MitraClip in the Management of Heart Failure

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Disclosure

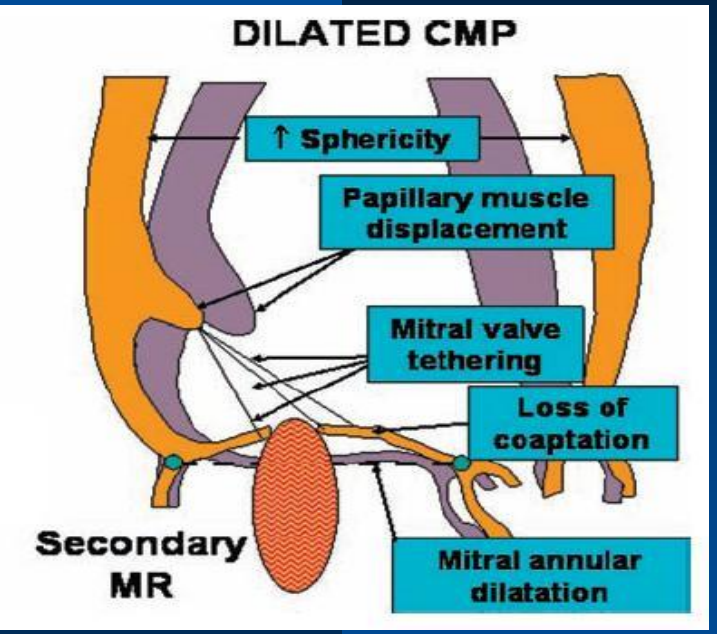
Consultancy fees and speaker's honoraria from:

ABBOTT VASCULAR

The Conundrum of Functional Mitral Regurgitation

- **Definition and Epidemiology**
  - ***Dimension of the problem***
- **Pathophysiology**
- **Clinical Consequences**
  - ***Natural history***
- **Management Options**
  - ***How and when to intervene ?***
  - ***Role of MitraClip***

Functional Mitral Regurgitation - definition



Secondary MR = 'functional MR' – valve leaflets and chordae are structurally normal and MR results from geometrical distortion of the subvalvular apparatus, secondary to LV enlargement and remodelling due to idiopathic cardiomyopathy or CAD

ESC Guidelines 2012

Functional MR - ventricular disease, characterized by restricted mitral valve leaflet motion in the setting of segmental wall motion abnormalities or dilated cardiomyopathies or normal leaflet motion in the setting of annular dilatation and LV dysfunction

Punnoose L et al. J Card Fail 2014

Functional Mitral Regurgitation - epidemiology

- HF patients who underwent cardiac catheterization; N=2057;
  MR: mild – 39%, moderate-severe – 17%

  Trichon BH et al. Am J Cardiol 2003;91:538-43

- patients with incident MI; echo within 30 days; N=773;
  MR: mild – 38%, moderate-severe – 12%

  Bursi F et al. Circulation 2005;111:295-301

- HF outpatients; N=469;
  MR: grade 1-2 – 51%, grade 3-4 – 45%

  Bursi F et al. Eur J Heart Fail 2010;12:382-388

- CRT recipients; N=794;
  MR: mild-moderate – 36-73%, advanced – 17-54%

  Di Biase L et al. Europace 2011;13:829-38

The Conundrum of Functional Mitral Regurgitation

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  - ***Dimension of the problem***
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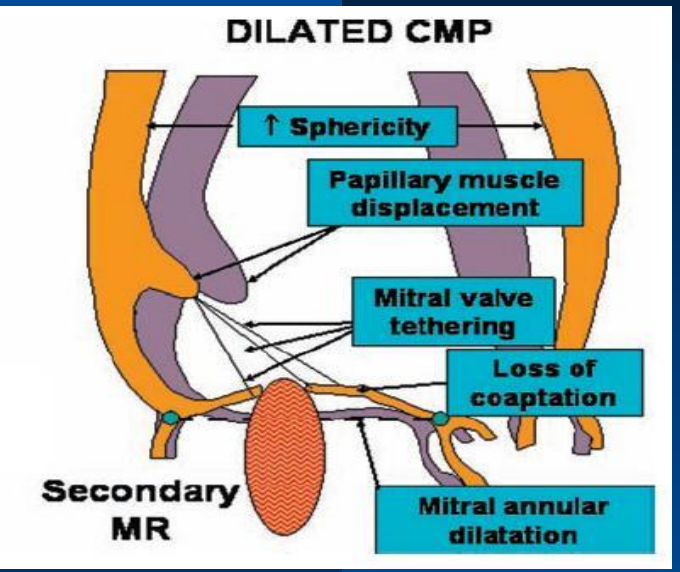
Functional Mitral Regurgitation – pathophysiology



Myocardial damage

↓

LV remodeling
- LV dilation
- ↑ LV sphericity
- local remodeling of MV apparatus

↓ → **FMR**

↓

LV dysfunction
HF symptoms

- Volume overload
- ↑LV wall stress
- ↑ workload

FMR begets LV remodeling
LV remodeling begets FMR

FMR contributes to LV dysfunction

Is this concept proven ?

