A new solution to the old problem of functional mitral regurgitation

Francesco Maisano

Edwards Cardioband Mitral Repair System
Potential conflicts of interest

Speaker's name: Francesco Maisano

☑ I have the following potential conflicts of interest to report:

Founder: 4Tech Cardio, Perifect, TSP Medical

Receipt of grants / research support: Abbott, Bioventrix, Direct Flow Medical, Medtronic

Receipt of honoraria or consultation fees: Abbott, Edwards Lifesciences, Medtronic, Mitraltech, Xeltis

Stock shareholder: Mitraltech
Types of Mitral Regurgitation

**Functional Mitral Regurgitation (FMR)**
- Loss of leaflet coaptation due to:
  - Annular enlargement
  - Papillary muscle displacement causing leaflet tethering/tenting
- Etiologies:
  - Advanced Barlow’s Disease
  - Fibroelastic deficiency
- LA Dysfunction Dilated Annulus (Chronic atrial fibrillation, hypertension)
- LV Dysfunction Dilated Annulus (Non-ischemic or ischemic dilated cardiomyopathy)

**Degeneratve Mitral Regurgitation (DMR)**
- Etiologies:
  - Advanced Barlow’s Disease
  - Fibroelastic deficiency
- Leaflet prolapse due to:
  - Leaflet deformities or lesions
  - Ruptured/elongated chordae
  - Papillary muscle muscle rupture

Medically Managed Patients with Severe MR Have Poor Outcomes

20% One year mortality rate

50% Five year mortality rate

Very high rate of heart failure hospitalization

<table>
<thead>
<tr>
<th>% of Patients</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>20</td>
<td>29</td>
<td>37</td>
<td>46</td>
<td>50</td>
</tr>
<tr>
<td>Proportion of surviving patients hospitalized for heart failure</td>
<td>41</td>
<td>50</td>
<td>58</td>
<td>68</td>
<td>90</td>
</tr>
</tbody>
</table>

*Sachin S. Goel, JACC Volume 63, Issue 2, January 2014*
Most Patients with Isolated FMR are Conservatively Managed Today*

*Duke Databank: 1,538 pts with echocardiographic 3+ to 4+ FMR and LVEF ≥20% between 2000 and 2010 not undergoing CABG

* Curtesy of Dr. Michael Mack
Transcatheter treatment of functional MR patients remains a challenge

Figure 1. Percentage of patients with ≤2+ mitral regurgitation (MR) at baseline and 12 months after percutaneous MitraClip placement. The smaller cohorts represent the subset of patients from each registry who had MR qualified by imaging and were available for follow-up. Certain registries were able examine only those with follow-up and compare baseline MR; others measured baseline MR in all comers. ACCESS-EU, A Two-Phase Observational Study of the MitraClip System in Europe; GRASP, Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation; EVEREST II, Endovascular Valve Edge-to-Edge Repair Study II; HRR+REALISM, High Risk Registry/Real World Expanded Multicenter Study of the MitraClip System.\(^{11,26,31,34}\)
Recurrence of mitral regurgitation after transcatheter therapy

- Matched-pair data analysis of 68 patients
- FMR grade $\geq 3+$ and severe HF symptoms at baseline
- Pre-discharge echocardiography showed residual MR $\leq 2+$ in 84%
- MR 3+ and 4+ showed again an uptake at 6 months

Changes from baseline to 6 months in mitral regurgitation (MR) grade. Data refer to 68 patients with paired echocardiographic data at baseline and 6-month follow-up.

In the match-pair analysis the number of patients with MR 1+ decreased substantially at one year.

MR 3+/4+ increase from 11.3% at discharge to 16.6%
SENTINEL Study
Recurrence of mitral regurgitation at one year in matched-pair analysis

**Figure 4** Severity of Mitral Regurgitation at Baseline and Follow-Up (Discharge and 1-Year Follow-Up) After TMVR

Nickenig et al. Percutaneous Mitral Valve Edge-to-Edge Repair, J Am Coll Cardiol 2014;64:875–84
Sustained reduction of mitral valve annular diameter has been associated with favorable outcomes in FMR.

“Patients with SMR and sustained reduction in MV AP-diameter above the cut off value showed lower grades of MR after one year when compared to patients without a stable reduction of AP-diameters (p=0.03).”

