Natural History of Mitral Regurgitation
(degenerative and ischemic)

Indications for Surgery

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Temporal Changes in the Etiology of Pure MR

Edwards WD. In Harrison’s Advances in Cardiology, Braunwald ed. 2003, p 317
**Mitral Regurgitation - Pathophysiology**

- Chronic MR is a preload burden on the LV
- LVEDV increases - eccentric LVH
- ↑ LV stroke volume = Effective SV + Regurg SV
- ↑ LA pressure → ↑ left atrium
- Pulmonary hypertension - late in the course

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**End systolic pressure volume relationship**

![Diagram](image)

**Mitral Regurgitation - Effect of Change in Contractility**
Overall Survival - Mitral Valve Repair vs Replacement For Severe MR


Clinical Outcome of Mitral Regurgitation Due to Flail Leaflet

229 patients with isolated MR due to flail leaflets - Dx 1980-'89
NYHA class I-II 162 (71%) Class III-IV 66 (28%)

86 patients treated medically

Survival by NYHA class - Rx medically

Mortality 6.3%/yr

Independent determinants of mortality
Older age, NYHA class, and lower EF


Long-Term Survival with Medical Treatment, According to the Ejection Fraction (EF)

Surgery in Patients With MR Due to Flail Leaflets

Surgery performed in 143 patients 23±32 months after diagnosis
MV repair in 95 patients. MVR in 47 patients
Concomitant CABG 29 patients
Indications for surgery:
- NYHA Class III-IV dyspnea 107 (75%)
- Physician’s preference 24 (17%)
- Infective endocarditis 5 (4%)
- Angina pectoris 4 (3%)
- Thromboembolism 1 (0.7%)
- Undetermined 2 (1.4%)

Perioperative mortality 4%


Flail Leaflet Mitral Regurgitation-
Long-Term outcome

Ling LH. Circulation 1997; 96:1819

221 patients (1980-1989) Age 65 +/- 13 years
Gr I Surg <= 1 month 63 patients (Op Mort- 1.6%)
Gr II Med Rx 158 patients (80 later surg - Op Mort- 6.3%)

Baseline
Age 61.1 +/- 14 66.5 +/- 12 .009
NYHA III-IV 40 (63%) 20 (13%) <.0001
At Fib at Start 20 (32%) 25 (16%) .02
Comorbid index 0.4 +/- 0.79 0.73 +/- 0.1 .01
EF 65% +/- 9% 65% +/- 9% ns

P value

Flail Leaflet Mitral Regurgitation - Over-all Outcome

Ling LH. Circulation 1997; 96:1819

<table>
<thead>
<tr>
<th>Gr I</th>
<th>Gr II</th>
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<tbody>
<tr>
<td>Survival 10 years</td>
<td>79 +/- 8%</td>
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<tr>
<td>CHF at 10 years</td>
<td>27 +/- 7%</td>
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Multivariate predictors for Survival

<table>
<thead>
<tr>
<th>Risk Ratio (95% CI)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Age 1.1 (1.06-1.13)</td>
<td>0.0001</td>
</tr>
<tr>
<td>EF 0.95 (0.93-0.98)</td>
<td>0.0002</td>
</tr>
<tr>
<td>NYHA Class 1.65 (1.21-2.25)</td>
<td>0.002</td>
</tr>
<tr>
<td>Early Surg 0.31 (0.13-0.72)</td>
<td>0.006</td>
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Same order for CV death, CHF, new-onset at fib

Overall Survival From Time of Diagnosis - Patients With Flail Leaflets - Early Surgery vs Conservative Management


Survival adjusted to age and ejection fraction according to the management strategy selected at baseline for patients in New York Heart Association class I or II (left) and for those in class III or IV (right)

Cardiac Death - MR With Flail Leaflets - Management Selected at Baseline


Overall Survival - Patients With Ax MR - Medical Rx - ERO


Cardiac Events - Ax MR Stratified by ERO

Overall Survival - Patients With Asx Organic MR - Medical Rx
Death From Cardiac Causes

N=456 pts
Age 63±14 yrs
LVEF 70±8%


Late Survival after MV Repair or Replacement at Reoperation for Recurrent MR

Survival (%)

Re-repair
Replacement

P=0.05


Mortality and Morbidity - MVP First Diagnosed Between 1989 and 1998
Natural History of Asx MVP in the Community

Cardiac mortality
CHF
Endocarditis
MV surgery

CV mortality

Overall mortality

Events (%)

Baseline Risk Stratification Used in 833 Olmsted County, Minn, Residents First Diagnosed With MVP Between 1989 and 1998

