What has changed since the introduction of mitral clip

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What has changed ?

- 1.- Diagnosis

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European Heart Journal – Cardiovascular Imaging
doi:10.1093/ehjci/jet105

RECOMMENDATIONS

Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging

Patrizio Lancellotti[1]*, Christophe Tribouilloy[2], Andreas Hagendorff[3], Bogdan A. Popescu[4], Thor Edvardsen[5], Luc A. Pierard[1], Luigi Badano[6], and Jose L. Zamorano[7], On behalf of the Scientific Document Committee of the European

VALVULAR HEART DISEASE

Quantification of mitral regurgitation by echocardiography

JL. Zamorano, C. Fernández-Golfín, A. González-Gómez

Heart 2014

Table 1 Echocardiography assessment of MR severity: main approaches

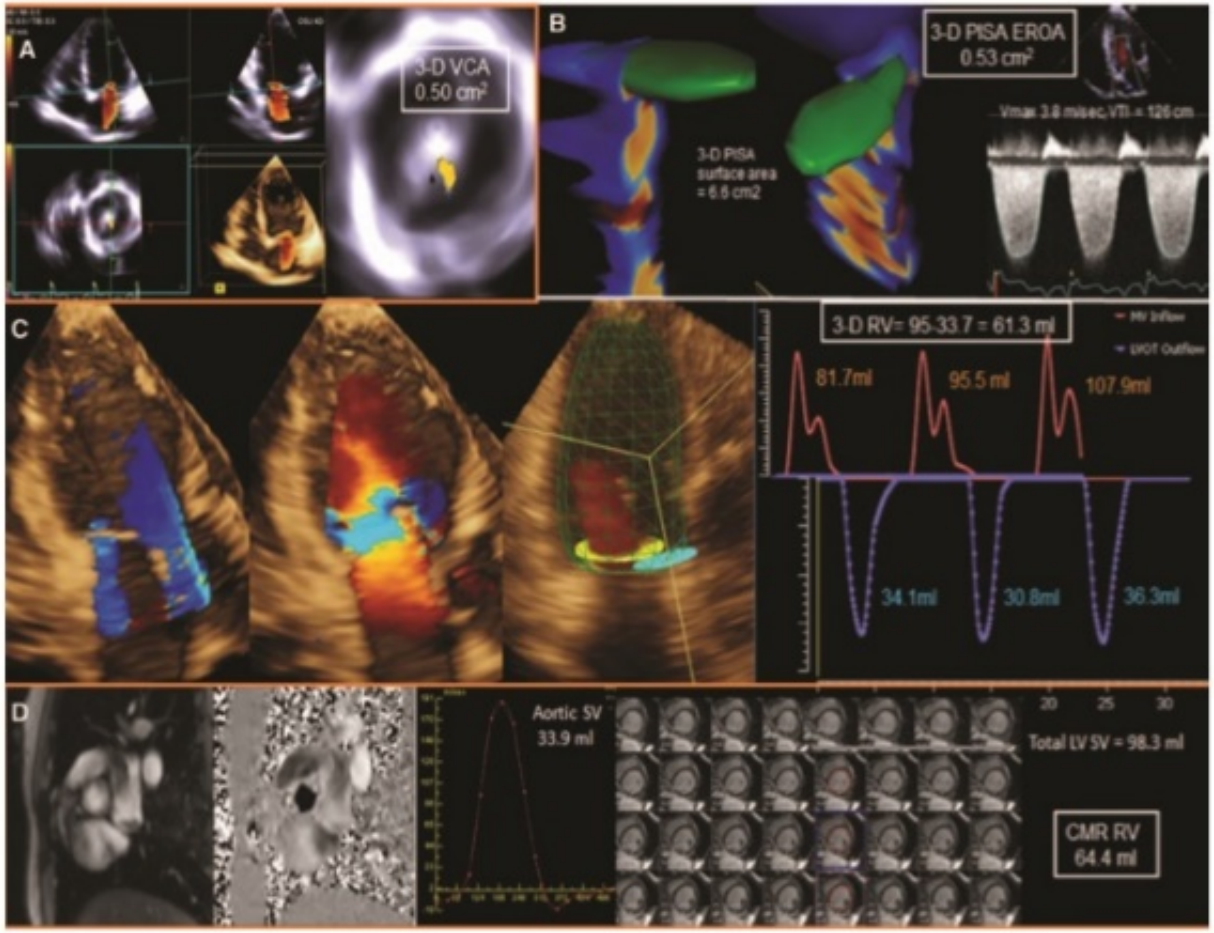
Method	Recording technique/equation	Strengths	Limitations
Colour jet area	Apical image, includes LA Nyquist limit 50–60 cm/s Trace maximum regurgitant jet MR jet/LA area	MR screening	Dependent on technical and haemodynamic factors Correlation with severity is poor Currently not recommended to quantify severity
Vena contracta width	Colour flow through the MV in PLAX or apical 4C view Identify the image with maximal flow through the valve VCW is the narrowest region of the regurgitant jet	Simple method Independent of haemodynamics, pressure and flow rate	Low colour gain, poor acoustic window, failure to assess multiple jets, non-circular EROA: underestimate VCW High colour gain, AF: overestimate VCW Dynamic behaviour of MR
PISA method	Apical 4C view Nyquist limit ≈15–40 cm/s Mid systole Peak CW MR velocity $EROA=2\pi r^2 \times Va/peak\ MRV$ $RVol=EROA \times VTI_{MR}$	Independent of haemodynamics, pressure and flow rate Preferred quantitative approach	Assumption of a hemispheric shape and a circular EROA Dynamic behaviour of MR
Volumetric method	Apical 4C view/apical 5C view PW at the MV/PW at the LVOT Mitral annulus diameter/LVOT diameter Mitral inflow volume=MV $d \times 0.785 \times VTI_{MV}$ LVOT volume=LVOT $d \times 0.785 \times VTI_{LVOT}$ RVol=Mitral inflow volume−LV outflow volume RF=RVol ×100/mitral inflow volume $EROA=RVol/VTI_{MR}$	Integration of the systolic behaviour of MR Alternative method if PISA or VCW are not accurate or applicable	Time consuming Inaccurate if significant AR Less reproducible Not recommended as first line method
3D echocardiography	Full volume colour Doppler or 3D zoom acquisitions of the MR jet: dataset cropping with MPR tools for evaluation of VCA	Diagnosis of location and extent of disease No geometrical assumptions Functional MR, multiple or eccentric jets	Poor acoustic window Poor spatial and temporal resolution of live acquisition of 3D colour Doppler Off line manipulation Dynamic behaviour of MR

Imaging Challenges in Secondary Mitral Regurgitation

Unsolved Issues and Perspectives

Patrizio Lancellotti, MD, PhD; Jose-Luis Zamorano, MD, PhD; Mani Vannan, MBBS

8 *Circ Cardiovasc Imaging* July 2014



What has changed ?

