Mitraclip in 2016

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Abnormal Valve Function

- Valve Stenosis
  - Obstruction to valve flow during that phase of the cardiac cycle when the valve is normally open.
  - Hemodynamic hallmark: “pressure gradient” = flow/VA
- Valve Regurgitation, Insufficiency, Incompetence
  - Inadequate valve closure → back leakage
- Combinations of valve lesions can coexist
  - Single disease process
  - Different disease processes
  - One valve lesion may cause another
  - Certain combinations are particularly burdensome (AS & MR)

Mitral Valve Competence:

- Integrated function of several anatomic elements
  - Posterior LA wall
  - Anterior & Posterior valve leaflets
  - Chordae tendineae
  - Papillary muscles
  - Left ventricular wall where the papillary muscles attach
Mitral Valve Disease: Etiology

- **Mitral Stenosis**
  - Rheumatic – 95%
  - Congenital
  - Prosthetic valve stenosis
  - Mitral Annular Calcification
  - Left Atrial Myxoma
- **Acute Mitral Regurgitation**
  - Ischemic Heart disease
  - Papillary muscle rupture
  - Mitral valve prolapse
  - Chordal rupture
  - Chest trauma
- **Chronic Mitral Regurgitation**
  - Ischemic Heart disease
  - Papillary muscle dysfunction
  - Intra & posterior MI
  - Mitral Valve prolapse
  - Infective endocarditis
  - Rheumatic
  - Prosthetic
  - Mitral annular calcification
  - Cardiomyopathy
  - 18 or ablation
  - IGS
Mitral Regurgitation: Pathophysiology

- MR: Leakage of blood into LA during systole
- 1st Abnormality - Loss of forward SV into LA
- Compensatory Mechanisms
  - Increase in SV (ventricle)
  - Forward SV + regurgitant volume
  - LV (LA) dilatation
  - Left Ventricular Volume Overload (LVVO)

Mitral Regurgitation: Physical Findings

- Auscultatory Findings
  - S1, S2: Soft or normal
  - S3: Increased
  - Holosystolic blowing murmur @ apex
  - MVP: mid-systolic click
  - IHSS: Murmur increases with Valsalva
  - Acute MR: Decreased systolic murmur
  - S3 gallop & diastolic flow rumble

- Hyperdynamic Left Ventricle
  - Brisk carotid upstrokes
  - Hyperdynamic LV apical impulse
  - LA lift; RV tap
Mitral Regurgitation Etiologies

**Causes**

- Degenerative MR (also known as primary or organic MR) is usually due to anatomic abnormality of the mitral valve itself, including the leaflets, and/or the subvalvular apparatus, such as the chordae or papillary muscles.

- Functional MR (also known as secondary MR) is the result of left ventricular dilation, which can be secondary to ischemic heart disease. Left ventricular dysfunction leads to annular dilatation and incomplete coaptation of the mitral valve resulting in MR.

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Moderate or Severe Valvular Disease is Common and Increases With Age

Moderate or Severe Valvular Disease is the most common type of heart valve insufficiency in the US. Prevalence increases with increasing age, from 2.0% for 18-44 yr olds rising to 9.3% for 75+ year olds. (CVD) 8:

![Graph showing prevalence of valvular heart disease by age](image)

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MR Progresses to Heart Failure

MR initiates a cascade of events progressing to heart failure, then death, if untreated.

- Diseased Left Ventricle
- Valve Damage
- Dilation of Left Ventricle
- Increased Load/Loss
- 1 year mortality up to 57%
2014 AHA/ACC Guidelines for the Management of Patients with Valvular Heart Disease

"Class Ib:
2. Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for HF (I28).

(Level of Evidence: B)

An RCT of percutaneous mitral valve repair using the MitraClip device versus surgical mitral repair was conducted in the United States. The clip was found to be safe but less effective than surgery. However, in a report from the Mayo Clinic, clip procedures were performed for both non-surgical and surgical indications. In the non-surgical group, the clip did not reduce severity of MR, improved symptoms, or reduce renal LV remodeling. Percutaneous mitral valve repair should only be considered for patients with chronic primary MR who remain severely symptomatic with NYHA class III to IV HF symptoms despite optimal GDMT for HF and who are considered inoperable."

Multidisciplinary Team
Success Requires Bridging Multiple Cardiac Specialties

Case Study: University Heart Center Hamburg
Transcatheter Mitral Valve Repair is an important part of a comprehensive valve center serving patients
Indications

- **Indications for Use**

  **MitraClip Clip Delivery System**

  The MitraClip Clip Delivery System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus (degenerative MR) in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.

- **For Functional MR: Caution: Investigational device. Limited by Federal (US) law to investigational use only.**

Strong Echo Team is Essential

Echocardiographic Assessment is Critical for MitraClip!

- **Patient Selection**
  - Determination of MR severity
  - Analysis of valvular apparatus and LV responsible for MR

- **Procedural Guidance**
  - Transseptal puncture guidance
  - Steering and grasping of the Implant
  - Determination of final result

- **Post-procedural follow-up**
  - Determination MR severity
  - Durability of Implant

The Mitral Valve Anatomy

The mitral valve apparatus includes the annulus, the leaflets, the chordae tendineae, and papillary muscles.

The leaflets are normally asymmetric—the anterior leaflet has a larger surface area, but occupies a smaller amount of annular circumference.
Mitral Regurgitation – A Review

Degenerative MR usually caused by an anatomic defect of one or more structures comprising the mitral valve apparatus.

Functional MR results from left ventricular (LV) dysfunction and dilation, which causes otherwise normal valve components to fail and produce MR.

