Mitral Regurgitation-Diagnosis and Treatment

- Indications for Surgery
- Percutaneous MitraClip Repair

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Disclosure Information

Mitral Regurgitation - Diagnosis and Treatment

Robert Siegel, M.D.

As a faculty member for this program, I disclose the following relationships with industry:

(GRS): Grant/Research Support (C): Consultant (SB): Speaker’s Bureau
(MSH): Major Stock Holder (AB): Advisory Board (E): Employment
(O): Other Financial or Material Support

Name of company: Philips Ultrasound;
Nature of Relationship: Speaker’s Bureau
Chronic Severe MR – Surgery if

**Symptoms**

- MV Repairable
- MV not Repairable

Echocardiography

- EF < 0.30
- EF ≥ 0.30

MV Surgery Repair Preferred

**Clinical Rx?**

MV Replacement

ACC/AHA ‘98/06
Chronic Severe MR

No Symptoms

Echocardiography

I a) LV EF ≤ 0.60 or LVSD ≥ 40mm

IIa) New onset A. fib; PASP >50

or >60 mmHg with exercise

MV Surgery

Repair Preferred

ACC/AHA '98/06
ACC/AHA Guidelines Chronic Severe MR 2006 IIa Indications *

MV repair “reasonable” in asymptomatic chronic severe MR & normal LVEF & LV Size

- If likelihood of repair is > 90% in experienced surgical centers*
  (Based on no objective DATA or clinical trial)
456 pts chronic MR assessed by quantitative Doppler

5 yr Mortality 22%, major determinant of survival was severity of MR by regurgitant orifice area (ERO)

Pts with ERO $\geq 0.40\text{cm}^2$ had 5yr survival of 58%

MVR independent predictor for better survival

Recommended if pts have an ERO $\geq 0.40\text{ cm}^2$ should be promptly considered for MVR
Are the Mayo studies applicable?

- Pts were managed by their individual M.D.’s
- No criteria given for timing of surgery
- Mayo studies did not use the ACC/AHA guidelines to refer to surgery when pts had CHF, Pulm HTN or A fib
- The development of CHF or A fib was listed as an adverse event, not as an indicator for surgery. Data shows poor outcome associated with not following 1998 guidelines
- These data offer insight into natural history of MR, but little information on effectiveness of guidelines
- Use of PISA & VC for surgical referral based solely on EROA in asymptomatic pts is problematic

Biner/Siegel JACC 2010
Reproducibility of PISA, VC, & Jet Area for Identifying Severe MR

- 16 pts with ≥ moderate MR studied- PISA & VC for EROA, & Jet Area evaluated for severe MR- Yes / No

- 18 echocardiologists (2 to 40 yrs post fellowship)
- 11 academic institutions
- 1 sonographer, 1 echo system (Philips iE33)
- Moving echo clips posted & reviewed on a website

Interobserver agreement-
Substantial ≥ 80%; Fair 60-79%; Poor < 60%
The least possible is 50%

Biner / Siegel JACC Imaging 2010
Interobserver agreement for assessment of MR severity

Qualitative & quantitative Doppler methods:

- Limited reproducibility
  - Only 38 to 44% had Substantial agreement

- Potentially difficult to differentiate severe From non-severe MR

- Use of PISA & VC for surgical referral based solely on EROA in asymptomatic patients is problematic

Biner / Siegel JACC Imaging 2010
• 132 asymptomatic pts with severe MR prospectively studied clinically and with echo-Doppler

• 5yr follow-up, 1998 ACC/AHA guidelines used to determine surgical referral

• Overall mortality not increased over control population

• Only 30% pts required surgery @ 5yrs, <50% pts required surgery @8yrs
Clinical implications:

- Asymptomatic pts with severe MR can be safely followed until develop Sx’s or guideline values for LV Fxn, size (LVSD- 4.5cm), or pulmonary hypertension.

- Strategy had excellent medical survival, as well as post-op outcome for MV surgery.

- However requires careful clinical f/u and closely monitored serial echoes (@12mo, q 3 to 6mo prn).
Predictability of MV Repair and Results

MV repair “reasonable” for asx chronic severe MR & normal LVEF & LV Size
If likelihood of repair is > 90%

- Pre-op echo assessment of repairability correct 80-95% → 5-20% MV prosthesis

Hellemans Am J Cardiol 1997;
Muratori J. Hrt Valve Dz 2001;
Monin JACC 2005
Predictability of MV repair and results variability in surgical & echo expertise

- **STS** 2000-2007 Pure MR → 31% Prosthesis
- EuroHeart 2001 → 53% Prosthesis
- “Best centers” up to 20% → replacement

Schwartz/Gilliam Circ 2010

- Ability to predict repair rate of > 90% in experienced surgical centers is limited-
- Does not support operating asymptomatic pt with normal LV FXN - as no symptomatic, LV function or survival benefit
ACC/AHA Guidelines Chronic Severe MR 2006 IIa Indications

MV repair “reasonable” in asymptomatic chronic severe MR & normal LVEF & LV Size

- If likelihood of repair is > 90% in experienced surgical centers*

- MV Repair = a valve for life & improved lifestyle
# MV Repair – does it last for Life?

