MHIF FEATURED STUDY:

REPAIR-MR

Coming soon!

EPIC message: *Research MHIF Patient Referral*

CONDITION:	PI:	RESEARCH CONTACT:	SPONSOR:
Severe primary MR who are at moderate surgical risk	Paul Sorajja, MD	Jane Fox Jane.fox@allina.com | 612-863-6289	Abbott

DESCRIPTION:

Purpose: to **compare the clinical outcome of MitraClip™ device versus open surgical repair in patients with severe primary MR who are at moderate surgical risk.**

Primary endpoint: survival, free of stroke and any cardiovascular hospitalization at 2 years; MR ≤ mild at 30 days; QOL improvement of at least 5 points at 2 years compared to baseline; hospital length of stay; rate of mitral valve replacement at index procedure

CRITERIA LIST/ QUALIFICATIONS:

Inclusion: severe primary MR (Grade III or greater mitral regurgitation mixed etiology is acceptable if principal mechanism is a degenerative mitral valve); symptomatic NHYA class II, III, or asymptomatic with EF ≤ 60%, PAS >50 mm HG, or LVESD >40 mm; 75 years or if < 75 years subject with STS predicted risk of mortality repair score >2%, or presence of comorbidities

Exclusion: ischemic or non-ischemic secondary MR; EF <30%; severe TR; severe annular calcification; valve anatomy which would preclude reducing MR to mild or less

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Minneapolis Heart Institute Foundation®
Creating a world without heart and vascular disease

MHIF FEATURED STUDY:

HighLife

OPEN AND ENROLLING:

EPIC message: *Research MHIF Patient Referral*

CONDITION:	PI:	RESEARCH CONTACT:	SPONSOR:
Symptomatic mitral regurgitation	Paul Sorajja, MD	Jane Fox Jane.fox@allina.com | 612-863-6289	HighLife Medical, Inc.

DESCRIPTION:

Purpose: to **evaluate the safety and efficacy of the HighLife trans-septal access 28mm Transcatheter Mitral valve and its delivery system (*transfemoral venous access and interatrial puncture*) in patients with moderate-severe or severe mitral regurgitation who are at a high risk for surgical treatment.**

Primary Feasibility endpoint: technical success

Safety: all cause mortality at 30 days

Performance: total MR reduction to 1+ or less as assessed by core lab

CRITERIA LIST/ QUALIFICATIONS:

Inclusion: moderate-severe or severe mitral regurgitation; NHYA class II, III; or ambulatory class IV

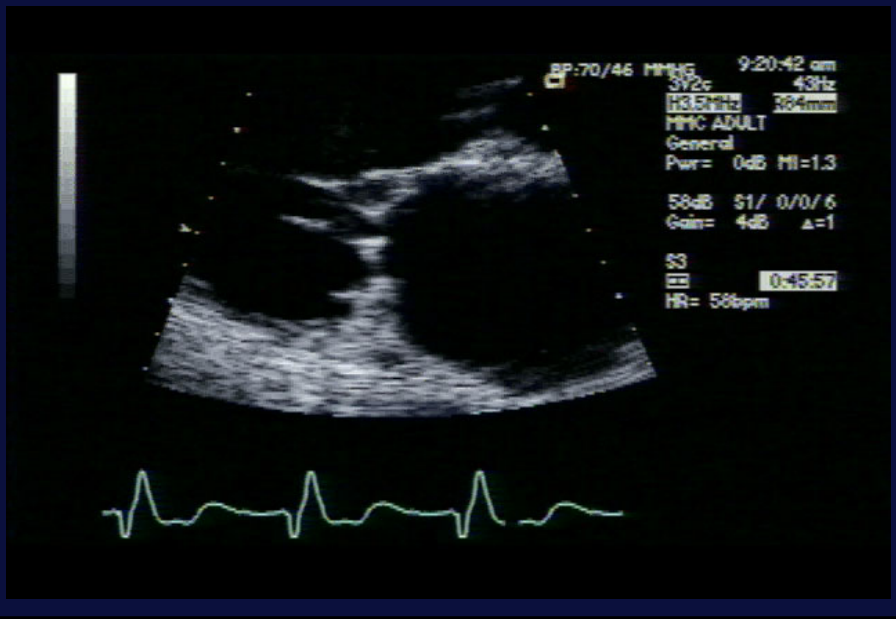
Exclusion: mitral stenosis; Flail Leaflet or prolapse; severe calcification; prior mitral intervention; mitral annulus <30 mm & >45 mm; Aortic prosthesis; LVEF<30%; PAS >70mmHg; TR requiring intervention

Functional MR

MHIF-2020

Maurice E. Sarano, MD, FACC

Functional MR (secondary)



ESC European Society of Cardiology

European Heart Journal (2019) **40**, 2194–2202
doi:10.1093/eurheartj/ehz314

CLINICAL RESEARCH
Valvular heart disease

Causes and mechanisms of isolated mitral regurgitation in the community: clinical context and outcome

Volha Dziadzko, Mikhail Dziadzko, Jose R. Medina-Inojosa, Giovanni Benfari, Hector I. Michelena, Juan A. Crestanello, Joseph Maalouf, Prabin Thapa, and Maurice Enriquez-Sarano*

FMR in the community

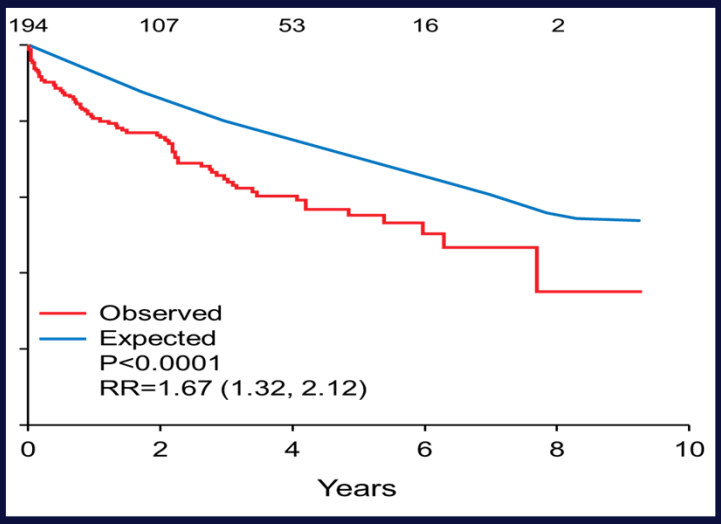
65% of all MR cases

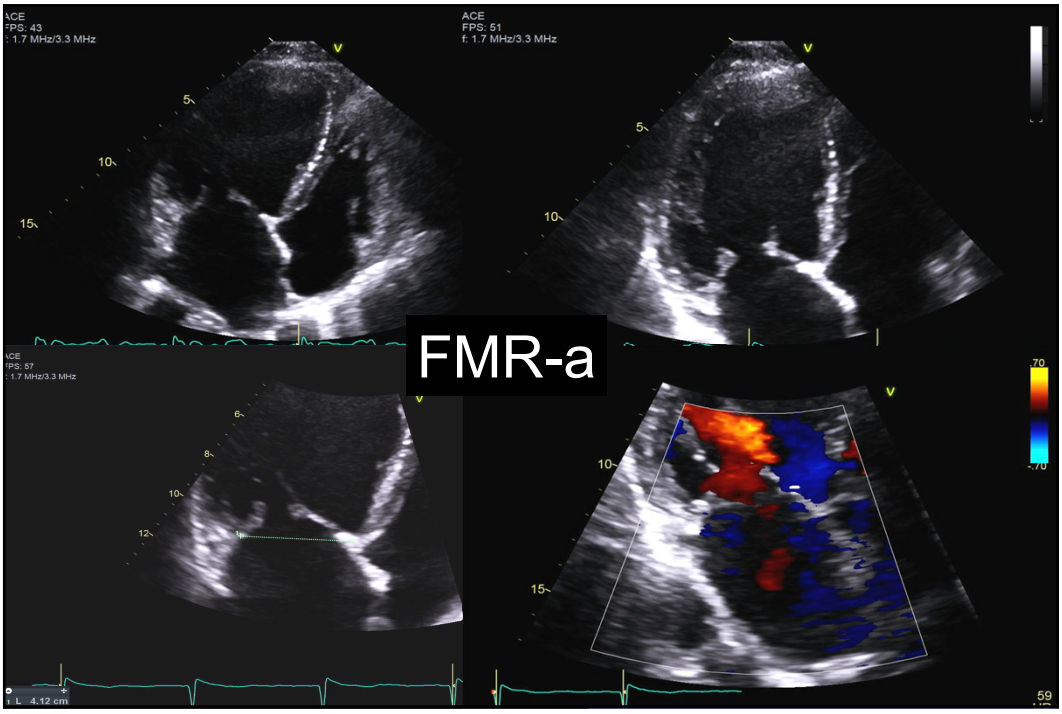
Structurally normal mitral valve
+
Mitral Regurgitation ≥moderate

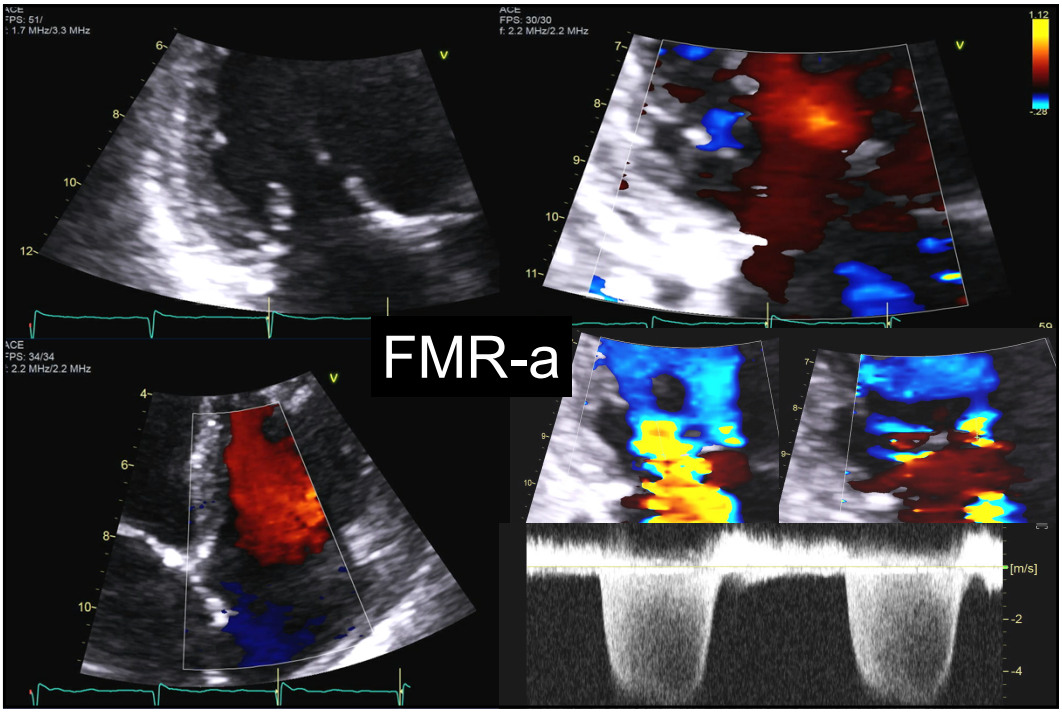
LV Remodeling — **38 %**

Atrial Enlargement — **27 %**

Functional MR-Atrial enlargement







Clinical characteristics according to MR etiology

	FMR ventricular remodeling	FMR isolated atrial dilatation	OMR	p-value
Total number of cases (%)	278 (38)	194 (27)	233 (32)	
Age at diagnosis, years	73±14	80±10	68±21	<.0001
Sex, male, %	59	32	51	<.0001
Dyspnea, %	74	66	49	<.0001
Atrial fibrillation/flutter,%	28	54	13	<.0001
History of Heart failure,%	49	32	12	<.0001
History of MI,%	17	9	3	<.0001
Diabetes,%	29	24	9	<.0001
Charlson index, median	3.5[2-5]	3[2-5]	2[0-3]	<.0001

ESC Congress
Munich 2018

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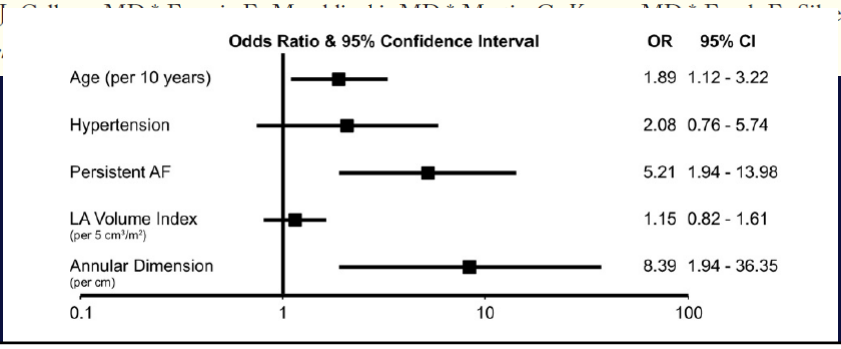
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.06.032

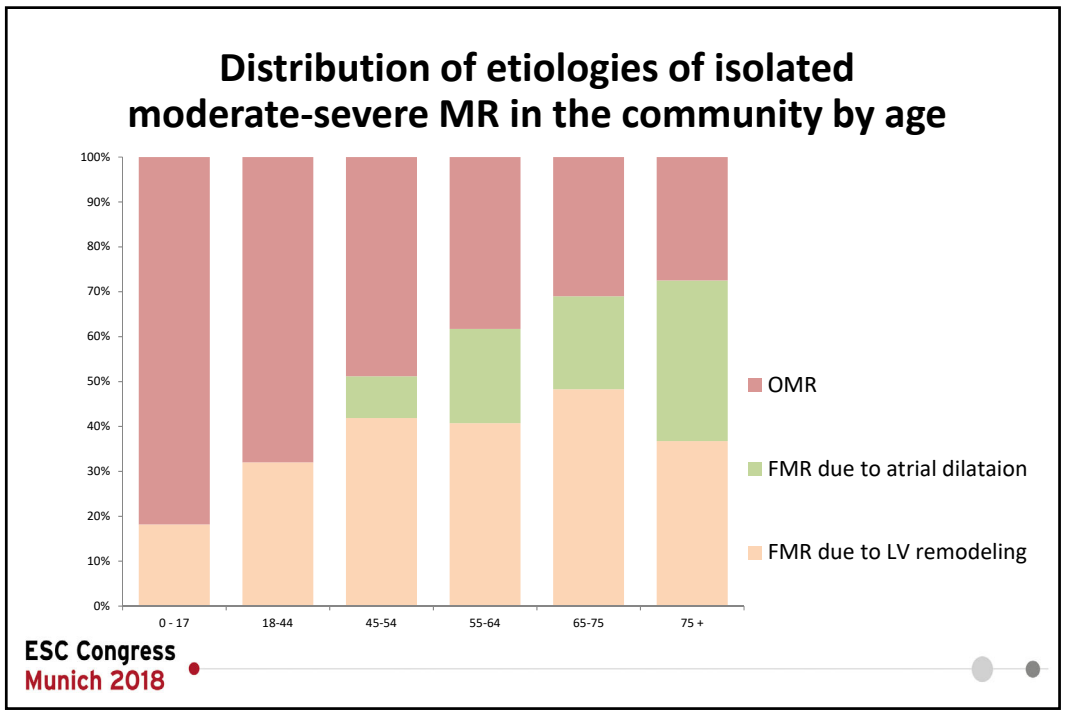
Heart Rhythm Disorders

Evidence of Atrial Functional Mitral Regurgitation Due to Atrial Fibrillation

Reversal With Arrhythmia Control

Zachary M. Gertz, MD,* Amresh Raina, MD,* Laszlo Saghy, MD,† Erica S. Zado, PA-C,*
David J [illegible] stry, MD*
Philade[illegible]