The Conundrum of Functional Mitral Regurgitation

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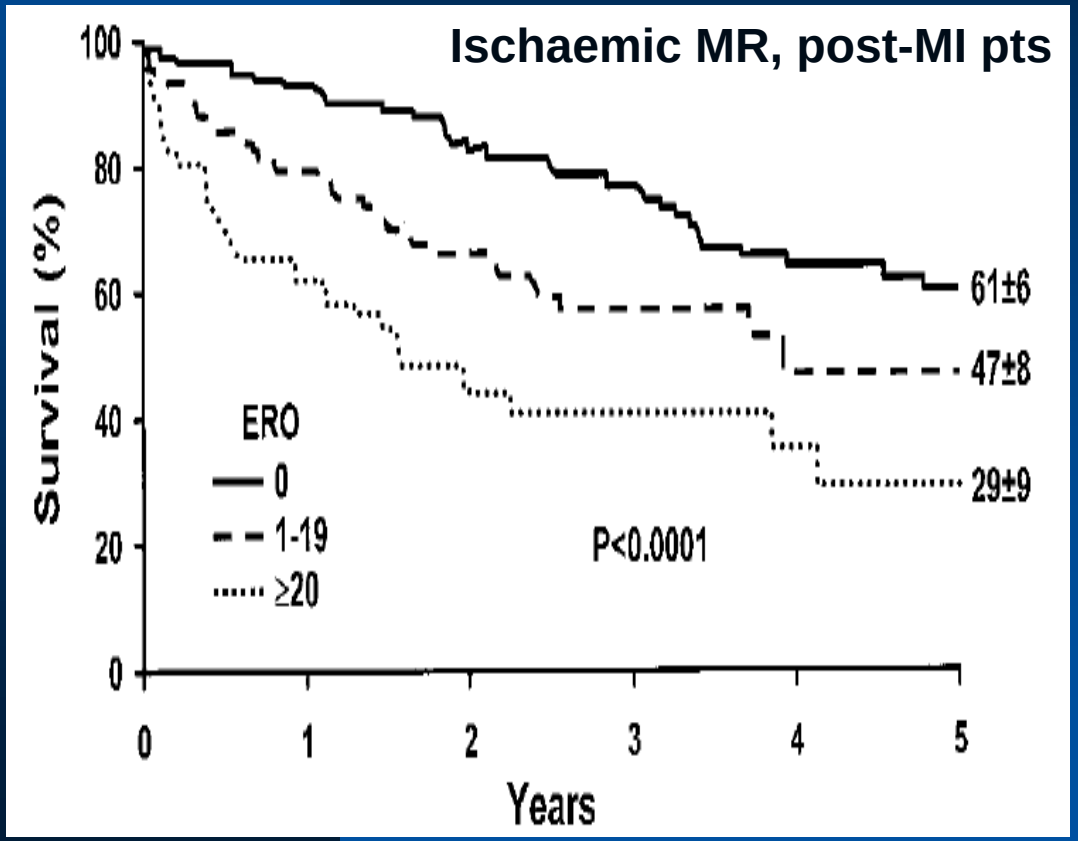
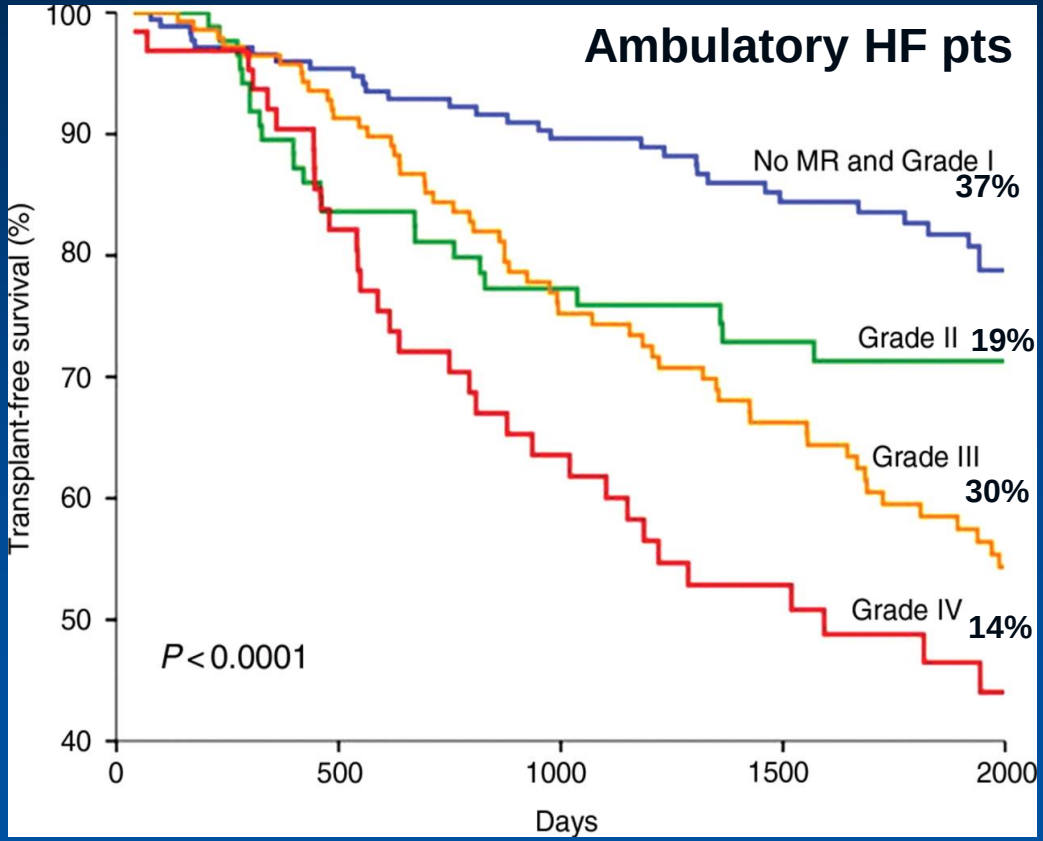
Functional Mitral Regurgitation – clinical consequences

FMR in ischemic & non-ischemic cardiomyopathies is associated with more severe symptoms and predicts (independently) poor outcome





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

Bursi F et al. Eur J Heart Fail 2010;12:382-388

The Conundrum of Functional Mitral Regurgitation

- **Epidemiology**
  - ***Dimension of the problem***
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Primary vs functional MR:
key question for the current management

- **Primary MR** – derangement of one or more components of MV itself

  MR → LV volume overload → remodeling with subsequent clinical consequences

  „correction of primary MR in a timely fashion reverses these consequences"

- **Functional MR** – damaged LV causes MR

  „primarily a ventricular problem it is less obvious that correcting the MR by itself will be curative or even beneficial"

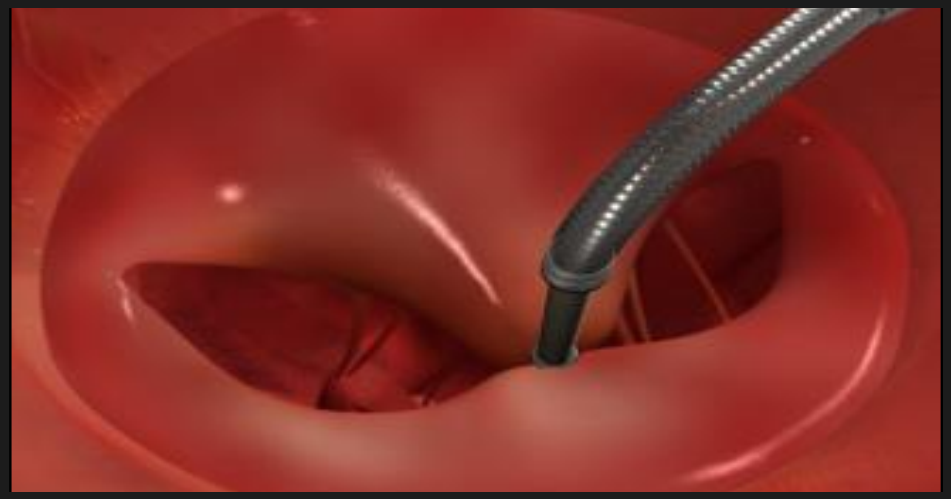
Carabello BA, JACC 2008;52:319-26

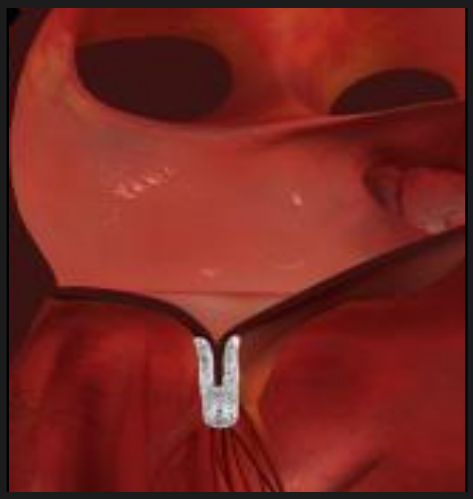
The Conundrum of Functional Mitral Regurgitation

- **Epidemiology**
  - *Dimension of the*
- **Pathophysiology**
- **Clinical Consequ**
  - *Natural history*
- **Management Options**
  - *How and when to intervene ?*

- **Optimal medical therapy**
  - **comorbidities**
- ***CRT***
- ***Surgery***
  - ***MV surgery***
  - ***Surgical treatment of LV***
- ***Percutaneous techniques***

