Defining mitral regurgitation (MR)

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

Images: www.mayoclinic.com
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

A common disease that increases with age

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

![Graph showing prevalence of MR vs. age](chart.png)


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

Severe MR leads to increased hospital admissions

Markwick et al, TCT 2012

Physician testimonials

Patients with severe MR feel like...
- Very weak
- Do not feel in control
- Desperate
- Difficult in breathing
- Have no life
Physician testimonials

Recommended therapeutic solutions

2012 ESC/EACTS guidelines on management of valvular heart disease

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

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

• 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

Filling a treatment gap MitraClip therapy

Less Invasive

Medical Therapy  MitraClip  MV Surgery

Increased MR Reduction

MitraClip procedure and device
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.


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
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

MitraClip procedure
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

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
  - Biotronix catheter in place
  - Hemostasis during procedure to ACT > 250
  - System is preassembled, and after sheath is in the lumen of the Clip Delivery System and Biotronix 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 Guide and Clip Delivery System are then inserted. The sheath is advanced into the left atrium over a wire. Once the Guide is in place and secured, the Clip Delivery System is advanced using 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 is performed with the Guide and CDS to align the clip perpendicular to the native valve plane, and the Clip Delivery System is advanced using the guide in the left atrium. The maneuvers are done under fluoroscopic and transesophageal guidance.
The MitraClip Procedure is Primarily Guided by Transesophageal Echo (TEE)

**Procedural Overview**

**Advancing into Left Ventricle and Leaflet Grasping**
After the Clip is aligned over the regurgitant jet in the left atrium, the sheath is then advanced into the left ventricle to begin the grasping procedure. Leaflet grasping is done by slowly retracting the system back until the leaflet is grasped by the leaflet grasping system. The Clip is then rotated to 90° on the Clip arms and then the leaflet is grasped.

**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 retracted and secured into the Clip. In addition, hemodynamic assessments are conducted to ensure regurgitation reduction without stress.

**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 MV reduction. The system is then removed from the patient. Careful management and continued medical therapy are recommended per the institution’s guidelines.

**TEE Procedural Echo Views**

- **Transseptal #1 Bi Cavit (80-110°)**: Proper superior/inferior leaflet alignment
- **Transseptal #2 SAX at Base (30-45°)**: Proper anterior/posterior leaflet location
- **Transseptal #3 4 Chamber (20°)**: Confirmation of proper height above line of coaptation

- **Positioning & Trajectory #1 Intercommissural - 2C**: Proper medial-lateral alignment
- **Positioning & Trajectory #2 LVOT (180-190°)**: Proper anterior/posterior alignment

**HEALTH 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

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.
**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

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\(^1\) 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.

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**Reimbursement and Funding Overview**

- **Israel**: Reimbursement as of Jan 2014
- **Italy**: Regional or innovation funding ongoing
- **Device**: reimbursed on top of DRG in Lombardy (80%)
- **UK**: Commissioning through Evaluation
- **Belgium**: New reimbursement submission July 2013
- **Germany**: DRG since Jan 2013
- **TUR**: SGK coverage in public hospitals
- **Poland**: Reimbursement in 6 centers
- **Netherlands**: DRG as of Jan 2014
- **Belgium**: DRG for the procedure as of Jan 2014
- **France**: PHRC/MitraFR study granted (1st patient in by Q4 2013)
- **Austria**: Temporary code in place. DRG will be requested when RCT data available
- **Czech Republic**: 2 Private Insurances agreement
- **UK**: Commissioning through Evaluation
- **Belgium**: New reimbursement submission July 2013
- **France**: PHRC/MitraFR study granted (1st patient in by Q4 2013)

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\(^*\) conditions apply
Growing Body of Clinical Evidence

- **EVEREST II RCT**
  - Demonstrated overall concept, clinical safety and effectiveness
- **ACCESS EU, REALISM, EVEREST II HR cohort Registries**
  - Addressed specific patient populations
- Franzen, Schillinger, Sven, Treede, Auricchio, Baldus, Van den Branden, Velasques
- *large cohort is defined as >50 patients
- COAPT and RESHAPE-HF Randomized trials of MitraClip versus optimal medical therapy