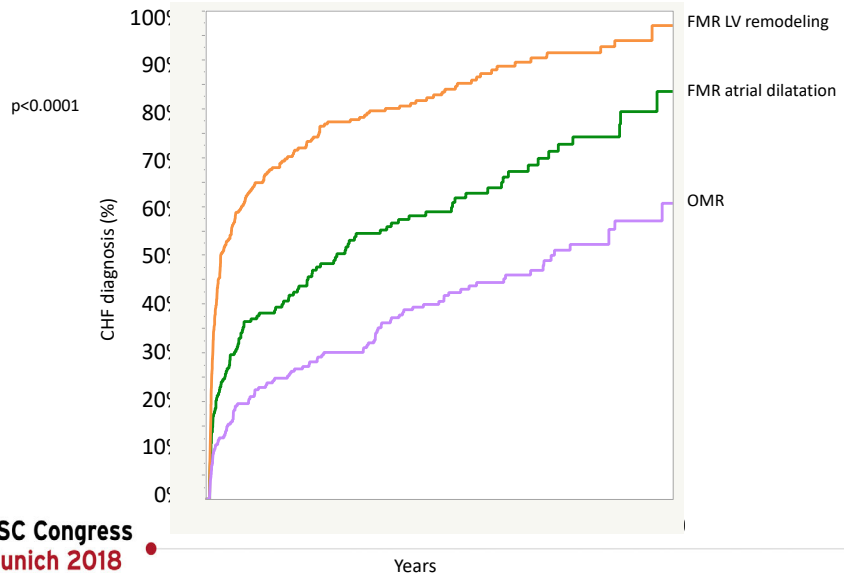


Echocardiographic differences by MR etiology

	FMR ventricular remodeling	FMR isolated atrial dilatation	OMR	p-value
LA volume, ml	102±33	94±30	91±35	0.005
MV RVol, ml	38±13	37±11	51±24	<.0001
MV ERO, cm²	0.24±0.10	0.20±0.08	0.31±0.19	<.0001
LVEF, %	33±14	57±11	61±10	<.0001
LV EDD, mm	59±8	48±5	51±8	<.0001
LV ESD, mm	49±10	32±6	32±7	<.0001
LV mass index, g/m²	135±34	106±30	108±29	<.0001
PASP, mmHg	52±14	48±14	44±18	<.0001

ESC Congress
Munich 2018

Outcomes of MR by etiology



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MR and surgery

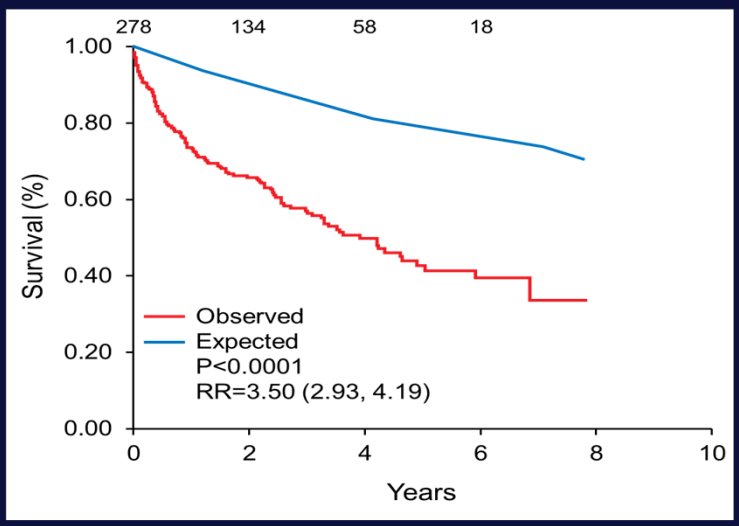
	FMR isolated atrial dilatation (n=194)	OMR (n=233)	Total (n=705)
MV repair/ replacement, (%)	6(3%)	86(37%)	102(14%)
Any cardiac surgery, n(%)	12(6%)	86(37%)	123(17%)
MV repair/ replacement by MR severity			
Moderate MR, n(%) in subset	5(3%) (n=175)	22(18%) n=124	31(6%) (n=491)
Severe MR, n(%) in subset	1(5%) (n=19)	64(59%) (n=109)	71(33%) (n=214)

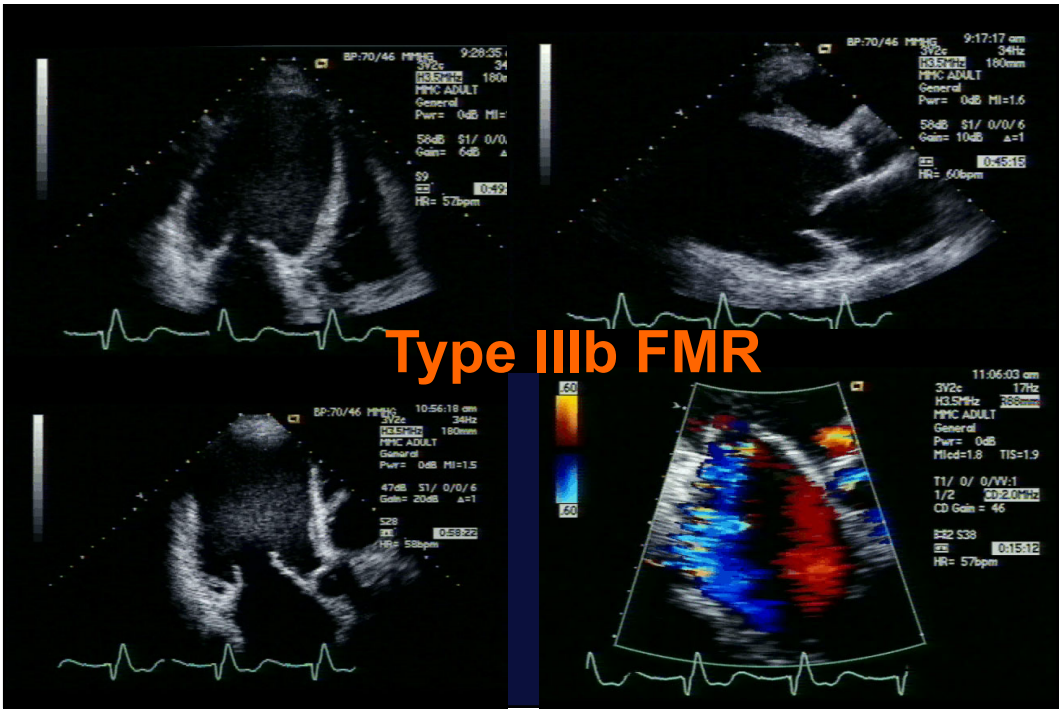
ESC Congress
Munich 2018

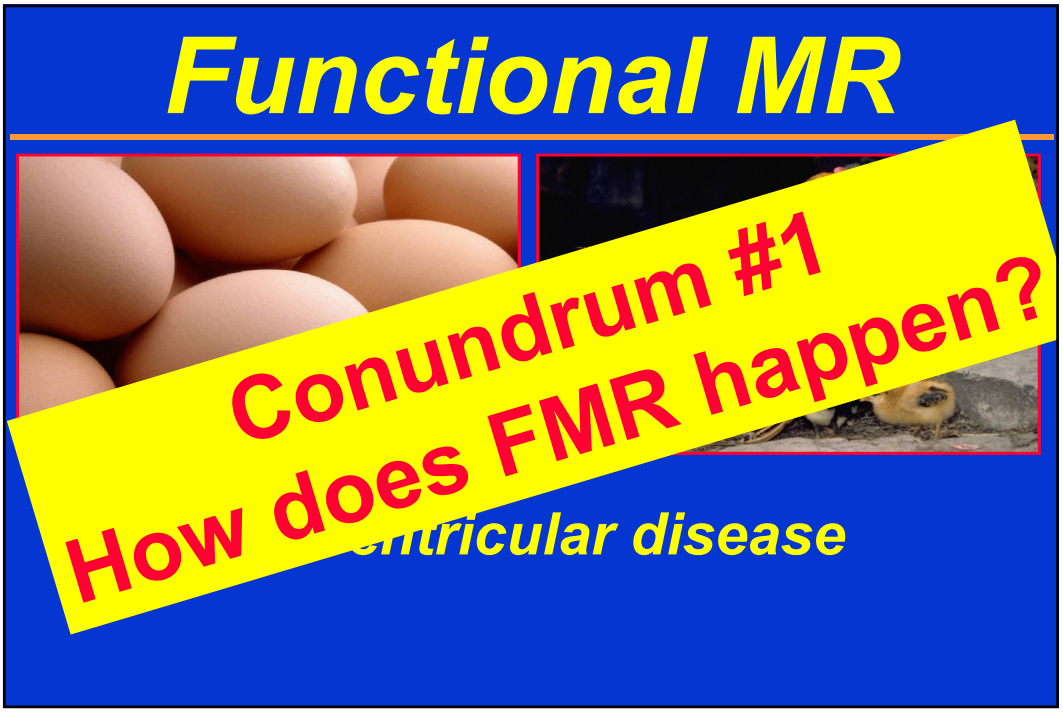
FMR-Atrial Dilatation

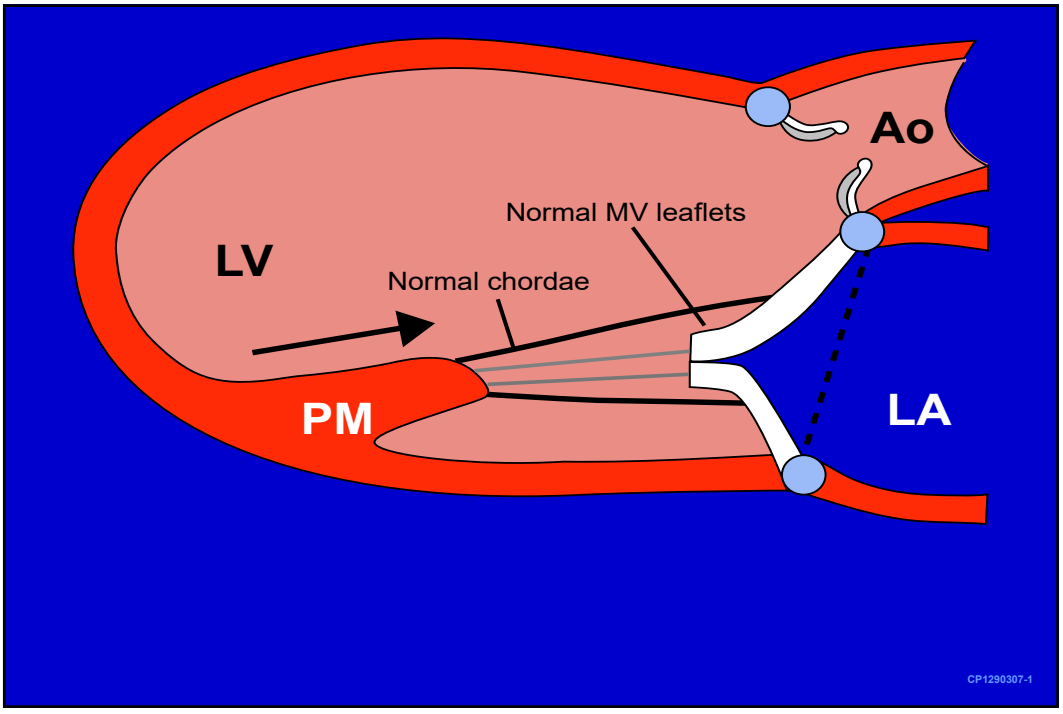
- An entity almost completely ignored despite representing ~1/3 of all MR
- Affecting mostly elderly women often with AF
- Peculiar hemodynamics: Low Rvol, normal LV, PHTN
- Very frequent HF preceding excess mortality
- Almost never mitral surgery
- Role of the MR ???

