

Secondary MR phenotypes/stages

Do they inform better than proportionate vs. disproportionate MR?

Philippe B. Bertrand, MD PhD

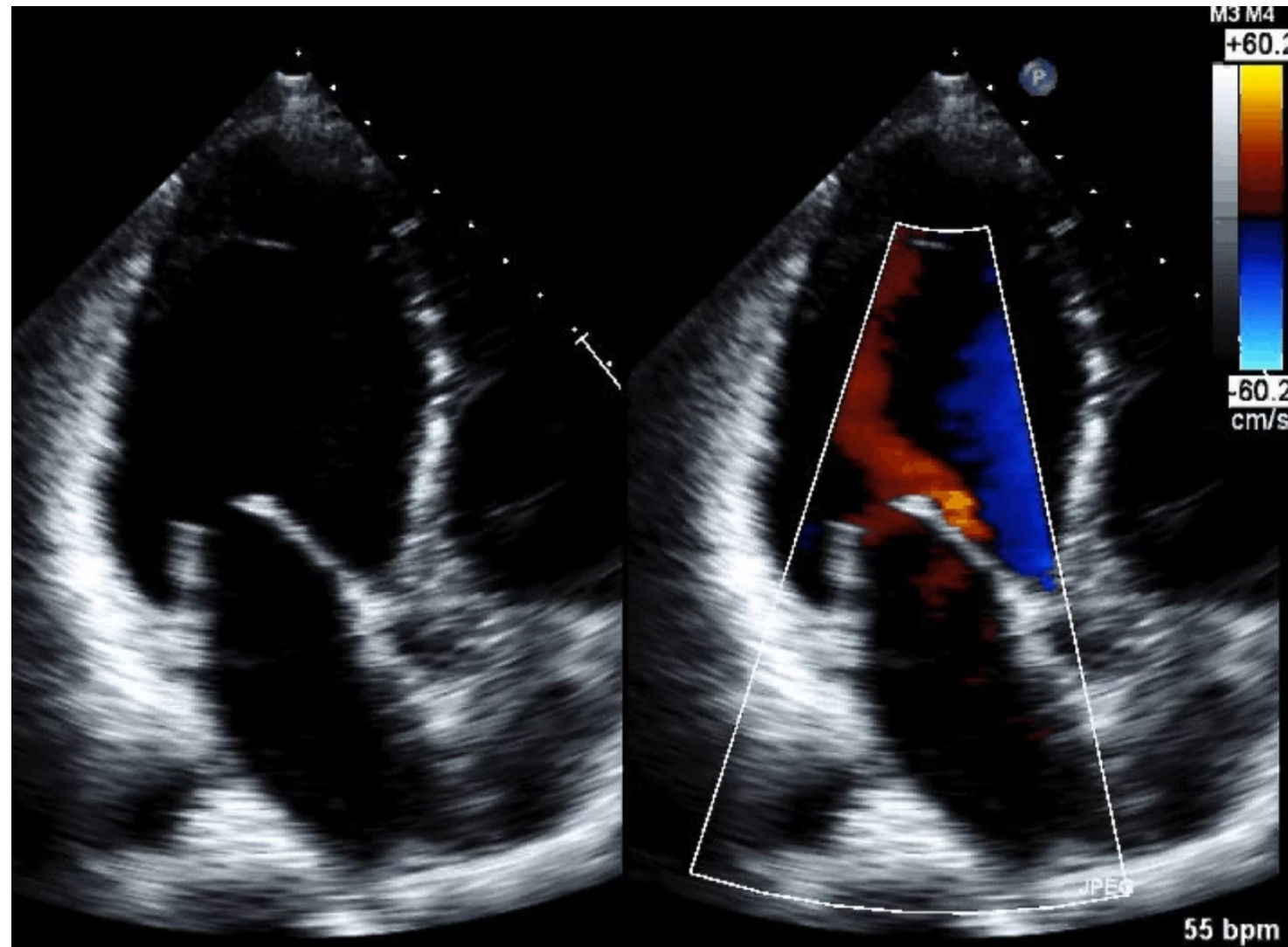
 @Ph_Bertrand

EuroValve 2023

Milan, 22 September 2023

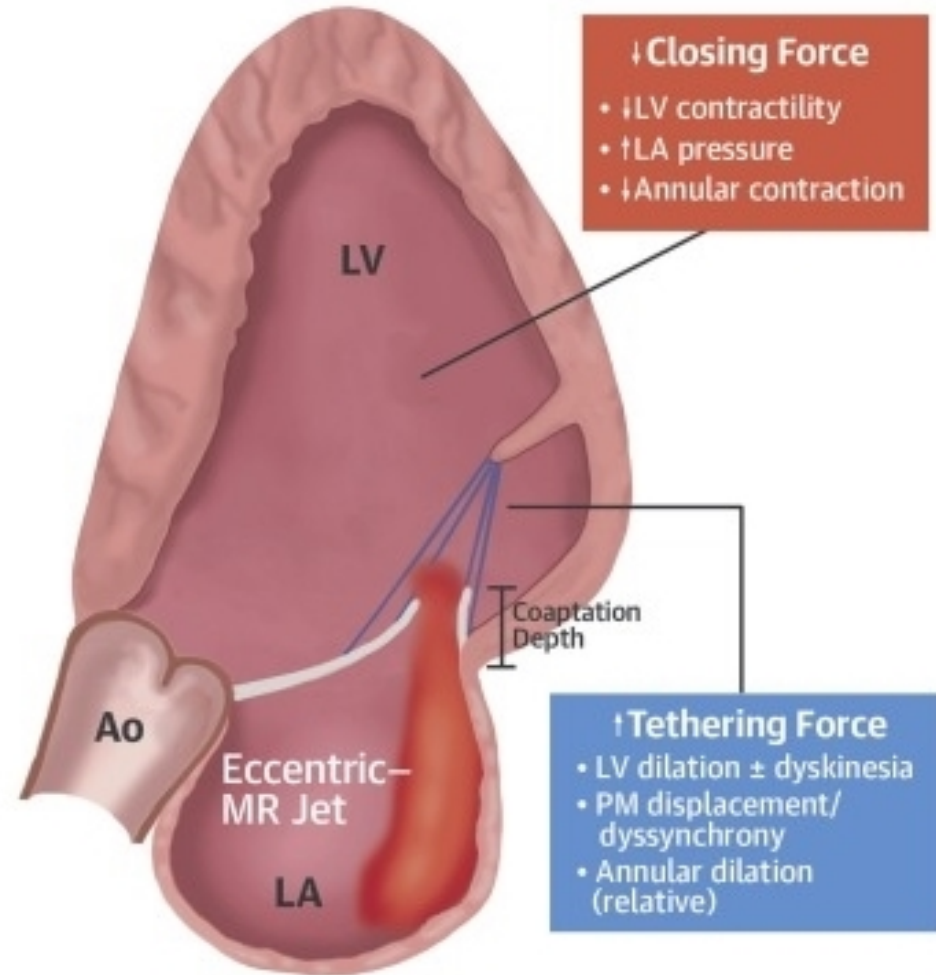
No disclosures

Secondary (Functional) Mitral Regurgitation

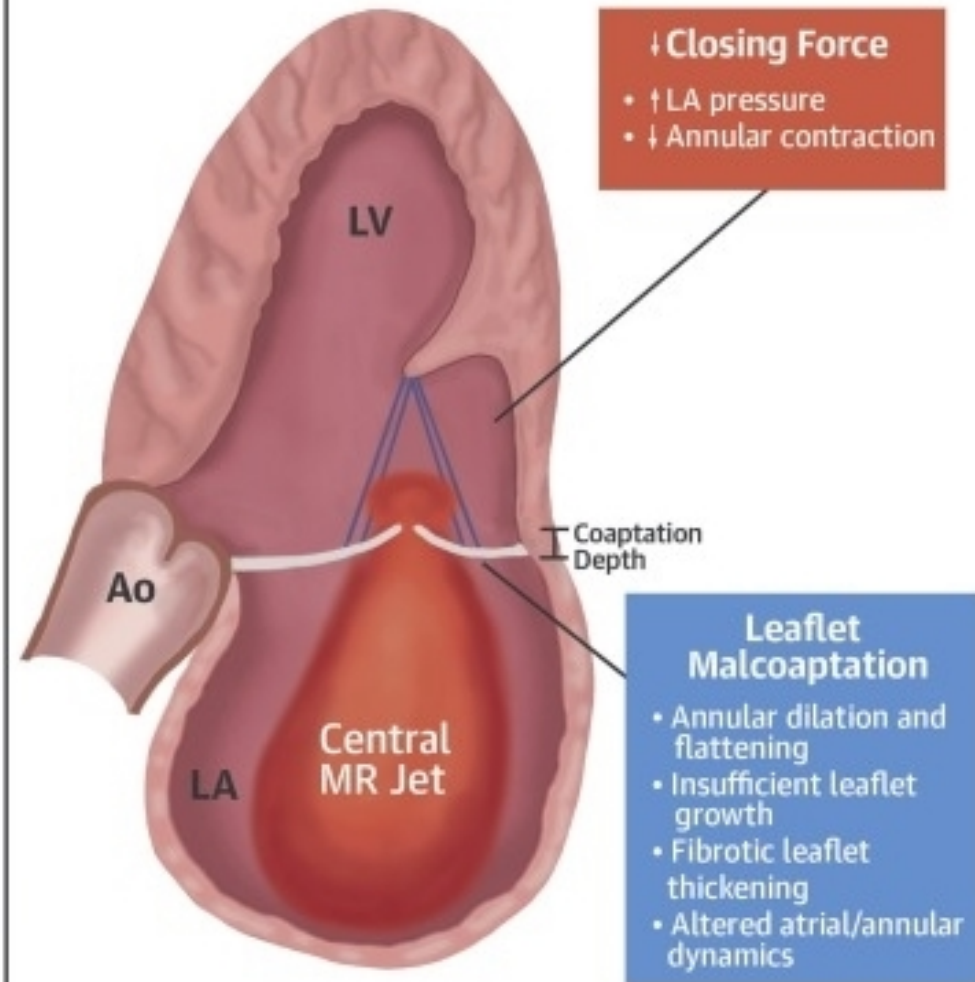


Secondary MR Phenotypes

“Ventricular” Functional MR



“Atrial” Functional MR



Secondary MR Phenotypes

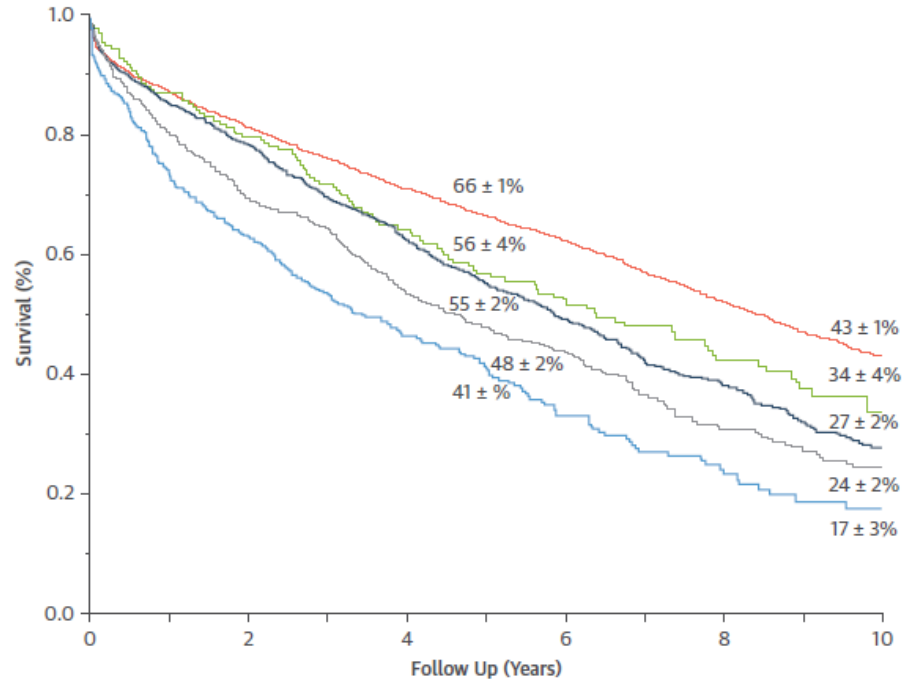
“Ventricular” Functional MR

“Atrial” Functional MR

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

