Insuffisance mitrale secondaire et insuffisance cardiaque : quels mécanismes ?

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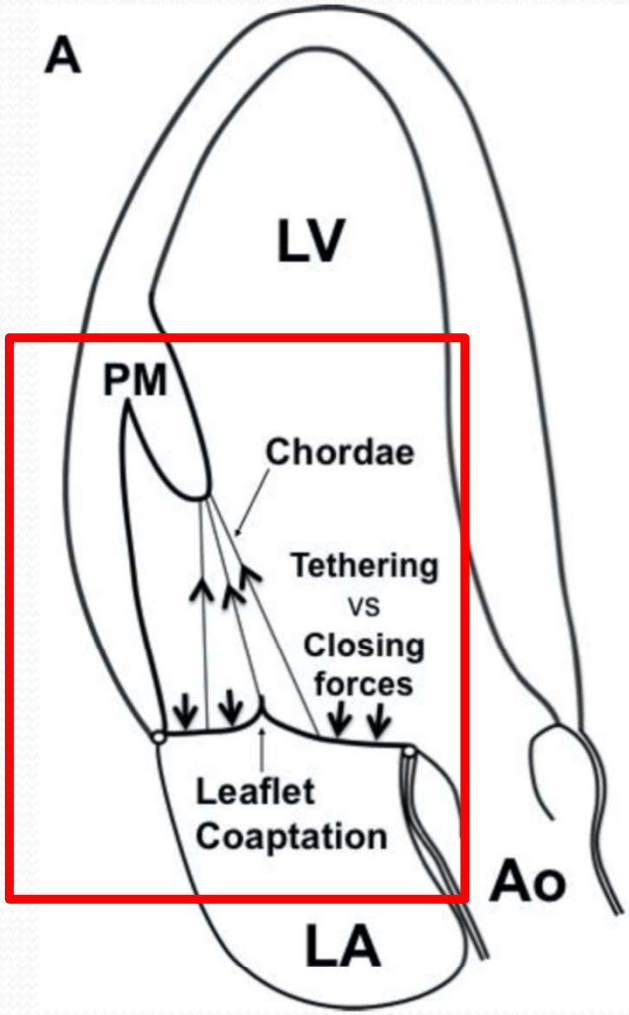
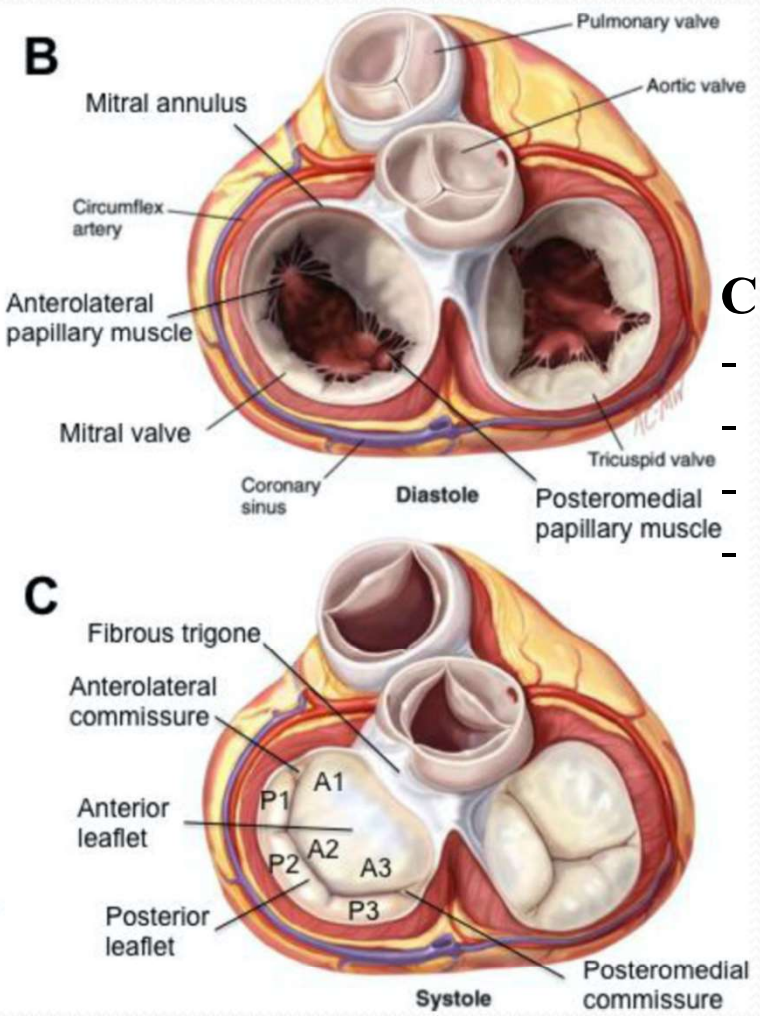


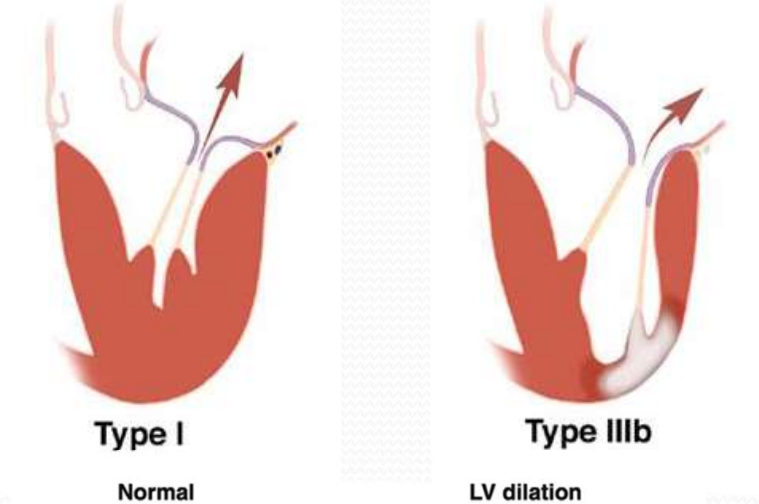


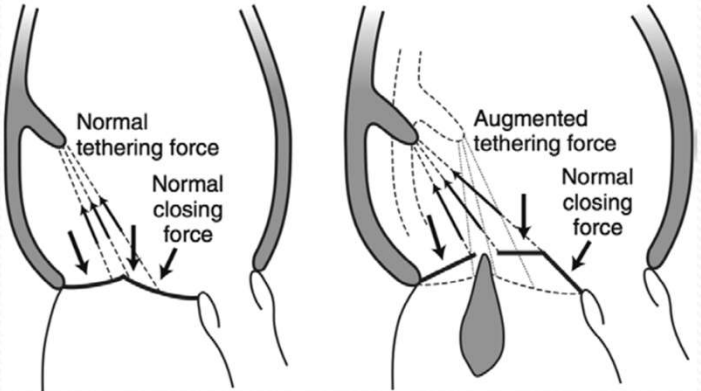
Components of the mitral valve

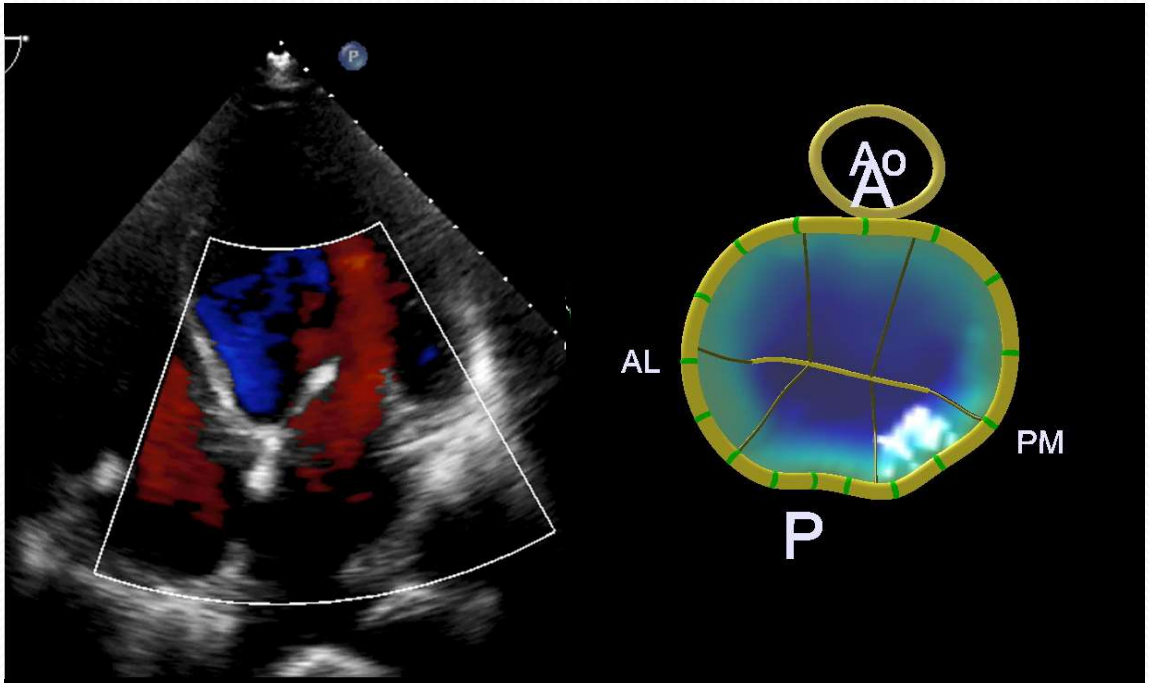
- the mitral annulus
- the MV leaflets
- the chordae tendineae
- and the LV wall with its attached papillary muscles

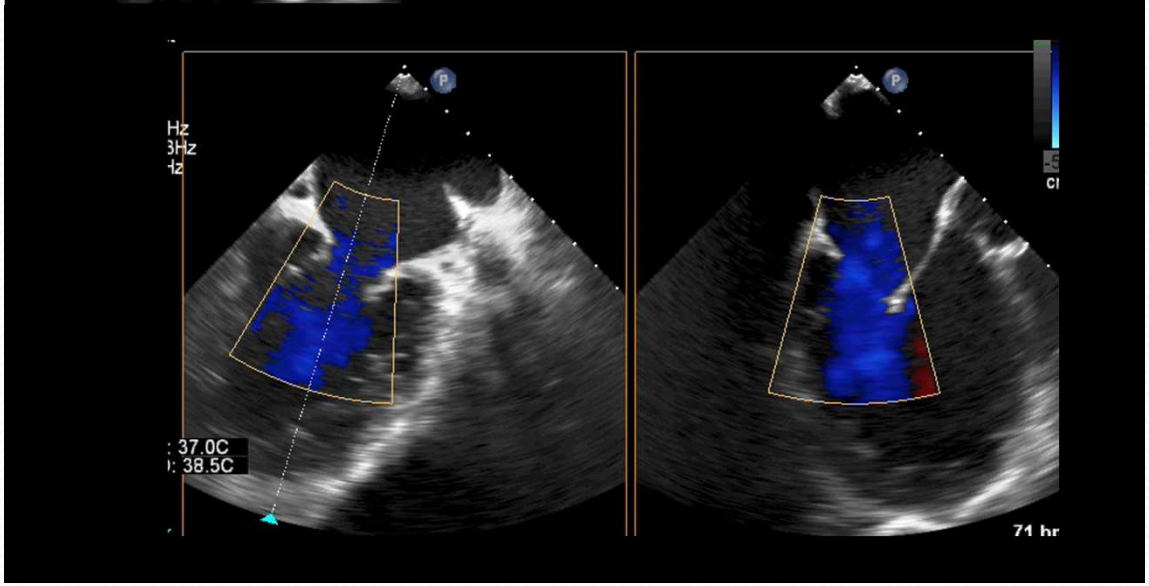
IM fonctionnelle (secondaire)

- CMD
- Post-ischémique
- Dilatation annulaire (FA)

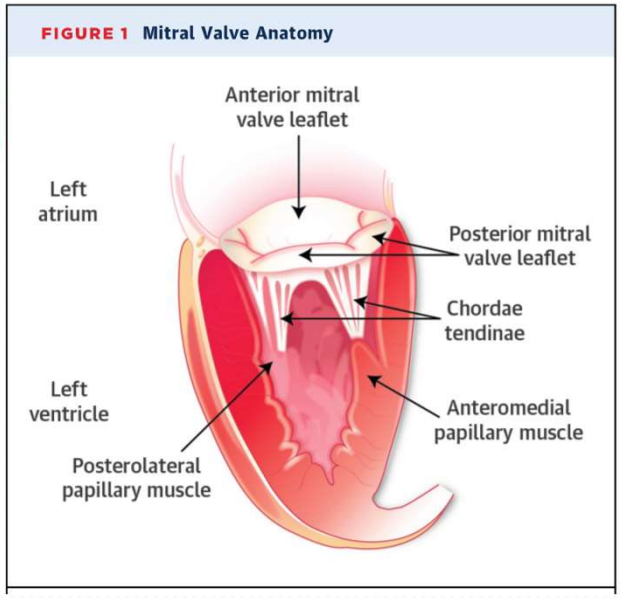








Multiple mechanisms



- Mitral leaflet tethering secondary to left ventricular (LV) dilatation/deformation with papillary displacement/discoordination ++++++
  - ❑ principal lesion of SMR
  - ❑ subsequent apical and lateral displacement of papillary muscles, which, in turn, draws the chordae tendineae away from the line of coaptation
  - ❑ results in restriction of systolic leaflet motion, namely type IIIb of Carpentier's classification.
  - ➔ Impact of geometric deformation ++++

- Insufficient LV-generated closing forces attributable to reduction of LV contractility
- Global LV/ papillary muscle dyssynchrony (➔QRS)
- Annular dilatation/dysfunction

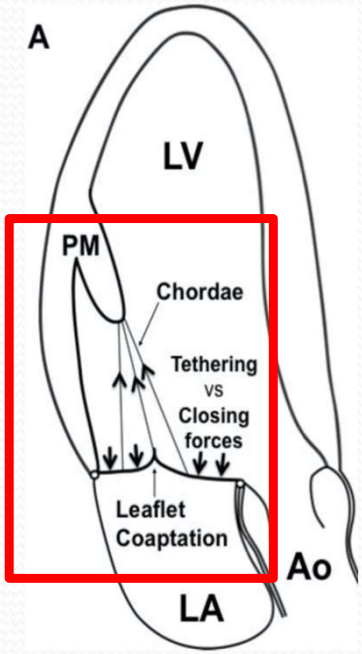
Because these changes are dependent on loading conditions and the phase of the cardiac cycle, secondary MR is dynamic in nature.

Mécanismes multiples

Tenting des feuillets mitraux secondaire à la dilatation/déformation du VG, avec déplacement/désynchronisation des piliers ++++

- Lésion principale de l'IM fonctionnelle.
- Déplacement apical et latéral des piliers qui engendre une tension sur les cordages et un défaut de coaptation des 2 feuillets mitraux
- Entraine une restriction systolique des feuillets (classe IIIb Carpentier)

➔ Importance de la déformation géométrique du VG ++++

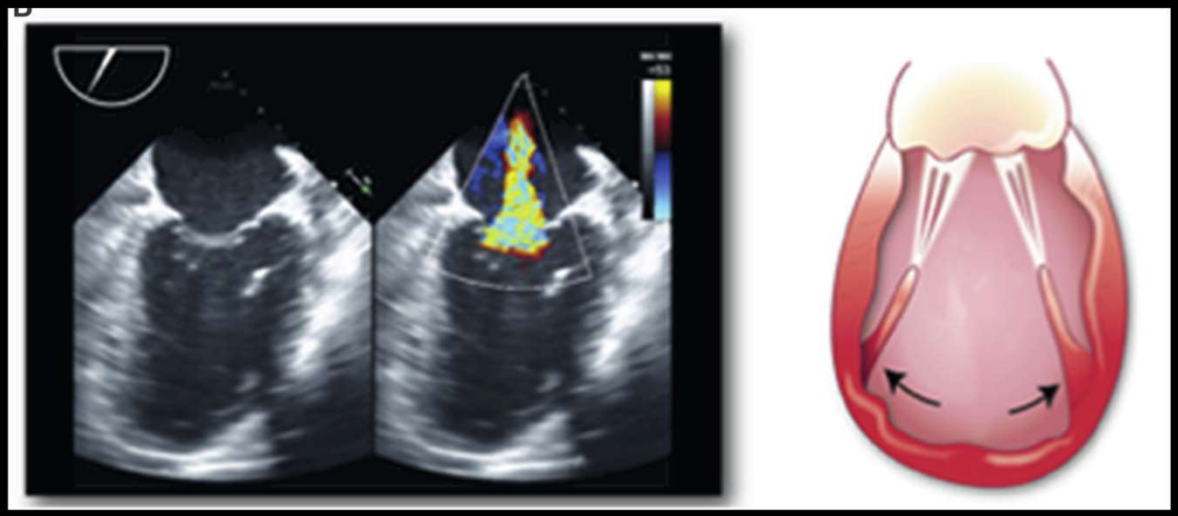


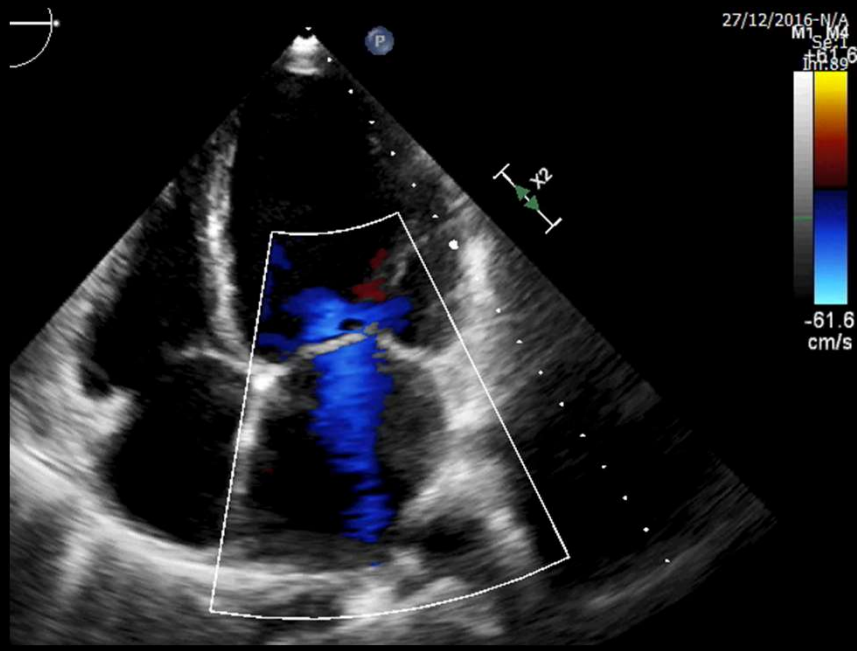
Differences between SMR due to dilated cardiomyopathy and to ischemic heart disease

The tethering shape varies
according to the site and extent of LV remodeling

SMR due to dilated cardiomyopathy

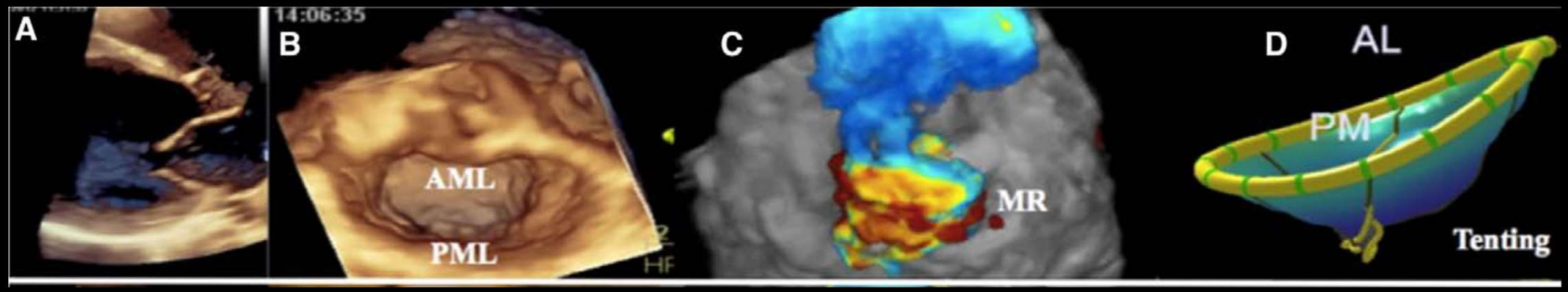
- Longstanding hypertension or idiopathic DCM
- Substantial systolic dysfunction, global remodeling, and increased LV sphericity
- Symmetrical tethering
- Coaptation point of the mitral valve moved apically, with a large tenting and both leaflets involved to a similar degree, causing a central regurgitant jet.
- Tethering is thus higher in patients with global LV remodeling
- Symmetric mitral annular dilation greatest in the septal-lateral direction, and correlates with the severity of LV dysfunction