Evolution of mitral valve annular dimension from one to five years

Septal Lateral Annular Dimension (SLAD)

Echo Core Lab Assessed

<table>
<thead>
<tr>
<th>Mean SLADDiastolic (cm)</th>
<th>Mean SLADsystolic (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL Paired Data (N=159)</td>
<td>BL Paired Data (N=91)</td>
</tr>
<tr>
<td>3.86</td>
<td>3.88</td>
</tr>
<tr>
<td>3.75</td>
<td>3.97</td>
</tr>
<tr>
<td>Δ = -0.11 cm</td>
<td>Δ = 0.09 cm</td>
</tr>
<tr>
<td>p = 0.0003</td>
<td>p = 0.13</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean SLADDiastolic (cm)</th>
<th>Mean SLADsystolic (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL Paired Data (N=156)</td>
<td>BL Paired Data (N=89)</td>
</tr>
<tr>
<td>3.54</td>
<td>3.56</td>
</tr>
<tr>
<td>3.41</td>
<td>3.44</td>
</tr>
<tr>
<td>Δ = -0.13 cm</td>
<td>Δ = -0.12 cm</td>
</tr>
<tr>
<td>p &lt; 0.0001</td>
<td>p = 0.042</td>
</tr>
</tbody>
</table>

Survival after undersized MVA

Surgical vs Medical Rx in DCM-MR

CABG alone vs CABG+MVA in IMR

• Comorbidities and operative risk
• Recurrent MR and MS
• Lack of reverse remodeling

• Less invasive therapy
• Tailored approach and off pump adjustments
• Early treatment

Edwards Cardioband Mitral Repair System
CE Mark Trial

Single arm, multicenter, prospective study with intra-subject comparisons to evaluate the performance and safety of the Edwards Cardioband Mitral Repair System for repair of functional mitral regurgitation

Edwards Cardioband Mitral CE Mark Trial

Patient Flow

Intent-To-Treat (ITT)
N=62

- Patient out of the device indication; n=1

Full Analysis Set (FA)
N=61

- No implantation; n=1

Per Protocol (PP)
N=60

- Death; n=7*
- Incomplete follow up; n=8
- Secondary Intervention; n=6

1-Year Follow-up
63% (39/62)**

* 2/7 patients died due to complications of elective open heart surgery.
** 39 patients completed echo follow up at 1 year. 38 patients completed clinical follow up at 1 year.

### Edwards Cardioband Mitral CE Mark Trial
#### Study Demographics (Full Analysis Set N=61)

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%) or Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>72 ± 7</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Male 44 (72%)</td>
</tr>
<tr>
<td></td>
<td>Female 17 (28%)</td>
</tr>
<tr>
<td><strong>Euroscore II (%)</strong></td>
<td>7.1</td>
</tr>
<tr>
<td><strong>Baseline NYHA Class of III or IV</strong></td>
<td>52 (85%)</td>
</tr>
<tr>
<td><strong>Ischemic</strong></td>
<td>36 (59%)</td>
</tr>
<tr>
<td><strong>Non Ischemic</strong></td>
<td>25 (41%)</td>
</tr>
<tr>
<td><strong>LVEDD (mm) Avg±SD</strong></td>
<td>60 ± 6</td>
</tr>
<tr>
<td><strong>EF (%) Avg±SD</strong></td>
<td>33 ± 11</td>
</tr>
<tr>
<td><strong>Previous CABG</strong></td>
<td>19 (31%)</td>
</tr>
<tr>
<td><strong>COPD</strong></td>
<td>13 (21%)</td>
</tr>
<tr>
<td><strong>Moderate to Severe Renal Failure</strong></td>
<td>46 (75%)</td>
</tr>
<tr>
<td><strong>Severe Pulmonary Hypertension</strong></td>
<td>15 (25%)</td>
</tr>
<tr>
<td><strong>Atrial Fibrillation</strong></td>
<td>46 (75%)</td>
</tr>
</tbody>
</table>

Edwards Cardioband Mitral CE Mark Trial
28% average reduction in septolateral diameter by core lab*

N=31

*Dr. Paul Grayburn – Baylor University

Edwards Cardioband Mitral CE Mark Trial
Septolateral reduction maintained at 1 year in paired analysis
Edwards Cardioband Mitral CE Mark Trial
MR reduction sustained at 1 year in paired analysis by core lab*

Edwards Cardioband Mitral CE Mark Trial
Significant functional improvement at 12 months

6MWT – Six Minute Walk Test; MLHFQ - Minnesota Living With Heart Failure Questionnaire; NYHA Class - New York Heart Association (NYHA) Functional Classification

Edwards Cardioband Mitral CE Mark Trial

Conclusions

- Transcatheter mitral repair using the Edwards Cardioband Mitral Repair System is safe and feasible
- Provides significant and consistent reduction in septolateral diameter
- Delivers a significant and consistent reduction in mitral regurgitation
- Provides functional improvement in most patients
- Further studies are warranted
Thank You
**Edwards Cardioband Mitral CE Mark Trial**

