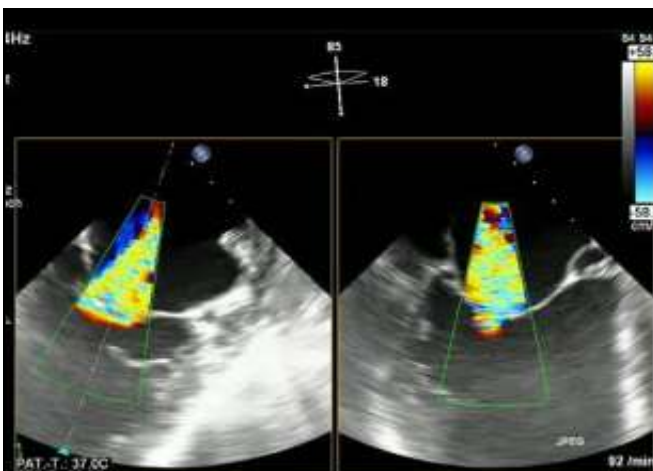


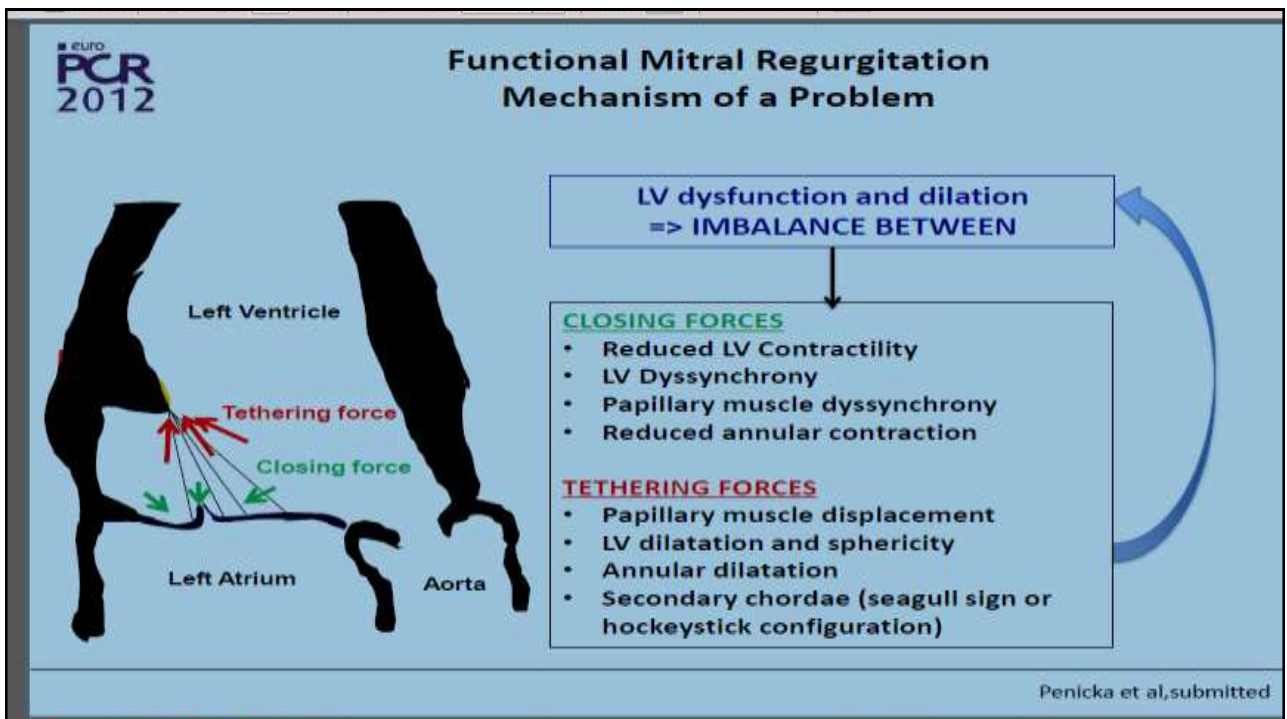
Mitraclip For Heart Failure: Who Is The Right Candidate?



