Percutaneous Mitral Valve Therapies: State of the Art in 2020
LA ACP Annual Meeting

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>Grant/Research Support</td>
<td>None</td>
</tr>
<tr>
<td>Consulting Fees/Honoraria</td>
<td>BSCI, Abbot DSMB</td>
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<tr>
<td>Intellectual Property Rights</td>
<td>UTHSCSA</td>
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<tr>
<td>Other Financial Benefit</td>
<td>CCI Editor In Chief</td>
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</tbody>
</table>
The 30,000 Ft View

Bogoslof Volcano, AK

Maria
3 Ft View of Valvular Heart Disease in Cardiology
Mitral Stenosis

• The most common etiology of MS is rheumatic fever, with a latency of approximately 10 to 20 years after the initial streptococcal infection. Symptoms usually appear in adulthood.

• Other etiologies are rare but include:
  - congenital MS
  - radiation exposure
  - atrial myxoma
  - mucopolysaccharidoses

• MS secondary to calcific annular disease is increasingly seen in elderly patients, and in patients with advanced chronic kidney disease.
Mitral Stenosis

- Mitral stenosis most commonly results from rheumatic heart disease
  - fusion of the valve leaflet cusps at the commissures
  - thickening and shortening of the chordae
  - calcium deposition within the valve leaflets
- Characteristic “fish-mouth” or “hockey stick” appearance on the echocardiogram (depending on view)
Mitral Stenosis: Natural History

- The severity of symptoms depends primarily on the degree of stenosis.

- Symptoms often go unrecognized by patient and physician until significant shortness of breath, hemoptysis, or atrial fibrillation develops.

- Do not tolerate tachycardia or volume overloads well.

- At high risk for development of left atrial-appendage thrombus formation, and subsequent stroke.

- Symptoms can be managed medically initially.
Mitral Stenosis Hemodynamics

- As the mitral valve area gets progressively smaller, a higher pressure in the LA is needed to “push” blood from LA to LV.

- LA enlarges markedly. Atrial fibrillation commonly results.

- ↑ LA pressure → ↑ pulmonary pressures → RV Hypertrophy

- Eventually, right heart failure will occur

- LV function is usually normal at rest, but may fail to increase normally with exercise.
Findings in Mitral Stenosis

- **EKG:** LAE; RVH; Eventually atrial fibrillation
- **CXR:** LAE; straightened left heart border; straightened right mainstem bronchus

Lateral CXR: Bulging of left atrium against esophagus
# Clinical Stages of Mitral Stenosis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Valve Anatomy</th>
<th>Valve Hemodynamics</th>
<th>Hemodynamic Consequences</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At risk of MS</td>
<td>• Mild valve doming during diastole</td>
<td>• Normal transmitral flow velocity</td>
<td>• None</td>
<td>• None</td>
</tr>
</tbody>
</table>
| B     | Progressive MS | • Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets  
• Planimetered MVA >1.5 cm² | • Increased transmitral flow velocities  
• MVA >1.5 cm²  
• Diastolic pressure half-time <150 msec | • Mild-to-moderate LA enlargement  
• Normal pulmonary pressure at rest | • None |
| C     | Asymptomatic severe MS | • Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets  
• Planimetered MVA ≤1.5 cm²  
• (MVA ≤1 cm² with very severe MS) | • MVA ≤1.5 cm²  
• (MVA ≤1 cm² with very severe MS)  
• Diastolic pressure half-time ≥150 msec  
• (Diastolic pressure half-time ≥220 msec with very severe MS) | • Severe LA enlargement  
• Elevated PASP >30 mm Hg | • None |
## Clinical Stages of Mitral Stenosis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Valve Anatomy</th>
<th>Valve Hemodynamics</th>
<th>Hemodynamic Consequences</th>
<th>Symptoms</th>
</tr>
</thead>
</table>
| D     | Symptomatic severe MS    | • Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets  
• Planimetered MVA ≤1.5 cm² | • MVA ≤1.5 cm²  
• (MVA ≤1 cm² with very severe MS)  
• Diastolic pressure half-time ≥150 msec  
• (Diastolic pressure half-time ≥220 msec with very severe MS) | • Severe LA enlargement  
• Elevated PASP >30 mm Hg | • Decreased exercise tolerance  
• Exertional dyspnea |