Secondary MR Phenotypes

“Ventricular” Functional MR

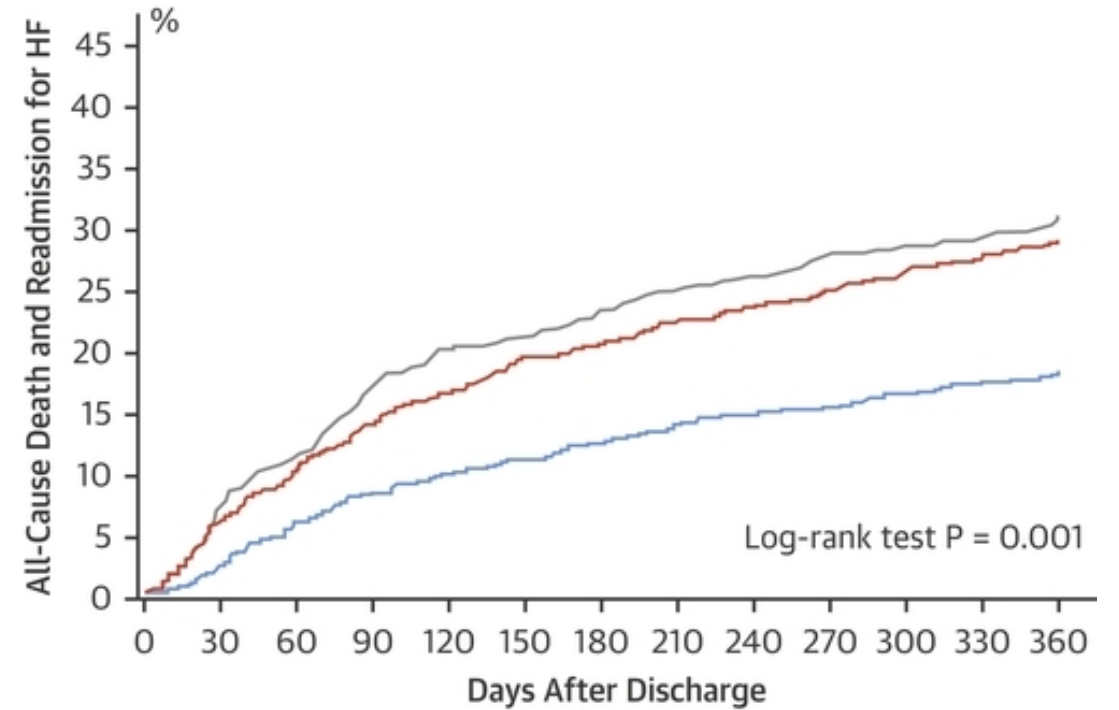


No FMR						
EROA 0.01-0.09	3,823	2,852	2,201	1,481	888	426
EROA 0.10-0.19	195	142	107	77	48	23
EROA 0.20-0.29	1,067	732	520	320	187	82
EROA ≥0.30	793	426	293	161	82	44
	503	218	131	67	30	11

— No FMR — EROA 0.01-0.09 mm² — EROA 0.1-0.19 mm² — EROA 0.2-0.29 mm² — EROA ≥0.30 mm²

Benfari et al, JACC img, 2021

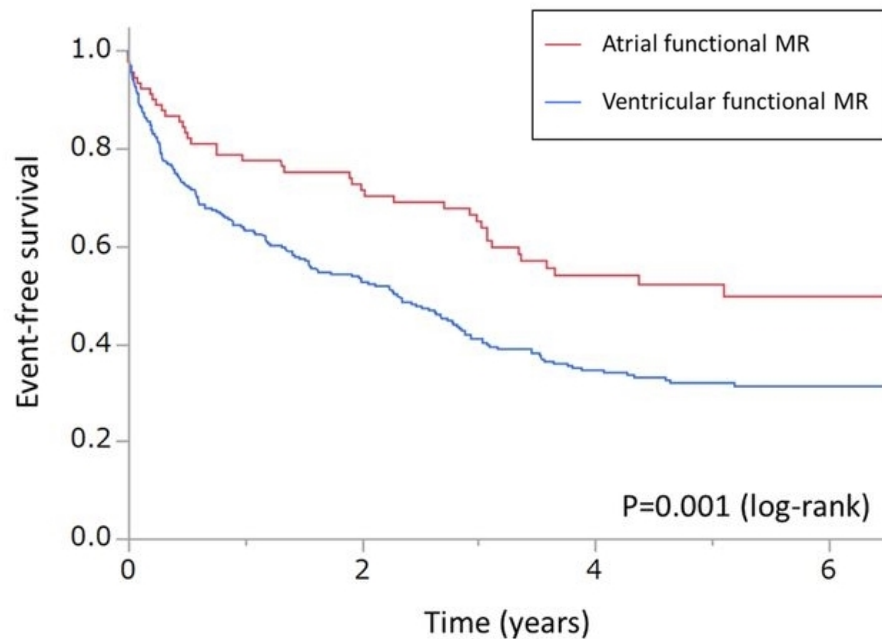
“Atrial” Functional MR



- No MR at Discharge (n = 515)
- Mild MR at Discharge (n = 974)
- Moderate to Severe MR at Discharge (n = 336)

