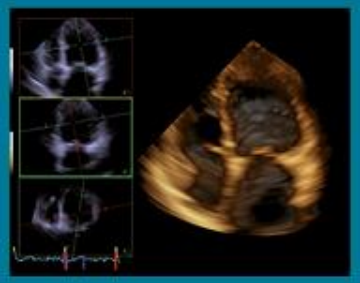


EuroValve

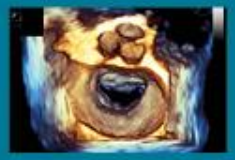
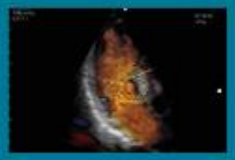
October 24-25, 2014

MitraClip and CRT in mitral regurgitation: a good marriage?

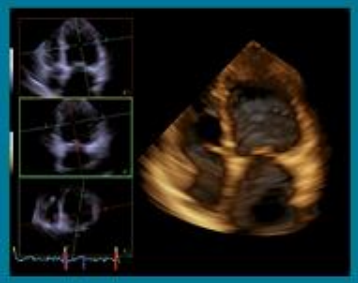
Victoria Delgado, MD, PhD

Leiden University Medical Center



www.eurovalvecongress.com



EuroValve

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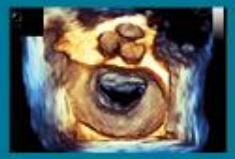
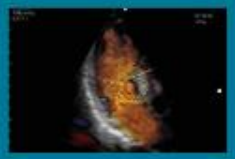
Faculty disclosure

Victoria Delgado

I disclose the following financial relationships:

Paid speaker for Abbott Vascular



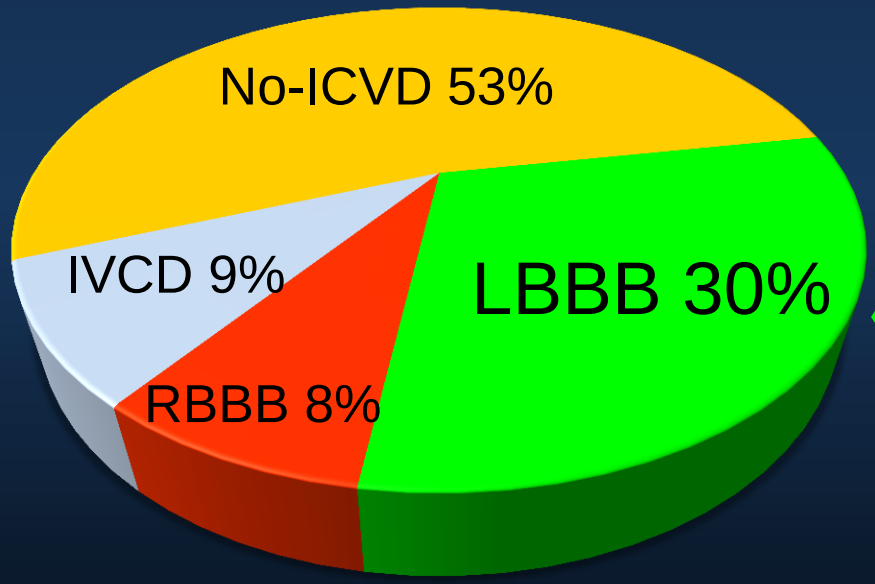
www.eurovalvecongress.com

CRT and MitraClip

- Prevalence of severe MR in HF patients candidates to CRT?
- Which patients improve after CRT?
- Impact of MR reduction on outcome?
- What comes first: CRT or MitraClip?