## Failure of repair- by Echo - 3 to 4+ MR

<table>
<thead>
<tr>
<th>Study</th>
<th>Follow-up</th>
<th>Failure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gillinov</td>
<td>@ 1.5 yrs</td>
<td>9%</td>
</tr>
<tr>
<td>Tanaka</td>
<td>@ 3.5 yrs</td>
<td>7%</td>
</tr>
<tr>
<td>Flameng</td>
<td>@ 7 yrs</td>
<td>29%</td>
</tr>
<tr>
<td></td>
<td>@ 10 yrs</td>
<td>35%</td>
</tr>
<tr>
<td>David</td>
<td>@ 12 yrs*</td>
<td>20% PML, 35% AML</td>
</tr>
<tr>
<td>Re-op rate</td>
<td>@10-12 yrs</td>
<td>7-12%</td>
</tr>
</tbody>
</table>

- MV repair durability not constant,
- Myxomatous valves: physically, structurally, biochemically & mechanically abnormal
MJ  An asymptomatic 38 yr woman with MVP, Severe MR, Normal LV function

Referred for MR Repair

80-95% MR Repair

5-20% MR Replacement
MJ had a repair recommended but she was one of 5- 20% → Mitral Replacement

- Major complications 25%
- Op mortality 4 - 6%
- Mechanical: CVA/bleed risk 0.6-2.3%/yr
- Bioprosthetic: re-operation in 10-20 yrs
- LV dysfunction
- Endocarditis risk: 2.2%/yr
80 - 95% MV Repair

- Peri-op MI 5%, CVA 1%
- Recurrent severe MR at 10 yrs - 35%
- Major complications 12.8%
- Op mortality 1.5 - 3.4%

BT asymptomatic 42 yr man with MVP, Severe MR, Normal LV function
Beware of Guides
Severe MR in the Asymptomatic Patient

Asymptomatic
Normal LV size
LVEF >0.60
NSR
Normal Pulm art Pr
Regular F/U feasible

Symptoms +/-
LVESD >4.0/4.5cm
LVEF <0.60
A fib &/or PHTN
Abn Stress Echo
Elevated BNP ??

Observe  MV Repair
Edge-to-Edge Mitral Valve Repair Technique

Alfieri pioneered intra-op in early 1990s MV repair by suturing the free edges of mid-part of MV leaflets → double orifice MV
80% from re-operation & recurrent MR > 2+ @ 12yrs

Alfieri method can be done transcatheter
FRED ST GOAR

1st patient treated in Caracas – June 27, 2003
The MitraClip Procedure

CSMC Mitraclip Team: Screened over 900 & 127 pts treated, F/U upto 6yrs
Case Selection

- No rheumatic MR Originating from the central 2/3 of the valve
- Etiology: degenerative or functional
- Sufficient leaflet tissue for mechanical coaptation
- Protocol anatomic exclusions
  - Flail gap $>10$mm
  - Flail width $>15$mm
  - LVIDs $>55$mm
  - MVA $<4$ sq cm
EVEREST II Randomized Clinical Trial

Study Design
279 Patients enrolled at 37 sites

- Significant MR (3+-4+)
- Specific Anatomical Criteria
- Randomized 2:1

Device Group
MitraClip System
n=184

Control 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

Feldman et al, NEJM 2011
MitraClip vs. MV Surgery

279 pts 2:1 Clip v. Surgery Feldman et al

- 23% had 3-4+MR after attempted clip → referred for elective MVR

- MAE @30days- death, MI, re-op, CVA, renal failure, infection, bleeding, AF, transfusion ≥2u, sepsis
  
  Clip had 15% v. MVR 48% (p<0.001)

- ≤ 2+MR @12mo: 72.4% clip v. 87.8% MVR (p=0.001)
  
  12mo LVEDV: ↓ 21cc in clip v. 40cc in MVR (p<0.001); LVESV & LVEF similar

- NYHA Class I & II: 97.6% clip v. 87.9% MVR (p<0.0001)
  & also better quality of life score with clip

- 37 centers- only 4 had done ≥ 20 clips *
Percutaneous Mitral Repair System

- 22 Fr Steerable Guide Catheter
- 24 Fr Sheath
- Clip Delivery System with the MitraClip
Estimates of worldwide clinical experience as of March 31, 2011

* High Surgical Risk estimate based on: logistic EuroSCORE ≥ 20%; or STS calculated or surgeon estimated mortality ≥ 12% or pre-specified comorbidities

No acute procedural mortality in > 3,000 cases as of 6/2011
Case 1. 76 yr, M (in 2006)