**SRB March 2020**
Medical Therapy of Mitral Stenosis

• Limit/minimize left atrial (LA) pressure elevation*
  – Diuretic
  – Slow heart rate (increases LA emptying time)
  – Maintain sinus rhythm (i.e., atrial contraction)

• Management of atrial fibrillation (Afib)
  – Prevent atrial fibrillation
  – Control heart rate when Afib occurs

• Prevent thromboembolic events
  – anticoagulation

* LA pressure ↑ when there is (a) ↑intravascular volume, cardiac output or heart rate or (b) loss of atrial contraction (i.e., pregnancy, infection, hyperthyroidism, and atrial fibrillation)
Indications for Intervention for Rheumatic Mitral Stenosis

Rheumatic MS

Very severe MS
MVA ≤1 cm²
T ½ ≥220 ms

Asymptomatic (stage C)
Favorable valve morphology
No LA clot
No or mild MR

YES

Favorable valve morphology
No LA clot
No or mild MR

NO

NO

Periodic Monitoring
PMBC (IIa)
PMBC (I)
MVR (I)
PMBC (IIb)
PMBC (IIb)
Periodic Monitoring

Severe MS
MVA ≤1.5 cm²
T ½ ≥150 ms

Symptomatic (stage D)
Favorable valve morphology
No LA clot
No or mild MR

YES

NYHA class III-IV symptoms with high surgical risk

NO

Periodic Monitoring

Asymptomatic (stage C)
New onset AF

YES

NO

Progressive MS
MVA >1.5 cm²
T ½ <150 ms

Symptomatic with no other cause
PCWP >25 mm Hg with exercise

YES

NO
Mitral Stenosis Surgery

Open commissurotomy

Closed commissurotomy

Valve replacement
Mitral Valvuloplasty Technique
Outcomes After PBMC 19 year Followup

Fazway et al EHJ Volume 66, Issue 2, June 2014, Pages 133-138
Percutaneous Mitral Valve Replacement for MAC
Anatomy of the Atrioventricular Valves

- Papillary muscles arise from the ventricular wall, and give rise to multiple fibrous chordae tendinae.
- Chordae attach to the edges of the valve leaflets, maintaining constant tension.
- Mitral valve: 2 leaflets. Tricuspid valve: 3 leaflets.
- Leaflets attach to the fibrous annulus.
- Annulus more oval/ horseshoe shaped.
- Valve opening, closure much more dynamic
Mitral Regurgitation
Brief Case Presentation

• 62 year old male college professor with a “heart murmur when I entered the Army” who is admitted for evaluation of subacute onset of shortness of breath over the preceding 3 months. No recent illness or hospitalization

• Vital Signs BP 138/74 HR 88 Regular RR 18 WT 167 lb HT 6’1”

• Physical Exam remarkable for JVP at 8cm with lungs that were clear. Cardiac Exam shows Gr III/IV HSM that radiated to the left axilla with + S4 No S3. S1, A2 normal P2 increased.
MR Etiologies

Normal
Degenerative MR Prolapse
Degenerative MR Flail
Functional MR Ischemic vs. nonischemic
Objectives Mitral Regurgitation

- Understand the mechanisms and classification of Mitral Regurgitation
- Review guidelines and outcomes for management strategies of mitral valve disease
- Discuss new techniques for monitoring mitral valvular heart disease
- Review percutaneous mitral valve procedures
- Discuss outcomes and opportunities for new percutaneous therapies
Identification of Mitral Regurgitation

There are a large number of patients who have MR that are unrecognized

- MR is due to multiple etiologies/mechanisms
- Patients are often minimally symptomatic
- Physical exam may be difficult
- Imaging studies require additional skill
2020 Management of MR


SRB March 2020
Prevalence of VHD in USA
2.5% of the overall population

Relationship between MR Severity and Mortality in Secondary MR

(Grigioni, Circulation 2001;103:1759-63)
How Are Patients with Isolated FMR Treated?