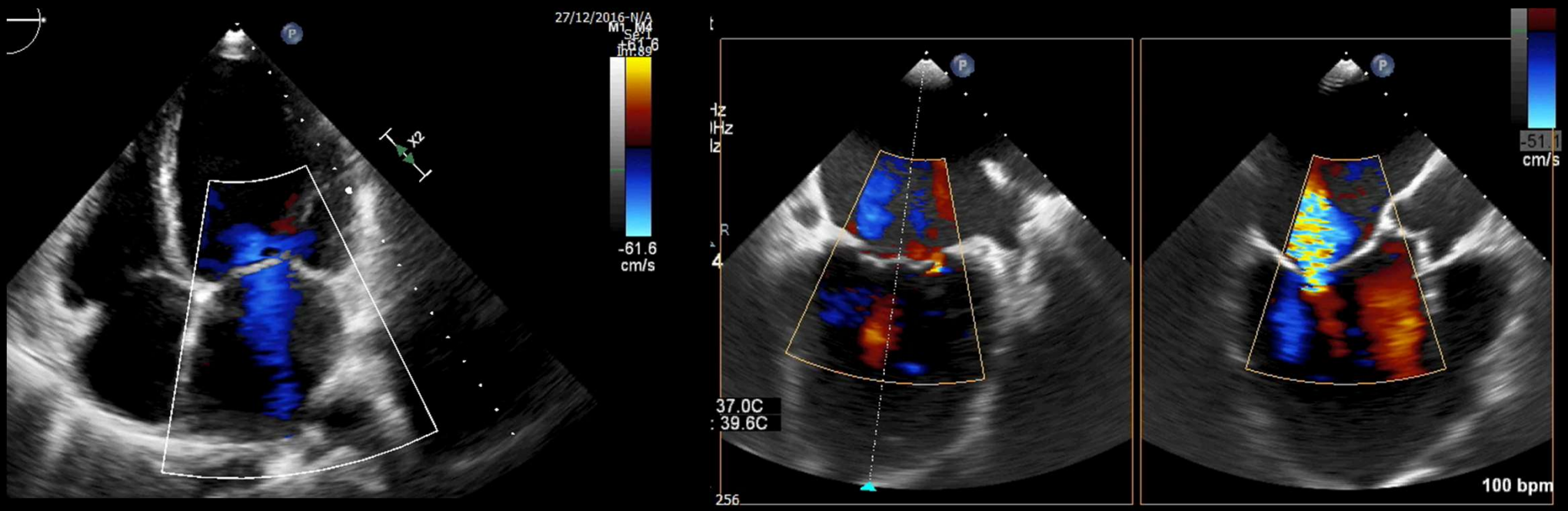


Asgar et al. JACC 2015

SMR due to dilated cardiomyopathy



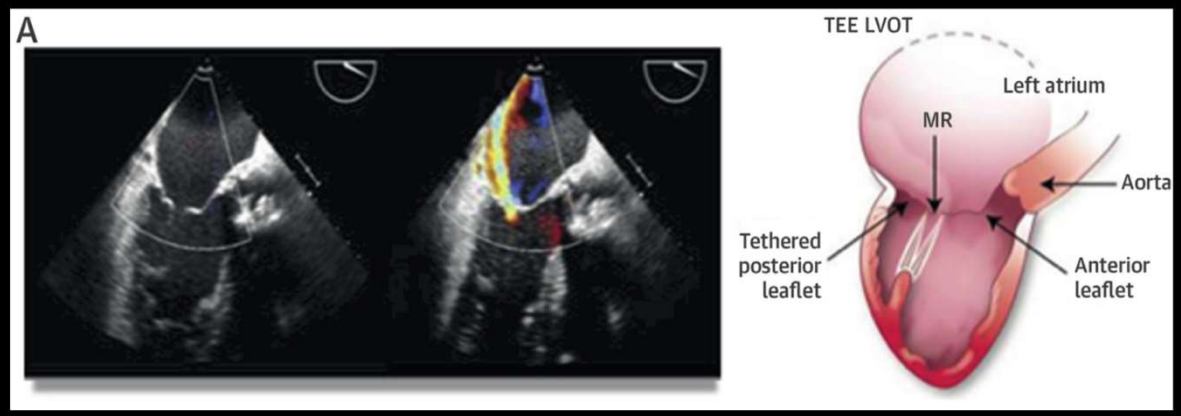
Lancelotti et al. Circ Cardiovasc Imaging 2014



SMR due to ischemic heart disease

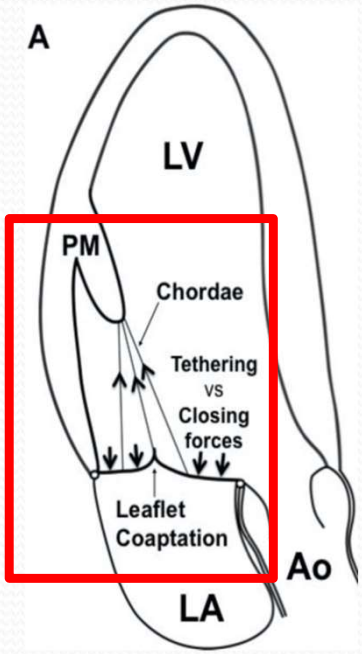
- Asymmetrical tethering
- Tenting typically predominates in the region of the posterior-medial scallop of the posterior leaflet (P2-P3) because of apically and posteriorly displaced posterior papillary muscle secondary to localized LV remodeling
- Tethering of secondary chords contributes to development of a hockey-stick deformity of the anterior leaflet, sometimes called « pseudo-prolapsus »
- the coaptation point of the leaflets is displaced posteriorly with respect to the center of the LV cavity.
- The consequence is anterior leaflet over-ride with a posterior

FIGURE 2 Secondary MR Due to Left Ventricular Dilation



Mécanismes multiples

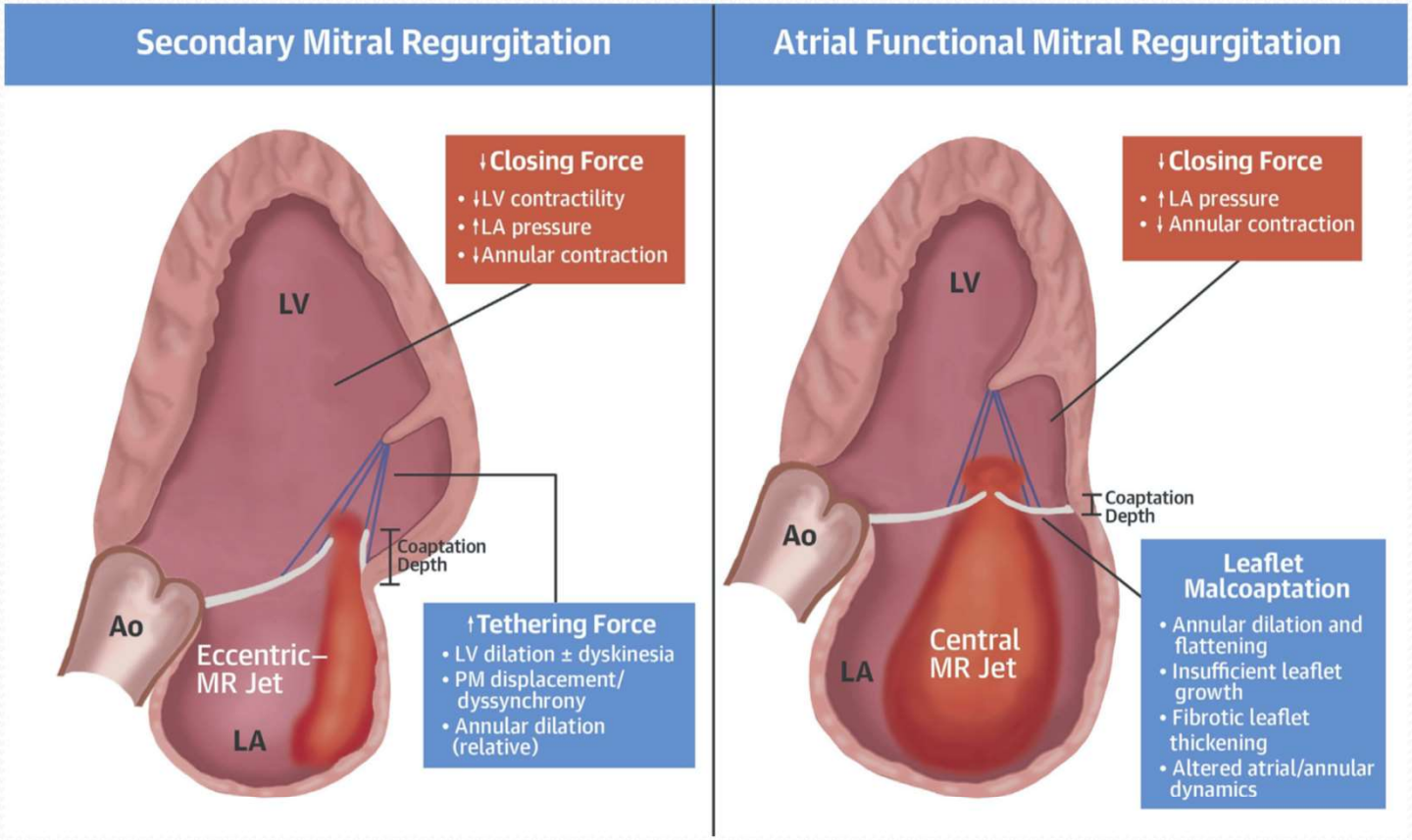
- Diminution des forces de fermeture de la valve mitrale en raison de la diminution de la contractilité VG.
- Désynchronisation VG/muscles papillaires (➔QRS)
- Dilatation annulaire, dysfonction annulaire.



Mécanismes variant beaucoup avec les conditions de charge et le long du cycle cardiaque ➔ l'IM fonctionnelle est dynamique et variable dans le temps.

Dilatation annulaire, dysfonction annulaire.

FIGURE 1 Mechanism of Functional MR



Reproduced with permission from Deferm et al.[1] Ao = aorta; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; PM = papillary muscle.

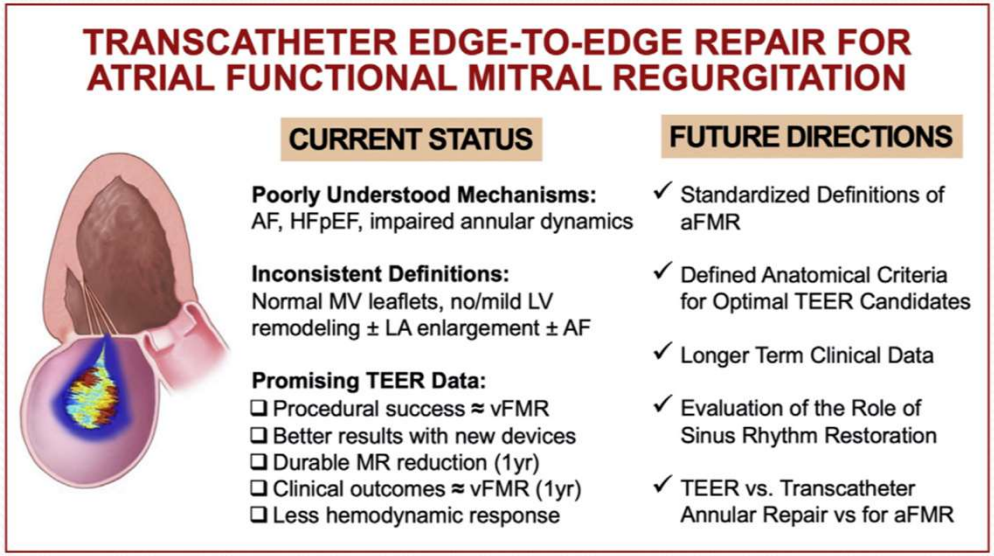
Alkhouli et al. JACC Itvn 2022

TABLE 2 Proposed Parameters for Phenotyping of FMR

	Atrial FMR	Ventricular FMR	Primary MR	
Parameter	Carpentier I	Carpentier IIIB	Carpentier II	Carpentier IIIA
MV tethering	–	+++	+	–
Leaflet restriction	–	Systole	–	Diastole
LA/annular dilatation	+++	+	++	++
LV dilatation	±	+++	±	±
LV dysfunction	±	+++ (±regional)	±	±

Abbreviations as in Table 1.

FIGURE 2 Current Status and Future Directions With TEER for aFMR



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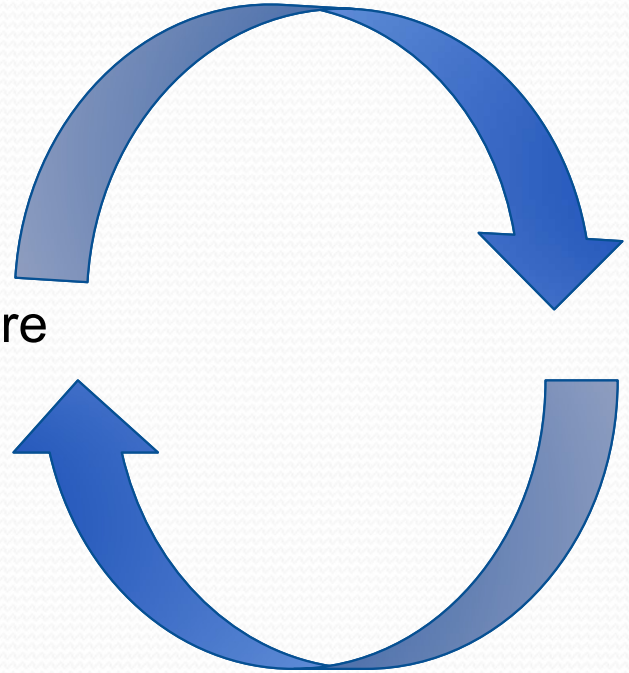
CMD ou CP. Ischémique

FEVG altérée

Surcharge volumétrique VG



Dilatation progressive du VG

IM secondaire

Adaptation de la valve mitrale

Influence of Chronic Tethering of the Mitral Valve on Mitral Leaflet Size and Coaptation in Functional Mitral Regurgitation

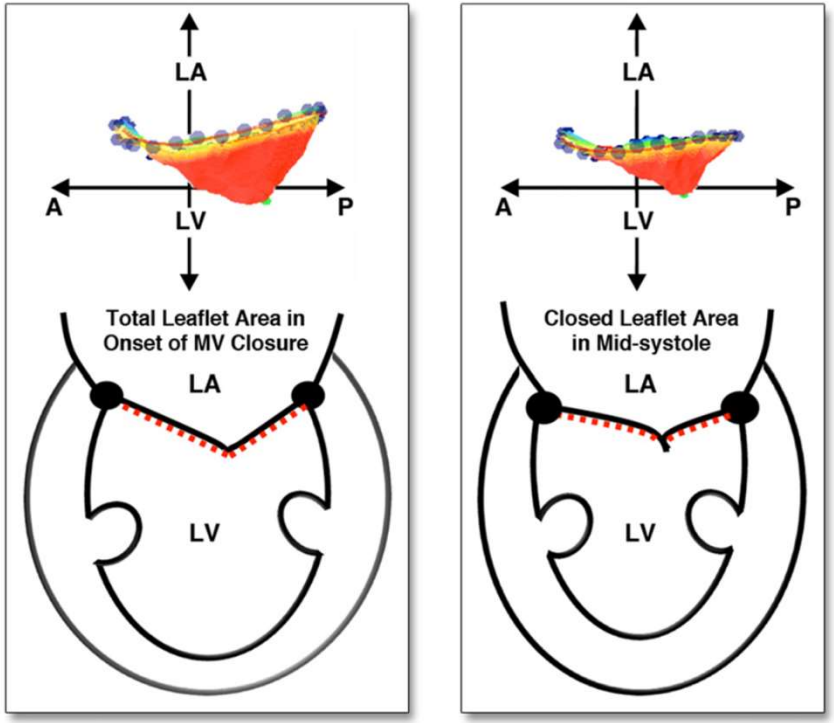
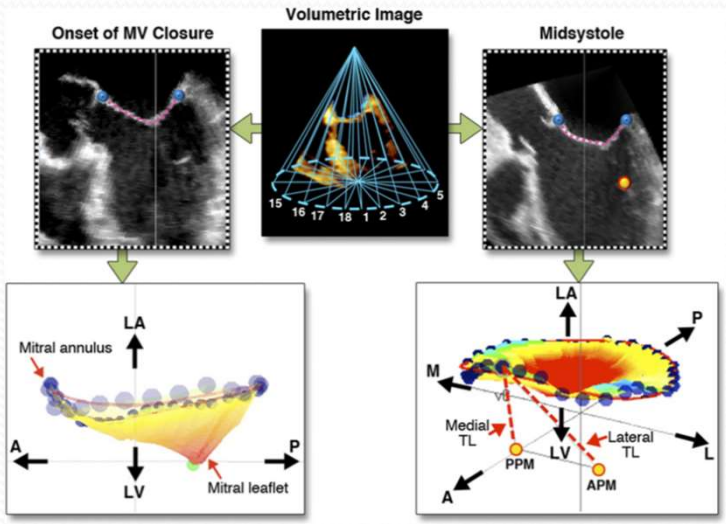


Figure 4. MV Apparatus Geometry

MV apparatus geometry in the onset of mitral leaflet closure **(left)** and the timing of maximum closure of mitral leaflet **(right)**. The 3-dimensional tenting closed leaflet area does not include coapted leaflet area in this study. Abbreviations as in Figure 1.



Saito et al. JACC: CARDIOVASCULAR IMAGING 2012

Influence of Chronic Tethering of the Mitral Valve on Mitral Leaflet Size and Coaptation in Functional Mitral Regurgitation

Table 2. Geometric Measurements of Mitral Complex and Coaptation

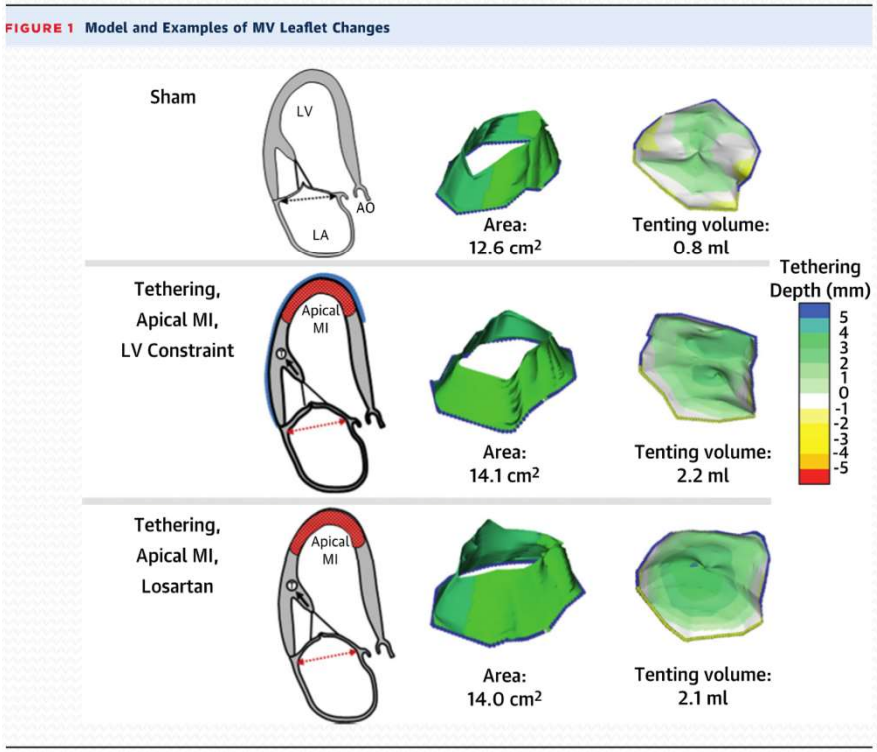
	FMR Group (n = 44)	Control Group (n = 56)	p Value
Annular area, cm^2/m^2	6.0 ± 2.5	4.5 ± 0.6	<0.0001
Leaflet area, cm^2/m^2	8.7 ± 1.8	6.7 ± 0.9	<0.0001
Leaflet to annular area ratio	1.45 ± 0.16	1.50 ± 0.11	0.09
Tenting volume, ml/m^2	1.3 ± 0.7	0.5 ± 0.3	<0.0001
Tethering length, mm/m^2			
Medial	23.0 ± 2.2	18.4 ± 2.8	<0.0001
Lateral	20.5 ± 3.2	17.1 ± 2.6	<0.0001
Coaptation length, mm			
Medial	3.2 ± 0.9	4.8 ± 0.6	<0.0001
Middle	3.8 ± 1.3	5.8 ± 0.7*†	<0.0001
Lateral	3.3 ± 0.9	4.8 ± 0.6	<0.0001
Coaptation area, cm^2/m^2	1.3 ± 0.4	1.6 ± 0.4	0.005
Coaptation index, %	15.6 ± 3.3	23.6 ± 4.8	<0.0001

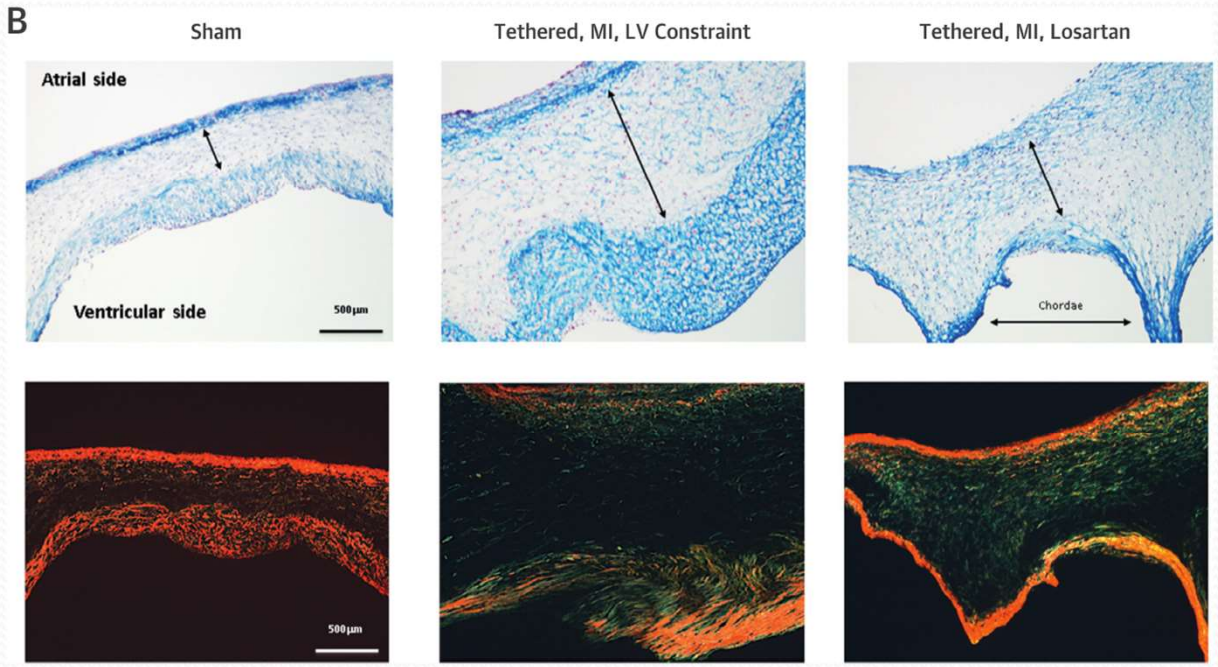
Values are mean ± SD. *$p < 0.05$ versus medial. †$p < 0.05$ versus lateral.
Abbreviation as in Table 1.