Mod-severe MR in HF patients

N= 1762, 66 year old, 68% men, LVEF 36%



Mod-severe MR 27%

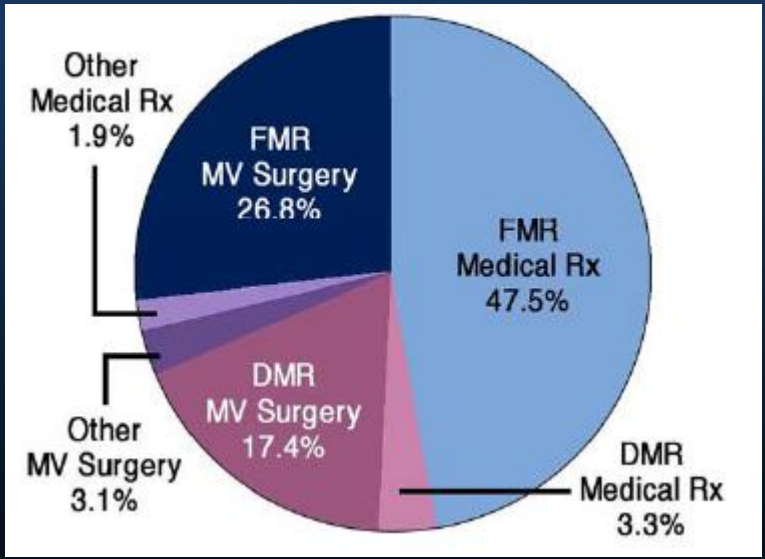
…CRT 14%

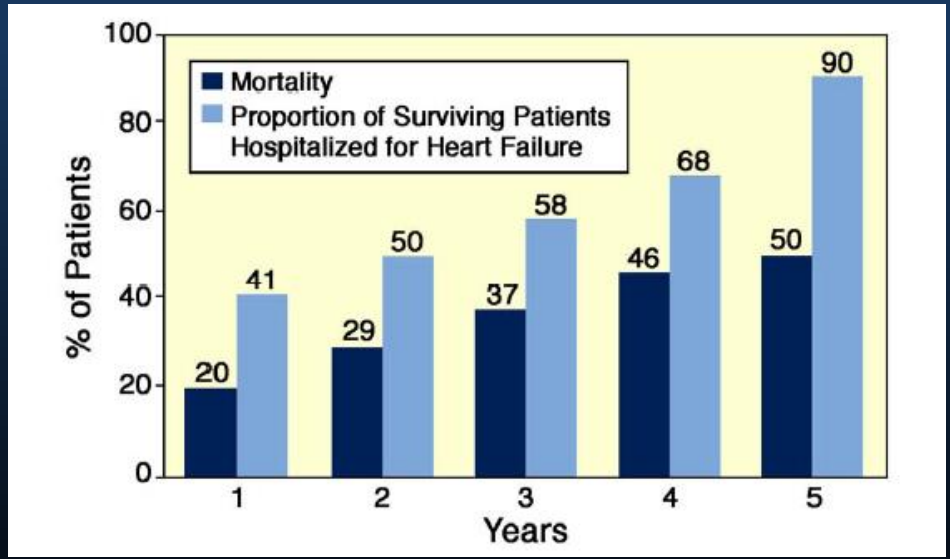
Cinca et al. Eur J Heart Fail 2013

MR in HF and MV repair/replacement

1095 patients with severe MR and HF 2000-2008

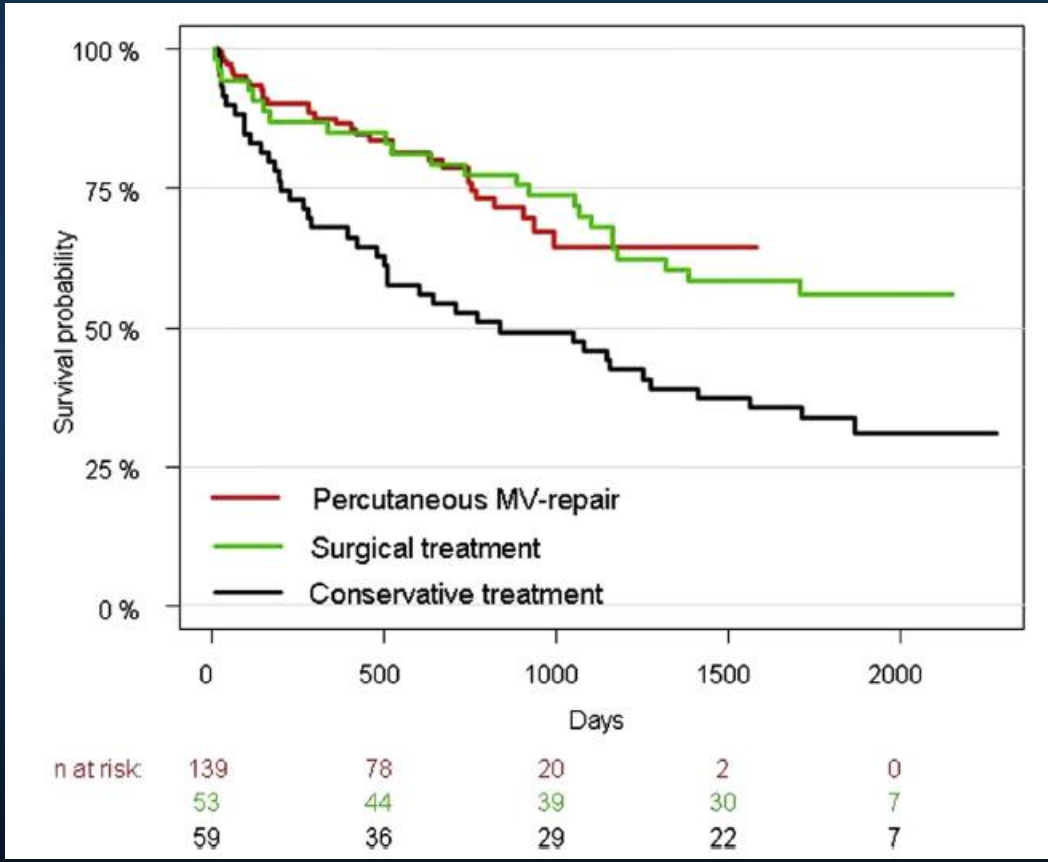
557 left unoperated
90% FMR and 6% DMR





Goel et al. J Am Coll Cardiol 2013 in press

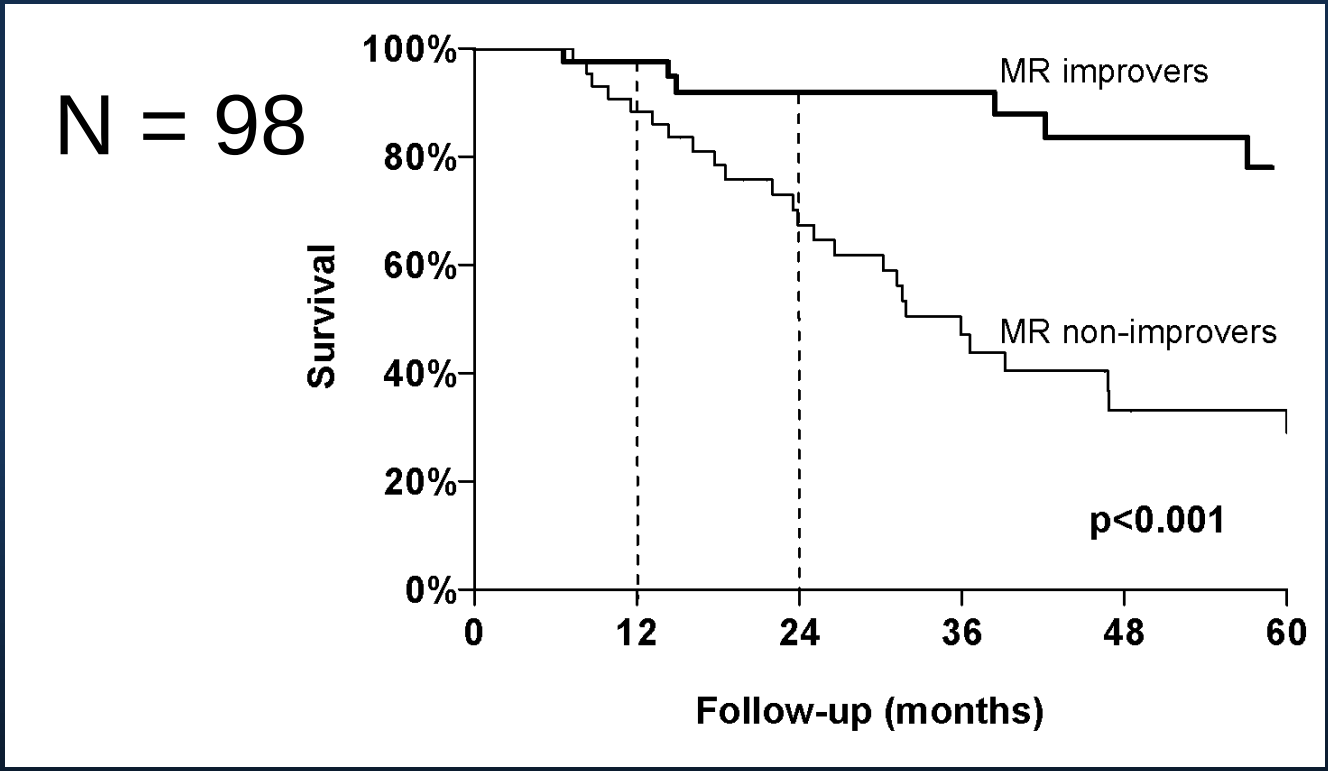
Outcomes of PMVR vs. surgery vs. MT



MitraClip:
77% FMR, LogEuroSCORE 24%
Surgery:
58% FMR, LogEuroSCORE 14%
Medical treatment:
87% FMR, LogEuroSCORE 19%

Swaans et al. JACC Intervent 2014

CRT and FMR: outcomes



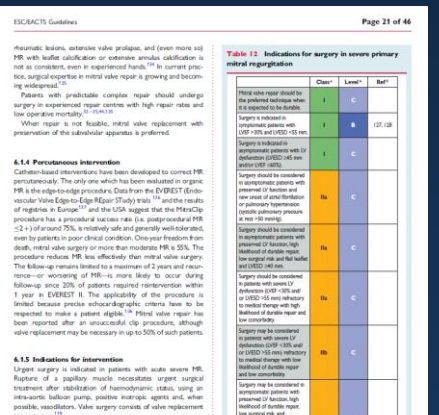
HR: 0.35 (95% CI 0.13-0.94); p = 0.043

van Bommel et al. Circ 2011

ESC Guidelines for treatment of MR

Primary (Degenerative)

Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfil the echo criteria of eligibility, are judged inoperable or at high surgical risk by a ‘heart team’, and have a life expectancy greater than 1 year (class IIbC).


ESC/EACTS Guidelines Page 21 of 46

rheumatic lesions, extensive valve prolapse, and (even more so) MR with leaflet calcification or extensive annulus calcification is not as consistent, even in experienced hands.[106] In current practice, surgical expertise in mitral valve repair is growing and becoming widespread.[105]

Patients with predictable complex repair should undergo surgery in experienced repair centres with high repair rates and low operative mortality.[82–85,443,5]

When repair is not feasible, mitral valve replacement with preservation of the subvalvular apparatus is preferred.

6.1.4 Percutaneous intervention

Catheter-based interventions have been developed to correct MR percutaneously. The only one which has been evaluated in organic MR is the edge-to-edge procedure. Data from the EVEREST (Endovascular Valve Edge-to-Edge REpair STudy) trial[104] and the results of registries in Europe[107] and the USA suggest that the MitraClip procedure has a procedural success rate (i.e. postprocedural MR ≤2+) of around 75%, is relatively safe and generally well-tolerated, even by patients in poor clinical condition. One-year freedom from death, mitral valve surgery or more than moderate MR is 55%. The procedure reduces MR less effectively than mitral valve surgery. The follow-up remains limited to a maximum of 2 years and recurrence—or worsening of MR—is more likely to occur during follow-up since 20% of patients required reintervention within 1 year in EVEREST II. The applicability of the procedure is limited because precise echocardiographic criteria have to be respected to make a patient eligible.[106] Mitral valve repair has been reported after an unsuccessful clip procedure, although valve replacement may be necessary in up to 50% of such patients.

6.1.5 Indications for intervention

Urgent surgery is indicated in patients with acute severe MR. Rupture of a papillary muscle necessitates urgent surgical treatment after stabilization of haemodynamic status, using an intra-aortic balloon pump, positive inotropic agents and, when possible, vasodilators. Valve surgery consists of valve replacement in most cases.[105]

The indications for surgery in severe chronic primary MR are shown in *Table 12* and *figure 3*.

The decision of whether to replace or repair depends mostly on valve anatomy, surgical expertise available, and the patient's condition.

Surgery is indicated in patients who have symptoms due to chronic MR, but no contraindications to surgery.

