Update - Mitral Valve - 2017

Sean R. Wilson, MD, FACC
Structural Interventional Cardiology
Outline

- Prevalence of Mitral Valve Disease
- The Mitral Valve Apparatus
- Classification of Mitral Valve Disease
- Transcatheter Mitral Valve Interventions
  - Repair
  - Replacement
- Technical Issues With Transcatheter Mitral Valve Technology
Changing Pattern of Valvular Disease in Industrialized Countries

![Graph showing the changing pattern of valvular disease over time, with lines for rheumatic valve disease, degenerative valve disease, and emerging valve disease.](image)
Prevalence of Valvular Heart Disease by Age

Lancet 2006;368:1005-11
A Largely Untreated Patient Population

Mitral Regurgitation 2009 U.S. Prevalence

Total MR Patients\textsuperscript{1,2} \quad 4,100,000

Eligible for Treatment\textsuperscript{3,4} (MR Grade $\geq 3+$) \quad 1,670,000

Untreated Large and Growing Clinical Unmet Need

14\% Newly Diagnosed Each Year

Annual Incidence\textsuperscript{3} (MR Grade $\geq 3+$)

Annual MV Surgery\textsuperscript{5} \quad 30,000

Only 2\% Treated Surgically
Complexity In Structure
Summary of Mitral Valve Apparatus

- Mitral valve anulus
- Mitral leaflets with commissures
- Chordae tendinae
- Papillary muscles
- Supporting left ventricular wall
MV Pathologies: Degenerative Disease

- Leaflets and chordae in myxomatous degeneration become thickened and redundant
- Results in leaflet prolapse beyond plane of the annulus and MR
- Body of the leaflet may be billowing, but the valve will be competent if the chordae are normal length
- When the chords are elongated, it causes prolapse beyond the opposing segment, and when the chords are ruptured/flail, MR is typically severe
- Pathophysiology of myxomatous disease is poorly understood at the cellular and molecular level
- Result from a defect either congenital or acquired in fibroelastic connective tissue homeostasis
MV Pathologies: Functional Disease

- Caused by geometric ventricular remodeling without primary valve leaflet pathology
- Secondary to ventricular dilatation and is seen in idiopathic dilated cardiomyopathy and in postinfarction ventricular remodeling
- Mechanisms of chronic ischemic MR are more complex
  - Posterior infarction with ventricular scar is present in the distribution of the circumflex or right coronary artery. Leads to localized regional wall-motion abnormalities associated with ventricular dilatation, a drop in ejection fraction, an increase in ventricular volumes, and remodeling to a globular heart
- Valve leaflets and chordae appear “normal.” Recent studies indicate that mitral leaflets in functional disease are stiffer than normal.
<table>
<thead>
<tr>
<th>Dysfunction</th>
<th>Lesions</th>
<th>Etiology</th>
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<tbody>
<tr>
<td><strong>Type I</strong></td>
<td></td>
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<tr>
<td>Normal leaflet motion</td>
<td>Annular dilatation</td>
<td>Dilated cardiomyopathy</td>
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<tr>
<td></td>
<td>Leaflet perforation / tear</td>
<td>Endocarditis</td>
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<tr>
<td><strong>Type II</strong></td>
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<tr>
<td>Excess leaflet motion (leaflet prolapse)</td>
<td>Elongation / rupture chordae</td>
<td>Degenerative valve disease</td>
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<td></td>
<td>Elongation / rupture of papillary muscle</td>
<td>Fibroelastic deficiency</td>
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<td>Barlow’s disease</td>
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<td>Marfan disease</td>
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<td></td>
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<td>Endocarditis</td>
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<td>Trauma</td>
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<td></td>
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<td>Ischemic cardiomyopathy</td>
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<tr>
<td><strong>Type IIIa</strong></td>
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<tr>
<td>Restricted leaflet motion (Diastole and Systole)</td>
<td>Leaflet thickening / retraction</td>
<td>Rheumatic heart disease</td>
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<tr>
<td></td>
<td>Leaflet calcification</td>
<td>Carcinoid heart disease</td>
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<tr>
<td></td>
<td>Chordal thickening / retraction / fusion</td>
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<tr>
<td></td>
<td>Commissural fusion</td>
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<tr>
<td><strong>Type III b</strong></td>
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<tr>
<td>Restricted leaflet motion (Systole)</td>
<td>Left ventricular dilatation/ aneurysm</td>
<td>Ischemic / Dilated cardiomyopathy</td>
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<td></td>
<td>Papillary muscle displacement</td>
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<tr>
<td></td>
<td>Chordae tethering</td>
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## Stages of Primary MR