Kajimoto K et al, Eur J Heart Fail, 2016

“Ventricular” versus “Atrial” Functional MR

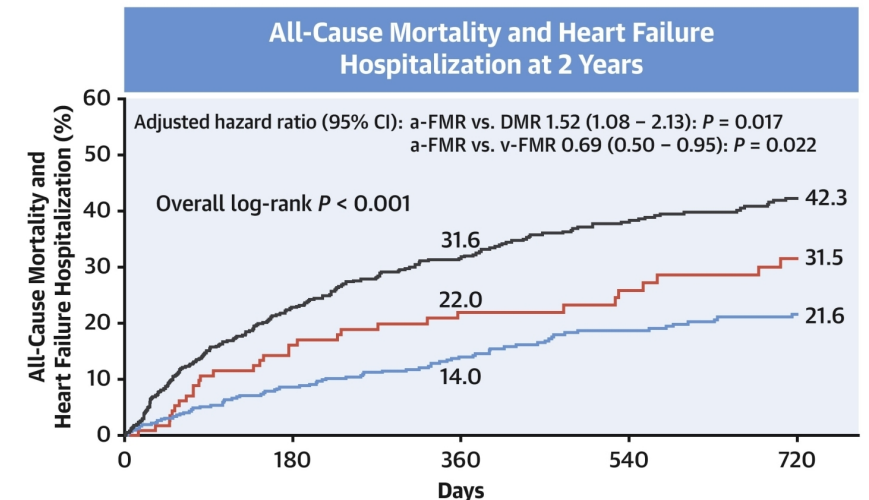


No. at risk

Atrial functional MR	90	60	33	17
Ventricular functional MR	288	134	75	32

HF population

CENTRAL ILLUSTRATION: Time-to-Event Curves According to Mitral Regurgitation Etiology and Cardiac Remodeling



No. at Risk:

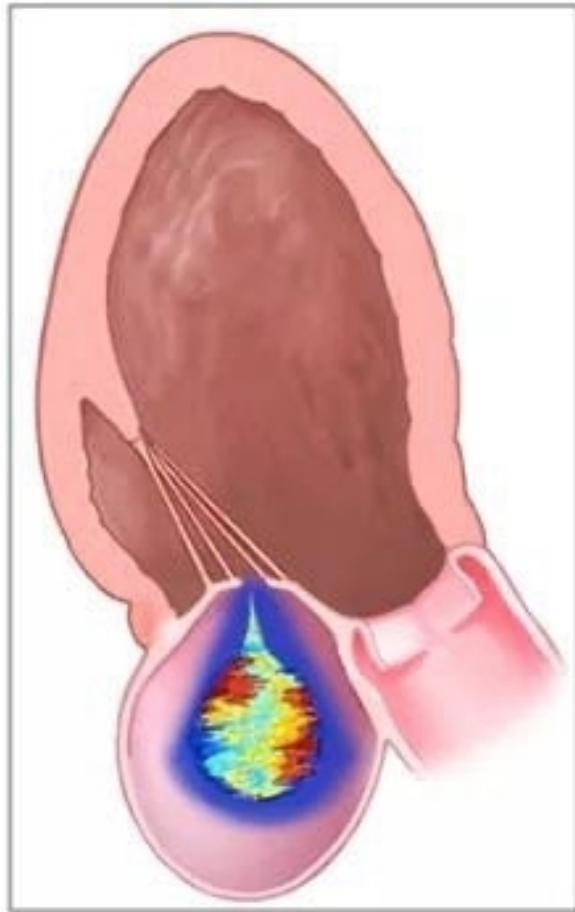
Atrial Functional MR	116	75	47
Ventricular Functional MR	505	294	159
Degenerative MR	423	310	168

Yoon S-H, et al. *J Am Coll Cardiol Intv.* 2022;15(17):1711-1722.

