

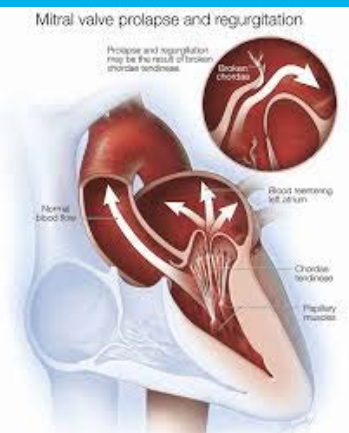


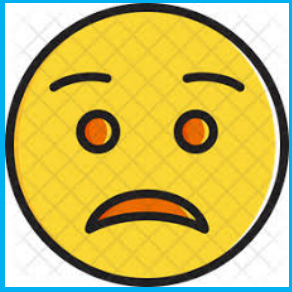
“How serious is it to have a leaking mitral valve?”

Dr. Andrew L. Morris

Professor of Medicine (Cardiology)

University of Manitoba





Your new patient

- Sandra Most-Worried is a healthy, 68 year-old woman, new to your practice, who is found to have a mitral regurgitation murmur.
- She is certain that her previous doctor never told her about any murmur. She is glad she now has a younger, and more ‘up-to-date,’ doctor.
- She wonders how she could have developed this new murmur and wonders how it can be “fixed.”
- Her daughter, a nurse working in San Francisco, told her mom she needs to see a ‘good cardiologist’ to get this thing “clipped.”



Case Presentation (cont'd)

Plan: You get an EKG and you try to locate previous medical records. You request an echocardiogram

And you ask yourself:

1. Is this really a new murmur?
2. Is this really a MR murmur?
3. Does anything really need to be done?
4. What's her daughter talking about? What's "clipping?" American medical overcharging?
5. Does she need surgical and/or cardiac consultation?
6. Is there an internist or a cardiologist in an adjacent office?
7. Does she need to be literally "seen" for an opinion?
8. Does your view change if she needs to travel 1500 miles for an opinion?









Types of mitral valve regurgitation:

Primary vs. secondary MR

- Classification of MR into primary vs. secondary (functional):
 - Primary MR-is due to intrinsic disease of the mitral apparatus. *Example*: Rheumatic fever, prolapse
 - Secondary MR-is due to dysfunction of the mitral supporting apparatus without intrinsic valve disease. *Example*: myocardial infarction. CHF.

Primary vs. secondary MR

CENTRAL ILLUSTRATION Classification of the Etiology of MR

	Carpentier Type I (normal leaflet motion and position)	Carpentier Type II (excess leaflet motion)	Carpentier Type IIIa (restricted leaflet motion in systole and diastole)	Carpentier Type IIIb (restricted leaflet motion in systole)
PRIMARY MR	 <p>Leaflet Perforation Cleft</p>	 <p>Mitral Valve Prolapse</p>	 <p>Rheumatic Valve Disease Mitral Annular Calcification Drug Induced MR</p>	
SECONDARY MR	 <p>Atrial MR</p>	 <p>Nonischemic Cardiomyopathy</p>		 <p>Ischemic Cardiomyopathy</p>

El Sabbagh, A. et al. J Am Coll Cardiol Img. 2018;11(4):628-43.

Primary and secondary mitral valve regurgitation (MR) groupings with their respective Carpentier's functional classification. Carpentier type I represents normal leaflet motion and position. Carpentier type II represents excess leaflet motion. Carpentier type IIIa represents restricted leaflet motion in systole and diastole. Carpentier type IIIb represents restricted leaflet motion in systole.

Primary

Secondary

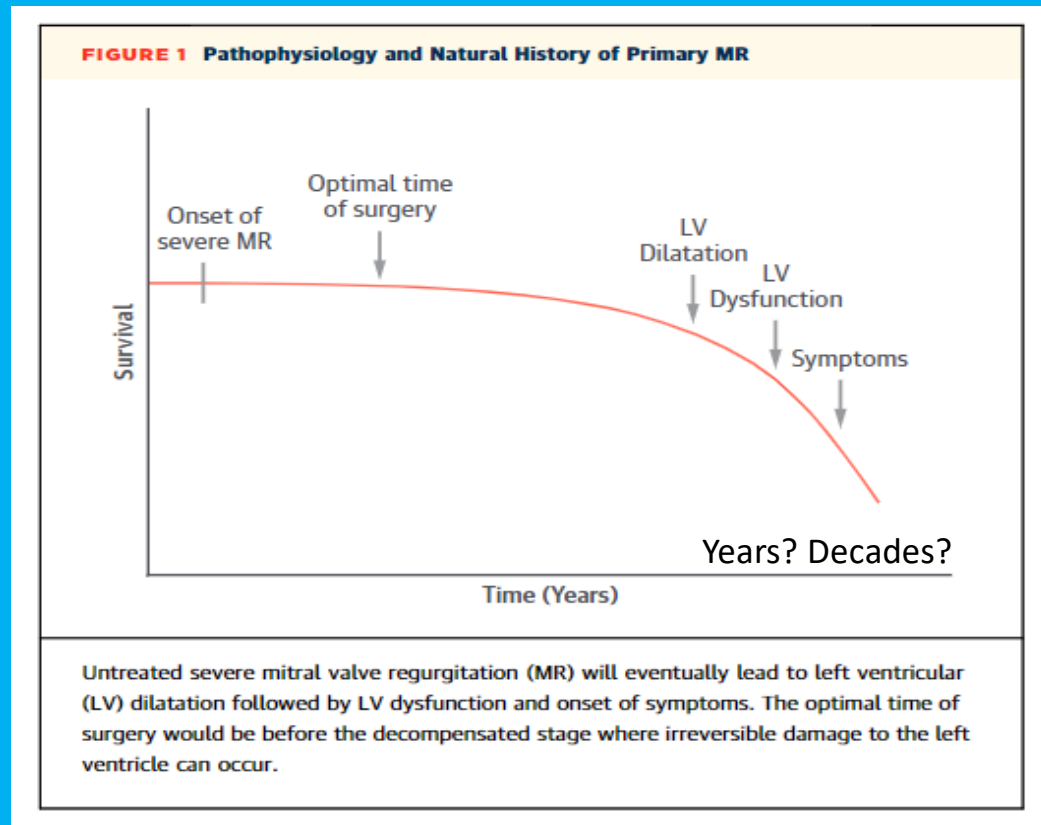
Leaflet perforation
MV Prolapse
Rheumatic, MAC

Atrial MR
Non-ischemic CMP

Ischemic CMP

Natural history of primary MR: When should we intervene?

