# *The Pathophysiology and Management of Functional Mitral Regurgitation*

## *What are the questions?*

*Banff 17*

# Differences between Primary vs Secondary M. Regurgitation

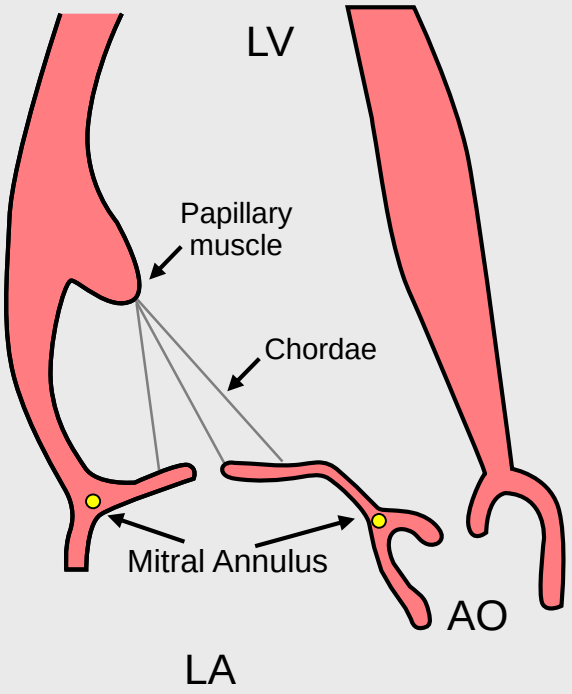
## Primary

- Pathological abnormalities of the **mitral apparatus**

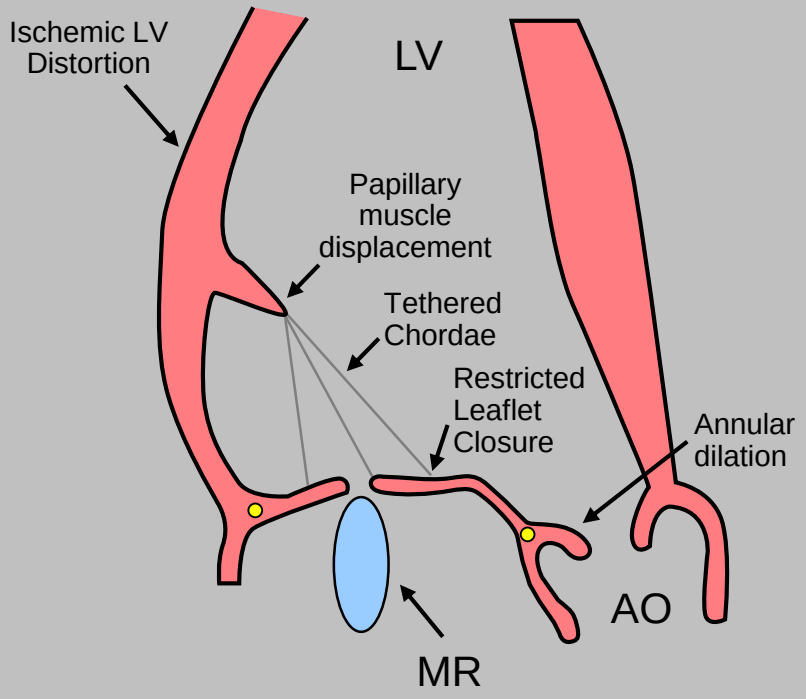
## Secondary (“Functional”)

- Normal or nearly normal mitral leaflets are prevented from proper coaptation by underlying LV dysfunction producing tethering, mitral annular dilation, or both

## Normal Mitral Valve




## Functional Mitral Regurgitation





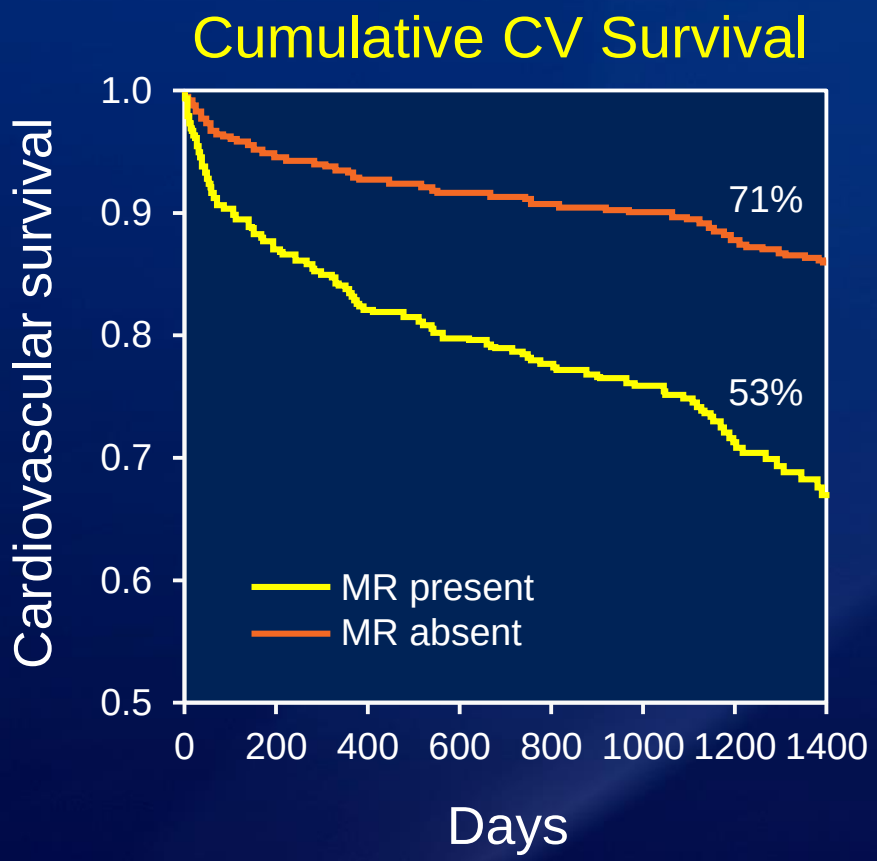
# Clinical Significance of *Mild* MR after MI

