Mitral Regurgitation

Hong Kong Core Cardiology Certificate Course

7/4/2019 11:10am to 11:45am

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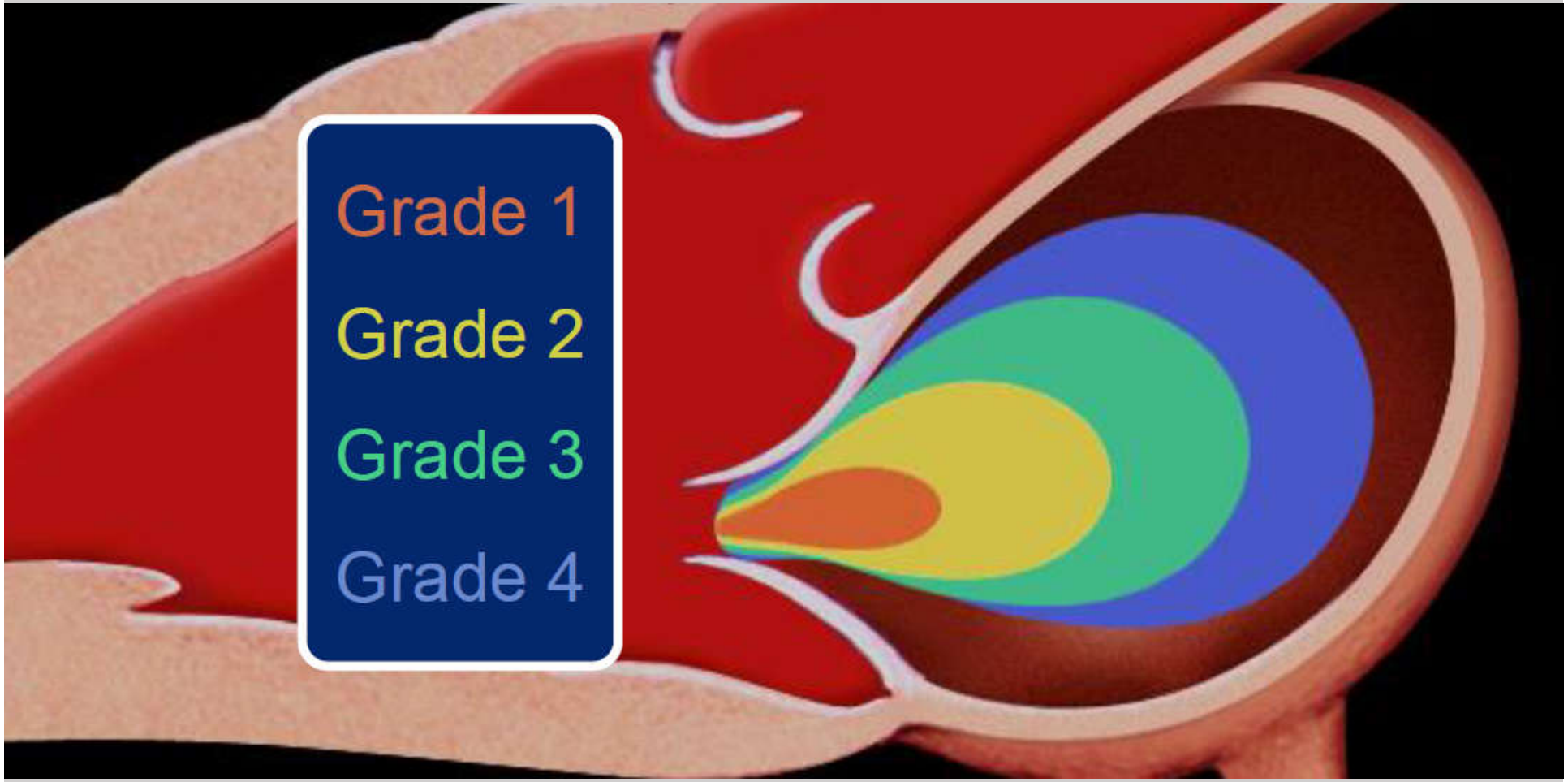
Echocardiographic Assessment of MR

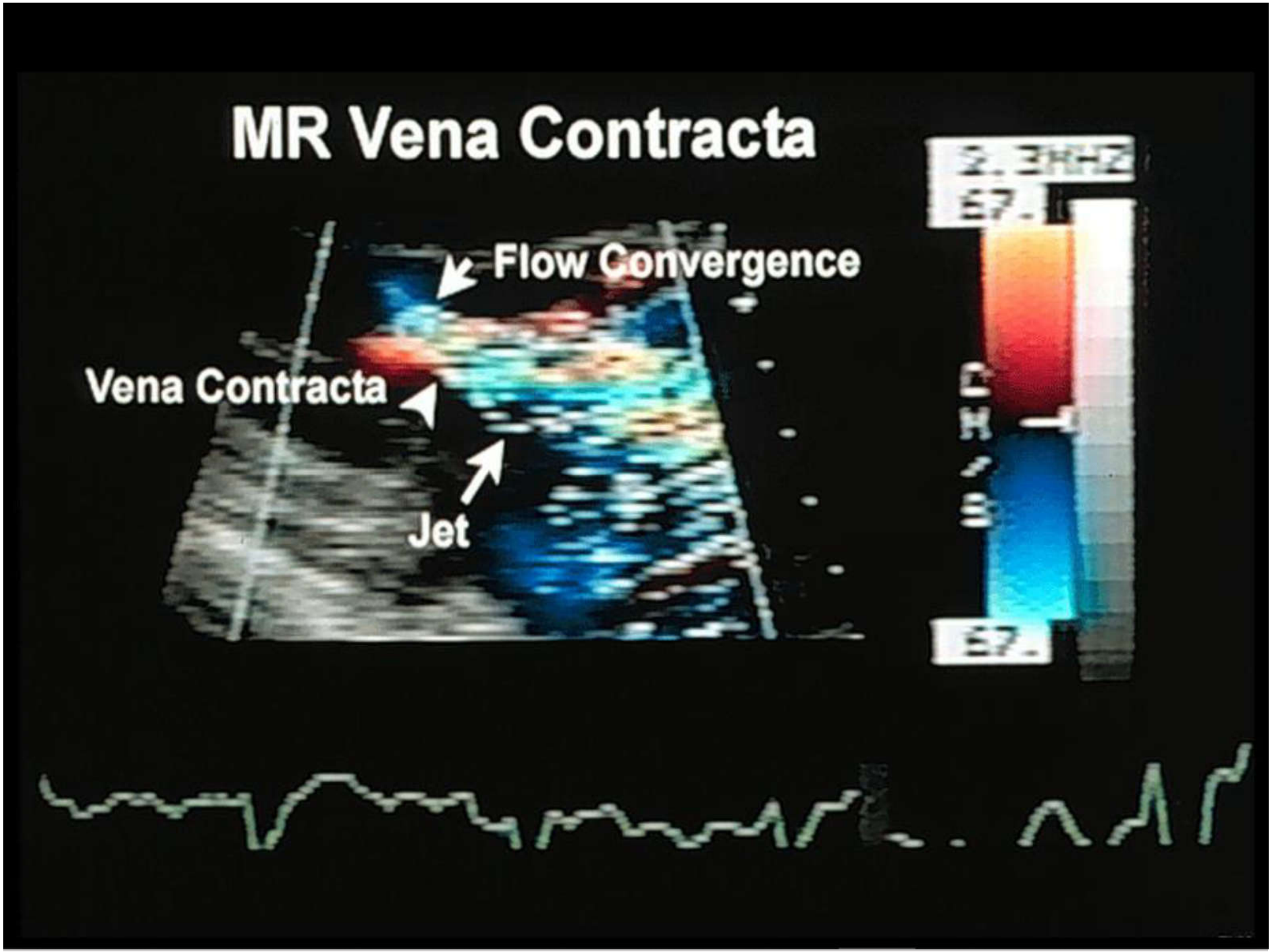
Echocardiographic Parameters for MR

	MR severity*			
	Mild	Moderate		Severe
Structural				
MV morphology	**None or mild leaflet abnormality** (e.g., mild thickening, calcifications or prolapse, mild tenting)	Moderate leaflet abnormality or moderate tenting		**Severe valve lesions** (primary: flail leaflet, ruptured papillary muscle, severe retraction, large perforation; secondary: severe tenting, poor leaflet coaptation)
LV and LA size†	Usually normal	Normal or mild dilated		Dilated‡
Qualitative Doppler				
Color flow jet area§	**Small, central, narrow, often brief**	Variable		Large central jet (>50% of LA) or eccentric wall-impinging jet of variable size
Flow convergence‖	**Not visible, transient or small**	Intermediate in size and duration		**Large throughout systole**
CWD jet	Faint/partial/parabolic	Dense but partial or parabolic		Holosystolic/dense/**triangular**
Semiquantitative				
VCW (cm)	<0.3	Intermediate		≥0.7 (>0.8 for biplane)¶
Pulmonary vein flow#	**Systolic dominance** (may be blunted in LV dysfunction or AF)	Normal or systolic blunting#		Minimal to no systolic flow/ **systolic flow reversal**
Mitral inflow**	**A-wave dominant**	Variable		E-wave dominant (>1.2 m/sec)
Quantitative††,‡‡				
EROA, 2D PISA (cm^2)	<0.20	0.20-0.29	0.30-0.39	≥0.40 (may be lower in secondary MR with elliptical ROA)
RVol (mL)	<30	30-44	45-59††	≥ 60 (may be lower in low flow conditions)
RF (%)	< 30	30-39	40-49	≥50

Colour Flow Doppler Qualitative Assessment

- Spatial distribution of velocities
- Sometimes misleading especially with eccentric jets




MR Vena Contracta
Flow Convergence
Vena Contracta
Jet

Pulmonary Vein Flow Reversal

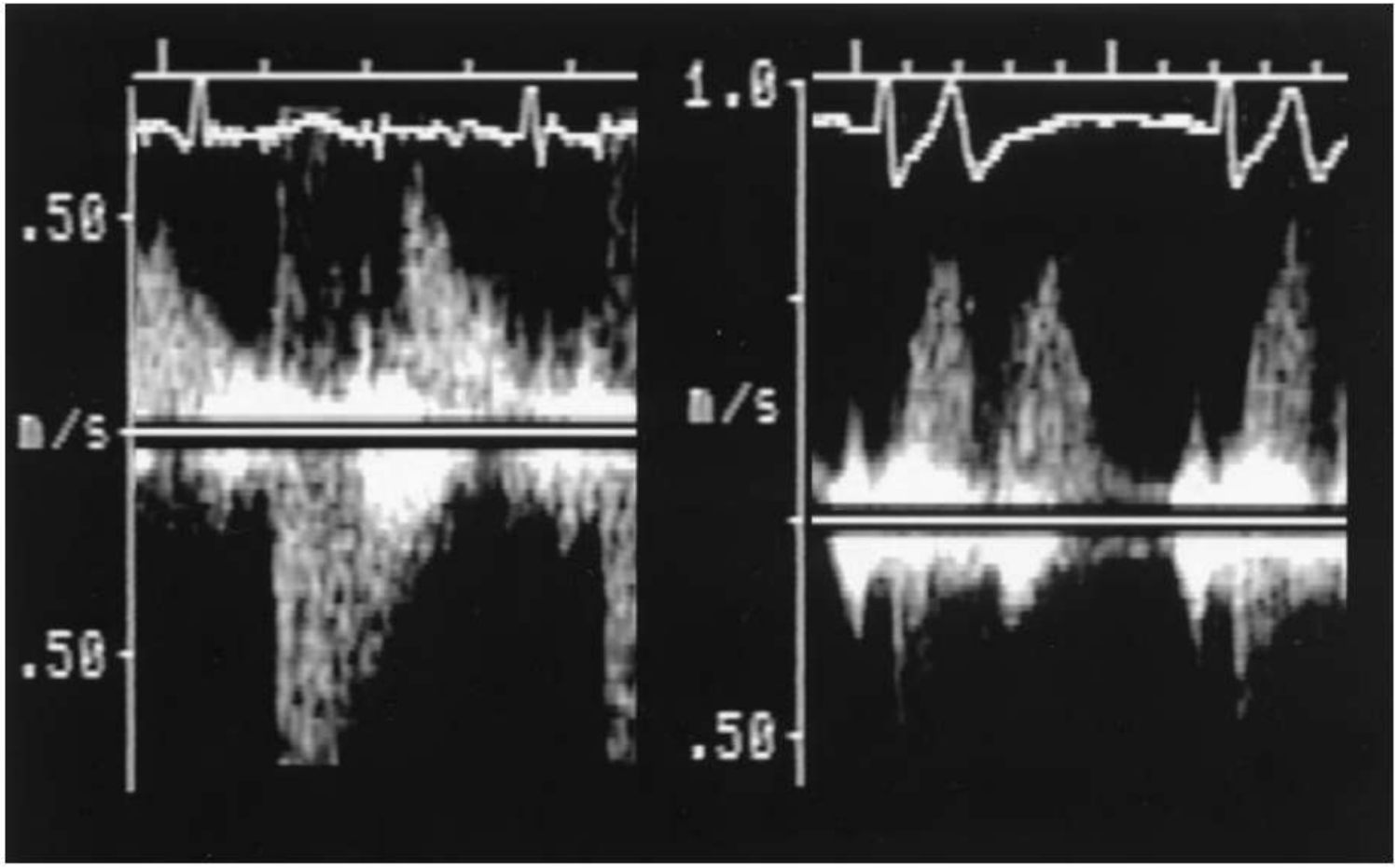
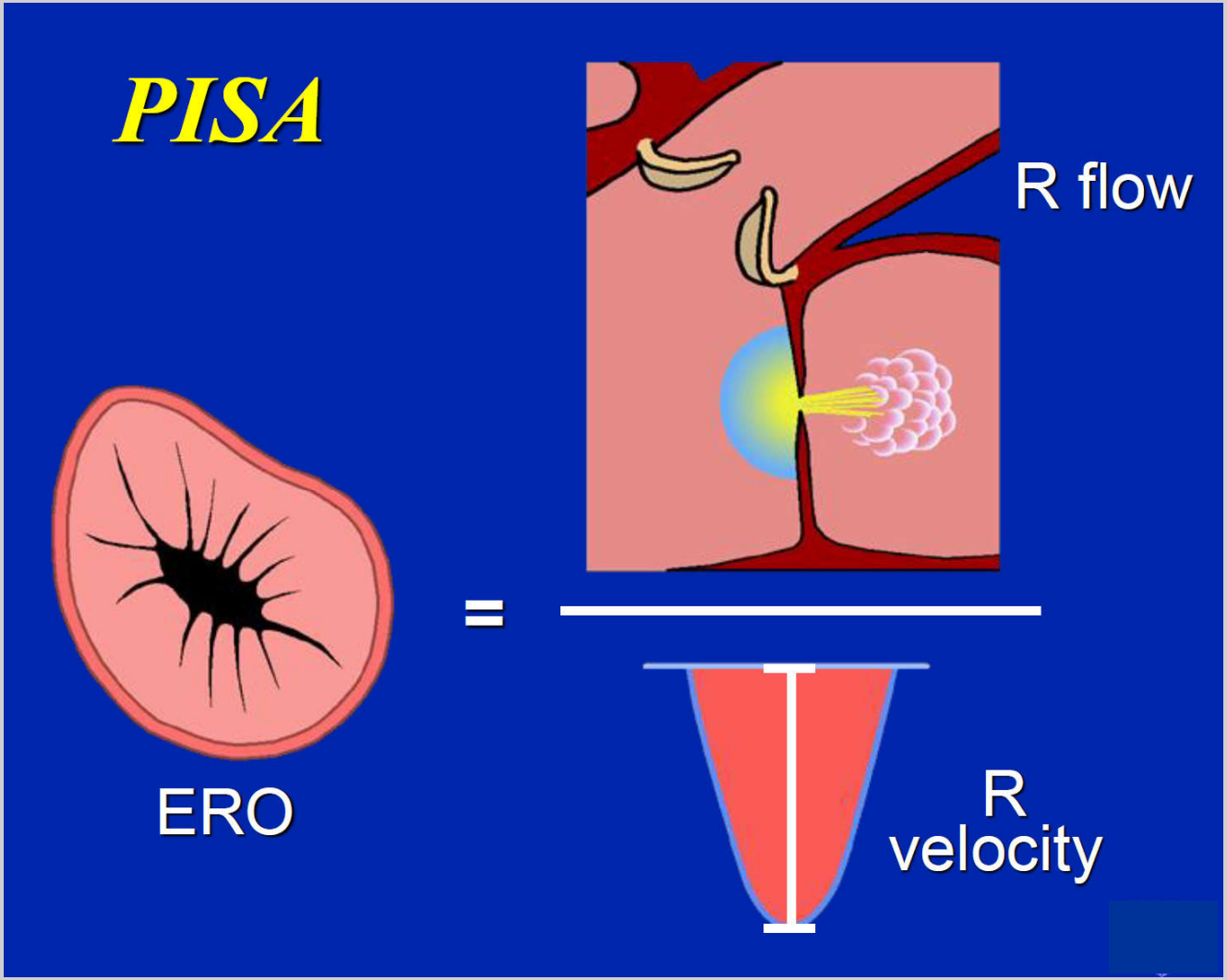


FIGURE 1. Pulmonary venous flow in 2 patients with a similar regurgitant volume (approximately 65 ml/beat), but 1 has systolic flow reversal (*left*) and the other has normal flow (*right*).

PISA Method Proximal Isovelocity Surface Area

- Blood rushes into an orifice
- Formation of hemispheres
- Increasing velocity and decreasing surface area



Calculation of EROA [Effective Regurgitant Orifice Area], Rvol [Regurgitation Volume], RF [Regurgitant Fraction]

$$EROA\ (\mathrm{cm}^2) = 2 \times \pi \times r^2 \times V_{alias} / V_{\max}$$

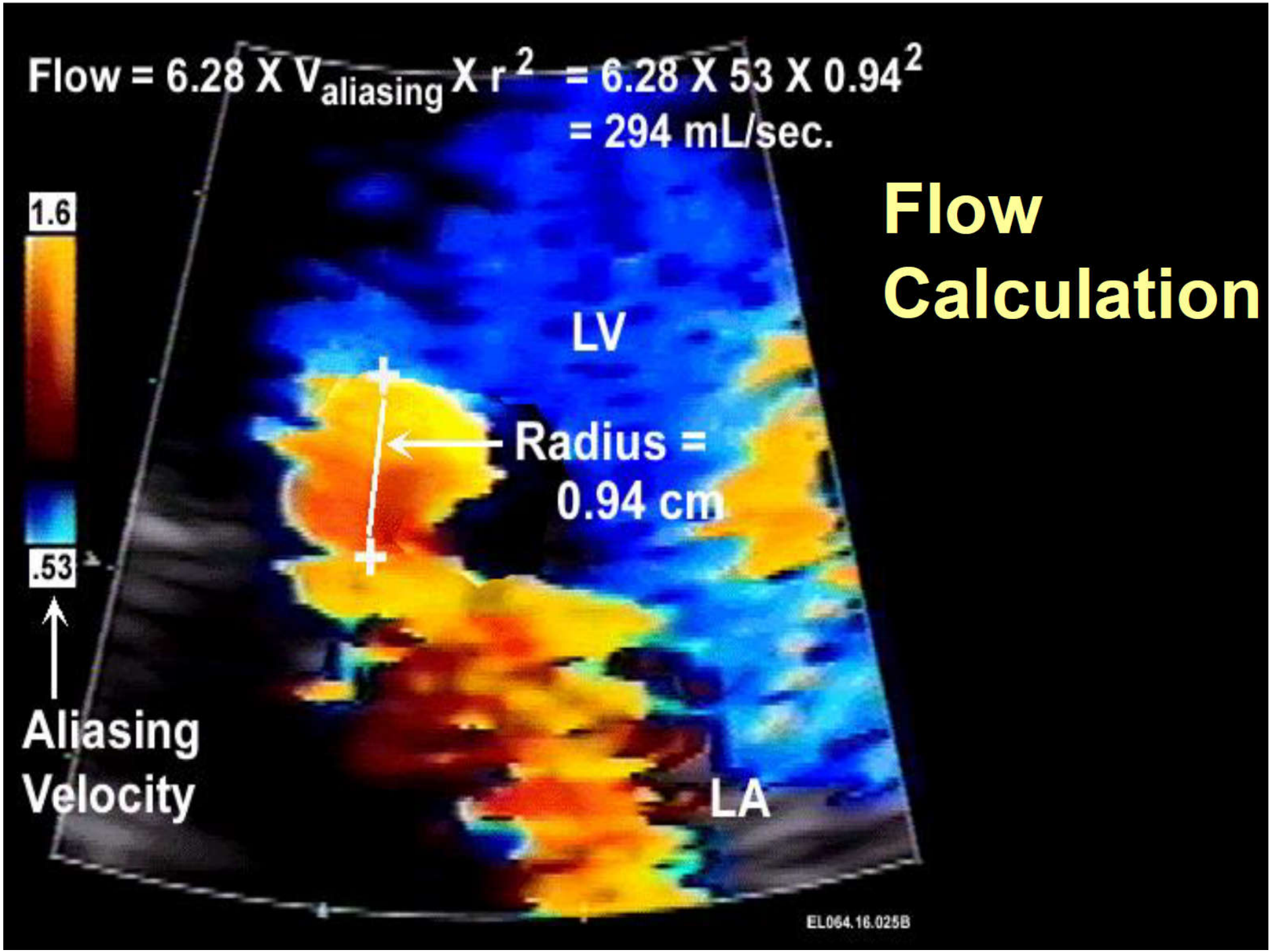
where r = PISA radius, V_{alias} = aliasing velocity, and $V_{\max}$ = peak velocity through the regurgitant orifice.

$$\text{R Vol} = EROA \times \text{VTI}$$

where VTI = regurgitant jet velocity-time integral (VTI)

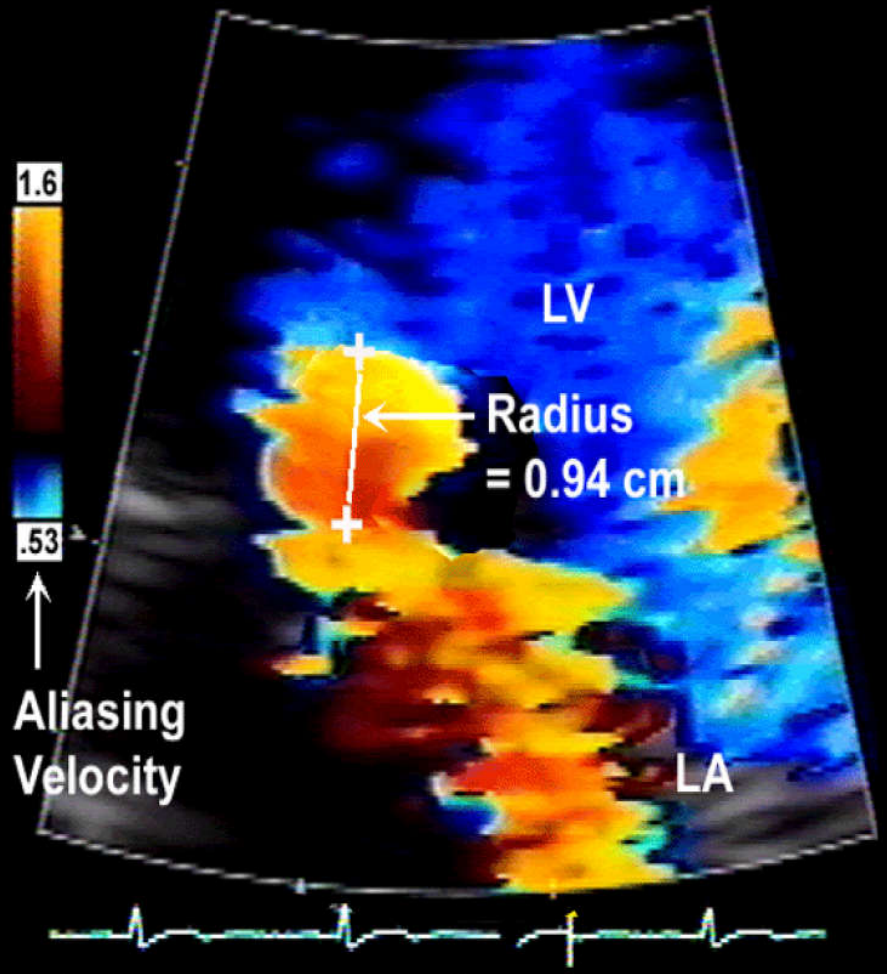
$$\text{RF} = (\text{R Vol}/\text{SV}_{\text{MV}}) \times 100$$

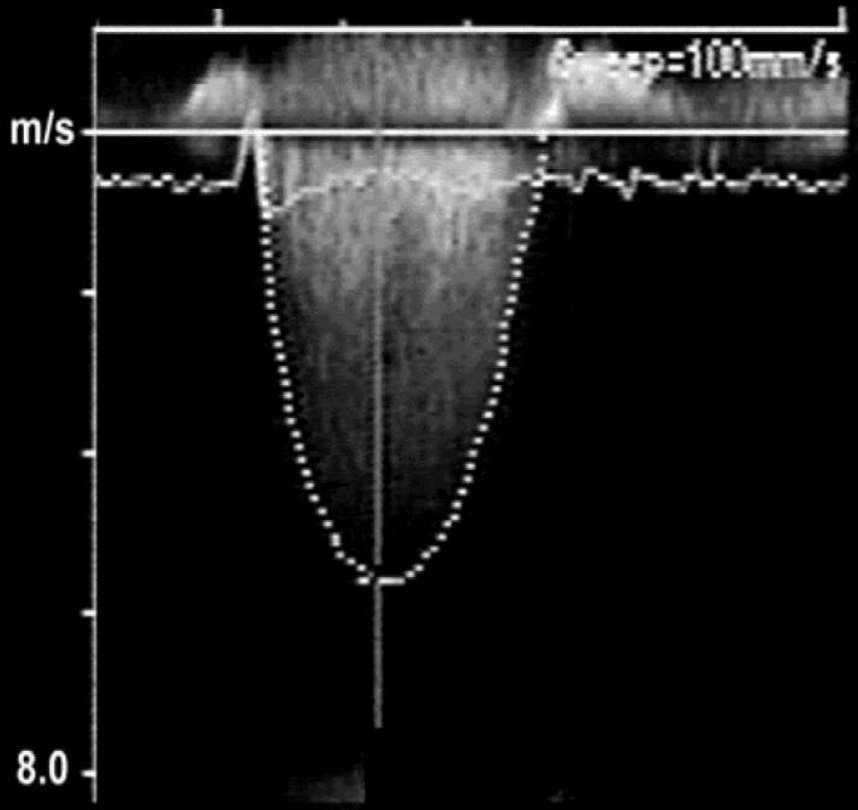
where SV_{MV} = mitral valve stroke volume = $\pi \times$ MV annulus radius^2 (cm^2) $\times$ MV inflow VTI (cm)



Flow Calculation

ERO Calculation





Flow = 294 mL/sec. MR velocity = 557 cm/sec.

