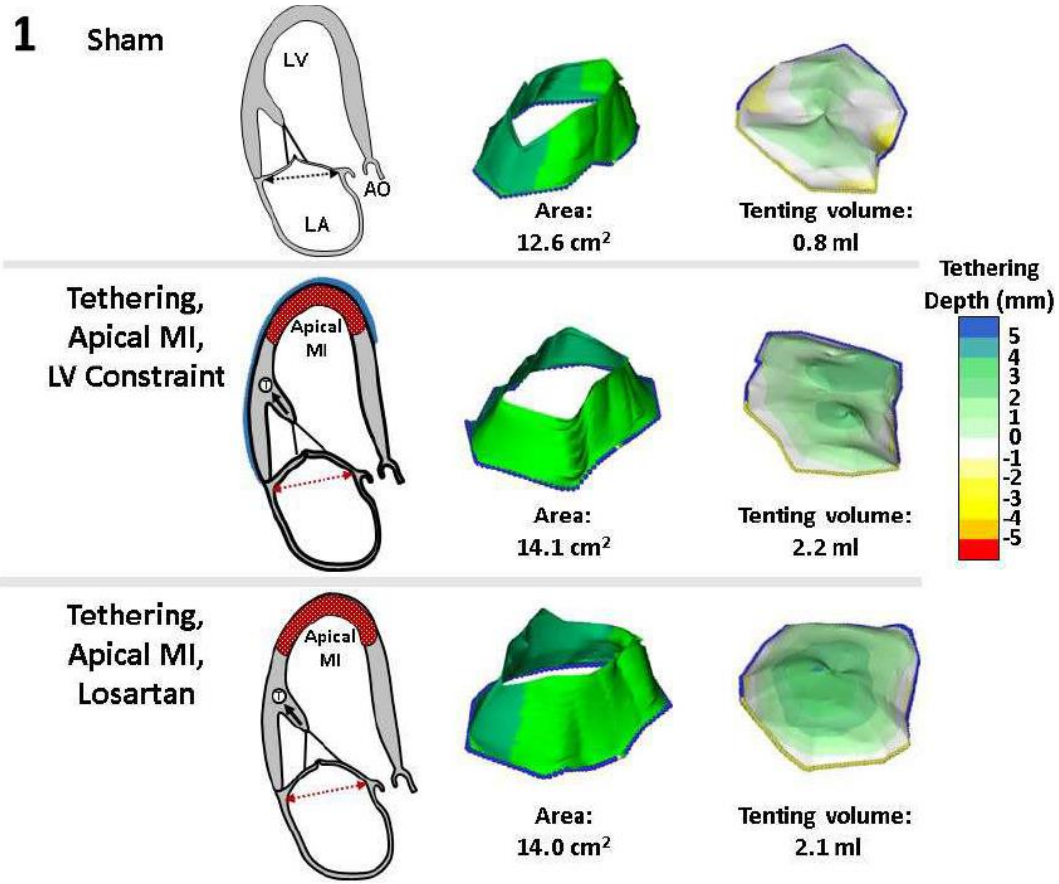
Dal-Bianco JP. Circulation. 2009;120:334-342