- 727 pts
- SAVE trial
- MI ≤16 days
- LVEF ≤40%

M. Regurg. on Angiography
|
141 pt 19.4%

Severity

1+ – 14.6%
2+ – 4.5%
3+ – 2 pts




Lamas: Circ, 1997

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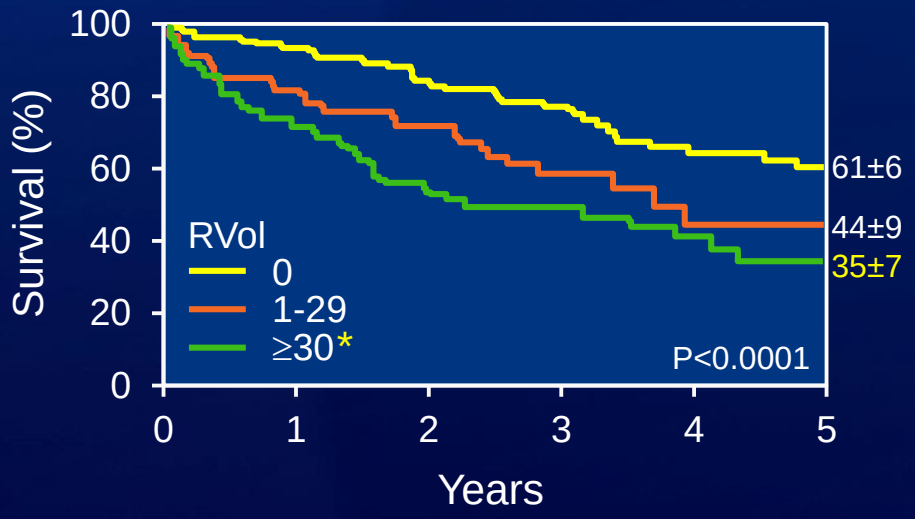
# Ischemic MR: Outcomes Stratified by the Degree of MR

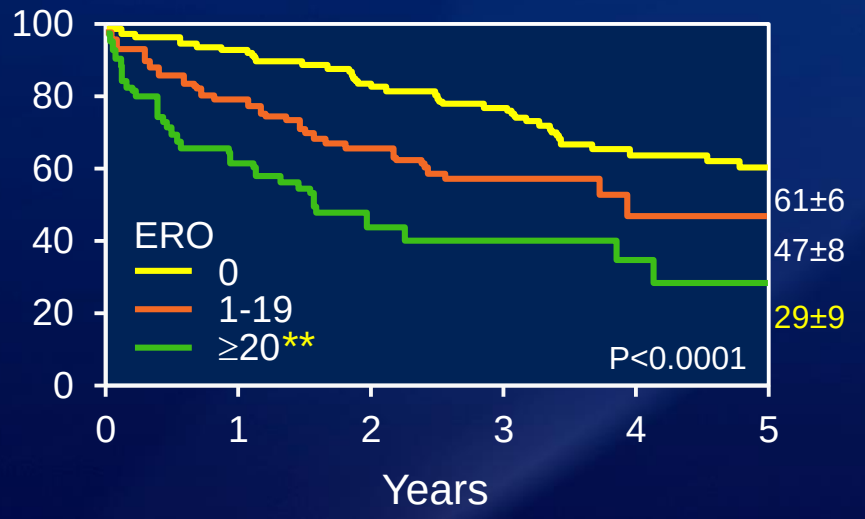
- 303 patients
- Prior (>16 days) QMI
- Mayo Clinic