49 y old male patient
 NYHA (III-) IV°
 Dilated cardiomyopathy
 EF: 15-20%
 Pro-BNP: 12169 pg/ml
 Pulmonary hypertension
 - PA_{sys} 49mmHg
 - CI 1,4 l/min/sqm
 - PVR 6 WE
 ICD System 2010
 EuroScore: 19,6%

How should this patient be treated?

- Can we estimate the prognosis in this patient?
- Should we improve the mitral regurgitation by surgery or an interventional procedure?
Will this improve prognosis?
- How effective are interventional procedures such as the edge-to-edge repair method? Other devices?
- Which patient characteristics & comorbidities will impact outcome? Which patients will benefit?
- How fit interventional procedures into established treatment strategies for heart failure?



Who Will I Refer for Mitraclip?

- Symptomatic
- Inoperable/High Risk
- Borderline indication for surgery
- Decline surgery

Borderline Surgical Indication

- MR < severe
- NYHA I – II, preserved LV
- Isolated Secondary MR, no viability or revascularisation option

"Inoperable"

- Porcelain Aorta



- Life Expectancy < 1 year

"High Risk"



Severe Kyphoscoliosis



“High Risk”

- Severe Vasculopathy
- Chest Irradiation
- Previous cardiac surgery / patent grafts
- ESRF
- Multiple pre-morbidities
- “Eyeball test”



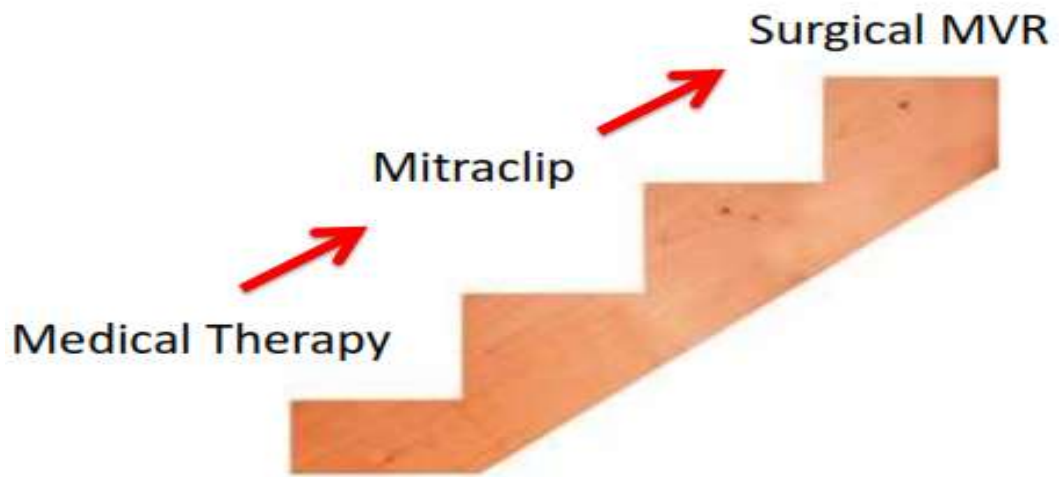
“Symptomatic”

- NYHA > I
- ≥ 1 hospitalisation for CCF
- Unacceptable Quality of Life
- Patient Expectations