2.- Anatomy / ethiology / Implications of clinical factors

1. Introduction
2. Quantifying severity:
1. **Assessing consequences**
2. What about daily practice?

ANTICIPATING

↓

Decision making

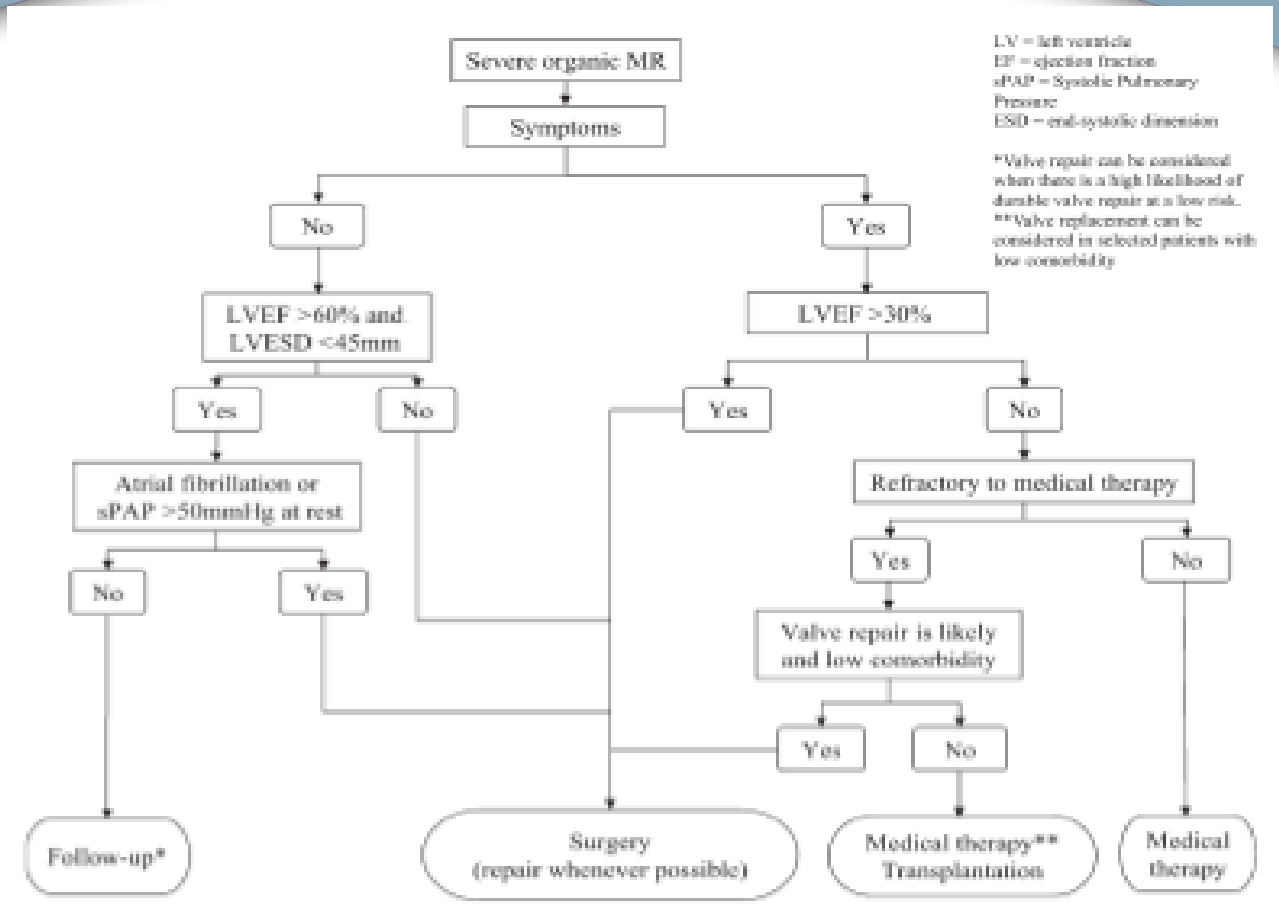
↓

Table 8 Indications for surgery in severe chronic organic mitral regurgitation

	Class
Symptomatic patients with LVEF >30% and ESD <55 mm	IB
Asymptomatic patients with LV dysfunction (ESD >45 mm[a] and/or LVEF ≤60%)	IC
Asymptomatic patients with preserved LV function and atrial fibrillation or pulmonary hypertension (systolic pulmonary artery pressure >50 mmHg at rest)	IIaC
Patients with severe LV dysfunction (LVEF <30% and/or ESD >55 mm)[a] refractory to medical therapy with high likelihood of durable repair, and low comorbidity	IIaC
Asymptomatic patients with preserved LV function, high likelihood of durable repair, and low risk for surgery	IIbB
Patients with severe LV dysfunction (LVEF <30% and/or ESD >55 mm)[a] refractory to medical therapy with low likelihood of repair and low comorbidity	IIbC

Severity is based on clinical and echocardiographic assessment.
ESD = end-systolic dimension, EF = ejection fraction, LV = left ventricular, MR = mitral regurgitation.
[a]Lower values can be considered for patients of small stature.

1. Introduction
2. Quantifying severity
3. **Assessing consequences**
4. What about daily practice?



Should surgery be advised for assymptomatic patients with severe MR before the appearance of AF, PHT or ventricular disfunction ?

Dutch AMR

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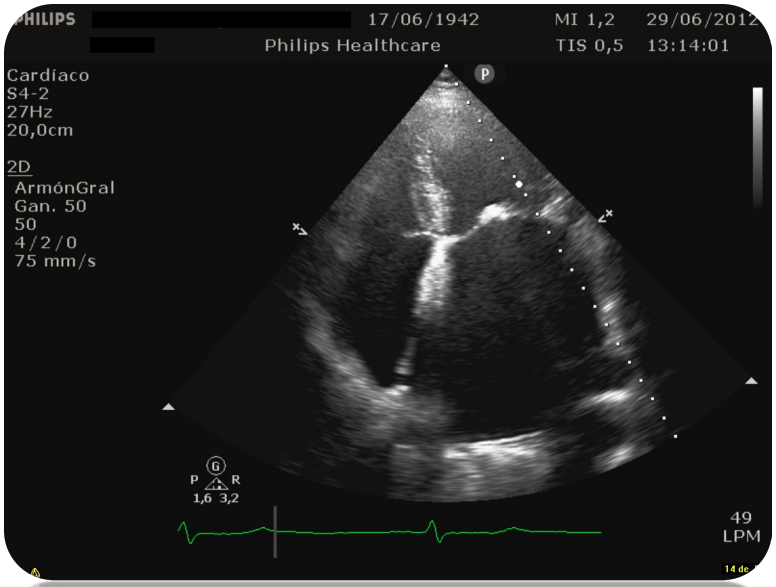
Vahanian A et al. Eur Heart J 2007
Tietge, WJ. Neth Heart J. 2012

1. Introduction
2. Quantifying severity
3. **Assesssing consequences:**
   - **LA**
   - LV
   - Stress test
4. What about daily practice?