Survival Stratified by R. Vol




*P=0.002 on multivariate analysis

Survival Stratified by ERO




**P>0.004 on multivariate analysis

Grigioni Circ, 2001

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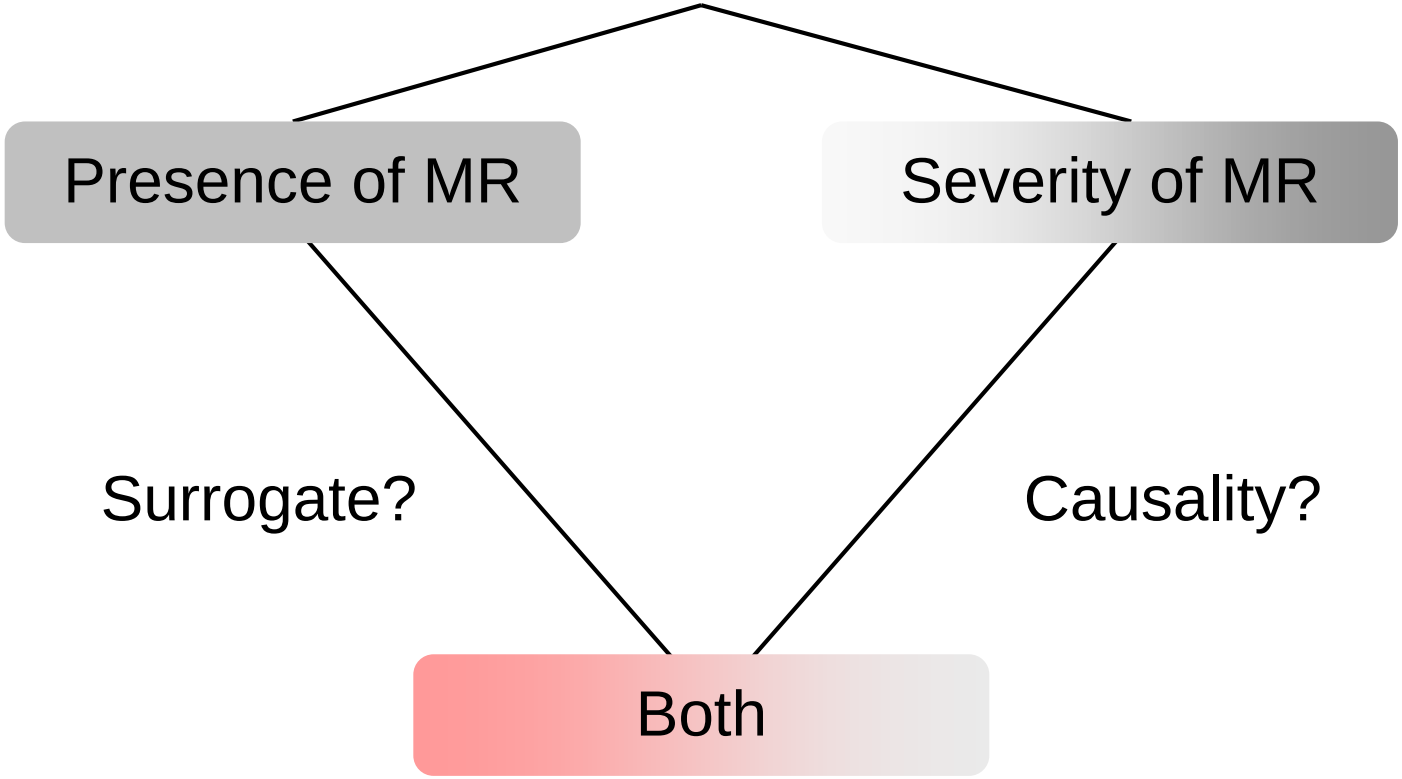
# Prognostic Impact of Functional MR