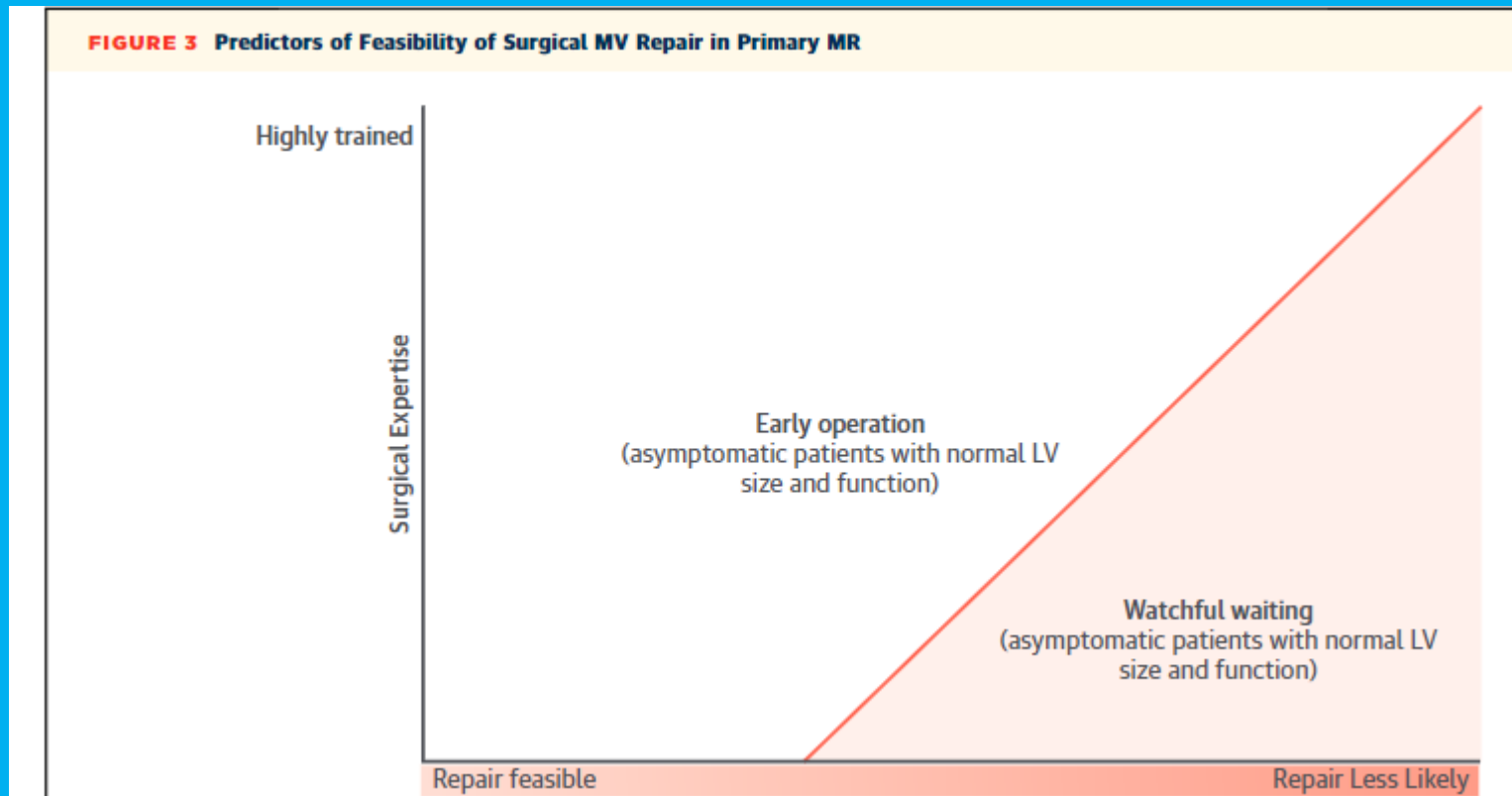
Survival



Too early is too early; too late is too late. When is just right?

Dx. and Mgt. of MR. JACC cardiovasc. Imaging. 2018;11 (4):631

Suitability for repair & operator experience affects consideration of treatment strategy



Where's your patient?

Factors Affecting the Prognosis of Primary MR.

TABLE 4 Factors Affecting Prognosis in Primary MR

Factor Type	Specific Factors
1. Factors related to the LV or LA	<ul style="list-style-type: none">■ Systolic dysfunction (EF <60%)■ LV enlargement (LVESD >4cm)■ LA enlargement (LA systolic volume index ≥ 60 ml/m²)
2. Clinical factors	<ul style="list-style-type: none">■ Age■ Presence/absence of heart failure■ Functional class■ Presence/absence of CAD
3. Rhythm/hemodynamic factors	<ul style="list-style-type: none">■ AF■ Arrhythmic MVP*■ Pulmonary hypertension
4. Factors related to MR, timing of intervention	<ul style="list-style-type: none">■ Severity of regurgitation■ Flail leaflet■ Delay in MV intervention after onset of LV dysfunction

Factors related to the LV or LA

Clinical factors

Rhythm/hemodynamic factors

Factors related to MR, timing of intervention.

*Characteristics include inferior T-wave inversions on 12-lead ECG, complex ventricular ectopy, spiked configuration of lateral annular tissue Doppler velocity (Pickelhaube sign), and late gadolinium enhancement (myocardial fibrosis) on cardiac magnetic resonance imaging.

AF – atrial fibrillation; CAD – coronary artery disease; EF – ejection fraction; LA – left atrium; LV – left ventricle; LVESD – left ventricular end-systolic diameter; MR – mitral regurgitation; MV – mitral valve; MVP, mitral valve prolapse.

Do all leaking valves need to be “fixed?”

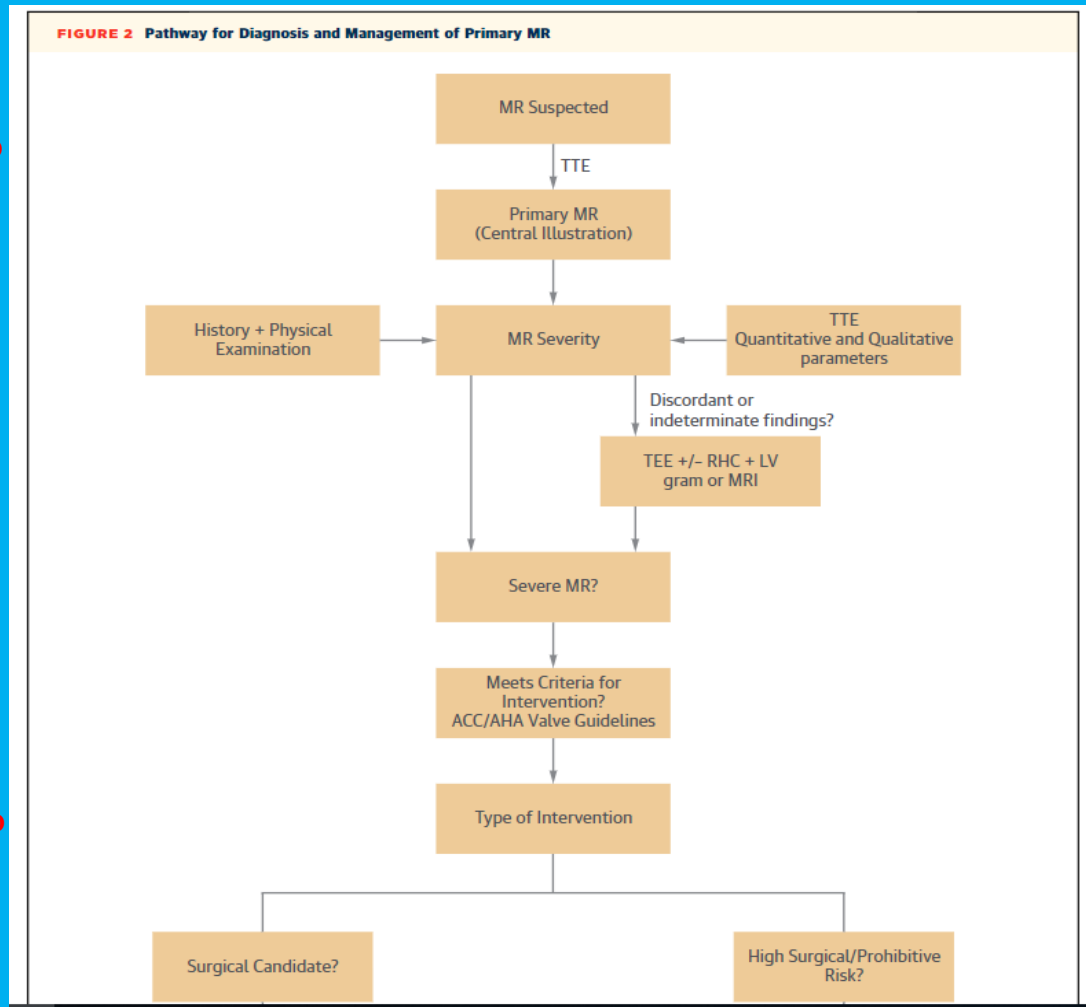
- Questions:

- How severe is the leak?
- What is the mechanism of the leak?
- What is the natural history of such leaks?
- What medical options exist for this type of MR?
- What type of surgical options are available?
- What type of interventional options are available?
- How much benefit has been shown for each type of treatment as compared to controls (interventional vs. ‘watchful waiting?’)

Mitral valve insufficiency

- When to intervene?
 - Symptoms vs. no symptoms?
 - Left atrial volume?
 - Dilated LV vs. normal-sized LV?
 - Reduced LV ejection fraction (EF) vs. normal EF?
 - Elevated RV systolic pressure vs. normal RVSP?
 - None of the above? How sure are we?
 - How good is the data?
 - Which is the treatment method proposed?
 - How good are the short-term and long-term outcomes?
 - What is the local experience?

Approach to mitral valve regurgitation



Mitral regurgitation?