Biologically active adaptative mechanism

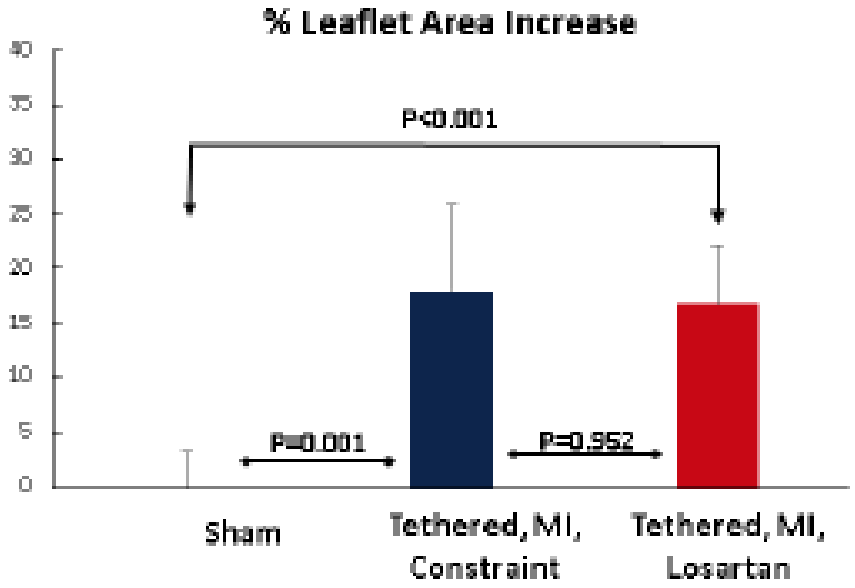
- Human valves maintain cell plasticity
- Mechanical stresses upregulate TGF-β
- TGF-β induces endothelial-mesenchymal transformation
- High prevalence of α-smooth muscle actin cells
- Penetration of these cells from the atrial surface in stretched valves
- Infiltration by cells + for CD45, resulting in fibroblasts, releasing more TGF-β

