

# **Intervention for Mitral Regurgitation: Catheter-based, Surgery, Medical Therapy**

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**Relevant RWI: None**

# Case Report 1

**79 yo male, Ischemic CMP**

**Admitted with acute HF 3 times in last year**

**Hx CABG: 3-VD (no options for revascularization)**

**Good GDMT**

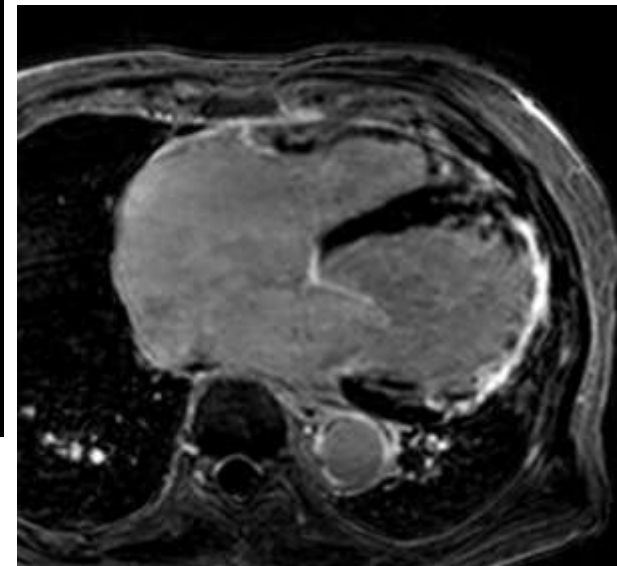
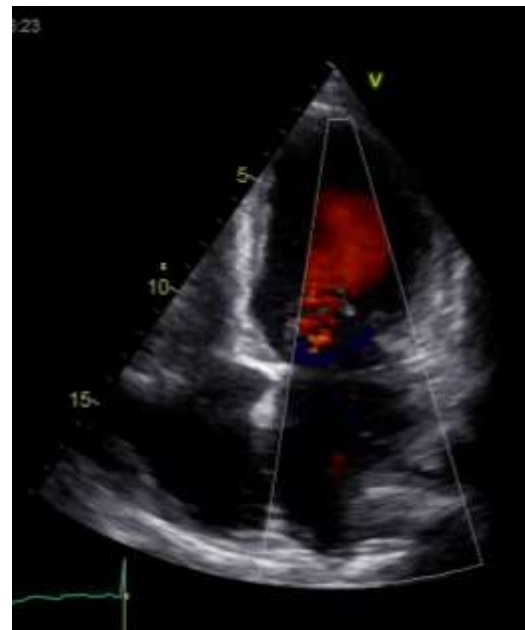
**LVEDV 170 ml**

**LVESV 115 ml**

**LVEF 32%**

**Severe MR**

**EROA 37 mm<sup>2</sup>**



## Case Report 2

**74 yo male, Non-ischemic cardiomyopathy,  
ICD, CRT-D, good GDMT  
NYHA IV**

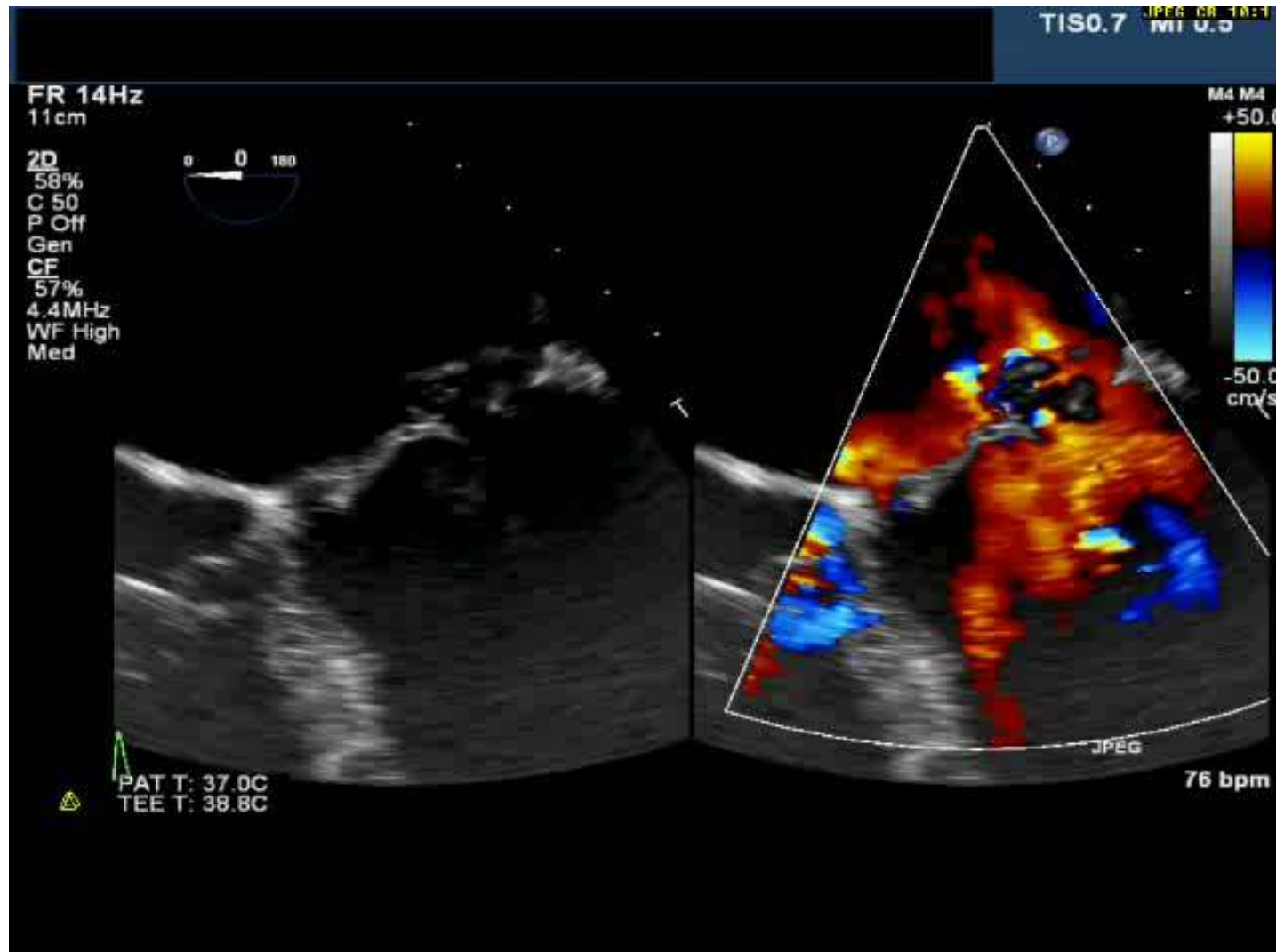
**LVEDV 505 ml  
LVESV 399 ml  
LVEF 21%  
Mod-severe MR  
EROA 22 mm<sup>2</sup>**



- **Classification, epidemiology, outcomes**
- **Indications for interventions**
  - **Primary MR**
  - **Secondary MR**

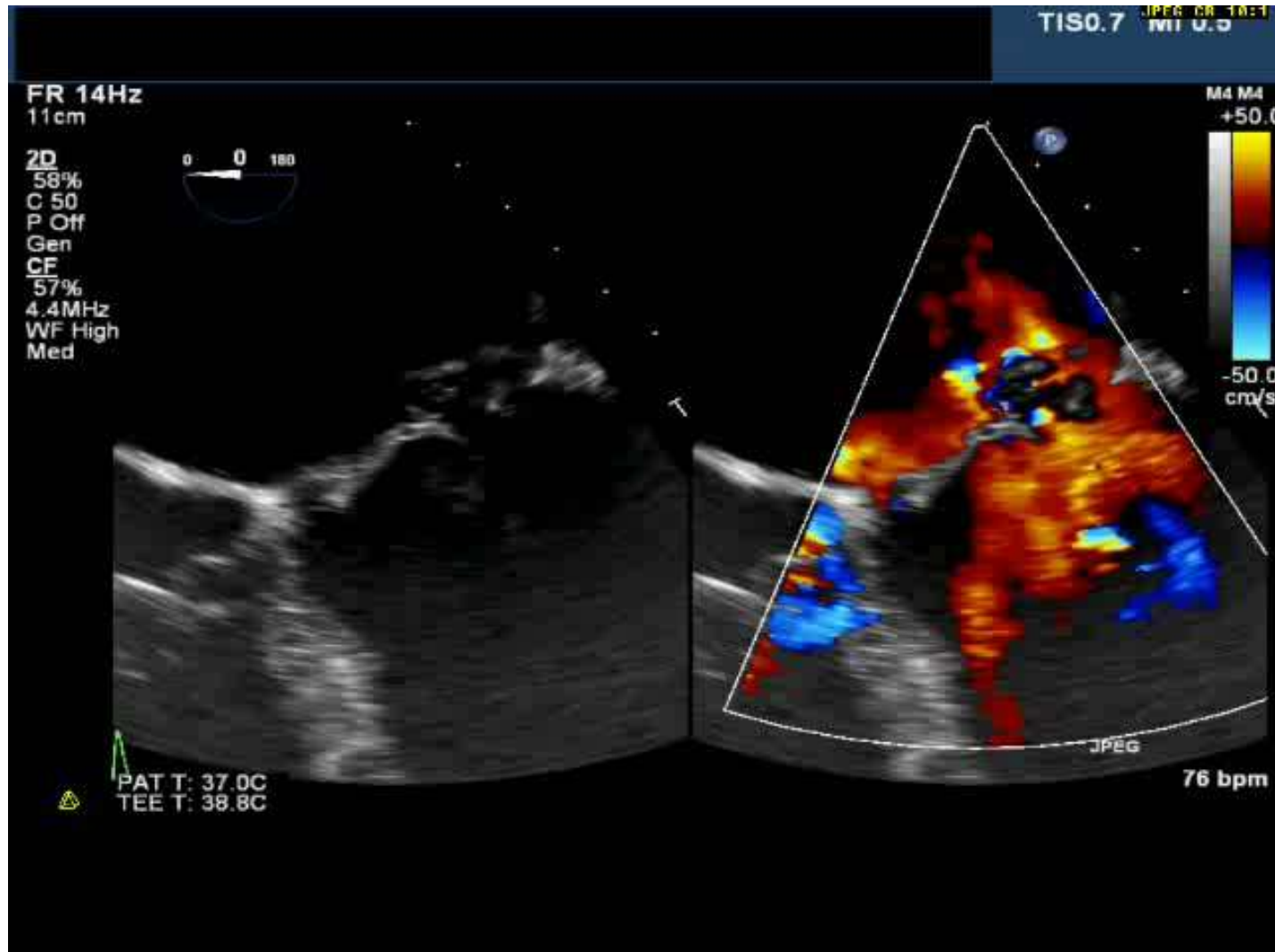
# Primary MR (Degenerative, Organic)