Normal, Prolapse, Flail, Functional MR

Degenerative Mitral Regurgitation Defined

- Flail is defined as when a leaflet has both ruptured chordae and a free edge that extends above the opposing leaflet or above the plane of the annulus during systole.

- Prolapse is characterized by the displacement of an abnormally thickened leaflet into the left atrium during systole.

TEE Assessment

- Focus on Mitral Valve leaflets and sub-valvular apparatus
  - Determine Etiology: DMR vs FMR
  - Leaflets: Flail, prolapse, restricted, cleft, etc.
  - Chordal Relationships
  - Papillary Muscles
  - Jet Origin
    - Location of Primary Jet
    - Presence/Locat of Secondary Jet
  - LV function: EF and LV size
  - LA size: MR acute vs. chronic
  - Atrial Septum: ASD, PFO, fossa size, aneurysm, etc.
  - Other: Intracardiac thrombus, vegetation, calcium, Rheumatic MV disease, etc.

- See clinical trial and/or commercial contraindications for anatomical exclusion details
Additional 3D data may be useful when available.

3D images should be used to supplement and confirm the initial diagnosis.

Flail Gap (DMR)

- Flail gap is defined as the greatest distance between the ventricular side of the flail leaflet segment to the atrial side of the opposing leaflet edge.
- This distance is measured perpendicular to the plane of the annulus in two views and the largest measurement is used.
- The TEE views for measurement are the:
  - 4 Chamber long axis (LAX)
  - LVOT
- Measure Flail Gap during Systole.

Flail Width (DMR)

- Flail width is defined as the width of flail leaflet segment as measured along the line of coaptation in the transgastric short axis view.
- TEE View for measurement is transgastric SAX.
- Measure during systole.
**Background**

- Degenerative MR is common, affecting ~600,000 persons in the U.S.
- Surgery is the standard of care, and is indicated for patients with symptoms or LV dysfunction
- However, there are patients in whom the risk of surgery is prohibitive

**Outcome Definitions**

- **Procedure success**
  - Post-implant MR grade S2, without CV surgery and without in-hospital mortality
- **Procedure complications**
  - Cardiac perforation, major bleeding, stroke, MI, mitral injury, or death
- **Device-related adverse events**
  - Single leaflet device attachment, complete clip detachment, device thrombosis, device or delivery component embolization

**Study Population**

- **564 Patients**
  - Median age (% men)----------------- 83 yrs (56%)
  - NYHA III/IV------------------------------- 83.9%
  - HF hospitalization prior yr------------------- 51.6%
  - Atrial fibrillation----------------------------- 83.6%
  - Prior CVA--------------------------------- 8.7%
  - Diabetes--------------------------------- 26.0%
  - Prior CABG--------------------------------- 32.4%
  - Prior MI---------------------------------- 24.8%
  - Creatinine ≥ 2 g/dL------------------------- 16.7%
  - O2-dependency-------------------------- 14.7%
  - Median STS-PROM MV repair--------------- 7.9% (4.7, 12.2)
  - Median STS-PROM MV replacement--------- 10.9% (8.3, 14.5)
Other Procedure Indications

- Frailty: 67.2%
- Hostile chest: 6.0%
- Porcelain aorta: 3.4%
- RV dysfunction with severe TR: 2.3%
- Immobility: 1.2%
- Severe liver disease (MELD >12): 0.5%
- IMA at high risk of injury: 1.4%
- Unusual extenuating circumstances: 25.3%

Echocardiographic data

- LV ejection fraction: 56% (45, 63%)
- MR severity grade 3 or 4: 94.9%
- LV EDD: 5.2 cm (4.6, 5.8 cm)
- LV ESV: 3.4 cm (3.0, 4.5 cm)
- Degenerative MR: 85.5%
  - Posterior prolapse: 28.9%
  - Posterior flail: 28.9%
  - Functional MR: 14.4%
- Mitral annular calcification: 38.4%
- Leaflet calcification: 17.2%
- Mitral gradient ≥5 mmHg: 8.0%
- MVA <4 cm²: 19.7%
- Severe TR: 14.7%

Change in Mitral Regurgitation

Clip implantation occurred in 94%

- 93% MR ≤2
- 63.7% MR ≤1
- p < 0.001
Clinical Outcomes

- Procedure success.... 91.8%
- Complications........ 7.8%
- Length-of-stay........ 3 d (1,6 d)
- Home discharge........ 81.9%

Adverse Events

- In-hospital mortality....................... 2.3%
- 30-day mortality......................... 5.8%
- Cardiac surgery......................... 0.5%
- Stroke........................................ 1.8%
- Myocardial infarction.................... 0%
- Major bleeding............................ 3.9%
- Cardiac perforation...................... 0.7%
- Device-related events................... 2.7%
  - Single leaflet device attachment....1.1%
  - Device embolization................... 0.4%
  - Other........................................ 1.2%

Commercial TMVR with MitraClip
Data Summary

- Prohibitive risk population with 86% DMR
- 91.8% procedure success
- Device-related adverse events: 2.7%
- Mortality: 2.3% in-hospital, 5.8% at 30-days
- Procedure complications: 7.8%
- EDD, MR, volume, clip site related to success
Conclusions

1) In this first report of the U.S. commercial experience with TMVR, procedure success, clinical outcomes, and adverse events were favorable in comparison to pre-approval studies and other national registries.

2) These data demonstrate effectiveness and safety of TMVR with MitraClip for the treatment of prohibitive risk patients with symptomatic MR.

MitraClip® Therapy Filling a Treatment Gap

- Medical therapy is limited to symptom management
- MV surgery has been the only option that reliably reduces MR
- A significant gap exists between medical and surgical options
- MitraClip® therapy is a first-in-class, percutaneous option to reduce MR