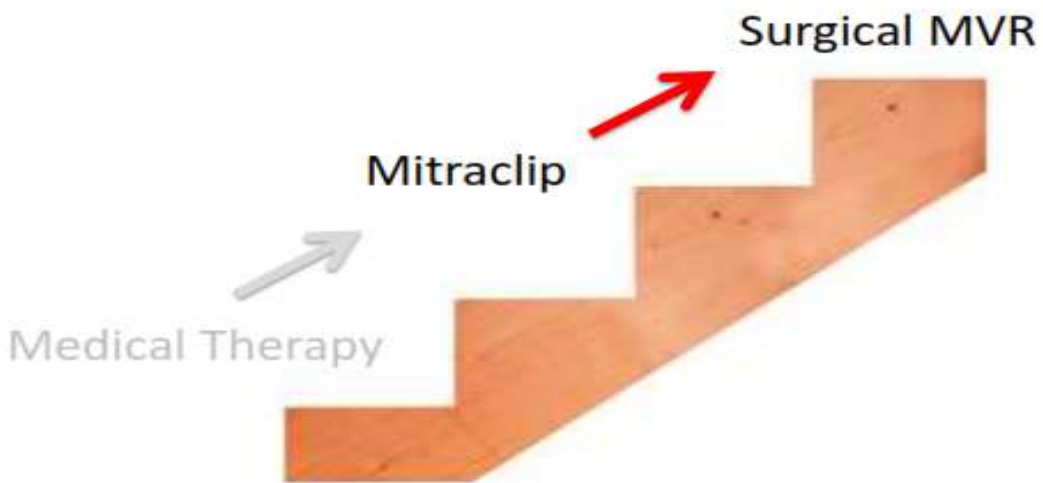
Big Step

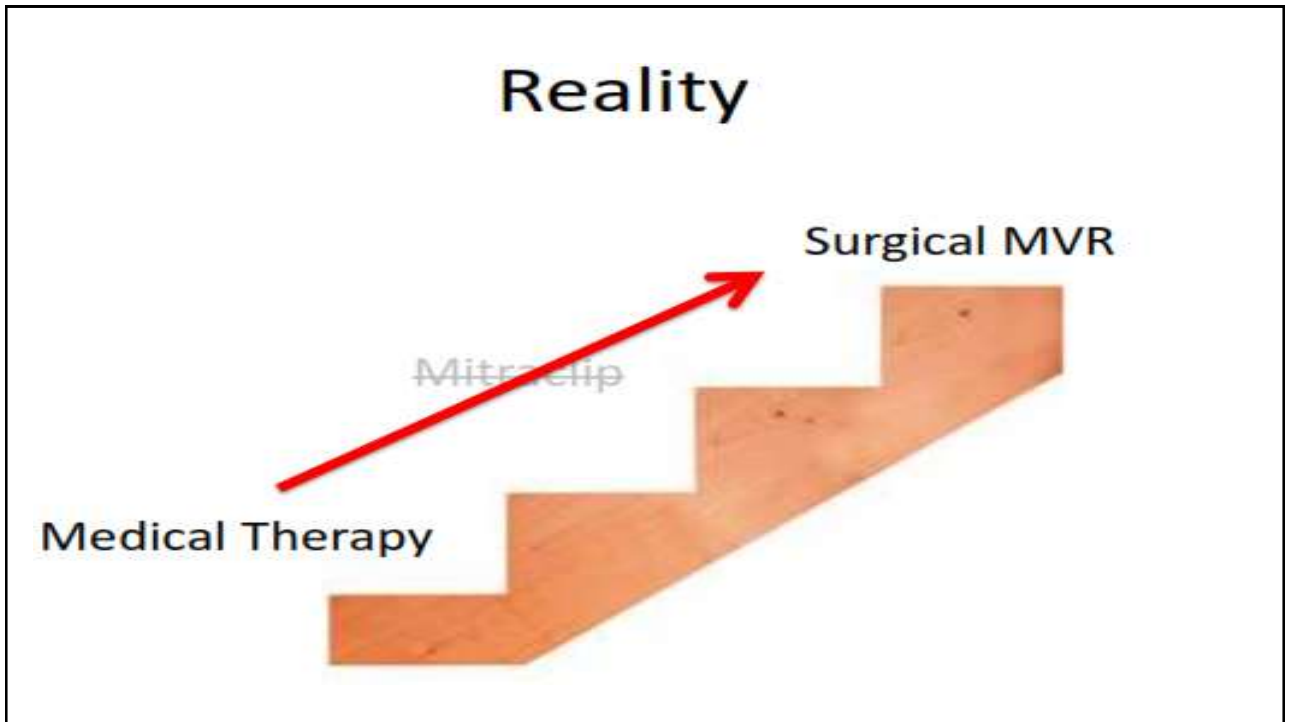


Small Steps



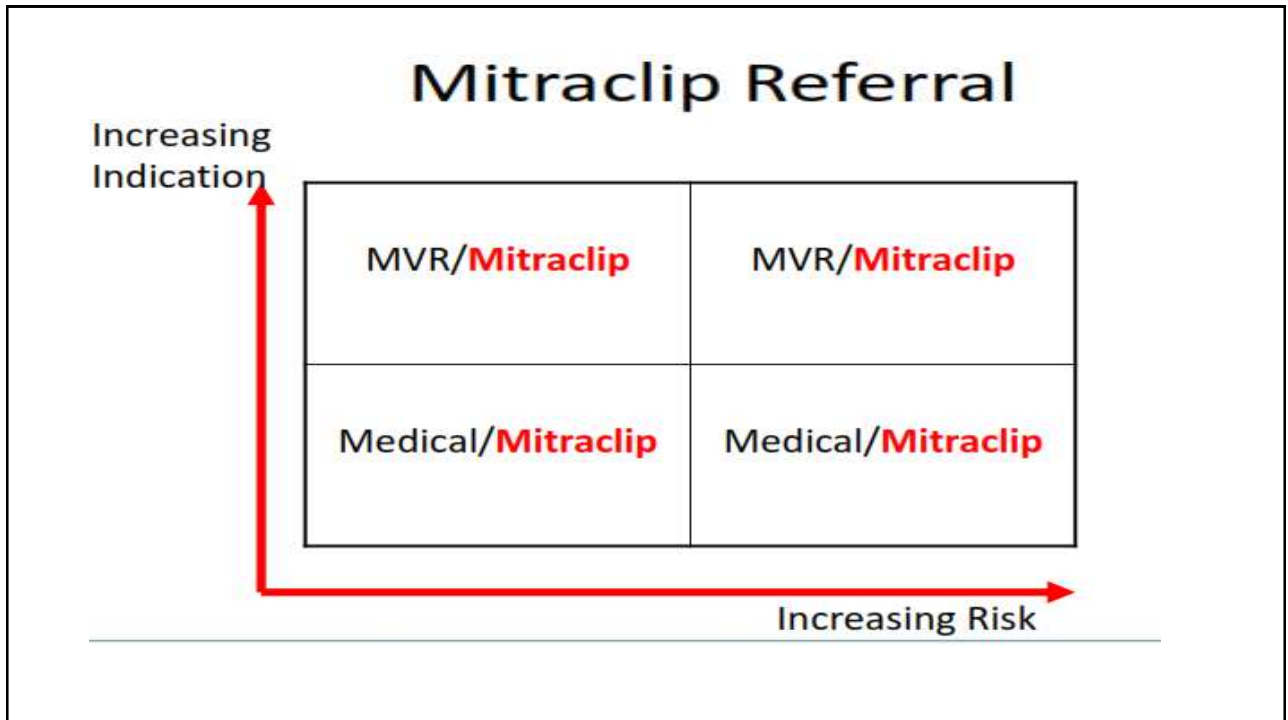
Perception





Impact on Surgical MVR

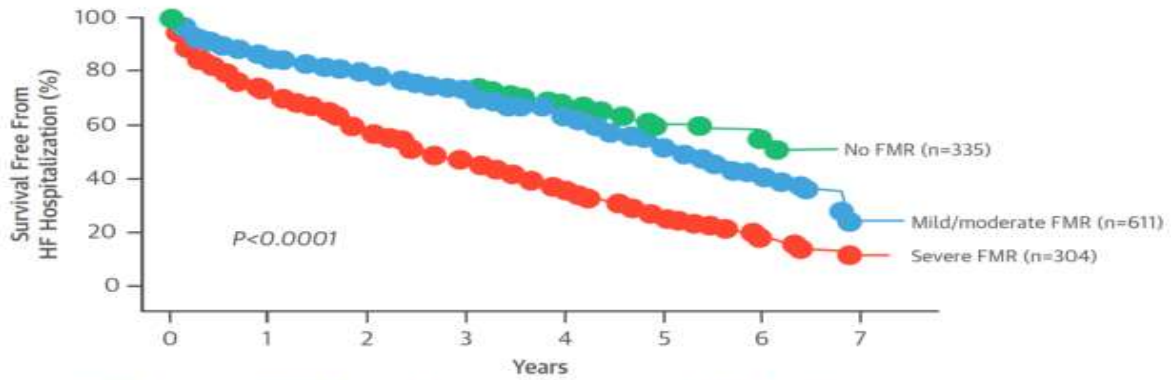
- Mitraclip programme likely to increase surgical referrals
- Patients more amenable to surgical MVR after discussing mitraclip option