<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptoms</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>A</td>
<td>At risk of MR</td>
<td>- Mild mitral valve prolapse with normal coaptation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Mild valve thickening and leaflet restriction</td>
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<tr>
<td></td>
<td></td>
<td>- No MR jet or small central jet area &lt;20% LA on Doppler</td>
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<tr>
<td></td>
<td></td>
<td>- Small vena contracta &lt;0.3 cm</td>
</tr>
<tr>
<td>B</td>
<td>Progressive MR</td>
<td>- Severe mitral valve prolapse with normal coaptation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Rheumatic valve changes with leaflet restriction and loss of central coaptation</td>
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<td></td>
<td></td>
<td>- Prior IE</td>
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<tr>
<td></td>
<td></td>
<td>- Central jet MR 20%–40% LA or late systolic eccentric jet MR</td>
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<td></td>
<td></td>
<td>- Vena contracta &lt;0.7 cm</td>
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<tr>
<td></td>
<td></td>
<td>- Regurgitant volume &lt;60 mL</td>
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<tr>
<td></td>
<td></td>
<td>- Regurgitant fraction &lt;50%</td>
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<tr>
<td></td>
<td></td>
<td>- ERO &lt;0.40 cm²</td>
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<tr>
<td></td>
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<td>- Angiographic grade 1–2+</td>
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<tr>
<td>C</td>
<td>Asymptomatic severe MR</td>
<td>- Severe mitral valve prolapse with loss of coaptation or flail leaflet</td>
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<tr>
<td></td>
<td></td>
<td>- Thickening of leaflets with radiation heart disease</td>
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<td></td>
<td></td>
<td>- Central jet MR &gt;40% LA or holosystolic eccentric jet MR</td>
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<td>- Vena contracta ≥0.7 cm</td>
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<td>- ERO ≥0.40 cm²</td>
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<tr>
<td></td>
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<td>- Angiographic grade 3–4+</td>
</tr>
<tr>
<td>D</td>
<td>Symptomatic severe MR</td>
<td>- Severe mitral valve prolapse with loss of coaptation or flail leaflet</td>
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ACC/AHA – Mitral Valve Guidelines

Mitral Regurgitation

Primary MR

Severe MR
Vena contracta ≥0.7 cm
RVol ≥60 mL
RF ≥50%
ERO ≥0.4 cm²
LV dilation

Symptomatic (stage D)
LVEF >30%

NO
YES

MV Surgery* (IIb)
MV Surgery* (I)

Asymptomatic (stage C)
LVEF 30% to ≤60%
or LVESD ≤40 mm (stage C2)

LVEF >60% and
LVESD <40 mm (stage C1)

New onset AF or PASP >50 mm Hg (stage C1)

Likelihood of successful repair >95% and Expected mortality <1%

YES
NO

MV Repair (IIa)
Periodic Monitoring

Secondary MR

CAD Rx
HF Rx
Consider CRT

Symptomatic severe MR (stage D)
Asymptomatic severe MR (stage C)
Progressive MR (stage B)

Persistent NYHA class III-IV symptoms

MV Surgery* (IIb)
Periodic Monitoring

*Mitral valve repair is preferred over MVR when possible.
Mitral regurgitation

Indications for mitral valve surgery for primary MR?