Percutaneous Mitral Valve Repair
MitraClip® System





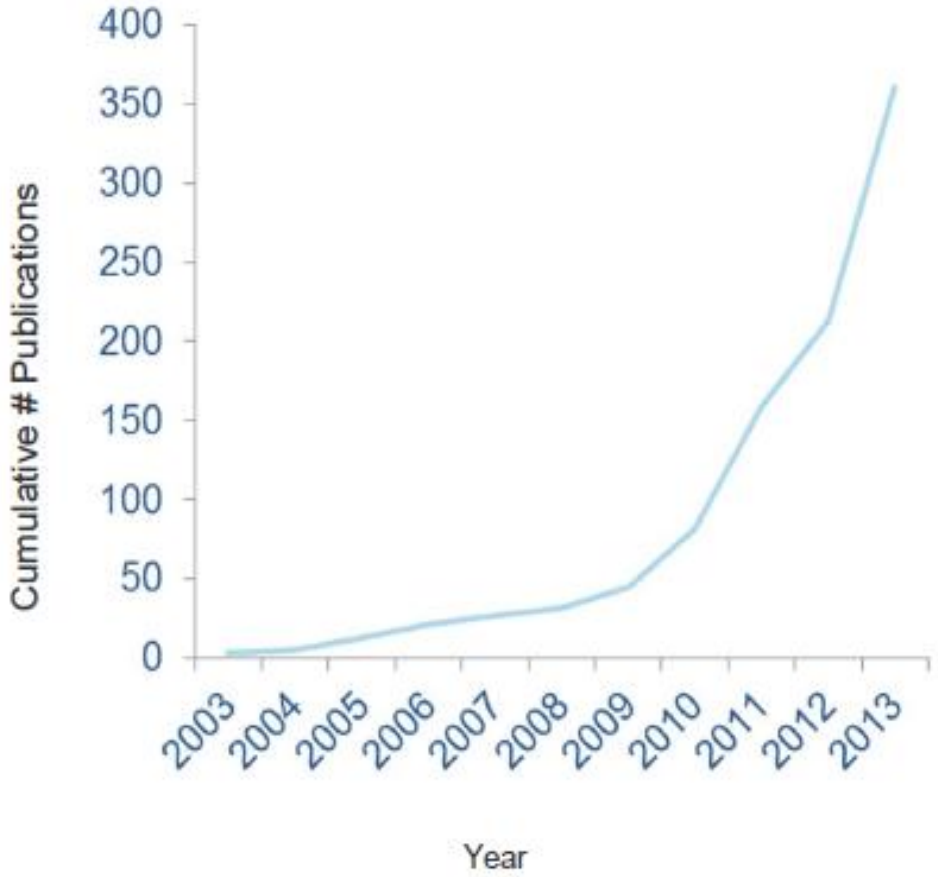
Worldwide Clinical Experience

- Over 12,000 patients have been treated with the MitraClip Therapy worldwide.[1]
  - 75% are considered high risk* for mitral valve surgery
  - 67% have functional mitral regurgitation (MR)
  - 96% Implant Rate
- The use of the MitraClip is supported by a rigorous clinical trial program.[1]
  - 50% are considered high risk* for mitral valve surgery
  - 60% have functional MR

1. Data as of 30/01/2014. Source: Abbott Vascular.
* Determination of high surgical risk based on: logistic EuroSCORE ≥ 20%, or STS calculated mortality ≥ 12%, or pre-specified high surgical risk co-morbidities specified in EVEREST II High Risk Study protocol.

Growing Number of Clinical Publications

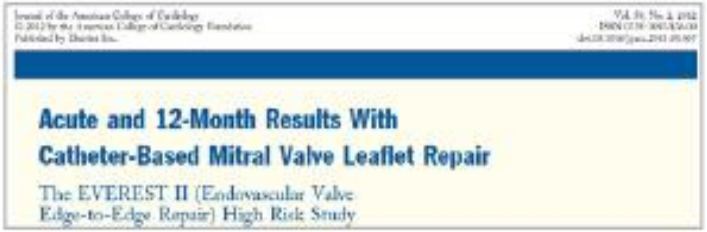
361 total publications on MitraClip therapy (2003-2013)




The NEW ENGLAND JOURNAL of MEDICINE

APRIL 14, 2011

Percutaneous Repair or Surgery for Mitral Regurgitation


Acute and 12-Month Results With Catheter-Based Mitral Valve Leaflet Repair

The EVEREST II (Endovascular Valve Edge-to-Edge Repair) High Risk Study


ESC/EACTS GUIDELINES

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)

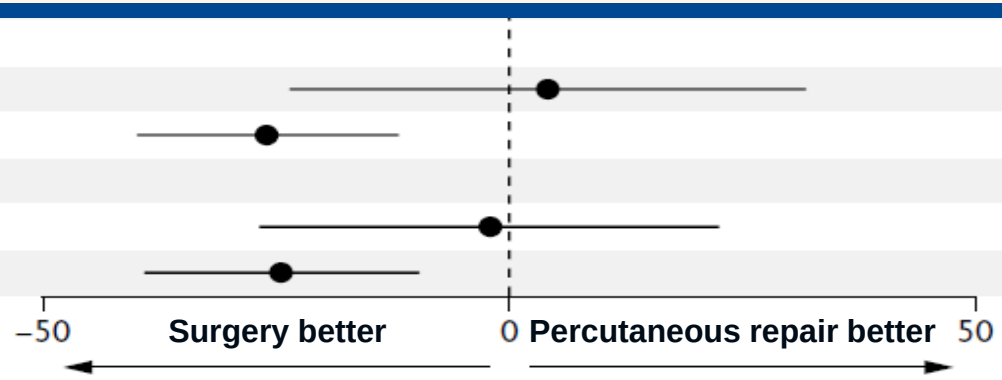

MitraClip therapy in daily clinical practice: initial results from the German transcatheter mitral valve interventions (TRAMI) registry

MitraClip as therapeutic option for MR first (and strong) evidence

EVEREST II: 279 patients with moderately severe or severe (grade 3+ or 4+) MR randomized in a 2:1 ratio to percutaneous repair or conventional surgery
LVEF – 60%, functional MR – 27%

Event	12 months	Percutaneous Repair	Surgery	P Value
		no. (%)		
Primary efficacy end point				
Freedom from death, from surgery for mitral-valve dysfunction, and from grade 3+ or 4+ mitral regurgitation†		100 (55)	65 (73)	0.007
Death		11 (6)	5 (6)	1.00
Surgery for mitral-valve dysfunction‡		37 (20)	2 (2)	<0.001
Grade 3+ or 4+ mitral regurgitation		38 (21)	18 (20)	1.00

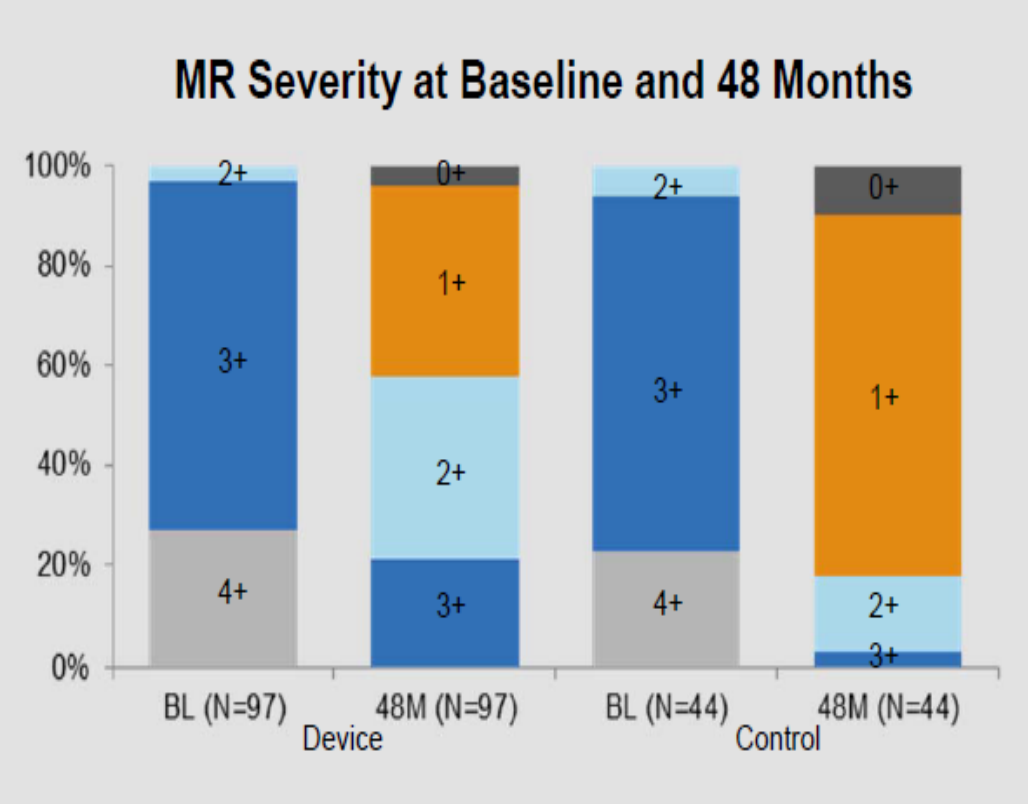
MR			
Functional	26/48 (54)	12/24 (50)	0.02
Degenerative	74/133 (56)	53/65 (82)	
LVEF			0.06
<60%	35/68 (51)	15/28 (54)	
≥60%	64/111 (58)	50/61 (82)	