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

- 11.4% for All pts (N=1538)
- 5.9% for 20%-30% LVEF (N=440)
- 8.4% for 30%-40% LVEF (N=298)
- 11.8% for 40%-50% LVEF (N=313)
- 18.4% for 50%-60% LVEF (N=479)
A Largely Unmeet Need in a Large Patient Population

Mitral Regurgitation 2009 U.S. Prevalence

Total MR Patients\(^1,2\)

4,100,000

Eligible for Treatment\(^3,4\)

(MR Grade ≥3+)

1,670,000

Annual Incidence\(^3\)

(MR Grade ≥3+)

30,000

Untreated Large and Growing Clinical Unmet Need

14% Newly Diagnosed Each Year

Annual MV Surgery\(^5\)

Only 2% Treated Surgically

---

2020 Management of MR

- Define
  - Imaging expert

- Assess
  - Imaging expert

- Etiology
  - Primary
  - Secondary
  - Mixed

- Carpentier Classification/Mechanism

- Determine severity:
  - Quantitation: EROA, RVol, RF
  - Associated findings: LV/LA size, PASP, TR, PV flow reversal
  - Other testing: TEE, CMR, ETT, exercise echo, cath/angio

- Mild
- Moderate
- Severe
Defining the Etiology
Valve Structure & MR Jet Characteristics

Primary

Secondary
# Echo Assessment of MR

**Table 1: Suggested Qualitative and Quantitative Parameters for Standardized Echo Reporting**

**Mitral Regurgitation Assessment**

<table>
<thead>
<tr>
<th>Qualitative Parameters</th>
<th>Quantitative Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mitral Stenosis</strong></td>
<td></td>
</tr>
<tr>
<td><em>Resistive</em></td>
<td></td>
</tr>
<tr>
<td><em>Degenerative</em></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td><strong>Carpentier Classification</strong></td>
<td></td>
</tr>
<tr>
<td>Normal leaflet motion (Type I) may be seen in primary MR due to endocarditis, perforation, or clefts, or in secondary MR due to pure annular dilation.</td>
<td></td>
</tr>
<tr>
<td>Excessive leaflet motion (Type II) is most commonly seen with mitral valve prolapse or flail leaflet.</td>
<td></td>
</tr>
<tr>
<td>Restricted leaflet motion (Type III) subdivided into:</td>
<td></td>
</tr>
<tr>
<td>- IL: restriction during both systole and diastole</td>
<td></td>
</tr>
<tr>
<td>- II: restricted during systole only (e.g., ischemic etiology)</td>
<td></td>
</tr>
<tr>
<td><strong>Subaortic Morphology</strong></td>
<td></td>
</tr>
<tr>
<td><em>Thickening</em></td>
<td></td>
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<tr>
<td><em>Calcification</em></td>
<td></td>
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<tr>
<td><em>Retraction</em></td>
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<tr>
<td><em>Tumor</em></td>
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<tr>
<td><em>Vegitation</em></td>
<td></td>
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<tr>
<td><strong>MR Mechanism</strong></td>
<td></td>
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<tr>
<td>Primary</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
</tr>
<tr>
<td>- Dilated Cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>- Ischemic Cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td><strong>Mitral Jet Duration (CW Doppler and frame-by-frame analysis of color flow Doppler)</strong></td>
<td></td>
</tr>
<tr>
<td>Isoelectric</td>
<td></td>
</tr>
<tr>
<td>Early systolic</td>
<td></td>
</tr>
<tr>
<td>Mid systolic</td>
<td></td>
</tr>
<tr>
<td>Late systolic</td>
<td></td>
</tr>
<tr>
<td>Biphasic</td>
<td></td>
</tr>
<tr>
<td>CW Doppler density</td>
<td></td>
</tr>
<tr>
<td><strong>MR Jets</strong></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td></td>
</tr>
<tr>
<td><strong>MR Jet Direction</strong></td>
<td></td>
</tr>
<tr>
<td>Centrally directed</td>
<td></td>
</tr>
<tr>
<td>Eccentric</td>
<td></td>
</tr>
<tr>
<td>Posteriorly directed</td>
<td></td>
</tr>
<tr>
<td>Anteriorly directed</td>
<td></td>
</tr>
<tr>
<td>Lateral directed</td>
<td></td>
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<tr>
<td>Anteriorly directed</td>
<td></td>
</tr>
<tr>
<td>AnteroMedially directed</td>
<td></td>
</tr>
<tr>
<td>Medially directed</td>
<td></td>
</tr>
<tr>
<td><strong>Pulmonary Vena Flow Profile</strong></td>
<td></td>
</tr>
<tr>
<td><em>Normal</em></td>
<td></td>
</tr>
<tr>
<td><em>Syndrome flow blunting</em></td>
<td></td>
</tr>
<tr>
<td><em>Syndrome flow reversal</em></td>
<td></td>
</tr>
<tr>
<td>Number of veins exhibiting syndrome reversal</td>
<td></td>
</tr>
</tbody>
</table>