- Symptomatic patients
- Asymptomatic patients
  - LV systolic dysfunction
  - Pulmonary hypertension
  - Atrial fibrillation
- Normal LV function, repair feasible?

class I

class I

class IIa

class IIa
Asymptomatic Degenerative Mitral

- LVEF < 60 %
- PAP > 50
- LVESd > 40 mm
- AF

If > 95% repair, < 1% mort
Wait for CHF Symptoms?

Mitral Regurgitation Survival After Mitral Valve Surgery

- FC I-II: 81% (n=488, p<0.001)
- FC III-IV: 58%

David et al, J Thorac Cardiovasc Surg 2003;126:1143-1152
Wait for CHF Symptoms?

Surgery for Acquired Cardiovascular Disease

**Mitral Regurgitation**

**Survival After Mitral Valve Surgery**

- FC I-II: 81%
- FC III-IV: 58%

**n=488**

**p<0.001**

**BAD!**

David et al, *J Thorac Cardiovasc Surg* 2003;126:1143-1152
Reduction in EF

![Graph showing survival vs. ejection fraction]

Reduction in EF

Wait until EF falls – Bad!

Pulmonary Artery Pressure

Echocardiography predictors and prognostic value of pulmonary artery systolic pressure in chronic organic mitral regurgitation

Thierry Le Tourneau, Marjorie Richardson, Francis Juthier, Thomas Modine, Georges Fayad, Anne-Sophie Polge, Pierre-Vladimir Ennezat, Christophe Bauters, André Vincentelli, Ghislaine Deklunder
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BAD!
Predictors of Mitral Valve Repair

The more you do the better you are.

Predictors of Mitral Valve Repair: Clinical and Surgeon Factors

Steven F. Bolling, MD, Shuang Li, MS, Sean M. O’Brien, PhD, J. Matthew Brennan, MD, Richard L. Prager, MD, and James S. Gammie, MD

Section of Cardiac Surgery, University of Michigan, Ann Arbor, Michigan; Duke Clinical Research Institute, Durham, North Carolina; and Division of Cardiac Surgery, University of Maryland, Baltimore, Maryland
To Repair or Replace: Degenerative Mitral Regurgitation

Overall survival (%)

Serano Circulation

Expected
Repair
Replacement

P=0.0004

Years

68%
52%
Asymptomatic Degenerative Mitral

- LVEF < 60%
- PAP > 50
- LVESd > 40 mm
- AF
- Surgical volume

If > 95% repair, < 1% mort

All are bad and associated with worse outcomes!
Mitral regurgitation

Indications for MV repair for asymptomatic primary MR:

- Chronic severe MR
- Preserved LV function
- Experienced surgical center
- Likelihood of durable repair without residual MR > 95%