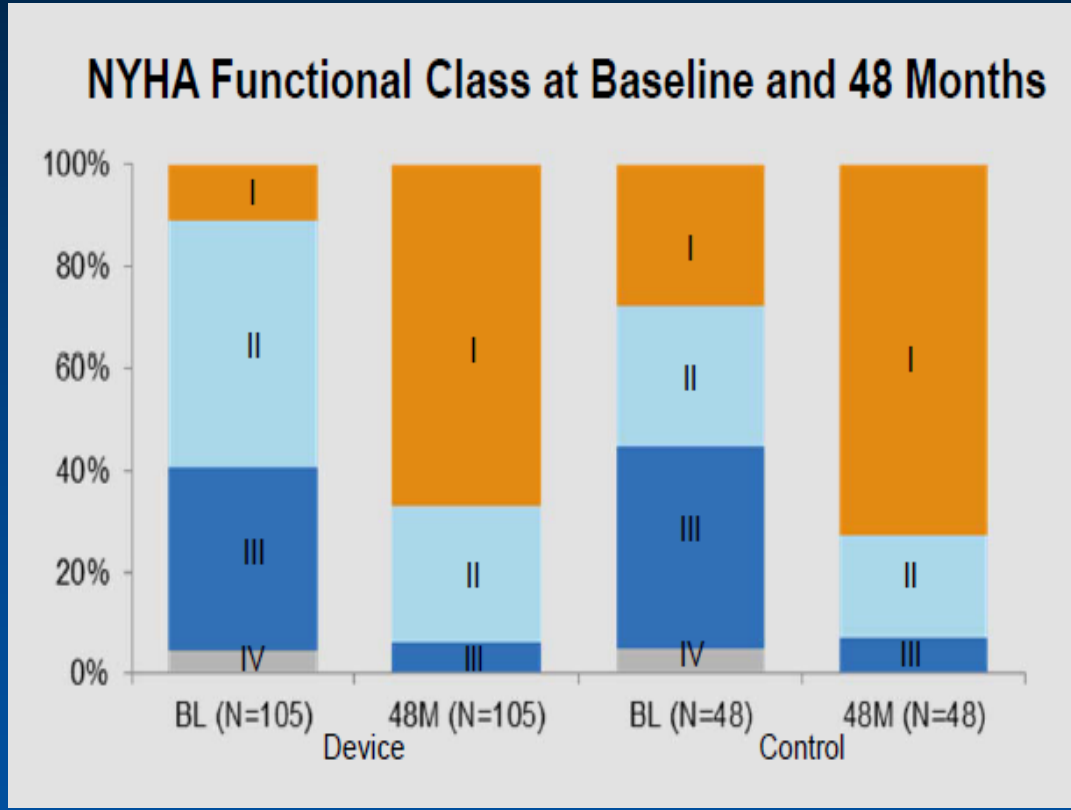


Feldman T et al., N Engl J Med 2011

MitraClip as therapeutic option for MR first (and strong) evidence

EVEREST II: 4-year results



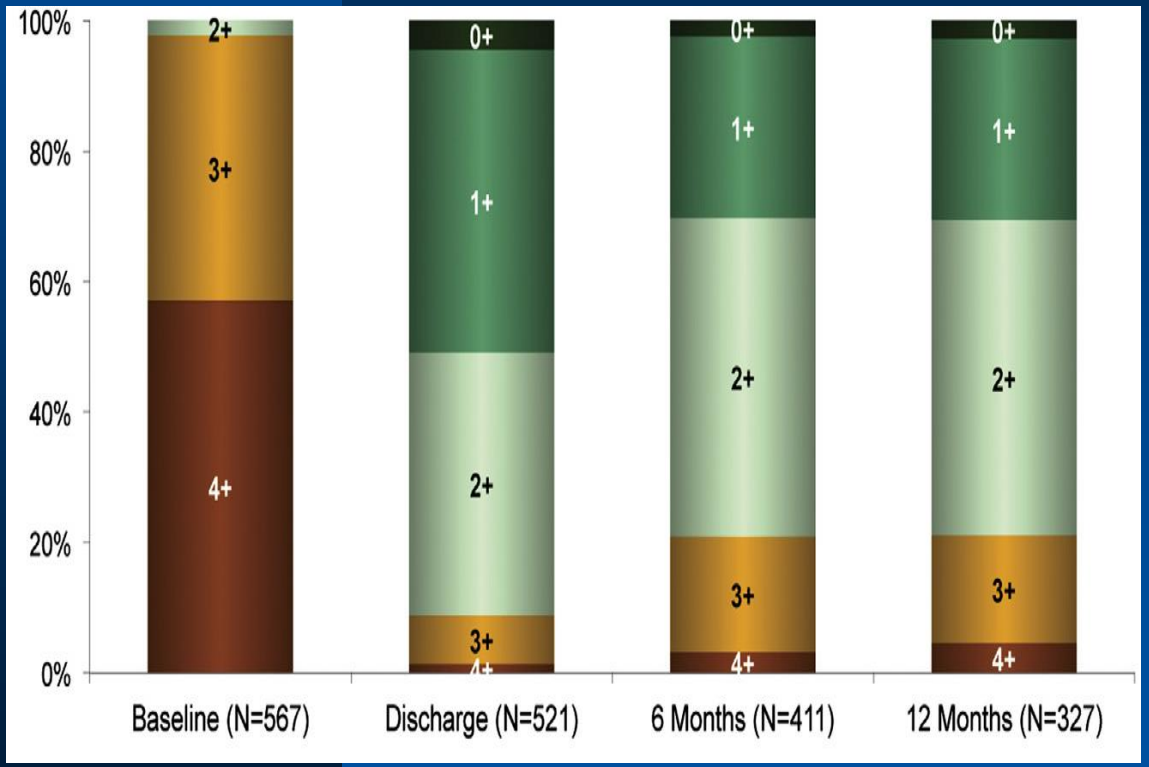


Sustained clinical benefits comparable to those after surgery
Improvement in MR durable through 4 years