## Excessive motion of the leaflets



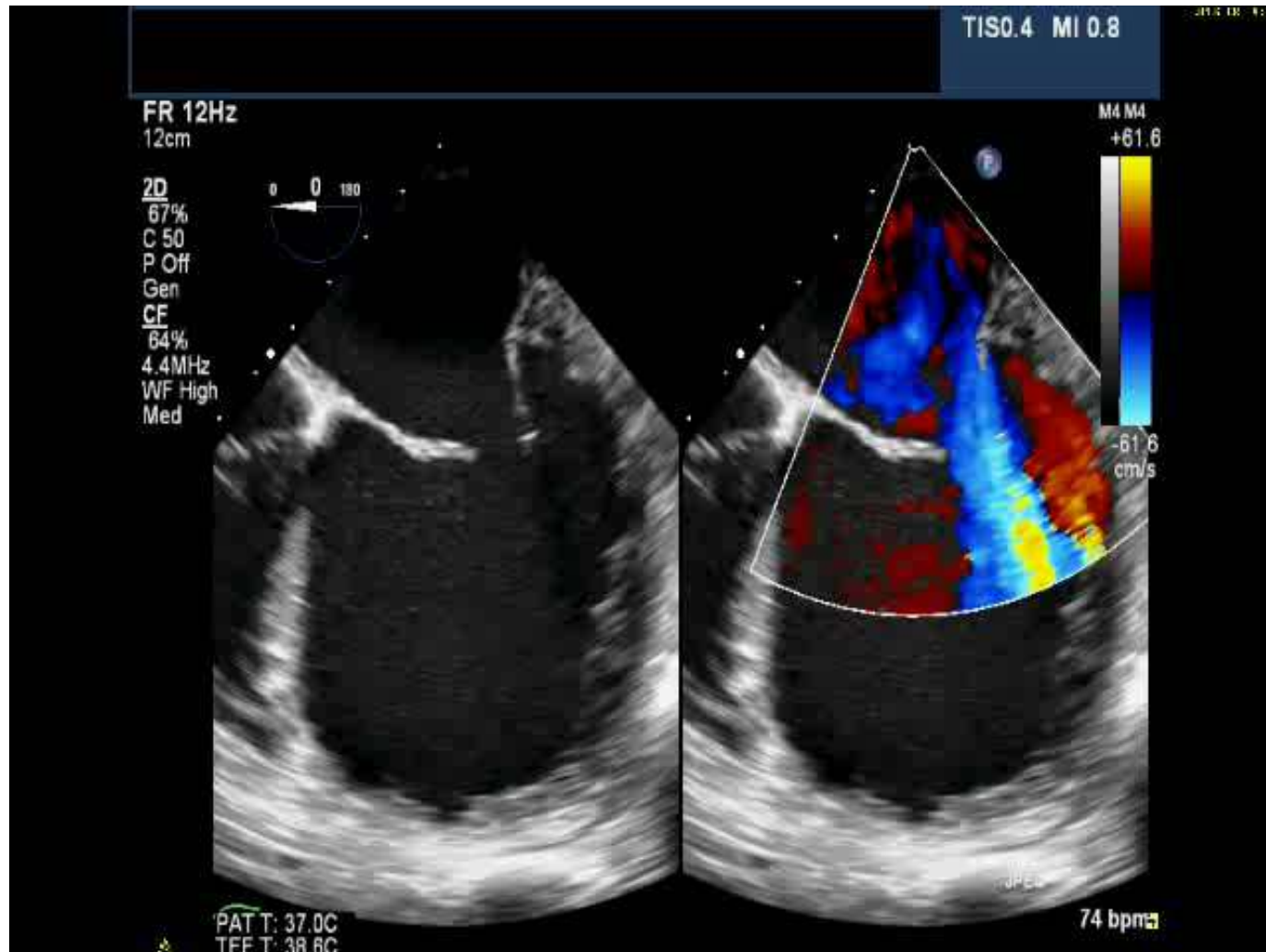
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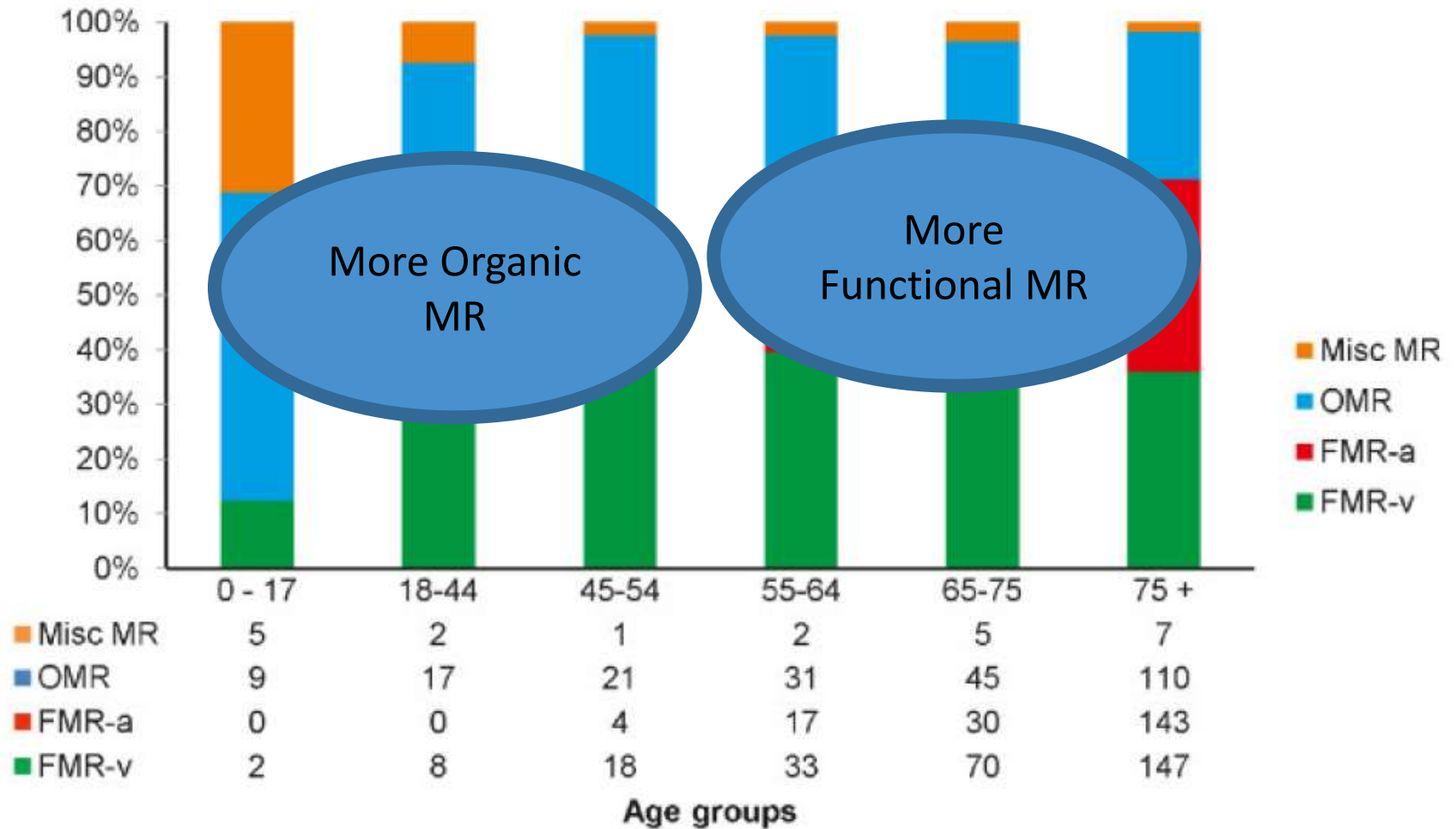
# Secondary MR (Functional)

## LV (or LA) remodeling



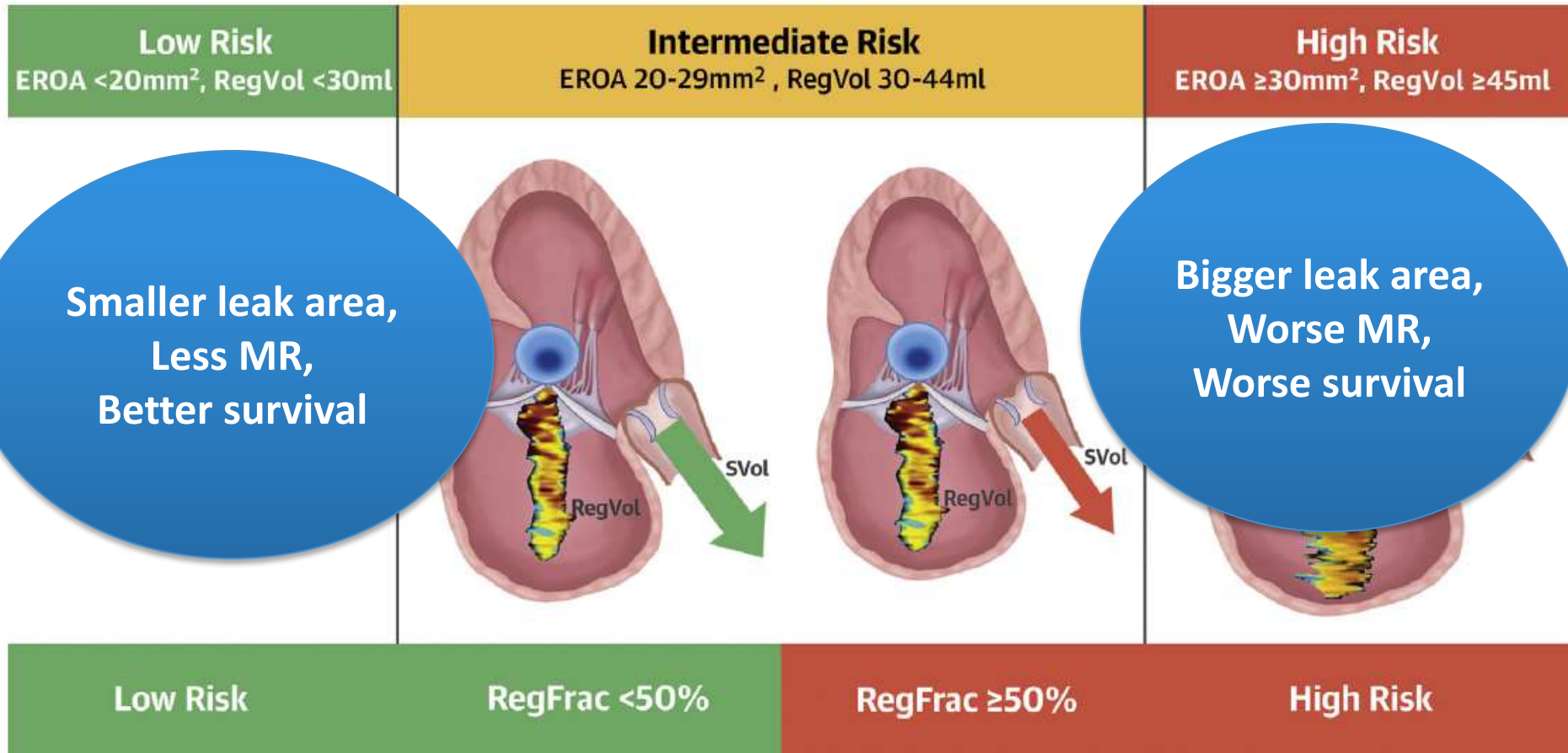


# MR Prevalence in the Community





**CENTRAL ILLUSTRATION** A Unifying Concept for the Quantitative Assessment of sMR



- Classification, epidemiology, outcomes
- ***Indications for interventions***
  - ***Primary MR***
  - Secondary MR

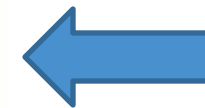
# Intervention in Primary (Degenerative) MR

Recommendations for Medical Therapy for Chronic Primary MR		
Referenced studies that support the recommendations are summarized in Online Data Supplement 29.		
COR	LOE	Recommendations
2a	B-NR	1. In symptomatic or asymptomatic patients with severe primary MR and LV systolic dysfunction (Stages C2 and D) in whom surgery is not possible or must be delayed, GDMT for systolic dysfunction is reasonable. <sup>10</sup>
3: No Benefit	B-NR	2. In asymptomatic patients with primary MR and normal LV systolic function (Stages B and C1), vasodilator therapy is not indicated if the patient is normotensive. <sup>10-12</sup>

# Intervention in Primary (Degenerative) MR

## Recommendations on indications for intervention in severe primary mitral regurgitation

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Mitral valve repair is the recommended surgical technique when the results are expected to be durable. <sup>293–296</sup>	I	B
Surgery is recommended in symptomatic patients who are operable and not high risk. <sup>293–296</sup>	I	B
Surgery is recommended in asymptomatic patients with LV dysfunction (LVESD $\geq 40$ mm and/or LVEF $< 60\%$ ). <sup>277,286,292</sup>	I	B
Surgery should be considered in asymptomatic patients with preserved LV function (LVESD $< 40$ mm and LVEF $> 60\%$ ) and AF secondary to mitral regurgitation or pulmonary hypertension <sup>c</sup> (SPAP at rest $> 50$ mmHg). <sup>285,289</sup>	IIa	B



...air should be considered in asymptomatic patients with LVEF $< 50\%$ and significant LA dilatation ( $> 40$ mm <sup>2</sup> or diameter $> 40$ mm) and in whom a Heart Valve repair is likely. <sup>285,288</sup>	IIa	B
...in symptomatic patients who meet echocardiographic criteria of eligibility, are judged inoperable or at high surgical risk by the Heart Team and for whom the procedure is not considered futile. <sup>299–302</sup>	IIb	B



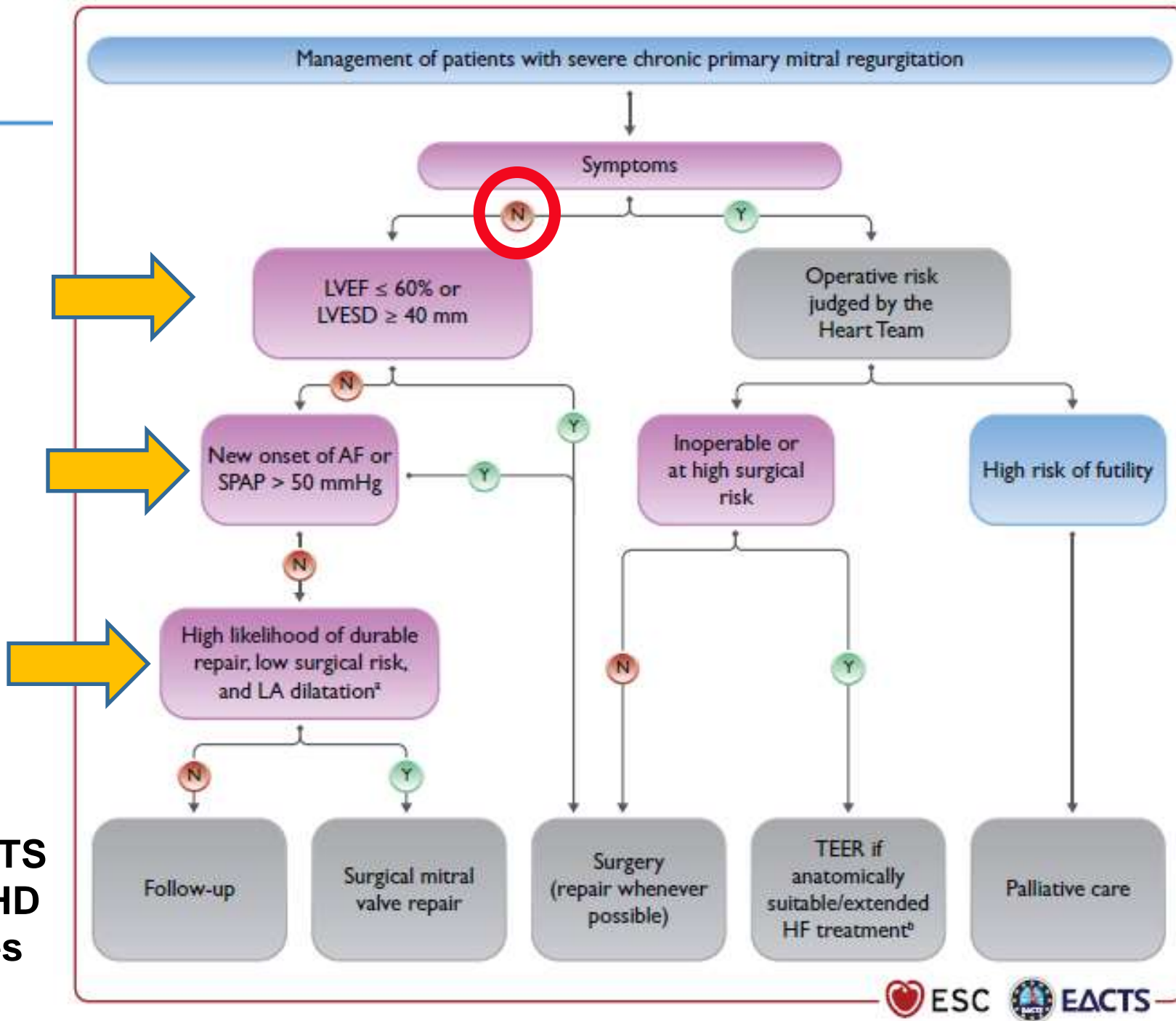
# Intervention in Primary (Degenerative) MR