When LVEF is <30%, a durable surgical repair can still improve symptoms, although the effect on survival is largely unknown. In this situation, the decision on whether to operate will take into account the response to medical therapy, comorbidity, and the likelihood of successful valve repair.

Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfil the echo criteria of eligibility, are judged inoperable or at high surgical risk by a heart team, and have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).

Table 12 Indications for surgery in severe primary mitral regurgitation

	Class[a]	Level[b]	Ref[c]
Mitral valve repair should be the preferred technique when it is expected to be durable.	I	C	
Surgery is indicated in symptomatic patients with LVEF >30% and LVESD <55 mm.	I	B	127,128
Surgery is indicated in asymptomatic patients with LV dysfunction (LVESD >45 mm and/or LVEF ≤60%).	I	C	
Surgery should be considered in asymptomatic patients with preserved LV function and new onset of atrial fibrillation or pulmonary hypertension (systolic pulmonary pressure at rest >50 mmHg).	IIa	C	
Surgery should be considered in asymptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk and flail leaflet and LVESD ≥40 mm.	IIa	C	
Surgery should be considered in patients with severe LV dysfunction (LVEF <30% and/or LVESD >55 mm) refractory to medical therapy with high likelihood of durable repair and low comorbidity.	IIa	C	
Surgery may be considered in patients with severe LV dysfunction (LVEF <30% and/or LVESD >55 mm) refractory to medical therapy with low likelihood of durable repair and low comorbidity.	IIb	C	
Surgery may be considered in symptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk, and: • left atrial dilatation (volume index ≥60 ml/m² BSA) and sinus rhythm, or • pulmonary hypertension on exercise (SPAP ≥60 mmHg at exercise).	IIb	C	

BSA = body surface area; LV = left ventricle; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; SPAP = systolic pulmonary artery pressure.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting class I (A + B) and IIa + IIb (A + B) recommendations.

The management of asymptomatic patients is controversial as there are no randomized trials to support any particular course of action; however, surgery can be proposed in selected asymptomatic patients with severe MR, in particular when repair is likely.[108,109]


ESC/EACTS Guidelines Page 25 of 46

LV function, who cannot be revascularized or who present with cardiomyopathy, are questionable. Repair may be considered in selected patients if comorbidity is low, in order to avoid or postpone transplantation. In the other patients, optimal medical treatment is currently the best option, followed, in the event of failure, by extended MV treatment [cardiac resynchronization therapy (CRT); ventricular assist devices; cardiac restraint devices heart transplantation].

The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfil the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).

There is continuing debate regarding the management of moderate ischaemic MR in patients undergoing CABG. In such cases, valve repair is preferable. In patients with severe EF, mitral valve surgery is more likely to be considered if myocardial viability is present and if comorbidity is low. In patients capable of exercising, exercise echocardiography should be considered whenever possible. Exercise-induced dyspnoea and a large increase in severity and systolic pulmonary artery pressure favour combined surgery.

There are no data to support surgical correction of mild MR.

6.2.6 Medical treatment

Optimal medical therapy is mandatory: it should be the first step in the management of all patients with secondary MR and should be given in line with the guidelines on the management of HF.[111] This includes ACE inhibitors and beta-blockers, with the addition of an aldosterone antagonist in the presence of HF. A diuretic is required in the presence of fluid overload. Nitrates may be useful for treating acute dyspnoea, secondary to a large dynamic component.

The indications for resynchronization therapy should be in accordance with related guidelines.[111] In responders, CRT may immediately reduce MR severity through increased closing force and resynchronization of papillary muscles.[86] A further reduction in MR and its dynamic component can occur through a reduction in tethering force in relation to LV reverse remodelling.

7. Mitral stenosis

Rheumatic fever, which is the predominant aetiology of MS, has greatly decreased in industrialized countries; nevertheless, MS still results in significant morbidity and mortality worldwide.[112] Percutaneous mitral commissurotomy (PMC) has had a significant impact upon the management of rheumatic MS.

7.1 Evaluation

The patient with MS may feel asymptomatic for years and then present with a gradual decrease in activity. The diagnosis is usually established by physical examination, chest X-ray, ECG, and echocardiography.

The general principles for the use of invasive and non-invasive investigations follow the recommendations made in the *General comments* (Section 3).[11]

Specific issues in MS are as follows:

- Echocardiography is the main method used to assess the severity and consequences of MS, as well as the extent of anatomic lesions.

Valve area should be measured using planimetry and the pressure half-time method, which are complementary. Planimetry, when it is feasible, is the method of choice, in particular immediately after PMC. Continuity equation and proximal isovelocity could be used when additional assessment is needed. Measurements of mean transvalvular gradient, calculated using Doppler velocities, are highly rate- and flow-dependent, but are useful to check consistency in the assessment of severity, particularly in patients in sinus rhythm. MS does not usually have clinical consequences at rest when valve area is >1.5 cm² (*Table 4*).[15]

A comprehensive assessment of valve morphology is important for the treatment strategy. Scoring systems have been developed to help assess suitability, taking into account valve thickening, mobility, calcification, subvalvular deformity, and commissural area.[113,114]

Echocardiography also evaluates pulmonary artery pressures, associated concomitant valve disease, and LA size. Due to the frequent association of MS with other valve diseases, a comprehensive evaluation of the tricuspid and aortic valves is mandatory. TTE usually provides sufficient information for routine management.

TOE should be performed to exclude LA thrombus before PMC or after an embolic episode, if TTE provides suboptimal information on anatomy or, in selected cases, to guide the procedure.

3DE improves the evaluation of valve morphology (especially visualization of commissures),[115] optimizes accuracy and reproducibility of planimetry, and could be useful in monitoring (TOE) and monitoring (TTE) PMC in difficult cases.

Echocardiography also plays an important role in monitoring the results of PMC during the procedure.

- Stress testing is indicated in patients with no symptoms or symptoms equivocal or discordant with the severity of MS. Dobutamine or, preferably, exercise echocardiography may provide additional information by assessing changes in mitral gradient and pulmonary pressures.[20]

7.2 Natural history

Survival in asymptomatic patients is usually good up to 10 years, progression being highly variable with sudden deterioration, which is usually precipitated by pregnancy or complications such as AF or embolism.[442] Symptomatic patients have a poor prognosis without intervention.[15]

7.3 Results of intervention

7.3.1 Percutaneous mitral commissurotomy

Technical success and complications are related to patient selection and the operator's experience.[116] Good initial results, defined as valve area >1.5 cm² with no MR >2/4, are achieved in over 80% of cases. Major complications include procedural mortality 0.5–4%, haemopericardium 0.5–10%, embolism 0.5–5%, and

Secondary (Functional)

MitraClip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfil the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (class IIbC).

Vahanian et al. Eur Heart J 2012

MR improvement after CRT

Tethering ≠ Closing forces
Changes in LV and mitral geometry

↑Closing forces
Restoring LV and mitral geometry
(reverse remodeling)