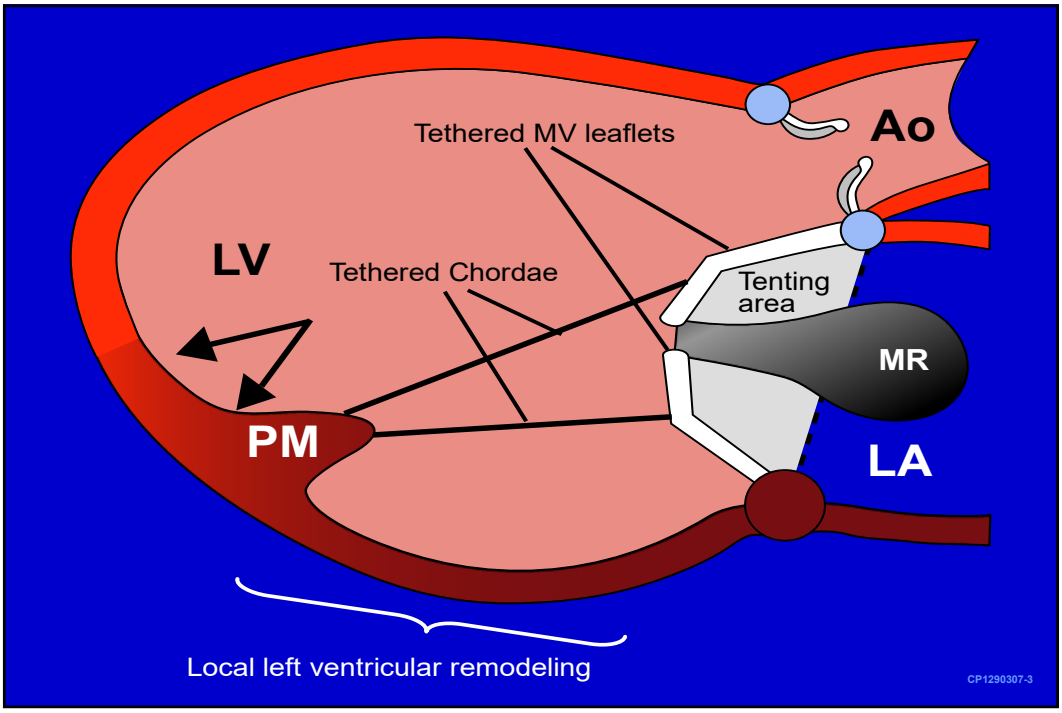
Functional MR-LV Remodeling

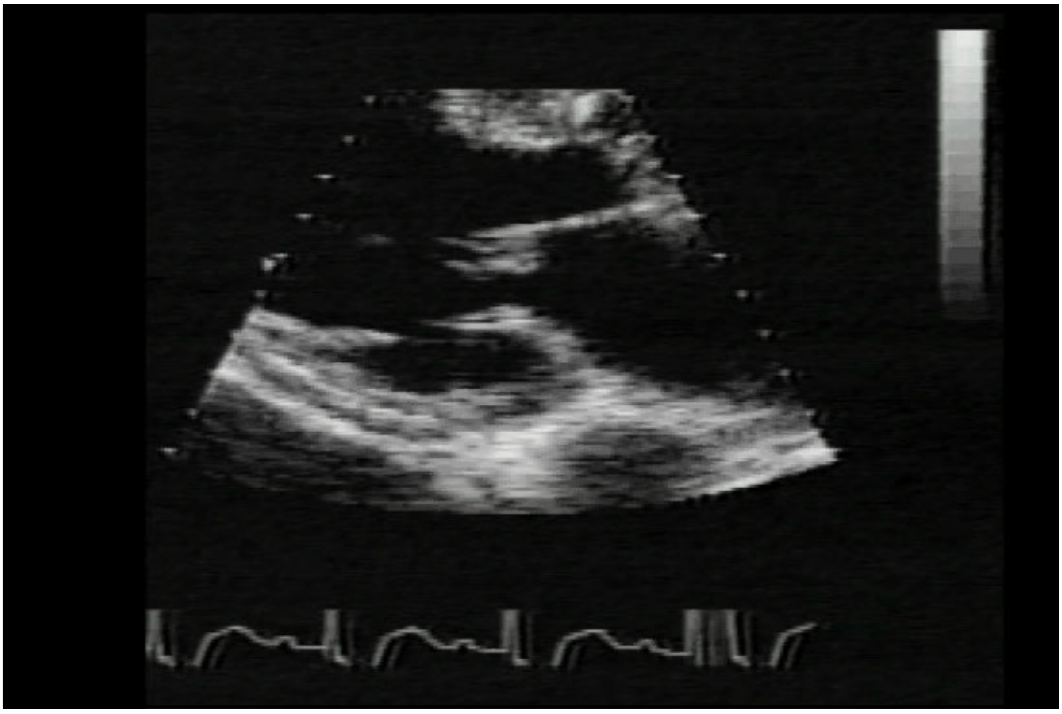




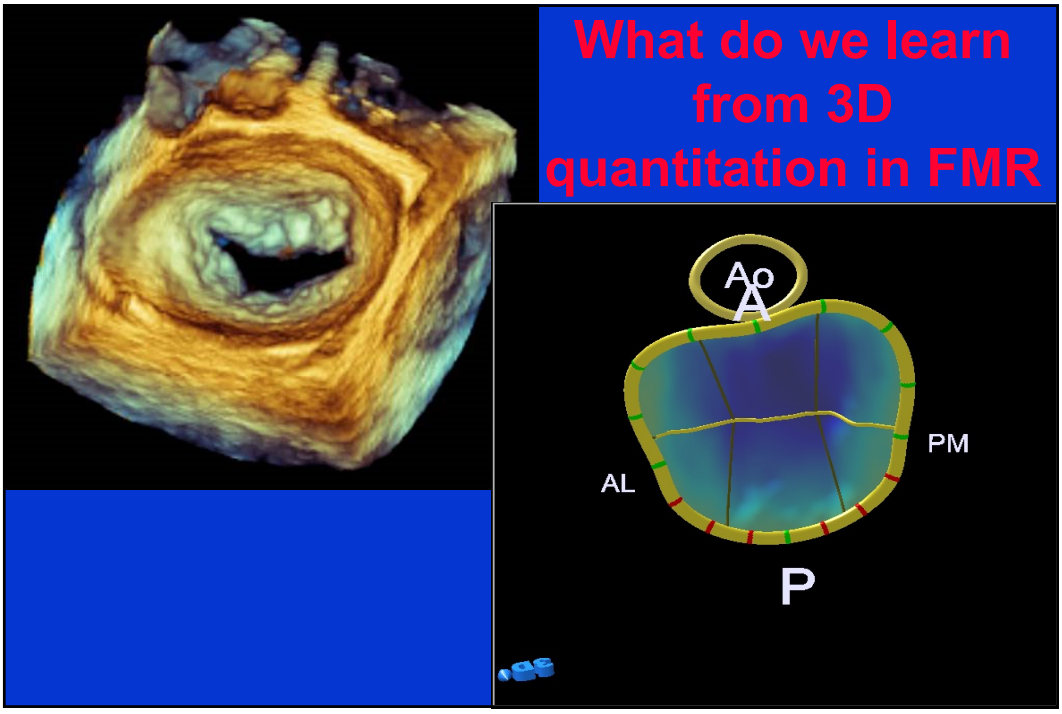

Functional MR
Conundrum #1
How does FMR happen?
ventricular disease

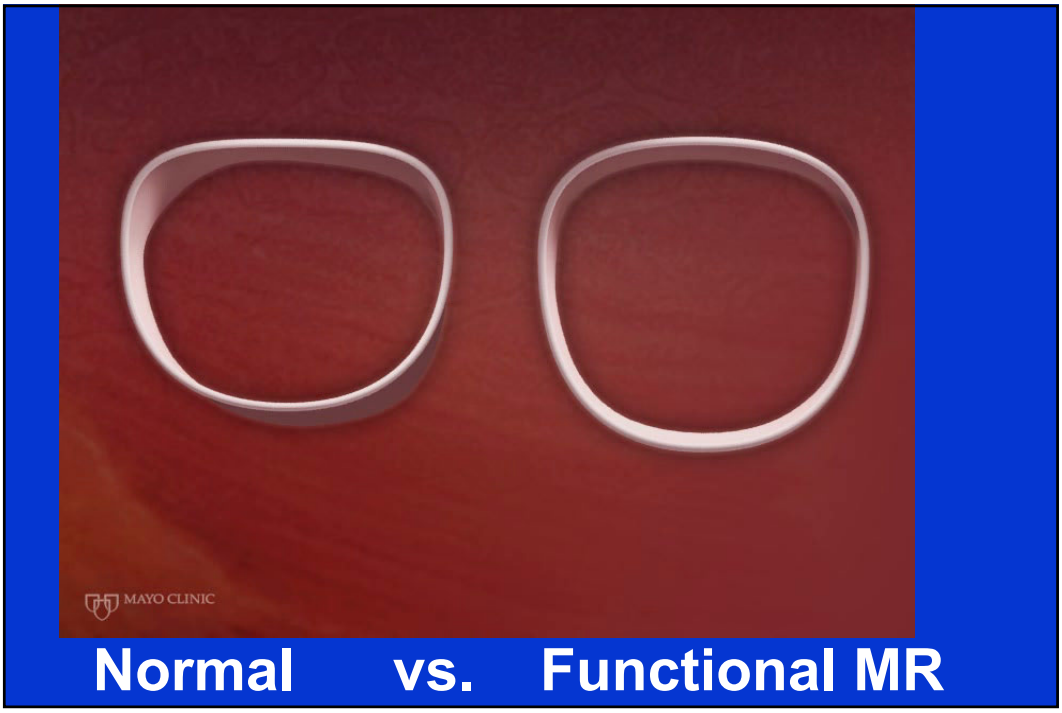

Ao
Normal MV leaflets
LV
Normal chordae
PM
LA
CP1290307-1

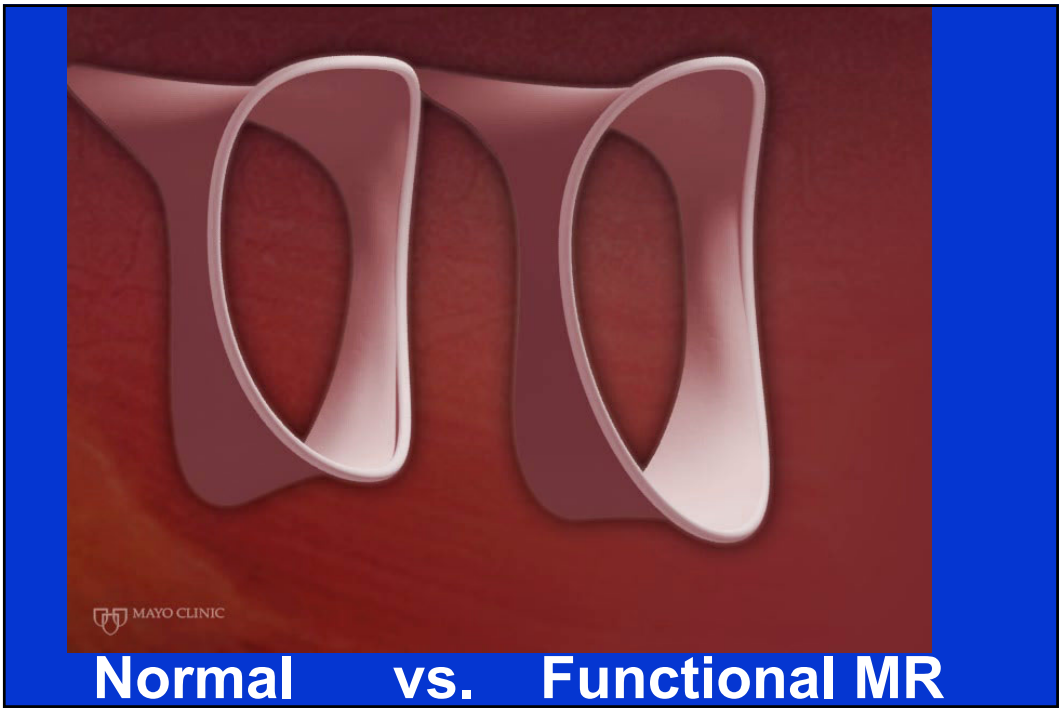

Tethered MV leaflets
Ao
LV
Tethered Chordae
Tenting area
MR
PM
LA
Local left ventricular remodeling
CP1290307-3




Try to close
The orifice !


What do we learn from 3D quantitation in FMR
Ao
A
PM
AL
P


MAYO CLINIC
Normal vs. Functional MR

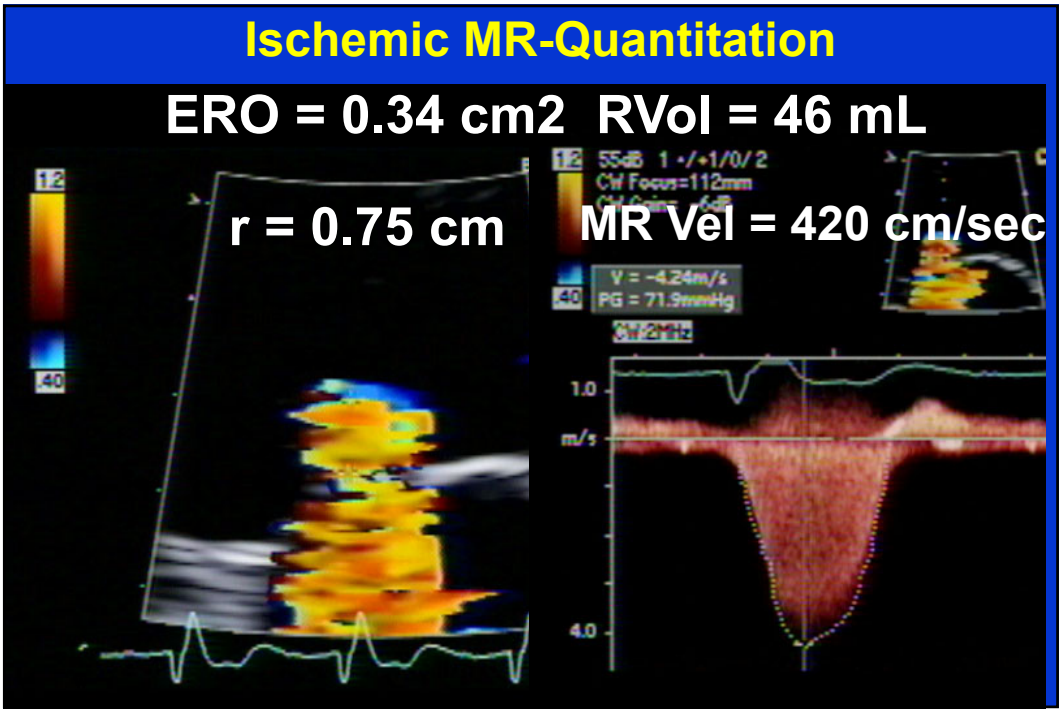

MAYO CLINIC
Normal vs. Functional MR

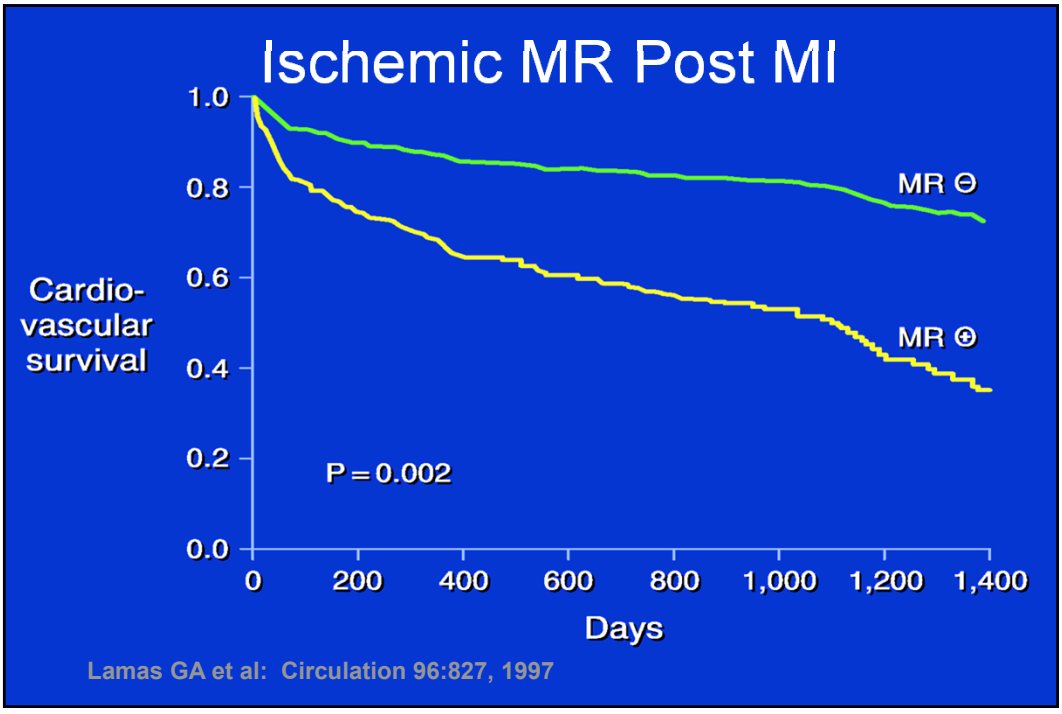
Functional MR

Conundrum #2
Is FMR significant ?
How to grade FMR ?

disease

Functional MR type IIIb


Ischemic MR-Quantitation
ERO = 0.34 cm2
RVol = 46 mL
r = 0.75 cm
MR Vel = 420 cm/sec
12
40
1.0
m/s
4.0


Ischemic MR Post MI
Cardio-vascular survival
1.0
0.8
0.6
0.4
0.2
0.0
MR ⊖
MR ⊕
P = 0.002
0
200
400
600
800
1,000
1,200
1,400
Days
Lamas GA et al: Circulation 96:827, 1997

Ischemic Mitral Regurgitation

Long-Term Outcome and Prognostic Implications With Quantitative Doppler Assessment

Francesco Grigioni, MD; Maurice Enriquez-Sarano, MD; Kenton J. Zehr, MD; Kent R. Bailey, PhD; A. Jamil Tajik, MD

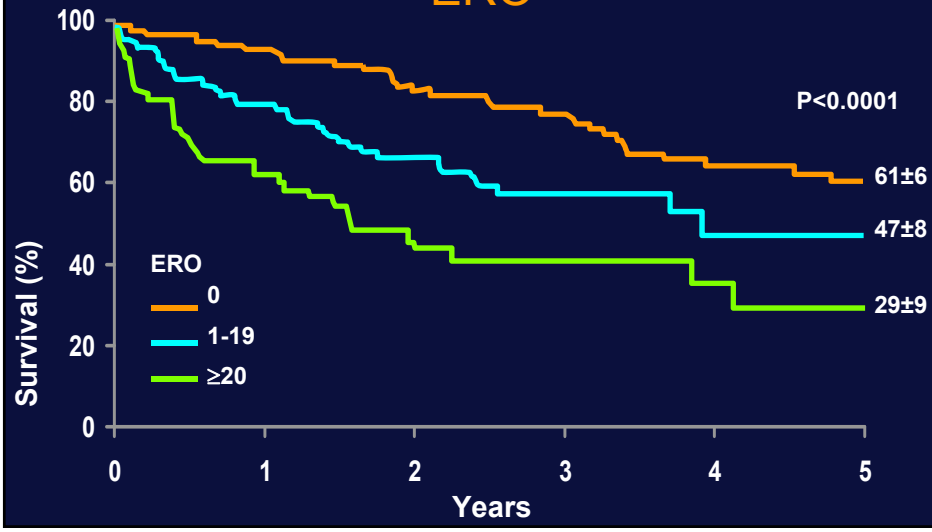
Background—Myocardial infarction (MI) can directly cause ischemic mitral regurgitation (IMR), which has been touted as an indicator of poor prognosis in acute and early phases after MI. However, in the chronic post-MI phase, prognostic implications of IMR presence and degree are poorly defined.

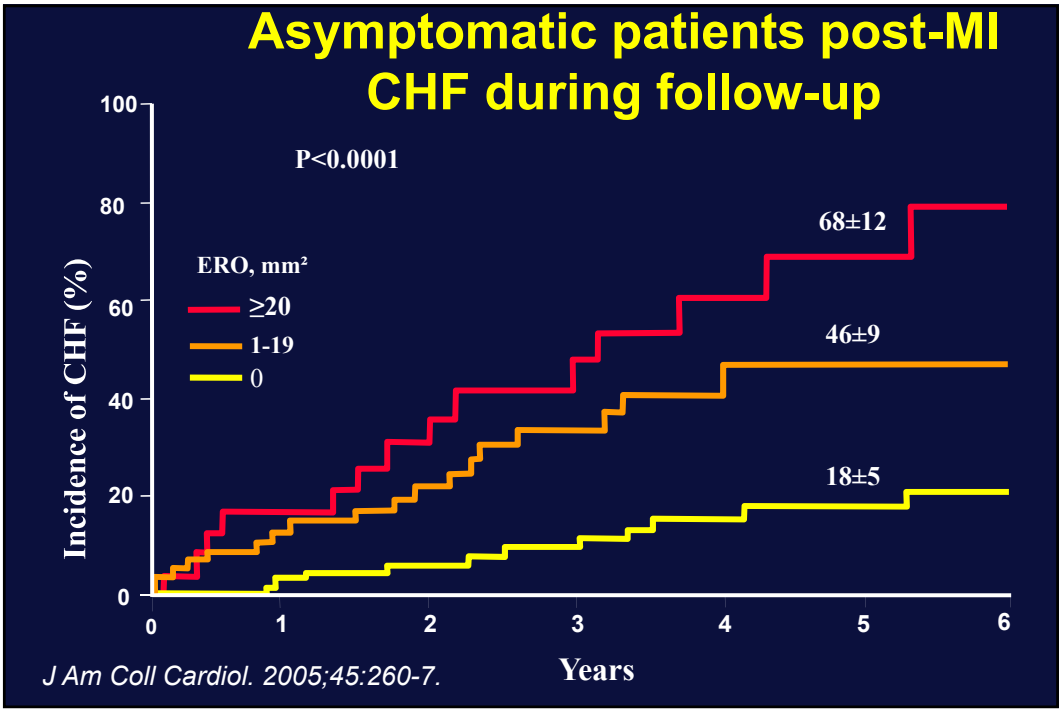
Methods and Results—We analyzed 303 patients with previous (>16 days) Q-wave MI by ECG who underwent transthoracic echocardiography: 194 with IMR quantitatively assessed in routine practice and 109 without IMR matched for baseline age (71±11 versus 70±9 years, P=0.20), sex, and ejection fraction (EF, 33±14% versus 34±11%, P=0.14). In IMR patients, regurgitant volume (RVol) and effective regurgitant orifice (ERO) area were 36±24 mL/beat and 21±12 mm^2, respectively. After 5 years, total mortality and cardiac mortality for patients with IMR (62±5% and 50±6%, respectively) were higher than for those without IMR (39±6% and 30±5%, respectively) (both P<0.001). In multivariate analysis, independently of all baseline characteristics, particularly age and EF, the adjusted relative risks of total and cardiac mortality associated with the presence of IMR (1.88, P=0.003 and 1.83, P=0.014, respectively) and quantified degree of IMR defined by RVol ≥30 mL (2.05, P=0.002 and 2.01, P=0.009) and by ERO ≥20 mm^2 (2.23, P=0.003 and 2.38, P=0.004) were high.