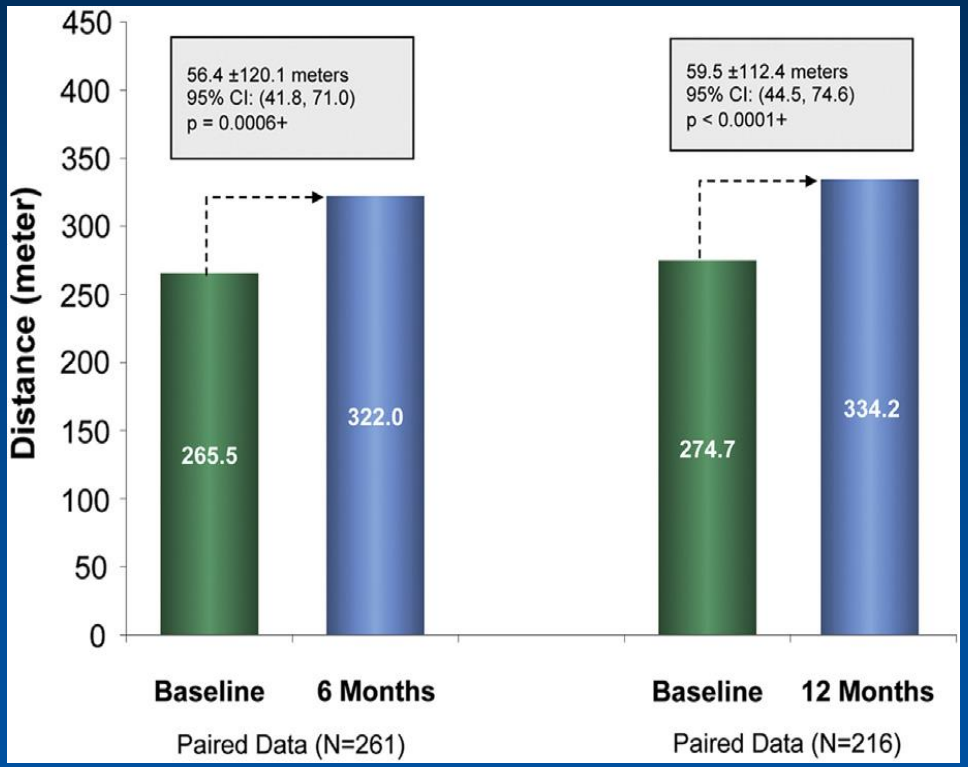
Mauri et al., JACC (in press)

MitraClip as therapeutic option for MR Real World Experience

ACCESS-EU: 567 pts with significant MR who underwent MitraClip therapy at 14 European sites; 69% functional MR, 85% NYHA III-IV, 53% LVEF <40%
Implant rate – 99.6%; mortality: 30-day – 3.4%,1-year – 81.8%



Severity of MR at baseline and during follow-up

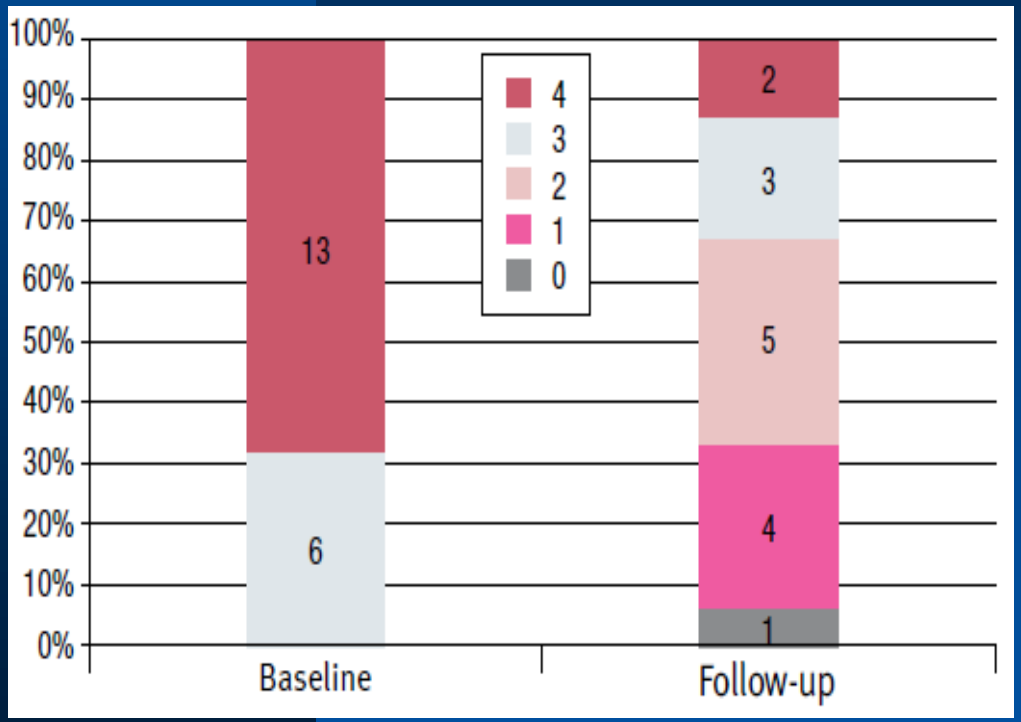


Changes in 6MWT in patients with MitraClip

Maisano F et al., JACC 2013;62:1052–61

MitraClip as therapeutic option for MR Real World Experience

Data from Israel: 20 pts with significant MR who underwent MitraClip therapy
90% functional/mixed MR, 90% NYHA III-IV, 68% LVEF <40%
In 18 reduction of MR to ≤ 2 ; during follow-up 2 pts died



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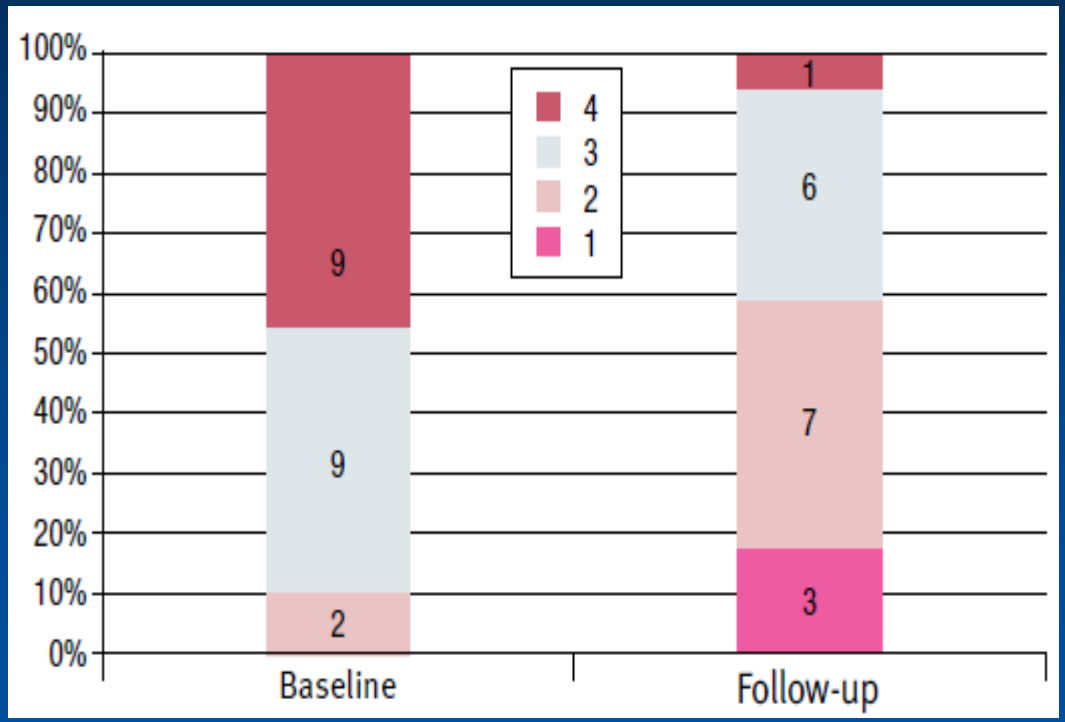


