Percutaneous Intervention in Mitral Valve Disease

Alec Vahanian, FESC, FRCP (Edin.)
Bichat Hospital, Paris
University Paris VII
<table>
<thead>
<tr>
<th>Relationship</th>
<th>Manufacturer(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speaker's Honoraria</td>
<td>Edwards Lifesciences</td>
</tr>
<tr>
<td>Consultant (Advisory Board)</td>
<td>Abbott, Medtronic, Saint Jude Medical, Valtech</td>
</tr>
</tbody>
</table>
Percutaneous Mitral Commissurotomy

Percutaneous Mitral Valve Repair

Transcatheter treatment after surgical failure

Final comments
Percutaneous Mitral Commissurotomy

“The Proof of Concept for Percutaneous Valve Intervention”

(D. Harken, 1948)

(K. Inoue, 1984)
Follow-up

- FU was concluded in 2008
- FU was complete in 923 patients (90%)
- Median FU: 11 years [interquartile range 5 - 16]
- Clinical endpoints: - death
  - need for surgery or re-PMC
  - NYHA class III-IV

Good Functional Results: patient alive, not operated on, and in NYHA class I or II at last follow-up

(Bouleti et al. Circulation 2012;125:2119-27)
20-Year Results
Survival without Surgery or Re-PMC

(Bouleti et al. Circulation 2012;125:2119-27)
20-Year Results
Survival without Surgery or Re-PMC, and in NYHA class I or II

(Bouleti et al. Circulation 2012;125:2119-27)
20-Year Results
Survival without re-intervention or surgery (pts <50 years)

(Bouleti et al. Circulation 2012;125:2119-27)
## Prediction of Long-Term Results of PMC

<table>
<thead>
<tr>
<th>Age (y) and final mitral valve area (cm²)</th>
<th>HR [95% CI]</th>
<th>p</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 and MVA ≥ 2.00</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>&lt;50 and MVA 1.50-2.00 or 50-70 and MVA &gt;1.75</td>
<td>2.1 [1.6-2.9]</td>
<td>&lt;0.0001</td>
<td>2</td>
</tr>
<tr>
<td>50-70 and MVA 1.50-1.75 or ≥70 and MVA ≥1.50</td>
<td>5.1 [3.5-7.5]</td>
<td>&lt;0.0001</td>
<td>5</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Valve anatomy and sex</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No valve calcification</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Valve calcification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- female</td>
<td>1.2 [0.9-1.6]</td>
<td>0.18</td>
<td>0</td>
</tr>
<tr>
<td>- male</td>
<td>2.3 [1.6-3.2]</td>
<td>&lt;0.0001</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rhythm and NYHA class</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus rhythm or A. fib. and NYHA class I-II</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Atrial fibrillation and NYHA class III-IV</td>
<td>1.8 [1.4-2.3]</td>
<td>&lt;0.0001</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Final mean mitral gradient (mm Hg)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 3</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>3-6</td>
<td>1.1 [1.0-1.8]</td>
<td>0.05</td>
<td>1</td>
</tr>
<tr>
<td>≥ 6</td>
<td>2.5 [1.8-3.5]</td>
<td>&lt;0.0001</td>
<td>3</td>
</tr>
</tbody>
</table>
ESC/EACTS Guidelines: Management of clinically significant mitral stenosis

**MS \( \leq 1.5 \text{ cm}^2 \)**

- Symptoms
  - Yes
    - Cl to PMC
    - No
      - Cl or high risk for surgery
        - Yes (Favourable anatomical characteristics)
        - No (Favourable clinical characteristics)
        - PMC
        - Surgery
  - No (High risk of embolism or haemodynamic decompensation)
    - Yes
      - Exercise testing
        - Symptoms
      - No symptoms
        - Cl to or unfavourable characteristics for PMC
          - No
          - Yes (Favourable clinical characteristics)
          - PMC
          - Follow-up
The Role of PMC

5001 Patients admitted in 92 centres from April to July 2001

N = 512 119 112 155

(lung. Eur Heart J 2003;24:1231)
Percutaneous Mitral Commissurotomy

_Percutaneous Mitral Valve Repair_

Transcatheter treatment after surgical failure

Final comments
Mitral Valve Apparatus

- Annulus
- Leaflets
- Subvalvular apparatus
- Papillary muscles
- Commissures

Complex interaction
Principles of a reconstructive valve operation

- Preserve or restore full leaflet motion
- Create a large surface of coaptation
- Remodel and stabilise the entire annulus
Surgery in Mitral Regurgitation

- In expert centres, in patients with primary MR, the repair rate is >90% and >90% of patients are alive and free from reoperation after 10-15 years.