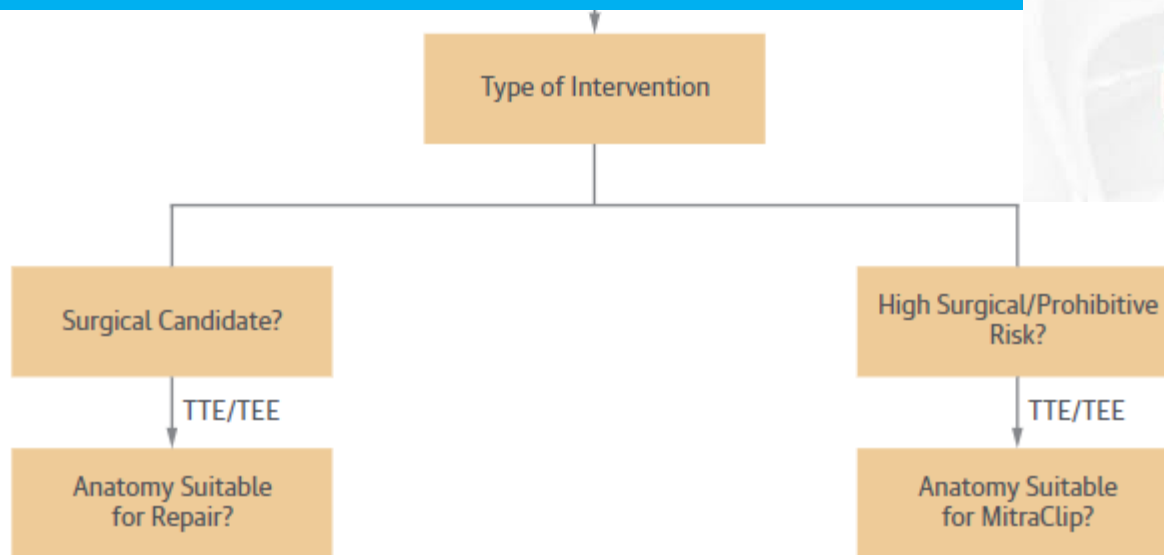
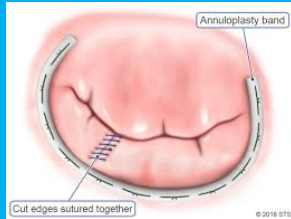
MR severity?

If Severe...

Surgery? Other?

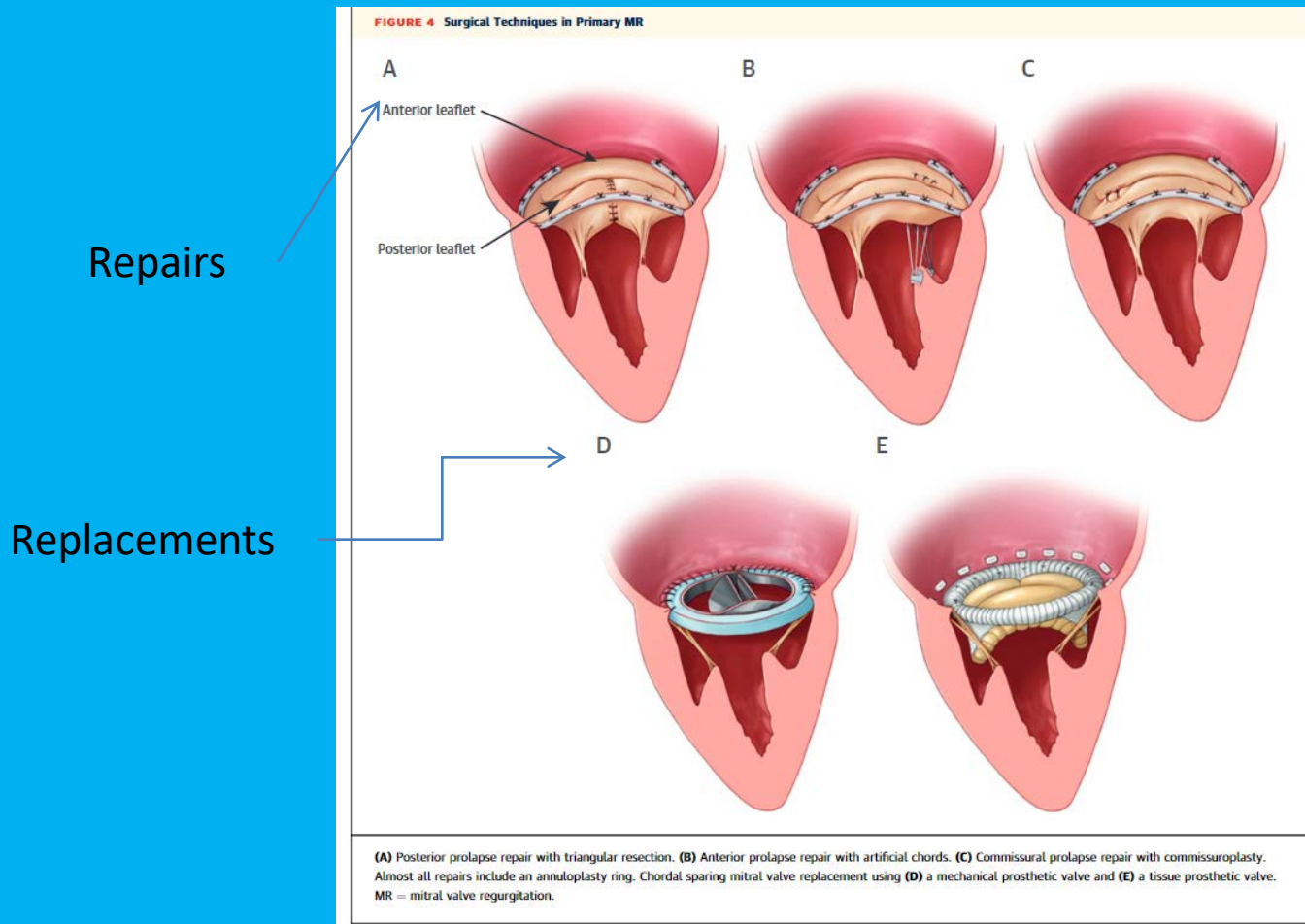
Surgical risk?

Interventions: surgical repair or non-surgical repair?