Dilation of LA **preceeds** (and is more intense) than LV

LA dilation (diameter > 40–50 mm or indexed vol > 60 mL/ m^2) is **independently** associated with **higher all cause and CV mortality**



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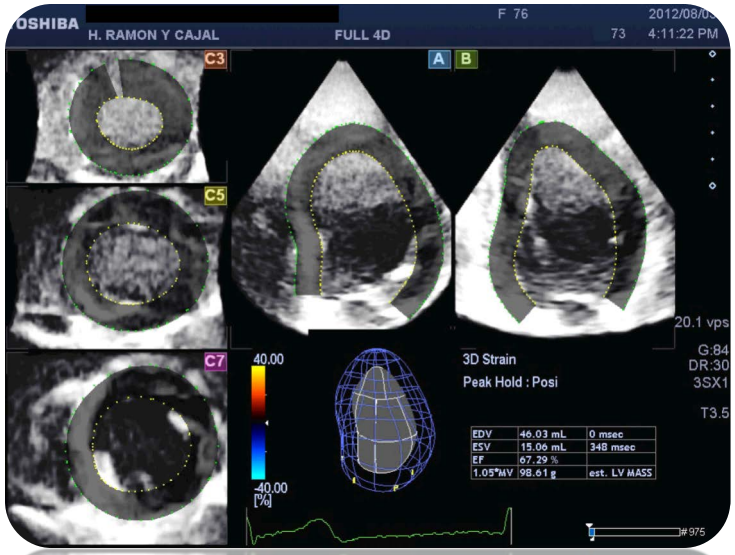
Messika-Zeitoun. Eur Heart J 2007
Le Tourneau T. J Am Coll Cardiol 2010
Hanna N. Cardiovasc Res 2004

1. Introduction
2. Quantifying severity
3. **Assesssing consequences:**
   - LA
   - **LV**
   - Stress test
4. What about daily practice?

Worst post-surgical outcome if LV disfunction is established



Parameters of subclinical LV disfunction:

- Diminished torsion
- Global long. Strain
- **BNP**
- Others…

Tribouilloy C. J Am Coll Cardiol 2009
Enriquez-Sarano M. Circulation 1994
Lancellotti P et al. J Am Soc Echocardiogr 2008

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1. Introduction
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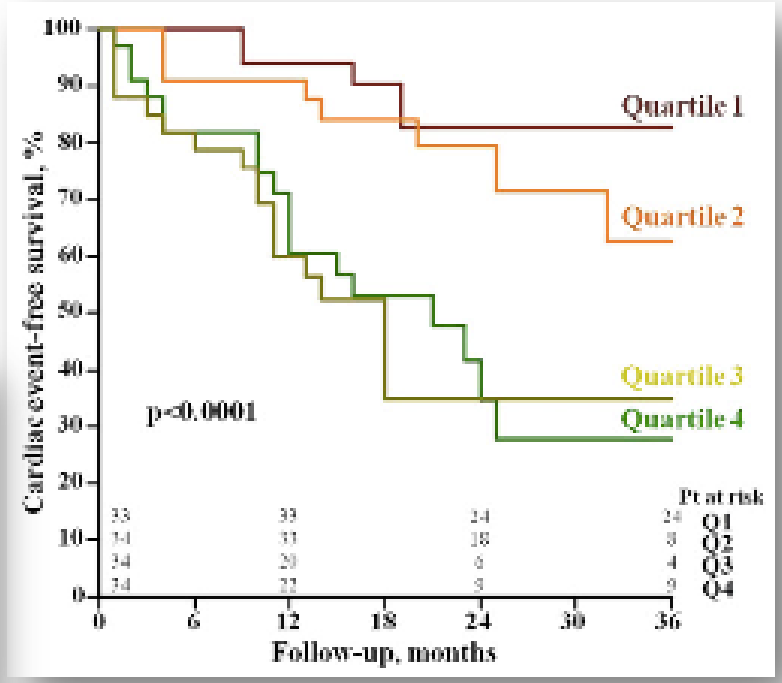
4. What about daily practice?

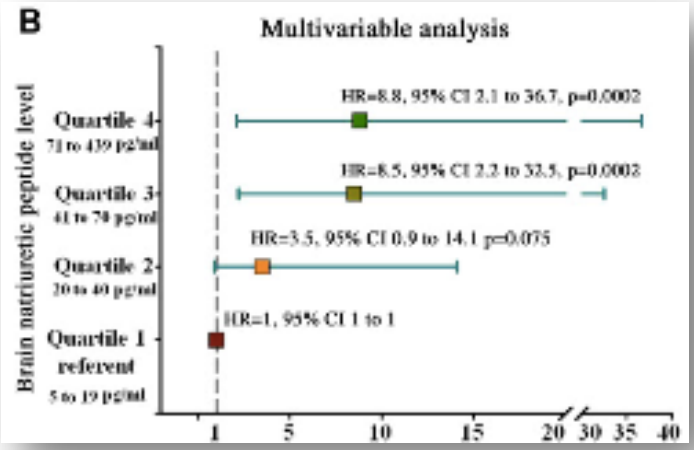
BNP

- Independent predictor of symptom-free survival
- Values: >31 pg/ml, >44 pg/ml, >105 pg/ml (incl dilated LV)

- 135 assymptomatic patients; sinus rythm;
- Mod-severe MR; non-dilated LV;

- BNP > 40 pg/ml
→x4 rise in cardiac events after 3 y.





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Magne et al. Heart 2012

1. Introduction
2. Quantifying severity
3. **Assessing consequences:**
   - LA
   - LV
   - **Stress test**
4. What about daily practice?

- **LV contractile reserve**

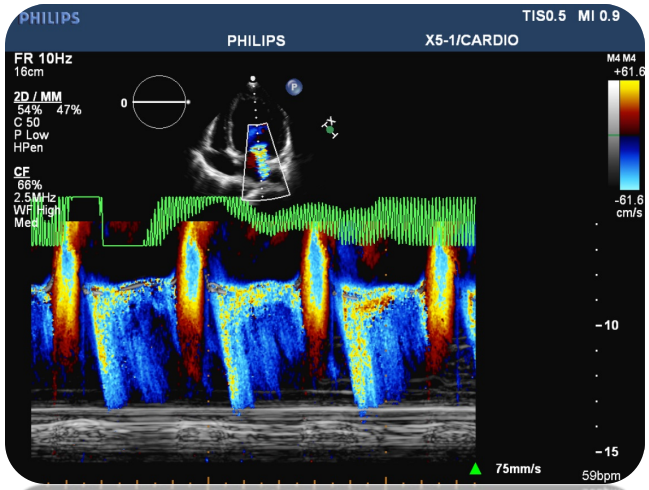
[Decrease in contractile reserve (LVEF < +4%) → Higher post-surgical morbility]

- **PHT**

[PSP raise during exercise → shorter symptom-free period]

- **Severity**

[Exercise-induced increase in ERO > 13 mm² → Increased morbi-mortality]