- With chronic MR, the mitral leaflet area may increase up to 35% over time, an adaptive response that minimizes the degree of regurgitatioN
- Insufficient leaflet remodeling may contribute to severe MR
- However, even in patients with increased mitral leaflet area, papillary muscle displacement with subsequent decreased coaptation length may still result in significant MR.

Saito et al. JACC: CARDIOVASCULAR IMAGING 2012

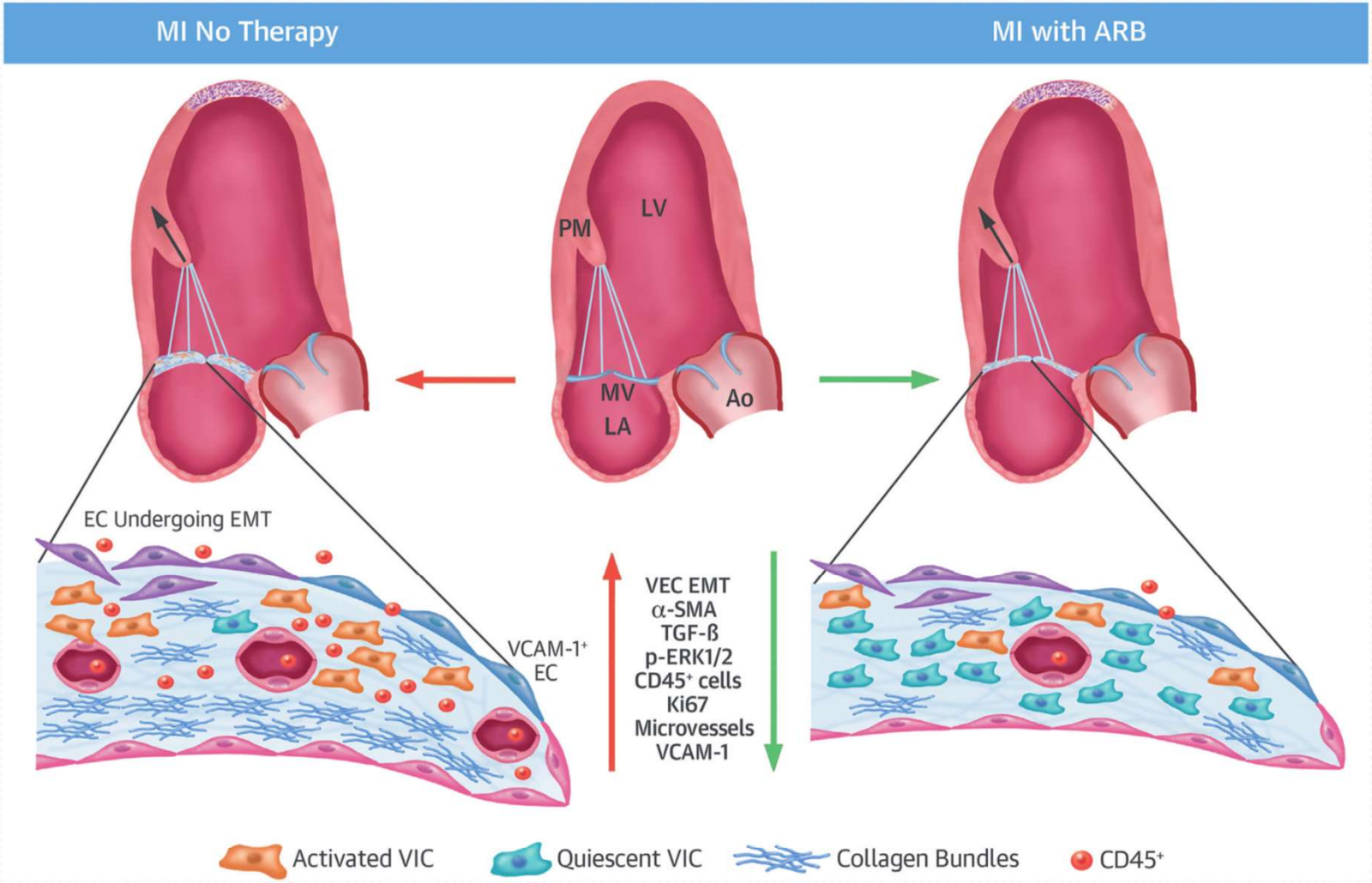
- After myocardial infarction (MI), mitral valve (MV) tethering stimulates adaptive leaflet growth but counterproductive leaflet thickening and fibrosis augment mitral regurgitation (MR).
- MV fibrosis post-MI is associated with excessive endothelial-to-mesenchymal transition (EMT), driven by transforming growth factor (TGF)-b overexpression.



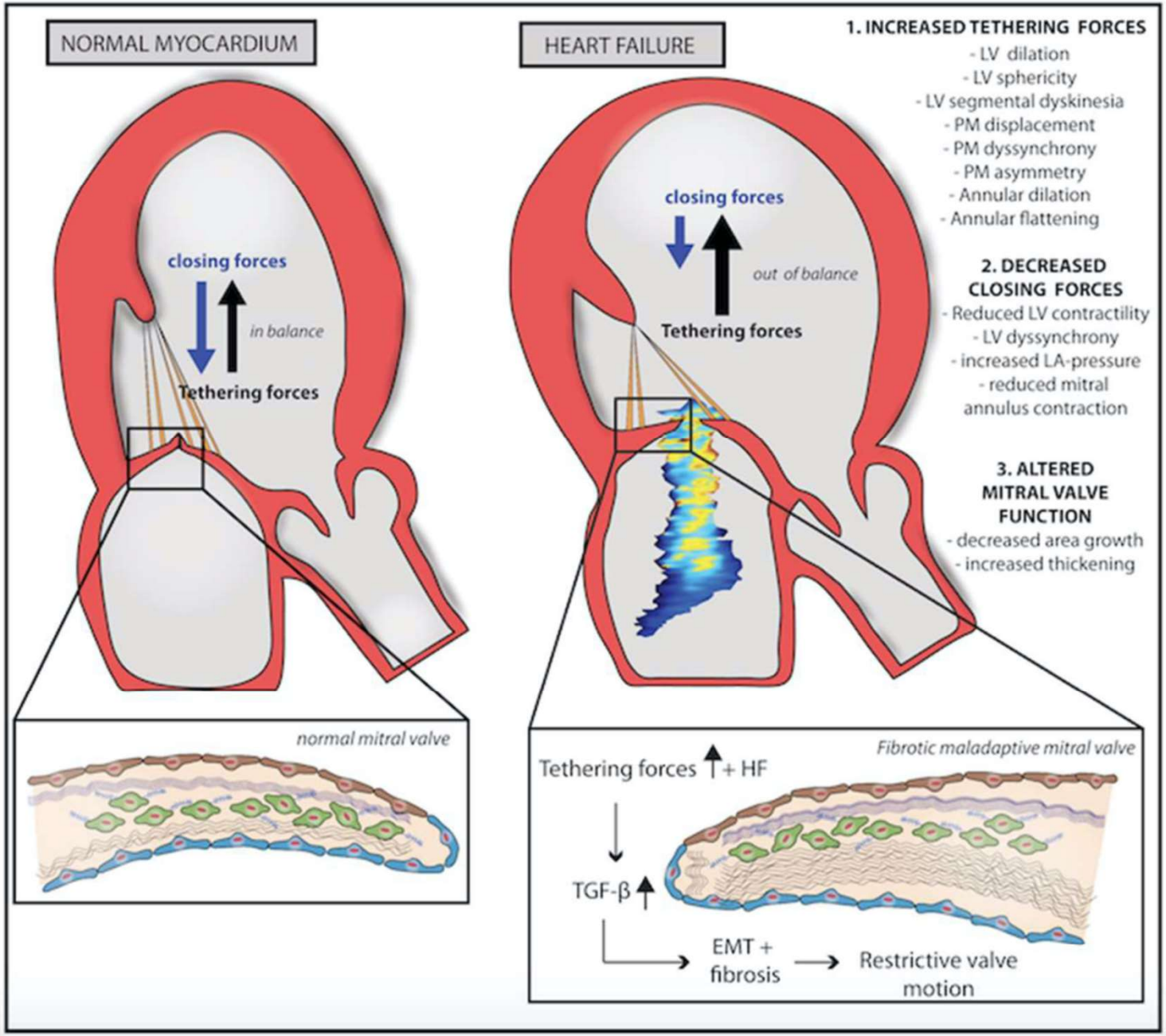


Bartko et al. JACC 2017

CENTRAL ILLUSTRATION **Losartan Reduces Post-MI Profibrotic Mitral Valve Changes Without Eliminating Adaptive Leaflet Growth**



Bartko, P.E. et al. J Am Coll Cardiol. 2017;70(10):1232–44.

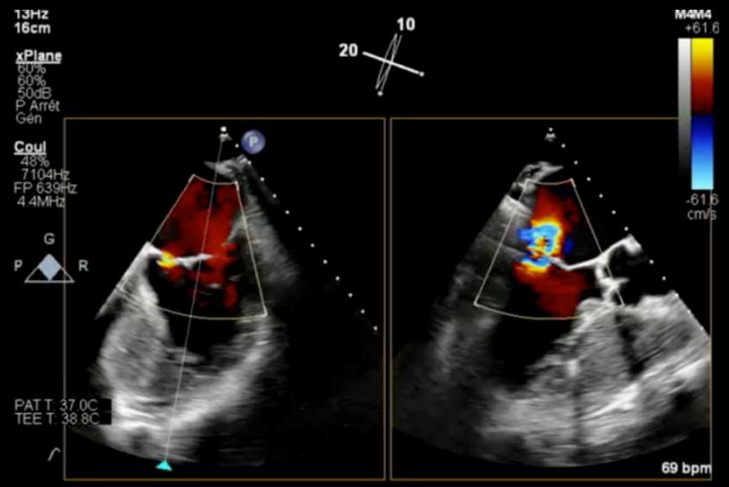


Coats et al. EHJ 2021

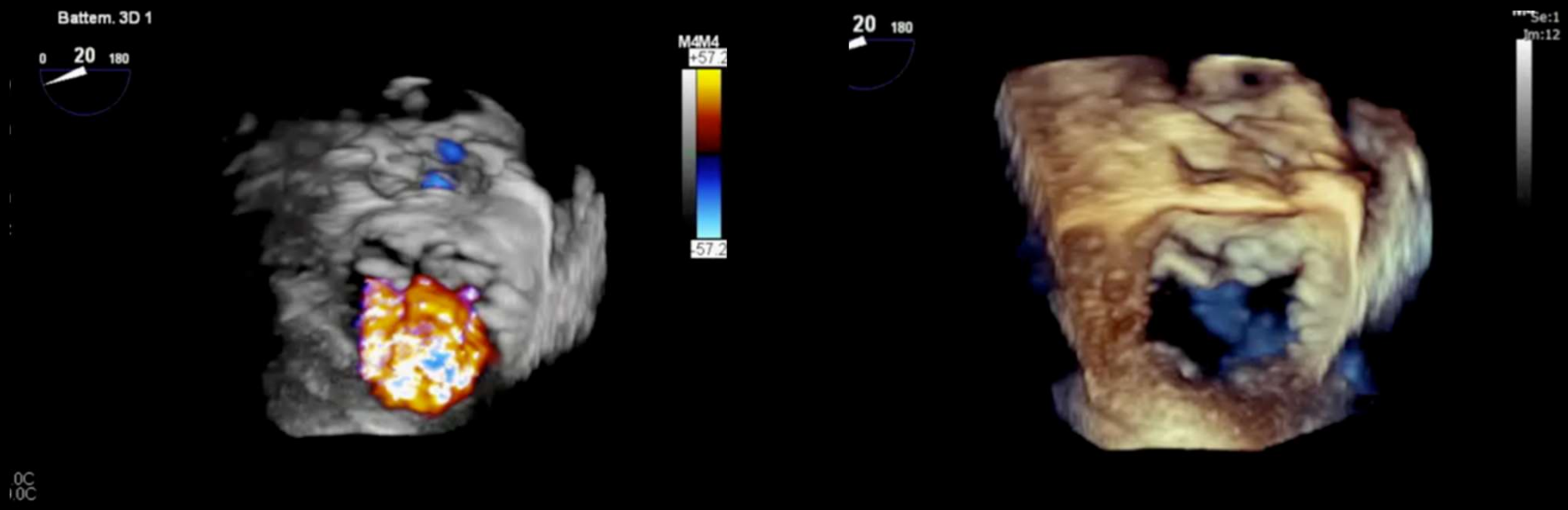
How to evaluate secondary MR?

Is it really severe ?

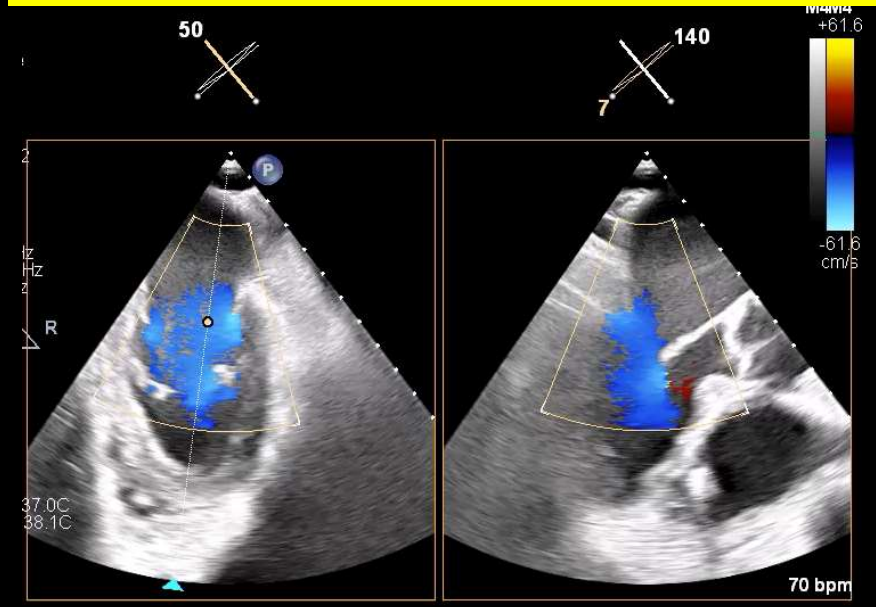
Mécanismes variant beaucoup avec les conditions de charge et le long du cycle cardiaque ➔ l'IM fonctionnelle est dynamique et variable dans le temps.

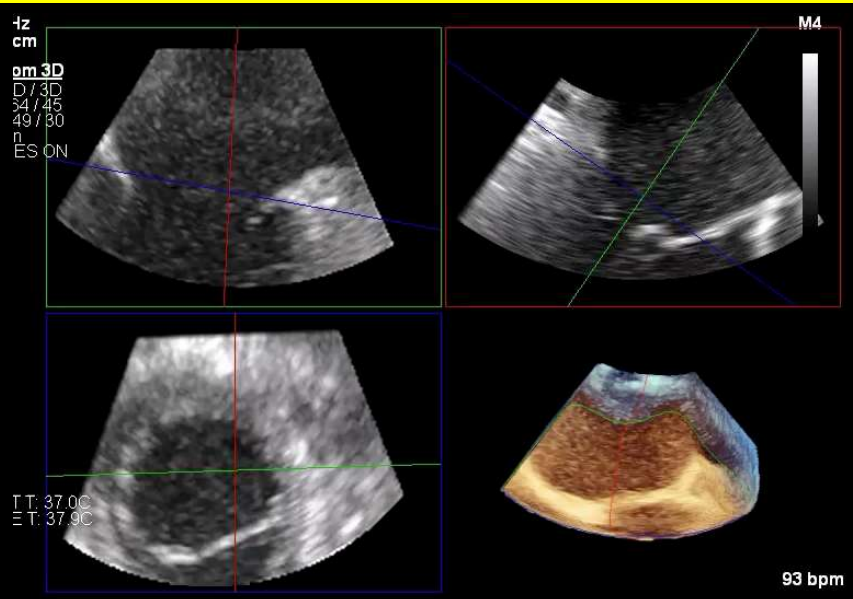


- TEER NOT PERFORMED
- PROCEDURE STOPPED BEFORE TS PUNCTURE



Mécanismes variant beaucoup avec les conditions de charge et le long du cycle cardiaque ➔ l'IM fonctionnelle est dynamique et variable dans le temps.

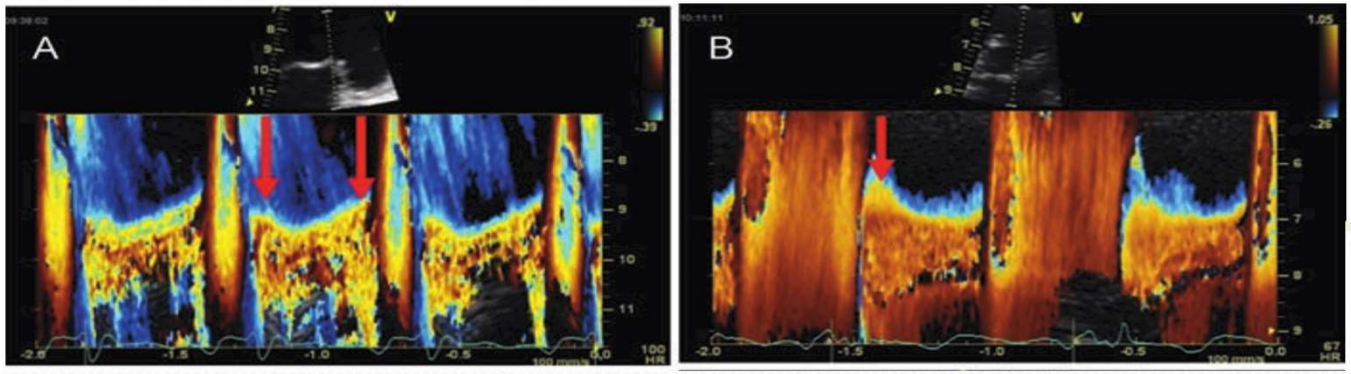


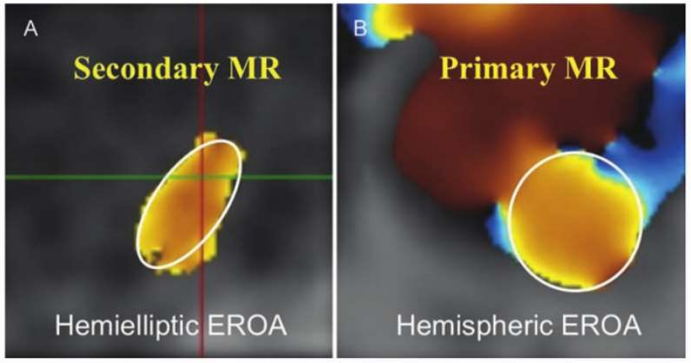


2nd procedure 1 month later : IV loop-diuretics 5 days before procedure ; NT-proBNP ↘↘

Pitfalls for PISA method in SMR

- Dynamic changes in MR : there is a dynamic variation of the regurgitant orifice area with early and late systolic peaks and a mid-systolic decrease.