## Recommendations on indications for intervention in severe primary mitral regurgitation

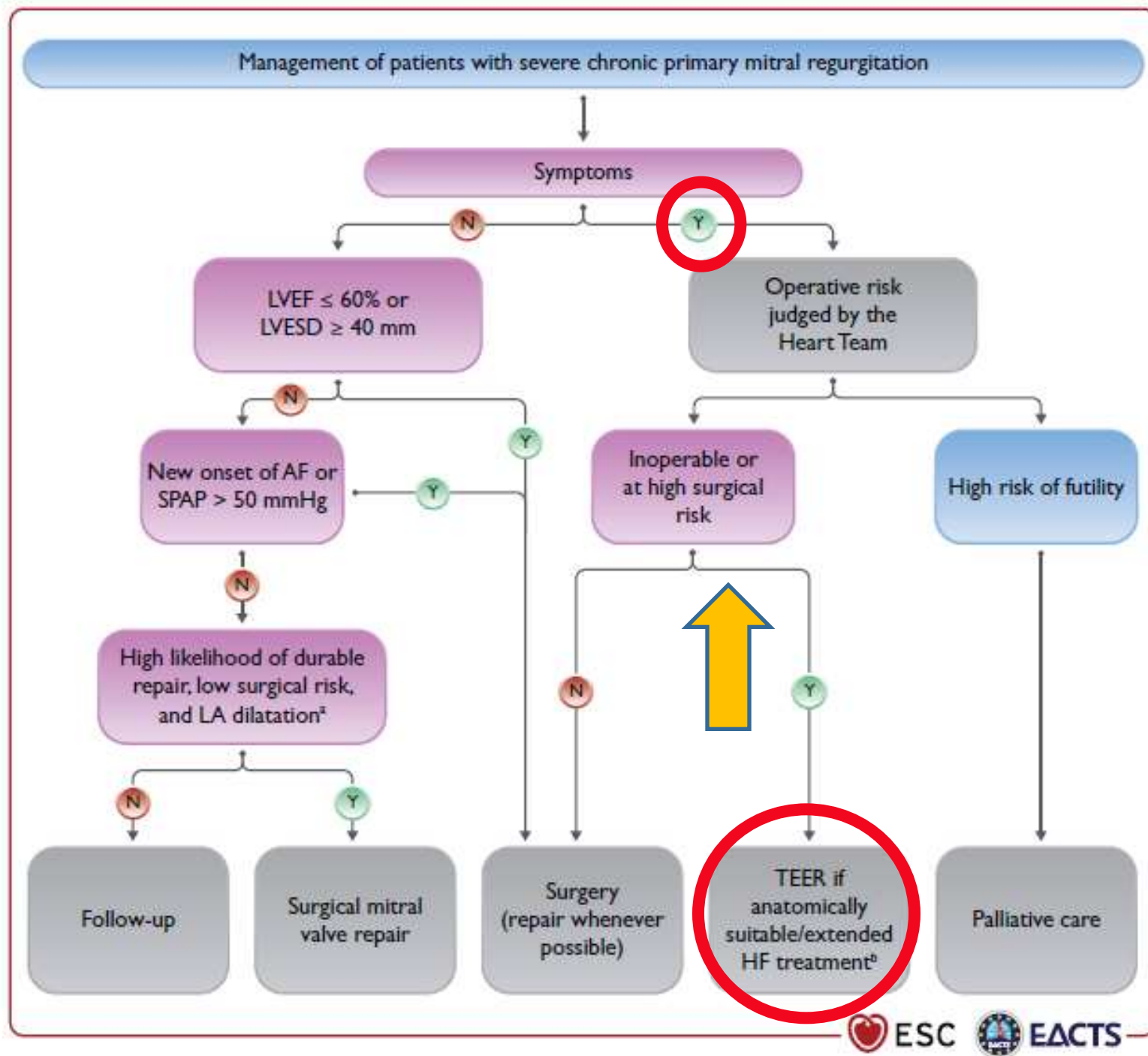
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Surgery is recommended in asymptomatic patients with LV dysfunction (LVEF ≤50% and/or LVESD ≥40 mm) and/or LVEF ≤60%. <sup>277,286,292</sup>	I	B
Surgery should be considered in asymptomatic patients with preserved LV function (LVEF >50% and LVESD <40 mm) and AF with mitral regurgitation or pulmonary hypertension (SPAP at rest >50 mmHg). <sup>285,289</sup>	IIa	B
TEER may be considered in symptomatic patients who fulfil the echocardiographic criteria of eligibility, are judged inoperable or at high surgical risk by the Heart Team and for whom the procedure is not considered futile. <sup>299–302</sup>	IIb	B

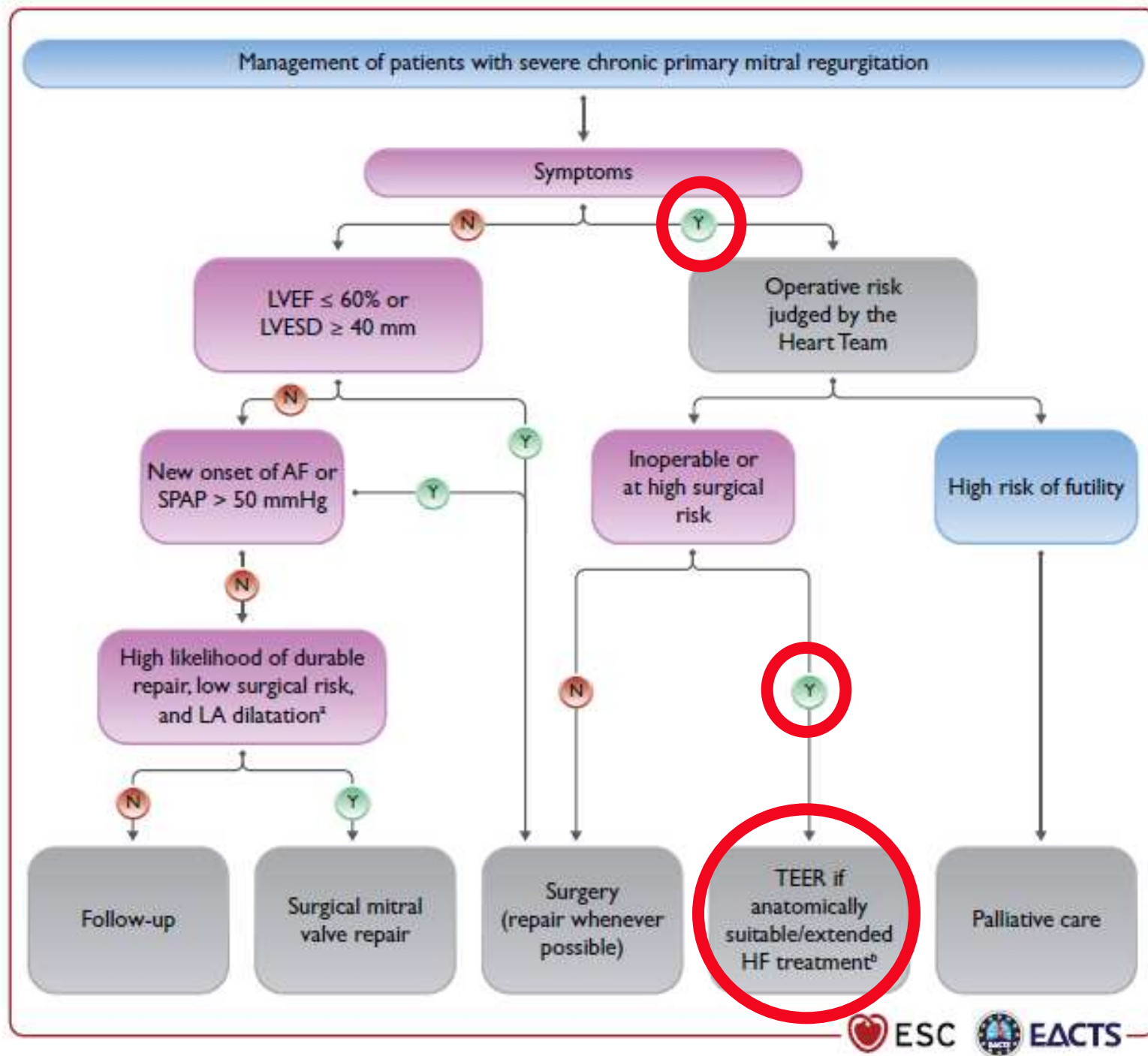
# Intervention in Primary (Degenerative) MR

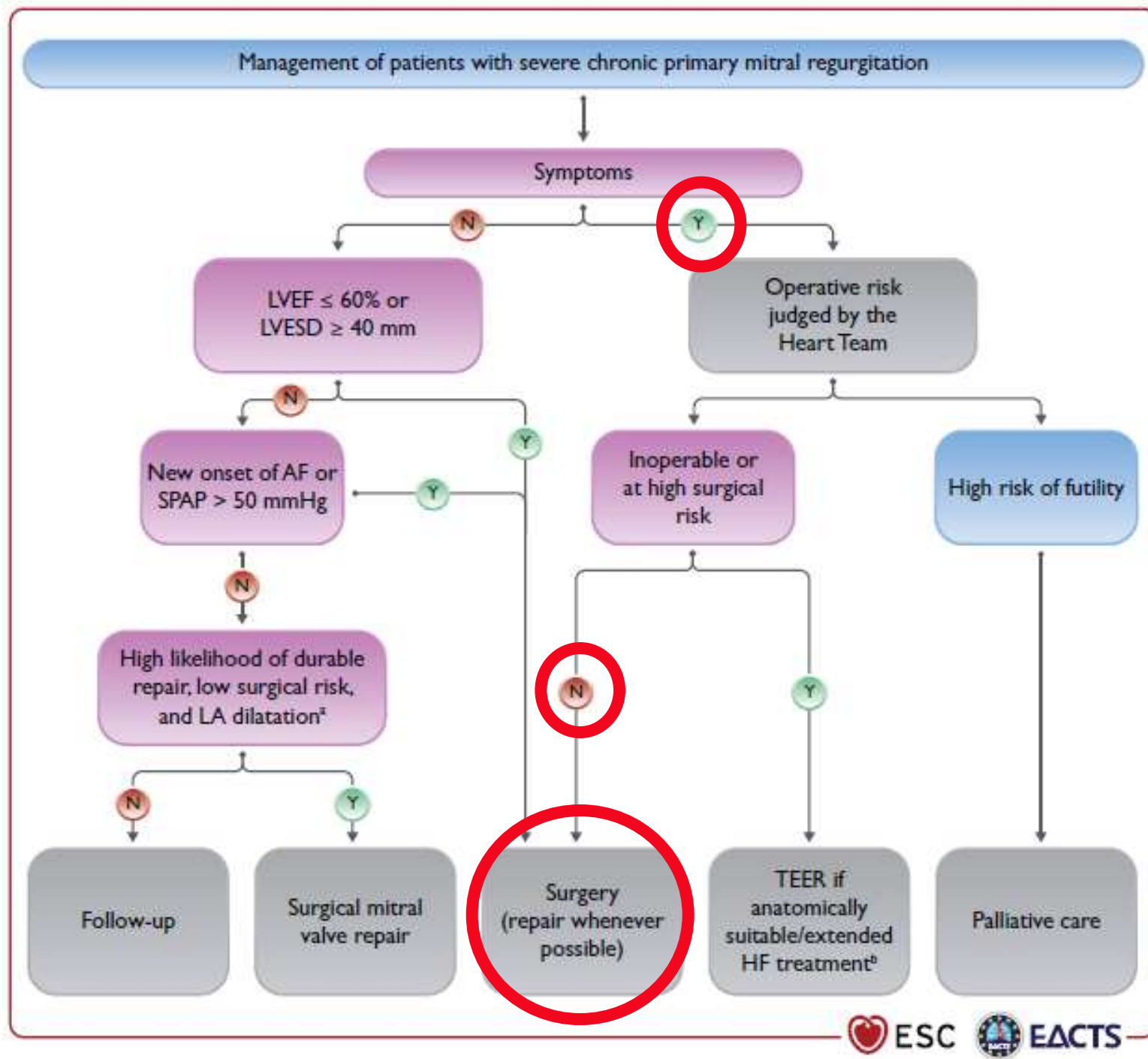
2b	C-LD	5. In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF >60% and LVESD <40 mm) (Stage C1) but with a progressive increase in LV size or decrease in EF on ≥3 serial imaging studies, mitral valve surgery may be considered irrespective of the probability of a successful and durable repair. <sup>16</sup>
2a	B-NR	6. In severely symptomatic patients (NYHA class III or IV) with primary severe MR and high or prohibitive surgical risk, transcatheter edge-to-edge repair (TEER) is reasonable if mitral valve anatomy is favorable for the repair procedure and patient life expectancy is at least 1 year. <sup>17,18</sup>
2b	B-NR	7. In asymptomatic patients with severe primary MR attributable to rheumatic valve disease, mitral valve repair may be considered at a Comprehensive Valve Center by an experienced team when surgical treatment is indicated, if a durable and successful repair is likely. <sup>19</sup>
3: Harm	B-NR	8. In patients with severe primary MR where leaflet pathology is limited to less than one half the posterior leaflet, mitral valve replacement should not be performed unless mitral valve repair has been attempted at a Primary or Comprehensive Valve Center and was unsuccessful. <sup>11-14,20-22</sup>