Role of an Angiotensine II receptor inhibitor
Experimental design

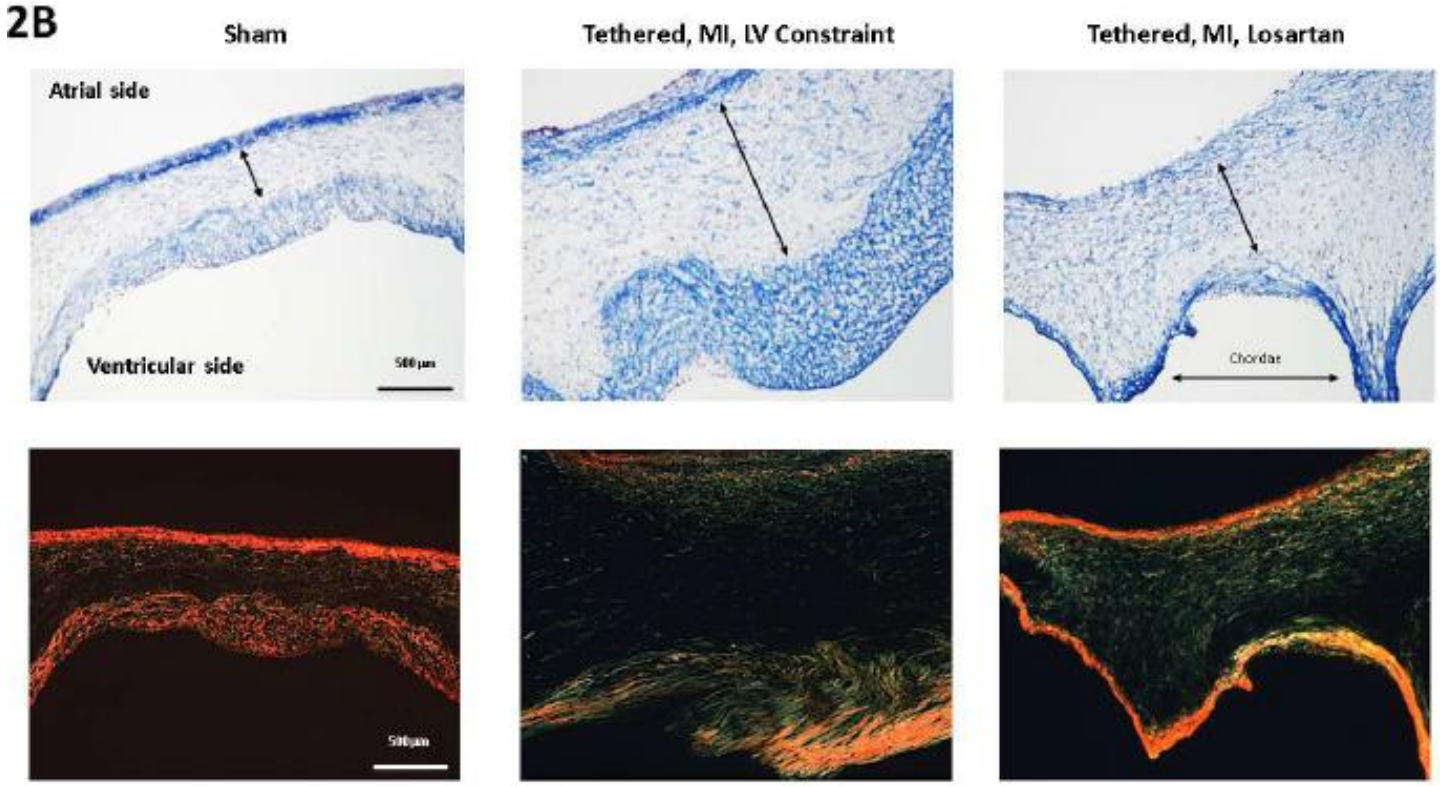


Bartko, Levine et al JACC 2017