- The PISA might look like an ellipsoidal, irreguliar or linear shape.
- In SMR, vertical PISA often < horizontal PISA ➔ When the shape of the flow convergence zone is not a hemisphere, the PISA method may underestimate the degree of functional MR ➔ lower threseholds to define severe MR in SMR.

- Constrained PFCR in the setting of regional myocardial deformity and leaflet tethering can limit the use and accuracy of the PFCR-based EROA computation in SMR.

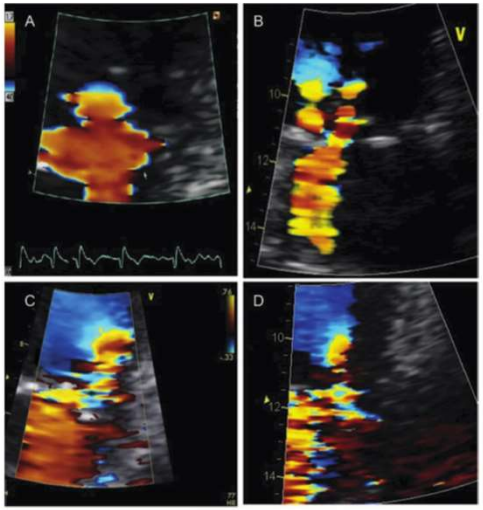
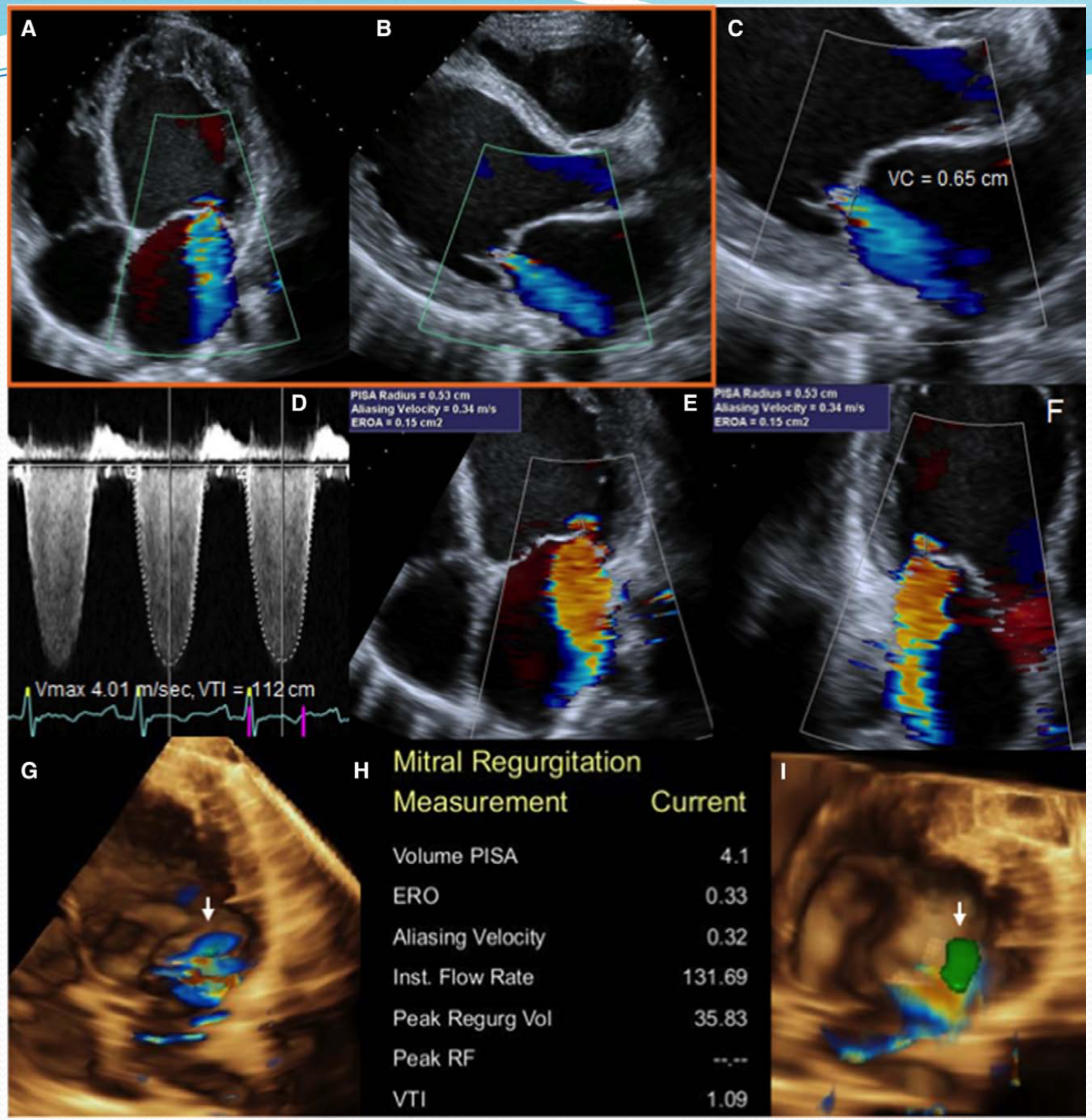
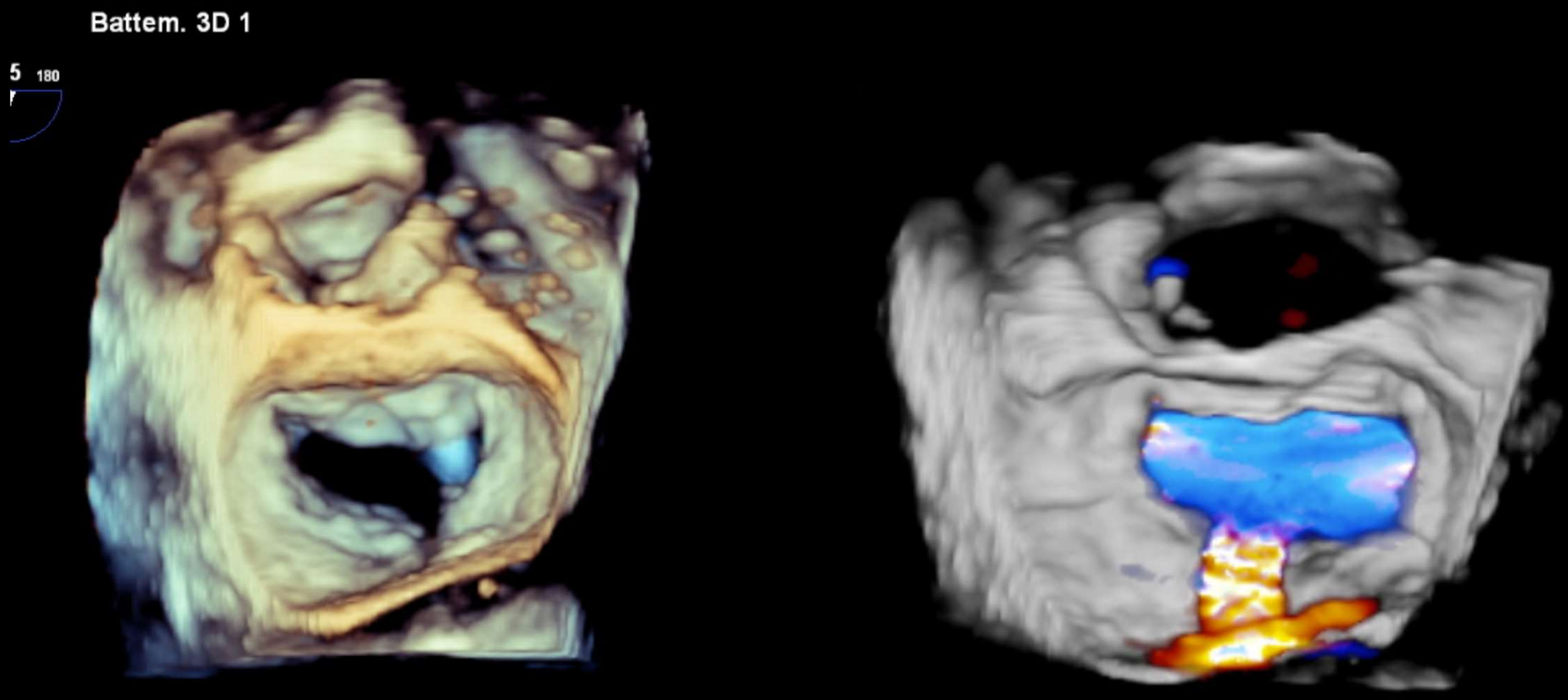


Figure 28 (*A*) Example of a flat flow convergence zone; (*B*) presence of two jets; (*C* and *D*) distorted and constrained flow convergence zone by the lateral myocardial wall.


A
B
C
VC = 0.65 cm
D
Vmax 4.01 m/sec, VTI = 112 cm
PISA Radius = 0.53 cm
Aliasing Velocity = 0.34 m/s
EROA = 0.15 cm2
E
PISA Radius = 0.53 cm
Aliasing Velocity = 0.34 m/s
EROA = 0.15 cm2
F
G
H
Mitral Regurgitation
Measurement Current
Volume PISA 4.1
ERO 0.33
Aliasing Velocity 0.32
Inst. Flow Rate 131.69
Peak Regurg Vol 35.83
Peak RF --.--
VTI 1.09
I

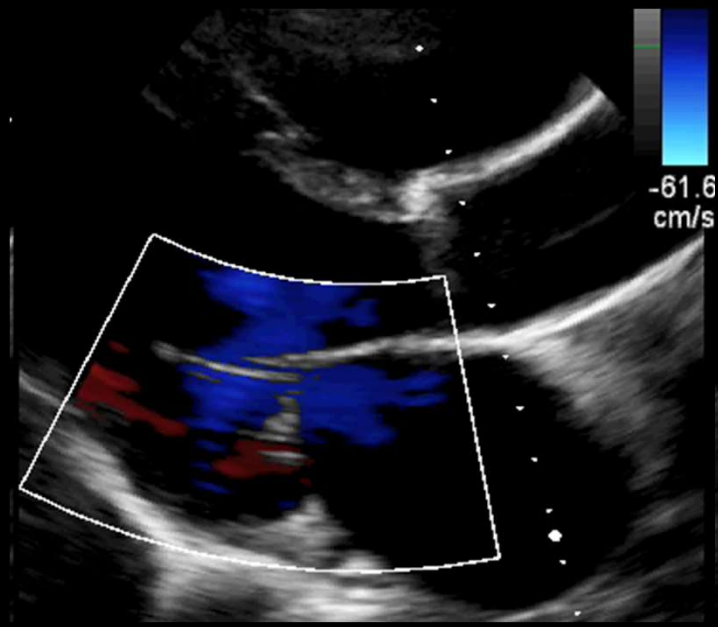
Description anatomique précise

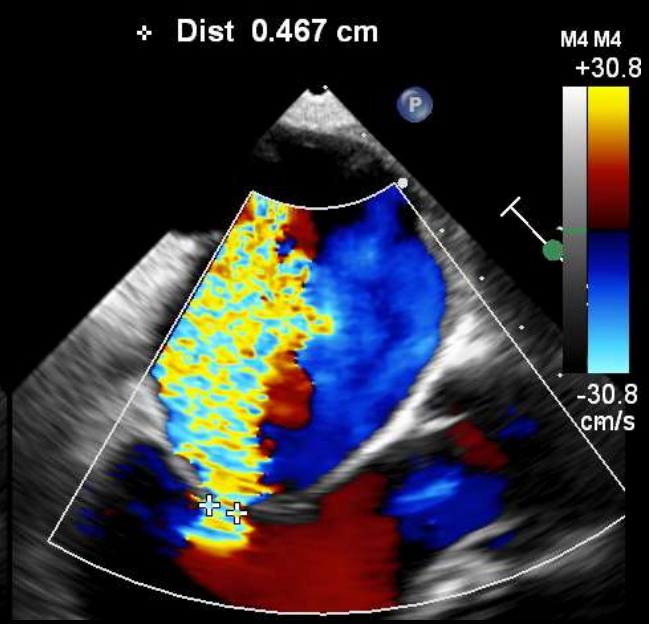
Utilisation du mode 3D live couleur

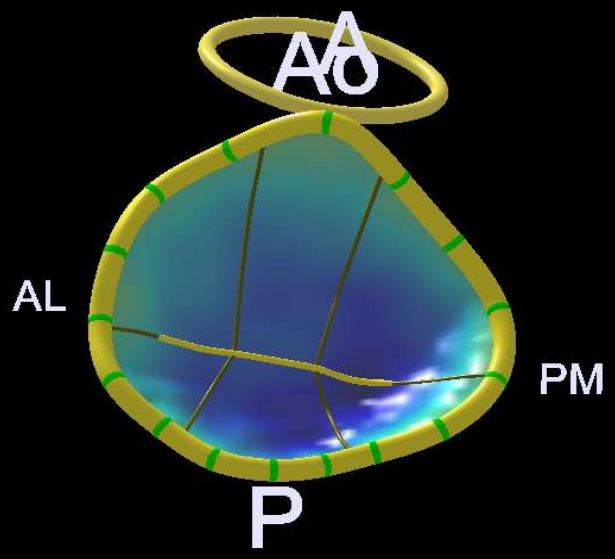


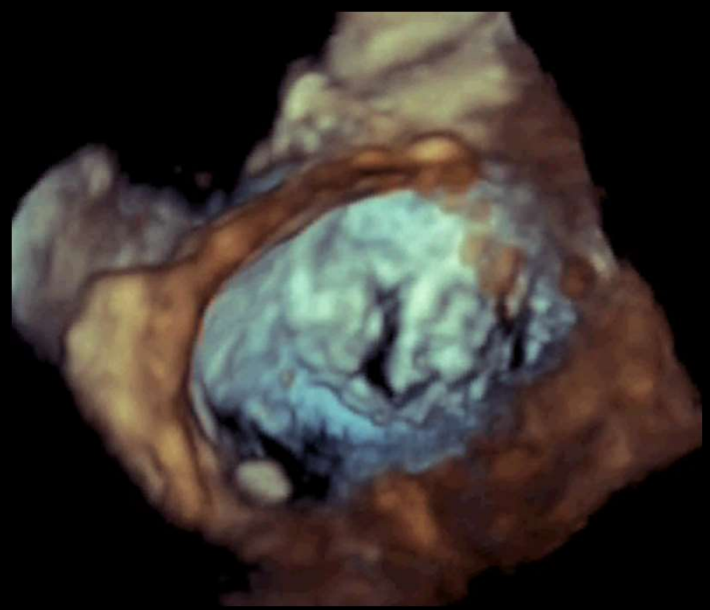
IM fonctionnelle sévère, sur CP ischémique évoluée (FEVG à 20%) avec un jet central en A2-P2.
Patient traité par MitraClip dans le cadre de Mitra-FR.

- Mr fa, 70 ans
- PAC en 2016 pour lésions 3TC sévère avec occlusion CD
- Hospi pour choc cardiogénique à nette prédominance droite avec bas débit.
- FEVG 25%, séquelle inférieure, IM fonctionnelle sévère (SOR à 0.22 cm2, volume régurgité 25 ml)
- Discussion MitraClip









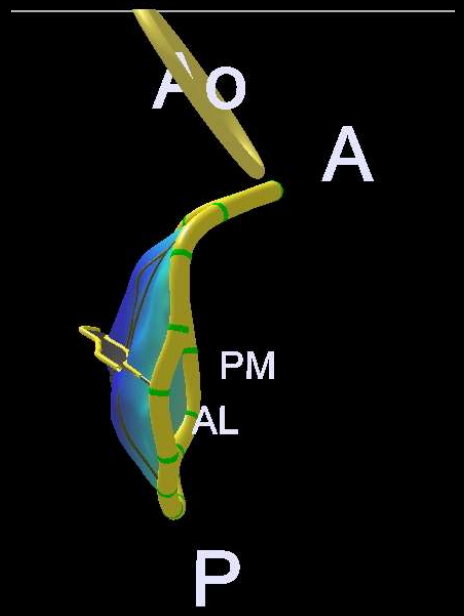
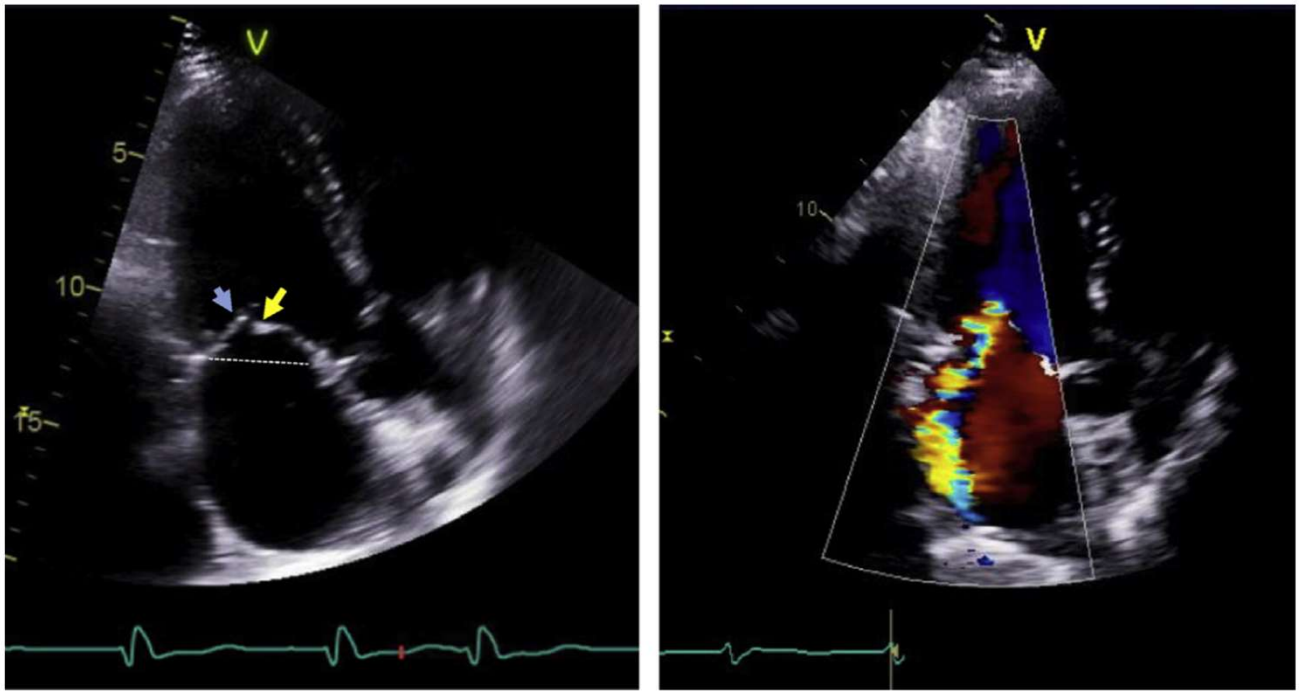
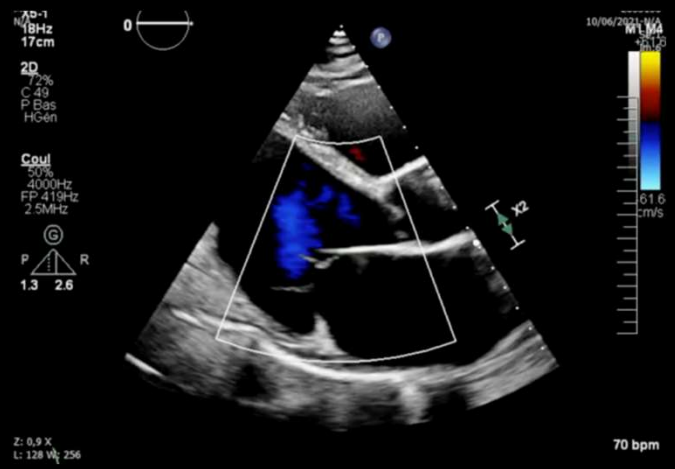