class IIa
# Stages of Secondary Mitral Regurgitation

<table>
<thead>
<tr>
<th></th>
<th>At risk of MR</th>
<th>Progressive MR</th>
<th>Asymptomatic severe MR</th>
<th>Symptomatic severe MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>• Normal valve leaflets, chords, and annulus in a patient with coronary disease or cardiomyopathy</td>
<td>• Regional wall motion abnormalities with mild tethering of mitral leaflet</td>
<td>• Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet</td>
<td>• Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet</td>
</tr>
<tr>
<td></td>
<td>• No MR jet or small central jet area &lt;20% LA on Doppler</td>
<td>• Annular dilation with mild loss of central coaptation of the mitral leaflets</td>
<td>• Annular dilation with severe loss of central coaptation of the mitral leaflets</td>
<td>• Annular dilation with severe loss of central coaptation of the mitral leaflets</td>
</tr>
<tr>
<td></td>
<td>• Small vena contracta &lt;0.30 cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Progressive MR</td>
<td>• ERO &lt;0.20 cm²†</td>
<td>• ERO ≥0.20 cm²†</td>
<td>• ERO ≥0.20 cm²†</td>
</tr>
<tr>
<td></td>
<td>• Regional wall motion abnormalities with mild tethering of mitral leaflet</td>
<td>• Regurgitant volume &lt;30 mL</td>
<td>• Regurgitant volume ≥30 mL</td>
<td>• Regurgitant volume ≥30 mL</td>
</tr>
<tr>
<td></td>
<td>• Annular dilation with mild loss of central coaptation of the mitral leaflets</td>
<td>• Regurgitant fraction &lt;50%</td>
<td>• Regurgitant fraction ≥50%</td>
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## Recommendations for Chronic Severe Secondary Mitral Regurgitation:
### Medical Therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with chronic secondary MR (stages B to D) and HF with reduced LVEF</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>should receive standard GDMT therapy for HF, including ACE inhibitors, ARBs,</td>
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<td>beta blockers, and/or aldosterone antagonists as indicated</td>
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<tr>
<td>Noninvasive imaging (stress nuclear/positron emission tomography, CMR, or stress</td>
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<tr>
<td>echocardiography), cardiac CT angiography, or cardiac catheterization, including</td>
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<tr>
<td>coronary arteriography, is useful to establish etiology of chronic secondary MR</td>
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<tr>
<td>(stages B to D) and/or to assess myocardial viability, which in turn may influence</td>
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<tr>
<td>management of functional MR</td>
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</table>
Here are the Class I recommendations for surgery in secondary mitral regurgitation.
# Recommendations for Chronic Severe Secondary Mitral Regurgitation: Intervention Medical Therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR</td>
<td>Ila</td>
<td>C</td>
</tr>
<tr>
<td>MV surgery may be considered for severely symptomatic patients (NYHA class III-IV) with chronic severe secondary MR (stage D)</td>
<td>Iib</td>
<td>B</td>
</tr>
<tr>
<td>MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery</td>
<td>Iib</td>
<td>C</td>
</tr>
</tbody>
</table>
Needed: Randomized Clinical Trials in Secondary Mitral Regurgitation

- Cardiothoracic Surgical Trials Network
- Severe Chronic Ischemic MR Protocol
  - MV repair vs replacement

Acker et al. NEJM 2014; 370: 23-32
Needed: Randomized Clinical Trials in Secondary Mitral Regurgitation

- Cardiothoracic Surgery
- Severe Mitral Regurgitation
- MV repair vs replacement

![Graph A: Death](image)

- MV repair vs replacement

![Graph B: Composite Cardiac End Point](image)

- MV repair vs replacement

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Months</th>
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<tbody>
<tr>
<td>MV repair</td>
<td>126</td>
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<tr>
<td>MV repair</td>
<td>116</td>
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<tr>
<td>MV repair</td>
<td>114</td>
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<tr>
<td>MV repair</td>
<td>109</td>
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<tr>
<td>MV repair</td>
<td>106</td>
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</table>

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Months</th>
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<tbody>
<tr>
<td>MV replacement</td>
<td>125</td>
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<tr>
<td>MV replacement</td>
<td>109</td>
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<td>MV replacement</td>
<td>104</td>
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<td>MV replacement</td>
<td>103</td>
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<tr>
<td>MV replacement</td>
<td>101</td>
</tr>
</tbody>
</table>
To Repair or Replace: Functional Mitral Regurgitation

Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation

Michael A. Acker, M.D., Michael K. Parides, Ph.D., Louis P. Perrault, M.D.,
Alan J. Moskowitz, M.D., Annetine C. Gelijns, Ph.D., Pierre Voisine, M.D.,
Peter K. Smith, M.D., Judy W. Hung, M.D., Eugene H. Blackstone, M.D.,
John D. Kopchick, M.D., Michael Kontny, M.D., Edward J. Greene, M.D.