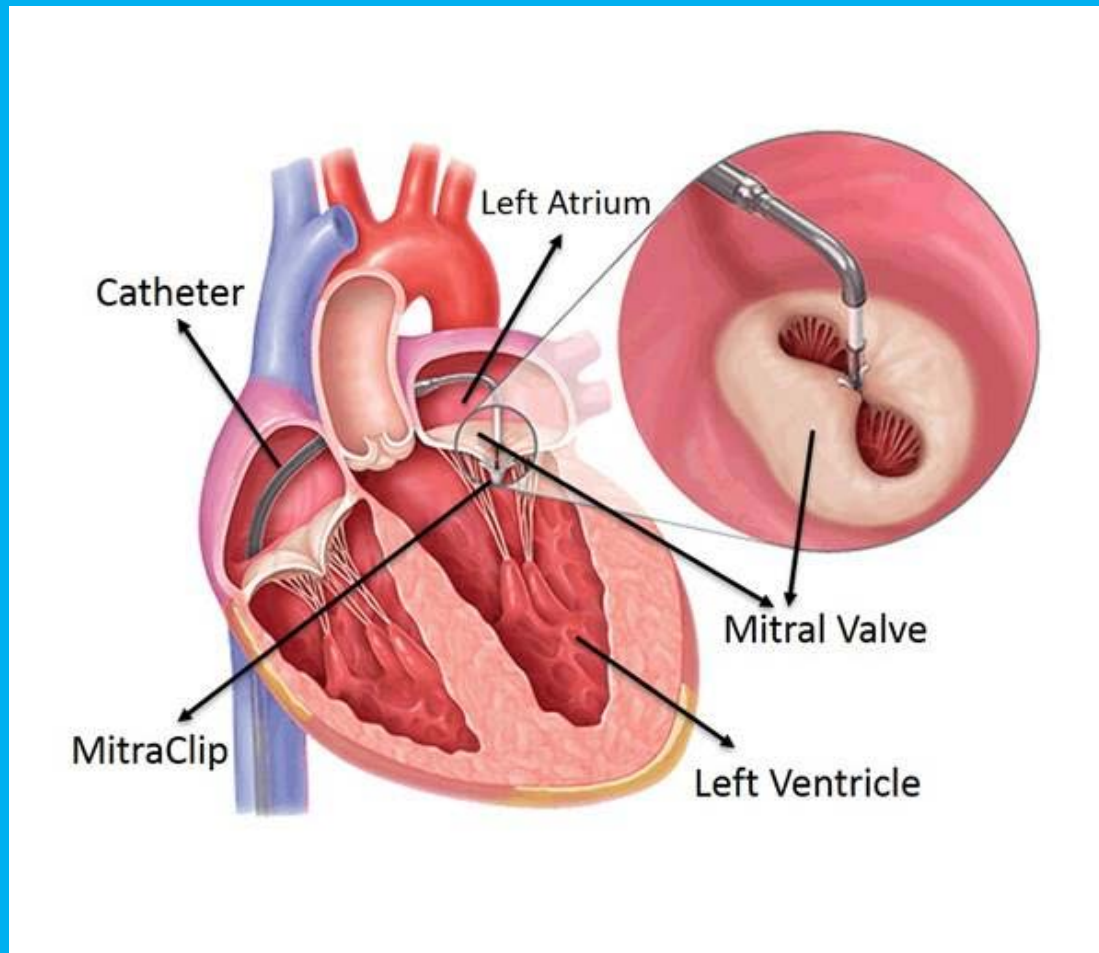


When primary mitral valve regurgitation (MR) is suspected based on history and physical examination, transthoracic echocardiography (TTE) is required to identify the etiology by using the Carpentier classification and to quantify severity. If there are discordant or indeterminate findings regarding severity, further quantification with transesophageal echocardiography (TEE), right heart catheterization (RHC) and left ventriculogram (LV gram), or magnetic resonance imaging (MRI) is then warranted. If severe, the next step would be to determine if any of the criteria for intervention are met based on the American College of Cardiology/American Heart Association (ACC/AHA) valve guidelines and to then determine surgical candidacy and feasibility of repair. If the patient is not a surgical candidate, an assessment for suitability for MitraClip intervention can be considered.

Surgical approaches: repair or replacement (mechanical vs. bioprosthetic)



Percutaneous clipping to narrow the regurgitant orifice



What evidence do we have regarding the timing of MR intervention and the type of intervention?

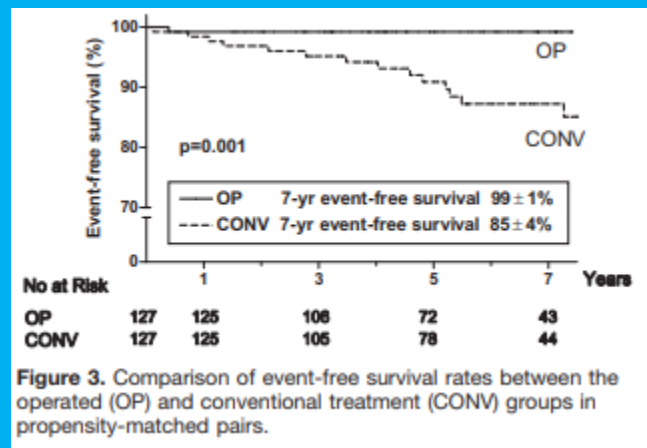
- *Randomized trials in valvular heart disease are few-and-far-between.*
- *Most of the data is from observational studies and non-randomized trials.*

Comparison of early surgery vs. conventional treatment in asymptomatic severe mitral regurgitation

- Prospective patients with severe MR with prolapse or flail mitral leaflet identified in the Echo Lab
- Surgery vs. no-surgery at the discretion of the physician
- MV repair in 94%; MV replacement in 6%.
- CABG in 12%
- **End-point:** Operative death (30 days), cardiac death, repeat MV surgery, HF hospitalization during follow-up.
- **Crossover** to surgery if: LVEF < 60%, LVESD > 45%, PAP > 50 mmHg, AFib or exertional dyspnea.

7-year event-free survival in operated vs. conventional treatment groups

Event-free survival-%



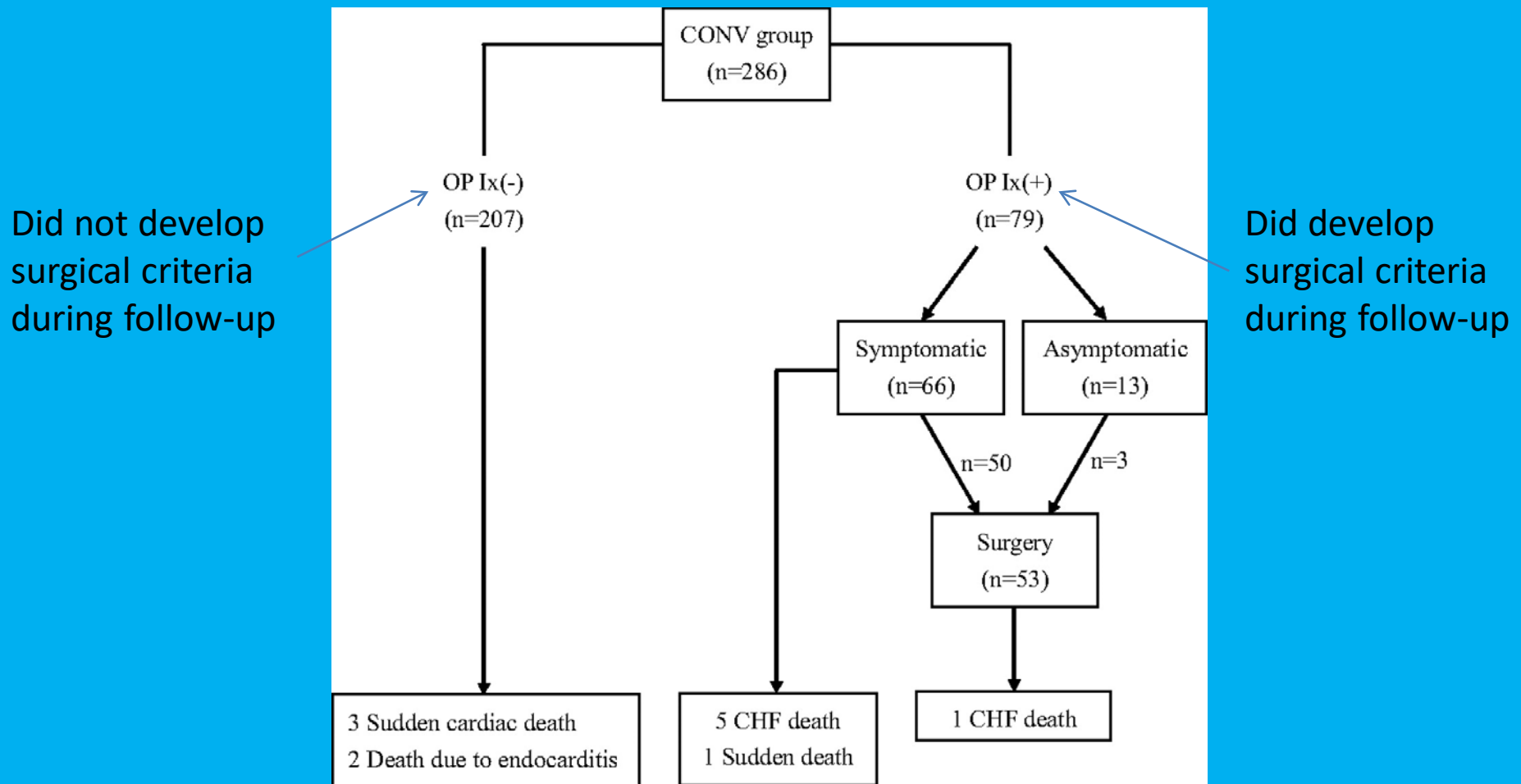
Years

Events:

- Operative death
- Cardiac death
- Repeat MV surgery
- HF hospitalization

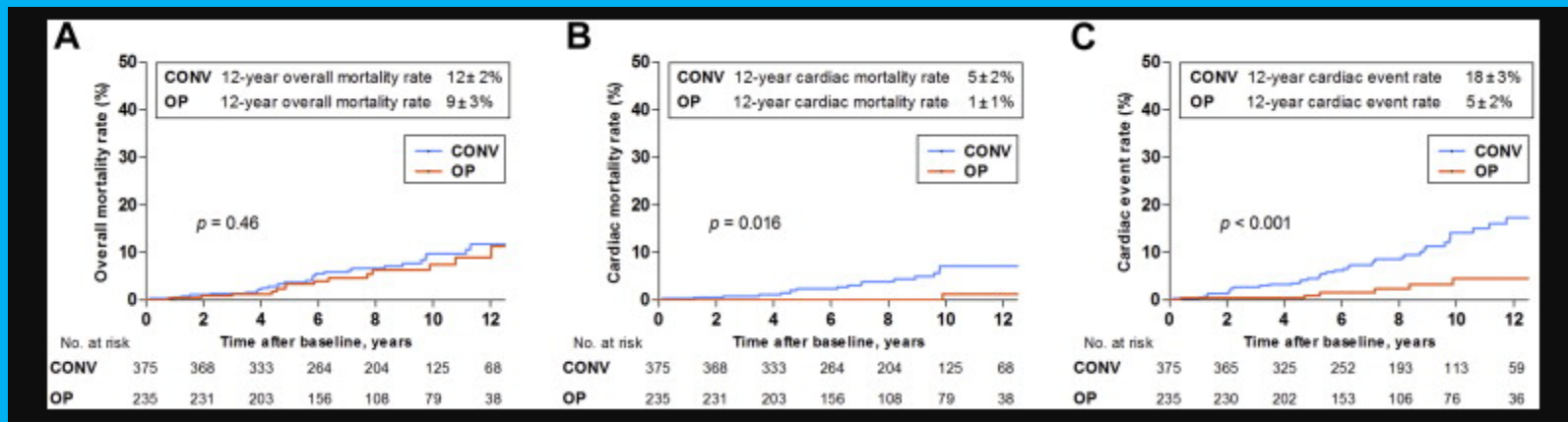
Are these end-points those of most importance to patients and to physicians?

Outcomes in the conventional care group (CONV)



Early surgery versus conventional treatment for asymptomatic severe mitral regurgitation: a propensity analysis

- Severe degenerative MR.
- Treatment groups determined by physicians' and patients' choices.



Mortality rate

Cardiac mortality rate

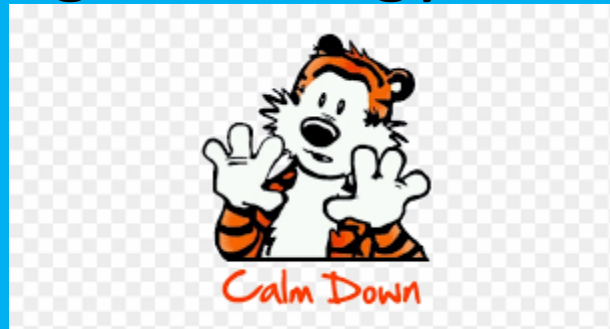
Cardiac event rate

Conclusions

- Severe, primary mitral valve insufficiency is an increasingly common disorder in our practices.
- Its evaluation requires an H&P and, oftentimes, an echocardiogram and a phone call.
- The decision to proceed with valve repair and/or replacement depends upon the presence or absence of symptoms and/or high-risk markers, the size and function of the LV, and the local experience with surgical and non-surgical mitral valve interventions.

Conclusions

- Asymptomatic, severe MR is rarely a medical/surgical emergency and the best decision regarding intervention can be made without a feeling of urgency.
- This is very comforting to patients and to their families. No single strategy fits all patients.



Questions?

Will be addressed in the Q&A session to follow.

Clinical trials in progress

- Dutch AMR Trial-asymptomatic
- REVERSE MR -asymptomatic
- Reshape HF2-CHF; randomized trial of mitral clip vs. standard treatment.

Early surgery for asymptomatic severe MR: ACC/AHA & ESC

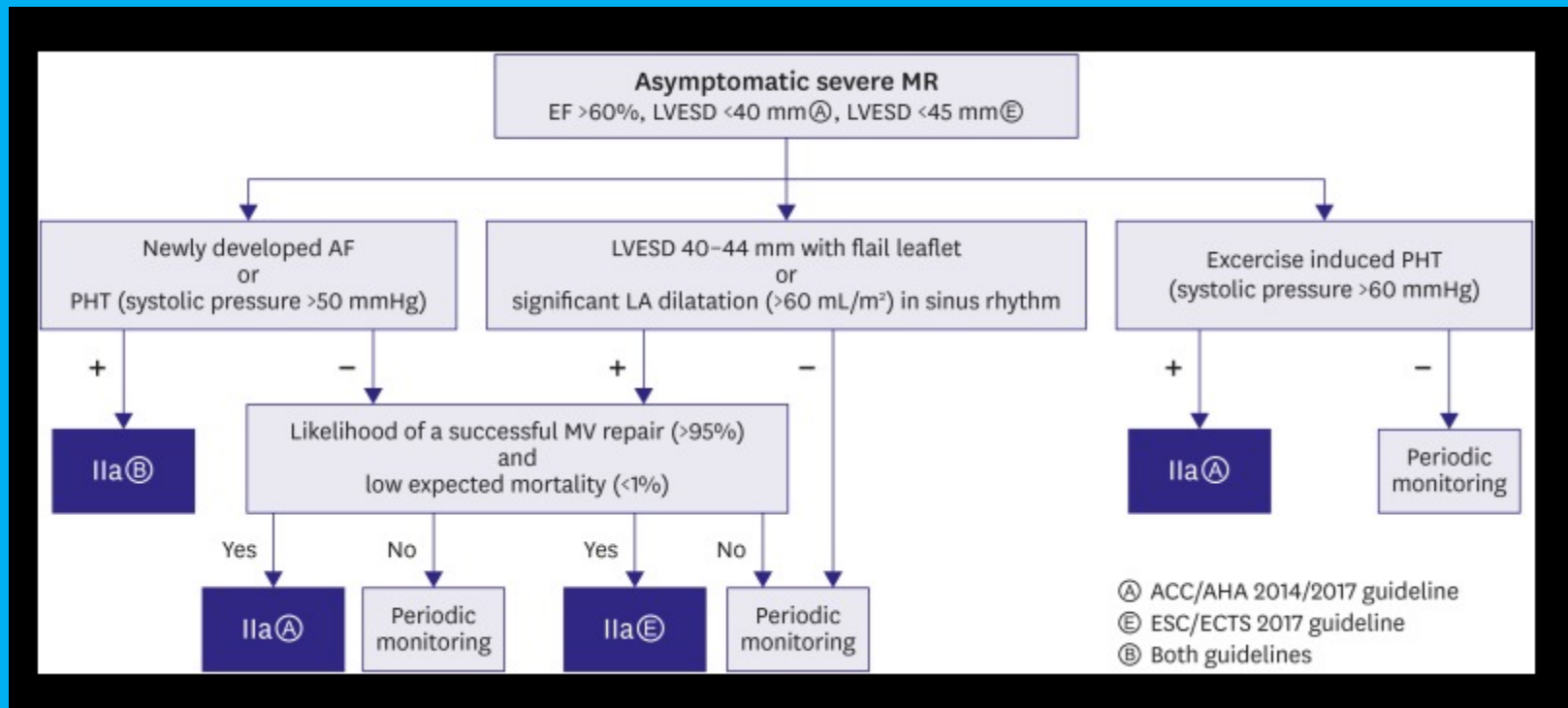


Figure 1. Early surgical indications for asymptomatic patients with severe MR. Adapted from ACC/AHA 2014/2017 and ESC/ECTS 2017 guidelines.

Korean Circ J. 2018 Nov;48(11):964-973. doi: 10.4070/kcj.2018.0308

Dutch AMR Trial

Dutch asymptomatic mitral regurgitation trial

Initiation: 2013; est. termination, 2021.

Method: Early valve repair vs. “watchful waiting.”

Subjects: 18 to 75 yrs; no symptoms; severe primary MR, LVEF above 60%; LVESD below 45 mm; 90% probability of valve repair.

Primary end-point: CV death, CHF, hospitalization for non-fatal CV events.

Mitral valve repair vs. watchful waiting for asymptomatic severe degenerative mitral regurgitation due to leaflet prolapse (REVERSE MR).

- Study initiation, 2018; termination, 2026
- N=424 pts.
- Randomized; parallel assignment.
- Early repair (< 3 months after randomization) vs. non-surgical treatment.
- Crossovers to surgery if: LVESD > 40 mm, LVEF < 60%, recurrent AFib, RVSP >50 mmHg.
- End-points: Death, CHF, AFib, SBE, TIA/CVA.