*Above criteria applicable for native mitral valve disease only and not for assessing MR post mitral valve repair (surgical or transcatheter).*

**Abbreviations:**
- AML = anterior mitral leaflet
- CW = continuous wave
- EROA = effective regurgitant orifice area
- EROA + = effective regurgitant orifice gradient
- LV = left ventricle
- MR = mitral regurgitation
- PA = pulmonary artery
- PISA = proximal isovelocity surface area
- PML = posterior mitral leaflet
- RA = right atrial
- RF = regurgitant fraction
- SAA = systolic anterior migration

**Sections:**
- Hemodynamic and Rhythm Parameters
- Qualitative Parameters
- Quantitative Parameters

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**LSU Health Shreveport**

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<table>
<thead>
<tr>
<th>Carpentier</th>
<th>Definition</th>
<th>Echocardiographic Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>normal leaflet motion with isolated annular dilation, leading to poor leaflet coaptation</td>
<td><img src="image1" alt="Echocardiographic Examples" /></td>
</tr>
<tr>
<td>Type II</td>
<td>excess motion of the margin of a leaflet segment above the annular plane</td>
<td><img src="image2" alt="Echocardiographic Examples" /></td>
</tr>
<tr>
<td>Type IIIa</td>
<td>restricted leaflet motion during diastole and systole</td>
<td><img src="image3" alt="Echocardiographic Examples" /></td>
</tr>
<tr>
<td>Type IIIb</td>
<td>restricted leaflet motion predominantly during systole</td>
<td><img src="image4" alt="Echocardiographic Examples" /></td>
</tr>
</tbody>
</table>

Case Presentation
Functional Mitral Regurgitation

- 68 year old male with a three year history of progressive dyspnea on exertion with two hospitalizations in the last 2 months for poorly controlled congestive heart failure
- 4V CABG (SVG with LIMA) eight years ago with LVEF 40% and patent grafts by cath at OSH 3 months ago.
- On maximal tolerated doses of ACE, Carvedilol and diuretics
MITRAL REGURGITATION REFERRAL TOOLKIT

REFERRAL ALGORITHM

Severity
Morphology
Symptoms
Treatment
Follow-up

SRB March 2020
Mitral Regurgitation
Brief Case Presentation
TEE of the Mitral Valve

Management of Severe MR in patients with HF (CCF)

1,095 pts* with 3+/4+ MR and HF between 2000 and 2008 (74% FMR, 21% DMR)

* Excluded MVA ≤ 2 cm², AR ≥ 2+, aortic peak velocity ≥ 2.5 m/s, HCM, endocarditis, concomitant AV, Ao or pericardial surgeries, LVAD or OHT.

171 of 474 (36%) un-operated pts with FMR and good echos would have been eligible for MitraClip based on published criteria.

Goel SS et al. JACC 2014;63,:185–90
2020 Management of MR

MDT:
- HF expert
- Imaging expert
- Valve expert
- Interventionalist
- Mitral surgeon
- Cardiac anesthesia
- Nurse coordinator and team
- Other specialists as needed
  - EP
  - Neurology, etc.