ERO = flow/velocity = .53 cm^2 or 53 mm^2

EL064.16.025A-22B

Indicator of MR severity

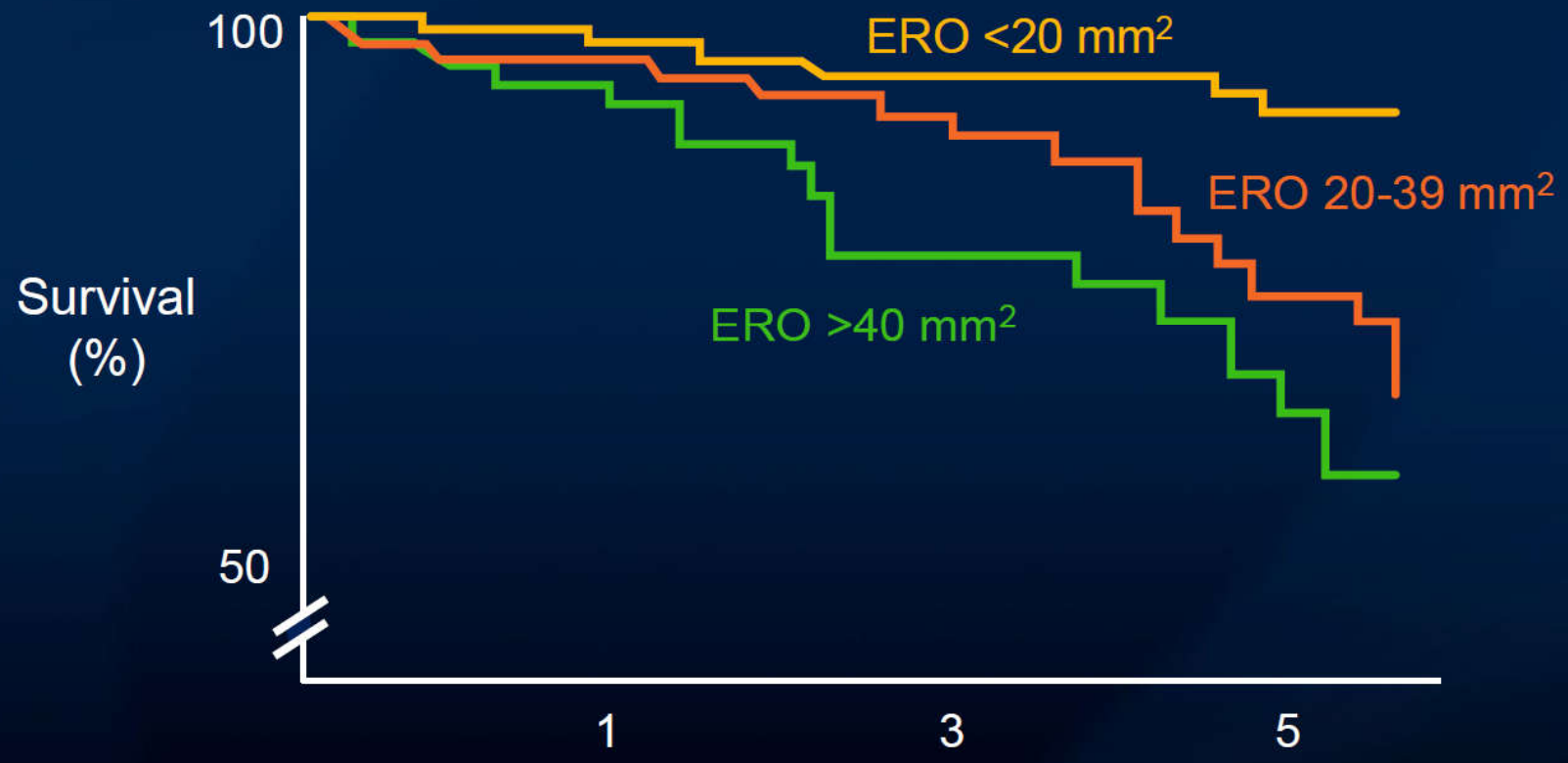
- Colour Jet Area >1/2 LA Area
- Regurgitation Volume >= 60 ml
- Regurgitation Fraction > 50%
- ERO >= 0.4cm2

Regurgitation Volume and ERO

ASE Grading

		Rvol (mL)	ERO (mm^2)
Mild	Grade I	<30	<20
Moderate	Grade II	30-44	20-29
	Grade III	45-59	30-39
Severe	Grade IV	>=60	>=40

The more severe the regurgitation The poorer the prognosis

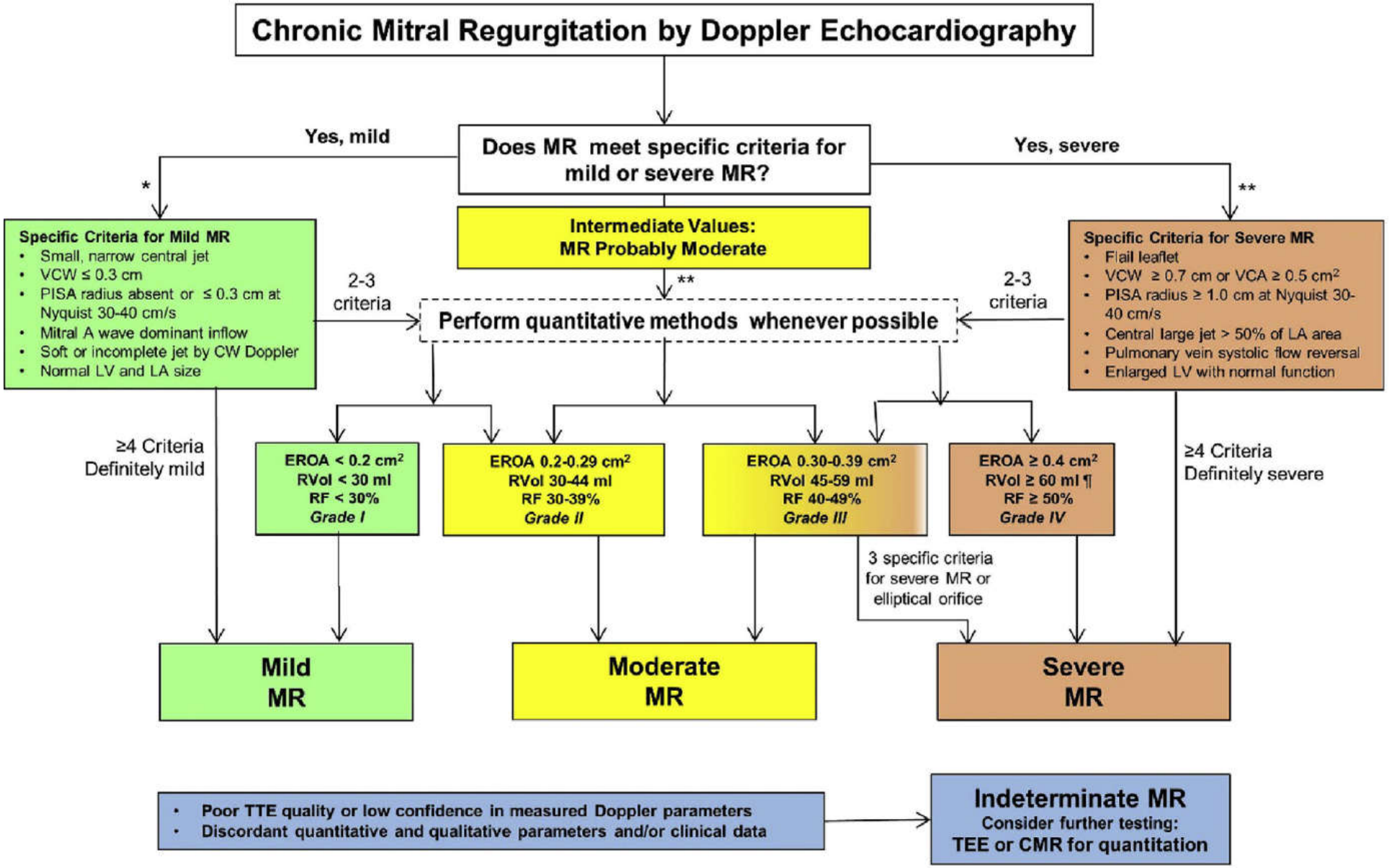


Enriquez-Sarano, M. et al: N Engl J Med; 352:875, 2005

TABLE 2 Strengths and Limitations of Common Echocardiographic Parameters of MR Severity

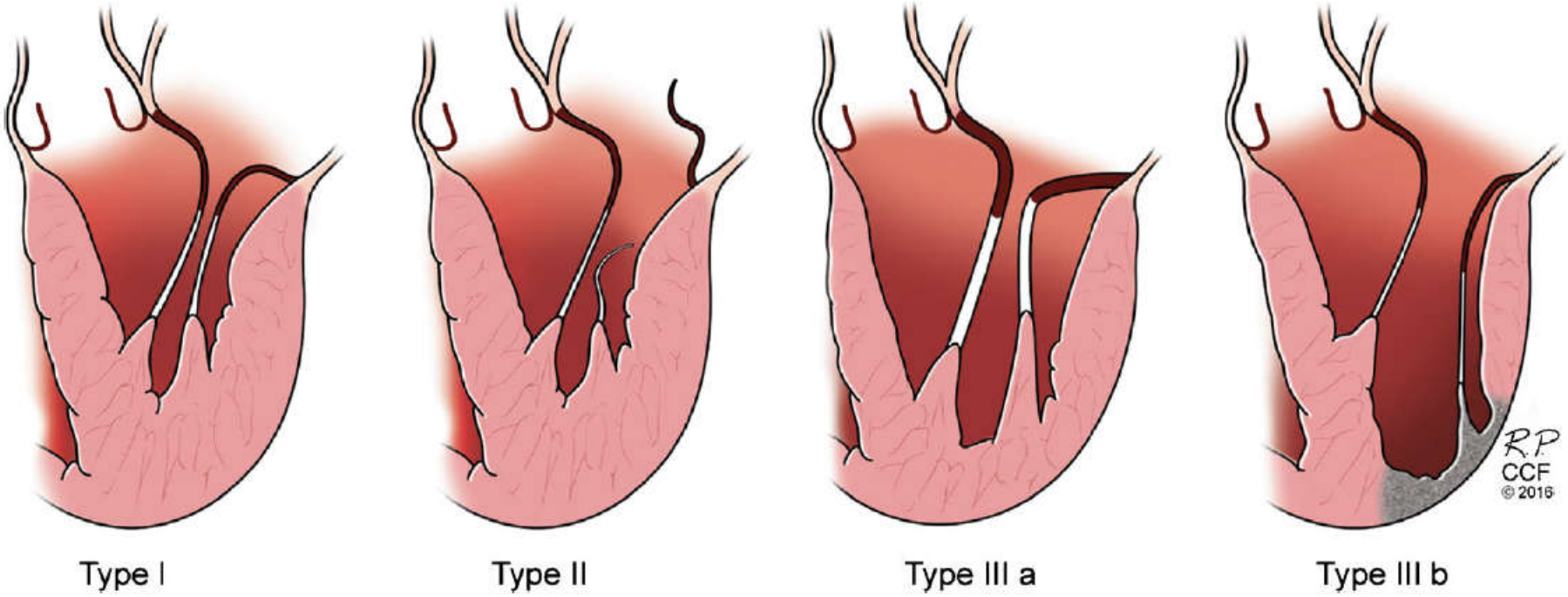
Parameter	Strengths	Limitations
Valve morphology	Flail leaflets or ruptured papillary muscles are specific for severe MR	Other findings are nonspecific
Regurgitant color flow	Easy to use, evaluates spatial orientation of MR jet, differentiates mild versus severe	Subject to technical and hemodynamic variation; can be underestimated with wall-impinging jets; image quality–dependent
Vena contracta width	Quick and easy to use; independent of hemodynamic and instrumentation factors; applies to eccentric jets; can differentiate mild versus severe MR	Not applicable to multiple jets; intermediate values require confirmation; small measurement errors can lead to big changes; 2D measure of a 3D structure; limited lateral resolution
PISA	Can be applied to eccentric jets (when angle-corrected); not affected by etiology of MR; quantitative; provides both lesion severity (EROA) and volume data (RVol); flow convergence at Nyquist limit of 50–60 cm/s alerts reader to significant MR	Not valid with multiple jets; provides peak flow and maximal EROA; interobserver variability; errors in radius measurement are squared; multiple potential sources of measurement error
Flow quantitation—PW	Quantitative; valid in multiple jets and eccentric jets; provides both lesion severity (EROA, RF) and volume data (RVol)	Time consuming; measurement of flow at MV annulus less reliable with calcified MV and/or annulus; not valid with concomitant significant AR unless pulmonic site is used; requires measurement at multiple sites, which introduces errors
Jet profile—CW	Simple, readily available; easy assessment of MR timing	Qualitative; complementary data; complete signal difficult to obtain in eccentric jet; gain dependent
Peak mitral E velocity	Simple, readily available, A-wave dominance excludes severe MR	Influenced by LA pressure/compliance, LV relaxation, MV area, and AF; complementary data only, does not quantify MR severity
Pulmonary vein flow	Simple; systolic flow reversal is specific for severe MR	Influenced by LA pressure, AF; not accurate if MR jet directed into the sampled vein; absence does not rule out severe MR
LA and LV size	Enlargement sensitive for chronic severe MR, important for outcomes; normal size virtually excludes severe chronic MR	Enlargement seen in other conditions (nonspecific); may be normal in acute severe MR

AF = atrial fibrillation; AR = aortic regurgitation; CW = continuous wave; EROA = effective regurgitant orifice area; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; MV = mitral valve; PISA = proximal isovelocity surface area; PW = pulsed wave; RF = regurgitant fraction; RVol = regurgitant volume.



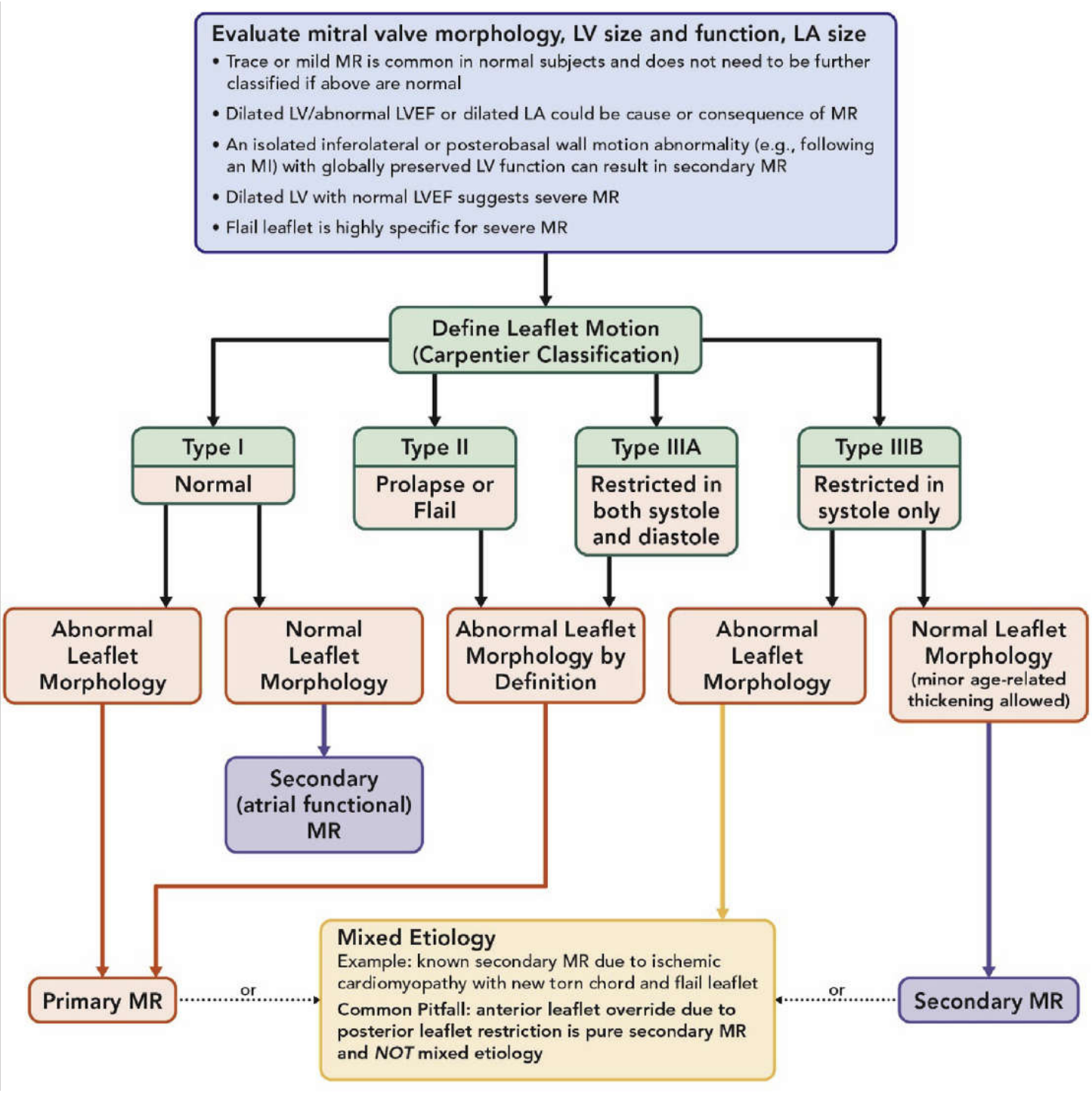
*	Beware of underestimation of MR severity in eccentric, wall impinging jets; quantitation is advised
**	All values for EROA by PISA assume holosystolic MR; single frame EROA by PISA, VCW, and VCA overestimate non-holosystolic MR
¶	Regurgitant volume for severe MR may be lower in low flow conditions.