MR improvement after CRT

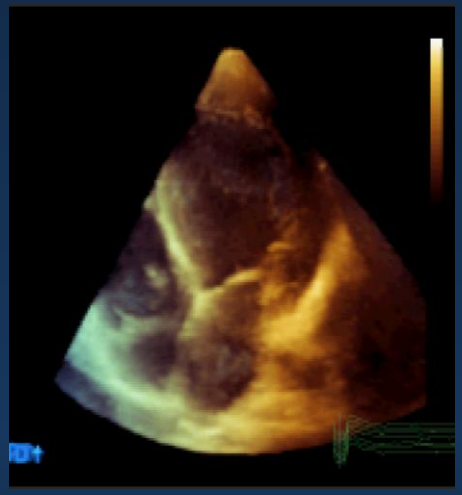
N = 34 HF patients

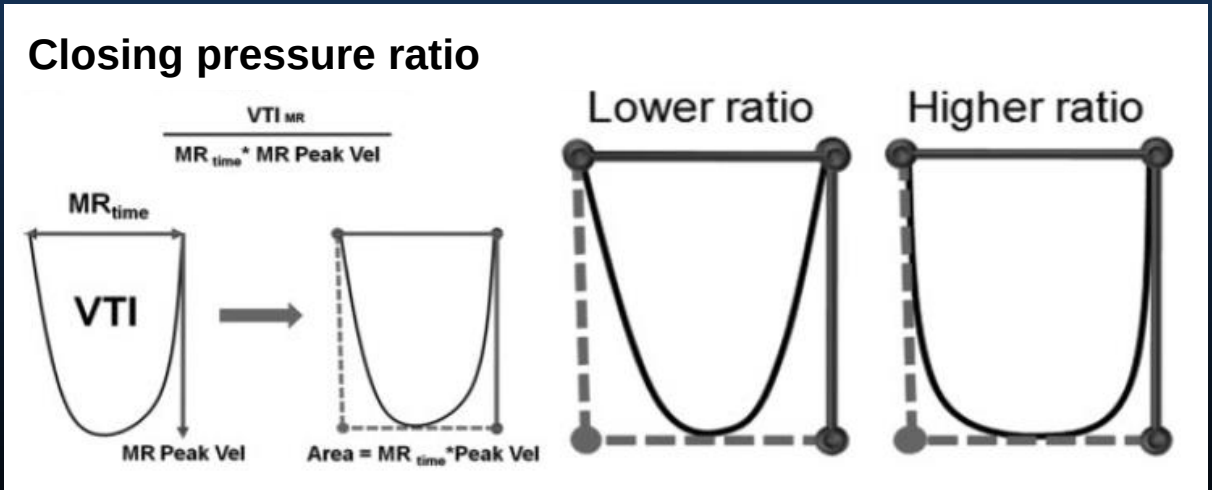
66±12 years

47% ischemic

LVEF 19±6%

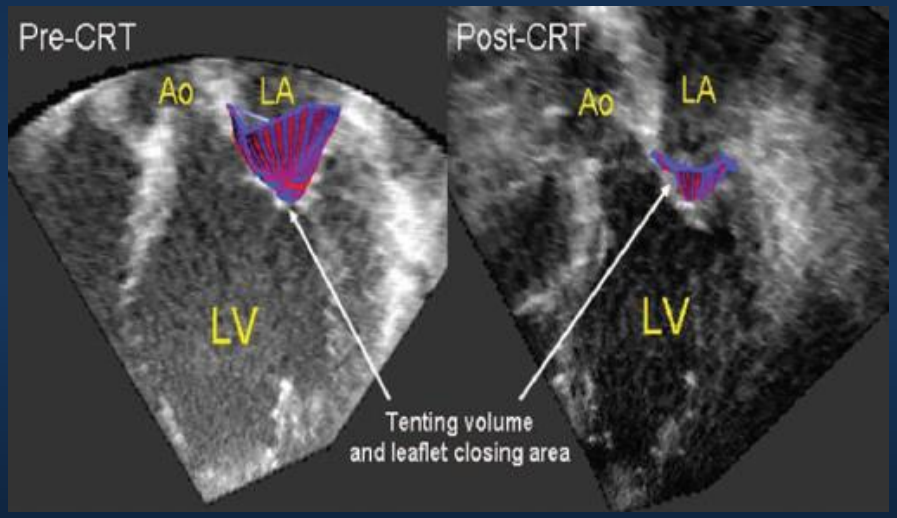
Yu-index 36±13 ms

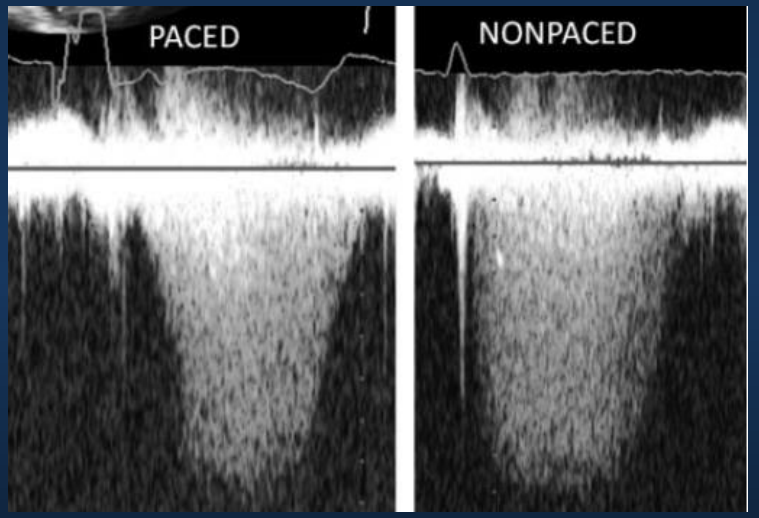




Solís et al. Circ cardiovasc Imag 2009

MR improvement after CRT





Changes in mitral valve geometry and closing forces at 6 months after CRT

Solís et al. Circ cardiovasc Imag 2009

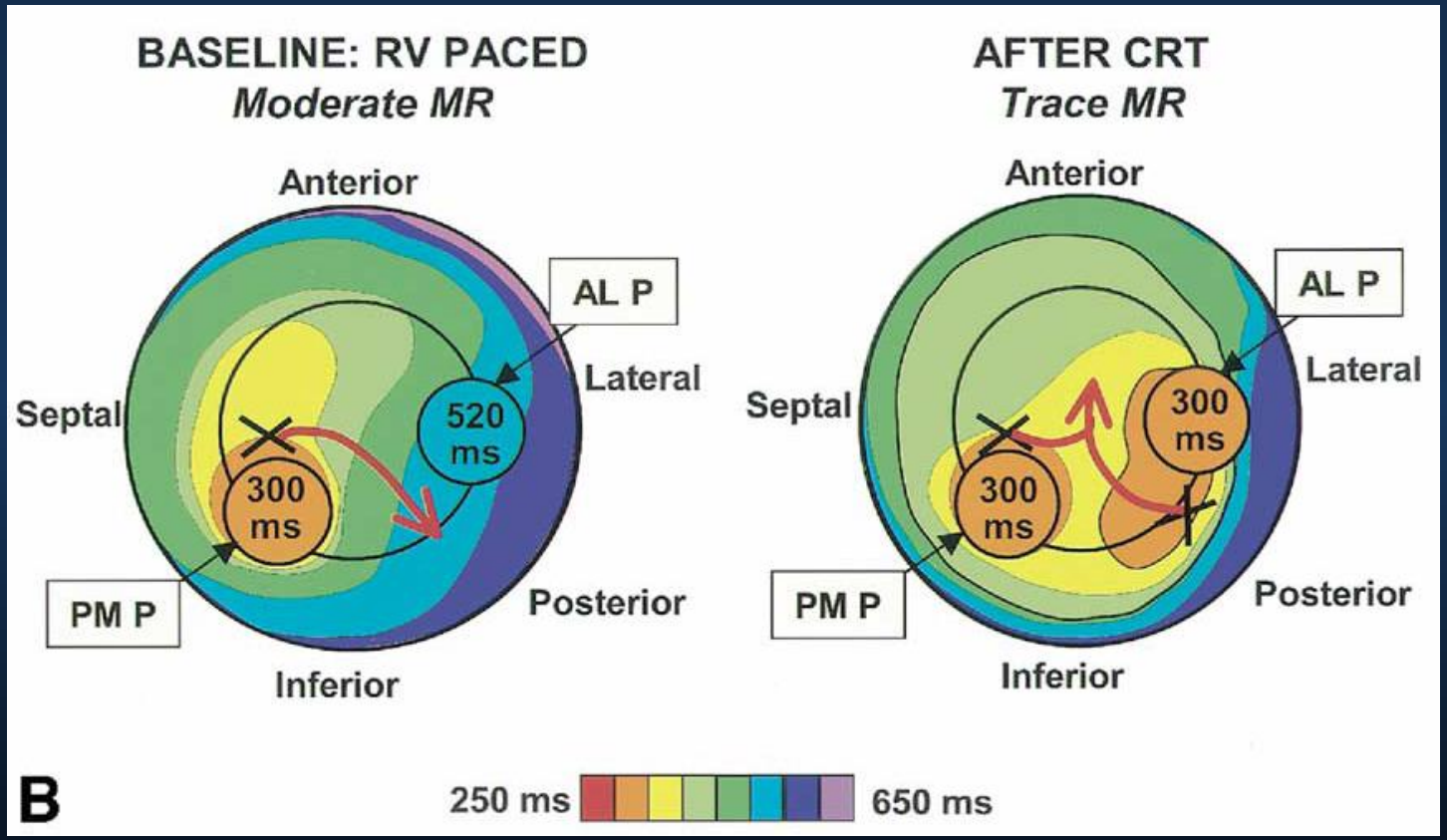
MR improvement after CRT

	MR improvement (n=18)		No MR improvement (n=16)	
	Pre-CRT	**Post-CRT**	**Pre-CRT**	**Post-CRT**
LVEDV, mL	265±88	228±77*	239±134	215±134*
LVESV, mL	216±78	167±81*	195±118	168±113*
LVEF, %	19±5	28±10*	20±7	24±12*
MAA, cm^2	12.4±3.2	11±3.4*	10.8±3.9	10±2.8
Leaflet closing area, cm^2	16.9±3.8	14.5±4.1*	14.2±4	13.1±3.6
Closing pressure ratio	0.77±0.04	0.85±0.1*	0.78±0.1	0.81±0.1