Changes in NYHA class in patients with MitraClip

Koifman E et al., IMAJ 2014;16:91-95

MitraClip as therapeutic option for functional MR – current experience

MitraClip® therapy in patients with end-stage systolic heart failure

Olaf Franzen[1*], Jan van der Heyden[2], Stephan Baldus[1], Michael Schlüter[1], Wolfgang Schillinger[3], Christian Butter[4], Rainer Hoffmann[5], Roberto Corti[6], Giovanni Pedrazzini[7], Martin J. Swaans[2], Michael Neuss[4], Volker Rudolph[1], Daniel Sürder[7], Jürg Grünenfelder[6], Christine Eulenburg[8], Hermann Reichenspurner[9], Thomas Meinertz[1], and Angelo Auricchio[7]

2011

- 50 CHF pts with severe FMR
- NYHA III-IV, EF – 19%
- optimally managed (74% with ICD/CRT)
- logistic EuroSCORE of 34%

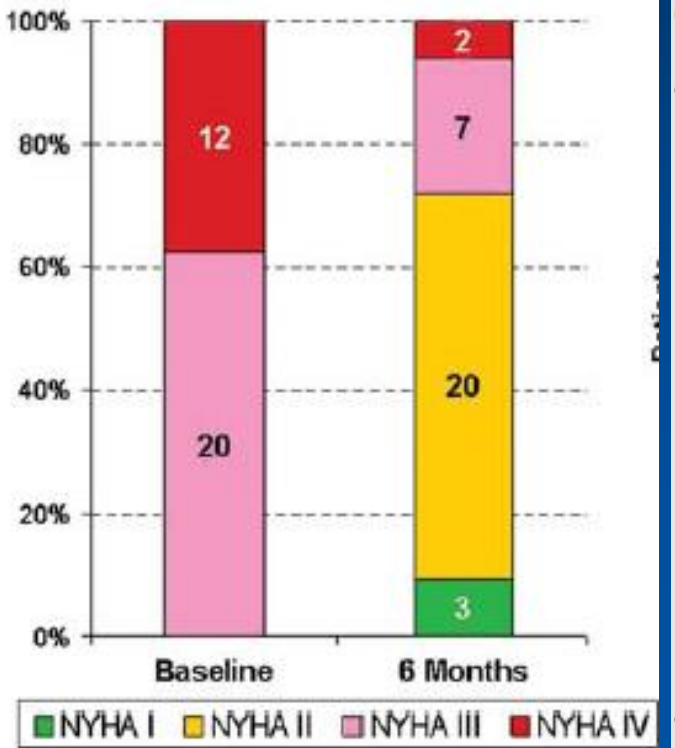
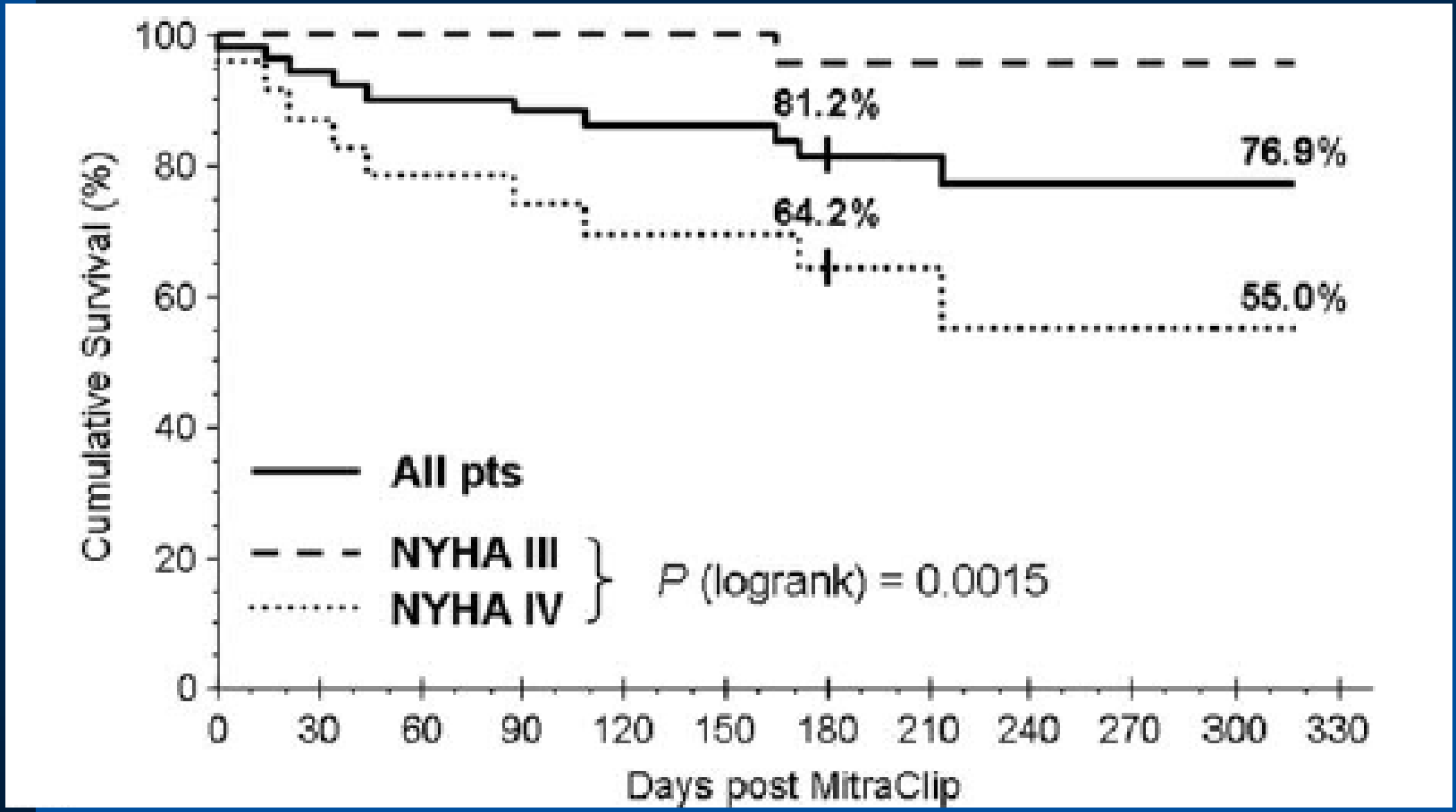


Table 2 Changes from baseline to 6 months in echocardiographic variables of successfully treated patients

	n	Baseline	6 months	Δ	*P*
Mitral valve orifice area (cm^2 ± SD)	12	4.9 ± 1.6	3.2 ± 0.9	−1.7 ± 1.4	0.002
Mean transmitral gradient (mmHg ± SD)	19	1.7 ± 1.4	3.0 ± 2.6	1.3 ± 2.3	0.018
LV ejection fraction (% ± SD)	28	20 ± 4	25 ± 9	6 ± 9	0.003
LV end-diastolic diameter (mm ± SD)	30	71 ± 8	69 ± 8	−2 ± 6	0.051
LV end-systolic diameter (mm ± SD)	30	62 ± 9	61 ± 8	−1 ± 6	0.083
LA diameter (mm ± SD)	20	51 ± 7	45 ± 9	−6 ± 9	0.023
LV end-diastolic volume (mL ± SD)	27	253 ± 73	237 ± 66	−15 ± 35	0.010
LV end-systolic volume (mL ± SD)	26	196 ± 65	172 ± 55	−24 ± 39	0.003