- Surgery for secondary MR remains a challenge. Most studies failed to demonstrate improved long-term clinical outcome following surgical correction.
Edge-to-Edge Technique
Surgical Edge-to-Edge technique

Percutaneous Mitral Valve Repair
MitraClip® System
The Procedure

Line of coaptation
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

Key Inclusion/Exclusion Criteria
EVEREST II RCT

**Inclusion**
- Candidate for MV Surgery
- Moderate to severe (3+) or severe (4+) MR
  - Symptomatic
    - >25% EF & LVESD ≤55mm
  - Asymptomatic with one or more of the following
    - LVEF 25-60%
    - LVESD ≥40mm
    - Pulmonary hypertension
    - Atrial fibrillation

**Exclusion**
- AMI within 12 weeks
- Need for other cardiac surgery
- Renal insufficiency
  - Creatinine >2.5mg/dl
- Endocarditis
- Rheumatic heart disease
- MV anatomical exclusions
  - Mitral valve area <4.0cm²
  - Leaflet flail width (≥15mm) and gap (≥10mm)
  - Leaflet tethering/coaptation depth (>11mm) and length (<2mm)

ACC/AHA Guidelines
JACC 52:e1-e142, 2008

# Safety Endpoint: 30 Day MAE

## Intention to Treat

<table>
<thead>
<tr>
<th>30 Day MAE</th>
<th>Percutaneous (N=180)</th>
<th>Surgery (N=94)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>2 (1.1%)</td>
<td>2 (2.1%)</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>2 (1.1%)</td>
<td>2 (2.1%)</td>
</tr>
<tr>
<td>Re-operation of Mitral Valve</td>
<td>0</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>Urgent / Emergent CV Surgery</td>
<td>4 (2.2%)</td>
<td>4 (4.3%)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>1 (0.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Deep Wound Infection</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ventilation &gt; 48 hrs</td>
<td>0</td>
<td>4 (4.3%)</td>
</tr>
<tr>
<td>New Onset Permanent Atrial Fib</td>
<td>2 (1.1%)</td>
<td>0</td>
</tr>
<tr>
<td>Septicemia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>GI Complication Requiring Surgery</td>
<td>2 (1.1%)</td>
<td>0</td>
</tr>
<tr>
<td>Transfusions ≥ 2 units</td>
<td>24 (13.3%)</td>
<td>42 (44.7%)</td>
</tr>
</tbody>
</table>

**TOTAL % of Patients with MAE**

- **Percutaneous**: 15.0%
- **Surgery**: 47.9%

Difference (Percutaneous - Surgery) = -32.9%

p<0.001; (95% CI: -20.7%, -45.0%)

Freedom from MV Surgery or Re-operation in EVEREST

P > 0.001

(Mauri L et al. J Am Coll Cardiol 2013. Online)
Mitral Regurgitation Severity in EVEREST

MR Severity at Baseline and 48 Months

(Mauri L et al. J Am Coll Cardiol 2013. Online)
NYHA Functional Class in EVEREST

NYHA Functional Class at Baseline and 48 Months

(Mauri L et al. J Am Coll Cardiol 2013. Online)
# MitraClip Therapy
## UHC experience

17 Sep 2008 – 31 Aug 2012

<table>
<thead>
<tr>
<th></th>
<th>EVEREST II</th>
<th>Hamburg</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>184</td>
<td>340</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>67 ± 13</td>
<td>75 ± 9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Men</td>
<td>55 (30%)</td>
<td>216 (64%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Functional MR</td>
<td>49 (27%)</td>
<td>230 (68%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NYHA III/IV</td>
<td>94 (51%)</td>
<td>320/333 (96%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>60 ± 10</td>
<td>43 ± 16</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Log. EuroSCORE, % [median (IQR)]</td>
<td>33 (18%)</td>
<td>22 (12 – 38)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>86/183 (47%)</td>
<td>241/328 (73%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>40/183 (22%)</td>
<td>218/337 (65%)</td>
<td>0.0031</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>59/175 (34%)</td>
<td>220/337 (65%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>14 (8%)</td>
<td>102/336 (30%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>COPD</td>
<td>27/183 (15%)</td>
<td>69/337 (21%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MR 3+/4+</td>
<td>176 (96%)</td>
<td>340 (100%)</td>
<td>0.1633</td>
</tr>
</tbody>
</table>

80% of patients would not have fulfilled EVEREST criteria
## Safety Results

**German TRAMI Registry n=1064**

<table>
<thead>
<tr>
<th></th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural Success</td>
<td>95.3</td>
</tr>
<tr>
<td>Patient with MACCE (death, MI, Stroke)</td>
<td>3.5</td>
</tr>
<tr>
<td>Death</td>
<td>2.9</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.2</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.4</td>
</tr>
<tr>
<td>Severe bleeding, transfusion</td>
<td>14.5</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>1.4</td>
</tr>
<tr>
<td>Vascular injury</td>
<td>6.9</td>
</tr>
<tr>
<td>Clip embolism</td>
<td>0</td>
</tr>
</tbody>
</table>

