



MitraClip

An additional treatment option for patients with moderate to severe Mitral regurgitation

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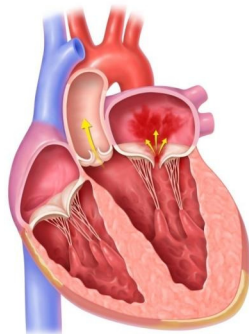


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Defining mitral regurgitation (MR)

MR occurs when the mitral valve fails to close completely, causing blood flow to move backward



Mayo Clinic (www.mayoclinic.com)



Degenerative MR — Prolapse



Degenerative MR — Flail



Functional MR

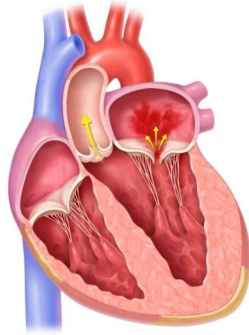
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Patients symptoms

MR occurs when the mitral valve fails to close completely, causing blood flow to move backward



Symptoms may include:

- Shortness of breath
- Heart palpitations
- Fatigue
- Lightheadedness
- Cough
- Swollen feet or ankles
- Excessive urination

Mayo Clinic (www.mayoclinic.com)

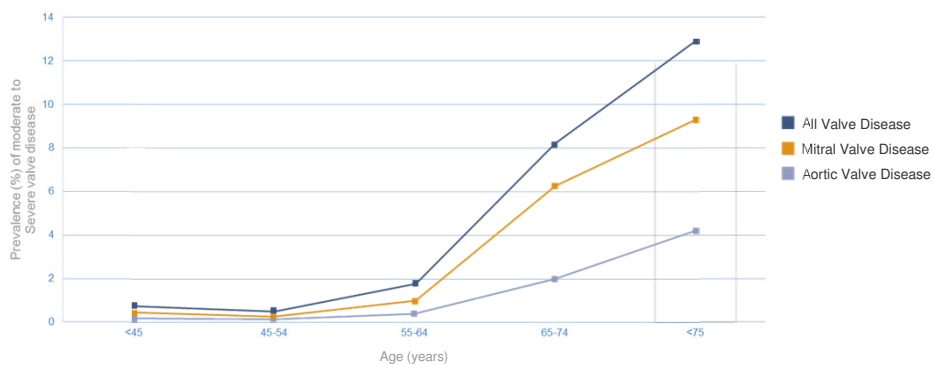
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A common disease that increases with age

MR affects approximately **1 in 10 people** after the age of 75



¹ Heart Disease and Stroke Statistics 2010 Update: A Report From the American Heart Association. Circulation. 2010;121:e46-e215.

² Nkomo et al. Burden of Valvular Heart Diseases: A Population-based Study. Lancet. 2006; 368: 1005-11.

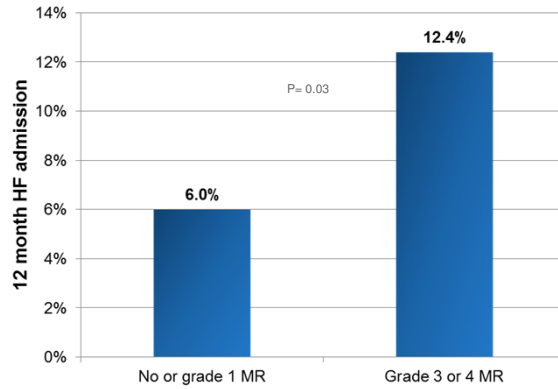
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Severe MR leads to increased hospital admissions

Significantly higher heart failure hospital admissions experienced by patients with moderate to severe MR



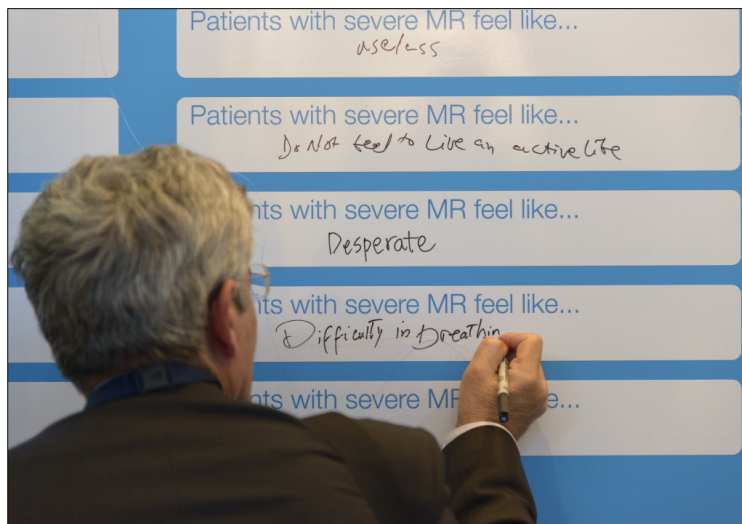
Markwick et al, TCT 2012

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Physician testimonials



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Physician testimonials



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Recommended therapeutic solutions

2012 ESC/EACTS guidelines on management of valvular heart disease

Medical Therapy	Mitral Valve Surgery	CRT	Percutaneous Mitral Valve Repair
First line treatment, limited to symptom management	Reliable reduction of MR to be considered based on patient risk status	Option for patients who fail to respond to medical therapy	Less invasive therapy to be considered in patients judged inoperable or at high surgical risk*
			2012 Update

Source: <http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/valvular-heart-disease.aspx>

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Limitations in regard to medical management

- **No medications are indicated to treat MR**, only to manage patients' symptoms.
- For the asymptomatic patients with chronic MR, there is no indicated medical therapy.
- In acute severe MR, medical therapy has a limited role and is aimed primarily to stabilize hemodynamics in preparation for surgery.
- If left ventricular systolic dysfunction is present, treatment with ACE inhibitors or beta blockers (particularly carvedilol) have been shown to reduce severity of functional MR.

Bonow et al. Circulation 2008

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Limitations in regard to current surgical management

- Many patients are not considered appropriate candidates for mitral valve surgery. **Up to 50%** of patients with severe symptomatic MR **are not referred to surgery**, even if a surgical indication exists.
- Reasons for denying surgery include impaired LVEF, a high operative risk, multiple co-morbidities, and advanced age.¹
- Nearly 1/3 of patients who are older and have more co-morbidities, still are likely to receive a replacement valve.²

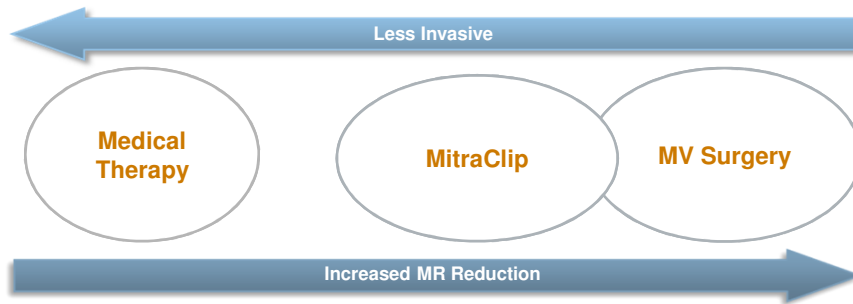
Mirabel et al. European Heart Journal 2007 / 2. Gammie et al. Ann Thorac Surg 2009

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Filling a treatment gap MitraClip rtherapy



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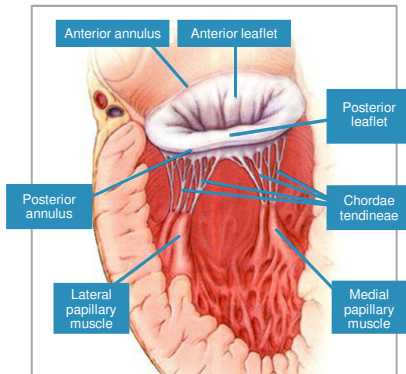


MitraClip procedure and device

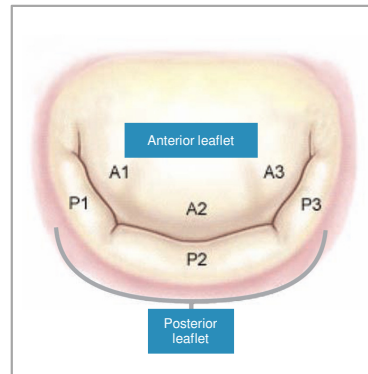


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A Promise for Life

The Mitral Valve Anatomy



The mitral valve apparatus includes the annulus, the leaflets, the chordae tendineae, and papillary muscles.