*=$p<0.05$

Solís et al. Circ cardiovasc Imag 2009

MR improvement after CRT



Kanzaki et al. J Am Coll Cardiol 2004

MR improvement after CRT

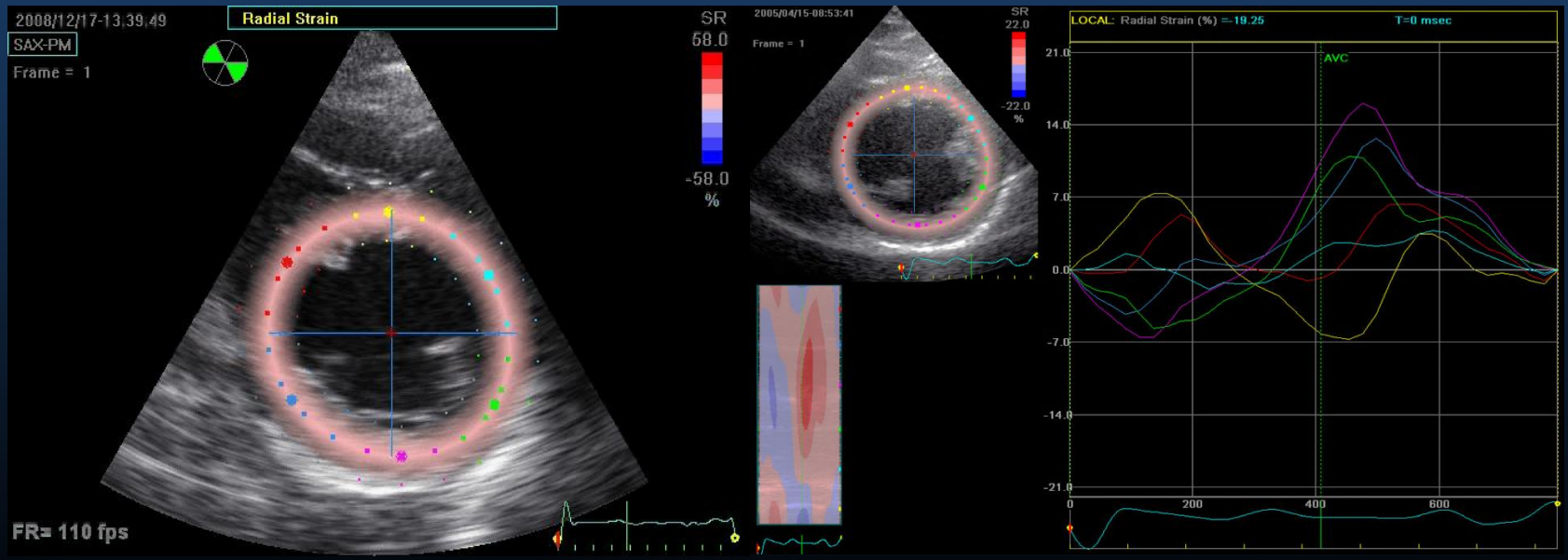
N = 25 HF patients

68±10 years, 64% ischemic

80% LBBB

LVEF 23±8%

Dyssynchrony between PMs: 169±69 ms

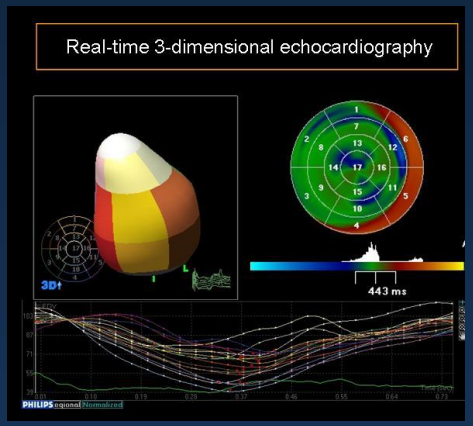


Ypenburg et al. J Am Coll Cardiol 2007

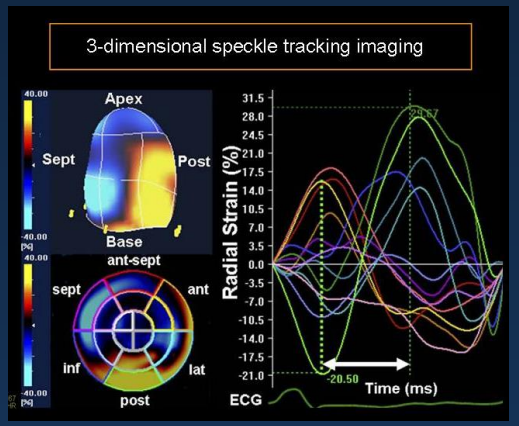
MR improvement after CRT

	Pre-CRT	Post-CRT	6 months	OFF
MR grade None/mild/mod/severe	0/0/16/9	0/10/15/0	3/8/13/0	2/2/17/3
LVEDV, mL	251±85	249±87	205±97	210±101
LVESV, mL	196±85	183±85	145±89	163±88
LVEF, %	23±8	28±9	33±10	29±10
MV tenting area, cm^2	7.8±1.0	7.2±1.0	6.7±1.2	6.9±1.3
Dyssynchrony, ms	169±69	25±26	26±28	134±51

Ypenburg et al. J Am Coll Cardiol 2007

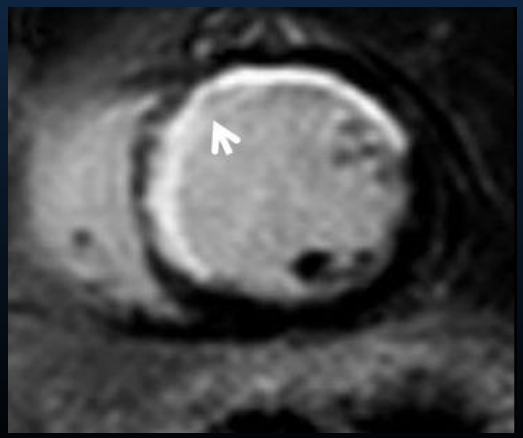


LV dysysnchrony?



CRT Response

Location and extent of scar tissue?



Suitable cardiac vein?