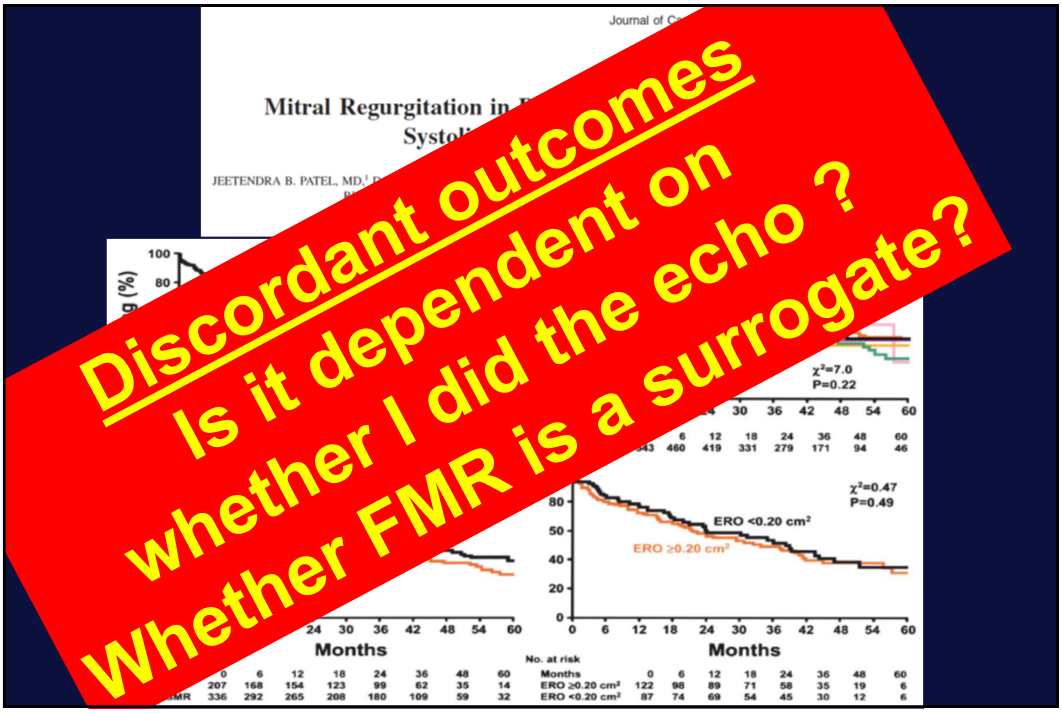
Conclusions—In the chronic phase after MI, IMR presence is associated with excess mortality independently of baseline characteristics and degree of ventricular dysfunction. The mortality risk is related directly to the degree of IMR as defined by ERO and RVol. Therefore, IMR detection and quantification provide major information for risk stratification and clinical decision making in the chronic post-MI phase. (***Circulation***. **2001;103:1759-1764.**)

Outcome after Q-MI

Impact of Quantified IMR on Survival: ERO

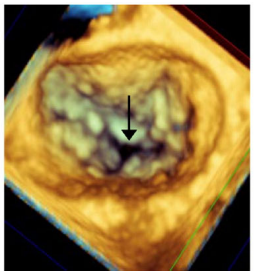


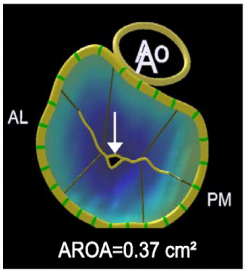

Asymptomatic patients post-MI
CHF during follow-up
P<0.0001
ERO, mm²
≥20
1-19
0
68±12
46±9
18±5
Incidence of CHF (%)
100
80
60
40
20
0
0
1
2
3
4
5
6
Years
J Am Coll Cardiol. 2005;45:260-7.

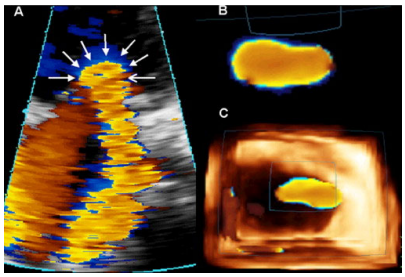

Mitral Regurgitation in
Systoli
JEETENDRA B. PATEL, MD.
Discordant outcomes
Is it dependent on
whether I did the echo ?
Whether FMR is a surrogate?
χ²=7.0
P=0.22
χ²=0.47
P=0.49
ERO <0.20 cm²
ERO ≥0.20 cm²
Months
Months
No. at risk

Limits of quantification: PISA

- Non circular orifice



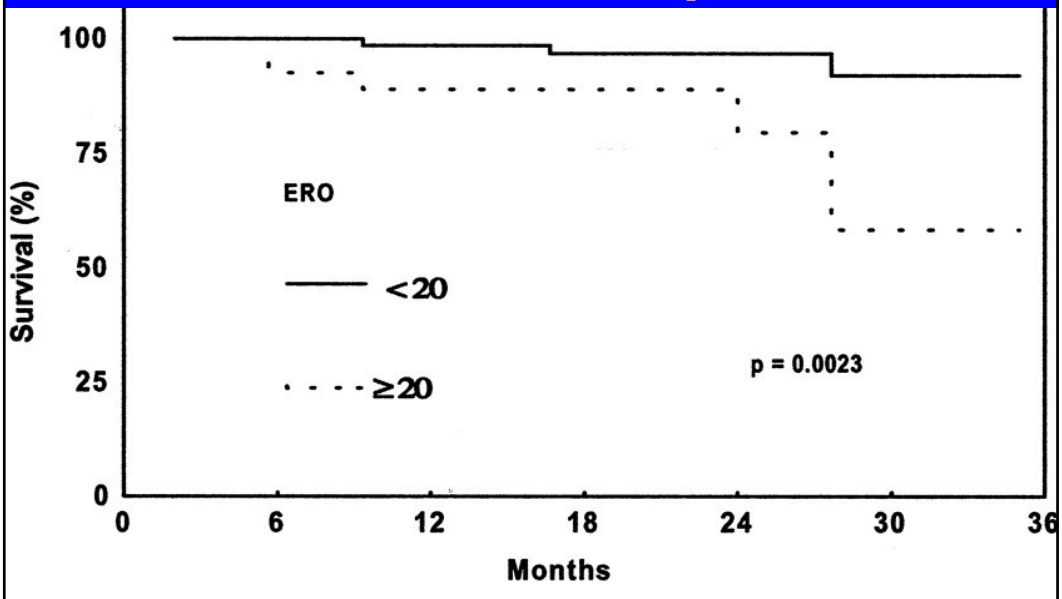




Chandra S, Am J Physiol Heart Circ Physiol 2011 Sep;301(3):

Yosefy C, Journal of the American Society of Echocardiography 2007;20:389-96.

FMR in Europe

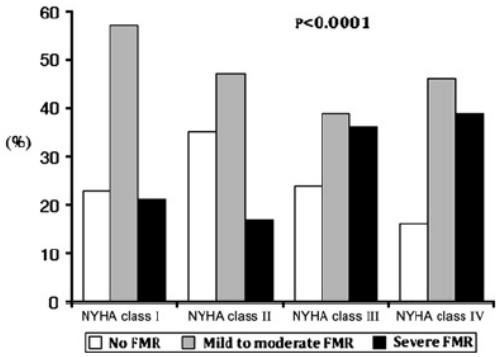


Lancelloti et al; Circulation 2003;108:1713

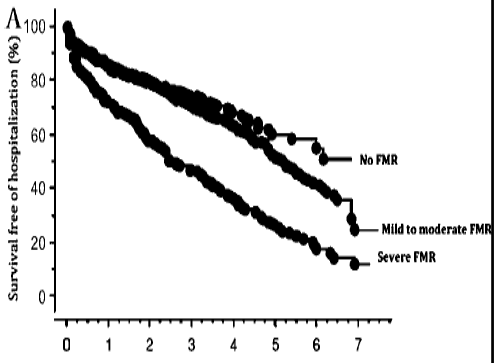
FMR in Europe

Impact on Outcome

Functional Class



Survival



Rossi et al, Heart 2011;97:1675

Recent FMR Studies ?

2018

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 72, NO. 23, 2018

Philipp E. Bartko, MD, PhD
Martin Hülsmann, MD
*Georg Goliasch, MD, PhD

*Department of Internal Medicine II
Division of Cardiology
Medical University of Vienna
Währingergürtel 18-20
Vienna 1090
Austria

Letters

Quantitative Definition of Severe Functional Mitral Regurgitation

Recent divergence between the American Heart Association/American College of Cardiology (AHA/

confidence interval [CI]: 1.13 to 2.43; p = 0.009) (Figure 1A) and RegVol (HR: 2.02; 95% CI: 1.34 to 3.05; p = 0.001) (Figure 1A). In contrast, the ESC/EACTS definition of sFMR was related to outcome exclusively if quantified by RegVol (HR: 1.46; 95% CI: 1.05 to 2.05; p = 0.026) (Figure 1B), but not if quantified by EROA (HR: 1.30; 95% CI: 0.91 to 1.86; p = 0.15) (Figure 1B).

2019

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 73, NO. 20, 2019
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A Unifying Concept for the Quantitative Assessment of Secondary Mitral Regurgitation

Philipp E. Bartko, MD, PhD,[a] Henrike Arfsten, MD,[b] Gregor Heitzinger,[a] Noemi Pavo, MD, PhD,[a] Aurel Toma, MD,[a] Guido Strunk, PhD,[b] Christian Hengstenberg, MD,[a] Martin Hülsmann, MD,[a] Georg Goliasch, MD, PhD[a]

Figure from Bartko letter JACC 2018[9]

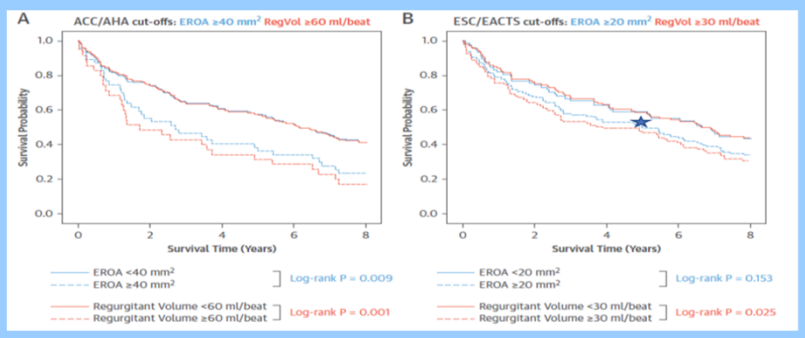
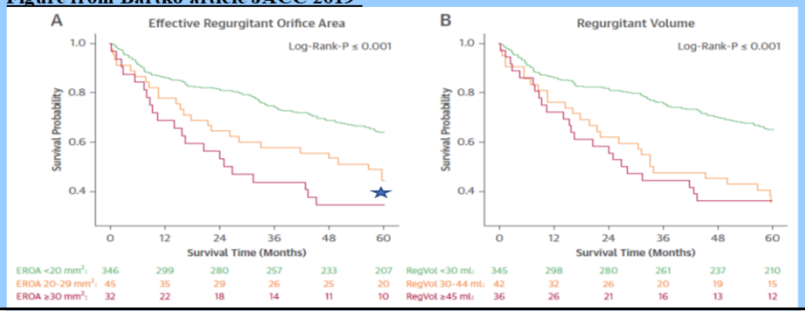
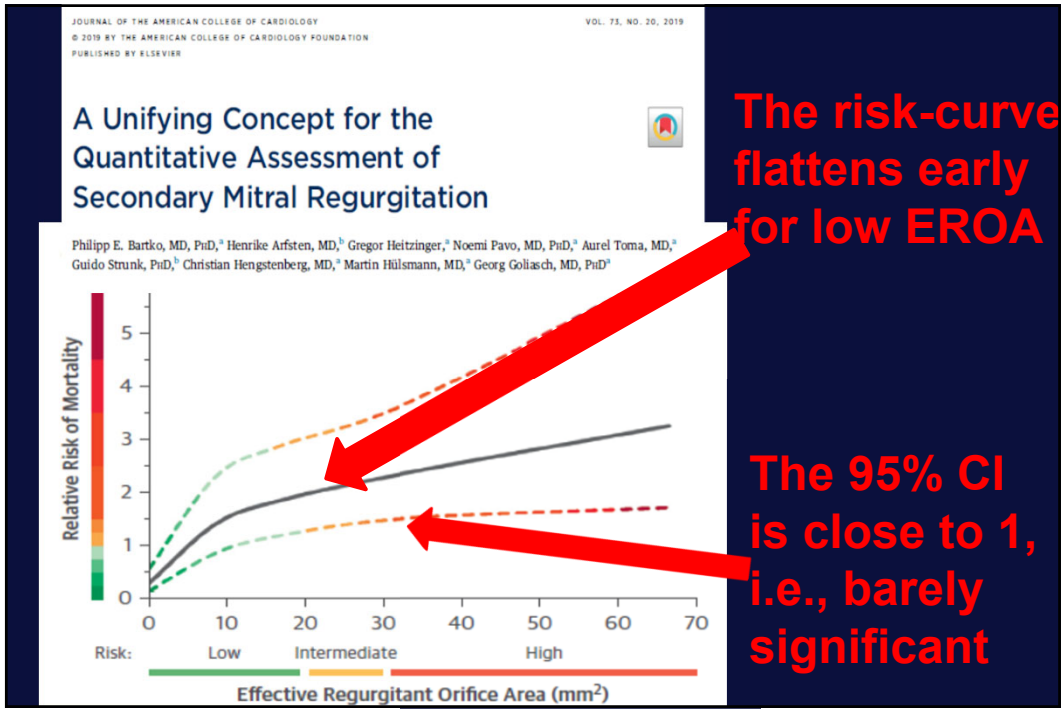


Figure from Bartko article JACC 2019[8]





Previous Cohorts display Discordant results regarding FMR outcome

Interactions between FMR and other determinants of outcome ?