Recurrent MR at 12 Months

P<0.001)
Needed: Randomized clinical trials in secondary MR

- Cardiothoracic Surgical Trials Network
- Moderate Ischemic MR Protocol
- MV repair vs CABG alone

Smith PK et al. NEJM 2014; 371: 2178-88
Needed: Randomized Clinical Trials in Secondary Mitral Regurgitation

- Cardiothoracic Surgical Trials Network
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Smith PK et al. NEJM 2014; 371: 2178-88
Transcatheter Mitral Valve Intervention

- Leaflet repair
- Indirect Annuloplasty
- Direct Annuloplasty
- Chordal Implantation
- MV Implantation
Transcatheter Mitral Valve Intervention

- Leaflet repair

<table>
<thead>
<tr>
<th>Leaflet repair</th>
<th>MitraClip (Abbott Vascular, USA)</th>
<th>TV-TS (24Fr)</th>
<th>Clip-based edge-to-edge repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>MitraFlex (TransCardiac Therapeutics, USA)</td>
<td>TA</td>
<td>Automatic capturing and connection of the approximate midpoint of the leaflets/implantation of an artificial chordae tendinae</td>
<td></td>
</tr>
</tbody>
</table>

- Chordal Implantation

- MV Implantation
The MitraClip System

- Commercial approval October 24, 2013
- Indicated for symptomatic patients with primary MR ≥3 and prohibitive surgical risk
“Prohibitive risk” is due to the presence of one or more of the following documented surgical risk factors:

- 30-day STS predicted operative mortality risk score of
  - ≥8% for patients deemed likely to undergo MV replacement or
  - ≥6% for patients deemed likely to undergo MV repair
- Porcelain aorta or extensively calcified ascending aorta
- Frailty (assessed by in-person cardiac surgeon consultation)
- Hostile chest
- Severe liver disease / cirrhosis (MELD Score > 12)
- Severe pulmonary hypertension (systolic pulmonary artery pressure > 2/3 systemic pressure)
- Unusual extenuating circumstance, such as
  - Right ventricular dysfunction with severe tricuspid regurgitation
  - Chemotherapy for malignancy
  - Major bleeding diathesis
  - Immobility
  - AIDS
  - Severe dementia
  - High risk of aspiration
  - Internal mammary artery (IMA) at high risk of injury, etc.
EVEREST II: MitraClip vs. Surgery

Study Design
EVEREST II Randomized Controlled Trial (RCT)

279 Patients enrolled at 37 sites
Significant MR (3+ or 4+)
Specific Anatomical Criteria
Randomized 2:1

Percutaneous Group
MitraClip System
N=184

Surgery Group
Surgical Repair or Replacement
N=95

Echocardiography Core Lab and Clinical Follow-Up:
Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years
EVEREST II: Primary Endpoints

Safety Major Adverse Events (30 days)
- Device Group, n=136: 9.6%
- Control Group, n=79: 57.0%

Effectiveness Clinical Success Rate (12 months)
- Device Group, n=134: 72.4%
- Control Group, n=74: 87.8%

Met superiority hypothesis:
- Pre-specified margin = 6%
- Observed difference = 47.4%
- 97.5% LCB = 34.4%

Met non-inferiority hypothesis:
- Pre-specified margin = 31%
- Observed difference = 15.4%
- 95% UCB = 25.4%

*Freedom from the combined outcome of death, MV surgery or re-operation for MV dysfunction, MR >2+ at 12 months.

LCB = lower confidence bound
UCB = upper confidence bound
Kaplan-Meier curves depict (A) freedom from the composite of death, mitral valve (MV) surgery, or reoperation, (B) freedom from death, (C) freedom from MV surgery or reoperation, and (D) landmark analysis of freedom from MV surgery or reoperation beyond 6 months after percutaneous repair or surgery. Although patients were followed for 5 years, only data from the first 6 months are shown here.
FIGURE 2 Severity of MR and Heart Failure Symptoms Post-Treatment