N = 277 HF patients treated with CRT

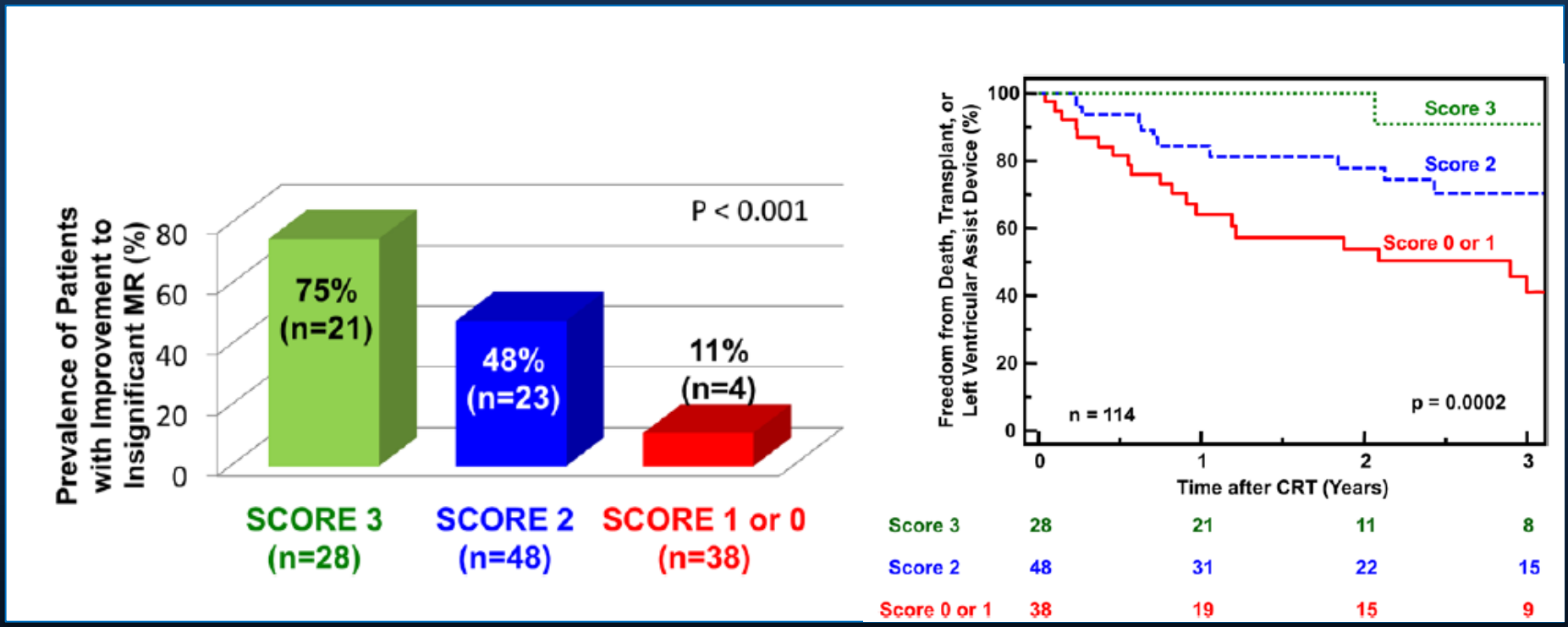
N = 114 (48%) severe MR

At 6 months follow-up ☞42% improved

Associates of MR improvement after CRT	
	OR (95% CI), p-value
LV radial dyssynchrony >200 ms	2.65 (1.1-6.3), p=0.03
LV end-systolic diameter index <29mm/m^2	2.53 (1.0-6.2), p=0.04
Papillary muscle site WMSI≤2.5	2.59 (1.0-6.3), p=0.04

Onishi et al. Circulation Heart Failure 2013

MR improvement after CRT and prognosis



Onishi et al. Circulation Heart Failure 2013

What comes first: MitraClip or CRT?

Surgery may be considered in patients with severe MR, LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.	IIb	C

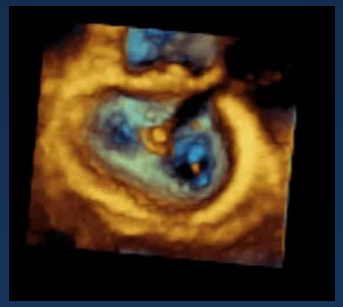
Indications for CRT in patients in sinus rhythm	Class	Level
1) LBBB with QRS duration >150 ms. CRT is recommended in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment (*)	I	A
2) LBBB with QRS duration 120-150 ms. CRT is recommended in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment (*)	I	B

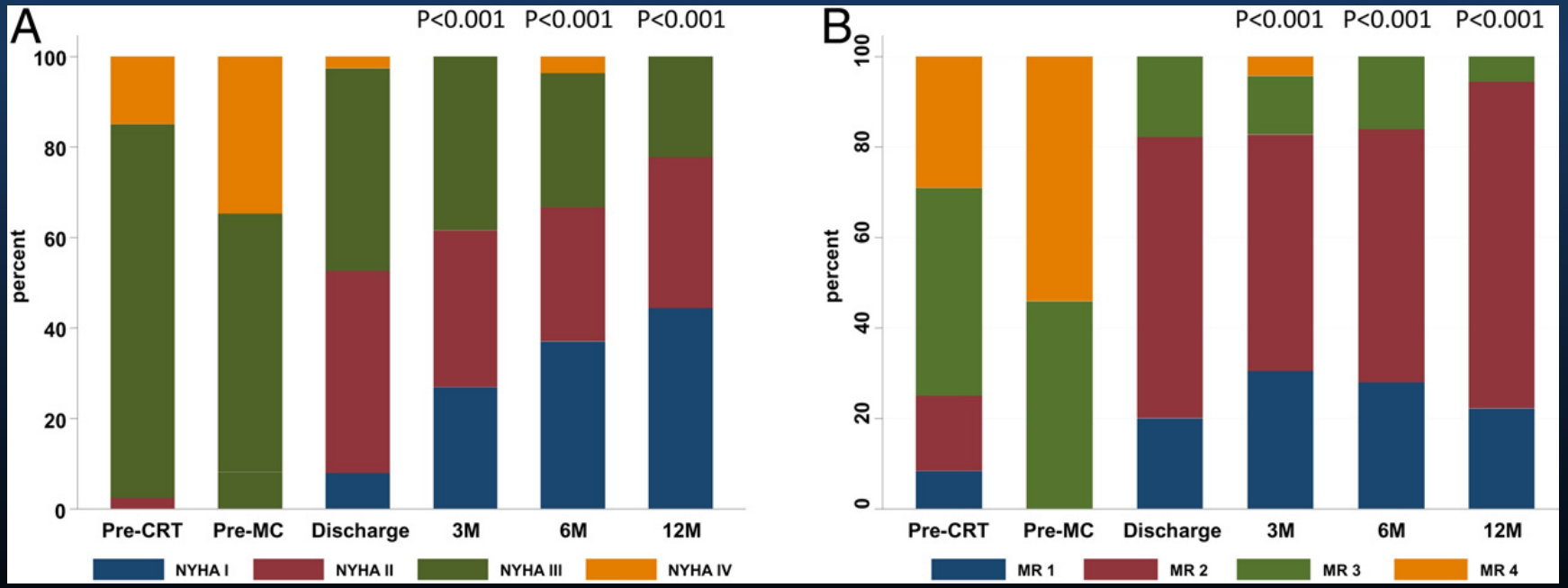
Vahanian et al. Eur Heart J 2012; Brignole et al. Eur Heart J 2013