# Secondary MR (Functional)

## LV (or LA) remodeling





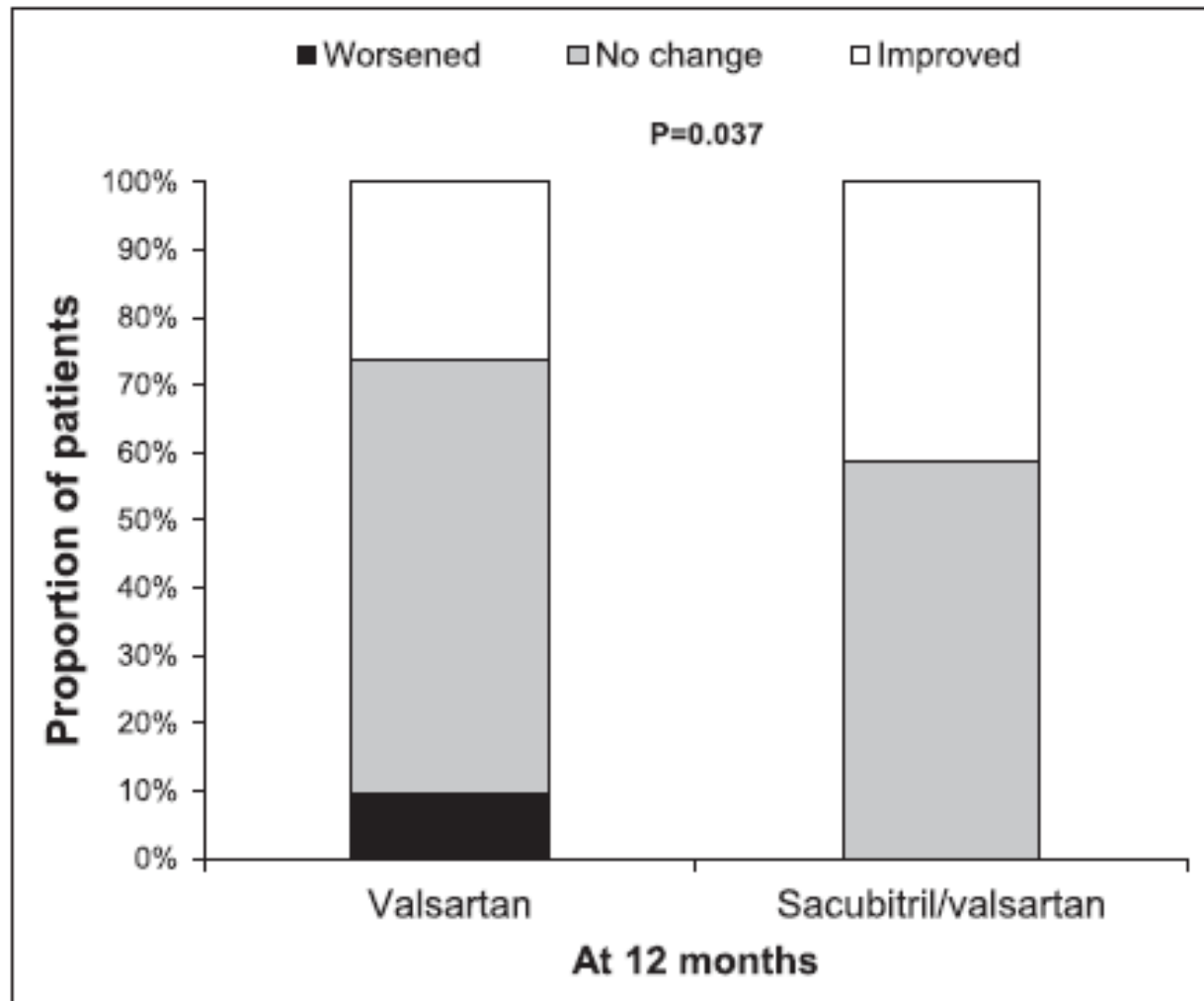
# Intervention in Secondary (Functional) MR

**Recommendations for Medical Therapy for Secondary MR**  
Referenced studies that support the recommendations are summarized in Online Data Supplement 31.

COR	LOE	Recommendations
1	A	1. Patients with chronic severe secondary MR (Stages C and D) and HF with reduced LVEF should receive standard GDMT for HF, including ACE inhibitors, ARBs, beta blockers, aldosterone antagonists, and/or sacubitril/valsartan, and biventricular pacing as indicated. <sup>1-11</sup>
1	C-EO	2. In patients with chronic severe secondary MR and HF with reduced LVEF, a cardiologist expert in the management of patients with HF and LV systolic dysfunction should be the primary MDT member responsible for implementing and monitoring optimal GDMT. <sup>9,12</sup>

# Effect of Sacubitril/Valsartan on Secondary MR

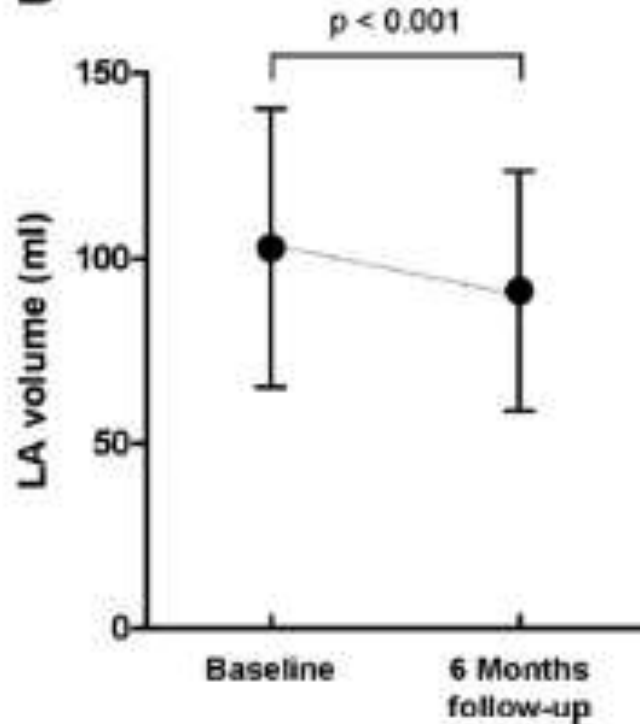
- 118 pts w mod-severe FMR, EF  $34 \pm 7\%$ , randomized to sacubitril/valsartan vs valsartan, 12 months follow-up



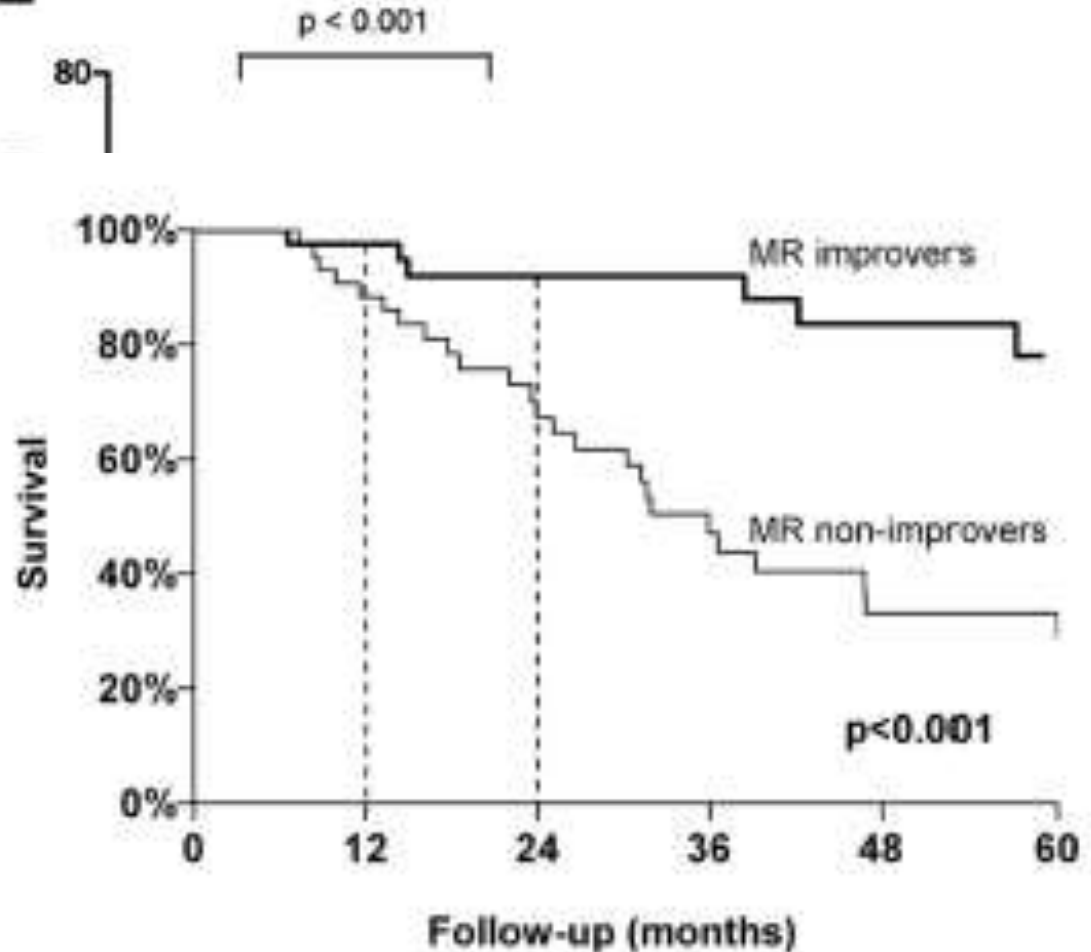
# Effect of CRT on Secondary MR

- 98 pts w mod-severe FMR, EF  $23 \pm 7\%$ , QRSd  $166 \pm 29$  ms  $\Rightarrow$  CRT
- 49% improved MR at 6 months by echo

**D**



**E**





# Intervention in Secondary (Functional) MR

## Recommendations on indications for mitral valve intervention in chronic severe secondary mitral regurgitation<sup>a</sup>

Recommendations	Class <sup>b</sup>	Level <sup>c</sup>
Valve surgery/intervention is recommended only in patients with severe SMR who remain symptomatic despite GDMT (including CRT if indicated) and has to be decided by a structured collaborative Heart Team. <sup>247,323,336,337</sup>	<b>I</b>	<b>B</b>
<b>Patients with concomitant coronary artery or other cardiac disease requiring treatment</b>		
Valve surgery is recommended in patients undergoing CABG or other cardiac surgery. <sup>329,330,333</sup>	<b>I</b>	<b>B</b>
In symptomatic patients, who are judged not appropriate for surgery by the Heart Team on the basis of their individual characteristics, <sup>d</sup> PCI (and/or TAVI) possibly followed by TEER (in case of persisting severe SMR) should be considered.	<b>IIa</b>	<b>C</b>

<b>Patients without concomitant coronary artery or other cardiac disease requiring treatment</b>		
TEER should be considered in selected symptomatic patients, not eligible for surgery and fulfilling criteria suggesting an increased chance of responding to the treatment. <sup>337,338,356,357 e</sup>	<b>IIa</b>	<b>B</b>
Valve surgery may be considered in symptomatic patients judged appropriate for surgery by the Heart Team.	<b>IIb</b>	<b>C</b>
In high-risk symptomatic patients not eligible for surgery and not fulfilling the criteria suggesting an increased chance of responding to TEER, the Heart Team may consider in selected cases a TEER procedure or other transcatheter valve therapy if applicable, after careful evaluation for ventricular assist device or heart transplant. <sup>e</sup>	<b>IIb</b>	<b>C</b>

**ESC/EACTS Valvular HD Guidelines 2021**

# Intervention in Secondary (Functional) MR

Recommendations on indications for mitral valve intervention in chronic severe secondary mitral regurgitation

Recommendations	Class
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Patients with concomitant coronary artery or other disease requiring treatment	
Valve surgery is recommended in patients undergoing CABG or other cardiac surgery. <sup>329,330,333</sup>	I
In symptomatic patients, who are judged not appropriate for surgery by the Heart Team on the basis of their individual characteristics, <sup>d</sup> PCI (and/or TAVI) possibly followed by TEER (in case of persisting severe SMR) should be considered.	IIb

Patients without concomitant coronary artery or other cardiac

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TEER should be considered in selected symptomatic patients, not eligible for surgery and fulfilling criteria suggesting an increased chance of responding to the treatment.<sup>337,338,356,357 e</sup>

IIa

B

Valve surgery may be considered in symptomatic patients judged appropriate for surgery by the Heart Team.