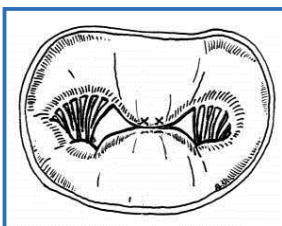
The leaflets are normally asymmetric—the anterior leaflet has a larger surface area, but occupies a smaller amount of annular circumference.

Images modified from Carpentier, A. et al. *Carpentier's Reconstructive Valve Surgery*. Saunders Elsevier; 2010.
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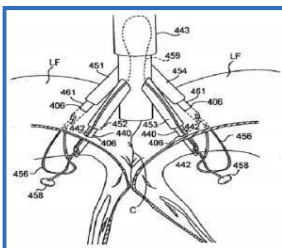
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Concept: Percutaneous Mitral Valve Repair



- Double-orifice suture technique developed by Prof. Ottavio Alfieri
- First published results in 1998 illustrated proven benefit in selected pathologic conditions



- Dr. Fred St. Goar, interventional cardiologist had patient successfully treated with edge-to-edge surgery
- Conceived several ideas for percutaneous valve repair
- Founded Evalve 1999 in to develop minimally invasive approach to treat mitral regurgitation based on the Alfieri technique

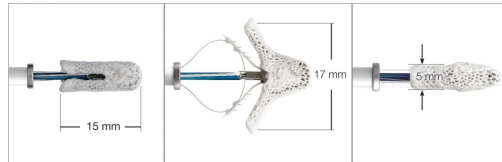
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The MitraClip System

- Percutaneous repair of the MV
- Beating heart procedure—no cardiopulmonary bypass
- Allows for real-time positioning and repositioning to optimize MR reduction
- Designed to preserve surgical options
- Femoral venous access
- Limited hospital length of stay compared to that after surgery

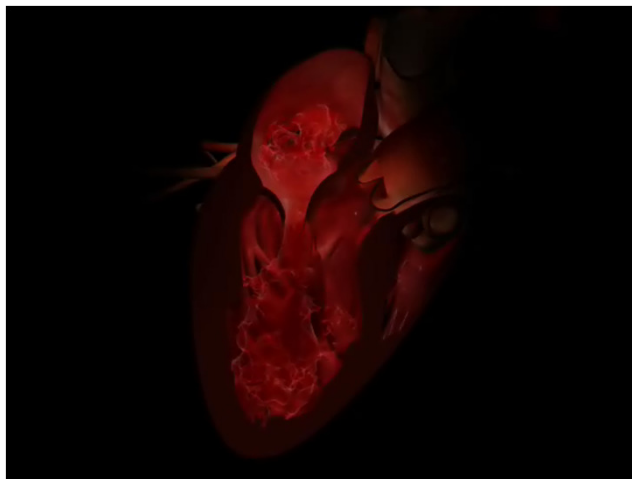


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MitraClip procedure



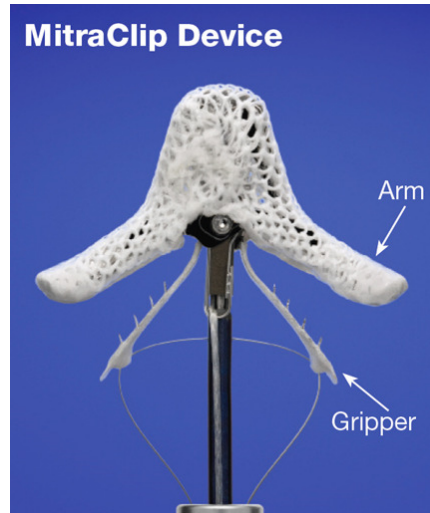
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A Closer Look at the MitraClip Device

- Implant made of cobalt chromium
- Polyester-covered to promote healing
- MRI Safe to 3 Tesla
- Real-time positioning during procedure
- Surgically removable when required

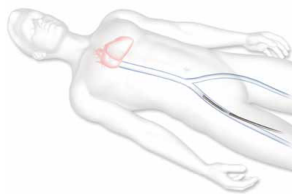


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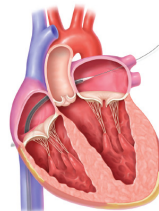
Procedural Overview

Patient and System Preparation



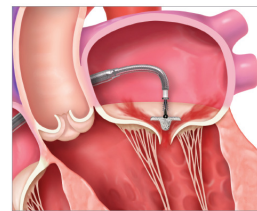
- The following considerations should be accounted for:
 - TEE probe will be in place for an extended period of time
 - Intubation under general anesthesia
 - 24 French sheath in femoral vein
 - Bladder/urinary catheter in place
 - Heparinization during procedure to ACT > 250
- System is prepared by removing all the air in the lumens of the Clip Delivery System and Steerable Guide Catheter
- System is functionally tested prior to use

Transseptal Crossing and Guide Insertion



A transseptal procedure is performed to gain access from the right atrium to the left atrium. The Steerable Guide Catheter (Guide) and Dilator are then carefully advanced into the left atrium over a wire. Once the Guide is in place and secured, the wire and Dilator are removed leaving the Guide in the left atrium.

Clip Delivery System Insertion and Steering in the Left Atrium



To introduce the Clip, the Clip Delivery System (CDS) is advanced through the Guide into the left atrium. A series of steering maneuvers and manipulations with the Guide and CDS are required to align the Clip perpendicular to the mitral valve plane, and the Clip Arms perpendicular to the line of coaptation. These maneuvers are done under echocardiographic and fluoroscopic guidance.

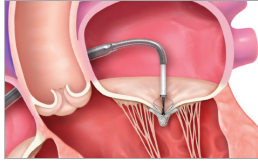
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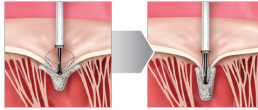
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Procedural Overview

Advancing into Left Ventricle and Leaflet Grasping

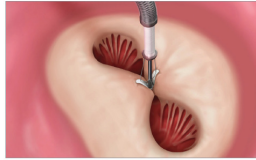


After the Clip is aligned over the regurgitant jet in the left atrium, the System is then advanced into the left ventricle to begin the grasping procedure. Leaflet grasping is done by slowly retracting the System back towards the left atrium to allow the leaflets to come to rest on the Clip Arms and then dropping the Grippers.



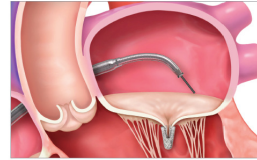
Clip Arms closed to 120° Clip Arms closed to 20°

Leaflet Insertion Assessment and Hemodynamic Measurements



Prior to Clip closure and deployment, a leaflet insertion and hemodynamic assessment must be performed. The leaflet insertion assessment ensures both leaflets are fully inserted and secure into the Clip. In addition, the MR reduction and pressure gradients are assessed to ensure regurgitation reduction without stenosis.

Deployment and System Removal



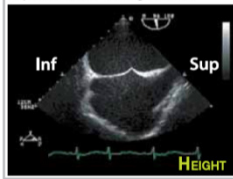
Once the assessments are positive, the Clip can be fully closed and deployed in a multistep process. The physician may also decide to place a second Clip to optimize MR reduction. The System is removed by releasing deflections on the catheter and slowly removing from the patient. Groin management and continued medical therapy are recommended per the institution's guidelines.