Carpentier Classifications



Type I | Type II | Type III a | Type III b

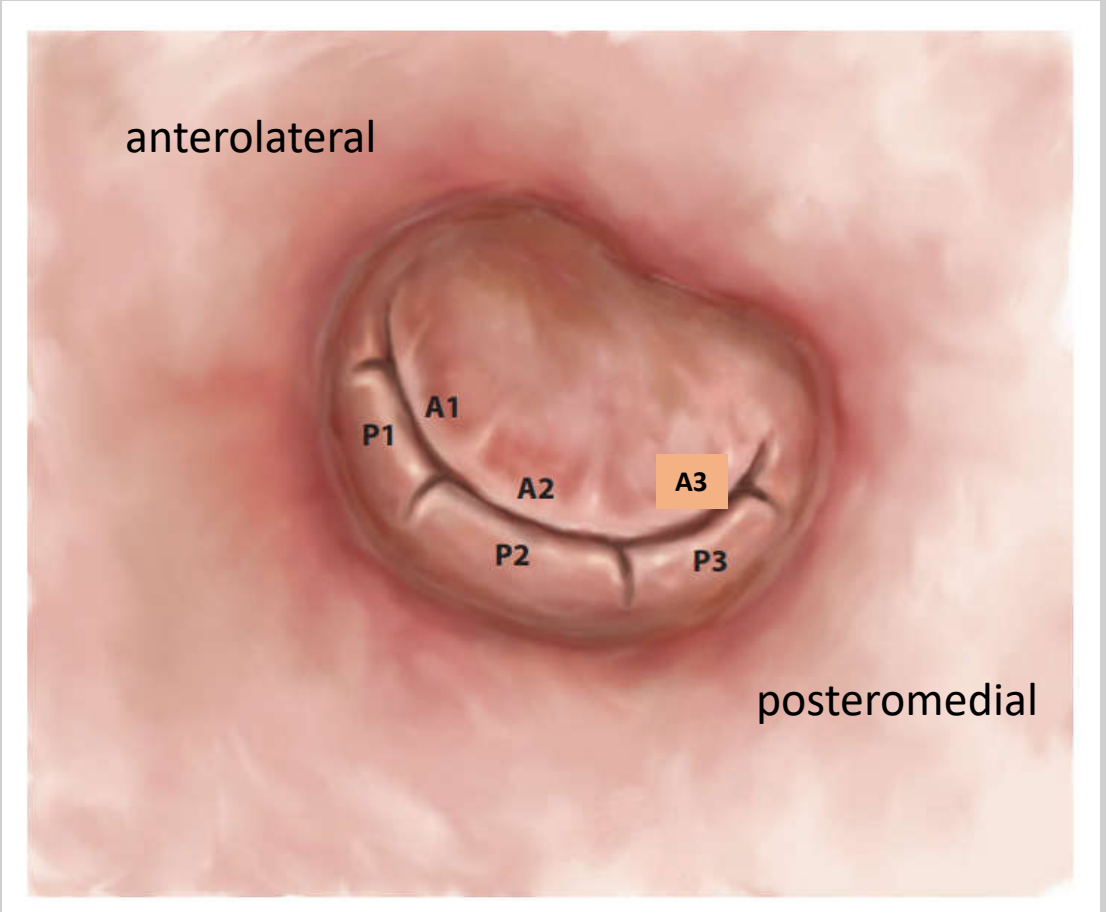
- Type I Normal leaflet motions (annular dilatation, leaflet perforation)
- Type II Excess leaflet motion (prolapse, frail, papillary muscle rupture)
- Type IIIa Restricted leaflet motion during systole and diastole (thickening, retraction)
- Type IIIb Restricted leaflet motion during systole only (tethering)

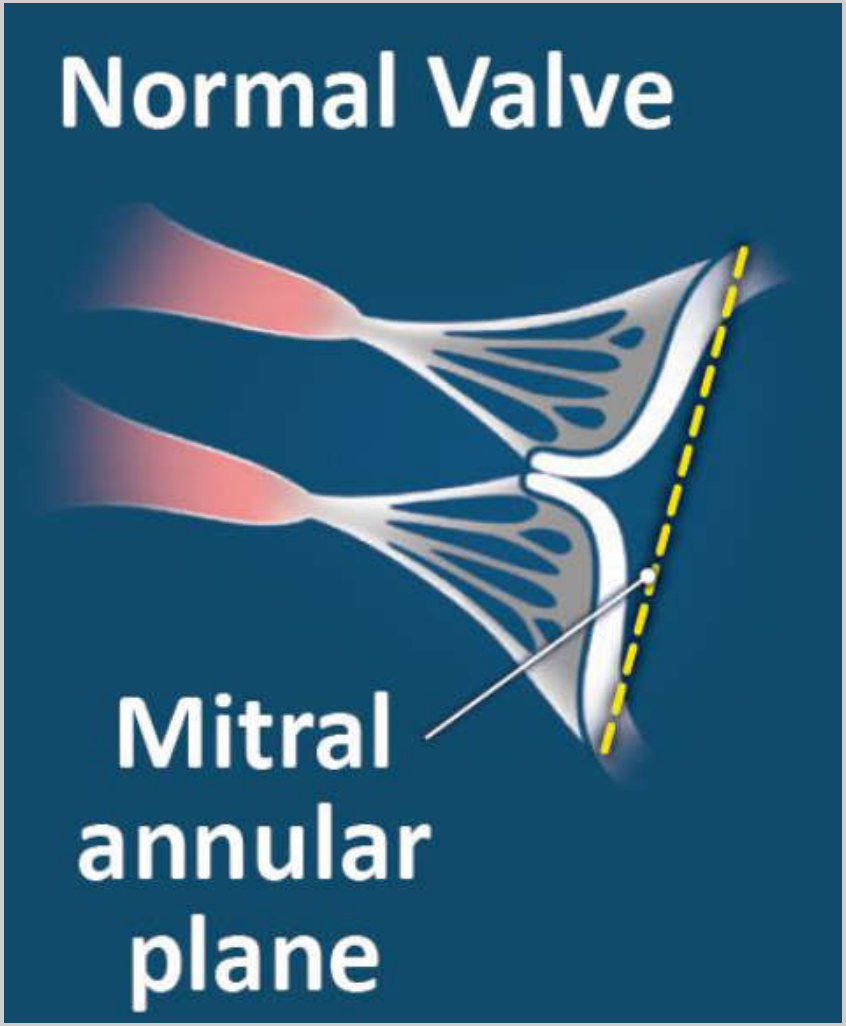

Evaluate mitral valve morphology, LV size and function, LA size
• Trace or mild MR is common in normal subjects and does not need to be further classified if above are normal
• Dilated LV/abnormal LVEF or dilated LA could be cause or consequence of MR
• An isolated inferolateral or posterobasal wall motion abnormality (e.g., following an MI) with globally preserved LV function can result in secondary MR
• Dilated LV with normal LVEF suggests severe MR
• Flail leaflet is highly specific for severe MR
Define Leaflet Motion (Carpentier Classification)
Type I
Normal
Type II
Prolapse or Flail
Type IIIA
Restricted in both systole and diastole
Type IIIB
Restricted in systole only
Abnormal Leaflet Morphology
Normal Leaflet Morphology
Abnormal Leaflet Morphology by Definition
Abnormal Leaflet Morphology
Normal Leaflet Morphology (minor age-related thickening allowed)
Secondary (atrial functional) MR
Primary MR
or
Mixed Etiology
Example: known secondary MR due to ischemic cardiomyopathy with new torn chord and flail leaflet
Common Pitfall: anterior leaflet override due to posterior leaflet restriction is pure secondary MR and NOT mixed etiology
or
Secondary MR

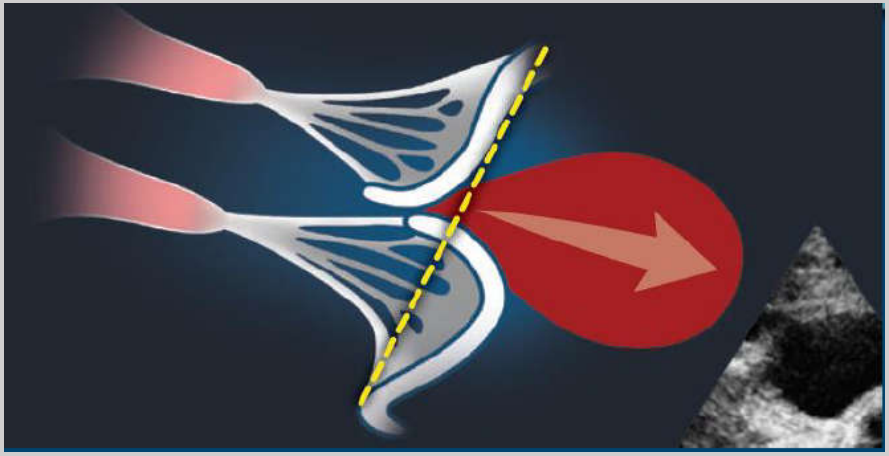
Etiology of Mitral Regurgitation: Primary MR

Mitral Valve Prolapse

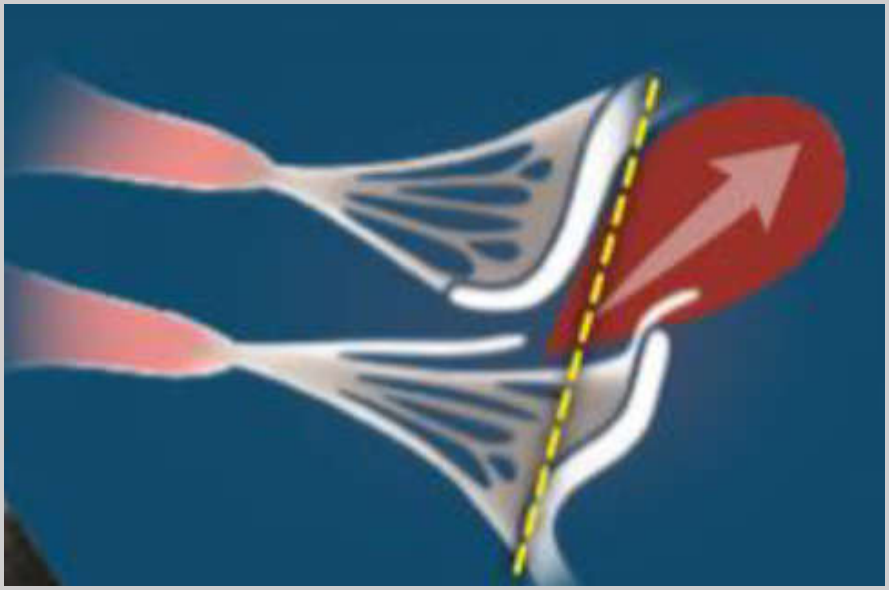
- Carpentier Classifications
- P2 most common site of localized prolapse and frail
- Defined as
  - abnormal leaflet displacement >= 2mm above MA in a long-axis view







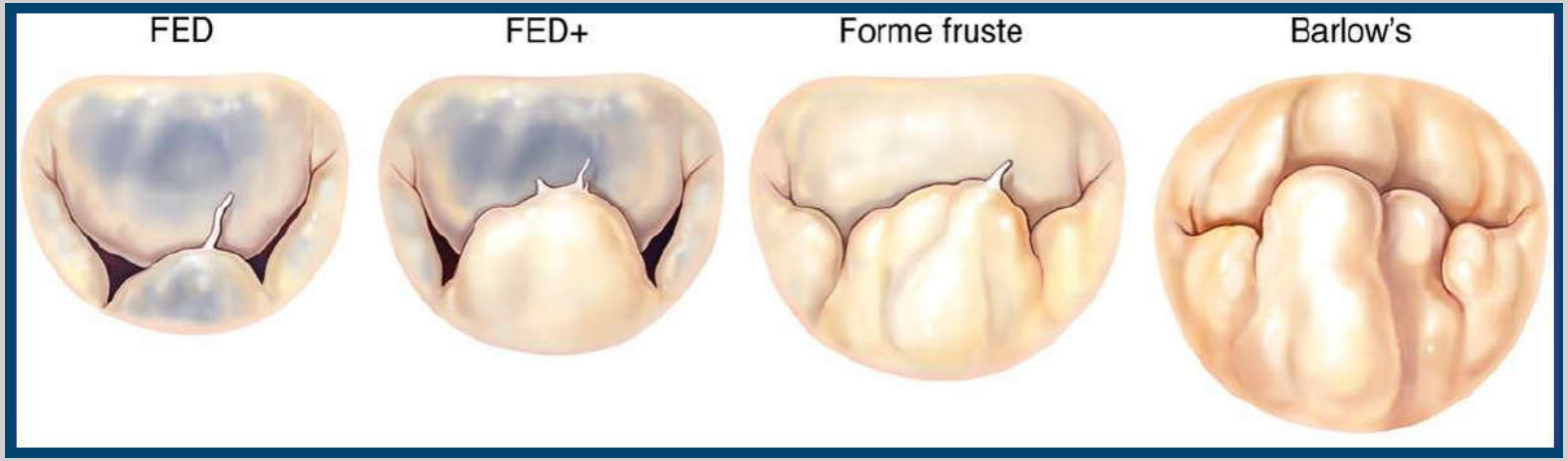
MV Prolapse Leaflet displacement >= 2mm above mitral annulus into LA



MV Frail Leaflet tip everted into LA

Degenerative MR

- Myxomatous degeneration
  - Abnormal accumulation of mucopolysaccharides
  - Altered extracellular matrix/matrix metalloproteinase, cysteine endoproteases, tenomodulin
  - Barlow disease
- Fibroelastic deficiency
  - Abnormal connective tissue structure leads to loss of mechanical integrity



- Etiology – complex and viable
  - Acquired
  - Genetic cause
- Myxomatous degeneration
  - Genetic disorder of connective tissue
  - Heterogenous
    - Autosomal dominant
    - X-linked
    - Variable penetrance
    - Sex- and age- dependent

- Abnormal bulging of mitral valve leaflets during systole
- Frail – segments of leaflet protrusion into atrium
  - Typically associated with torn chordae or ruptured papillary muscle
  - Loss of leaflet restraint
- Most recent studies – Incidence 2-3%

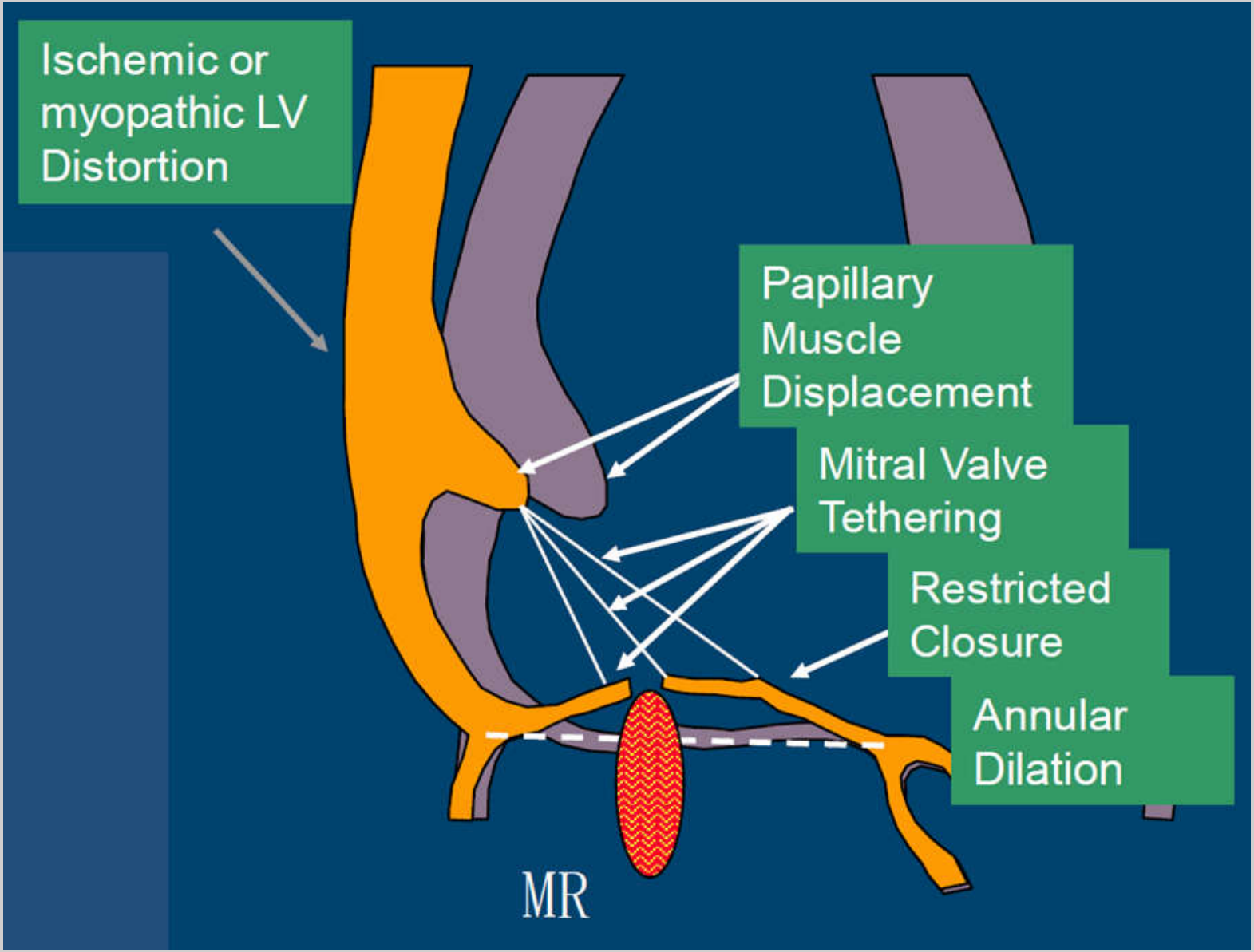
Acquired causes	Genetic causes
Rheumatic	Myxomatous degeneration
Endocarditis	Marfan syndrome
Trauma (penetrating or blunt)	Ehlers-Danlos syndrome
Ischemic (papillary muscle dysfunction or rupture)	Osteogenesis imperfecta

Etiology of Mitral Regurgitation: Secondary MR

Secondary MR

- Functional MR
- Valve leaflets, chordae – structurally normal
- Imbalance between
  - Closing force
  - Tethering force
  - Altered LV geometry
  - LV gradient
- Annular dilatation
  - Chronic AF/LA enlargement
- Proposed lower threshold -
  - EROA 20mm^2
  - Regurgitation Volume 30ml

Mechanism of Secondary MR



Mitral regurgitation and Chronic Atrial Fibrillation


Mitral Regurgitation
Atrial Fibrillation

Journal of the American College of Cardiology

Volume 40, Issue 1, July 2002
DOI: 10.1016/S0735-1097(02)01922-8

PDF Article

Atrial fibrillation complicating the course of degenerative mitral regurgitation

Determinants and long-term outcome

Francesco Grigioni, Jean-François Avierinos, Lieng H Ling, Christopher G Scott, Kent R Bailey, A.Jamil Tajik, Robert L Frye and Maurice Enriquez-Sarano

Author + information

Abstract

Objectives The study was done to define the incidence, determinants and prognostic implications of onset of atrial fibrillation (AF) during follow-up of mitral regurgitation (MR) initially in sinus rhythm.

Incidence of New AF after DMR Diagnosis

JACC Vol. 40, No. 1, 2002
July 3, 2002:84–92

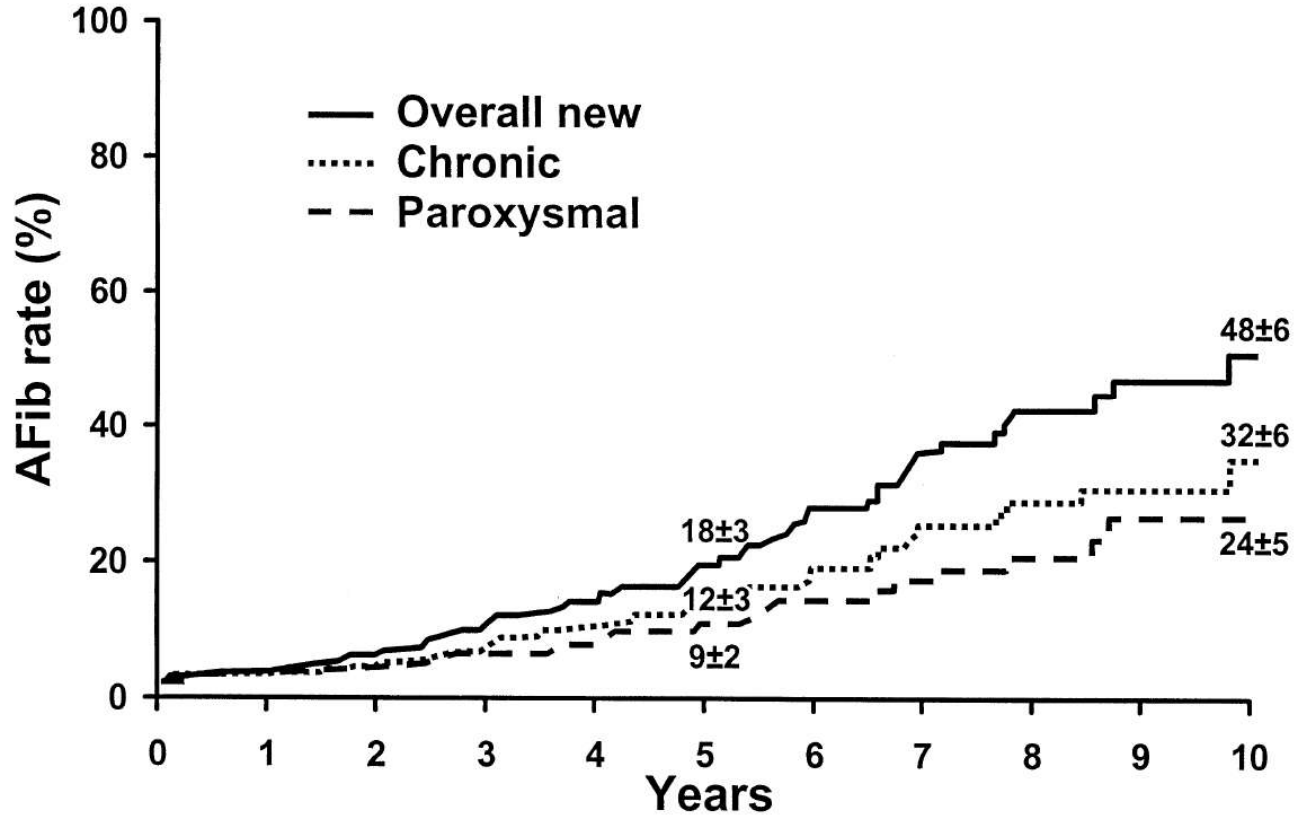


Figure 1. Incidence of atrial fibrillation (AFib) under conservative (medical) management among patients with mitral regurgitation due to flail leaflets diagnosed with the patient in sinus rhythm. The overall rates of new atrial fibrillation and of permanent and paroxysmal atrial fibrillation are presented as Kaplan-Meier curves.

Increased Incidence of New AF with Age

JACC Vol. 40, No. 1, 2002
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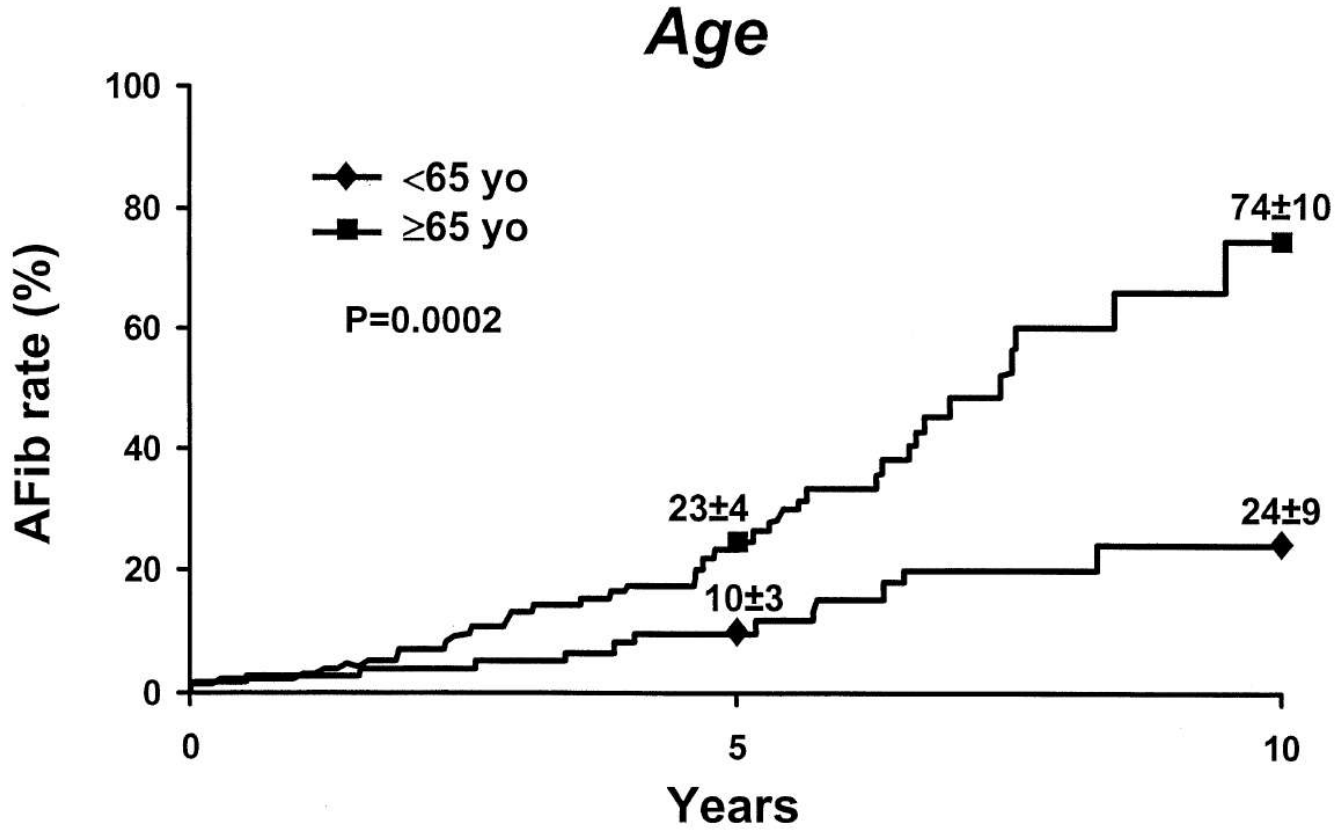


Figure 2. Atrial fibrillation (AFib) rate in patients with mitral regurgitation due to flail leaflets diagnosed with the patient in sinus rhythm, according to age at diagnosis, <65 or ≥65 years old (yo). Note the considerably higher rate in older patients.