Who Will I **Not** Refer for Mitraclip?

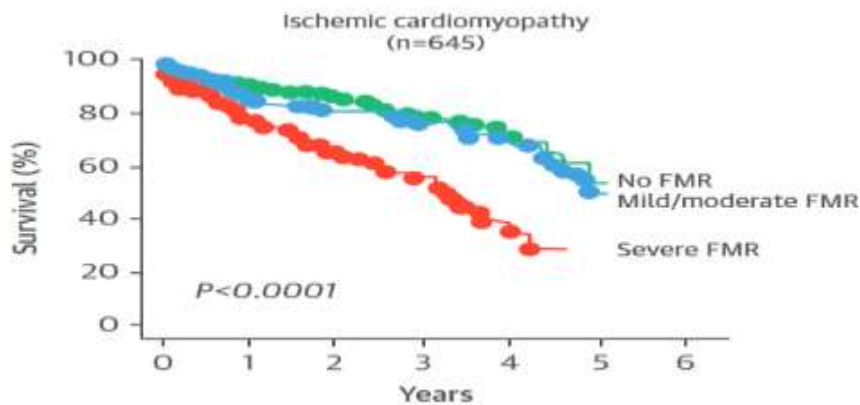
- Asymptomatic
- Complex pathology
- Patient Preference
 - (Low surgical risk, eminently repairable)

Prognosis of secondary MR



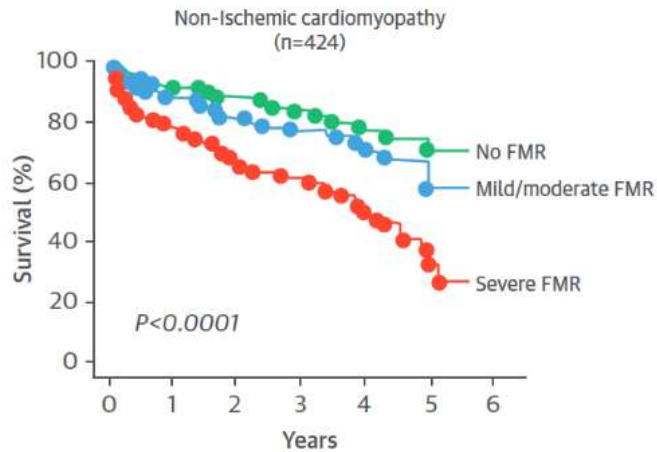
- 1256 patients with HF due to ischemic and non-ischemic dilated cardiomyopathy
- 24 % had severe secondary MR
- **Independent, powerful predictor of death or hospitalization for HF**
(HR 2.7 (95% CI 2.1 to 3.5; $p < 0.0001$))

Prognosis of secondary MR



Rossi A et al, *Heart*; 97(20), 2011

Prognosis of secondary MR



Rossi A et al, *Heart*; 97(20), 2011

Therapeutic Options

- **Goals of therapy are :**
 - ✓ to improve symptoms and quality of life
 - ✓ to reduce HF hospitalizations
 - ✓ to improve survival