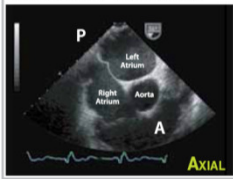
The MitraClip Procedure is Primarily Guided by Transesophageal Echo (TEE)

TEE Procedural Echo Views

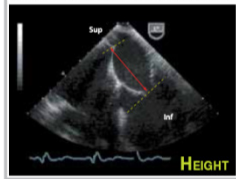
Transeptal #1
Bi Caval (80-110°) – Proper superior-inferior tenting location



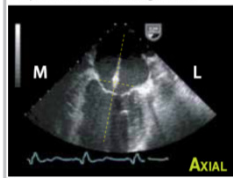
Transeptal #2
SAX at Base (30-60°) – Proper anterior-posterior tenting location



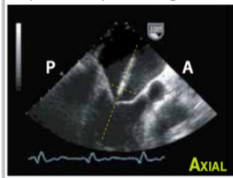
Transeptal #3
4 Chamber (0°) – Confirmation of proper height above line of coaptation



Positioning & Trajectory #1
Intercommissural - 2C (55-75°)
Proper medial-lateral alignment



Positioning & Trajectory #2
LVOT (100-160°)
Proper anterior-posterior alignment



HEIGHT above valve

For proper Delivery Catheter travel during grasping and adequate tension on leaflets.

AXIAL alignment

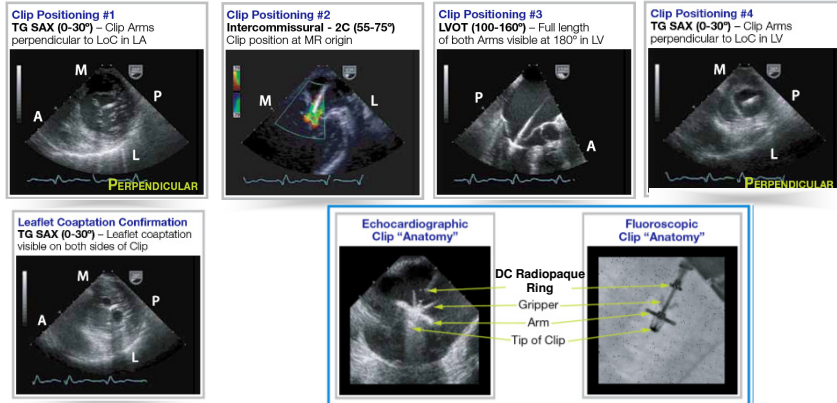
For proper grasping and symmetrical leaflet capture.

PERPENDICULAR to line of coaptation (LoC)

For symmetrical leaflet capture and adequate leaflet insertion.

The MitraClip Procedure is Primarily Guided by Transesophageal Echo (TEE)

TEE Procedural Echo Views



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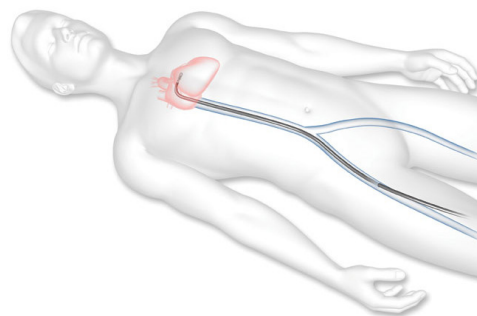
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Post-procedure Considerations

Post-Procedure Recovery Instructions

- Patient might have to be intubated, procedure performed under general anesthesia
- Patient may have Femoral Arterial and/or Venous access
- Patient will have had 24 French sheath in Femoral Vein during procedure
- Patient will have Foley catheter in place
- Patient will have had TEE probe in place for extended period of time
- Antibiotic Therapy
 - Administer prophylactic antibiotics per institutional guidelines for implanted devices
- Groin Access
 - Per institutional guidelines and similar to other catheterization procedures
- Anticoagulation Therapy
 - Short-term anticoagulation therapy may be necessary after cardiac valve repair with the MitraClip device. Prescribe anticoagulation and other medical therapies per institutional guidelines.



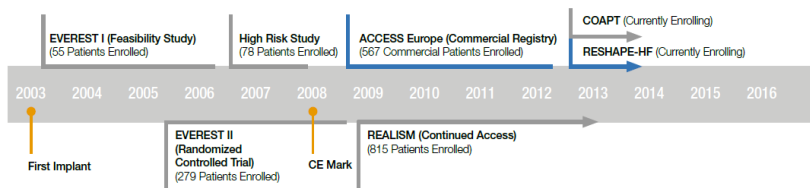
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Worldwide Clinical Experience

- Over 13,000 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 \geq 20%, or STS calculated mortality \geq 12%, or pre-specified high surgical risk co-morbidities specified in EVEREST II High Risk Study protocol.

Reimbursement and Funding Overview

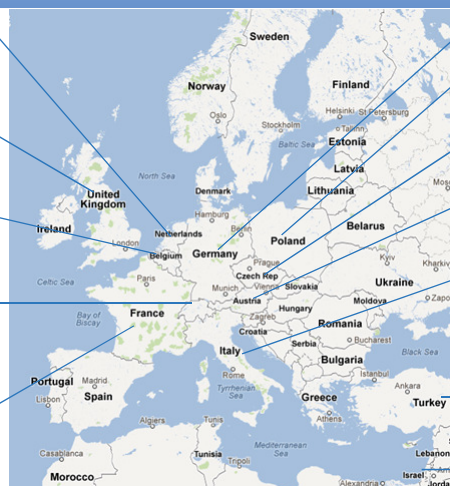
Netherlands: DRG as of Jan 2014

UK: Commissioning through Evaluation

Belgium: New reimbursement submission July 2013

Switzerland: DRG for the procedure as of Jan 2014*

France: PHRC/MitraFR study granted (1st patient in by Q4 2013)



Germany: DRG since Jan 2013

Poland: Reimbursement in 6 centers

Czech Republic: 2 Private insurances agreement

Austria: Temporary code in place. DRG will be requested when RCT data available

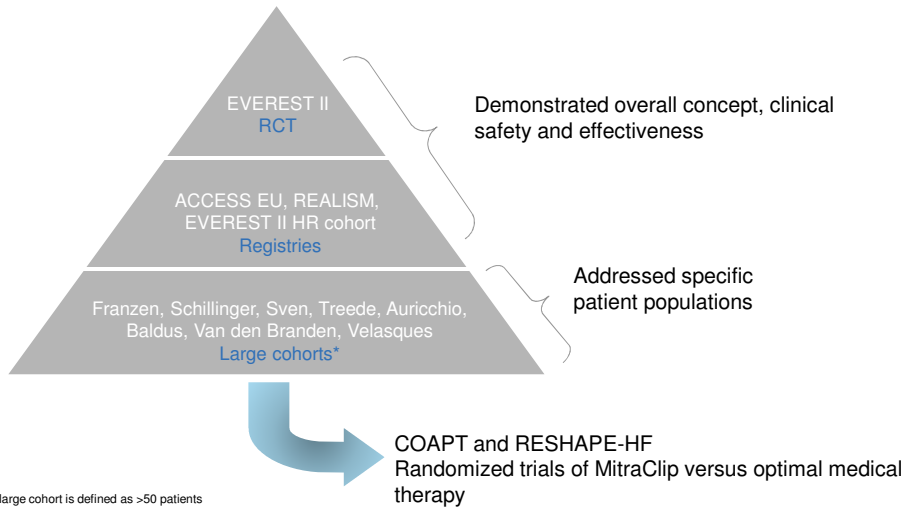
Italy: Regional or innovation funding ongoing. Device reimbursed on top of DRG in Lombardy (80%)

Turkey: SGK coverage in public hospitals

Israel: Reimbursement as of Jan 2014

*conditions apply

Growing Body of Clinical Evidence



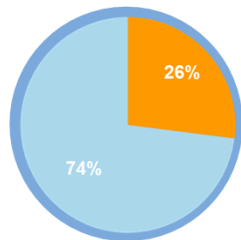
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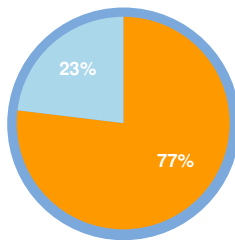
MitraClip Therapy Broad Spectrum of Experience

EVEREST II
(Randomized Controlled Trial)