Increased Incidence with LA dimension

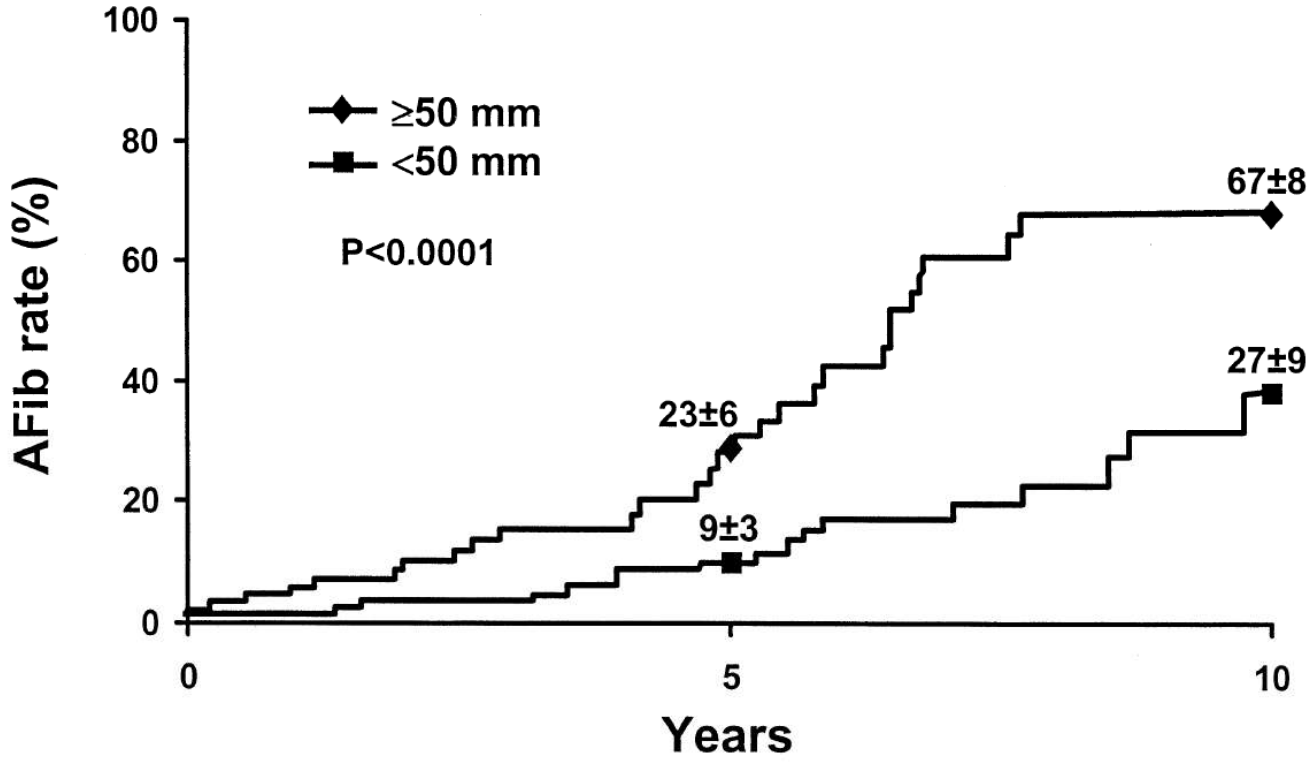


Figure 3. Atrial fibrillation (AFib) rate in patients with mitral regurgitation due to flail leaflets diagnosed with the patient in sinus rhythm, according to left atrial diameter at diagnosis <50 or ≥50 mm. Note the considerably higher rate in patients with a markedly dilated left atrium.

Survival in Relation to AF in DMR

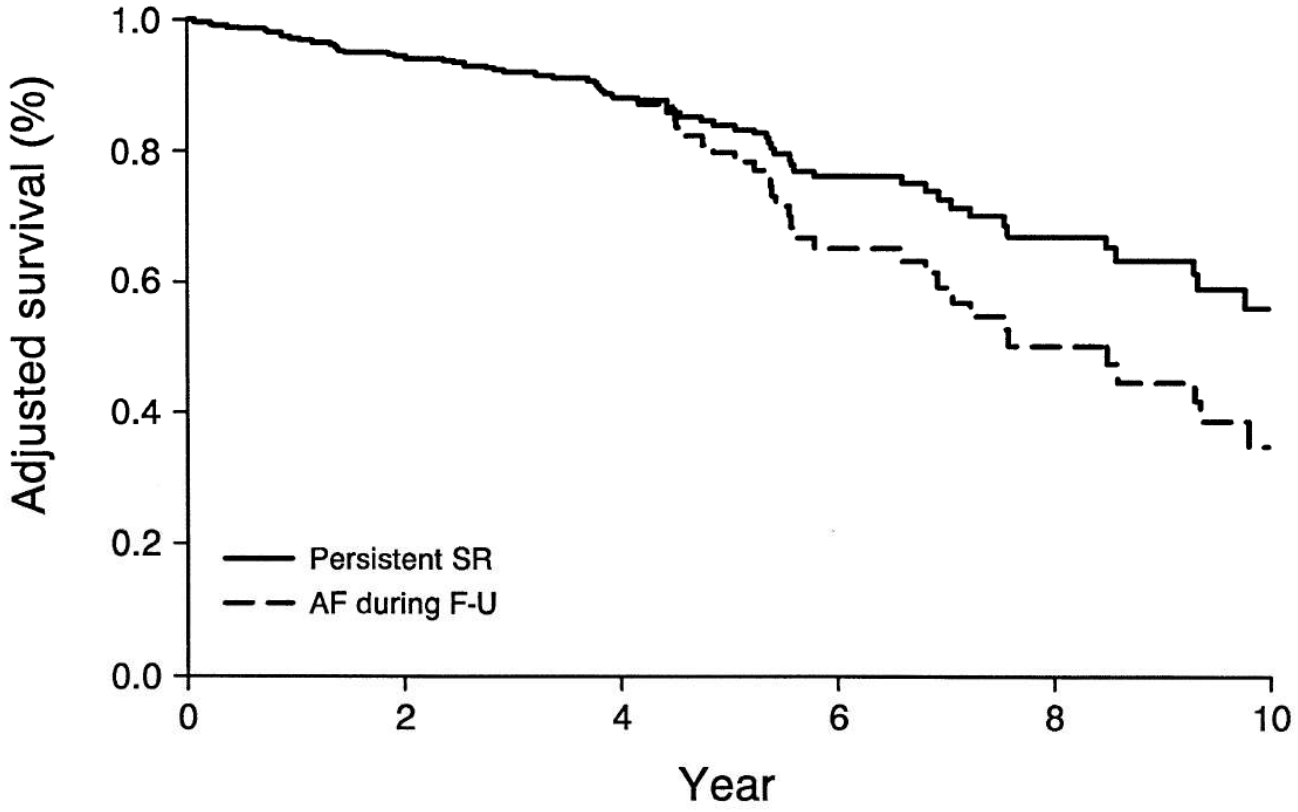
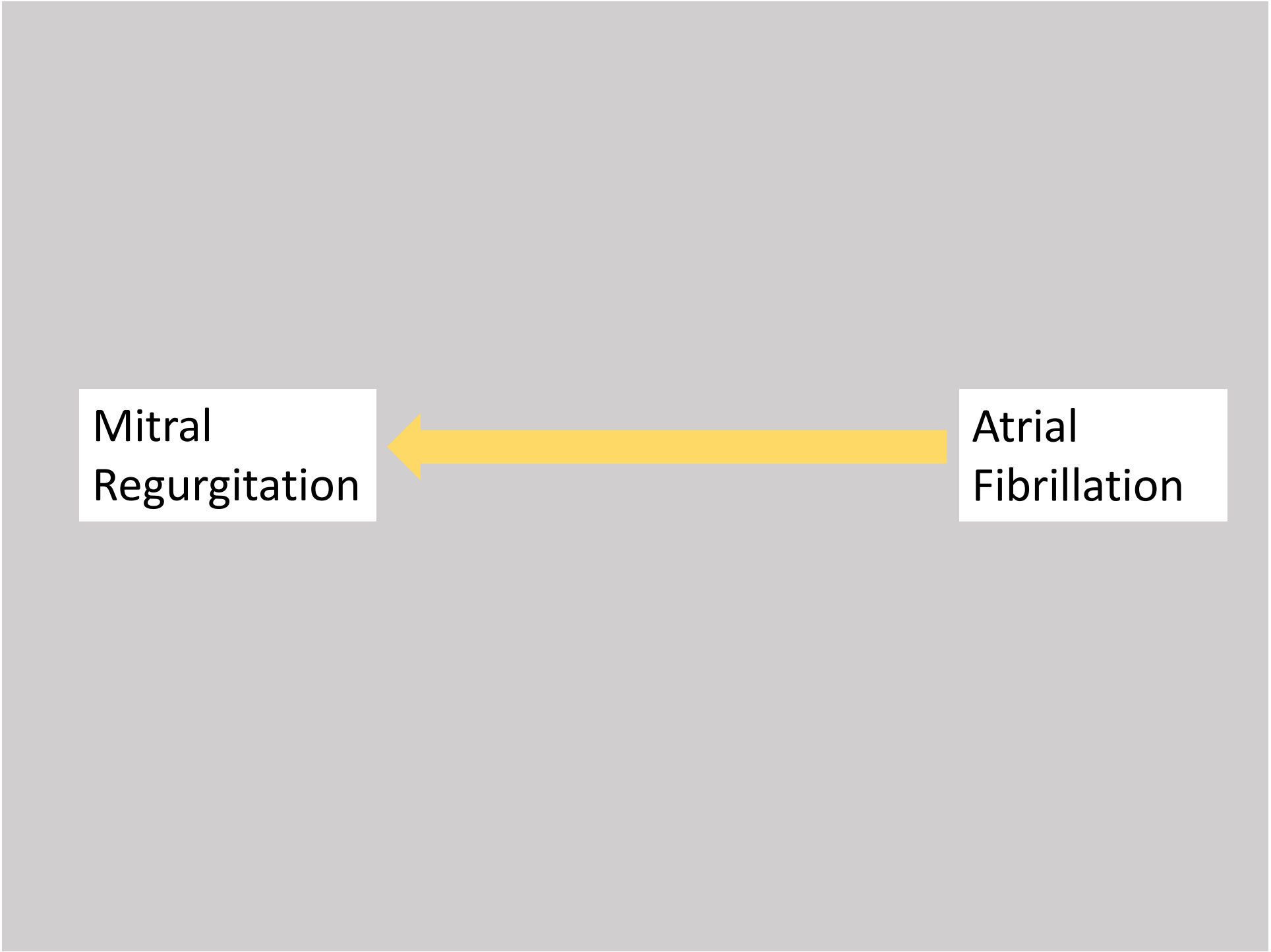


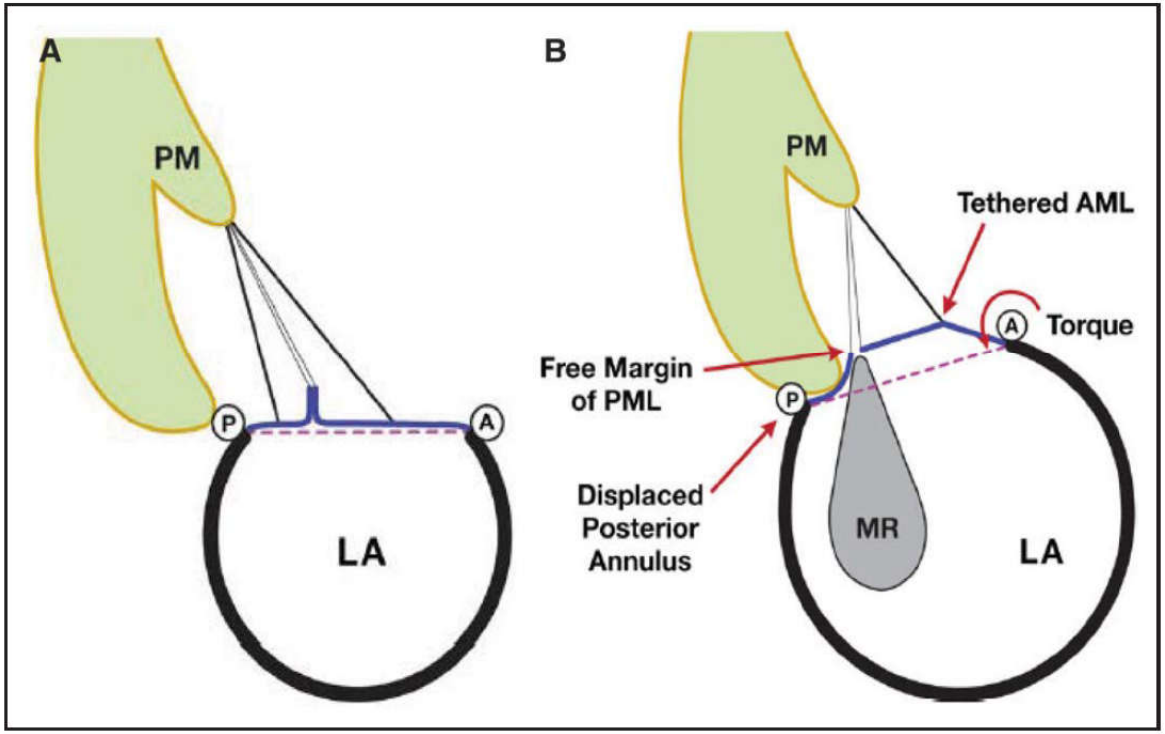
Figure 4. Survival of patients with mitral regurgitation due to flail leaflets adjusted for age, gender, ejection fraction and symptoms at baseline, and separating at the fourth year after diagnosis those patients with and those without postdiagnosis atrial fibrillation. Note the excess mortality in patients with follow-up atrial fibrillation. SR = sinus rhythm; AF = atrial fibrillation; F-U = follow-up.


Mitral Regurgitation
Atrial Fibrillation

- Between 14% and 26.4% of the patients included in the landmark clinical trials on NOAC showed significant valvular heart disease other than moderate and severe mitral stenosis or mechanical valve prostheses
- Most common is **MR** (73 to 90%)

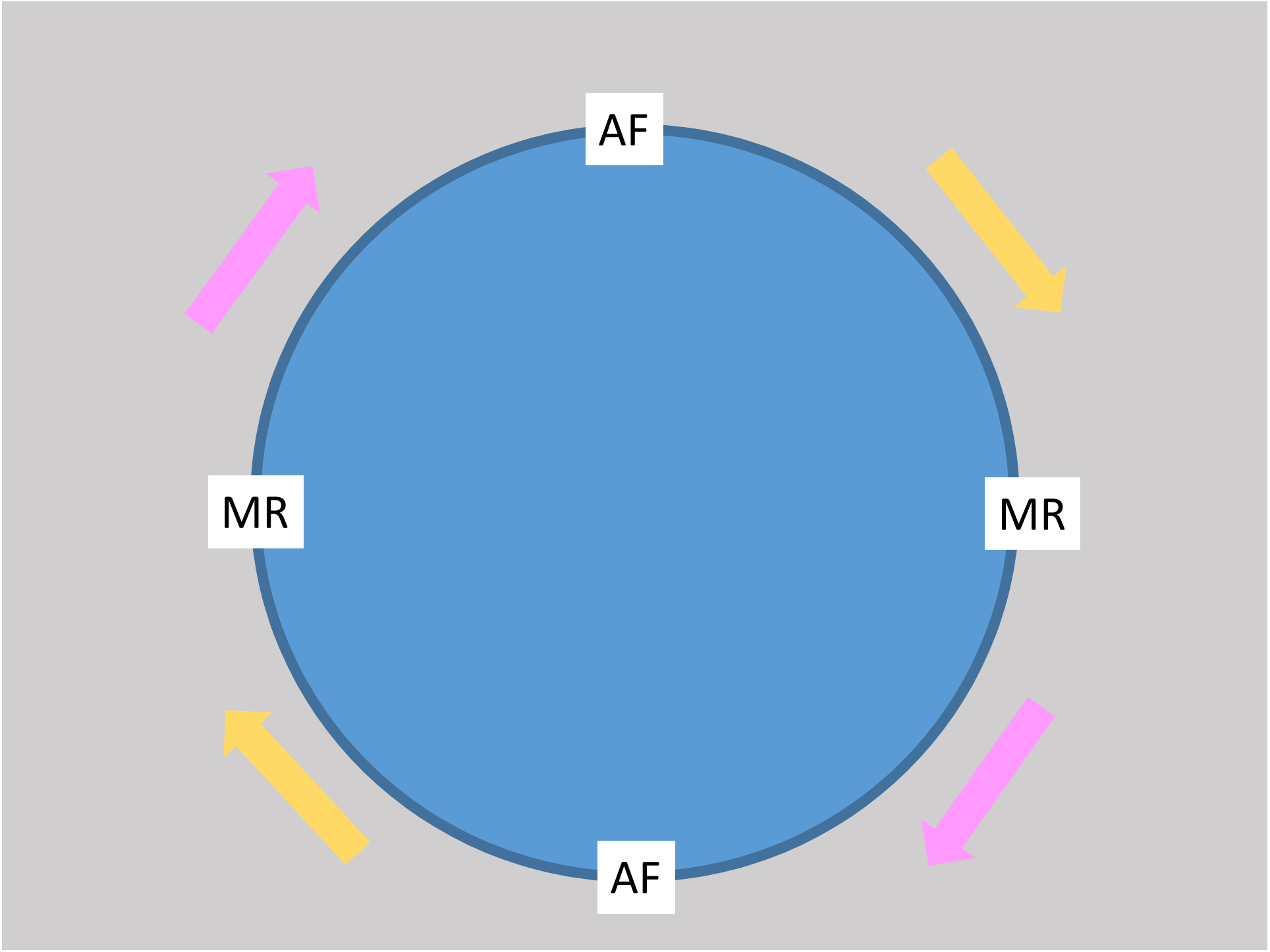
Mechanism of Atrial Functional MR

Normal



AF

- LA and MA dilatation displace the posterior MA above the crest of LV, pressing the PML against
- Leaving little leaflet surface for coaptation
- PML tethering
- Counterclockwise torque across intertrigonal axis – AML tethering

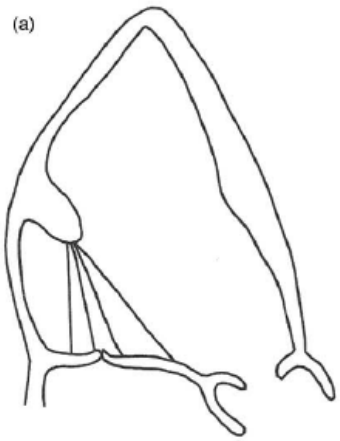

AF
MR
MR
AF

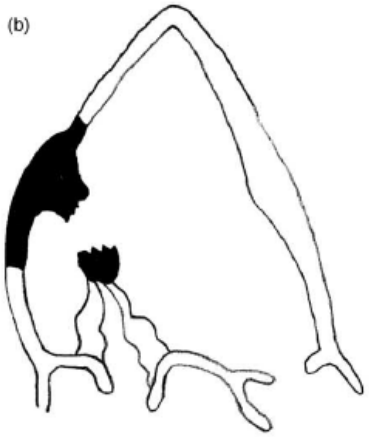
Etiology of Mitral Regurgitation: MR following AMI

Major causes of MR following AMI

- Papillary muscle rupture
- Rupture of a head of a chordae tendineae
- Ischaemia/Scar of the papillary muscle
- Mitral annulus dilatation
- Change in global geometry of the left ventricle with tethering of the mitral leaflets
- Preexisting MR

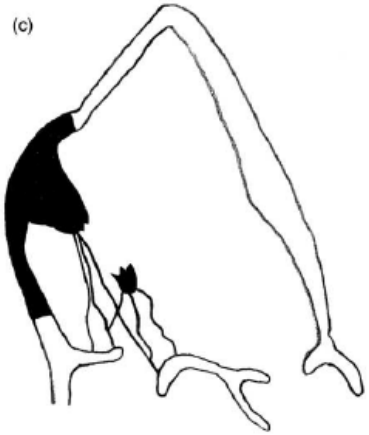
Normal mitral apparatus

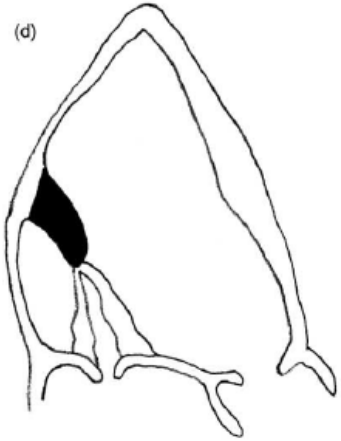




Complete rupture papillary muscle

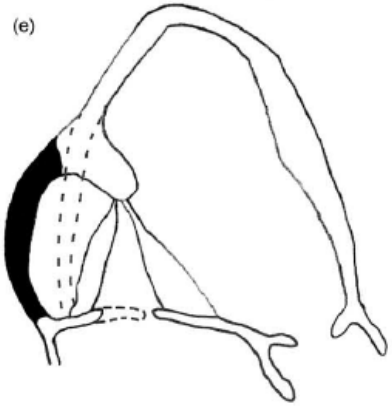
Partial rupture papillary muscle

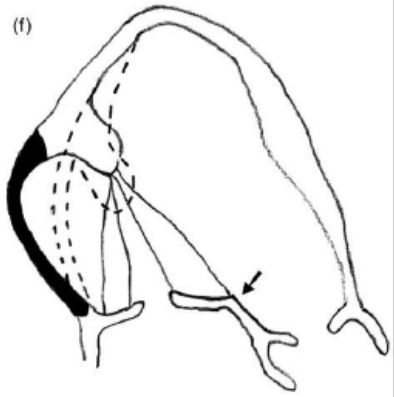




Ischaemia/ Infarction/Scarring

Infarction in non-PM areas





Inferobasal infarction leads to change in LV geometry

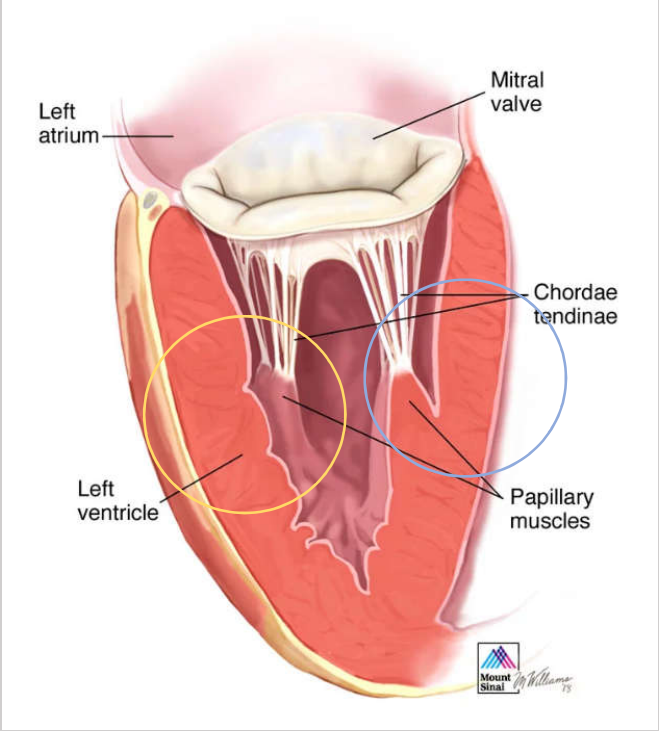
Papillary Muscle Rupture

- Rare 1-5% of patients with AMI
- Literature first identifies papillary muscle rupture as early as 1948
- Visualization via TTE first reported 1981
- First report identification with TTE in 1985
- Main causes
  - STEMI
  - NSTEMI
  - Trauma
  - Endocarditis
  - Autoimmune

- Mostly PosteroMedial papillary muscle
  - Single blood supply from PDA (RCA > LCx)
- AnteroLateral papillary muscle
  - Dual blood supply