MitraClip as therapeutic option for functional MR – current experience

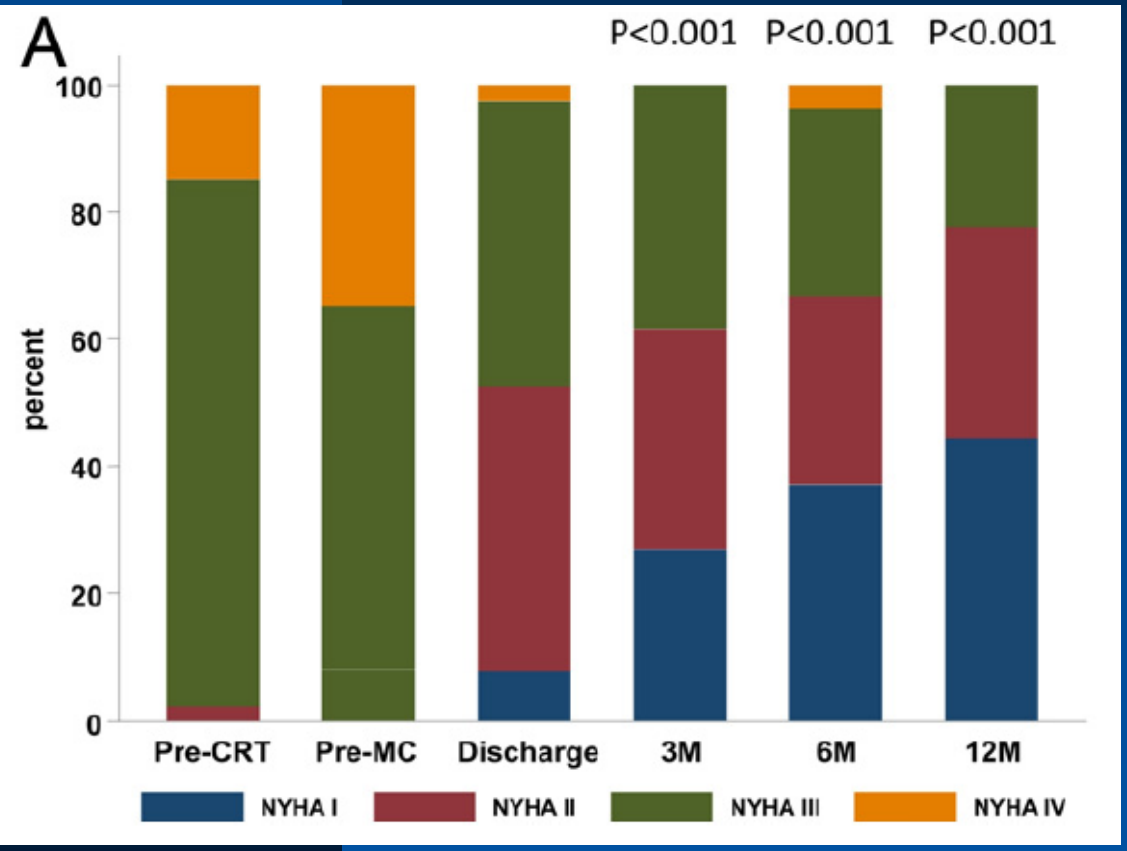


Franzen O et al., Eur J Heart Fail 2011

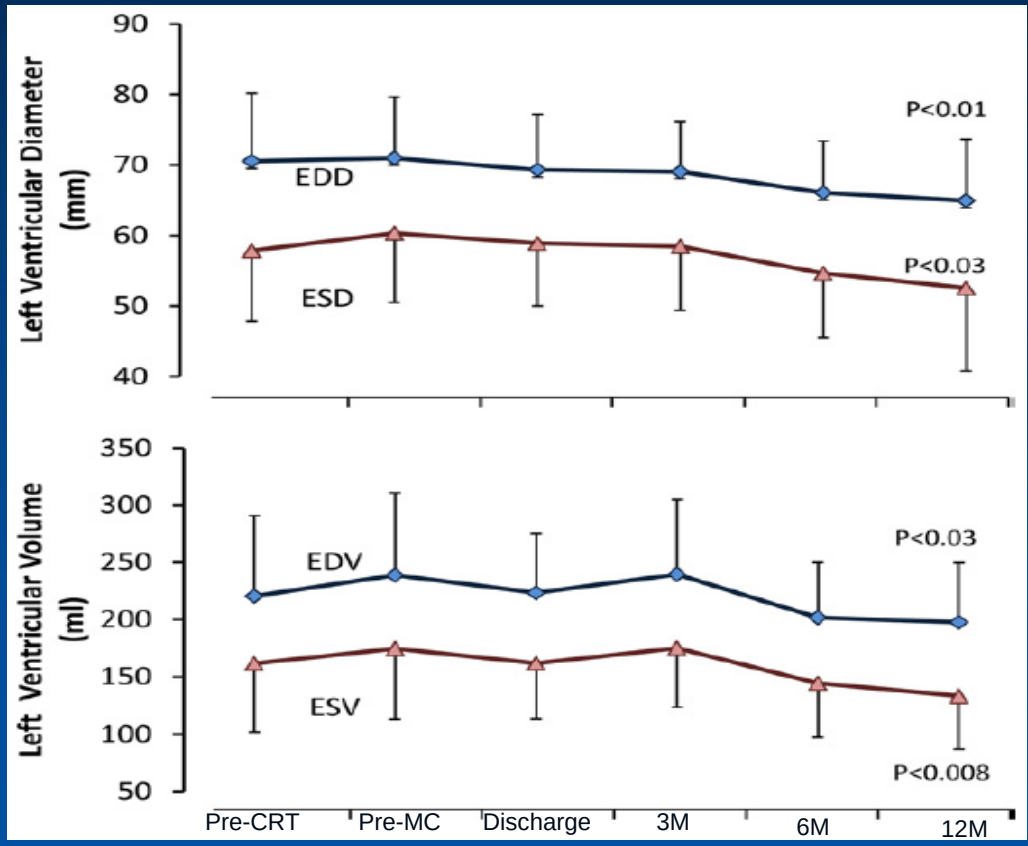
MitraClip as therapeutic option for functional MR – current experience