A

<table>
<thead>
<tr>
<th></th>
<th>Device (n=101)</th>
<th>Surgery (n=40)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>98% 2+</td>
<td>93% 2+</td>
<td>0.11</td>
</tr>
<tr>
<td>12 Months</td>
<td>18% 1+</td>
<td>0% 0+</td>
<td>0.004</td>
</tr>
<tr>
<td>5 Years</td>
<td>19% 3+</td>
<td>3% 3+</td>
<td>0.01</td>
</tr>
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B

<table>
<thead>
<tr>
<th></th>
<th>Device (n=105)</th>
<th>Surgery (n=40)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>1</td>
<td>40% I</td>
<td>40% I</td>
<td>0.99</td>
</tr>
<tr>
<td>2</td>
<td>1% II</td>
<td>8% II</td>
<td>0.03</td>
</tr>
<tr>
<td>3</td>
<td>9% III</td>
<td>13% III</td>
<td>0.19</td>
</tr>
</tbody>
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Etiology and Worldwide Experience of MitraClip - 2015

Number of implantation procedures

- DMR, 22%
- FMR, 65%
- Mixed, 13%

Western Europe
Emerging Europe
APAC
CALA
USA
US commercial
Transcatheter Mitral Valve Intervention

- Leaflet repair
- Indirect Annuloplasty

<table>
<thead>
<tr>
<th>Indirect annuloplasty</th>
<th>Carillon (Cardiac Dimensions, USA)</th>
<th>TJ (9Fr)</th>
<th>Coronary sinus reshaping</th>
<th>CE mark approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral Cerclage</td>
<td>(NIH, USA)</td>
<td>TJ</td>
<td>Coronary sinus-right atrial encircling</td>
<td>Preclinical study underway</td>
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<tr>
<td>Valicare (Valicare Medical, Israel)</td>
<td></td>
<td>TJ</td>
<td>Rigid D-shaped annuloplasty</td>
<td>Preclinical study underway</td>
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</tbody>
</table>
Transcatheter Mitral Valve Intervention

- Leaflet repair
- Indirect Annuloplasty
- Direct Annuloplasty

<table>
<thead>
<tr>
<th>Direct annuloplasty</th>
<th>Mitralign (Mitralign, USA)</th>
<th>TF</th>
<th>2x2 plicating anchors through posterior annulus</th>
<th>CE mark trial completed USA feasibility trial planned</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardioband (Valtech, Israel)</td>
<td>TV-TS</td>
<td>Plicating anchors on atrial side of mitral annulus</td>
<td>CE mark trial underway</td>
</tr>
<tr>
<td></td>
<td>Accucinch (Guided Delivery Systems, USA)</td>
<td>TF</td>
<td>Plicating anchors on ventricular side of mitral annulus</td>
<td>International feasibility trial underway</td>
</tr>
<tr>
<td></td>
<td>Millipede (Millipede, USA)</td>
<td>TV-TS</td>
<td>Semirigid circumferential annular ring</td>
<td>Preclinical study underway</td>
</tr>
</tbody>
</table>

- Mitralign Bident
  - Arterial access
  - Transannular cinching
- GDS Accucinch
  - Arterial access
  - Subannular cinching
- Valtech Cardioband
  - Venous access
  - Annular fixation
Transcatheter Mitral Valve Intervention

- Leaflet repair
- Indirect Annuloplasty
- Direct Annuloplasty
- Chordal Implantation

<table>
<thead>
<tr>
<th>Chordal Implantation</th>
<th>NeoChord (NeoChord, USA)</th>
<th>TA</th>
<th>Synthetic chordae tendinae</th>
<th>CE mark approved</th>
</tr>
</thead>
</table>
Transcatheter Mitral Valve Repair