PM – 6-12 times more common

Usually 2-7 days post ischaemic events



Acute MR - Management

Overall goal

Stabilization → Mitral surgery/Intervention

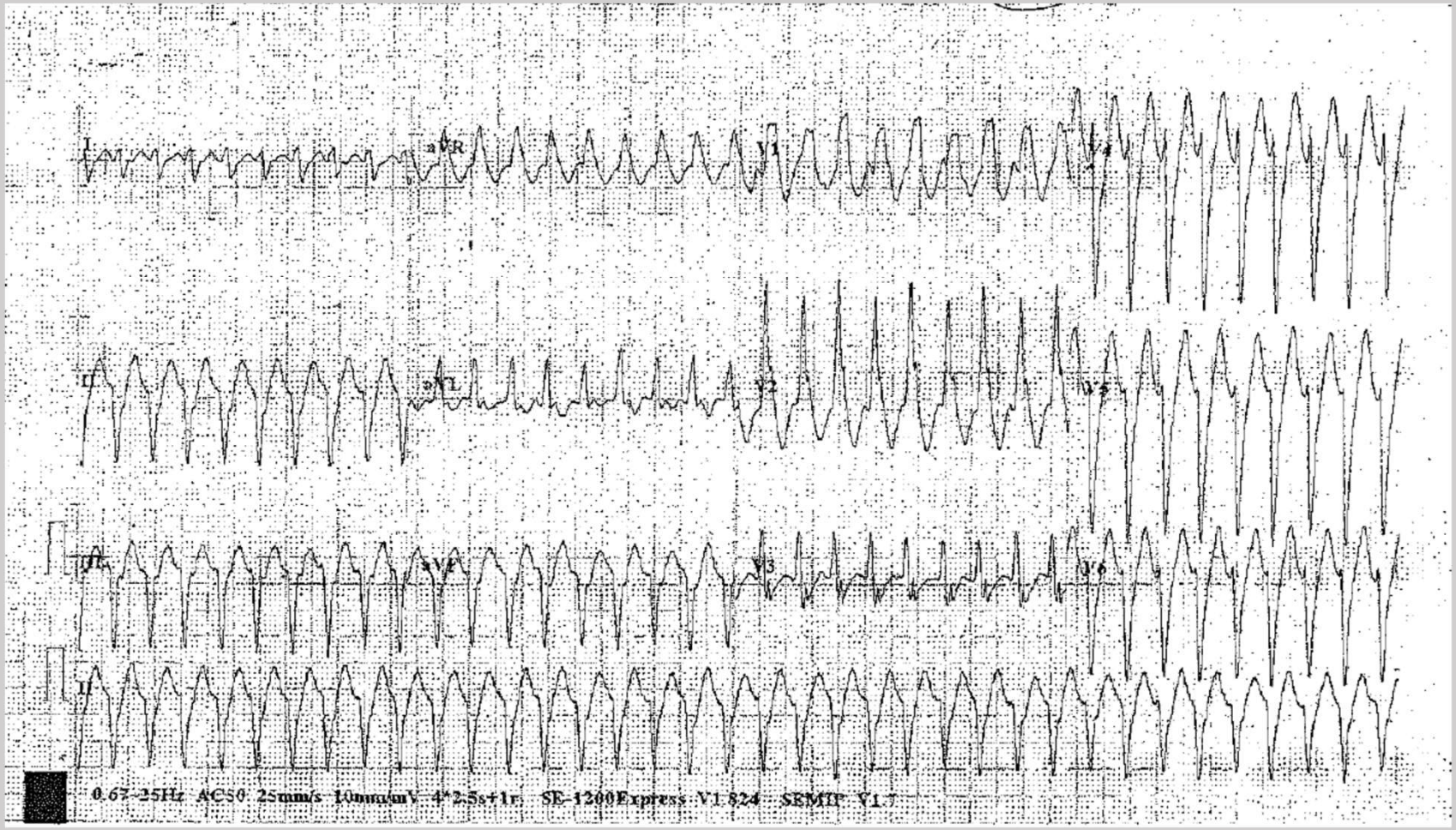
- Vasodilators
- Inotropes
- IABP
- Mechanical haemodynamic support
- Diuretics

Other Special Forms of MR

What could be the presenting symptom of severe MR?

- Incidental finding of a heart murmur
- Chest pain
- Shortness of breath, decreased exercise tolerance suggestive of heart failure
- Palpitation
- Fever or embolic complications due to underlying infective endocarditis
- VT/VF/Sudden cardiac death (SCD)

1st ECG


0.67-25Hz ACS0 25mm/s 10mm/mV 4*2.5s+1r SE-1200Express V1.824 SEMII V1.7

CMR

- LVDd 6.2 cm, LVSd 4.5 cm, EF 52.6%
- LGE in the posterior papillary muscle compatible with scar
- Small intramural scar also seen in mid inferior wall

Electrophysiology Studies

- Coro N
- Spontaneous PVC of (1) RBBB inferior axis
- Transition of V4 (2) RBBB superior asix
- Transition of V3 noticed
- Double potentials at posterior papillary muscle
- Voltage map: scarring + double potentials extending form the tip to base of posterior papillary muscle to 2 cm towards the septum
- Inducible VT of clinical morphology confirmed exceeding from the base of posterior papillary muscle

MVP and SCD

- Prevalence of MVP in general population ~ 2-3%
- Estimated rate of SCD in MVP ~ 0.2-0.4% per yrear
- High risk subgroup – LV dysfunction due to severe MR
- SCD may occur in patients with no or trivial MR

Malignant MVP Syndrome

- MV repair and ablation
- SICD/ICD

Management Guidelines

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EXPERT CONSENSUS DECISION PATHWAY

2017 ACC Expert Consensus Decision Pathway on the Management of Mitral Regurgitation

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

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Management Guidelines for MR

- 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

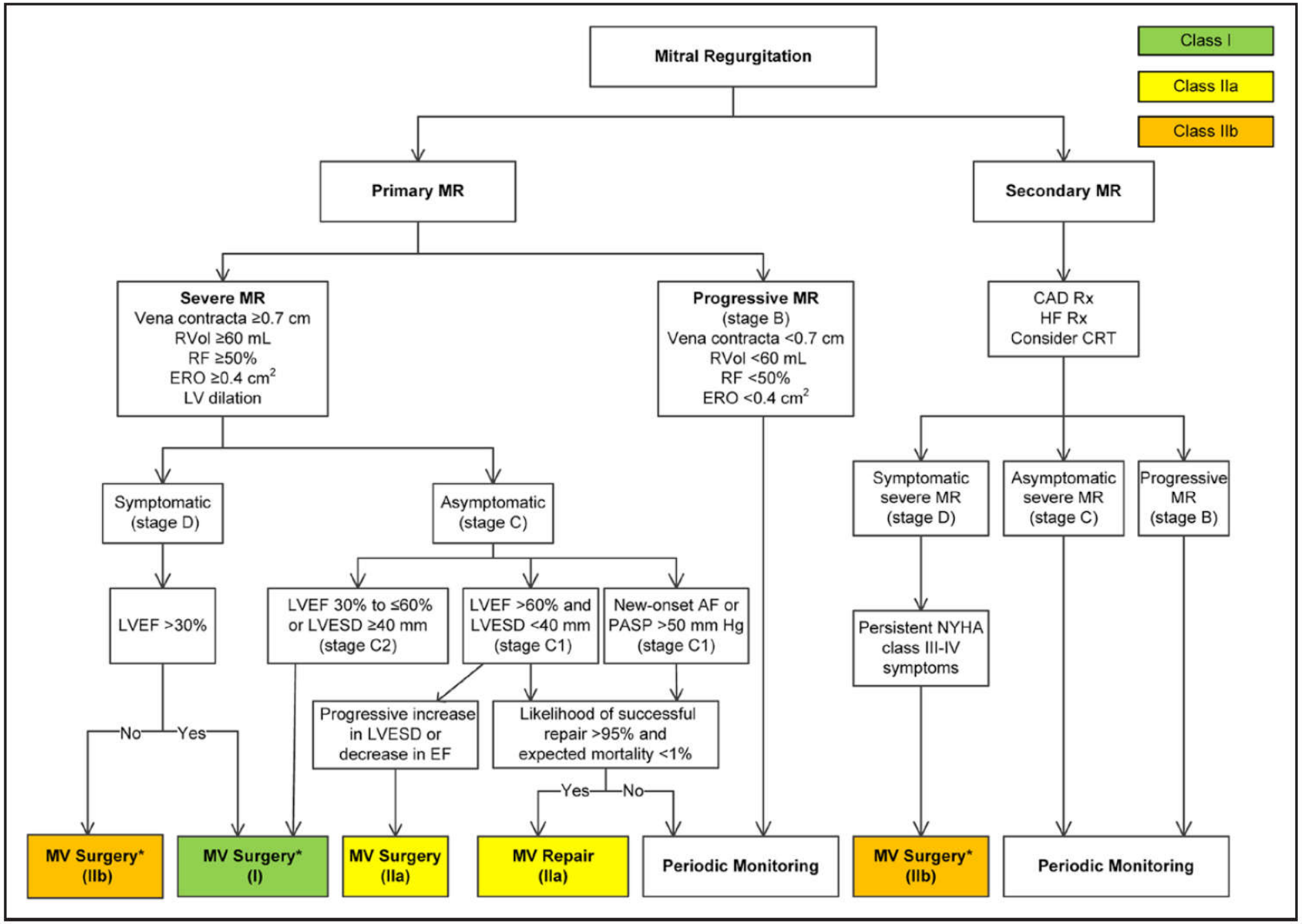


Figure 2. Indications for Surgery for MR (Updated Figure 4 From the 2014 VHD guideline).
*MV repair is preferred over MV replacement when possible.

Intervention: Primary MR

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. Symptoms + EF > 30%
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] ≥40 mm, stage C2).[76–82]	2014 recommendation remains current. No Symptoms + impaired/dilated LV
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. MV repair preferred
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.[84,89,95,100–104]	2014 recommendation remains current. MV repair preferred
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. Concomitant Severe Primary MR

MR begets MR
MV surgery in anticipated progression

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 ≤60% or LVESD ≥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)			
There is concern that the presence of MR leads to progressively more severe MR ("mitral regurgitation begets mitral regurgitation"). The concept is that the initial level of MR causes LV dilatation, which increases stress on the mitral apparatus, causing further damage to the valve apparatus, more severe MR and further LV dilatation, thus initiating a perpetual cycle of ever-increasing LV volumes and MR. Longstanding volume overload leads to irreversible LV dysfunction and a poorer prognosis. Patients with severe MR who develop an EF ≤60% or LVESD ≥40 have already developed LV systolic dysfunction.[112–115] One study has suggested that for LV function and size to return to normal after mitral valve repair, the left ventricular ejection fraction (LVEF) should be >64% and LVESD <37 mm.[112] Thus, when longitudinal follow-up demonstrates a progressive decrease of EF toward 60% or a progressive increase in LVESD approaching 40 mm, it is reasonable to consider intervention. Nonetheless, the asymptomatic patient with stable LV dimensions and excellent exercise capacity can be safely observed.[116]			
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. Asymptomatic + New onset AF/Resting PTH

Recommendations for Chronic Primary MR Intervention (Continued)			
COR	**LOE**	**Recommendations**	**Comment/Rationale**
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. Concomitant moderate primary MR
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. EF < 30
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. MitraClip
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. MV repair vs MVR

Table 2. Stages of Secondary MR (Table 16 in the 2014 VHD Guideline)

Grade	Definition	Valve Anatomy	Valve Hemodynamics*	Associated Cardiac Findings	Symptoms
A	At risk of MR	Normal valve leaflets, chords, and annulus in a patient with coronary disease or cardiomyopathy	No MR jet or small central jet area <20% LA on Doppler Small vena contracta <0.30 cm	Normal or mildly dilated LV size with fixed (infarction) or inducible (ischemia) regional wall motion abnormalities Primary myocardial disease with LV dilation and systolic dysfunction	Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
B	Progressive MR	Regional wall motion abnormalities with mild tethering of mitral leaflet Annular dilation with mild loss of central coaptation of the mitral leaflets	ERO <0.40 cm^2† Regurgitant volume <60 mL Regurgitant fraction <50%	Regional wall motion abnormalities with reduced LV systolic function LV dilation and systolic dysfunction due to primary myocardial disease	Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
C	Asymptomatic severe MR	Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet Annular dilation with severe loss of central coaptation of the mitral leaflets	ERO ≥0.40 cm^2† Regurgitant volume ≥60 mL Regurgitant fraction <50%	Regional wall motion abnormalities with reduced LV systolic function LV dilation and systolic dysfunction due to primary myocardial disease	Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
D	Symptomatic severe MR	Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet Annular dilation with severe loss of central coaptation of the mitral leaflets	ERO ≥0.40 cm^2† Regurgitant volume ≥60 mL Regurgitant fraction ≥50%	Regional wall motion abnormalities with reduced LV systolic function LV dilation and systolic dysfunction due to primary myocardial disease	HF symptoms due to MR persist even after revascularization and optimization of medical therapy Decreased exercise tolerance Exertional dyspnea

Intervention: Secondary MR

Recommendations for Secondary MR Intervention

COR	LOE	Recommendations	Comment/Rationale
IIa	C	Mitral valve surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR.	2014 recommendation remains current.
IIa	B-R	It is reasonable to choose chordal-sparing MVR over downsized annuloplasty repair if operation is considered for severely symptomatic patients (NYHA class III to IV) with chronic severe ischemic MR (stage D) and persistent symptoms despite GDMT for HF.[69,70,125,127,130–139]	**NEW:** An RCT has shown that mitral valve repair is associated with a higher rate of recurrence of moderate or severe MR than that associated with mitral valve replacement (MVR) in patients with severe, symptomatic, ischemic MR, without a difference in mortality rate at 2 years' follow-up.
See Online Data Supplement 18 (Updated From 2014 VHD Guideline)			

In an RCT of mitral valve repair versus MVR in 251 patients with severe ischemic MR, mortality rate at 2 years was 19.0% in the repair group and 23.2% in the replacement group (P=0.39).[70] There was no difference between repair and MVR in LV remodeling. The rate of recurrence of moderate or severe MR over 2 years was higher in the repair group than in the replacement group (58.8% versus 3.8%, P<0.001), leading to a higher incidence of HF and repeat hospitalizations in the repair group.[70] The high mortality rate at 2 years in both groups emphasizes the poor prognosis of secondary MR. The lack of apparent benefit of valve repair over valve replacement in secondary MR versus primary MR highlights that primary and secondary MR are 2 different diseases.[69,125,127,130–139]

Concomitant Severe Secondary MR

Chordal-sparing MVR preferred over downsized annuloplasty repair

IIb	**B**	Mitral valve repair or replacement may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe secondary MR (stage D) who have persistent symptoms despite optimal GDMT for HF.[125,127,130–140]	2014 recommendation remains current. MVR/Replacement NYHA III/IV GDMT
IIb See Online Data Supplement 18 (Updated From 2014 VHD Guideline)	**B-R**	In patients with chronic, moderate, ischemic MR (stage B) undergoing CABG, the usefulness of mitral valve repair is uncertain.[71,72]	**MODIFIED: LOE updated from C to B-R.** The 2014 recommendation supported mitral valve repair in this group of patients. An RCT showed no clinical benefit of mitral repair in this population of patients, with increased risk of postoperative complications.
In an RCT of 301 patients with moderate ischemic MR undergoing CABG, mortality rate at 2 years was 10.6% in the group undergoing CABG alone and 10.0% in the group undergoing CABG plus mitral valve repair (HR in the combined-procedure group=0.90; 95% CI: 0.45 to 1.83; *P*=0.78).[71] There was a higher rate of moderate or severe residual MR in the CABG-alone group (32.3% versus 11.2%; *P*<0.001), even though LV reverse remodeling was similar in both groups.[71] Although rates of hospital readmission and overall serious adverse events were similar in the 2 groups, neurological events and supraventricular arrhythmias were more frequent with combined CABG and mitral valve repair. Thus, only weak evidence to support mitral repair for moderate secondary MR at the time of other cardiac surgery is currently available.[71,72]			

MV Repair in Moderate ischaemic MR undergoing CABG - Uncertain

Moderate MR undergoing CABG

- There is continuing debate regarding the management of moderate ischaemic mitral regurgitation in patients undergoing CABG
- A randomized controlled trial could not show a benefit of concomitant valve surgery

Michler RE, Smith PK, Parides MK, Ailawadi G, Thourani V, Moskowitz AJ, Acker MA, Hung JW, Chang HL, Perrault LP, Gillinov AM, Argenziano M, Bagiella E, Overbey JR, Moquete EG, Gupta LN, Miller MA, Taddei-Peters WC, Jeffries N, Weisel RD, Rose EA, Gammie JS, DeRose JJ Jr, Puskas JD, Dagenais F, Burks SG, El-Hamamsy I, Milano CA, Atluri P, Voisine P, O'Gara PT, Gelijns AC, CTSN. Two-year outcomes of surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med 2016;374:1932–1941

Management Guidelines for MR

- 2017 ESC/EACTS Guidelines for the management of valvular heart disease

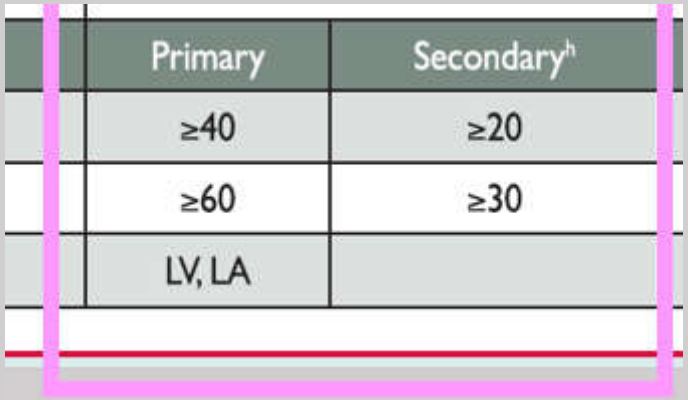
Table 4 Echocardiographic criteria for the definition of severe valve regurgitation: an integrative approach (adapted from Lancellotti *et al.*[2,6,7])

	Aortic regurgitation	Mitral regurgitation		Tricuspid regurgitation
Qualitative				
Valve morphology	Abnormal/flail/large coaptation defect	Flail leaflet/ruptured papillary muscle/ large coaptation defect		Abnormal/flail/large coaptation defect
Colour flow regurgitant jet	Large in central jets, variable in eccentric jets[a]	Very large central jet or eccentric jet adhering, swirling, and reaching the posterior wall of the LA		Very large central jet or eccentric wall impinging jet[a]
CW signal of regurgitant jet	Dense	Dense/triangular		Dense/triangular with early peaking (peak <2 m/s in massive TR)
Other	Holodiastolic flow reversal in descending aorta (EDV >20 cm/)	Large flow convergence zone[a]		–
Semiquantitative				
Vena contracta width (mm)	>6	≥7 (>8 for biplane)[b]		≥7[a]
Upstream vein flow[c]	–	Systolic pulmonary vein flow reversal		Systolic hepatic vein flow reversal
Inflow	–	E-wave dominant ≥1.5 m/s[d]		E-wave dominant ≥1 m/s[e]
Other	Pressure half-time <200 ms[f]	TVI mitral/TVI aortic >1.4		PISA radius >9 mm[g]
Quantitative		Primary	Secondary[h]	
EROA (mm^2)	≥30	≥40	≥20	≥40
Regurgitant volume (mL/beat)	≥60	≥60	≥30	≥45
+ enlargement of cardiac chambers/vessels	LV	LV, LA		RV, RA, inferior vena cava

In secondary MR, lower thresholds have been proposed to define severe mitral regurgitation compared with primary mitral regurgitation [20mm^2 for effective regurgitant orifice area (EROA) and 30mL for regurgitant volume], owing to their association with prognosis

- Grigioni F, Enriquez-Sarano M, Zehr KJ, Bailey KR, Tajik AJ. Ischemic mitral regurgitation: long-term outcome and prognostic implications with quantitative Doppler assessment. Circulation 2001;103:1759–1764.

ESC Guidelines



	Primary	Secondary[h]
	≥40	≥20
	≥60	≥30
	LV, LA	

2014 AHA/ACC Guidelines - yes

2017 AHA/ACC Guidelines – going back to same definition

Indications for intervention in asymptomatic severe primary mitral regurgitation	
IIb C Surgery may be considered in asymptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk, and: • Left atrial dilatation (volume index ≥60 mL/m² BSA) and sinus rhythm	**IIa C (modified!)** Surgery should be considered in asymptomatic patients with preserved LVEF (>60%) and LVESD 40–44 mm when a durable repair is likely, surgical risk is low, the repair is performed in heart valve centres, and the following finding is present: presence of significant LA dilatation (volume index ≥60 mL/m² BSA) in sinus rhythm.
Pulmonary hypertension on exercise (SPAP ≥ 60 mmHg at exercise)	Taken out
Indications for mitral valve intervention in secondary mitral regurgitation	
IIa C Surgery should be considered in patients with moderate secondary mitral regurgitation undergoing CABG	Moderate Secondary MR + CABG X *
IIb C When revascularization is not indicated, surgery may be considered in patients with severe secondary mitral regurgitation and LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated).	**IIb C (modified)** When revascularization is not indicated, surgery may be considered in patients with severe secondary mitral regurgitation and LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have a low surgical risk. When revascularization is not indicated and surgical risk is not low, a percutaneous edge-to-edge procedure may be considered in patients with severe secondary mitral regurgitation and LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and who have a suitable valve morphology by echocardiography, avoiding futility. In patients with severe secondary mitral regurgitation and LVEF <30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have no option for revascularization, the Heart Team may consider percutaneous edge-to-edge procedure or valve surgery after careful evaluation for ventricular assist device or heart transplant according to individual patient characteristics. **Additional statement:** The lower thresholds defining severe MR compared to primary MR are based on their association with prognosis. However, it is unclear if prognosis is independently affected by MR compared to LV dysfunction. For isolated mitral valve treatment in secondary MR, thresholds of severity of MR for intervention still need to be validated in clinical trials. So far, no survival benefit has been confirmed for reduction of secondary MR.