MitraClip in Nonresponders to CRT: PERMIT-CARE Survey

NYHA class

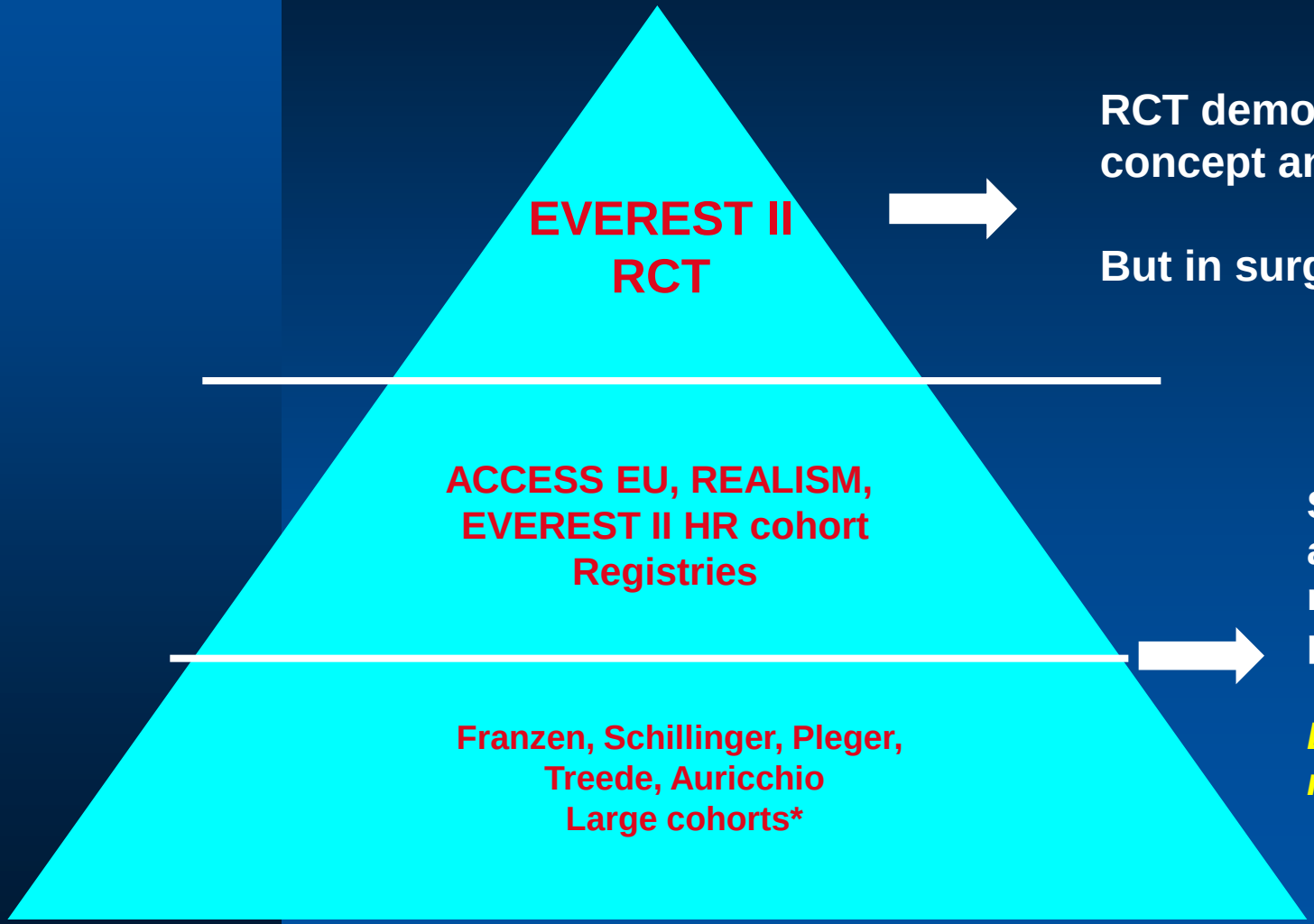


Echocardiographic parameters



Auricchio A et al. JACC 2011;58:2183-9

MitraClip as therapeutic option for functional MR – current experience



RCT demonstrated overall concept and clinical safety

But in surgical population only

Specific patient populations addressed (high risk, HF, CRT non-responders, ...) with positive outcomes

But observational non randomized only

MitraClip in the 2012 Heart Failure Guidelines

The role of isolated mitral valve surgery in patients with severe functional mitral regurgitation and severe LV systolic dysfunction who cannot be revascularized or have non-ischaemic cardiomyopathy is questionable, and in most patients conventional medical and device therapy are preferred. In selected cases, repair may be considered in order to avoid or postpone transplantation.

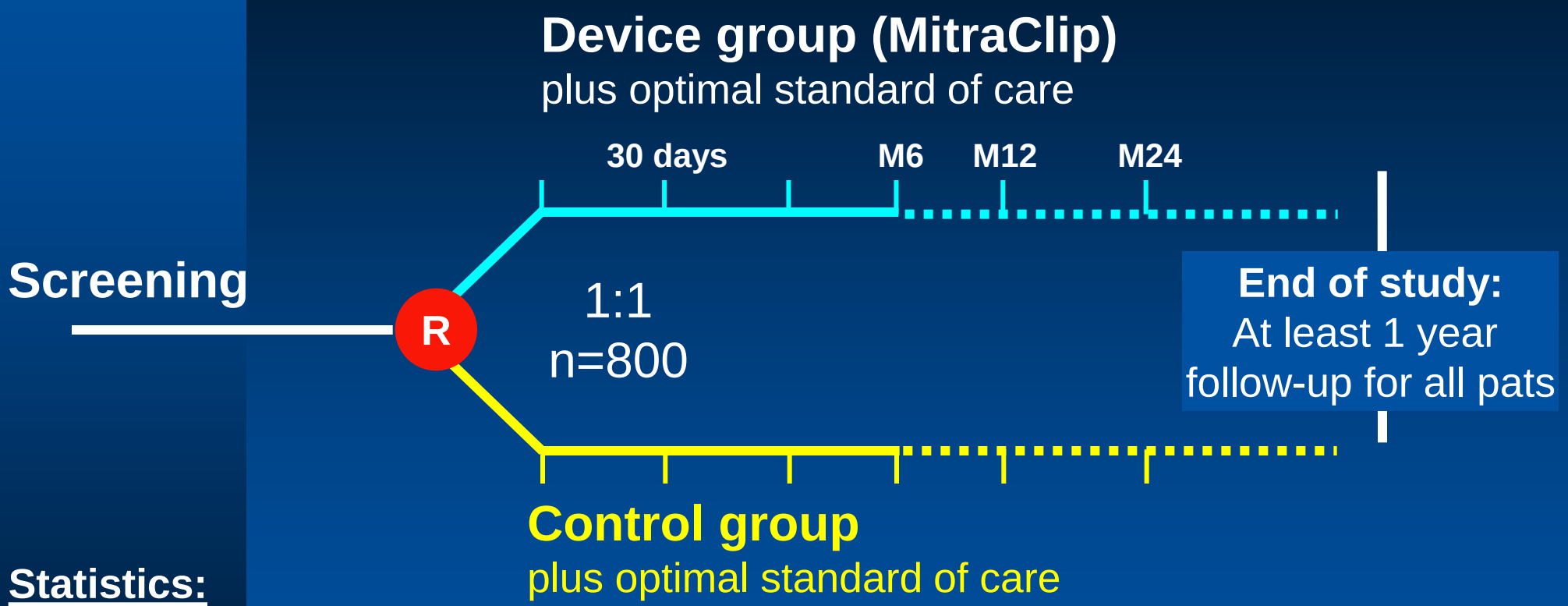
In patients with an indication for valve repair but judged inoperable or at unacceptably high surgical risk, percutaneous edge-to-edge repair may be considered in order to improve symptoms.[250]

A RandomizEd Study of tHe MitrACliP DEvice in Heart Failure Patients with Clinically Significant Functional Mitral Regurgitation

RESHAPE-HF: objectives

1. To further study the safety and effectiveness of the MitraClip System for the treatment of clinically significant functional mitral regurgitation in NYHA Functional Class III or Class IV chronic heart failure (CHF) patients.
2. The trial is designed to provide the evidence necessary to determine appropriate recommendations for use of the MitraClip System in the ESC Guidelines on the treatment options for CHF patients with functional mitral regurgitation.
3. Additionally, the trial will evaluate cost-effectiveness of be MitraClip System and gather data to support reimbursement of the device for use in CHF patients.

RESHAPE-HF clinical trial



Statistics:

- Prospective, randomized, parallel-controlled, multi-center
- 800 CHF patients
- NYHA III-IV

Primary endpoint:
Composite of all-cause mortality and recurrent heart failure hospitalizations during 12 months

Future of MR Management ?

	RESHAPE MitraClip vs. medical therapy	COAPT MitraClip vs. medical therapy
Patients (n)	800	420
FMR grade	≥ 3+	≥ 3+
NYHA	III, IV	II, III, IV
LVEF	≥ 15% - ≤ 40%	≥20% - ≤60%
Primary endpoint	Death or HF Rehospitalization at 1 year	HF Rehospitalization at 1 year
Primary safety endpoint		Death, stroke LVAD, cardiac transplant
Follow up	2 years	5 years

Future of MR Management ?

Sunrise or sunset ?