A Clinical Evaluation of the Safety and Effectiveness of the MitraClip System in the Treatment of Clinically Significant Functional Mitral Regurgitation (Reshape-HF2)

A Randomized Study of the MitraClip Device in Heart Failure Patients With Clinically Significant Functional Mitral Regurgitation

- Mitral clip vs. standard care for patients with chronic CHF and functional MR.
- Initiated 2015; completed 2021.
- NYHA II, III, IV
- Hospitalized at least once in prior 12 months.
- BNP >300 or NT-BNP >1000
- LVEF $\geq 15\%$ to $\leq 35\%$ if Class II; 15% to 45% if Class III/IV.

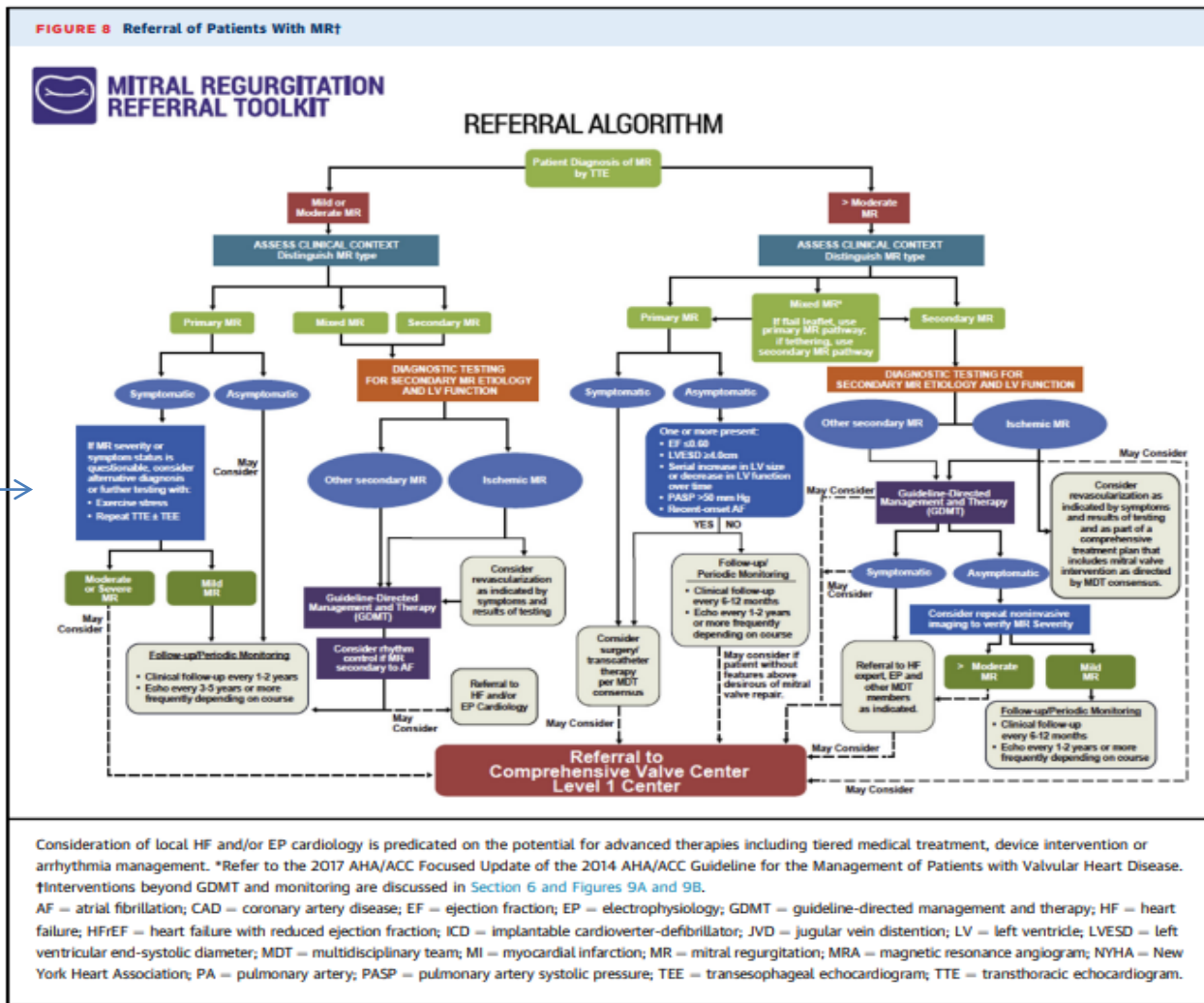
Goettingen, Germany

What sayeth the guidelines?



Really??

You've got to be kidding!



AHA/ACC Guidelines for primary MR

MVR=mitral valve replacement

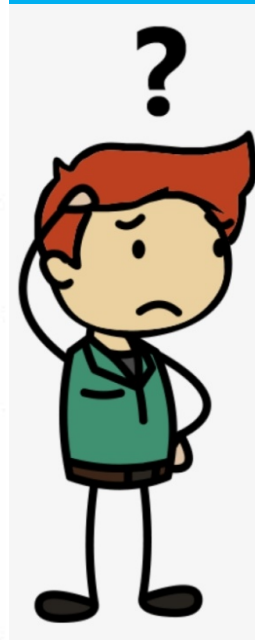
Recommendations for Chronic Primary MR Intervention			
COR	LOE	Recommendations	Comment/Rationale
I	B	Mitral valve surgery is recommended for symptomatic patients with chronic severe primary MR (stage D) and LVEF greater than 30%. ⁷³⁻⁷⁵	2014 recommendation remains current.
I	B	Mitral valve surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30% to 60% and/or left ventricular end-systolic diameter [LVESD] \geq 40 mm, stage C2). ⁷⁶⁻⁸²	2014 recommendation remains current.
I	B	Mitral valve repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet. ⁸³⁻⁹⁹	2014 recommendation remains current.
I	B	Mitral valve repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving the anterior leaflet or both leaflets when a successful and durable repair can be accomplished. ^{84,88,95,100-104}	2014 recommendation remains current.
I	B	Concomitant mitral valve repair or MVR is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications. ¹⁰⁵	2014 recommendation remains current.
IIa	B	Mitral valve repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF $>$ 60% and LVESD $<$ 40 mm) in whom the likelihood of a successful and durable repair without residual MR is greater than 95% with an expected mortality rate of less than 1% when performed at a Heart Valve Center of Excellence. ^{101,106-112}	2014 recommendation remains current.
IIa	C-LD	Mitral valve surgery is reasonable for asymptomatic patients with chronic severe primary MR (stage C1) and preserved LV function (LVEF $>$ 60% and LVESD $<$ 40 mm) with a progressive increase in LV size or decrease in ejection fraction (EF) on serial imaging studies. ¹¹²⁻¹¹⁵ (Figure 2)	NEW: Patients with severe MR who reach an EF \leq 60% or LVESD \geq 40 have already developed LV systolic dysfunction, so operating before reaching these parameters, particularly with a progressive increase in LV size or decrease in EF on serial studies, is reasonable.

See Online Data Supplement 17 (Updated From 2014 VHD Guideline)