ESC European Society of Cardiology
European Heart Journal (2018) **39**, 39–46
doi:10.1093/eurheartj/ehx402
CLINICAL RESEARCH
Heart failure/cardiomyopathy

Refining the prognostic impact of functional mitral regurgitation in chronic heart failure

Georg Goliasch[1]*, Philipp E. Bartko[1], Noemi Pavo[1], Stephanie Neuhold[2], Raphael Wurm[1], Julia Mascherbauer[1], Irene M. Lang[1], Guido Strunk[3], and Martin Hülsmann[1]

Subgroups	Patients/events	Crude HR (95% CI)	*P*-value	Adjusted HR (95% CI)[a]	*P*-value
NYHA functional class					
NYHA I	66/22	1.20 (0.40–3.55)	0.75	0.83 (0.27–2.49)	0.73
NYHA II	153/58	1.89 (0.95–3.77)	0.07	2.17 (1.07–4.44)	**0.03**
NYHA III	236/110	1.81 (1.18–2.79)	**0.007**	1.80 (1.17–2.77)	**0.008**
NYHA IV	121/81	1.02 (0.65–1.60)	0.93	1.09 (0.69–1.72)	0.71
Echocardiographic LV function					
Moderately reduced (LVEF 30–40%)	159/76	2.15 (1.25–3.69)	**0.006**	2.37 (1.36–4.12)	**0.002**
Severely reduced (LVEF <30%)	325/171	1.29 (0.94–1.79)	0.12	1.31 (0.95–1.81)	0.10
Quartiles of NT-proBNP (pg/mL)					
1st quartile (<863 pg/mL)	144/39	0.43 (0.06–3.17)	0.41	0.56 (0.07–4.05)	0.56
2nd quartile (871–2360 pg/mL)	145/64	2.07 (1.19–3.62)	**0.01**	2.16 (1.22–3.86)	**0.009**
3rd quartile (2368–5159 pg/mL)	143/67	1.33 (0.78–2.26)	0.30	1.36 (0.79–2.32)	0.26
4th quartile (>5167 pg/mL)	144/101	1.17 (0.78–1.76)	0.45	1.18 (0.78–1.77)	0.43

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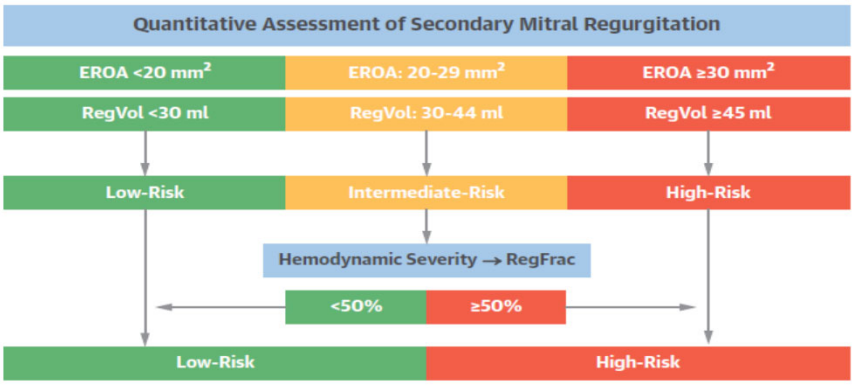
A Unifying Concept for the Quantitative Assessment of Secondary Mitral Regurgitation

Philipp E. Bartko, MD, PhD,[a] Henrike Arfsten, MD,[b] Gregor Heitzinger,[a] Noemi Pavo, MD, PhD,[a] Aurel Toma, MD,[a] Guido Strunk, PhD,[b] Christian Hengstenberg, MD,[a] Martin Hülsmann, MD,[a] Georg Goliasch, MD, PhD[a]

FIGURE 3 A Risk-Based Algorithm for Quantitative Assessment of sMR



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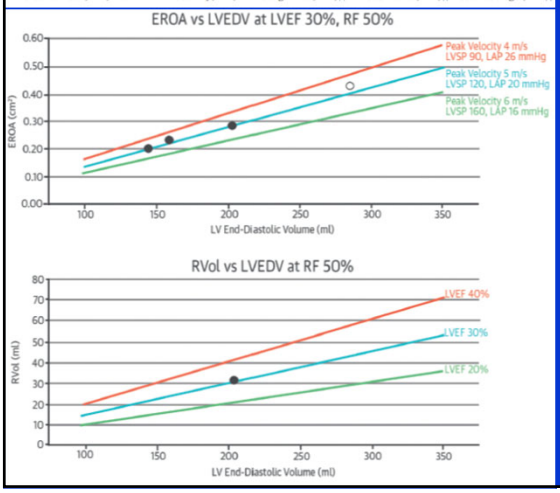
REVIEW TOPIC OF THE WEEK

Defining "Severe" Secondary Mitral Regurgitation

Emphasizing an Integrated Approach

Paul A. Grayburn, MD,*† Blasé Carabello, MD,‡ Judy Hung, MD,§ Linda D. Gillam, MD,‖ David Liang, MD,¶ Michael J. Mack, MD,# Patrick M. McCarthy, MD,** D. Craig Miller, MD,†† Alfredo Trento, MD,†† Robert J. Siegel, MD‡‡

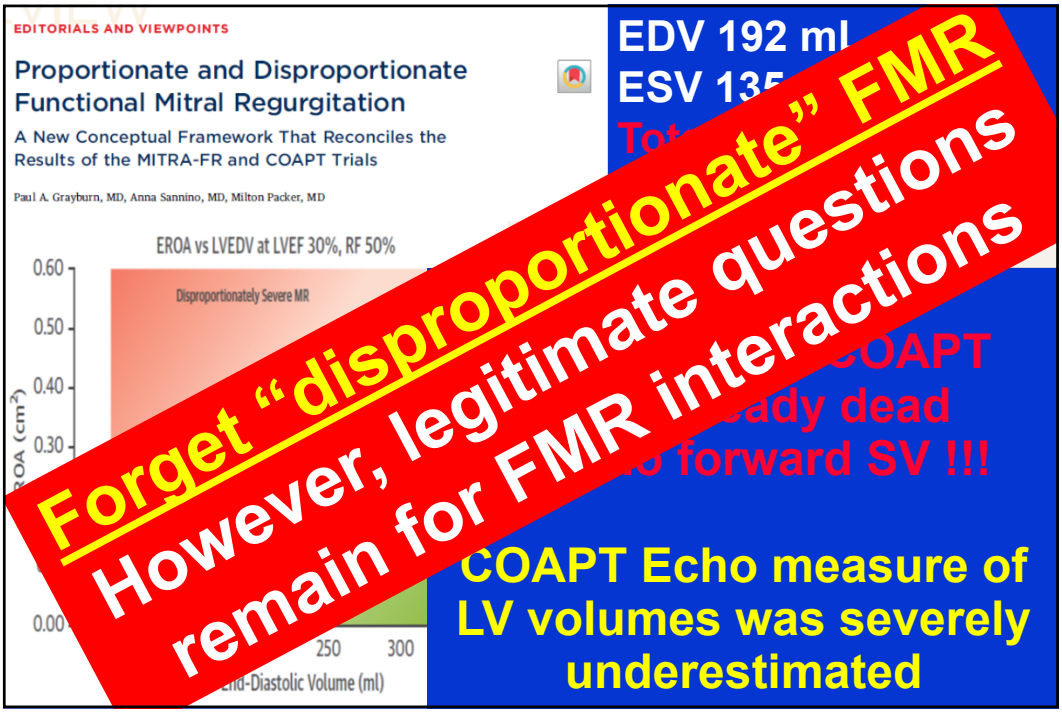


What did Paul forget?

RF = RVol/Total LV SV
Rvol/(Rvol+FSV)
RVol= ERO*RTVI

RTVI =
High with compliant LA
Low with non-compliant LA

FSV=50 mL, ERO=0.30 cm²
LA compliant RTVI=150 cm
RVol 45 mL, RF 47%
LA non-Compliant RTVI 100
RVol 30 mL, RF 38%



Previous Cohorts display Discordant results regarding FMR outcome

What about surgical data ?

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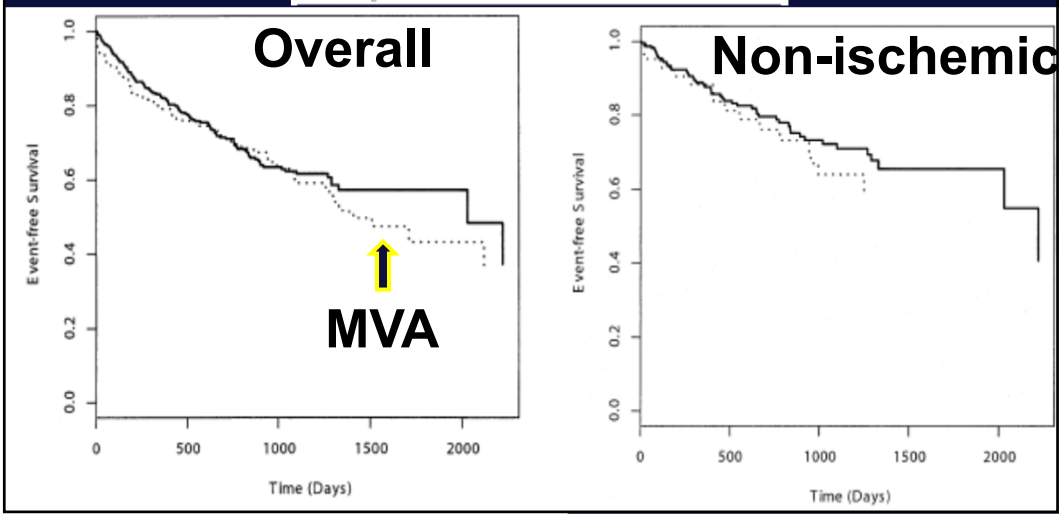
Left Ventricular Dysfunction

Impact of Mitral Valve Annuloplasty on Mortality Risk in Patients With Mitral Regurgitation and Left Ventricular Systolic Dysfunction

Audrey H. Wu, MD, MPH,* Keith D. Aaronson, MD, MS,* Steven F. Bolling, MD, FACC,† Francis D. Pagani, MD, PhD, FACC,† Kathy Welch, MS, MPH,‡ Todd M. Koelling, MD, FACC*
Ann Arbor, Michigan



Coronary Artery Bypass Surgery With or Without Mitral Valve Annuloplasty in Moderate Functional Ischemic Mitral Regurgitation

Final Results of the Randomized Ischemic Mitral Evaluation (RIME) Trial

K.M. John Chan, FRCS CTh; Prakash P. Punjabi, FRCS CTh; Marcus Flather, MD, FRCP; Riccardo Wage, DCR (R); Karen Symmonds, DCR (R); Isabelle Roussin, MD; Shelley Rahman-Haley, MD, FRCP; Dudley J. Pennell, MD, FRCP; Philip J. Kilner, MD, PhD; Gilles D. Dreyfus, MD; John R. Pepper, MChir, FRCS; for the RIME Investigators

Patients with CAD referred to CABG with moderate MR with EF >30%, NYHA I-III

Randomized 1/1 to CABG alone or CABG + Mitral repair

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Variable	CABG (n=39)	CABG+MVR (n=34)
Age, y	70.4±7.9	70.9±10.5
Female sex, n (%)	10 (26)	9 (26)
Body mass index	27.4±5.0	25.3±6.4
Medical history, n (%)		
Atrial fibrillation	4 (10)	2 (6)
Previous myocardial infarction	28 (72)	25 (74)
Previous stroke	1 (3)	2 (6)
Peripheral vascular disease	5 (13)	4 (12)
Hypertension	23 (59)	17 (50)
Diabetic on treatment	15 (38)	12 (35)
Chronic pulmonary disease	1 (3)	2 (6)
NYHA class, n (%)		
I	1 (3)	1 (3)
II	25 (64)	22 (65)
III	13 (33)	11 (32)
Mitral regurgitation*		
Effective regurgitant orifice area, cm^2	0.18±0.10	0.21±0.09
Regurgitant volume, mL/beat	30.3±13.8	35.5±13.3
Vena contracta width, cm	0.4±0.1	0.4±0.1
Tricuspid regurgitation,* n (%)		
None	18 (46)	12 (36)
Mild	18 (46)	18 (52)
Moderate	3 (8)	4 (12)
Left ventricle*		
LVESD, mm	43.3±9.5	45.7±7.4
LVEDD, mm	56.5±12.0	56.5±12.6
Ejection fraction, %	40.3±16.1	40.0±17.3

Coronary Artery Bypass Surgery With or Without Mitral Valve Annuloplasty in Moderate Functional Ischemic Mitral Regurgitation

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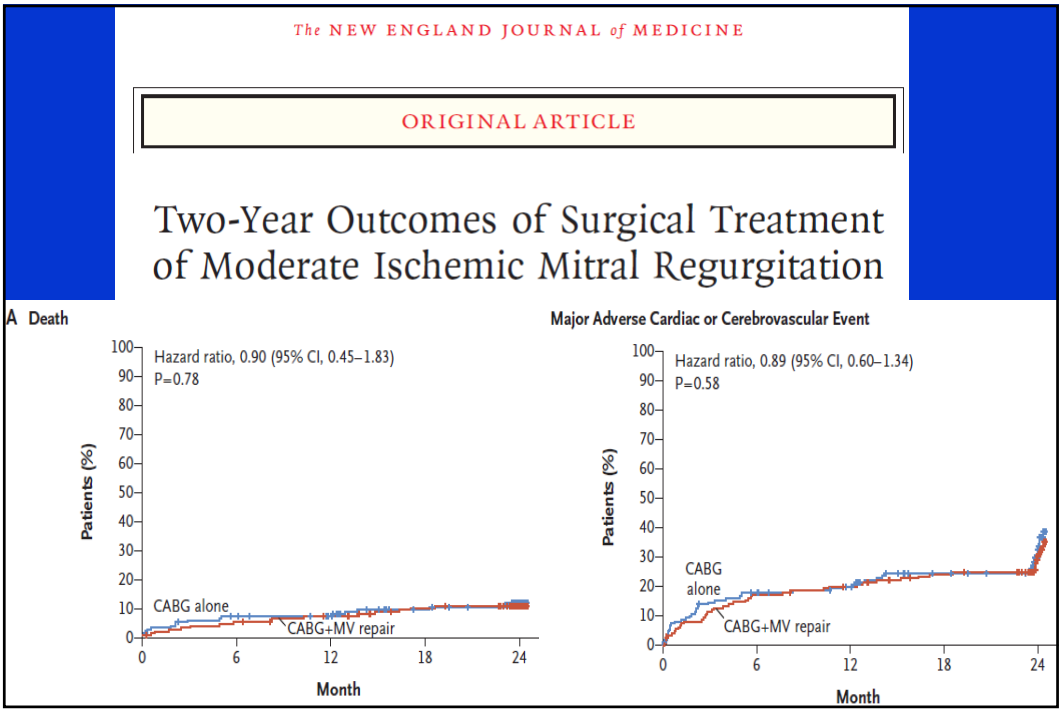
Results

Table 3. Study End Points at 1 Year

	CABG (n=32)			CABG+MVR (n=27)			
End Points	Baseline	1 Year	Δ	Baseline	1 Year	Δ	*P* Value*
Primary end point							
Peak VO_2, ml/kg/min	15.1±3.3	15.9±2.5	0.8±2.9	14.8±3.2	18.1±2.9	3.3±2.3	<0.001
Secondary end points							
LV ESVI, ml/m^2†	71.8±16.1	67.4±20.4	−4.4±17.4	78.4±26.5	56.2±14.9	−22.2±25.6	0.002
MR volume, ml/beat†	31.9±14.8	22.7±14.6	−9.2±19.1	35.4±24.0	7.2±3.5	−28.2±24.6	0.001
BNP (pg/ml)	681.4±197.3	286.7±132.0	−394.7±213.6	748.1±158.3	190.7±117.8	−557.4±182.9	0.003



MR and surgery

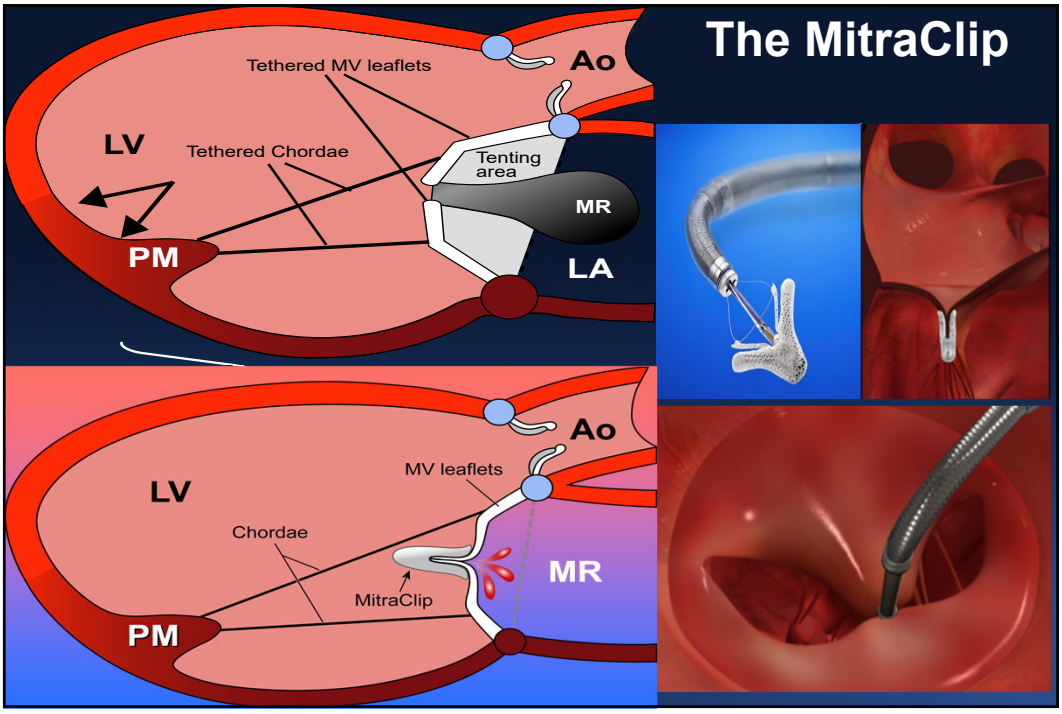
	FMR ventricular remodeling (n=278)	FMR isolated atrial dilatation (n=194)	OMR (n=233)	Total (n=705)
MV repair/ replacement, (%)	10(4%)	6(3%)	86(37%)	102(14%)
Any cardiac surgery, n(%)	25(9%)	12(6%)	86(37%)	123(17%)
MV repair/ replacement by MR severity				
Moderate MR, n(%) in subset	4(2%) (n=192)	5(3%) (n=175)	22(18%) n=124	31(6%) (n=491)
Severe MR, n(%) in subset	6(7%) (n=86)	1(5%) (n=19)	64(59%) (n=109)	71(33%) (n=214)

ESC Congress
Munich 2018

Severe Undertreatment of FMR

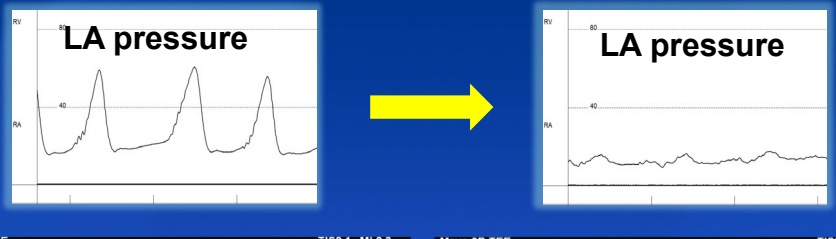
Previous Cohorts display Discordant results regarding FMR outcome

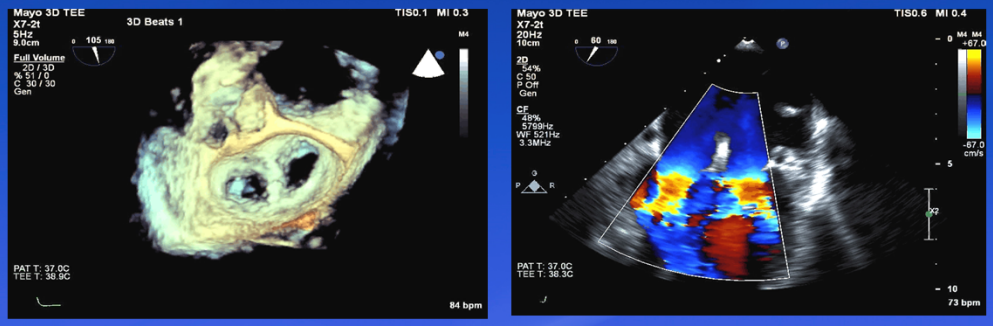
What about Interventional data ?