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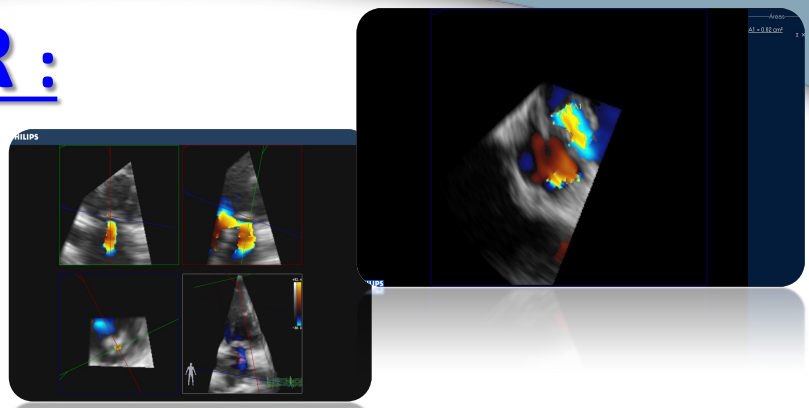
Barbieri A. Eur Heart J 2011
Magne J. Circulation 2010
Lee R. Heart 2005
Lancellotti. Eur Heart J 2005

RE - DEFINING

SEVERE MR :



1. Introduction
2. Quantifying severity:
1. Assessing consequences
2. **What about daily practice?**

I:

- **ROA ≥ 0.4 cm² by 3D planimetry**

- **EROA ≥ 0.3 cm² by PISA**

II:

- **ROA ≥ 0.3 but < 0.4 cm² by 3D planimetry**

- **EROA ≥ 0.2 but < 0.3 cm² by PISA**

+ one of the following:

- RVol ≥ 45 ml
- RF ≥ 40%
- VC ≥ 0.5 cm

III:

- **EROA not measurable, + two of the following:**
  - RVol ≥ 45 ml
  - RF ≥ 40%
  - VC ≥ 0.5 cm
  - PISA radius > 0.9 cm (for a Nyq. Lim. 50-60 cm/s)
  - large holosystolic jet with coanda effect
  - picotransmitral peak E vel ≥ 1,5 m/s
  - systolic flow reversal in PV

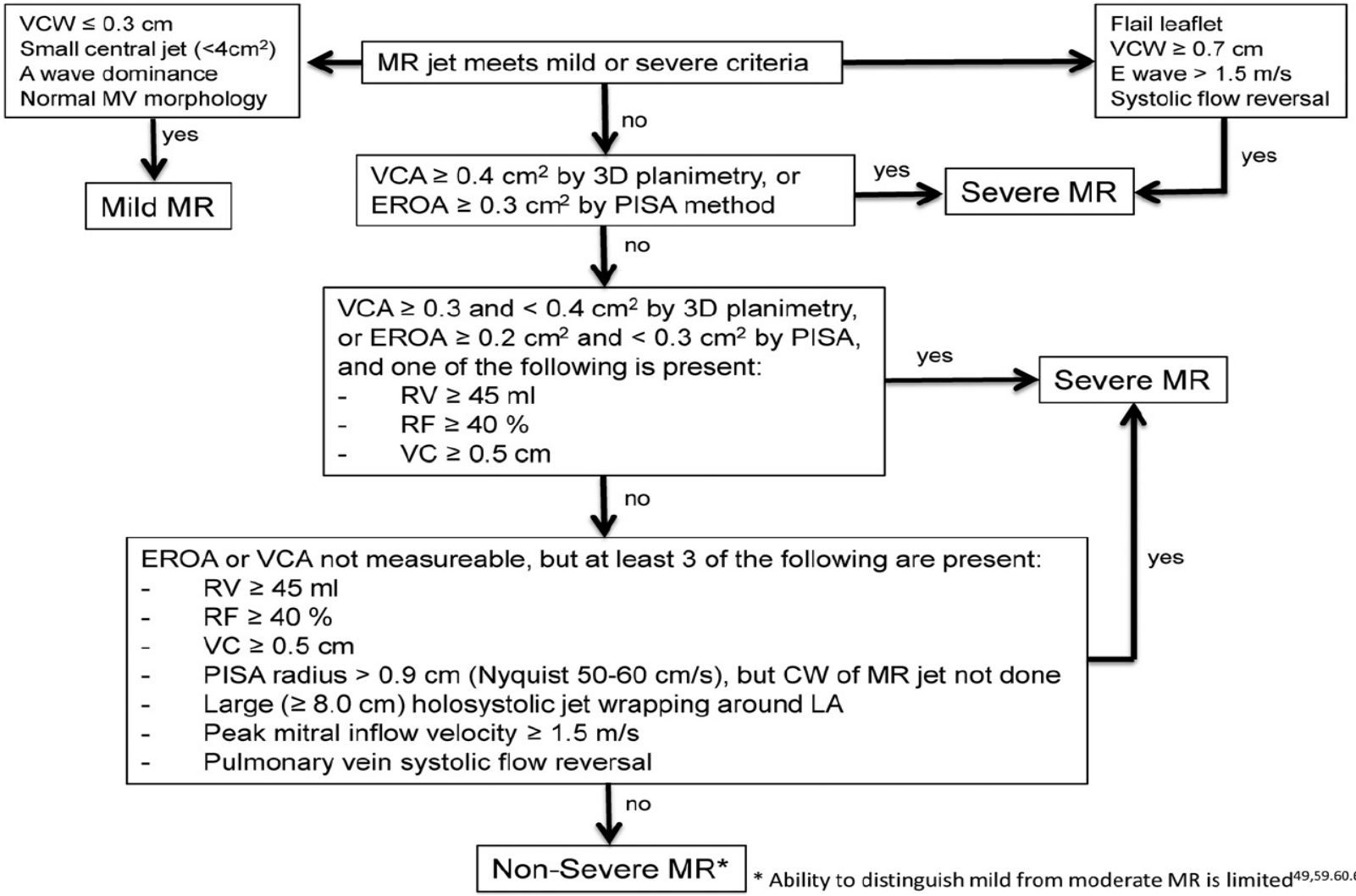
Grayburn P, Weissman N, Zamorano JL. Circulation,. 2012

Quantitation of Mitral Regurgitation

Paul A. Grayburn, Neil J. Weissman and Jose L. Zamorano

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Circulation. 2012



EuroIntervention 2014;10:U10-U0

Mitral valve anatomy: implications for transcatheter mitral valve interventions

Jose L. Zamorano[1]*, MD, PhD; Ariana González-Gómez[1], MD; Patrizio Lancellotti[2], MD, PhD

1. University Hospital Ramón y Cajal, Madrid, Spain; 2. University Hospital of Liege, Liege, Belgium

ovale depicted. The accepted anatomic measurements and characteristics for MitraClip patient selection are summarised in **Table 1**.

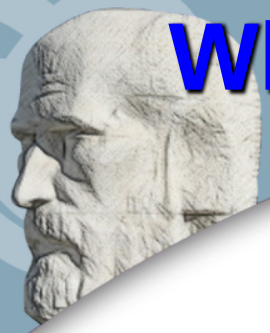
Table 1. Anatomical criteria for selection of patients for MitraClip implantation.