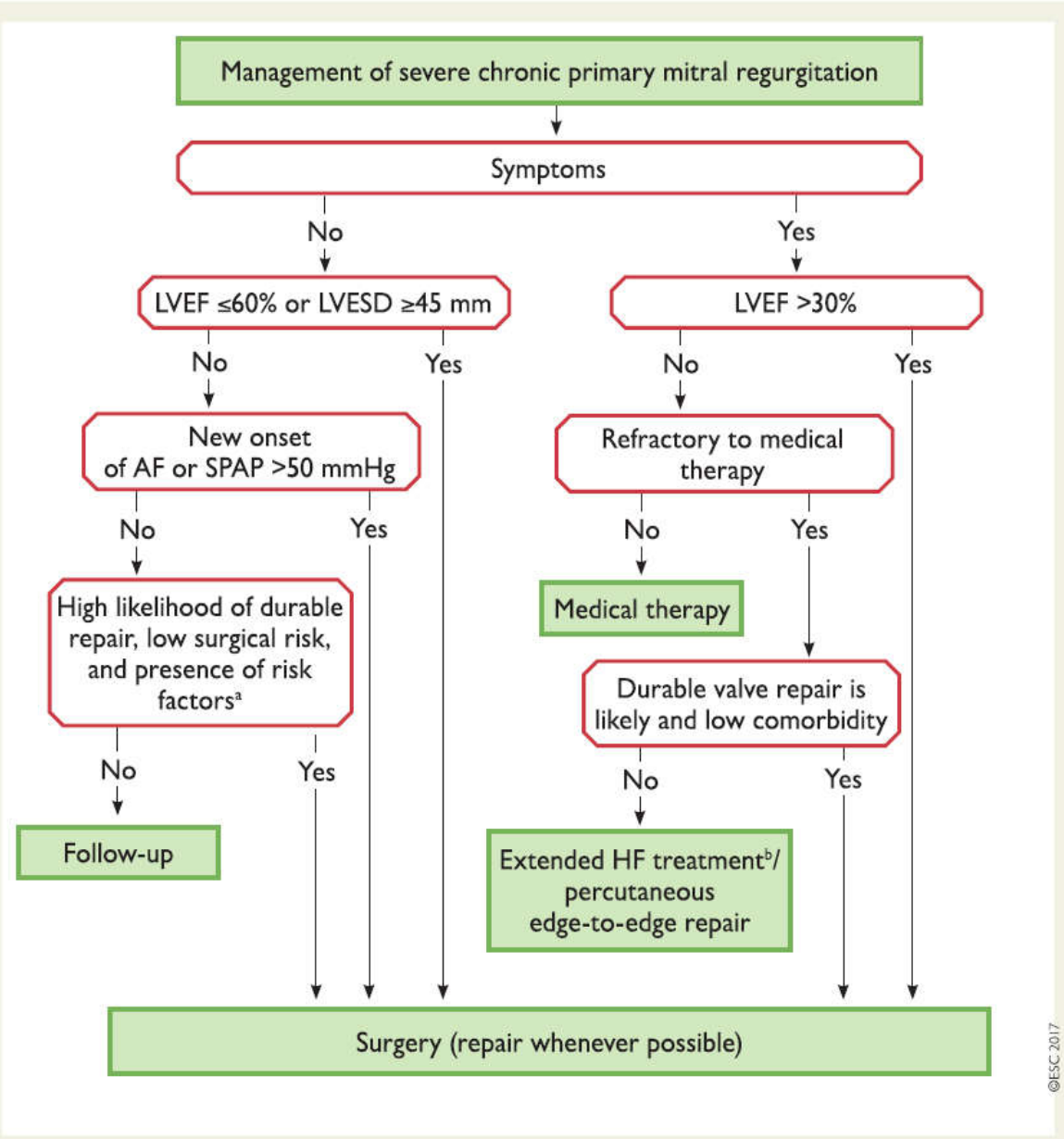


Figure 4 Management of severe chronic primary mitral regurgitation. AF = atrial fibrillation; BSA = body surface area; CRT = cardiac resynchronization therapy; HF = heart failure; LA = left atrial; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; SPAP = systolic pulmonary arterial pressure.

[a]When there is a high likelihood of durable valve repair at a low-risk, valve repair should be considered (IIa C) in patients with LVESD ≥40 mm and one of the following is present: flail leaflet or LA volume ≥60 mL/m^2 BSA at sinus rhythm.

[b]Extended HF management includes the following: CRT; ventricular assist devices; cardiac restraint devices; heart transplantation.

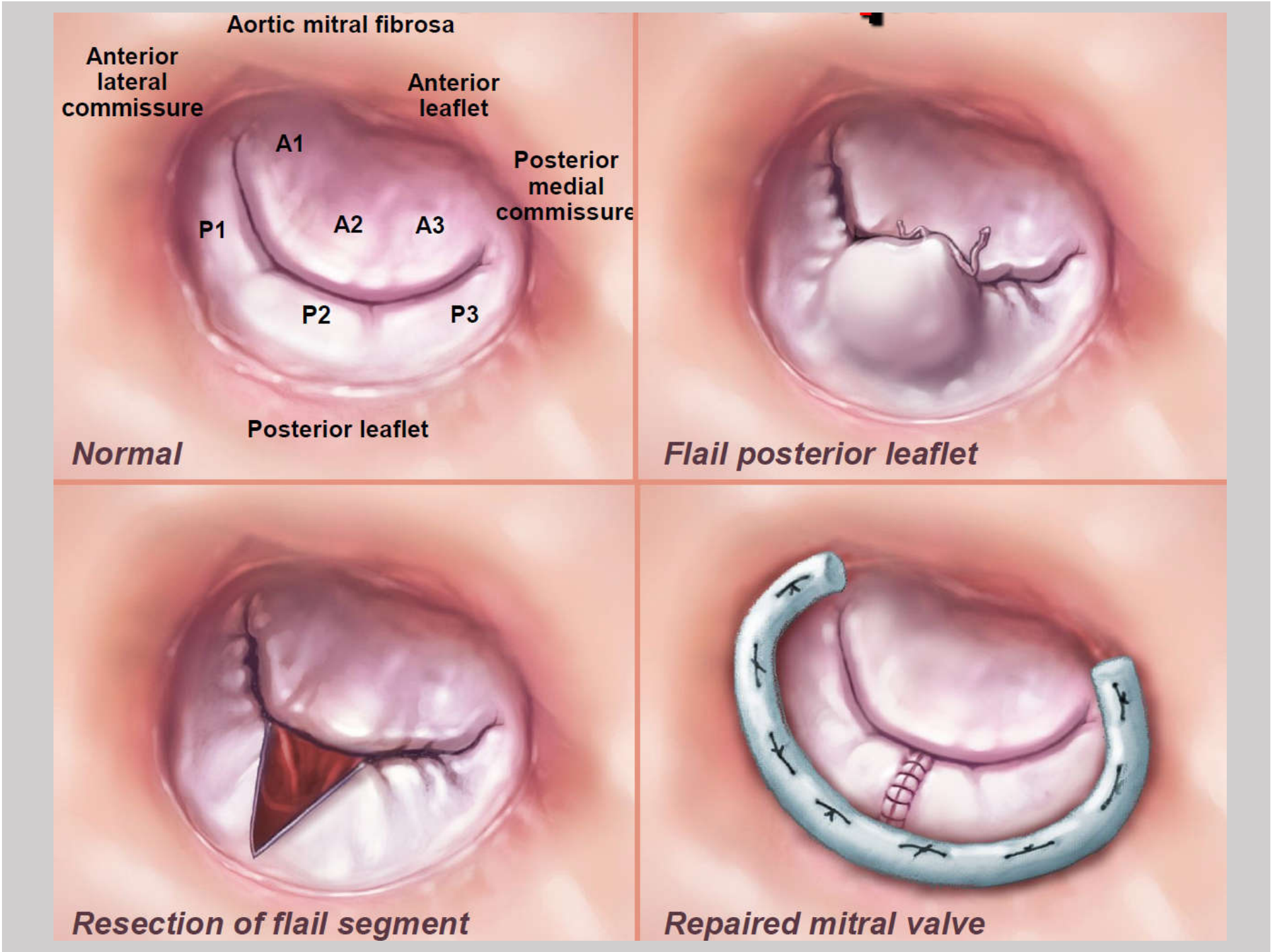
Intervention: Primary MR

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 ≥45 mm[c] and/or LVEF ≤60%).[122,131]	I	B
Surgery should be considered in asymptomatic patients with preserved LV function (LVESD <45 mm and LVEF >60%) and atrial fibrillation secondary to mitral regurgitation or pulmonary hypertension[d] (systolic pulmonary pressure at rest >50 mmHg).[123,124]	IIa	B
Surgery should be considered in asymptomatic patients with preserved LVEF (>60%) and LVESD 40–44 mm[c] when a durable repair is likely, surgical risk is low, the repair is performed in a heart valve centre and at least one of the following findings is present: • flail leaflet or • presence of significant LA dilatation (volume index ≥60 mL/m^2 BSA) in sinus rhythm.	IIa	C
Mitral valve repair should be considered in symptomatic patients with severe LV dysfunction (LVEF <30% and/or LVESD >55 mm) refractory to medical therapy when the likelihood of successful repair is high and comorbidity low.	IIa	C
Mitral valve replacement may be considered in symptomatic patients with severe LV dysfunction (LVEF <30% and/or LVESD >55 mm) refractory to medical therapy when the likelihood of successful repair is low and comorbidity low.	IIb	C
Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary mitral regurgitation who fulfil the echocardiographic criteria of eligibility and are judged inoperable or at high surgical risk by the Heart Team, avoiding futility.	IIb	C

Intervention: Secondary MR

Recommendations	Class[b]	Level[c]
Surgery is indicated in patients with severe secondary mitral regurgitation undergoing CABG and LVEF >30%.	I	C
Surgery should be considered in symptomatic patients with severe secondary mitral regurgitation, LVEF <30% but with an option for revascularization and evidence of myocardial viability.	IIa	C
When revascularization is not indicated, surgery may be considered in patients with severe secondary mitral regurgitation and LVEF >30% who remain symptomatic despite optimal medical management (including CRT if indicated) and have a low surgical risk.	IIb	C
When revascularization is not indicated and surgical risk is not low, a percutaneous edge-to-edge procedure may be considered in patients with severe secondary mitral regurgitation and LVEF >30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have a suitable valve morphology by echocardiography, avoiding futility.	IIb	C
In patients with severe secondary mitral regurgitation and LVEF <30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have no option for revascularization, the Heart Team may consider a percutaneous edge-to-edge procedure or valve surgery after careful evaluation for a ventricular assist device or heart transplant according to individual patient characteristics.	IIb	C

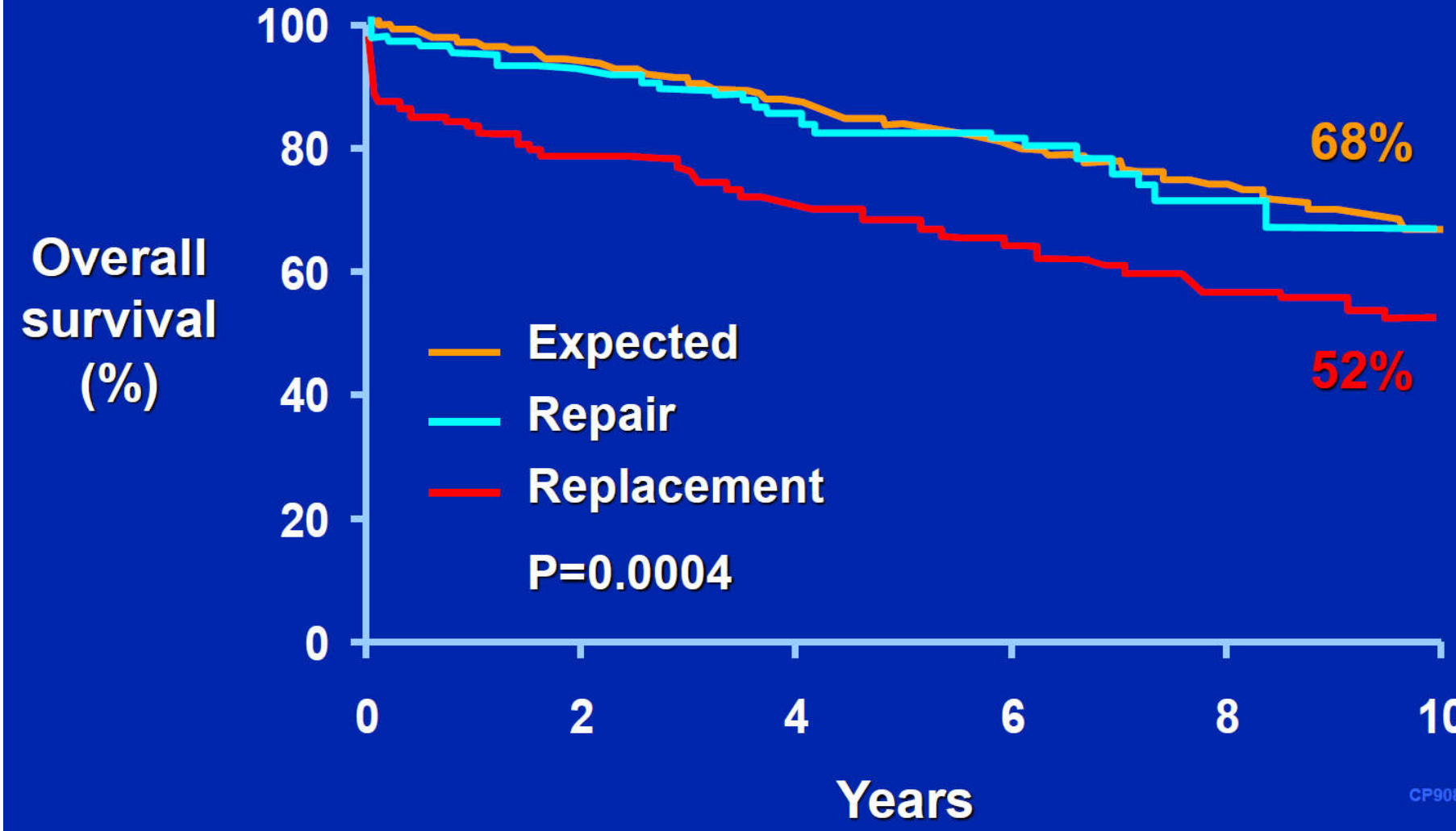
Open Mitral Valve Repair


Aortic mitral fibrosa
Anterior lateral commissure
Anterior leaflet
A1
Posterior medial commissure
P1
A2
A3
P2
P3
Posterior leaflet
Normal
Flail posterior leaflet
Resection of flail segment
Repaired mitral valve

Features suggestive of a high likelihood of successful repair

- Posterior leaflet prolapse
- Commissural prolapse
- Rupture chordae to the posterior leaflet
- Congenital cleft
- Small perforation