Primary RFs (Excess Mortality)  Secondary RFs (CV Morbidity)
EF ≤50%  Slight MR
MR moderate  Flail leaflet
LA diameter >40 mm  AF
Age >50 y


MVP - Survival According to Categories of Baseline Risk Factors

Overall Survival  Cardiac Survival

P(exp) = probabilities; difference between observed and expected mortality
P(dif) = difference in total mortality between subgroups

Cardiovascular Morbidity - Baseline Risk Factors

MVP-related Events - Baseline Risk Factors


MVP-related events
- Death
- CHF
- Endocarditis
- MV surgery

447 consecutive ASx patients with MVP or flail leaflets
Severe MR and preserved EF (>60%)

2 Groups: Conventional management - 286
early surgery - 161

Follow-up - median 5.4 years

Operative Group
- no operative mortality
- no cardiac deaths
- 2 repeat surgeries

Conventional Rx Group
- 12 cardiac deaths
- 1 repeat surgery
- 22 admissions for CHF

127 propensity score-matched pairs

Cox multivariate analysis in the Conventional Rx group:
Independent variables predicting late CHF or indications for surgery: baseline grade of pulmonary hypertension (HR 1.9)
Age (HR 1.02)
ERO (HR 2.1)


Conventional Rx vs Early Surgery - Severe MR


Cardiac Death - Conventional Rx Group of MR Patients

Comparison of event-free survival rates between the operated (OP) and conventional treatment (CONV) groups in propensity-matched pairs.

Events = operative death, cardiac death, repeat MV surgery, CHF hospitalization


Prognostic Usefulness of BNP in Severe Asx MR - LVEF > 60%

269 consecutive patients
First 167 - Derivation Group - mean F-U 36 ± 8 mo.
Second 102 - Validation Group - mean F-U 31 ± 9 mo.

Combined endpoint:
CHF symptoms, LV dysfunction, death (LVDSD) on follow-up

ROC characteristics - optimal cut-off value 105 pg/ml BNP
discriminated high risk patients in both cohorts:
Derivation Gr - 76% vs 5.4%
Validation Gr - 66% vs 4.0%

BNP was strongest independent predictor

Severe MR - BNP Levels Predict Combined Endpoint

Survival Free of LVDSD According to BNP Levels


Incremental Value - When BNP Added to Echo Variables


Kaplan-Meier analysis according to clinical course in 128 patients

Symptom or LV Systolic Dysfunction (SLVSD) - Free Survival


Asymptomatic Severe Mitral Regurgitation
Is Watchful Waiting Good Enough?

132 asymptomatic consecutive patients - severe MR due to MVP or flail leaflet
Age 55 ± 15 years

Referred to surgery:
- Symptoms
- LV enlargement (LVESD > 45 mm or ESDI > 26 mm/m²)
- LV dysfunction (LVEF < 60 or Fractional shortening < 0.32)
- Pulmonary hypertension (Systolic pressure > 50 mm Hg)
- Recurrent atrial fibrillation

Followed up 62 ± 26 months.
Reevaluated at 3, 6, 12 months, then yearly

38 (29%) patients developed criteria for surgery,
- Symptoms 24 (63%)
- LV criteria 9 (24%)
- Pulm hyper or atrial fib 5 (13%)


Event-Free Survival

34 had surgery
4 refused surgery
Survival free of:
- any event
- symptoms
- asympt. LV-dysfunction
- new onset Afib/PHT

**Survival of Ax Patients with Severe Degenerative MR Followed Medically**

- **All patients**
- **Patients with flail leaflet**
- **Expected survival**

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**Mitral Regurgitation - Indications For Surgery**

**Class I**
- 1. Symptomatic patient with acute severe MR (B)
- 2. Chronic severe MR - NYHA II-IV, with EF > 0.30 and/or ESD > 55 mm (B)
- 3. Ax chronic severe MR, EF 0.30-0.60 and/or ESD > 40 mm (B)
- 4. MV repair preferred over MVR when surgery needed [C]

**Class IIa**
- 1. Ax patients with chronic severe MR with EF >0.60 and ESD < 40 mm where successful repair is > 90% (B)
- 2. Ax patients with chronic severe MR, EF >0.60, and new-onset atrial fibrillation [C]
- 3. Ax patients with chronic severe MR, EF>0.60 and PASP > 50 mm Hg at rest or > 60 mm Hg with exercise [C]
- 4. Chronic severe MR due to primary valve disease, NYHA III-IV, and EF < 0.30 and/or ESD > 55 mm where repair is likely [C]