Percutaneous treatment of MR as bail-out therapy for non-responders to CRT

PERMIT-CARE

N = 51

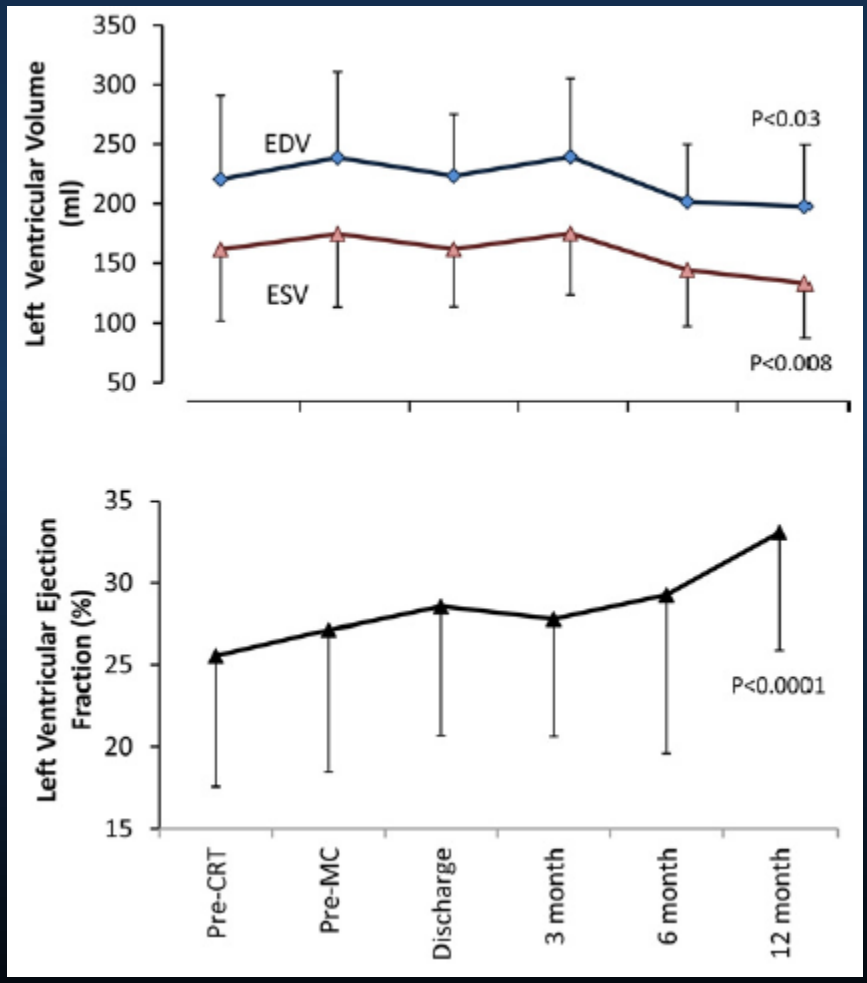




Auricchio et al. J Am Coll Cardiol 2011

Percutaneous treatment of MR as bail-out therapy for non-responders to CRT

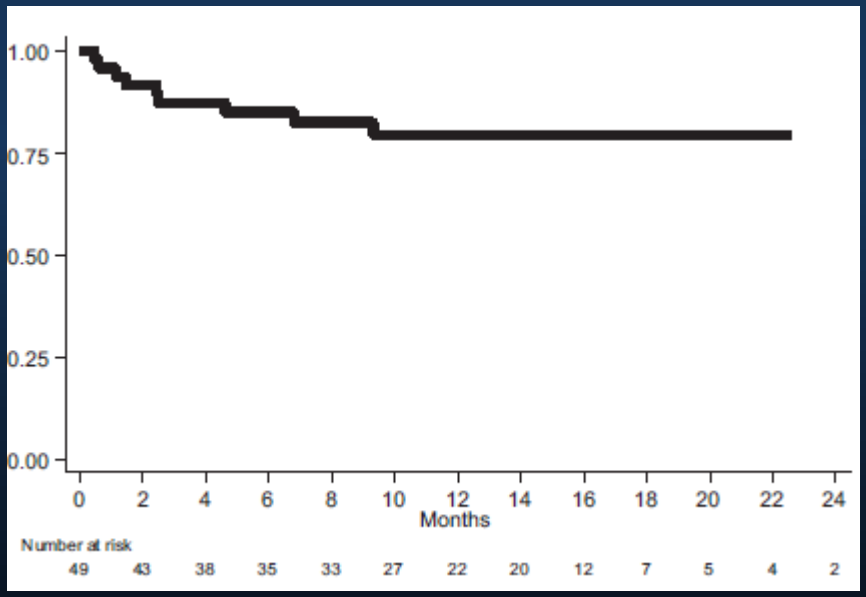
Total procedure time (min)	172.1 ± 82.9
Total device time (min)	102.8 ± 62.9
Fluoroscopy time (min)	31.6 ± 18.1
Deployment of >1 clip	25 (49)
Use of inotropic drugs	35 (67)
Complications	
Acute heart failure	7 (14)
Cardiac tamponade	1 (2)
Acute bleeding requiring transfusion	5 (10)
Urgent surgical valve repair/replacement	1 (2)
Death	1 (2)



Auricchio et al. J Am Coll Cardiol 2011

Percutaneous treatment of MR as bail-out therapy for non-responders to CRT

PERMIT-CARE



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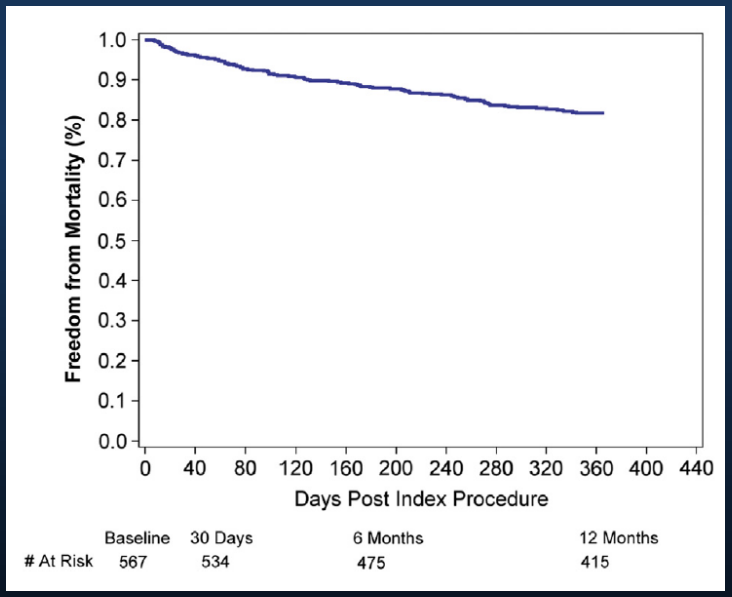
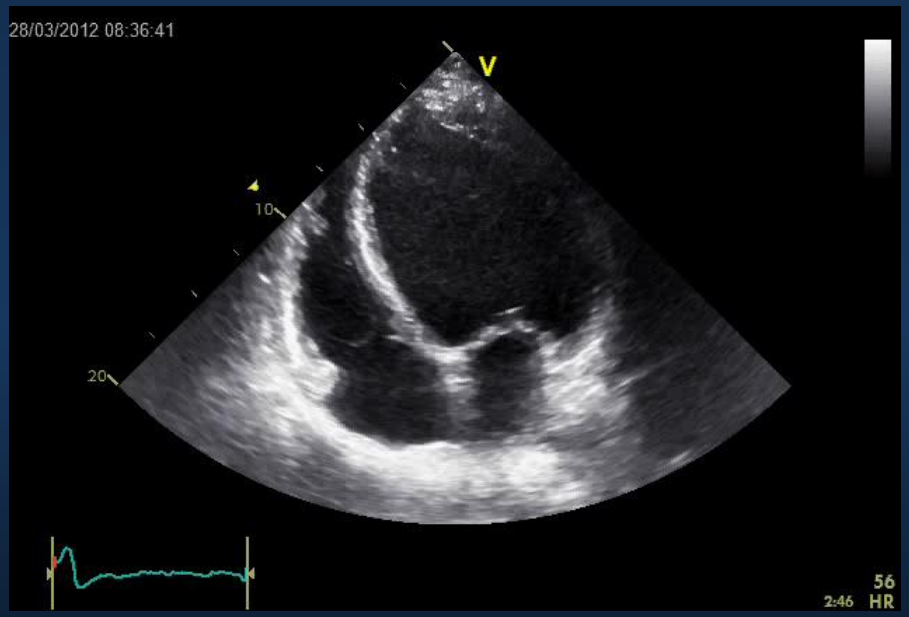
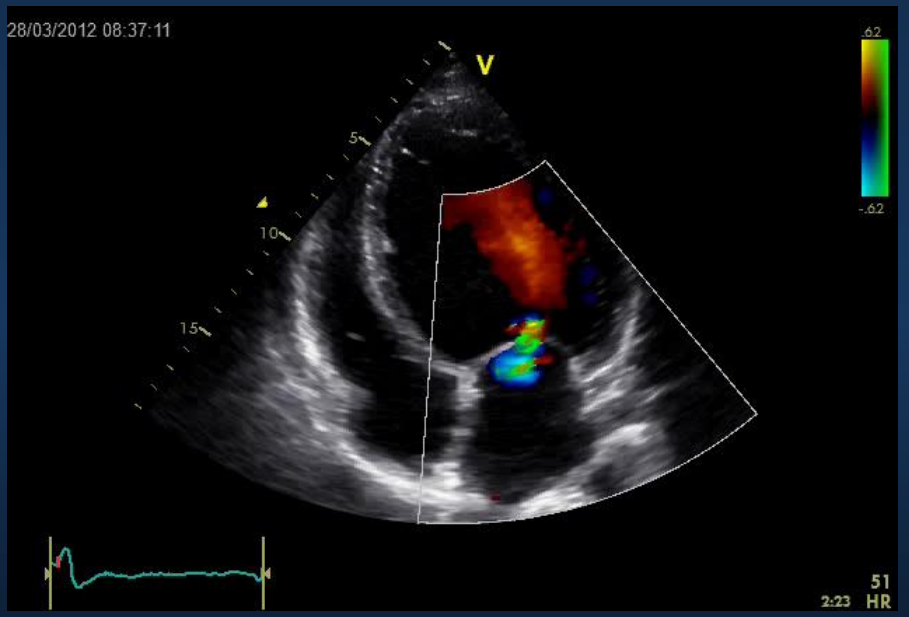