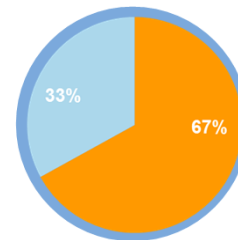
- 178 patients
- Device time – 146 minutes
- Implant rate – 89%

ACCESS EU
(Europe)



- 567 patients
- Procedure time – 117 minutes
- Implant rate – 99%

Commercial
(APJ, CALA, Europe, US)



- 10,614 patients
- Device time – 91 minutes
- Implant rate – 96%

■ = DMR ■ = FMR

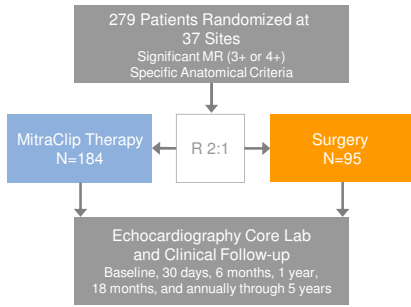
Data on file Abbott Vascular, December 31, 2013.
Source: Schillinger, W. ACCESS-EUROPE Phase I: A Post Market Study of the MitraClip System for the Treatment of Significant Mitral Regurgitation in Europe: Analysis of Outcomes at 1 Year. ESC 2012; August 25-29, 2012; Munich, Germany.
Lim, S. The EVEREST II High Surgical Risk Cohort: Effectiveness of Transcatheter Reduction of Significant Mitral Regurgitation in High Surgical Risk Patients. ACC 2013; San Francisco, CA

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EVEREST II Randomized Controlled Trial Design



Patient Demographics	MitraClip Therapy (n=184)	Surgery (n=95)	P-value
Age (mean)	67 years	66 years	0.32
Male	63%	66%	0.60
History of CHF	91%	78%	0.005
Degenerative MR Etiology	74%	73%	0.81
Functional MR Etiology	26%	27%	0.81
Mean Ejection Fraction	60%	61%	0.65
Previous Coronary Artery Bypass Grafting (CBAG)	21%	19%	0.54
NYHA Functional Class III/IV	51%	48%	0.61
Atrial Fibrillation	34%	39%	0.42

Source: Feldman T, Foster E, Qureshi M, et al. The EVEREST II Randomized Controlled Trial: Three Year Outcomes Transcatheter Cardiovascular Therapeutics; October 22-26, 2012; Miami, FL.

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EVEREST II RCT

- Positive Safety Profile

Major Adverse Events at 30 Days All Treated Patients (N=258)

Description of Event	# (%) Patients experiencing event	
	MitraClip (N=178)	Surgery (N=80)
Death	2 (1.1%)	2 (2.5%)
Myocardial Infarction	0	0
Re-operation of Mitral Valve	0	1 (1.3%)
Urgent / Emergent CV Surgery	4 (2.2%)	4 (5.0%)
Stroke	1 (0.6%)	2 (2.5%)
Renal Failure	1 (0.6%)	0
Deep Wound Infection	0	0
Ventilation > 48 hrs	0	4 (5.0%)
GI Complication Requiring Surgery	2 (1.1%)	0
New Onset Permanent AFib	2 (1.1%)	0
Septicemia	0	0
MAE Major Bleeding Complication*	9 (5.1%)	37 (46.3%)
TOTAL % of Patients with MAE	7.9%	50.0%

Source: Feldman T, Foster E, Qureshi M, et al. The EVEREST II Randomized Controlled Trial: Three Year Outcomes Transcatheter Cardiovascular Therapeutics; October 22-26, 2012; Miami, FL.

*Major Bleeding Complications included in this table required surgery or transfusions ≥ 2 units of blood; does not include bleeding events already reported in other categories in this table.

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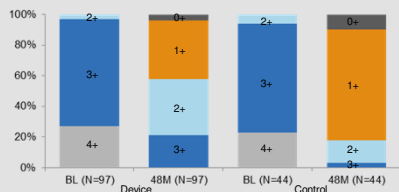
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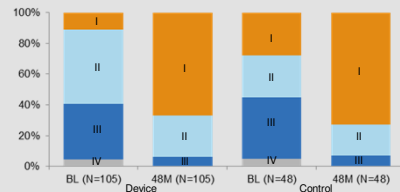
EVEREST II RCT 4-year Results

- Sustained clinical benefits comparable to those seen after surgery
 - Improvements in NYHA class: only 5.7% of patients in NYHA III-IV in the MitraClip group and 6.3% in the surgical group at 4 years
- Improvement in MR durable through 4 years

MR Severity at Baseline and 48 Months



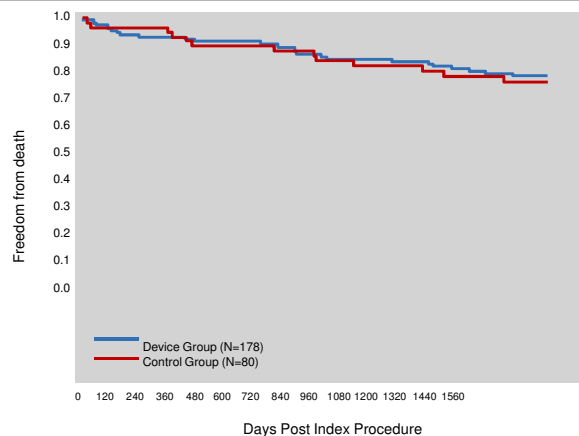
NYHA Functional Class at Baseline and 48 Months



Source: Mauri et al EVEREST II 4 years JACC manuscript 2013

EVEREST II RCT 4-year Results

- Freedom from death comparable to surgery

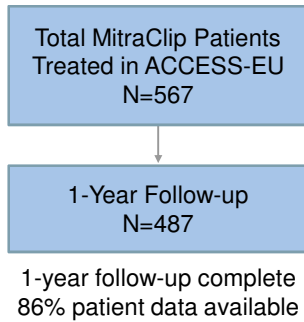


Source: Mauri et al EVEREST II 4 years JACC manuscript 2013

ACCESS EU - Real-World Clinical Experience

ACCESS-EU Cohort: The majority of patients have functional MR and extensive co-morbidities

Study Design



Baseline Demographics and Comorbidities	ACCESS-EU MitraClip Patients, N=567
Age (mean ± SD), years	74 ± 10
Logistic EuroSCORE, (%)	
Mean ± SD	23 ± 18
Logistic EuroSCORE ≥20, (%)	45
Male Gender, (%)	64
Mitral Regurgitation Grade 3+, (%)	98
NYHA Functional Class III or IV, (%)	85
Ejection Fraction <40%, (%)	53

Source: Schillinger, W. ACCESS-EUROPE Phase I: A Post Market Study of the MitraClip System for the Treatment of Significant Mitral Regurgitation in Europe: Analysis of Outcomes at 1 Year. ESC 2012; August 25-29, 2012;

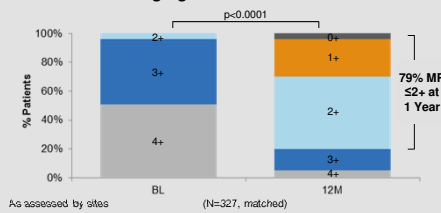
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ACCESS EU - Real-World Clinical Experience

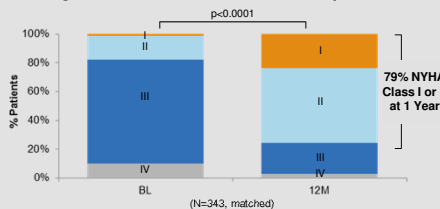
Mitral Regurgitation Grade Reduction



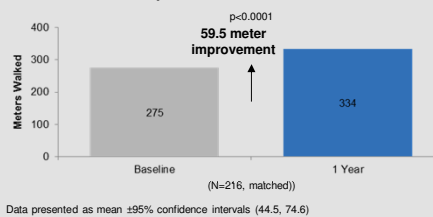
Demonstrated safety with low adverse event rates

Description of Event	Site Reported Safety Events at 30 Days
Death	19 (3.4)
Stroke	4 (0.7)
Myocardial Infarction	4 (0.7)
Renal Failure	27 (4.8)
Respiratory Failure	4 (0.7)
Need for Resuscitation	10 (1.8)
Cardiac Tamponade	6 (1.1)
Bleeding Complications	22 (3.9)

Significant NYHA Functional Class Improvements



Functional Improvement in 6-Minute Walk Test



Source: Schillinger, W. ACCESS-EUROPE Phase I: A Post Market Study of the MitraClip System for the Treatment of Significant Mitral Regurgitation in Europe: Analysis of Outcomes at 1 Year. ESC 2012; August 25-29, 2012; Munich, Germany.