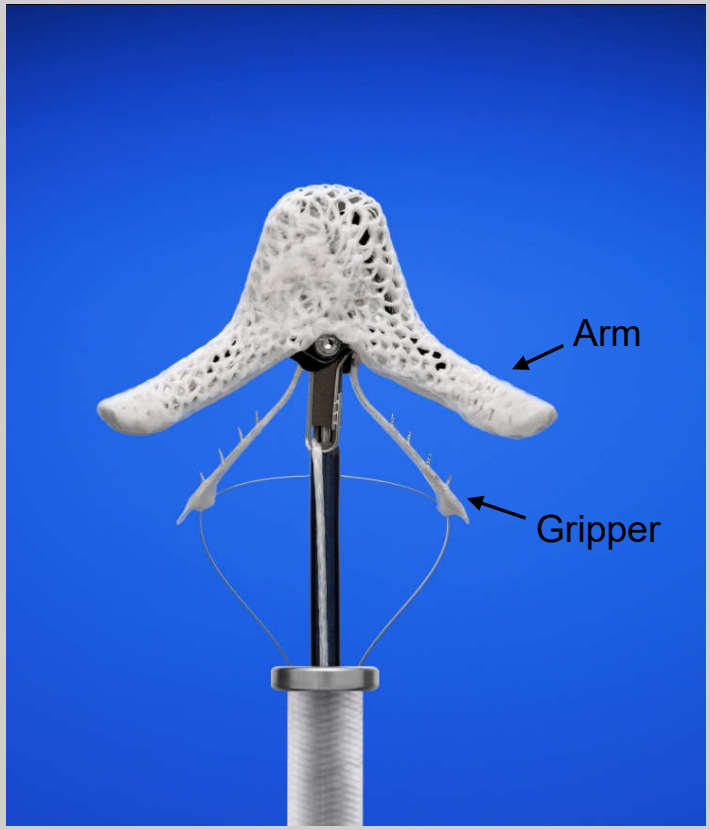
MR: Mitral Valve Repair

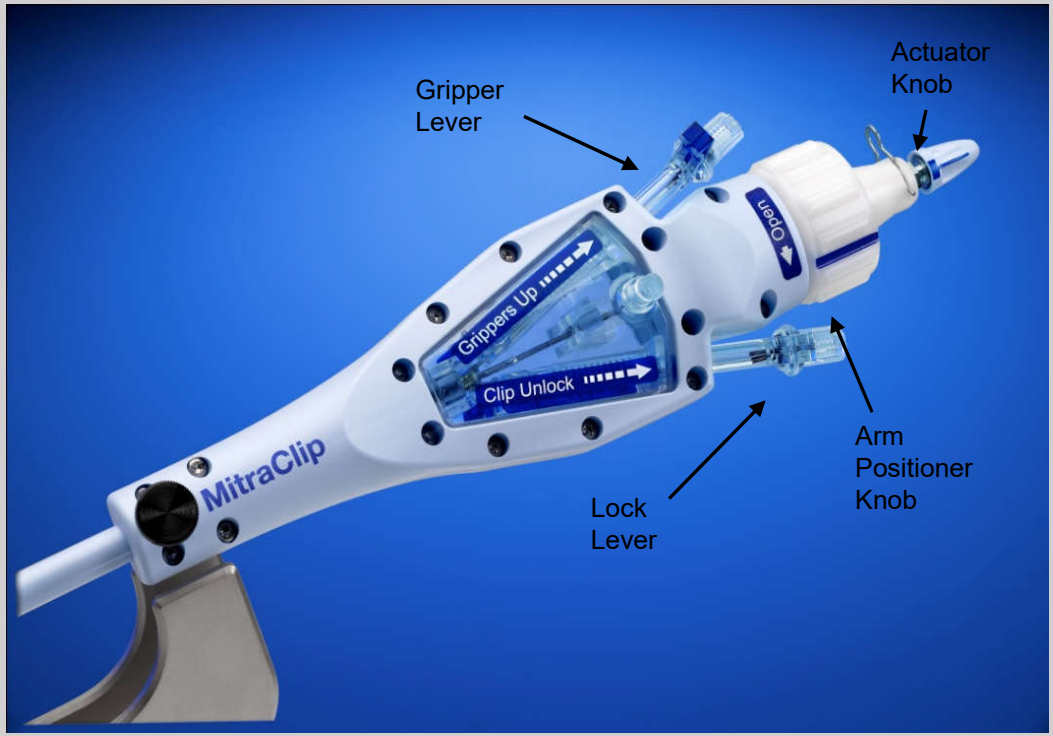


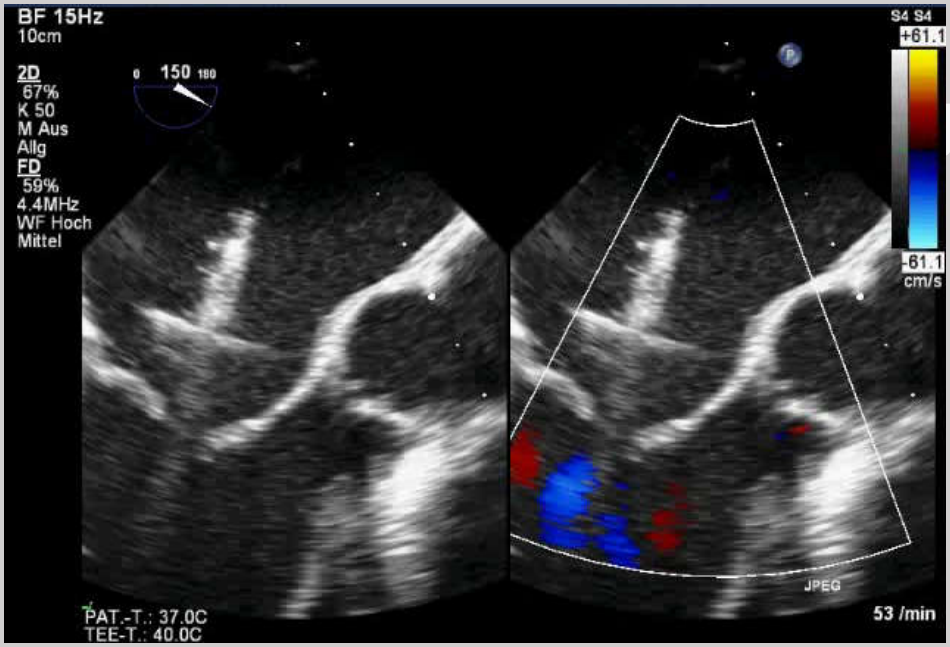
Transcatheter Mitral Valve Repair

Abbott MitraClip System

- Percutaneous Mitral Repair with MitraClip



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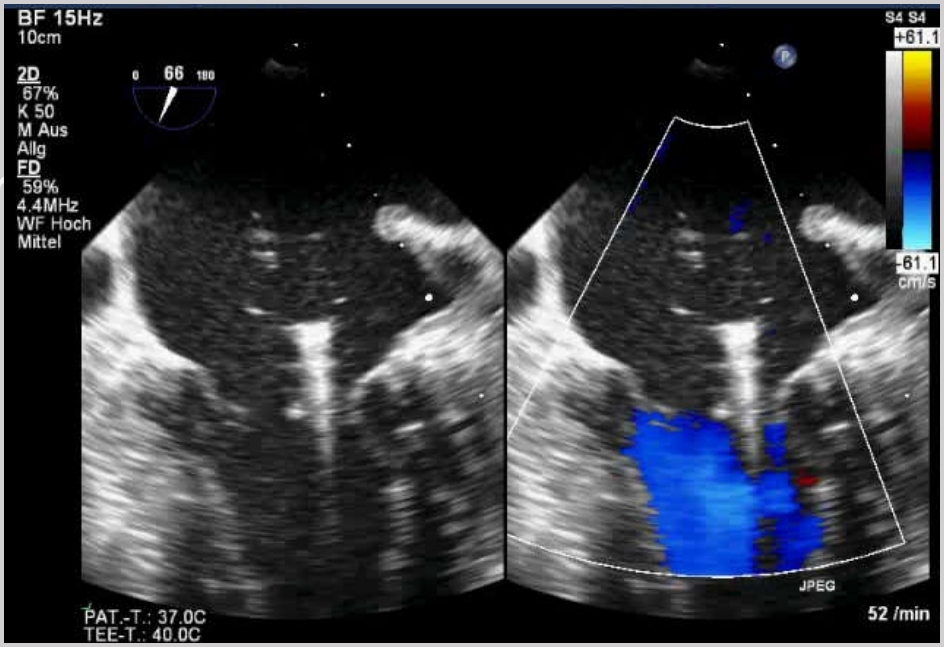
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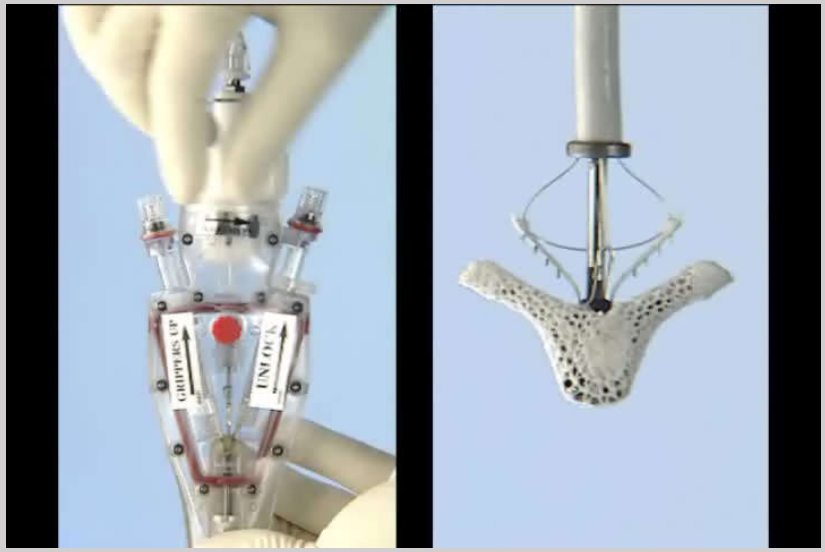
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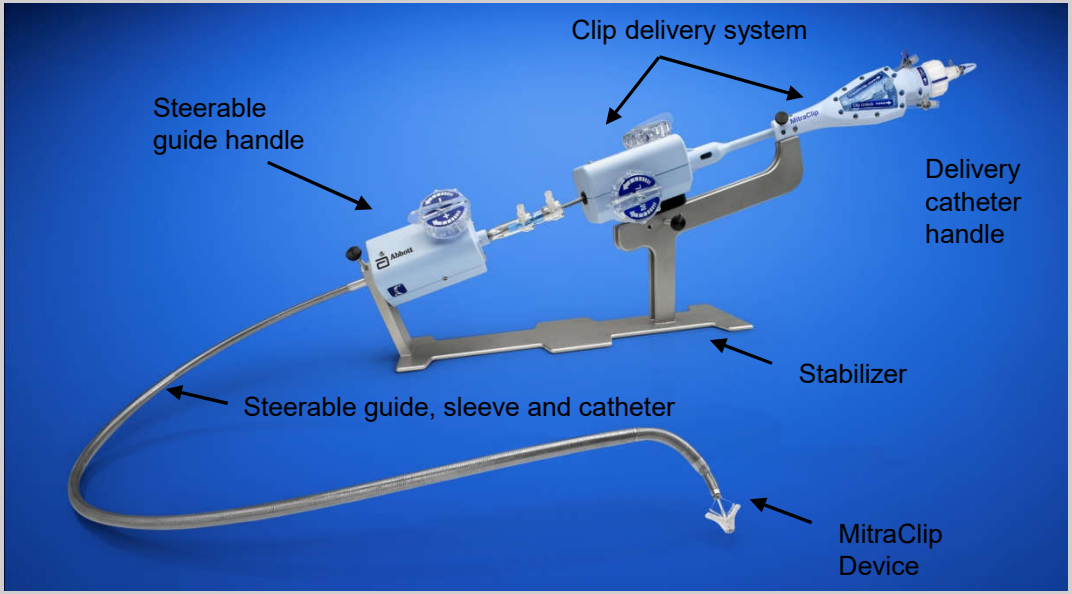
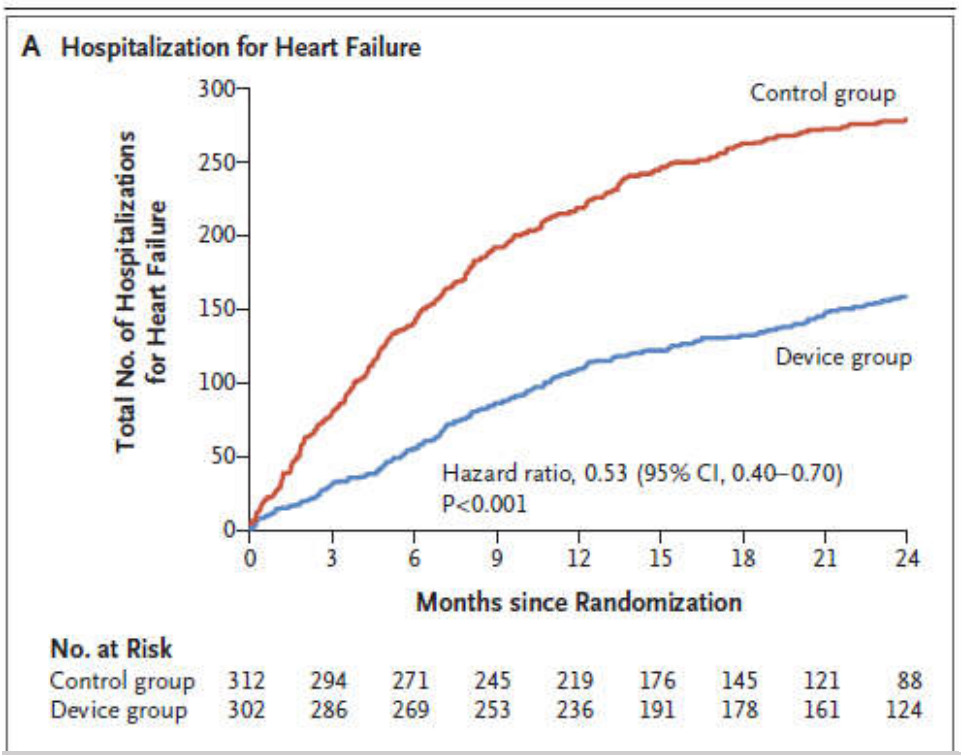
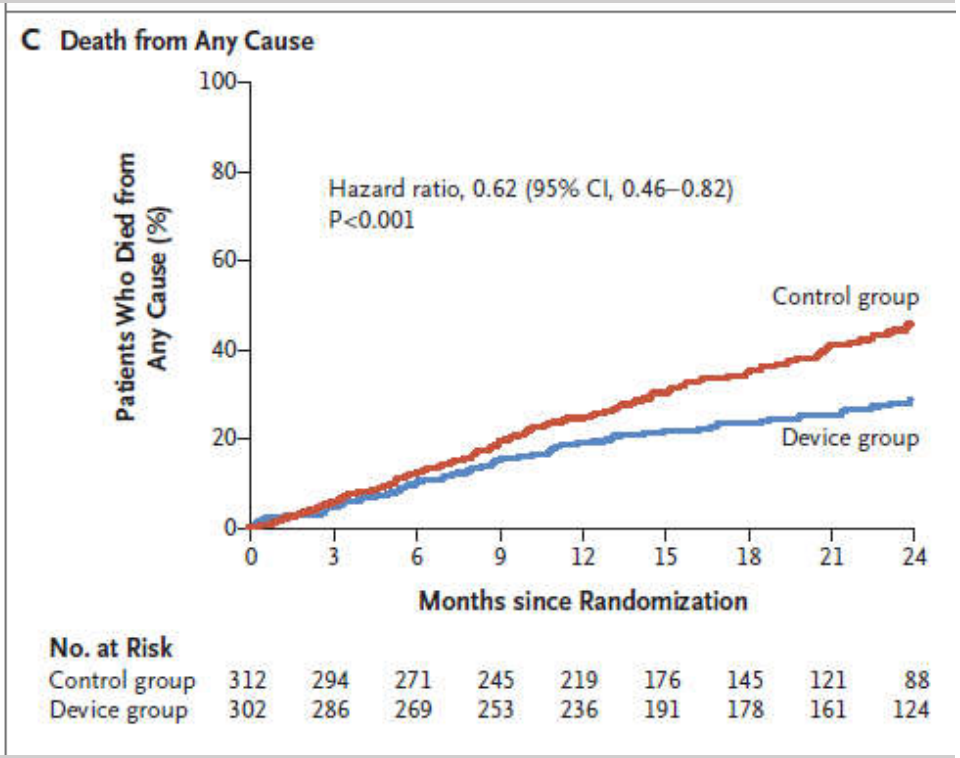

Clip delivery system
Steerable
guide handle
Delivery
catheter
handle
Stabilizer
Steerable guide, sleeve and catheter
MitraClip
Device

COAPT Trial for Functional MR

- 614 patients, 78 sites
- GDMT vs MitraClip+GDMT





NEMJ 2018

COAPT – Study Design

Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

A parallel-controlled, open-label, multicenter trial in 614 patients with heart failure and moderate-to-severe (3+) or severe (4+) secondary MR who remained symptomatic despite maximally-tolerated GDMT

Primary endpoints:

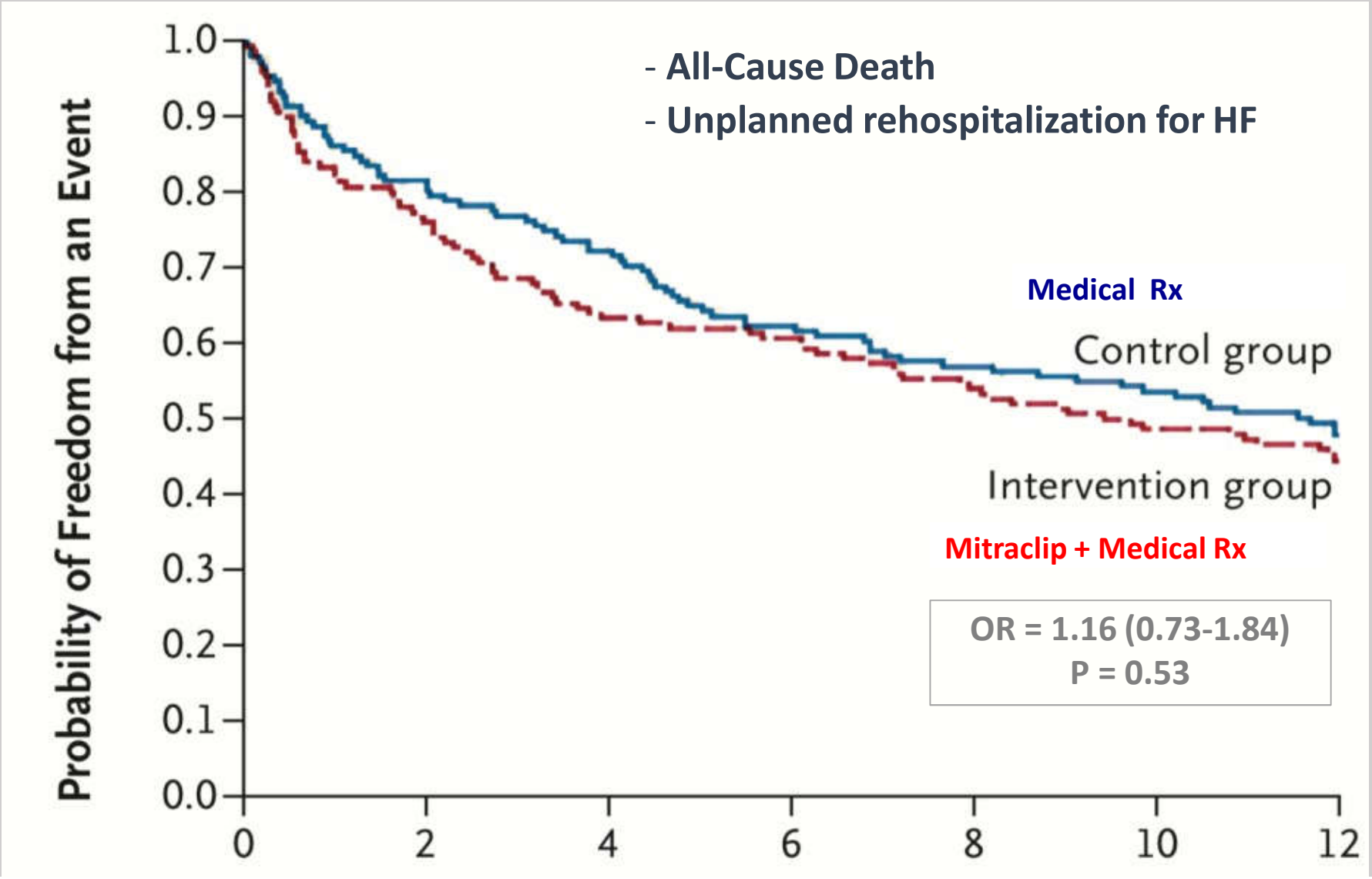
Effectiveness: All HF hospitalizations through 24 mos, analyzed when last pt completes 12-mo FU

Safety: Freedom from device-related complications through 12 months

COAPT Investigators. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. N Engl J Med 2018; 379:2307-2318

Primary composite endpoint

(99% follow-up)



MITRA-FR vs COAPT

	MITRA-FR (n=304)	COAPT (n=614)
Severe MR entry criteria	Severe FMR by EU guidelines: EROA >20 mm^2 or RV >30 mL/beat	Severe FMR by US guidelines: EROA >30 mm^2 or RV >45 mL/beat
EROA (mean ± SD)	31 ± 10 mm^2	41 ± 15 mm^2
LVEDV (mean ± SD)	135 ± 35 mL/m^2	101 ± 34 mL/m^2
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 ≥3+ MR	17%	5%

*MITRA-FR defn: device implant failure, transf or vasc compl req surg, ASD, card shock, cardiac embolism/stroke, tamponade, urg card surg

FDA approval MitraClip Secondary MR

14/3/2019

FDA expands MitraClip indication to include patients with secondary mitral regurgitation

Posted: 03/14/2019 **Author:** Jason Wermers, CRTonline.org **2019 NEWS**

The U.S. Food and Drug Administration (FDA) approved a new indication for MitraClip (Abbott Vascular) on Thursday, several months after COAPT trial results showed that the device plus optimal medical therapy was a significantly more effective treatment for patients with heart failure (HF) and moderate to severe secondary mitral regurgitation (MR) than optimal medical therapy alone was.

Those trial results were presented at Transcatheter Cardiovascular Therapeutics (TCT) 2018 in San Diego in September and were published in December in the *New England Journal of Medicine*.

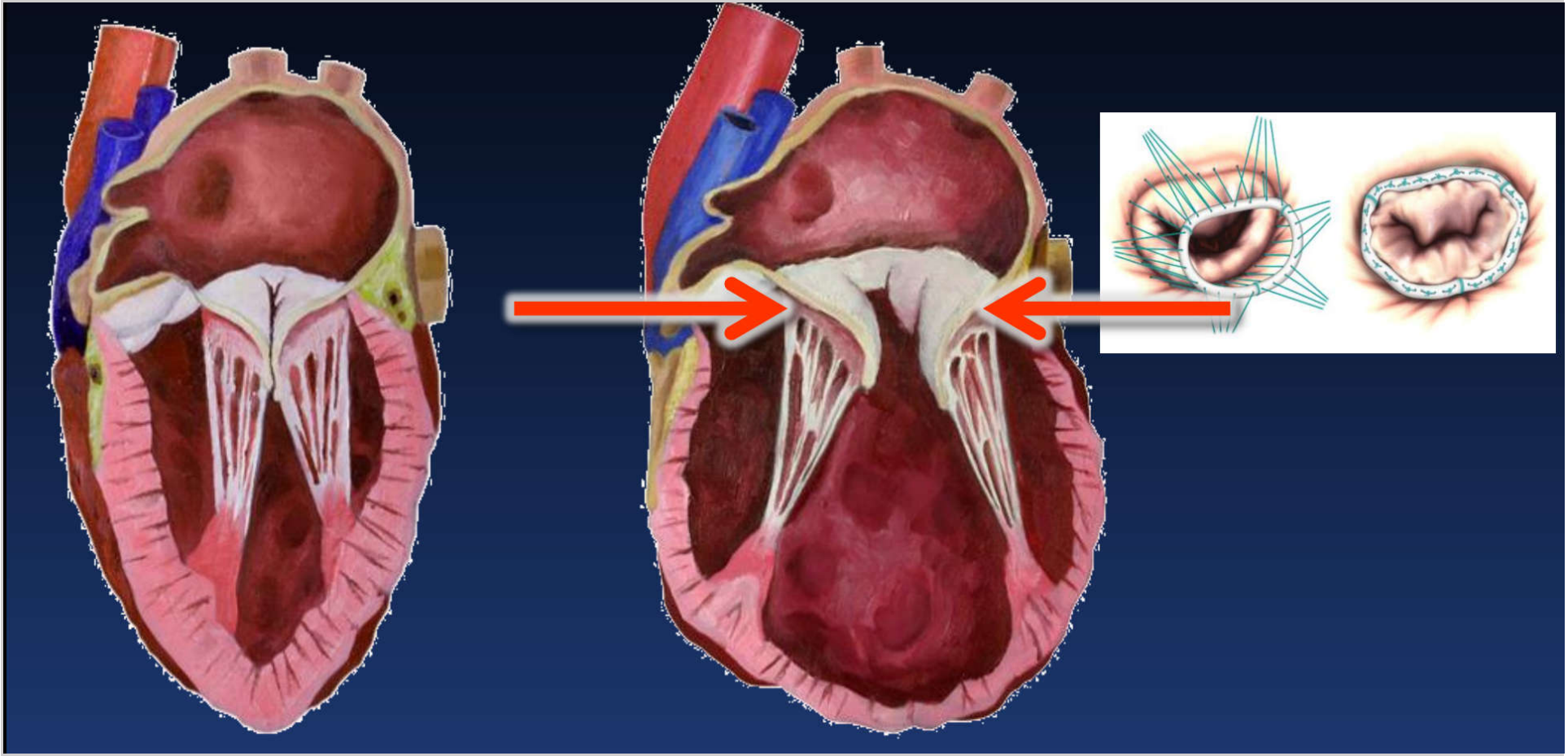
When first approved in 2013, the MitraClip Clip Delivery System was indicated to reduce mitral regurgitation in patients with primary MR and whose risks for mitral valve surgery are prohibitive. The new indication, approved Thursday, is for treatment of patients with HF and secondary MR despite being treated with optimal medical therapy, the FDA said in a news release.

“Expanding the approval of this device to heart failure patients with significant secondary mitral regurgitation, who have failed to get symptom relief from other therapies, provides an important new treatment option,” Bram D. Zuckerman, MD, director of the Division of Cardiovascular Devices in the FDA’s Center for Devices and Radiological Health, said in the news release. “Careful evaluation by a team of specialists is essential to determining whether a particular patient is an appropriate candidate for this procedure.”

About 6.5 million American adults live with HF. A small percentage of these patients also have moderate-to-severe or severe secondary MR, increasing the risks and complicating the treatment of their HF. With the new approval, this small percentage of patients could be indicated as candidates for treatment with the MitraClip device when combined with optimal medical therapy, the FDA said.

The MitraClip is inserted in a minimally invasive procedure through the femoral vein in the leg and guided into the heart’s left ventricle where