- **To date, the most effective therapies target the causal LV dysfunction:**
 - ✓ GDMT for HF (Beta blockers, ACEi, aldosterone antagonists)
 - ✓ CRT with biventricular pacing
 - ✓ Revascularization (large ischemia, viability)

Therapeutic Options

• Recommendations for surgical treatment :

| Recommendations | COR | LOE |
|---|-----|-----|
| MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR | IIa | C |
| MV surgery may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D) | IIb | B |

Therapeutic Options

• Recommendations for surgical treatment :

| | Class ^a | Level ^b |
|--|--------------------|--------------------|
| Surgery is indicated in patients with severe MR ^c undergoing CABG, and LVEF >30%. | I | C |
| Surgery should be considered in symptomatic patients with severe MR, LVEF <30%, option for revascularization, and evidence of viability. | IIa | C |
| 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 |

2012 ESC/EACTS Valvular Heart Disease Guidelines

Therapeutic Options

• Large-scale MitraClip registries :

| Registry (Ref. #) | N | Mean Age (yrs) | NYHA Functional Class III/IV | FMR Etiology | ≤2+ MR Post | Procedural Success* |
|-----------------------------|-------|----------------|------------------------------|--------------|-------------|---------------------|
| | | | | | | |
| TRAMI (90) | 1,064 | 75 | 87% | 71% | 96% | 95% |
| ACCESS-EU (91) | 567 | 78 | 85% | 77% | 91% | 99.6% |
| European Sentinel (92) | 628 | 74 | 86% | 72% | 98% | 95% |
| EVEREST II and REALISM (93) | 351 | 76 | 85% | 70% | 86% | – |

Therapeutic Options

• Recommendations for transcatheter treatment:

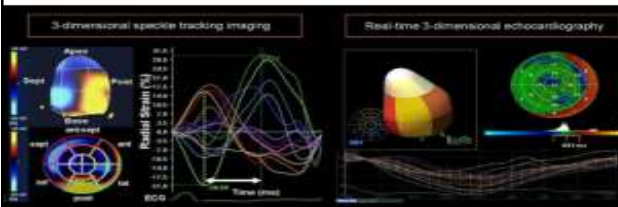
Percutaneous mitral valve repair provides a less invasive alternative to surgery but is not approved for clinical use in the United States

2014 ACC/AHA Valvular Heart Disease Guidelines

The MitraClip procedure may be considered in patients with symptomatic severe secondary MR despite optimal GDMT, judged inoperable or at high surgical risk by the heart team

recommendation **Class IIb**, level of evidence **C**

CRT responders and Mitralinsufficiency



Mechanism MR improvement after CRT:

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



Three **echocardiographic** features associated with amelioration of significant MR after CRT :

N=277, QRS >120 ms, EF <35%

1. anteroseptal to posterior wall radial strain dyssynchrony >200 ms,

2. lack of Natural history CRT non responders, NYHA III
Ypenburg et al; JACC 2009

3. lack of Mortality@3Y **30-75%**
Onishi et

CRT **NON**-responders and Mitralinsufficiency

Role of MitraClip



FOCUS ISSUE: STRUCTURAL HEART DISEASE

Clinical Research

Correction of Mitral Regurgitation in Nonresponders to Cardiac Resynchronization Therapy by MitraClip Improves Symptoms and Promotes Reverse Remodeling