Mitral Regurgitation

What can the MitraClip achieve



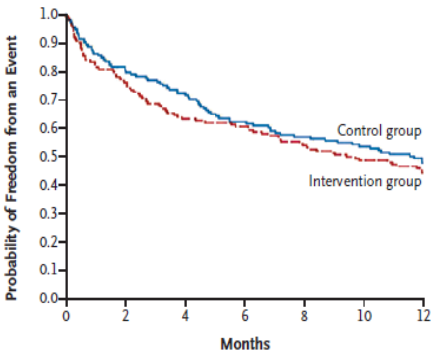


The NEW ENGLAND JOURNAL of MEDICINE

MITRA-FR

Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

J.-F. Obadia, D. Messika-Zeitoun, G. Leurent, B. Iung, G. Bonnet, N. Piriou, T. Lefèvre, C. Piot, F. Rouleau, D. Carrié, M. Nejjari, P. Ohlmann, F. Leclercq, C. Saint Etienne, E. Teiger, L. Leroux, N. Karam, N. Michel, M. Gilard, E. Donal, J.-N. Trochu, B. Cormier, X. Armoiry, F. Boutitie, D. Maucort-Boulch, C. Barnel, G. Samson, P. Guerin, A. Vahanian, and N. Mewton, for the MITRA-FR Investigators*



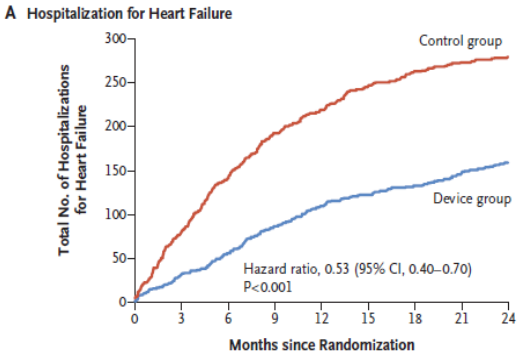
No. at Risk							
Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

The NEW ENGLAND JOURNAL of MEDICINE

COAPT

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

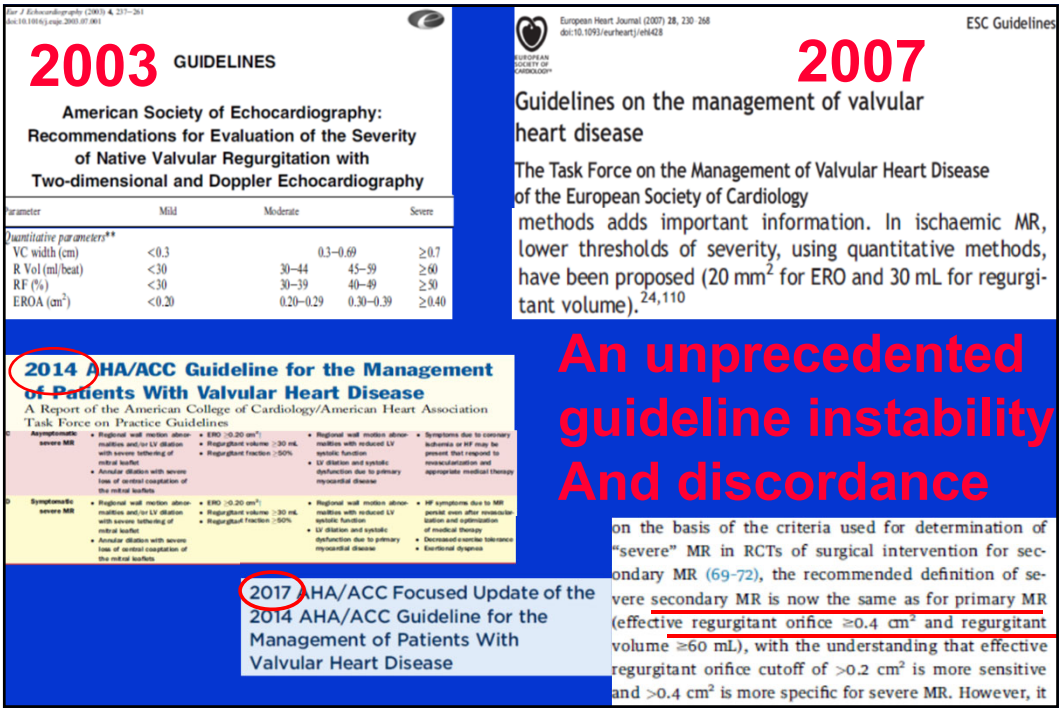
G.W. Stone, J.A. Lindenfeld, W.T. Abraham, S. Kar, D.S. Lim, J.M. Mishell, B. Whisenant, P.A. Grayburn, M. Rinaldi, S.R. Kapadia, V. Rajagopal, I.J. Sarembock, A. Brieke, S.O. Marx, D.J. Cohen, N.J. Weissman, and M.J. Mack, for the COAPT Investigators*



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

Previous RCTs display Discordant results regarding FMR outcome

What about Guidelines ?



MR severity

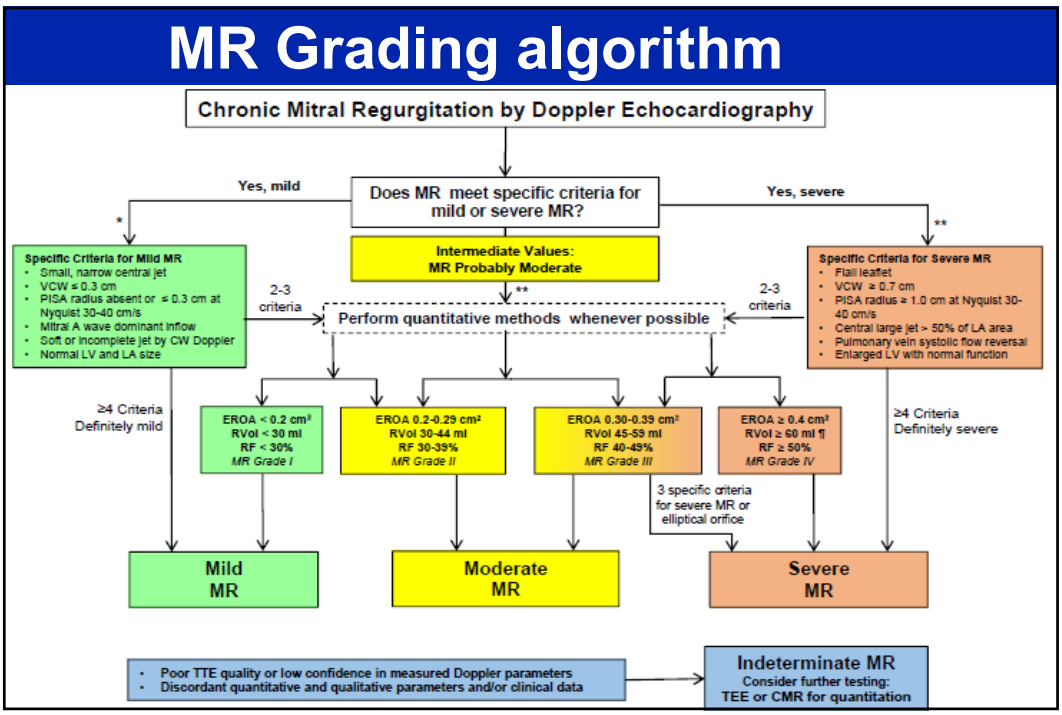
ASE GUIDELINES AND STANDARDS

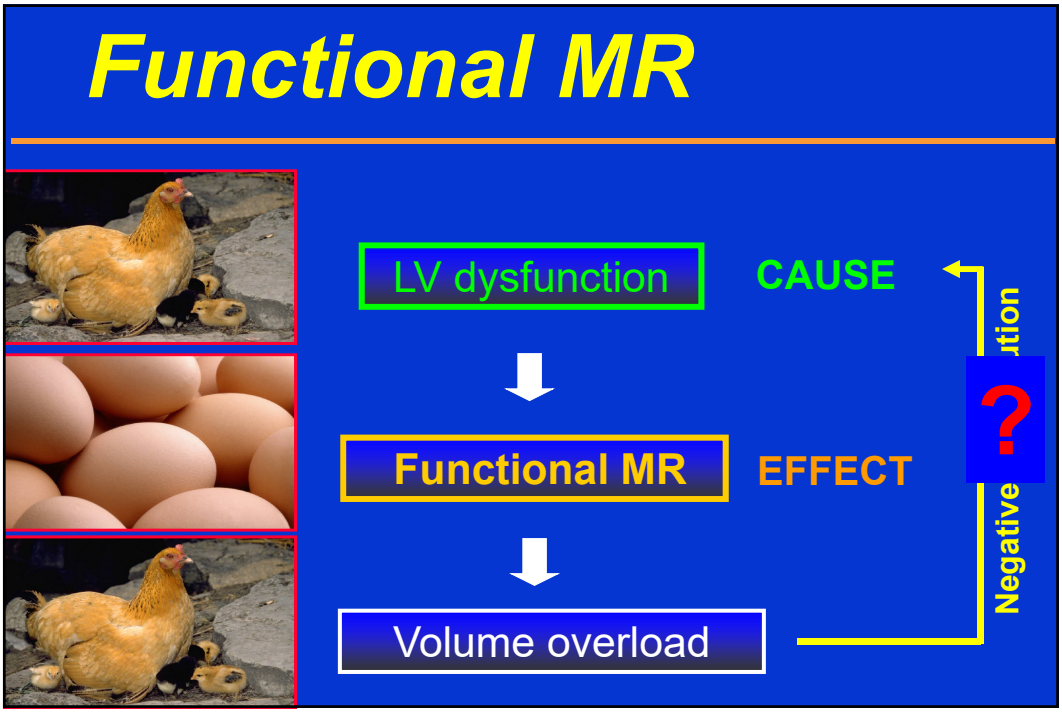
Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation

A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance

William A. Zoghbi, MD, FASE (Chair), David Adams, RCS, RDCS, FASE, Robert O. Bonow, MD, Maurice Enriquez-Sarano, MD, Elyse Foster, MD, FASE, Paul A. Grayburn, MD, FASE, Rebecca T. Hahn, MD, FASE, Yuchi Han, MD, MMSc,* Judy Hung, MD, FASE, Roberto M. Lang, MD, FASE, Stephen H. Little, MD, FASE, Dipan J. Shah, MD, MMSc,* Stanton Shernan, MD, FASE, Paaladinesh Thavendiranathan, MD, MSc, FASE,* James D. Thomas, MD, FASE, and Neil J. Weissman, MD, FASE, *Houston and Dallas, Texas; Durham, North Carolina; Chicago, Illinois; Rochester, Minnesota; San Francisco, California; New York, New York; Philadelphia, Pennsylvania; Boston, Massachusetts; Toronto, Ontario, Canada; and Washington, DC*

ASE Regurgitation committee meeting


MR Grading algorithm
Chronic Mitral Regurgitation by Doppler Echocardiography
Does MR meet specific criteria for mild or severe MR?
Yes, mild
Yes, severe
Specific Criteria for Mild MR
Small, narrow central jet
VCW ≤ 0.3 cm
PISA radius absent or ≤ 0.3 cm at Nyquist 30-40 cm/s
Mitral A wave dominant inflow
Soft or incomplete jet by CW Doppler
Normal LV and LA size
Intermediate Values: MR Probably Moderate
Specific Criteria for Severe MR
Flail leaflet
VCW ≥ 0.7 cm
PISA radius ≥ 1.0 cm at Nyquist 30-40 cm/s
Central large jet > 50% of LA area
Pulmonary vein systolic flow reversal
Enlarged LV with normal function
2-3 criteria
2-3 criteria
Perform quantitative methods whenever possible
≥4 Criteria Definitely mild
≥4 Criteria Definitely severe
EROA < 0.2 cm² RVol < 30 ml RF < 30% MR Grade I
EROA 0.2-0.29 cm² RVol 30-44 ml RF 30-39% MR Grade II
EROA 0.30-0.39 cm² RVol 45-59 ml RF 40-49% MR Grade III
EROA ≥ 0.4 cm² RVol ≥ 60 ml ¶ RF ≥ 50% MR Grade IV
3 specific criteria for severe MR or elliptical orifice
Mild MR
Moderate MR
Severe MR
Poor TTE quality or low confidence in measured Doppler parameters
Discordant quantitative and qualitative parameters and/or clinical data
Indeterminate MR
Consider further testing: TEE or CMR for quantitation


Functional MR
LV dysfunction
CAUSE
Functional MR
EFFECT
Volume overload
Negative
?

Resolving the FMR Conundrum

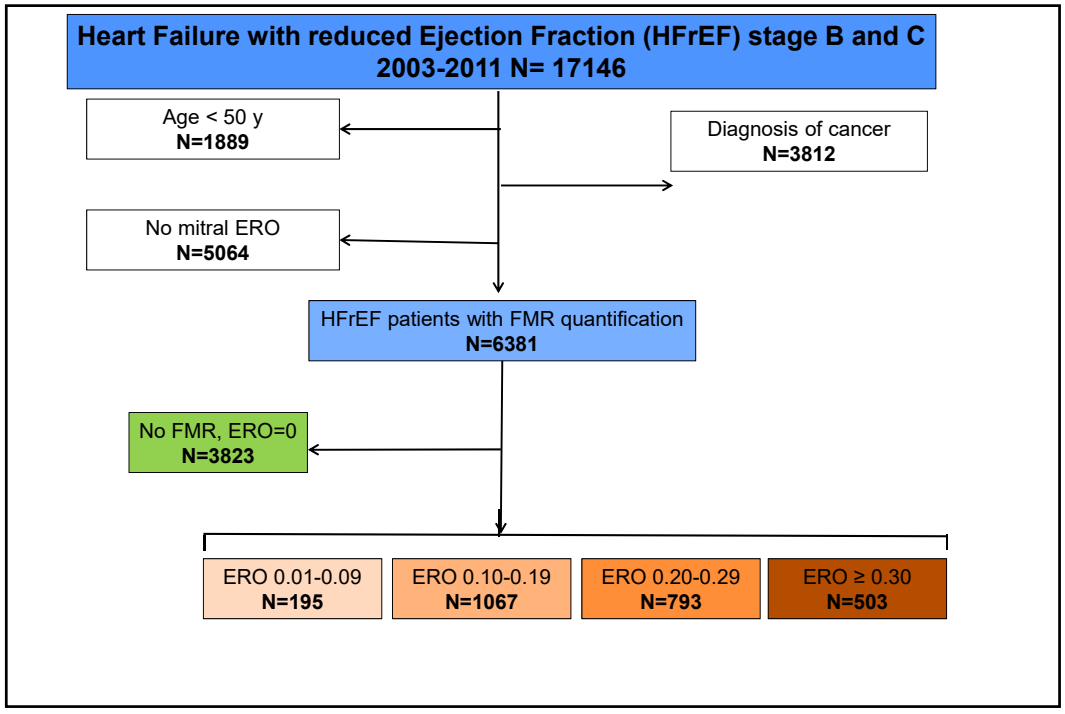
We need new data

Very large cohorts

Comprehensively characterized

With long-term outcome

With comparison FMR-DMR



Resolving the FMR Conundrum

Comprehensive Characterization

-Doppler-Echo: All MR, LV, LA, hemodynamics, RV, TR as entered at initial diagnosis in routine practice

-Clinical: Vitals, symptoms (NLP), PMH, ECG, Comorbidity, ADL, Meds per Clinician notes