# Management of Functional MR

issues

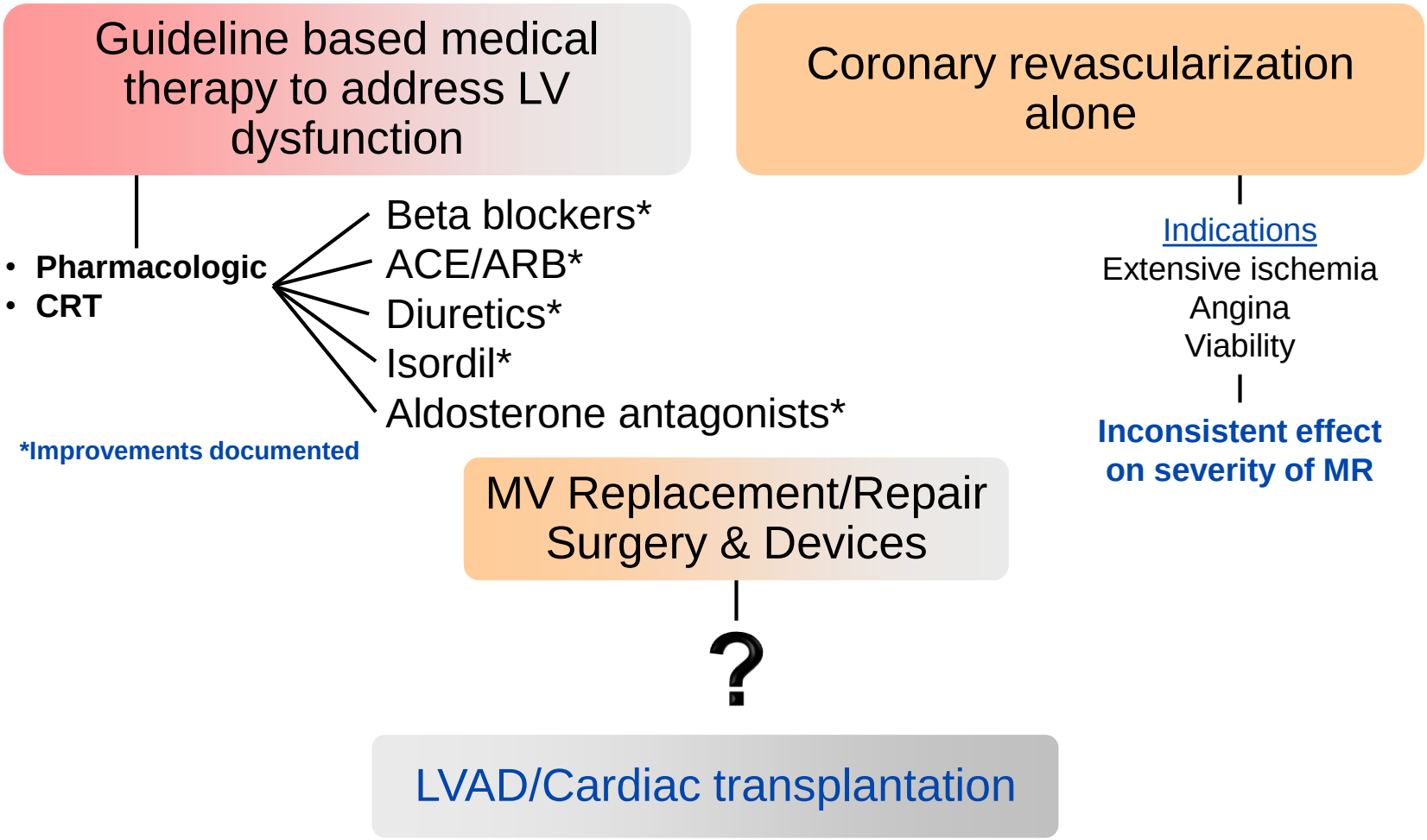
In pts with moderate MR

- CABG alone vs CABG + mitral annuloplasty/repair

In pts requiring a mitral valve procedure (moderate to severe MR)

- Mitral valve repair
- Mitral valve replacement

# Therapeutic Considerations for Ischemic MR in Patients With LV Dysfunction



The results of mitral valve repair for functional mitral regurgitation are much inferior to those in patients with degenerative MR

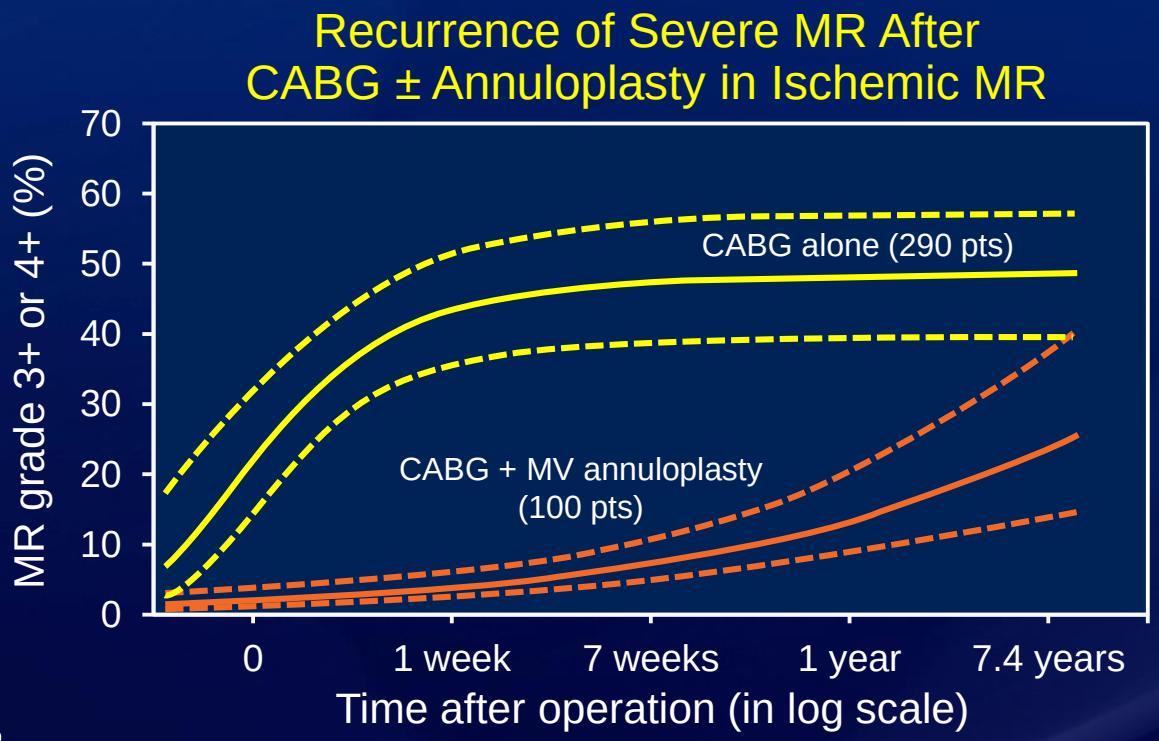

 