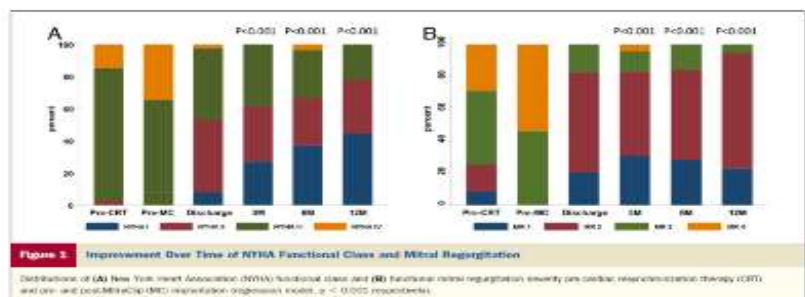
Angelo Auricchio, MD, PhD,* Wolfgang Schillinger, MD,† Sven Meyer, MD,‡
 Francesco Maisano, MD,§ Rainer Hoffmann, MD,|| Gian Paolo Ussia, MD,¶
 Giovanni B. Pedrazzini, MD,* Jan van der Heyden, MD,# Simona Fratini, MD, PhD,**
 Catherine Klersy, MD, MSc,†† Jan Komtebedde, DVM,* Olaf Franzen, MD,‡
 on behalf of the PERMIT-CARE Investigators

Lugano, Switzerland; Göttingen, Hamburg, and Aachen, Germany;
 Milan, Catania, L'Aquila, and Pavia, Italy; and Nieuwegein, the Netherlands

Permit-Care – CRT non-responders

- Prospectively conducted survey reporting the outcomes in 51 symptomatic patients consecutively treated with the MitraClip at 7 European institutions with CRT for at least 6 months and remained classified as NYHA functional class III or IV.

| Table 1 Demographic Characteristics (N = 51) | |
|--|---------------------|
| Age (yrs) | 70.26 ± 9.58 |
| Male | 44 (89) |
| Diagnosis (%) | |
| Ischemic cardiomyopathy | 37 (73) |
| Nonischemic cardiomyopathy | 14 (27) |
| Previous infarction (%) | |
| CAD or PVD | 24 (47) |
| Valve surgery | 4 (8) |
| New York Heart Association functional class | |
| III | 32 (63) |
| IV | 17 (33) |
| Previous CRT-D (%) | 47 (92) |
| CRT-P | 4 (8) |
| Comorbidities | |
| Previous stroke | 8 (16) |
| Diabetes | 11 (22) |
| CORD | 15 (29) |
| Renal insufficiency | 30 (70) |
| Logistic EuroSCORE | 29.7 ± 19.4 |
| STS score | 13.9 ± 14.5 |
| Laboratory findings | |
| Creatinine (μmol/l) | 149.5 ± 63.2 |
| Sodium (mmol/l) | 139.74 ± 4.2 |
| Potassium (mmol/l) | 4.25 ± 0.43 |
| Hemoglobin (g/l) | 132.34 ± 1.5 |
| NT-proBNP (ng/l) | 3,702 (1,794–8,248) |
| Match since CRT | 32.9 ± 26.7 |



Auricchio A et al; PERMIT-CARE Investigators. Correction of Mitral Regurgitation in Nonresponders to Cardiac Resynchronization Therapy by MitraClip Improves Symptoms and Promotes Reverse Remodeling. *J Am Coll Cardiol*. 2011 Nov 15;58(21):2183-9.

MitraClip intervention improves survival in Heartfailure patients

JACC: CARDIOVASCULAR INTERVENTIONS
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VOL. 7, NO. 8, 2014
ISSN 1936-8796/\$36.00
<http://dx.doi.org/10.1016/j.jcin.2014.07.171>

STRUCTURAL

Survival of Transcatheter Mitral Valve Repair Compared With Surgical and Conservative Treatment in High-Surgical-Risk Patients

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Jan A. S. Van der Heyden, MD, PhD*



Chronic secondary MR

- **Class I**
 - Medical heart failure therapy (diuretics, betablockers, ACE-I/ARBs)
 - Cardiac resynchronization therapy, (if indicated)
- Mitral repair/replacement is equivalent