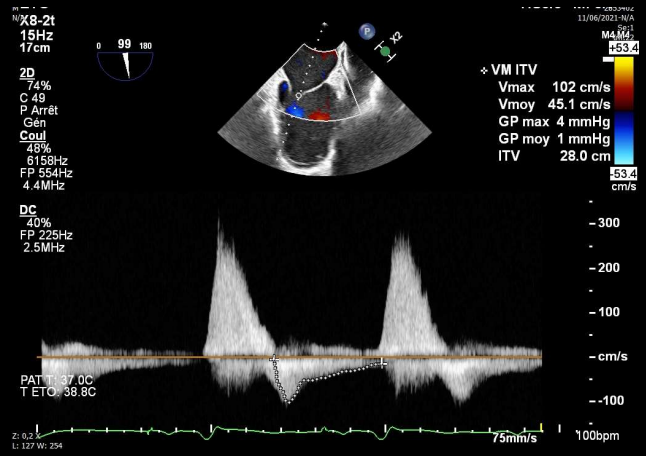
FIGURE 3 **Anterior Leaflet Override in Functional MR**

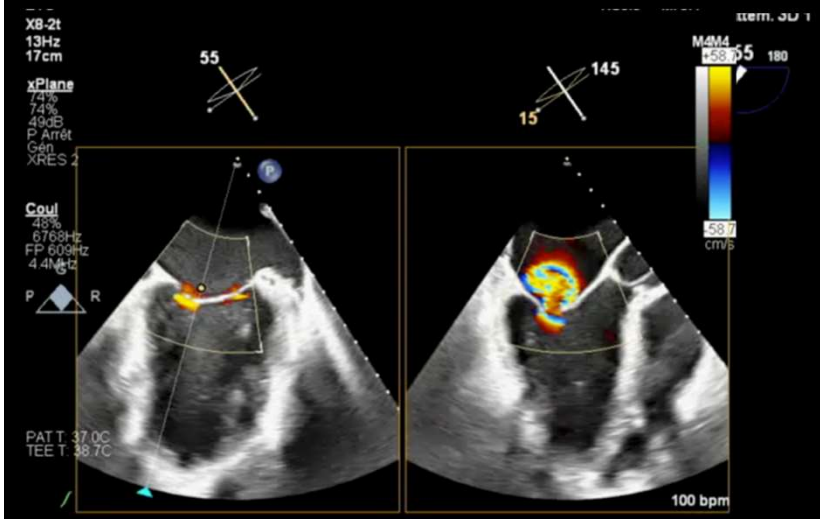


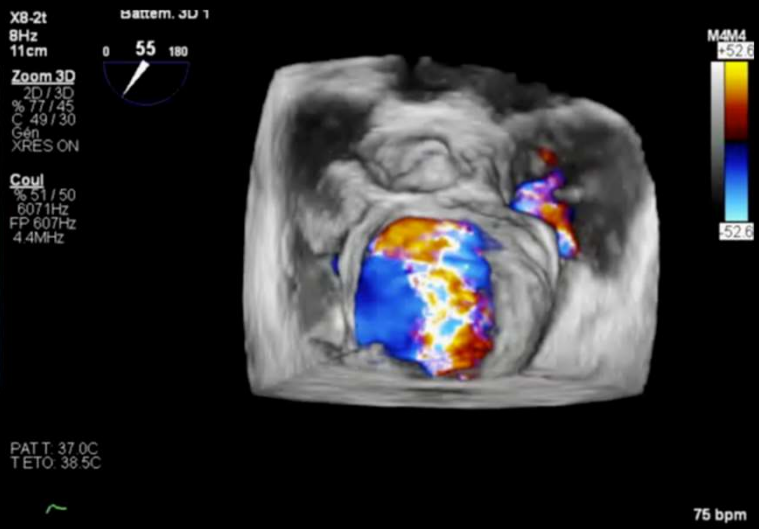
Anterior leaflet override in secondary MR due to ischemic cardiomyopathy. Apical long-axis views showing fixed posterior mitral leaflet (PML) **(blue arrow)** with an overriding anterior mitral leaflet (AML) **(yellow arrow)**. Coaptation is absent with a large "wrap-around" color Doppler jet directed posteriorly by the fixed PML **(right panel)**. This is commonly misdiagnosed as mitral valve prolapse, but cannot be such because the AML never moves superiorly to the mitral annulus **(dotted line)**. AML = anterior mitral leaflet; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; PML = posterior mitral leaflet.


X5-1
18Hz
17cm
2D
72%
C 49
P Bas
HGén
Coul
50%
4000Hz
FP 419Hz
2.5MHz
1.3 2.6
61.6
cm/s
70 bpm


X5-1
30Hz
14cm
2D
78%
C 49
P Bas
HGén
Coul
50%
4000Hz
FP 419Hz
2.5MHz
1.3 2.6
Dist 1.12 cm
+92.4
-30.8
cm/s
69bpm


X8-2t
15Hz
17cm
2D
74%
C 49
P Arrêt
Gén
Coul
48%
6158Hz
FP 554Hz
4.4MHz
DC
40%
FP 225Hz
2.5MHz
99
VM ITV
Vmax 102 cm/s
Vmoy 45.1 cm/s
GP max 4 mmHg
GP moy 1 mmHg
ITV 28.0 cm
+53.4
-53.4
cm/s
300
200
100
cm/s
-100
PAT T: 37.0C
T ETO: 38.8C
75mm/s
100bpm

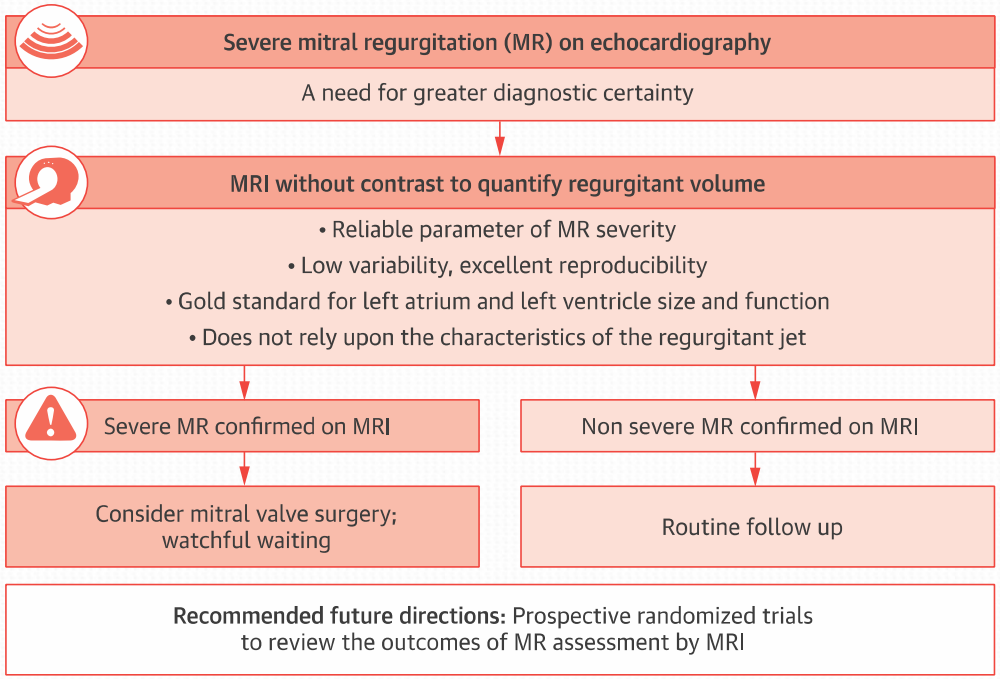

X8-2t
13Hz
17cm
xPlane
74%
74%
49dB
P Arrêt
Gén
XRES 2
Coul
48%
6768Hz
FP 609Hz
4.4MHz
55
145
15
180
M4M4
+58.7
-58.7
cm/s
PAT T: 37.0C
TEE T: 38.7C
100 bpm


X8-2t
8Hz
11cm
Zoom 3D
2D / 3D
% 77 / 45
C 49 / 30
Gén
XRES ON
Coul
% 51 / 50
6071Hz
FP 607Hz
4.4MHz
Battem. 3D 1
0 55 180
M4M4
+52.8
-52.8
PAT T: 37.0C
T ETO: 38.5C
75 bpm

Complementary role of cardiac MRI

- To confirm the severity of MR ++++

CENTRAL ILLUSTRATION **Proposed Clinical Pathway and Rationale for the Use of Cardiac MRI in the Assessment of Patients With Severe Mitral Regurgitation**



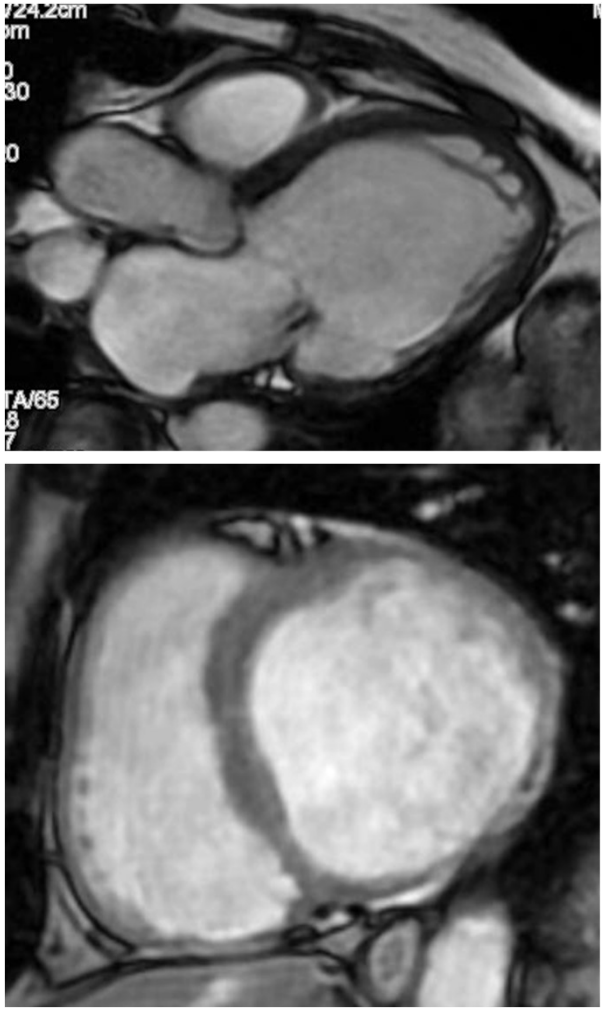
Uretsky, S. et al. J Am Coll Cardiol. 2018;71(5):547–63.

MRI = magnetic resonance imaging.

parameters used to grade mitral regurgitation are inconsistent, CMR is a valid alternative to quantify the regurgitant volume and is the reference standard to quantify LV and LA volumes.[278] In addition, quantification of mitral regurgitation with CMR has shown prognostic implications.[277] Finally, preliminary data show that myocardial fibrosis assessed with CMR is frequent in PMR and has been associated with sudden cardiac death and ventricular arrhythmias.[279]

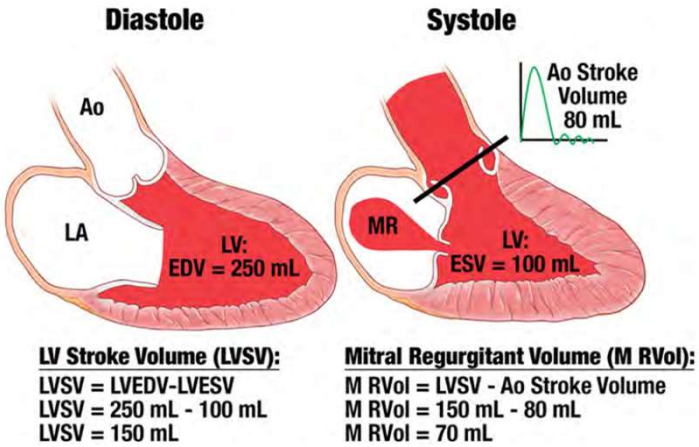
Vahanian et al. ESC Guidelines VHD 2021

Complementary role of CMR in secondary MR



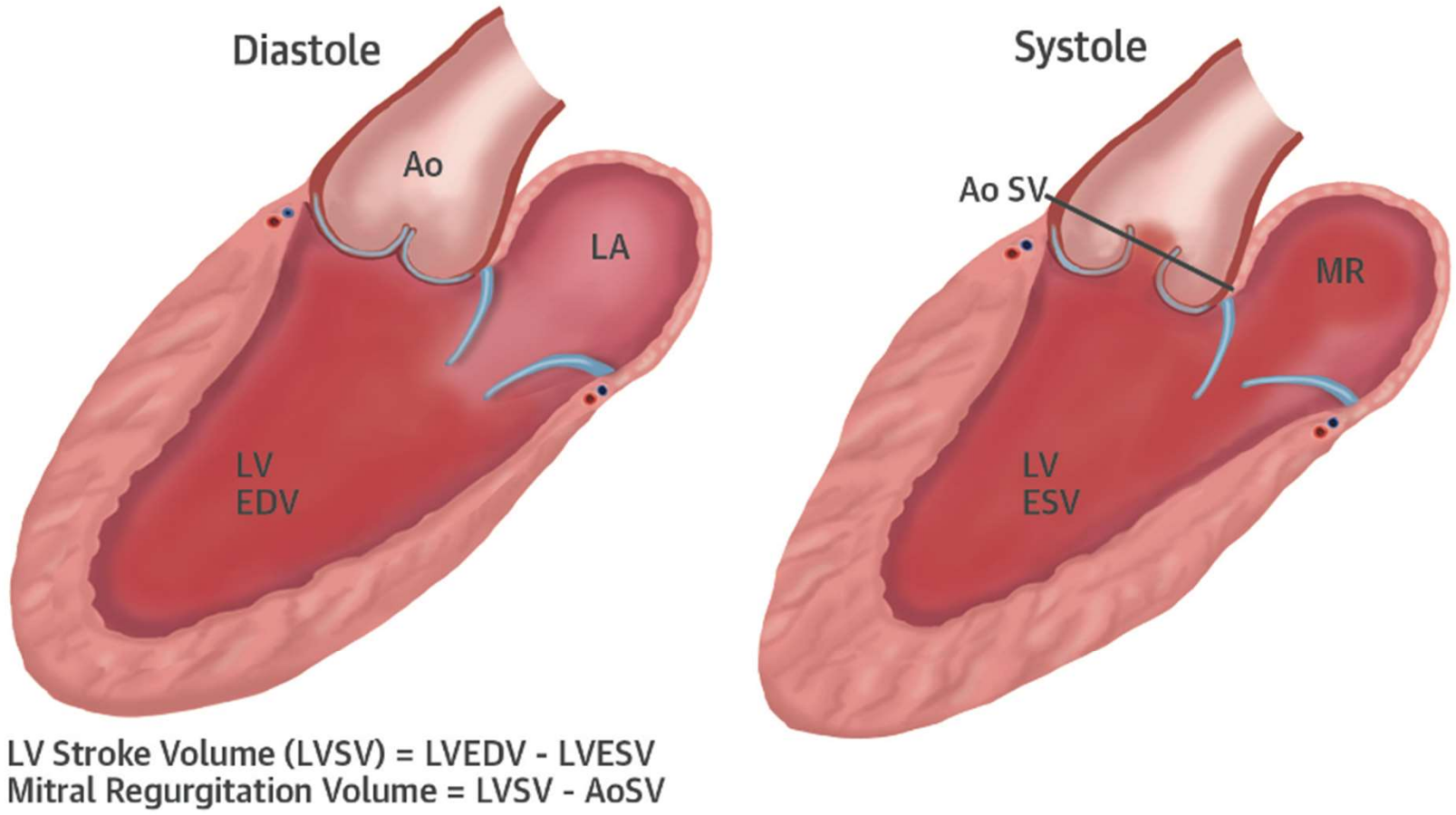
Courtesy to Juliette Rousseau, CCN

- **LV analysis :**
  - LV volume and LV remodeling
  - Scar of MI
  - LV Viability
  - LVEF
- +/- mechanisms of MR
- **Reliable and reproducible quantification of regurgitant volume and regurgitant fraction**
- **LA volume**
- RV function



How to assess MR severity by CMR?

FIGURE 1 Schematic Diagram Showing the Principle of Estimation of Mitral Regurgitant Volume Using Cardiac MRI



Example of the method used to calculate mitral regurgitant volume (see text for details). Ao = aorta; EDV = end-diastolic volume; ESV = end-systolic volume; LA = left atrium; LV = left ventricular; MR = mitral regurgitation; MRI = magnetic resonance imaging; SV = stroke volume.

Kar et al. JACC 2015

JACC: CARDIOVASCULAR IMAGING
VOL. ■, NO. ■, 2018

PUBLISHED BY ELSEVIER

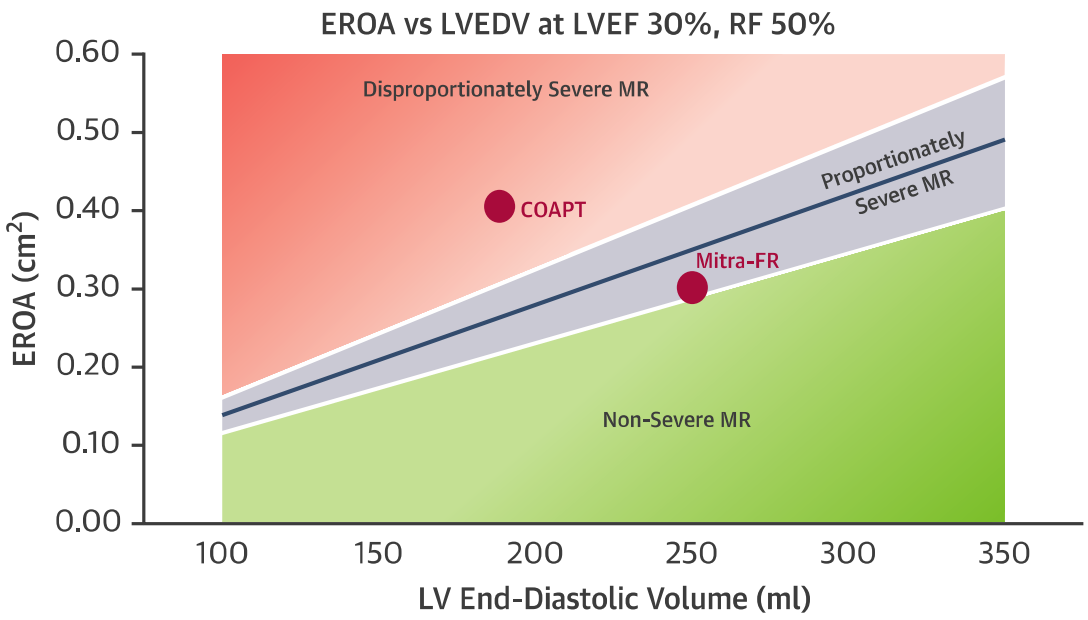
EDITORIAL VIEWPOINT

Proportionate and Disproportionate Functional Mitral Regurgitation

A New Conceptual Framework That Reconciles the Results of the MITRA-FR and COAPT Trials

Paul A. Grayburn, MD, Anna Sannino, MD, Milton Packer, MD

FIGURE 2 Relationship Between EROA and LVEDV Illustrating Domains That Define Disproportionately Severe, Proportionately Severe, and Nonsevere Functional Mitral Regurgitation



THE DISPROPORTIONATE SUCCESS OF THE DISPROPORTIONATE CONCEPT

TABLE 1. If we assume a similar flow and cardiac frequency in COAPT than in MITRA-FR, with a measured regular volume of 60 mL, the left ventricular end-diastolic volume should be 290 mL, which is more than in MITRA-FR

	MITRA-FR data	COAPT data	COAPT EDV recalculation
EDV	245 mL	193 mL	290 mL
EF	31%	31%	31%
Total LVSV	(EDV × 0.31) = 76 mL	(EDV × 0.31) = 59 mL	(Regular volume + efficiency stroke volume) 90 mL 88
Regular volume (PISA method)	45 mL	60 mL	60 mL
Effective LVSV	(LVSV – RV) = 31 mL	(LVSV – RV) = −1 mL	(2200 mL/73) = 30 mL
Regular fraction	59%	102%	59%
Fc	73 beats/min	?	73 beats/min
Q	2.2 L/min	Impossible	2.2 L/min

MITRA-FR, French Prospective Randomized Trial; *COAPT*, Cardiovascular Assessment of the Mitraclip Percutaneous Therapy; *EDV*, end-diastolic volume; *EF*, ejection fraction; *LVSV*, left ventricular stroke volume; *PISA*, proximal isovelocity surface area; *RV*, right ventricle.