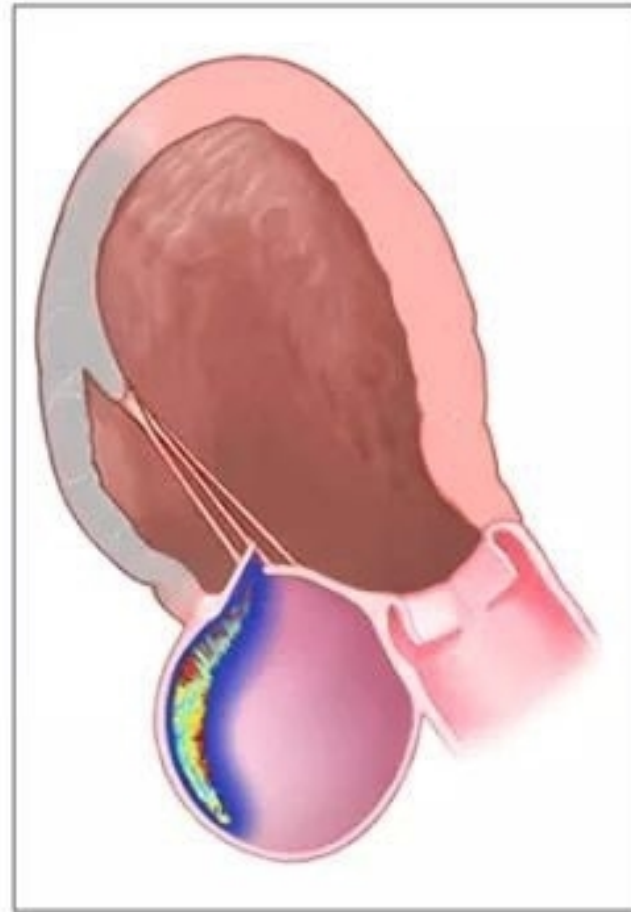
Post-TEER

Secondary MR Phenotypes

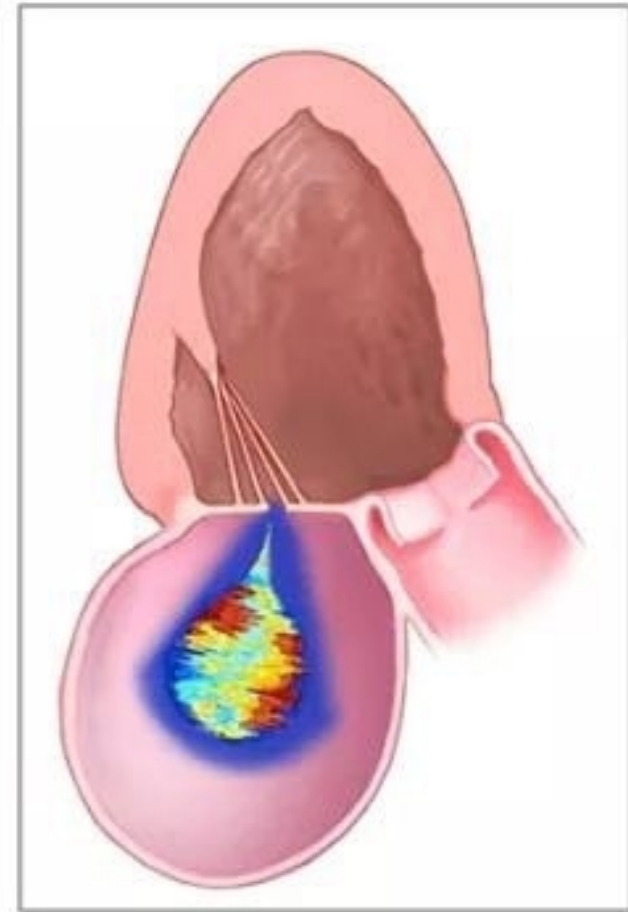
A Ventricular functional MR



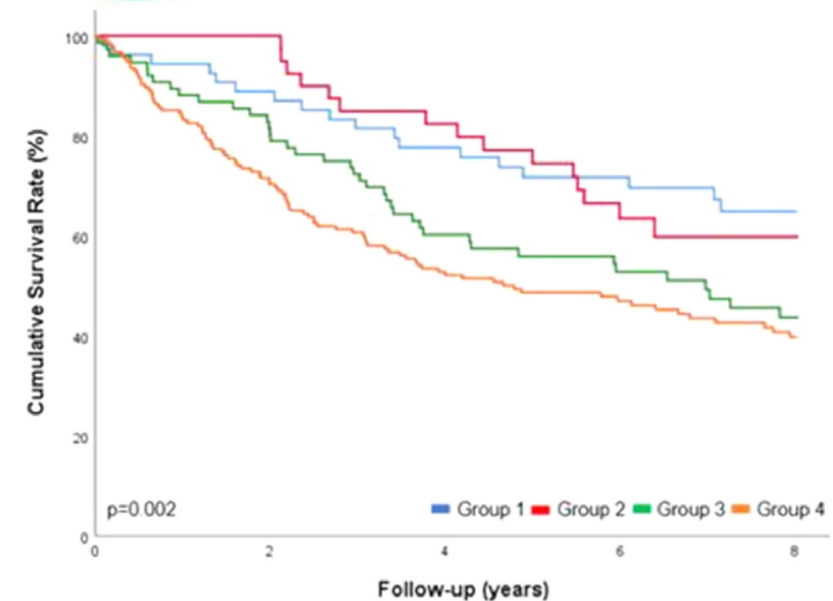
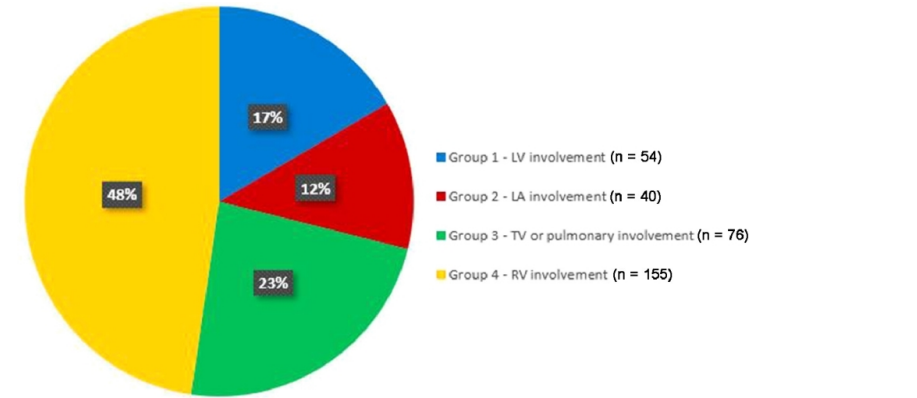
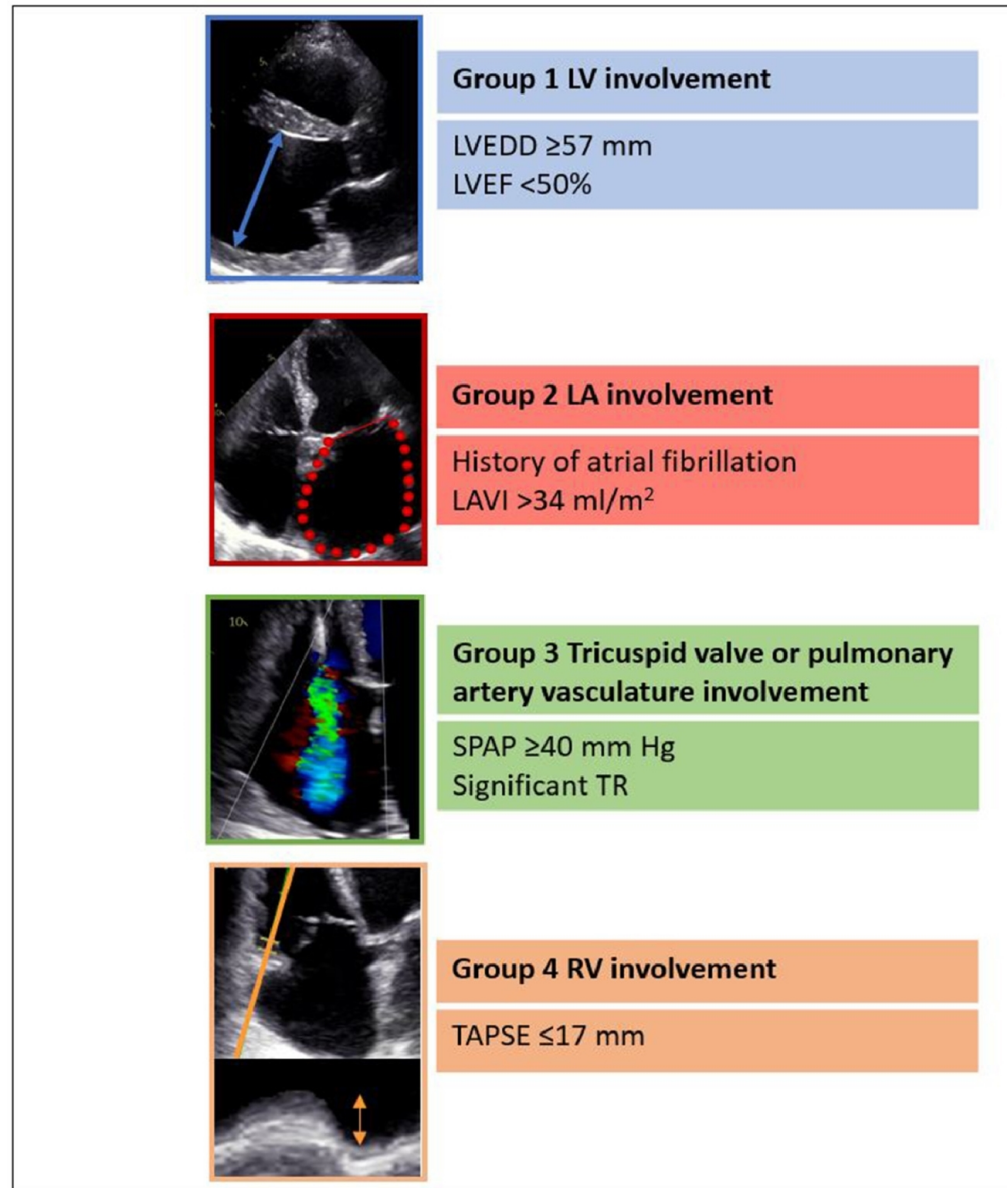
B Ischemic MR



C Atrial functional MR



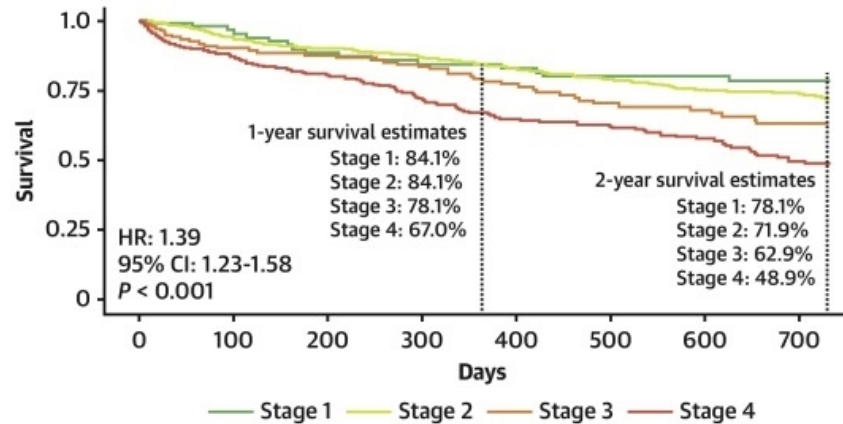
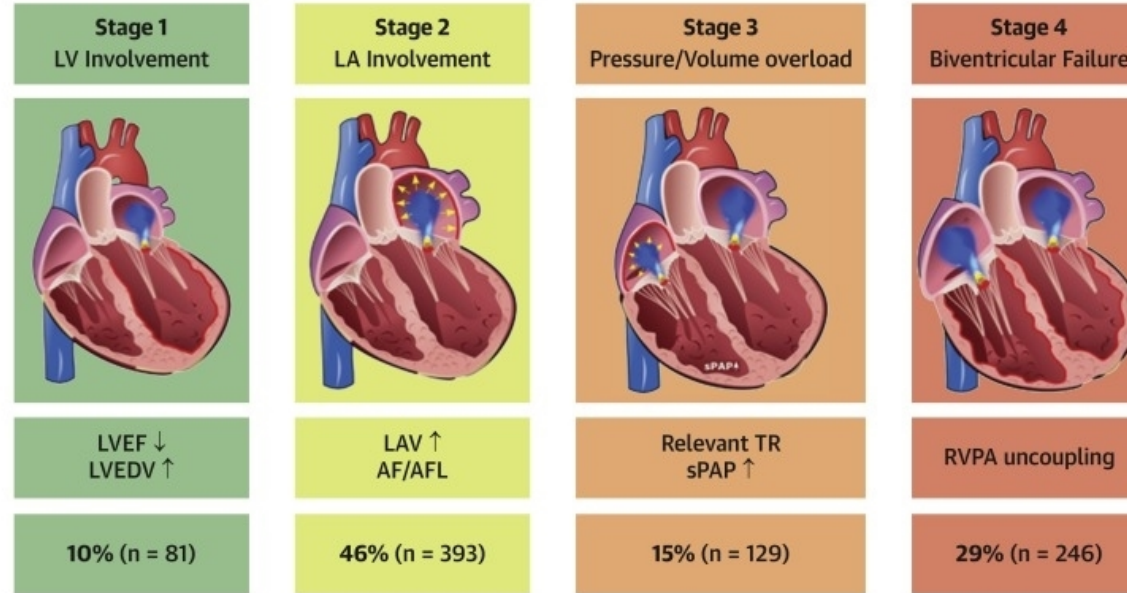
Stages of “Extramitral Cardiac Involvement” in SMR



Patients at risk	0	2	4	6	8
Group 1	54	48	41	33	28
Group 2	40	40	32	21	16
Group 3	76	61	43	34	23
Group 4	155	109	78	56	41

Stages of Secondary MR: Impact on Prognosis post-TEER

CENTRAL ILLUSTRATION: Distribution of Secondary Mitral Regurgitation Stages Within the Overall Population (n = 849) and its Impact on Survival Prognosis



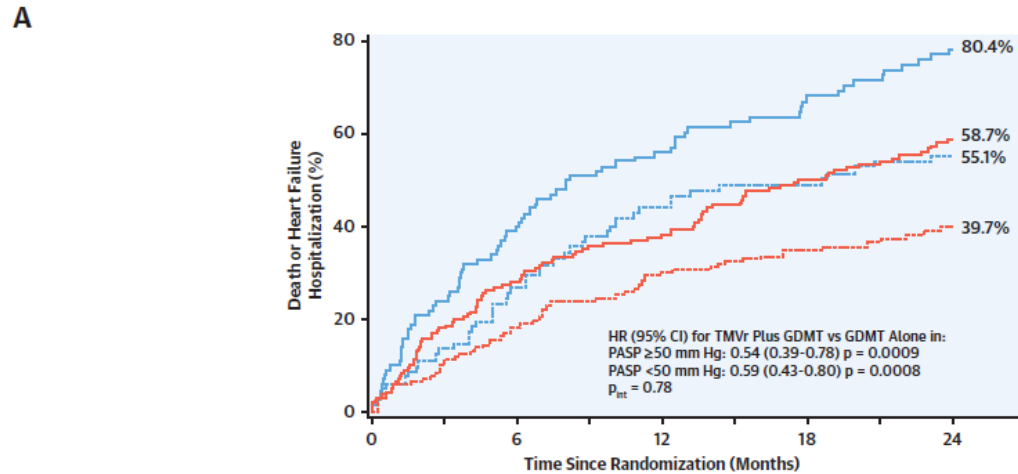
Stages of Secondary MR & Outcome in COAPT trial