Efficacy Results in ACCESS EU

**Mitral Regurgitation Grade***
- Baseline: 2+ (24%); 3+ (4%); 4+ (4%)
- 1 Year: 0 (100%); 2+ (0%); 3+ (0%); 4+ (0%)
- 79% MR ≤ 2+ at 1 Year

*As assessed by the sites
N = 327 Matched Cases

**NYHA Functional Class***
- Baseline: II (100%); III (0%); IV (0%)
- 1 Year: I (100%); II (0%); III (0%); IV (0%)
- p<0.0001

N = 343 Matched Cases

**MLHFQ**
- Baseline: Mean QOL Score (MLHFQ) = 41.6
- 1 Year: Mean QOL Score (MLHFQ) = 28.1
- Mean improvement - 13.5 points
  95% CI: (-16.0, -11.0)

N = 264 Matched Cases

**6MWT**
- Baseline: Mean Meters Walked = 275
- 1 Year: Mean Meters Walked = 334
- Mean improvement 59.5 meters
  95% CI: (44.5, 74.6)

N = 216 Matched Cases

(ACCESS EU Maisano In Press JACC)
The percutaneous Mitraclip procedure may be considered in symptomatic patients with severe primary or secondary MR despite optimal medical therapy, who fulfil the echo criteria of eligibility, are judged inoperable or at high risk for surgery by a heart team, and who have a life expectancy greater than one year.

*(Recommendation class IIb, level of Evidence C)*

The current findings have to be confirmed in larger series with longer follow-up and with a randomized design.
The Trials we need in Secondary MR

HF patients with Severe MR and Low EF

RESHAPE, COAPT just started
Mitra-FR will start

Management
(including Revascularisation and/or CRT)

Edge-to-Edge
Medical therapy
Coronary Sinus Annuloplasty
Limitations of Percutaneous Coronary Sinus Annuloplasty
The Devices

- The Edwards MONARC system*

- The CARILLON device

- The PTMA Implant System*

* abandoned
Percutaneous Mitral Commissurotomy

Percutaneous Mitral Valve Repair

Transcatheter treatment after surgical failure

Final comments
Mitral Bioprosthesis vs Mechanical Prostheses

Primary dysfunction

Reoperations

(Hammermeister et al. J Am Coll Cardiol 2000;36:1152-8)
Transcatheter « Valve in Valve » for Mitral Bioprosthesis Failure
Persistence/Recurrence of MR following Restrictive Annuloplasty

(Magne et al. Cardiology, 2008)
Transcatheter « Valve in a Ring »

Transsseptal

Transapical
Transcatheter « Valve in a Ring »

(De Weger. Eur J Cardio-thorac Surg. 2010.)
(D Himbert. J Am Coll Cardiol. 2012;60:1205-6.)
Percutaneous Mitral Commissurotomy

Percutaneous Mitral Valve Repair

Transcatheter treatment after surgical failure

Final comments
The «Heart Team»

- Surgeons
- Cardiologists
- Anaesthesiologists
- Other specialists: HF, EP, Geriatricians, …
- Imaging specialists (Echo, CT, MRI)

Treatment of Mitral Valve Disease
Patient Selection for Intervention on the Mitral Valve

Medical Rx

PMVR

Surgery (Repair, Replacement, LVAD, Transplantation)

« Futility > Utility »
Because of cardiac and extra cardiac factors
Where Shall we Perform Percutaneous Valve Intervention?