- Etiology, severity
- Symptoms
- LV function
- Associated conditions
  - AF, CAD, IE

- Comorbidities
- Risk assessment
- Functional assessment
- Shared decision making

GDMT for:
- HF*
- CAD
- AF
- HTN
- Lipids, etc.

Surgical Treatment
- Repair
- Replacement
- CABG
- AF surgery
- LAA management

Transcatheter Treatment
- Edge-to-Edge clip repair
- Other repair systems if when approved
- Replacement†
- AF ablation
- LAA management

* HF: Heart Failure
† Replacement: Valve replacement

Follow Up of Chronic MR

• Clinical Evaluation
  ▪ Functional Status/ETT

• Laboratory Evaluation
  ▪ BNP level

• Echo Follow-up
  ▪ LV Function
  ▪ Global Longitudinal Strain
# Frequency of Echocardiograms in Asymptomatic Patients With VHD and Normal Left Ventricular Function

<table>
<thead>
<tr>
<th>Stage</th>
<th>Valve Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage</strong></td>
<td>Aortic Stenosis</td>
</tr>
</tbody>
</table>
| Progressive    | Every 3–5 y  
(mild severity  
$V_{\text{max}}$ 2.0–2.9 m/s)  
Every 1–2 y  
(moderate severity  
$V_{\text{max}}$ 3.0–3.9 m/s) | Every 3-5 y (mild severity)  
Every 1-2 y (moderate severity) | Every 3–5 y  
(MVA >1.5 cm$^2$) | Every 3–5 y  
(mild severity)  
Every 1–2 y (moderate severity) |
| Severe         | Every 1 y  
($V_{\text{max}}$ ≥4 m/s) | Every 1 y  
Dilating LV–more frequent | Every 1–2 y  
(MVA 1.0–1.5 cm$^2$)  
Every 1 y  
(MVA <1 cm$^2$) | Every 6 months to 1 y  
Dilating LV–more frequent |
Global Longitudinal Strain

Evaluation of Regional Myocardial Function

Higher Value is Better
Kaplan–Meier survival curves
BNP Combined with GLS in MR

Exercise and Global Strain

Abnormal GLS and Exercise

Normal GLS and Exercise

Mentias et al J AM Coll Cardiol 2016:69:1974-86
2020 Management of MR

**GDMT for:**
- HF*
- CAD
- AF
- HTN
- Lipids, etc.

**Surgical Treatment**
- Repair
- Replacement
- CABG
- AF surgery
- LAA management

**Transcatheter Treatment**
- Edge-to-Edge clip repair
- Other repair systems if/when approved
- Replacement†
- AF ablation
- LAA management

**Follow Up‡**
- HF expert*
- Clinical cardiologist
- Primary care clinician

**MR Symptoms or Signs**

* DOI: 10.1016/j.jacc.2020.02.005
† O'gara et al 2020 Focused Update of the 2017 ACC Expert Consensus Decision Pathway on the Management of Mitral Regurgitation
Surgical Techniques and Outcomes for DMR

Established techniques

(A) Ring annuloplasty
(B) Quadrangular resection and sliding leaflet plasty
(C) Chordal transfer
(D) Cleft closure
(E) Mitral replacement

Newer techniques

(A) Chordal replacement (PTFE)
(B) Posterior leaflet augmentation
(C) Edge-to-edge Alfieri stitch
(D) Papillary muscle approximation
(E) Posterior wall reduction

Glower DD. JACC 2012;60:1315–22
Long-term Outcomes after Isolated MV Repair vs. Replacement

Median age 75 yrs; 36.7% MV repair, 63.3% MV replacement

MV repair by age

- 1-year Mortality: <75 < 75% < 75%
- 5-year Mortality: <75 16.7% ≥75 29.3%
- 10-year Mortality: <75 33.6% ≥75 59.7%

MV replacement by age

- 1-year Mortality: <75 14.1% ≥75 20.3%
- 5-year Mortality: <75 29.3% ≥75 40.5%
- 10-year Mortality: <75 52.6% ≥75 71.9%