**Major Inclusion/Exclusion Criteria**

**Inclusion Criteria**
- Age > 18 years
- **Symptomatic patients** (NYHA Class II-IV) despite optimal medical therapy, including CRT if indicated
- LVEF ≥ 25%, LVEDD ≤ 70mm
- **Moderate to severe functional MR**
- **Subject is high risk to undergo MV surgery**
  (as assessed by a cardiac surgeon and a cardiologist, at the site and according to ESC/EACTS guidelines on the management of valvular heart disease)

**Exclusion Criteria**
- Untreated clinically significant CAD requiring revascularization
- Pulmonary hypertension >70mmHg at rest
- Renal insufficiency requiring dialysis
- Right-sided congestive heart failure with echocardiographic evidence of severe right ventricular dysfunction and severe tricuspid regurgitation
- Heavily calcified annulus or leaflets
- Any recent cardiovascular intervention
- CVA or TIA within 6 months or severe carotid stenosis (>70% by ultrasound)
- **Mitral valve anatomy which may preclude proper device treatment**

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## Edwards Cardioband Mitral CE Mark Trial Endpoints

<table>
<thead>
<tr>
<th>Safety</th>
<th>Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td><strong>Primary</strong></td>
</tr>
<tr>
<td>• Overall rate of <strong>Major Serious Adverse Events</strong> (SAEs) and Serious Adverse Device Effects (SADE) until hospital discharge and at post-operative 30 days</td>
<td>• <strong>Technical success</strong> rate of the implantation of the Edwards Cardioband system</td>
</tr>
<tr>
<td>• <strong>Major SAEs</strong>: Death, myocardial infarction, cardiac tamponade, device related cardiac surgery, stroke</td>
<td>• <strong>Technical feasibility</strong> of Edwards Cardioband system adjustment</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td><strong>Secondary</strong></td>
</tr>
<tr>
<td>• Overall rate of <strong>Major Serious Adverse Events</strong> (SAEs) and Serious Adverse Device Effects (SADE) up to 24 months</td>
<td>• <strong>MR severity at 6, 12 and 24 months</strong></td>
</tr>
<tr>
<td></td>
<td>• <strong>Change in 6 MWT</strong> in 6, 12 and 24 months</td>
</tr>
<tr>
<td></td>
<td>• <strong>Change in quality of life</strong> (MLWHFQ) at 6, 12 and 24 months</td>
</tr>
</tbody>
</table>

Events defined according to VARC-2 guidelines  
MLHDFQ - Minnesota Living With Heart Failure Questionnaire

Edwards Cardioband Mitral CE Mark Trial
Participating Sites

**Edwards Cardioband Mitral CE Mark Trial Study Outcomes (Full Analysis Set N=61)**

<table>
<thead>
<tr>
<th>Implant rate</th>
<th>98.4% (60/61)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Device success (at discharge)</strong></td>
<td>78.3% (47/60)</td>
</tr>
<tr>
<td>• Death (non-device related)*</td>
<td>n=2</td>
</tr>
<tr>
<td>• Device failures:</td>
<td></td>
</tr>
<tr>
<td>- No implant size adjustment**</td>
<td>n=2</td>
</tr>
<tr>
<td>- Anchor detachment with MR reduction***</td>
<td>n=5</td>
</tr>
<tr>
<td>- Anchor detachment with no MR reduction***</td>
<td>n=5****</td>
</tr>
</tbody>
</table>

*CEC adjudicated.
**Contraction wire protection is now available in commercialized device.
***Anchor detachment occurred early in the series. Anchor has since been modified to avoid detachment.
****MR did not improve at discharge for 4/5; MR recurrence at 6 months for 1/5

## Edwards Cardioband Mitral CE Mark Trial

### Adjudicated major safety events at 30 Days

<table>
<thead>
<tr>
<th>30 Day Events</th>
<th>Patients Experiencing Event, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Full Analysis Set N=61</td>
</tr>
<tr>
<td>Death</td>
<td>2 (3.3%)</td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Need for elective Mitral Operation</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>2 (3.3%)</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>4 (6.6%)</td>
</tr>
<tr>
<td>Respiratory Failure</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Cardiac Tamponade</td>
<td>1 (1.6%)</td>
</tr>
</tbody>
</table>

Events defined according to VARC-2 Guidelines (European Heart Journal, 2012, 33:2403-2414). One additional death case per ITT.

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