-Cath, Surgery if performed

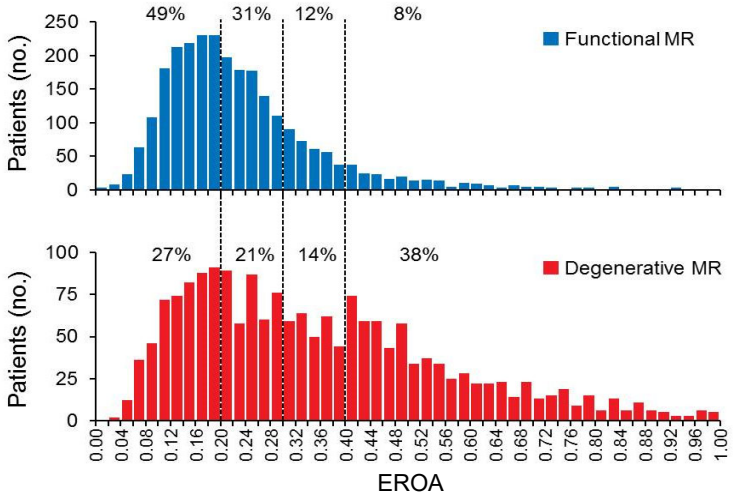
-Labs: Creatinine, Hb, BNP

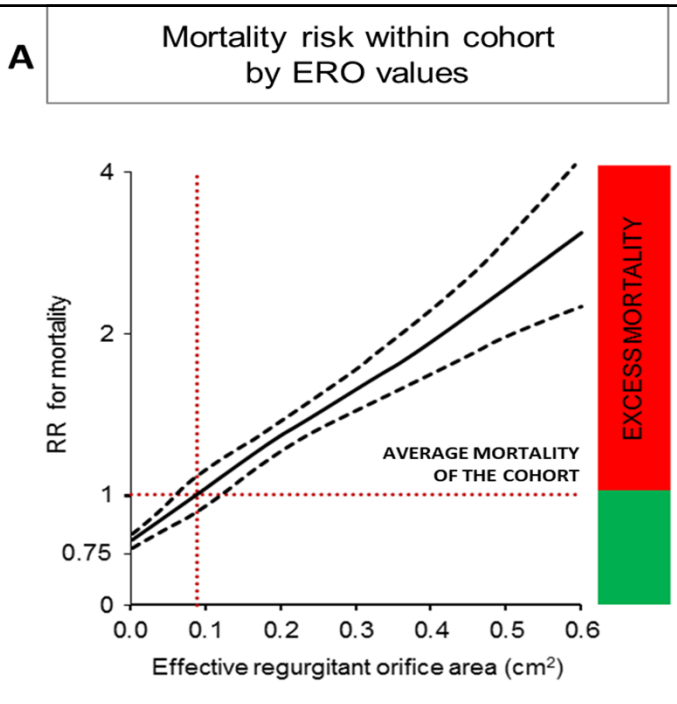
-Mortality: by Accurint

Baseline Characteristics

	Overall (6381)	NO FMR (60%, 3823)	FMR-EROA 0.01-0.19 (20%, 1262)	FMR-EROA 0.20-0.39 (17%, 1103)	FMR-EROA >/= 0.40 (3%, 193)	p-value for trend
Clinical characteristics						
Age (years)	70 ± 11	68±7	73±11	72±10	70±10	0.2
Female (%)	31	25	45	34	31	<0.0001
BMI (kg/m^2)	29.1±6.5	29.9±6.8	27.9±6.0	28.1±5.5	28.2±6.9	0.002
Atrial fibrillation (%)	20 (1239)	14	26	33	30	<0.0001
Heart Rate (bpm)	76±18	75 ±18	75 ±17	78±17	80±16	<0.0001
Systolic BP (mmHg)	121±21	122±21	128±22	118±19	106±18	<0.0001
Diastolic BP (mmHg)	69±12	69±13	71±14	68±13	65±13	<0.0001
Diabetes (N, %)	1724 (28)	1058 (28)	294 (24)	324 (30)	48 (25)	0.8
Systemic hypertension (N,%)	3716 (58)	2293 (60)	749 (59)	591 (54)	83 (43)	<0.0001
Dyslipidemia (N, %)	3196 (50)	2034 (53)	601 (48)	484 (44)	77 (40)	0.0001
CAD (N, %)	4379 (69)	2613 (68)	865 (69)	761 (69)	140 (73)	0.2
Charlson-Comorbidity-index	2.44±1.94	2.36±1.94	2.44±1.89	2.70±1.98	2.72±1.91	0.002
Symptoms						
Dyspnea (N, %)	3363 (53)	1702 (45)	734 (58)	744 (67)	160 (83)	<0.0001
Angina (N, %)	1722 (27)	1132 (30)	302 (24)	236 (21)	52 (27)	0.3
Palpitation (N, %)	787 (12)	439 (12)	163 (13)	157 (14)	28 (15)	0.2
Echocardiographic characteristics						
LV EDD (mm)	59±9	54±7	58±9	61±9	66±10	<0.0001
LV ESD (mm)	46±10	43±7	43±8	52±10	57±12	<0.0001
LV EDD-index (mm/m2)	29±5	27±4	31±5	32±5	34±6	<0.0001
LV ESD-index (mm/m2)	24±5	21±4	25±5	27±6	29±7	<0.0001
LV-EF (%)	36±10	38±9	33±10	30±10	28±10	<0.0001
WMS-index	2.01±0.44	1.91±0.42	2.11±0.44	2.22±0.43	2.30±0.36	<0.0001
LV SV-index (ml/m2)	38 ±10	39±10	37±11	34±10	31±9	<0.0001
E (m/sec)	0.81±0.29	0.70±0.25	0.90±0.26	0.96±0.26	1.17±0.33	<0.0001
E/A	1.22±0.86	0.94±0.57	1.46±0.97	1.88±1.03	2.52±1.30	<0.0001
DTE (msec)	193±63	213±62	180±58	157±46	147±37	<0.0001
E/e'	17.13±9.47	14±7	21±10	22±10	28±11	<0.0001
EROA (cm2)	0.09±0.13	0	0.14±0.04	0.28±0.05	0.51±0.11	<0.0001
RVol (mL)	14±19	0	24±8	42±11	67±19	<0.0001
MR severe by integrative grading, %	11	0	3	42	94	<0.0001
S-PAP (mmHg)	42±15	36±12	45±15	50±14	57±14	<0.0001
Medical therapy						
Ace-inhibitors / ARB (N,%)	5008 (78)	2922 (76)	1026 (81)	903 (82)	157 (81)	<0·0001
Beta Blockers (N,%)	5928 (83)	3063 (80)	1098 (87)	969 (88)	168 (87)	<0·0001
Diuretics (N,%)	4316 (68)	2243 (59)	963 (76)	931 (84)	179 (93)	<0·0001
Aspirin (N,%)	4999 (78)	3018 (79)	987 (78)	843 (76)	151 (78)	0·12
Statin (N,%)	4109 (64)	2513 (66)	783 (62)	699 (63)	114 (59)	0·01
Spironolactone (N, %)	1024 (17)	473 (12)	227 (18)	256 (23)	68 (35)	<0·0001
Cardiac Resynchronization Therapy (N	170 (2.7)	59 (1.5)	33 (2.6)	57 (5.2)	21 (10.9)	<0.0001

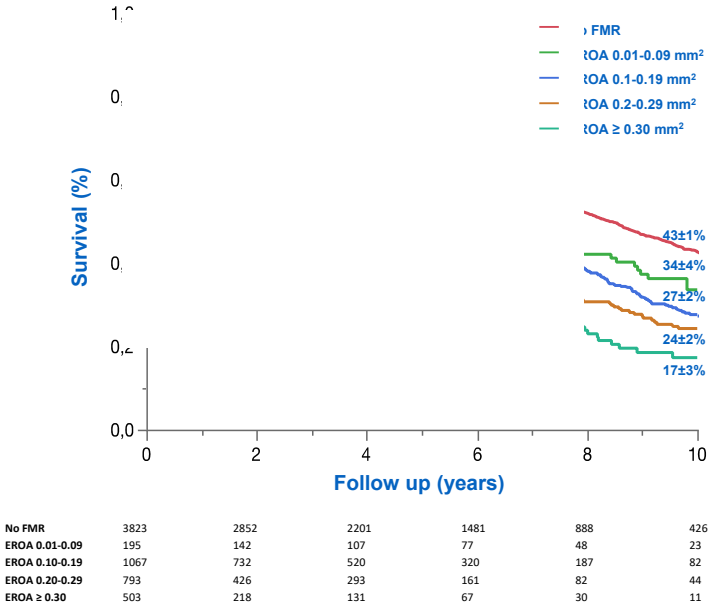
Distribution of MR severity



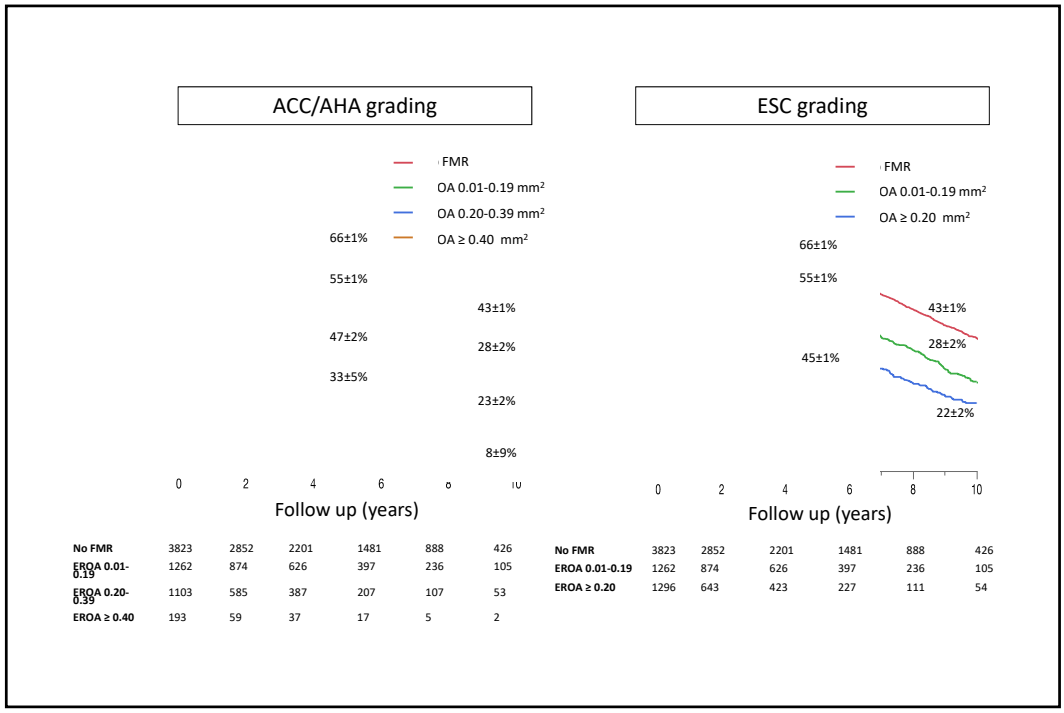


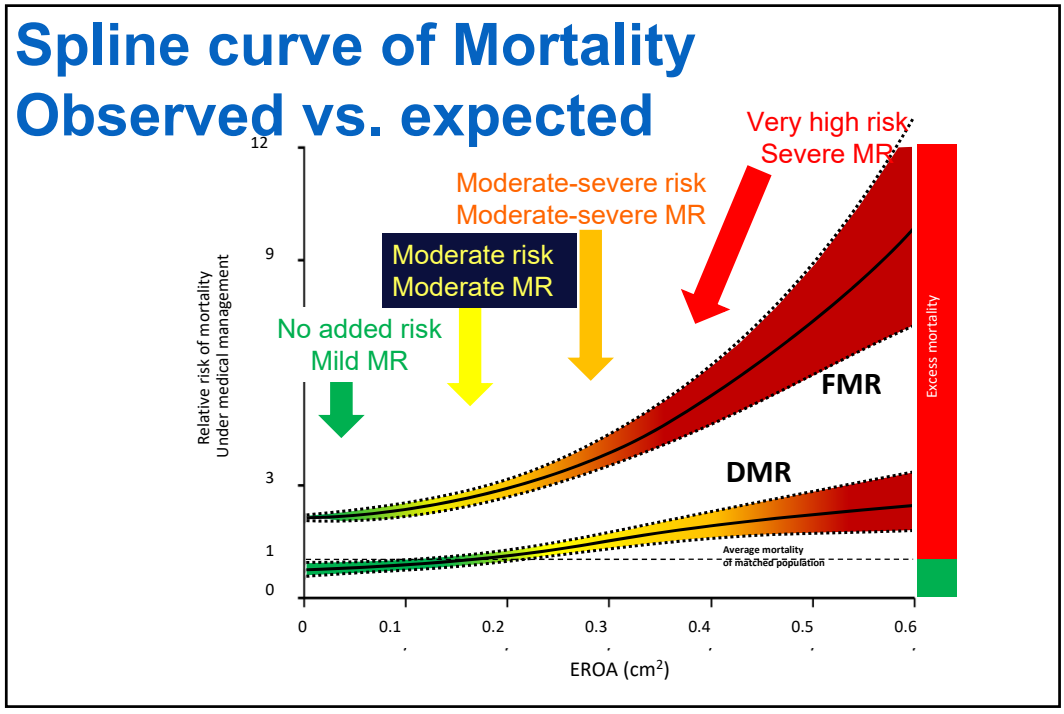
Long-term mortality risk under medical management

Model	ERO groups vs. No FMR						ERO continuous increase vs. No FMR	
	PROPOSED GRADING	HR (95% CI); p value	ACC/AHA GRADING	HR (95% CI); p value	ESC GRADING	HR (95% CI); p value	increase	HR (95% CI); p value
Unadjusted	**0.01-0.09 cm²**	1.28 [1.05-1.55]; 0.01	**0.01-0.19 cm²**	1.39 [1.27-1.52]; p<0.0001	**0.01-0.19 cm²**	1.39 [0.27-1.52]; P<0.0001	**per 0.1 cm²**	1.24[1.20-1.27] <0.0001
	0.10-0.19 cm²	1.41 [1.29-1.55] ; <0.0001						
	0.20-0.29 cm²	1.69 [1.52-1.89] ; <0.0001	**0.20-0.39 cm²**	1.76 [1.60-1.94]; p<0.0001	**≥ 0.20 cm²**	1.86 [1.70-2.03]; p<0.0001		
	>/= 0.30 cm²	2.20 [1.93-2.51] ; <0.0001	**>/= 0.40 cm²**	2.77 [2.23-3.41]; p<0.0001				
Adjusted	**0.01-0.09 cm²**	1.08 [0.88-1.33]; 0.4	**0.01-0.19 cm²**	1.09 [0.99-1.20], p=0.07	**0.01-0.19 cm²**	1.09 [0.99-1.20]; P=0.07	**per 0.1 cm²**	1.11[1.08-1.15]; <0.0001
	0.10-0.19 cm²	1.09 [0.98-1.21]; 0.08						
	0.20-0.29 cm²	1.13 [1.01-1.27]; 0.04	**0.20-0.39 cm²**	1.21 [1.09-1.34], p=0.0005	**≥ 0.20 cm²**	1.27 [1.15-1.41]; p<0.0001		
	>/= 0.30 cm²	1.61 [1.40-1.86]; <0.0001	**>/= 0.40 cm²**	2.00 [1.61-2.48]; p<0.0001				

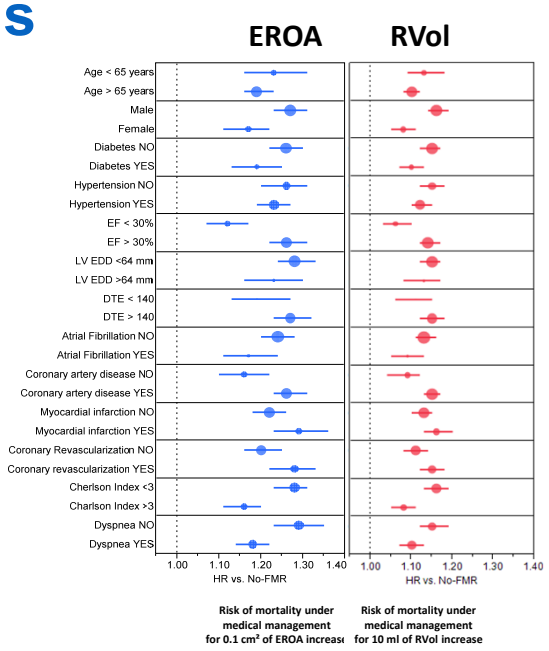


No FMR	3823	2852	2201	1481	888	426
EROA 0.01-0.09	195	142	107	77	48	23
EROA 0.10-0.19	1067	732	520	320	187	82
EROA 0.20-0.29	793	426	293	161	82	44
EROA ≥ 0.30	503	218	131	67	30	11