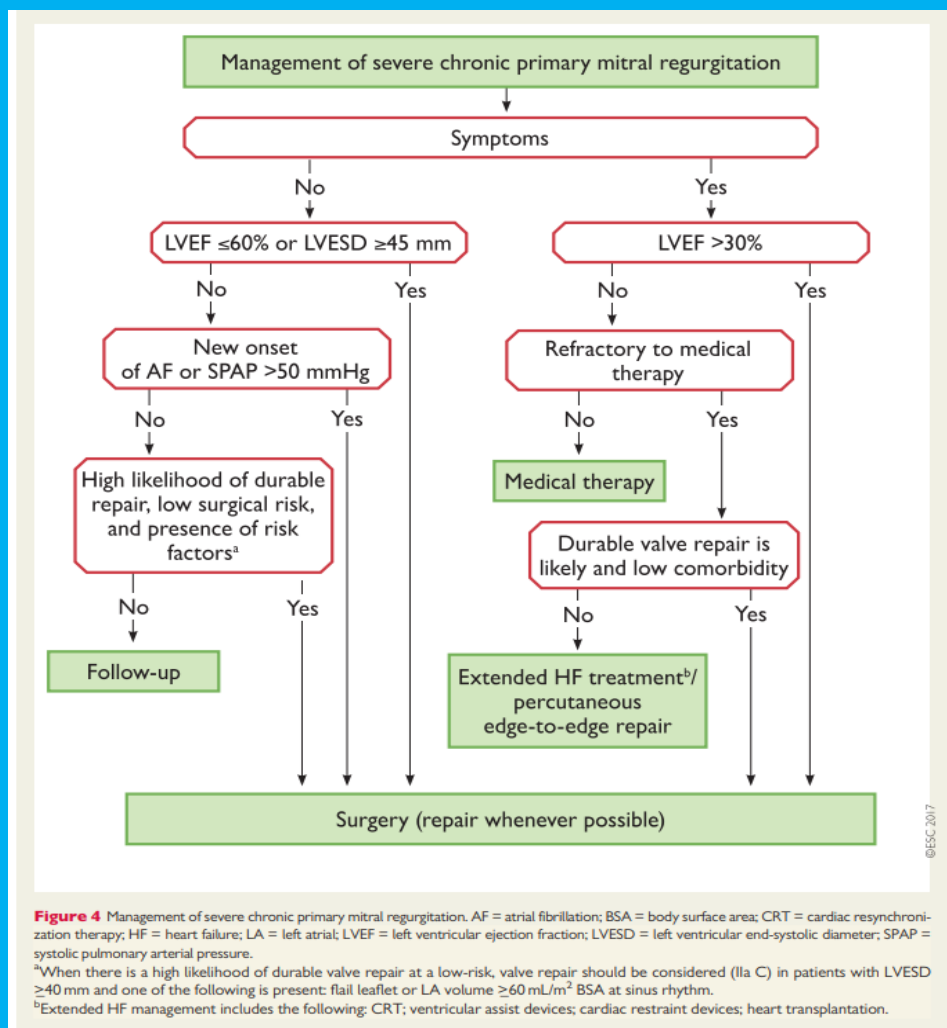


AHA/ACC Guidelines for primary MR

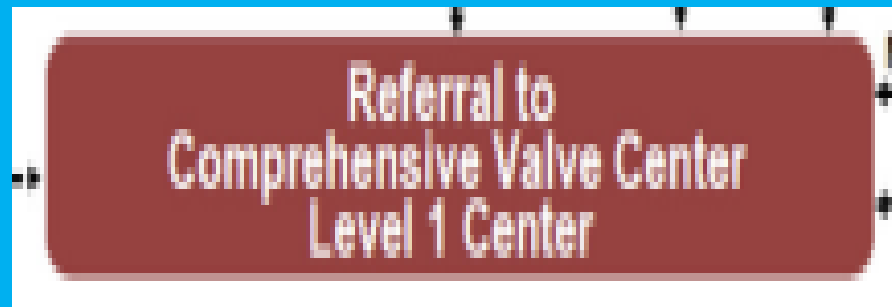
IIa	B	Mitral valve repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function (LVEF >60% and LVESD <40 mm) in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (pulmonary artery systolic arterial pressure >50 mm Hg). ^{111,117-123}	2014 recommendation remains current.
IIa	C	Concomitant mitral valve repair is reasonable in patients with chronic moderate primary MR (stage B) when undergoing cardiac surgery for other indications.	2014 recommendation remains current.
IIb	C	Mitral valve surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF less than or equal to 30% (stage D).	2014 recommendation remains current.
IIb	B	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 heart failure (HF). ¹²⁴	2014 recommendation remains current.
III: Harm	B	MVR should not be performed for the treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless mitral valve repair has been attempted and was unsuccessful. ^{84,89,90,95}	2014 recommendation remains current.



ESC/EACTS Guidelines



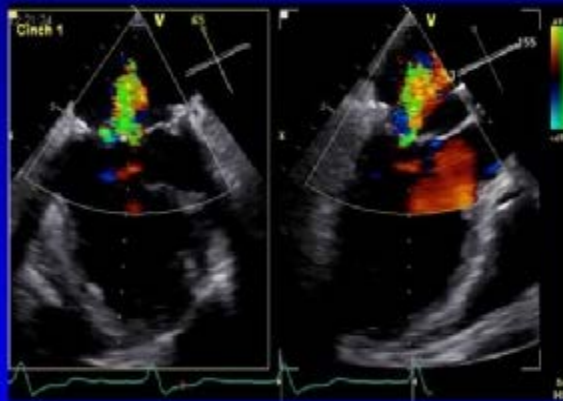
Bottom Line



1) Is the regurgitation severe ?

2) What is the mechanism of the regurgitation?

3) Is the patient symptomatic ?



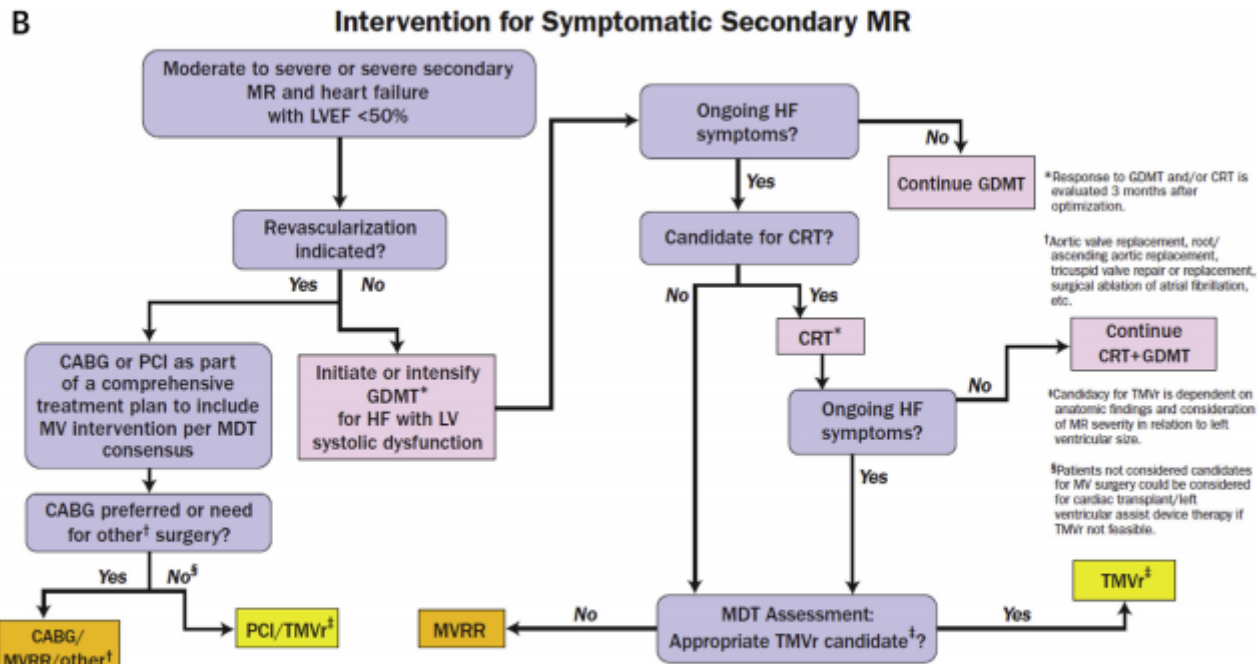
4) Are there contra-
indications to any
intervention
on the valve ?

6) Is a transcatheter intervention
feasible?

5) Is surgery contraindicated /high risk ?