	Suitable for MC	Unsuitable for MC
Aetiology	Degenerative or functional.	Perforated mitral leaflets or clefts, lack of primary and secondary chordal support, rheumatic or endocarditic
MV area	>4 cm²	Significant mitral stenosis
MR jet	Central	Eccentric and multiple jets
Calcification	None (grasping area)	Severe (grasping area)
Specific measurements	Flail width <15 mm Flail gap <10 mm Coaptation depth <11 mm Coaptation length >2 mm	Gap between leaflets >2 mm

MC: MitraClip; MR: mitral regurgitation; MV: mitral valve

During the procedure, understanding and consideration of anat-

Figure 3. *A 3DE en face view of the mitral valve from the left atrium perspective allows visualisation in one image of the whole mitral valve for correct orientation of the MitraClip device.*



3.- Guidelines

MitraClip as Tx option for high risk surgical patients in ESC Heart Failure 2012 guidelines

ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: John J. V. McMurray (Chairperson) (UK)*, Stamatis Adamopoulos (Greece), Stefan D. Anker (Germany), Angelo Auricchio (Switzerland), Michael Böhm (Germany), Kenneth Dickstein (Norway), Volkmar Falk (Switzerland), Gerasimos Filippatos (Greece), Cândida Fonseca (Portugal), Miguel Angel Gomez Sanchez (Spain), Tiny Jaarsma (Sweden), Lars Køber (Denmark), Gregory Y. H. Lip (UK), Aldo Pietro Maggioni (Italy), Alexander Parkhomenko (Ukraine), Burkert M. Pieske (Austria), Bogdan A. Popescu (Romania), Per K. Rønnevik (Norway), Frans H. Rutten (The Netherlands), Juerg Schwitter (Switzerland), Petar Seferovic (Serbia), Janina Stepinska (Poland), Pedro T. Trindade (Switzerland), Adriaan A. Voors (The Netherlands), Faiez Zannad (France), Andreas Zeiher (Germany).

...“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.”.....

although its effect on survival is unknown. In this situation, the decision to operate should take account of response to medical therapy, co-morbidity, and the likelihood that the valve can be repaired (rather than replaced).

Secondary mitral regurgitation

This occurs because LV enlargement and remodelling lead to reduced leaflet closing. Effective medical therapy leading to reverse remodelling of the LV may reduce functional mitral regurgitation, and every effort should be made to optimize medical treatment in these patients.

Ischaemic mitral regurgitation is a particular type of secondary mitral regurgitation that may be more suitable for surgical repair. As it is often a dynamic condition, stress testing is important in its evaluation. An exercise-induced increase of effective regurgitant orifice ($\geq$13 mm^2) is associated with a worse prognosis. Combined valve and coronary surgery should be considered in symptomatic patients with LV systolic dysfunction, coronary arteries suitable for revascularization, and evidence of viability. Predictors of late failure of valve repair include large interpapillary muscle distance, severe posterior mitral leaflet tethering, and marked LV dilatation (LV end-diastolic diameter >65 mm). In these patients, mitral valve replacement, rather than repair, may be advisable. In the presence of AF, atrial ablation and left atrial appendage closure may be considered at the time of mitral valve surgery.

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]

13.4 Heart transplantation

Heart transplantation is an accepted treatment for end-stage HF.[251,252] Although controlled trials have never been conducted, there is consensus that transplantation—provided that proper selection criteria are applied—significantly increases survival, exercise capacity, quality of life, and return to work compared with conventional treatment.

Apart from the shortage of donor hearts, the main challenges in transplantation are the consequences of the limited effectiveness and complications of immunosuppressive therapy in the long term (i.e. antibody-mediated rejection, infection, hypertension, renal failure, malignancy, and coronary artery vasculopathy). The indications for and contraindications to heart transplantation are summarized in *Table 23*.

13.5 Mechanical circulatory support

MCS is an umbrella term describing a number of different technologies used to provide both short- and longer term assistance in patients with either chronic HF or AHF. A variety of terms have been used to describe the use of these technologies (*Table 24*).[211,253] The most experience is with MCS in end-stage

Table 23 Heart transplantation: indications and contraindications

Patients to consider	End-stage heart failure with severe symptoms, a poor prognosis, and no remaining alternative treatment options
	Motivated, well informed, and emotionally stable
	Capable of complying with the intensive treatment required post-operatively
Contraindications	Active infection
	Severe peripheral arterial or cerebrovascular disease
	Current alcohol or drug abuse
	Treated cancer in previous 5 years
	Unhealed peptic ulcer
	Recent thrombo-embolism
	Significant renal failure (e.g. creatinine clearance <50 mL/min)
	Significant liver disease
	Systemic disease with multiorgan involvement
	Other serious co-morbidity with poor prognosis
	Emotional instability or untreated mental illness
	High, fixed pulmonary vascular resistance (>4–5 Wood Units and mean transpulmonary gradient >15 mmHg)

HF = heart failure.

Table 24 Terms describing various uses of mechanical circulatory support (MCS)

Bridge to decision (BTD):	Use of MCS in patients with drug-refractory acute circulatory collapse and at immediate risk of death to sustain life until a full clinical evaluation can be completed and additional therapeutic options can be evaluated.
Bridge to candidacy (BTC):	Use of MCS to improve end-organ function in order to make an ineligible patient eligible for transplantation.
Bridge to transplantation (BTT):	Use of MCS to keep a patient at high risk of death before transplantation alive until a donor organ becomes available.
Bridge to recovery (BTR):	Use of MCS to keep patient alive until intrinsic cardiac function recovers sufficiently to remove MCS.
Destination therapy (DT):	Long-term use of MCS as an alternative to transplantation in patients with end-stage heart failure ineligible for transplantation.

MCS = mechanical circulatory support.

Source: ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012 published on ESC web-site: http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/acute-chronic-heart-failure.aspx?hit=dontmiss

European Heart Journal
doi:10.1093/eurheartj/ehs109

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)

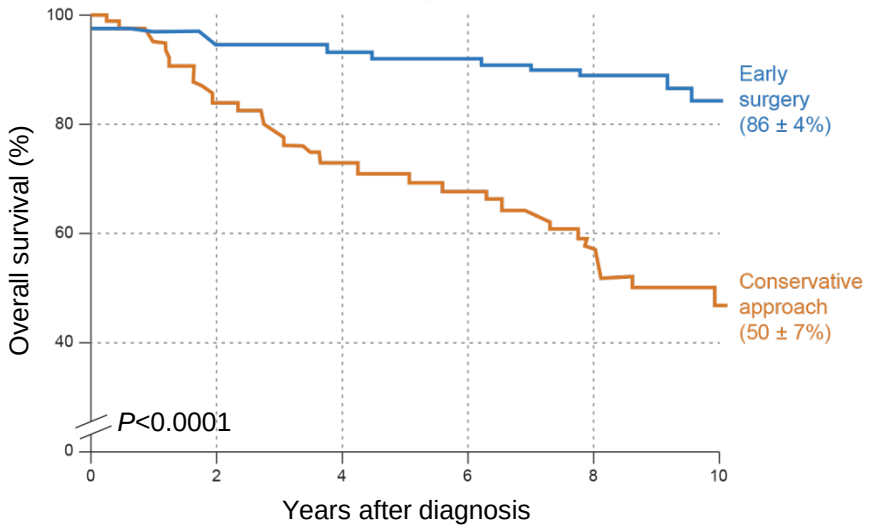
> ***Indication for primary MR:*** *Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a 'heart team', and have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).* (page 21)