The Journal of Thoracic and Cardiovascular Surgery https://doi.org/10.1016/j.jtcvs.2020.06.114

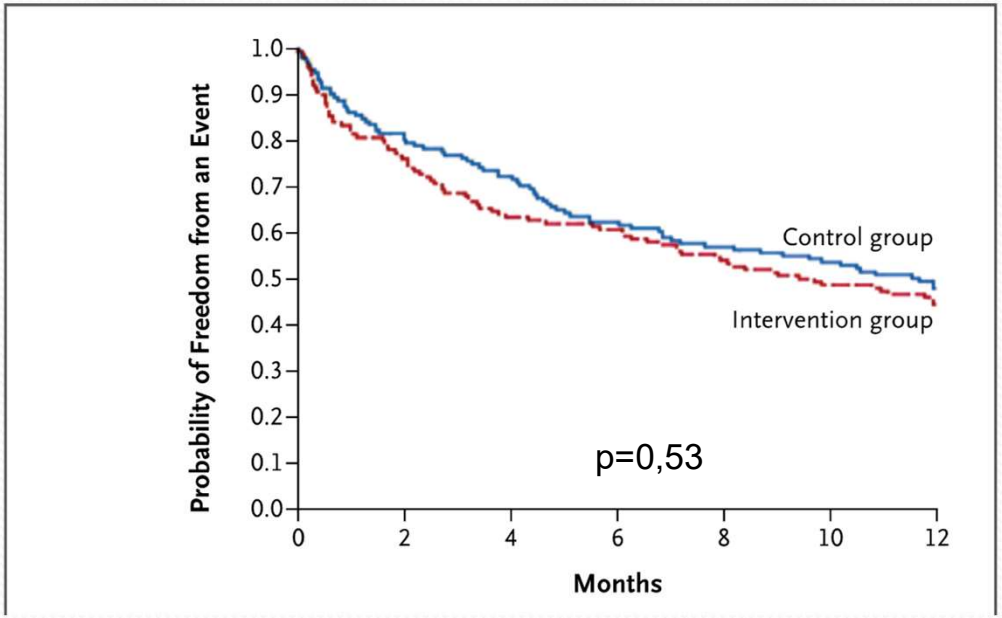
STROKE VOLUME = -1 ML

Not so easy to accurately evaluate secondary MR…even for high-quality centers involved in RCT trials…..

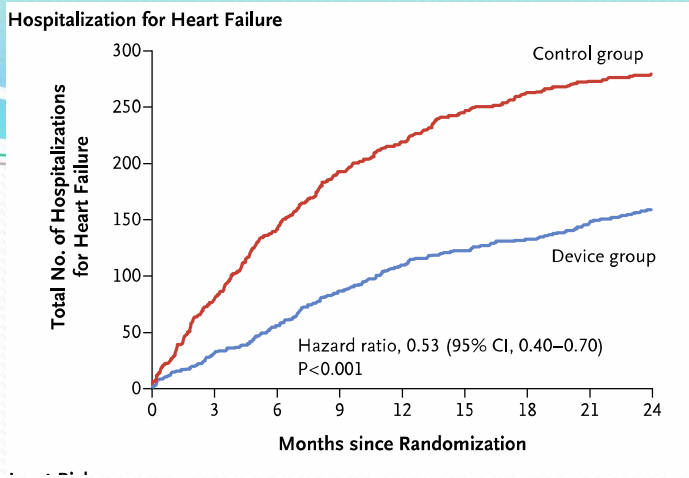
Concerning SMR mechanisms, what did we learn from randomized trials of SMR treatments ?

MITRA-FR

Primary outcome : death or unplanned HF hospitalization

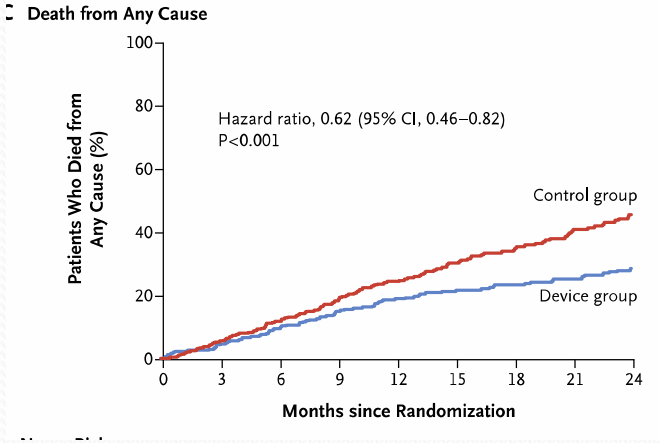


Obadia et al. NEJM 2018



COAPT

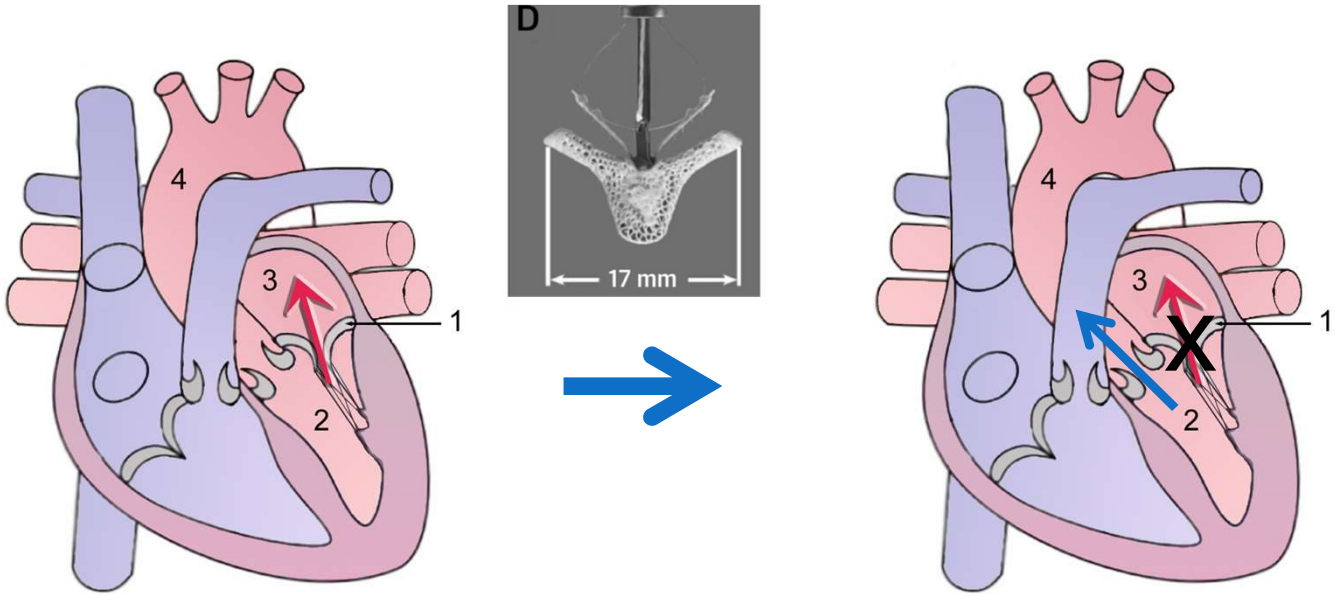
Stones et al. NEJM 2018



One month later

COAPT paradigm
« Effective and sustainable treatment of secondary MR improves prognosis »
➔ To avoid recurrence of the MR +++

To treat SEVERE secondary MR
EROA 0,4 cm^2 for COAPT (vs. 0,3 cm^2 for Mitra-FR)



ORIGINAL ARTICLE

Surgical Treatment of Moderate Ischemic Mitral Regurgitation

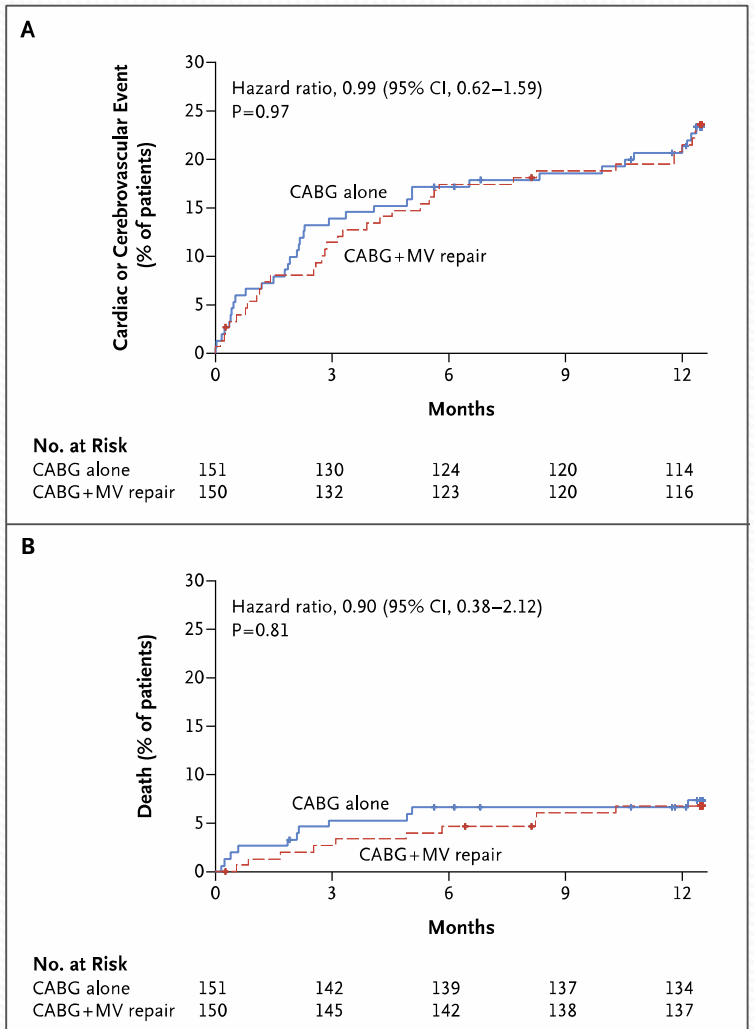


Figure 1. Time-to-Event Curves for the Composite End Point of Cardiac or Cerebrovascular Events and Death, According to Treatment Group.
The composite end point of major adverse cardiac or cerebrovascular events included death, stroke, subsequent mitral-valve (MV) surgery, hospitalization for heart failure, and an increase of one or more classes in the New York Heart Association (NYHA) classification. Crosses indicate censoring of data at the indicated time point. CABG denotes coronary-artery bypass surgery.

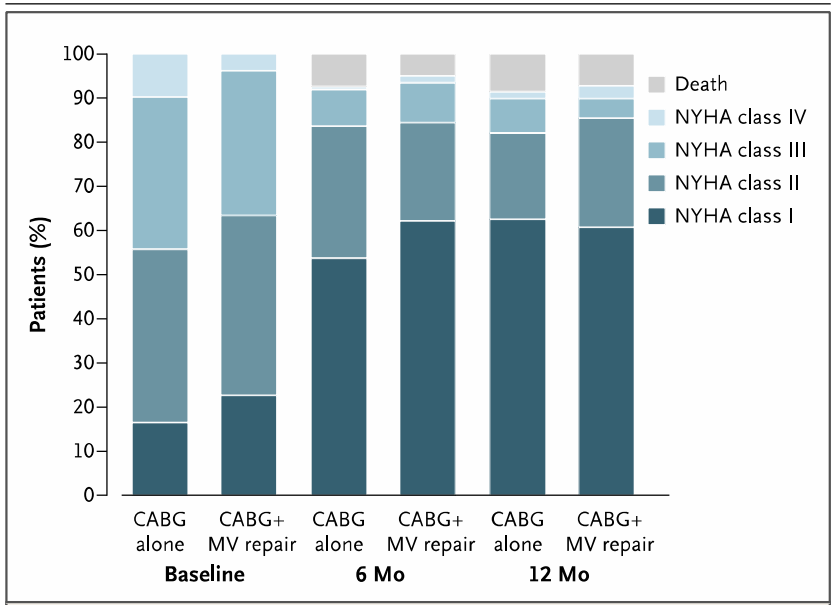


Figure 2. NYHA Class and Death, According to Treatment Group.
The proportions of patients in each NYHA class are shown at baseline and at 6 and 12 months; the proportions of patients who died are shown at 6 and 12 months.

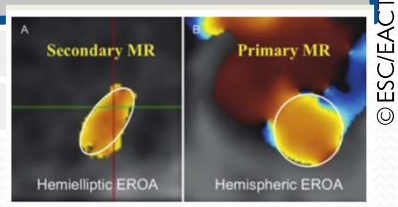
Baseline :
- 65 years, LVEF 40%
- Moderate MR ➔SOR 0,2 cm2

Smith et al. NEJM 2014

MITRAL REGURGITATION :
same definition of severity for primary and secondary MR

Table 7 **Severe mitral regurgitation criteria based on 2D echocardiography**

	Primary mitral regurgitation	Secondary mitral regurgitation
Qualitative		
Mitral valve morphology	Flail leaflet, ruptured papillary muscle, severe retraction, large perforation	Normal leaflets but with severe tenting, poor leaflet coaptation
Colour flow jet area	Large central jet (>50% of LA) or eccentric wall impinging jet of variable size	Large central jet (>50% of LA) or eccentric wall impinging jet of variable size
Flow convergence	Large throughout systole	Large throughout systole
Continuous wave Doppler jet	Holosystolic/dense/triangular	Holosystolic/dense/triangular
Semiquantitative		
Vena contracta width (mm)	≥7 (≥8 mm for biplane)	≥7 (≥8 mm for biplane)
Pulmonary vein flow	Systolic flow reversal	Systolic flow reversal
Mitral inflow	E-wave dominant (>1.2 m/s)	E-wave dominant (>1.2 m/s)
TVI mitral/TVI aortic	>1.4	>1.4
Quantitative		
EROA (2D PISA, mm^2)	≥40 mm^2	≥40 mm^2 (may be ≥30 mm^2 if elliptical regurgitant orifice area)
Regurgitant volume (mL/beat)	≥60 mL	≥60 mL (may be ≥45 mL if low flow conditions)
Regurgitant fraction (%)	≥50%	≥50%
Structural		
Left ventricle	Dilated (ESD ≥40 mm)	Dilated
Left atrium	Dilated (diameter ≥55 mm or volume ≥60 mL/m^2)	Dilated



ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2022) **00**, 1–62
https://doi.org/10.1093/ehjci/jeab253
EACVI DOCUMENT

Multi-modality imaging assessment of native valvular regurgitation: an EACVI and ESC council of valvular heart disease position paper

Table 10 Grading the severity of MR

MR severity classes	Mild	Moderate		Severe
MR Severity sub-classes[j]	**Mild (Grade 1 or 1+)**	**Mild-to-moderate (Grade 2 or 2+)**	**Moderate-to-severe (Grade 3 or 3+)**	**Severe (Grade 4 or 4+)**
Qualitative parameters				
MV morphology	None or mild leaflet abnormality or minimal tenting	Moderate leaflet abnormality or moderate tenting	Moderate leaflet abnormality or moderate tenting	**Flail leaflet/large coaptation defect/severe tenting**
Colour flow MR jet	Small, central (usually <4 cm^2 or <20% of LA area)	Intermediate (usually 4–6 cm^2 or 20–30% of LA area)	Intermediate (usually 6–8 cm^2 or 30–40% of LA area)	**Large central jet** (usually >8 cm^2 or >50% of LA area) or eccentric jet swirling and reaching the posterior wall of the LA
Flow convergence zone[a] CW signal of MR jet	No or small faint/parabolic	Dense, partial or parabolic	Dense, parabolic or triangular	• **Large throughout systole** • Holosystolic/dense/triangular
Semi-quantitative parameters				
VC width (mm)	<3	3 to <5	5 to <7	**≥7 (≥8 for biplane)**[b]
Pulmonary vein flow	Systolic dominance[e]	Normal or systolic blunting	Systolic blunting	Minimal to no systolic flow/**systolic flow reversal**[d]
Mitral inflow	A wave dominant[b]	Variable	E-wave dominant (Peak E > 1.2 m/s)[f]	E wave dominant (Peak E > 1.2 m/s)[f]
VTI mitral/VTI LVOT	<1	Intermediate	>1.2[f]	**>1.4**[f]
Quantitative parameters[h,i,k]				
EROA (mm^2)	<20	20–29	30–39	≥40
R Vol (mL)[l]	<30	30–44	45–59	≥60
RF (%)	<30	30–39	40–49	≥50
CMR parameters				
RF (%)	<30	30–39	40–49	≥50
Structural parameters				
LV and LA size[g]	Usually normal	Normal or dilated	Usually dilated	**Usually dilated**
PA pressures[g]	Usually normal	Normal or elevated	Normal or elevated	**Usually elevated**

COAPT paradigm
"Effective and sustainable treatment of secondary MR improves prognosis »
➔ To avoid recurrence of the MR +++

Most complete correction of SMR during the procedure:

- ✓ Center experience
- ✓ High number of procedures
- ✓ More clips implanted per patient

To treat SEVERE secondary MR EROA 0,4 cm^2 for COAPT (vs. 0,3 cm^2 for Mitra-FR)

ORIGINAL ARTICLE

Two-Year Outcomes of Surgical Treatment of Severe Ischemic Mitral Regurgitation

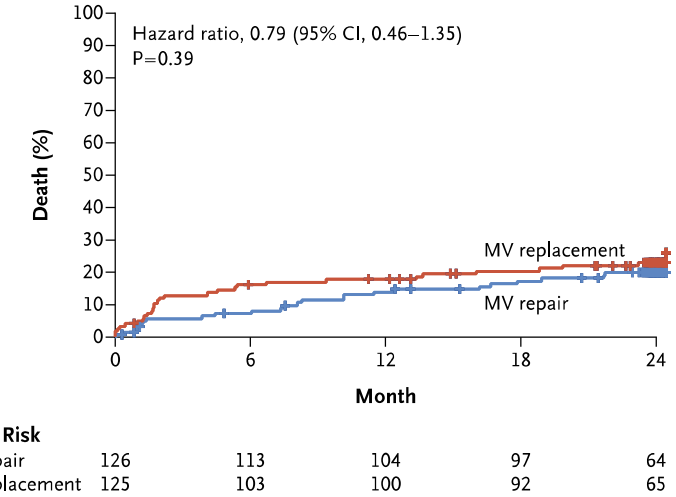


Figure 1. Time-to-Event Curves for Death.
Shown are the proportions of patients who died in the mitral-valve (MV) repair group and the mitral-valve replacement group at 2 years. The most frequent underlying causes of death were multisystem organ failure (in 20.8% of patients), heart failure (in 17.0%), and sepsis (in 13.2%). The tick marks indicate censored data.

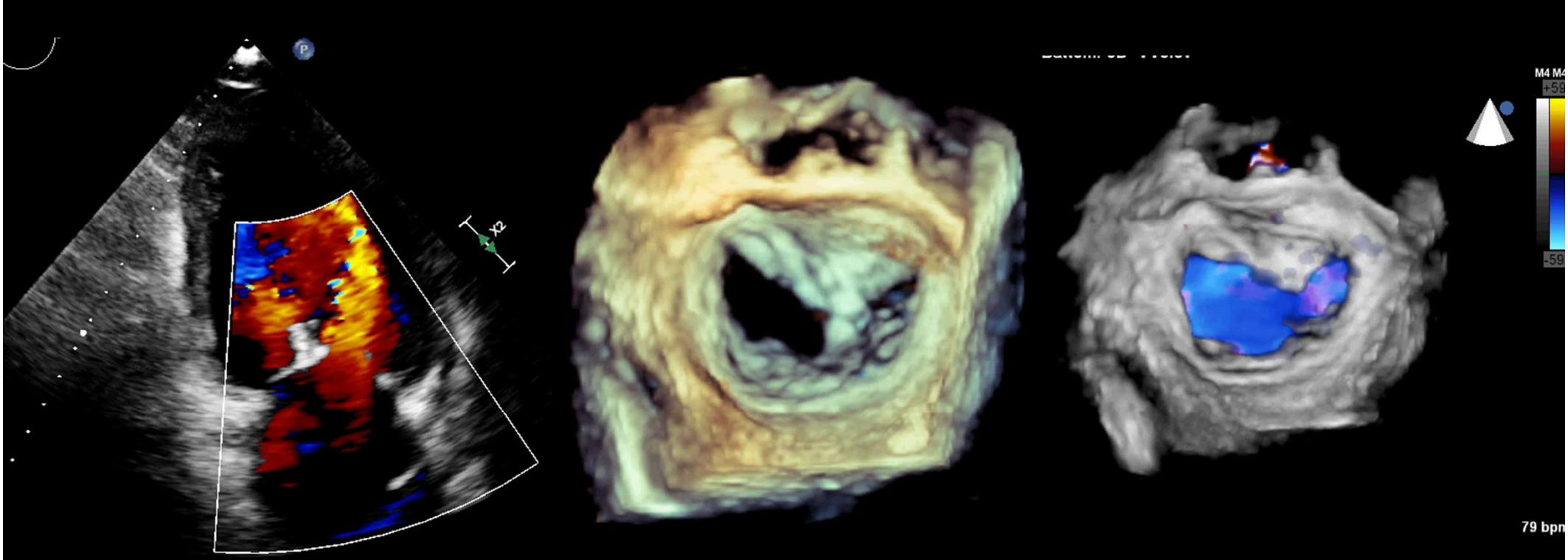
Table 1. Clinical End Points, Serious Adverse Events, and Hospitalizations at 2 Years.