Auricchio et al. J Am Coll Cardiol 2011; Maisano et al. J Am Coll Cardiol 2013

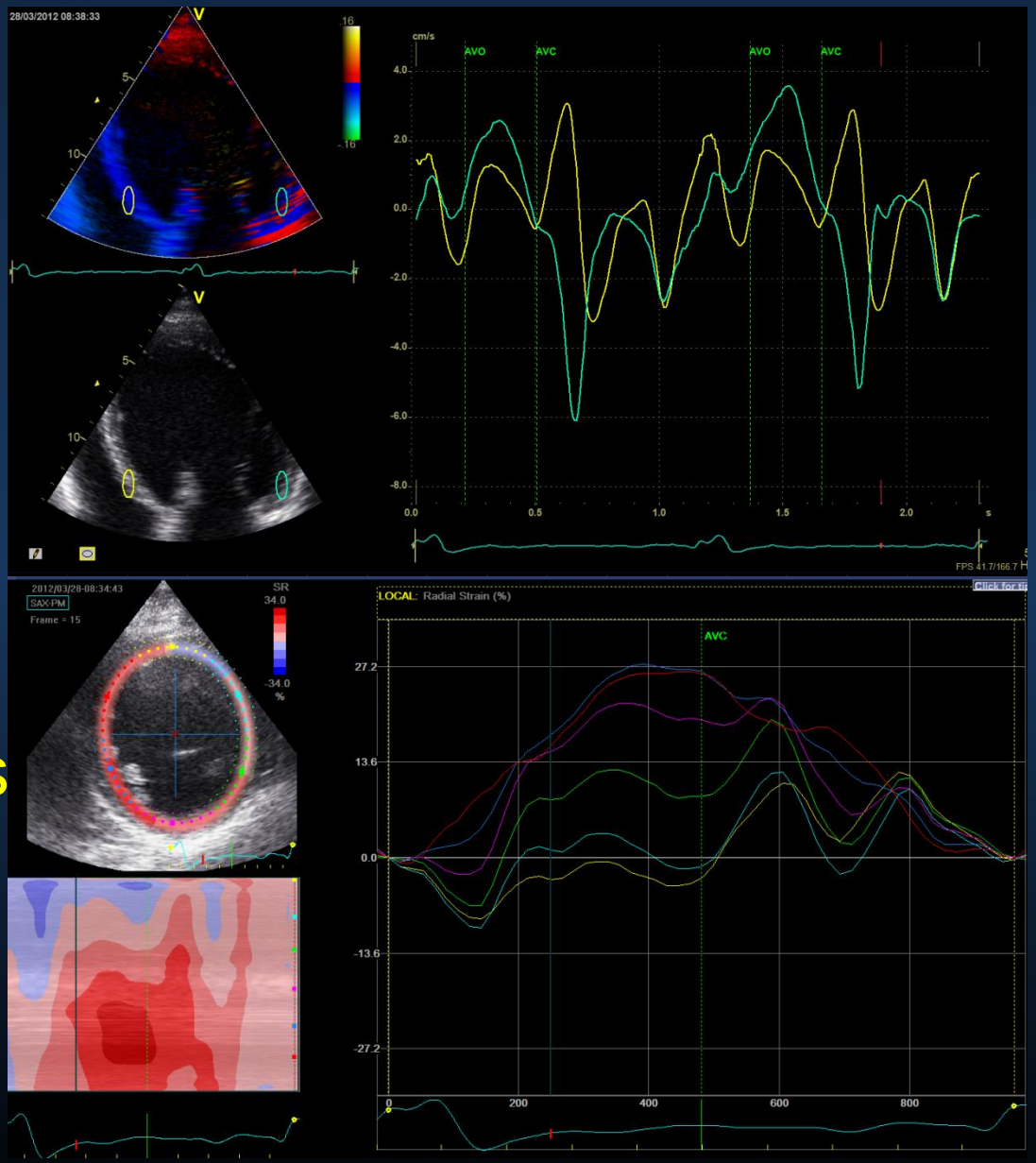
What comes first: mitraclip vs. CRT?

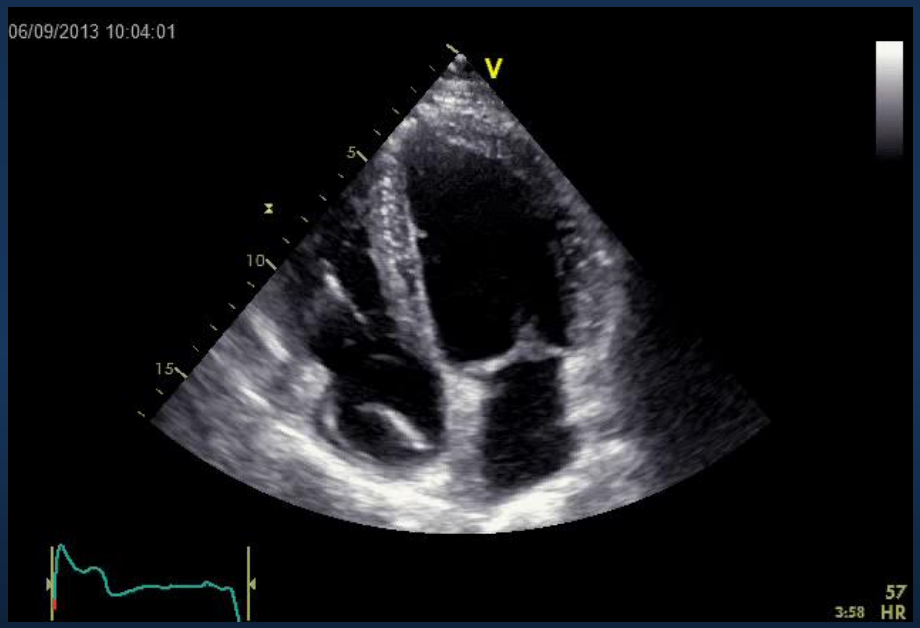


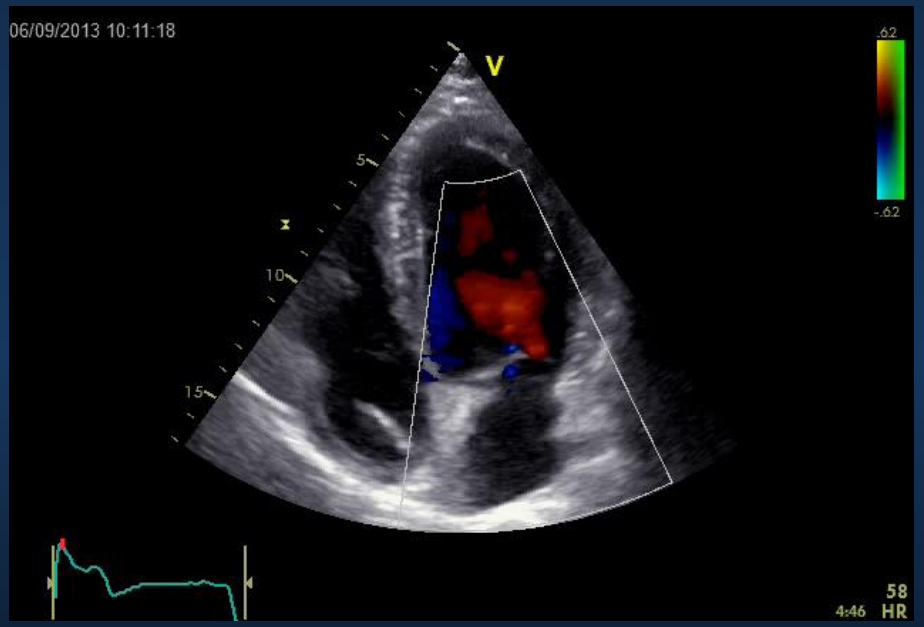


SL delay 67 ms

PPM-APM 200 ms




06/09/2013 10:04:01
V
5
10
15
57
3:58
HR


06/09/2013 10:11:18
V
.62
-.62
5
10
15
58
4:46
HR

Conclusions

- MR is frequent among patients candidates for CRT
- Response to CRT $\leftrightarrow$ Improvement in MR
  - Improvement in closign forces
  - LV reverse remodeling
  - Restoration of MV geometry
- Percutaneous mitral valve repair feasible after CRT