Functional MR Staging	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
	No Cardiac Impairment	LA Abnormality	Significant LV Dysfunction/Dilation	Significant Pulmonary Hypertension	Substantial Right Heart Involvement
Staging Criteria		LA volume index >34 ml/m ² , or LA dimension >4.5cm Or atrial fibrillation	LVEF ≤30% or Or severe LV dilation (LVEDD >7.5 cm)	PASP ≥45 mmHg	≥ Moderate RV dysfunction (RV FAC <28% or RV FWS <15%) Or ≥ moderate tricuspid regurgitation
<u>2-year death or HFH</u>	-	N=65	N=77	N=76	N=169
TEER+GDMT (n=183)	-	34.8% (13/39)	41.1% (16/39)	60.0% (21/35)	41.5% (28/70)
GDMT alone (n=204)	-	47.9% (12/26)	63.5% (24/38)	78.0% (32/41)	73.6% (70/99)

Prognostic Impact of SPAP and TR in COAPT

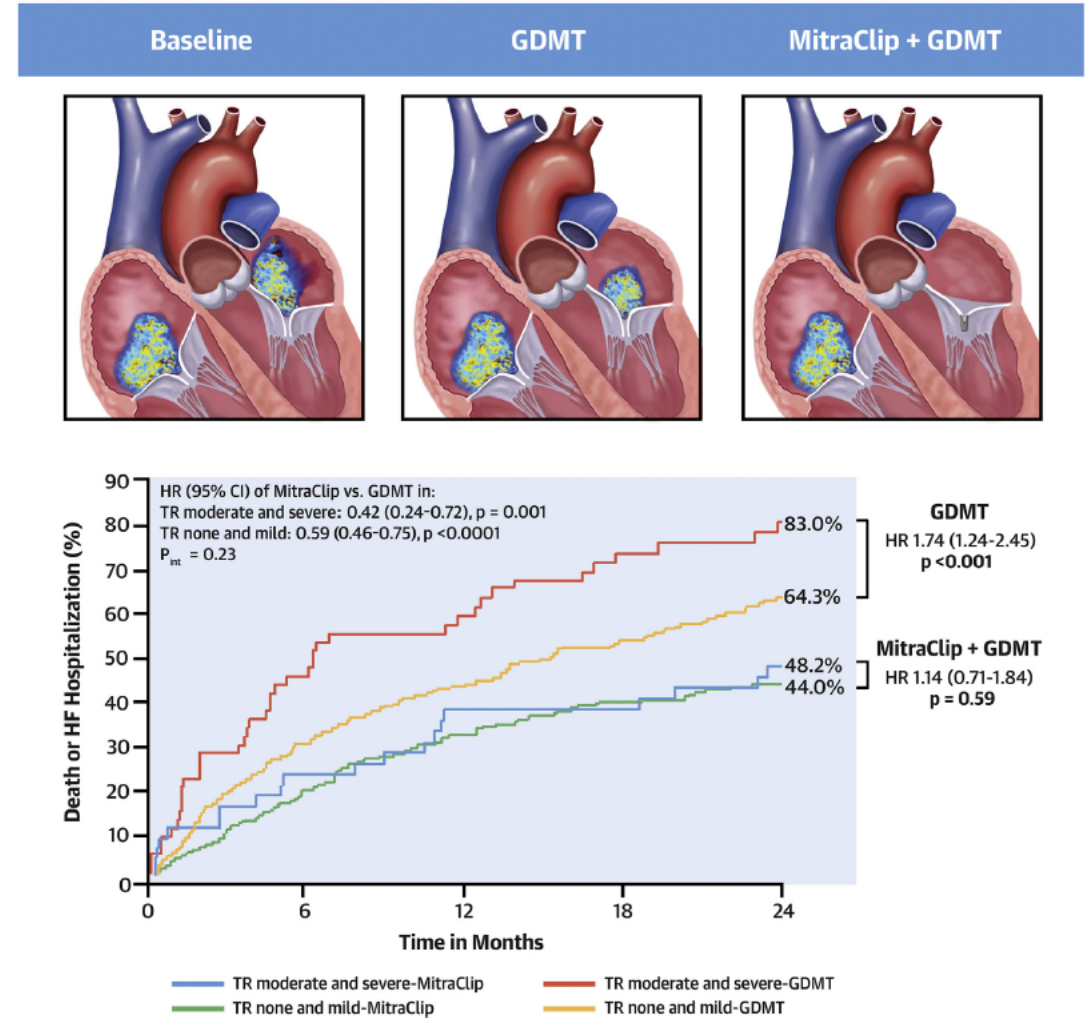
CENTRAL ILLUSTRATION 2-Year Rates of the Composite Outcome of Death or Heart Failure Hospitalization in Patients With Heart Failure With Secondary Mitral Regurgitation Randomized to Transcatheter Mitral Valve Repair Plus Guideline-Directed Medical Therapy Versus Guideline-Directed Medical Therapy Alone



No. at risk:

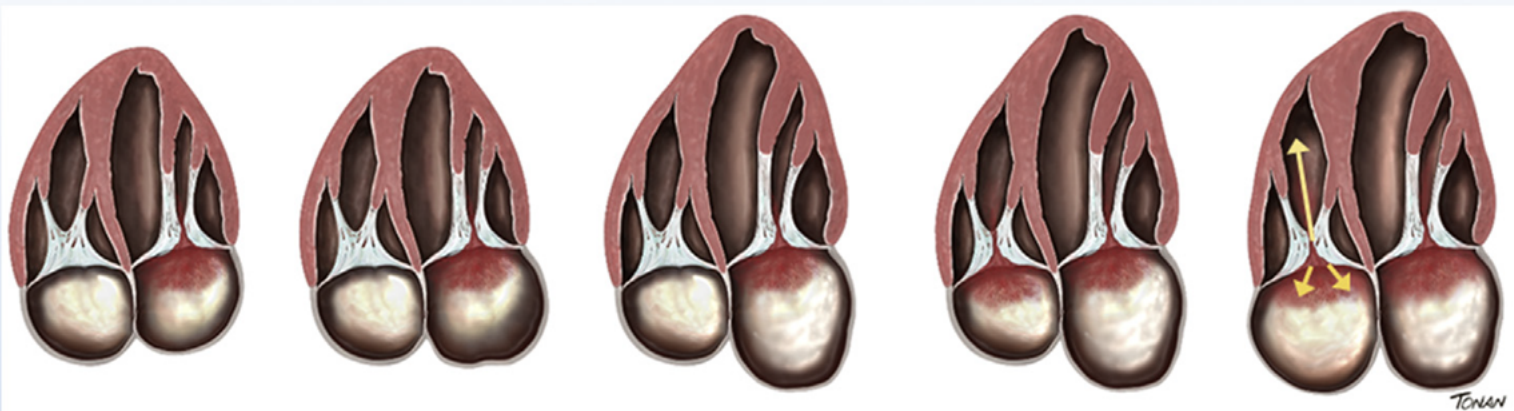
	0	6	12	18	24
--- PASP ≥50 mm Hg TMVr Plus GDMT	82	60	45	41	34
— PASP ≥50 mm Hg GDMT Alone	102	61	41	30	19
--- PASP <50 mm Hg TMVr Plus GDMT	171	137	117	107	92
— PASP <50 mm Hg GDMT Alone	173	124	99	77	58

Ben-Yehuda, O. et al. J Am Coll Cardiol. 2020;76(22):2595-606.



Hahn, R.T. et al. J Am Coll Cardiol. 2020;76(11):1305-14.