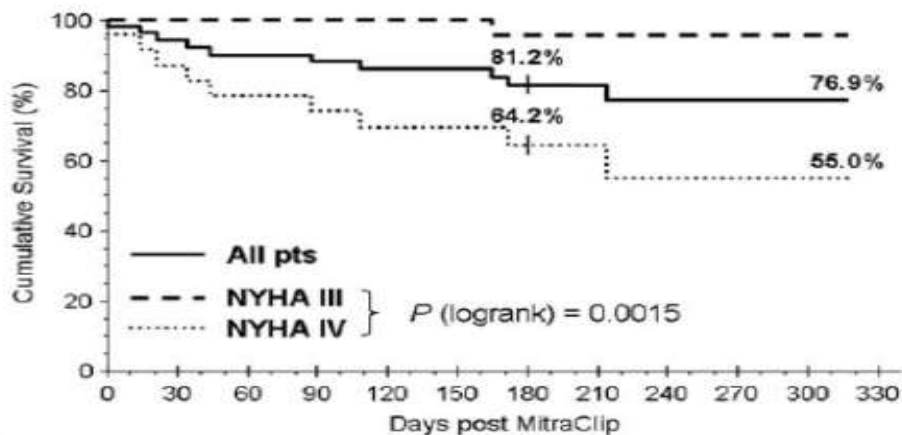
- **Class II**

| Recommendations | COR | LOE |
|--|-----|-----|
| MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR | IIa | C |
| MV surgery may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D) | IIb | B |
| MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery | IIb | C |

ACC/AHA guidelines 2014

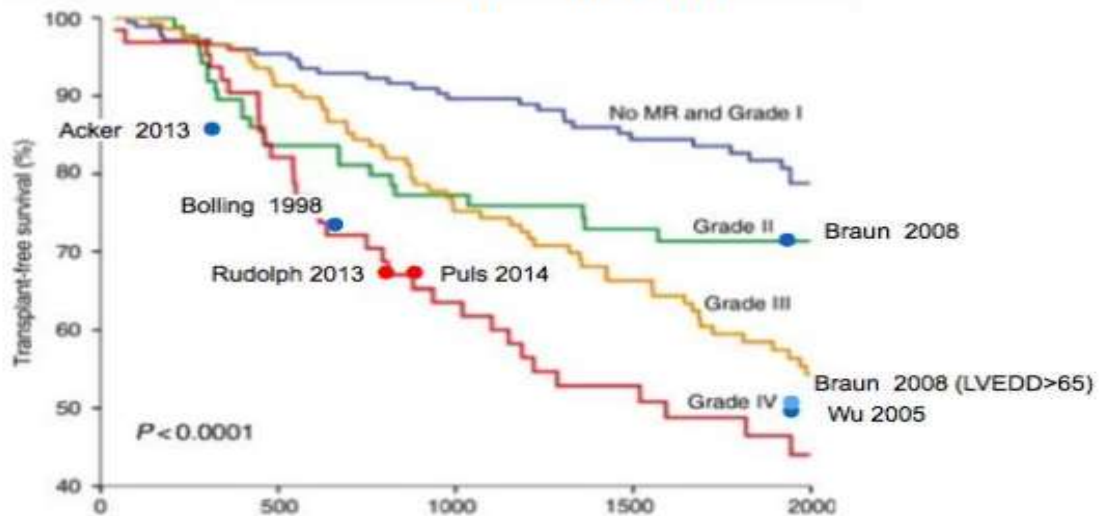
Survival after MitraClip therapy in end stage heart failure

N=50
MR III-IV°
EF < 25%



Survival after mitral valve reconstruction¹

Functional MR



Conclusion

- Secondary MR is a strong, independent predictor of worse prognosis in patients with HF, whatever the etiology
- GDMT, CRT and/or revascularization if indicated are the keystone of therapeutic options
- For persistent severe secondary MR, MV surgery or transcatheter MV repair are feasible and their respective indications have to be discussed by a multidisciplinary heart team including HF specialists, interventional cardiologists, cardiac surgeons, imaging experts.
- However neither MV surgery nor MitraClip therapy have demonstrated that they could modify the natural evolution of the underlying LV disease and that they could improve survival.
- Ongoing randomized trials (COAPT, RESHAPE-HF, MITRA-FR) will hopefully help to clarify MitraClip indication for such patients