Median Number of Repairs per hospital per year = 5

Vassileva CM et al. Circ 2013;127:1870-6
Usefulness of Valve Surgery during CABG in Secondary MR

- 301 pts with multivessel CAD and ischaemic MR (ERO 0.2 to 0.4 cm², vena contracta 3 to 7 mm)
- Randomized to CABG + valve repair vs. CABG
- **Primary End point**: LVESVI at 1 yr: 49.6 ± 31.5 ml vs. 46.1 ± 22.4 ml/m² (NS)

Recurrence of Severe MR After CABG +/- Annuloplasty in Ischemic MR

- Recurrent severe MR lower with annuloplasty, but still 20% at 5 years

Mihaljevic et al, JACC 2007;49:2191
# Current Mitral Regurgitation related Devices

## Leaflet/Chordal Solutions
- **MitraClip, PASCAL**
- **Neochord, Harpoon**
- **Cardiosolutions, Middle Peak Medical**

## Direct Annular Shape Change
- **Millipede IRIS**
- **Edwards/Valtech Cardioband**
- **ValCare Amend**

## Indirect Annuloplasty
- **Ancora Accucinch**
- **Carillon, MVRx ARTO**
- **Mitral Valve Cerclage**

## Mitral Valve Replacement
- **Tendyne**
- **Intrepid**
- **HighLife, Cephea, Caisson**

---

*Leaflet Repair*  
*Direct Annular Reshaping*  
*Indirect/CS Annuloplasty*  
*TMV Replacement*
MitraClip anatomical patient selection considerations

Recommended criteria

• Pathology in A2-P2 area
• Coaptation length > 2 mm (depending on leaflet mobility)
• Coaptation depth < 11 mm
• Flail gap < 10 mm
• Flail width < 15 mm
• Mitral valve orifice area > 4cm² (depending on leaflet mobility)
• Mobile leaflet length > 1 cm

Figure 3  Key Anatomic Eligibility Criteria

The coaptation length must be at least 2 mm. Coaptation depth must be <11 mm. If a flail leaflet exists, the flail gap must be ≤10 mm and width must be ≤15 mm. These anatomic characteristics are necessary for sufficient leaflet tissue for mechanical coaptation when the...
Delivery System

Post Clip Placement
Figure of Eight

The COAPT Trial

Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

A parallel-controlled, open-label, multicenter trial in 614 patients with heart failure and moderate-to-severe (3+) or severe (4+) secondary MR who remained symptomatic despite maximally-tolerated GDMT

Randomize 1:1*

MitraClip + GDMT
N=302

GDMT alone
N=312

*Stratified by cardiomyopathy etiology (ischemic vs. non-ischemic) and site

Primary Effectiveness Endpoint
All Hospitalizations for HF within 24 months

67.9%/yr vs. 35.8%/yr
HR (95% CI] = 0.53 [0.40-0.70], P=0.000006
NNT (24 mo) = 3.1 [95% CI 1.9, 8.2]
**All-Cause Mortality**

- **HR [95% CI] = 0.62 [0.46-0.82]**
- **P=0.0007**

- **NNT (24 mo) = 5.9 [95% CI 3.9, 11.7]**

<table>
<thead>
<tr>
<th>Time After Randomization (Months)</th>
<th>MitraClip + GDMT</th>
<th>GDMT alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>302</td>
<td>312</td>
</tr>
<tr>
<td>3</td>
<td>286</td>
<td>294</td>
</tr>
<tr>
<td>6</td>
<td>269</td>
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<tr>
<td>9</td>
<td>253</td>
<td>245</td>
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<td>21</td>
<td>161</td>
<td>121</td>
</tr>
<tr>
<td>24</td>
<td>124</td>
<td>88</td>
</tr>
</tbody>
</table>

No. at Risk:
- MitraClip + GDMT: 302
- GDMT alone: 312

The Mortality Benefit of Therapies for HFrEF

- ACE inhibitor or ARB: 16%
- Sacubitril / valsartan: 32%
- Beta-blockers: 36%
- Mineralocorticoid receptor antagonists: 28%
- Isordil / hydralazine: 28%
- ICD: 24%
- CRT (COAPT): 37%
- MitraClip: 42%