ACC/AHA grading
FMR
OA 0.01-0.19 mm²
OA 0.20-0.39 mm²
OA ≥ 0.40 mm²
66±1%
55±1%
47±2%
33±5%
43±1%
28±2%
23±2%
8±9%
0 2 4 6 8 10
Follow up (years)
No FMR 3823 2852 2201 1481 888 426
EROA 0.01-0.19 1262 874 626 397 236 105
EROA 0.20-0.39 1103 585 387 207 107 53
EROA ≥ 0.40 193 59 37 17 5 2
ESC grading
FMR
OA 0.01-0.19 mm²
OA ≥ 0.20 mm²
66±1%
55±1%
45±1%
43±1%
28±2%
22±2%
0 2 4 6 8 10
Follow up (years)
No FMR 3823 2852 2201 1481 888 426
EROA 0.01-0.19 1262 874 626 397 236 105
EROA ≥ 0.20 1296 643 423 227 111 54

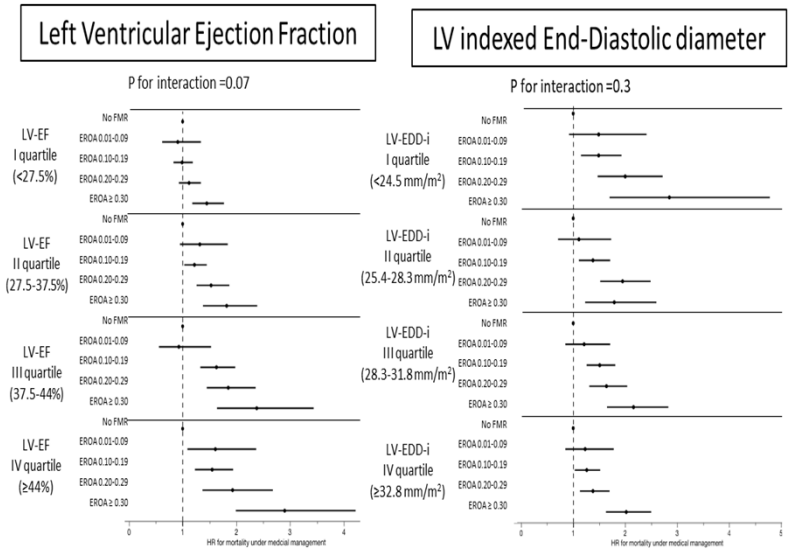

Spline curve of Mortality
Observed vs. expected
Very high risk
Severe MR
Moderate-severe risk
Moderate-severe MR
Moderate risk
Moderate MR
No added risk
Mild MR
FMR
DMR
Excess mortality
Average mortality of matched population
Relative risk of mortality
Under medical management
12
9
3
1
0
0 0.1 0.2 0.3 0.4 0.5 0.6
EROA (cm²)

Interactions



Interactions

B
Mortality-risk LV interaction Analysis



FMR Outcome

-Despite criticisms of the methods FMR severity measured by EROA measured in routine practice is a strong and independent determinant of survival in HFrEF

-There is no evidence of modulation of risk, in particular by LV size or function

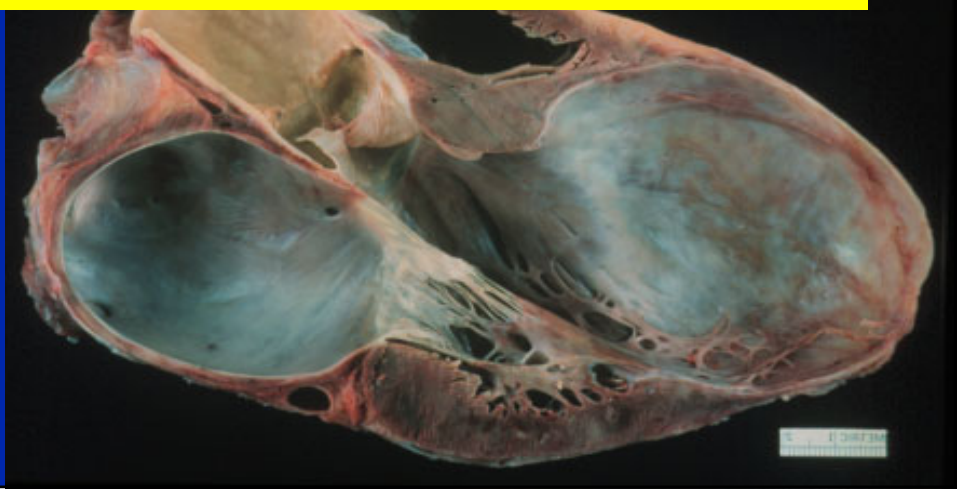
-The risk of mortality appears for low EROA (0.1 cm2) and increases exponentially with higher EROA thereafter compared to expected mortality

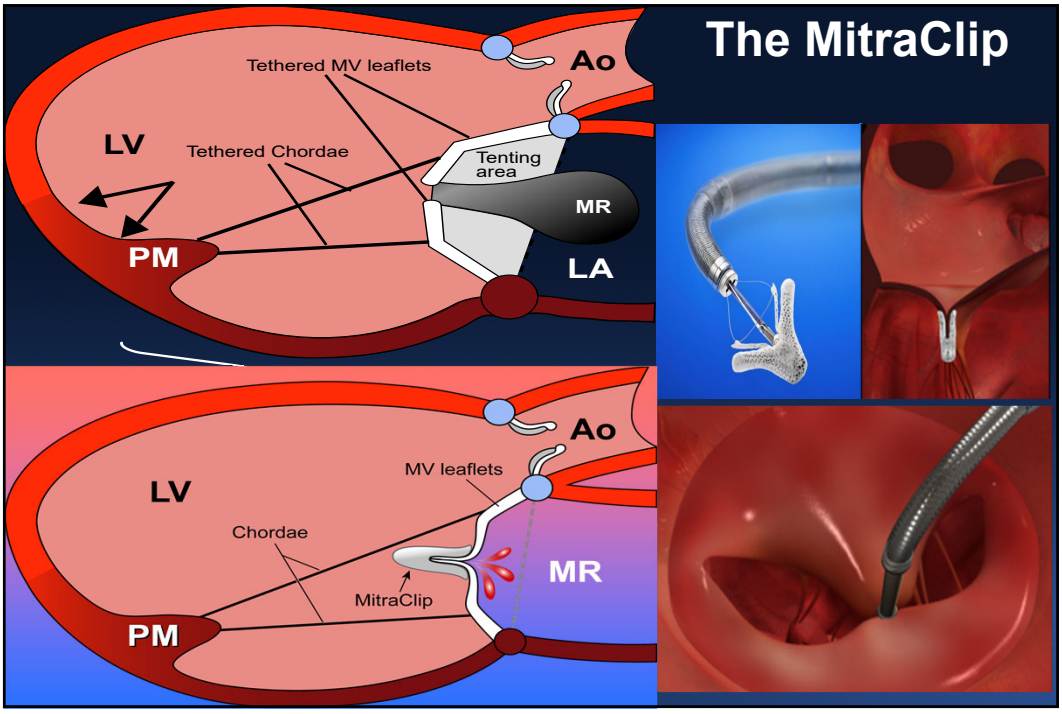
FMR Gradin

Despite what the g
FMR type IIIb h
severity a
-com and
-
with outcome with
an grading scale

It is time to harmonize FMR grading between ACC/AHA and ESC around an expanded grading scale

Conundrum #3
How to treat FMR-v ?





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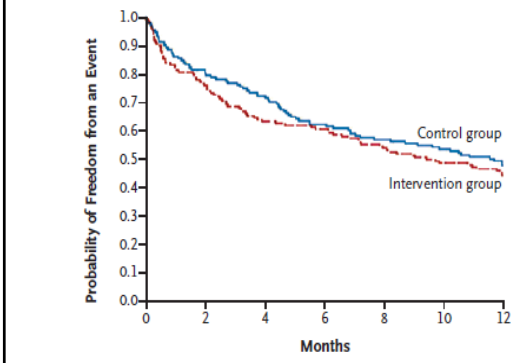
MITRA-FR

Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

J.-F. Obadia, D. Messika-Zeitoun, G. Leurent, B. Iung, G. Bonnet, N. Piriou, T. Lefèvre, C. Piot, F. Rouleau, D. Carrié, M. Nejjari, P. Ohlmann, F. Leclercq, C. Saint Etienne, E. Teiger, L. Leroux, N. Karam, N. Michel, M. Gilard, E. Donal, J.-N. Trochu, B. Cormier, X. Armoiry, F. Boutitie, D. Maucort-Boulch, C. Barnel, G. Samson, P. Guerin, A. Vahanian, and N. Mewton, for the MITRA-FR Investigators*



No. at Risk

Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

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COAPT

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

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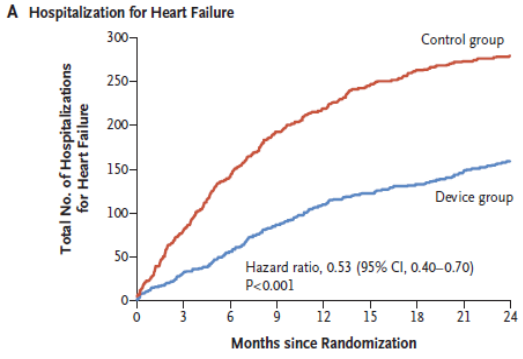

No. at Risk

Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

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Similar populations ?

	MITRA-FR	COAPT
Condition	Symptomatic FMR due to LVD	Symptomatic FMR due to LVD
Device	Standard MitraClip	Standard MitraClip
Intervention/center	~4	~4
Age	71 yrs	72 yrs
Male sex	75%	65%
Ischemic	60%	61%
EF	33%	31%
GFR	50 mL/min	50 mL/min
STS/Euroscore	6.5%	8%

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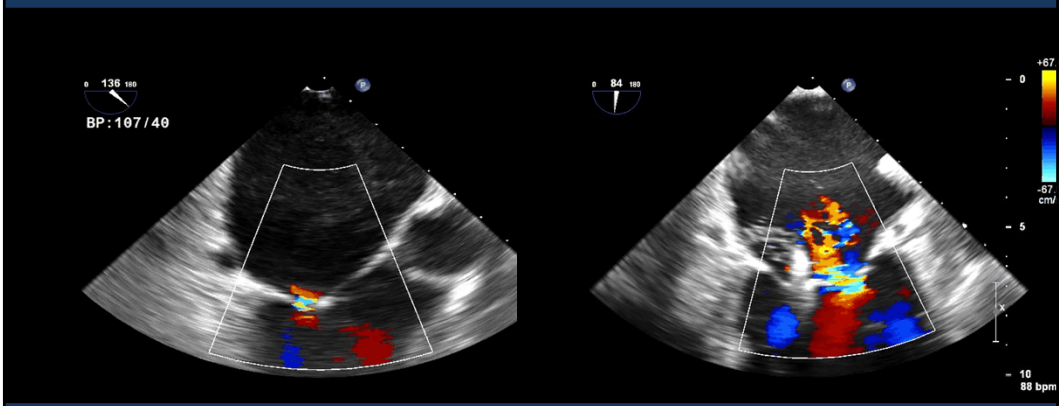
What is different ?

	MITRA-FR	COAPT
Case selection: EDVI	135 mL/m2	101 mL/m2
LV ED diameter	69 mm	62 mm
ERO	0.31 cm2	0.41 cm2
NT-ProBNP	3300 pg/mL	5500 pg/mL
Intervention: Achieved Implant	90.7%	95%
2 Clips	45%	55%
Complications	14.6%	8.5%
MR discharge ≤1+	75.6%	82.3%
MR 1-year ≤2	~80%	~95%
Process	Serious Med Rx Local	Intensive Med Rx pre-randomization by panel

Mitral Regurgitation

What determines the success of repair ?



Residual MR

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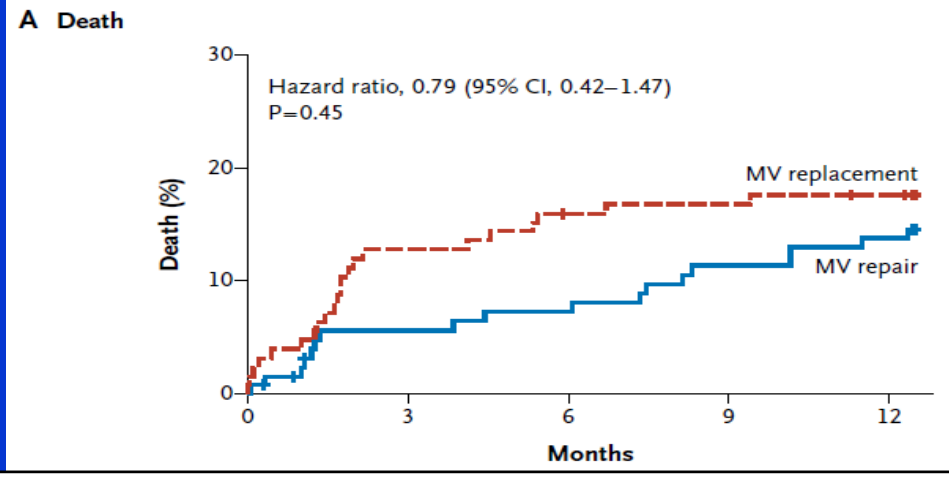
ORIGINAL ARTICLE

Mitral-Valve Repair versus Replacement



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ORIGINAL ARTICLE

Two-Year Outcomes of Surgical Treatment

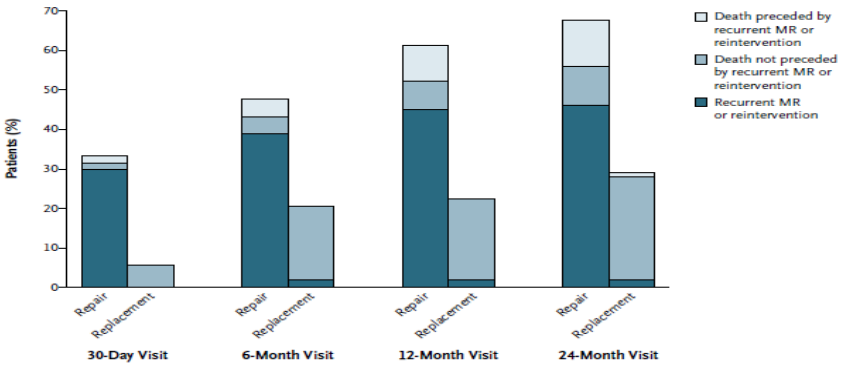
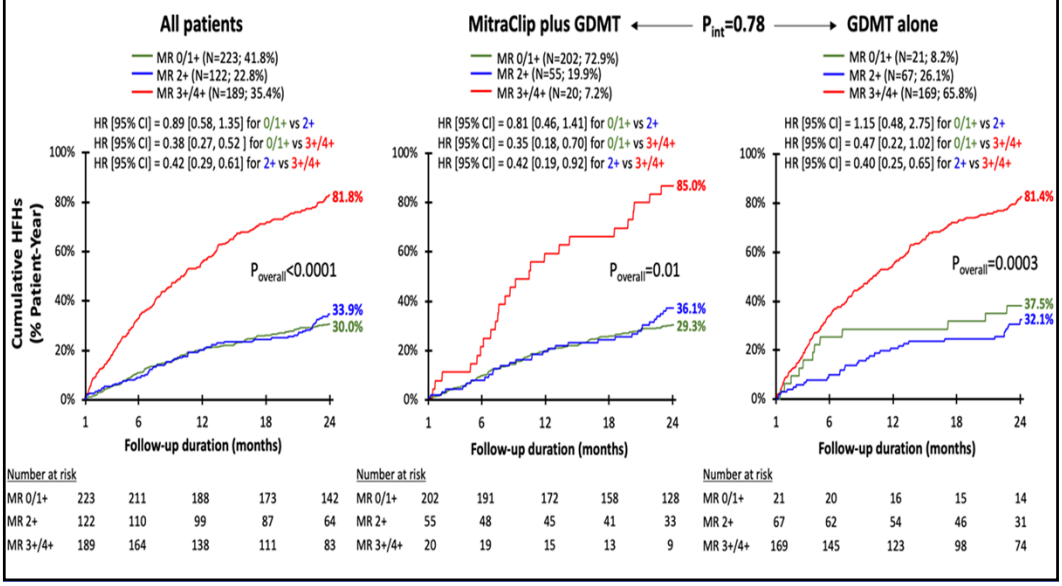


Figure 2. Cumulative Failure of Mitral-Valve Repair or Replacement.
Failure of the intervention was defined as death, moderate or severe mitral regurgitation (MR) as seen on transthoracic echocardiography, or mitral-valve reintervention.

COAPT Trial—Impact of residual MR



FMR-LV dysfunction

- Represents ~1/3 of all MR
- An independent determinant of survival and HF
- Specific scale of grading
- Profoundly Undertreated
- We have now a potentially successful method of MR treatment, but the result has to be "perfect"


Thank
You