# Durability of Ischemic Mitral Valve Repair

- 78 patients
- Ischemic MR
- Mean follow-up 28 mo

Recurrent MR (2+) – 32%

Severe MR (3-4+) – 20%




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

Jerri: JTCVS, 2006

Mihaljevic et al: JACC 49:2191, 2007

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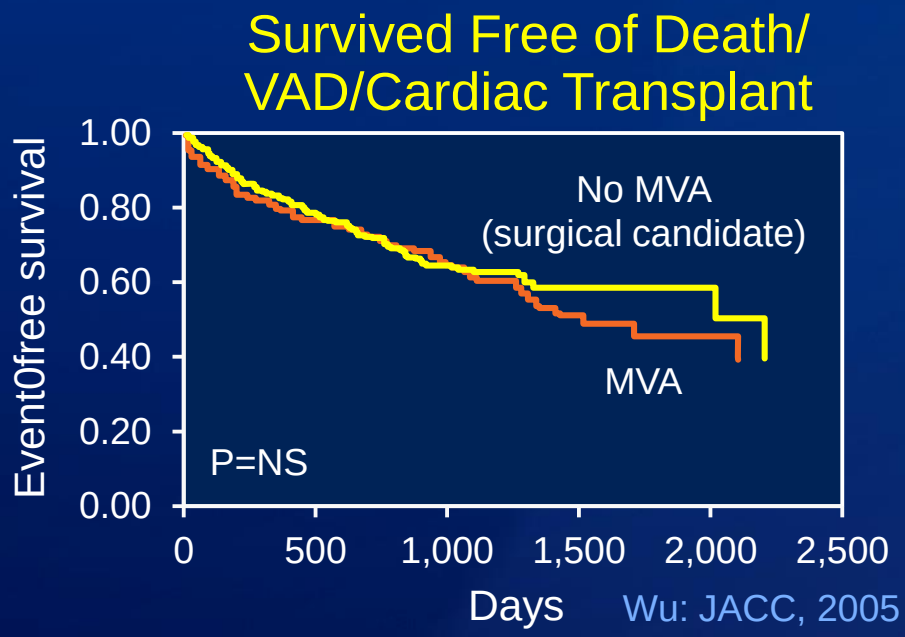
# Effect of Mitral Valve Annuloplasty in Patients With LVEF ≤30%

- 419 patients
- Retrospective analysis
- Consecutive series




Wu: JACC, 2005

Effectiveness of Surgical Mitral Valve Repair Versus Medical Treatment for People With Significant Mitral Regurgitation and Non-Ischemic Congestive Heart Failure (SMMART-HF)

This study has been terminated (unable to recruit sufficient numbers of patients

Clinical Trials.gov NCT 00608140

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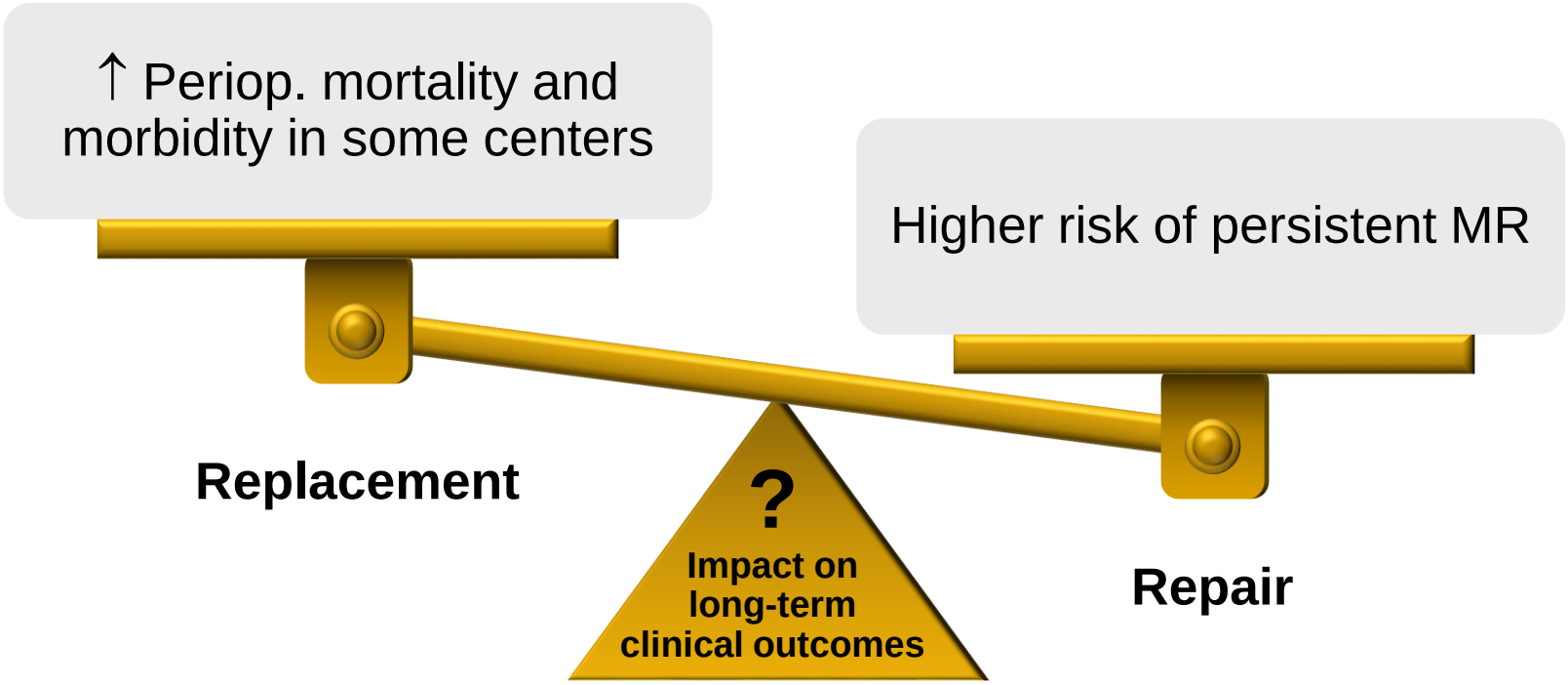
# Randomized Trials of Surgical Treatment in Moderate Ischemic Functional MR