All class I guideline recommendations

c/o J Lindenfeld
**Time to Death or First HF Hosp**

Randomization groups stratified by 30-day residual MR

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**MitraClip + GDMT**

- **MR 0/1+ (N=202; 72.9%)**: 73.3%
- **MR 2+ (N=55; 19.9%)**: 47.5%
- **MR 3+/4+ (N=20; 7.2%)**: 38.3%

Follow-up Duration (Months)

- **P=0.001 Overall**
  - HR [95% CI] = 0.75 [0.48, 1.18] for 0/1+ vs 2+
  - HR [95% CI] = 0.36 [0.20, 0.64] for 0/1+ vs 3+/4+
  - HR [95% CI] = 0.48 [0.25, 0.92] for 2+ vs 3+/4+

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**GDMT Only**

- **MR 0/1+ (N=21; 8.2%)**: 73.6%
- **MR 2+ (N=67; 26.1%)**: 53.0%
- **MR 3+/4+ (N=169; 65.8%)**: 42.1%

Follow-up Duration (Months)

- **P<0.001 Overall**
  - HR [95% CI] = 0.84 [0.38, 1.84] for 0/1+ vs 2+
  - HR [95% CI] = 0.44 [0.21, 0.90] for 0/1+ vs 3+/4+
  - HR [95% CI] = 0.50 [0.34, 0.76] for 2+ vs 3+/4+

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**MR At Risk**

- **MitraClip + GDMT**
  - MR 0/1+: 202
  - MR 2+: 55
  - MR 3+/4+: 20

- **GDMT Only**
  - MR 0/1+: 21
  - MR 2+: 67
  - MR 3+/4+: 169
The MITRA-FR Trial

304 pts with SMR due to LV dysfunction with LVEF 15-40%, NYHA II-IVa, hospitalization for HF within the previous 12 mos, not eligible for mitral surgery

MR defined by EU “severe” criteria as EROA >20 mm² or RVol >30 mL/beat

Both groups with “real-world” HF meds (not maximally-tolerated GDMT)

Randomize 1:1 at 37 French centers

MitraClip + MT  
N=152

MT alone  
N=152

Primary endpoint: Freedom from death or HF hospitalizations through 12 months

MITRA-FR: 12-Month Outcomes

<table>
<thead>
<tr>
<th></th>
<th>MitraClip + MT</th>
<th>MT alone</th>
<th>OR [95% CI] or HR [95% CI]*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1° EP: Death or HF hosp</td>
<td>54.6%</td>
<td>51.3%</td>
<td>1.16 [0.73–1.84]</td>
<td>0.53</td>
</tr>
<tr>
<td>Death</td>
<td>24.3%</td>
<td>22.4%</td>
<td>1.11 [0.69–1.77]*</td>
<td>0.65</td>
</tr>
<tr>
<td>CV death</td>
<td>21.7%</td>
<td>20.4%</td>
<td>1.09 [0.67–1.78]*</td>
<td>0.74</td>
</tr>
<tr>
<td>HF hosp</td>
<td>48.7%</td>
<td>47.4%</td>
<td>1.13 [0.81–1.56]*</td>
<td>0.59</td>
</tr>
<tr>
<td>MACE*</td>
<td>56.6%</td>
<td>51.3%</td>
<td>1.22 [0.89–1.66]*</td>
<td>–</td>
</tr>
</tbody>
</table>

* MACE = Death, MI, CVA, HF hosp

## Why are the COAPT Results so Different from MITRA-FR? Possible Reasons

<table>
<thead>
<tr>
<th></th>
<th>MITRA-FR (n=304)</th>
<th>COAPT (n=614)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe MR entry criteria</td>
<td>Severe FMR by EU guidelines: EROA &gt;20 mm$^2$ or RV &gt;30 mL/beat</td>
<td>Severe FMR by US guidelines: EROA &gt;30 mm$^2$ or RV &gt;45 mL/beat or PSVFR or other</td>
</tr>
<tr>
<td>EROA (mean ± SD)</td>
<td>31 ± 10 mm$^2$</td>
<td>41 ± 15 mm$^2$</td>
</tr>
<tr>
<td>LVEDV (mean ± SD)</td>
<td>135 ± 35 mL/m$^2$</td>
<td>101 ± 34 mL/m$^2$</td>
</tr>
</tbody>
</table>