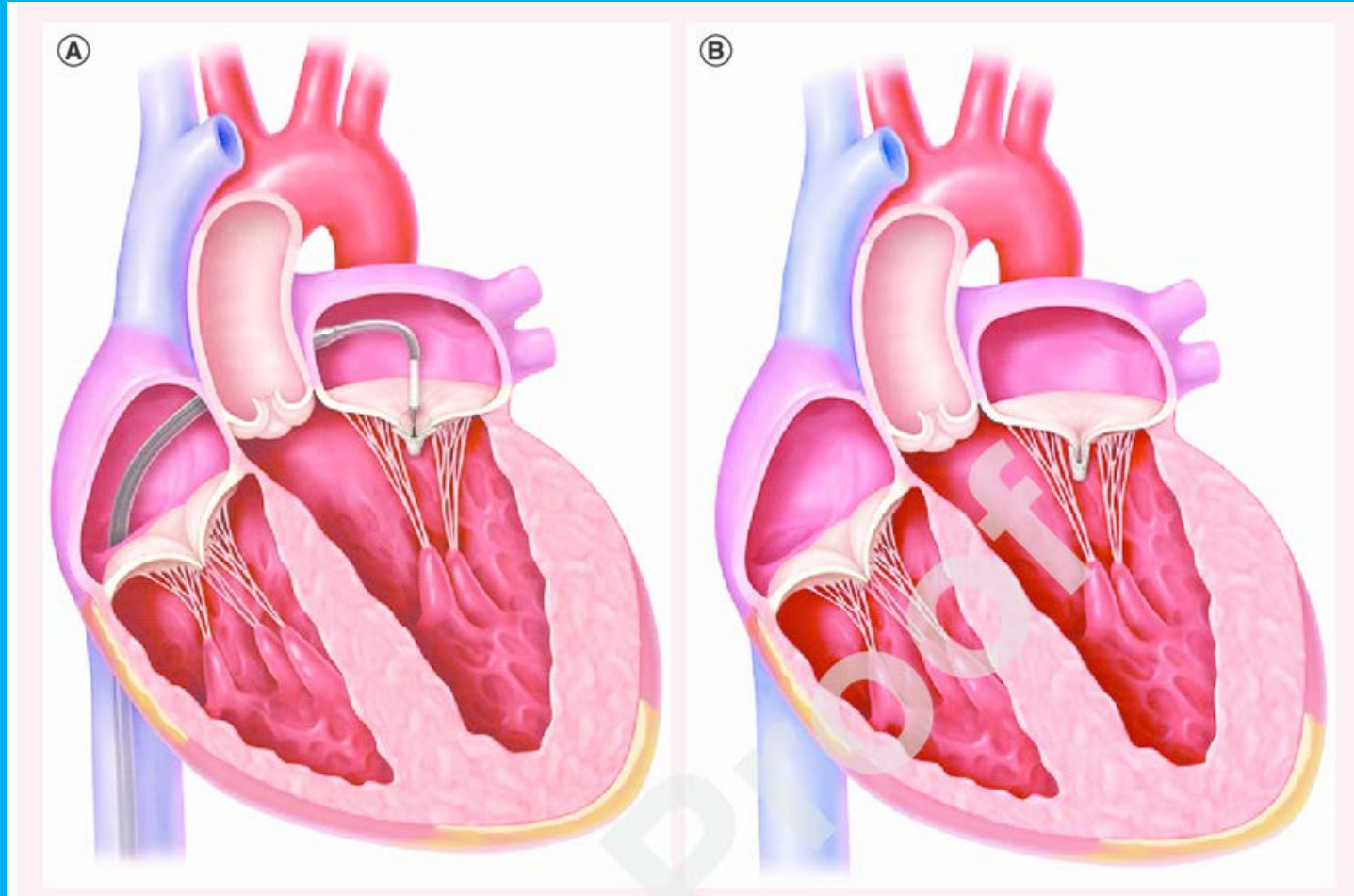
7) What is the final decision
of the heart team ?

FIGURE 9B Intervention for Symptomatic Secondary MR



AAD = antiarrhythmic drug; AF, atrial fibrillation; CABG = coronary artery bypass graft; CRT = cardiac resynchronization therapy; GDMT = guideline-directed management and therapy; HF = heart failure; LVEF = left ventricular ejection fraction; MDT = multidisciplinary team; MR = mitral regurgitation; MV = mitral valve; MVRR = mitral valve repair or replacement; PCI = percutaneous coronary intervention; TMVr = transcatheter mitral valve repair.

A percutaneous clip for primary MR: Two orifices rather than one

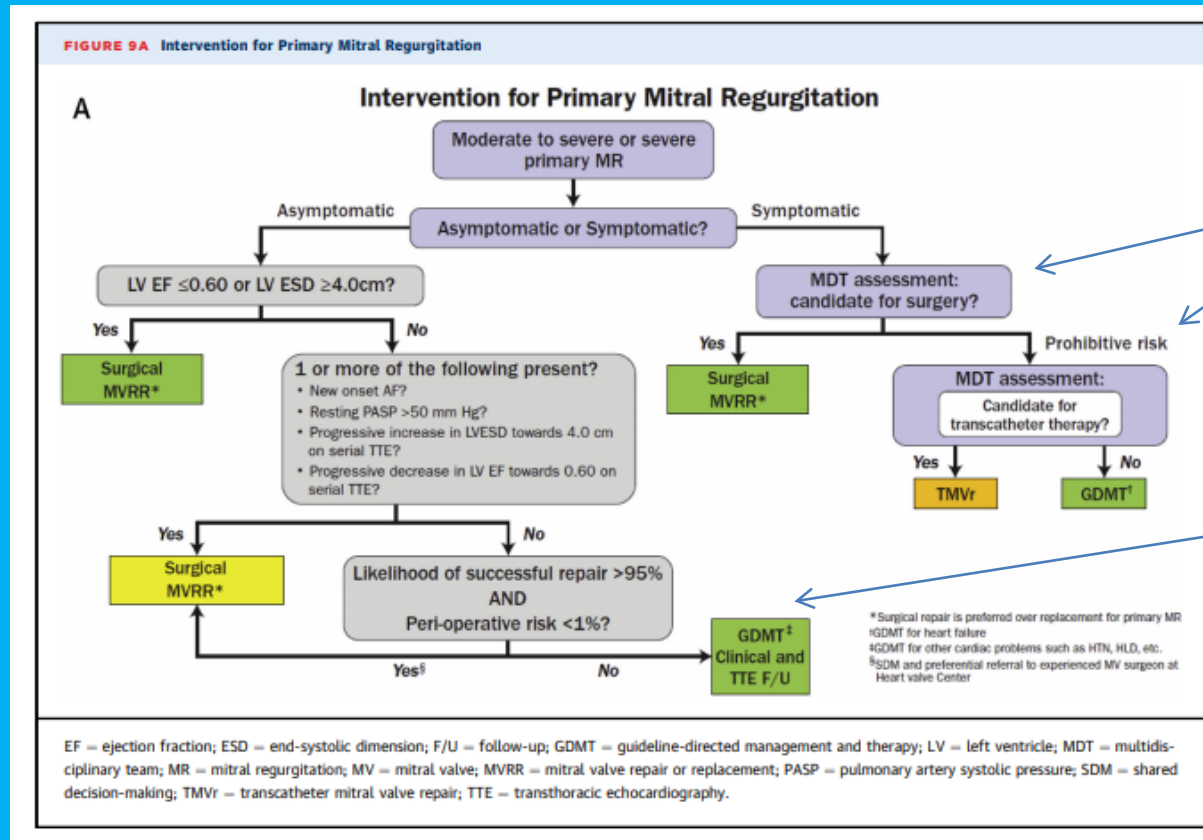




Indications for intervention in severe primary mitral regurgitation

Recommendations	Class ^a	Level ^b
Mitral valve repair should be the preferred technique when the results are expected to be durable.	I	C
Surgery is indicated in symptomatic patients with LVEF >30%. ^{121,131,132}	I	B
Surgery is indicated in asymptomatic patients with LV dysfunction (LVESD \geq 45 mm ^c and/or LVEF \leq 60%). ^{122,131}	I	B

Roadmap for primary MR



MDT=multi-disciplinary team

GDMT=Guideline-directed Medical therapy.

Is early surgery beneficial?

Early Surgery in Valvular Heart Disease

Kim DH, Kang DH

Korean Circ J. 2018 Nov;48(11):964-973.

doi: [10.4070/kcj.2018.0308](https://doi.org/10.4070/kcj.2018.0308).

Surgery vs medical management of symptomatic severe MR

Initial surgery vs. conservative management of symptomatic severe mitral regurgitation in the elderly.

Kang DH, Heo R, Lee S, Baek S, Kim DH, Song JM, Song JK, Lee JW.

Heart. 2018 May;104(10):849-854. doi: 10.1136/heartjnl-2017-311759. Epub 2017 Oct 5.

Early report of surgery for MR

A method for the surgical correction of mitral insufficiency. I. Preliminary considerations

DAVILA, J.C., MATTSON, W.W., Jr, O'NEILL, T.J., GLOVER, R.P.

Surgery, gynecology & obstetrics. Volume 98, Issue 4, 1 April 1954, Pages 407-412

Severe MR in symptomatic elderly patients

- More than 70 years old; N=157
- Severe primary MR with mild symptoms
- Prospective, consecutive series.
- Follow-up=5.4 years
- End-points: total mortality, cardiac mortality, cardiac events.
- Results: significant reduced in all end-points