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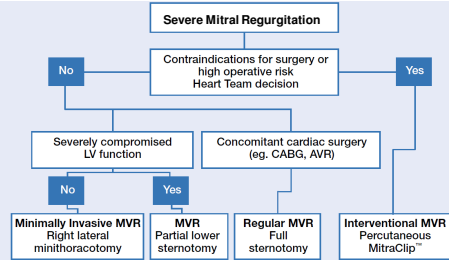


Hamburg UKE Experience – High Risk Patients

- 202 consecutive patients: No prior mitral valve intervention
- FMR 65%, DMR 27%, mixed 8%
- Mean logistic EuroScore of 36%

Baseline characteristics 202 patients

Baseline characteristics	
Age	75 ± 9
FMR etiology (%)	65
LVEF (%)	44 ± 16
NYHA III-IV (%)	98
Logistic EuroSCORE (%)	36 (21-54)
Ischemic Cardiomyopathy (%)	41



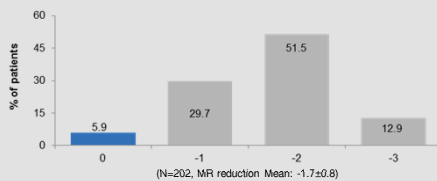
Heart Team Treatment Decision matrix:

MitraClip patients: "severe mitral valve regurgitation patients with contraindications for surgery or high operative risk"

Treede H et al. A heart team's perspective on interventional mitral valve repair: Percutaneous clip implantation as an important adjunct to a surgical mitral valve program for treatment of high-risk patients. J Thorac Cardiovasc Surg. 2011 Oct 26

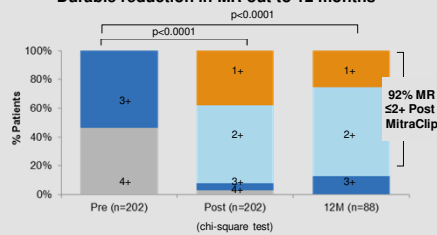
Hamburg UKE Experience – High Risk Patients

Acute reduction in MR by grade

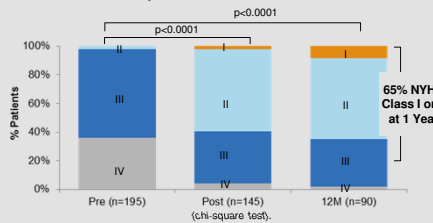


Data presented as mean ± 95% confidence intervals (44.5, 74.6)

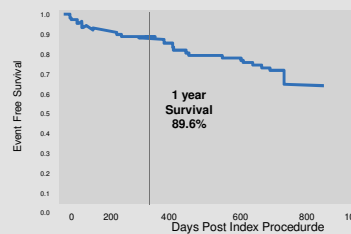
Durable reduction in MR out to 12 months



Durable improvement in NYHA classification



Overall survival at 12 months was 89.6%



Treede H et al. A heart team's perspective on interventional mitral valve repair: Percutaneous clip implantation as an important adjunct to a surgical mitral valve program for treatment of high-risk patients. J Thorac Cardiovasc Surg. 2011 Oct 26

MitraClip in Specific Patient Populations

Patient groups in which significant clinical benefits have been reported:

- Degenerative MR, declined for surgery¹
- Severe LV dysfunction refractory to medical therapy²
- Severe Heart Failure, despite optimal medical therapy³
- CRT non-responders⁴
- Bivalvular Disease: Severe Aortic Stenosis and Mitral Regurgitation⁵

The following parameters should be taken into consideration by the Heart Team⁶:

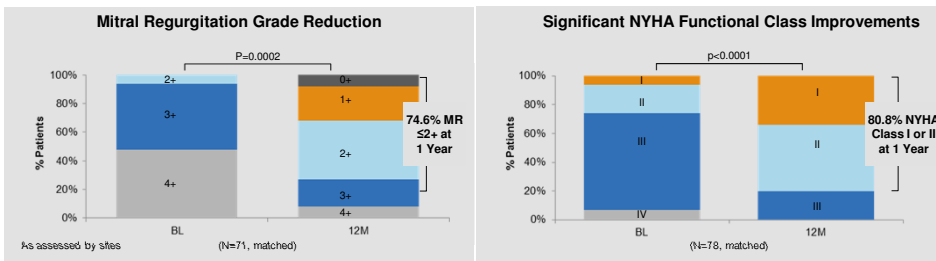
- Moderate to severe or severe MR (Functional or Degenerative)
- Echocardiographic criteria for eligibility
- Level of surgical risk
- Greater than one year life expectancy

1. Reichenspurner, H. et al. Clinical Outcomes through 12 months in patients with Degenerative Mitral Regurgitation treated with the MitraClip device in the ACCESS-Europe Phase I trial. Eur J Cardiothoracic Surgery. 2013; 44:e 280-288. 2. Franzen O, Baldus S, Rudolph V, et al. Acute outcomes of MitraClip therapy for mitral regurgitation in high-surgical-risk patients: Emphasis on adverse valve morphology and severe left ventricular dysfunction. Eur Heart J. 2010; 31:1373-1381. 3. Franzen et al. MitraClip Therapy In Patients With End-Stage Systolic Heart Failure. Eur J Heart Failure. 2011; 13: 569-576. 4. Auricchio et al. Correction of Mitral Regurgitation in Nonresponders To Cardiac Resynchronization Therapy By MitraClip Improves Symptoms And Promotes Reverse Remodeling. JACC 2011; 58: 2183-2189. 5. Rudolph V, Schirmer J, Franzen O, Schlüter M, Seifert M, Treede H, Reichenspurner H, Blankenbreg S, Baldus S. Bivalvular transcatheter treatment of high-surgical-risk patients with coexisting severe aortic stenosis and significant mitral regurgitation. Int J Cardiol. 2013; 167(3):716-20. 6. ESC/EACTS 2012 Guidelines on the management of valvular heart disease. Eur Heart J (2012) 33, 2451-2496.

The data is not from prospective studies and study results should be interpreted with caution

Degenerative MR, Declined for Surgery

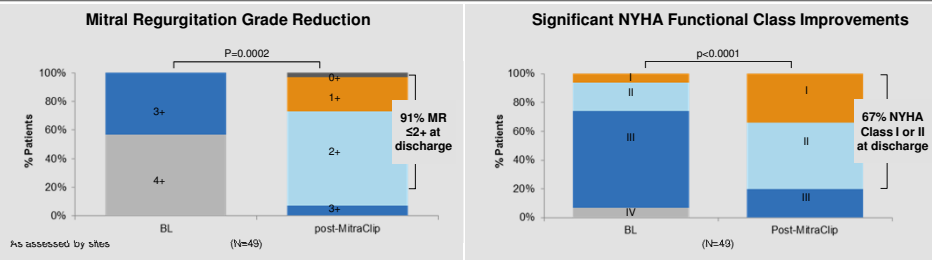
- ACCESS-EU DMR patients cohort: 117 elderly patients, 74% in NYHA class III-IV
- Significant reduction in MR and clinical improvements reported at 12 months
- Implant rate of 94.9%
- MitraClip therapy reduced symptoms and enhance quality of life in patients deemed inoperable or at high surgical risk
- Survival rate of 82.9% reported at 12 months



Reichenspurner, H. et al. Clinical Outcomes through 12 months in patients with Degenerative Mitral Regurgitation treated with the MitraClip device in the ACCESS-Europe Phase I trial. Eur J Cardiothoracic Surgery. 2013; July 17

Severe LV Dysfunction Refractory to Medical Therapy

- 51 patients with MR $\geq 3+$: adverse MV morphology and/or severe LV dysfunction in 69%
- Procedural success achieved in 96% of patients
- Reduction in MR, although moderate in most patients, was acceptable given high surgical risk and corresponding clinical benefits



“Mitral valve repair using the MitraClip system was shown to be feasible in patients at high surgical risk primarily determined by an adverse mitral valve morphology and/or severe LV dysfunction.”