IIb

C

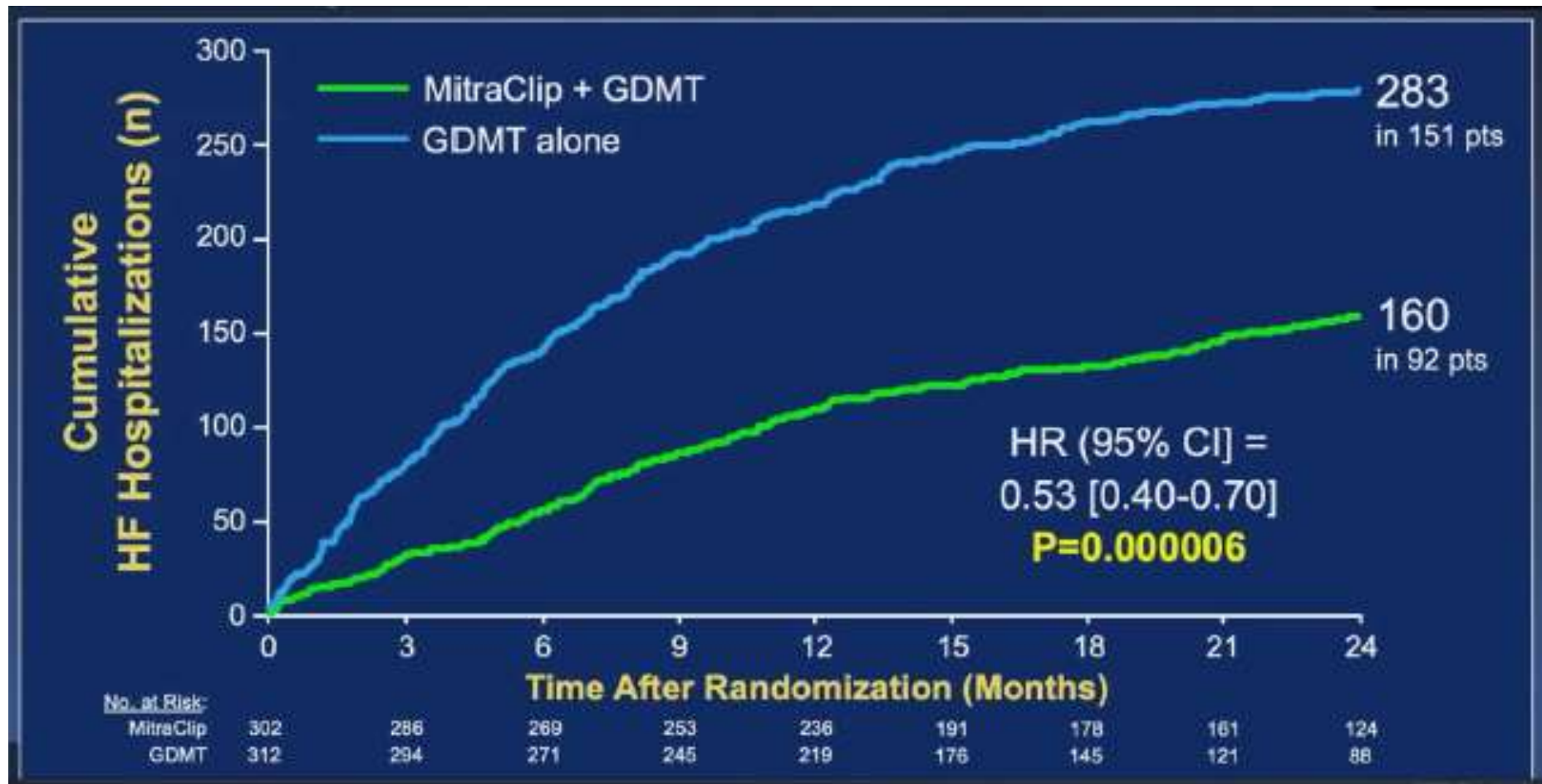
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IIb

C

# COAPT Primary Endpoint: All-HF Hospitalizations Within 24 Months

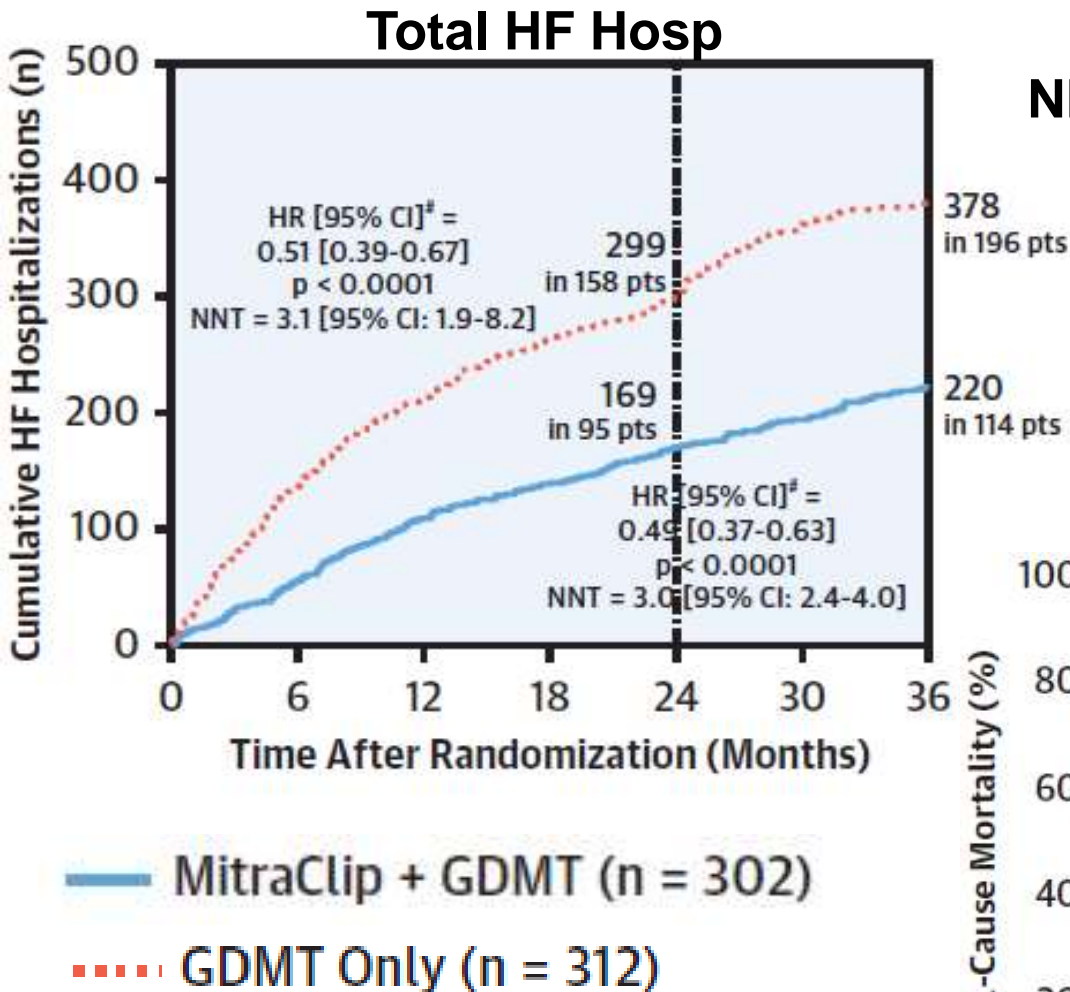
- 614 pts w 3-4+ secondary MR, EF 20-50%, LVESD $\leq$ 7 cm
- HF sx despite max GDMT
- Rand to GDMT or MitraClip + GDMT