MitraClip Therapy
Broad Spectrum of Experience

- **EVEREST II** (Randomized Controlled Trial)
  - 178 patients
  - Device time – 146 minutes
  - Implant rate – 89%
  - 26% DMR = FMR
- **ACCESS EU** (Europe)
  - 567 patients
  - Procedure time – 117 minutes
  - Implant rate – 99%
  - 23% DMR = FMR
- **Commercial** (APJ, CALA, Europe, US)
  - 10,614 patients
  - Device time – 91 minutes
  - Implant rate – 96%
  - 33% DMR = FMR


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.
**EVEREST II**

**Randomized Controlled Trial Design**

279 Patients Randomized at 37 Sites

Significant MR (3+ or 4+)

Specific Anatomical Criteria

![MitraClip Therapy](N=184)

R 2:1

![Surgery](N=95)

**Patient Demographics**

<table>
<thead>
<tr>
<th></th>
<th>MitraClip Therapy (n=184)</th>
<th>Surgery (n=95)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>67 years</td>
<td>66 years</td>
<td>0.32</td>
</tr>
<tr>
<td>Male</td>
<td>63%</td>
<td>66%</td>
<td>0.60</td>
</tr>
<tr>
<td>History of CHF</td>
<td>91%</td>
<td>78%</td>
<td>0.005</td>
</tr>
<tr>
<td>Degenerative MR Etiology</td>
<td>74%</td>
<td>73%</td>
<td>0.81</td>
</tr>
<tr>
<td>Functional MR Etiology</td>
<td>26%</td>
<td>27%</td>
<td>0.81</td>
</tr>
<tr>
<td>Mean Ejection Fraction</td>
<td>60%</td>
<td>61%</td>
<td>0.65</td>
</tr>
<tr>
<td>Previous Coronary Artery Bypass Grafting (CABG)</td>
<td>21%</td>
<td>19%</td>
<td>0.54</td>
</tr>
<tr>
<td>NYHA Functional Class III/IV</td>
<td>51%</td>
<td>48%</td>
<td>0.61</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>34%</td>
<td>33%</td>
<td>0.42</td>
</tr>
</tbody>
</table>

**EVEREST II RCT**

- **Positive Safety Profile**

**Major Adverse Events at 30 Days**

All Treated Patients (N=258)

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

**TOTAL % of Patients with MAE**

7.9% 50.0%
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

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

Study Design

Total MitraClip Patients Treated in ACCESS-EU N=567

1-Year Follow-up N=487

1-year follow-up complete 86% patient data available

Baseline Demographics and Comorbidities

<table>
<thead>
<tr>
<th>ACCESS-EU MitraClip Patients, N=567</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD), years</td>
<td>74 ± 10</td>
</tr>
<tr>
<td>Logistic EuroSCORE, (%)</td>
<td>23 ± 18</td>
</tr>
<tr>
<td>Logistic EuroSCORE ≥20, (%)</td>
<td>45</td>
</tr>
<tr>
<td>Male Gender, (%)</td>
<td>64</td>
</tr>
<tr>
<td>Mitral Regurgitation Grade 3+, (%)</td>
<td>98</td>
</tr>
<tr>
<td>NYHA Functional Class III or IV, (%)</td>
<td>85</td>
</tr>
<tr>
<td>Ejection Fraction &lt;40%, (%)</td>
<td>53</td>
</tr>
</tbody>
</table>


ACCESS EU - Real-World Clinical Experience

Demonstrated safety with low adverse event rates

<table>
<thead>
<tr>
<th>Description of Event</th>
<th>Site Reported Safety Events at 30 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>19 (3.4)</td>
</tr>
<tr>
<td>Stroke</td>
<td>6 (1.1)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>6 (1.1)</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>27 (4.8)</td>
</tr>
<tr>
<td>Respiratory Failure</td>
<td>6 (1.1)</td>
</tr>
<tr>
<td>Need for Resuscitation</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Cardiac Tamponade</td>
<td>6 (1.1)</td>
</tr>
<tr>
<td>Bleeding Complications</td>
<td>28 (5.2)</td>
</tr>
</tbody>
</table>

Data presented as mean ±95% confidence intervals (4.4, 7.4).