Franzen O, Baldus S, Rudolph V, et al. Acute outcomes of MitraClip therapy for mitral regurgitation in high-surgical-risk patients: Emphasis on adverse valve morphology and severe left ventricular dysfunction. Eur Heart J. 2010; 31:1373-1381

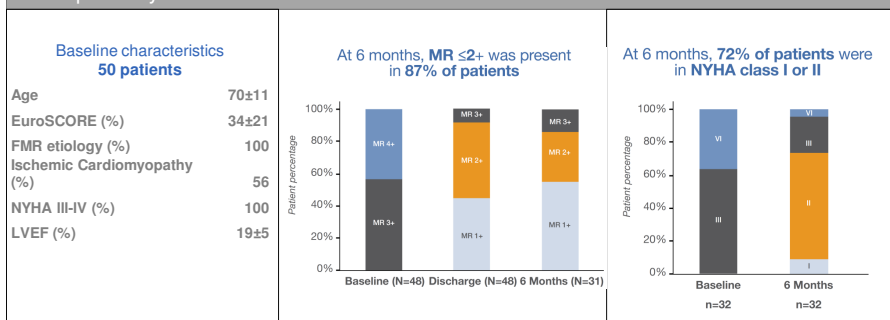
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Severe HF, Despite Optimal Medical Therapy

- Retrospective analysis of 50 patients with LVEF $\leq 25\%$, MR $\geq 3+$ and NYHA III or IV
- Significant clinical improvements reported at 6 months
- Cumulative survival at 6 months in NYHA-III and NYHA-IV patients was 81.2% and 64.2% respectively



“Patients with end-stage heart failure and marked LV dysfunction can be treated by the MitraClip as successful therapy promotes clinical benefits at 6 months.”

Franzen O, et al. MitraClip(R) therapy in patients with end-stage systolic heart failure. Eur J Heart Fail 2011; 13(5):569-576

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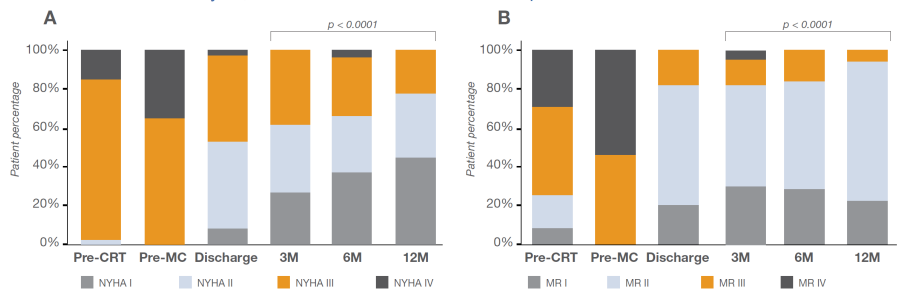
38



PERMIT-CARE – CRT Non-responders

- Prospective survey of 51 “CRT nonresponders”, with FMR and NYHA III or IV
- Implant rate of 95%
- At discharge 73% patients had an improved functional NYHA class; the proportion of NYHA I & II increased overtime.
- LVEF significantly increased at 6 and 12 months
- Reverse LV remodeling occurred even in the presence of MR 2+ - reduced LV volume in 70% of patients

Results: at 1 year, sustained reduction in MR and improvement in NYHA functional class



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.
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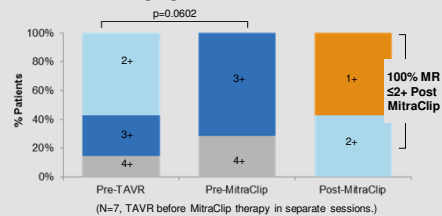
Bivalvular Disease: Severe Aortic Stenosis and Mitral Regurgitation

- 11 patients with bivalvular AS and MR 3+ treated with TAVR followed by MitraClip
- TAVR preceded MitraClip therapy in 10 patients; 3 patients undergoing both interventions in a single session.
- Reduction in MR severity to 2+ or less in 10 patients; 100% of patients who underwent TAVR before MitraClip in separate session achieved MR ≤ 2+

Baseline characteristics 11 patients

Baseline characteristics	
Age	78 ± 6
FMR etiology (%)	45
LVEF (%)	36 ± 13
NYHA III-IV (%)	91
Logistic EuroSCORE (%)	25
Ischemic Cardiomyopathy (%)	45

Mitral Regurgitation Grade Reduction



“Complete transcatheter treatment of coexisting severe AS and significant MR in high-surgical-risk patients is technically feasible, regardless of which prosthesis and what access route is chosen for TAVR, and regardless of whether both procedures are performed in separate sessions or in a single session.”

Rudolph V, Schirmer J, Franzen O, Schlüter M, Seiffert M, Treede H, Reichenspurner H, Blankenberg S, Baldus S. Bivalvular transcatheter treatment of high-surgical-risk patients with coexisting severe aortic stenosis and significant mitral regurgitation. Int J Cardiol. 2013; 167(3):716-2

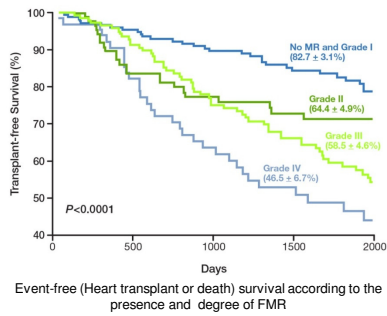
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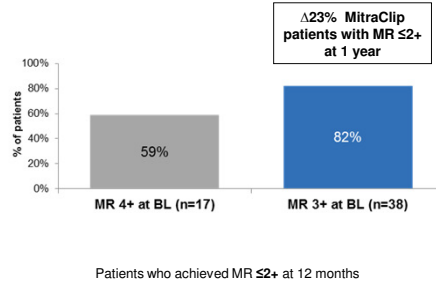


Earlier Referral Saves Lives

Event – free survival decreases with increasing MR severity^{1,2,3}



MitraClip intervention in less severe MR results in better outcomes⁴



1. Bursi F et al. Eur J Heart Failure 2010; 12:382-88; 2. Enriquez-Sarano M, Avierinos J-F, Messika-Zeitoun D, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Eng J Med*. 2005;352(9):875-883.; 3. Grigioni F, Tribouilloy C, Avierinos JF, et al. Outcomes in mitral regurgitation due to flail leaflets: a multicenter European study. *J Am Coll Cardiol* 2008;1(2):133-141. 4. Whitlow et al. JACC Vol. 59, No. 2, 2012:130-9

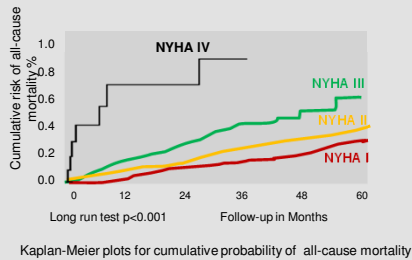
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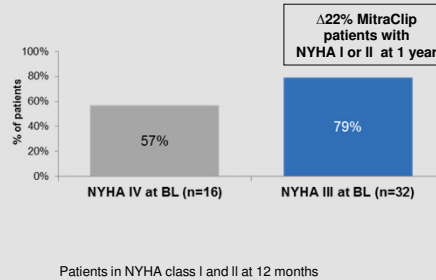


Earlier Referral Saves Lives

Risk of mortality increases with increasing NYHA class



For patients with MR≥3+, MitraClip intervention in less severe NYHA class results in better outcomes



Ahmed A et al. Am Heart J. 2006 151: 444-50; Whitlow et al. EII High Risk Study (JACC 2012) Vol. 59, No. 2, 2012:130-9