Stone et al. NEJM 2018



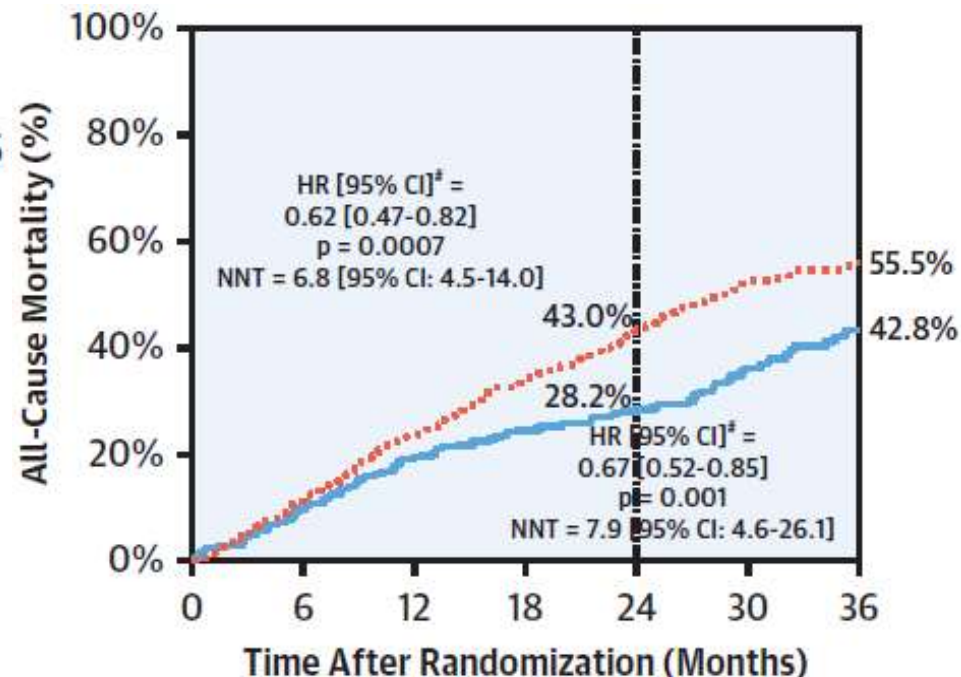
# COAPT: 3 Year Outcomes



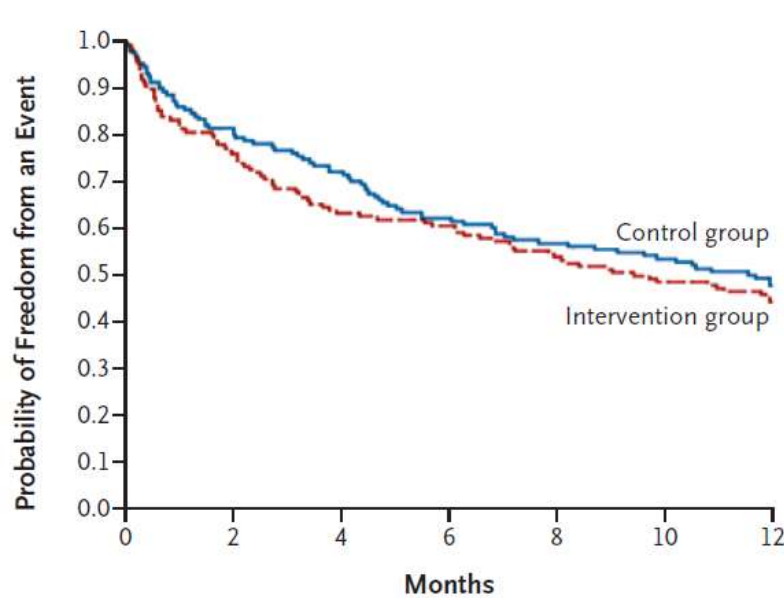
**NNT = 3**

**NNT = 8**

## All-cause Mortality



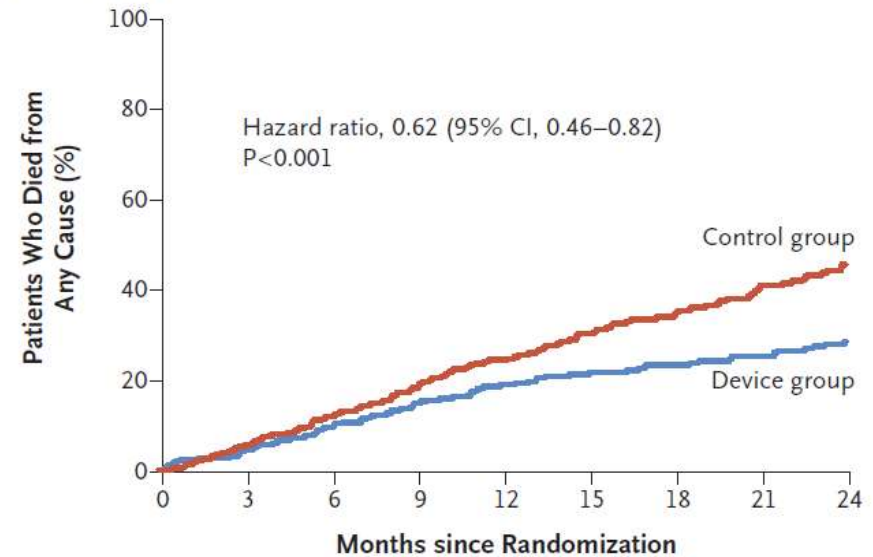
# MitraClip Trials and Survival



No. at Risk							
Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

**MITRA-FR**  
**Obadia et al NEJM 2018**

Death from Any Cause



No. at Risk									
Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

**COAPT**  
**Stone et al NEJM 2018**

# Case Report 1

**79 yo male, Ischemic CMP**

**Admitted with acute HF 3 times in last year**

**Hx CABG: 3-VD (no options for revascularization)**

**Good GDMT**

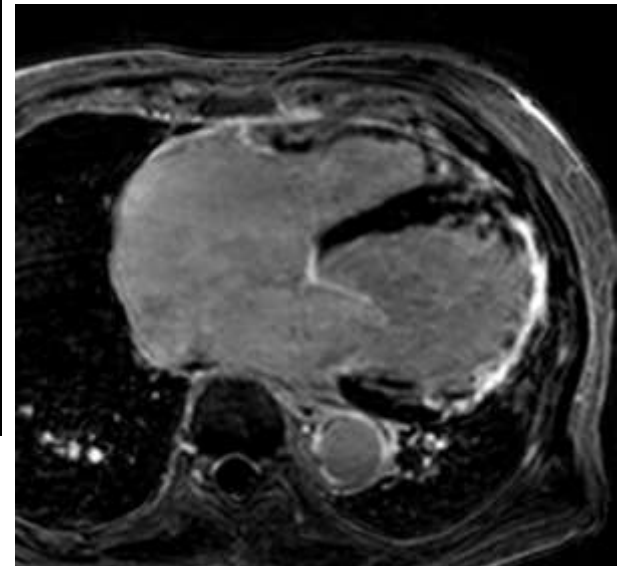
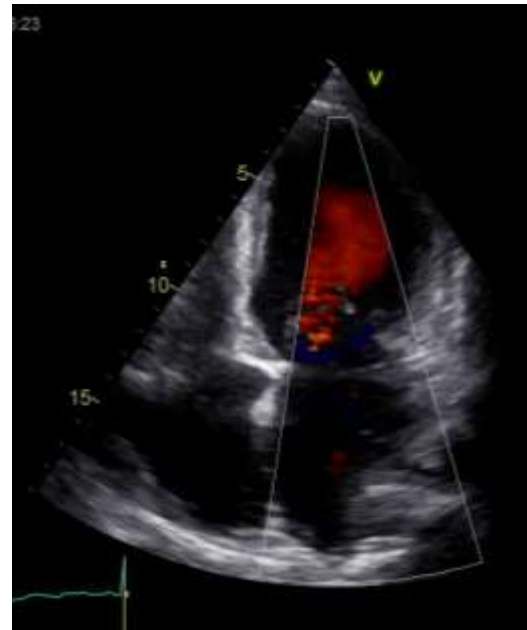
**LVEDV 170 ml**

**LVESV 115 ml**

**LVEF 32%**

**Severe MR**

**EROA 37 mm<sup>2</sup>**



## 2 MitraClip implantations, NYHA I No more admissions



**LVEDV 161 ml**  
**LVESV 116 ml**  
**LVEF 28%**



## Case Report 2

**74 yo male, Non-ischemic cardiomyopathy,  
ICD, CRT-D, good GDMT  
NYHA IV**

**LVEDV 505 ml  
LVESV 399 ml  
LVEF 21%  
Mod-severe MR  
EROA 22 mm<sup>2</sup>**



**MitraClip implantation  
NYHA IV  
Patient died at 9 months of follow-up**

**6 months after  
MitraClip  
LVEDV 446 ml  
LVESV 399 ml  
LVEF 11%**



# **WHY ARE THESE 2 PATIENTS DIFFERENT?**

# COAPT vs Mitra-FR: Why Different Results?

	MITRA-FR (n=304)	COAPT (n=614)
Severe MR entry criteria	Severe FMR by EU guidelines: EROA >20 mm <sup>2</sup> or RV >30 mL/beat	Severe FMR by US guidelines: EROA >30 mm <sup>2</sup> or RV >45 mL/beat or PSVFR or other
EROA (mean ± SD)	31 ± 10 mm <sup>2</sup>	41 ± 15 mm <sup>2</sup>
LVEDV (mean ± SD)	135 ± 35 mL/m <sup>2</sup>	101 ± 34 mL/m <sup>2</sup>
GDMT at baseline and FU	Receiving HF meds at baseline – allowed variable adjustment in each group during follow-up per “real-world” practice	CEC confirmed pts were failing maximally-tolerated GDMT at baseline – few major changes during follow-up
Acute results: No clip / ≥3+ MR	9% / 9%	5% / 5%
Procedural complications*	14.6%	8.5%
12-mo MitraClip MR ≤2+ / ≥3+	83% / 17%	95% / 5%

Adapted from Stone, G

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Acute results: No clip / ≥3+ MR	0% / 0%	5% / 5%
Procedural complications*	14.6%	8.5%
12-mo MitraClip MR ≤2+ / ≥3+	83% / 17%	95% / 5%

Adapted from Stone, G

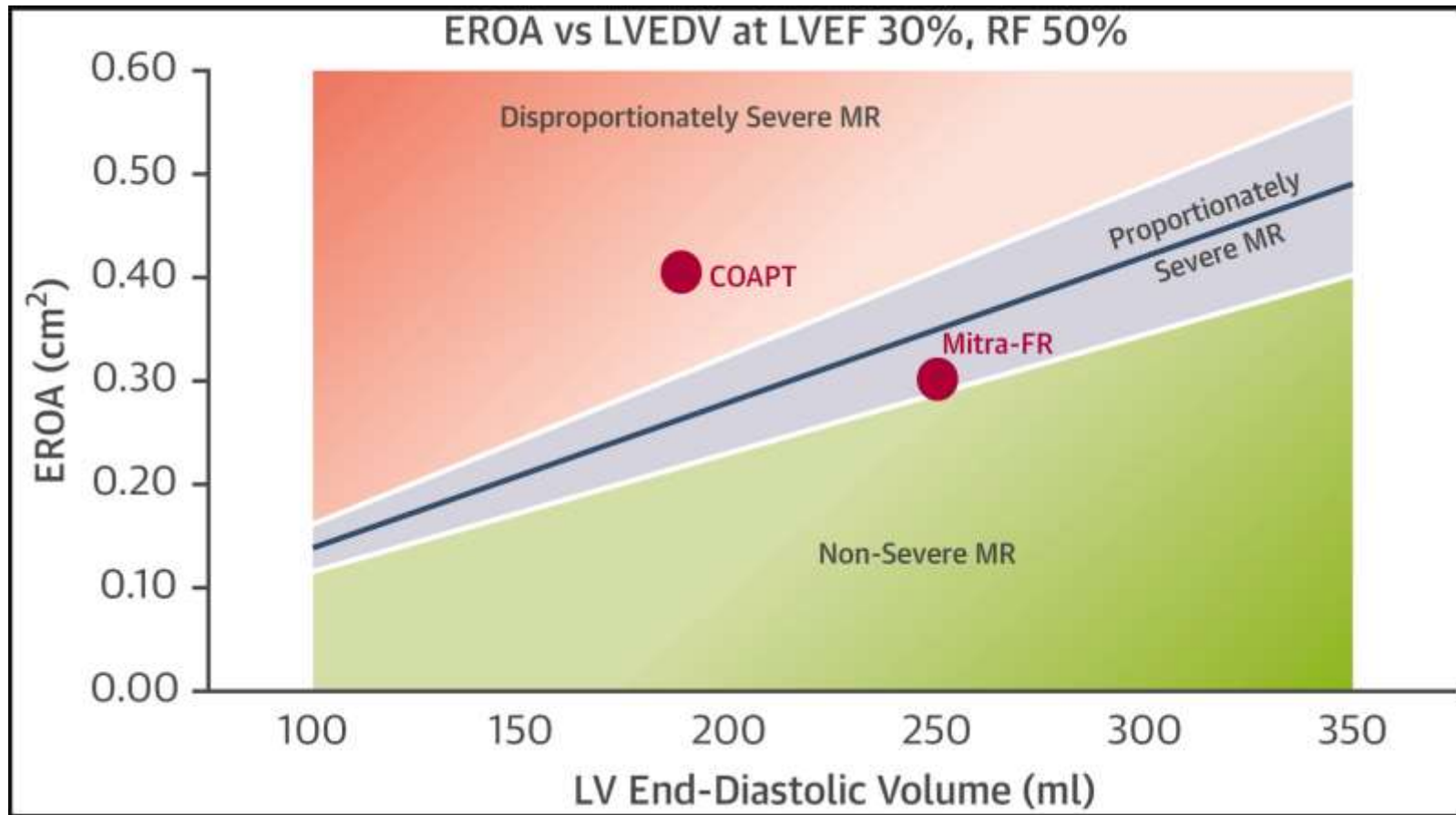


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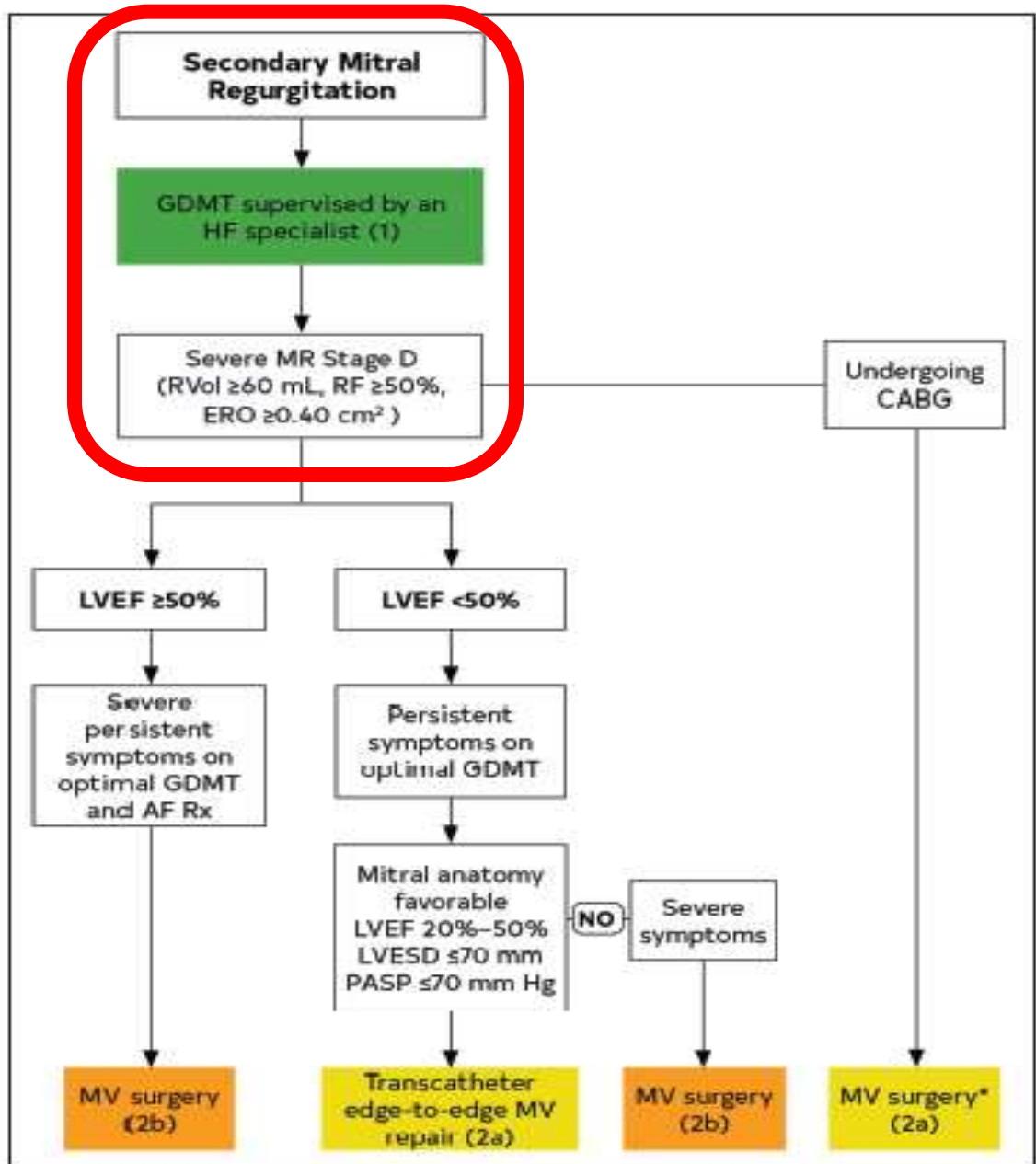
Adapted from Stone, G

