Edwards Cardioband
Mitral Reconstruction System

Introduction and overview
Two-year follow up of CE trial
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Mitral Reconstruction System

Disease state background
Functional mitral regurgitation
Types of mitral regurgitation

**Functional Mitral Regurgitation (FMR)**
- LV dysfunction
dilated annulus
  - Non-ischemic or ischemic
dilated cardiomyopathy
- LA dysfunction
dilated annulus
  - Chronic atrial fibrillation,
hypertension

**Degenerative Mitral Regurgitation (DMR)**
- Etiologies
  - Advanced Barlow’s Disease
  - Fibroelastic deficiency

**Loss of leaflet coaptation due to:**
- Annular dilatation
- Papillary muscle displacement
  causing leaflet tethering / tenting

**Leaflet prolapse due to:**
- Leaflet deformities or lesions
- Ruptured / elongated chordae
- Papillary muscle rupture

FMR – a vicious cycle that is associated with advanced Chronic Heart Failure

- Annular-ventricular dilatation
- MR
- Volume overload
50% of patients with mitral regurgitation are managed medically

Distribution of patients with isolated MR

- Isolated MR (n=877)
  - No severe MR (n=331)
  - Severe MR (n=546)
    - Symptoms missing (n=6)
    - No symptoms (n=144)
    - Symptoms (n=396)
      - No intervention (n=193 (49%))
      - Intervention (n=203 (51%))

Medically treated patients with severe MR

- FMR Medical Rx (47.5%)
- FMR MV Surgery (26.8%)
- Other Medical Rx (1.9%)
- Other MV Surgery (3.1%)
- DMR Medical Rx (3.3%)
- DMR MV Surgery (17.4%)

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

Sustained reduction of mitral valve annular diameter may lead to 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).”
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System description and functionality
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- A transcatheter device designed to reduce mitral regurgitation through annular reduction
Cardioband Mitral System key advantages

**Annular reduction**
Restores valve to a more functional state, facilitating leaflet coaptation, thereby reducing MR

**Adjustable implantation**
Enables annular reduction based on each patient’s anatomy

**Real-time confirmation**
Allows real-time adjustment and confirmation of MR reduction
Cardioband Mitral System procedure

1. Access via transseptal puncture & system insertion
2. Deploy implant via steerable catheter
3. Adjust and confirm real-time reduction of MR
Dynamic size adjustment results in significant reduction in annular diameter

Pre-adjustment

Partial adjustment

Final adjustment

Courtesy of Georg Nickenig, MD, Robert Schueler, MD, Heart Center University of Bonn, Germany.
Cardioband Mitral System delivers a significant and consistent reduction in mitral regurgitation

Baseline

Final size post-adjustment
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European CE mark trial
Cardioband Mitral System CE mark trial

- Single arm, multicenter, prospective study with intra-subject comparisons to evaluate the performance and safety of the Cardioband mitral system for repair of functional mitral regurgitation.
Key study admission criteria

**Inclusion**
- 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**
- 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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# Cardioband Mitral System CE mark trial

## Study endpoints

### Safety

**Primary Endpoints**
- Overall rate of **Major Serious Adverse Events** (SAEs) and Serious Adverse Device Effects (SADE) until hospital discharge and at post-operative 30 days
- **Major SAEs:** Death, myocardial infarction, cardiac tamponade, device related cardiac surgery, stroke

### Performance

**Secondary Endpoints**
- Overall rate of **Major Serious Adverse Events** (SAEs) and Serious Adverse Device Effects (SADE) up to 24 months

<table>
<thead>
<tr>
<th>Events Defined According to VARC Guidelines (European Heart Journal. 2012;33:2403-2414.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6MWT – Six Minute Walk Test</td>
</tr>
<tr>
<td>MLHFQ – Minnesota Living with Heart Failure Questionnaire</td>
</tr>
</tbody>
</table>

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Participating sites

Bichat Hospital
(n=13)

San Raffaele Hospital
(n=10)

Zurich University Hospital
(n=4)

Presidio Ospedaliero Ferrarotto
(n=1)

St. Antonius Hospital
(n=1)

Heart Center, University Hospital Bonn
(n=16)