*MITRA-FR defn: device implant failure, transf or vasc compl req surg, ASD, card shock, cardiac embolism/stroke, tamponade, urg card surg
Proportionate vs. Disproportionate MR

Grayburn PA et al. JACC CV Im 2019;12:353–62
MitraClip for Severe MR Recurrence after Surgical Rings

6/6 successful cases (≤2+ MR) without procedural complications days - 12 years post surgery (1 clip in all cases due to smaller MVOA)

Pre 4+

Post trace

Cosgrove-Edwards ring

Double orifice

Grasso C et al. JACC 2014;63:834–9
# A Sampling of Mitral Annuloplasty Devices

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Cardiac Dimensions Carillon</th>
<th>MVRx ARTO</th>
<th>Mitralign TAMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>N pts treated</td>
<td>~600 (113 in studies)</td>
<td>45</td>
<td>71 (51 with 2nd gen)</td>
</tr>
</tbody>
</table>

- **Coronary sinus mediated posterior annulus cinching**
- **A-P shortening via coronary sinus - LA band**
- **Retrograde aortic pledget-mediated annular plication**

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Edwards Cardioband</th>
<th>Ancora Heart Accucinch</th>
<th>Millipede IRIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N pts treated</td>
<td>~100</td>
<td>39 (6 versions)</td>
<td>11</td>
</tr>
</tbody>
</table>

- **LA semi-rigid posterior partial annuloplasty band with anchor cinching**
- **LV postero-basal annuloventriculoplasty via anchor cinching**
- **Complete circumferential semi-rigid direct annuloplasty ring**

*CE mark*
Clinical Presentation of TR
Mild TR; Consider Repair if L-sided Surgery or Clip

Nishimura et al. J Am Coll Cardiol. 2014;63:e57-185
**Central Illustration**  Transcatheter Therapies for TR

**Transcatheter Therapies for Tricuspid Regurgitation**

**Challenges of Transcatheter Therapies for Tricuspid Regurgitation**

- Large tricuspid annulus dimensions
- Nonplanar and elliptical annulus shape
- Absence of calcium
- Right ventricular morphology
- Proximity of other structures (coronary sinus, AV node and HIS bundle, vena cava, right coronary artery)
Internal Jugular Approach

Common Femoral Approach
TEE: Pre and Post MitraClip
Percutaneous Mitral Valve Replacement for MAC
Mitral Valve-in-Valve / Valve-in-Ring
TMVR Landscape 2019

Braile Biomedica

Direct Flow Medical

Navigate

SATURN TMVR

Braile Biomedica

Twelve Medtronic

Neovasc Tiara

Mitraltech

CardiAQ 1st G

M-Valve

PermaValve MID

Caisson

Cephea

CardiAQ Edwards

Edwards Fortis

Sinomed

Tendyne Abbott

AND Many Others...
Transcatheter MVR with Human Use

From Greg Stone

CardiAQ Edwards
Neovasc Tiara
Edwards Fortis
Abbott Tendyne
HighLife
Medtronic Intrepid
Caisson
“It’s Difficult to Make Predictions, Especially About the Future”

Mark Twain
(November 30, 1835 – April 21, 1910)
MR and Percutaneous Device Therapy

- The presence of MR predicts increasing mortality and health care expenses in patients, especially those with Heart Failure
- Requires a multidisciplinary team to provide optimal care
- Less invasive treatments of MR are emerging as a viable and effective method to improve survival and contain costs
- MitraClip is the most common therapy today, but more options will become available in the next future including “surgical like” percutaneous annuloplasty and replacement
Any Questions?

sbail8@lsuhsc.edu