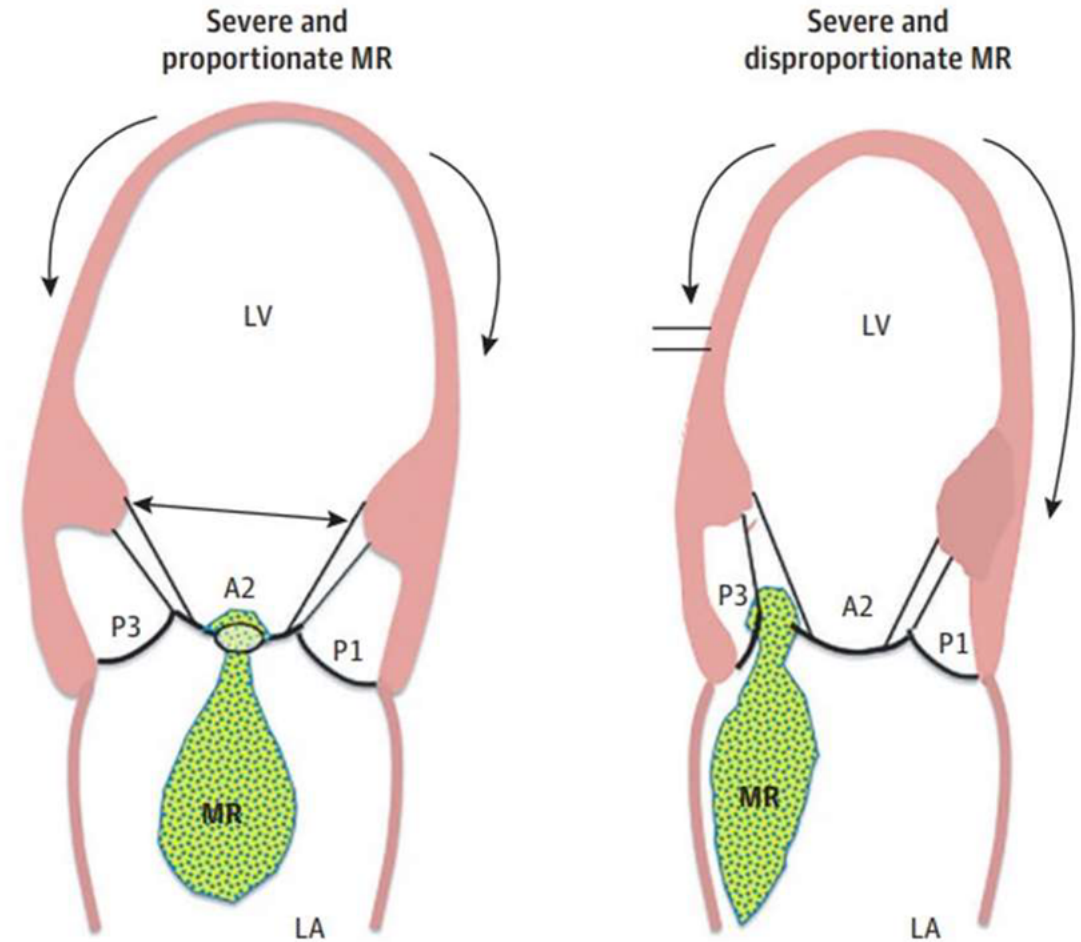
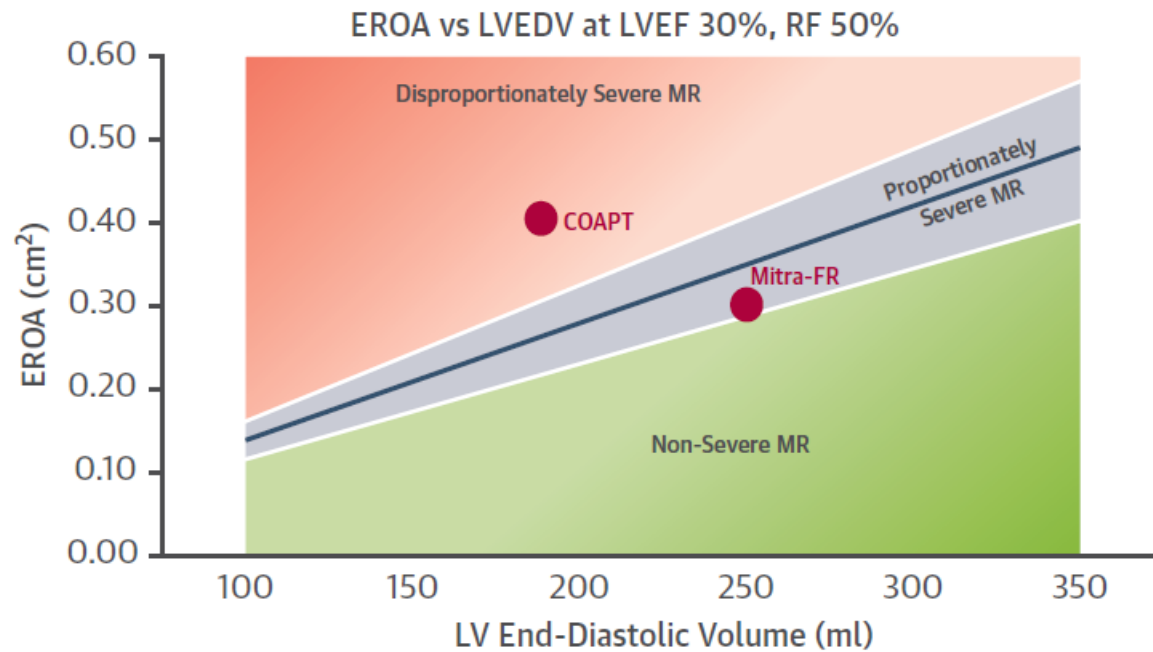
Stages of Secondary MR Do Not Predict Response to Rx



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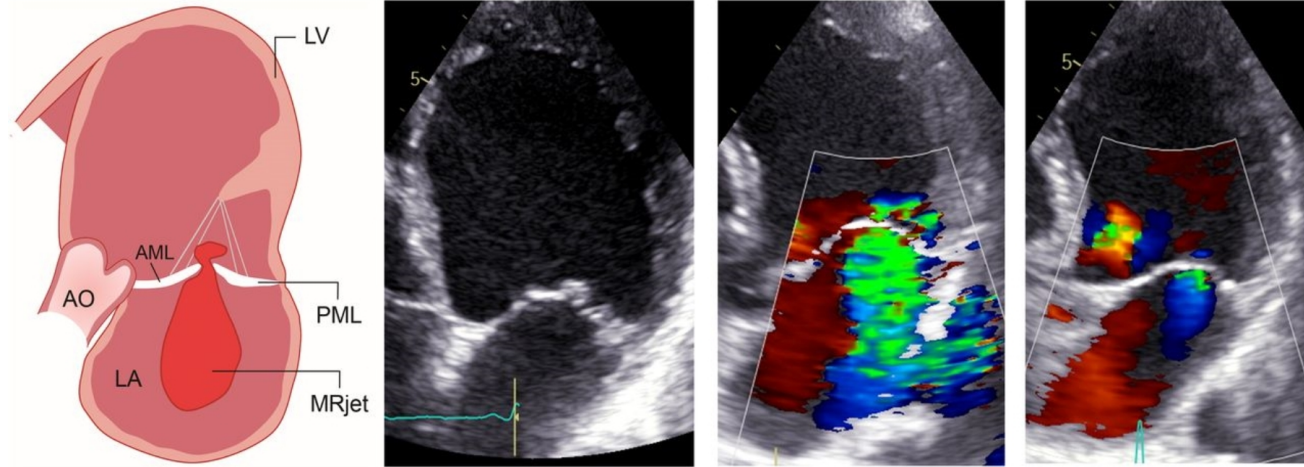
Proportionality Concept in Secondary MR

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

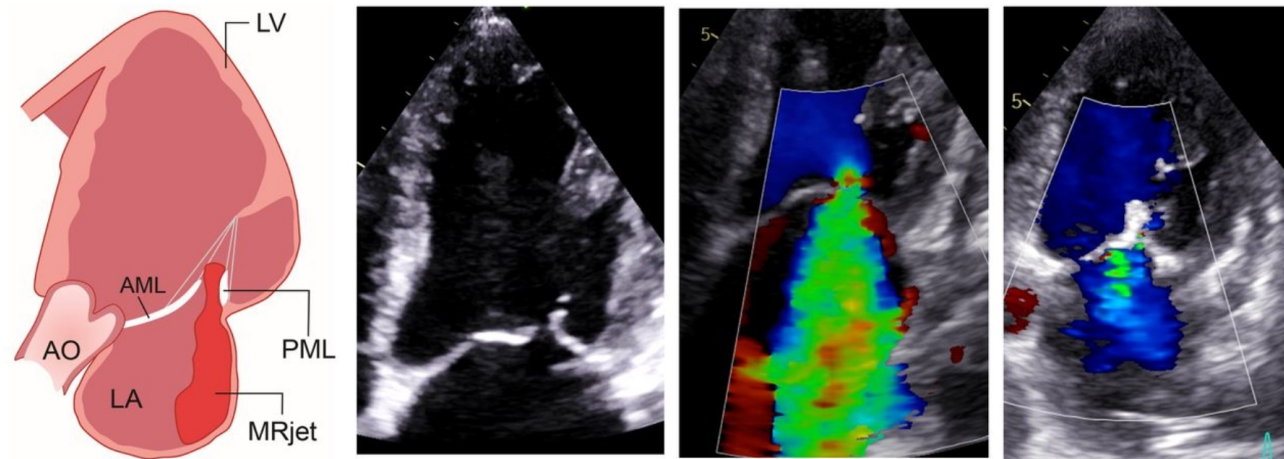


Proportionality Concept in Secondary MR

Proportionate SMR



Disproportionate SMR



FMR passive bystander or active driver of disease?



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

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FMR passive bystander or active driver of disease?