**Class IIb**
- Chronic severe secondary MR due to severe LV dysfunction (EF < 0.30), with NYHA III-IV despite Rx + bivent pacing [C]

**Class III**
- 1. Ax patients with MR, EF>0.60 and ESD<40 mm, needing MVR [C]
- 2. MV surgery not indicated for mild - moderate MR [C]

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**Mechanism of Ischemic and PostInfarction MR**

- Normal mitral apparatus
- Local LV remodeling and papillary muscle displacement
- Global LV remodeling and dilatation
Ischemic MR Increases Future CV Events

Ischemic MR occurs in up to 40% of patients after AMI


SAVE study - CV mortality:
- Mild IMR on medical Rx at 3.5 yrs - 29%
- No MR on medical Rx at 3.5 yrs - 12%
- Presence of MR independent predictor of CV mortality
- Odds Ratio 2.0 (95% CI 1.23-3.04)

Severe heart failure:
- Mild IMR - 24%
- No IMR - 15%
- P<0.001

Severe heart failure:
- Mild IMR as No IMR
- Hazard Ratio 2.83 (95% CI 1.8-4.2) P<0.001

Outcome worse as severity of IMR increases

5-year survival:
- Mild IMR - 47%
- Moderate - severe IMR - 29%

Severe heart failure:
- Mild IMR - 24%
- No IMR - 16%

P=0.015

Severe heart failure:
- Mild IMR vs No IMR
- Hazard Ratio 2.8 (95% CI 1.8-4.2) P<0.001

Course of IMR After Isolated CABG is Variable

Moderate IMR at 6 weeks post CABG
- Improved (0 - trace) 8%
- Improved to mild 52%
- Persisted moderate 37%
- Developed severe 3%

Improved from moderate to none-mild 51%
Remained moderate 25%
Progressed to moderate to severe 12%

Six weeks post CABG
- 22% of patients with moderate MR became severe

Predictors of Improvement of Unrepaired Moderate MR
After Elective Isolated CABG

121 patients - Age 65 ± 9 yrs
12 month follow-up
- 57 no or mild MR (improved group)
- 64 failed to improve

Predictors of Improvement before surgery
- By Tech-99 and F18-FDG ≥ 3 segments of viable myocardium (OR 1.45)
- Absence of dyssynchrony (<60 ms) (OR 1.49)
- 98% of patients with both had improvement
- Only 34% with dyssynchrony and 18% with non-viable myocardium had improvement
- 32% with dyssynchrony and 45% with non-viable myocardium had worsening of MR

Penktsa et al. Circulation 2006;120:1474
Predictors of Improvement of Unrepaired Moderate MR After Elective Isolated CABG

Asynchrony between Papillary Muscles

Events:
Death - any cause or Hosp - worsening HF

Penicka et al. Circulation 2009;120:1474

Course of IMR After Isolated CABG is Variable
Cardiac function, Functional Class, and Survival all have varied after CABG compared to those without IMR. Depends on amount of revascularized ischemic vs nonviable myocardium and on ventricular geometry.

Survival after CABG patients with IMR
Actuarial survival 88% - EF 36.2 ± 10% - 87% for isolated CABG
Mortality higher with MV repair (12% vs 2%)
Kang DH. Circulation 2006;114:1499
Matched patients with and without IMR - no difference in survival
Mallidi HR. J Thorac Cardiovasc Surg 2004;127:636

Large studies with multivariate analysis
2242 patients - CABG - mild-moderate IMR independent predictor of survival at 5 years
Odds Ratio: Mild IMR 1.34 p=0.033, Moderate IMR 1.49 p=0.007
Grossi EA. Circulation 2006;114:1573
3264 patients - IMR severity ↑ risk of death after CABG
Hazard ratio 1.44 p<0.001
Even mild IMR ↑ risk HR 1.34 p<0.01
Schroder JN. Circulation 2005;112:(Suppl 1) I-293

Ischemic Mitral Regurgitation
Valve Repair vs Replacement

n = 482 pts with ischemic MR 1985 - '97
Survival - multivariable, multiphase hazard function analysis
Propensity-matched better-risk group
Valve Repair Valve Replacement
397 85
30 day 94% 81%
1 yr 82% 56% p = 0.03
5 yr 58% 36%

High risk group - repair = replacement p = 0.4
Freedom from repair failure at 5 yrs = 91%
Risk factors - older age, higher FRC, greater WM abn, renal dysfunction

Moderate Ischemic MR - CABG With and Without MV Repair


Thanks for Listening