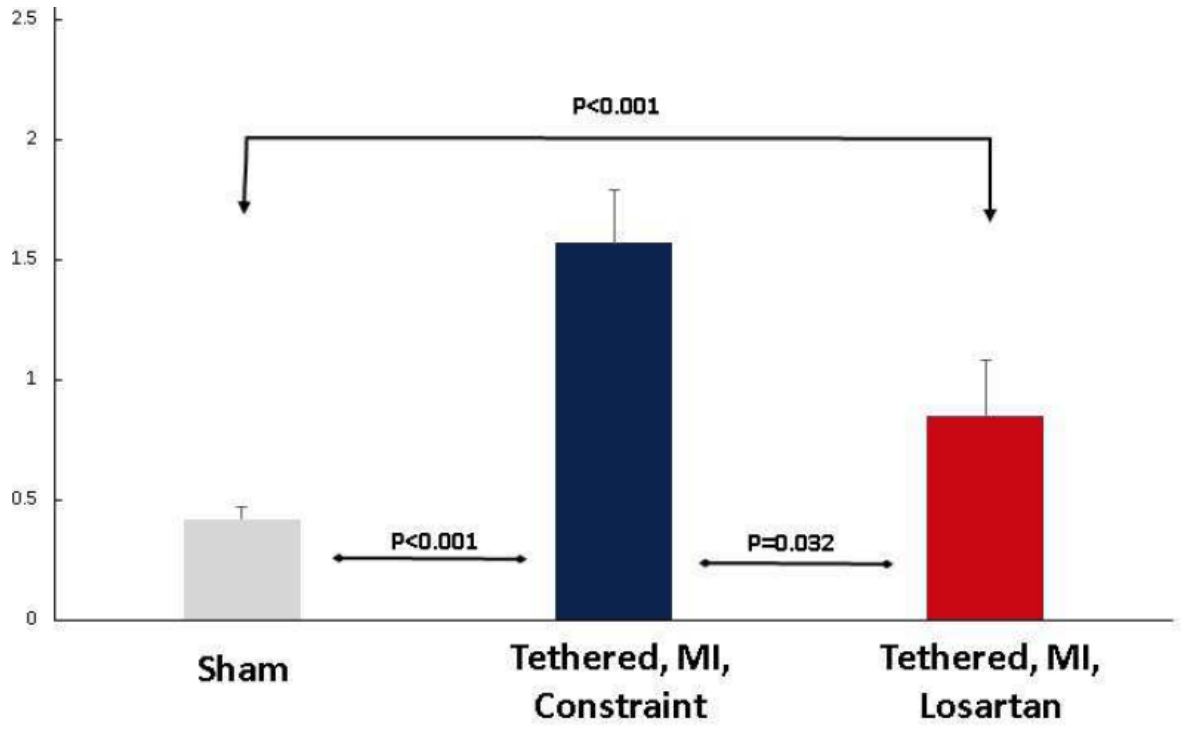
Similar % leaflet area increase



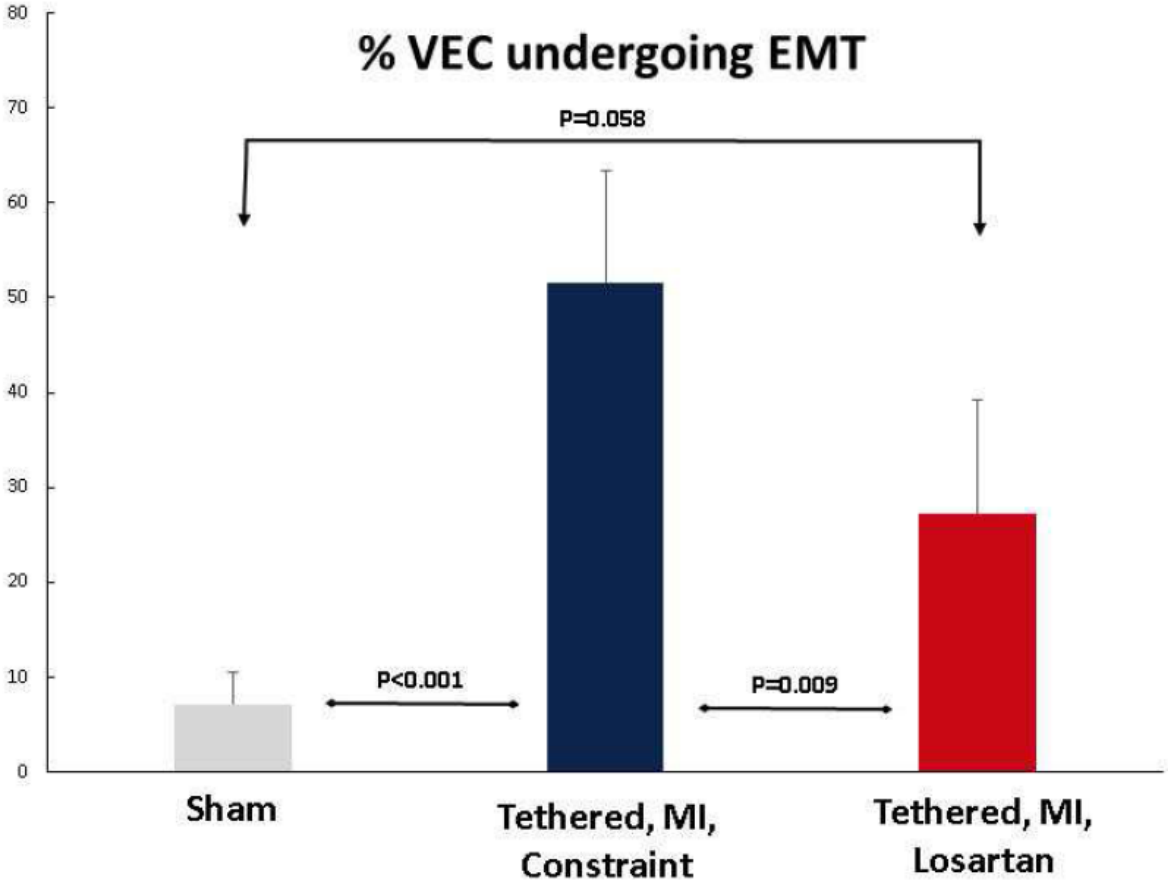
Reduced expansion of the spongiosa layer with losartan