Asklepios, St. Georg
(n=10)

Heart Center University of Köln
(n=4)

LMU Klinikum der Universität München, Campus Großhadern
(n=1)

Universitätsmedizin der Johannes Gutenberg Universität Mainz
(n=1)

Rambam Health Care Campus
(n=1)

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Patient flow

Full analysis set (FA)  
N=61

- No implantation n=1

Implanted  
N=60

- Death n=7 (1 device-related)
- Discontinued follow-up n=5
- Study exit due to secondary intervention n=6

1-year follow up  
N=42

- Death n=4 (none device or procedure-related)
- Discontinued follow up n=1
- Study exit due to secondary intervention n=3

2-year follow up  
N=34

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## Study demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=61</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72 ± 7</td>
</tr>
<tr>
<td>Male</td>
<td>72%</td>
</tr>
<tr>
<td>Euroscore II</td>
<td>7%</td>
</tr>
<tr>
<td>NYHA functional class III or IV</td>
<td>87%</td>
</tr>
<tr>
<td>Ischemic etiology of regurgitation</td>
<td>60%</td>
</tr>
<tr>
<td>LVEF</td>
<td>33 ± 11</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>32%</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>75%</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>77%</td>
</tr>
</tbody>
</table>
Early learnings led to device improvements

Technical success at discharge 78.3% (47/60)

- Death¹  n=2
- Device failures:
  - No implant size adjustment  n=2
  - Anchor disengagement with MR reduction  n=5
  - Anchor disengagement with no MR reduction  n=5

Early learnings led to device improvements in second half of the study and in commercially available device.

¹1 intracranial hemorrhage; 1 multi-organ failure and sepsis (this patient also experienced anchor disengagement). None device or procedure related; CEC adjudicated. Presented by Francesco Maisano, MD at PCR London Valves 2018.
### Cardioband Mitral System CE mark trial

#### Favorable safety profile

<table>
<thead>
<tr>
<th>Adjudicated 30 Day Events¹</th>
<th>Full analysis set N=61</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Death</strong></td>
<td>2 (3.3%)</td>
</tr>
<tr>
<td>Intracranial hemorrhage²</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Multi-organ failure and sepsis following elective mitral surgery²</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td><strong>Myocardial infarction</strong></td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td><strong>Major bleeding complications</strong></td>
<td>2 (3.3%)</td>
</tr>
<tr>
<td><strong>Renal failure</strong></td>
<td>4 (6.6%)</td>
</tr>
<tr>
<td><strong>Respiratory failure</strong></td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td><strong>Cardiac tamponade</strong></td>
<td>1 (1.6%)</td>
</tr>
</tbody>
</table>

- No device migration or embolization
- No mitral stenosis

¹Events defined according to VARC Guidelines (European Heart Journal, 2012, 33:2403-2414.).

²None device or procedure related; CEC adjudicated.

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79% survival at 2 years

Kaplan-Meier analysis
Presented by Francesco Maisano, MD at PCR London Valves 2018.
Cardioband Mitral System CE mark trial

96% of patients with mitral regurgitation reduced to ≤ 2+ sustained at two years by core lab

1

Dr. Paul Grayburn – Baylor University
Presented by Francesco Maisano, MD at PCR London Valves 2018.
Cardioband Mitral System CE mark trial

96% of patients with mitral regurgitation reduced to ≤ 2+ sustained at two years in paired analysis (core lab¹)

¹Dr. Paul Grayburn – Baylor University
Presented by Francesco Maisano, MD at PCR London Valves 2018.
Cardioband Mitral System CE mark trial

Septolateral reduction sustained at 2 years in paired analysis (core lab\(^1\))

\[ N.S. ^a \]

\[ p<0.01 ^a \]

Septolateral Diameter (mm)

<table>
<thead>
<tr>
<th>Time</th>
<th>Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>36.8</td>
</tr>
<tr>
<td>Discharge</td>
<td>25.9</td>
</tr>
<tr>
<td>1 Year</td>
<td>25.9</td>
</tr>
<tr>
<td>2 Years</td>
<td>26.3</td>
</tr>
</tbody>
</table>