Variable	Repair (N=126)	Replacement (N=125)	P Value*
	no./total no. of patients (%)		
Clinical end point			
Death	24/126 (19.0)	29/125 (23.2)	0.42
Stroke	10/126 (7.9)	7/125 (5.6)	0.46
Worsening New York Heart Association class†	5/85 (5.9)	5/84 (6.0)	1.0
Rehospitalization for heart failure	27/126 (21.4)	22/125 (17.6)	0.44
Failed index mitral-valve procedure	6/126 (4.8)	0	0.03
Mitral-valve reoperation	4/126 (3.2)	1/125 (0.8)	0.37
Moderate or severe recurrent mitral regurgitation	57/97 (58.8)	3/79 (3.8)	<0.001
MACCE‡	53/126 (42.1)	53/125 (42.4)	0.96
Canadian Cardiovascular Society class III or IV	4/82 (4.9)	0/80	0.19
	no. of events (rate/100 patient-yr)		
Serious adverse event			
Any event	291 (145.6)	247 (129.8)	0.18
Heart failure	48 (24.0)	29 (15.2)	0.05

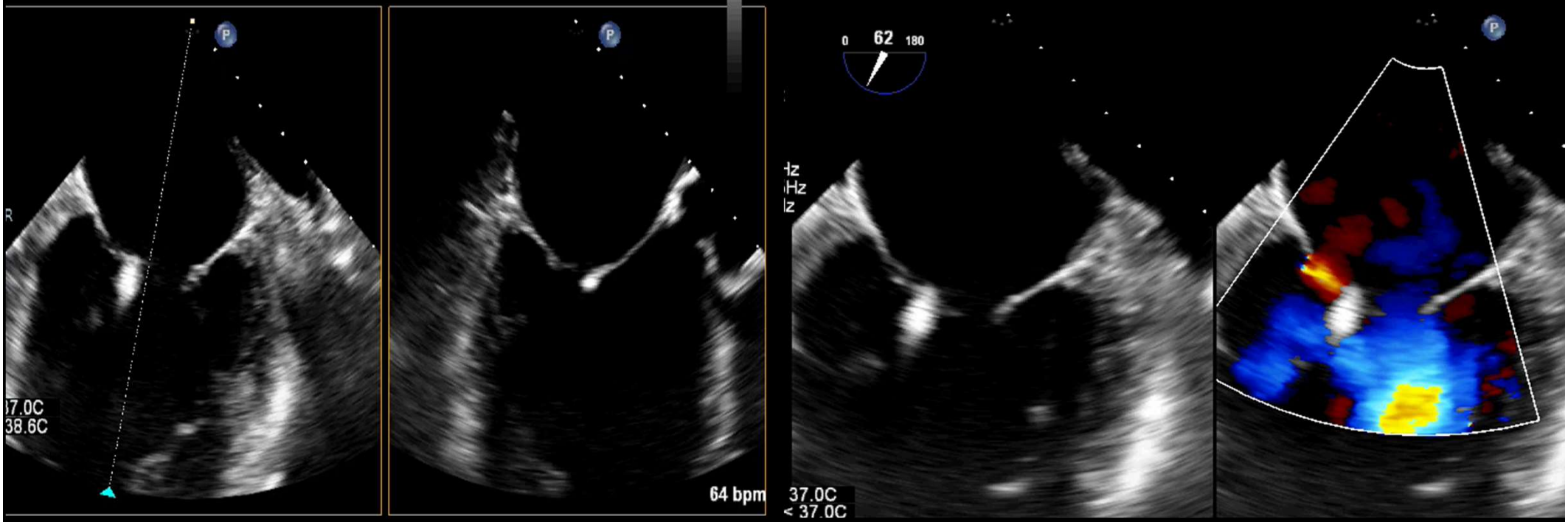
Baseline :
- 77 years, LVEF 40%
- Severe ischemic MR ➔ SOR 0,4 cm2
- CABG in 75% of each group

No significant between-group difference in left ventricular reverse remodeling or survival at 2 years.

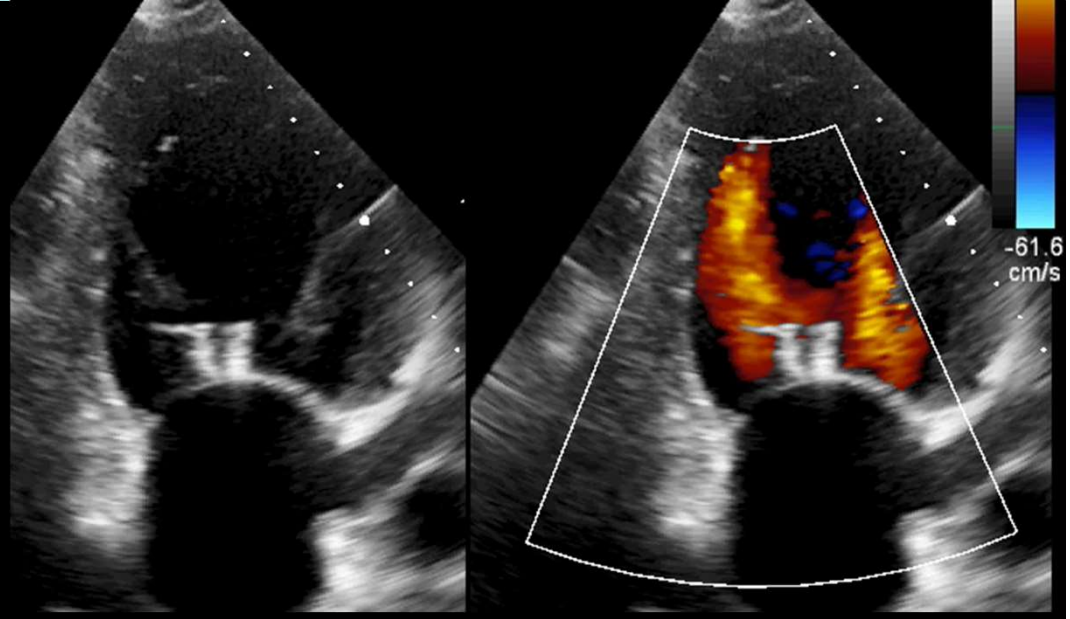
Goldstein et al. NEJM 2016

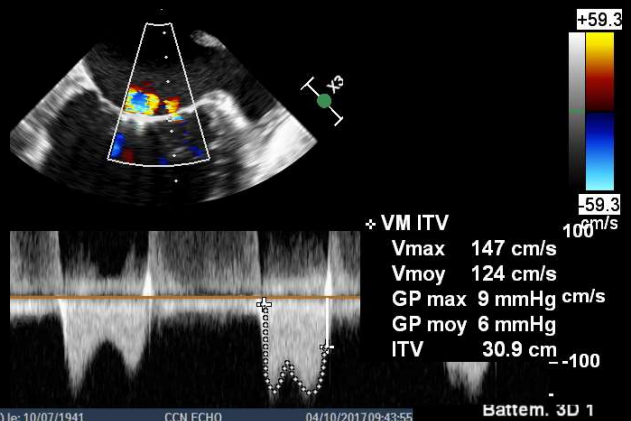


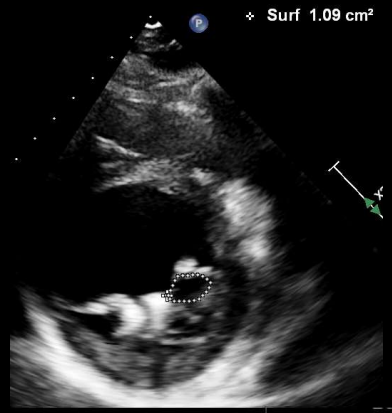
TEE at 6 months : no detachement of the clip,
new severe MR with a rupture of chordae tendinae. LVEF : 30%, sPAP 70 mmHg.

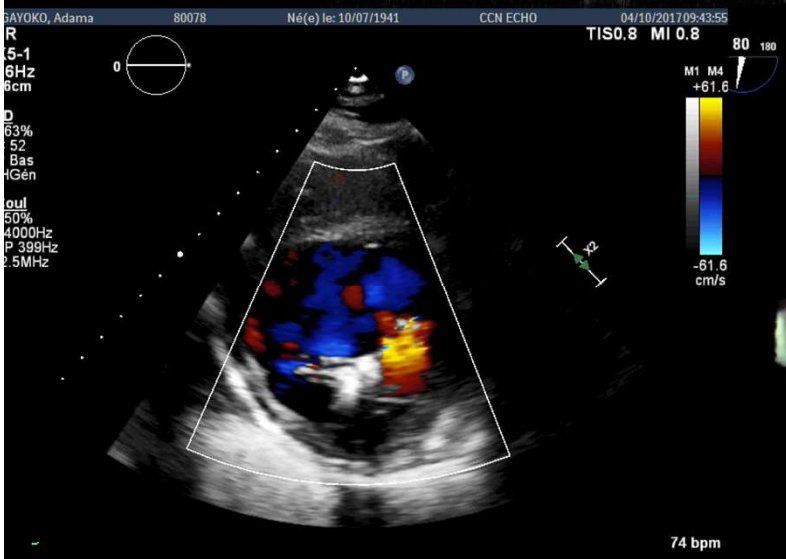


- Mr BA, 75 years-old
- Successful redo mitraclip procedure with implantation of a second clip (lateral)
- Final mitral area : 0.6 + 1.1 = 1.7 cm2
- Mean gradient : 4-5 mmHg.
- LVEF 25%, sPAP 50 mmHg.

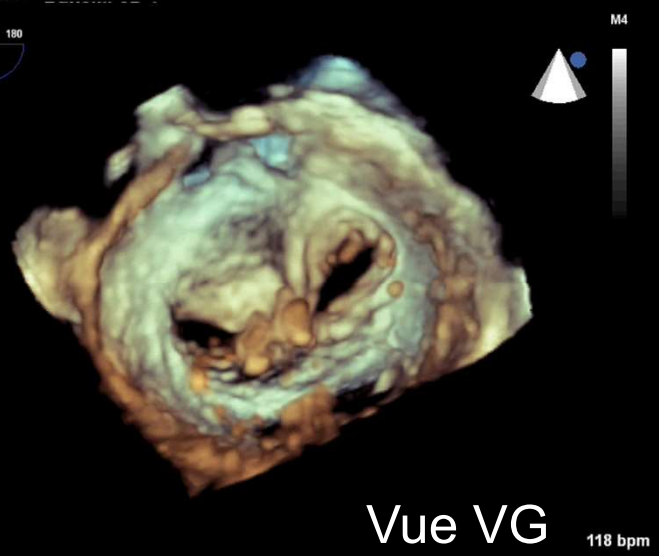








Vue OG



Vue VG

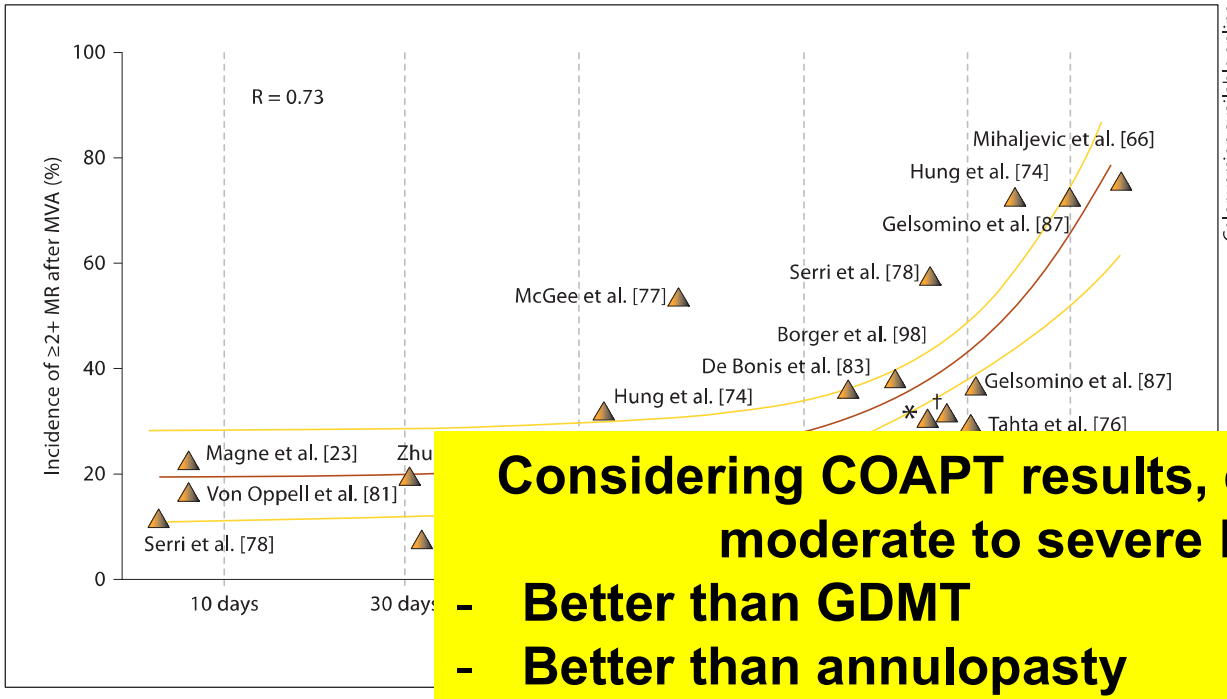


Fig. 8. Incidence of postoperative ≥2+

Magne et al. Cardiology 2009

Considering COAPT results, concerning recurrence of moderate to severe MR, Mitraclip is :

- **Better than GDMT**
- **Better than annulopasty**
- **Better than MVR**

…. → to be confirmed

Table 1. Clinical End Points, Serious Adverse Events, and Ho

Variable	Repair (N=126)	Replacement (N=125)	P Value*
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Heart failure	48 (24.0)	29 (15.2)	0.05

Goldstein et al. NEJM 2016

Baseline			3+-4+				
MitraClip (n=302)	-	-	49.0%	51.0%	-	-	-
GDMT (n=311)	-	-	55.3%	44.7%		-	
30 days			7.4%				
MitraClip (n=273)	72.9%	19.8%	5.9%	1.5%	<0.001	92.7%	<0.001
GDMT (n=257)	8.2%	26.1%	37.4%	28.4%		34.2%	
6 months			6.3%				
MitraClip (n=240)	66.7%	27.1%	4.6%	1.7%	<0.001	93.8%	<0.001
GDMT (n=218)	9.2%	28.9%	42.2%	19.7%		38.1%	
12 months			5.3%				
MitraClip (n=210)	69.1%	25.7%	4.3%	1.0%	<0.001	94.8%	<0.001
GDMT (n=175)	11.4%	35.4%	34.3%	18.9%		46.9%	
24 months			0.9%				
MitraClip (n=114)	77.2%	21.9%	0%	0.9%	<0.001	99.1%	<0.001
GDMT (n=76)	15.8%	27.6%	40.8%	15.8%		43.4%	

Most complete correction of SMR during the procedure:

- ✓ Center experience
- ✓ High number of procedures
- ✓ More clips implanted per patient

To treat SEVERE secondary MR EROA 0,4 cm^2 for COAPT (vs. 0,3 cm^2 for Mitra-FR)

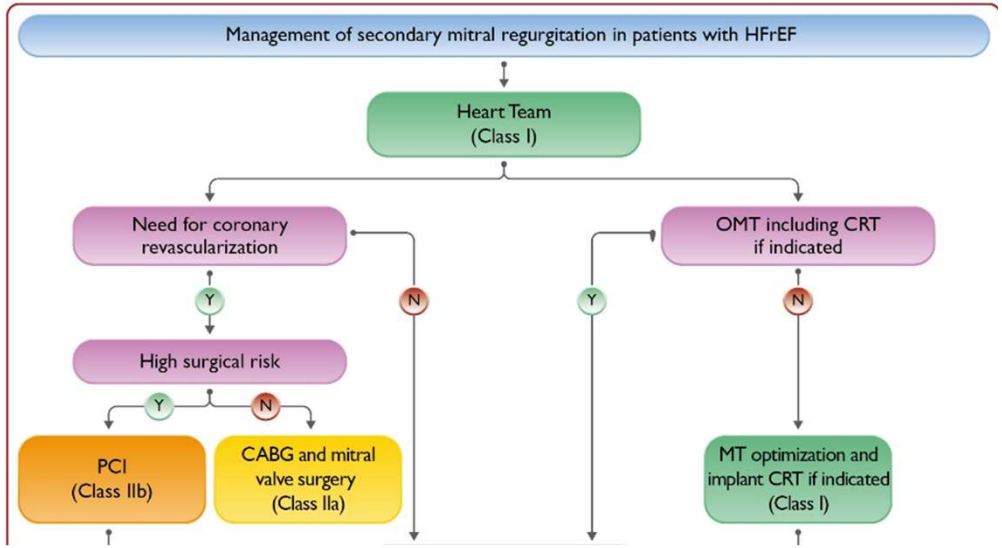
COAPT paradigm
"Effective and sustainable treatment of secondary MR improves prognosis »
➔ To avoid recurrence of the MR +++

↓

Optimal medical treatement +++
in association with the MitraClip

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)



Management of secondary mitral regurgitation in patients with heart failure and reduced ejection fraction

First treat underlying LV dysfunction ++

- OMT
- CRT
- Revascularisation

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2022) **23**, 755–764
https://doi.org/10.1093/ehjci/jeac068

ORIGINAL PAPER

Guideline directed *medical* therapy and reduction of secondary mitral regurgitation

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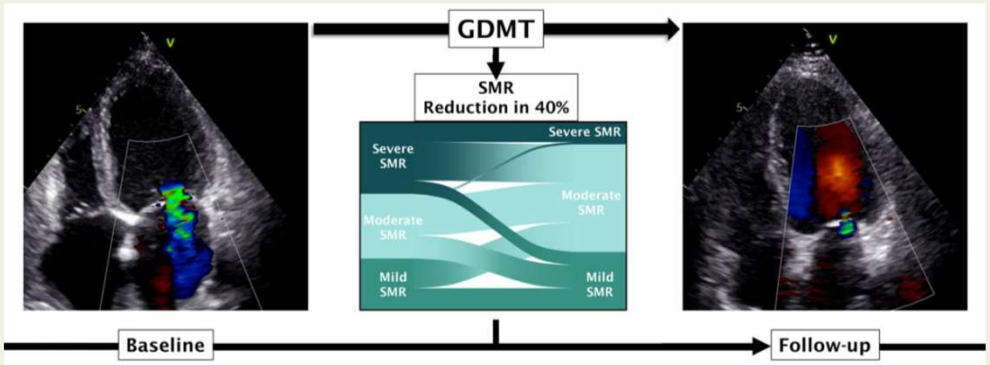
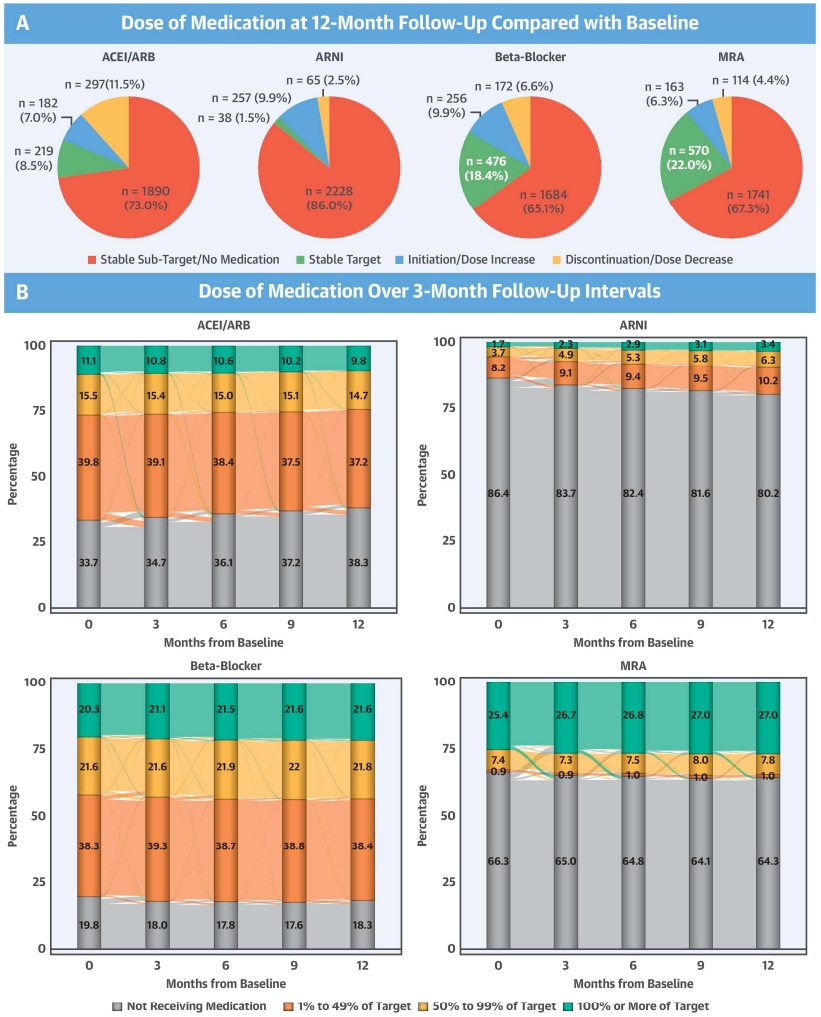
Graphical Abstract



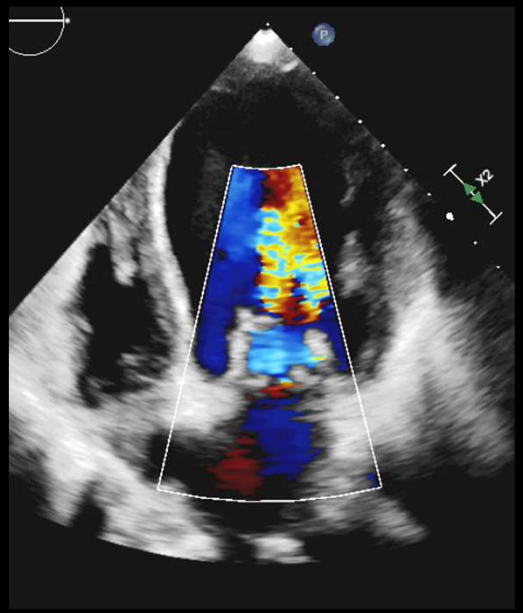
Conclusion The present study provides comprehensive evidence for the effectiveness of contemporary GDMT to specifically improve SMR. Our data indicate that GDMT titration conveys a three-fold increased chance of reducing SMR severity. Moreover, the dosage effects of ARNi, as well as the combination of RASi and MRA, BB and MRA, and all three substances in the aggregate are able to significantly improve SMR.