| Trial | Pt (no.) | Follow-up (years) | Outcomes (CABG + MVR vs CABG alone) |
|---|---|---|---|
| **Fattouche** e | 102 | 5 | ↑ EF<br>↓ Volumes<br>Improved NYHA class |
| **Chan (RIME Trial)** | 73 | 1 | ↓ LV reverse remodeling<br>↑ Peak $O_2$ consumption<br>↓ M regurgitation<br>↓ BNP |
| **Smith (CTS Network)** | 301 | 2 | No change in LVESV<br>↓ Moderate → severe MR<br>↑ Bypass time and hospital stay<br>↑ Perioperative neurologic events |

No trial powered for major clinical outcomes

JTCVS, 2009; Circ, 2012; NEJM, 2014

# Mitral Annuloplasty vs Replacement for Functional MR

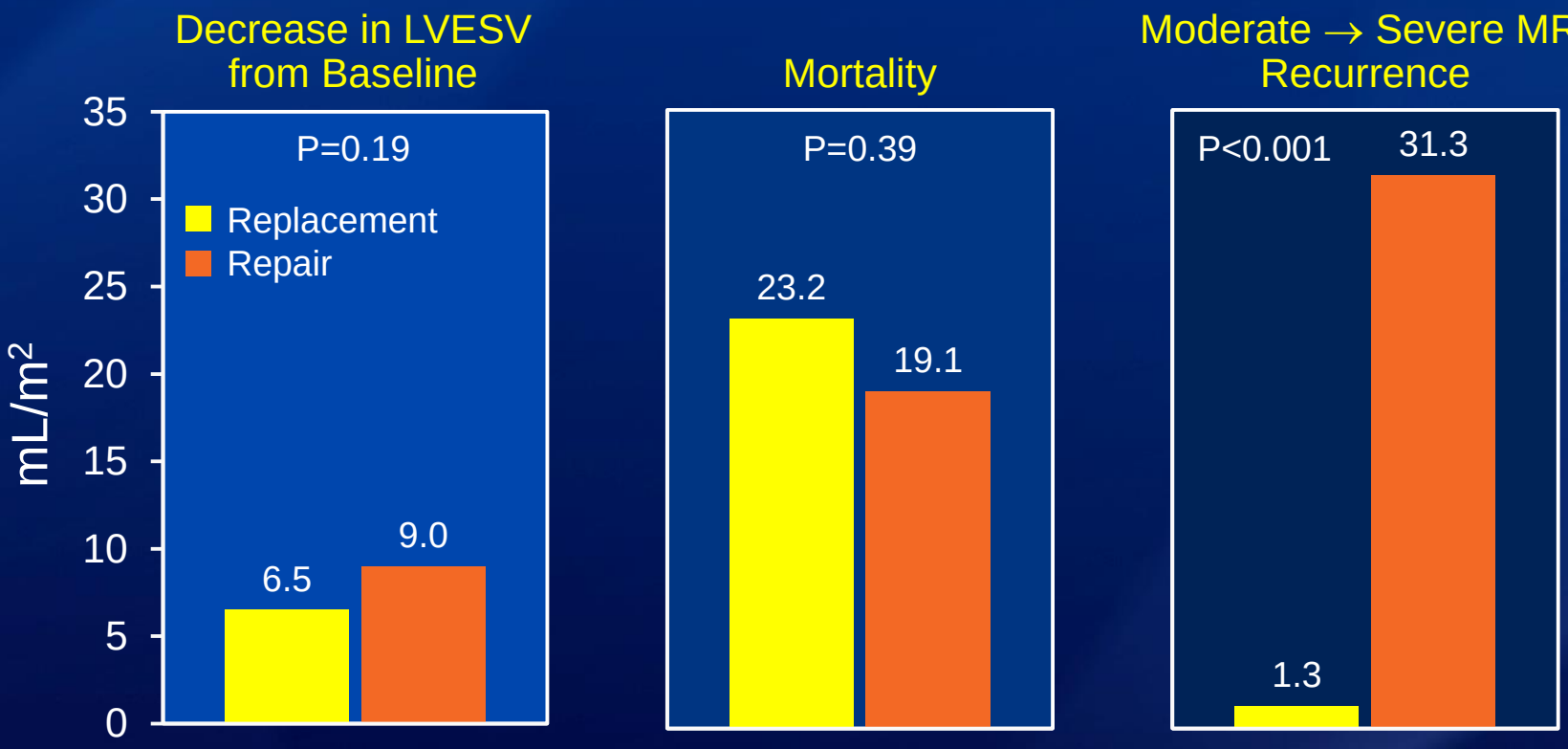




# Mitral Valve Repair vs Replacement for Severe Ischemic MR

## CTSN Trial – 2-Year Outcomes (251 Patients)




Repair patients - higher rate of serious heart failure, 24% vs 15% (P=0.05) and more CV readmissions 48.3 vs 32.2 (P=0.01)

Goldstein: NEJM, 2015

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# Should Moderate to Severe Functional MR be Corrected?

**Intuitively– Yes**

**Caveats**

- No concrete evidence that surgery alters natural history
- High risk of recurrence after MV Repair — Annuloplasty vs Other techniques
- Significant morbidity and mortality with MV replacement in some series

**Ongoing trials are important for *both* approaches**

| Surgery vs Medical | Percutaneous vs Medical | Percutaneous vs Surgery |
|---|---|---|

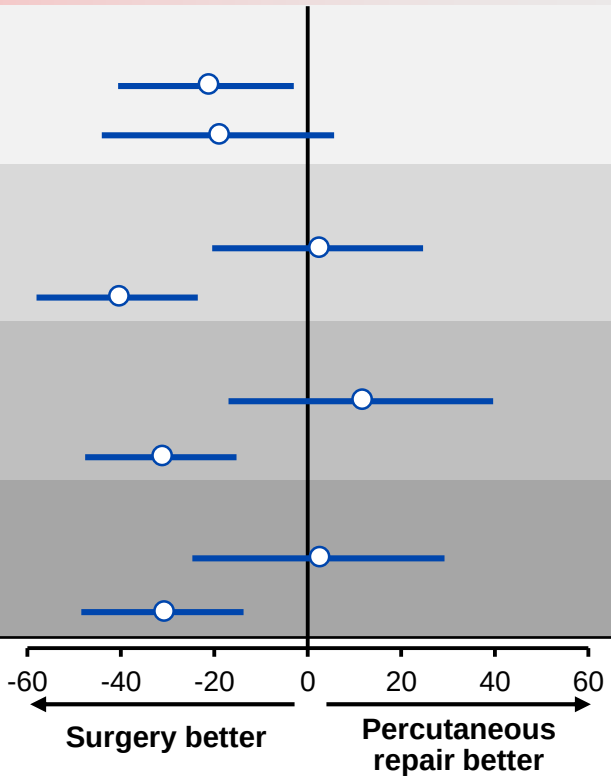

 