> ***Indication for secondary MR:*** *The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfill 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).* (page 25)

Early surgical intervention improves outcomes

EARLIER TREATMENT

10-year overall survival of asymptomatic MR patients was significantly greater with early Surgery vs. medical management

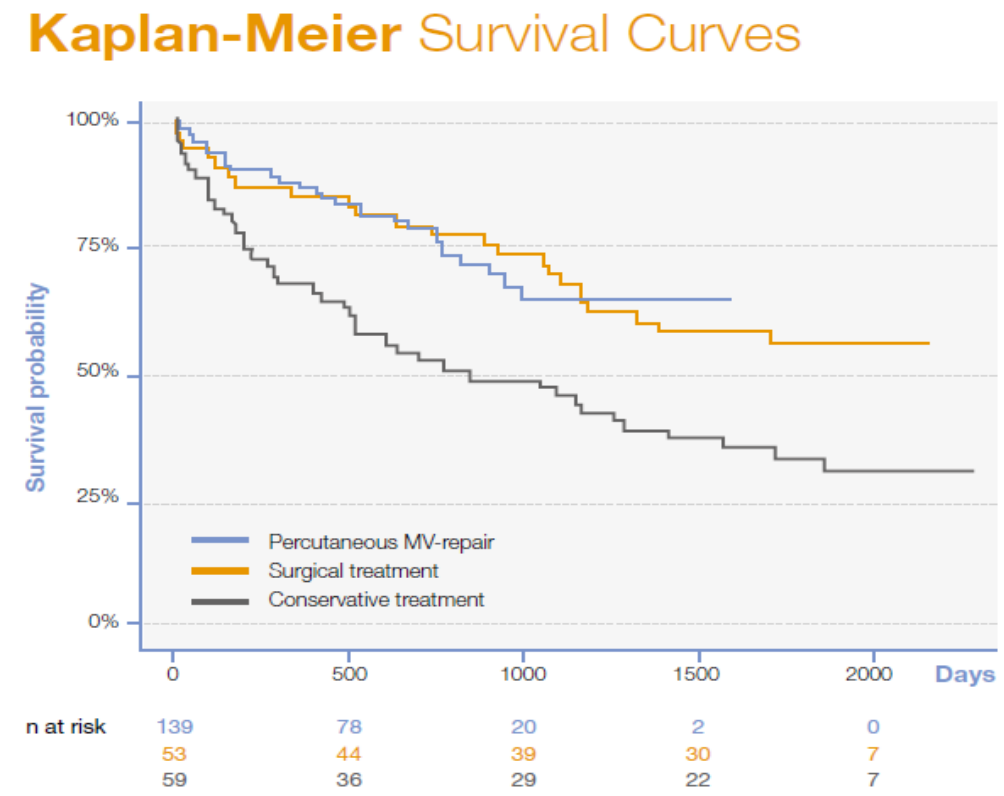


Otto, C. Heart 2003

*"**early intervention** to prevent left ventricular systolic dysfunction or pulmonary hypertension **provides optimal clinical outcomes".***

1. Otto, C. – Timing of surgery in mitral regurgitation - Heart 2003;89:100–105
Montant P, Chenot F, Robert A, et al. Long-term survival in asymptomatic patients with severe degenerative mitral regurgitation: a propensity score-based comparison between an early surgical strategy
and a conservative treatment approach. J Thorac Cardiovasc Surg. 2009;138(6):1339-1348.

MitraClip intervention improves survival



MitraClip therapy* is superior to conservative treatment and survival rates are comparable to surgery in high-surgical-risk patients with symptomatic MR (DMR and FMR)

*Swaans - Survival of Transcatheter Mitral Valve Repair Compared With Surgical and Conservative Treatment in High-Surgical-Risk Patients – JACC, 2014(7); 8 : 875-881

What has changed ?

4.- Experience

Worldwide Experience

Study	Population	N*
EVEREST I (Feasibility)	Feasibility patients	55
EVEREST II (Pivotal)	Pre-randomized patients	60
EVEREST II (Pivotal)	Non-randomized patients (High Risk Study)	78
EVEREST II (Pivotal)	Randomized patients (2:1 Clip to Surgery)	279 184 Clip 95 Surgery
REALISM (Continued Access)	Non-randomized patients	899
Compassionate/Emergency Use	Non-randomized patients	66
ACCESS Europe Phase I	Non-randomized patients	567
ACCESS Europe Phase II	Non-randomized patients	286
Commercial Use	Commercial patients	18,338
Total		**20,533** **+95 surgery**