In cardiology and cardiac surgery centres
Multimodality Imaging

Linked Live 3DTEE and fluoroscopic images

Volume location of 3D Echo
# Transcatheter Mitral Valve Landscape

<table>
<thead>
<tr>
<th>Approach</th>
<th>Commercial</th>
<th>In Development</th>
<th>Abandoned</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edge-to-Edge Repair</td>
<td>Abbott Vascular</td>
<td>St. Jude Medical</td>
<td>QuantumCor</td>
</tr>
<tr>
<td>Direct Annuloplasty</td>
<td>Kardium mitralis</td>
<td>Valcare Medical</td>
<td>ReCor Medical</td>
</tr>
<tr>
<td>Indirect Annuloplasty</td>
<td>Cardiac Dimensions</td>
<td>Valtech</td>
<td>St. Jude Medical</td>
</tr>
<tr>
<td>Chordal Repair</td>
<td>neoCHORD</td>
<td>Valtech</td>
<td>Edwards</td>
</tr>
<tr>
<td>Ventricular Remodeling</td>
<td>CardioKinetix Inc.</td>
<td>MARDIL MEDICAL</td>
<td>Myocor</td>
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<tr>
<td>Enhanced coaptation</td>
<td>middle peak</td>
<td>cardiosolutions</td>
<td>Acorn</td>
</tr>
<tr>
<td>MV Replacement</td>
<td>Medtronic</td>
<td>endoValve</td>
<td>Highlife</td>
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<tr>
<td></td>
<td>Valtech</td>
<td>MitrAssist</td>
<td>Edwards</td>
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<td></td>
<td>CardiAQ</td>
<td>TENDYNEI</td>
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<tr>
<td></td>
<td>Medtronic</td>
<td>ValtXchange Inc.</td>
<td></td>
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</table>
New Devices: Direct Annuloplasty

Mitralign

In clinical trial (n=40)

GDS

In clinical trial (n=10)

Cinching cable

P1

P3

P2
New Devices: Direct Annuloplasty

Millipede

Valtech Cardioband

In clinical trial (n=8)
Transfemoral FIM

Patient C1-05, San-Raffaele Hospital, February 19th, 2013
- 69 years old male
- NYHA Class II, underwent CABG in 2000
- Ongoing Atrial Fibrillation
- Severe MR

- Implanted with the Cardioband transfemoral system
- Total Procedure time: 2.5 hours
- MR Reduced to MILD by cinching the implant
- Patient was discharged after 2 days with no safety issues

<table>
<thead>
<tr>
<th></th>
<th>Before Adjustment</th>
<th>After Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR Grade</td>
<td>Severe</td>
<td>Mild</td>
</tr>
<tr>
<td>Septo-Lateral Dimension</td>
<td>29.5mm</td>
<td>19mm (34% decrease)</td>
</tr>
<tr>
<td>Coaptation Length</td>
<td>7mm</td>
<td>9.9mm</td>
</tr>
<tr>
<td>Anterior-Posterior Dimension</td>
<td>35mm</td>
<td>30mm</td>
</tr>
</tbody>
</table>
New Devices: Chordal Implant

NeoChord

Valtech V-Chordal

MitraFlex

In clinical trial

In clinical trial
Combination of Techniques

= Fully Percutaneous Mitral Repair

IRVINE, Calif., June 14, 2012—CardiAQ Valve Technologies, the world’s first self-conforming and self-anchoring transcatheter mitral valve implantation (TMVI), today announced the world’s first TMVI implantation. This cardiovascular medicine milestone: a bioprosthetic mitral heart valve treatment into an 86-year-old male suffering from severe mitral regurgitation and severe heart failure. The breakthrough TMVI procedure was performed on June 12 at Rigshospitalet University Hospital, Copenhagen, Denmark, by interventional cardiology professor Niels Christiansen, M.D., and Olaf Franzen, M.D., cardiovascular surgeon Steen Hansen, M.D., and echocardiographer Nikolaj Ihlemoe.
Challenges

- Positioning
- Fixation
- Paravalvular leaks
- Valve gradient and LV outflow track obstruction
- Thrombosis
- Durability
- Feasibility of reintervention
- ......
Transcatheter Mitral Valve Replacement in a Patient with Calcified Native Mitral Valve Stenosis

(Sinning et al. Eur Heart J 2013; In Press)
Conclusions

- **Percutaneous Mitral Commissurotomy** shows good immediate and long-term clinical results and carries a low risk when performed by experienced teams. Patient selection must be based on anatomy as well as other characteristics.

- The current results of *the Edge-to-Edge technique* suggest that it may be useful in selected high risk patients. Long-term FU and RCT in secondary MR are needed.

- The results with *coronary sinus annuloplasty* are disappointing.

- Preliminary data on *transcatheter treatment after surgical failure* show that it is feasible.

- *In the future improvement is expected from:*
  - New devices aimed at reproducing surgical techniques
  - Combination of repair techniques
  - Valve replacement
The Future of the Treatment of Mitral Regurgitation

A larger number of patients will be treated by less invasive surgery and interventional Cardiology

(Figure 7. Volume of surgical and percutaneous mitral valve treatment at the University Heart Center Hamburg 2002–2010.)
« We need to be sure that we do not sacrifice proven long-term effectiveness for short-term issues, such as convenience, invasiveness, or irreversible procedural complications »

C. Otto

Mitral transcatheter techniques may represent a satisfactory palliation in patients who are at high surgical risk or inoperable, however it is unlikely that they will ever reach the success of TAVI.
Keep the well proven .......

... and be open-minded for something new
10,000 extra hours

Talent & Innovation Engagement

Outliers: The Story of Success
Malcolm Gladwell