# Randomized Trial Data of Mitra-Clip vs Surgery in Functional vs Degenerative MR

## EVEREST II Trial

**Subgroup Analyses for Freedom From Death, MV Surgery or Reoperation, and 3+ or 4+ MR at 5 Years**

| Subgroup | Percutaneous Repair, % | Surgery, % | P value | Interaction P value |
|---|---|---|---|---|
| **Sex** | | | | 0.89 |
| Male | 42.9 | 63.9 | 0.03 | |
| Female | 46.4 | 65.0 | 0.15 | |
| **Age** | | | | 0.005 |
| Age ≥70 yrs | 45.1 | 42.3 | 0.81 | |
| Age <70 yrs | 43.4 | 83.3 | <0.001 | |
| **Type of MR** | | | | **0.02** |
| Functional MR | 40.5 | 28.6 | 0.43 | |
| Degenerative MR | 45.5 | 76.2 | <0.001 | |
| **LVEF** | | | | **0.04** |
| LVEF <60% | 44.1 | 41.2 | 0.83 | |
| LVEF ≥60% | 44.1 | 74.4 | 0.001 | |




Feldman: JACC, 2015

# ESC/EACTS Guidelines for Mitra-Clip

Class IIB LOE-C

Approved for Both Primary and Secondary MR

**MitraClip System for the Treatment of FMR:**
Ongoing Randomized Trials vs Medical Therapy

| | COAPT | RESHAPE | MITRA-FR |
|---|---|---|---|
| Design/location | Multicentre and randomized; US | Multicentre and randomized; EU | Multicentre and randomized; France |
| No of patients | 430 | 800 | 288 |
| LVEF, % | ≥20%–≤50% | ≥15%–≤40% | ≥15%–≤40% |

Del Trigo: Circ CV Intv, 2015

# Functional Mitral Regurgitation – Conclusions

- FMR is primarily a disorder of the LV
- FMR is common in CHF and after MI
- FMR predicts increased mortality in a graded fashion
- Medical therapy including beta-blockers, ACE-1 ARB is effective
- CRT may be effective in some patients
- CABG alone can reduce FMR acutely in some patients – results unpredictable