# “Proportionate” vs “Disproportionate” MR

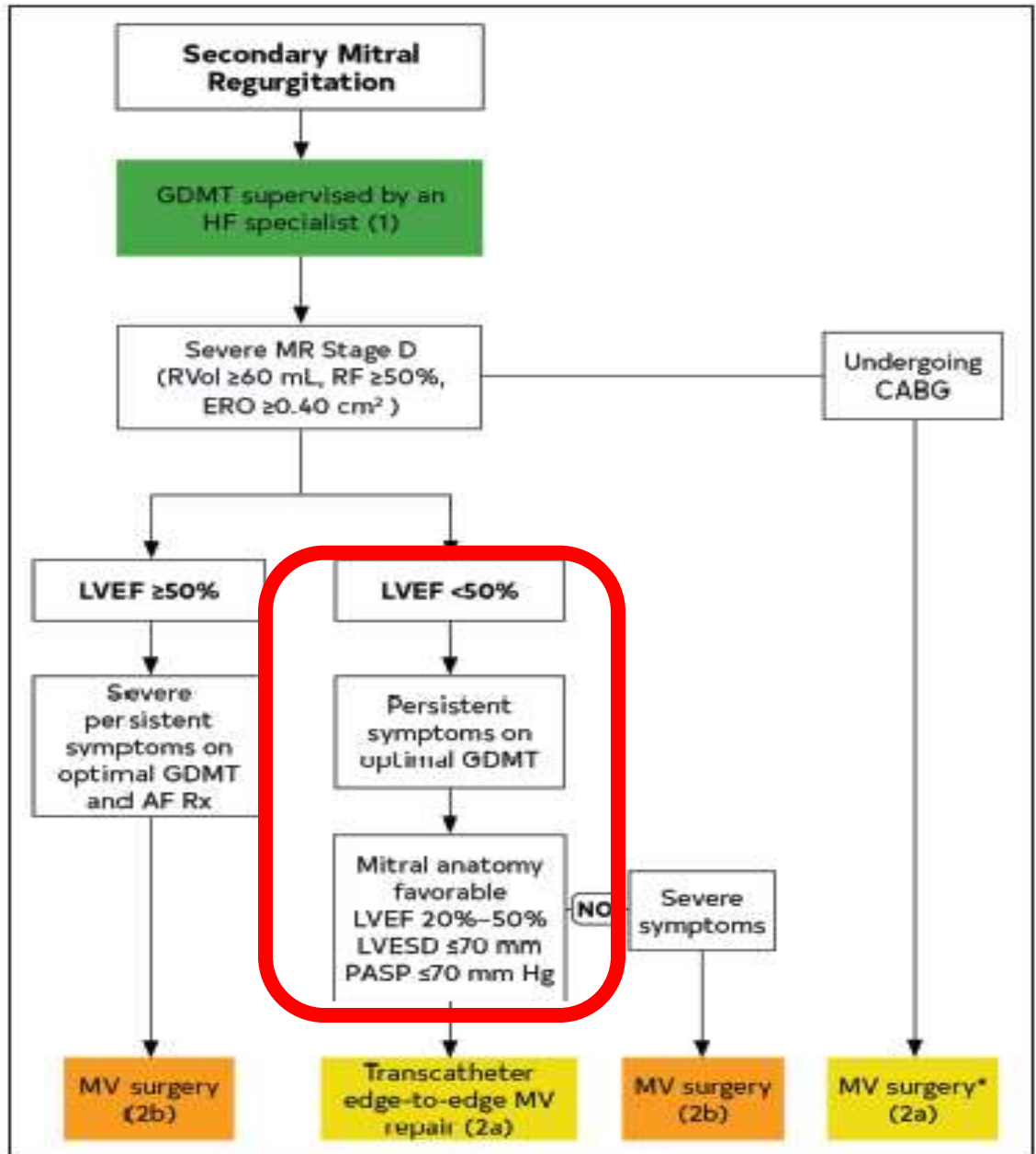




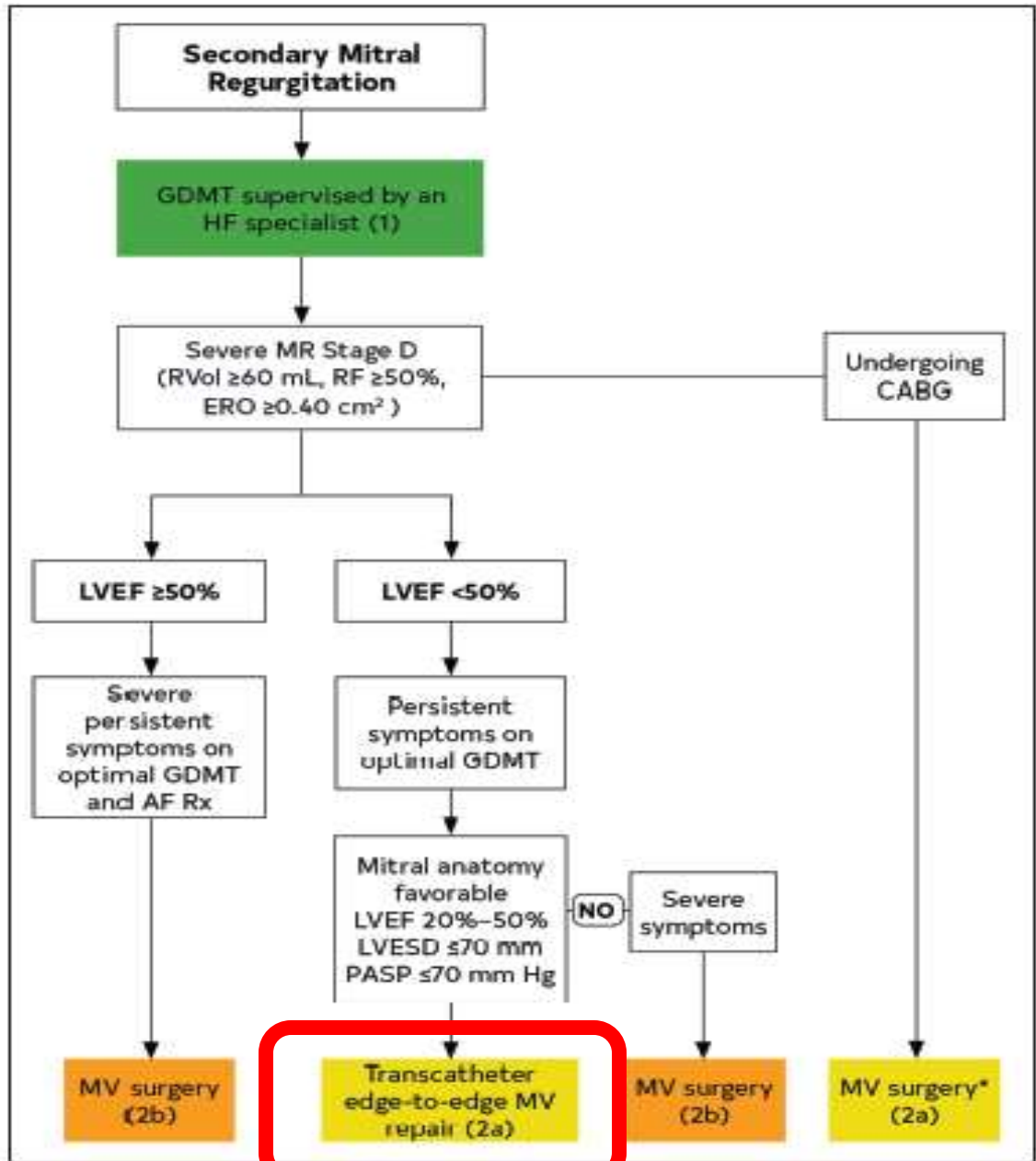
# Intervention in Secondary (Functional) MR



# Intervention in Secondary (Functional) MR



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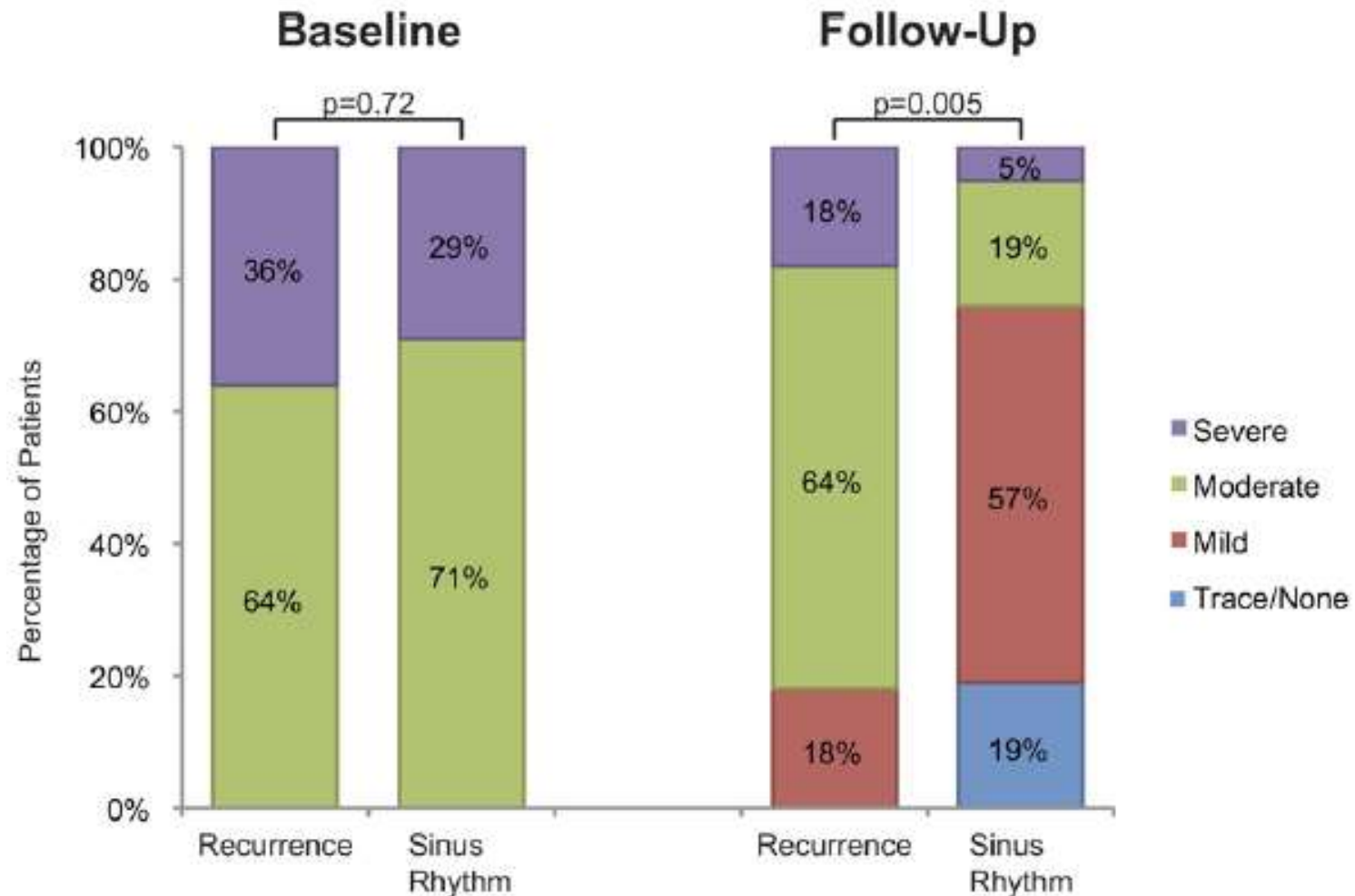


# Atrial FMR

Secondary Mitral Regurgitation	Atrial Functional Mitral Regurgitation
<b>Etiology and Prevalence</b> <ul style="list-style-type: none"> <li>• 11%-59% post myocardial infarction</li> <li>• &gt;50% in dilated cardiomyopathy</li> </ul>	<ul style="list-style-type: none"> <li>• 6%-7% in lone AF</li> <li>• Up to 53% in HFpEF</li> </ul>
<b>Diagnosis</b> <ul style="list-style-type: none"> <li>• Systolic LV dysfunction</li> <li>• Restricted leaflet motion and tethering</li> <li>• Eccentric jet &gt; central jet</li> <li>• Relative LA dilation</li> </ul>	<ul style="list-style-type: none"> <li>• Normal systolic LV function</li> <li>• Normal leaflet motion</li> <li>• Central jet</li> <li>• Severe LA dilation</li> </ul>
<b>Management</b> <ul style="list-style-type: none"> <li>• Optimal HF therapy</li> <li>• Cardiac resynchronization therapy</li> <li>• Revascularization</li> <li>• MitraClip</li> </ul>	<ul style="list-style-type: none"> <li>• Address AF/HFpEF risk factors and lifestyle</li> <li>• HF therapy, diuretics as indicated</li> <li>• Early sinus restoration strategy</li> <li>• ?Intervention, annuloplasty, MitraClip</li> </ul>

# Effect of Restoration of SR in Atrial Functional MR

- 53 pts w Afib scheduled for ablation and mod-severe atrial FMR
- Echo at 12 months in those with successful SR vs Recurrent Afib