\(^1\)Dr. Paul Grayburn – Baylor University
\(^a\)t-test

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Significant functional improvement at 2 years in paired analysis

NYHA Class

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 Year</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>100%</td>
<td>40%</td>
<td>83%</td>
</tr>
<tr>
<td>III</td>
<td>80%</td>
<td>60%</td>
<td>17%</td>
</tr>
<tr>
<td>II</td>
<td>60%</td>
<td>50%</td>
<td>0%</td>
</tr>
<tr>
<td>I</td>
<td>40%</td>
<td>30%</td>
<td>0%</td>
</tr>
</tbody>
</table>

P<0.01<sup>a</sup>

MLHFQ Score

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 Year</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>36</td>
<td>19</td>
<td>20</td>
</tr>
</tbody>
</table>

P<0.01<sup>b</sup>

6MWT

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 Year</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meters Walked</td>
<td>335</td>
<td>407</td>
<td>355</td>
</tr>
</tbody>
</table>

P=N.S.<sup>b</sup>

<sup>a</sup>McNemar's test

<sup>b</sup>t-test

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

Presented by Francesco Maisano, MD at PCR London Valves 2018.
Study conclusions

Transcatheter mitral valve reconstruction using the Cardioband mitral system:

- Allows for safe and feasible procedural success supported by real-time confirmation of results
- Provides significant and durable reduction in septolateral diameter and consequently in mitral regurgitation (96% MR ≤ 2+ at 2 years)
- Results in clinically significant improvements in functional status, quality of life and exercise capacity sustained at 2 years
- Preserves patient’s native anatomy, keeping future options open
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Case report with 24-month follow up
Courtesy of Azeem Latib, MD
EMO-GVM Centro Cuore Columbus and
San Raffaele Scientific Institute, Milan, Italy
Baseline patient characteristics

Clinical Background

- 75 year-old male
- Ischemic Cardiomyopathy
  - Prev. CABG (LIMA-LAD; RIMA-RI; SVG-OM)
  - Prev. PCI on PL, Ramus
- Permanent AF
- VVI pacemaker
- NYHA III

Baseline Echo

- Moderate-to-severe MR
- Annular dilatation & dysfunction
  - AP Diameter = 33 mm
  - IC Diameter = 41 mm
  - Coaptation depth = 4 mm
- EF=45%
Cardioband Mitral System procedure

LAO View
Cardioband Mitral System
MR reduced and sustained at 24 months

- At 2-year follow-up:
  - MR remains mild
  - NYHA reduced from III to I
  - No admissions for Heart Failure
  - LVEF stable at 40%
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How to get started
Patient screening process

- Edwards offers additional echo support for interested centers
- A center has the option to submit both echo and CT scans simultaneously
Opening a Cardioband Mitral System center

In general, training will be scheduled after at least 2-3 patients were screened and found eligible for the procedure.

After full training at least 2-3 procedures should take place in the following three weeks in order to ensure best outcomes for the patient.
Cardioband Mitral System training occurs in the hospital and concludes with device implantation

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Theoretical training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 2</td>
<td>Cath lab practice (Cardioband mitral system and echo simulators)</td>
</tr>
<tr>
<td>Day 3</td>
<td>Cardioband device implantation</td>
</tr>
</tbody>
</table>

A total of **two days** to complete site training and first procedure

- An additional echo simulator training will be available separately
Startup center training details
Mandatory training for new users

Schedule
- One and a half day training program:
  - Half day theoretical training
  - One full day cath lab simulator practice
- Immediately followed by Cardioband implantation

Requirements
- Attendees
  - 1st and 2nd operator
  - Echocardiographist
- Equipment
  - Human grade structural heart cath lab
  - 3D TEE machine
  - Meeting room with projector

Topics
- Device introduction
- Device functionality
- Procedure steps
- Troubleshooting management
- Clinical study results
- Echo navigation
- Camera simulator deployment
- Guided echo simulator deployment (fluoroscopy and echo)
- Solo echo simulator deployment (fluoroscopy and echo)

Certificates
- 1st operator
- 2nd operator
- Echocardiographist
- System preparation
For professional use. See instructions for use for full prescribing information, including indications, contraindications, warnings, precautions, and adverse events.

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