Table 3 Impact of severe mitral regurgitation on outcome compared with the remaining study population by various subgroups of heart failure defined functionally by New York Heart Association stage, biochemically by quartiles of NT-proBNP, and echocardiographically by left ventricular ejection fraction

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

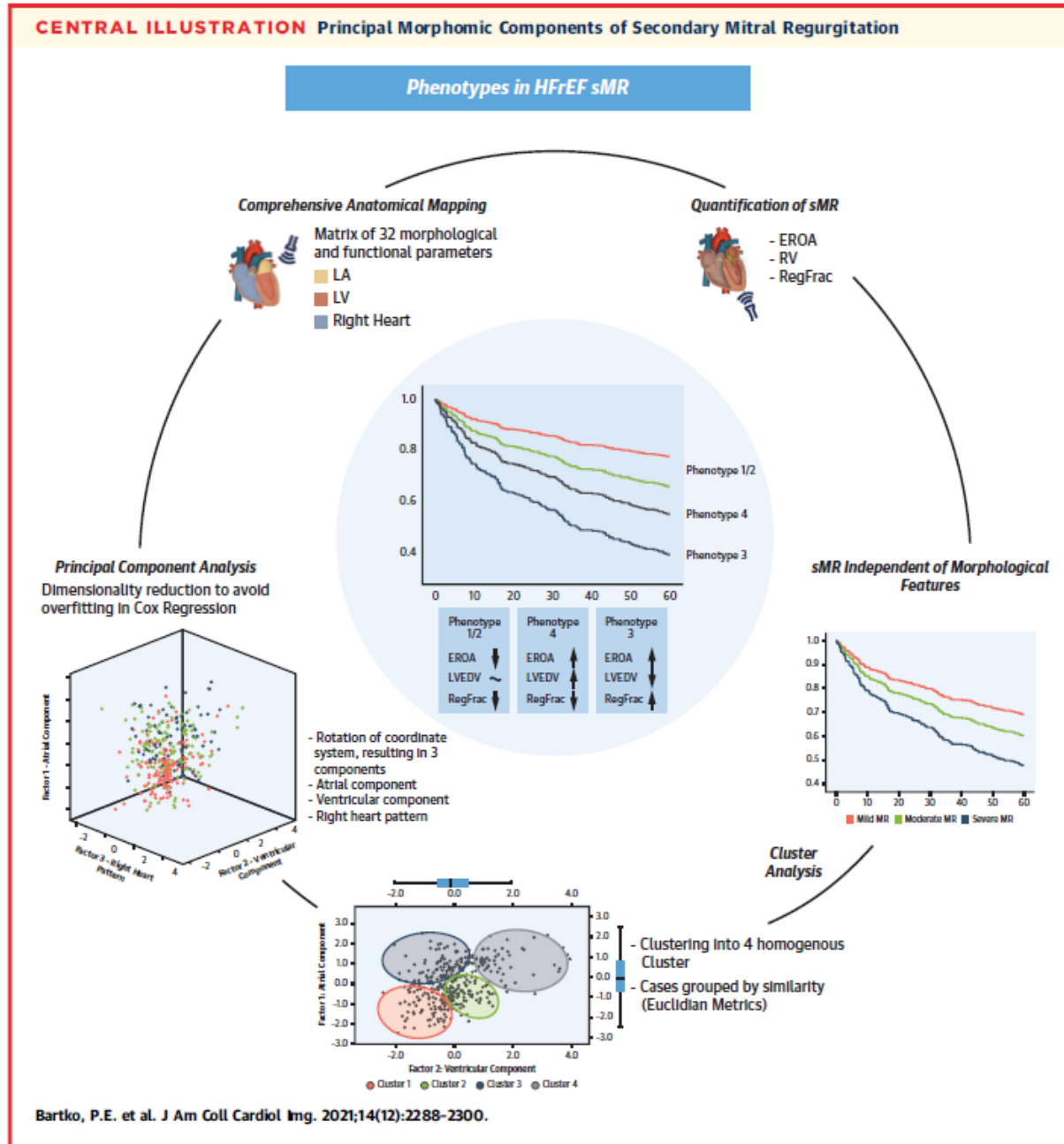
Bold values indicates statistical significance.

NYHA, New York Heart Association; HR, hazard ratio; CI, confidence interval; LV, left ventricular; LVEF, LV ejection fraction.

^aAdjusted for: age, sex, and ischaemic aetiology of heart failure.

Adverse prognostic impact of FMR in an “intermediate-failure phenotype, with NYHA II or III, moderately reduced EF and NT-proBNP in 2nd quartile

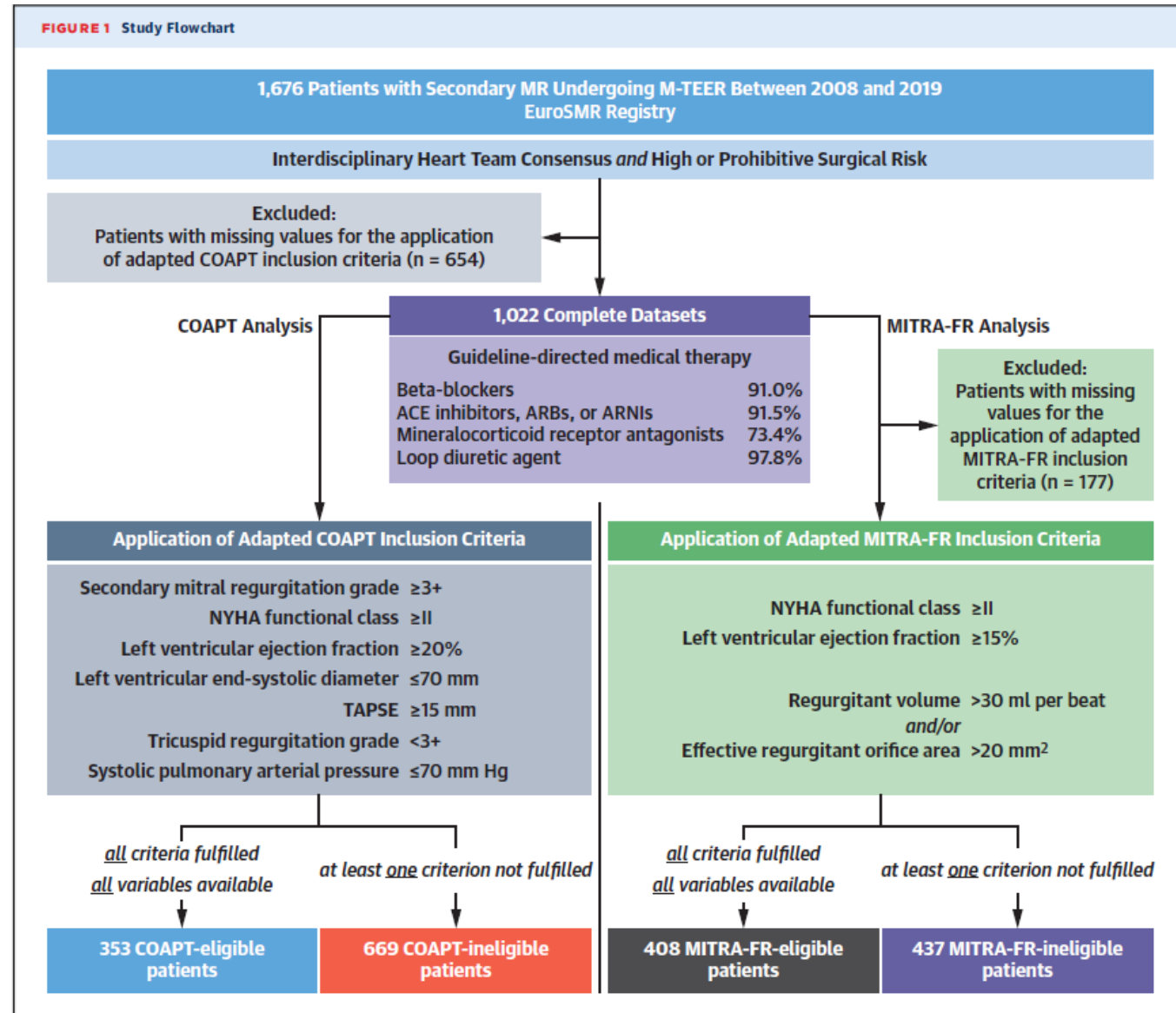
FMR passive bystander or active driver of disease?