Cardioband

Carillion

Nitinol Stiffeners
Radiopaque (RO) Markers
Adjustment Mechanism

8mm

Great Cardiac Vein Anchor
Coronary Sinus Anchor

Bottom view

Mitraclip
Transcatheter Mitral Valve Intervention

- Leaflet repair
- Indirect Annuloplasty
- MV Implantation

<table>
<thead>
<tr>
<th>MV Implantation</th>
<th>CardiAQ (CardiAQ, USA)</th>
<th>TV-TS/TA (32Fr)</th>
<th>Self-positioning, self-anchoring, and self-conforming system for TMVI</th>
<th>First-in-man study completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fortis (Edwards, USA)</td>
<td>TA/TV-TS</td>
<td>TMVI technology designed to minimize PVL</td>
<td>First-in-man study completed</td>
<td></td>
</tr>
<tr>
<td>Tiaara (Neovasc, USA)</td>
<td>TA/TV-TS (32Fr)</td>
<td>Self-expanding bovine pericardial, D-shaped trileaflet MV</td>
<td>First-in-man study completed</td>
<td></td>
</tr>
<tr>
<td>Tendyne (Tendyne Holdings, USA)</td>
<td>TA (30Fr)</td>
<td>Fully retrievable, self-expanding trileaflet porcine pericardial valve sewn onto a nitinol frame/atrial and ventricular fixation system</td>
<td>First-in-man study completed</td>
<td></td>
</tr>
<tr>
<td>Medtronic TMVR (Medtronic, USA)</td>
<td>TAI/TV-TS</td>
<td>Self-expanding nitinol scaffold and a bovine pericardial valve with 3 cusps/ recapturable and retrievable</td>
<td>Preclinical study underway</td>
<td></td>
</tr>
<tr>
<td>Cardiovalve (Valtech, Israel)</td>
<td>TV-TS (26Fr)</td>
<td>TMVI system that can be delivered using a TF delivery system in a 2-step implantation procedure</td>
<td>Preclinical study underway</td>
<td></td>
</tr>
</tbody>
</table>
Transcatheter Mitral Valve Replacement

Leaflet Attachment

Atrial Flange

Pre-clinical Animal Models

"Transcatheter Mitral Valve Implantation is Complex"
Variability in Design

- Atrial skirt
- Posterior anchor
- Anterior anchors

CardiaQ

Outflow ("ventricular portion")

Tiara

Medtronic device

Edwards FORTIS

Inflow ("atrial portion")

Outflow ("ventricular portion")
Goals of a Prosthetic Valve

- Simple and reproducible implant (high immediate success rate with)
- Absence of transvalvular gradient
- Absence of peri-valvular regurgitation
- No LVOT, coronary sinus, or LCX obstruction
- Preservation of LV contractility, haemodynamics, and blood flow pattern
- Non-thrombogenic (no need for chronic anti-coagulation)
- Low infection rates
- No acute or delayed embolization
- Durable
- Ability to grow (in paediatric patients)

## Comparison of Transcatheter Mitral Valve Implantation versus Repair

<table>
<thead>
<tr>
<th>Transcatheter Mitral Valve Replacement</th>
<th>Transcatheter MV Repair</th>
</tr>
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<tbody>
<tr>
<td>Dynamic mitral structure</td>
<td>More natural hemodynamics</td>
</tr>
<tr>
<td>Asymmetric anatomy</td>
<td>No need for long-term anti-coagulation</td>
</tr>
<tr>
<td>Deliverability (profile, rigidity)</td>
<td>Need for advanced imaging</td>
</tr>
<tr>
<td>Fixation</td>
<td>Variability of disease/need for multiple devices</td>
</tr>
<tr>
<td>Need for chronic oral anti-coagulation</td>
<td>Possible need for combined therapies</td>
</tr>
<tr>
<td>Risk of LVOT, CS, and LCX obstruction</td>
<td>Residual/recurrent regurgitation</td>
</tr>
<tr>
<td>Risk of para-valvular leak</td>
<td></td>
</tr>
</tbody>
</table>

Questions That Need To Be Answered

- If the patient is young....

  Durability → Materials, Design, Process

- If the patient can not tolerate anti-coagulants

  Hemodynamics → Fluid Mechanics

- If the patient a high risk surgical candidate

  Implantation → Anatomy
Thank You