CENTRAL ILLUSTRATION: Changes in Use and Dose of GDMT Over 12 Months Among Patients With Chronic Heart Failure With Reduced Ejection Fraction in Contemporary U.S. Outpatient Practice

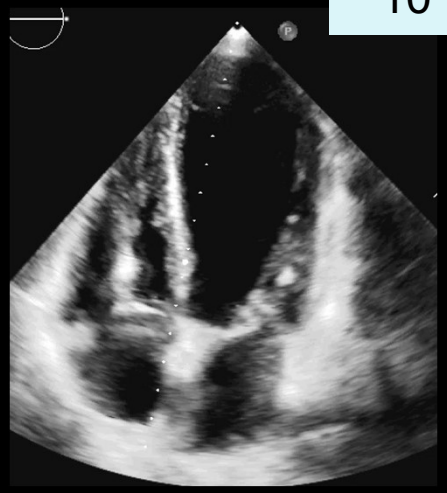


Greene, S.J. et al. J Am Coll Cardiol. 2019;73(19):2365–83.

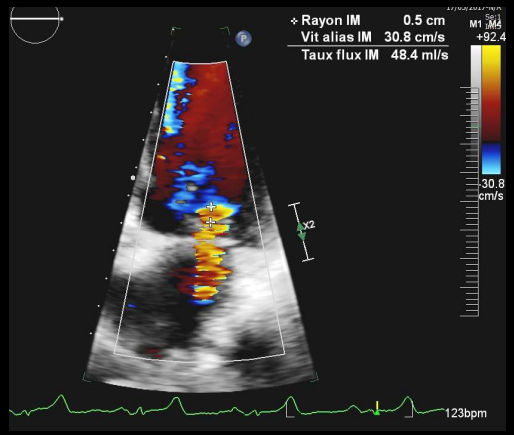
- 65 y-old woman
- Previous rheumatic MR grade ¼
- Recent large LBBB
- NYHA III
- LVEDD 64 mm ;
- LVESD 56 mm
- LVEF 33%
- Severe SMR : EROA 0.31 cm2, vol reg 50 ml
- Dilated LA
- Normal sPAP



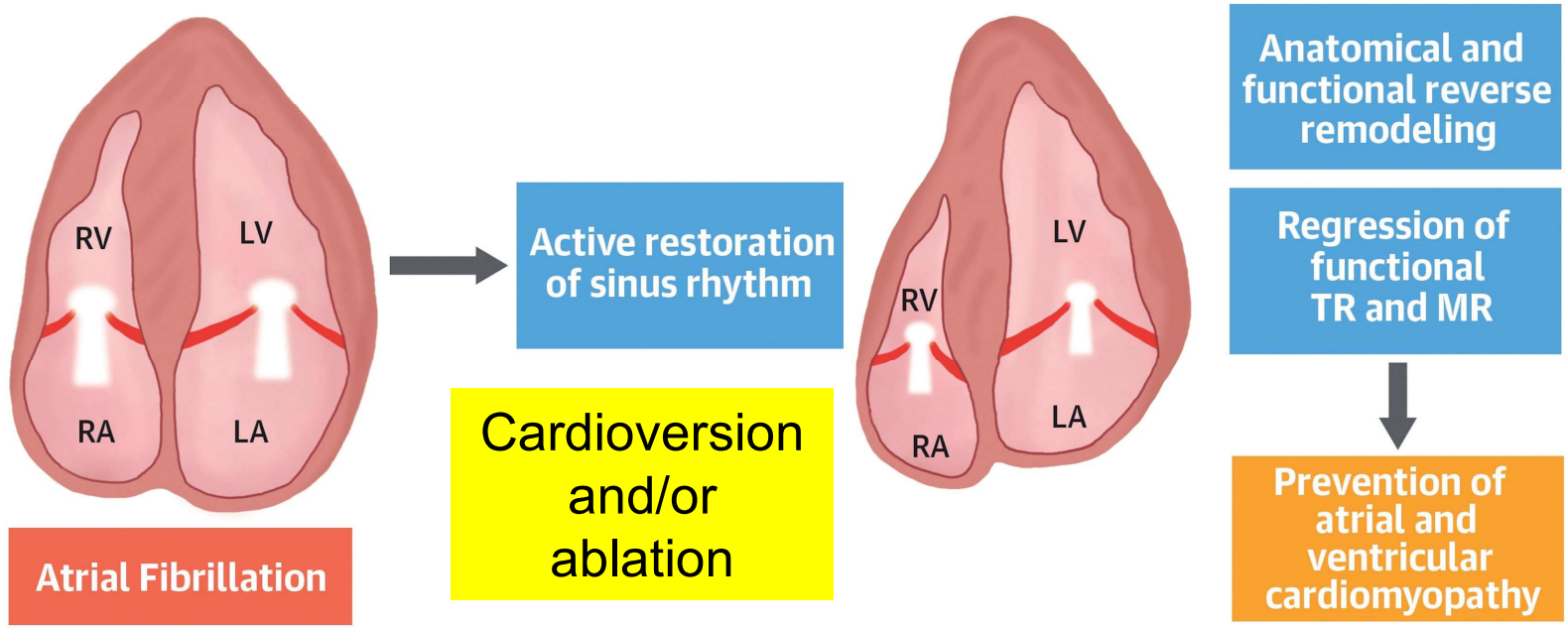
10 months after CRT-D, NYHA I



- LVEDD 44 mm ;
- LVESD 32 mm
- LVEF 60%
- IM ¼
- Dilated LA
- Normal sPAP



CENTRAL ILLUSTRATION: Reverse Cardiac Remodeling/Improvement of Regurgitation After Restoration of Sinus Rhythm

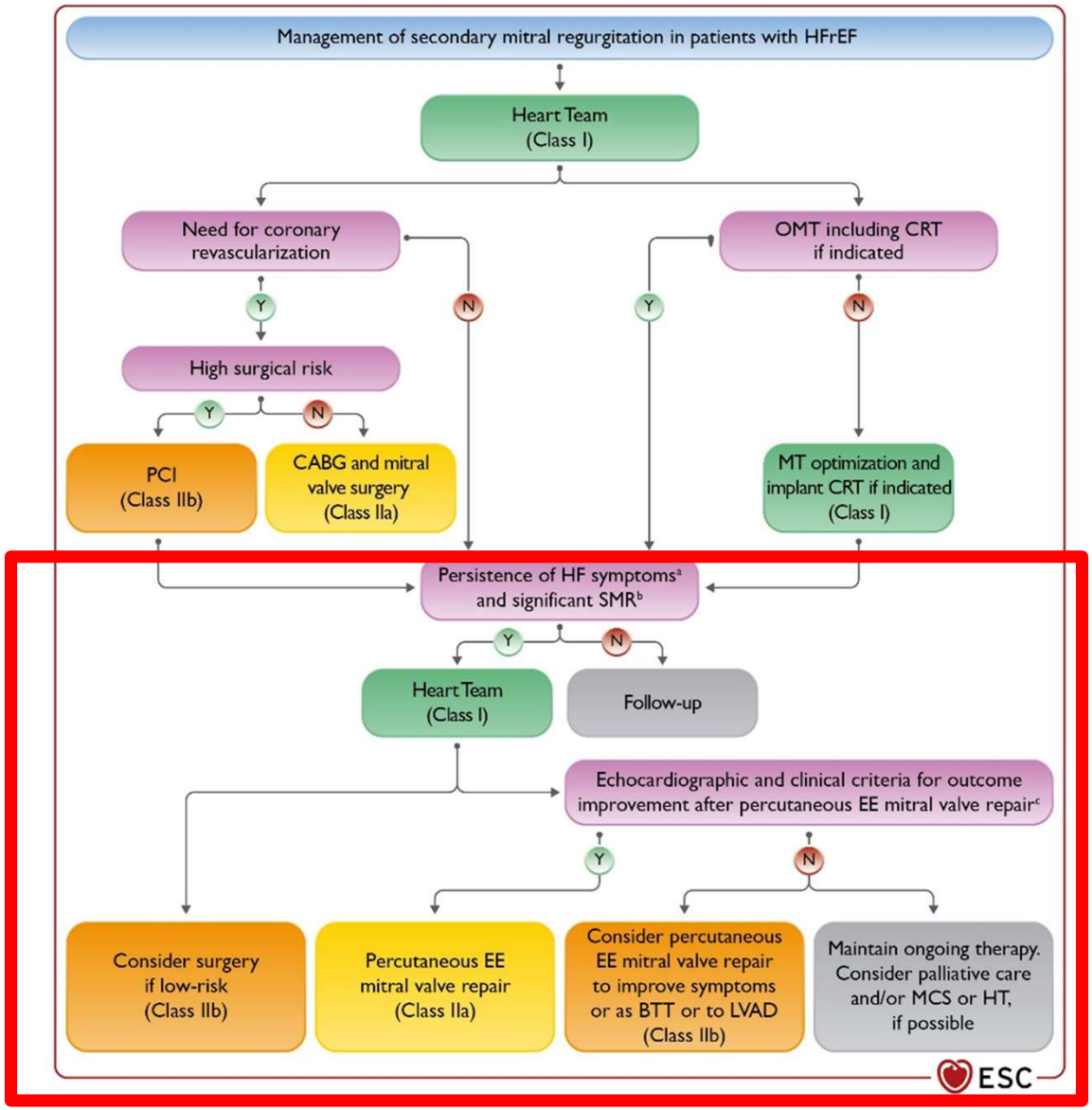


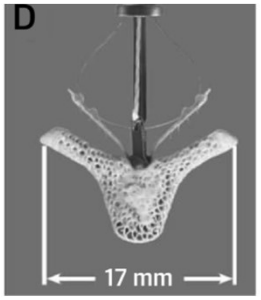
Soulat-Dufour, L. et al. . 2022;79(10):951-961.

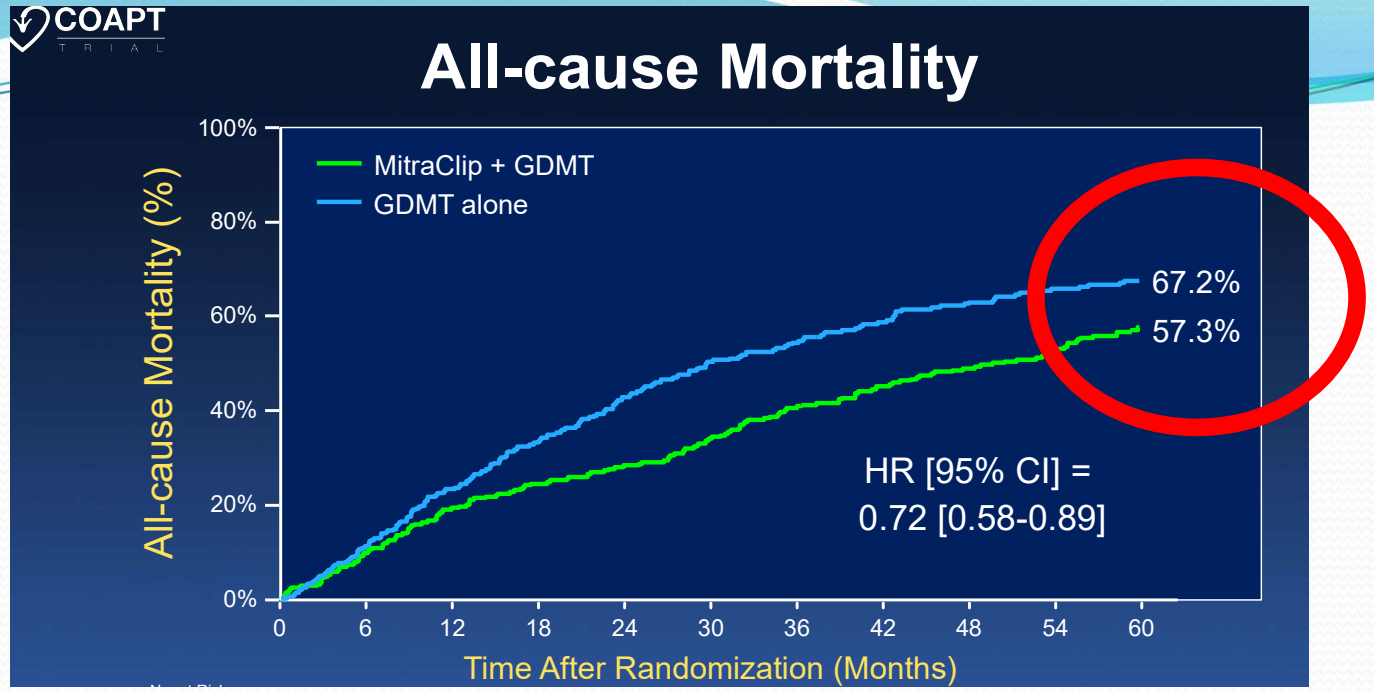
CONCLUSIONS Management of AF should focus on restoration of SR to induce anatomical (all atrial Vi, ES RV Vi) and/or functional (4 chambers) cardiac cavity reverse remodeling and reduce severity of functional regurgitation. (Thromboembolic and Bleeding Risk Stratification in Patients With Non-valvular Atrial Fibrillation [FASTRHAC]; NCT02741349) (J Am Coll Cardiol 2022;79:951-961) © 2022 by the American College of Cardiology Foundation.

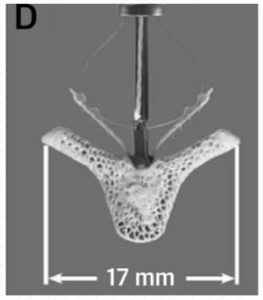
2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

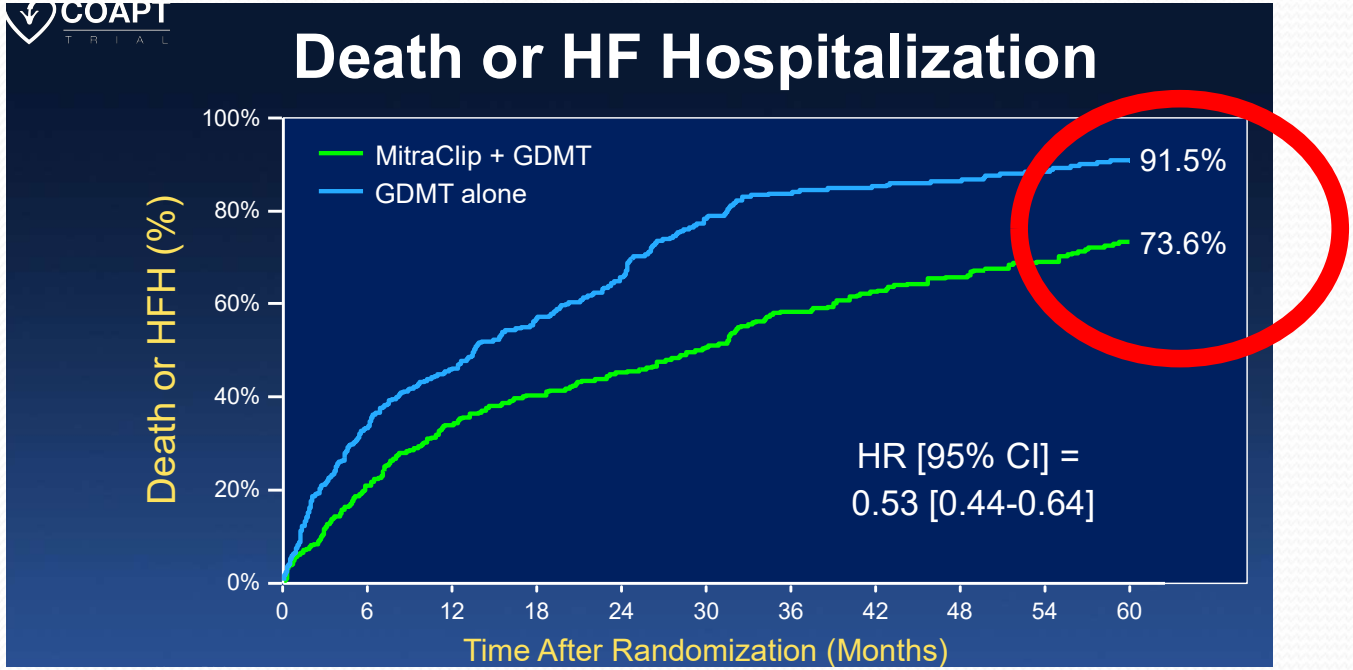
Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)











Severe prognosis (control or TEER) +++++

Impact of Transcatheter Edge-to-Edge Mitral Valve Repair on Guideline-Directed Medical Therapy Up-Titration

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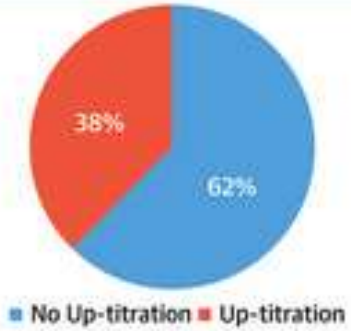
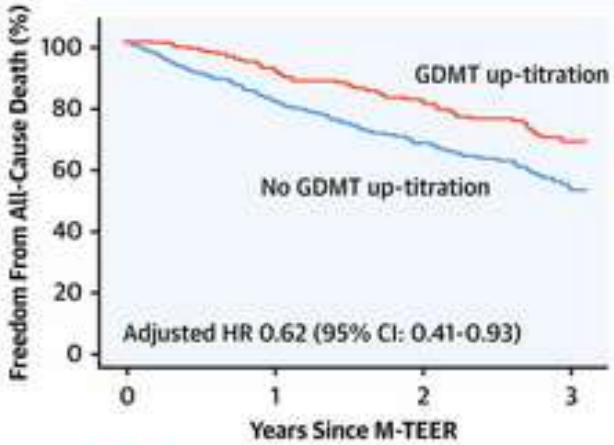
GDMT Up-titration After M-TEER

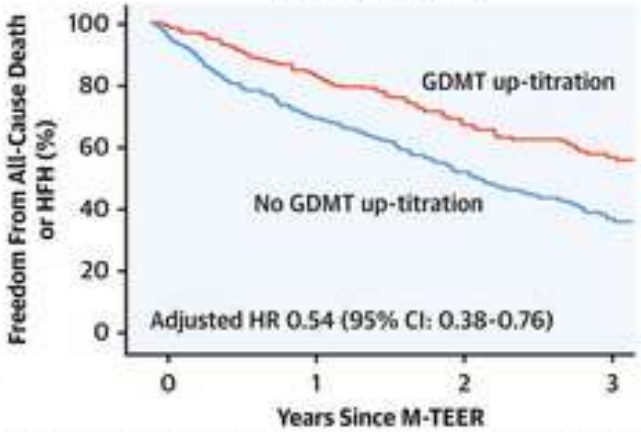


Predictors of GDMT Up-titration

Variables*	OR (95% CI)	*P*-Value
NT-proBNP	1.16 (0.56-2.41)	0.695
Systolic pulmonary artery pressure	0.99 (0.97-1.02)	0.513
Previous myocardial infarction	0.81 (0.38-1.75)	0.593
Mean arterial blood pressure	1.00 (0.98-1.02)	0.868
Glomerular filtration rate	1.01 (0.99-1.02)	0.280
MR reduction of at least 3 grades	1.71 (1.08-2.71)	**0.022**
NYHA improvement (≥1 class)	0.66 (0.35-1.25)	0.200

Association Between GDMT Up-titration and Outcomes





ADAMO et al. JACC ITVN 2023

CONCLUSION

- Impact of LV geometry on secondary MR mechanisms
- Assess severity : TTE, TEE, CMR
- Symptomatic secondary severe MR:

- Treat underlying LV disease +++ : GDMT, CRT, revascularisation, concomitant AS, AF ablation
- TEER > > surgery if COAPT phenotype.
- Continue to optimize GDMT ++++

Merci !