Reduced leaflet thickness with Losartan

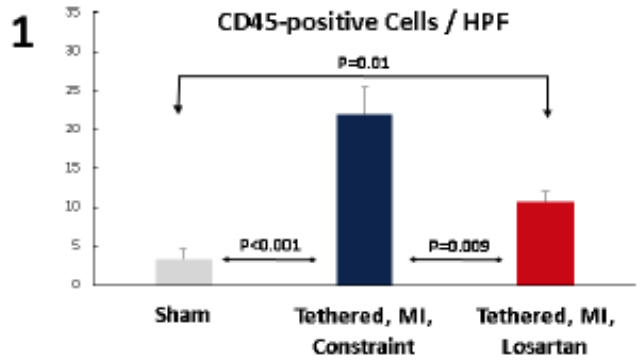


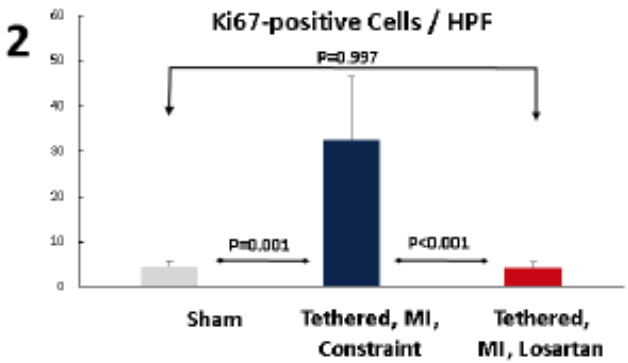
3A

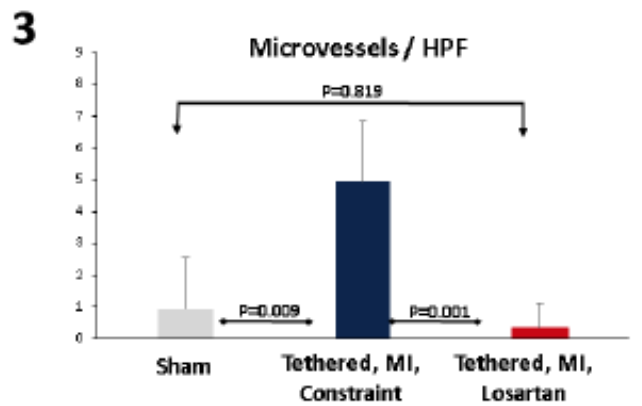

% VEC undergoing EMT
80
70
60
50
40
30
20
10
0
P=0.058
P<0.001
P=0.009
Sham
Tethered, MI, Constraint
Tethered, MI, Losartan

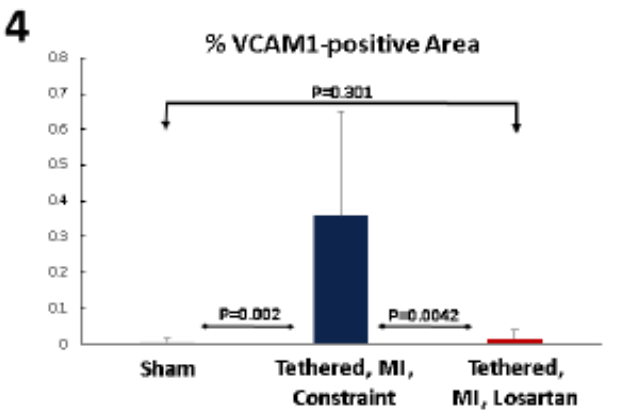
Effects of Losartan on CD45+ cells, cellular proliferation, endothelial activation, and microvessels