*Data as of 02/28/2015. Source: Abbott Vascular

Growing body of clinical evidence – over 20.000 patients treated

Overall clinical feasibility & safety

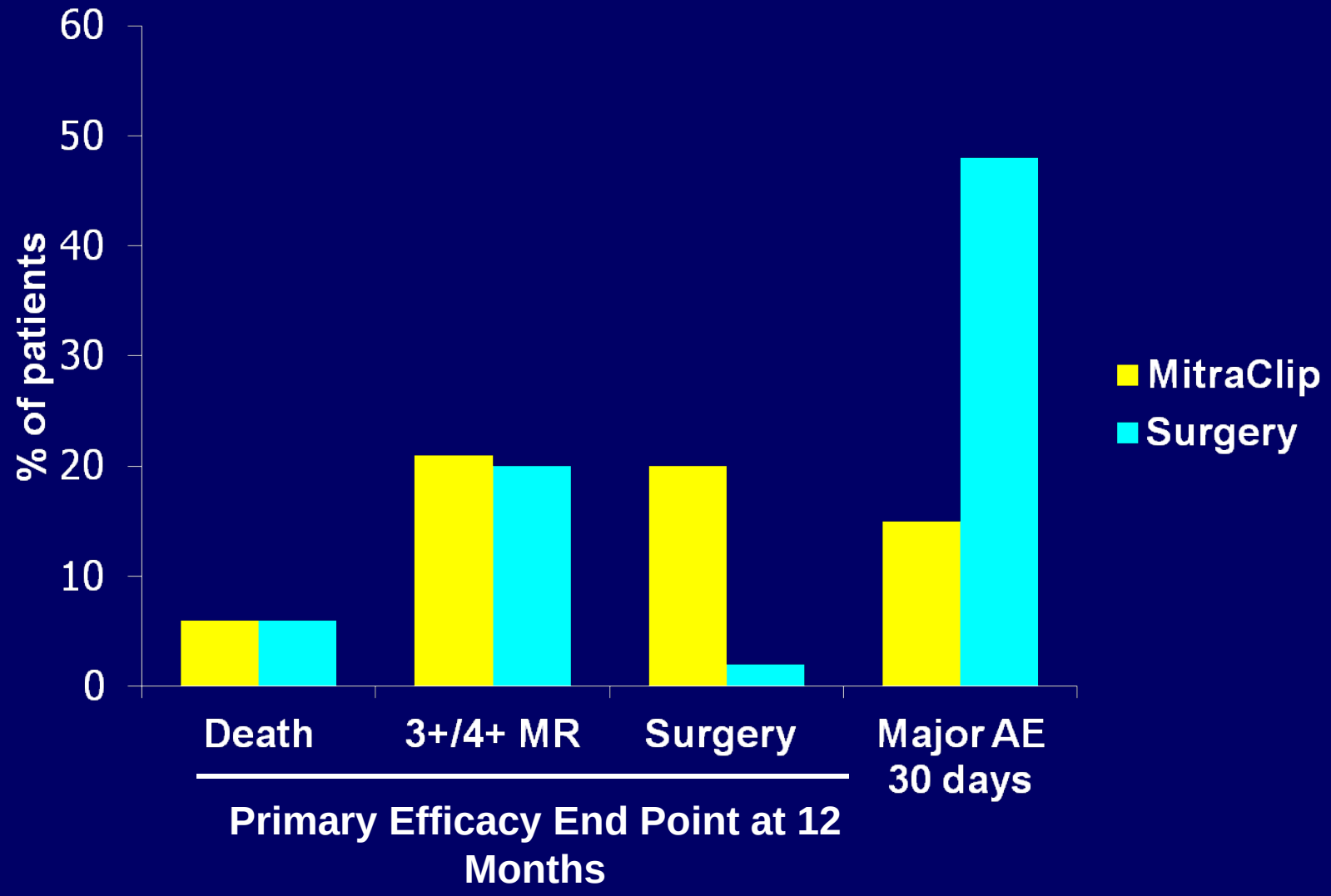
↓

Efficacy & safety in clinical practice

↓

Address specific patient populations

EVEREST II: Components of the Primary Efficacy end-point and major adverse events



Feldman T et al. N Engl J Med 2011;364:1395-1406

Growing body of clinical evidence – over 20.000 patients treated

Overall clinical feasibility & safety

↓

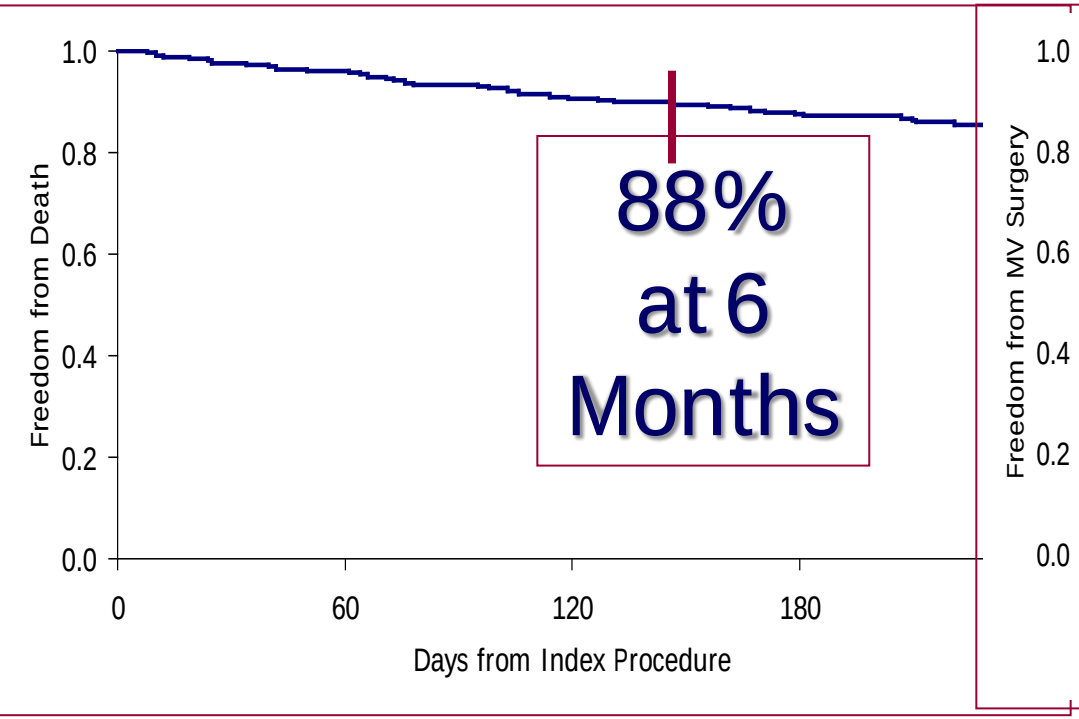
Efficacy & safety in clinical practice

↓

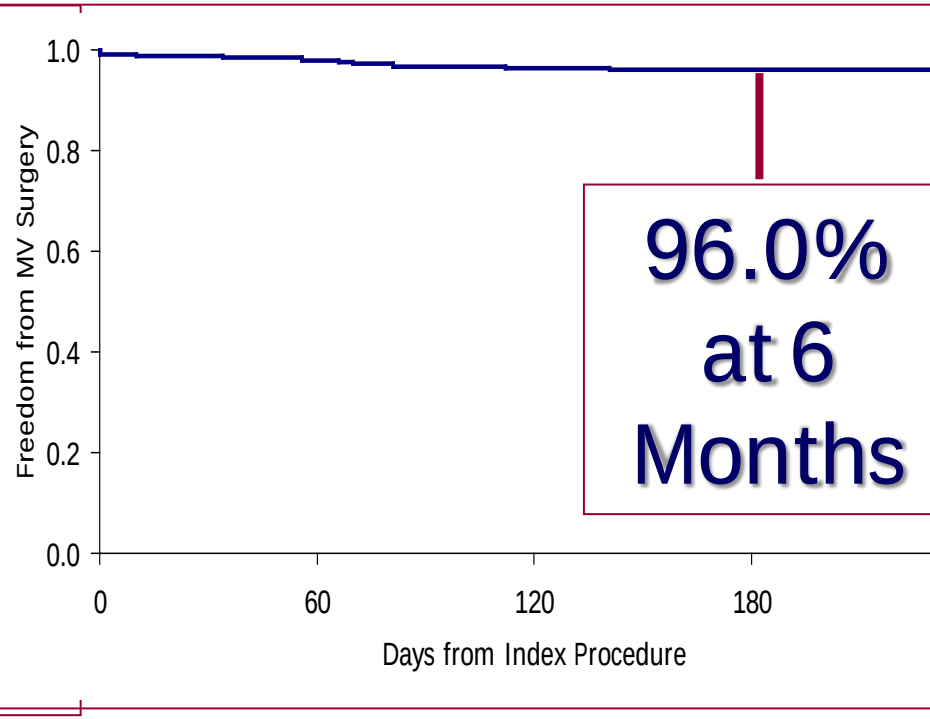
Address specific patient populations

Outcomes in ACCESS EU

Freedom from death



Freedom from MV Surgery



Source: Maisano, F. ACCESS EUROPE: A Post Market Study of the MitraClip System for the Treatment of Significant M
Regurgitation in Europe: Analysis of Outcomes at 6 Months. ACC 2012; March 24-27, 2012; Chicago, IL.