# Functional (Secondary) MR
## "Evidence and Uncertainties"

- **Does correcting FMR prolong or improve the quality of life?**
  **May depend upon presence of CHF symptoms**
- **Trials with Mitraclip / Devices will help inform the field**
- If correcting FMR is demonstrated to help: then providing the most complete and durable correction is desirable

Predictors of recurrences after repair

- Severe tethering
- Inferobasal aneurysm
- Severe LV dilatation

Valve-sparing mitral valve replacement should be used more liberally in these patients

# When to Intervene on the Mitral Valve in a Patient Undergoing CABG

**Mild → moderate MR**

**Dominant Symptom – Angina**

CABG alone
or
CABG plus
mitral annuloplasty

**Severe MR**

**Dominant symptom – CHF**

Valve sparing
MV replacement
vs
Repair ❓

**Trials suggest replacement is preferred over repair**

Annuloplasty ❓ Other techniques

# Evolving Concepts in regard to the Management of Functional MR

We now understand much more about what we do not know

**2016 update to The American Association for Thoracic Surgery consensus guidelines: Ischemic mitral valve regurgitation**

The American Association For Thoracic Surgery Ischemic Mitral Regurgitation Consensus Guidelines Writing Committee: Irving L. Kron, MD,[a] Damien J. LaPar, MD, MSc,[a] Michael A. Acker, MD,[b] David H. Adams, MD,[c] Gorav Ailawadi, MD,[a] Steven F. Bolling, MD,[d] Judy W. Hung, MD,[e] D. Scott Lim, MD,[f] Michael J. Mack, MD,[g] Patrick T. O'Gara, MD,[h] Michael K. Parides, PhD,[i] and John D. Puskas, MD[c]

## Existing Association Guidelines

### Moderate Ischemic MR

A. MV repair may be considered at time of other cardiac surgery, including CABG (COR IIb, LOE B)

### Mitral Valve Replacement (MVR) vs Repair

Not available

## AATS Guidelines

### Moderate Ischemic MR

**A.** **MV replacement** is reasonable in patients with severe IMR who remain symptomatic despite guideline directed medial and cardiac device therapy, and who have a basal aneurysm/ dyskinesis, significant leaflet tethering, and/or severe LV dilation (EDD >6.5 cm) (COR IIa, LOE B)

### Mitral Valve Replacement (MVR) vs Repair

A. MVR for IMR is performed with complete preservation of both anterior and posterior leaflet chords (COR I, LOE B)

B. MV repair for IMR is performed with small undersized complete rigid annuloplasty ring (COR IIa, LOE B)

Kron: JTCVS, 2017

# Updated AATS Guidelines

## Existing Association Guidelines
## Severe Ischemic MR

A. MV surgery is reasonable at time of other cardiac surgery (eg, CABG, AVR) (COR IIa, LOE C)

B. MV surgery may be considered as an isolated procedure for treatment of patients with severe symptoms (NYHA III/IV) despite GDMT (COR II, LOE C)

## AATS Guidelines
## Severe Ischemic MR

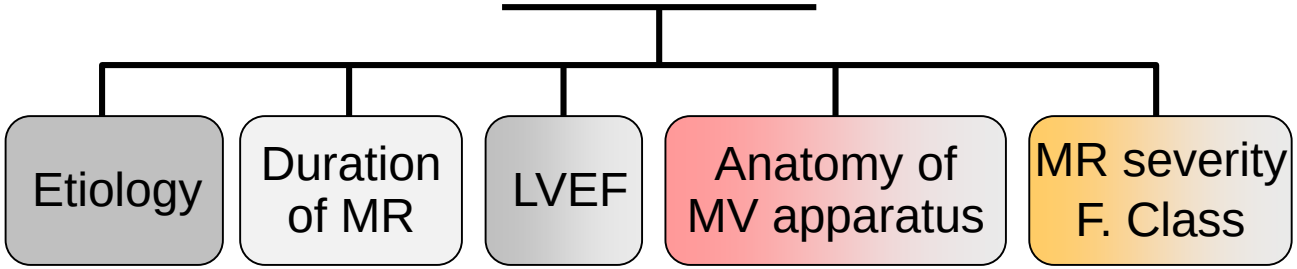
**A.** **MV replacement** is reasonable in patients with severe IMR who remain symptomatic despite guideline directed medial and cardiac device therapy, and who have a basal aneurysm/dyskinesis, significant leaflet tethering, and/or severe LV dilation (EDD >6.5 cm) (COR IIa, LOE B)

**B.** **MV repair** with an undersized complete rigid annuloplasty ring may be considered in patient with severe IMR who remain symptomatic despite guideline directed medical and cardiac device therapy and who do not have a basal aneurysm/dyskinesis, significant leaflet tethering, or severe LV enlargement (COR IIb, LOE B)

Kron: JTCVS, 2017

# Why is the Benefit of MR Reduction so Hard to Prove?

- MR recurrence ≥20%; perioperative mortality 1.5-15%
- The benefit may be limited to specific pt subgroups that have not been pre-defined in CV datasets




- Perhaps there is no benefit ? – *MR is a surrogate not causally related to outcome ?*
- *"Things may not be as they seem"*

*Gersh And Frye NEJM 2008*

M. Mack (Pers. Comm), 2016