Significant NYHA Functional Class Improvements

79% NYHA Class I or II at 1 Year

59.5 meter improvement

p<0.0001

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

<table>
<thead>
<tr>
<th>Baseline characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>75±9</td>
</tr>
<tr>
<td>FMR etiology (%)</td>
<td>65</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>44±16</td>
</tr>
<tr>
<td>NYHA III-IV (%)</td>
<td>98</td>
</tr>
<tr>
<td>Logistic EuroSCORE (%)</td>
<td>36 (21-54)</td>
</tr>
<tr>
<td>Ischemic Cardiomyopathy (%)</td>
<td>41</td>
</tr>
</tbody>
</table>

Heart Team Treatment Decision matrix:
MitraClip patients: “severe mitral valve regurgitation patients with contraindications for surgery or high operative risk”


Acute reduction in MR by grade

<table>
<thead>
<tr>
<th>Grade</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6.0</td>
</tr>
<tr>
<td>1</td>
<td>20.7</td>
</tr>
<tr>
<td>2</td>
<td>51.5</td>
</tr>
<tr>
<td>3</td>
<td>12.9</td>
</tr>
</tbody>
</table>

Data presented as mean ±95% confidence intervals (4.5, 74.6)

Durable reduction in MR out to 12 months

Overall survival at 12 months was 89.6%

65% NYHA Class I or II at 1 Year

0% NYHA Class III or IV

80% NYHA Class I or II at 1 Year

Severe Mitral Regurgitation

Contraindications for surgery or high operative risk: Heart Team decision

Severely compromised LV function

Concomitant cardiac surgery (eg. CABG, AVR)

Minimally invasive MV repair: Partial/total sternotomy

Regular MV repair: Full sternotomy

Interventional MV repair: MitraClip

p<0.0001

Durable improvement in NYHA classification

Overall survival at 12 months was 89.6%

% Survive

0 200 400 600 800 1000 Days Post/Index Procedure

1 year Survival 89.6%
MitraClip in Specific Patient Populations

**Patient groups in which significant clinical benefits have been reported:**
- Degenerative MR, declined for surgery\(^1\)
- Severe LV dysfunction refractory to medical therapy\(^2\)
- Severe Heart Failure, despite optimal medical therapy\(^3\)
- CRT non-responders\(^4\)
- Bivalvular Disease: Severe Aortic Stenosis and Mitral Regurgitation\(^5\)

The following parameters should be taken into consideration by the Heart Team\(^6\):
- Moderate to severe or severe MR (Functional or Degenerative)
- Echocardiographic criteria for eligibility
- Level of surgical risk
- Greater than one year life expectancy

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**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

---

**MitraRegurgitation Grade Reduction**

- No therapy 80%
- Therapy 88%
- P<0.002
- 76.8% MR 2+ or 3+ at 1 Year

**Significant NYHA Functional Class Improvements**

- No therapy 25%
- Therapy 72%
- P<0.001
- 82.2% NYHA Class I or II at 1 Year
Severe LV Dysfunction Refractory to Medical Therapy

- 51 patients with MR ≥ 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 Regurgitation Grade Reduction

- Reduction in MR, although moderate in most patients, was acceptable given high surgical risk and corresponding clinical benefits.

Significant NYHA Functional Class Improvements

- Significant NYHA functional class improvements at 6 months.

"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."

Severe HF, Despite Optimal Medical Therapy

- Retrospective analysis of 50 patients with LVEF ≤25%, MR ≥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."

**References**


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 III 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

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

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>11 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>78 ± 6</td>
</tr>
<tr>
<td>FMR etiology (%)</td>
<td>45</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>36 ± 13</td>
</tr>
<tr>
<td>NYHA III-I (%)</td>
<td>91</td>
</tr>
<tr>
<td>Log odds EuroSCORE (%)</td>
<td>65</td>
</tr>
<tr>
<td>Ischemic Cardiomyopathy (%)</td>
<td>45</td>
</tr>
</tbody>
</table>

Mitral Regurgitation Grade Reduction

100% MR ≤ 2+ Post MitraClip

"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."