4B





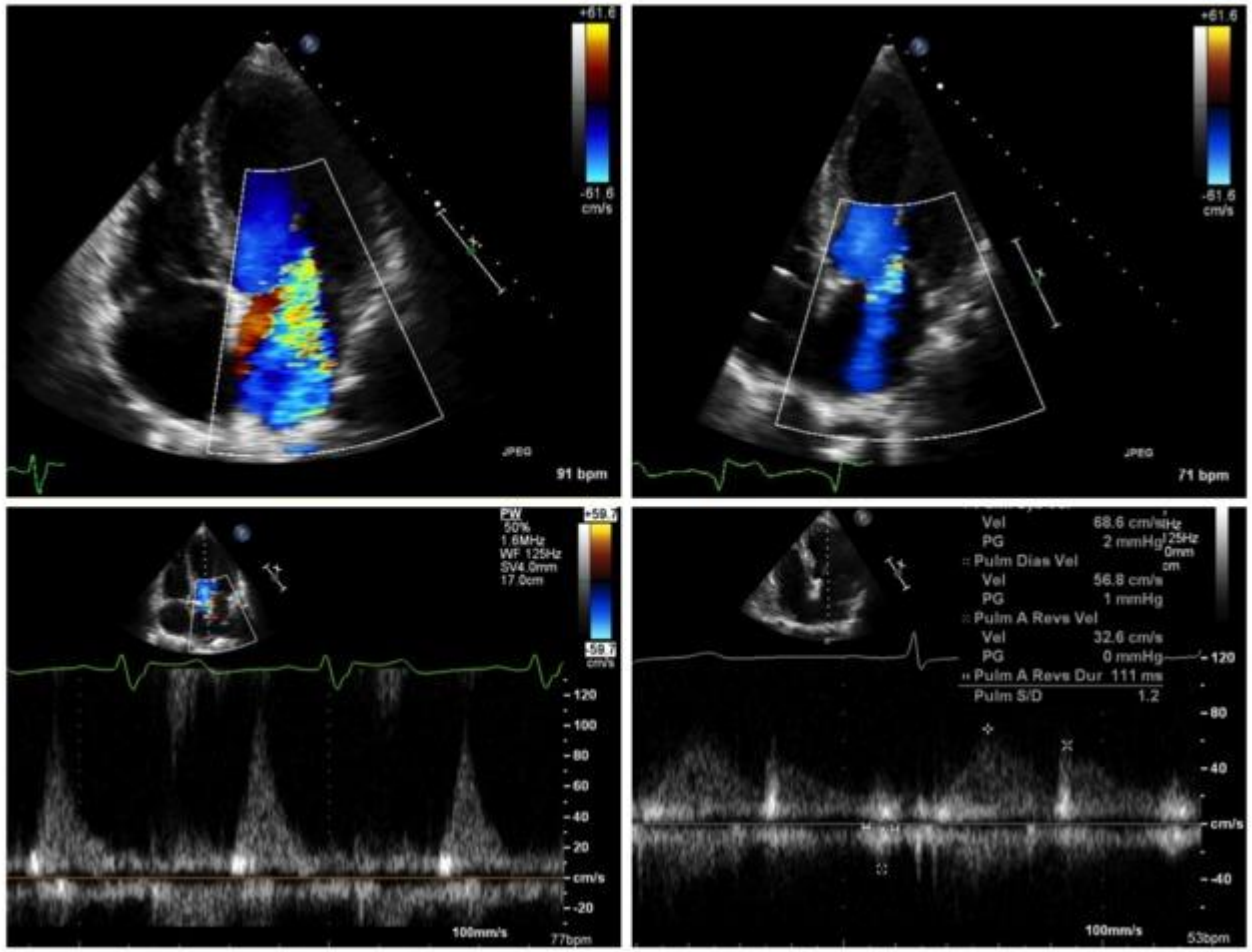




Remaining questions

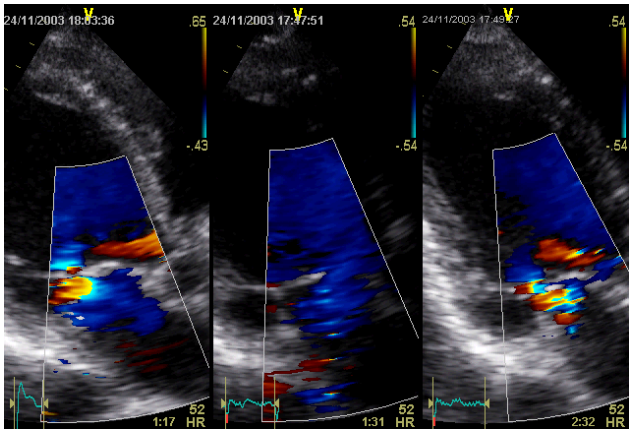
- Would these results be sustained?
- Would, despite losartan, MV fibrosis and stiffness ultimately occur later?
- Similar data need to be reported in the presence of MR
- Other scenari of MI size and location should be tested
- Time course and dose effect in clinical settings
- Potential effects of angiotensin receptor+neprilysin inhibitors?