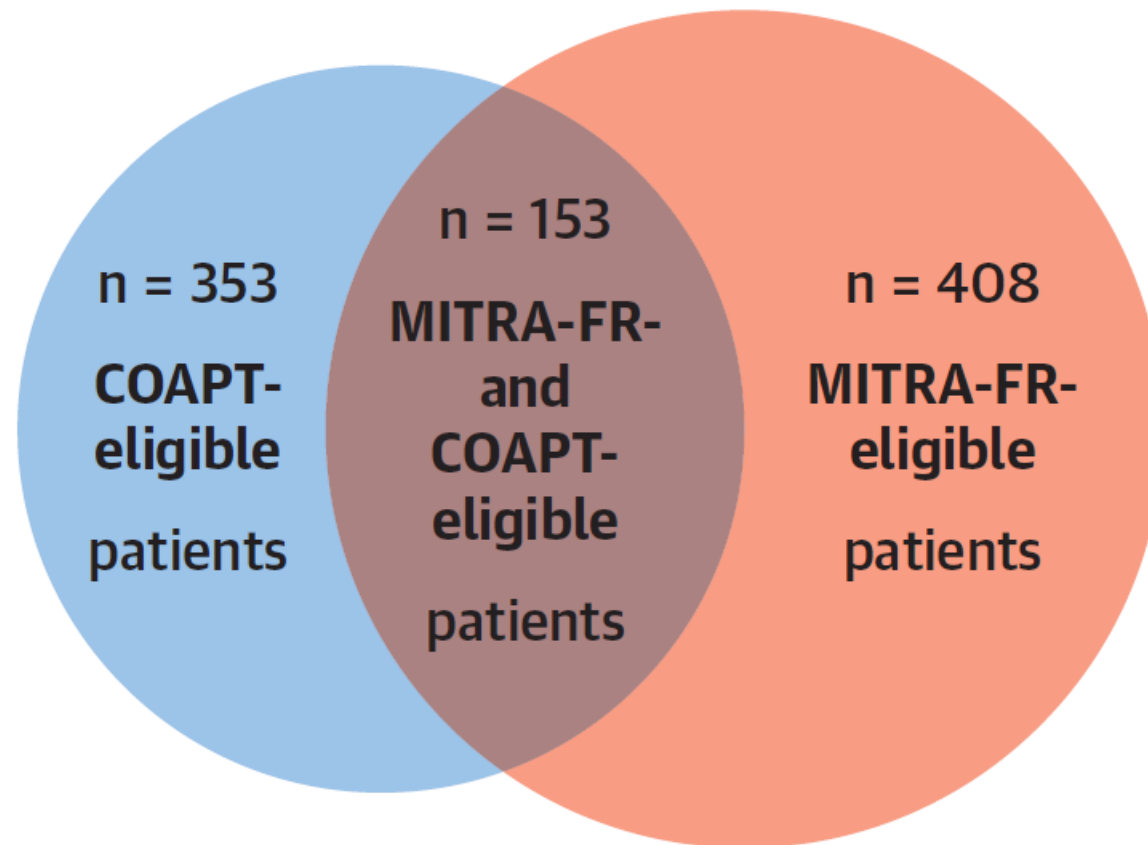
Bartko, P.E. et al. J Am Coll Cardiol Img. 2021;14(12):2288-2300.

Bartko P et al, JACC img, 2021

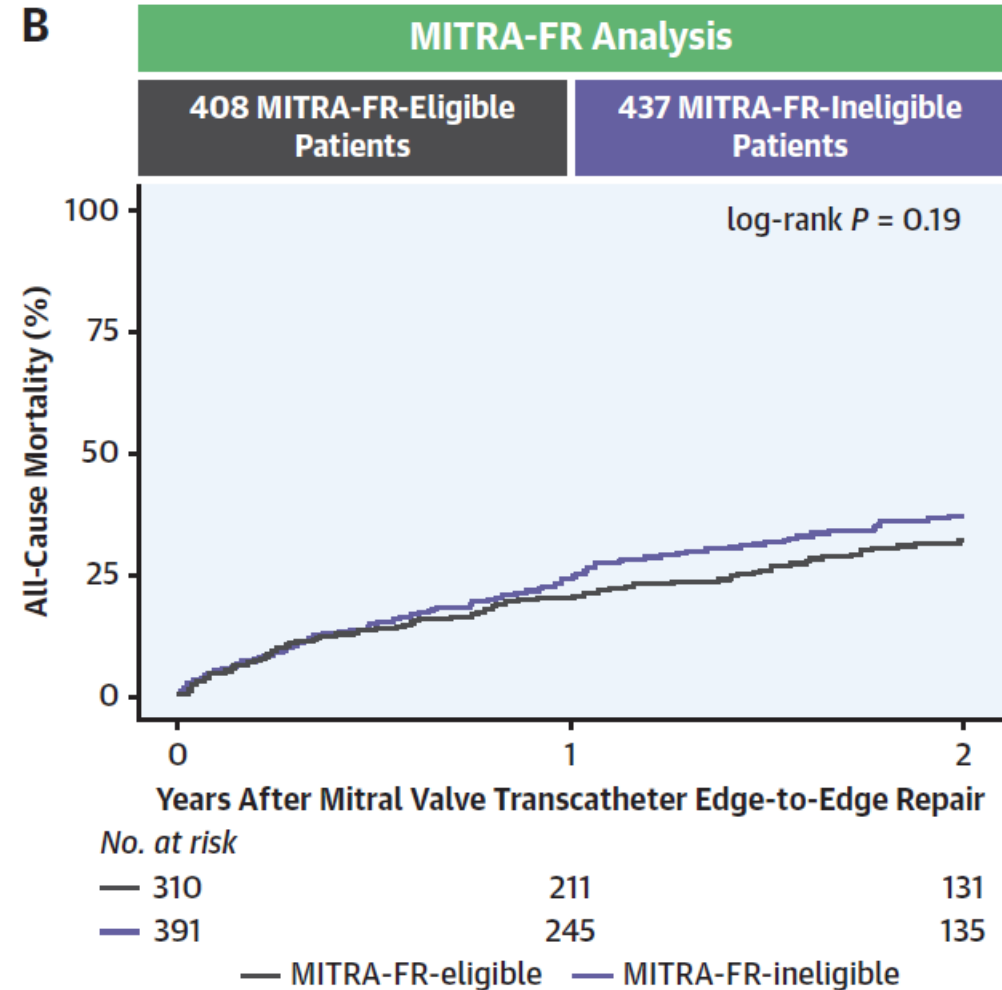
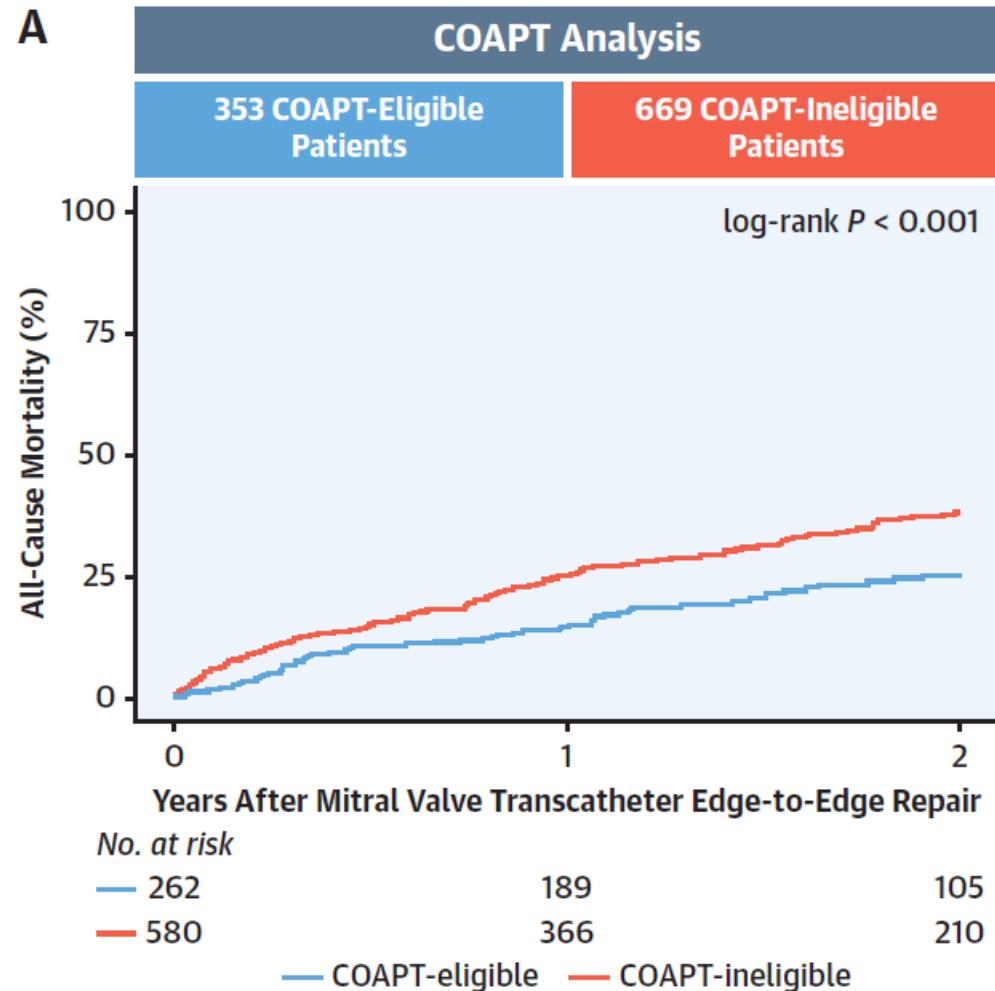
COAPT vs MITRA-FR in the EuroSMR registry



COAPT vs MITRA-FR in the EuroSMR registry



COAPT vs MITRA-FR in the EuroSMR registry



Summary

Do they inform better?

Phenotypes/stages of secondary MR:

- pathophysiology / mechanistic insights
- extent of extravalvular cardiac damage
→ prognostication & risk stratification

Proportionality concept of secondary MR

- MR as active driver of outcome or passive bystander?
- expected benefit from MV intervention?
→ higher level of complexity in SMR; more research needed



Thank you

Philippe B. Bertrand, MD PhD

 @Ph_Bertrand

EuroValve, Milan, 22 September 2023