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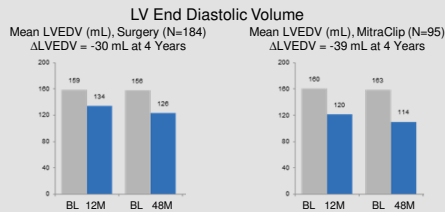
42



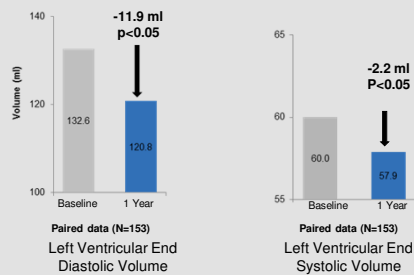
Reverse LV Remodeling

- EVEREST II 4 year outcomes – reverse LV remodeling
- REALISM Non-High Risk Cohort 1 year outcomes - significant improvements in LV reverse remodeling

Reverse LV remodeling - EVEREST II RCT 4 years outcomes



REALISM Non-High Risk Cohort 1 year outcomes



Mauri et al EVEREST II 4 years JACC manuscript 2013
S. Kar, S. Lim, REALISM Non-High Risk – ACC 2013

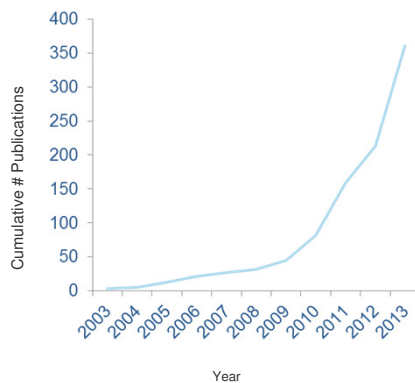
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Growing Number of Clinical Publications

361 total publications on MitraClip therapy (2003-2013)



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED 1912 APRIL 14, 2011 VOL 364 NO 15

Percutaneous Repair or Surgery for Mitral Regurgitation

Reif Feldman, M.D., Elyse Frerking, M.D., Donald C. Glines, M.D., Stefan Erbe, M.D., Michael J. Brindley, M.D., Peter S. Fain, M.D., Richard W. Smalling, M.D., Ph.D., Robert Siegel, M.D., Geoffrey A. Rose, M.D., Erik Engstrom, M.D., Carlos Legido, M.D., Alfredo Torrealba, M.D., Eric S. Siegen, M.D., Yoonmi Fodge, M.D., George V. Lantieri, M.D., Joseph M. Mazzone, Ph.D., and Laura Mauri, M.D., for the EVEREST II Investigators*

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

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

European Heart Journal 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)

European Journal of Heart Failure

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

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ESC Heart Failure 2012 Guidelines


 European Heart Journal
 doi:10.1093/eurheartj/ehs104

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

“ 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 ”

(page 48 from ESC 2012 guidelines)

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>

German AGIK and ALKK 2013 Recommendations

Morphology for a MitraClip therapy

Optimal valve morphology	Conditionally suitable valve morphology	Unsuitable valve morphology
Central pathology in Segment 2 No leaflet calcification	Pathology in Segment 1 or 3 Mild calcification outside of the grip-zone of the clip system; ring calcification, post annuloplasty	Perforated mitral valve leaflet or cleft Severe calcification in the grip-zone
Mitral valve opening area >4 cm ²	Mitral valve opening area >3 cm ² with good residual mobility	Haemodynamically significant mitral stenosis (valve opening area <3 cm ² , MPG≥5 mmHg)
Mobile length of the posterior leaflet ≥10 mm	Mobile length of the posterior leaflet 7–10 mm	Mobile length of the posterior leaflet <7 mm
Coaption depth <11 mm	Coaption depth ≥11 mm	
Normal leaflet strength and mobility	Leaflet restriction in systole (Carpentier IIIB)	Rheumatic leaflet thickening and restriction in systole and diastole (Carpentier IIIA)
Flail-width <15 mm Flail- Gap <10 mm	Flail-width >15 mm only with a large ring width and the option for multiple clips	Barlow's syndrome with multisegment flail leaflets

Indications for the MitraClip therapy

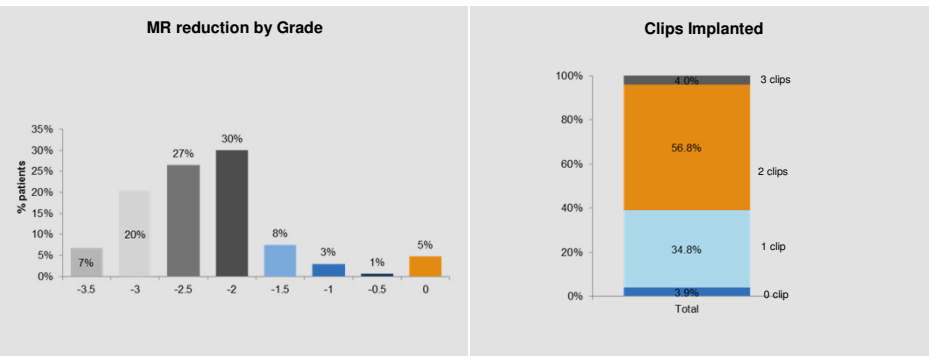
Ideal for Mitraclip treatment	MitraClip to be considered	MitraClip not recommended or only in exceptional cases
Severe mitral regurgitation and Optimal valve morphology and FMR with LVEF<30 % or DMR (with operation-indication following guidelines) and A high operative risk or other risk-constellations	Moderate to severe mitral regurgitation and Optimal valve morphology and FMR or DMR (with operation-indication following guidelines) and High operative risk, very high age or other risk-constellations	Moderate to severe mitral regurgitation and Conditionally suitable valve morphology or Life expectancy <12 months or LVEF<15 % or cardiothoracic operation planned due to other indications or Previously operated mitral valve or As surgical/interventional hybrid procedure or At low operative risk

Source: Boekstegers P, et al. Percutaneous interventional mitral regurgitation treatment using the Mitra-Clip system. Clin. Res. Cardiol. 2013

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European Patient Profiles Outcomes

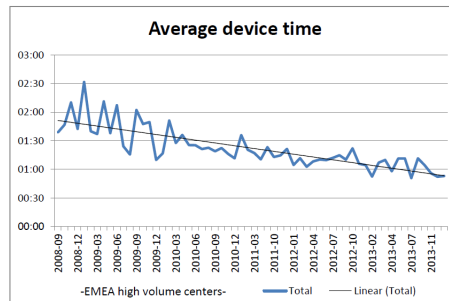
- More than 80% of patients achieved MR reduction of 2 grades or more
- More than 90% were treated with 2 clips or fewer



Data sources: Data on file at Abbott Vascular, December 2013 This includes all submitted and reviewed procedures, including successful and unsuccessful procedures as reported. .

Importance of the Learning Curve

- The MitraClip learning curve is characterized by¹:
 - Procedure time reduction: 180min to 55min
 - Acute procedural success* from 80% to 92%
- Significant device time reduction is observed across the MitraClip centers of excellence²



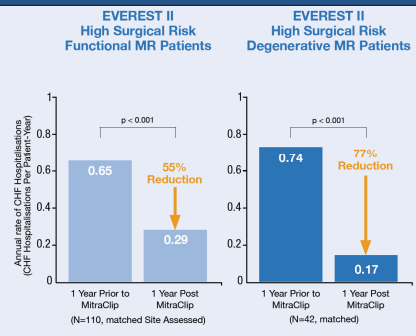
*Acute procedural success: implanted MitraClip device and MR ≤2+

1. Schillinger W et al. Impact of the learning curve on outcomes after percutaneous mitral valve repair with MitraClip and lessons learned after the first 75 consecutive patients? - European Journal of Heart Failure Advance Access October 24, 2011 3
2. Data sources: Data on file at Abbott Vascular, December 2013 This includes all submitted and reviewed procedures, including successful and unsuccessful procedures as reported.