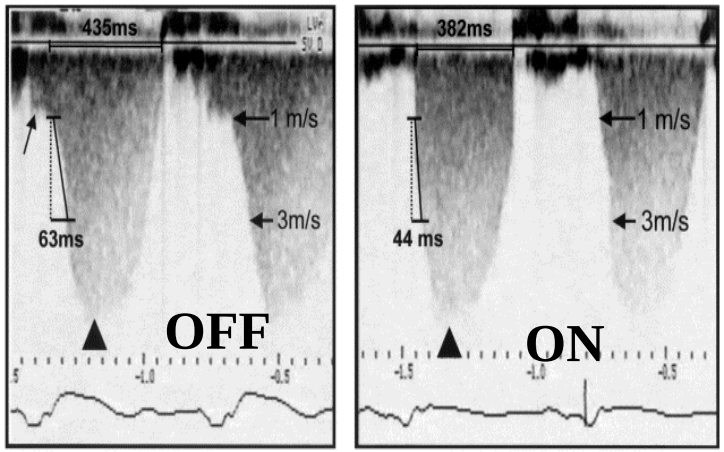
Effect of optimizing medical treatment

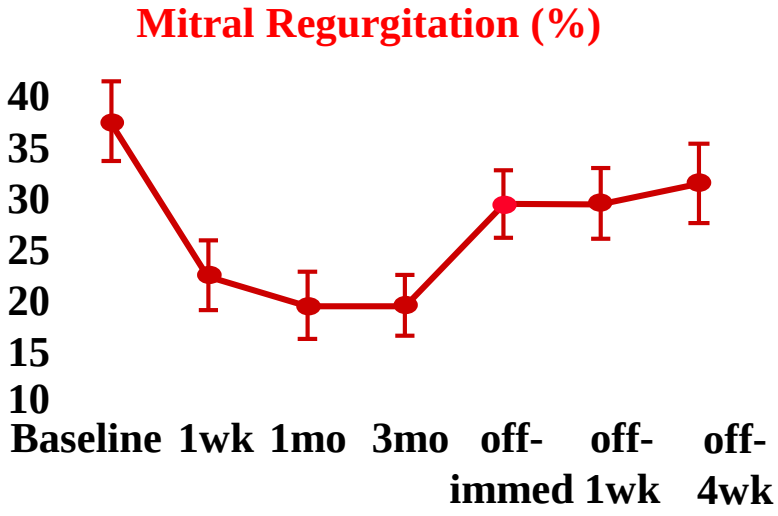


Effects of CRT on secondary MR

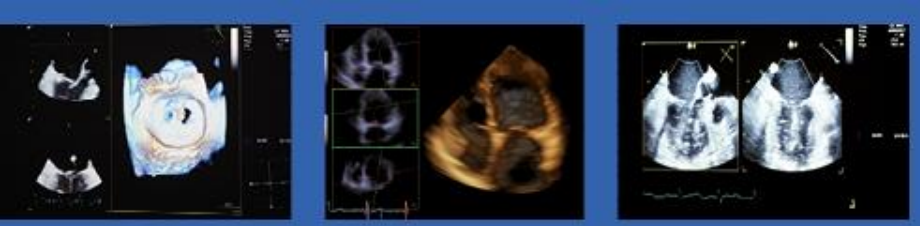
Before Early Late







Breithardt et al JACC 2003; 41: 765 - 770



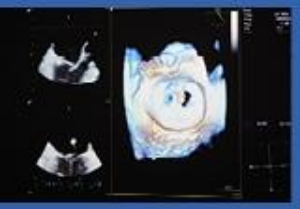
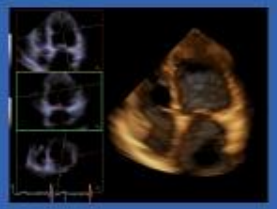
Repair or Replacement

Repair appears to be associated with lower mortality

Better long-term correction of MR with replacement

Recent randomized trial (Acker et al N Engl J Med 2014)

- **No significant difference in**
  - major cardiac or cerebrovascular events
  - functional status
  - quality of life
  - LV reverse remodeling
- **More durable correction of MR with replacement**

Take Home message

Secondary MR has an organic component: MV adaptation

Quantitation by 2D PISA underestimates the severity of MR

Secondary MR is dynamic: varies with exercise, medical treatment and CRT

Secondary MR should be considered severe after optimization
of medical therapy and resynchronization when indicated

Repair or replacement should be chosen according to the number of markers of repair failure