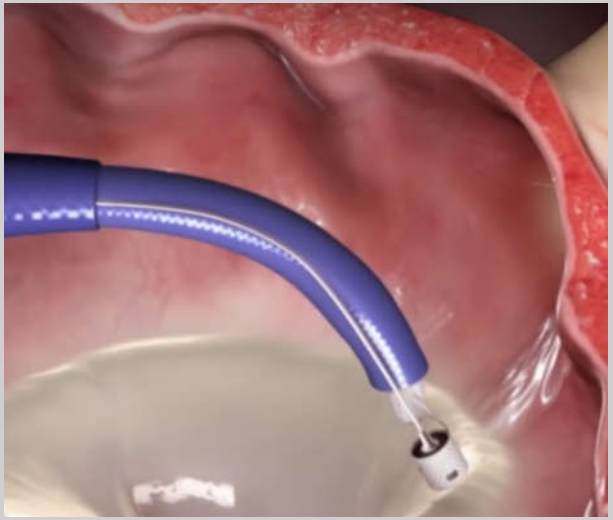
Surgical Annuloplasty for Functional MR

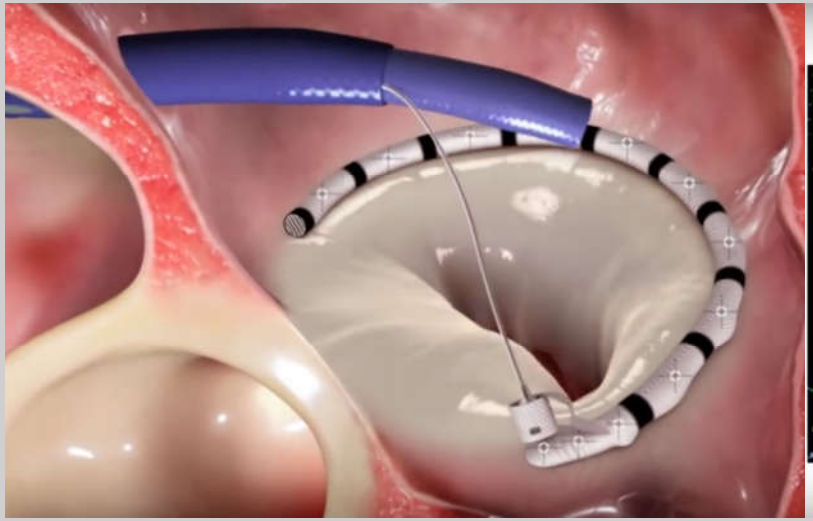


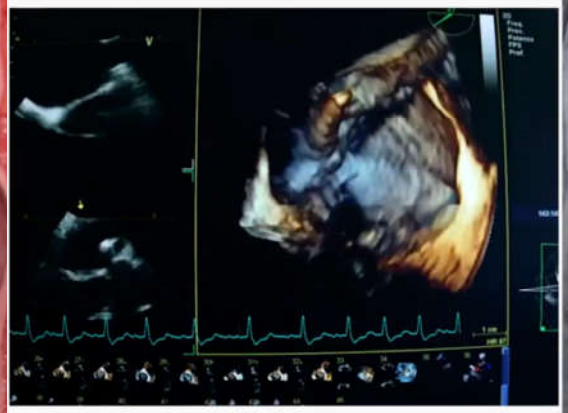
Edwards Cardioband

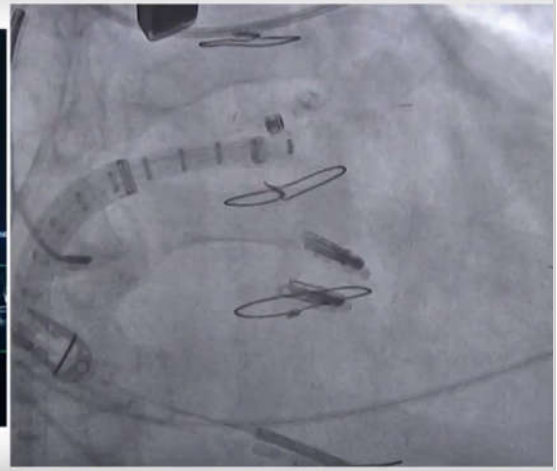
Direct Annuloplasty

Edwards Cardioband



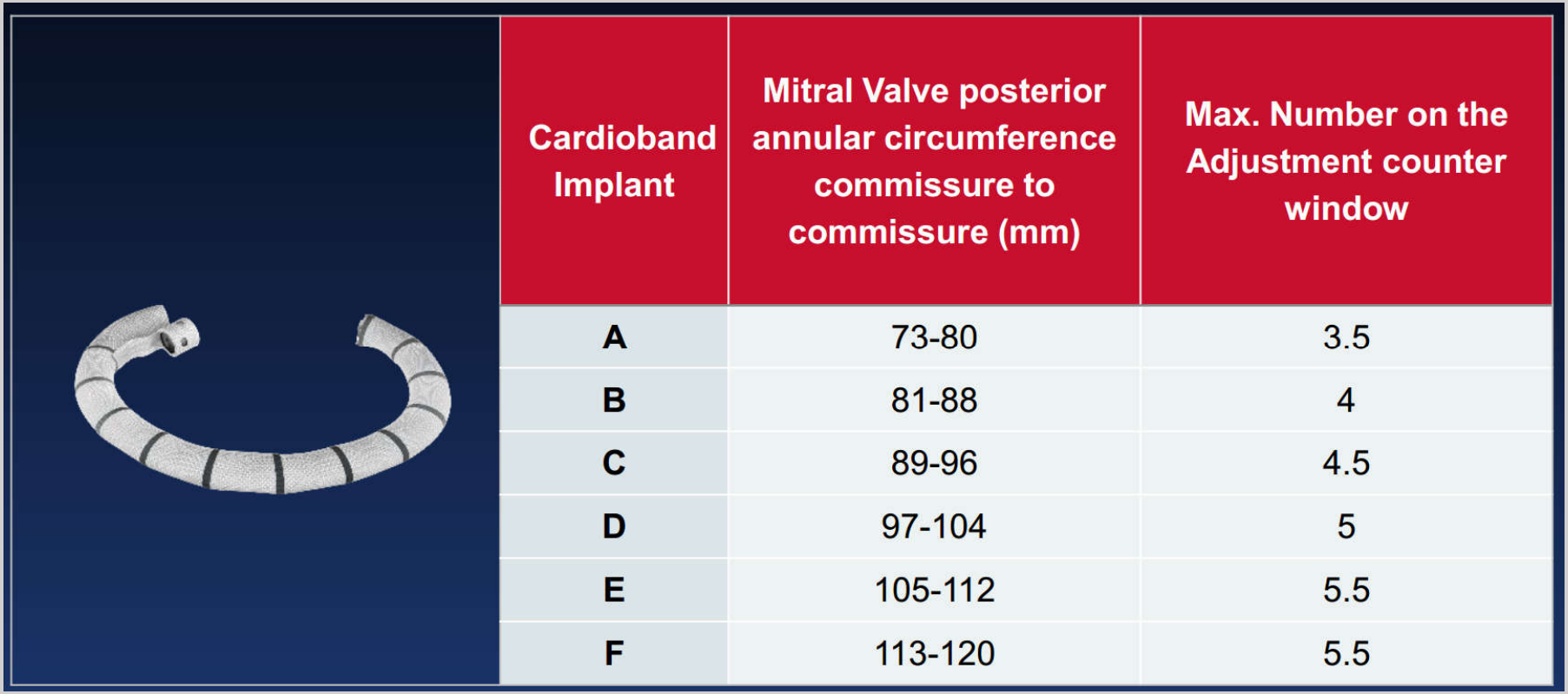






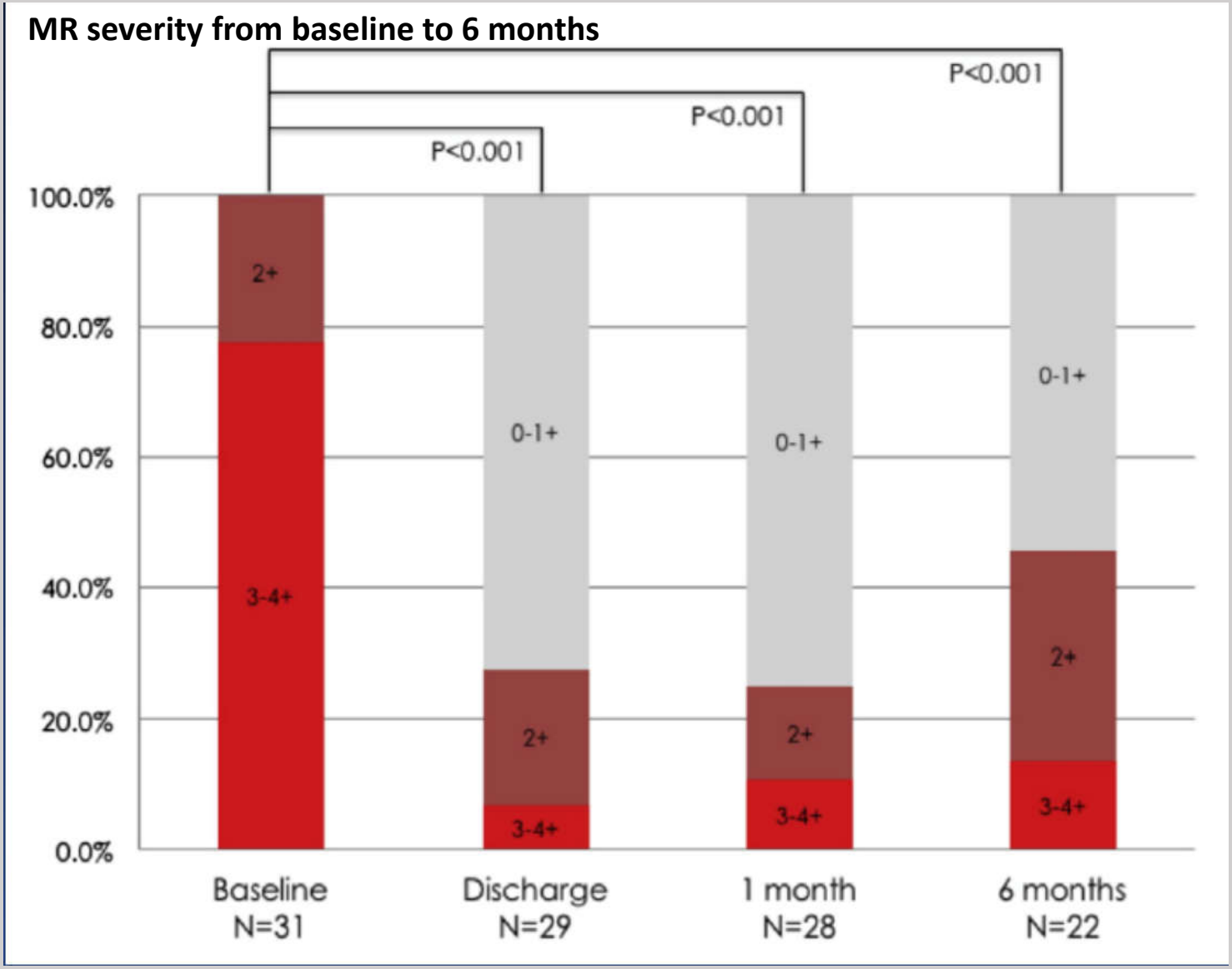
Edwards Cardioband

- 6 sizes
- CT assessment of annulus size



Cardioband Implant	Mitral Valve posterior annular circumference commissure to commissure (mm)	Max. Number on the Adjustment counter window
A	73-80	3.5
B	81-88	4
C	89-96	4.5
D	97-104	5
E	105-112	5.5
F	113-120	5.5

6-Month Results with the Cardioband Percutaneous MV Repair System

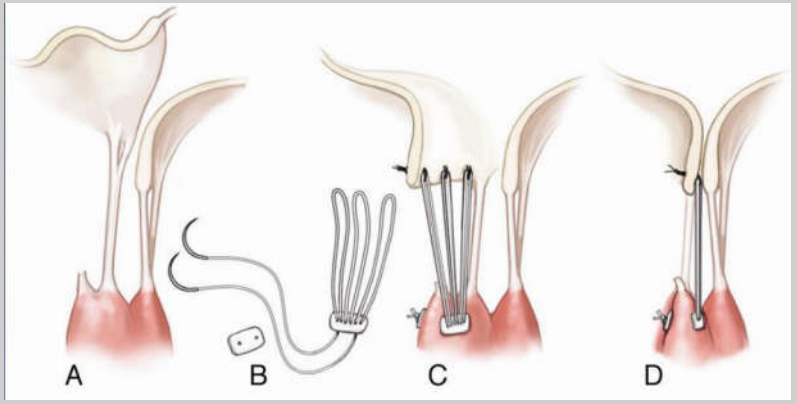


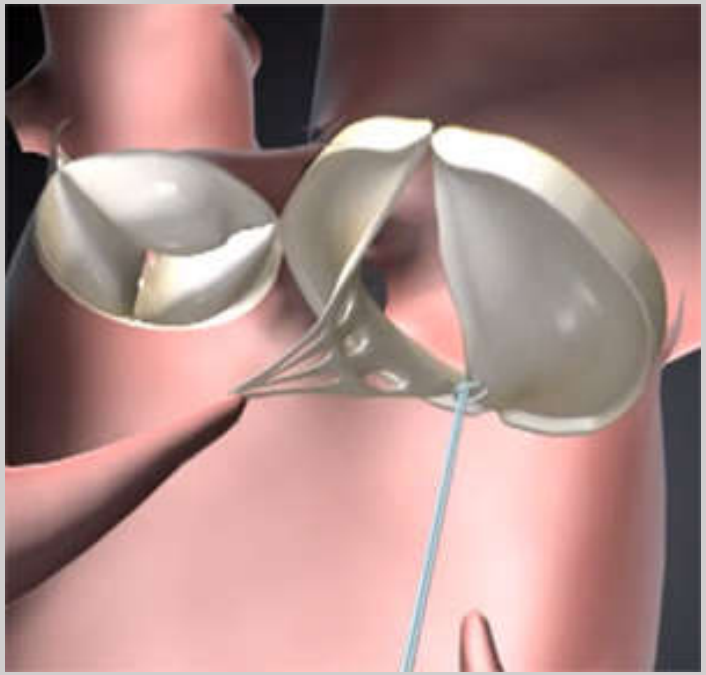
Nickenig.

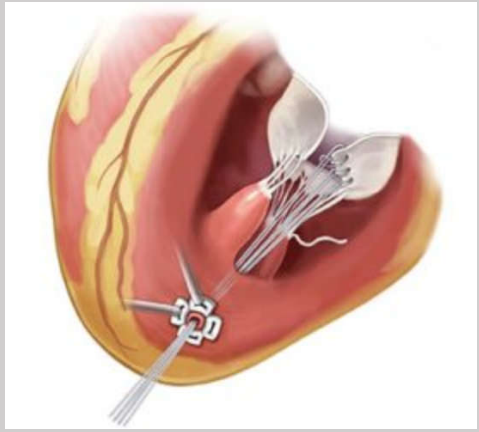
JACC Intv 2016

NeoChord DS100

- Artificial chord implantation
- ePTFE material
- Transpical system

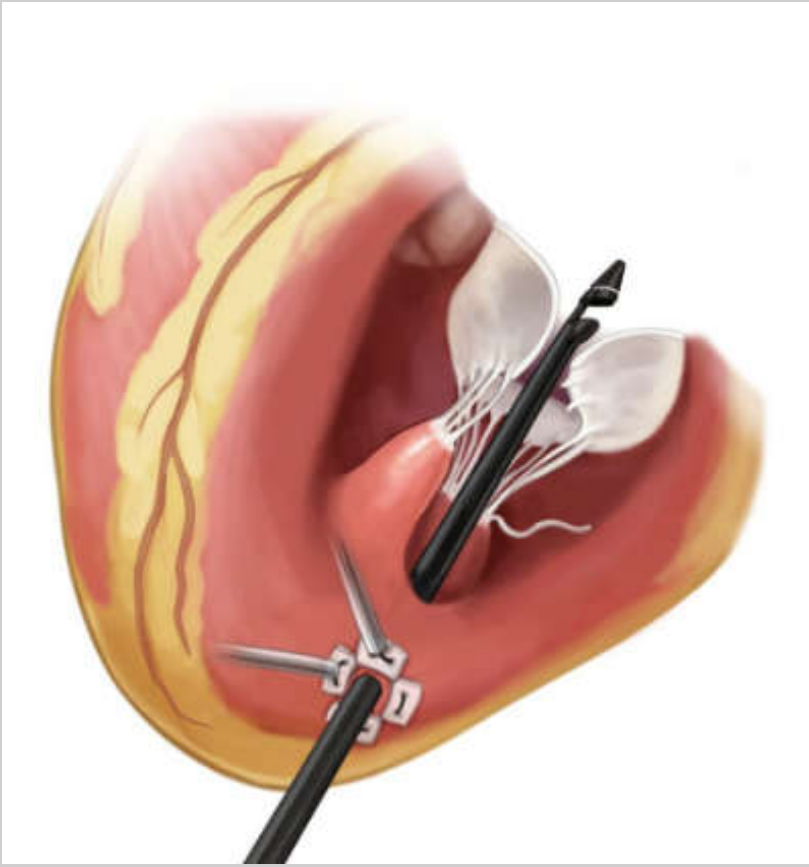


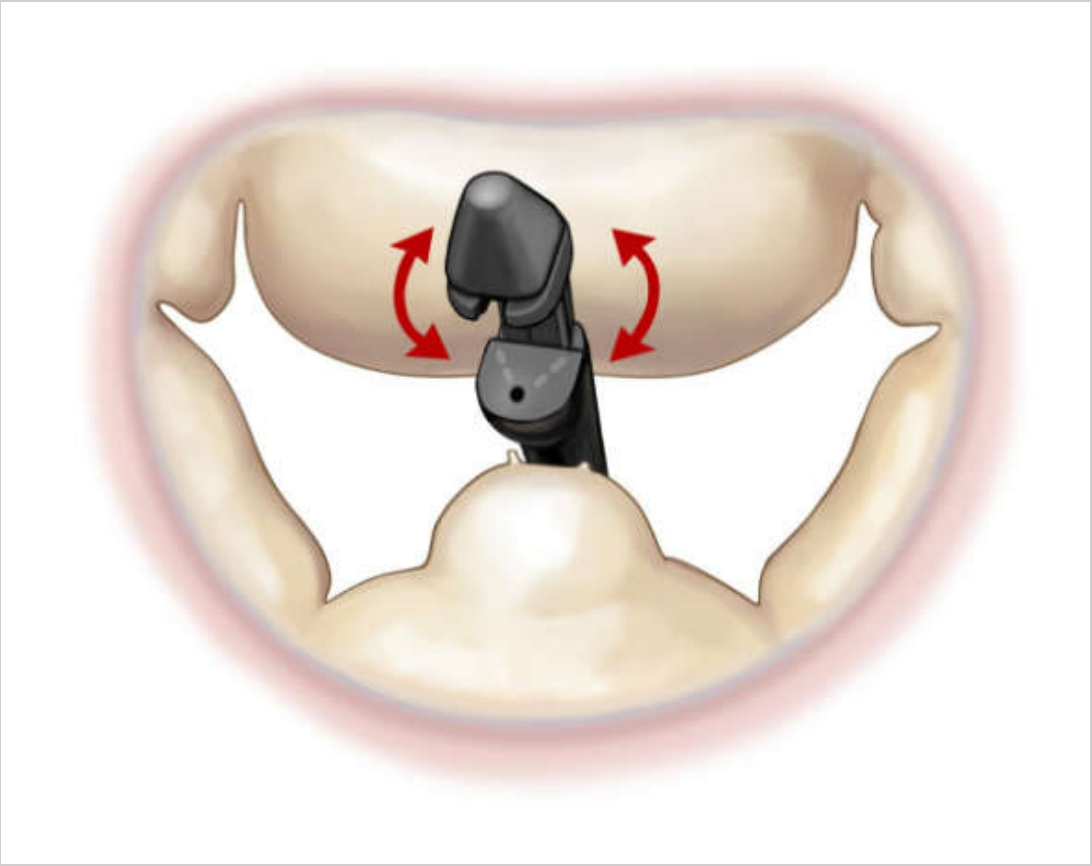




NeoChord
Transforming Mitral Valve Repair


NeoChord DS1000



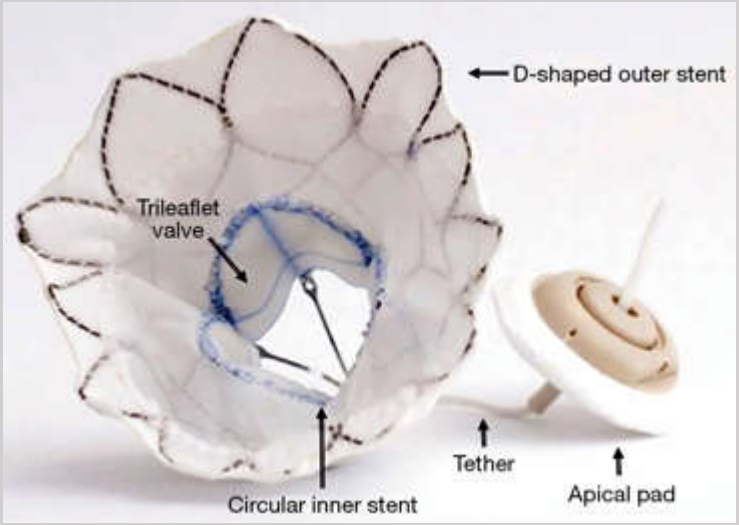


Transcatheter Mitral Valve Replacement

Transcatheter Mitral Valve Implantation

- Edwards CardiAQ

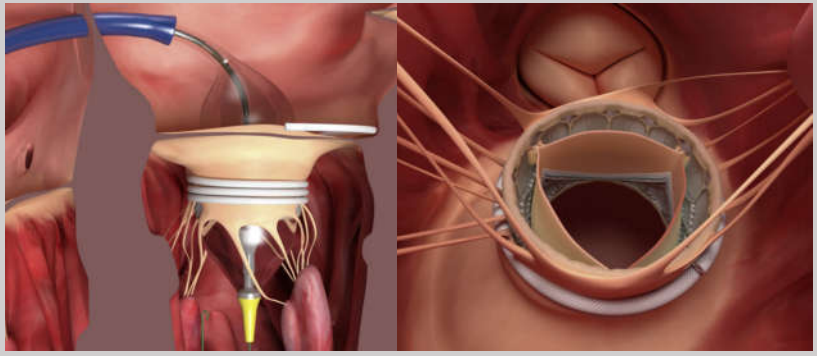
- Medtronic Intrepid



- Abbott Tendyne

Edwards SAPIEN M3

- Leverages SAPIEN 3 Valve tissue and frame
- Knitted PET skirts aids in sealing
- 29mm Valve
- 20Fr eSheath compatibility
- Transseptal system



Dock Delivery

SAPIEN M3 Dock

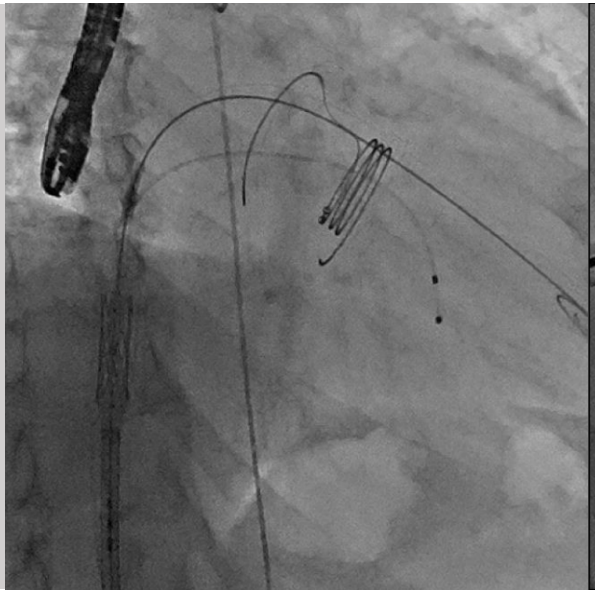
SAPIEN M3 Dock Delivery System

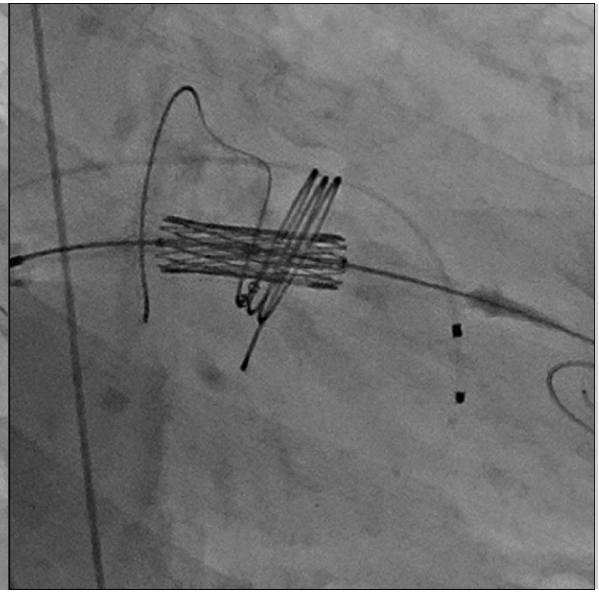
Valve Delivery

SAPIEN M3 Valve

Commander Delivery System

Final Implant





Percutaneous Transcatheter Mitral Valve Replacement

First-in-Human Experience With a New Transseptal System

John G. Webb, MD, Dale J. Murdoch, MBBS, Robert H. Boone, MD, Robert Moss, MBBS, Adrian Attinger-Toller, MD, Philipp Blanke, MD, Anson Cheung, MD, Mark Hensey, MB, BCh, BAO, Jonathon Leipsic, MD, Kevin Ong, MD, Janarthanan Sathananthan, MBChB, David A. Wood, MD, Jian Ye, MD, Paolo Tartara, MD

ABSTRACT

BACKGROUND Severe mitral regurgitation (MR) conveys significant morbidity and mortality, and surgical repair or replacement may not be a desirable option.

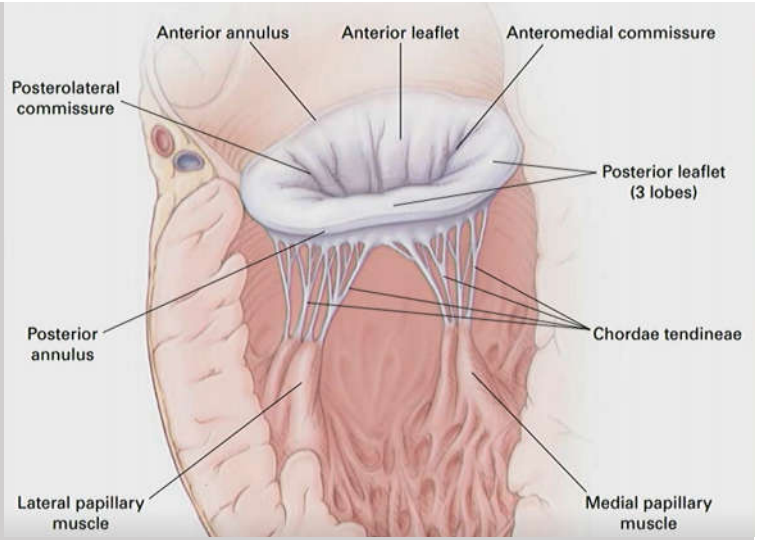
OBJECTIVES The purpose of this study was to evaluate the feasibility of a percutaneous transseptal transcatheter mitral valve replacement (TMVR) system.

METHODS This first-in-human study was conducted between August 2017 and August 2018. The system comprises a nitinol dock, which encircles the chordae tendineae, and a balloon-expandable transcatheter heart valve. The dock and transcatheter heart valve form an ensemble, with the native mitral valve leaflets secured in between, thereby abolishing MR. Key inclusion criteria were severe symptomatic MR and high surgical risk; exclusion criteria included left ventricular ejection fraction <30% or screening suggesting unfavorable anatomy. The primary endpoint was technical success as defined by Mitral Valve Academic Research Consortium (MVARC) criteria at completion of the index procedure. The secondary endpoint was freedom from mortality, stroke, and device dysfunction (MR grade >1, mitral gradient >6 mm Hg, left ventricular outflow tract gradient >20 mm Hg) at 30 days.

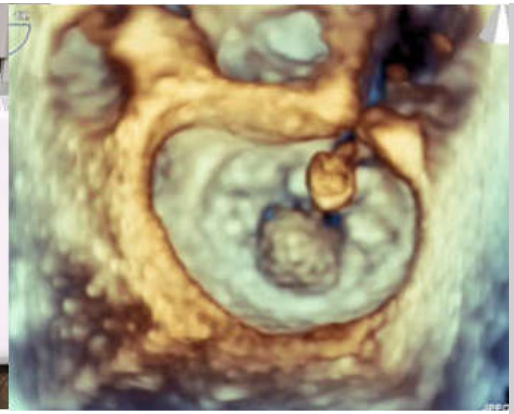
RESULTS Ten patients with severe MR of various etiologies (4 degenerative, 4 functional, and 2 mixed) were treated. The device was successfully implanted and the primary endpoint was achieved in 9 of 10 patients (90%). By transesophageal echocardiography, total MR was reduced to ≤ trivial in all implanted patients, and mean transmitral gradient was 2.3 ± 1.4 mm Hg. A pericardial effusion occurred in 1 patient: pericardiocentesis was performed, and the device was not implanted. Median length of hospital stay was 1.5 days. At 30 days, there was no stroke, myocardial infarction, rehospitalization, left ventricular outflow tract obstruction, device migration, embolization, or conversion to mitral surgery. One patient had recurrent regurgitation due to a paravalvular leak, treated with a closure device. All other treated patients had ≤1+ MR. No patients died.

CONCLUSIONS Percutaneous transvenous transseptal TMVR is feasible and safe in patients with severe MR who are at high risk for mitral valve surgery. Further evaluation is warranted. (J Am Coll Cardiol 2019;73:1239–46)

Conclusion



- Mitral Valve
  - complex structure
  - more of apparatus than valves
  - pathologies in one level can affect the other levels
  - cascade of events into vicious cycle
- MR has significant impact on morbidities and mortality
- Challenges in quantifications
- Primary and Secondary MR very distinct entities
- Mixed etiologies
- Dynamic degree of MR
- Updated evidence in clinical management guidelines and evolving minimal invasive intervention techniques



HONG KONG VALVE
HEART TEAM CONFERENCE

First Announcement

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Cheung Kung Hai Lecture Theatre,
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- Live case demonstrations from Queen Mary Hospital
- Plenary lectures by overseas & local experts
- Hands-on, didactic workshops
  - Cardiac catheterization skills for cardiothoracic surgeons
  - Cardiac surgical basics for interventional cardiologists
  - Cardiothoracic anaesthesiology and TEE essentials for Hybrid Heart Valve Interventions
  - Transcatheter heart valve crimping and loading for nurses

Conference Secretariat
hkvalve@hku.hk
http://hkvalve.org


HONG KONG VALVE 2018
15-16TH SEPTEMBER 2018
Thank you!