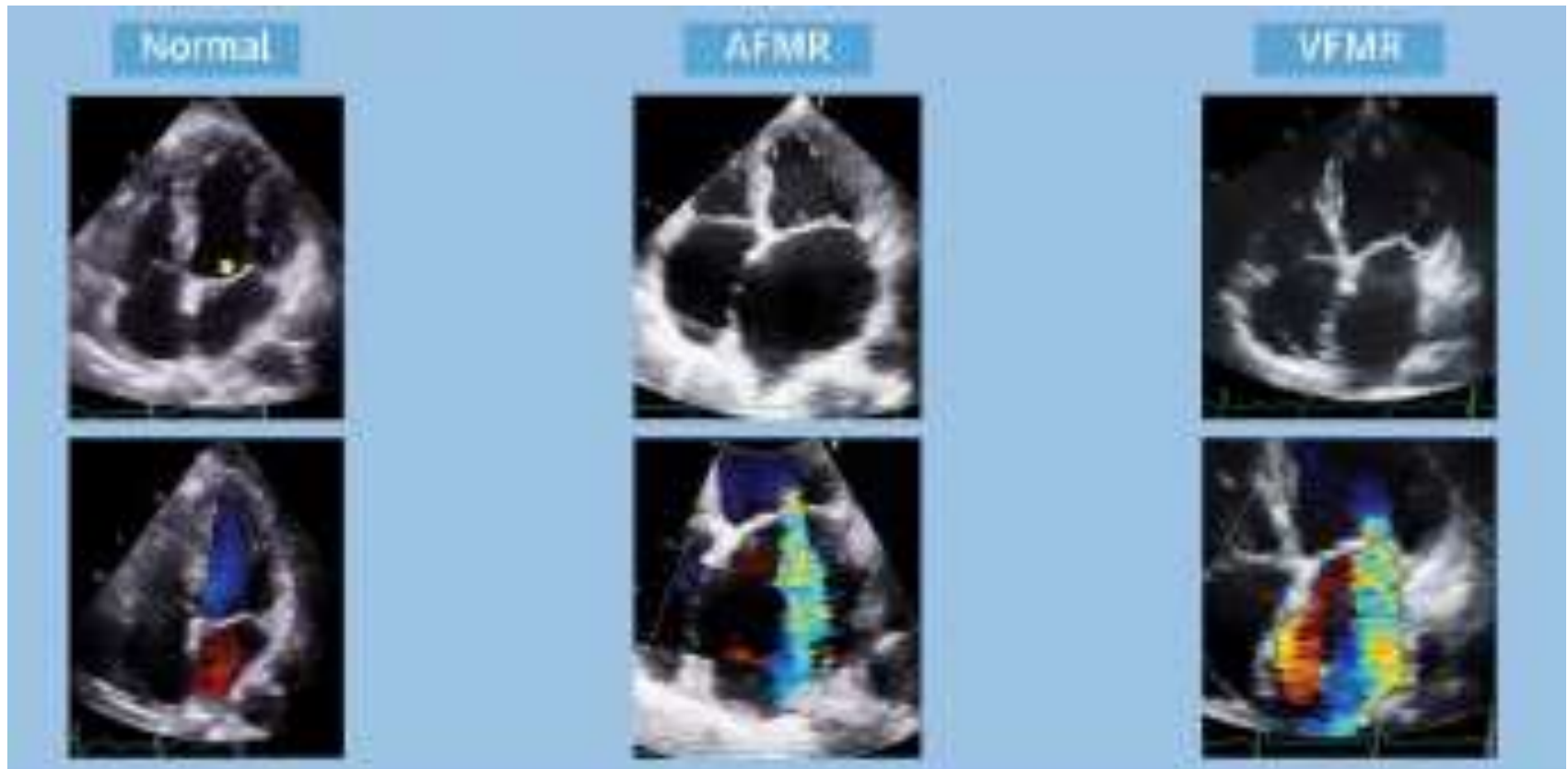
# Intervention in Secondary (Functional) MR

2b	B-NR	3. In patients with chronic severe secondary MR from atrial annular dilation with preserved LV systolic function (LVEF $\geq 50\%$ ) who have severe persistent symptoms (NYHA class III or IV) despite therapy for HF and therapy for associated AF or other comorbidities (Stage D), mitral valve surgery may be considered. <sup>16-20</sup>
2b	B-NR	4. In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF $< 50\%$ ) who have persistent severe symptoms (NYHA class III or IV) while on optimal GDMT for HF (Stage D), mitral valve surgery may be considered. <sup>9,12,21-43</sup>
2b	B-R	5. In patients with CAD and chronic severe secondary MR related to LV systolic dysfunction (LVEF $< 50\%$ ) (Stage D) who are undergoing mitral valve surgery because of severe symptoms (NYHA class III or IV) that persist despite GDMT for HF, chordal-sparing mitral valve replacement may be reasonable to choose over downsized annuloplasty repair. <sup>9,12,21-32,44-47</sup>

- **Classification, epidemiology, outcomes**
- **Indications for interventions**
  - **Primary MR**
  - **Secondary MR**



# Atrial FMR



Zoghbi et al. JACC Img 2022





# Carpentier Classification



**Type I**



**Type II**



**Type IIIa**



**Type IIIb**

## Etiology

**Atrial Functional MR**  
AF, annular and LA dilation

**MVP**  
Flail leaflet

**Rheumatic Disease**  
Radiation

**Ischemic CM**  
Dilated CM

Legend: The Carpentier Classification defines mitral regurgitation (MR) in relation to mitral leaflet motion. Type I signifies normal motion ( as in atrial functional MR), Type II excessive motion (prolapse/flail) and Type III restricted motion (secondary MR due to underlying cardiomyopathy). Adapted from reference 4.

# Intervention in Primary (Degenerative) MR

Recommendations for Intervention for Chronic Primary MR		
Referenced studies that support the recommendations are summarized in Online Data Supplement 10.		
COR	LOE	Recommendations
1	B-NR	1. In symptomatic patients with severe primary MR (Stage D), mitral valve intervention is recommended irrespective of LV systolic function. <sup>1,2</sup>
1	B-NR	2. In asymptomatic patients with severe primary MR and LV systolic dysfunction (LVEF ≤60%, LVESD ≥40 mm) (Stage C2), mitral valve surgery is recommended. <sup>3-10</sup>
1	B-NR	3. In patients with severe primary MR for whom surgery is indicated, mitral valve repair is recommended in preference to mitral valve replacement when the anatomic cause of MR is degenerative disease, if a successful and durable repair is possible. <sup>11-15</sup>
2a	B-NR	4. In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF ≥60% and LVESD ≤40 mm) (Stage C1), mitral valve repair is reasonable when the likelihood of a successful and durable repair without residual MR is >95% with an expected mortality rate of <1%, when it can be performed at a Primary or Comprehensive Valve Center. <sup>4,13,16</sup>

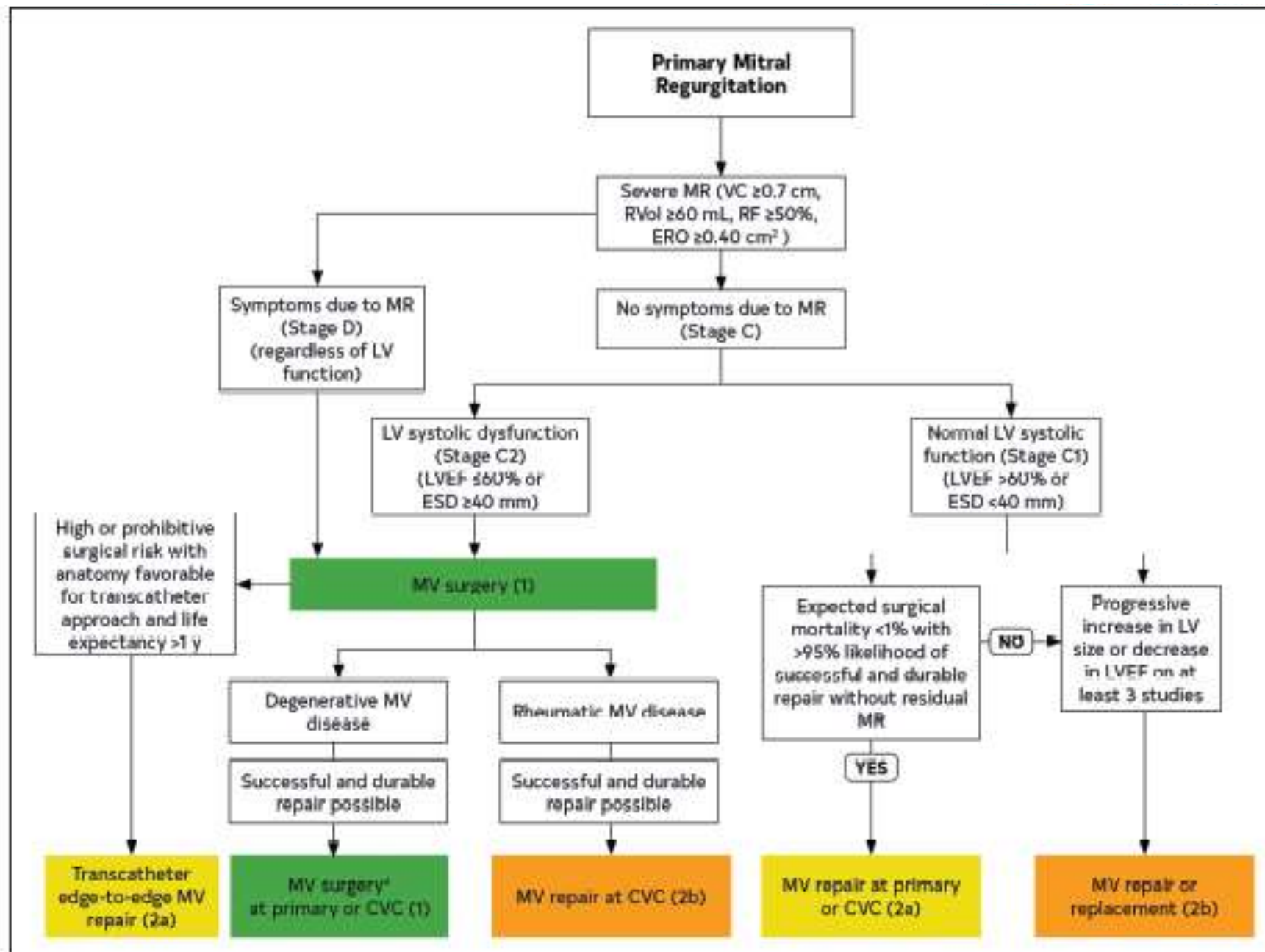
2b	C-LD	5. In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF >60% and LVESD <40 mm) (Stage C1) but with a progressive increase in LV size or decrease in EF on ≥3 serial imaging studies, mitral valve surgery may be considered irrespective of the probability of a successful and durable repair. <sup>16</sup>
2a	B-NR	6. In severely symptomatic patients (NYHA class III or IV) with primary severe MR and high or prohibitive surgical risk, transcatheter edge-to-edge repair (TEER) is reasonable if mitral valve anatomy is favorable for the repair procedure and patient life expectancy is at least 1 year. <sup>17,18</sup>
2b	B-NR	7. In symptomatic patients with severe primary MR attributable to rheumatic valve disease, mitral valve repair may be considered at a Comprehensive Valve Center by an experienced team when surgical treatment is indicated, if a durable and successful repair is likely. <sup>19</sup>
3: Harm	B-NR	8. In patients with severe primary MR where leaflet pathology is limited to less than one half the posterior leaflet, mitral valve replacement should not be performed unless mitral valve repair has been attempted at a Primary or Comprehensive Valve Center and was unsuccessful. <sup>11-14,20-22</sup>

# Intervention in Primary (Degenerative) MR

Recommendations for Intervention for Chronic Primary MR		
Referenced studies that support the recommendations are summarized in Online Data Supplement 10.		
COR	LOE	Recommendations
1	B-NR	1. In symptomatic patients with severe primary MR (Stage D), mitral valve intervention is recommended irrespective of LV systolic function. <sup>1,2</sup>
1	B-NR	2. In asymptomatic patients with severe primary MR and LV systolic dysfunction (LVEF $\leq$ 60%, LVESD $\geq$ 40 mm) (Stage C2), mitral valve surgery is recommended. <sup>3-10</sup>
1	B-NR	3. In patients with severe primary MR for whom surgery is indicated, mitral valve repair is recommended in preference to mitral valve replacement when the anatomic cause of MR is degenerative disease, if a successful and durable repair is possible. <sup>11-15</sup>
2a	B-NR	4. In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF $\geq$ 60% and LVESD $\leq$ 40 mm) (Stage C1), mitral valve repair is reasonable when the likelihood of a successful and durable repair without residual MR is $>$ 95% with an expected mortality rate of $<$ 1%, when it can be performed at a Primary or Comprehensive Valve Center. <sup>4,13,16</sup>

2b	C-LD	5. In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF $>$ 60% and LVESD $<$ 40 mm) (Stage C1) but with a progressive increase in LV size or decrease in EF on $\geq$ 3 serial imaging studies, mitral valve surgery may be considered irrespective of the probability of a successful and durable repair. <sup>16</sup>
2a	B-NR	6. In severely symptomatic patients (NYHA class III or IV) with primary severe MR and high or prohibitive surgical risk, transcatheter edge-to-edge repair (TEER) is reasonable if mitral valve anatomy is favorable for the repair procedure and patient life expectancy is at least 1 year. <sup>17,18</sup>
2b	B-NR	7. In symptomatic patients with severe primary MR attributable to rheumatic valve disease, mitral valve repair may be considered at a Comprehensive Valve Center by an experienced team when surgical treatment is indicated, if a durable and successful repair is likely. <sup>19</sup>
3: Harm	B-NR	8. In patients with severe primary MR where leaflet pathology is limited to less than one half the posterior leaflet, mitral valve replacement should not be performed unless mitral valve repair has been attempted at a Primary or Comprehensive Valve Center and was unsuccessful. <sup>11-14,20-22</sup>





# Intervention in Secondary (Functional) MR

## Recommendations for Intervention for Secondary MR

Referenced studies that support the recommendations are summarized in [Online Data Supplement 31](#).

COR	LOE	Recommendations
2a	B-R	1. In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) who have persistent symptoms (NYHA class II, III, or IV) while on optimal GDMT for HF (Stage D), TEER is reasonable in patients with appropriate anatomy as defined on TEE and with LVEF between 20% and 50%, LVESD ≤70 mm, and pulmonary artery systolic pressure ≤70 mm Hg. <sup>1-8</sup>
2a	B-NR	2. In patients with severe secondary MR (Stages C and D), mitral valve surgery is reasonable when CABG is undertaken for the treatment of myocardial ischemia. <sup>9-15</sup>



# Mitral Valve Anatomy: Complex