Earlier Referral Saves Lives

Event – free survival decreases with increasing MR severity\(^1,2,3\)

MitraClip intervention in less severe MR results in better outcomes\(^4\)

\(\Delta 23\%\) MitraClip patients with MR \(\leq 2+\) at 1 year

Patients who achieved MR \(\leq 2+\) at 12 months

\(59\%\) vs 82%

Patients who achieved MR \(\leq 2+\) at 1 year


———

Earlier Referral Saves Lives

Risk of mortality increases with increasing NYHA class

For patients with MR\(\geq 3+\), MitraClip intervention in less severe NYHA class results in better outcomes

\(\Delta 22\%\) MitraClip patients with NYHA I or II at 1 year

Patients in NYHA class I and II at 12 months

57% vs 79%

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

Mean LVEDV (mL), Surgery (N=184)
\[ \Delta \text{LVEDV} = -30 \text{ mL at 4 Years} \]

Mean LVEDV (mL), MitraClip (N=95)
\[ \Delta \text{LVEDV} = -39 \text{ mL at 4 Years} \]

\[ P < 0.05 \text{ for all changes from Baseline within groups.} \]

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

Growing Number of Clinical Publications

361 total publications on MitraClip therapy (2003-2013)
### Morphology for a MitraClip therapy

<table>
<thead>
<tr>
<th>Central pathology in Segment 2</th>
<th>Conditionally suitable valve morphology</th>
<th>Unsuitable valve morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>No leaflet calcification</td>
<td>Pathology in Segment 1 or 3</td>
<td>Perforated mitral valve leaflet or cleft</td>
</tr>
<tr>
<td>Mitral valve opening area &lt;4 cm²</td>
<td>Mild calcification outside of the grip-zone of the clip system; ring calcification, post annuloplasty</td>
<td>Severe calcification in the grip-zone</td>
</tr>
<tr>
<td>Mobile length of the posterior leaflet ≥10 mm</td>
<td>Mobile length of the posterior leaflet 7-10 mm</td>
<td>Haemodynamically significant mitral stenosis (valve opening area &lt;3 cm², MPA &gt;5 mmHg)</td>
</tr>
<tr>
<td>Coaptation depth &lt;1.1 mm</td>
<td>Coaptation depth &gt;1.1 mm</td>
<td>Mobile length of the posterior leaflet &lt;7 mm</td>
</tr>
<tr>
<td>Normal leaflet strength and mobility</td>
<td>Leaflet restriction in systole (Carpentier IIIb)</td>
<td>Rheumatic leaflet thickening and restriction in systole and diastole (Carpentier IIA)</td>
</tr>
<tr>
<td>Mitral valve opening area &gt;3 cm²</td>
<td>Mobile length of the posterior leaflet 7-10 mm</td>
<td>Barlow’s syndrome with multisegment flail leaflets</td>
</tr>
<tr>
<td>Flail-width &lt;15 mm</td>
<td>Flail- Gap &lt;10 mm</td>
<td>Flail-width &gt;15 mm only with a large ring width and the option for multiple clips</td>
</tr>
</tbody>
</table>

### Indications for the MitraClip therapy

<table>
<thead>
<tr>
<th>Ideal for MitralClip treatment</th>
<th>MitraClip to be considered</th>
<th>MitraClip not recommended or only in exceptional cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe mitral regurgitation and FMR with LVEF &lt;30%</td>
<td>Moderate to severe mitral regurgitation and FMR or DMR (with operation indication following guidelines) and High operative risk, very high age or other risk-constellations</td>
<td>Moderate to severe mitral regurgitation and Conditionally suitable valve morphology and Life expectancy &lt;12 months or LVEF &lt;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</td>
</tr>
</tbody>
</table>

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

Importance of the Learning Curve

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

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

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

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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

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¹ Markwick et al. Prognostic implications of moderate and severe mitral regurgitation in contemporary clinical care. TCT 2012
³ Markwick et al. Prognostic implications of moderate and severe mitral regurgitation in contemporary clinical care. TCT 2012
⁴ Markwick et al. Prognostic implications of moderate and severe mitral regurgitation in contemporary clinical care. TCT 2012
Quality of life improvements experienced by patients

**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

### Significant improvement with high-risk patients

- **PCOS**
  - Baseline: 35.41
  - 6 months: 46.67

- **MCS**
  - Baseline: 36.07
  - 6 months: 46.94

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


### 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
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

Multi-disciplinary Team
Bridging Traditional Silos

Collaboration across specialties is critical to MitraClip Therapy Success

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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