Growing body of clinical evidence – over 20.000 patients treated

Overall clinical feasibility & safety

↓

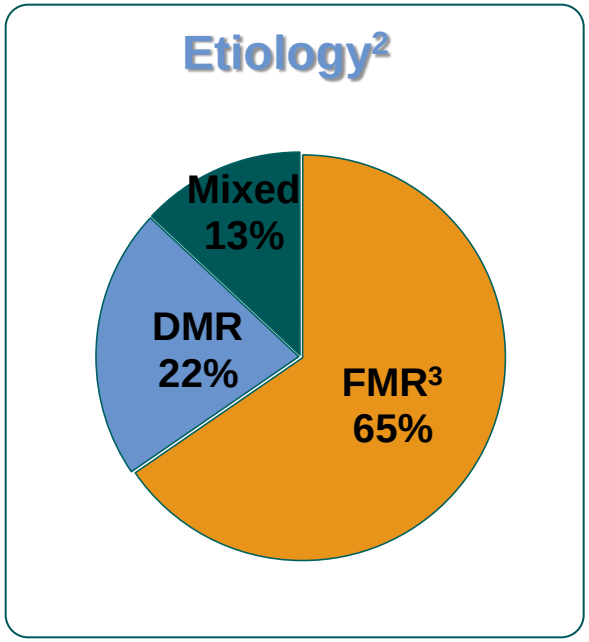
Efficacy & safety in clinical practice

↓

Address specific patient populations

Worldwide Commercial MitraClip Implant Experience

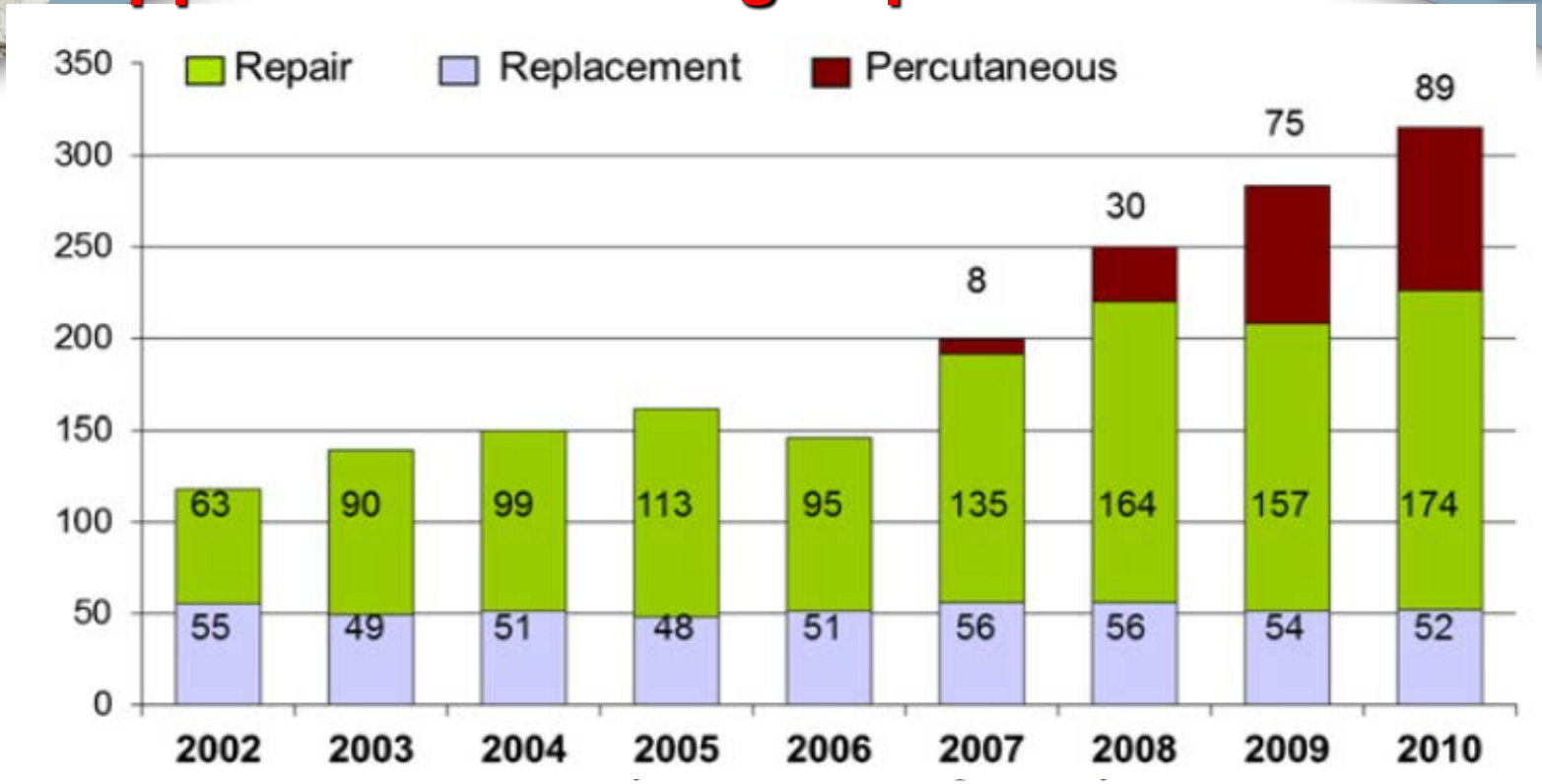
- Treating Centers: 476
- Patients[1]: 19,191
- Implant Rate[1]: 96%
- Etiology[2]
  - **Functional MR[3]** **65%**
  - Degenerative MR 22%
  - Mixed 13%



1. First-time procedures only. Includes commercial patients, ACCESS I and ACCESS II patients
2. Etiology not inclusive of U.S. cases as of 04/14/2014
3. Represents OUS use

Data as of 02/28/2015. Source: Abbott Vascular.

Surgical volumes with a Heart Team Approach. Hamburg experience



In contrast with concerns of many cardiac surgeons, the implementation of a percutaneous mitral valve program did not have a negative influence on our center's surgical mitral valve volume. To the contrary, the surgical volume even increased because of a positive impact of patients who were referred for interventional treatment but turned out to be good surgical candidates and therefore consequently underwent surgical MVR .

A heart team's perspective on interventional mitral valve repair . Treede et. al. JTCVS 2011

Conclusion
What has change

- MR is a complex poblem. Better Tools for assessment
- Multifactorial facts affects prognosis. We know more
- Data from RCT, registries and cohorts indicate MitraClip as a safe and effective option
- Efficacy & safety confirmed in
  - Patients at high risk for surgery
  - CRT non-responders
  - Patients with severe heart failure