DOE, CABG x2, Angina, CTO of RCA
COPD, 30 pack yr smoker, HTN, Hyperlipidemia, Fe-deficiency anemia

1-5<sup>th</sup> of Scotch/night
76 yr old male with shortness of breath, CABG x2; RCA occluded, Flail posterior leaflet- High surgical risk, ? Durability of MitraClip– MV flail & old inferior MI
TEE following placement of 2 MitraClips
F/U Echo 4 year after MitraClip procedure
Now 80 yrs old - Asymptomatic, no DOE, Wheezing improved, Angina is now gone. Resumed physical activities bike ≥ 1hr. Works >6 hrs in garden. Multiple visits to Argentina to pursue Tango dancing
Functional Mitral Regurgitation

A MitraClip can be used where MR is due to malcoaptation due to leaflet tethering in patients with reduced LVEF.

However a concern-
Post op LV dysfunction in surgical MV repair
  LVEF < 55% → 38% pts
  LVSD ≥ 40mm → 23% pts

Matsumura T., et al. JACC 2003
Case 2. 81-yr-old lady, NYHA Class III
Dilated, non-ischemic cardiomyopathy
On CHF Meds; LVEF 19%
Case 2. TTE LVEF 19%

Severe MR - Would you Clip the MR?
Case 2. Improved symptoms

Post clip trace MR- sustained for 3 ½ yrs at present
Case 2 s/p 3.5 year MitraClip procedure
Reduced LV dimensions

**LVEDD**: from 60 mm to 57 mm

**LVESD**: from 54 mm to 49 mm
Case 3, 55y F
SOB - Functional MR
LVEF - 27%

Would you clip it?
18mo f/u - NYHA I

LVEDD
Pre:  62 mm  
Post:  52 mm

LVESD
Pre:  52 mm  
Post:  38 mm
80 yr F, Flail Post MV leaflet, CHF

Pre clip Cardiac output 2.15 L/min; post 2 clips C.O.4.6 L/min
Pre Left atrial Vwave 27mmHg; post - V wave 10mmHg;
Post clip - mean grad 1.5mmHg; MVA 3.4cm²
Acute hemodynamic effects of MitraClip

- Evaluated 107 pts pre/post clip - Lt / Rt heart hemodynamics & 2D echo-Doppler
- 96 pts (90%) had a clip deployed
- Successful clip deployment: * p<0.001
  \[ \downarrow \text{MR grade from 3.3 } \rightarrow 1.6 \]
  \[ \downarrow \text{Regurg vol 52 } \rightarrow 30\text{ml} \]
  \[ \downarrow \text{LVEDV 172 } \rightarrow 158\text{ml} \]

No patient developed post-procedural low C.O.

Siegel et al JACC 2011
Acute hemodynamic effects of MitraClip

Successful clip deployment:  p<0.001

↑ C.O 5.0 → 5.7L/min (low C.O. pts had > increase)
↑ SV 57 → 65ml
↓ LVEDP 11.4 to 8.8 mmHg (hi EDP had >decrease)
↓ LVEDV 172 →158 ml;
↓ LVEF 60 → 56%

No patient developed post-procedural low C.O.
53% age >70yrs ; 46% NYHA class III - IV

Siegel et al JACC 2011
Percutaneous Mitral Repair
MitraClip: CSMC Results (n=127)

• In total 125 of 127 MitraClips placed

• Acute results from last 72 patients (Realism trial – open registry)

Reduction of MR
from 3 - 4+ to $\leq 2+$ MR 96%

to $\leq 1+$ MR 75%
Percutaneous MitraClip for MR

CSMC Results (n=127 patients)

Complications during the procedure

• 1 - card tamponade; 1 hemothorax d/t IJ line
• No secondary mitral stenosis
• No deaths
• Major Complications rare
• 8 patients → MVR
• Excellent risk benefit ratio
Conclusions: MitraClip repair for MR

- Very safe and less morbidity than surgery
- Effective for reducing MR in selected patients with functional & degenerative MR
- Reduction of MR leads to reverse modeling, ↑ cardiac output, and ↓ LVEDP
- Improves symptoms & NYHA class
New era for treatment of Mitral Regurgitation

Thanks!

CSMC Team
K.P. 92y, practicing psychiatrist, admitted with acute pulmonary edema; severe MR; intubated, high risk for intervention
Aortic arch complex mobile atheroma
SEVERE MR

On screening TEE for mitraclip
Screening TEE

Pulmonary vein: systolic flow reversal
P2 +/- P3 Flail?
3D TEE Surgical view from LA  aortic valve anterior

Based on 3D – Probably need to treat middle and medial scallops (P2 / P3) - 2 clips
Mild residual MR

Improved pulmonary vein inflow
TTE at 12-month F/U after 2 MitraClips
93 yr-old Psychiatrist – returned to work!!

Apical 4-chamber view: no MR
At 1 year NYHA II

Not only returned to work!
After 18 mo post MitraClip !!!!!
Thanks Again!