Economic Value

- **Hospitalizations** accounts for approximately **60% of total heart failure cost** in the US.¹
- Significantly reduced **post-procedural hospital length of stay** with MitraClip vs surgery (EVEREST II RCT). The average length of stay for the MitraClip group was 2.6 days versus 7.5 days in the surgical control group. In the high risk surgical cohort, only a slight increase of up to 3 days was observed.²
- Analysis of high surgical risk patients demonstrated significant decrease in CHF hospitalizations.^{3, 4}

Significantly Decreased CHF Hospitalizations



1. Braunschweig F, Cowie MR, Auricchio A. What are the costs of heart failure? Europace 2011
2. Data on file at Abbott Vascular, November 2011
3. Argemiano, M et al. EVEREST II High Surgical Risk Cohort: Effectiveness of Percutaneous Reduction of Significant Mitral Regurgitation in Functional Etiology. Transcatheter Cardiovascular Therapeutics Annual Conference; November 7-11, 2011; San Francisco, CA
4. Feldman, T. EVEREST II High Surgical Risk Cohort: Effectiveness of Percutaneous Reduction of Significant Mitral Regurgitation in Degenerative Etiology. Transcatheter Cardiovascular Therapeutics Annual Conference; November 7-11, 2011; San Francisco, CA.

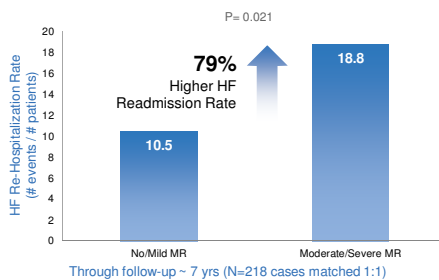
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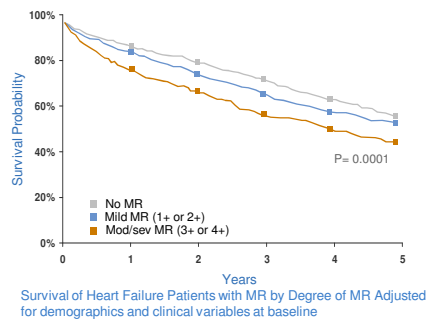


Severe MR leads to increased hospital admissions and lower survival rates

Significantly higher hospital admissions experienced by patients with moderate to severe MR¹



Significantly lower survival rates experienced by patients with moderate to severe MR²



1. Markwick et al. Prognostic Implications of Moderate and Severe Mitral Regurgitation in Contemporary Clinical Care. TCT 2012
2. Trichon BH et al. Am J Card. 2003;91:538-43

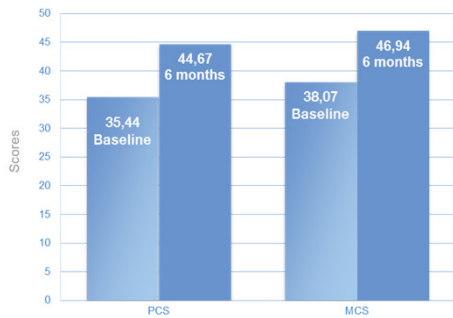
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Quality of life improvements experienced by patients

Significant improvement with high-risk patients



High Surgical Risk Patients with Severe MR: Results of Physical Component Summary (PCS) and Mental Component Summary (MCS) at 6 months post MitraClip procedure

G.P. Ussia et al. International Journal of Cardiology 155 (2012) 194–200

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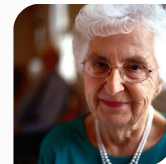
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Before MitraClip: “I couldn’t get my breath... I couldn’t even lie down. My doctor told my daughter that if I didn’t have MitraClip, there was no more to be done, and I would just gradually slip out of life.”

After MitraClip: “I feel so much better because I can walk now. I live alone. I like to get out... and do everything. I’m on the ball.”

-79 yr old MitraClip patient



Patient testimonials

“When I got home the first thing I did was sit down and cry. I was so happy and relieved that I had been given my independence back.”

Ethel Partington, 72, with a 20 year history of heart problems



“As Dr. Berens told my family, the MitraClip was my only hope. Without the MitraClip, my time was limited. For me, I believe the MitraClip should be called the “MiracleClip”. I left the hospital about 24 hours later.”

Kato Pomer, 92, one of the oldest, highest-risk patients to receive the MitraClip



“It’s made a lot of difference -- I was on oxygen for about 6 months (before the procedure) and I got rid of the oxygen the day after, and haven’t been on it since.”

Merv Hislop, 68, got the clip after suffering half a dozen minor heart attacks that left doctors warning he might not survive



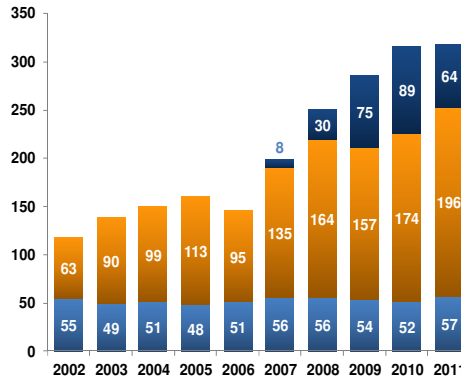
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Percutaneous Mitral Valve Repair is an Important Part of a Comprehensive Valve Center Serving Patients

Case study: Patient volume increases after introduction of MitraClip therapy

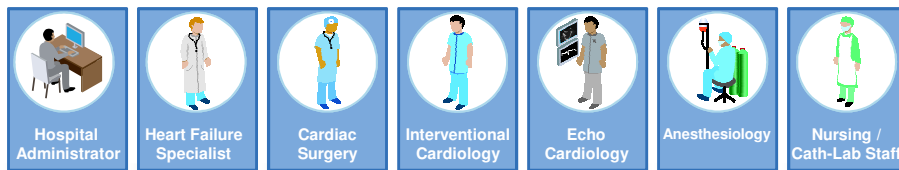


* Voluntary recall of MitraClip for 6 months
 - Hendrik Treede et al. A Heart Team's Perspective on Interventional Mitral Valve Repair: Percutaneous clip implantation as an important adjunct to a surgical mitral valve program for treatment of high-risk patients; The Journal of Thoracic and Cardiovascular Surgery, 2011; Conrad, L et al. Towards an integrated approach to mitral valve disease: implementation of an interventional mitral valve programme and its impact on surgical activity. European Journal of Cardio-Thoracic Surgery 44 (2013)



Multi-disciplinary Team Bridging Traditional Silos

Collaboration across specialties is critical to MitraClip Therapy Success



Optimal Patient Care

Summary

- Patients treated in a real world, commercial setting in Europe are elderly, have predominantly functional MR and a majority present with significant LV dysfunction
- The MitraClip procedure is performed consistently with a high implant rate and acute MR reduction achieved in a majority of patients
- Significant clinical improvements are achieved in majority of patients with results consistent with controlled clinical trials
 - Improvement in NYHA class
 - Durable improvement of MR grade
 - Functional improvement in 6 min walk test
 - Reverse LV remodeling
- Earlier referral saves lives
 - Survival decreases with increasing MR severity
 - MitraClip intervention at earlier MR disease stage results in better outcomes
- Significantly decreased CHF hospitalizations and length of stay

Thank you for your attention

Abbott Vascular International BVBA

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Abbott Vascular Sponsored Studies (EVEREST I, EVEREST II, REALISM, ACCESS-EU, RESHAPE-HF & COAPT) TRAMI, GRASP, PERMIT-Care are independent studies

Product is subject to prior training requirement as per the Instruction for Use. This product is intended for use by or under the direction of a physician. Prior to use, it is important to read the package insert thoroughly for instructions for use, warnings and potential complications associated with use of this device.

Information contained herein is for presentation for Europe, Middle East and Africa ONLY. Please check the regulatory status of the device before distribution in areas where CE marking is not the regulation in force.

The following needs to be considered by French healthcare professionals only. Clip de réparation mitrale MitraClip et accessoires. Dispositifs médicaux de classe III et I, organisme notifié Dekra. Fabriqué par Evolve Inc, mandataire européen MedPass. Se référer aux informations de la notice d'instructions qui décrivent les informations de bon usage du dispositif. Veuillez lire attentivement les instructions figurant dans la notice. Non pris en charge par les organismes d'assurance maladie.

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